Coeliac disease: Health-related quality of life and patients' experiences of health care services

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A thesis submitted to the University of Oxford in fulfilment of the requirement for the degree of

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Diagnosis and management of coeliac disease: Health-related quality of life and patients' experiences of health care services

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ABSTRACT

Coeliac disease (CD) is a chronic gastrointestinal condition, the only treatment for which is a gluten-free diet (GFD). Following a GFD is restrictive, burdensome, and can impact health-related quality of life (HRQOL). People with CD can experience long delays to diagnosis and evidence suggests large variations in follow-up care, but the relationship between health care experiences and HRQOL is unknown.

The main aim of this research was to develop a patient-reported outcome measure and patient experience questionnaire, and use these to investigate the relationship between adults' experiences of health care services and HRQOL in CD. The questionnaires, named the Coeliac Disease Assessment Questionnaire (CDAQ) and the Coeliac Disease Patient Experience Questionnaire (CD-PEQ), were developed following qualitative interviews with adults with CD, and refined with input from experts, and cognitive interviews. The CDAQ was also subject to a translatability assessment to assess its linguistic and cultural

translatability, and a cross-sectional survey to assist with item reduction and scale generation. Members of Coeliac UK (n=267) completed the CDAQ and CD-PEQ, together with the SF-36v2 and demographic questions as part of a postal survey.

Psychological health, vitality, general health, and dietary burden were found to have the greatest impact on HRQOL, with physical health and social isolation the least affected. HRQOL was found to have a strong correlation with patients' experiences of health care services. Aspects most strongly related were: the provision of information; communication with HCPs; difficulty obtaining prescriptions; and GPs' knowledge.

This research has identified aspects of health care services that are strongly related to HRQOL in CD. Health care providers are recommended to focus service improvement efforts on these areas. A reliable and valid disease-specific patient-reported outcome measure and patient experience questionnaire have been developed as part of this study. The CDAQ is suitable for use in research studies, including clinical trials, to assess HRQOL in CD.

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LIST OF ABBREVIATIONS

ALSAQ	Amyotrophic Lateral Sclerosis Assessment Questionnaire
BDI	Beck Depression Inventory
BME	Black and Minority Ethnic
BSG	British Society of Gastroenterology
BSI-18	Brief Symptom Inventory
CCG	Clinical Commissioning Group
CD	Coeliac Disease
CD-PEQ	Coeliac Disease Patient Experience Questionnaire
CD-QOL	Coeliac Disease Quality of Life Survey
CDAQ	Coeliac Disease Assessment Questionnaire
CDQ	Celiac Disease Questionnaire
DH	Dermatitis Herpetiformis
FDA	Food and Drug Administration (US)
GBB 24	Gießener Symptom Check List
GFD	Gluten-Free Diet
GIQLI	Gastrointestinal Quality of Life Index
GSRS	Gastrointestinal Symptom Rating Scale
HADS	Hospital Anxiety and Depression Scale
HCP	Health Care Professional
HRQOL	Health-Related Quality of Life
IBS-QOL	IBS Quality of Life
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NPSP	National Patient Survey Programme
PCA	Principal Components Analysis
PCSG	Primary Care Society of Gastroenterology
PDQ	Parkinson's Disease Questionnaire
PGWBI	Psychological General Well-Being Index
PROM	Patient-Reported Outcome Measure
QOL	Quality of Life
SIP	Sickness Impact Profile
STAI	State-Trait Anxiety Inventory
TA	Translatability Assessment
VAS	Visual Analogue Scale
WHOQOL	World Health Organization Quality of Life assessment instrument
Z-SDS	Zung Self-rating Depression Scale

PUBLICATIONS AND PRESENTATIONS

Publications

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Note: presenter underlined

CHAPTER 1:
Introduction

1.1 Overview

Coeliac disease (CD) is a chronic autoimmune condition that affects the small intestine, for which the only treatment at present is a gluten-free diet (GFD). Following a GFD can be burdensome, with difficulties faced in various aspects of daily life, including travelling, shopping, and eating meals outside of the home (Sverker et al., 2005). A UK survey of people with CD found that on average, patients consulted their GP about their symptoms on 13 occasions before receiving a diagnosis (Gray and Papanicolas, 2010). Following diagnosis, it is recommended that people are followed up on an annual basis (National Institute for Health and Care Excellence (NICE), 2015), however, there are indications that the frequency and type of follow-up care people receive varies greatly (Bebb et al., 2006; Ciacci, Ciclitira et al., 2015). Despite a growing body of research measuring the health-related quality of life (HRQOL) of people with CD, few studies have explored the relationship between patients' experiences of health care services and HRQOL. Therefore, it is not known whether variations in care are related to HRQOL (i.e. whether poor experiences of care, such as lack of support following diagnosis, are related to HRQOL).

Researching patients' experiences of health care services will allow a fuller understanding of how care received during diagnosis and management varies between people with CD, and the relationship between health care experiences and HRQOL to be explored. Assessing patients' experiences of health care services and identifying aspects of services

that are significantly related to HRQOL will allow key areas for improvement to be identified, while also providing the much needed evidence to inform guidelines about the diagnosis and management of CD. Therefore, the main aim of this research study is to investigate patients' experiences of health care services and determine whether they are related to HRQOL. To achieve this, appropriate measurement tools will be developed through mixed methods and used in a cross-sectional survey. The research design is set out in full at the end of this chapter, and methodology described in detail in subsequent relevant chapters.

The remainder of this chapter provides an introduction to CD and a review of the literature on HRQOL and patients' experiences of health care services in CD. Following this, the study's aims, objectives and research design are set out. The chapter concludes by outlining the structure of this thesis.

1.2 Coeliac disease

1.2.1 Epidemiology and pathogenesis

Coeliac disease is a chronic gastrointestinal autoimmune condition triggered by the consumption of gluten, a protein found in wheat, barley and rye. The prevalence of CD in the UK and Europe is 1% (Mustalahti et al., 2010; van Heel and West, 2006) and is increasing in Western countries (Lionetti and Catassi, 2015). The condition occurs in approximately twice as many women as men (Freeman et al., 2011). Many people remain undiagnosed, with studies estimating that only 1 in 8 people with CD have received a diagnosis (van Heel and West, 2006).

The consumption of gluten within this population results in damage to the small intestine, leading to villous atrophy, i.e. flattening of the finger-like projections that line the small intestine. As a result, symptoms are often experienced prior to diagnosis, and include diarrhoea, abdominal discomfort, fatigue, unplanned weight loss, and persistent mouth ulcers. However, some people do not experience symptoms (asymptomatic CD), or only recognise symptoms retrospectively once treatment has commenced (subclinical CD) (Ludvigsson, Leffler et al., 2013).

Coeliac disease can develop at any age, with adults most frequently diagnosed in their fourth to sixth decade (i.e. aged 30-59) (Green, Stavropoulos et al., 2001; Ludvigsson, Card et al., 2015). The development of CD has a genetic factor, with almost all people with CD having the genes HLA-DQ2 or HLA-DQ8 (Sollid, 2002). As such, family members of those diagnosed have an increased risk of developing the condition, with the risk ranging from 2-20% depending on the relationship and the number of HLA-DQ2 copies present (Ludvigsson, Bai et al., 2014). The development of CD also has environmental factors, of which a key factor is the presence of gluten in the diet. However, as approximately 30% of the population are genetically susceptible to CD, the majority of which consume gluten, it is thought that other environmental factors are also important (Green, Lebwohl and Greywoode, 2015). Although this field of research is in its infancy (Ludvigsson and Green, 2014), it is thought that factors such as the composition of intestinal microbiota (which may be determined by factors such as genetics, antibiotics and other drugs), experiencing intestinal infections such as rotavirus or Campylobacter, and the age at which gluten is introduced may play a role (Lionetti and Catassi, 2015). It was previously thought that introducing gluten between 4-6 months of age, and

breastfeeding were protective against the development of CD (Lionetti and Catassi, 2015). However, two recent studies, 'PreventCD' and 'Celiprev', found no association between the timing of gluten introduction or duration of breastfeeding and the development of CD (Ludvigsson and Green, 2014). The presence of other autoimmune conditions is another factor that increases the risk of developing CD (Mooney, Hadjivassiliou et al., 2014).

1.2.2 Diagnosis

To diagnose CD in accordance with the National Institute for Health and Care Excellence (NICE) guidelines (NICE, 2015), adults with suspected CD should first undergo serological testing (i.e. have their blood tested for antibodies that are produced in response to the consumption of gluten in people with CD). If the blood test is positive (i.e. antibodies are present) or clinical suspicion remains despite a negative blood test result, it is recommended that adults are referred to a specialist for an endoscopy (NICE, 2015; Coeliac UK, n.d., d). An endoscopy is a medical procedure in which a thin tube with a camera is passed via the mouth into the intestine in order to examine it. During the procedure, an intestinal biopsy is normally taken for closer examination. While the focus of this thesis is adults, it is worth noting that the process for diagnosing children is slightly different, as outlined in joint guidelines produced by the British Society of Paediatric Gastroenterology, Hepatology and Nutrition (BSPGHAN) and Coeliac UK (Murch et al., 2013). While a biopsy showing evidence of villous atrophy is necessary to confirm a diagnosis of CD in adults (Hopper et al., 2007), in the circumstance where a child has symptoms of CD and high levels of antibodies in their blood, then a second antibody

blood test along with a genetic test can be carried out in place of an endoscopy (Murch et al., 2013)[1]. It is possible that a similar approach may be adopted for adults in the future.

1.2.3 Treatment – the gluten-free diet

At present, the only treatment for CD is a life-long GFD (Green and Cellier, 2007), i.e. a diet free of wheat, barley, and rye. The inclusion of oats within a GFD is controversial due to a lack of evidence regarding their suitability. Oat products are often contaminated with gluten-containing grains (Ciacci, Ciclitira et al., 2015), but pure uncontaminated oats are available, and a small quantity, eaten daily, is thought to be safe. However, a small number of people with CD are intolerant to oats, and the long-term risks of oat consumption are unknown (Ciacci, Ciclitira et al., 2015). Labelling regulations (EU 41/2009) issued by the European Commission state that food products containing 20 parts per million of gluten or less can be labelled 'gluten-free' (European Commission, 2009).

The cost of gluten-free products is at least four times more expensive than their gluten-containing counterparts, with limited availability in budget supermarkets and corner shops (Burden et al., 2015). In the UK, gluten-free staple foods, such as bread and pasta, are available on prescription. However, the provision of prescriptions and range of products available varies geographically, with some Clinical Commissioning Groups[2] (CCGs) restricting availability (e.g. to children and pregnant women) or stopping them altogether. This raises concerns in relation to the affordability of gluten-free food for

[1] Flowcharts showing the diagnostic pathways for symptomatic and asymptomatic children can be found in the joint BSPGHAN and Coeliac UK guidelines (Murch et al., 2013).

[2] Clinical Commissioning Groups are bodies responsible for commissioning local health care services in England.

lower socio-economic groups, and raises questions about whether changes in prescribing policy will affect adherence to the GFD.

The burden of following a GFD has been found to be greater than the treatment burden of chronic conditions such as hypertension and gastroesophageal reflux disease, and comparable to end stage renal disease (Shah et al., 2014). Sverker et al. (2005) found people faced particular difficulties when eating outside of the home and at work.

A systematic review by Hall et al. (2009) investigated factors associated with adherence to a GFD, and found that strict adherence ranged from 42-91%. Adherence was found to be most strongly associated with membership of a support group and regular dietetic follow-up, and to a lesser extent with sociocultural factors (e.g. cultural differences between White and South Asian groups), and emotional factors (i.e. depression and anger) (Hall et al., 2009). Hall et al's conclusions are limited as methods of measuring adherence vary between studies, with no gold standard currently available.

The difference in adherence between South Asians and White Caucasians was investigated by Butterworth, Banfield et al. (2004). They found fewer South Asians followed a fairly strict or strict GFD compared with White Caucasians (66.6% compared with 74% respectively), and suggested that this may be due to South Asians having difficulty understanding or complying with the diet.

1.2.4 Alternative treatments

While a GFD is the only current treatment for CD, there are a growing number of complementary or alternative therapies in development. Some treatments are designed to be administered alongside a GFD, for example, ALV003 (Alvine Pharmaceuticals) is an enzyme which aims to break up small amounts of gluten (i.e. gluten consumed inadvertently) to prevent intestinal damage and symptoms from occurring. Other treatments are designed to alter the immune response, allowing people to return to a gluten-containing diet (e.g. ImmusanT's Nexvax2 vaccine). To date, no therapies have reached Phase III clinical trials (Wungjiranirun et al., 2016), which assess a drug's effectiveness, and therefore the GFD is likely to remain the only treatment in the near future, 'and probably longer' (Ludvigsson, Card et al., 2015).

1.2.5 Complications

Following diagnosis, a GFD is effective in the majority of patients, with intestinal damage typically repairing once the diet has commenced (Ludvigsson, Leffler et al., 2013). However, symptoms and villous atrophy sometimes persist (non-responsive CD). In the majority of cases this is due to inadvertent gluten consumption or the presence of an associated condition, such as small bowel bacterial overgrowth (Mooney, Evans et al., 2012), while in a small number of cases, the cause is unknown and is referred to as refractory CD. Further information about refractory CD can be found in Rishi et al. (2016).

Coeliac disease is associated with a small increased risk of malignancy and mortality compared with the general population (Hopper et al., 2007). In particular, there is a small increased risk of developing lymphoma (Abdul Sultan et al., 2015), with estimates

suggesting approximately 7-8 in every 10,000 people with CD will develop lymphoma each year (Ludvigsson, Card et al., 2015; Mooney, Hadjivassiliou and Sanders, 2014).

Undiagnosed CD is associated with fertility problems and adverse pregnancy outcomes (e.g. miscarriage) (Hopper et al., 2007), however, women with diagnosed CD have been found to have the same fertility as the general population (Ludvigsson, Card et al., 2015).

At diagnosis, coeliac disease is associated with reduced bone mineral density in 50-70% of patients and increased fracture risk (Malamut and Cellier, 2015). Bone mineral density has been shown to improve on a strict GFD (Mooney, Hadjivassiliou and Sanders, 2014), however the risk of fractures, both before and after diagnosis, is more common in people with CD (Ludvigsson, Michaelsson et al., 2007).

People with CD are more likely to develop other autoimmune diseases, with type I diabetes and autoimmune thyroiditis the most common (Malamut and Cellier, 2015). The risk of developing complications is reduced by strict adherence to a GFD (Mooney, Hadjivassiliou and Sanders, 2014). A wider discussion of complications associated with CD is beyond the scope of this thesis, but further information can be found in Malamut and Cellier (2015) and Abdul Sultan et al. (2015).

1.2.6 Other gluten-related disorders

Coeliac disease is one of a number of health conditions related to the consumption of gluten (Figure 1) (Sapone et al., 2012). Other autoimmune conditions that sit alongside CD are dermatitis herpetiformis (DH), a skin manifestation of CD affecting 1 in every

3,300 people in the UK (i.e. a prevalence of 0.03%) (West et al., 2014), and gluten ataxia, a neurological manifestation of CD (Ludvigsson, Leffler et al., 2013). Reactions to gluten can also be allergic (i.e. wheat allergy), or neither autoimmune nor allergic (i.e. 'non-coeliac gluten sensitivity'). There is currently no standard diagnostic approach for 'non-coeliac gluten sensitivity' (Ludvigsson, Leffler et al., 2013).

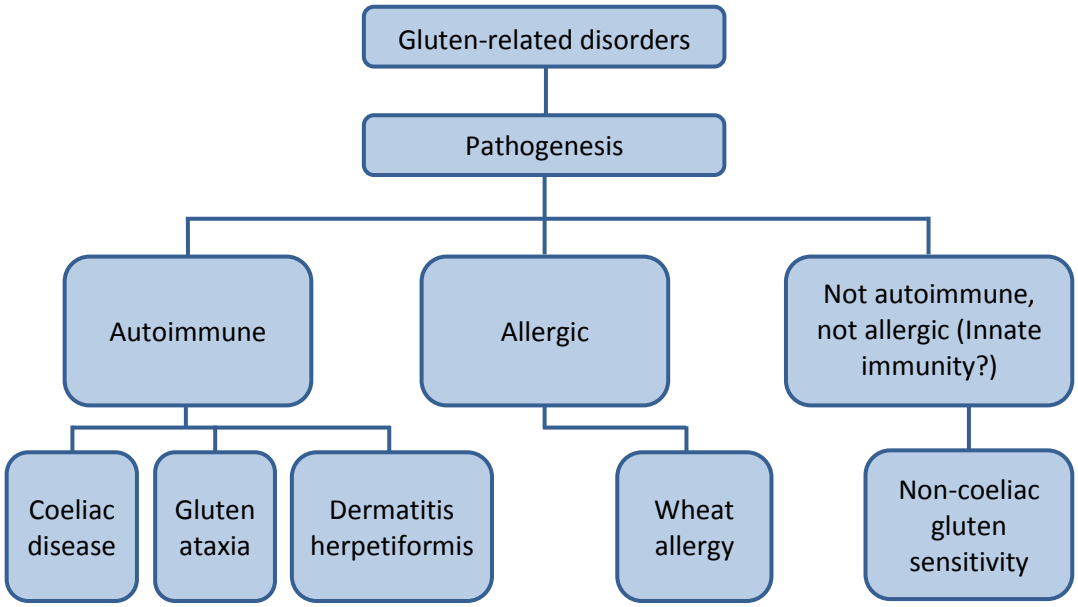


Figure 1. Classification of gluten-related disorders (adapted from Sapone et al., 2012)

1.3 Health-related quality of life

1.3.1 Introduction

Traditionally, health has been measured from a biomedical perspective, using measures of mortality and morbidity, and as such, the broader impact of health conditions on psychological and social factors have been ignored. Over the last few decades, there has been a move towards evaluating health care from the patient's perspective (Black and

Jenkinson, 2009), with reports from patients now considered a reliable and important source of information (Jenkinson and Morley, 2016).

Health-related quality of life can be defined as an individual's 'subjective perception of the effects of the disease and treatment(s) on daily life; well-being; and psychological, physical, and social functioning' (Patrick et al., 2011), and covers aspects of general health, cognitive function, mental health, emotional state, subjective well-being, life satisfaction, and social support (Jenkinson and McGee, 1998). Quality of life (QOL) is also referred to in the literature, and is generally a broader concept than HRQOL, covering additional aspects such as personal wealth, level of safety, and opportunity (McDowell, 2006).

1.3.2 Patient-reported outcome measures

HRQOL is typically measured using patient-reported outcome measures (PROMs), short questionnaires that the patient completes. PROMs can be defined as 'any report of the status of a patient's health condition that comes directly from the patient without interpretation of the patient's response by a clinician or anyone else' (U.S. Food and Drug Administration, 2009). They can be categorised according to the population for which they are intended or their content. The main categories are: disease-specific (e.g. Parkinson's Disease Questionnaire), site or region specific (e.g. Oxford Knee Score), dimension-specific (e.g. Beck Depression Inventory), or generic (e.g. SF-36v2). There are advantages associated with each type of measure, for example, disease-specific measures may be more responsive to change (Patrick and Deyo, 1989), whereas generic measures

allow results to be compared across conditions and with that of the general population (Jenkinson and Morley, 2016).

In addition to the above categories, there are preference-based measures, which allow for the valuation of health states (Feeny, 2005). 'Societal preferences' of different health states allow utility scores to be calculated (York Health Economics Consortium, 2016), which can be used for the economic evaluation of health care. The most widely used utility measure is the EQ-5D (Jenkinson and Fitzpatrick, 2013).

The number of PROMs has grown rapidly since the early 1990s (Garratt et al., 2002), to the extent that there are often multiple disease-specific measures available. In order to aid users to select an appropriate PROM, criteria for their evaluation have been developed (e.g. by Terwee et al., 2007), and are utilised in Chapter 2 to evaluate coeliac disease-specific PROMs.

Use of PROMs

There are many ways in which PROMs can be used, for example, within clinical trials to assess the effectiveness of newly-developed treatments; as a screening tool to identify patients requiring treatment; and to aid doctor-patient communication in clinical practice. PROMs can be used to assess health at one point in time, or changes in health, by administering the measure on two or more occasions.

Health policy

The UK government's commitment to improving the HRQOL of people with long-term conditions is set out in the National Health Service (NHS) Outcomes Framework (i.e. a set

of indicators by which the health service is measured), with one of the five domains focusing on this issue (Great Britain. Department of Health, 2014). Within England, the government has driven the collection of PROMs data to allow the comparison of the performance of health care service providers (Black, 2013). As part of this initiative, since 2009, the English NHS has routinely collected PROMs data from people undergoing the following four elective surgical procedures: hip replacements, knee replacements, groin hernia surgery, and varicose vein surgery (Black, 2013).

1.3.3 Health-related quality of life in coeliac disease

There have been no systematic reviews assessing HRQOL in CD to date. However, Kurppa, Collin, Mäki et al. carried out an expert review in 2011. They reviewed articles about HRQOL in both adults and children with CD, and concluded that reduced HRQOL was, or may be, associated with the presence of symptoms at diagnosis, co-morbidities, poor adherence, and female gender. They also found that HRQOL typically improves on commencement of a GFD. A limitation of the review is the lack of detail regarding the methodology used to conduct it, for example, the authors provide no details of their search strategy, and therefore it is hard to assess how comprehensive the review was. As such, it was necessary to conduct a further review of the literature as part of this thesis.

A scoping review, as defined by Grant and Booth (2009), was conducted to identify and summarise research assessing HRQOL in CD. A systematic search to identify relevant literature was conducted in PubMed, EMBASE, PsycINFO, CINAHL, and the BNI (from inception to 31st May 2016) using the same search strategy and inclusion and exclusion criteria as used for the systematic review, reported in Chapter 2 (see Section 2.2). This

was supplemented with further searches of PubMed and Google Scholar to identify relevant qualitative studies and reviews. This approach was taken to identify the majority of literature in the field to provide an overview of research investigating HRQOL in CD, and was not intended to be an all-inclusive and systematic review.

A summary of the findings of the review follows.

HRQOL compared with the general population

The HRQOL of people with newly-diagnosed CD has been found to be worse than healthy controls (Gray and Papanicolas, 2010; Kurppa, Collin, Sievänen et al., 2010; Mustalahti, Lohiniemi et al., 2002; Tontini et al., 2010; Ukkola et al., 2011; Viljamaa et al., 2005; Zingone, Siniscalchi et al., 2010). Studies following up people with newly-diagnosed CD after one year of following a GFD found HRQOL had improved to a level comparable with controls (Tontini et al., 2010; Ukkola et al., 2011).

Many studies (Barratt, Leeds, Robinson et al., 2011; Barratt, Leeds and Sanders, 2011; Cranney, Zarkadas, Graham, Butzner et al., 2007; Cranney, Zarkadas, Graham, and Switzer, 2003; Fera et al., 2003; Gray and Papanicolas, 2010; Norström et al., 2011; O'Leary, Wieneke, Buckley et al., 2002; Usai, Minerba et al., 2002; Viljamaa et al., 2005; Zarkadas et al., 2006; Zingone, Siniscalchi et al., 2010) have also compared the HRQOL of people with CD who have been diagnosed for varying lengths of time with healthy controls. The majority of these studies (Barratt, Leeds and Sanders, 2011; Cranney, Zarkadas, Graham, Butzner et al., 2007; Cranney, Zarkadas, Graham, and Switzer, 2003; Gray and Papanicolas, 2010; Norström et al., 2011; O'Leary, Wieneke, Healy, et al., 2004;

Viljamaa et al., 2005; Zarkadas et al., 2006) found that the HRQOL of people with CD was comparable with healthy controls. However, five studies (Barratt, Leeds, Robinson et al., 2011; Fera et al., 2003; Usai, Minerba et al., 2002; Wieneke, Buckley et al., 2002; Zingone, Siniscalchi et al., 2010) found the HRQOL of people with CD to be worse when compared with healthy controls. In two of these studies (Barratt, Leeds, Robinson et al., 2011; Wieneke, Buckley et al., 2002), it is not clear whether the finding was statistically significant. It is possible that the difference in findings is due to the recruitment method. The majority of studies finding people with CD to have a reduced HRQOL recruited participants through hospitals while also recruiting healthy participants to act as a control group. This is in contrast to the studies finding the HRQOL of people with CD to be similar to that of controls, which mostly obtained participants through support groups and compared their HRQOL with normative population data. It is possible that participants recruited through hospital settings may be experiencing more difficulties in relation to their CD and require more care as a result. In contrast, participants that are members of a support group may feel more able to cope with the condition as a result of the support that they receive.

Finally, some studies compared the HRQOL of people with CD with that of healthy controls, by gender (Hallert, Grännö, Grant et al., 1998; Roos, Kärner, and Hallert, 2006; Tontini et al., 2010). The HRQOL of women with CD was found to be worse than female controls as measured by the SF-36, significantly so in the general health, vitality, and role emotional domains (Hallert, Grännö, Grant et al., 1998) and MCS and PCS scores (Tontini et al., 2010). The psychological well-being of women diagnosed for between 8 and 12 years, as measured by the PGWB, was also worse than female controls, although this did

not reach statistical significance (Roos, Kärner, and Hallert, 2006). Conversely, the HRQOL of males with CD was found to be comparable with or better than male controls (Hallert, Grännö, Grant et al., 1998; Roos, Kärner, and Hallert, 2006; Tontini et al., 2010).

Psychological health

A large number of studies have explored the impact of CD on aspects of psychological health, specifically anxiety and depression (Addolorato, Stefanini et al., 1996; Addolorato, Capristo et al., 2001; Addolorato, De Lorenzi et al., 2004; Addolorato, Mirijello et al., 2008; Ciacci, Iavarone et al., 1998; Fera et al., 2003; Zingone, Siniscalchi et al., 2010), and social phobia (Addolorato, Mirijello et al., 2008). Significantly more depression was found in people with untreated CD (i.e. those not following a GFD) compared with the general population (Addolorato, Stefanini et al., 1996; Addolorato, Capristo et al., 2001; Addolorato, Mirijello et al., 2008; Zingone, Siniscalchi et al., 2010). All four studies recruited small samples (ranging from 16 to 40 participants) through hospital clinics in Italy.

There is mixed evidence regarding anxiety levels, with some studies finding significantly more anxiety in those with untreated CD compared with healthy controls (Addolorato et al., 2001; Zingone, Siniscalchi et al., 2010), while others found it to be comparable (Addolorato et al., 1996). While all studies measured anxiety using the State-Trait Anxiety Inventory (STAI), one potential factor affecting the conclusions drawn may be due to the way in which high levels of anxiety were defined. Some compared mean anxiety scores of those with CD with healthy controls, while others calculated the percentage of respondents with scores above a certain cut-off point.

Studies comparing depression between people with CD following a GFD and the general population found significantly higher levels of depression in people with CD (Addolorato et al., 2001; Addolorato, Mirijello et al., 2008; Ciacci, Iavarone et al., 1998; Fera et al., 2003). The mean duration of diagnosis ranged from 1 year to 9.1 years across the studies, which may suggest that length of diagnosis is not a factor in the presence of depression. Fera et al. (2003) also found significantly higher anxiety scores in people with CD on a GFD compared with healthy controls. The presence of social phobia has also been explored by Addolorato et al. (2008) in a sample of 40 people with CD, finding a higher percentage of social phobia in people with CD when compared with healthy controls. All four studies were conducted in Italy and measured depression using the modified Zung Self-rating Depression Scale (Z-SDS) in hospital samples.

Addolorato et al. (2001) followed a group of patients from diagnosis up until they had been following a GFD for one year. They found that the percentage of people with depression and trait anxiety remained similar following one-year of treatment, while the percentage of people with state anxiety reduced significantly to that similar to controls. Addolarato et al.'s findings lead them to speculate that depression may indeed be a feature of CD.

Gender and age

Several studies have compared the HRQOL of men and women with CD using generic and disease-specific measures, generally by surveying support group members. The majority of studies found that men with CD report a significantly better HRQOL than women with

CD (Norström et al., 2011; Roos, Kärner, and Hallert, 2006; Zampieron, 2011; Zarkadas et al., 2006). In contrast, two studies found the HRQOL of men and women with CD were comparable (Black and Orfila, 2011; Ciacci, D'Agate et al., 2003), however, both measured HRQOL with unvalidated questionnaires. There is some evidence to suggest that men in the general population also report better HRQOL than women (Norström et al., 2011; Roos, Kärner, and Hallert, 2006), although, this difference appears to be more pronounced in CD. The reason for this difference is unclear but Sverker et al. (2009) suggest that women experience greater responsibility for work carried out within the household, including the preparation of food, which together with other responsibilities (e.g. paid work) can have a greater impact on daily life.

There is mixed evidence regarding the relationship between HRQOL and age in people with CD. An evaluation of 89 patients following a GFD for approximately 10 years found HRQOL did not differ significantly by age (Hallert, Grännö, Grant et al., 1998). The results of a second study (Fera et al., 2003), in which 100 patients were recruited through a hospital, support these findings. This contrasts with a study by Gray and Papanicolas (2010), which found HRQOL before diagnosis was related to the age of the patient at diagnosis, i.e. the younger the patient at diagnosis, the lower their HRQOL. While the first two studies used the SF-36 to assess HRQOL, the third study (Gray and Papanicolas, 2010) assessed HRQOL using the EQ-5D. It is questionable whether the EQ-5D is a good choice of measure in people with CD as its constructs are less relevant to people with CD, in particular, CD would not be expected to impact on the respondent's 'mobility' or ability to 'self-care'.

Impact of treatment

As stated previously, the only treatment currently available for people with CD is a GFD. Many studies (Casellas, Rodrigo, López Vivancos et al., 2008; Ciacci, Maiuri et al., 2009; Kurppa, Collin, Sievänen et al., 2010; Leeds et al., 2011; Mustalahti, Lohiniemi et al., 2002; Peräaho, Kaukinen, Paasikivi et al., 2003; Tontini et al., 2010; Vilppula et al., 2011) have evaluated the impact of following a GFD on the HRQOL of people with CD. The majority of studies compared participants' change in HRQOL over a one year period by administering questionnaires at two points in time, once at diagnosis and again after 12 months on a GFD.

The majority of studies (Casellas, Rodrigo, López Vivancos et al., 2008; Ciacci, Maiuri et al., 2009; Kurppa, Collin, Sievänen et al., 2010; Mustalahti, Lohiniemi et al., 2002; Peräaho, Kaukinen, Paasikivi et al., 2003; Tontini et al., 2010) found that a GFD improved HRQOL, although one study (Ciacci, Maiuri et al., 2009) did not report whether this improvement was significant, and a second study (Tontini et al., 2010) found that improvements were confined to women. The remaining two studies (Vilppula et al., 2011; Leeds et al., 2011) found that a GFD did not have an impact on HRQOL. Both of these studies evaluated the impact of a GFD in people diagnosed through screening programmes. It is likely that screen-detected patients suffer no or few symptoms prior to diagnosis, and therefore are less likely to perceive the benefits of a GFD. Improvements in any symptoms that are experienced may be offset by managing a more complicated diet (Leeds et al., 2011).

In addition to the prospective studies discussed above, two studies (Gray and Papanicolas, 2010; Norström et al., 2011) measured HRQOL before diagnosis retrospectively through the administration of cross-sectional surveys to members of support groups. Both studies found significant improvements in HRQOL at the time of the survey compared with before diagnosis, as measured by the EQ-5D. While a retrospective approach allowed for much larger sample sizes, it is possible that the collection of data was affected by recall bias.

A further study (Green, Stavropoulos et al., 2001) asked people with CD to rate their HRQOL on a scale before diagnosis (i.e. bad, fair, good, and excellent), again this was a retrospective assessment, and after diagnosis (i.e. worse, unchanged, and improved). Seventy-seven per cent of people with CD reported their HRQOL as improved. A limitation of this study is that it did not use a validated HRQOL measure.

The above findings indicate that the HRQOL of people with CD improves upon commencement of a GFD. However, improvements may not occur or may be limited in certain groups (e.g. screen-detected patients and women) (Kurppa, Collin, Mäki et al., 2011).

Impact of support programmes

Two studies have developed and trialled support programmes for people with CD and assessed their impact on psychological health and well-being (Addolorato, De Lorenzi et al., 2004; Jacobsson, Friedrichsen et al., 2012a).

In the first study, Jacobsson, Friedrichsen et al. (2012a) assessed the impact of a patient education programme on the psychological well-being of women with CD who had followed a GFD for at least five years. Fifty women completed the patient education programme (10 weekly sessions), while a further 52 women were allocated to a control group (information sheets only). Women attending the education programme reported a significant improvement in overall well-being, a change that was significantly greater than the control group. After six months, only a significant improvement in vitality remained. Furthermore, women attending the patient education programme found interactions with others empowering, providing them with greater self-confidence (Jacobsson, Milberg et al., 2016).

In the second study, Addolorato et al. (2004) evaluated the effectiveness of psychological support counselling in 33 patients with newly-diagnosed CD experiencing anxiety and depression. Patients commenced a GFD and received counselling for six months, while a control group commenced a GFD only. After the intervention, significantly fewer patients reported depression compared with the control group, while the number of patients with anxiety was comparable.

A recent study found face-to-face support to be associated with better HRQOL, whereas support received online was associated with worse HRQOL (Lee, Wolf et al., 2016).

This evidence suggests that support programmes can be beneficial in terms of improving aspects of HRQOL in people with CD. However, further research is needed to explore the

longer term impacts of such initiatives and determine the best method (i.e. the type and timing of the intervention) and mode for intervention.

1.4 Patients' experiences of health care services

1.4.1 Introduction

Asking patients about their experiences of health care services as a method of gaining information to indirectly improve the quality of health care has become common practice. Within a UK context, the government, in particular, have expressed their commitment to collecting patient experience data in reports (e.g. Great Britain. Department of Health, 2010a; Great Britain. Department of Health, 2010b) and government initiatives, such as the National Patient Survey Programme (NPSP). Regular patient experience surveys are conducted as part of the NPSP to assess the quality of NHS services from the patient's perspective. These surveys focus on the factual aspects of the processes of care, which allows areas for service improvement to be identified (Coulter et al., 2009; Sizmur and Redding, 2009).

The NHS Outcomes Framework (Great Britain. Department of Health, 2014), introduced in Section 1.3.2 is further evidence of the English government's commitment to providing patients with a positive experience of care, with one of the five domains focusing on this aspect.

Several conceptual frameworks of patient experience have been developed, including the NHS Patient Experience Framework (Great Britain. Department of Health, 2012), and the Picker Institute's 'Picker principals' (Picker Institute Europe, n.d.), which include

dimensions such as: access to care; information provision; communication; continuity of care; and emotional support.

The information provided by patients about their experiences of health care services can be categorised as 'reports' (i.e. their accounts of what happened) or 'evaluations' (i.e. their rating or satisfaction) of care (Ahmed et al., 2014). Historically, research has focused on patients' evaluations of their care, but there has been a move towards asking patients about specific experiences of care (Fitzpatrick, 2002) in order to obtain information that can be used to improve the quality of services. By asking patients to report accounts of their experiences (e.g. 'Have you had a follow-up appointment in the past 12 months?'), clear factual results that are linked to follow-up actions can be obtained (Coulter, 2006). Despite the predominance of 'report'-type questions, the value of evaluative questions should still be recognised. For example, the inclusion of evaluation-type questions can help to identify problematic aspects of health care that are most important to patients (Fitzpatrick, 2002), or allow the acceptability of issues, such as waiting times, to be assessed (Ahmed et al., 2014).

1.4.2 Health care services related to coeliac disease

Guidelines outlining recommended practices for the diagnosis and management of CD have been developed by various bodies, including NICE (NICE, 2009; NICE, 2015), the British Society of Gastroenterology (BSG) (Ciclitira et al., 2010; Ludvigsson, Bai et al., 2014), and the Primary Care Society of Gastroenterology (PCSG) (Primary Care Society for Gastroenterology, 2006).

A scoping review of literature examining patients' experiences of health care services in CD was conducted (see Appendix A for search strategy). The aim of this review was to identify key literature in the field and provide an overview of research investigating patients' experiences of health care services in CD. Of the studies identified, of particular interest is a UK study, which found that the mean duration of symptoms before diagnosis was 13.2 years (Gray and Papanicolas, 2010). Studies conducted in Canada (Cranney et al., 2007) and Switzerland (Vavricka et al., 2016) also found long delays to diagnosis of 11.7 years and 7.3 years respectively. Vavricka et al. (2016) found the delay to diagnose females was significantly longer than males.

Long-term management of coeliac disease

Guidelines recommend that people with CD are followed-up on an annual basis (NICE, 2015; Ciclitira et al., 2010). However, there are indications that the frequency and type of follow-up care varies greatly, with some patients receiving no medical care while others are reviewed annually (Ciacci, Ciclitira et al., 2015). Kurien et al. (2016) suggest that these significant variations have developed following the introduction of CCGs. A UK study found 62% of participants received regular follow-up care (Bebb et al., 2006).

Nelson et al. (2007) also found the provision of dietetic services to be inadequate, with current provision (approximately 2.9 hours per 100,000 patients) much less than that estimated to be required to provide a basic level of care (i.e. a 30 minute review per patient per year).

There is a lack of evidence regarding the value of providing follow-up care to patients, as well as who should conduct this follow-up (Haines et al., 2008; Ciclitira et al., 2010). Bardella et al. (1994) found those receiving regular follow-up were more adherent to the GFD. Patients' preference for follow-up is with a dietitian with a doctor available (Bebb et al., 2006). Follow-up by a dietitian or trained physician could help ensure adequate nutrient intake and avoid potential complications (Ciacci, Ciclitira et al., 2015). Sanders et al. (2005) recommend that every hospital have a specialist coeliac dietitian available to empower patients to better manage their condition when outside of the home. With regards to determining which patients should receive follow-up care, Haines et al. (2008) warn that symptoms alone should not guide this decision. Kurien et al. (2016) suggest that both symptom and histological status could be used to classify patients and determine the level of support required. Due to a lack of evidence surrounding these issues, two of five recommendations made by NICE, published in the most recent guidelines (NICE, 2015), encourage further research on these topics, specifically, the frequency of follow-up and the role of the dietitian.

1.5 Relationship between patients' experiences of health care services and outcomes

Surprisingly, few studies have investigated associations between patients' experiences of health care services and HRQOL in relation to CD. A USA study (Mahadev et al., 2013) found that dietitian use was not associated with HRQOL. However, relationships have been found between information provision and outcomes. Häuser, Stallmach et al. (2007) found a significant association between HRQOL and dissatisfaction with GPs' provision of information about CD. A Finnish study (Ukkola et al., 2012) also found the

provision of sparse information and unsatisfactory doctor-patient communication was related to negative attitudes towards CD and the GFD, although they did not specifically measure HRQOL. This suggests the need for further research investigating the relationship between patients' experiences of health care services and HRQOL.

1.6 Research aims and objectives

The scoping reviews conducted to identify the majority of literature investigating HRQOL and patients' experiences of health care services in CD (discussed in sections 1.3.3, 1.4.2, and 1.5), found very little research exploring experiences of health care services of people with CD. Furthermore, the relationship between health care experiences and HRQOL within this population group is unknown. This is a cause for concern as the frequency and type of health care received varies considerably. This study will provide information about whether health care services are meeting the needs of people with CD, and whether there is a relationship between patients' experiences of health care and HRQOL. It is anticipated that the outcomes of the study will be used to inform relevant policies and guidelines, and ultimately, improve patient care.

The overall aim of this study was to investigate the relationships between the HRQOL of people with CD and their experiences of health care services. This is achieved by the following objectives:

- To assess the quality of health care services from the patients' perspective and identify areas for service quality improvement.
- To understand how CD impacts on HRQOL and identify determinants of HRQOL.

- To undertake a review of measurement instruments used to assess HRQOL in adult CD and select an appropriate measure for use in this study. On the basis of this review, which indicated no suitable measure is available, the development of a new measure will be documented.
- To develop a patient experience questionnaire to assess experiences of health care services for the diagnosis and management of CD.

1.7 Research design

The research design used to investigate the above aims and objectives is set out in Figure 3 and is comprised of the five phases described below. The primary method of investigation was a cross-sectional survey, conducted in Phase 5, which incorporated a HRQOL measure and a questionnaire about experiences of health care services. The previous four phases of research focused on the development of these questionnaires, using both qualitative and quantitative methods.

In **Phase 1**, a review of PROMs was conducted to determine which measures have been used to assess HRQOL in CD, and ascertain whether an existing measure was suitable for use in this study. The review concluded that no measures were suitable and therefore, the development of a new measure was built into the study design.

Phases 2-4 focused on the development of a new PROM and patient experience questionnaire, named the Coeliac Disease Assessment Questionnaire (CDAQ) and Coeliac Disease Patient Experience Questionnaire (CD-PEQ) respectively. In **Phase 2**, qualitative interviews were conducted and analysed to inform the development of candidate items

for the questionnaires. These were refined in **Phase 3** with input from experts, in the form of meetings and interviews, and people with CD through cognitive interviews. The CDAQ was also subject to two further stages of development, firstly, a translatability assessment, which aimed to reduce problems arising in future translations, and secondly, in **Phase 4**, a cross-sectional survey ('Survey 1') to reduce the number of items in the measure and identify its dimensions.

A cross-sectional survey was conducted in the final Phase (**Phase 5)**, which incorporated both the CDAQ and CD-PEQ. The survey data was analysed using regression analysis and conclusions in relation to the research aims were drawn.

The US Food and Drug Administration (U.S. FDA, 2009) have produced guidance on the development of PROMs used in clinical trials to make label claims about products (see Figure 2 for development diagram). There is potential for the CDAQ to be used beyond this study, for example, in clinical trials assessing new treatments for CD, and therefore, the research design to develop the CDAQ followed FDA guidance. FDA guidelines are seen as best practice for the development of PROMs regardless of their intended use (Speight and Barendse, 2010).

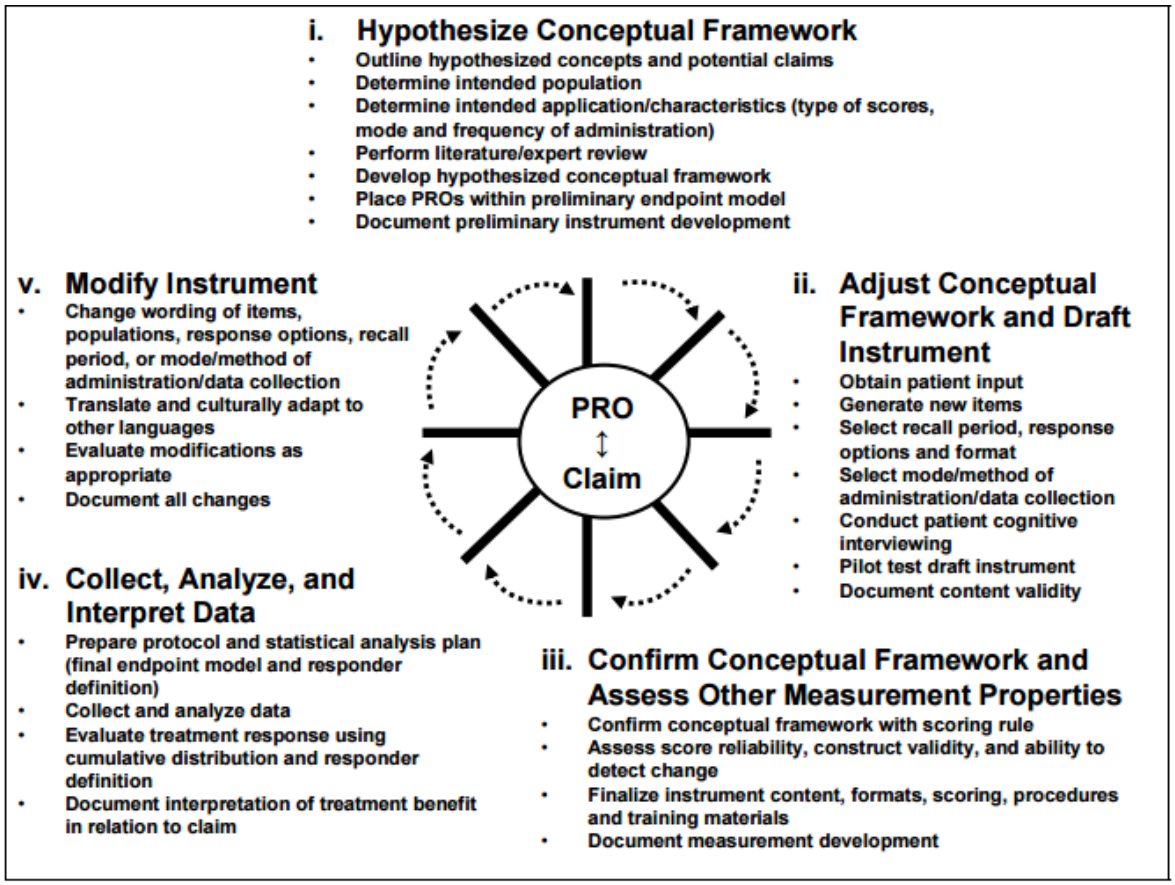


Figure 2. FDA guidance process diagram for the development of a PRO instrument (U.S. FDA, 2009)

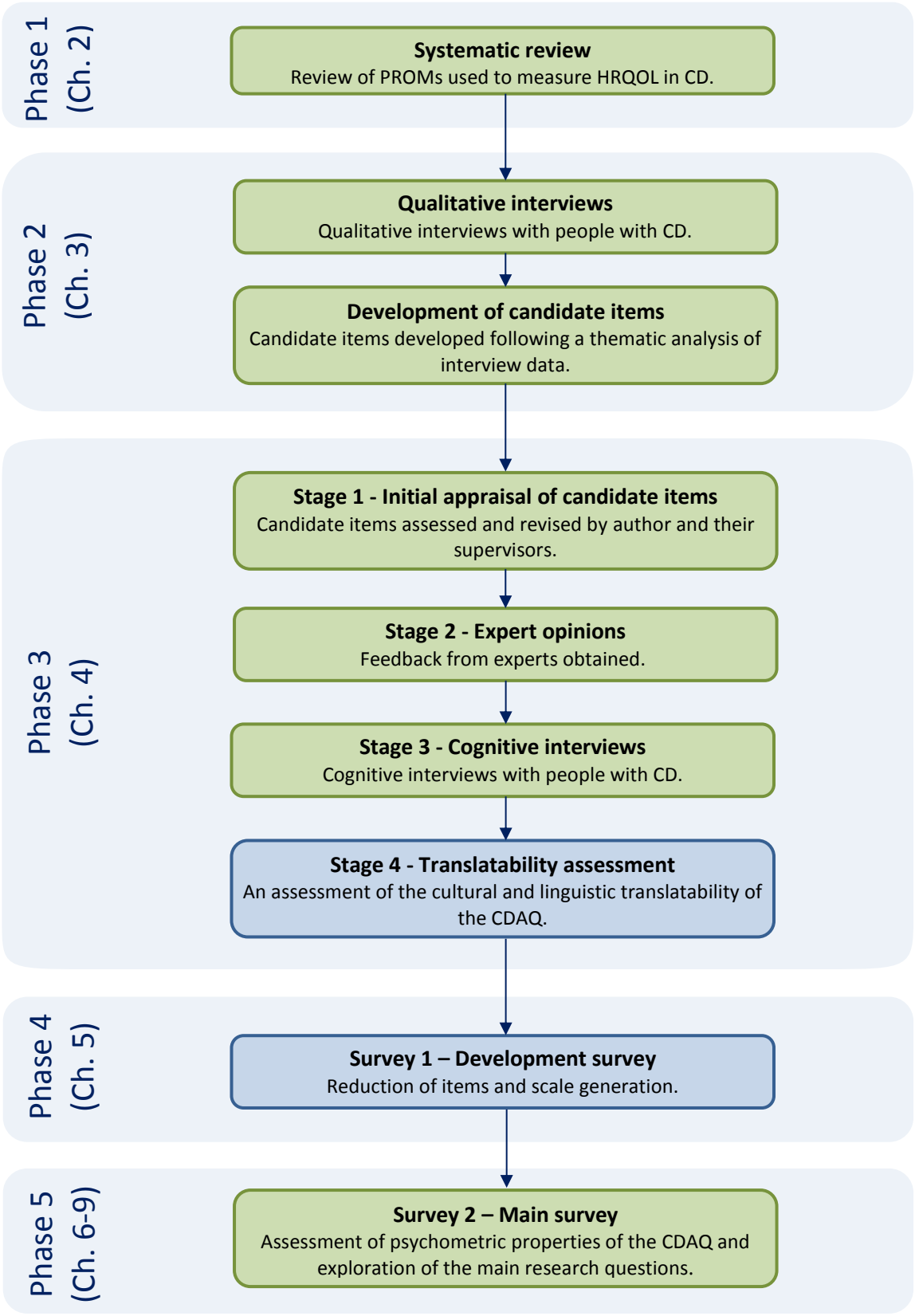


Figure 3. Research methodology

Green boxes show steps applicable to both the CDAQ and CD-PEQ. Blue boxes show steps relevant to the CDAQ only. Phase 1: Review of PROMs in CD; Phase 2: The qualitative development of items; Phase 3: Refining and pre-testing the questionnaires; Phase 4: Survey 1 – Development survey; Phase 5: Survey 2 – Main survey.

1.8 Thesis structure

The first chapter of this thesis has provided some background information about CD, presented a summary of the current literature about HRQOL in CD and patients' experiences of health care services, and set out the aims and design of this research. The remaining nine chapters describe the research undertaken and present the results and conclusions of the study.

Chapter 2 presents a systematic review of existing PROMs that have been used to assess HRQOL in adults with CD. The psychometric properties of each disease-specific measure identified are evaluated. The chapter concludes that there are no suitable coeliac disease-specific PROMs to investigate the aims of this research and that a new PROM is needed.

The development of the new PROM (the CDAQ) and patient experience questionnaire (CD-PEQ) are presented in chapters three, four and five. **Chapter 3** discusses the qualitative interviews that were conducted to explore peoples' experiences of using health care services to diagnose and manage CD, and to identify the impact of CD on HRQOL. The main themes identified are discussed and candidate items for both questionnaires presented.

Chapter 4 discusses the stages undertaken to refine candidate items, and produce a draft version of the CDAQ and final version of the CD-PEQ. A four-stage process was followed, of which the first three stages applied to both questionnaires: stage one - an initial appraisal of items by researchers; stage two – experts reviewed and commented on

items; and stage three - cognitive interviews with people with CD. Stage four, a translatability assessment, was conducted for the CDAQ only.

Chapter 5 discusses the results of a cross-sectional survey (Survey 1) to identify the most suitable items for inclusion in the final version of the CDAQ. Statistical methods are applied to identify the dimensions of the CDAQ and their internal reliability is evaluated. The final version of the CDAQ is presented.

Following the finalisation of the CDAQ and CD-PEQ, the questionnaires were used in a second cross-sectional survey (Survey 2) to explore the aims of this thesis. Firstly, the data was used to evaluate the psychometric properties of the CDAQ (**Chapter 6**). Next, the results of Survey 2 are presented in Chapters 7 to 9. **Chapter 7** describes patients' experiences of health care services; **Chapter 8** presents the HRQOL of people with CD; and **Chapter 9** investigates the relationships between HRQOL and patients' experiences of services.

The final chapter, **Chapter 10**, discusses the findings of the research and describes its contribution to the field. The strengths and limitations of the study and areas for further research are also discussed.

CHAPTER 2:

A systematic review of patient-reported outcome measures used to assess health-related quality of life in coeliac disease

2.1 Introduction

The aims and objectives of this thesis and the methodology by which they were achieved is set out in the previous chapter. The main aim of the study is to investigate associations between HRQOL and patients' experiences of health care services in people with CD through a cross-sectional survey. To achieve this, an appropriate and valid PROM was needed for inclusion in the survey to assess HRQOL. The U.S. Food and Drug Administration (U.S. FDA, 2009) recommend reviewing available measures to assess their suitability, prior to the development of any new measure. At the time of the review, no existing reviews assessing CD-specific PROMs could be found. Therefore, it was necessary to conduct a systematic review of outcome measures used in CD as part of this research to determine whether an existing PROM was available for use in this study.

Systematic reviews gather the available evidence for decision-making purposes through the identification, evaluation and summary of relevant individual studies (Centre for Reviews and Dissemination, 2009). Guidelines on the conduct of systematic reviews have been set out by the Centre for Reviews and Dissemination (Centre for Reviews and Dissemination, 2009) and the Cochrane Collaboration (Higgins and Green, 2011). In addition, guidance for the reporting of systematic reviews has been developed by the PRISMA group (Moher et al., 2009). In brief, good quality systematic reviews should

include a comprehensive search strategy, clear criteria for the inclusion or exclusion of studies, and well-documented processes for assessing the quality of studies and extracting and synthesising the data (Centre for Reviews and Dissemination, 2009).

There are many examples of systematic reviews assessing the quality of PROMs in the literature. For example, Harris et al. (2016) reviewed PROMs used with patients undergoing hip or knee replacement surgery, while Kearney et al. (2012) reviewed PROMs used to assess and manage Achilles tendon rupture. The purpose of both studies was to identify the most promising PROMs for their respective health conditions.

2.1.1 Aims and objectives

The aim of this chapter was to conduct a systematic review of studies using PROMs to assess HRQOL in adults with CD. This was achieved by the following objectives:

- To identify PROMs that have been used to measure HRQOL in adults with CD;
- To evaluate the instruments identified;
- And to select an appropriate measure, for use in a cross-sectional survey, to allow the research aims of this thesis to be investigated.

2.2 Methods

A systematic literature search to identify studies assessing HRQOL in adults with CD was conducted in PubMed, EMBASE, PsycINFO, CINAHL, and the BNI to include publications up until 31st May 2016 (i.e. the date the search was conducted), with no defined start date. The search strategy was developed by the author, and reviewed by my supervisors and a subject-specialist librarian. The search strategy for PubMed is shown in Box 1 (with

strategies for the remaining databases available in Appendix B). Duplicate results were removed.

Firstly, the titles and abstracts of retrieved articles were reviewed against the inclusion and exclusion criteria (Box 2) to identify potentially relevant studies. Next, the full-text papers of these studies were retrieved and assessed against the criteria. Articles identified as relevant were included in the review. For this review and throughout this research, adults were defined as persons aged 18 years or older, following the legal definition within the UK and many other countries (University of Oxford, 2017).

Box 1. Search strategy (PubMed)

("Celiac Disease"[Mesh] OR "Diet, Gluten-Free"[Mesh] OR "Coeliac disease" OR "Celiac disease" OR Gluten sensitiv* OR Gluten-sensitiv* OR Gluten enteropath* OR "celiac sprue" OR "coeliac sprue" OR "nontropical sprue" OR "non-tropical sprue" OR "gluten intolerance" OR "gluten induced enteropathy" OR "gluten-induced enteropathy" OR "gluten free diet" OR "gluten-free diet")
AND
("Quality of Life"[Mesh] OR "Health Status"[Mesh] OR "Quality of life" OR QOL OR HRQOL OR HR-QOL OR HRQL OR HR-PRO OR HRPRO OR PROM OR PROMs OR PROs OR "Health Index" OR "Health Indices" OR "Functional Index" OR "Functional Indices" OR "Health Profile" OR "Health Status" OR "Health State" OR "Life Quality" OR "Well Being" OR Well-being OR Wellbeing OR Health level* OR "Level of health" OR Patient report* OR Patient-report* OR "Patient Rated" OR "Patient-rated" OR "Patient Rating" OR SF-36 OR SF36 OR SF-12 OR SF12 OR EQ-5D OR EQ5D OR GSRS OR PGWB OR HADS OR STAI OR BDI OR CDQ OR CD-QOL OR CDQOL OR GIQLI OR "Zung self-rating" OR M-SDS)
Limitations: "title/abstract"

Box 2. Inclusion and exclusion criteria

Inclusion criteria

Articles were included if:

- They reported empirical data from a research study **AND**
- They measured HRQOL from the patient's perspective using a questionnaire **AND**
- Participants were adults (aged 18 years or older) **AND**
- Participants have CD (clinically diagnosed or self-reported)

OR

- The article is a review of studies utilising a questionnaire to measure HRQOL, from the patient's perspective, in adults with CD.

Exclusion criteria

Articles were excluded if:

- All participants were children (under the age of 18) **OR**
- Questionnaires were completed by someone other than the person with CD (e.g. a clinician) **OR**
- They were opinion pieces or qualitative studies **OR**
- They were only available in a foreign language.

In order to address the first aim of the review (i.e. the identification of PROMs used to assess HRQOL in CD), key details of each included study (i.e. country of origin, PROMs used, study sample) were extracted. In the second stage of the review (the identification of an appropriate and valid PROM for use in the current study), relevant data (i.e. study aim, sample, evidence of psychometric properties) was extracted using a data extraction form for any disease-specific measures identified. Only disease-specific measures were evaluated as they are more able to capture details of health conditions than generic measures (Devlin and Appleby, 2010), as they include items of specific importance to the target population. In contrast, generic measures may have low content validity as they cover a broader range of issues, some of which may not be relevant to the target population (Patrick and Deyo, 1989).

Following data extraction, the evidence gathered was evaluated according to criteria set out by Terwee et al. (2007), which allows evidence of each psychometric property to be summarised as 'positive', 'indeterminate', 'negative', or 'no information available'. It is important to evaluate the psychometric properties of measurement instruments to ensure that they are reliable (i.e. the extent to which the measure is free from measurement error), valid (i.e. measures what it purports to measure), and responsive to change (i.e. able to measures changes that occur over time). A description of each psychometric property, how it is measured, and what warrants a positive rating is described next.

2.2.1 Psychometric properties

Missing data

Missing data occurs when respondents fail to answer one or more items on a questionnaire. This can occur for a number of reasons, such as items not being understandable or applicable to respondents, no appropriate response options, respondents not wishing to answer items due to their sensitive nature (e.g. items about sexual activity), or being skipped by mistake (de Vet et al., 2011; Streiner and Norman, 2008). Pilot studies during questionnaire development should resolve many of the above problems (de Vet et al., 2011), although it is typical for between 0.5 and 2 per cent of items within a questionnaire to be missing data (Fairclough, 2005).

De Vet et al. (2011) state that although a precise figure outlining an acceptable amount of missing data is arbitrary, they consider an acceptable level as less than 3 per cent, while greater than 15 per cent is unacceptable. In concurrence, Fairclough (2005) recommends

that items with more than 3-4 per cent of missing data should be investigated. However, Terwee et al. (2007) do not provide any guidance on missing data and therefore, the above guidance will be used to discuss missing data for each instrument, but a rating will not be given.

Floor and ceiling effects

A floor or ceiling effect occurs when a high proportion of respondents achieve the lowest or highest possible score. Floor and ceiling effects can affect the instrument's responsiveness, as they are unable to measure improvement in those at the ceiling, or deterioration in those at the floor of the scale (de Vet et al., 2011). Terwee et al. (2007) state that a positive rating is given when 15% or fewer respondents score at the extremes of the scale, in a sample of at least 50 people.

Content validity

Content validity is an assessment of how comprehensively the construct of interest is covered by the questionnaire's items (McDowell, 2006). Evidence to support content validity is best collected through interviews or focus groups with people from the target population (Brod et al., 2009). For a positive rating, the measurement aim, target population, constructs, and procedures for item selection should be clearly stated, with experts and the target population involved in the generation of items (Terwee et al., 2007).

Construct validity

Construct validity assesses the extent to which the questionnaire is measuring the construct of interest. There is no single measure to prove construct validity, instead

evidence is built up by comparing constructs within the questionnaire to similar domains on other measures. These measures are often generic (Jenkinson and Fitzpatrick, 2013). Prior hypotheses setting out expected correlations should be developed and tested (Terwee et al., 2007), with both strong ('convergent validity') and weak ('divergent validity') correlations examined, i.e. domains of the target instrument expected to correlate most and least with domains on other measures.

Predefined hypotheses about 'known groups' can also be set out and tested (Terwee et al., 2007), where one group is expected to achieve a significantly higher score than the other (Streiner and Norman, 2008). For example, those known to have the health condition of interest would be expected to achieve a higher score (indicating worse HRQOL) than those that do not. 'Known groups' validity is also referred to as 'discriminative validity' (Streiner and Norman, 2008). A positive rating for construct validity is awarded if hypotheses are set out in advance and at least 75% are proved correct (Terwee et al., 2007).

Internal consistency reliability

Internal consistency measures the extent to which each item within a dimension is measuring the same underlying construct. Internal consistency is typically measured using Cronbach's alpha, with acceptable values between 0.70 and 0.95 (Terwee et al., 2007). To achieve a positive rating, alpha values must be in the acceptable range, and factor analysis should have been used to explore the dimensions of the construct. The recommended sample size on which to conduct factor analysis varies between 4 and 10 respondents per item (de Vet et al., 2011), with a minimum sample size of 100

respondents (Kline, 2000; Terwee et al., 2007). For the purposes of this research, the quality criteria produced by Terwee et al. (2007) were followed, which recommends a sample size of at least 100 respondents or seven times the number of items, whichever the greatest.

Item-total correlations provide further information about the contribution of each item to the scale score. Correlations < 0.3 (Kline, 2000; Nunnally and Bernstein, 1994), are considered to contribute little to discriminate between respondents on the construct of interest (de Vet et al., 2011).

Test-retest reliability

Test-retest reliability measures the stability of test scores over time (Kline, 2000). To assess this, the instrument is administered at two points in time to a group of people in which no change is expected to have occurred during this period. As no change is anticipated, if the measure is reliable, scores are expected to be very similar or the same. Intraclass correlation coefficients (ICC) or weighted Kappa coefficients should be calculated to assess this property. Instruments are rated positively if coefficients are 0.70 or above in a sample of 50 or more people (Terwee et al., 2007).

Responsiveness to change

A measure is responsive if it is able to detect changes in health status over time (Revicki et al., 2006), when changes have occurred. To assess responsiveness, a longitudinal study is required which incorporates people in which a change in the construct to be measured is expected to occur (de Vet et al., 2011), and an appropriate timeframe to measure this change. For example, the questionnaire could be administered before and after an

intervention designed to improve health. Predefined hypotheses should be set out detailing expected changes between known groups and expected correlations between change scores on the instrument being assessed with other valid instruments (Terwee et al., 2007).

There is no consensus regarding the measurement of responsiveness, and therefore, a positive rating is given if an appropriate measure has been used. The most frequently used measures of responsiveness are effect size (ES), standardized response mean (SRM), and the responsiveness statistic (RS) (Hays and Revicki, 2005). Effect size is calculated by dividing the mean change score by the standard deviation of the baseline score, and is a measure of the magnitude of change (Hays and Revicki, 2005). Cohen (1992) has outlined the following criteria for interpreting effect size: 0.2 (small change), 0.5 (moderate change), and 0.8 (large change). Standardized response mean is calculated by dividing the mean change score by the standard deviation of the change score (de Vet et al., 2011). Finally, the responsiveness statistic is calculated as the smallest change in scores considered important by patients, divided by the standard deviation of the change score for those who have not changed (de Vet et al., 2011).

Interpretability

Interpretability refers to the extent to which scores and change scores have meaning (de Vet et al., 2011). Terwee et al. (2007) suggest that the provision of means and standard deviations of scores of known groups can aid interpretations. In addition, Minimal Important Change (MIC) can be calculated to aid the interpretation of change scores, and is defined as 'the minimal amount of change in the (sub)scale that is considered to be

important' (Terwee et al., 2007). A positive rating is given if mean and standard deviations are given for four or more known groups and the MIC has been calculated.

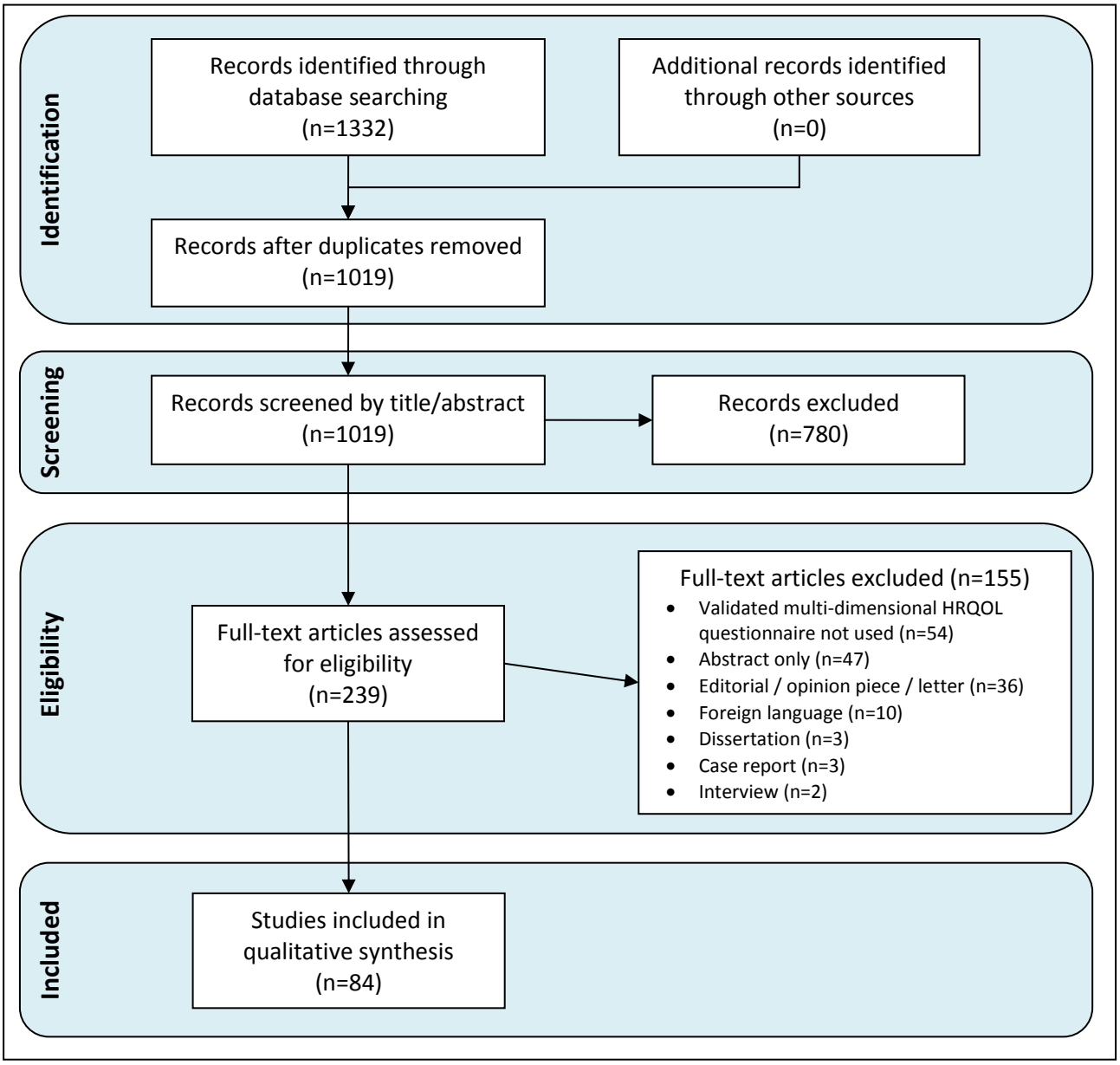
2.3 Results

The database searches retrieved 1332 articles (PubMed n=346; EMBASE n=778; PsycINFO n=33; CINAHL n=157; BNI n=18), of which, 313 were removed as duplicates (Figure 4)[3]. A further 780 articles were removed after screening the titles and abstracts. Broadly, studies were excluded as: 1) participants were children or adolescents; 2) participants did not have CD; 3) the study did not include PROMs; or 4) the article was a case report.

The full-text papers of the remaining 239 articles were retrieved and assessed against the inclusion and exclusion criteria, identifying a further 155 for exclusion. Fifty four articles were excluded as studies had not used validated multi-dimensional HRQOL questionnaires. Some studies had used PROMs that assessed one or two aspects of HRQOL, such as anxiety and depression (e.g. Beck Depression Inventory (BDI) and the State-Trait Anxiety Inventory (STAI)), while others assessed constructs other than HRQOL, for example, symptoms (e.g. Gastrointestinal Symptom Rating Scale (GSRS)) or coping (e.g. COPE). The aim of this review was to identify questionnaires that assess multi-dimensional HRQOL, and therefore, articles utilising measures such as those described above, were excluded.

[3] Flow diagram is based on PRISMA (Liberati et al., 2009), which sets out reporting guidelines for systematic reviews and meta-analyses.

Figure 4. PRISMA Flow diagram - Systematic review process



A further 47 articles were excluded as only an abstract was available, which often contained limited information, for example, not stating which HRQOL measures had been used. The remaining articles were excluded because they did not report results of a study (i.e. editorial, opinion pieces and letters to the editor) (n=36), they were written in a

foreign language (n=10), they reported individual patient cases (n=3), they were not peer-reviewed (n=3), or they were interviews with experts (n=2).

The remaining studies (n=84) were reviewed to identify PROMs used to measure HRQOL in adults with CD.

2.3.1 HRQOL PROMs used in coeliac disease

The review identified eight measures in 84 articles that have been used to measure HRQOL in adults with CD (Table 1). Disease-specific (Celiac Disease Questionnaire (CDQ), Coeliac Disease Quality of Life Survey (CD-QOL)), region-specific (Gastrointestinal Quality of Life Index (GIQLI)), domain-specific (Psychological General Well-being Index (PGWBI)) and generic (SF-36 Health Survey, SF-12 Health Survey, Euroqol EQ-5D, World Health Organization Quality of Life assessment instrument (WHOQOL-BREF)) measures have all been used to measure HRQOL in CD (Table 2 - Table 5).

Interest in measuring HRQOL in CD has increased over the last decade, with the majority of articles (n=70, 82.4%) included in this review published during this period. The majority of studies (n=62, 72.9%) were conducted in Europe. To date, HRQOL in CD has predominantly been assessed using generic measures, the most commonly used being the SF-36, with 38 articles reporting its use. However, disease-specific measures are increasingly being used, following the development of the first measure in 2007, and will be discussed in detail next.

Table 1. Patient-reported outcome measures used to assess HRQOL in coeliac disease

PROM	PROM type	No of articles	Items	Dimensions	Recall period	Response options and scoring
CDQ (Häuser, Gold, Stallmach et al., 2007)	Disease-specific	9	28	Four dimensions: emotion (7 items); social (7 items); worries (7 items); gastrointestinal (7 items).	Past two weeks	Items are scored from 1 (most dysfunction) to 7 (no dysfunction). Dimension scores (0-49) and a total score (0-196) can be calculated. Higher scores indicate better HRQOL.
CD-QOL (Dorn et al., 2010)	Disease-specific	11	20	Four dimensions: limitations (9 items); dysphoria (4 items); health concerns (5 items); inadequate treatment (2 items).	Past month (30 days)	Items are scored from 1 ('Not at all') to 5 ('A great deal'). Dimension scores and a total score can be calculated. Higher scores indicate better HRQOL.
GIQLI (Eypasch et al., 1995)	Region-specific	2	36	Five dimensions: core symptoms, physical functioning, psychological functioning, social relations, disease-specific.	Past two weeks	All items are scored from 0 ('least desirable response') to 4 ('most desirable response'). Dimension scores and an overall score can be calculated. Higher scores indicate better HRQOL.
PGWBI (Dupuy, 1984)	Domain-specific	26	22	Six dimensions: anxiety (5 items); depressed mood (3 items); well-being (4 items); self-control (3 items); general health (3 items); vitality (4 items).	Past month (standard version)	Items are scored from 0-5. Dimension scores and an overall index (0-110) can be calculated. Higher scores represent higher HRQOL.
WHOQOL-BREF (The WHOQOL Group, 1998)	Generic	2	26	Four dimensions: physical health (7 items); psychological (6 items); social relationships (3 items); and environment (8 items). A further two items assess overall QOL, and general health.	Past two weeks (standard version)	Four dimension scores can be calculated and transformed to a 0-100 scale. Higher scores indicate higher QOL.

PROM	PROM type	No of articles	Items	Dimensions	Recall period	Response options and scoring
SF-36 (Ware and Sherbourne, 1992)	Generic	38	36	Eight dimensions: physical functioning (10 items); role-physical (4 items); bodily pain (2 items); general health (5 items); vitality (4 items); social functioning (2 items); role-emotional (3 items); mental health (5 items), plus a single item asking about change in health status.	Past four weeks (standard version)	Dimension scores and a Mental Component Summary (MCS) and Physical Component Summary (PCS) can be calculated. Scores can be calculated on a 0-100 metric or as *T* scores. Higher scores indicate higher QOL.
SF-12 (Ware et al., 1996)	Generic	5	12	Eight dimensions (as the SF-36): physical functioning (2 items); role-physical (2 items); bodily pain (1 item); general health (1 item); vitality (1 item); social functioning (1 item); role-emotional (2 items); mental health (2 items).	Past four weeks (standard version)	As with the SF-36, a Mental Component Summary (MCS) and Physical Component Summary (PCS) can be calculated.
EQ-5D (Rabin and de Charro, 2001)	Generic	11	5 plus VAS	Five dimensions (each containing 1 item): mobility; self-care; usual activities; pain/discomfort; anxiety/depression. Visual Analogue Scale (VAS) measures self-rating of overall health.	Today	3L (three-level) version: Items are scored from 1 ('no problems') to 3 ('severe problems') and combined to produce a health profile (243 possible combinations). An overall score can also be calculated by applying weights.

Table 2. Studies included in the systematic review that report using disease-specific measures

Author, date	Country	Sample (recruitment method)	Other PROMs used
CDQ			
Aksan et al., 2015	Turkey	205 people with CD (support association)	SF-36
Ford et al., 2012	UK	288 people with CD (support association)	PGWBI
Häuser, Gold, Stallmach et al., 2007	Germany	488 people with CD (support association)	SF-36
Häuser, Stallmach et al., 2007	Germany	446 people with CD (support association)	SF-36
Lähdeaho et al., 2014	Finland	34 patients with CD	SF-36v2
Marchese et al., 2013	Italy	171 patients with CD (hospital)	SF-36
Pouchot et al., 2014	France	211 patients with CD (hospital)	SF-36
Tack et al., 2013	The Netherlands	16 patients with CD on a strict GFD (hospital)	-
Zampieron et al., 2011	Italy	187 people with CD (support group)	-
CD-QOL			
Casellas, Rodrigo, Lucendo et al., 2015	Spain	366 patients with CD diagnosed > 1 yr (hospital)	EQ-5D
Casellas, Rodrigo, Molina-Infante et al., 2013	Spain	298 people with CD	EQ-5D
Castilhos et al., 2015	Brazil	96 women with CD (support association)	-
Croese et al., 2015	Australia	12 people with CD (participants of previous clinical trial)	-
Dorn et al., 2010	USA	387 people with CD (support groups; hospital)	-
Lee et al., 2012	USA	1743 people with CD (support groups)	SF-12; Not clear if all CD-QOL questions used
Mahadev, Gardner et al., 2016	USA	211 people with CD (hospital; support groups)	PGWBI
Mahadev, Simpson et al., 2013	USA	413 patients with CD (hospital)	-
Nazareth et al., 2015	USA	423 people with CD (support group, hospital)	-
Tennyson et al., 2013	USA	365 people with CD (hospital, support group)	-
Zingone, Iavarone et al., 2013	Italy	230 patients with CD on GFD ≥ 1 yr (hospital)	SF-36

Table 3. Studies included in the systematic review that report using region-specific measures

Author, date	Country	Sample (recruitment method)	Other PROMs used
GIQLI			
Casellas, López Vivancos and Malagelada, 2005	Spain	54 patients with CD on a GFD; 9 untreated patients (Hospital)	EQ-5D
Casellas, Rodrigo, López Vivancos et al., 2008	Spain	163 patients with CD on a GFD; 177 untreated patients (Hospital)	EQ-5D

Table 4. Studies included in the systematic review that report using domain-specific measures

Author, date	Country	Sample (recruitment method)	Other PROMs used
PGWBI			
Baiardini et al., 2012	Italy	104 patients with CD (hospital)	-
Ford et al., 2012	UK	288 people with CD (support association)	CDQ
Hallert, Svensson et al., 2009	Sweden	57 patients with CD aged 45-64 years old on a GFD for a minimum of 8 years (hospital)	-
Jacobsson et al., 2012a	Sweden	102 women with CD on a GFD for ≥ 5 years (hospital)	-
Jacobsson et al., 2012b	Sweden	106 women with CD on a GFD ≥ 5 years	-
Kurppa, Collin et al., 2010	Finland	46 patients with CD (hospital)	-
Kurppa, Paavola et al., 2014	Finland	40 people with screen-detected CD (newspaper advertisements; support groups)	SF-36
Leffler, Kelly et al., 2012	USA	86 patients with CD (10 clinical sites)	-
Lohiniemi et al., 2000	Finland	53 patients with CD diagnosed between 9 and 11 years ago (hospital)	-
Mahadev, Gardner et al., 2016	USA	211 people with CD (hospital; support groups)	CD-QOL
Mustalahti, Lohiniemi et al., 2002	Finland	40 patients with CD (19 screen-detected; 21 symptom-detected) (hospital)	-
Paarlahti et al., 2013	Finland	596 people with CD (support group, newspaper advertisements)	-

Author, date	Country	Sample (recruitment method)	Other PROMs used
Paavola et al., 2012	Finland	466 people with CD (370 symptom-detected; 96 screen-detected) (support group, newspaper advertisements)	SF-36
Pekki et al., 2015	Finland	263 patients with CD (178 normal mucosal morphology, 85 incomplete mucosal recovery)	-
Peräaho et al., 2003	Finland	49 newly-diagnosed patients with CD (23 natural GFD; 26 wheat-starch-based GFD) (hospital)	-
Peräaho et al., 2004	Finland	39 patients (23 included oats in diet; 16 excluded oats) (hospital)	-
Picarelli et al., 2013	Italy	30 people with CD (hospital)	-
Roos, Kärner and Hallert, 2006	Sweden	51 patients with CD aged 45-64 yrs on a GFD ≈ 10 years (hospital)	-
Roos, Kärner and Hallert, 2009	Sweden	108 patients with CD aged 43-64 yrs	-
Roos, Wilhelmsson et al., 2011	Sweden	162 women with CD on a GFD > 5 yrs (hospital)	-
Simrén et al., 2006	Sweden	23 patients with CD (hospital)	SF-36
Smith and Goodfellow, 2011	USA	156 people with CD (support group)	-
Tuire et al., 2012	Finland	177 people with CD on a GFD ≥ 2 yrs (support association, newspaper advertisements)	-
Ukkola et al., 2011	Finland	698 people with CD diagnosed < 1 yr (support association)	-
Viljamaa et al., 2005	Finland	151 patients with CD (53 screen-detected; 44 symptom-detected; 54 untreated) (hospital)	SF-36
Vilppula et al., 2011	Finland	35 screen-detected patients with CD (hospital)	-

Table 5. Studies included in the systematic review that report using generic measures

Author, date	Country	Sample (recruitment method)	Version	Other PROMs used
SF-36 and derivatives				
Aksan et al., 2015	Turkey	205 people with CD (support association)	SF-36	CDQ
Arigo et al., 2012	USA	177 women with CD (support groups; online)	SF-36	-
Bakker et al., 2013	The Netherlands	57 patients with CD and Type I diabetes (hospital)	RAND-36	-
Barratt, Leeds, Robinson et al., 2011	UK	225 patients with CD (hospital)	SF-36	-
Barratt, Leeds and Sanders, 2011	UK	225 patients with CD (hospital)	SF-36	-
Black and Orfila, 2011	UK	146 people with CD (support association)	SF-36 (adapted)	-
Brottveit et al., 2012	Norway	22 patients with CD	SF-36	-
Carta et al., 2015	Italy	60 patients with CD	SF-12	-
Ciacci, Peluso et al., 2007	Italy	47 newly-diagnosed patients with CD (hospital)	SF-36	EQ-5D
Cranney, Zarkadas, Graham, Butzner et al., 2007	Canada	2,681 people with CD or DH (support association)	SF-12	-
Cranney, Zarkadas, Graham and Switzer, 2003	Canada	266 people with CD or DH (support association)	SF-12	-
Fera et al., 2003	Italy	100 patients with CD on a GFD for ≥ 1 year (hospital)	SF-36	-
Hallert, Grännö, Grant et al., 1998	Sweden	89 patients with CD on a GFD for ≈ 10 years (hospital)	SF-36	-
Hallert, Grännö, Hultén et al., 2002	Sweden	68 patients with CD in remission 8-12 years after diagnosis (hospital)	SF-36	-
Häuser, Gold, Stallmach et al., 2007	Germany	488 people with CD (support association)	SF-36	CDQ
Häuser, Gold, Stein et al., 2006	Germany	446 people with CD (support association)	SF-36	-
Häuser, Musial et al., 2007	Germany	412 people with CD on a GFD for ≥ 1yr (support association)	SF-36	-
Häuser, Stallmach et al., 2007	Germany	446 people with CD (support association)	SF-36	CDQ
Hopman et al., 2009	Netherlands	53 people with CD diagnosed for ≥ 10 years (hospital)	SF-36	-
Johnston et al., 2004	UK	14 patients with screen-detected CD; 17 patients with symptom-detected CD (hospital)	SF-36	-

Author, date	Country	Sample (recruitment method)	Version	Other PROMs used
Kurppa, Paavola et al., 2014	Finland	40 people with screen-detected CD (newspaper advertisements; support groups)	SF-36	PGWBI
Lähdeaho et al., 2014	Finland	34 patients with CD	SF-36v2	CDQ
Lee et al., 2012	USA	1743 people with CD (support groups)	SF-12	CD-QOL
Lee and Newman, 2003	USA	253 people with CD (support group)	SF-36 (adapted)	-
Leeds et al., 2011	UK	33 patients with CD and Type I Diabetes (12 of whom were newly-diagnosed) (hospital)	SF-36	
Leeds et al., 2014	UK	22 people with Type I diabetes and potential CD; 14 people with Type I diabetes and newly-diagnosed CD; 16 people with CD (hospital)	SF-36v2	-
Leffler, Dennis et al., 2009	USA	206 people with CD (hospital)	SF-36	EQ-5D
Marchese et al., 2013	Italy	171 patients with CD (hospital)	SF-36	CDQ
Nachman, del Campo et al., 2010	Argentina	53 patients with CD (hospital)	SF-36	-
Nachman, Mauriño et al., 2009	Argentina	132 newly-diagnosed patients with CD (97 classic CD; 35 atypical CD) (hospital)	SF-36	-
O'Leary, Wieneke, Buckley et al., 2002	Ireland	118 patients with CD (‘computerised database')	SF-36	-
O'Leary, Wieneke, Healy et al., 2004	Ireland	50 adults diagnosed with CD in childhood (hospital)	SF-36	-
Paavola et al., 2012	Finland	466 people with CD (370 symptom-detected; 96 screen-detected) (support group, newspaper advertisements)	SF-36	PGWBI
Pouchot et al., 2014	France	211 patients with CD (hospital)	SF-36	CDQ
Rajpoot, Sharma et al., 2015	India	146 patients with CD (92 on a GFD, 54 not receiving treatment) (hospital)	SF-36	-
Simrén et al., 2006	Sweden	23 patients with CD (hospital)	SF-36	PGWBI
Tontini et al., 2010	Italy	43 newly-diagnosed patients with CD (hospital)	SF-36	-
Usai, Manca et al., 2007	Italy	129 patients with CD (80 strictly adhere to GFD; 49 partial adhere to GFD)	SF-36	-
Usai, Minerba et al., 2002	Italy	68 patients with CD	SF-36	-

Author, date	Country	Sample (recruitment method)	Version	Other PROMs used
Viljamaa et al., 2005	Finland	151 patients with CD (53 screen-detected; 44 symptom-detected; 54 untreated) (hospital)	SF-36	PGWBI
Zarkadas et al., 2006	Canada	2,681 people with CD (support association)	SF-12	-
Zingone, Iavarone et al., 2013	Italy	230 patients with CD on GFD ≥ 1 yr (hospital)	SF-36	CD-QOL
Zingone, Siniscalchi et al., 2010	Italy	30 newly-diagnosed patients with CD on a GFD; 30 patients with CD on a GFD ≥ 1 yr (hospital)	SF-36	-
EQ-5D				
Casellas, López Vivancos and Malagelada, 2005	Spain	54 patients with CD on a GFD; 9 untreated patients (Hospital)	-	GIQLI
Casellas, Rodrigo, López Vivancos et al., 2008	Spain	163 patients with CD on a GFD; 177 untreated patients (Hospital)	-	GIQLI
Casellas, Rodrigo, Lucendo et al., 2015	Spain	366 patients with CD diagnosed > 1 yr (hospital)	-	CD-QOL
Casellas, Rodrigo, Molina-Infante et al., 2013	Spain	298 people with CD	-	CD-QOL
Ciacci, Peluso et al., 2007	Italy	47 newly-diagnosed patients with CD (hospital)	-	SF-36
Gray and Papanicolas, 2010	UK	697 people with CD (support association)	-	-
Jordá and Lopez Vivancos, 2010	Spain	38 patients with CD on a GFD; 13 patients not on a GFD (12 pre-treatment, 1 non-adherer) (hospital)	-	-
Leffler, Dennis et al., 2009	USA	206 people with CD (hospital)	-	SF-36
Norström et al., 2011	Sweden	1,031 people with CD (support association)	-	-
Ramírez-Cervantes et al., 2015	Mexico	80 patients with CD (hospital)	-	-
Whitaker et al., 2009	UK	147 patients on a GFD ≥ 1 yr (89 classical symptoms; 51 other symptoms; 7 unclassified) (hospital)	-	-
WHO-QOL BREF				
Sainsbury and Mullan, 2011	Australia	265 people with CD (support association)	-	-
Sainsbury, Mullan and Sharpe, 2013	Australia	189 people with CD (support association)	-	-

2.3.2 Disease-specific measures

Celiac Disease Questionnaire (CDQ)

The Celiac Disease Questionnaire (CDQ) (Häuser, Gold, Stallmach et al., 2007) is a 28-item self-administered questionnaire developed in Germany to measure HRQOL in adults with CD. The review identified nine articles (see Table 2) reporting studies that have utilised the CDQ. The development of the CDQ is reported in Häuser, Gold, Stallmach et al. (2007), with subsequent papers reporting the translation and validation of the CDQ into Italian (Marchese et al., 2013), French (Pouchot et al., 2014), and Turkish (Aksan et al., 2015). A further two papers (Lähdeaho et al., 2014; Tack et al., 2013) report the use of the CDQ in clinical trials to assess the impact of new treatments, and finally, three studies (Ford et al., 2012; Häuser, Stallmach et al., 2007; Zampieron et al., 2011) explore factors affecting HRQOL. Participant samples for these studies were drawn from both hospitals and support groups.

A brief description of the development of the CDQ follows. Candidate items (n=52) for the CDQ were devised following a review of the literature and existing measures, and asking members of the German Coeliac Society (n=10) and gastroenterologists (n=4) to complete a questionnaire about the impact of CD. Next, the relevance of candidate items were rated by people with CD (n=10) and medical experts (n=4), with relevant items (n=40) included in a preliminary version. This version was reviewed by members of the German Coeliac Society (n=10) and, in addition, five experts and two translators checked the questionnaire for readability and ease of completion. A revised version (40 items) was sent to 1000 members of the German Coeliac Society. Item reduction, using

principal components analysis, was performed on the first 100 responses, with 12 items removed as they did not meet predefined criteria, leaving 28 items in the final version. The CDQ takes less than 20 minutes to complete, which was found to be acceptable (Häuser, Gold, Stallmach et al., 2007). The CDQ has four dimensions: emotion, social, worries, and gastrointestinal. Dimension scores and an overall score can be calculated, with higher scores indicating better HRQOL.

The questionnaire was developed in German, and subsequently translated into English (Häuser, Gold, Stallmach et al., 2007), Italian (Marchese et al., 2013), Dutch (Tack et al., 2013), French (Pouchot et al., 2014), and Turkish (Aksan et al., 2015). Validation studies assessing the translated versions are reported for all but the Dutch version. The psychometric properties of the CDQ are assessed next.

Missing data

Missing data is reported to be low (Häuser, Gold, Stallmach et al., 2007; Zampieron et al., 2011). In one study, Häuser, Gold, Stallmach et al. (2007) found the amount of missing data per item to range from 0.2 – 11.2%, with the most frequently unanswered items asking about sex, lack of understanding by colleagues, professional career, and problems with health insurance providers. Within a French sample (Pouchot et al., 2014), some of these items were left unanswered by a larger proportion of people (e.g. professional career (31%), sex (26%)).

Floor and ceiling effects

A ceiling effect was reported for the 'social' dimension, with between 15.7% and 32.0% of participants reporting no social restrictions (Hauser, Gold et al., 2007; Marchese et al., 2013; Pouchot et al., 2014). No floor effects have been reported.

Content validity

The developers provide clear descriptions of the questionnaire's measurement aim and target population. Some information is provided about the concepts measured and item selection procedures.

Experts and people with CD were involved in the generation and selection of items through the completion of an open-ended questionnaire, and the review of preliminary versions. The diversity of participants in the item generation phase is unknown as socio-demographic data is not reported. While people with CD were involved in the generation of items, this did not take the form of interviews or focus groups as recommended (e.g. by the U.S. FDA, 2009).

Construct validity

In the development and validation study (Häuser, Gold, Stallmach et al., 2007), in addition to the CDQ, patients also completed the SF-36, Hospital Anxiety and Depression Scale (HADS), and the Gießener Symptom Check List (GBB 24). The authors hypothesised that CDQ dimensions would correlate (between 0.4 and 0.8) with similar dimensions on the other measures. Correlations were as expected for the CDQ Emotion, Social, and Worries domains. Correlations of the CDQ Gastrointestinal domain with similar SF-36 domains were weaker than hypothesised (Physical Function dimension (r=0.26), Role

Physical dimension (r=0.32)), but in accordance with hypotheses for the Bodily Pain dimension (0.48) (Häuser, Gold, Stallmach et al., 2007). Finally, correlation of the CDQ Total Score and the SF-36 General Health Perception dimension was 0.61 (Häuser, Gold, Stallmach et al., 2007).

Evidence regarding the CDQ's discriminative validity was also gathered. As expected, most studies found that women report significantly lower CDQ total scores than men (Ford et al., 2012; Zampieron et al., 2011; Marchese et al., 2013). However, a study of 446 members of the German Coeliac Society did not find an association between reduced HRQOL and gender (Häuser, Gold, Stallmach et al., 2007). The CDQ total score and some domain scores have also been found to discriminate by other factors including marital status, symptom status (Zampieron et al., 2011), social class index, and presence of co-morbidities (Häuser, Gold, Stallmach et al., 2007).

Internal consistency reliability

Five studies (Pouchot et al., 2014; Marchese et al., 2013; Ford et al., 2012; Aksan et al., 2015; Häuser, Gold, Stallmach et al., 2007) have assessed the internal consistency of the CDQ, with Cronbach's alpha values found to range between 0.73 and 0.93 for all subscales. The developers conducted a principal components analysis on 100 survey responses to explore the CDQ's structure. The analysis identified a four-factor solution explaining 49.1% of the variance (Häuser, Gold, Stallmach et al., 2007). According to Terwee's criteria, the minimum necessary sample size on which to perform this analysis (i.e. 7*40=280) was not reached.

Test-retest reliability

Four studies (Häuser, Gold, Stallmach et al., 2007; Marchese et al., 2013; Pouchot et al., 2014; Aksan et al., 2015) have assessed the test-retest reliability of the CDQ, with retest intervals ranging from seven days to one month. Intraclass correlation coefficients ranged from 0.72 to 0.94 for all scales (Pouchot et al., 2014; Marchese et al., 2013). While sufficient, the sample size of one study is not reported, and two further studies (Häuser, Gold, Stallmach et al., 2007; Aksan et al., 2015) do not report sufficient detail about the study design (i.e. how they measured test-retest reliability) or the design was inadequate (i.e. small sample size (n=47) and inadequate methods (i.e. Pearson correlation coefficients)).

Responsiveness to change

One study (Pouchot et al., 2014) has assessed the CDQ's responsiveness to change by inviting adults registered at a referral centre for CD to complete the French version of the CDQ at baseline and again after a period of six months. Respondents had been diagnosed for a mean of 13.3 years and of those completing both questionnaires, 51 people reported a change (i.e. that they had improved or worsened). Small to moderate effect sizes were found across the four subscales and the total score, ranging from 0.01 to 0.36 for those who had improved, and -0.03 to -0.54 for those who had worsened. Few conclusions can be drawn about the responsiveness of the CDQ from this study due to the lack of an intervention and small sample sizes.

Interpretability

The developers of the CDQ state that a minimally important clinical difference can be regarded as half a standard deviation (Häuser, Gold, Stallmach et al., 2007). They also

recommend that scores are controlled for co-morbidities. In one study, the authors regarded a reduced HRQOL as scores ≤ 10th percentile within the study sample (Häuser, Stallmach et al., 2007). Some articles report means and standard deviations of CDQ scores of population groups and sub-groups.

Discussion

The psychometric properties of the CDQ, which measures HRQOL in adults with CD, were assessed, and while there is some evidence to support the reliability and validity of the measure, some major limitations have been identified. The CDQ appears to be acceptable to respondents, with low levels of missing data reported. The internal consistency of the measure is also adequate, with reported Cronbach's alpha values within the acceptable range. An appropriate method (i.e. principal components analysis) was used to explore the dimensionality of the CDQ, however, the sample size was small, and only 49.1% of the variance was explained; a figure of 60-65% would normally be expected.

The test-retest reliability of the CDQ also appears to be sufficient, however, many of the studies assessing this property had a poor design or were reported inadequately, and therefore, further evidence is needed.

CDQ scores were correlated with scores on similar domains of other measures, including the SF-36, providing evidence to support construct validity. In addition, the CDQ was able to discriminate between men and women.

Limitations

A major limitation in the development of the CDQ is the lack of input from people with CD. Although participants completed open-ended questionnaires as part of the item generation phase, guidelines (e.g. U.S. FDA, 2009) recommend that interviews or focus groups form part of this process. The diversity of those participating in the item generation phase is unknown. As a result, it is possible that the questionnaire does not cover all issues that are important to people with CD (i.e. reduced content validity).

A further potential limitation of the measure relates to its recall period, asking respondents about their experiences in relation to CD over the past two weeks. The impact of CD on HRQOL is variable, for example, inadvertent gluten consumption and social impacts are unlikely to occur on a very frequent basis, and therefore, it is important that the recall period is long enough to capture the full impact of the condition. As such, a recall period of two weeks may be insufficient.

The use of the CDQ within a British population, and possibly other populations, could be problematic due to the irrelevance of some items (e.g. the item about health insurance providers). Finally, a ceiling effect within the 'social' dimension means that the questionnaire is limited in its ability to capture further improvements within this construct.

Coeliac Disease Quality of Life Survey (CD-QOL)

The Coeliac Disease Quality of Life Survey (CD-QOL) (Dorn et al., 2010) is a 20-item disease-specific questionnaire developed in the United States of America. The review identified 11 articles (see Table 2) which report the use of the CD-QOL, however, one of

the studies (Lee, Ng et al., 2012) was excluded as they had not used the CD-QOL in its validated form (i.e. they report the use of 19 disease-specific questions). The development of the measure is reported in Dorn et al. (2010), with subsequent papers reporting the translation and validation of the CD-QOL into Spanish (Casellas, Rodrigo, Molina-Infante et al., 2013) and Italian (Zingone, Iavarone et al., 2013). Croese et al., (2015) used the CD-QOL in a study exploring the use of hookworms to treat CD. Castilhos et al. (2015) investigated HRQOL in a Brazilian sample using the CD-QOL, while the remaining studies explored the relationship between HRQOL and adherence (Casellas, Rodrigo, Lucendo et al., 2015), type of detection (i.e. screen- or symptom- detected) (Mahadev, Gardner et al., 2016), dietitian use (Mahadev, Simpson et al., 2013), the use of supplements (Nazareth et al., 2015), and interest in new drug treatments (Tennyson et al., 2013). The studies recruited people from both support association and hospital samples. With the exception of the development and translation studies, very little information regarding the psychometric properties of the CD-QOL were found.

The CD-QOL was developed as follows. Forty-eight candidate items were developed following two focus groups in which participants were asked about the impact of CD. The focus group participants (n=12) were all Caucasian, predominantly female (n=10), and recruited from one CD support group. Five experts (4 gastroenterologists and 1 nutritionist) reviewed and eliminated candidate items that were considered redundant or not 'needs-based', leaving 24 items to form a draft version. The eliminated items are not reported. The draft version was completed by 17 people with CD during cognitive interviews, which resulted in some items being re-worded. The revised version was piloted in 44 members of a support group, and items further re-worded if less than 50%

of members reported the item as moderately or significantly bothersome. The revised version (24 items) was administered to 387 people with CD (support groups and hospital patients) to assess its psychometric properties. A further four items were removed as a result of the validation process, leaving the final version with 20 items. The final measure has four dimensions: limitations (9 items), dysphoria (4 items), health concerns (5 items), and inadequate treatment (2 items). The measure presents statements to which respondents report how much they associate with them on a scale of 1 ('Not at all') to 5 ('A great deal'). Dimension scores and an overall score can be calculated.

The questionnaire was developed in American English and has subsequently been translated into Spanish (Casellas, Rodrigo, Molina-Infante et al., 2013) and Italian (Zingone, Iavarone et al., 2013). To date, the measure has mostly been used in the USA. An evaluation of the available evidence follows.

Missing data

The CD-QOL appears to be acceptable to respondents, as two studies report the amount of missing data to be low (between 0 and 2 people did not complete all items) (Casellas, Rodrigo, Molina-Infante et al., 2013; Zingone, Iavarone et al., 2013).

Floor and ceiling effects

During the development of the CD-QOL, three items were removed due to ceiling effects (> 60% reporting no limitation), however, the items removed are not reported. Two studies evaluated the floor and ceiling effects of the final validated scale, of which one study identified ceiling effects in the 'dysphoria' (28.7%) and 'inadequate treatment' (27.4%) dimensions. No floor effects were reported.

Content validity

The authors utilised a 'needs-based' conceptual model to develop the CD-QOL, which they define as including questions which 'relate to perceptions and concerns relating to the impact of the disease rather than to specific symptoms or functional limitations' (Dorn et al., 2010). The intention for the measure to be relevant to a clinical sample is stated.

People with CD were involved in the development of the CD-QOL, initially during the item generation phase, through focus groups, and subsequently, through cognitive interviews. While the cognitive interviews allowed the interpretation of each item to be explored, it is not clear whether the comprehensiveness of the measure from the patients' perspective was assessed at this stage. The final version of the CD-QOL does not include items relating to the physical impact of CD as focus group participants did not report these issues as salient (Dorn et al., 2010).

Construct validity

In the development study, the authors hypothesised relationships between the CD-QOL and a single-item HRQOL question, the Brief Symptom Inventory (BSI-18), Sickness Impact Profile (SIP), IBS Quality of Life (IBS-QOL), and an abdominal pain visual analogue scale (VAS). Correlations were expected to range between 0.4 and 0.7. All correlations, with the exception of abdominal pain, were within the hypothesised range and in the hypothesised direction. The validation study of the Italian translation (Zingone, Iavarone et al., 2013) reported correlations between the CD-QOL overall score and SF-36 MCS (r=0.55) and PCS (r=0.26).

The CD-QOL has been found to discriminate by level of adherence (Casellas, Rodrigo, Lucendo et al., 2015), and age (i.e. respondents > 60 years report better HRQOL than those < 30 years) (Castilhos et al., 2015). Worse HRQOL was also associated with interest in a medicinal treatment for CD (Tennyson et al., 2013), and long delays to diagnosis (Mahadev et al., 2013).

Internal consistency reliability

Internal consistency was assessed during the development of the CD-QOL, with Cronbach's alpha exceeding 0.7 for all dimensions (actual values not reported). Two further studies report Cronbach's alpha values of 0.88 (Zingone, Iavarone et al., 2013) and 0.90 (Casellas, Rodrigo, Molina-Infante et al., 2013) for the overall scale. A factor analysis (method not specified) with a Varimax rotation was performed on a sufficient sample size (n=387) as part of the CD-QOL's development. The analysis identified a four-factor solution, but the authors do not state the percentage of variance explained.

Test-retest reliability

One study (Zingone, Iavarone et al., 2013) has assessed test-retest reliability, administering the CD-QOL at two points in time, with a two-week interval. Cohen's Kappa coefficient was lower than desired (0.63) and the sample size was inadequate (n=31).

Responsiveness to change

No studies have formally evaluated the CD-QOL's responsiveness to change. However, one study (Croese et al., 2015) administered the measure before and after administering

a trial treatment, and found the overall CD-QOL score had improved significantly following the intervention.

Interpretability

While the developers of the CD-QOL do not provide any guidance regarding the interpretation of scores, other authors have interpreted a poor QOL as the 25th percentile (Mahadev et al., 2013) or 40th percentile (Casellas, Rodrigo, Lucendo et al., 2015).

Discussion

The psychometric properties of the CD-QOL have been assessed, finding limited evidence of reliability, validity and responsiveness to change. Studies reported low levels of missing data, indicating that it is acceptable to people with CD. Evidence supporting the measure's construct validity was found, with the measure able to discriminate by level of dietary adherence. Various concerns regarding the content validity of the measure were identified. Firstly, while people with CD were involved in the generation of items through focus groups, there was limited diversity in the sample. This could mean that issues affecting those not represented are not included in the questionnaire. Content validity may be further reduced by the item reduction strategy used, with half of the candidate items removed by health care professionals (HCP) alone. It is therefore possible that issues of importance to people with CD were removed, resulting in the final items of the measure not comprehensively covering the construct of interest. Finally, the final measure does not include any items addressing symptoms. People with CD can experience severe symptoms as a result of their condition, and the absence of such items reduces the content validity of the measure.

Evidence of poor test-retest reliability was found, which raises questions about the stability of scores over time. No evidence of responsiveness to change was found; this is a particularly important property if the measure is to be used to assess the impact of interventions in clinical trials. Finally, ceiling effects within two of the dimensions were found, meaning that for a proportion of respondents, improvements in those aspects of HRQOL cannot be measured.

Summary of evidence

The CDQ and CD-QOL were evaluated against criteria developed by Terwee et al. (2007) as set out previously. The results of the evaluation are shown in Table 6.

While there is evidence to support certain psychometric properties, there is insufficient or negative evidence with regards to many aspects of both measures. A comparison of the disease-specific measures will be discussed next.

Table 6. Psychometric properties of outcome measures in coeliac disease

Property	CDQ	CD-QOL
Floor / ceiling	-[a]	-[b]
Content validity	?	?
Construct validity	+	+
Internal consistency	?	?
Test-retest reliability	?	-
Responsiveness	?	0
Interpretability	+	?

No information available (0); negative rating (-); indeterminate rating (?); positive rating (+)
[a]CDQ: social dimension exceeded 15%.
[b]CD-QOL: 'dysphoria' and 'inadequate treatment' dimensions exceeded 15%.

2.4 Discussion

A systematic review was carried out to identify PROMs used to evaluate HRQOL in CD and select a disease-specific PROM for use in a cross-sectional survey to explore the aims of this thesis. The review identified eight measures, two of which were disease-specific. An evaluation of these measures in accordance with quality criteria established by Terwee et al. (2007) concluded that neither measure was acceptable for use in this research.

A systematic, well-documented literature search utilising an extensive search strategy was employed to identify relevant literature. The search was restricted to peer-reviewed publications to reduce the inclusion of poor quality studies. It is possible that additional searches (e.g. though Google Scholar or of the grey literature) would have identified further studies providing additional psychometric evidence, however, it is highly unlikely that further measures would have been identified.

Inclusion and exclusion criteria were clearly defined and followed when selecting articles eligible for inclusion in the review. Furthermore, the number of articles included at each stage of the review (i.e. identification, screening, eligibility, and inclusion) were clearly documented using PRISMA's flow diagram. To increase the reliability of the article selection process, it is recommended that all articles are reviewed by more than one researcher when determining articles for inclusion in the review (Centre for Reviews and Dissemination, 2009). In this review, study selection was performed by one researcher only, and therefore, this should be acknowledged as a limitation which may have led to eligible studies being 'missed'.

Included studies were evaluated against established criteria, which have been used to evaluate PROMs in previous reviews (e.g. Kearney et al., 2012). Other methods of assessment were considered, for example, the COSMIN checklist (Mokkink et al., 2010), however, this was designed to evaluate the methodological quality of studies rather than the quality of measures (Mokkink et al., 2010), and therefore, was not appropriate for this review.

In total, eight measures were identified as having been used to measure HRQOL in adults with CD. Four of these measures were generic, two disease-specific, and a further two were region- or domain- specific. The psychometric properties of the disease-specific measures, the CDQ and CD-QOL, were evaluated. Major limitations in their development were found, specifically regarding their content validity. During development, the use of interviews or focus groups with participants from the target population is considered good practice and 'essential' for establishing content validity (Patrick et al., 2011). It is also required if data collected from instruments is to be used to support labelling claims (U.S. FDA, 2009). Qualitative data did not form the development of the CDQ, and therefore, there is limited evidence that the measure comprehensively covers issues that are important to people living with CD. While focus group data was used to inform the development of the CD-QOL, there was limited diversity within the sample. It is important that qualitative interviews involve a diverse sample in terms of both the patients' experiences, and demographic and clinical factors, to ensure that the resulting PROM covers the construct of interest (Patrick et al., 2011). A second key concern was that item reduction was conducted by experts alone, who removed half of the candidate items to produce a draft. The development paper does not report the content of

eliminated items, and it is unclear whether people with CD had the opportunity to review the reduced questionnaire to assess the comprehensiveness of the remaining items. Content validity of the CD-QOL is further limited as it does not include items about symptoms.

In addition to the major limitations described above, further limitations were identified, including a relatively short recall period and items not relevant to a British population in the CDQ, and ceiling effects in two of the four domains of the CD-QOL. Evidence of test-retest reliability was lacking for both measures and therefore, the stability of test scores over time is unclear.

Due to the limitations identified, neither disease-specific measure was considered appropriate for use in this research. Therefore, a new disease-specific measure to assess HRQOL in adults with CD was developed as part of this study. As there is potential for the new measure to be used beyond this research, for example in clinical trials to assess new treatments for CD, it was developed in accordance with current best practice guidelines, specifically, those produced by the FDA. The methodology by which the PROM was developed is set out in Chapter One (Figure 3, p. 29).

Since this review, Canestaro et al. (2016) have conducted a systematic review of CD-specific PROMs with the specific aim of evaluating their suitability for use in clinical trials of therapeutic treatments. While the purpose of the two reviews differ, both reviewed CD-specific PROMs and both concluded that, at present, none of the PROMs available are suitable.

CHAPTER 3:

The development of the Coeliac Disease Assessment Questionnaire (CDAQ) and the Coeliac Disease Patient Experience Questionnaire (CD-PEQ): a qualitative study

3.1 Introduction

In the previous chapter, a review of PROMs assessing HRQOL in CD found there is no suitable disease-specific measure available. Therefore, a process to develop and validate a new disease-specific measure was set out (Figure 3, p. 29). In addition, a process to develop a patient experience questionnaire, for use in Survey 2, was also set out, and developed concurrently with the PROM. This chapter presents the first stage of development, which aims to generate candidate items for the new questionnaires. In accordance with the literature, qualitative methods were used to achieve this aim.

Historically, PROMs were developed following a review of literature, examining the content of existing questionnaires, and input from experts (i.e. clinicians and researchers) (McColl, 2005). However, the importance of involving patients in their development is now recognised to ensure the resulting measures comprehensively cover the concepts of interest, i.e. to ensure the content validity of the PROM (Jenkinson and Fitzpatrick, 2013). It also allows the researcher to gain an appreciation of the language and terminology used by the population group, and incorporate this into the measure (McColl, 2005). The involvement of patients is particularly important in conditions such as CD, where social and psychological factors are prominent as a result of managing a GFD on a daily basis.

Guidelines (U.S. FDA, 2009) recommend the generation of candidate items includes the involvement of people from the target population through qualitative interviews or focus groups. Qualitative methods typically address questions of 'how' and 'why' (Ziebland, 2013), which allow us to understand what it is like to live with a chronic illness from the perspective of those with the condition (Flick et al., 2004). A diverse sample, in terms of factors such as disease severity, time since onset of the condition, and ethnicity, should be included in the qualitative interviews (Patrick et al., 2011). Many valid questionnaires have been developed in this way (e.g. The Endometriosis Health Profile-30 (Jones et al., 2001) and The Mild Cognitive Impairment Questionnaire (Dean et al., 2014)).

3.1.1 Aims and objectives

The aim of this stage of the research was to develop candidate questionnaire items for a PROM to assess HRQOL in adults with CD (the CDAQ), and a questionnaire to assess experiences of health care services in adults with CD (the CD-PEQ). This was achieved by the following objectives:

- To understand how living with CD impacts on the HRQOL of adults;
- To explore patients' experiences of health care services in relation to the diagnosis and management of CD;
- To identify the main themes of HRQOL and experiences of health care services;
- And to develop candidate questionnaire items based on the themes identified.

Ethics clearance for this aspect of the study was received from the University of Oxford Central University Research Ethics Committee (REC Reference No:

MSD/IDREC/C1/2012/38). While participating in a qualitative interview was considered a low risk activity in terms of potential harm, it was recognised that participants may find discussing their experiences of CD distressing. As such, all participants were provided with contact information for Coeliac UK's helpline and advised that further information about CD and available support could be accessed on Coeliac UK's website.

3.2 Methods

Qualitative research methods, specifically individual interviews and focus groups, are regarded as the key means of data collection when involving patients in the generation of items (McColl, 2005; Brod et al., 2009). Interviews conducted as part of the item generation phase are exploratory, allowing for key domains and sub-domains of the concept of interest to be identified and a conceptual model developed (Brédart et al., 2014). An in-depth semi-structured approach, allowing for both broad and more specific questions, is recommended to capture both an unbiased patient perspective as well as eliciting specific information about the health condition of interest (Brod et al., 2009).

In accordance with guidelines, in-depth, semi-structured interviews were conducted with adults with CD to achieve the aims and objectives outlined above. An advantage of individual interviews is that it allows for a private environment for individuals to discuss sensitive issues (Brod et al., 2009). This is salient in conditions such as CD, in which those affected may experience impacts (e.g. relationships) or symptoms (e.g. gastrointestinal) which individuals may find awkward or embarrassing to discuss in larger groups.

Guidelines regarding the diagnosis and management of CD, were also reviewed and incorporated into CD-PEQ items to allow an exploration of whether experiences were in line with best practice.

3.2.1 Recruitment

Interview participants were recruited through Coeliac UK, a charity for people with CD, and snowballing.

Sixty Coeliac UK members (approximately 50% men, 50% women) were selected from Coeliac UK's membership database and invited to take part in an interview. Members were eligible for selection if they met the inclusion criteria (Figure 5).

Figure 5. Coeliac UK database search criteria (search one)[4]

- aged 18 years or older,
- report that they have CD,
- have agreed to be contacted for research purposes,
- and live in one of the following geographical areas:
    - Yeovil area (i.e. postcode areas within 20 miles of Yeovil)[5]
    - Oxford area (i.e. postcode areas within 20 miles of Oxford)
    - Birmingham (i.e. postcode areas within 5 miles of Birmingham)

Participant recruitment was limited to three geographical areas (Oxford, Birmingham, and Yeovil) for pragmatic reasons (i.e. due to time and costs involved in travelling to the interviews). The geographical regions chosen were selected to maximise variability between people living in rural and urban areas, different counties, and more and less

[4] Coeliac UK database searches were conducted in June and July 2012.

[5] Postcode areas were identified using http://www.freemaptools.com on 1st June 2012. This online tool allows the identification of postcode areas within a specified radius of a location. Postcode areas included in the search are found in Appendix F.

socially deprived areas. Twenty members from each geographical region were invited by Coeliac UK to participate.

Members selected were sent a letter of invitation (Appendix C), a participant information sheet (Appendix D), a consent form (Appendix E), and a stamped addressed return envelope. Those interested in taking part returned a completed consent form to the Health Services Research Unit at the University of Oxford. On receipt of the consent form, the researcher contacted the respondent to obtain demographic details and brief information about their CD.

To capture a wide range of perspectives and experiences, maximum variation sampling (Patton, 1990) was adopted, with variation sought across gender, age, ethnicity, duration of diagnosis, and clinical presentation (i.e. symptomatic or asymptomatic).

A review of the demographic and disease characteristics of respondents who had returned consent forms, highlighted limited, or an absence of, representation of certain groups, i.e. younger members, members diagnosed more recently, members belonging to black and minority ethnic groups, and members living in central urban locations. In an attempt to include individuals from these groups, a further 30 members were selected from Coeliac UK's database and invited to participate. Details of this search are in Appendix F.

Four adults with CD were recruited through snowballing; two through the author's colleagues, and two through interview participants.

3.2.2 Interviews

The interviews were semi-structured and covered the following: the period prior to diagnosis; the diagnostic process; treatment received following diagnosis; follow-up care; HRQOL; the GFD; and information and support. The interviews also utilised narrative methods (as described in Ziebland, 2013), by commencing with a broad, open question, such as, 'Can you tell me about when you first suspected that something was wrong?'. This provided participants with the opportunity to share issues of importance to themselves. The interview guide (Appendix G) was developed following a review of relevant literature, pilot tested with a colleague, and modified as the interviews progressed. Modifications were minor, with several sub-questions added to fully explore emerging themes.

All interviews were conducted by the author between June and October 2012 and lasted between 50 minutes and two and a half hours. Interviews took place at the participant's home, workplace, or the University of Oxford. Interviews were audio-recorded with the participant's consent and transcribed verbatim by the author or a professional transcriber. All transcripts were checked against the audio recording. Further demographic details were collected at the end of each interview (see Appendix H for demographics form).

3.2.3 Analysis

Interview data was coded and analysed in NVivo 9 using a thematic approach (Braun and Clarke, 2006). An initial coding framework was developed by coding the transcripts of the first four interviews, and evolved further as the analysis progressed, with new codes

added as new themes arose and similar codes collapsed (see Appendix I for final coding framework). This approach allowed categories to emerge from the data, rather than be imposed on it, ensuring that the researcher does not "confuse what s/he sees in the data with what s/he expects to find" (Tesch, 1990). The author and a second researcher (Dr Michele Peters) coded two of the transcripts; results were compared and amendments made to the coding framework as appropriate. The author used the revised framework to code the remainder of the transcripts.

Interviews were conducted until data saturation was reached. Data saturation is broadly defined as the point at which no new information is obtained (Morse, 1995). The achievement of data saturation is important to ensure the relevant constructs are sufficiently mapped (Kerr et al., 2010). This provides evidence to support construct validity. A data saturation table (Table 7) was constructed, showing the emergence of themes across interviews, in order to assess when data saturation had been reached (as outlined in Kerr et al., 2010).

In order to summarise the data, a 'one sheet of paper' (OSOP) analysis (Ziebland and McPherson, 2006) was conducted for each analytical code identified. This process involved identifying narrative of similar experiences (e.g. all narrative describing pain in relation to CD), considering how these experiences could be grouped into broader themes, and exploring relationships between these themes. Twenty-eight OSOP analyses were conducted in total, an example of which can be found in Appendix J.

Table 7. Qualitative interviews - data saturation table

		Interview (participant ID)[2]																						
Category[1]	**Code**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**
GFD	Acceptability of gluten-free food	X	X	X	X	X			X			X	X	X	X	X	X	X	X	X			X	
GFD	Cross-contamination	X		X	X				X	X	X	X	X		X	X	X	X	X	X	X	X	X	X
GFD	Risk		X	X		X		X		X		X				X				X			X	
GFD	Dietary adherence	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X			X	X
GFD	Eating outside of the home	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
GFD	Food choice	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X		X	X		X	X
GFD	Food shopping	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X		X	X	X	X	X	X
EH	Feelings	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
EH	Concerns and worries	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
EH	Isolation and exclusion			X					X		X			X	X	X							X	
EH	Unwanted visibility	X			X	X		X	X	X	X	X	X		X				X	X	X	X		
IA	Holidays	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
IA	Travelling				X	X				X		X	X	X	X	X				X	X		X	
IA	Work	X	X		X	X		X	X	X				X	X	X		X	X	X	X	X	X	X
IA	Planning ahead			X	X	X			X	X		X	X		X	X		X	X	X	X	X	X	
IA	Other social activities	X	X			X					X		X		X	X		X	X	X	X	X		
IA	Avoiding social activities				X	X		X		X			X		X	X			X	X			X	
IA	Time							X			X			X					X	X			X	
R	Lack of understanding from others					X	X		X	X	X			X	X	X		X	X	X	X	X	X	
R	Support	X	X	X	X	X			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
R	Trust	X		X		X		X	X		X		X	X		X	X		X	X	X	X		
S	Gastrointestinal	X	X			X		X		X	X	X	X	X	X	X	X	X	X	X			X	X
S	Weight	X	X	X				X		X	X		X	X	X	X			X	X			X	
S	Energy				X			X			X		X	X	X	X		X						
S	Pain					X		X		X	X	X		X										X

Category[1]	Code	Interview (participant ID)[2]																						
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
S	Other symptoms	X	X	X	X	X		X			X	X		X	X	X		X		X			X	
S	*Nausea / vomiting*	X									X	X												
S	*Ravenous*		X																					
S	*Anaemia*			X								X			X			X					X	
S	*Pale appearance*															X								
S	*Osteoporosis*			X																				
S	*Low calcium*													X										
S	*Brain fog / difficulty thinking*				X			X			X									X				
S	*Rash*					X																		
S	*Mind - body disconnection*							X																
S	*Heart arrhythmia*													X										
S	*Fainting*													X										
S	*Restlessness*											X		X										
S	*Mouth ulcers*														X									
S	*Increased sensations (hands/mouth)*														X									
FIN	Impact on finances	X	X	X	X	X		X	X	X			X	X	X	X		X		X	X		X	X
HE	Access to services	X	X	X	X	X		X	X	X		X	X	X	X			X	X	X	X	X	X	X
HE	Diagnosis	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
HE	Follow-up consultations	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
HE	Integrated care and continuity of care	X			X	X			X			X		X		X	X		X		X	X	X	X
HE	Prescriptions	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X
HE	Relationships with HCPs	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
HE	Satisfaction with healthcare		X		X	X		X	X	X		X	X	X		X		X	X	X	X	X	X	X
HE	Information provision	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

[1]Category Abbreviations: GFD - Gluten-free diet; EH - Emotional health; IA - Impact on activities; R - Relationships; S - Symptoms; FIN - Financial issues; HE - Health care experience. [2]'X' indicates that the participant spoke about the sub-theme (with 'X' indicating the first time the issue was raised across the interviews)

3.3 Results

Forty six per cent (n=41) of members invited by Coeliac UK returned a consent form agreeing to participate, and four participants were recruited through snowballing. In total, 23 interviews were conducted. It was not necessary to interview all respondents who had agreed to participate as data saturation was reached after 15 interviews. However, interviews continued past this point to include a larger sample of diverse participants thus ensuring all issues of relevance were captured, and to allow a sufficient depth of understanding of relevant constructs to be achieved. Participants were aged between 29 and 90 years old, had been diagnosed with CD for between three months and 40 years, and two-thirds were female (Table 8).

The analysis identified seven main themes (Figure 6). Six themes related to quality of life, while the final theme was about health care experiences. Interview extracts illustrating themes are presented, followed by participant identification numbers in parenthesis (e.g. CD4).

Table 8. Demographic and disease characteristics of interview participants

ID	Age	Gender	Marital status	Ethnic origin	Occupational status	Duration since diagnosis (years)	Geographical area
1	82	M	Married	White British	Retired	40	Oxfordshire
2	90	M	Married	White Irish	Retired	35	Berkshire
3	87	M	Married	White British	Retired	2	Buckinghamshire
4	71	F	Married	White British	Part-time work	7	Oxfordshire
5	77	M	Married	White British	Retired	9	Staffordshire
6	75	F	Married	White British	Retired	10	Staffordshire
7	66	M	Married	White British	Part-time work	15	Worcestershire
8	59	F	Widowed	White Irish	Unemployed	11	Birmingham
9	77	F	Widowed	White British	Retired	35	Somerset
10	76	F	Divorced	White British	Retired (volunteer)	18	Somerset
11	89	M	Widowed	White British	Retired	6	Somerset
12	77	F	Divorced	White British	Retired	8	Somerset
13	70	M	Married	White British	Retired	13	Dorset
14	46	F	Married	White British	Full-time work	2	Oxfordshire
15	65	F	Married	White British	Part-time work	30	Oxfordshire
16	66	M	Married	White British	Part-time work	5	London
17	69	F	Married	White British	Retired	10	Buckinghamshire
18	70	F	Married	White British	Retired (volunteer)	7	Birmingham
19	37	F	Married	White British	Full-time work	37	Birmingham
20	38	F	Married	White British	Part-time work	6	Oxfordshire
21	29	F	Married	White British	Full-time work	1	Northamptonshire
22	48	F	Married	Asian/British Indian	Part-time work	6	Oxfordshire
23	32	F	Single	White Irish	Full-time work	<1	Oxfordshire

Figure 6. Qualitative interview themes and sub-themes

Gluten-free diet
- Acceptability of gluten-free food
- Cross-contamination
- Eating outside of the home
- Food choice
- Food shopping
- Risk

Emotional health
- Concerns and worries
- Feelings
- Isolation and exclusion
- Unwanted visibility

Impact on activities
- Avoiding social activities
- Holidays
- Other social activities
- Planning ahead
- Time
- Travelling
- Work

Relationships
- Lack of understanding
- Support
- Trust

Symptoms
- Concentration
- Energy
- Gastrointestinal
- Pain
- Weight

Financial issues
- Cost of gluten-free food

Health care experience
- Diagnosis
- Follow-up consultations
- Access to services
- Prescriptions
- Integrated care and continuity of care
- Relationships with health care professionals
- Information provision

3.3.1 Quality of Life themes

The analysis found the following six quality of life themes: gluten-free diet, emotional health, impact on activities, relationships, symptoms, and financial issues.

Gluten-free diet

The first theme, GFD, captures the challenges faced by participants following a gluten-free diet, both in terms of practical difficulties, and the poor palatability of gluten-free alternatives.

Cross-contamination (i.e. the contamination of gluten-free food with gluten) was discussed as one of the key difficulties faced in relation to the GFD. Attitudes towards cross-contamination varied, with some participants greatly concerned about its

occurrence. Participants were particularly concerned about cross-contamination when eating out, due to their lack of control regarding the preparation of food, and concern about restaurants' lack of knowledge. Two participants discussed choosing food that is less likely to be contaminated to minimise the likelihood of consuming gluten. Specific measures were also taken to avoid cross-contamination within the home, such as using separate toasters and cooking utensils, and washing up separately using separate cloths. Some participants described taking fewer measures to avoid it, with the level of concern appearing to relate to the severity of symptoms experienced following gluten consumption. An 87 year old male, diagnosed two years ago, commented:

> *'I shouldn't really use the same toaster, but um, we just keep it clean … I'm not so worried, about the um, slight contamination, which um, someone who's got it [CD] really badly would need to'* (CD3, 87 years old, male)

A closely related concept was the level of risk participants were willing to take when determining whether or not to eat certain foods. A 65 year old female, diagnosed for 30 years, commented:

> *'I tell you what's awkward when people [um]; [name] brought me back a cake that … and I just think what baking powder did she use, she's not got the baking powder. And I suppose if I'm feeling, if I'm on a good phase I'll think, 'Oh I'll risk it, it's fine, I know what it is.' … So things like that, so you're put in an awkward social situation because something, something is probably OK but may not be. I do find that slightly awkward … because I'd actually rather not have it'* (CD15, 65 years old, female)

Another difficulty participants experienced with following a GFD was obtaining gluten-free food. Participants commented that supermarkets did not always have products in stock, and that certain items were only available in specific supermarkets. Because of this, it was sometimes necessary for participants to visit numerous supermarkets or the same supermarket on more than one occasion to buy the items needed. Other

difficulties many faced when shopping was finding gluten in products they would not expect, and gluten-free products' ingredients changing, making them no longer suitable. This was 'disappointing', 'a nightmare', and 'a never-ending surprise' for participants. Despite an increase in the range of gluten-free foods available, participants also discussed having a limited choice, particularly when eating out, with some describing this as 'upsetting', 'a problem', and 'difficult'.

When participants purchased gluten-free items, many were disappointed with their taste and texture, particularly bread, describing it as 'absolutely vile', 'disagreeable', and 'too crumbly to make a sandwich'.

Some participants described their difficulties with cooking and baking gluten-free alternatives. For example, one 48 year old Asian British woman described her struggle with making gluten-free chapattis for her family.

Emotional health

As well as the practical aspects of managing CD, the condition also impacted on emotional health, with participants discussing various worries and concerns. While a key concern was whether family members, particularly children or grandchildren, would develop CD, the remaining concerns were about the participants' own health. Concerns were raised about issues such as receiving medical test results, developing symptoms after mistakenly consuming gluten, and the possibility of developing associated conditions such as osteoporosis.

Four participants described their experiences of depression and while all participants related their depression to CD, the extent of depression varied. In an extreme case, a 60 year old man recalls '*waking up in the mornings and just being filled with utter gloom*' (CD7). Other negative emotions experienced by some participants were isolation and exclusion. Feelings of isolation occurred when participants took part in an activity but were somewhat removed, for example, eating a packed lunch while others purchased food from a café. Participants described this as feeling 'alone', 'out there in the wilderness', 'an outsider', and 'at sea'. Participants also discussed feeling excluded from social activities, for example, not able to attend an event as their diet was not catered for.

Participants generally disliked receiving attention because of their CD. This was a common scenario when eating out, but also occurred elsewhere, for example, receiving a different wafer during communion. Some found this embarrassing, and disliked having to 'make a fuss' to ensure that their GFD was catered for. As well as unwanted attention, several participants felt like a 'nuisance' to others, especially when catered for by family and friends. Participants adopted strategies to avoid drawing attention to their CD, such as accepting offers of sweets or biscuits 'for later' to avoid having to explain their condition.

Impact on activities

Impact on activities was another area of HRQOL impacted by CD, which refers to work, social activities, travelling and holidays. Participants' ability to attend work and perform while there was impacted by gastrointestinal symptoms and tiredness. This impact on

work varied greatly between participants, some were simply late on occasion or took days off due to ill health, whereas in extreme cases, two participants resigned from their job.

When participants were able to attend work, some felt that their performance was impeded on occasion by the symptoms they experienced. For example, a 71 year old female describes the difficulties she faced with decision-making while working in the legal profession:

> *"To make a decision … I think, I'd actually make quite a point of that decision because that does affect you quite profoundly and certainly workwise, you know, you shilly shally around and you don't want to commit yourself to writing this letter or, or something because you know it's hard to make the decision whether you've, whether you've covered all the points"* (CD4, 71 years old, female)

The impact of CD extended to feeling excluded when socialising with colleagues, due to being unable to eat foods people had brought in to share, or not being catered for at work events (e.g. Christmas lunch).

Coeliac disease also impacted on participants ability to travel (e.g. to work or on holiday). For example, a 38 year old female recalls:

> *'I'd have stomach-ache, umm and lots of trips to the bathroom, I mean it got to a ridiculous stage where I couldn't <u>even</u> get to work, I couldn't make the journey from home to work without having to go to the bathroom'* (CD20, 38 years old, female)

As before, this was primarily related to symptoms experienced prior to diagnosis, but instances of impeded travel following diagnosis, due to gluten consumption, were

described. Activities were also impacted by the difficulty of finding gluten-free food, leaving some participants hungry as they had to skip lunch.

In an attempt to reduce the impact of CD on activities, participants had developed strategies to maintain their GFD and cope with symptoms. One of the main strategies used was planning ahead, for example, eating before attending a party, taking food on holiday, and carrying toilet paper or spare underwear to cope with symptoms. Planning ahead was described as 'a nuisance', 'awkward', and 'not convenient'.

In some circumstances, participants chose not to attend activities, or selected an alternative activity, due to difficulties explaining their dietary needs, a dislike of 'fuss', and to avoid becoming ill. This made some feel excluded, sad or that they were missing out. Avoidance was selective, for example, one participant only attended church functions in which she was involved in the food preparation. Another participant, a 32 year old female, described how her CD may affect her choice of future holiday destinations:

> *'I'm a bit scared about travelling, not around Europe maybe, but I was half thinking of going to Morocco next year and half of me's afraid to go because of my stomach, just in case there's no there's not a lot of option and I don't want to be diarrhoea and sick on holidays and just not feeling well'* (CD23, 32 years old, female)

While in most cases, it was the participant who chose whether or not to attend an activity, two participants (husband and wife both with CD) described one occasion where they were not invited to an event specifically because of their need to follow a GFD.

Relationships

Participants discussed how CD affects their relationships with others, in particular, the support and understanding that others provide, the impact CD has on others, and trust in relationships.

Most participants found their family and friends to be supportive and understanding, for example, accommodating their diet during visits, and choosing restaurants that would cater. A 29 year old participant, who had been recently diagnosed, explained how her husband helps communicate her dietary needs when she feels less able to do so:

> *'Sometimes I don't feel like I want to, you know I don't want to force the issue but because [husband's name] is like my wingman so every time I feel like I can't mention it [the GFD] he'll say "you know this is just the way it has to be, and you know I'm sorry it's a faff but, that's just it"'* (CD21, 29 years old, female)

However, not all relationships were supportive and understanding, with many participants recalling negative experiences or comments, such as being called 'faddy' or 'too fussy', told it '*won't hurt you just this once*', or friends not catering for them at parties. This lack of support and understanding was annoying and frustrating for participants. Describing her frustration, one female participant said,

> *'you kind of wish that if you ate it [gluten] you'd collapse down on the floor clasping at your stomach and get whisked off to hospital because then people would see a reaction'* (CD8, 59 years old, female)

As well as impacting on themselves, participants also perceived their CD to impact on family and friends. Most frequently mentioned was the need for family and friends to cater for their diet, and limitations on restaurant choice. In a few cases, the impact was greater, with other family members following a GFD within the home. Several participants also discussed the general disruption to family life, resulting from issues such

as the need for all family members to take precautions to avoid cross-contamination. Participant's also reported family members concern and worry for both the participant (e.g. about the suitability of food when eating out) and themselves (e.g. that they may develop the condition).

Participants discussed the level of trust they put in others to provide gluten-free food, with one participant describing it as '*a bit nerve-wracking because you're just putting your health in someone else's hands and trusting them to know*' (CD21, 29 years old, female). Several participants discussed instances where they had been told their food was gluten-free, but were subsequently unwell. Participants discussed strategies to minimise the risk of becoming ill when eating food prepared by others, such as, choosing a meal that is known to be gluten-free, or eating small quantities of food.

Symptoms

Participants experienced a range of symptoms in relation to their CD. While the majority of the discussion related to experiences prior to diagnosis, symptoms were also experienced post-diagnosis as a result of gluten consumption.

Many participants experienced gastrointestinal symptoms, such as loose bowel movements, diarrhoea, abdominal bloating and discomfort, stomach pain, stomach cramps, nausea, and vomiting. Participants described these symptoms using words such as 'continual', 'severe', 'tiresome', 'embarrassing', and 'horrendous'. The impact of symptoms could be severe, with some describing how they would spend all day on or near the toilet.

While gastrointestinal symptoms were most common, some participants experienced other symptoms such as tiredness, poor concentration or 'brain fog', and pain. Pain was not limited to the stomach and intestine, with some describing a more general muscular pain. Feelings of tiredness and exhaustion were experienced by several participants and had a detrimental impact on relationships and activities. One 70 year old man, diagnosed for 15 years, described his tiredness and how he started using alcohol as a way of coping:

> *'And [um] so I was literally, all I was able to do was to maybe take the washing out of the washing machine and put it, hang it up or go down to the shop just down the road, get a bit of shopping then I'd come back here and I'd spend the rest of the day asleep in the chair literally, just asleep and the only things that stimulated me physically at all were sugar and alcohol.'* (CD13, 70 years old, male)

Other symptoms experienced were reported by one participant only, for example, heart arrhythmia, fainting, mouth ulcers, and rashes.

While not a symptom as such, participants also tended to comment on their weight, as many had gained weight following diagnosis. They described this as 'frustrating', 'concerning', and 'hard to come to terms with'. Conversely, a few experienced weight loss or were very thin, although only one participant described this as a worry. In general, participants talked about weight loss prior to diagnosis, and weight gain post-diagnosis.

Symptoms often impacted on participants' daily activities, such as their ability to commute to work and focus on tasks. Past experiences of symptoms also had an impact on attitudes to risk surrounding gluten consumption.

Financial issues

The last theme, 'financial issues', captured the cost implications of living with CD. The main concern within this theme, and something mentioned by the majority of participants, was the high cost of gluten-free alternatives such as bread. This caused a great deal of frustration, with participants calling prices 'ridiculous', 'extortionate', 'outrageous', and 'unfair'. Several participants felt guilty that family and friends had bought expensive gluten-free alternatives for them to eat when visiting. Several participants raised concerns that those on low incomes may struggle to afford the additional cost of following a GFD.

While the above issue relates to the post-diagnostic period, two participants experienced financial impacts of their CD prior to diagnosis. These participants had to stop working due to their ill health, with the resulting impact on their finances severe. The longer term implications were stressed by one married male participant:

> *'Fourteen years undiagnosed coeliac, two to three years towards recovery, [um] that's seventeen years to largely to a greater extent taken out of your earning thingummy, run on impact on pension etc, etc, etc. [um] Impact on family, on the children, on their education and [um] so on'* (CD13, 70 years old, male)

3.3.2 Health care experience themes

The analysis identified a 'health care experience' theme comprising eight sub-themes, which captured various aspects of the participants' experiences of health care services used in relation to CD. Each of the sub-themes will be discussed next.

Diagnosis

All participants reported that they had been diagnosed with CD and discussed how their diagnosis came about, with many participants developing symptoms of CD, for which

they sought medical help within a year of their onset. The time it took to receive a diagnosis of CD varied considerably, from a matter of weeks to many years. A 70 year old woman commented:

> *'I was in and out of hospital with various problems with my stomach but no-one ever found it. I was going to specialists and what have you for a long time…it's hard to understand why it wasn't found before'* (CD18, 70 years old, female)

While most participants report being diagnosed following a blood test and endoscopy, some report only having one of these tests[6]. In one case, an endoscopy was not conducted as the 38 year old woman '*chickened out*', with others also expressing concern about having the procedure. Some older participants report prolonged periods of extensive testing which, in addition to endoscopies and blood tests, included barium meals and enemas, hospital stays, and x-rays.

While the majority of diagnoses resulted from investigations into symptoms, seven participants were diagnosed following investigations into the cause of another illness (e.g. osteoporosis or anaemia). In a few cases, participants suspected CD and asked to be tested for the condition, with suspicions arising following the diagnosis of a family member, or positive results of a self-directed trial GFD.

Participants were informed of their diagnosis by a GP, consultant, nurse, or receptionist. A few participants felt their diagnosis was communicated poorly, for example, a 75 year old woman was not told of her diagnosis until a year after her doctor received positive blood test results:

[6] Current diagnostic guidelines and procedures are described in Section 1.2.2.

> *'"I've done tests on you" he [GP] said "for that" [CD] … I said, "Well what was the results?" … he got all the paperwork … he said, "Here it is, here's the test I sent you for." "Oh," he said, "this come back it was coeliac, indicates it's coeliac," he said, "This is my fault this is."'* (CD6, 75 years old, female)

Some participants were dissatisfied with the care they received prior to diagnosis, with two participants either making a complaint or feeling that they should have. Some were dissatisfied as they felt their symptoms had not been taken seriously by their doctor, with two participants told or it being implied that '*it's in your head*'. Dissatisfaction also arose due to long delays to diagnosis, with four participants diagnosed with IBS prior to CD.

Follow-up consultations

Participants discussed the health care they had received following diagnosis, both the immediate post-diagnostic period and ongoing care. Following diagnosis, the majority of participants were referred to a dietitian, with some seen on more than one occasion. In some cases, participants were referred to a consultant or specialist to discuss their diagnosis. In an extreme case, a female participant was admitted to hospital due to ill health as a result of CD.

While many participants were invited for a bone scan, one participant only received the scan after requesting it. Some participants were also offered a second biopsy to confirm their diagnosis, while others mentioned it was not offered or not something they wanted.

With regards to ongoing follow-up care, there were large variations between participants, with some receiving annual follow up and others receiving no care at all. Those receiving care were seen at the hospital or their GP surgery by a GP, hospital consultant, dietitian,

or nurse. Appointments were either self-managed, with participants arranging appointments when they felt necessary (e.g. one participant would note when their annual appointment was due in their diary), or they would receive an invitation from their health care provider. The content of follow-up appointments varied. Most participants had blood samples taken at or before their follow-up appointment, and for some, this was the extent of their follow-up care. For others, activities such as being weighed, asked questions (e.g. how they are managing their diet, and whether they have any symptoms), and having the opportunity to ask questions also occurred.

For participants not receiving ongoing care, there were mixed views about whether they would like to attend follow-up appointments. Some felt it would be useful as they had questions about their CD, whereas others felt it would be a waste of HCPs time as they felt OK. One participant was surprised they had not received any further tests or follow-up care following a positive blood test for CD, while others were uncertain about the care they should receive. A male diagnosed for nine years commented:

> *'Dr [GP's name] is new, um when I go there to see him, now that I've got an appointment to see him I'll say, "By the way you know I'm a coeliac, um, blah, blah, blah? I haven't seen the coeliac specialist here, er, do I need one or don't I and if I don't why?" […] because what's the difference between this and somebody who's got cancer or anything else wrong with them. I know cancer's more serious but it's as though you're dumped in a forgotten world'* (CD5, 77 years old, male)

Access to services

Another aspect of health care experience that participants discussed was the ability to access services when they were needed, with problems described at all stages of the illness journey.

During diagnosis, several participants had a long delay between receiving a positive blood test and having an endoscopy. While one woman waited seven months and felt *'there wasn't really much I could do about it'* (CD10, 76 years old, female), another woman, aged 29 years, went private to have the procedure more quickly:

> *'I was fortunate enough to have private health care so after my blood test we looked at the NHS waiting list and it was I think 44 days to, um, to see a to have an endoscopy on the NHS to get my final final diagnosis. But with my work's private health care provider it was, I think it was a Thursday that I got my blood test results and they said if you come in on Monday, we can test you on Monday. And so for me it was really quick after that because, I just wanted to be able to, I wanted to stop eating gluten but I knew I couldn't stop eating gluten until I'd had the endoscopy and I thought I can't keep eating something for another month and a bit, when I know it's making me ill.'* (CD21, 29 years old, female)

Following diagnosis, several participants described difficulties accessing health care appointments, medical tests and advice about their CD. A 46 year old participant described her upset on learning that her son had also been diagnosed with CD. She felt a strong need to discuss his diagnosis with a doctor or gastroenterologist, but was unable to access the support that she needed from within the health care service.

Several participants self-managed their CD and requested or arranged medical appointments and tests themselves (e.g. follow-up and dietetic appointments, DEXA scans, and bowel cancer tests). Some felt these appointments or tests would not have occurred without their initiation.

Prescriptions

Prescriptions were another aspect of health care experience on which participants often commented. While the process of obtaining gluten-free food on prescription worked well for some, others described the difficulties they had encountered, such as receiving

large quantities of food which was difficult to store, products not being available on time, and HCPs lacking knowledge of the prescription process. A 32 year old female, who had been recently diagnosed, discussed the difficulties she had encountered when arranging her first prescription:

> *'I went to a pharmacy but I had to go to three pharmacies because a lot of them didn't have the list [of gluten-free food] and eventually I went to [pharmacy] and she gave me a list and I picked some stuff and I dropped it back in [to the GP surgery], I did it all on the one day I dropped it back in to the doctors, then I collected it and I went for my prescription and I thought everything would be £8 and they told me to pay forty something pound and obviously I wasn't going to pay forty pound for my list so that was a disaster.'* (CD23, 32 years old, female)

While the above participant, and others, found the cost of prescriptions expensive, others found they helped with the overall cost of following a GFD.

As well as discussing the process of obtaining gluten-free food on prescription, participants also commented on how the availability of food on prescription has changed over time, with many now only able to receive bread and flour. Of particular concern for some was the uncertainty surrounding the future of prescriptions, as some CCGs have stopped prescribing gluten-free food.

Integrated care and continuity of care

'Integrated care' aims to improve the patient's experience of health care through improved co-ordination of its delivery (Shaw et al., 2011), for example, improving co-ordination across primary and secondary care. 'Continuity of care' is a related term defined as comprising continuity both in terms of patients' relationships with clinicians ('relationship continuity') and clinical management, which incorporates the sharing of information ('management continuity') (Freeman and Hughes, 2010). The analytical

theme 'integrated care and continuity of care' presented here, has arisen from an analysis of the qualitative data and incorporates aspects of both integrated care and continuity of care as defined above.

A few participants described instances of poor information sharing and communication within the NHS, and between the NHS and private health care providers. For example, tests requested by the GP were not conducted by the hospital, and blood tests conducted privately were not made available to the NHS. Poor communication also extended to patients, with some participants stating they had not been informed of test results or had received conflicting information. A 70 year old female described receiving different interpretations of her blood test results:

> *'I've been to see my doctor since I've had the blood tests and he said again they're fine and after that I've had a letter from the hospital saying they want to do further investigations because something is low. Blood count or something. So I don't know why the doctor thinks it isn't but the hospital thinks it is, that's a bit of a problem at the moment … And the fact that my doctor is saying there's nothing but they're saying there's something is a bit of a worry really.'* (CD18, 70 years old, female)

With regards to continuity of care, participants rarely saw the same HCP more than once, but the majority did not state this as a problem.

Relationships with health care professionals

Another aspect of health care experience that participants discussed was their relationship with HCPs, with many describing HCPs as supportive, empathetic and understanding. Some also mentioned the trust and confidence that they have in their GP or GP surgery. However, some participants described instances where HCPs did not listen

to them, did not take their symptoms seriously, or were unsupportive, as a 38 year old female recalls:

> *'There was one doctor who even said to me "oh you know look on the bright side it'll [symptoms] keep your weight down keep you slim", and I was so angry I was absolutely furious um, but that was the sort of attitude that he had'* (CD20, 38 years old, female)

The manner or method of communication used by HCPs was problematic for some. For example, one woman received blood test results without an accompanying explanation of what the results meant, while another recalls receiving a copy of a letter that her GP wrote to the consultant describing her as a 'difficult patient', she continues:

> *'I saw this letter and said, "I'm not a difficult patient, there's something the matter with me, it's just that you don't know what it is." Well that upset me, that really annoyed me that phraseology and so he wrote me a letter of apology.'* (CD4, 71 years old, female)

Information provision

The provision of information was an area of health care experience often commented on by participants. The point of diagnosis was a time when many participants described receiving a lot of information, particularly during their first dietetic appointment. The breadth of information provided varied with only some participants informed of potential associated issues, such as lactose intolerance, and the acceptability of oats within the diet. Some participants discussed their desire for more detailed information from dietetic appointments, such as information about magnesium and calcium, with a few mentioning they would have liked to have a food diary checked to ensure their diet is sufficient.

A few participants described instances where the manner of information provision was inappropriate. A 29 year old female describes the information she was provided with at diagnosis:

> *'my doctor first off said this is the gastroenterologist said "some people get cancer" um, lymphatic cancer if it goes untreated and I think what he was trying to say was, as a scare tactic really, if you don't stop eating gluten then, the cells in your intestine can be dividing all the time and it can cause lymphatic cancer ... but I went away feeling a little bit like, basically a little bit like I was going to die because I was going to get cancer because he said "oh it's lymphatic cancer and that's one of the cancers we can't treat so it's usually terminal'* (CD21, 29 years old, female)

A few participants commented positively about the knowledge of dietitians and other HCPs, describing them as '*excellent*', '*very helpful and knowledgeable*', and '*able to give me more, specific advice if I needed it*'. However, others had more negative opinions, with one female commenting that the dietitian was '*absolutely useless … you know um so I felt that my limited knowledge was better than hers*' (CD8, 59 years old, female).

3.4 Development of candidate items

Following an analysis of interview data, 64 candidate items were developed for the CDAQ and 57 items for the CD-PEQ. While the majority of candidate items were developed from the analysis of qualitative interview data, a few items for the CD-PEQ arose following a review of relevant guidelines for the diagnosis and management of CD (PCSG, 2006; NICE, 2009; Ciclitira et al., 2010; Bai et al., 2013)[7]. For example, the question, '*Since your diagnosis of coeliac disease, have you had a pneumococcal vaccination (sometimes called the 'pneumo jab')?*' was added as guidelines from both the British Society for Gastroenterology (BSG, 2010) and Coeliac UK (Coeliac UK, n.d., c) state that the

[7] Note that since the review occurred, the following guidelines have been updated: NICE (NICE, 2015) and BSG (Ludvigsson, Bai et al., 2014).

vaccination should be offered. Guidelines were also used to help shape the wording and response options of existing items.

To date, very little has been documented about how the results of qualitative analysis link to the concepts underlying items of PROMs (Lasch et al., 2010). To overcome this, a diagram, referred to as a draft conceptual framework was developed for the CDAQ, showing how the items developed relate to the qualitative themes (domains), and the overall concept of HRQOL (Figure 7). A full list of candidate items, with item wording in full, for the CDAQ and CD-PEQ can be found in Appendix K and Appendix L respectively.

The CDAQ asks respondents how frequently they have experienced various issues related to their CD during the past four weeks, with respondents answering on a five-point response scale: 'never', 'rarely', 'sometimes', 'often', and 'always'. This is a preferred response set for frequency (PROMIS, 2013), which is widely used by other instruments (e.g. The Parkinson's Disease Questionnaire (PDQ-39) (Jenkinson, Fitzpatrick, Peto et al., 1997)).

A recall period of four weeks was selected in order to capture the full impact of living with CD. Longer recall periods are more appropriate when assessing disease-specific HRQOL, as shorter periods could underestimate the impact of the condition (Norquist et al., 2012). The qualitative interviews have highlighted how the impact of CD can fluctuate according to periods of gluten consumption and the social activities undertaken. Asking patients to average symptoms over longer periods of time may provide good estimates of health status in conditions where symptoms come and go (Norquist et al., 2012).

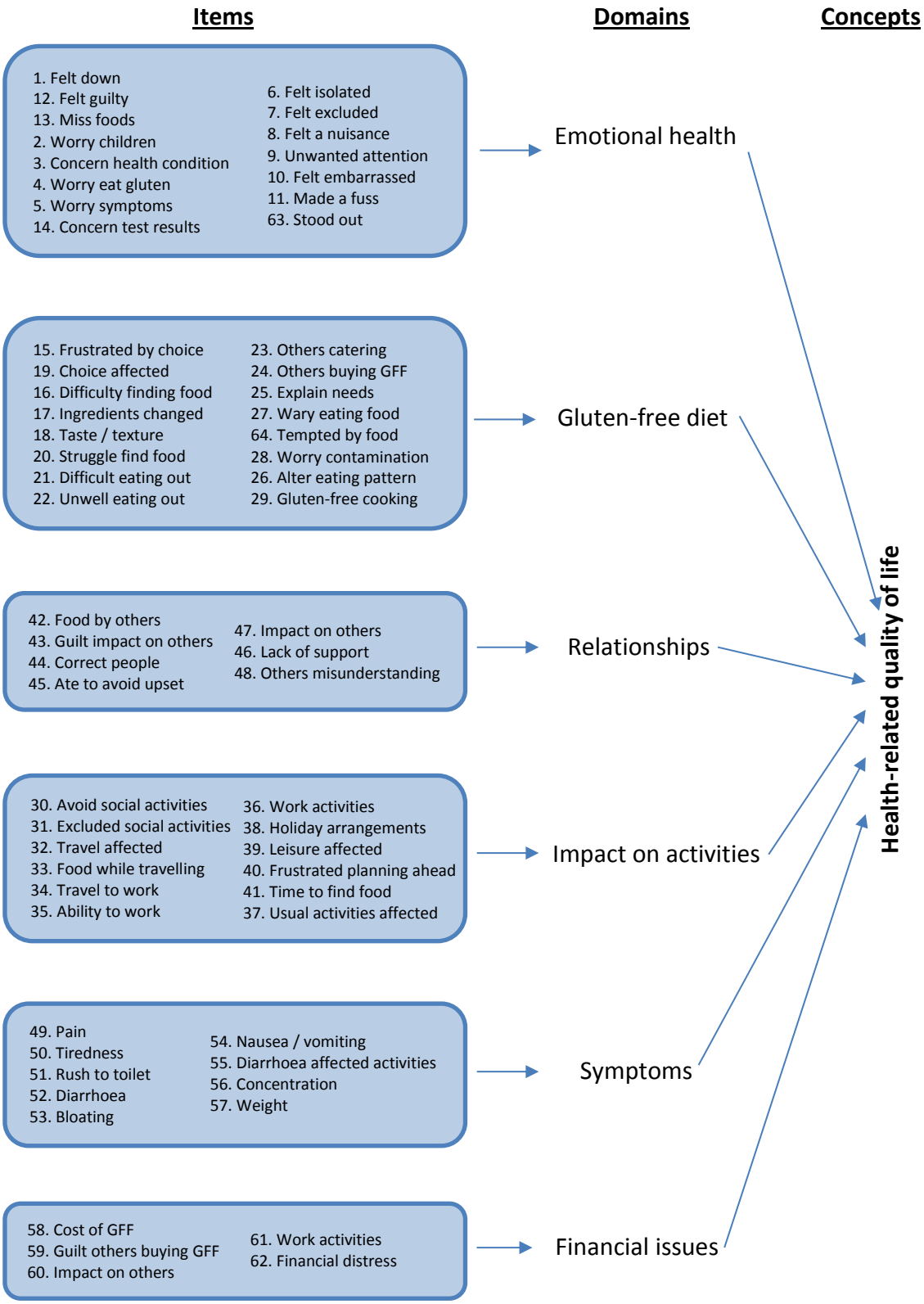


Figure 7. Draft conceptual framework for the CDAQ

Item numbers refer to those stated in the item tracking matrix (Appendix K), where full item wording can also be found.

3.5 Discussion

In order to generate candidate items for the CDAQ and CD-PEQ, 23 qualitative interviews were conducted and analysed, producing 64 and 57 candidate items for the CDAQ and CD-PEQ respectively. A maximum variation sample was sought in an attempt to include a diverse group of individuals in the interviews, in terms of their demographic background, health, and experiences of health care. This sampling method allows variation in experiences to be understood and themes common to all individuals to be identified (Patton, 1990), thus maximising opportunities for the resulting measures to be comprehensive.

Interview participants were primarily recruited through Coeliac UK, a charity for people with CD. This allowed targeted recruitment according to various factors held on Coeliac UK's membership database, such as, geographical location, age, length of diagnosis, and ethnicity. Thus, recruiting through Coeliac UK was a pragmatic and efficient way to recruit a diverse sample (as shown in Table 8), which allowed for common themes to be robustly addressed. Furthermore, recruiting through a charity may make it more likely that those recruited are engaged with their health condition and willing to discuss the impacts of their condition at length. This is important as qualitative interviews rely on participants providing in-depth information.

Although there is no evidence to suggest that members of Coeliac UK are systematically different in the experience of their illness to people with CD who do not have membership, the recruitment of participants primarily through Coeliac UK must be noted

as a possible limitation of the study. For example, those unable to pay the Coeliac UK membership fee were not reached.

Alternative approaches were considered, such as the recruitment of participants through clinical settings. However, limitations were identified with this approach. Firstly, patients attending a coeliac clinic are likely to be newly-diagnosed or suffering with ongoing issues, therefore the diversity of a sample recruited in this way may have been limited. Furthermore, the number of clinical settings it would have been feasible to involve would be small, which may have resulted in less varied experiences of health care services being captured, for example, patients belonging to the same GP practice or clinic are likely to receive the same type of follow-up care. Finally, pragmatic issues such as cost must be considered. It is likely that recruiting through a clinical setting would incur greater associated costs, for example, paying for staff to search their databases to identify patients with CD and send out letters of invitation.

While variation in terms of participants' demographic characteristics and experiences was achieved, fewer younger participants and those from black and minority ethnic groups were included. While there is little evidence specifically about the HRQOL of people with CD from black and minority ethnic groups, it is possible that cultural issues or religious beliefs may impact HRQOL. This study included one female from an Asian background, and while perhaps certain issues, such as the time taken to prepare foods was greater than the other participants in the study, there were no themes identified that were specific to this interview.

A possible limitation of this phase of the research is that candidate items were not developed for every symptom raised by participants. Specifically, items were not developed for associated conditions mentioned (i.e. anaemia, osteoporosis, and low calcium levels) or symptoms mentioned by only one or two people (e.g. being ravenous, of pale appearance, having a rash, heart arrhythmia, fainting). The reason for this was twofold, firstly, the purpose of this research was to develop a PROM to assess the impact of CD on HRQOL rather than a symptom checklist; and secondly, these symptoms were reported by very few people, and therefore, it is most likely that any items developed would have been removed in the following stages of development due to floor effects (i.e. many people indicating that the symptom does not affect them). As an example, one participant mentioned experiencing a rash due to having a condition associated with CD, namely, dermatitis herpetiformis (DH). Few people have DH, a prevalence of 0.03% in the UK, (West et al., 2014) compared with a prevalence of 1% for CD (Mustalahti et al., 2010), and therefore, rashes are unlikely to affect many people with CD. In fact, an item regarding DH was removed during the development of the Celiac Symptom Index, a scale to assess symptoms in CD, due to 80.5% reporting this as a problem 'none of the time' (Leffler, Dennis et al., 2009).

CHAPTER 4:
Refining and pretesting the CDAQ and CD-PEQ

4.1 Introduction

Candidate CDAQ and CD-PEQ items were developed following qualitative interviews with people with CD as discussed in the previous chapter. As well as involving patients in the item generation phase of instrument development, their participation in the refinement of items is important and contributes towards the production of reliable and valid measures.

Involving patients in the refinement of questionnaire items allows their understanding of the items, response options, and recall periods to be assessed (U.S. FDA, 2009). Furthermore, how comprehensively a questionnaire is covering the concept of interest (i.e. content validity) can also be assessed (Brod et al., 2009). Content validity is considered one of the most important measurement properties (Terwee et al., 2007), without the establishment of which, the evaluation of other measurement properties is not considered useful (Terwee et al., 2007; U.S. FDA, 2009). To gather evidence to support content validity, it is recommended that cognitive interviews are conducted with patients (Brod et al., 2009; U.S. FDA, 2009).

It is increasingly common for newly-developed questionnaires to utilise cognitive interviews along with other methods, such as expert opinion, to gather evidence supporting content validity and ensure patient understanding. For example, the refinement of candidate items as part of the development of the Long-Term Conditions

Questionnaire (LTCQ) involved interviews with professionals, cognitive interviews with people with long-term conditions, and a translatability assessment (Kelly et al., 2016).

This chapter describes the extensive process undertaken to refine the candidate items for the CDAQ and CD-PEQ and develop draft questionnaires. This process, referred to as Phase Three, was comprised of four stages (see Figure 3, p. 29), each of which is described below.

Firstly (stage one), items were reviewed by the author using the Question Appraisal System (QAS-99), amended following discussions with the author's supervisors, and formatted into questionnaires. Applying the QAS-99 tool allows common problems with questionnaires (e.g. poor question clarity) to be resolved at an early stage of development. The QAS-99 has been successfully used in the refinement of previous outcomes and experiences measures (e.g. Togher et al., 2016). Further information about the QAS-99 can be found in Section 4.2.1.

Next (stage two), feedback on the revised questionnaires was obtained from a range of experts (including clinicians and researchers) in meetings and interviews, and the questionnaires were further revised. The involvement of both patients and experts can help to ensure that the content of newly-developed PROMs is relevant and comprehensive (Reeve et al., 2013).

Thirdly (stage three), the questionnaires were pretested through cognitive interviews with people with CD to identify and resolve problems occurring during their completion.

Conducting cognitive interviews with patients contributes towards evidence supporting content validity, and is recommended by both the U.S. Food and Drug Administration (U.S. FDA, 2009) and the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) (Patrick et al., 2011).

In the final stage of refinement (stage four), a translatability assessment (TA) was conducted to identify and address any cultural or linguistic translatability issues with the CDAQ. Conducting a TA as part of the development of a PROM is a relatively new approach (Conway, Acquadro, and Patrick, 2014), however, it is becoming increasingly applied in the development of new measures. For example, the recently developed Irritable Bowel Syndrome with Diarrhoea (IBS-D) instrument (Delgado-Herrera et al., 2016) and the Long-Term Conditions Questionnaire (LTCQ) (Kelly et al., 2016) both included TAs as part of their development process.

Revisions were made to the questionnaires following each of these stages (note that Stage Four was conducted for the CDAQ only). Further details of the purpose of each of the stages is available in the relevant section introductions (see Sections 4.2.1, 4.3.1, 4.4.1 and 4.5.1).

4.1.1 Aims and objectives

The aim of Phase Three was to refine the candidate questionnaire items and produce a draft version of the CDAQ for use in Survey 1, and a final version of the CD-PEQ for use in Survey 2. This was achieved by the following objectives:

- To refine the wording of candidate items;

- To obtain feedback from experts and people with CD to ensure the comprehensiveness of candidate items;
- And to pre-test the questionnaire with people with CD to resolve issues with completion.

Each of the four stages of Phase Three are described in detail below. An item tracking matrix showing which CDAQ items were revised following each stage can be found in Appendix K.

4.2 Stage 1 - Initial appraisal of candidate items

4.2.1 Introduction

An initial appraisal of CDAQ and CD-PEQ items was conducted in two parts. Firstly, the author revised items using Willis and Lessler's (1999) Question Appraisal System (QAS-99), and secondly, items were further revised following discussions with the author's supervisors. The QAS-99 is a tool that aids the systematic review of questionnaires to identify and resolve common problems with questionnaire design prior to their use. The system aids the identification of problems with various aspects of questionnaires, including instructions and response categories, question clarity, and the likelihood that respondents will be able to recall the knowledge required to answer questions. The appraisal system categorises problems in to eight headings (Table 9). The aim of this stage was to resolve common problems with questionnaire items and improve wording prior to their review by experts in Stage 2.

Table 9. Problem categories and descriptions of the QAS-99

Problem category	Description
Reading	Reading the questionnaire to respondents in a uniform manner is difficult for interviewers.
Instructions	Instructions are conflicting or difficult to follow.
Clarity	Question wording impedes respondent understanding, for example, due to vague or awkward wording, unclear technical terms or reference periods.
Assumptions	Questions are double-barrelled or based on unfounded or problematic assumptions about the respondent, or assumes the respondent's behaviour is constant.
Knowledge / memory	The respondent is unable to recall the information needed to answer questions, is unable to calculate responses, or has not formed an attitude about the topic of enquiry.
Sensitivity / bias	Questions enquire about a sensitive topic, contain sensitive or 'loaded' words, or imply a socially acceptable response.
Response categories	Response categories are problematic, for example, due to overlapping or missing response options, mismatches between the question and response options, or response options being displayed in an illogical order.
Other	Problems identified by the reviewer not identified in another category.

4.2.2 Method

QAS-99 coding forms (Appendix M) were completed by the author for all candidate CDAQ (n=64) and CD-PEQ (n=57) items. Each form contains 27 questions addressing the eight problem categories. Items were not assessed for problems with 'reading', as the questionnaires have been designed for self-completion. Following the identification of problems, revisions were made.

4.2.3 Results

Findings from the application of the QAS-99 to CDAQ and CD-PEQ candidate items are described below, starting with the CDAQ.

CDAQ

In total, 140 problems were identified across 64 draft CDAQ items, with problems found in all of the categories assessed (Table 10). Following a review of the problems, 42 items were amended and 8 items deleted (see Appendix K).

Table 10. Problems identified with the CDAQ using the QAS-99

QAS-99 problem category	n
Clarity	54
Assumptions	52
Response categories	16
Sensitivity / bias	10
Instructions	3
Knowledge / memory	3
Other problems	2
Total	**140**

The largest number of problems (n=54) were due to a lack of 'clarity', with most problems arising due to vague, and lengthy or awkward question wording. Question clarity was also reduced because of undefined technical terms such as 'gluten', 'contaminated', and 'nausea'.

The 'assumptions' category held the second largest number of problems (n=52). Problems arose due to assumptions being made about respondents or questions being double-barrelled (Example 1).

Example 1. CDAQ candidate item 2 contains assumptions and is double-barrelled

Original item	…were you worried that your children or grandchildren may develop coeliac disease?
Author's comments	This question makes two assumptions, firstly, that the respondent has children or grandchildren and secondly, that they do not currently have coeliac disease. The question is double-barrelled as it asks about both 'children' and 'grandchildren'; it is possible that the respondent may worry about one family group, but not the other.
Revised item	…were you worried that a family member may have or develop coeliac disease?

Problems were also identified with the CDAQ's response categories (n=16), with some items having an insufficient number of response options. For example, some questions were not relevant to all respondents (e.g. questions asking about the workplace), and therefore, a response of 'never' to 'always' did not apply. To address this, a 'not applicable' response category was added where appropriate and scored as missing data.

Some items (n=10) were deemed to be of a sensitive nature, for example, items asking about bowel movements, satisfaction with weight, mood, and the financial impact of treatment. Item wording was amended, where possible, to minimise sensitivity to respondents. Few issues were found in the remaining categories.

Following an initial appraisal of the CDAQ's items using the QAS-99, the revised items were discussed with the author's supervisors. Discussions resulted in further amendments to 33 items, with 2 items added and 8 items deleted. Many of the amendments were to ensure consistency in the tense used. Items added addressed specific aspects of constructs currently addressed by broader items, while deleted items were removed due to similarities with other items.

CD-PEQ

In total, 107 problems were identified across the 57 draft CD-PEQ items reviewed (Table 11).

Table 11. Problems identified with the CD-PEQ using the QAS-99

QAS-99 problem category	n
Clarity	41
Assumptions	23
Knowledge / memory	22
Response categories	18
Instructions	2
Other problems	1
Sensitivity / bias	0
Total	**107**

The largest number of problems was with the clarity of questions (n=41), with many appearing vague or missing reference periods (e.g. '*Did your doctor listen carefully to your concerns about your health and take them seriously?*'). Phrases, such as 'Before your diagnosis', were added to questions to add clarity. It was not necessary to add reference periods to all questions as some asked about all experiences to date (e.g. '*Have you received enough information about which gluten-free foods are available on prescription?*').

Many problems were also identified within the 'assumptions' category (n=23), in particular, due to inappropriate assumptions made about the respondent, such as an assumption that all respondents receive all services. Not all respondents receive dietetic and follow-up appointments, and therefore, filter questions and questionnaire 'skips' were added to ensure respondents are only asked questions that are relevant to them.

Problems were also identified within the 'knowledge/memory' category (n=22), with most problems arising due to the possibility that respondents are no longer able to recall the information needed to answer questions (e.g. duration between first visiting their GP about their symptoms to receiving a diagnosis). Response options such as 'I can't remember' were added to allow those unable to recall the necessary information to answer questions.

Eighteen problems were identified with the CD-PEQ's response options, including vague wording, illogical ordering, and missing categories. Few problems (n=3) occurred in the remaining categories.

Candidate items and the results of the QAS-99 assessment were discussed with the author's supervisors, resulting in 34 amendments, with 13 questions added and 23 questions deleted. Questions were added for three reasons, firstly, to ensure respondents are only asked questions relevant to them through the addition of filter questions; secondly, to obtain more detailed information about experiences already enquired about; and finally, to address aspects of guidelines about the diagnosis and management of CD not already covered. Deleted items were sufficiently addressed by one or more of the remaining items (i.e. duplicated) and were therefore removed.

During the appraisal, guidelines for the diagnosis and management of CD (PCSG, 2006; NICE, 2009; Ciclitira et al., 2010; Bai et al., 2013; Coeliac UK, n.d., a; Coeliac UK, n.d., b) were reviewed and used to inform the questionnaire, in particular the wording of questions and response options. By ensuring that the questionnaire is informed by

guidelines, the interpretation of survey results, in terms of assessing how experiences compare with recommended practice, will be possible. Four additional items were generated following the review.

4.2.4 Summary

An initial appraisal of the CDAQ and CD-PEQ's candidate items was conducted and common problems with survey questions were resolved. This was achieved by utilising Willis and Lessler's (1999) Question Appraisal System and through discussions with the author's supervisors. In total, 64 CDAQ items were reviewed, of which 46 were amended, 2 were added, and 16 were deleted. For the CD-PEQ, 57 items were reviewed, of which 34 were amended, 13 were added, and 23 were deleted.

In total, 140 problems were identified with the CDAQ and 107 with the CD-PEQ. The largest number of problems, for both questionnaires, arose within the 'clarity' and 'assumptions' categories due to questions being unclear or containing inappropriate assumptions. While the proportion of problems arising with the CDAQ and CD-PEQ was similar for most categories, the number of problems with knowledge and memory were greater for the CD-PEQ (n=22, compared with 3 for the CDAQ). This is explained by the recall periods within the questionnaires. While the CDAQ only asks participants to recall experiences from the past four weeks, the CD-PEQ asks questions relating to periods which could have occurred many years ago, for example, the period prior to diagnosis.

The changes made to the questionnaires during this stage of development have made them easier for respondents to understand and complete, and therefore, the acceptability of the questionnaires to respondents might be enhanced.

4.3 Stage 2 - Expert opinions

4.3.1 Introduction

The previous stage of questionnaire development sought to conduct an initial appraisal of the CDAQ and CD-PEQ's candidate items to resolve common problems and format items to produce draft questionnaires. To ensure questionnaires are relevant and comprehensive in relation to their target concept, population, and aim of measurement, it is recommended that both patients and experts assess their content (Reeve et al., 2013). Stage 2 of questionnaire development, presented here, sought feedback on the draft CDAQ and CD-PEQ from multi-disciplinary experts, with the purpose of improving the questionnaires, ensuring they are comprehensive, and that the information gathered is of use to HCPs.

4.3.2 Methods

Feedback from experts was sought through meetings and qualitative interviews.

Recruitment

Twenty experts, including clinicians, researchers, and Coeliac UK employees, were invited to participate in a meeting in Oxford or High Wycombe (see Appendix N for invitation letter). Experts located near these locations were identified through an internet search and snowball sampling. Those with a particular interest in CD were sought, but this was not essential to participate. Experts were sent an information sheet (Appendix O) about

the study along with their invitation. Nine experts participated in a meeting and three experts who were unable to attend the meetings participated in in-depth interviews (Table 12).

Table 12. Meeting and interview participants

	Participant job title
Meeting 1	• Dietitian and Director of Policy, Research and Campaigns, Coeliac UK • Health Policy Lead, Coeliac UK • Dietitian (CD and Diabetes specialist)
Meeting 2	• Chief Executive, Coeliac UK • Dietitian (Gastroenterology specialist) • Dietitian (Gastroenterology) • Dietitian (Oncology Dietetic Team Leader) • University Research Lecturer and Senior Research Scientist (PROMs expert) • Senior Research Scientist (Health Services Researcher and PROMs expert)
Interviews	• Consultant Gastroenterologist • GP (specialist interest in gastroenterology and CD) • GP

Prior to the meetings and interviews, experts were sent a copy of the questionnaires and made aware of the key points for discussion.

The meetings

Two face-to-face meetings, held in Oxford and High Wycombe, took place in June 2013, lasting 2 hours 46 minutes and 2 hours 2 minutes respectively. Both meetings were audio-recorded. The author took brief notes during the meetings, which were elaborated using the audio-recordings.

Meetings commenced with a short presentation about the study, followed by discussions about the CDAQ and CD-PEQ. Participants were provided with copies of the

questionnaires and a list of questions to aid discussion (Appendix P). The key points for discussion were:

- Does the questionnaire cover all areas of health care experiences and quality of life in people with CD? Are there questions that you would like to add?
- Are any of the questions particularly problematic (e.g. poorly worded, irrelevant to people with CD, or ambiguous)?

The interviews

Three semi-structured interviews were conducted by the author between June and July 2013, and addressed the same questions as the meetings described above. Two interviews were conducted in-person (at the University of Oxford and expert's home) and one via telephone. Interviews lasted between 18 and 28 minutes and were audio-recorded with the expert's consent.

Analysis

A matrix was developed showing the original item wording and a summary of comments from the meetings and interviews. Comments were reviewed by the author and suggestions for amendments to items made. The suggested changes were discussed and agreed with the author's supervisors.

4.3.3 Results

An analysis of meeting and interview data identified a number of areas in which both the CDAQ and CD-PEQ could be improved. Examples of experts' comments and changes made can be found in Appendix Q. For a full list of items amended, see the item tracking

matrix in Appendix K. Issues raised in relation to each of the questionnaires will be discussed below, starting with the CDAQ.

CDAQ

Following a review of experts' comments, amendments were made to 13 CDAQ items. Experts made a number of suggestions to improve the CDAQ, such as re-wording items, expanding items to incorporate additional aspects, and adding statements specifying the item's relevance to CD. A couple of concerns regarding the cultural translatability of items, and negative image of CD that the questionnaire may portray were also raised. In addition, experts commented on the CDAQ's content validity. The issues identified along with examples of amendments are discussed below.

Rewording items

For several items, experts recommended that alternative wording would better convey the item's meaning. For example, for item 20 ('*…did you worry that you would be unwell while out of the house?*'), experts thought that '*out of the house*' could be taken too literally (e.g. being in the garden) and therefore, it was reworded to '*away from the home*'.

Expansion of items

Several comments focused on expanding items to include additional relevant aspects. For example, experts commented that gluten can be present in drinks as well as food and recommended that items were expanded to reflect this. As a result, four items were amended, including item 32 which was reworded to read '…did you feel awkward about refusing unsuitable food **or drink** from other people?' (*amendment highlighted in bold*).

Items' relevance to CD

Experts noted that some items explicitly state they are related to CD, whereas others do not. This was raised generally and in relation to specific items, such as item 39 ('*…were your finances strained (for example, due to the cost of following a gluten-free diet, or inability to work)?*'). Where it was felt that clarity was needed, as in the above example, a statement such as 'due to your coeliac disease' was added. However, it was not felt appropriate or necessary to add this statement to all items, as firstly, it would make the length of items very long, and secondly, an introduction at the start of the questionnaire already states that the questionnaire is about CD.

Cultural translatability

Experts commented on the cultural translatability of some items. For example, item 1 ('*…did you worry that you might be unwell after eating out (for example, at a friend's house, restaurant, or café)?*') refers to '*eating out*', which experts suggested may not occur in all cultures. As such, the phrase was replaced with '*eating food prepared by others*' to maximise the applicability of the item to different populations. Translatability issues were explored in full towards the end of pre-testing (see Chapter 4.4).

Questionnaire portraying a negative image of CD

Some experts felt that overall, the questionnaire provided a negative image of CD, particularly to those recently diagnosed, and it was suggested that some items could be phrased positively to overcome this. While rephrasing some items in a positive manner may provide a more positive view of CD, it could cause problems for respondents when completing the questionnaire as the direction of scoring would change, which would also complicate scoring. For these reasons, items were not rephrased.

Content validity

Experts felt the questionnaire was comprehensive, but commented that further items about bone health and the consumption of calcium could be added. However, opinion was divided, with some concerned about listing specific health problems of which people may be unaware. It was also noted that knowledge of bone density levels relies on clinical tests. As issues surrounding bone health and calcium consumption are broadly covered by items 9 ('*…have you felt concerned about developing a health condition related to your coeliac disease?*') and 10 ('*…have you felt concerned about the results of medical tests?*'), and for the reasons identified by experts, it was felt inappropriate to add additional items addressing these topics.

CD-PEQ

Following a review of experts' comments about the CD-PEQ, amendments were made to 31 questions or their associated response options, one item was added, and one deleted. The deleted item resulted from merging two similar items ('*Have you received enough information from health care professionals about how to get gluten-free food on prescription*' and '*Have you received enough information from health care professionals about gluten-free food available on prescription?*'). Experts provided suggestions to improve the formatting of the questionnaire and clarity of questions, and avoid obtaining biased answers or invoking anxiety. Some suggestions were made as a result of the clinical knowledge held by HCPs, which are highlighted separately. Each of these themes will be discussed below.

Formatting the questionnaire

Experts suggested several changes to the format of the questionnaire, such as emboldening words to improve question clarity, combining questions to reduce the questionnaire's length, and changing the order of questions to improve the flow of the questionnaire.

Improving question clarity

Experts felt that some questions needed clarification in order for respondents to interpret them as intended, and in the same way to each other. For example, question 4 ('*How would you rate the length of time it took to diagnose your coeliac disease?*') was revised ('*How would you rate the length of time from when you first sought medical advice about your symptoms to receiving a definite diagnosis?*') to provide clarification about the time period of interest.

Avoiding bias

Experts thought that the wording of question 7 ('*Before your diagnosis of coeliac disease, did you receive an incorrect diagnosis (for example, Irritable Bowel Syndrome (IBS))?*') could lead to bias as only one example of an incorrect diagnosis was provided. As it is possible for CD to be misdiagnosed as other conditions, such as gastroenteritis, the example of IBS was removed to encourage respondents to interpret the question more broadly.

Avoiding invoking anxiety

Experts were concerned about one question (question 16), which asks respondents to report which medical tests they have received since diagnosis. It was thought that the

provision of a list of tests may be perceived as tests that should have been conducted, causing anxiety for those who have not received some or all of the tests. To overcome this, the following preface was added to the question, '*Following diagnosis, some people have some additional tests or vaccinations*'.

Suggestions based on clinical knowledge

Experts recommended changes to several questions based on their clinical knowledge of CD and its diagnosis and management within health care services. For example, the response options for some questions were amended to more accurately reflect referral times that are encountered in practice, as opposed to those detailed in clinical guidelines. Clinical knowledge was also useful in identifying missing response options. For example, experts identified two additional response options ('*My bone density was discussed*' and '*My emotional well-being was assessed*') to include in the list of activities that may occur during follow-up appointments.

Content validity

In general, experts felt that the questionnaire was comprehensive. Some suggestions on extending the prescriptions section were made to ask about the respondent's perception of the role of prescriptions, knowledge of prescribing policy, and how the respondent pays for their prescriptions. While the first two suggestions were considered too specific for the purposes of this questionnaire, a question enquiring about the payment of prescriptions was added.

4.3.4 Summary

Experts provided feedback on the CDAQ and CD-PEQ questionnaires, which was used to improve them and ensure their comprehensiveness. This was achieved by holding meetings and interviews, in which 12 experts, including GPs, dietitians, Coeliac UK employees, and researchers with expertise in questionnaire development participated. Following a review of experts' comments, amendments were made to 13 CDAQ items and 31 CD-PEQ items. In addition, one item was added and a further item deleted from the CD-PEQ.

Amendments to the CDAQ made the intended meaning of items clearer, improved their cultural translatability, and expanded their breadth to include other relevant aspects. In general, experts considered the content of the CDAQ was comprehensive, suggesting only one topic area be covered in more depth.

Amendments to the CD-PEQ improved the questionnaire's formatting, the clarity of questions, and reduced the potential for bias and the generation of anxiety. Again, experts considered the questionnaire comprehensive, but in response to their suggestions, a further item regarding the payment of prescriptions was added.

A broad range of professionals contributed to the discussions, many of which had a particular interest in CD. The contribution of feedback from HCPs, in particular, was useful, as they were able to draw on knowledge and experience gained from working with people with CD in a health care setting. Their comments, in particular, helped revise

questions and response options which asked about the practical aspects of diagnosing and managing CD, such as usual waiting times and follow-up procedures.

4.4 Stage 3 - Cognitive interviews

4.4.1 Introduction

In the previous section of this chapter, feedback from experts was used to improve the CDAQ and CD-PEQ and assess their content validity. Stage 3, described next, assessed content validity from the perspective of those with CD, and pre-tested the completion of questionnaires through the conduct of cognitive interviews.

Cognitive interviewing is a methodology used to aid the identification of sources of response error within questionnaires (Willis, 1999; Willis, 2015), such as incomprehensive or unanswerable questions. During cognitive interviews, participants complete survey questions and verbalise their thought processes of doing so. As well as exploring respondents' cognitive processes, the content validity (i.e. the comprehensiveness of the questionnaire's content) of questionnaires can be assessed (Patrick et al., 2011). Both the US Food and Drug Administration (U.S. FDA, 2009) and the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) (Patrick et al., 2011) recommend conducting cognitive interviews to provide evidence for content validity as part of the development of PROMs. As such, it is typical for PROMs developed more recently to incorporate cognitive interviewing in to their development process, as did the Thyroid-specific Patient Reported Outcome (ThyPRO) measure (Watt et al., 2008) for example. Finally, interviews also provide an opportunity to identify structural or logical problems within the questionnaire (Willis, 1999).

The aim of this stage of questionnaire development was to identify and resolve sources of response error within the CDAQ and CD-PEQ, more specifically:

- To ascertain whether people with CD understood all aspects of the questionnaires (i.e. instructions, items, and response options) as intended;
- To identify aspects of the questionnaires that people with CD found difficult to complete;
- To identify structural and logical errors within the questionnaires (e.g. errors in skip patterns);
- And to assess the questionnaires' content validity.

This aspect of the study has been reviewed by, and received ethics clearance through, the University of Oxford Central University Research Ethics Committee (REC Reference No: MSD-IDREC-C1-2013-142).

4.4.2 Methods

To achieve the above aims and objectives, cognitive interviews were conducted as described below.

Recruitment

Participants were recruited at two time points (August 2013 and February 2015[8]). People were eligible to participate if they had CD, were aged 18 years or over, lived in England,

[8] Cognitive interview rounds one and two for the CDAQ, and round one for the CD-PEQ were conducted in August 2013. Cognitive interview round two for the CD-PEQ was conducted in February 2015.

and had access to a telephone or Skype. Prospective participants were sent an information sheet (Appendix R) and a consent form (Appendix S).

Recruitment method one – recruitment letters sent to those previously expressing an interest in the research

In August 2013, 10 people (3 males, 7 females) who had expressed an interest in participating in a qualitative interview, but were not interviewed, were invited to take part in a cognitive interview (see Appendix T for letter of invitation), eight of which (3 males, 5 females) took part.

In February 2015, four respondents to Survey 1 who had expressed an interest in participating in further research were invited to take part in a cognitive interview, two of which (1 male, 1 female) participated[9].

Recruitment method two – online social networking groups

To reach younger people and non-Coeliac UK members, a recruitment advert (Appendix U) was posted on the message boards of online social networking groups for people with CD at two time points (August 2013 and February 2015). The number of members belonging to each group at the time of recruitment is shown in Table 13. The total number of adults with CD that the advert reached is likely to be less than the sum of the groups' members. This is because some members may belong to more than one group; may be less than 18 years old; may not have CD, but joined the groups for other reasons (e.g. to gain information about CD to support a family member); or may not view the message boards frequently or at all. Twelve respondents took part in an interview.

[9] Note that Survey 1 included the CDAQ only. Cognitive interviews conducted following Survey 1 were to further refine the CD-PEQ.

Table 13. Cognitive interview recruitment from online social networking groups

Social networking group	Number of members (August 2013)	Number of members (February 2015) [a]
Facebook		
Coeliac disease – not just a food preference	30,569	-
Coeliac UK	16,732	-
Coeliac London	6,187	-
Gluten Free Guerrillas	3,276	-
Coeliacs in the UK	3,074	8,158
Coeliac Yorkshire	2,002	-
Yahoo Groups		
UK-Coeliac	374	-

[a] Number of members only provided for groups on to which the recruitment advertisement was posted.

Cognitive interviews

In total, 22 cognitive interviews were conducted across two rounds, with revisions to the questionnaires occurring after each round. Twenty interviews were conducted over the telephone and two interviews were face-to-face at the participant's request. Interviews lasted approximately one hour (ranging from 50 to 90 minutes) to minimise participant burden, as advised by Willis (1999). Interviews were audio-recorded with the participant's consent, with the recordings used to write detailed notes. Participants were selected to complete the CDAQ (n=10) or CD-PEQ (n=12), and were sent the relevant questionnaire prior to the interview with instructions not to complete the questionnaire beforehand (Appendix V).

Interviews began with the researcher providing some background information about the study and explaining the interview procedure. Participants were then asked to start completing the questionnaire. In order to explore the participant's cognitive processes

during questionnaire completion, a 'verbal probing' technique, more specifically 'immediate retrospective probing', as described by Watt et al. (2008), was selected.

Verbal probing is a method which allows the interviewer to ask the participant questions, known as 'probes', to explore how they arrived at their answer. This method was selected as it allowed participants to answer the questionnaire as usual, and was less burdensome than 'think-aloud' interviews, as the interviewer takes a larger role. This approach also provided the researcher with greater control of the interviews than the 'think-aloud' method, allowing greater focus on areas of particular interest (McColl, 2005; Willis, 1999).

Participants completed the CDAQ or CD-PEQ one page or section at a time. Having done so, the researcher asked a series of cognitive probes. This retrospective probing approach ensured that disruption to the flow of the questionnaire was minimised. Demographic data was collected at the end of each interview.

To ensure interview probes addressed all aspects of survey response, their development was guided by Tourangeau's 'question and answer' response model (described in Willis, 2015). The model sets out the four-stage sequence of cognitive processes experienced when responding to a survey question: comprehension, retrieval, judgement, and response.

Both general and item-specific probes were developed, and are discussed further below.

General cognitive probes

The interviewer asked four general probes (Table 14) following completion of the first page or section of the questionnaire. Asking these broad questions provided the participant with the opportunity to highlight any difficulties encountered, and provided them with an idea of the type of information required. In order to reduce burden, at the end of subsequent pages or sections, the researcher asked the following general probe, '*Did you have difficulty understanding or answering any of the questions on this page?*'.

Table 14. General probes asked during cognitive interviews

Question-response phase	Probe
Comprehension	Were any of the questions difficult to understand?
Retrieval	Did you have difficulty remembering the information needed to answer any of the questions?
Judgement	Were you uncertain of any of your answers?
Response	Were you able to find appropriate response options to match your answers?

At the end of the questionnaire, a series of general probes (Table 15) were asked to obtain feedback on the questionnaires' instructions, recall period(s), response options, formatting and length. To conclude, participants were asked whether any aspects of HRQOL or experiences of health care were missing, to allow an assessment of whether constructs were adequately addressed.

Item-specific cognitive probes

Item-specific probes explored cognitive processes in relation to individual items. Some probes made use of paraphrasing techniques, i.e. asking the participant to rephrase a question in their own words, which allowed participants' comprehension of questions to be assessed. Examples are shown in Table 16.

Table 15. Examples of general cognitive probes asked at the end of each cognitive interview

Area assessed	Probe	CDAQ / CD-PEQ[a]
Instructions	Did you have any difficulties understanding the instructions?	Both
	What would you change about or add to the instructions?	Both
Recall period	Overall, do you think asking these questions in relation to the **past 4 weeks** provided an accurate picture of how your quality of life is affected by your coeliac disease?	CDAQ
	Do you think you would have answered differently if it had been a shorter or longer time period?	CDAQ
Response options	How easy or difficult did you find it to distinguish between the response categories?	Both
	What is the difference between 'rarely' and 'sometimes'?	CDAQ
Formatting and length	How do you think the questionnaire could be changed to make it easier to complete?	Both
	How did you find the length of the questionnaire?	Both
Content coverage	Are there any areas in which your coeliac disease affects your quality of life that you do not feel have been covered by the questionnaire?	CDAQ
	Are there any areas of your health care experiences in relation to your coeliac disease that you do not feel have been covered by the questionnaire?	CD-PEQ

[a]Indicates whether the probe was asked in relation to the CDAQ, CD-PEQ or both.

To reduce participant burden, the researcher restricted the length of interviews to approximately one hour, and therefore it was not possible to administer all probes in each interview. However, this did not impact on the value of the cognitive interviews.

Table 16. Examples of item-specific cognitive probes asked during cognitive interviews

	Item	Item-specific probes
CDAQ	…have you felt that people misunderstood your condition or dietary needs (for example, referring to your gluten-free diet as a personal choice)?	Can you give me an example of when this has happened within the last 4 weeks?
	…did you find it difficult to let people know they have misunderstood your condition or dietary needs?	Can you rephrase this question in your own words?
	…have you been concerned about cross-contamination (gluten-free food coming into contact with food containing gluten)?	What does the term 'cross-contamination' mean to you?
CD-PEQ	How long was it from when you first sought medical advice about your symptoms to receiving a definite diagnosis?	When, to you, was the point at which you received a 'definite diagnosis'?
	Which of the following symptoms did you have before you were diagnosed with coeliac disease?	Did you experience any symptoms that are not on the list?
	Instructions – 'To diagnose coeliac disease, an endoscopy is often conducted. An endoscopy…'	Can you explain 'endoscopy' in your own words?

Analysis

The audio recordings and written field notes for interviews were used to create a summary of participants' comments, which were organised in to two matrices, one for each questionnaire. Each matrix was comprised of one row per item, and documented the following (in columns): item number, original item wording, participants' responses (e.g. 'never', 'sometimes'), and a summary of participants' comments. In addition, two further tables were produced summarising comments made about each questionnaires' instructions, recall period, content coverage, response options, and formatting. The researcher systematically reviewed each item within the matrices and suggested revisions to the questionnaires. As part of the review for the CDAQ, the participants' comprehension of items against their intended meaning, as documented in a concept elaboration document (Appendix W), was also assessed. The concept elaboration document describes each CDAQ item in detail, elaborating on the meaning of key words

and phrases. Suggested revisions were discussed with my supervisors and a consensus reached prior to any changes being made. Items requiring further consideration were flagged in order to investigate these in more detail in a second round of interviews, which were analysed as above.

4.4.3 Results

In total, 22 cognitive interviews were conducted, 10 for the CDAQ (round one, n=6; round two, n=4) and 12 for the CD-PEQ (round one, n=5; round two, n=7). Participant characteristics are shown in Table 17. Overall, two-thirds (68%) of participants were female, participants had been diagnosed for between one and 40 years, with the majority reporting strictly adhering to a GFD. Four participants were not members of Coeliac UK.

Table 17. Demographic and disease characteristics of cognitive interview participants (n=22)

Questionnaire commented on, round 1 or 2	ID	Age	Gender	Marital status	Ethnic origin	Occupational status	Duration since diagnosis (years)	Consume gluten on purpose?	Coeliac UK member?	Recruitment[a]
CDAQ R1	50	66	M	Widowed	White British	Retired	16	Never	No	Social network
	51	71	M	Married	White British	Part-time work	6	Never	Yes	Qualitative interviews
	52	53	F	Divorced	White British	Self-employed	9	Rarely	Yes	Social network
	53	24	F	Single	White British	Full-time work	3	Sometimes	No	Social network
	54	28	F	Single	White Irish	Full-time work	5	Never	Yes	Qualitative interviews
	55	57	F	Divorced	White British	Full-time work	7	Never	Yes	Social network
CD-PEQ R1	56	71	M	Married	White British	Part-time work	2	Never	Yes	Qualitative interviews
	57	52	F	Married	White British	Part-time work	2	Never	No	Social network
	58	80	M	Married	White British	Retired	18	Never	Yes	Qualitative interviews
	59	61	F	Married	White British	Full-time work	11	Never	Yes	Social network
	60	64	F	Divorced	White British	Retired	7	Rarely	Yes	Qualitative interviews
CDAQ R2	61	72	F	Married	White British	Retired	10	Never	Yes	Qualitative interviews
	62	49	M	Married	White British	Full-time work	16	Rarely	Yes	Social network
	63	72	F	Married	White British	Full-time work	11	Rarely	Yes	Qualitative interviews
	64	80	F	Married	White British	Retired	15	Never	Yes	Qualitative interviews

Questionnaire commented on, round 1 or 2	ID	Age	Gender	Marital status	Ethnic origin	Occupational status	Duration since diagnosis (years)	Consume gluten on purpose?	Coeliac UK member?	Recruitment[a]
CD-PEQ R2	65	28	M	Single	White British	Full-time work	27	Never	Yes	Survey 1
	66	56	M	Married	White British	Self-employed	3	Never	No	Social network
	67	41	F	Single	White British	Full-time work	40	Never	Yes	Social network
	68	23	F	Single	White British	Full-time education	6	Never	Yes	Social network
	69	45	F	Single	White British	Self-employed	4	Never	Yes	Social network
	70	40	F	Married	White British	Looking after the home	2	Never	Yes	Survey 1
	71	58	F	Married	White British	Doing something else	1	Never	Yes	Social network

[a]**Social network** – participants recruited through adverts posted on online social media networks; **Qualitative interviews** – participants who had previously expressed an interest in participating in a qualitative interview, but were not invited to take part in an interview; **Survey 1** – participants responding to survey 1 expressing an interest in participating in further research.

CDAQ results

In total, 50 CDAQ items were reviewed, of which 11 items were revised, one was deleted, and two were added. The questionnaire's instructions and formatting were also revised.

Sources of response error identified in the cognitive interviews were categorised as follows: (1) participants answered items in general rather than in relation to their CD; (2) different interpretations of words or phrases between participants; and (3) items not interpreted as intended. Each of these categories, along with examples, are discussed further below, with a full list of issues and amendments available in Appendix X. The item tracking matrix, mentioned previously and found in Appendix K, provides an overview of which items changed following rounds one and two.

Category 1 – participants answered items in general rather than in relation to their coeliac disease

Participants answered some questions in general rather than specifically about their CD. For example, when asked if they had been affected by nausea or vomiting, some considered their overall experience, rather than experiences relating only to their CD. To address this, the item was revised to '*…have you been affected by nausea or vomiting that you think was caused by your coeliac disease?*'. In total, four items were identified as problematic and revised where appropriate. In addition to amending the wording of individual items, amendments were made to the instructions to further highlight that all questions relate to CD. The introductory sentence was revised to read, '*This questionnaire asks how you feel your coeliac disease has affected your life during the past*

4 weeks', with '*These questions relate to your coeliac disease*' added to the top of each subsequent page.

Category 2 – different interpretations of words or phrases between participants

Problems occurring due to participants interpreting items in different ways to each other were found for six items. For example, specific words and phrases, such as 'isolation', 'excluded', and 'out of the house' had different meanings for different people (see Example 2). Amendments were made to clarify item wording.

Category 3 – participants interpreted items not as the developer intended

A final category of problems occurred due to participants interpreting items in a different way than intended. For example, when asked about financial strain due to CD, several participants interpreted this question as asking whether they spend more on a GFD than they would a gluten-containing diet, or whether gluten-free food is expensive, rather than its intended meaning (i.e. whether CD has had a severe impact on the individual's finances). To address this, the item was reworded to, '*…did you struggle financially due to your coeliac disease (for example, due to the cost of following a gluten-free diet, or inability to work)?*' and moved to appear before an item specifically asking about frustrations in relation to the cost of gluten-free substitute foods.

In total, three items had been misinterpreted by participants. Two items were re-worded and one item deleted ('*…was your choice of food affected?*') as it could not be reworded to reflect its intended meaning.

CDAQ items with which issues were raised were flagged as problematic, and marked as requiring specific consideration in the remaining stages of development. Items were flagged if they were either not relevant to all participants (e.g. those asking about work activities), were considered potentially ambiguous, or were one of a number of items addressing the same concept.

Participants also commented on instructions, the recall period, response options, formatting and length, and comprehensiveness. These are discussed below.

Example 2. Example of different interpretations of 'excluded' between participants

Original item	…did you feel excluded from social activities?
Participants' comments	**Participant 54:** The participant felt that feeling excluded was not feeling part of a group, for example, if everyone was eating a certain food but she could not, e.g. a speciality food of a country. **Participant 55:** When asked about the difference between feeling isolated and excluded, the participant commented that exclusion was more about not being able to go to an event because they couldn't cater for you.
Author's comments	'Excluded' was interpreted by participants as either meaning partial exclusion (i.e. feeling like an outsider or 'not part of the group') or complete exclusion (i.e. not being able to attend). The latter interpretation is the intended concept and the item was revised to reflect this.
Revised item	…did you feel excluded from attending social activities?

Instructions

In general, participants reported that they were able to understand the questionnaire's instructions. However, as already described, some participants were unsure whether certain items should be answered in general or in relation to their CD. To address this, small amendments were made to the instructions to emphasise that all items are asking about the respondent's CD.

Recall period

The CDAQ instructed participants to answer questions in relation to the past four weeks. This is something that participants struggled with to varying degrees (e.g. one participant included experiences occurring five weeks ago). Many commented that certain experiences, such as having medical tests or going on holiday, were unlikely to have occurred within the past four weeks. However, participants regarded these issues as important, with some recommending a longer recall period to capture these issues. Despite this, participants generally felt that the CDAQ provided an accurate picture of the impact of CD on their HRQOL and stated that their answers would not be vastly different given a longer recall period.

Response options

The CDAQ has five response options, 'Never', 'Rarely', 'Sometimes', 'Often', and 'Always'. The majority of participants reported that they did not have any trouble differentiating between response categories, however, participants occasionally had difficulty choosing between adjacent categories. One participant struggled to interpret 'rarely' as she felt that something occurring within the past four weeks was not a rare occurrence.

Formatting and length

Few concerns were raised regarding the formatting and length of the CDAQ. Many commented that some items were duplicated, with one participant mentioning that the questionnaire was quite long. These issues were addressed in later stages of the CDAQ's development when some items were removed to produce a final version following statistical analysis (see Chapter 5).

Content validity

In general, participants felt that the CDAQ comprehensively covered all areas of HRQOL in relation to CD. However, two participants commented that personal relationships were not specifically covered. One participant described her recent decision not to move in with her partner as he did not take her condition seriously enough, which resulted in her lacking trust in his cooking. While relationships are not addressed specifically, many of the issues faced are addressed by other items, e.g. concern about food prepared by others, lack of support from family and friends, and embarrassment surrounding the discussion of CD and dietary needs. Additional items specifically addressing relationships were not added as the resulting items would not be applicable to all respondents (i.e. those that are single). The inclusion of such items could therefore result in missing data.

CD-PEQ results

In total, 48 items were reviewed, of which 32 items were amended, 4 items added, and 8 items deleted (Round 1: 25 amended, 1 added and 4 deleted; Round 2: 21 amended, 3 added and 4 deleted). Examples of amendments made are discussed below, with a full list of amendments available in Appendix Y.

The cognitive interviews identified a variety of issues with the CD-PEQ, which were broadly classified as problems with: (1) capturing the diversity of experiences; (2) information retrieval; (3) question clarity; (4) lack of knowledge; and (5) judgement. Each of these areas, including examples of amendments made, are described next.

Category 1 – capturing the diversity of experiences

The cognitive interviews highlighted the diversity of people's experiences, particularly regarding how and when CD was diagnosed. There was particular diversity in terms of the participants' age at diagnosis, symptoms experienced prior to diagnosis, and how the diagnosis occurred (e.g. some were diagnosed following many years of symptoms and visits to the GP, while others were diagnosed as a result of blood tests conducted due to a related condition). Due to this diversity, it was necessary to amend some questions and their response options, and introduce questionnaire 'skips' to maximise the applicability of the questionnaire to all respondents. For some questions, participants were unable to map their experience to an appropriate response category, and therefore, new response options were added to overcome this.

As an example, it became apparent that those diagnosed as young children would not be able to answer questions asking about the period prior to diagnosis and the diagnosis itself. To address this, a filter question was added at the beginning of the questionnaire, which directed those to skip these sections if they were diagnosed at aged 15 or less.

Category 2 - information retrieval

For some participants, retrieving the information needed to answer some of the questions was difficult as the events of enquiry (e.g. diagnosis) occurred many years ago. For example, none of the participants were certain of their answer to the question, 'How long did you have to wait for an endoscopy?'. Although exact timings were no longer retrievable from memory, most participants were able to recall roughly how long they had to wait saying it was 'pretty quick' or happened 'quite quickly'. As a result, a few questions enquiring about the timescales of experiences were amended to ask more

broadly about how people felt about the amount of time they took on a scale from 'very quick' to 'very slow'.

Category 3 – question clarity

There were several instances where participants were unable to interpret or misinterpreted questions. This was demonstrated by participants disregarding timescales (e.g. 'Were you offered a second appointment to speak to a dietitian within 6 months of your first appointment?'), not selecting the most appropriate response option, and stating their uncertainty about a question's meaning (Example 3). Question wording was amended and formatting used (e.g. emboldening key words) to enhance the clarity of questions.

Example 3. Example of problems with question clarity

Original question	In the last 12 months, have you been able to speak to the following health care professionals about your coeliac disease when you needed?
Participants' comments	**Participant 57:** The participant was unsure what the question was asking. She has been able to speak to her dietitian at appointments, but does not feel that she could call the dietitian at any time for help. **Participant 59:** The participant was unsure what the question was asking. She has spoken with hospital doctors in pre-arranged appointments, but has not called them up when needed. When she has had questions to ask, she waited for her annual appointment.
Author's comments	Participants commented that there was a difference between raising an issue during an appointment and being able to ring a health care professional for advice when needed. The question was re-worded to improve clarity.
Revised item	In the last 12 months, have you been able to get information and advice about your coeliac disease from a health professional when you wanted to do so?

Category 4 – lack of knowledge

Participants demonstrated a lack of knowledge about certain medical tests, procedures, and terminology (e.g. 'pneumococcal vaccination' and 'health care professional'). Where appropriate, explanations were provided or amendments to terminology were made. Where this was not possible, items were deleted. For example, participants were asked if they had received a genetic test as part of their diagnosis. As many participants were not familiar with this test, and it had not been commonly used to date, the question was removed.

Category 5 – judgement

Participants felt unable to make the judgements needed to provide answers for a couple of questions. This was either due to a lack of knowledge the participant perceived was needed (e.g. about usual diagnosis and treatment pathways), or simply because they were unable to make the judgements requested (e.g. how often HCPs appeared informed about themselves and their medical history). Where possible, question wording was revised, but where the cognitive demands placed on respondents were regarded as too complex, questions were deleted.

Content validity and general comments

Overall, participants were positive about the questionnaire, with one commenting that it was clear the researchers understood what it was like to have CD. While participants felt the questionnaire was extensive, there were some suggestions for additional questions, including further items about associated conditions, medication, and support received outside the health service (e.g. through social networking groups). In response to these comments, a list of associated conditions within the NICE guidelines (NICE, 2009) was

reviewed and the existing list of associated conditions within the questionnaire was expanded. A question asking participants about other sources of support was added, and while it is recognised that other sources of support play a role, the questionnaire's focus is to explore experiences of health care services, and therefore, other sources of support will not be explored in depth.

Participants found the instructions clear and felt the length of the questionnaire was acceptable, with some commenting that the large number of questions was necessary to cover people's experiences in sufficient detail.

4.4.4 Summary

The CDAQ and CD-PEQ were pre-tested with people with CD to identify and resolve problems with understanding or answering the questionnaires, while also assessing their comprehensiveness. This was achieved by conducting 22 cognitive interviews. Following a review of participants' comments, questions were revised, deleted from and added to both questionnaires, with the final versions of the CDAQ and CD-PEQ comprised of 51 items and 43 items respectively.

The majority of interviews were conducted over the telephone, which allowed the recruitment of participants from a wide geographical area. This was particularly important when enquiring about experiences' of health care services, as access and provision may vary between trusts. This approach helped ensure the resulting questionnaires are relevant to all.

A limitation with telephone interviews is that non-verbal behaviour cannot be observed, for example, crossing out one answer and selecting another. Where requested, interviews were conducted in person, which allowed an individual with hearing difficulties to participate.

A 'verbal probing' method of cognitive enquiry was used in preference to the alternative 'think-aloud' approach, which requires the respondent to be trained in how to perform the interview, and places significant cognitive burden on the respondent (Willis, 1999). A limitation of 'verbal probing' is the increased chance of recall errors and hindsight bias due to a longer gap between answering the question and verbalising cognitive processes (McColl, 2005). To minimise this, an 'immediate retrospective probing' approach was selected, reducing the time between answering a question and verbalising the associated cognitive processes, while minimising disruptions to the flow of the questionnaire.

The cognitive interviews were conducted in two rounds, with revisions occurring after each round. While a consensus regarding the number of interviews deemed sufficient has not been reached (Beatty and Willis, 2007), guidelines recommend that a new round of cognitive interviews is conducted if the current round results in revisions to the questionnaire (Patrick et al., 2011). While this approach is optimal, a more pragmatic approach, as set out by Willis (1999), was adopted, which recognises that a questionnaire could be tested forever and therefore, recommends conducting as many rounds as practical. Both questionnaires were included in a pilot survey (Chapter 6), which provided further opportunity for people with CD to raise any issues with questionnaire items prior to their use in Survey 2.

The results of the cognitive interviews conducted for the CDAQ found that participants occasionally answered questions in general, rather than in relation to their CD as instructed. They also interpreted words and phrases within questionnaires in different ways to each other, or not as intended.

Some participants would have liked a longer recall period to capture additional experiences, for example, holidays or periods of gluten consumption. This issue was also found by Watt et al. (2008) who used cognitive interviews during the development of a measure to assess quality of life in thyroid patients.

The results of the cognitive interviews conducted for the CD-PEQ identified one of the main problems as the difficulty of capturing the diversity of experiences across respondents, and correspondingly ensuring that the questionnaire was relevant for all. Participants had vastly different experiences, and the questionnaire required considerable thought to ensure that respondents were able to navigate it regardless of their experience, i.e. whether they were diagnosed as a child or adult, experienced symptoms prior to diagnosis, and receive follow-up care.

A limitation of the cognitive interviews is that while demographic and basic information about the participants' CD were collected and reported (including age, ethnicity, time since diagnosis, and adherence to a GFD), additional background information (such as method of diagnosis, and symptoms experienced prior to diagnosis) was not routinely collected or documented. As such, while the sample was known to include diversity

across these factors, as many participants touched on these issues during their interview, a formal analysis taking these factors into account was not conducted.

A second key issue, was the difficulty of information retrieval relating to distant events, in particular, timescales (e.g. waiting times). While it is recognised that data about timescales can prove more useful when collecting data about patients' experiences of health care, participants experienced difficulties recalling information about events occurring years ago. As a result, some questions were amended to ask the respondent how they felt about timescales attached to experiences (e.g. waiting times) as opposed to actual timescales. This is a difficulty when asking respondents about experiences related to the entire history of their disease, rather than a recent acute episode of care.

Further problems identified with the CD-PEQ were due to poor question clarity, respondents' lack of knowledge, and difficulties making the necessary judgements to answer questions.

Amendments were made to questions, response options, and instructions to address the issues identified.

4.5 Stage 4 - Assessment of the translatability of the Coeliac Disease Assessment Questionnaire

4.5.1 Introduction

The previous section described pre-testing the questionnaires through cognitive interviews. While this was the final stage of development for the CD-PEQ, an additional

stage was conducted for the CDAQ. Stage 4, described here, aimed to assess and revise the CDAQ to minimise cultural and linguistic problems that may arise in future translations.

It is common for PROMs, such as the CDAQ, to be used internationally, and therefore, it is often necessary for measures to be translated into different languages and adapted for different cultures. Translations typically occur after the original PROM has been finalised. As such, it may be difficult to produce other language versions that are conceptually equivalent to the original measure, for example, because equivalent words or expressions do not exist in the target language. If discrepancies between the source (i.e. the original language version) and target language (i.e. the languages into which the measure is to be translated) versions cannot be resolved, the aggregation of global data may be difficult (Wild et al., 2005).

To minimise these issues, it is increasingly common to carry out a Translatability Assessment (TA) as part of a PROM's development. A TA is 'the evaluation of the extent to which a PRO measure can be meaningfully translated into another language' (Conway, Acquadro and Patrick, 2014). As well as focussing on linguistic translatability, whether or not items are culturally relevant or appropriate is also assessed. For example, references to the respondent's ability to climb stairs may not be as relevant in a country where single-storey houses predominate. Essentially, the assessment considers whether a conceptually equivalent translation in each of the target languages is likely to be achieved.

A TA is typically carried out prior to the finalisation of the PROM to allow for revisions to the original version. Revisions aim to minimise translatability issues arising in future translations.

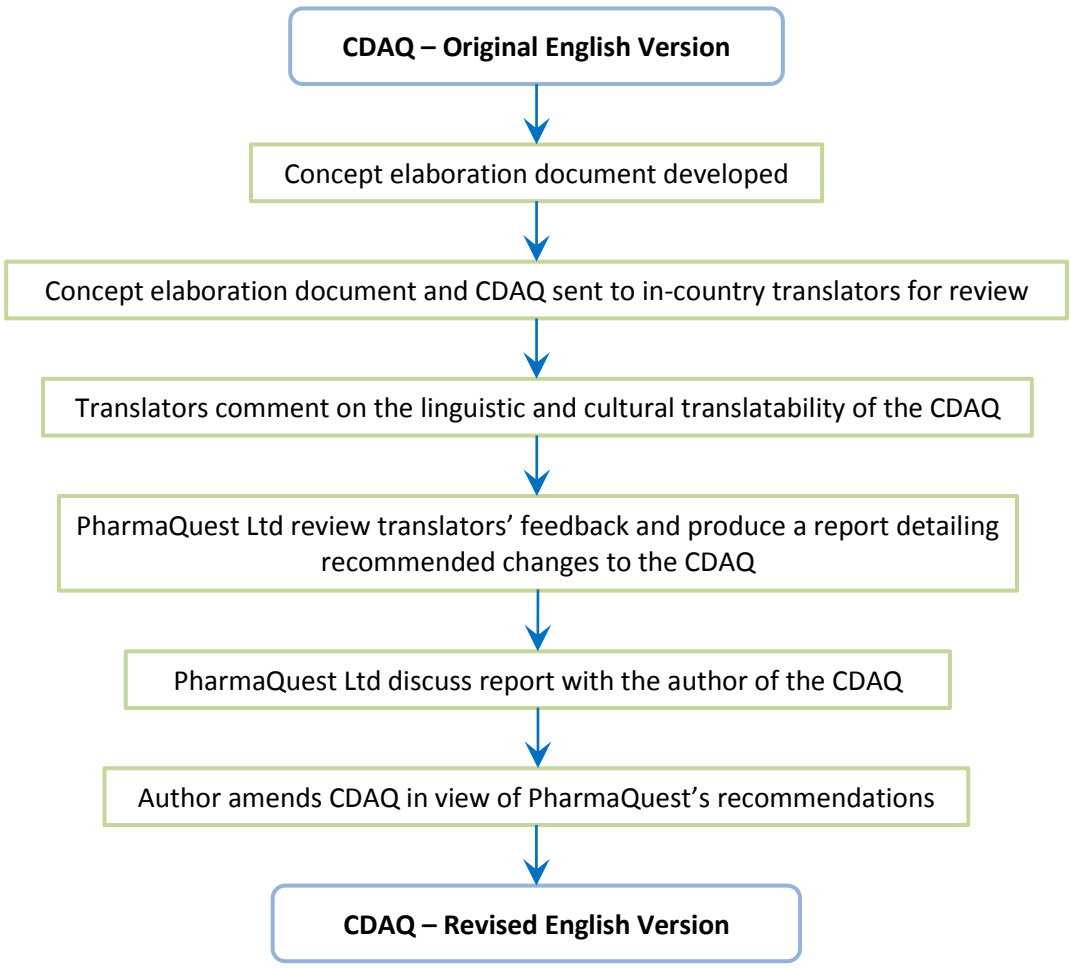
4.5.2 Methods

A TA of the CDAQ's candidate items (n=51) was conducted in collaboration with PharmaQuest Ltd (now Corporate Translations, Inc.), a translation company specialising in the translation and linguistic validation of PROMs. A wide variety of language-country combinations were selected in consultation with PharmaQuest Ltd to ensure broad coverage across continents and language families. The language-country combinations selected were: Arabic (Egypt), Finnish (Finland), French (France), German (Germany), Simplified Chinese (China), and Spanish (Argentina)[10]. The source version of the CDAQ is written in English.

The key steps of the TA are shown in Figure 8. A concept elaboration document (similar to that in Appendix W) was developed by PharmaQuest Ltd and reviewed by the author. The concept elaboration document was sent to in-country translators, together with the English version of the CDAQ. Translators commented on the translatability of the CDAQ's instructions, items and response options. Following a review of the translators' comments, PharmaQuest Ltd provided recommendations for improving the CDAQ, which were discussed with the author in a teleconference and detailed in a report. Amendments were made based on these recommendations.

[10] Language families for the selected languages in the format 'language (language family)': German (Indo-European (Germanic)); French and Spanish (Indo-European (Romance)); Arabic (Afro-Asiatic (Semitic)); Finnish (Uralic (Finno-Ugric)), and Simplified Chinese (Sino-Tibetan).

Figure 8. Translatability Assessment methodology



4.5.3 Results

Sixty-four changes were recommended to the English version of the CDAQ. The majority (97%, n=62) related to the CDAQ's items and two related to the instructions. The recommended changes address various translatability issues, which were broadly categorised as cross-cultural and grammatical (Table 18).

Table 18. Categorisation of translatability issues

Translatability issue category	Description
Cross-cultural issues	**Translatability issues arising due to differences between the source and target cultures or languages.**
Vocabulary	Specific words in the source version do not have an equivalent in the target language.
Semantic differences	Words or phrases in the source version are not conceptually equivalent in the target language.
Sociocultural differences	Concepts or cultural practices referenced within the source version are unfamiliar in the target culture.
Grammatical issues	**Translatability issues arising due to grammatical or structural problems within the source version.**
Structural issues	Problematic structuring of items within the source version, e.g. missing verbs, redundant words, or incomplete sentences.
Tenses	Inconsistent tenses used within the source version.
Wording-concept mismatch	Item wording does not accurately or adequately express the underlying concept in the source version, e.g. due to vague wording or incorrect use of vocabulary.

The number of recommended and implemented changes, by category of translatability issue, is shown in Table 19. The majority of recommendations were to address translatability issues arising due to a lack of equivalent vocabulary in the target languages, and inconsistent tenses used throughout the CDAQ. In total, 64 changes were recommended to 40 of the CDAQ's items.

The majority of recommended changes (97%, n=62) were implemented. The two recommendations not followed advised that examples of gluten-free products were added to clarify the phrase 'gluten-free substitute foods'. However, as cognitive interview participants understood this phrase, no changes were made.

In addition to the recommended changes, seven further amendments were made to improve readability. Therefore, in total, 69 amendments were made to 43 items (n=67) and the instructions (n=2). A summary of amendments can be found in Appendix Z.

Each category of translatability issue identified will be described further below.

Table 19. Changes to the CDAQ, by category of translatability issue

Translatability issue	Sub-category	No. of recommended changes	No. of recommended changes followed	No of additional changes	Total No of changes
Cross-cultural	Vocabulary issues	22	20	0	20
	Semantic differences	4	4	0	4
	Sociocultural differences	1	1	0	1
Grammatical	Structural issues	7	7	6	13
	Tenses	28	28	0	28
	Wording-concept mismatch	2	2	1	3
Total no. of changes		**64**	**62**	**7**	**69**
Total no. of items with changes recommended [a]		**40**	**40**	**7**	**43**

[a]Some items had more than one recommended change

Cross-cultural issues

Translatability issues arose due to cross-cultural differences, in particular, social and semantic differences between cultures.

a) Vocabulary issues

Problems with vocabulary were identified when it was not possible to directly translate certain words into one or more of the target languages. Vocabulary equivalent to 'unwell', 'condition', 'health condition', 'troubled', 'loose bowels', 'affected', 'awkward', and 'catering' did not exist in all of the target languages. Alternative vocabulary for the

English source version was suggested and 20 amendments were made. For example, references to the individual's 'condition' were not translatable in all languages, and therefore, the word 'condition' was replaced with 'coeliac disease'.

b) Semantic differences

Translations of certain words and phrases such as, 'out of the house', 'eating out', and 'struggle financially' would not necessarily be conceptually equivalent to the source version in one or more of the target languages. For example, 'travelling to work' was highlighted as difficult to translate as the word 'travel' is only used for longer journeys in many of the target languages. The item was revised to include the verbs 'to go' and 'to travel' to ensure a smoother translation process in future.

c) Sociocultural differences

One item was highlighted as potentially difficult to translate due to sociocultural differences. This item referred to the concept of following a GFD out of personal choice, for example, to lose weight. This concept would not be understood in all other cultures. The original and revised item wording can be found in Example 4.

Grammatical issues

Translatability issues were classified as grammatical where the tense used or item structure could cause difficulties with translation.

a) Structural issues

The structure of several items was considered problematic due to missing verbs or awkward wording, resulting in 13 amendments, which as well as aiding the future

translation of the CDAQ, also improved the readability of the English version (see Example 5).

Example 4. Sociocultural differences – following a gluten-free diet to lose weight

Original item	have you felt that people misunderstood your condition or dietary needs (for example, referring to your gluten-free diet as a personal choice)?
Comments from in-country linguists	**Arabic Translator:** *'… the fact that some people follow a gluten free diet to lose weight would not be understood from this phrase. This kind of diet is not very common in Egypt…'* **Finnish Translator:** *'… if one uses a direct translation of "personal choice" in Finnish it might not be imply exactly what you want to say'* (sic)
PharmaQuest's comments	*'"Personal choice" may be difficult to translate, especially in countries where the concept of using a gluten-free diet to lose weight may not have been considered. It may be better to say "personal preference" or expand on the item and say "referring to your gluten free diet as a personal choice, rather than a health related decision".'*
Revised item	have you felt that people misunderstood your coeliac disease or dietary needs (for example, thinking you follow a gluten-free diet as a personal choice rather than for your coeliac disease)?

Example 5. Grammatical issue – item missing a verb

Original item	…did you have difficulties with work-related tasks?
Comments from in-country linguists	**French Translator:** *'Could "with" be replaced by a verb? (performing, for example)'* **Simplified Chinese Translator:** *'… Direct translation of "have difficulties with work-related tasks?" can't work here. It is better to change it to "have difficulties in doing work-related tasks?"…'*
PharmaQuest's comments	*'The lack of verb in this question has raised an issue with two different language groups, however this can be resolved easily.'*
Revised item	…have you had difficulties carrying out work-related tasks?

b) Tenses

Translators identified inconsistencies in the tenses used, with some items written in the completed past tense (e.g. '*did you feel down or in low spirits?*'), and others in the continuous past tense (e.g. '*have you felt annoyed or frustrated about the cost of gluten-*

free substitute foods?'). Twenty-eight items were rewritten so that all items appear in the continuous past tense.

c) Wording-concept mismatch

A few translatability issues arose due to the item not accurately or adequately expressing the underlying concept. This was primarily due to incorrect use of vocabulary or vague item wording. For example, the phrase 'eating out' was used to convey all instances of going out to eat (e.g. in a restaurant or at a friend's house). However, the phrase is typically used to mean eating out in a public place only, such as a restaurant or café.

Instructions and response options

Minor amendments to the questionnaire's instructions were also made. For example, the instruction '*Please tick **one** box for each question and answer **all** questions*' was simplified to '*Please tick **one** box for **each** question*'. No changes were recommended for the response options.

4.5.4 Summary

A TA was conducted to identify and resolve cultural and linguistic translatability issues with the CDAQ. The TA identified 64 issues across 40 items, of which 62 changes were made to the CDAQ. In addition, a further seven amendments were made to improve readability, resulting in a total of 69 amendments to 43 items. Translatability issues were broadly categorised as cross-cultural and grammatical.

Cultural and linguistic issues should be considered when developing a PROM, and it is recommended that an expert in PROM translations reviews the measure to minimise

these issues (Patrick et al., 2011). Due to the expertise required to perform this activity, along with the access needed to in-country translators, the TA was conducted in collaboration with PharmaQuest Ltd., a company that specialises in the translation of PROMs.

The CDAQ was reviewed by six translators covering a broad range of languages and countries. A wide variety of countries and languages were selected to maximise the likelihood of identifying and resolving major translation issues prior to the finalisation of the measure.

The TA identified potential difficulties with the translation of the CDAQ due to the absence of equivalent vocabulary in the target languages, conceptual differences between interpretations of phrases, sociocultural differences, and grammatical issues (e.g. missing verbs and inconsistent tenses). The majority of issues arose due to difficulties with the translation of particular words or phrases, with very few issues arising due to cross-cultural differences.

The translatability issues identified by the translators were reviewed by the author, and amendments to the English source version were made. While it was expected that the TA would result in revisions that would improve the ease of future translations, many of the revisions made (e.g. the standardisation of tenses) also improved the English version of the CDAQ. Conway, Acquadro and Patrick (2014) also found that TAs can lead to improvements in the source version, for example, the identification and resolution of double negatives.

Feedback on the translatability of the CDAQ from people speaking a broad range of languages and located within different cultures, has resulted in 69 amendments to the CDAQ. While these amendments will make future translations of the CDAQ simpler, they have also improved the English source version.

4.6 Discussion

The aim of this chapter was to refine the CDAQ and CD-PEQ candidate items that were developed following qualitative interviews. This was achieved through a four-stage process that involved an initial appraisal of items by researchers, meetings and interviews with experts, cognitive interviews with people with CD, and a translatability assessment of the CDAQ. Candidate items were added, amended and deleted throughout these stages, resulting in 51 items in the draft CDAQ and 43 items in the final version of the CD-PEQ (Figure 9).

The refinement of candidate questionnaire items was conducted in accordance with guidelines (U.S. FDA, 2009). In particular, a thorough process involving a range of experts (i.e. researchers, clinicians, and Coeliac UK staff) and people with CD has been taken to maximise opportunities to gather evidence to support the content validity of the measure; a measurement property that is considered by some as the most important (Terwee et al., 2007). The sample of people with CD who were involved in the refinement of the questionnaires were diverse in many respects (i.e. age, gender, marital status, and time since diagnosis), but lacked diversity in terms of their ethnicity, with most of White British origin, and dietary adherence, with most strictly adhering to a GFD.

Further research exploring the content validity of the questionnaires in individuals from other ethnic backgrounds and those who follow a GFD less rigorously would be valuable.

The process used to develop the CDAQ has a number of advantages over that used to develop the existing CD-specific measures, namely the CDQ and CD-QOL (identified in Chapter 2). Firstly, while both the CDQ and CD-QOL included people with CD in their development, their role was limited. For the CDQ, people with CD contributed to item generation through the completion of a questionnaire as opposed to interviews or focus groups as recommended in guidelines (U.S. FDA, 2009). While the CD-QOL did utilise focus groups to inform item development, the diversity of participants was very limited, for example, all participants were recruited from the same local support group, were all Caucasian, and were predominantly female. Patrick et al. (2011) recommend involving a diverse sample in qualitative interviews to help ensure the content validity of the final PROM. As this has not been achieved, the content validity of the CD-QOL may be limited.

A further advantage of the CDAQ is that a translatability assessment was conducted and therefore, few problems are anticipated during future translations of the measure. Neither the CDQ nor CD-QOL conducted a formal translatability assessment, although translators were involved in the development of the CDQ, primarily to check the measure's readability and ease of completion for the purposes of creating an English version. Therefore, translations of the CDQ and CD-QOL may not be conceptually equivalent if appropriate words do not exist in the target language, hampering the aggregation of data collected on a global scale (Wild et al., 2005).

Thirdly, only the CDAQ has assessed items against the QAS-99, a tool specifically developed for identifying and resolving common problems with the design of questionnaires.

Finally, the CDAQ utilised cognitive interviews to further refine items and provide evidence for content validity, as recommended by Brod et al. (2009) and the U.S. Food and Drug Administration (2009). The developers of the CDQ did not utilise cognitive interviews as part of the measure's development. Conversely, Dorn et al. (2010) report conducting cognitive interviews as part of the CD-QOL's development, but provide no details of how the interviews were conducted or analysed, and therefore, the quality of the interviews and how comprehensive they were cannot be evaluated.

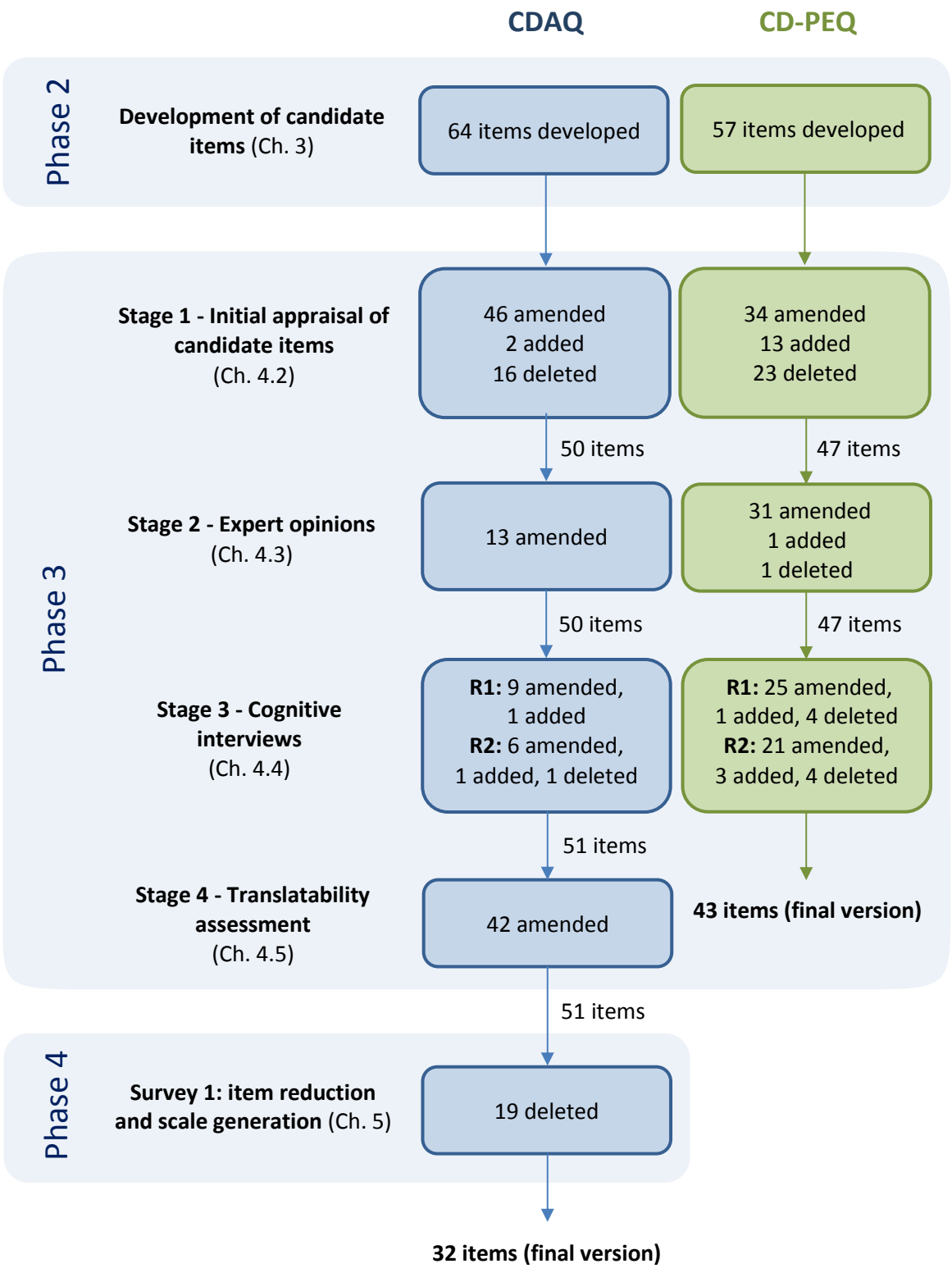


Figure 9. The stages of development of the CDAQ and CD-PEQ

Flowchart showing the number of items amended, added and deleted at each stage of questionnaire development. Phase 2: The qualitative development of items; Phase 3: Refining and pre-testing the questionnaires; Phase 4: Item reduction and scale generation (CDAQ only). 'R1' and 'R2' refer to rounds 1 and 2 of the cognitive interviews.

CHAPTER 5:
Item reduction and scale generation of the CDAQ

5.1 Introduction

The previous chapter describes an extensive process carried out to finalise items for the CDAQ and the CD-PEQ. This chapter describes how the preliminary 51-item CDAQ was reduced to the final version of the questionnaire, and how the dimensions of the CDAQ were determined.

The development of a PROM typically involves exploring its underlying structure using statistical methods. This is most commonly achieved through factor analysis (de Vet et al., 2011). Such exploration, particularly of more complex constructs, allows dimensions of the constructs to be identified and items that do not fit the constructs to be discarded. Items with floor or ceiling effects (i.e. a large proportion of respondents endorsing the extreme response options) should also be reviewed or considered for removal as they are uninformative and do not improve the psychometric properties of the scale (Fayers and Machin, 2007; Streiner and Norman, 2008). Furthermore, the reduction of items is also necessary at this stage to reduce the often large number of candidate items to a more appropriate number for a usable scale, thus enhancing acceptability of the PROM. Questionnaires should ideally be brief, while retaining comprehensive coverage of the construct of interest (i.e. while maintaining content validity) (Fayers and Machin, 2007). Thus, the overall aim of item reduction and scale generation is to produce homogenous, internally consistent, and univariate scales or sub-scales (Kline, 2000).

It is common practice for developers to utilise item reduction and scale generation methods when developing PROMs. For example, while developing the Parkinson's Disease Questionnaire (PDQ-39), Jenkinson et al. (2012) used item reduction methods and factor analysis to reduce the number of questionnaire items from 65 to 39, and identify eight factors.

5.1.1 Aims and objectives

The aim of this stage of the research was to reduce the number of items in the CDAQ and determine its dimensions. This was achieved by the following objectives:

- To reduce the number of items in the CDAQ to produce homogenous scales through the removal of redundant and ill-fitting items;
- To reduce the length of the CDAQ to improve the acceptability of the PROM to respondents;
- And to explore the dimensions of the CDAQ using factor analysis.

5.2 Methods

To achieve the above aim, a survey of adults with CD was conducted (hereafter referred to as 'Survey 1').

5.2.1 Recruitment

Eight hundred Coeliac UK members were invited to participate in Survey 1. Members were eligible for selection if they were aged 18 years or older, reported a medical diagnosis of CD, had not opted-out of being contacted for research purposes, and lived in the UK.

Coeliac UK's membership is skewed towards a more elderly population, contains fewer people from BME groups, and more females than males. As such, a stratified random sample, stratified by ethnicity, age, and gender (Table 20), was adopted to increase the likelihood of achieving a diverse sample, to assist in the development of a PROM that is applicable to all adults with CD.

It was not possible to precisely achieve the proposed stratified sample as Coeliac UK's database did not have a sufficient number of younger, male BME members[11]. Additional members were selected from other strata to account for this (see Table 20).

Table 20. Sampling stratum for Survey 1

Stratum	Ethnicity	Age group	Gender	Proposed (n)	Actual (n)
1	White	<= 40	Female	160	160
2	White	<= 40	Male	160	160
3	White	> 40	Female	160	160
4	White	> 40	Male	160	160
5	BME[a]	<= 40	Female	40	48
6	BME	<= 40	Male	40	24
7	BME	> 40	Female	40	40
8	BME	> 40	Male	40	48
			Total	**800**	**800**

[a]Black and Minority Ethnic (BME) Groups

5.2.2 Survey 1

Questionnaire packs were posted to 800 members of Coeliac UK in September 2014. Each pack included a personalised letter of invitation (Appendix AA), information sheet (Appendix BB), questionnaire (Appendix CC), and pre-paid return envelope. The questionnaire included the draft 51-item CDAQ along with demographic and disease-

[11] Coeliac UK had 47 male BME members aged 40 years old or less at the time of the database search. Half were invited to participate in Survey 1 and half were invited to participate in Survey 2.

related questions. Questionnaires were mailed from Coeliac UK and returned to the Health Services Research Unit at the University.

Although most experts recommend sending reminder letters as a way of increasing response rates (McColl et al., 2001), Coeliac UK did not support this. As an alternative, details of the study were placed on Coeliac UK's website (Appendix DD).

Ethics clearance to conduct Surveys 1 and 2 (described in Chapter Six) was received through the University of Oxford Central University Research Ethics Committee (REC Reference No: MSD-IDREC-C1-2014-031).

5.2.3 Statistical methods

This section outlines the methods used to reduce the number of items, determine the factor structure, and score the CDAQ.

Initial item reduction

Prior to determining the CDAQ's dimensions, items were removed from the draft CDAQ using the following criteria as a guide:

- Missing data > 5%
- Floor or ceiling effect > 50% (i.e. at least 50% of respondents selected 'never' or 'always')
- Inter-item correlations <0.2 or > 0.8 (assessed following review of a correlation matrix)

A correlation matrix showing a summary of the interrelationships among items in a scale (Pett et al., 2003) was generated as part of the above analysis. Correlations (r) between each pair of variables range between -1.00 and +1.00, with higher absolute values indicating a stronger relationship (Pett et al., 2003). Positive values indicate that people scoring highly on one item tended to score highly on the other item, while negative values indicate that those scoring highly on the first item tended to score low on the second item (Pett et al., 2003).

It is useful to review the correlation matrix during the development of a measure to identify items that are redundant or ill-fitting. Items that are very highly correlated are measuring almost the same thing (de Vet et al., 2011), while there is little common variance between items with a very low correlation (Pett et al., 2003), indicating that they are measuring different constructs. Values of what constitutes very high and low correlations varies, but for the purposes of this study, inter-item correlations <0.2 or >0.8 were reviewed and considered for removal.

Six items had a 'not applicable' response option available which respondents could select if they felt an item was not relevant to them. Missing data was calculated as the sum of respondents not endorsing any response option plus those selecting the 'not applicable' category (where available).

Assessing the factorability of the correlation matrix

Following the removal of items meeting the above criteria, two tests were performed to assess the factorability of the dataset, thus indicating the appropriateness of conducting

a factor analysis. The first test, Bartlett's Test of Sphericity (Bartlett, 1950), tests the null hypothesis that there are no relationships between the items in the correlation matrix, i.e. that each item is addressing a different underlying construct (Pett et al., 2003). A significant result indicates that the null hypothesis can be rejected and that factor analysis is an appropriate method.

The second test, the Kaiser-Meyer-Olkin (KMO) Measure of Sampling Adequacy (Kaiser and Rice, 1974) provides further information about the strength of the relationships between items (Pett et al., 2003). KMO values greater than 0.60 indicate the data is considered factorable (Kaiser and Rice, 1974).

Factor Analysis

Following the above checks, an exploratory factor analysis was conducted. Factor analysis is a statistical method that examines the relationships between items in a correlation matrix to identify the structure of the underlying construct(s) assessed by the items. The method aims to group items such that correlations between items within the same group are high, and correlations between items belonging to different groups are low (Fayers and Machin, 2007; de Vet et al., 2011). It is usual to rotate the initial factor solution to aid interpretation (Nunnally and Bernstein, 1994; de Vet et al., 2011).

A Principal components analysis (PCA) with Varimax rotation was used to identify the initial factors. 'Varimax' is an orthogonal rotation method of which an underlying assumption is that the factors extracted are uncorrelated (Fayers and Machin, 2007). This method was chosen as it tends to produce clearly defined domains (Nunnally and

Bernstein, 1994). Varimax is often considered the best orthogonal approach (Nunnally and Bernstein, 1994; Kline, 2000), as it provides clear, interpretable solutions (Pett et al., 2003). Components with an eigenvalue greater than one were extracted. Eigenvalues measure the amount of variation in the data explained by each factor (Fayers and Machin, 2007).

A higher order factor analysis was conducted to determine the appropriateness of combining dimension scores to create an overall score. Nunnally and Bernstein (1994) recommend an oblique solution is sought in relation to this type of analysis and therefore, principal axis factoring with direct oblimin rotation was used for the higher order factor analysis.

Sample size

Recommendations regarding the minimum sample size for factor analysis vary considerably, ranging from two to 10 respondents per item, with a minimum of 100 respondents (Kline, 2000). Quality criteria for the assessment of health status questionnaires state that an adequate sample size on which to perform factor analysis is seven respondents per item, with a minimum of 100 respondents (Terwee et al., 2007). Following this criterion, a minimum sample size of 357 respondents was required (i.e. 7*51 items). The number of respondents returning a completed questionnaire exceeded the minimum sample size required.

Item reduction

During the principal components analysis (PCA), items were considered for deletion if:

- they correlated highly with other items (>0.7), indicating item redundancy;

- or they did not load strongly on any component (all loadings <0.5), indicating a poor fit between the item and components within the measure.

Internal reliability

Internal reliability assesses the extent to which items within a dimension or scale are measuring the same underlying construct (Jenkinson and Fitzpatrick, 2013). The internal reliability of each CDAQ subscale was assessed using Cronbach's alpha. Cronbach's alpha values between 0.7 and 0.9 indicate good internal consistency (de Vet et al., 2011). Very high values of Cronbach's alpha indicate redundancy in the scale, i.e. one or more items are measuring the same concept (Terwee et al., 2007), while low values may indicate that the items within a scale are tapping different underlying constructs. It should be noted that while a minimum Cronbach's alpha coefficient of 0.70 is generally acceptable for group comparisons (Velikova and Wright, 2005), a minimum value of 0.90 is recommended when interpreting scores at the individual patient level (Nunnally and Bernstein, 1994).

Item-total correlations provide information about the contribution of each item to the scale score. Correlations < 0.3 (Nunnally and Bernstein, 1994), were considered for removal as they were contributing little to discriminate between respondents.

Items were deleted one at a time, with the PCA and assessment of internal reliability performed after each item deletion, thus allowing the impact of the item's removal on the factor structure and reliability of the scales to be assessed.

Data was analysed using IBM SPSS Statistics 20, hereafter referred to as SPSS. To check the accuracy of data, 20 per cent of questionnaires were entered twice. A comparison of the two datasets identified a small number of discrepancies (n=7, 0.10% of data entered). Amendments to the final dataset were made where necessary.

Scoring the CDAQ

Each item was scored from 1 ('Never') to 5 ('Always'). Item scores were inverted prior to the calculation of dimension scores[12]. Dimension scores were calculated by summing the scores of questions within each dimension and converting this score to a 0-100 metric, where 0 indicates poorest quality of life and 100 indicates highest quality of life. The formula used for calculating dimension scores was:

DIMENSION SCORE = (((SUM OF SCORES FOR ALL ITEMS WITHIN THE DIMENSION) – LOWEST POSSIBLE DIMENSION SCORE) / DIMENSION SCORE RANGE) * 100

If a respondent had not completed one or more questions, then the associated dimension score(s) could not be calculated.

5.3 Results

The survey achieved a 52% (n=412) response rate. One questionnaire was excluded from the analysis as only the demographics section had been completed. Response rates were calculated for each stratum of the sampling strategy, based on self-reported

[12] Scores were inverted so that higher scores indicate better HRQOL. This is more intuitive and fits with how other measures are commonly scored.

demographics. Response rates were higher in those aged 40 years or over, people from a white ethnic background, and females (Table 21).

Table 21. Survey 1 response rates – overall and by age, ethnicity and gender

Characteristic		Sent (n)	Received (n)	Response rate (%)
Age	n=411			
<=40		392	170	43.4
>40		408	241	59.1
Ethnicity	n=411			
White		640	361	56.4
BME		160	50	31.3
Sex	n=411			
Female		408	225	55.1
Male		392	186	47.4
Overall		**800**	**412**	**52**

Respondent characteristics can be found in Table 22. The mean age of respondents was 49.8 years (SD 18.9, range 18-87), with more females (54.7%) responding than males (45.3%). The majority of respondents were White British (84.7%), married (65.7%), and in full-time (41.1%) or part-time (10.7%) paid employment. The respondents' duration of diagnosis ranged from 1 month to 67 years (mean 8.2 years, SD 10.5). The majority of respondents were diagnosed by endoscopy (90.8%), had never purposefully consumed gluten within the last 12 months (67.6%), and feel that their CD has an impact on themselves and their health (88.8%).

Table 22. Characteristics of Survey 1 respondents (n=411)

Characteristic	*n*	*%*
Age (years)[a]	**49.8±18.9**	
18-29	69	16.8
30-39	101	24.6
40-49	40	9.7
50-59	49	11.9
60-69	63	15.3
70-79	70	17.0
80-89	19	4.6
Sex		
Female	225	54.7
Male	186	45.3
Marital status		
Married / civil partnership	270	65.7
Single	98	23.8
Widowed	21	5.1
Divorced	16	3.9
Separated	6	1.5
Ethnicity		
White British	348	84.7
Asian / Asian British	39	9.5
White Other	13	3.1
Mixed / Multiple ethnic groups	9	2.3
Black / African / Caribbean / Black British	1	0.2
Other ethnic group	1	0.2
Occupational status		
Full-time paid work	169	41.1
Fully retired	117	28.5
Part-time paid work	44	10.7
Doing something else	19	4.6
Looking after the home	18	4.4
Full-time education	14	3.4
Permanently sick or disabled	10	2.4
Unemployed	8	1.9
Duration since diagnosis (years)[a]	**8.2±10.5**	
<1	47	11.4
1-4	139	33.8
5-9	96	23.4
10-14	52	12.7
15-19	21	5.1
20-24	10	2.4
≥25	39	9.5

Table 22 (continued). Characteristics of Survey 1 respondents (n=411)

Impact of CD on health		
No impact	39	9.5
Mild impact	119	29.0
Moderate impact	168	40.9
Severe impact	66	16.1
Very severe impact	12	2.9
Purposeful gluten consumption in last 12 months		
Never	278	67.6
Rarely	68	16.5
Sometimes	44	10.7
Often	16	3.9
Always	1	0.2
Diagnosis		
Had endoscopy	373	90.8
Had blood test	318	77.4
Had other tests	25	6.1

a. Mean±SD.

5.3.1 Item response distribution

The distribution of responses for each CDAQ item was reviewed (Appendix EE). Responses to the majority of items were well-distributed across the five response options. However, a floor effect (i.e. more than 50% of respondents selecting 'Never') was present for eight items (items 13, 17, 18, 21, 23, 25, 28, 35)[13] and a ceiling effect (i.e. more than 50% of respondents selecting 'Always') occurred in one item (item 40).

The amount of missing data (i.e. non-response plus those selecting 'not applicable') ranged from 0% - 15.5% per CDAQ item. When considering the proportion of non-response separately, it was minimal, ranging from 0% to 1.2%. Five items (items 10, 17, 19, 28, 46) met the criteria for removal (i.e. missing data > 5%) (Table 23).

[13] Item numbers refer to those used in the Survey 1 questionnaire (Appendix CC)

A correlation matrix (Appendix FF) was reviewed and a high inter-item correlation (r=0.82) was found between items 24 (‘*felt depressed*’) and 36 (‘*felt down or in low spirits*’), suggesting multicollinearity.

5.3.2 Item reduction

Fourteen items met the exclusion criteria, of which eleven items were deleted from the CDAQ (Table 23). It follows that three items were retained. Item 40 (‘*felt annoyed about the cost of gluten-free food*’) was retained despite its ceiling effect, as respondents and qualitative participants strongly related to this issue and commented on its importance. Item 13 (‘*had nausea or vomiting*’) demonstrated a floor effect, but was retained as qualitative participants reported the impact of the symptom as severe. Items 24 (‘*felt depressed*’) and 36 (‘*felt down or in low spirits*’) were highly correlated. Item 24 was deleted as it was thought that respondents may interpret the item as clinical depression rather than ‘low mood’ as intended.

The decision to retain these three items was made in collaboration with my supervisors, who both have expertise in the development of PROMs.

After removal of the above items, item 8 (‘*worried family member could develop CD*’) was the only remaining item with a ‘not applicable’ response option. As this response option was rarely endorsed by respondents (1%, n=4), the ‘not applicable’ response option was removed.

The remaining 40 items were included in the factor analysis.

Table 23. CDAQ items removed prior to factor analysis

Item	Item description (abbreviated)	Reason for removing item
24	Felt depressed	Inter-item correlation between item 24 and item 36 >0.8
10	Concern about results of tests	Missing data (including N/A) > 5%.
19	Limited holiday / holiday choices	Missing data (including N/A) > 5%.
46	Difficulties cooking or baking	Missing data (including N/A) > 5%.
17	Difficulties with work-related activities	Missing data (including N/A) > 5% Floor effect > 50%
28	Limited work activities	Missing data (including N/A) > 5% Floor effect > 50%
18	Leisure activities limited	Floor effect > 50%
21	Unable to travel due to being ill	Floor effect > 50%
23	Excluded from attending activities	Floor effect > 50%
25	Difficulty concentrating	Floor effect > 50%
35	Lacked support of family and friends	Floor effect > 50%

5.3.3 Factor analysis

Bartlett's Test of Sphericity was statistically significant (X^2 (780) = 8963.46, p<0.001), and the Kaiser-Meyer-Olkin (KMO) Measure of Sampling Adequacy was 0.95. The results of these preliminary tests confirmed it was appropriate to conduct a factor analysis.

Principal components analysis with Varimax rotation

The PCA (conducted on the 40 retained items) identified six components with an eigenvalue > 1, explaining 58.6% of the variance. All items loaded on to at least one component with a loading > 0.40 (Table 24).

Table 24. Principal components analysis with Varimax rotation – rotated loadings of 40 CDAQ items

Item		Component					
No	Item description (abbreviated)	1	2	3	4	5	6
3	Appeared to be making fuss about dietary needs	**.76**	.19	.29	.15	.10	.03
2	Embarrassed discussing CD or dietary needs	**.75**	.13	.25	.13	.10	.03
38	Felt uncomfortable about others catering	**.71**	.25	.11	.13	.24	.29
5	Difficult to mention misunderstanding	**.67**	.13	.30	.23	.05	-.09
37	Felt you were a nuisance	**.67**	.23	.09	.20	.33	.22

Table 24 (continued). PCA with Varimax rotation – rotated loadings of 40 CDAQ items

39	Felt guilty about others buying GF food	**.61**	.27	.03	.14	.15	.33
32	Felt uncomfortable refusing food or drink	**.60**	.16	.24	.25	.29	-.02
6	Received unwanted attention	**.58**	.06	.15	.13	.15	-.01
4	Others misunderstood CD or dietary needs	**.52**	.16	.41	.24	.02	-.14
7	Felt guilty about impact on friends and family	**.52**	.21	.18	.18	.32	.31
33	Consumed as felt uncomfortable refusing	**.41**	.28	-.04	.20	.30	-.30
49	Frustrated by choice of suitable food	.08	**.72**	.33	.02	-.01	.08
48	Difficulty finding food when out of house	.30	**.66**	.33	.11	.12	-.09
42	Difficulty finding suitable food	.14	**.65**	.18	.19	.15	-.20
47	Burdened by time to find or make GF	.28	**.60**	.18	.06	.24	.20
45	Disappointed with taste or texture of GF	.06	**.59**	-.05	.14	.02	.27
50	Frustrated by planning ahead	.32	**.58**	.44	.04	.08	.12
40	Felt annoyed about cost of GF food	.15	**.57**	.20	.16	.01	.24
44	Craved food or drinks containing gluten	.09	**.53**	-.17	.16	.31	.02
43	Missed meals or snacks	.32	**.51**	.13	.29	.15	-.15
41	Financial difficulties due to CD	.18	**.41**	.16	.29	.36	-.12
31	Concerned about cross-contamination	.30	.19	**.68**	.18	.21	.23
30	Worried accidentally consume gluten	.31	.24	**.66**	.17	.17	.19
51	Concerned about food prepared by others	.30	.34	**.66**	.17	.17	.13
20	Worried become ill when not at home	.19	.12	**.63**	.35	.29	-.01
1	Worried become ill after eating food by others	.37	.16	**.62**	.33	.12	.07
34	Worried become ill at inconvenient time	.17	.11	**.54**	.40	.31	-.10
12	Had abdominal bloating	.20	.12	.10	**.74**	.05	.13
14	Had pain	.21	.14	.19	**.72**	.09	.00
11	Bothered by bowel movements	.11	.11	.23	**.70**	.03	.24
13	Had nausea or vomiting	.20	.12	.13	**.64**	.10	-.15
15	Had tiredness or a lack of energy	.14	.20	.17	**.61**	.32	.08
26	Felt bothered by your weight	.20	.14	.09	**.40**	.26	.20
27	Avoided social activities	.23	.09	.29	.17	**.72**	.04
22	Isolated from others	.34	.09	.23	.05	**.67**	.16
29	Avoided going out to eat	.22	.26	.42	.15	**.57**	.02
36	Felt down or in low spirits	.28	.20	.00	.36	**.52**	.19
16	Daily activities limited by CD	.05	.13	.30	.46	**.47**	.00
8	Worried family member could develop CD	.18	.16	.26	.18	.18	**.43**
9	Concern about developing related health problem	.17	.20	.31	.39	.23	**.42**

Values <0.40 are shown in grey. The highest loading for each item is shown in bold. Item numbers relate to those used in the questionnaire in Survey 1.

The components extracted assessed the following general areas: (1) stigma - 11 items; (2) dietary burden - 10 items; (3) worries and concerns - 6 items; (4) symptoms - 6 items; (5) social isolation - 5 items; and (6) future concerns - 2 items.

Following an exploration of the results, eight items were removed from the CDAQ (Table 25). In brief, four items (items 2, 34, 38, 51) had high inter-item correlations with other items within the same component; one item (item 26) had a poor fit conceptually with other items within its component; and finally, item 43 was removed as other items covered the issues it addressed and it was identified as potentially unreliable in cognitive interviews previously conducted.

To further reduce the length of the questionnaire, two additional items (items 33 and 41) were removed. These items had weak loadings (<0.5) as well as being close to meeting the criteria for a floor effect (49.9% and 46.7% selected 'Never' respectively). Removal of these items did not significantly affect the internal consistency of the subscales.

A further principal components analysis was performed on the remaining 32 items (Table 26). Again, the analysis identified six components with an eigenvalue > 1, explaining 61.0% of the variance. Items loaded on to the same components as the previous analysis.

Table 25. Items deleted during principal components analysis

Component	Item No	Item description	Reason for removing

1	2	have you felt embarrassed or uncomfortable discussing your coeliac disease or dietary needs?	• Highly correlated with item 3 (r=0.72)
			• Item 2 removed rather than item 3 due to:
			  ○ Higher Cronbach's alpha when item 2 was removed
			  ○ Item 3 was well distributed with more potential to be sensitive to change (20.0% selected 'Always')
			  ○ 'Making a fuss' (item 3) was identified in participant interviews as a key issue.

1	33	have you eaten or drunk something that you were uncertain was gluten-free because you felt uncomfortable refusing?	• Factor loadings < 0.5 on all factors • Close to meeting the criteria for a floor effect – 49.9% selected 'Never' • Cognitive interviews identified this item as an issue that is unlikely to affect many • Issue covered by item 32
1	38	have you felt uncomfortable about other people taking your dietary needs in to account when preparing food for you?	• Highly correlated with item 37 (r=0.74) • Item 37 and 38 have similar distributions across response options and similar Cronbach's alpha values regardless of which is deleted. • Item 38 removed as item 37 is a more general question and therefore applicable to more respondents. In addition, item 38 is partially covered by item 39.
2	41	have you had financial difficulties due to your coeliac disease (for example, due to the cost of following a gluten-free diet, or inability to work)?	• Factor loadings < 0.5 on all factors • Close to meeting floor effect criteria – 46.7% selected 'Never'
2	43	have you had to miss meals or snacks because suitable food was unavailable?	• Cognitive interviews identified that the item can be answered in different ways, therefore questioning its reliability. • Item covered by items 42 and 50 • Lowest loading item onto factor
3	34	have you worried that you would become ill at a difficult or inconvenient time (for example, while travelling or at a social event)?	• Highly correlated with item 20 (r=0.71) • While not mentioned in cognitive interviews, the item could be interpreted as there never being a convenient time to be unwell. • Cognitive interviews identified this item as an issue that is unlikely to affect many.

Component	Item No	Item description	Reason for removing
3	51	have you felt concerned that food prepared by others, and presented as gluten-free, may contain gluten?	• Highly correlated with item 1 (r=0.69) • The translatability assessment identified the wording of the item as problematic. • Item 51 (1.2%) had more missing data than item 1 (0%).
4	26	have you felt bothered by your weight?	• Factor loadings < 0.5 on all factors • Item does not fit with scale onto which it has loaded • Item is fairly generic and not necessarily a specific issue for people with coeliac disease.

Components: (1) Stigma, (2) Dietary burden, (3) Worries and concerns, (4) Symptoms, (5) Social isolation, and (6) Future concerns. Item numbers refer to those used in the Survey 1 questionnaire (Appendix CC)

Table 26. Principal Components Analysis with Varimax rotation – rotated loadings of the remaining 32 items

		Component					
Item no	**Item description (abbreviated)**	**1**	**2**	**3**	**4**	**5**	**6**
3	Appeared to be making fuss about dietary needs	**.75**	.21	.16	.15	.24	.05
5	Difficult to mention misunderstanding	**.73**	.14	.23	.06	.23	.01
37	Felt you were a nuisance	**.67**	.23	.18	.35	.00	.18
39	Felt guilty about others buying GF food	**.63**	.28	.12	.16	-.04	.20
6	Received unwanted attention	**.61**	.06	.12	.15	.07	.12
4	Others misunderstood CD or dietary needs	**.60**	.18	.27	.05	.34	-.11
32	Felt uncomfortable refusing food or drink	**.59**	.15	.23	.30	.20	.11
7	Felt guilty about impact on friends and family	**.52**	.23	.17	.34	.09	.29
49	Frustrated by choice of suitable food	.06	**.76**	.07	.06	.28	.04
48	Difficulty finding food when out of house	.29	**.67**	.15	.18	.29	-.07
42	Difficulty finding suitable food	.14	**.63**	.22	.18	.17	-.16
47	Burdened by time to find or make GF	.31	**.63**	.06	.24	.06	.21
50	Frustrated by planning ahead	.32	**.62**	.07	.13	.37	.10
45	Disappointed with taste or texture of GF	.06	**.60**	.15	.03	-.21	.29
40	Felt annoyed about cost of GF food	.18	**.57**	.14	.00	.14	.24
44	Craved food or drinks containing gluten	.12	**.51**	.15	.26	-.29	.07
12	Had abdominal bloating	.21	.12	**.74**	.10	.02	.10
14	Had pain	.23	.13	**.74**	.11	.12	.07
11	Bothered by bowel movements	.13	.13	**.69**	.05	.12	.29
13	Had nausea or vomiting	.18	.09	**.66**	.11	.15	-.06
15	Had tiredness or a lack of energy	.14	.19	**.62**	.35	.09	.14
27	Avoided social activities	.22	.10	.19	**.76**	.22	.06
22	Isolated from others	.35	.11	.04	**.69**	.10	.20
29	Avoided going out to eat	.22	.28	.18	**.62**	.34	.05
36	Felt down or in low spirits	.31	.21	.36	**.54**	-.14	.09
16	Daily activities limited by CD	.05	.15	.49	**.51**	.18	.07
31	Concerned about cross-contamination	.31	.22	.20	.27	**.62**	.32
30	Worried accidentally consume gluten	.30	.29	.20	.23	**.61**	.26
1	Worried become ill after eating food by others	.40	.19	.36	.19	**.55**	.13
20	Worried become ill when not at home	.22	.16	.36	.32	**.51**	.18
8	Worried family member could develop CD	.18	.12	.12	.13	.20	**.72**
9	Concern about developing related health problem	.19	.20	.35	.22	.18	**.57**

Item numbers refer to those used in the Survey 1 questionnaire (Appendix CC)

Internal reliability was calculated for each subscale (Table 27). Cronbach's alpha values were between 0.80 and 0.90 for all subscales, indicating good internal reliability, with the exception of the 'future concerns' subscale (α=0.63). Item-total correlations were >0.3.

Table 27. Item-total correlations and Cronbach's alpha statistics

Item no		Corrected Item-Total Correlation	Cronbach's alpha
	Stigma (8 items)		**0.88**
3	Appeared to be making fuss about dietary needs	0.76	
37	Felt you were a nuisance	0.72	
5	Difficult to mention misunderstanding	0.68	
32	Felt uncomfortable refusing food or drink	0.67	
7	Felt guilty about impact on friends and family	0.63	
39	Felt guilty about others buying GF food	0.61	
4	Others misunderstood CD or dietary needs	0.59	
6	Received unwanted attention	0.52	
	Dietary burden (8 items)		**0.83**
48	Difficulty finding food when out of house	0.69	
49	Frustrated by choice of suitable food	0.65	
47	Burdened by time to find or make GF	0.65	
50	Frustrated by planning ahead	0.65	
42	Difficulty finding suitable food	0.57	
40	Felt annoyed about cost of GF food	0.52	
45	Disappointed with taste or texture of GF	0.46	
44	Craved food or drinks containing gluten	0.40	
	Symptoms (5 items)		**0.82**
14	Had pain	0.68	
12	Had abdominal bloating	0.67	
11	Bothered by bowel movements	0.61	
15	Had tiredness or a lack of energy	0.58	
13	Had nausea or vomiting	0.57	
	Social isolation (5 items)		**0.82**
27	Avoided social activities	0.71	
29	Avoided going out to eat	0.65	
22	Isolated from others	0.63	
36	Felt down or in low spirits	0.55	
16	Daily activities limited by CD	0.53	
	Worries and concerns (4 items)		**0.87**
31	Concerned about cross-contamination	0.77	
30	Worried accidentally consume gluten	0.77	
1	Worried become ill after eating food by others	0.72	
20	Worried become ill when not at home	0.64	

Table 27 (continued). Item-total correlations and Cronbach's alpha statistics

	Future concerns (2 items)		**0.63**
8	Worried family member could develop CD	0.46	
9	Concern about developing related health problem	0.46	

As well as having low internal reliability (α=0.63), the 'future concerns' component comprised only two items. Ideally, each factor should comprise at least three items (de Vet et al., 2011) to create a reliable scale. Removal of these items would limit content validity. Interestingly, both of the existing CD disease-specific PROMs have items addressing these issues. Therefore, the two items comprising component six 'future concerns' were merged with items in component five 'worries and concerns'. The items in components five and six went together conceptually and statistically. Internal reliability for the combined scale was good (α=0.85) and item-total correlations sufficient (>0.3) (Table 28).

Table 28. Item-total correlations and Cronbach's alpha statistics for the revised 'Worries and concerns' scale

Item no		Corrected Item-Total Correlation	Cronbach's alpha
	Worries and Concerns (6 items)		**0.85**
31	Concerned about cross-contamination	0.76	
30	Worried accidentally consume gluten	0.73	
1	Worried become ill after eating food by others	0.69	
20	Worried become ill when not at home	0.63	
9	Concern about developing related health problem	0.57	
8	Worried family member could develop CD	0.47	

Higher order factor analysis

A higher order factor analysis was conducted on the five CDAQ dimensions to assess whether an overall score can be calculated. The analysis identified one factor with an eigenvalue > 1, explaining 68.0% of the variance. All domains loaded on to the factor with an eigenvalue of 3.40. This indicates that it is appropriate to combine the dimension scores to create an overall scale score. This overall score can be calculated as follows, where a score of 0 indicates poorest quality of life and 100 indicates highest quality of life:

$$\text{OVERALL INDEX SCORE} = (\text{SUM OF DIMENSION SCORES}) / 5$$

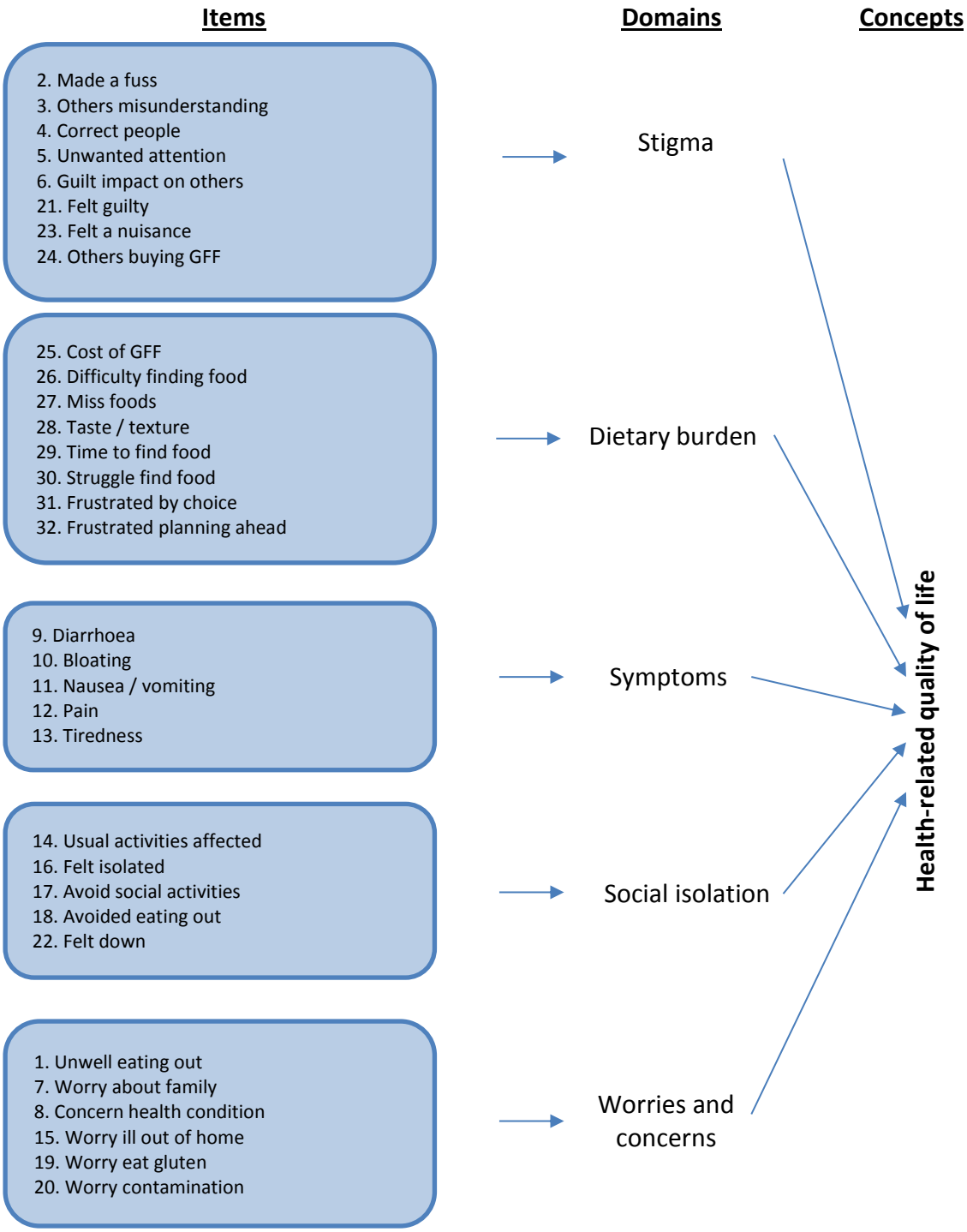
The CDAQ

The final version of the CDAQ consists of 32 items addressing the following five dimensions: stigma; dietary burden; symptoms; social isolation; and worries and concerns (see Table 29 for full descriptions).

Table 29. Descriptions of CDAQ dimensions

CDAQ Dimension	Description
Stigma	The perceived or actual burden felt in social situations where the individual's CD becomes visible.
Dietary burden	Practical difficulties encountered with and feelings about following a gluten-free diet.
Symptoms	Symptoms experienced in relation to CD, e.g. pain, tiredness.
Social isolation	Avoidance of and/or limited participation in social activities due to CD, and feelings of isolation from others.
Worries and concerns	Worries and concerns surrounding the consumption of gluten and subsequent consequences, also the genetic aspects of the condition.

The conceptual framework, first developed in Chapter 3 (see Figure 7, p. 98), was revised accordingly.



Note: Item numbers refer to the final version of the CDAQ (Appendix II, p. 432)

5.4 Discussion

The aim of this chapter was to determine the dimensions of the CDAQ and reduce the number of items to produce a final scale. Following the collection and analysis of survey data, 19 items were deleted, resulting in a scale of 32 items addressing the following five dimensions: stigma (8 items), dietary burden (8 items), symptoms (5 items), social isolation (5 items), and worries and concerns (6 items). The length of the final version of the CDAQ (i.e. 32 items) is similar to that of other PROMs which have been found to be acceptable to respondents, for example, the Parkinson's Disease Questionnaire (PDQ-39) (Jenkinson, Fitzpatrick, Peto et al., 1997) has 39 items, while the SF-36v2 (Ware and Sherbourne, 1992) has 36 items.

Data on which item reduction and scale generation was based was collected via a survey of Coeliac UK's members. A stratified random sample achieved a diverse sample for analysis, which increases the likelihood that the final CDAQ will be of relevance to adults from all demographic groups. Of particular note, 12.1% of the sample belonged to black and minority ethnic groups. A possible limitation is that all respondents are members of Coeliac UK, although there is no evidence to suggest that HRQOL in this population differs from that of the wider population of adults with CD.

Although a reminder letter could not be sent as it is against Coeliac UK's policy, a reminder was placed on Coeliac UK's website approximately two months after the survey mailing. The timing and placement of the advert was out of the author's control, and consequently, it is unlikely to have increased the response rate. Despite the lack of an

effective reminder, a good response rate of 52% was achieved. Reminder letters have been used in the development of other measures, such as the PDQ (Jenkinson, Fitzpatrick, Peto et al., 1997) and ALSAQ (Jenkinson, Fitzpatrick, Brennan et al., 1999), increasing the response rate only marginally.

Many of the items deleted during item reduction were removed due to their inability to discriminate between respondents, i.e. floor effects or larger amounts of missing data. Additionally, items were removed due to redundancy, or a poor conceptual fit within dimensions. The content of each deleted item is covered to varying extents by one or more of the retained items. For example, many of the items addressing specific activities (e.g. work-related) are covered by the broader item, '*have your daily activities been limited by your coeliac disease?'* (item 16). As such, the overall content validity of the questionnaire is not greatly reduced, but information about specific aspects of the impact of CD is lost.

There was some crossover between items removed from the CDAQ during item reduction and those removed from the CDQ. For example, item 19 of the CDAQ addresses the impact of CD on the choice of holiday and activities while holidaying. To an extent, this is covered by item 16 (above) and item 30 '*have you had difficulty finding something to eat when you were not at home?*'. However, the impact of CD on holiday choice is lost. The authors of the CDQ also removed an item about "problems in travelling/holidays", which they found particularly surprising (Häuser, Gold, Stallmach, et al., 2007). In the current author's opinion, it is not surprising that a PROM is unable to capture this impact. Most people tend to holiday infrequently and therefore, it is not possible to include items such

as this in a measure that asks about the last 2 (CDQ) or 4 weeks (CDAQ), as it will only ever apply to a small proportion of those asked and therefore, will not prove useful in discriminating between respondents. Dorn et al. (2010) do not report the content of items removed during the development of the CD-QOL, and therefore a comparison cannot be made with the CDAQ.

A comparison between items and domains between the final version of the CDAQ and existing CD-specific measures (i.e. the CDQ and CD-QOL) found some differences between the measures. A key difference was the paucity of items exploring the gluten-free diet (e.g. food shopping and food choice) in the CDQ and CD-QOL, when compared with the CDAQ. This is surprising given that it has been identified as a key issue for people with CD in the literature (Sverker et al., 2005) and within the qualitative interviews conducted as part of this study (see Chapter 3). Another fundamental difference is the lack of items addressing CD symptoms in the CD-QOL, while these were covered by both the CDAQ and CDQ.

Finally, the amount of missing data in the retained items of the CDAQ was very low and meets criteria set out by de Vet et al. (2011) of less than 3%. This suggests that respondents comprehend the items, feel they are relevant, and are able to find appropriate response options. The CD-QOL also had low levels of missing data (between 0 and 2 people did not complete all items) (Casellas, Rodrigo, Molina-Infante et al., 2013; Zingone, Iavarone et al., 2013), while the CDQ had much higher levels of missing data (up to 31%) for some items (i.e. professional career and sexual activity) (Pouchot et al., 2014).

Therefore, in terms of the amount of missing data, the CDAQ is comparable with the CD-QOL and appears superior to the CDQ.

CHAPTER 6:
Psychometric evaluation of the CDAQ

6.1 Introduction

In the previous chapter, analyses were conducted to produce the final version of the CDAQ and assess the internal consistency of its dimensions. Following this, a cross-sectional survey ('Survey 2') was conducted for two purposes: firstly, to further evaluate the psychometric properties of the newly-developed CDAQ; and secondly, to investigate HRQOL in CD, patients' experiences of health care services, and the relationship between HRQOL and patients' experiences of services (i.e. the main aims of this thesis). Findings related to the psychometric properties of the CDAQ are discussed in this chapter, while survey results discussing patients' experiences of health care services, HRQOL, and their relationship, are presented in chapters 7, 8 and 9 respectively.

It is important to assess the psychometric properties of instruments in order to evaluate their quality. Specifically, PROMs must be reliable, valid, and responsive to change (Jenkinson and McGee, 1997). The reliability of a measure refers to the reproducibility and internal consistency of scores (Fitzpatrick, Davey et al., 1998), evidence for which is gathered by assessing test-retest reliability and internal consistency reliability. Test-retest reliability measures the stability of test scores over time (Kline, 2000), while internal consistency reliability assesses the extent to which items within a scale or domain are all measuring the same underlying construct (de Vet et al., 2011).

The validity of a measure refers to the extent to which it measures what it purports to measure (Fitzpatrick, Davey et al., 1998). There are a number of ways to establish the validity of a measure, but this chapter will focus on the assessment of construct validity. Evidence for construct validity is generated by testing hypotheses regarding the direction and strength of expected relationships (Hays and Revicki, 2005), and, for PROMs, is often assessed by comparing scores on the measure of interest with scores on other well-validated measurement instruments.

Finally, responsiveness to change assesses whether the measure is able to detect changes over time when they have occurred (Revicki et al., 2006). Evaluating the CDAQ's responsiveness is outside the scope of this thesis, but work is currently underway to assess this measurement property.

A comprehensive list of psychometric properties and how they are measured is set out in section 2.2.1.

It is typical for authors of newly-developed measures to report evidence of their psychometric properties alongside details of their development (e.g. the Gastrointestinal Quality of Life Index (Eypasch et al., 1995) and the Celiac Disease Questionnaire (Häuser, Gold, Stallmach et al., 2007)). This chapter will evaluate and report findings regarding the reliability and validity of the CDAQ.

6.1.1 Aims and objectives

The aim of this chapter was twofold, firstly, to report the methodology used to collect the data necessary to address the aims of this thesis, and secondly, to further evaluate the psychometric properties of the CDAQ. This was achieved by the following objectives:

- To conduct a pilot survey of a questionnaire asking people with CD about their HRQOL and experiences of health care services;
- To amend the questionnaire following the results of the pilot survey and conduct a larger survey (Survey 2) exploring HRQOL and experiences of health care services in CD;
- To assess the construct validity of the CDAQ;
- And to assess the reliability (test-retest and internal consistency) of the CDAQ.

6.2 Methods

Prior to conducting Survey 2, a small pilot survey was carried out to ascertain whether people would complete and return a 26-page questionnaire about their CD, and identify and resolve any major problems with the questionnaires (e.g. incorrect skip patterns or questions with large amounts of missing data). Following the pilot survey, Survey 2 was sent to 800 adults with CD.

6.2.1 Survey 2 pilot

Twenty people who had responded to a social media advertisement, recruiting for cognitive interview participants but who were not selected for interview, were invited to take part in a pilot survey in March 2015. The pilot questionnaire included the CDAQ, the CD-PEQ, demographic questions, and the SF-36v2 (reasons for the inclusion of the SF-36v2 are discussed in section 6.2.3). A comments box at the end of the questionnaire

asked participants for feedback about the questionnaire. Questionnaires were mailed from and returned to the University of Oxford along with a personalised invitation letter, information sheet, and a pre-paid return envelope[14].

Results

The response rate to the pilot survey was 60% (n=12), indicating that people were willing to complete the questionnaire despite its length. Characteristics of respondents to the pilot survey are shown in Table 30.

Table 30. Characteristics of pilot survey respondents

ID	Age	Gender	Marital status	Ethnic origin	Occupational status	Duration since diagnosis (years)	Impact of CD on health
1902	51	Female	Separated	White British	Full-time paid work	1	Severe
1903	36	Female	Separated	White British	Part-time paid work	11	Moderate
1905	57	Female	Married	White British	Full-time paid work	16	Mild
1907	62	Male	Married	White British	Retired	22	Mild
1908	47	Female	Married	White British	Full-time paid work	19	Mild
1911	-	-	-	-	-	18	Mild
1913	39	Female	Single	White British	Doing something else	11	Moderate
1914	30	Female	Married	Asian Pakistani	Unemployed	1	Mild
1915	31	Female	Single	White British	Full-time paid work	7	Moderate
1916	68	Female	Married	White British	Retired	16	Moderate
1919	20	Female	Single	White British	Full-time education	<1	Severe
1920	24	Female	Single	White British	Full-time paid work	22	Moderate

Following a review of the completed questionnaires, some minor changes were made:

- The introductory wording to the SF-36v2 was amended to emphasise that these questions were not solely about CD (i.e. the wording was amended from '*This*

[14] The pilot questionnaire and accompanying literature was very similar to that used in Survey 2.

section of the questionnaire asks for your views about your health' to '*…your views about your health in general*').

- Instructions regarding how to complete the questionnaire were clarified (i.e. '*please tick <u>one</u> box only' and 'please tick all that apply*' were added where appropriate).

6.2.2 Survey 2

Following completion of the pilot survey, Survey 2 was conducted.

Recruitment

Eight hundred members of Coeliac UK were invited to participate in Survey 2. Members were eligible for selection if they were aged 18 years or older, lived in the UK, reported that they have a medical diagnosis of CD, had not opted out of being contacted for research purposes, and were not sent a questionnaire as part of Survey 1. The sampling strategy followed that taken for Survey 1, i.e. a stratified random sample, stratified by ethnicity, age, and gender. As before, it was not possible to achieve the proposed sample due to an insufficient number of younger, male, BME members. The proposed and actual number of members selected from each stratum is shown in Table 31.

Table 31. Sampling stratum for Survey 2

Stratum	Ethnicity	Age group	Gender	n (proposed)	n (actual)
1	White	<= 40	Female	160	160
2	White	<= 40	Male	160	160
3	White	> 40	Female	160	160
4	White	> 40	Male	160	160
5	BME[a]	<= 40	Female	40	44
6	BME	<= 40	Male	40	31
7	BME	> 40	Female	40	40
8	BME	> 40	Male	40	45
			Total	**800**	**800**

[a]Black and Minority Ethnic (BME) Groups

The Survey

Members were sent a questionnaire pack, which included a personalised invitation letter (Appendix GG), an information sheet (Appendix HH), a questionnaire (Appendix II), and a pre-paid return envelope. The questionnaire included the CDAQ, the CD-PEQ, the SF-36v2, and demographic questions. Questionnaires were mailed from Coeliac UK in April 2015 and returned to the University of Oxford.

Test-retest reliability

In order to assess test-retest reliability, members were asked to provide their name and address if they were willing to receive a second questionnaire. Follow-up questionnaires were sent to all respondents who provided their contact details. A test-retest interval of two weeks was selected as short enough that changes in HRQOL were unlikely to occur, but long enough to minimise the chances of respondents recalling their previous answers. A two-week interval period is commonly selected when assessing measures (de Vet et al., 2011).

The follow-up questionnaire (see Appendix JJ) included the CDAQ and the following question, 'Compared with two weeks ago, how would you rate the impact of your coeliac disease on you and your health now?'. Respondents answered on a five-point scale from 'Much better' to 'Much worse'. Questionnaires were sent with a covering letter (Appendix KK) and a pre-paid return envelope, and were sent from and returned to the University of Oxford. Each respondent was allocated an ID number. The respondent's ID number was written on their follow-up questionnaire before it was sent, in order to match follow-up responses with that of the first questionnaire.

6.2.3 Assessing the CDAQ's construct validity

To assess the CDAQ's construct validity, it was necessary to include a validated measure against which the CDAQ could be assessed. As there were no suitable existing disease-specific measures, generic measures previously used in CD were considered. These measures were identified in the systematic review in Chapter Two, and were as follows: the WHOQOL-BREF, EQ-5D, SF-36, SF-12, PGWBI, and the GIQLI (Table 1, p. 44).

Many of the generic measures contain domains or items that are irrelevant to the CD population and were therefore not considered appropriate. For example, the WHOQOL-BREF is a broader measure of QOL and includes domains such as 'environment', which addresses issues including safety and transportation, and 'spirituality'. The EQ-5D is also very broad and includes only five questions, of which those on 'self-care' and 'mobility' are less relevant. As such, it is unlikely that the EQ-5D would be a good choice as it has limited shared constructs with the CDAQ. The GIQLI also contains irrelevant items, such as, items about regurgitation and slow speed of eating, which aren't considered problems in those with CD. Finally, the PGWBI does not measure impact on social activities, which is of primary importance in CD as identified in the qualitative interviews.

The final measures, the SF-36 and SF-12, have been used in many studies of CD and other conditions worldwide, with the SF-36 considered to be the leading generic measure (McDowell, 2006). The SF-36v2 is a 36-item generic measure of HRQOL addressing the following eight domains (Table 32): Physical Functioning (PF), Role-Physical (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), Role-Emotional (RE), and Mental Health (MH). In addition to the calculation of dimension scores, two

summary scores can be calculated, the Physical Component Summary (PCS) and Mental Component Summary (MCS). All eight domains contribute to the PCS and MCS scores, with the PF, RP and BP domains contributing most to the PCS, and MH, RE and SF contributing most to the MCS. The SF-12 is a short form of the SF-36 and allows the calculation of the summary scores only.

Table 32. Descriptions of SF-36v2 dimensions

Dimension	Description
Physical Functioning (PF)	Limitations in the performance of physical activities.
Role-Physical (RP)	Problems carrying out work or other usual activities due to physical problems.
Bodily Pain (BP)	Pain and its impact on usual activities.
General Health (GH)	General health and expectations of health.
Vitality (VT)	Energy levels and feelings of fatigue.
Social Functioning (SF)	Impact of emotional or physical problems on social activities.
Role-Emotional (RE)	Problems carrying out work or other usual activities due to emotional problems.
Mental Health (MH)	Psychological well-being – feelings of depression and anxiety.
Physical Component Summary (PCS)	Pain, limited physical functioning and problems due to physical functioning. PF, RP and BP contribute most to the PCS score.
Mental Component Summary (MCS)	Psychological distress, emotional problems, and limitations due to emotional problems. MH, RE and SF contribute most to the MCS score.

The SF-36 was selected to validate the construct validity of the CDAQ as there are many shared domains, and domain scores can be calculated. The inclusion of a generic measure will also allow the HRQOL of people with CD to be compared with that of the general population. A licence to use the SF-36v2 in this research study was obtained from OptumInsight Life Sciences Inc.

6.2.4 Statistical methods

Test-retest reliability, internal consistency reliability, and construct validity of the CDAQ were assessed. Methods used to evaluate each of these properties are described next.

Descriptions of psychometric properties and how they are assessed is described in Chapter 2.

Test-retest reliability

Test-retest reliability was assessed using the intraclass correlation coefficient (ICC)[15]. The ICC "measures the strength of agreement between repeated measurements" (Fayers and Machin, 2007). An ICC of 0.70 or above is generally considered acceptable (Terwee et al., 2007; Kline, 2000).

Internal consistency reliability

The internal consistency of each CDAQ dimension was assessed using Cronbach's alpha as previously discussed in Chapter 5.

Construct validity

Convergent and divergent validity

Convergent and divergent validity was assessed by comparing dimensions of the CDAQ and the SF-36v2. As the metrics for scoring the CDAQ and SF-36v2 are the same (i.e. higher scores indicate better HRQOL for both measures), all correlations were expected to be positive. Broadly, dimensions of the CDAQ were expected to correlate more strongly with mental health dimensions rather than physical health dimensions of the SF-36v2, with the exception of the symptoms domain where the reverse was expected. The following hypotheses were developed outlining expected relationships between the two measures:

[15] $ICC_{agreement}$ with two-way random effects model was used.

- The CDAQ overall index score was expected to correlate more strongly with mental health dimensions of the SF-36v2 and the MCS score, rather than physical health dimensions and the PCS score.
- CDAQ stigma, dietary burden, social isolation, and worries and concerns dimensions were expected to have a moderate to strong ($r_s \geq 0.4$) correlation with the social functioning (SF) and mental health (MH) dimensions of the SF-36v2, and the MCS score. An association with general health (GH) was also expected if mental health was found to be impaired.
- Moderate to strong ($r_s \geq 0.4$) correlations were also expected between CDAQ worries and concerns and general health (GH), and CDAQ social isolation and vitality (VT).
- The CDAQ and SF-36v2 both include items about pain and energy and therefore, moderate to strong ($r_s \geq 0.4$) correlations were expected between the CDAQ symptoms dimension and bodily pain (BP), vitality (VT), and the PCS score.
- Correlations between CDAQ dimensions and the remaining SF-36v2 dimensions were expected to be weak to moderate ($r_s \leq 0.3$), with the weakest correlations expected with physical functioning (PF) and role-physical (RP).

As the data was not normally distributed, correlations were explored using Spearman's rank order correlation coefficient.

Discriminative (known groups) validity

Based on the literature, it was hypothesised that the CDAQ overall index score would vary by gender, with females expected to report lower scores than males, i.e. worse HRQOL.

CDAQ overall index scores broadly followed a normal distribution for males (p=0.325) and females (p=0.322), as assessed by Shapiro-Wilk's test of normality (p>0.05), and therefore, an independent samples t-test was run to explore this hypothesis.

It was also expected that the CDAQ overall index score would discriminate between groups based on their self-reported impact of CD (scored from 1 ('no impact') to 5 ('very severe impact')). It was hypothesised that CDAQ scores would be higher (i.e. better HRQOL) for those reporting that CD has a lower impact on themselves and their health, e.g. those reporting 'no impact' would have a higher CDAQ overall index score than those reporting a 'mild', 'moderate', 'severe', or 'very severe' impact. The CDAQ overall index score was normally distributed for all severity groups, with the exception of the 'severe impact' group (p=0.021), as assessed by Shapiro-Wilk's test for normality (p>0.05). In order to determine whether the differences between severity groups were statistically significantly different, a one-way ANOVA with Tukey-Kramer post-hoc test[16] was considered appropriate as it is robust to violations of normality.

The CDAQ

Dimension scores and an overall index score were calculated for all respondents (where possible) using the methods previously discussed. As a reminder, scores range from 0 to 100, where 0 indicates poorest HRQOL as measured by the CDAQ and 100 indicates highest HRQOL. If a respondent has not completed one or more questions, the associated dimension score(s) and overall index score cannot be calculated. A full scoring guide can be found in Appendix LL.

[16] The Tukey-Kramer post-hoc test was considered appropriate as population variances for the CDAQ overall index score were equal across groups, and groups were of an unequal size.

6.3 Results

Of the 800 questionnaires sent to members of Coeliac UK, 276 (34.5%) were returned before the survey closed. Eight questionnaires were excluded from the analysis as the respondent had not reported that a doctor informed them of their diagnosis[17], leaving 268 respondents.

Respondent characteristics are presented in Table 33. The mean age of respondents was 49.5 years (SD 18.9). The mean duration since diagnosis was 7.49 years (range 1 – 50 years). The majority of respondents were female (61.9%), married (59.3%), working (55.2%), and White British (84.0%). More than half of respondents (60.4%) considered their CD to have at least a moderate impact on themselves and their health. The majority (72.0%) had never purposefully consumed gluten within the last 12 months.

Table 33. Characteristics of Survey 2 respondents (n=268)

	Survey 2, Q1	
Characteristic	***n***	***%***
Age (years**)**[a]	**49.5 ± 18.9**	
18-29	45	16.8
30-39	59	22.0
40-49	30	11.2
50-59	38	14.2
60-69	33	12.3
70-79	47	17.5
80-89	11	4.1
Sex		
Female	166	61.9
Male	97	36.2

[17] Four respondents reported that they had not been informed of their diagnosis by a doctor, while four respondents had not answered the question.

Table 33 (continued). Characteristics of Survey 2 respondents (n=268)

Marital status		
Married / civil partnership	159	59.3
Single	75	28.0
Widowed	13	4.9
Divorced	11	4.1
Separated	5	1.9
Ethnicity		
White British	225	84.0
Asian / Asian British	23	8.6
White Other	9	3.4
Mixed / Multiple ethnic groups	5	1.8
Other ethnic group	1	0.4
Occupational status		
Full-time paid work	92	34.3
Fully retired	62	23.1
Part-time paid work	34	12.7
Self-employed	22	8.2
Looking after the home	14	5.2
Full-time education	12	4.5
Doing something else	7	2.6
Permanently sick or disabled	7	2.6
Unemployed	4	1.5
Missing / multiple data	14	5.2
Duration since diagnosis (years)[a]	**7.49 ± 9.67**	
<1	28	10.4
1-4	113	42.2
5-9	40	14.9
10-14	40	14.9
15-19	15	5.6
20-24	4	1.5
≥25	16	6.0
Impact of CD on health		
No impact	24	9.0
Mild impact	80	29.9
Moderate impact	107	39.9
Severe impact	38	14.2
Very severe impact	17	6.3
Purposefully consumed gluten in last 12 months		
Never	193	72.0
Rarely	40	14.9
Sometimes	28	10.4
Often	4	1.5
Always	1	0.4

[a]Mean ± SD

Note: Missing data <5% is not reported.

6.3.1 Item response distribution

Missing data for individual CDAQ items was very low, with a maximum of three respondents (1.1%) not completing any one item. One item (*'had nausea or vomiting'*) had a floor effect, with 51.9% (n=139) of respondents selecting 'never'. This effect was identified in Survey 1, but a decision was made to retain the item. None of the items had a ceiling effect. The distribution of responses for all individual items can be found in Appendix MM.

6.3.2 Reliability

Test-retest reliability

Seventy eight per cent of respondents (n=215) provided their name and address consenting to receive a follow-up questionnaire. The response rate to the follow-up questionnaire was 77.7% (n=167). Four respondents were removed as they had not reported a medical diagnosis of CD, leaving 163 cases in the analysis.

The majority of respondents (n=145, 89.0%) rated the impact of their CD as 'about the same' as when they had completed the first questionnaire (Table 34). As the test-retest reliability analysis aimed to assess the stability of the measure over time, only respondents within this group were included in the analysis. Mean CDAQ scores for these respondents are presented in Table 35. The mean test-retest interval was 18.93 days (min. 13 days - max. 43 days).

Table 34. Self-reported change in coeliac disease since completion of first questionnaire, n=163

	n	*%*
Much better	7	4.3
A little better	5	3.1
About the same	145	89.0
A little worse	5	3.1
Much worse	1	0.6

Table 35. CDAQ scores for respondents completing both questionnaires whose health was unchanged, n=145

	Questionnaire 1				*Questionnaire 2*			
	n	*Mean*	*SD*	*Min. – Max.*	*n*	*Mean*	*SD*	*Min. – Max.*
Overall score	140	56.15	17.43	21 - 98	139	57.07	18.54	12.79 - 100
Stigma	144	54.19	21.59	9 - 100	145	55.24	22.65	0 - 100
Dietary burden	143	41.24	19.27	0 - 100	140	42.83	20.07	0 - 100
Symptoms	145	61.72	22.46	10 - 100	143	63.46	23.27	0 - 100
Social isolation	143	70.28	21.80	15 – 100	144	69.48	22.98	15 - 100
Worries and concerns	144	53.62	20.65	8 – 100	144	55.50	20.56	13 - 100

ICCs for CDAQ dimensions were: stigma (0.85), dietary burden (0.83), symptoms (0.80), social isolation (0.87), worries and concerns (0.79), and overall index score (0.89). The results indicate stability of CDAQ scores over time. ICCs for all dimensions were statistically significant ($p<0.001$).

The mean CDAQ overall index score for those returning a follow-up questionnaire (55.87, SD 17.42) was statistically significantly higher (i.e. better HRQOL) than those not agreeing to be sent a follow-up questionnaire or choosing not to return it (49.87, SD 18.50), $p=0.010$.

Internal consistency reliability

Internal consistency was assessed for each CDAQ dimension. Cronbach's alpha values were: stigma (0.87), dietary burden (0.87), symptoms (0.86), social isolation (0.86), and worries and concerns (0.82), indicating good internal consistency reliability.

6.3.3 Construct validity

Convergent and divergent validity

Correlations between CDAQ dimensions and the SF-36v2 are shown in Table 36. All correlations were in the expected direction (i.e. positive).

Table 36. Spearman correlation coefficients between CDAQ dimensions and the SF-36v2

CDAQ Dimensions	SF-36v2 Components		SF-36v2 Dimensions							
	PCS	MCS	PF	RP	BP	GH	VT	SF	RE	MH
Overall index score	0.38*	0.60*	0.22*	0.34*	0.48*	0.60*	0.59*	0.58*	0.37*	0.60*
Stigma	0.18†	0.50*	0.06	0.20†	0.27*	0.41*	0.45*	0.46*	0.26*	0.49*
Dietary burden	0.31*	0.46*	0.22*	0.29*	0.36*	0.47*	0.42*	0.42*	0.33*	0.48*
Symptoms	0.42*	0.49*	0.21*	0.33*	0.51*	0.55*	0.54*	0.50*	0.31*	0.48*
Social Isolation	0.35*	0.63*	0.28*	0.35*	0.44*	0.61*	0.59*	0.61*	0.44*	0.63*
Worries and concerns	0.30*	0.42*	0.15‡	0.29*	0.37*	0.45*	0.43*	0.40*	0.27*	0.42*

*p<0.001; †p<0.01; ‡p<0.05

SF-36v2 dimensions: Physical Component Summary (PCS); Mental Component Summary (MCS); Physical Functioning (PF); Role-Physical (RP); Bodily Pain (BP); General Health (GH); Vitality (VT); Social Functioning (SF); Role-Emotional (RE); Mental Health (MH).

As expected, dimensions of the CDAQ correlated more strongly with mental health dimensions than physical health dimensions. The CDAQ overall index score and dimension scores were more strongly correlated with the MCS score than the PCS score. These correlations were as expected, with the exception of the CDAQ symptoms domain, which was expected to correlate more strongly with the PCS. The symptoms dimension was strongly correlated with both the PCS and MCS ($r_s \geq 0.4$, $p<0.001$). The SF-36v2 does not contain many questions specifically asking about symptoms, but focuses more on limited mobility and functioning. CD symptoms are generally not associated with mobility issues, but instead are more likely to limit social functioning and have an impact on

mental health. A higher correlation with the MCS than PCS is likely to be due to these reasons.

CDAQ stigma, dietary burden, social isolation, and worries and concerns were strongly correlated with mental health (MH) and social functioning (SF) as expected ($r_s \geq 0.4$, $p<0.001$). The CDAQ symptoms dimension was also strongly correlated with MH and SF. Limited social functioning and poor psychological well-being would reasonably be expected to coincide with increased symptoms.

As hypothesised, moderate to strong correlations ($r_s \geq 0.4$, $p<0.001$) were found between CDAQ worries and concerns and general health (GH), and CDAQ social isolation and vitality (VT). Moderate to strong correlations ($r_s \geq 0.4$, $p<0.001$) were also found between all other CDAQ dimensions and GH and VT. It is not unreasonable to expect those with poorer general health and lower energy levels to have poorer CD-related HRQOL (e.g. those with increased symptoms and who find the diet more burdensome to have lower energy and poorer perceptions of their health).

Strong correlations ($r_s \geq 0.4$, $p<0.001$) were also found between CDAQ symptoms and bodily pain (BP), vitality (VT), and the PCS score, as expected.

Weak correlations ($r_s \leq 0.3$) were found between CDAQ scores and physical functioning (PF). Weak to moderate correlations ($r_s \leq 0.35$) were found between CDAQ scores and Role-Physical (RP).

Discriminative (known groups) validity

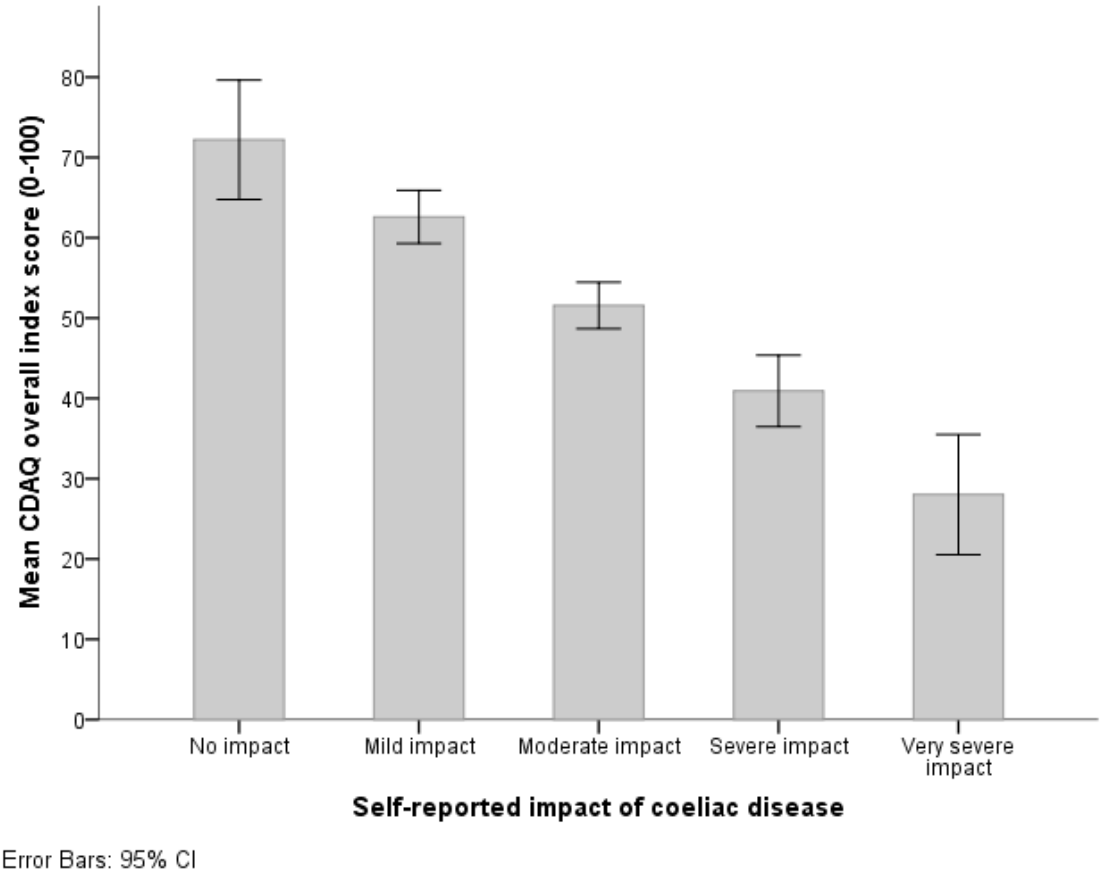
Gender

The mean CDAQ overall index score for males (60.91, SD=16.81, n=93) was 11.73 higher than females (49.18, SD=17.36, n=158), indicating that males report better HRQOL. This difference was statistically significant (95% CI, 7.32 to 16.15, $t(249)=5.232$, $p<0.001$).

Self-reported impact of coeliac disease

CDAQ overall index scores decreased from the 'no impact' (72.21 ± 16.32) through 'mild impact' (62.59 ± 14.38), 'moderate impact' (51.57 ± 14.93), 'severe impact' (40.92 ± 13.34), to 'very severe impact' (28.02 ± 13.53) groups (Figure 10). CDAQ overall index scores were significantly different between these groups ($F(4, 248)=34.70$, $p<0.001$).

Figure 10. Mean CDAQ overall index score by self-reported impact of coeliac disease



The decrease in CDAQ overall index scores between the groups is shown in Table 37. The decrease in scores was statistically significant for all comparisons ($p<0.05$), with the exception of the 'no impact' to 'mild impact' groups ($p=0.061$).

Table 37. Comparisons of CDAQ overall index scores by self-reported impact of coeliac disease groups

		CDAQ overall index score			
Group (a)	**Group (b)**	***Mean difference between (a) and (b)***	***SE***	***95% CI***	***p***
No impact	Mild impact	9.62	3.60	-0.28 to 19.51	0.061
Mild impact	Moderate impact	11.02	2.21	4.96 to 17.08	**<0.001**
Moderate impact	Severe impact	10.65	2.79	2.98 to 18.31	**0.002**
Severe impact	Very severe impact	12.90	4.47	0.63 to 25.17	**0.034**

6.4 Discussion

The aim of this chapter was to evaluate the psychometric properties of the newly-developed CDAQ, in particular, the reliability and validity of the measure. A survey (Survey 2) of adults with CD was conducted, in which the CDAQ was administered alongside the SF-36v2. The CDAQ was found to be a reliable and valid measure for assessing HRQOL in adults with CD.

A pilot survey was conducted prior to Survey 2 to test the acceptability of the questionnaire to respondents and identify any errors prior to its wider dissemination. The response rate indicated that the questionnaire was acceptable to respondents, while some minor amendments were made to the questionnaire's formatting following a review of the completed questionnaires.

The methods used to conduct Survey 2 followed that taken in Survey 1. The response rate to Survey 2 (34.5%) was similar to that achieved in other Coeliac UK surveys (personal communication with Coeliac UK's research manager), however, it was lower than that achieved in Survey 1 (52.0%). This difference is likely to be due to the much greater length of Survey 2 (26 pages) compared with Survey 1 (10 pages).

Missing data for CDAQ items was very low, with the maximum amount of missing data for any one item being 1.1% (n=3). This meets the PROMs quality criteria set out by Terwee et al. (2007), i.e. the criteria used to assess the quality of existing CD-specific measures in Chapter 2. The results are also consistent with the findings of Survey 1 (reported in Chapter 5), providing further evidence that adults with CD find the CDAQ acceptable.

Reliability

Cronbach's alpha values ranged from 0.82 to 0.87, which is consistent with findings from Survey 1 (α=0.82-0.88). Scores were within the ideal range (0.7-0.95) (Terwee et al., 2007) indicating CDAQ dimensions are internally consistent. These results are comparable with existing CD-specific measures, the CDQ (0.73 – 0.93 (Pouchot et al., 2014; Marchese et al., 2013; Ford et al., 2012; Aksan et al., 2015; Häuser, Gold, Stallmach et al., 2007)) and the CD-QOL (>0.7 (Dorn et al., 2010; Zingone, Iavarone et al., 2013)).

Test-retest reliability was assessed to examine the stability of test scores over time. Respondents completed the CDAQ at two time points, two weeks apart. The interval selected was appropriate, and a sufficient sample size on which to conduct the analysis was achieved (i.e. n=145). ICCs ranged from 0.79 to 0.89, indicating that the measure is

reliable. When assessed against Terwee's quality criteria the CDAQ received a positive rating. This indicates that the test-retest reliability of the CDAQ appears superior to the CD-QOL, for which negative evidence was found, and at least comparable with the CDQ, for which some evidence of sufficient test-retest reliability was found, but the quality of some of the studies was poor (see Section 2.3.2 for further details).

Validity

Construct validity was assessed by comparing CDAQ scores with the SF-36v2 and exploring differences in scores between known groups. It is common for construct validity to be assessed against generic measures (Jenkinson and Fitzpatrick, 2013) and the SF-36v2 is considered to be the leading generic measure (McDowell, 2006). When selecting an appropriate PROM against which to evaluate construct validity, it is important that there is evidence of its psychometric properties (de Vet et al., 2011). The SF-36v2 has been extensively validated and its use is well documented both in general and within the target population (as per the findings of the systematic review in Chapter 2), making it a suitable measure to include for the validation of the CDAQ's constructs.

In contrast, the systematic review conducted as part of this research (Chapter 2), found limited evidence supporting the psychometric properties of existing disease-specific measures (i.e. the CDQ and CD-QOL), while also highlighting limitations with their development. As such, it would not have been appropriate or valuable to assess the construct validity of the CDAQ against these measures. Furthermore, it is not common practice for newly-developed measures to be directly compared to existing disease-

specific measures, and indeed, may be bad practice if there is reason to believe that existing measures are flawed.

In general, correlations between the CDAQ and SF-36v2 were as expected, with dimensions of the CDAQ correlating more strongly with mental health dimensions of the SF-36v2 and the MCS score. Correlations between the CDAQ and certain dimensions of the SF-36v2, such as the general health (GH) and vitality (VT) domains, were stronger than expected. However, it is reasonable to expect that poorer CD-related HRQOL (e.g. increased dietary burden or symptoms) may have a moderate to strong association with decreased energy levels and a poorer view of one's health.

The literature shows that males with CD report a better HRQOL than females with CD (Norström et al., 2011; Zarkadas et al., 2006). The CDAQ was able to discriminate between males and females, and groups reporting varying levels of impact of their CD. These results provide evidence that the CDAQ is measuring the constructs that it purports to measure.

The CDAQ's responsiveness to change has not been assessed as part of this study, but work to assess this important measurement property is underway. To conclude, this chapter has presented evidence indicating that the CDAQ is a reliable and valid measure for the assessment of HRQOL in CD.

CHAPTER 7:
Patients' experiences of health care services

7.1 Introduction

The next three chapters present the results of the main cross-sectional survey (Survey 2) in relation to the aims of this thesis. The main aim was to explore the relationship between patients' experiences of health care services and HRQOL in CD (results presented in Chapter 9). In order to achieve this aim, it is first necessary to report the results of the patient experience questionnaire (Chapter 7) and HRQOL questionnaires (Chapter 8) separately.

The use of patient experience surveys is widespread, particularly in England where regular national surveys are conducted (e.g. the GP Patient Survey) (Graham and Woods, 2013). Patient experience surveys provide important information about what happened during the patient's episode(s) of health care, which can be utilised by health care providers, commissioners, and service users to improve the quality of health care services. Furthermore, the English government is committed to providing patients with a positive experience of health care, as set out in the NHS Outcomes Framework (Great Britain. Department of Health, 2014).

In CD, patient experience surveys to date have focused on specific aspects of health care, rather than the patient's broader experience, for example, follow-up care (i.e. whether patients were receiving follow-up care, the type of care received, and preferences for follow-up) (Bebb et al., 2006), dietitian use (Mahadev et al., 2013), and wider health care

use (Norström et al., 2011; Ukkola et al., 2012). While no studies in the field of CD have explored patients' experiences of health care services from diagnosis through to follow-up care, broader experiences of health care have been investigated in other conditions. For example, Peters, Fitzpatrick et al. (2013) investigated the experiences of health and social care of 5,209 people with neurological long-term conditions, asking questions about diagnosis, treatment, patient-centred care, professionals understanding about neurological long-term conditions, respect and dignity, and personal care and support.

7.1.1 Aims and objectives

There are very few studies exploring patients' experiences of health care services in CD, and those conducted have focused on limited aspects of health care. Exploring the broader health care experience (i.e. pre-diagnostic period through to follow-up) will provide a more comprehensive overview of patients' experiences. Therefore, the aim of this chapter was to investigate patients' experiences of health care services utilised in relation to CD, from diagnosis to the present, and report the results of the survey. This was achieved by the following objectives:

- To present the response distribution for individual patient experience questions;
- To calculate a summary score to represent the patient's overall experience of health care services;
- And to explore how experiences of health care services vary between respondents.

7.2 Methods

The findings presented in Chapters 7, 8 and 9 are based on data collected through Survey 2. Survey methodology is described in Chapter 6.

7.2.1 Dichotomous problem scores

Patient experience questions were coded as dichotomous problem scores (i.e. 'no problem' = 0 or 'a problem' = 1). This approach follows that taken in previous studies (e.g. Jenkinson, Coulter and Bruster, 2002; Hewitson et al., 2014), in which a problem was defined as "an aspect of health care that could, in the eyes of the patient, be improved upon" (Jenkinson, Coulter and Bruster, 2002). Examples of item coding are shown in Figure 11. The coding of items was set out by the author and finalised with supervisors. Not all questions lent themselves to being coded in this way, as some questions provided background information or context to answers of other questions. In total, 31 (out of 53) questions were coded as problem scores[18], details of which can be found in Appendix NN.

Figure 11. Coding patient experience questions as problem scores, an example

Q11. Did you receive enough information throughout the diagnostic process?

1 ☐ Yes, I received enough information
2 ■ No, I did not receive *enough* information
3 ■ No, I did not receive *any* information
4 ☐ I did not want any information
5 ☐ I can't remember

Q18. How helpful was your first appointment with a dietitian?

1 ☐ Very helpful
2 ☐ Fairly helpful
3 ■ Not very helpful
4 ■ Not at all helpful
5 ☐ I am not sure / I can't remember

Note: Boxes shaded black indicate a problem, unshaded boxes indicate no reported problem.

[18] Questions with multiple parts were treated as separate questions, and questions 21 and 29 were combined into one question.

7.2.2 Missing data

Missing data occurred due to non-response or as a result of 'skips' in the questionnaire (i.e. respondents were instructed not to complete certain questions if they were deemed not applicable based on previous answers). Missing data was coded as 'no problem' based on the following assumptions: (1) if problems had occurred they would have been reported, and (2) if questions weren't relevant for individuals then they could not have problems with those aspects of care. The same principle applied if the respondent answered 'do not remember'. This approach to treating missing data has been taken in previous studies (e.g. Peters, Fitzpatrick et al., 2013).

7.2.3 Overall experiences problem score

In order to explore how experiences varied between respondents, an overall experiences problem score was created for each respondent. Items were not included in the calculation of the score if missing data was greater than or equal to 20%. This approach was taken to minimise bias that may result from missing data due to questionnaire skips (i.e. data not missing at random). A figure of 20% was selected after reviewing the data; it allowed the removal of items with particularly high amounts of missing data while retaining as many items as possible.

Questions asking about aspects of dietetic and follow-up appointments were not applicable to all respondents, and therefore, the inclusion of these items in an overall score would result in an unequal weighting of problems. For example, those not currently receiving regular follow-up, but whom would like to, could only achieve a maximum problem score of 1 for follow-up care. However, those receiving follow-up care who had experienced problems with the service could achieve a maximum problem

score of 5. To address this, summary scores were created[19] to amalgamate experiences of dietary advice and follow-up in to two dichotomous scores (i.e. 'no problems' = 0 or 'one or more problems' = 1)[20]. This allowed details of experiences to be maintained, while minimising bias that could result from summing individual items (i.e. people experiencing more services have more problems).

The overall experiences problem score was calculated as the sum of problems for the remaining dichotomised items[21], and ranged from 0-21.

7.2.4 Statistical analysis

As an indicator of adherence, respondents were asked how frequently they had consumed gluten on purpose within the last 12 months, responding on a scale from 'Never' to 'Always'. For analysis purposes, response categories 'Often' and 'Always' were combined due to a low numbers of respondents consuming gluten frequently (n=5). There is currently no agreed gold standard for the measurement of GFD adherence (Hall et al., 2009), but similar approaches to that taken here (i.e. self-report) have been used in previous studies (e.g. Hallert et al., 1998; Häuser, Stallmach et al., 2007). With regards to marital status, only five respondents reported that they are 'separated'. Therefore, the 'separated' and 'divorced' categories were combined for analysis.

[19] The follow-up summary score was created by amalgamating items 21 and 29, 22, 26, 27 and 28. The dietary advice summary score was created by amalgamating items 15, 16, 18, and 19.
[20] For example, a follow-up summary score of 1 represents that the respondent does not have regular follow-up or the respondent has regular follow-up but has experienced one or more problems with the service (i.e. indicated a problem to one or more of the individual items).
[21] See Table 38 for details of which items contributed to the overall experiences problem score.

Bivariate analyses were conducted to explore the relationship between experiences of health care services (as measured by the overall experiences problem score) and gender, ethnicity, age, time since diagnosis, number of co-morbidities, gluten consumption, and marital status.

The overall experiences problem score was not normally distributed as assessed by Shapiro-Wilk's test of normality ($p<0.05$) and a visual inspection of a Normal Q-Q plot[22]. Therefore, non-parametric tests were appropriate. Data are reported as medians and inter-quartile ranges (25^{th} percentile – 75^{th} percentile). The Mann-Whitney U test and Kruskal-Wallis H tests were used to compare scores between groups, as appropriate. Where the Kruskal-Wallis H test was statistically significant, pairwise comparisons with a Bonferroni correction were performed. Spearman's correlation was used to assess associations between continuous variables.

The level of statistical significance for all analyses was set at $P < 0.05$ (two-sided). Data was analysed using IBM SPSS Statistics 20.

7.3 Results

The number of people reporting problems with aspects of health care services is presented in Table 38, along with missing data. Data presented in Sections 7.3.1 and 7.3.2 is based on individual item data. The overall experiences problem score is calculated and reported in Section 7.3.3.

[22] A normal Q-Q plot is a type of graph which displays a diagonal line showing expected values for the sample assuming that the data follows a normal distribution, overlaid with observed values. If the data is normally distributed, it is expected that the observed values should roughly follow the diagonal line.

7.3.1 Missing data

Missing data due to non-response is less than 5% for the majority of items, with the exception of items 9a (14.2%, "*Not offered blood test to diagnose CD*") and 20c (10.1%, "*Pneumococcal vaccination not offered*"). Higher amounts of missing data for these items may be due to a lack of information sharing or knowledge about the specifics of tests and treatments received. In addition, diagnostic blood tests for CD were introduced in 1983 (Losowsky, 2008) and therefore, they would not have been available to those diagnosed prior to this.

The majority of missing data was caused as a result of 'skips' in the questionnaire (referred to as 'not applicable' in Table 38), with 19 items missing data as a result. Assessing missing data as a whole (i.e. 'non-response' plus 'not applicable'), six items had missing data ≥ 20%. Of these, two items (items 9a, 36) were removed from further analysis, and four items (items 22, 26, 27, 28) were amalgamated in to summary variables.

Table 38. Number of respondents reporting problems with aspects of health care services, and missing data (n=268)

Q No	Item description	Respondents reporting problems		Missing data						Overall experiences problem score?[b]
				Non-response		Not applicable		Total missing[a]		
		n	%	n	%	n	%	n	%	
	Diagnosis									
6	Felt their diagnosis of CD was slow	110	41.0	3	1.1	39	14.6	42	15.7	Y
8b	HCP didn't always inspire confidence	105	39.2	8	3.0	39	14.6	47	17.5	Y
8a	HCP didn't always listen carefully	98	36.6	5	1.9	39	14.6	44	16.4	Y
8c	HCP didn't always take symptoms seriously	94	35.1	5	1.9	39	14.6	44	16.4	Y
14	Did not receive enough information at time of diagnosis	69	25.7	3	1.1	18	6.7	21	7.8	Y
13	Informed of diagnosis in a somewhat unprofessional or inappropriate manner	66	24.6	3	1.1	18	6.7	21	7.8	Y
11	Did not receive enough information throughout diagnostic process	50	18.7	3	1.1	18	6.7	21	7.8	Y
10	Slow wait to receive an endoscopy	32	11.9	7	2.6	18	6.7	25	9.3	Y
9a	Not offered blood test to diagnose CD	8	3.0	38	14.2	18	6.7	56	**20.9**	-
9b	Not offered an endoscopy to diagnose CD	4	1.5	8	3.0	18	6.7	26	9.7	Y
	Dietary advice									
	Dietary advice summary score	*99*	*36.9*	-	-	-	-	-	-	*Y*
16	Slow access to see dietitian following diagnosis	50	18.7	1	0.4	37	13.8	38	14.2	-
19	Not offered second appointment with dietitian when needed	40	14.9	3	1.1	37	13.8	40	14.9	-
18	Unhelpful first dietetic appointment	36	13.4	1	0.4	37	13.8	38	14.2	-
15	No access to dietitian following diagnosis when needed	9	3.4	3	1.1	18	6.7	21	7.8	-
	Follow-up appointments									
20c	Pneumococcal vaccination not offered	141	52.6	27	10.1	0	0	27	10.1	Y
	Follow-up summary score	*116*	*43.3*	-	-	-	-	-	-	*Y*

Q No	Item description	Respondents reporting problems		Missing data						Overall experiences problem score?[b]
				Non-response		Not applicable		Total missing[a]		
		n	%	n	%	n	%	n	%	
21,29	Follow-up appointments not occurring (but patients would like to have follow-up)	68	25.4	7	2.6	0	0	7	2.6	-
27	Questions at follow-up appointment not always answered adequately	31	11.6	1	0.4	131	48.9	132	**49.3**	-
28	Unhelpful follow-up appointment	23	8.6	0	0	109	40.7	109	**40.7**	-
22	Regular follow-up is infrequent	8	3.0	1	0.4	109	40.7	110	**41.0**	-
26	No opportunity to ask questions at follow-up appointment	5	1.9	0	0	109	40.7	109	**40.7**	-
	Prescriptions									
36	Expensive cost of prescriptions	31	11.6	2	0.7	203	75.7	205	**76.5**	-
32	Not given enough information about prescriptions	81	30.2	4	1.5	0	0	4	1.5	Y
33	Difficulties obtaining prescriptions	54	20.1	4	1.5	0	0	4	1.5	Y
	Knowledge and information									
41d	Felt GPs weren't always knowledgeable about CD	178	66.4	6	2.2	0	0	6	2.2	Y
40	GP didn't always have good understanding of CD	114	42.5	6	2.2	0	0	6	2.2	Y
38	Information and advice not always available from health professional when needed	82	30.6	10	3.7	0	0	10	3.7	Y
39	Not given enough information about medical test results	78	29.1	6	2.2	0	0	6	1.5	Y
41a	Felt dietitians lacked knowledge about CD	51	19.0	5	1.9	0	0	5	1.9	Y
42	Health professionals provided inconsistent information and advice	44	16.4	4	1.5	0	0	4	1.5	Y
41b	Felt specialist hospital doctors lacked knowledge about CD	29	10.8	6	2.2	0	0	6	2.2	Y

[a]Missing data ≥ 20% highlighted in bold.

[b]Indicates whether the item contributed towards the overall experiences problem score.

Item numbers refer to those used in Survey 2 (see questionnaire in Appendix II).

7.3.2 Patients' experiences of health care services

For reporting purposes, CD-PEQ items have been grouped into the following five categories: diagnosis; dietary advice; follow-up appointments; prescriptions; and knowledge and information. Where applicable, dichotomous problem scores are reported (i.e. items in Table 38). For items not coded as problem scores, frequency data is reported (Appendix OO).

Diagnosis

The majority (93.3%, n=250) of respondents were diagnosed aged 16 years or over. Respondents reported that it took an average of 4.00 ± 7.97 years (range <1 - 50 years) from when they first sought medical advice about their symptoms to receiving a definite diagnosis, with almost half (41.0%, n=110) reporting their diagnosis as slow. Most respondents (82.8%, n=222) were informed of their diagnosis by a hospital doctor/consultant or their GP, with a quarter (24.6%, n=66) reporting that their diagnosis was communicated in a somewhat unprofessional or inappropriate manner.

The most common symptoms experienced prior to diagnosis (i.e. by more than 50% of respondents) were: abdominal bloating (63.8%, n=171), diarrhoea/loose bowel movements (62.3%, n= 167), abdominal pain (57.1%, n=153), and chronic fatigue (51.5%, n=138) (a full table of symptoms is available in Appendix OO). A small proportion of respondents (2.2%, n=6) were asymptomatic.

In most cases, the respondent spoke to a GP (70.3%, n=161) or a hospital doctor/consultant (21.8%, n=50) the most often prior to their diagnosis. Many

respondents reported problems with this HCP, most commonly reporting a lack of confidence in them (39.2%, n=105).

The majority of respondents were offered the appropriate tests to diagnose their CD, however, some (11.9%, n=32) reported delays to receiving an endoscopy. Some respondents felt they did not receive enough information throughout the diagnostic process (18.7%, n=50) or at the time of diagnosis (25.7%, n=69).

Dietary advice

Overall, just over a third (36.9%, n=99) of respondents had one or more problems with the dietetic service or did not receive a dietetic appointment when they would have liked to. The majority of respondents (86.2%, n=231) had consultations with a dietitian about their CD after receiving a diagnosis, with 82.7% (n=191) finding their first dietetic appointment helpful. During the first appointment, dietitians generally explained the GFD (90.0%, n=208) and provided supporting written information about it (83.1%, n=192). Practical aspects surrounding how to obtain gluten-free foods were covered to varying degrees, with information about prescriptions (72.3%, n=167) more frequently covered than explanations of food labelling (52.4%, n=121) and tips on eating out (37.2%, n=86). Two-thirds (65.8%, n=152) of appointments covered cross-contamination, while one of the least frequently discussed issues was the suitability of oats (46.3%, n=107).

The most frequently reported problems were about access to the service, with 21.6% (n=50) reporting a long wait for their initial appointment, and 17.3% (n=40) were not offered a second appointment when they felt it was needed.

Follow-up appointments

Overall, 43.3% (n=116) experienced one or more problems with the follow-up care they received or did not receive care when they would have liked to. Over half (59.3%, n=159) of respondents report receiving regular follow-up appointments, with the majority (94.3%, n=150) last seen within the past two years. Appointments were generally with a hospital doctor/consultant (46.5%, n=74), GP (20.8%, n=33), or dietitian (18.9%, n=30).

Follow-up appointments most frequently involved (i.e. more than 50% reported) the taking of blood for testing (78.0%, n=124), weighing the patient (69.8%, n=111), and the discussion of symptoms (55.3%, n=88). Few reported that their appointment covered a review of prescriptions (21.4%, n=34), their emotional well-being (17.6%, n=28), or their understanding of food labelling (11.3%, n=18). Few respondents (14.5%, n=23) found follow-up appointments unhelpful or felt that they had received poor health care since their diagnosis (7.8%, n=21).

Despite a recommendation from Coeliac UK advising that all people with CD receive the pneumococcal vaccination, over half (52.6%, n=141) of respondents report not being offered the vaccination.

The majority (84%, n=225) of respondents would like to have follow-up appointments in the future, of which a quarter (25.4%, n=68) do not currently receive any care. The preferred option is to receive annual appointments (60.4%, n=136) with a hospital doctor/consultant (48.4%, n=109).

Prescriptions

Prescriptions for gluten-free food were obtained by 70.1% (n=188) of the sample during the last 12 months, over half (65.4%, n=123) of whom were entitled to free prescriptions. Of those who paid for their prescriptions, most (92%, n=60) had a pre-payment certificate[23]. Only 11.6% (n=31) of the sample considered the cost of prescriptions expensive. However, this increases to 47.7% when considering those who pay for their prescriptions only.

Some respondents (20.1%, n=54) reported difficulties obtaining prescriptions or felt they had not been given enough information about obtaining prescriptions (30.2%, n=81). Respondents were asked to provide reasons for not obtaining prescriptions in an open text box. Reasons were given by 63 respondents and categorised into eight categories (Table 39). Some commented on the complexity of the prescription process, with one writing, "*It requires a doctor's appointment and each item to be listed on my notes for me to have repeat prescriptions – basically a huge hassle*". Others felt it inappropriate to obtain food on prescription both for personal reasons, e.g. financial assistance not required, or for general reasons, e.g. "*When people are dying of cancer because the NHS can't afford drugs, it is immoral to get bread, etc on prescription*". Finally, some were unable to obtain prescriptions, for example, because they are not available in their area.

[23] The current prescription charge is £8.40 per item. Pre-payment certificates (PPCs) allow a single charge to cover all prescriptions received within a given period (3 or 12 months). PPCs for three months costs £29.10 or 12 months costs £104.00.

Table 39. Reasons for not obtaining gluten-free food on prescription

Reason category	n
Limited range of foods available	17
Complex prescription process	11
Unsure of prescription process	9
Buys products from supermarket	8
Expensive cost of prescriptions	8
Order size is too large	5
Prescriptions are inappropriate	4
Prescriptions not available	3
Unable to categorise / newly diagnosed	8

Note: some respondents provided more than one reason

The most commonly prescribed items were bread or rolls (61.6%, n=165), pasta (42.9%, n=115), and flour or bread mixes (41.4%, n=111) (see Appendix OO).

Knowledge and information

Two-thirds of respondents (66.4%, n=178) reported that their GP was not knowledgeable or knowledgeable 'to some extent' about CD. Fewer people felt dietitians (19.0%, n=51) or specialist hospital doctors (10.8%, n=29) lacked this knowledge.

Approximately two-thirds (67.5%, n=181) had spoken to a HCP specifically about their CD in the last 12 months. Most frequently, patients consulted their GP (41.0%, n=110), a hospital doctor/consultant (38.4%, n=103), or a dietitian (29.1%, n=78). During this period, approximately one third (30.6%, n=82) of respondents were not always able to get the general information and advice they needed, or information about the results of medical tests (29.1%, n=78). When information was received, 16.4% (n=44) reported problems with the consistency of information and advice.

7.3.3 Overall experiences problem score

An overall experiences problem score was calculated for all respondents, with an average of 5.5 problems reported (IQR: 3-10; range: 0-19) (Table 40).

Table 40. Number of problems reported with health care services, n=268

	No. of respondents	
Overall experiences problem score	**n**	**%**
0	24	9.0
1-5	110	41.0
6-10	80	29.9
11-15	46	17.2
16-21	8	3.0

The median number of problems was significantly higher for females (6.5, IQR: 3.0 – 10.0, n=166) than males (5.0, IQR: 2.0 – 8.0, n=97), p=0.003. Overall experiences problem scores were statistically significantly different between groups of different marital status ($\chi^2(3)=15.24$, p=0.002). Pairwise comparisons found significant differences between the 'married/civil partnership' and 'single' groups only (p=0.005), with single respondents reporting more problems (Table 41).

Younger age and a shorter time since diagnosis were significantly associated with an increase in the overall experiences problem score (i.e. more problems). The associations were weak to moderate (Table 42).

There was no significant correlation between overall experiences problem score and the number of co-morbidities. The median number of reported problems was similar for

white[24] (5.0, IQR = 2.0 – 10.0, n=234) and BME (6.0, IQR = 3.0 – 10.0, n=29) respondents (p=0.418), and between groups consuming different levels of gluten ($\chi^2(3)=4.09$, p=0.252) (Table 41).

Table 41. Overall experiences problem score by demographic and disease factors

	Overall experiences problem score		
Gluten consumption	**n**	**Median**	**IQR[a]**
Never	193	6.0	2.5 - 10.0
Rarely	40	5.0	2.0 - 7.8
Sometimes	28	5.5	3.0 - 9.8
Often / Always	5	11.0	2.5 – 15.5
Marital status			
Single	75	8.0	4.0 – 11.0
Married / civil partnership	159	5.0	2.0 – 9.0
Separated / divorced	16	4.5	2.0 – 7.0
Widowed / surviving partner	13	4.0	2.0 – 6.0
Satisfaction with health care since diagnosis			
Very good	80	2.0	1.0 – 5.0
Good	78	6.0	3.8 – 9.0
Fair	64	10.0	7.0 – 12.0
Poor	17	12.0	8.5 – 14.0
Very poor	4	10.0	4.8 – 17.5
Not received any health care since diagnosis	20	5.0	4.0 – 8.0

[a]25th and 75th percentiles

Table 42. Associations between overall experiences problem score and demographic and disease variables

Score	Variable	r_s	P (2-tailed)[a]
Overall experiences problem score	Age	-0.396	**<0.001**
	Time since diagnosis	-0.161	**0.010**
	No of comorbidities	0.100	0.108

[a]95% confidence interval. Statistically significant values are shown in bold.

Overall experiences problem scores were statistically significantly different between groups of respondents with different levels of satisfaction regarding health care since diagnosis ($\chi^2(5) = 104.76$, p<0.001) (Table 41). Pairwise comparisons found statistically

[24] Those reporting they are White British or White Irish.

significant differences in overall experiences problem score between the 'good' and 'fair' groups (p=0.005), 'good' and 'poor' groups (p=0.012), and between the 'very good' group with all other groups ('very poor', p=0.030; 'poor', p<0.001; 'fair', p<0.001; and 'good', p<0.001), with those experiencing fewer problems reporting greater satisfaction.

7.4 Discussion

This chapter has explored patients' experiences of health care services in relation to CD. Patients' experiences were mixed, with patients reporting both positive and negative experiences of care. Aspects of health care for which the largest number of problems (i.e. >40%) were reported were: 'GPs weren't always knowledgeable about CD' (66.4%), the Pneumococcal vaccination was not offered (52.6%), one or more problems with follow-up (43.3%), 'GPs didn't always have a good understanding of CD' (42.5%), and respondents felt their diagnosis of CD was slow (41.0%). The least number of problems (i.e. <10%) were reported for the following aspects of care: 'not offered an endoscopy to diagnose CD' (1.5%) and 'not offered a blood test to diagnose CD' (3.0%).

The biggest issue reported in this survey was the perceived lack of knowledge about CD by GPs. This is potentially cause for concern as GPs are a key point of contact for respondents both prior to diagnosis and following diagnosis. In 70.3% of cases, the GP was often the primary point of contact prior to diagnosis, with many respondents reporting these interactions as poor (i.e. the GP did not listen carefully or take their symptoms seriously). Following diagnosis, GPs were a key point of contact regarding the ongoing management of the condition, with many respondents (41%) having spoken to their GP specifically about their CD in the last 12 months.

In a Canadian study (Zarkadas et al., 2006), a similar proportion (40.0%) rated the provision of information from doctors as fair or poor. In contrast to these findings, Ukkola et al. (2012) found only 7% of respondents to a Finnish survey reported that they perceived physicians lacked knowledge of CD. However, when asked to suggest areas for future research, many commented that they would like the knowledge of physicians improved. These conflicting results within Ukkola's study may be due to survey design, as it is unclear whether respondents were able to select more than one reason for their dissatisfaction with physicians. Ukkola et al.'s sample was limited to those following a GFD for 1 year, whereas respondents in the current study and Zarkadas's study had been diagnosed for a mean of 7.49 years and 10 years respectively.

The speed of diagnosis was reported as another key problem, with respondents diagnosed, on average, four years after first seeking medical advice about their symptoms. However, very few respondents reported problems accessing the relevant diagnostic tests once CD was suspected, with most respondents reporting that they had or were offered blood tests and an endoscopy to diagnose CD. The time taken to diagnose CD was significantly less in the current study compared with a previous study (4.0 years compared with 13.2 years respectively) conducted by Gray and Papanicolas (2010), which may suggest that people are being diagnosed more quickly than previously. Both studies surveyed members of Coeliac UK, and the mean age and gender distribution of respondents were comparable. Factors which may be reducing the length of time to diagnose CD may include the introduction of the NICE guidelines in 2009 (NICE, 2009), which provide detailed guidance regarding the circumstances in which individuals should

be tested for CD. Furthermore, there is increased awareness of CD and the GFD in general, for example, the increased visibility and availability of gluten-free food in supermarkets and restaurants. It should be noted that part of the reason for the difference in durations may be due to differences in question wording; Gray and Papanicolas asked respondents about the duration of symptoms prior to diagnosis, whereas, the current study asked about the duration between first seeking medical advice and diagnosis.

In 2016, NICE published a quality standard for CD outlining priority areas of health care for improvement (NICE, 2016). The CD quality standard (QS134) lists five statements, with statements 1-3 focusing on aspects of diagnosis, and the final two statements focusing on the post-diagnostic period. Statement 3 requires those referred for an endoscopy to receive one within 6 weeks. While this study did not ask respondents to report timescales between referral and receipt of an endoscopy (for reasons identified in the cognitive interviews – see Section 4.4.3), respondents reported *how they felt* about this time period, with 11.9% reporting delays to receiving an endoscopy. This may suggest that this quality standard is not being met, and is supported by recent findings of a study conducted by FitzPatrick et al. (2017) who found only 17% of patients within an Oxford coeliac clinic received an endoscopy within this 6-week timescale. This is a particularly important issue as many find it difficult to remain on a gluten-containing diet for the period between receiving a positive blood test and an endoscopy to confirm diagnosis due to the symptoms that they are experiencing. However, it is important for patients to remain on a gluten-containing diet in order to get a confirmed diagnosis of

CD, thus allowing access to prescriptions for gluten-free food (where available) and ensuring the diagnosis is correct.

Many respondents also reported one or more problems with follow-up care. The main problem was respondents not receiving follow-up appointments when they would have liked to. These findings support those of another UK study (Bebb et al., 2006), which found a similar proportion of respondents received follow-up care (62.0% compared with 59.3% in this study), with no follow-up the least preferred option for future health care. Both the NICE guidelines (NICE, 2015) and NICE quality standard for CD (statement 5) (NICE, 2016) state that people with CD should be offered an annual review. Therefore, access to ongoing monitoring and support needs to be improved in accordance with these guidelines.

Respondents who were receiving follow-up care were seen regularly and were given the opportunity to ask questions, however, emotional well-being was only assessed in 17.6% of follow-up appointments. From the literature, it is known that there is a relationship between CD and mental health problems, such as depression and anxiety (Addolorato et al., 2001; Ciacci, Iavarone et al., 1998; Fera et al., 2003). Assessing emotional well-being as part of review appointments could help to improve the diagnosis and management of mental health problems in people with CD.

Bivariate analyses found the median number of problems with health care services was significantly higher for respondents that are female, single, a younger age, and more recently diagnosed.

Methodology

Throughout this chapter, percentages of those experiencing problems with services have been calculated as a proportion of the whole sample (i.e. 268 respondents) in accordance with the assumptions made (i.e. that problems experienced with services are reported). As a result, the percentages reported for questions not relevant to all respondents are conservative estimates. For example, 11.6% of all respondents had some questions answered inadequately during their most recent follow-up appointment. If we recalculate the percentage as a proportion of those eligible to answer the question (i.e. those receiving follow-up care), the percentage of people indicating a problem increases to 22.6%. In summary, problem scores are a useful way of summarising patient's experiences and provide an indication of what we know to be a problem, but may be an underestimate. The approach taken here to recode answers to patient experience questions into dichotomous problem scores to analyse the survey data has been used before, for example, Peters, Fitzpatrick et al. (2013) analysed the health and social care experiences of people with neurological long-term conditions in this way. Picker Institute Europe, a charity that uses patients' experiences of health care to drive quality improvement and a major provider of such data to the NHS, have also taken this approach when analysing patient experience data, for example, when developing the Picker Patient Experience Questionnaire (Jenkinson, Coulter and Bruster, 2002).

The creation of dimension scores to summarise different aspects of the patients' experience was explored, as this approach has been taken in previous work (e.g. Sizmur and Redding, 2009; Fitzpatrick, et al., 2010). Items were grouped into dimensions which broadly followed existing frameworks of patient experience (i.e. the NHS Patient

Experience Framework (Great Britain. Department of Health, 2012) and the Picker Institute Principles of Patient-Centered Care (Picker Institute Europe, n.d.)). The internal consistency of dimensions, as assessed by Cronbach's alpha, were low, suggesting that items within each dimension were not addressing aspects of the same underlying construct. As such, the use of dimension scores was deemed unreliable and not used in the analysis.

In order to explore how experiences varied between respondents, an overall experiences problem score was created. A key factor that was considered when creating this score was how best to handle the missing data that arose as a result of 'skips' in the questionnaire. A simple summation of all dichotomous problem scores would have resulted in bias, for example, those not in receipt of follow-up care may have had lower overall experiences problem scores because many of the questions regarding follow-up would not be relevant. In an attempt to overcome this, items with large amounts of missing data were removed and summary scores were created for services which had not been used by all. Although this helped to address the issue, some bias may remain, for example, it was not deemed appropriate to ask those diagnosed as children about their experiences of diagnosis due to problems with recall, and therefore, this group may have a lower overall experiences problem score as a result.

The issue of missing data as a result of irrelevant questions and recall problems is a prominent issue in surveys asking about a patient's history. Surveys focusing on recent experiences of illness (e.g. within the last 12 months) or a single episode of care (e.g. hospital admission) are less likely to be affected by these issues. This issue was

minimised in the CD-PEQ, as many items asked experiences within the past 12 months. Those that did not, asked about the period of diagnosis, which is likely to be remembered by respondents as it is an important event in people's lives.

To conclude, this survey is the most comprehensive survey of patients' experiences of health care services in CD conducted to date within the UK, and to the author's knowledge, worldwide. The results of the CD-PEQ will be explored further in Chapter Nine, which will consider the relationship between patients' experiences of health care services and HRQOL.

CHAPTER 8:
Quality of life in coeliac disease

8.1 Introduction

While the previous chapter presented the results of the CD-PEQ from Survey 2, the focus of this chapter is to describe how HRQOL is affected by CD. Firstly, CDAQ and SF-36v2 scores are presented, followed by an exploration of how HRQOL varies between respondents based on demographic and disease-related variables.

Traditionally, the evaluation of health and medical care was conducted by health care professionals (Jenkinson, 1997), however, the value of asking patients to report directly on aspects of their health, such as HRQOL, has gained greater recognition over the past few decades (Black and Jenkinson, 2009). HRQOL is typically measured using PROMs, with most instruments including items on physical, emotional, and social functioning (Fayers and Machin, 2007). Measuring the broader impact of health is particularly important in conditions such as CD, as much of the impact of living with CD is as a result of managing a GFD on a daily basis. The results of the qualitative interviews (see Chapter 3) have shown that the impact of CD can be wide ranging, thus further highlighting the importance of understanding the impacts on HRQOL from the patients' perspective (i.e. factors such as emotional functioning and social well-being) alongside more traditional clinical factors.

In CD, HRQOL prior to diagnosis has been found to be substantially reduced in comparison to the general population (Gray and Papanicolas, 2010). Upon

commencement of a GFD there is an improvement in HRQOL for the majority of patients (van de Water and Mulder, 2009). However, studies looking at the HRQOL of people following a GFD for eight years or more have found that HRQOL is lower than that of the general population, particularly in women (Hallert, Grännö, Grant et al., 1998; Hallert and Lohiniemi, 1999; Nachman, del Campo et al., 2010). Reasons for this disparity between genders is currently unknown (Hallert and Lohiniemi, 1999). At present, there is no consensus about whether HRQOL in patients with CD can reach levels comparable to that of the general population (Casellas, Rodrigo, López Vivancos et al., 2008). Several studies have shown an association between poor adherence to the GFD and a reduced HRQOL (Wagner, Berger et al., 2008; Nachman, del Campo et al., 2010), however, a systematic review by Hall et al. (2009) concluded that, overall, adherence to a GFD and HRQOL are not related. Other factors found to be associated with a reduced HRQOL are the presence of a mental disorder, active medical comorbidities, and dissatisfaction with doctor-patient communication (Häuser, Stallmach et al. 2007).

The majority of studies conducted to date have been carried out in mainland Europe using generic measures. More recently, disease-specific PROMs for CD have been developed (see Chapter 2). This chapter will analyse HRQOL data collected in a UK population with both generic and disease-specific measures, providing evidence to further understand the impact of CD on people living with the condition.

8.1.1 Aims and objectives

The aim of this chapter was to investigate the HRQOL of people with CD through the analysis of data collected from Survey 2. This was achieved by the following objectives:

- To report HRQOL data collected from the survey (i.e. CDAQ and SF-36v2 scores);
- To compare the HRQOL of people with CD to that of the general population;
- And to explore the relationships between HRQOL and demographic and disease-related variables.

8.2 Methods

The data that will be used to address the above aim was collected from Survey 2, which was sent to 800 members of Coeliac UK. The survey questionnaire included the CDAQ, SF-36v2, demographic questions, as well as the CD-PEQ. Full details of the survey methodology can be found in Chapter 6.

8.2.1 Statistical methods

SF-36v2 scores

SF-36v2 scores can be calculated on a 0-100 scale or as norm-based *T* scores. *T* scores have a mean of 50 and a standard deviation of 10, which allow comparisons to be made both across scores and with the general population. Due to the ease of interpreting *T* scores over the original 0-100 scoring metric, it is recommended that interpretations of SF-36v2 data are based on *T* scores (Maruish, 2011), and therefore, *T* scores are reported in this chapter. As UK population norms are more than 20 years old and therefore, unlikely to reflect current health status (Burholt and Nash, 2011), *T* scores based on the 2009 US general population norms are reported within this chapter. Original 0-100 scores are reported in Appendix PP to allow comparisons to be made with existing literature.

When analysing group level data, *T* scores within 0.3 standard deviations of the mean are considered within the normal range (i.e. between 47 and 53 for group data as a whole), with values below the lower limit indicating impaired functioning. QualityMetric Health Outcomes Scoring Software v4.5 was used to calculate SF-36v2 scores.

Bivariate analyses

Bivariate analyses were conducted to explore the relationship between HRQOL (i.e. CDAQ dimension scores, CDAQ overall index score, and SF-36v2 scores) and gender, ethnicity, age, time since diagnosis, number of co-morbidities, gluten consumption, marital status, and experience of health care services (as measured by the 'overall experiences problem score' developed in Chapter Seven).

Shapiro-Wilk's test of normality ($p<0.05$) and a visual inspection of Normal Q-Q plots were used to assess whether PROM scores were normally distributed. Not all scores followed a normal distribution and therefore, both parametric and non-parametric analyses were conducted. The results of these analyses were similar, and therefore, only the parametric results are reported (mean, standard deviation and range). Independent samples t-tests and one-way analysis of variance (ANOVA) were used to compare scores between groups, as appropriate. Where significant differences were found between variables with three or more groups, pairwise comparisons (Tukey-Kramer post hoc test) were run. Pearson's correlation was used to assess associations between continuous variables.

8.3 Results

Of the 268 respondents returning a questionnaire who had reported a diagnosis of CD, one participant had not completed the CDAQ and was therefore removed from this analysis, leaving 267 cases.

8.3.1 CDAQ scores

Missing data for CDAQ individual items was minimal, ranging from 0.4% (n=1) to 0.7% (n=2). CDAQ dimension scores and the overall index score could not be calculated for up to 1.9% (n=5) and 4.9% (n=13) of respondents, respectively. The mean CDAQ scores are shown in Table 43.

Table 43. Health-related quality of life in coeliac disease – CDAQ scores (n=267)

		Score[a]		
	n	***Mean***	***SD***	***Range***
CDAQ				
Overall index score	254	53.56	18.05	6 - 98
Stigma	262	52.58	21.55	0 - 100
Dietary burden	262	39.50	19.19	0 - 100
Symptoms	264	59.38	24.09	0 - 100
Social isolation	263	67.41	23.17	0 - 100
Worries and concerns	264	50.00	21.11	0 - 100

[a]CDAQ scores range from 0 (poorest quality of life) to 100 (highest quality of life).

The lowest mean CDAQ dimension score was 'dietary burden' (39.50) indicating that the burden of managing a GFD is the most important factor impacting on HRQOL. The highest mean CDAQ dimension score was 'social isolation' (67.41), indicating that the impact of CD on participating in social activities and feelings of isolation had the least impact on HRQOL, compared with the other dimensions.

CDAQ scores were also analysed by response bands, i.e. scores between 0 and 20, 21-40, 41-60, 61-80, and 81-100 (Table 44). These response bands were selected to reflect the CDAQ's response options, and so, in general, those scoring between 0 and 20 will mostly have selected 'always', indicating a greater impact of CD on HRQOL[25].

Table 44. CDAQ scores – number and proportion of respondents by response bands

	CDAQ score									
	0 - 20		21 - 40		41 - 60		61 - 80		81 - 100	
Dimension	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Overall index score	5	2.0	64	25.2	93	36.6	75	29.5	17	6.7
Stigma	16	6.1	62	23.7	87	33.2	66	25.2	31	11.8
Dietary burden	42	16.0	97	37.0	93	35.5	23	8.8	7	2.7
Symptoms	17	6.4	51	19.3	78	29.5	64	24.2	54	20.5
Social isolation	7	2.7	36	13.7	72	27.4	60	22.8	88	33.5
Worries and concerns	18	6.8	64	24.2	103	39.0	56	21.2	23	8.7

The greatest proportion of respondents (16.0%) scoring within the worst HRQOL response band (i.e. '0-20') was for the dietary burden dimension. This indicates that more people experience a severe impact on their HRQOL as a result of managing a GFD, than any other dimension. Furthermore, more than half (53.0%) of respondents scored between '0' and '40' for the dietary burden dimension, indicating that many experienced difficulties with managing a GFD on a frequent basis (i.e. often or always).

The greatest proportion of respondents scored within the best HRQOL response band (i.e. '81-100') for the social isolation dimension (33.5%), followed by the symptoms dimension (20.5%). This indicates that many respondents experience infrequent or no difficulties regarding participation in social activities, and few or no symptoms.

[25] Respondents scoring: 21-40 will mostly have selected 'often'; 41-60 will mostly have selected 'sometimes'; 61-80 will mostly have selected 'rarely'; and 81-100 will mostly have selected 'never' indicating good HRQOL.

8.3.2 SF-36v2 scores

Missing data for individual SF-36v2 items was minimal, ranging from 0 to 1.9% (n=5). Dimension and component summary scores could not be calculated for up to 0.7% (n=2). The mean SF-36v2 scores are shown in Table 45.

Table 45. Quality of life in coeliac disease – SF-36v2 scores (n=267)

		Scores[a]		
	n	***Mean***	***SD***	***Range***
SF-36v2				
Physical Component Summary Score (PCS)	265	49.46	9.23	15.41 – 67.21
Mental Component Summary Score (MCS)	265	47.11	10.71	14.51 – 66.28
Physical Functioning (PF)	267	50.84	9.30	19.26 – 57.54
Role-Physical (RP)	266	48.89	9.84	21.23 – 57.16
Bodily Pain (BP)	265	48.62	10.32	21.68 - 62.00
General Health (GH)	267	46.41	11.63	18.95 – 66.50
Vitality (VT)	266	47.03	10.85	22.89 – 70.42
Social Functioning (SF)	266	48.20	10.23	17.23 – 57.34
Role-Emotional (RE)	265	48.08	10.57	14.39 – 56.17
Mental Health (MH)	266	47.81	10.21	14.24 – 63.95

[a]Norm-based T scores (mean 50, SD 10). Scores range from 0 (poorest quality of life) to 100 (highest quality of life).

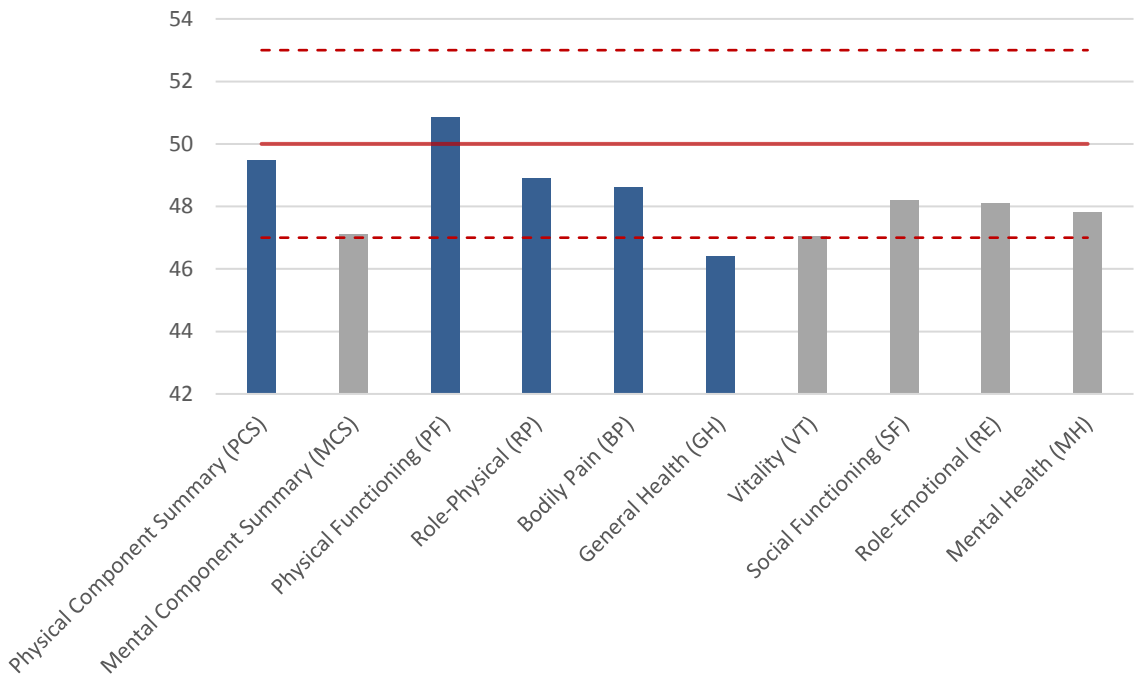
The mean MCS score and scores of domains most associated with psychological and mental health (i.e. MH, RE, SF, and VT) are lower than the PCS score and scores of domains most associated with physical health (PF, RP, and BP), with the exception of the general health (GH) domain, which scored the lowest. This indicates that CD impacts most greatly on psychological and mental health.

Comparison with the general population

SF-36v2 scores were compared with population norms (Figure 12). Scores were within the 'normal' range for all domains except general health (GH). The GH domain score (46.41) was slightly below the lower limit of 'normal', indicating that people with CD have a marginally poorer evaluation of their health than the general population. The MCS

(47.11) and vitality (47.03) scores were at the lower end of the normal range, indicating that the psychological health and vitality of people with CD is comparable with those within the general population who are towards the lower bound of the normal range. Aspects of physical health, particularly physical functioning, were comparable with the general population.

Figure 12. SF-36v2 Profile of *T* scores: Adults with coeliac disease compared with population norms



The solid line indicates the 2009 US general population norm (mean 50, SD 10), and the dashed lines indicate the lower (47) and upper (53) bounds of *T* scores within the normal population range. Blue columns are domains most associated with physical functioning. Grey columns are domains most associated with psychological and mental health.

Population norms were also available by gender. The mean dimension and component summary scores for males and females in the sample were compared with their respective norm scores (Table 46). As discussed previously, mean scores outside 0.3 standard deviations from the norm *T* score indicate that the sample is outside the normal range, with lower scores indicating impaired functioning.

Table 46. SF-36v2 Profile of *T* scores: Males and females with coeliac disease compared with population norms

	Male scores				*Female scores*			
	n	***Mean***	***Norm***	***SD[a]***	***n***	***Mean***	***Norm***	***SD[a]***
SF-36v2								
Physical Component Summary Score (PCS)	97	50.77	50.89	0.01	164	48.66	49.19	0.05
Mental Component Summary Score (MCS)	97	49.49	51.02	0.15	164	45.76	49.06	**0.33**
Physical Functioning (PF)	97	52.30	51.36	-0.09	166	49.92	48.74	-0.12
Role-Physical (RP)	97	49.75	50.76	0.10	165	48.31	49.29	0.10
Bodily Pain (BP)	96	50.57	50.95	0.04	165	47.53	49.12	0.16
General Health (GH)	97	48.74	50.56	0.18	166	45.17	49.48	**0.43**
Vitality (VT)	97	50.21	51.45	0.12	165	45.15	48.66	**0.35**
Social Functioning (SF)	97	50.41	50.88	0.05	165	46.92	49.19	0.23
Role-Emotional (RE)	97	49.28	51.06	0.18	164	47.34	49.02	0.17
Mental Health (MH)	97	50.27	51.00	0.07	165	46.46	49.07	0.26

[a]Standard deviation from the norm ((Norm *T* score – mean *T* score)/10) – values greater than 0.3 standard deviations from the norm (shown in bold) indicate that the group is not within the normal range for males or females in the 2009 US general population.

Mean scores for males were within the normal range of the general population (i.e. mean scores were less than 0.3 SDs from the norm). In females, the mean MCS, general health (GH) and vitality (VT) scores were greater than 0.3 SDs below the norm, indicating that females with CD report worse psychological and mental health, evaluate their health more poorly, and report lower amounts of energy than females in the general population. Although within the normal range, the mental health (MH) of females was towards the lower bound of the normal range.

8.3.3 Bivariate analysis

In order to explore how HRQOL varied between respondents, bivariate analysis was conducted, the findings of which are presented below.

Gender

Mean CDAQ and SF-36v2 scores were lower for females than males (Table 47). This difference was statistically significant for the majority of scores with the exception of the PCS score, and Role-Emotional (RE) and Role-Physical (RP) dimensions, indicating that in general, the HRQOL of females is worse than males. Table 46 shows that this is also true in a general population sample, with norm *T* scores of females lower than males for all scores.

Table 47. CDAQ and SF-36v2 scores by gender, n=263

	Male (n=97)			*Female (n=166)*			*Difference*	
	n	***Mean***	***SD***	***n***	***Mean***	***SD***	***Mean***	***p***
CDAQ								
Overall index score	93	60.91	16.81	158	49.18	17.36	11.73	**<0.001**
Stigma	97	61.02	18.28	161	47.05	21.37	13.97	**<0.001**
Dietary burden	96	44.30	20.35	162	36.15	17.43	8.15	**0.001**
Symptoms	95	68.58	21.99	165	54.15	23.50	14.43	**<0.001**
Social isolation	96	74.90	20.91	164	63.08	23.39	11.82	**<0.001**
Worries and concerns	96	54.60	21.76	164	46.77	19.88	7.83	**0.003**
SF-36v2								
PCS	97	50.77	8.20	164	48.66	9.82	2.11	0.064
MCS	97	49.49	9.99	164	45.76	10.77	3.74	**0.006**
Physical Functioning (PF)	97	52.30	7.87	166	49.92	10.04	2.38	**0.034**
Role-Physical (RP)	97	49.75	9.88	165	48.31	9.87	1.44	0.256
Bodily Pain (BP)	96	50.57	10.33	165	47.53	10.19	3.04	**0.022**
General Health (GH)	97	48.74	10.58	166	45.17	12.03	3.56	**0.016**
Vitality (VT)	97	50.21	9.91	165	45.15	10.99	5.06	**<0.001**
Social Functioning (SF)	97	50.41	9.02	165	46.92	10.68	3.50	**0.007**
Role-Emotional (RE)	97	49.28	10.59	164	47.34	10.49	1.94	0.151
Mental Health (MH)	97	50.27	9.74	165	46.46	10.12	3.81	**0.003**

Ethnicity

People belonging to BME groups reported lower mean HRQOL scores in all dimensions of the CDAQ and SF-36v2 (Table 48). This difference was statistically significant in all but three dimensions: stigma, social isolation, and physical functioning (PF). Proportionally,

the number of males and females is similar between the white (36.8% males) and BME (37.9% males) groups.

Table 48. HRQOL scores by ethnicity, n=263

	White (n=234)			*BME (n=29)*			*Difference*	
	n	***Mean***	***SD***	***n***	***Mean***	***SD***	***Mean***	***p***
CDAQ								
Overall index score	223	54.55	17.82	28	45.36	17.99	9.19	**0.011**
Stigma	230	53.03	21.16	28	46.32	22.23	6.71	0.116
Dietary burden	229	40.27	18.86	29	30.60	17.69	9.67	**0.009**
Symptoms	231	60.78	23.41	29	48.62	25.84	12.16	**0.010**
Social isolation	231	68.42	22.54	29	59.66	26.99	8.77	0.055
Worries and concerns	231	50.63	20.92	29	41.95	19.35	8.68	**0.035**
SF-36v2								
PCS	232	49.95	9.03	29	45.43	10.50	4.52	**0.013**
MCS	232	47.80	10.00	29	41.89	13.79	5.90	**0.033**
Physical Functioning (PF)	234	51.33	8.78	29	46.54	12.44	4.79	0.053
Role-Physical (RP)	233	49.43	9.35	29	44.15	12.64	5.28	**0.037**
Bodily Pain (BP)	232	49.23	10.08	29	44.02	11.27	5.21	**0.010**
General Health (GH)	234	47.05	11.45	29	41.96	12.20	5.09	**0.026**
Vitality (VT)	233	47.55	10.58	29	42.83	12.35	4.71	**0.027**
Social Functioning (SF)	233	48.88	9.84	29	42.82	11.71	6.07	**0.002**
Role-Emotional (RE)	232	48.79	9.83	29	42.24	13.99	6.54	**0.020**
Mental Health (MH)	233	48.46	9.50	29	43.11	13.51	5.35	**0.047**

Age and time since diagnosis

Weak positive correlations were found between age and HRQOL scores, and time since diagnosis and HRQOL scores, with the exception of the PCS score and some of the other physical domains of the SF-36v2 (i.e. PF and RP), which were negatively correlated (i.e. as age or time since diagnosis increases, physical health decreases) (Table 49). The correlations were statistically significant for all CDAQ dimensions and some SF-36v2 dimensions. The correlation was strongest (r=0.408) between age and CDAQ stigma, suggesting that as age increases, stigma reduces. In general, this indicates that those

who are older or who have had the condition for longer report a marginally better HRQOL.

Table 49. Associations between HRQOL and demographic and disease variables

Variable	Dimension	r	P (2-tailed)[a]
Age	**CDAQ**		
	Overall index score	0.342	**<0.001**
	Stigma	0.408	**<0.001**
	Dietary burden	0.189	**0.002**
	Symptoms	0.275	**<0.001**
	Social isolation	0.270	**<0.001**
	Worries and concerns	0.285	**<0.001**
	SF-36v2		
	PCS	-0.153	0.013
	MCS	0.284	**<0.001**
	Physical Functioning (PF)	-0.259	**<0.001**
	Role-Physical (RP)	-0.181	**0.003**
	Bodily Pain (BP)	0.010	0.871
	General Health (GH)	0.207	**0.001**
	Vitality (VT)	0.234	**<0.001**
	Social Functioning (SF)	0.133	**0.032**
	Role-Emotional (RE)	-0.001	0.989
	Mental Health (MH)	0.254	**<0.001**
Time since diagnosis	**CDAQ**		
	Overall index score	0.160	**0.013**
	Stigma	0.176	**0.005**
	Dietary burden	0.234	**<0.001**
	Symptoms	0.125	**0.048**
	Social isolation	0.155	**0.014**
	Worries and concerns	0.165	**0.009**
	SF-36v2		
	PCS	-0.057	0.365
	MCS	0.163	**0.009**
	Physical Functioning (PF)	-0.091	0.146
	Role-Physical (RP)	-0.037	0.560
	Bodily Pain (BP)	0.007	0.917
	General Health (GH)	0.096	0.125
	Vitality (VT)	0.135	**0.031**
	Social Functioning (SF)	0.122	0.052
	Role-Emotional (RE)	0.041	0.514
	Mental Health (MH)	0.138	**0.028**

[a]95% confidence interval. Statistically significant values are shown in bold.

Number of comorbidities

Weak negative correlations were found between the number of comorbidities[26] and HRQOL scores, with the strongest associations found with physical aspects of health (Table 50). The correlations were statistically significant in all cases, with the exception of the dietary burden dimension. This indicates that those with a greater number of comorbidities tend to report a slightly poorer HRQOL.

Table 50. Associations between HRQOL and number of comorbidities

Variable	Dimension	r	P (2-tailed)[a]
No of comorbidities	**CDAQ**		
	Overall index score	-0.261	**<0.001**
	Stigma	-0.179	**0.004**
	Dietary burden	-0.123	0.051
	Symptoms	-0.298	**<0.001**
	Social isolation	-0.264	**<0.001**
	Worries and concerns	-0.167	**0.007**
	SF-36v2		
	PCS	-0.380	**<0.001**
	MCS	-0.266	**<0.001**
	Physical Functioning (PF)	-0.363	**<0.001**
	Role-Physical (RP)	-0.371	**<0.001**
	Bodily Pain (BP)	-0.334	**<0.001**
	General Health (GH)	-0.313	**<0.001**
	Vitality (VT)	-0.287	**<0.001**
	Social Functioning (SF)	-0.356	**<0.001**
	Role-Emotional (RE)	-0.349	**<0.001**
	Mental Health (MH)	-0.231	**<0.001**

[a]95% confidence interval. Statistically significant values are shown in bold.

Adherence to the gluten-free diet

There were no significant differences in HRQOL scores between different levels of dietary adherence, with the exception of the CDAQ dietary burden dimension (Table 51). Pairwise comparisons found significant differences between the 'Never' (40.84, SD: 18.46, n=190) and 'Often/Always' (17.50, SD: 15.72, n=5) groups only (p=0.035; mean

[26] Note: 26.5% (n=71) had no co-morbidities, 29.1% (n=78) had one co-morbidity, 18.3% (n=49) had two co-morbidities, and 22.8% (n=61) reported three or more (up to a maximum of seven) co-morbidities.

difference: 23.34; CI: 1.14 – 45.54), indicating that those experiencing greater dietary burden consume gluten on a more frequent basis.

Table 51. ANOVA by gluten consumption

Variable	Dimension	F value	P value (2 sided)
Gluten consumption	**CDAQ**		
	Overall index score	1.280	0.282
	Stigma	0.763	0.516
	Dietary burden	3.527	**0.016**
	Symptoms	2.404	0.068
	Social isolation	1.421	0.237
	Worries and concerns	1.978	0.118
	SF-36v2		
	PCS	0.262	0.853
	MCS	0.307	0.820
	Physical Functioning (PF)	0.100	0.960
	Role-Physical (RP)	0.335	0.800
	Bodily Pain (BP)	0.252	0.860
	General Health (GH)	1.832	0.142
	Vitality (VT)	1.241	0.295
	Social Functioning (SF)	0.064	0.979
	Role-Emotional (RE)	0.399	0.754
	Mental Health (MH)	0.893	0.445

Marital status

HRQOL scores were statistically significant for different marital statuses in the following CDAQ dimensions: stigma, symptoms, and overall index score, and the following SF-36v2 dimensions: Physical Functioning (PF), General Health (GH), Social Functioning (SF), Role-Emotional (RE), and the MCS score (Table 52).

Table 52. ANOVA by marital status

Variable	Dimension	F value	P value (2 sided)
Marital status	**CDAQ**		
	Overall index score	3.314	**0.021**
	Stigma	5.616	**0.001**
	Dietary burden	1.356	0.257
	Symptoms	5.459	**0.001**
	Social isolation	1.999	0.115
	Worries and concerns	1.640	0.181
	SF-36v2		
	PCS	0.800	0.495
	MCS	3.287	**0.021**
	Physical Functioning (PF)	3.843	**0.010**
	Role-Physical (RP)	1.323	0.267
	Bodily Pain (BP)	1.305	0.273
	General Health (GH)	3.569	**0.015**
	Vitality (VT)	2.632	0.051
	Social Functioning (SF)	2.926	**0.034**
	Role-Emotional (RE)	3.000	**0.031**
	Mental Health (MH)	2.296	0.078

In order to explore where differences between HRQOL scores by marital status groups lay, pairwise comparisons were run. Table 53 shows the results of comparisons where statistical significant differences exist.

Table 53. Comparisons of HRQOL scores by marital status groups

			Score				
Score	**Group (a)**	**Group (b)** [a]	***Mean difference between (a) and (b)***	***SE***	***95% CI***		***p***
CDAQ							
Overall index score	Single	Married	-7.29	2.55	-13.89	-0.69	0.024
Stigma	Single	Married	-9.12	2.92	-16.67	-1.56	0.011
Stigma	Single	Widowed	23.17	6.71	-40.52	-5.82	0.004
Symptoms	Single	Married	-11.11	3.30	-19.64	-2.57	0.005
SF-36v2							
MCS	Single	Married	-4.53	1.47	-8.33	-0.73	0.012
PF	Single	Widowed	9.23	2.76	2.08	16.38	0.005
PF	Married	Widowed	8.34	2.65	1.48	15.21	0.010
GH	Single	Married	-5.01	1.60	-9.16	-0.86	0.011
SF	Single	Married	-3.85	1.42	-7.52	-0.19	0.035

[a]Married group also includes those in a civil partnership and the widowed group also includes surviving partners from a civil partnership. Note that comparisons between groups where HRQOL scores were not significantly different are not shown.

Pairwise comparisons found that the majority of statistically significant differences between HRQOL scores were between the 'single' group, and 'married' or 'widowed' groups. Mean HRQOL scores for the 'single' group were lower than the 'married' group, indicating poorer overall HRQOL, mental and psychological well-being, general health, and social functioning, and greater stigma and symptoms. However, the 'single' group reported significantly lower levels of stigma and better physical functioning than the 'widowed' group. The 'married' group also reported better physical functioning than the 'widowed' group.

Better HRQOL reported by 'married' respondents may be due to the support that they receive from their spouse. Mean age varied across groups (single 33.5 years, married 54.8 years, separated/divorced 52.1 years and widowed 73.4 years). It is likely that some of the differences identified, particularly aspects of physical functioning, are due to differences in age, rather than marital status itself. The relationships between HRQOL and demographic and disease-related variables are explored further through regression analyses in Chapter 9.

8.4 Discussion

The aim of this chapter was to explore HRQOL in CD as assessed by the CDAQ and SF-36v2. General HRQOL, as measured by the SF-36v2, was lowest for the mental component score (MCS) and domains most associated with aspects of psychological and mental health, particularly vitality (i.e. energy levels and feelings of fatigue). Poorest HRQOL was found for the general health dimension, indicating slightly poorer general health and expectations of health among people with CD. Aspects of physical functioning

were the least affected, with CD having limited impact on the performance of physical activities and pain. The conduct of work and other activities were also minimally impacted by physical problems.

One other UK study (Barratt, Leeds and Sanders, 2011) has explored the HRQOL of people with CD using the SF-36 in a larger sample (n=225). The MCS score of both studies was comparable (47.50 in the current study compared with 47.43), however, the PCS score reported by Barratt et al. was lower than the current study (49.32 in the current study compared with 47.34). Furthermore, Barratt et al. found the vitality, general health, and social functioning domains to be the most impaired. Vitality and general health, but not social functioning, were also the most impaired domains in the current study. It is possible that Barratt et al. found greater physical impairment and poorer vitality and general health scores than the present study due to recruiting through a hospital follow-up clinic.

The results of the current study support the findings of other cross-sectional studies conducted in Germany (Häuser, Gold, Stein et al., 2006) and Finland (Paavola et al., 2012), who also found the vitality and general health domains to be the most impaired.

When compared with a general population sample, HRQOL was generally comparable (i.e. within the 'normal' range), although, for many aspects, scores were towards the lower bound of normal, particularly for psychological and mental health (MCS score) and vitality. The general health and expectations of health reported by people with CD were marginally worse than the general population. When analysed by gender, aspects of

HRQOL remained outside the normal range for females only, with significantly worse psychological and mental health (MCS), general health, and vitality found in females with CD compared with females in the general population. The HRQOL of males was comparable to males in the general population. These findings are consistent with previous research (Hallert, Grännö, Grant et al., 1998; Tontini et al., 2010) which also found the HRQOL of females with CD was worse than the general female population.

An analysis of disease-specific HRQOL, as measured by the CDAQ, found the greatest impact on HRQOL was dietary burden, with many respondents experiencing frequent difficulties with managing a GFD. In a UK study, Whitaker et al. (2009) found that many people with CD regarded following a GFD as a substantial burden, even after being diagnosed for several years. Furthermore, Sverker et al. (2005) also highlighted the burden of managing daily life while following a GFD in a qualitative study of 43 people with CD. Social isolation had the least impact on HRQOL, with many respondents infrequently or never experiencing limitations to their participation in social activities or feelings of isolation. This was a surprising finding as Lee, Ng et al. (2012) found reduced HRQOL was particularly related to social aspects of living with CD, specifically dining out, travelling, and family life. A possible reason for these contradictory findings may be due to differences in the underlying constructs being assessed. For example, in the CDAQ, while avoidance of eating out is an item within the 'social isolation' domain, other items, such as feeling guilty about the impact CD has on friends and family form part of the 'stigma' domain. Lee, Ng et al. do not provide details of item wording used, and therefore, in the absence of this information, it is difficult to fully compare the results.

Analyses evaluating HRQOL by disease and demographic factors found HRQOL was significantly worse in females, those belonging to BME groups, those who are older, have had the condition for longer, and who have a greater number of co-morbidities. Some of these results support the findings of Kurppa, Collin, Mäki et al.'s (2011) review, which also found reduced HRQOL in those with increased co-morbidities and female gender. With regards to disease-specific HRQOL, respondents from a BME background experienced significantly more dietary burden, symptoms, and worries and concerns compared with those from a white background. Dietary adherence was not related to HRQOL, with the exception of dietary burden (i.e. those experiencing greater dietary burden consumed gluten on a more frequent basis). These results support the findings of a systematic review which investigated factors associated with adherence to the GFD (Hall et al. 2009). The review concluded that, overall, adherence to a GFD and HRQOL are not related.

CHAPTER 9:
Relationship between patients' experiences of health care services and HRQOL

9.1 Introduction

The previous two chapters have explored the results of the CD-PEQ and HRQOL questionnaires (the SF-36v2 and CDAQ) respectively. In this chapter, the focus turns to addressing the main research aim, namely, to investigate the relationships between patients' experiences of health care services and HRQOL.

Very few studies have investigated the relationship between patients' experiences of health care services and HRQOL in people with CD. Mahadev et al. (2013) conducted a survey to explore the relationship between dietitian use and HRQOL in an American study. They found that dietitian use was not associated with HRQOL, symptoms, or adherence to a GFD. The findings are limited by the smaller sample size of those who had not seen a dietitian (n=87), and bias of the sample towards those more highly educated and therefore, not representative of the wider population (Mahadev et al., 2013). The study also used the CD-QOL to assess HRQOL, the limitations of which are discussed in Chapter 2.

In a German sample, Häuser, Stallmach et al. (2007) conducted a survey to explore predictors of a reduced HRQOL in people with CD. In terms of the patients' experience, dissatisfaction with information provided from a doctor regarding CD and its treatment

was predictive of reduced HRQOL, as measured by the CDQ. Other predictive factors were poor adherence to the GFD, mental disorders, and co-morbidities.

A further study (Ukkola et al., 2012) also found a relationship between unsatisfactory communication with clinicians and the provision of sparse information, and negative attitudes towards CD and the GFD. This study explored the broader experiences (i.e. perceptions of CD, unmet health care needs, and treatment) of people with CD at diagnosis and again after following a GFD for one year in a Finnish sample. A limitation of the study is that it did not use a validated PROM to assess HRQOL.

While there is limited research exploring the relationship between patients' experiences of health care services and HRQOL in CD, research has been conducted in other conditions. For example, Fitzpatrick, Peters et al. (2010) investigated the relationships between the health and social care experiences of people with Motor Neurone Disease, Multiple Sclerosis, and Parkinson's Disease and their HRQOL, while also investigating the experiences and HRQOL of their carers (Peters, Jenkinson et al., 2013). Other research has focused on specific health care settings, for example, Sizmur and Redding (2009) explored the experiences of hospital inpatients, with the specific aim of identifying which aspects of the patients' experience were most strongly related to patient satisfaction.

In summary, limited research exploring the relationships between patients' experiences of health care services and HRQOL has been conducted in CD, with no research, to the author's knowledge, conducted within the UK. Of the research conducted, the focus, in terms of the patients' experience tends to be quite narrow, focusing on a small number

of aspects, such as the provision of information about CD and the GFD. Furthermore, not all studies have used validated measures to assess HRQOL. Interestingly, the research has found some relationships between patients' experiences and HRQOL, thus suggesting the need for the broader patients' experience and HRQOL to be investigated.

9.1.1 Aims and objectives

The aim of this chapter was to analyse the data (from Survey 2) to investigate the relationships between patients' experiences of health care services and HRQOL in CD. This will be achieved by the following objectives:

- To explore the relationship between the patients' overall experience and HRQOL;
- And to identify aspects of the patients' experience most strongly related to HRQOL.

9.2 Methods

The data that will be used to address the above aim was collected from Survey 2. The survey questionnaire included the CDAQ, CD-PEQ, SF-36v2, and demographic questions, and was sent to 800 members of Coeliac UK. Full details of the survey methodology can be found in Chapter 6.

9.2.1 Statistical methods

Firstly, Pearson's correlation was used to assess associations between HRQOL scores and the 'overall experiences problem score' (i.e. the number of problems experienced with health care services). Following this, backwards stepwise multiple linear regression analyses were conducted to explore the association between experiences of health care services and HRQOL. The models explored disease-specific HRQOL, and therefore, the

dependent variable used in analyses was either the CDAQ overall index score or CDAQ dimension scores. The main independent variable was the 'overall experiences problem score' (as developed in Chapter 7), which summarises the patients' experiences of health care services as a score between 0 and 21 (a higher score means a greater number of problems). The following additional independent variables were included in the model as potential confounders: age, time since diagnosis, number of comorbidities, gender, ethnicity, marital status, and gluten consumption. A list of variables can be found in Table 54.

Table 54. Multiple regression analysis variables

	Variable	Type
Dependent variable	CDAQ overall index score / CDAQ domain score	Continuous
Independent variables	Age (years)	Continuous
	Years since diagnosis	Continuous
	No of comorbidities	Continuous
	Gender	Binary
	0 – Female	
	1 – Male	
	Ethnicity	Binary
	0 – White	
	1 – BME	
	Marital Status[a]	Binary dummy variables
	Single (reference category)	
	Married	
	Separated or divorced	
	Widowed	
	Gluten consumption[a]	Binary dummy variables
	Never (reference category)	
	Rarely	
	Sometimes	
	Often or always	
	Overall experiences problem score	Continuous

[a]Marital status and gluten consumption were coded into dummy variables.

During the backwards stepwise regression analyses, to identify items for removal, the significance of variables in the model (p-value) and multicollinearity (as assessed by the Variance Inflation Factor (VIF)) were assessed. Items were removed one at a time, with the regression analyses re-run after each item removal. For each model, the regression coefficient (B), standard error of the coefficient (SE_B), confidence intervals, and significance values (p 2-sided) are reported. The proportion of variance in the dependent variable explained by the independent variables is reported using adjusted R^2. The residuals for all models were found to be normally distributed as assessed by a visual inspection of the Normal Q-Q Plot (Standardized Residuals). The level of statistical significance for all analyses was set at $P < 0.05$ (two-sided). Data was analysed using IBM SPSS Statistics 20.

9.3 Results

9.3.1 Correlations between 'overall experiences problem score' and CDAQ dimensions

Correlations between the 'overall experiences problem score' and CDAQ scores were investigated (see Table 55).

Table 55. Associations between experiences of health care services and HRQOL

Variable	CDAQ dimension	r	p (2-tailed)[a]
Overall experiences problem score	Overall index score	-0.508	**<0.001**
	Stigma	-0.477	**<0.001**
	Dietary burden	-0.347	**<0.001**
	Symptoms	-0.387	**<0.001**
	Social isolation	-0.477	**<0.001**
	Worries and concerns	-0.447	**<0.001**

[a]P<0.05

The results show that an increase in the number of problems experienced with health care services were statistically significantly related to greater stigma, increased dietary burden, more symptoms, greater social isolation, more worries and concerns, and worse overall disease-specific HRQOL (i.e. a decrease in CDAQ scores). All correlations were significant and moderate to strong, with the strongest correlation found between the 'overall experiences problem score' and the CDAQ overall index score (r=-0.508, p<0.001) (Figure 13).

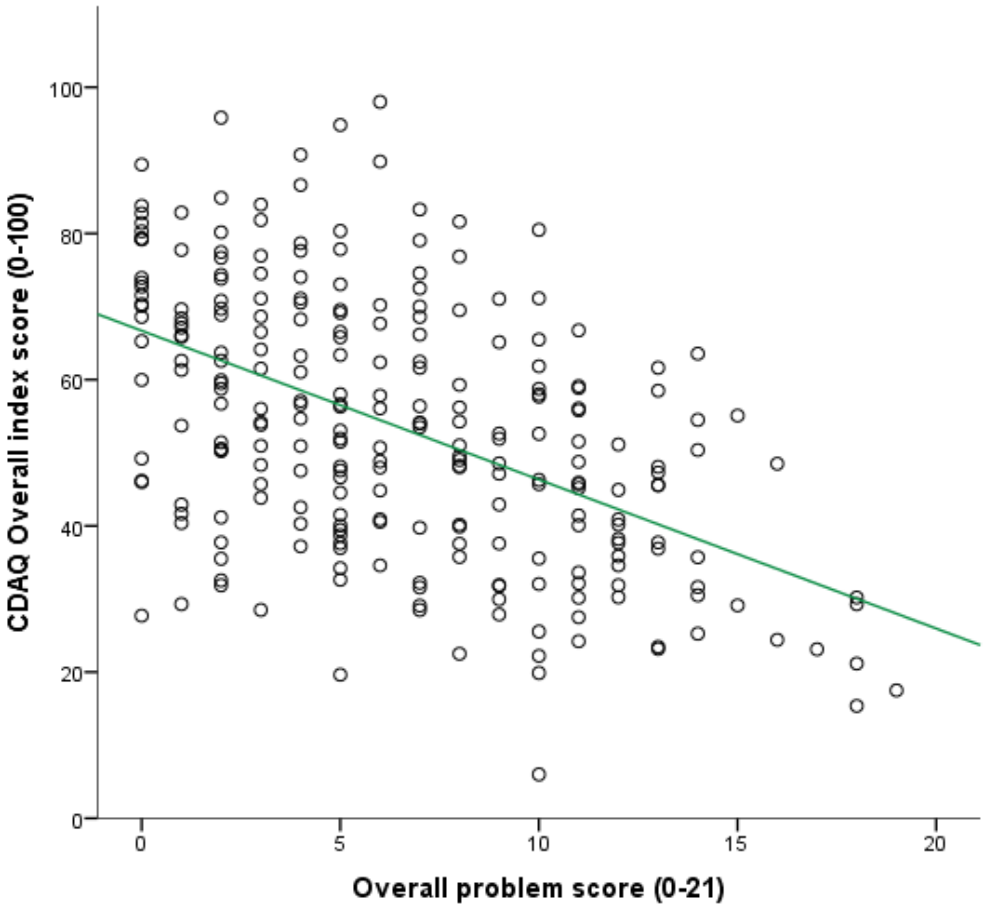


Figure 13. Correlation between patients' experiences of health care services and HRQOL

In order to explore whether these significant relationships between experiences of health care services and HRQOL remain while adjusting for demographic and disease-related variables, regression analyses were performed.

9.3.2 Regression analyses with 'overall experiences problem score' as an independent variable

Six regression models were built, one with the CDAQ overall index score as the dependent variable, and a further five with the CDAQ dimension scores as the dependent variable. The initial regression models showing all variables, prior to deleting any items, are found in Appendix QQ. The final model for each analysis, after deleting items to leave significant variables only, is presented below.

Association between 'overall experiences problem score' and CDAQ overall index score

The relationship between the overall experiences problem score and the CDAQ overall index score remained statistically significant ($p<0.001$) after adjusting for disease-related and demographic variables (i.e. confounding factors). Regression coefficients for significant variables are found in Table 56. More problems with health care services, younger age, a greater number of co-morbidities, female gender and BME ethnicity are statistically significantly associated with lower CDAQ overall index scores (i.e. poorer HRQOL). These variables accounted for 36.8% of the variability in the CDAQ overall index score.

Table 56. Multiple regression analysis - dependent variable: CDAQ overall index score (final model)

Variable	B	SE_B	95% Confidence Interval		p
Intercept	56.790	3.615	49.670	63.910	<0.001
Age	0.187	0.056	0.078	0.297	0.001
Gender (male)	6.035	1.982	2.130	9.940	0.003
No of comorbidities	-2.870	0.683	-4.215	-1.525	<0.001
Ethnicity (BME)	-6.473	2.905	-12.197	-0.750	0.027
Overall experiences problem score	-1.487	0.224	-1.929	-1.046	<0.001

R^2=0.381, Adjusted R^2=0.368, F(5,242) = 29.740, p<0.001

Association between 'overall experiences problem score' and CDAQ stigma score

The relationship between the overall experiences problem score and CDAQ stigma score remained statistically significant (p<0.001) after controlling for confounding variables (Table 57). More problems with health care services, younger age, a greater number of co-morbidities, and female gender are statistically significantly associated with lower stigma scores (i.e. greater feeling of stigma). Variables in the final model accounted for 33.3% of the variability in the CDAQ stigma score.

Table 57. Multiple regression analysis - Dependent variable: CDAQ stigma score (final model)

Variable	B	SE_B	95% Confidence Interval		p
Intercept	46.664	4.304	38.188	55.140	<0.001
Age	0.324	0.066	0.193	0.455	<0.001
Gender (male)	7.675	2.356	3.034	12.315	0.001
No of comorbidities	-2.455	0.813	-4.055	-0.855	0.003
Overall experiences problem score	-1.477	0.270	-2.009	-0.945	<0.001

R^2=0.344, Adjusted R^2=0.333, F(4,250) = 32.735, p<0.001

Association between 'overall experiences problem score' and CDAQ dietary burden score

After controlling for confounding factors, the relationship between the overall experiences problem score and CDAQ dietary burden score remained statistically significant (p<0.001) (Table 58). More problems with health care services, those diagnosed more recently, females, and those consuming gluten sometimes, often or always, are statistically significantly associated with lower dietary burden scores (i.e. greater dietary burden). Variables in the final model accounted for 18.0% of the variability in the CDAQ dietary burden score. All variables were significant in the final model (with the exception of the rarely consumes gluten group).

Table 58. Multiple regression analysis - Dependent variable: CDAQ dietary burden score (final model)

Variable	B	SE_B	95% Confidence Interval		p
Intercept	42.895	2.645	37.685	48.104	<0.001
Years since diagnosis	0.408	0.125	.161	.656	**0.001**
Gender (male)	6.303	2.332	1.709	10.897	**0.007**
Consumes gluten - rarely	-2.120	3.086	-8.199	3.959	0.493
Consumes gluten - sometimes	-8.781	3.717	-16.104	-1.458	**0.019**
Consumes gluten - often or always	-20.220	7.888	-35.758	-4.681	**0.011**
Overall experiences problem score	-1.163	0.255	-1.664	-.661	**<0.001**

R^2=0.200, Adjusted R^2=0.180, F(6,239) = 9.947, p<0.001

Association between 'overall experiences problem score' and CDAQ symptoms score

After controlling for confounding variables, the relationship between the overall experiences problem score and CDAQ symptoms score remained statistically significant (p<0.001) (Table 59). More problems with health care services, together with younger age, female gender, a greater number of co-morbidities, BME ethnicity, those consuming gluten sometimes, and those who are separated or divorced are statistically significantly associated with lower symptoms scores (i.e. greater symptoms). Significant variables accounted for 32.2% of the variability in the CDAQ symptoms score. All variables were significant in the final model (with the exception of the married and widowed categories of marital status, and rarely and often or always categories of gluten consumption).

Table 59. Multiple regression analysis - Dependent variable: CDAQ symptoms score (final model)

Variable	B	SE_B	95% Confidence Interval		p
Intercept	62.662	5.136	52.544	72.780	<0.001
Age	0.208	0.091	0.028	0.388	0.024
Gender (male)	8.202	2.715	2.854	13.550	0.003
No of comorbidities	-5.008	0.939	-6.858	-3.158	<0.001
Ethnicity (BME)	-8.599	4.110	-16.696	-0.502	0.037
Marital status – married	3.890	3.381	-2.769	10.549	0.251
Marital status – separated or divorced	-11.524	5.835	-23.018	-0.031	0.049
Marital status – widowed	6.095	7.454	-8.589	20.778	0.414
Consumes gluten - rarely	-0.680	3.555	-7.683	6.324	0.849
Consumes gluten - sometimes	-10.881	4.260	-19.273	-2.489	0.011
Consumes gluten - often or always	10.103	9.358	-8.332	28.537	0.281
Overall experiences problem score	-1.348	0.311	-1.960	-0.736	<0.001

R^2=0.351, Adjusted R^2=0.322, F(11,243) = 11.968, p<0.001

Association between 'overall experiences problem score' and CDAQ social isolation

The relationship between the overall experiences problem score and CDAQ social isolation score remained statistically significant (p<0.001) after controlling for confounding factors (Table 60). More problems with health care services, female gender, and a greater number of co-morbidities are statistically significantly associated with lower social isolation scores (i.e. greater social isolation), with variables accounting for 28.5% of the variability in the CDAQ social isolation score.

Table 60. Multiple regression analysis - Dependent variable: CDAQ social isolation score (final model)

Variable	B	SE_B	95% Confidence Interval		p
Intercept	84.525	2.816	78.980	90.071	<0.001
Gender (male)	5.736	2.616	0.584	10.887	0.029
No of comorbidities	-3.069	0.872	-4.785	-1.352	0.001
Overall experiences problem score	-2.269	0.277	-2.814	-1.723	<0.001

R^2=0.293, Adjusted R^2=0.285, F(3,252) = 34.837, p<0.001

Association between 'overall experiences problem score' and CDAQ worries and concerns score

The relationship between the overall experiences problem score and the CDAQ worries and concerns score remained statistically significant ($p<0.001$) after controlling for confounding factors (Table 61). More problems with health care services, younger age, and a greater number of co-morbidities are statistically significantly associated with lower worries and concerns scores (i.e. greater worry and concern). Variables accounted for 22.2% of the variability in the CDAQ worries and concerns score.

Table 61. Multiple regression analysis - Dependent variable: CDAQ worries and concerns score (final model)

Variable	B	SE_B	95% Confidence Interval		p
Intercept	54.943	4.459	46.160	63.725	<0.001
Age	0.180	0.069	0.043	0.317	0.010
No of comorbidities	-2.319	0.840	-3.974	-0.665	0.006
Overall experiences problem score	-1.677	0.284	-2.238	-1.117	<0.001

R^2=0.231, Adjusted R^2=0.222, F(3,252)= 25.206, p<0.001

The relationship between patients' experiences of health care services and HRQOL was statistically significant in all models, suggesting that, even after accounting for confounding factors, HRQOL decreases as the number of problems with health care services increase. Female gender, a greater number of co-morbidities and younger age were also frequently associated with lower CDAQ scores (i.e. worse HRQOL). While important and interesting, using an overall experiences problem score does not allow health care providers to identify which aspects of health care to change to improve HRQOL. In order to identify aspects of health care services that have the strongest relationship with HRQOL, further regression analyses were conducted, the results of which are presented next.

9.3.3 Regression analyses with individual patient experience items as independent variables

In total, a further six regression analyses were conducted. The dependent variables and confounding factors remained the same as in the previous analyses (see Table 54), but instead of including the 'overall experiences problem score' as the main independent variable, the 21 individual items that comprise the 'overall experiences problem score' were included in its place. For details of these individual items see Table 38, p. 213.

Association between individual patient experience items and the CDAQ overall index score

Aspects of health care services most strongly related to the CDAQ overall index score, after accounting for confounding factors, were HCPs not listening before diagnosis, difficulties obtaining prescriptions, receiving inconsistent information and advice, and problems with dietary advice. These variables, together with age, gender, number of co-morbidities, years since diagnosis, and ethnicity, accounted for 36.6% of the variability in the CDAQ overall index score (Table 62). Younger age, female gender, a greater number of co-morbidities, fewer years since diagnosis, BME ethnicity, and an increased number of problems with the above aspects of health care services are statistically significantly associated with lower CDAQ overall index scores (i.e. poorer HRQOL).

Table 62. Multiple regression analysis - Dependent variable: CDAQ overall index score (final)

Variable	B	SE_B	95% CI		p
Intercept	52.491	3.270	46.047	58.935	<0.001
Age	0.165	0.058	0.050	0.280	0.005
Gender (male)	8.006	2.055	3.955	12.056	<0.001
No of comorbidities	-2.679	0.719	-4.096	-1.262	<0.001
Years since diagnosis	0.225	0.108	0.013	0.438	0.038
Ethnicity (BME)	-7.161	2.984	-13.041	-1.282	0.017
8a – HCP didn't listen	-6.396	2.036	-10.408	-2.384	0.002
33 – Difficulties obtaining prescriptions	-5.714	2.435	-10.512	-0.917	0.020
42 – Inconsistent information and advice	-7.006	2.599	-12.126	-1.886	0.008
Dietary advice score	-5.050	2.022	0.013	-9.035	0.013

R^2=0.390, Adjusted R^2=0.366, F(9,228)= 16.196, p<0.001

Association between individual patient experience items and the CDAQ stigma score

After accounting for the confounding factors of age and gender, aspects of health care services most strongly related to the CDAQ stigma score were being informed of the CD diagnosis unprofessionally, receiving inconsistent information and advice, and a lack of confidence in HCPs. These variables accounted for 34.1% of the variability in the CDAQ stigma score (Table 63). Younger age, female gender, more co-morbidities, and problems with the above-mentioned aspects of care are statistically significantly associated with lower CDAQ stigma scores (i.e. greater feelings of stigma).

Table 63. Multiple Regression Analysis - Dependent variable: CDAQ Stigma score (final model)

Variable	B	SE_B	95% Confidence Interval		p
Intercept	40.872	3.644	33.695	48.050	<0.001
Age	0.384	0.062	0.261	0.507	<0.001
Gender (male)	6.948	2.357	2.305	11.591	0.004
No of comorbidities	-2.659	0.808	-4.250	-1.068	0.001
13 – Informed of diagnosis unprofessionally	-7.008	2.600	-12.129	-1.887	0.008
42 – Inconsistent information and advice	-11.834	2.969	-17.682	-5.985	<0.001
8b – Lack of confidence in HCP	-5.833	2.325	-10.413	-1.254	0.013

R^2=0.356, Adjusted R^2=0.341, F(6,248) = 22.867, p<0.001

Association between individual patient experience items and the CDAQ dietary burden score

The CDAQ dietary burden score was most strongly related to difficulties obtaining prescriptions, information and advice not being available when needed, a perception that GP's lack knowledge of CD, and problems with dietary advice. Together with significant confounding factors, these variables accounted for 19.7% of the variability in the CDAQ dietary burden score. Along with problems with the aspects of health care services mentioned above, female gender, a shorter time since diagnosis, and consuming gluten sometimes, often or always were statistically significantly associated with lower CDAQ dietary burden scores (i.e. greater dietary burden).

Table 64. Multiple regression analysis - Dependent variable: CDAQ dietary burden score (final model)

Variable	B	SE_B	95% Confidence Interval		p
Intercept	43.871	2.762	38.430	49.312	<0.001
Gender (male)	5.949	2.370	1.280	10.619	0.013
Years since diagnosis	0.408	0.125	0.162	0.653	0.001
Consumes gluten – rarely	-3.121	3.083	-9.195	2.953	0.312
Consumes gluten – sometimes	-7.813	3.750	-15.201	-0.424	0.038
Consumes gluten – often or always	-20.438	7.807	-35.817	-5.059	0.009
33 – Difficulties obtaining prescriptions	-5.563	2.783	-11.045	-0.081	0.047
38 – Information and advice not available	-5.836	2.507	-10.775	-0.898	0.021
41d –GPs lack knowledge of CD	-5.202	2.600	-10.324	-0.080	0.047
Dietary advice score	-4.810	2.384	-9.506	-0.113	0.045

R^2=0.226, Adjusted R^2=0.197, F(9,236) = 7.657, p<0.001

Association between individual patient experience items and the CDAQ symptoms score

Receiving inconsistent information and advice, and problems with dietary advice were strongly related to the CDAQ symptoms score. Younger age, female gender, BME ethnicity, sometimes consuming gluten, and a greater number of co-morbidities were statistically significantly associated with lower CDAQ symptoms scores (i.e. worse

symptoms) (Table 65). These variables accounted for 30.7% of variability in the CDAQ symptoms score.

Table 65. Multiple regression analysis - Dependent variable: CDAQ symptoms score (final model)

Variable	B	SE_B	95% Confidence Interval		p
Intercept	53.890	4.133	45.749	62.031	<0.001
Age (years)	0.329	0.073	0.186	0.472	<0.001
Gender (male)	9.721	2.734	4.336	15.107	<0.001
Ethnicity (BME)	-10.717	4.147	-18.885	-2.549	0.010
Consumes gluten – rarely	-0.474	3.565	-7.497	6.548	0.894
Consumes gluten – sometimes	-9.911	4.309	-18.397	-1.424	0.022
Consumes gluten – often or always	15.243	9.583	-3.633	34.119	0.113
No of comorbidities	-4.863	0.942	-6.720	-3.007	<0.001
42 – Inconsistent information and advice	-7.957	3.572	-14.993	-0.920	0.027
Dietary advice score	-8.818	2.739	-14.213	-3.422	0.001

R^2=0.332, Adjusted R^2=0.307, F(9,245) =13.532, p<0.001

Association between individual patient experience items and the CDAQ social isolation score

Health care professionals not listening prior to diagnosis, not enough information throughout diagnosis, difficulties obtaining prescriptions, and a lack of information and advice available when needed were aspects of health care services that were strongly related to CDAQ social isolation scores (Table 66). Problems with these aspects of health care, together with younger age, female gender, and a greater number of co-morbidities were statistically significantly related to lower CDAQ social isolation scores (i.e. greater social isolation). These variables accounted for 31.2% of the variability in the CDAQ social isolation score.

Table 66. Multiple regression analysis - Dependent variable: CDAQ social isolation score (final model)

Variable	B	SE_B	95% Confidence Interval		p
Intercept	69.441	4.219	61.131	77.751	<0.001
Age (years)	0.223	0.072	0.082	0.365	0.002
Gender (male)	5.181	2.598	0.064	10.298	0.047
No of comorbidities	-3.603	0.907	-5.390	-1.816	<0.001
8a – HCP did not listen	-11.205	2.613	-16.352	-6.058	<0.001
11 – Not enough information throughout diagnosis	-8.619	3.211	-14.943	-2.296	0.008
33 – Difficulties obtaining prescriptions	-6.650	3.146	-12.847	-0.453	0.036
38 – Information and advice not available	-7.132	2.807	-12.661	-1.603	0.012

R^2=0.331, Adjusted R^2=0.312, F(7,248) = 17.537, p<0.001

Association between individual patient experience items and the CDAQ worries and concerns score

Aspects of health care services most strongly related to the CDAQ worries and concerns score were problems with information and advice not being available when needed, inconsistent information and advice, being informed of the CD diagnosis unprofessionally, and problems with dietary advice (Table 67). These problems together with younger age, a greater number of co-morbidities, and frequency of gluten consumption were statistically significantly related to worse CDAQ worries and concerns scores (i.e. greater worry and concern). The variables accounted for 21.3% of variability in the CDAQ worries and concerns score.

Table 67. Multiple regression analysis - Dependent variable: CDAQ worries and concerns score (final model)

Variable	B	SE_B	95% Confidence Interval		p
Intercept	46.152	3.985	38.303	54.000	<0.001
Age (years)	0.247	0.067	0.115	0.379	<0.001
No of comorbidities	-2.435	0.849	-4.108	-0.762	0.005
Consumes gluten – rarely	7.227	3.290	0.747	13.708	0.029
Consumes gluten – sometimes	4.891	4.016	-3.019	12.802	0.224
Consumes gluten – often or always	4.491	8.631	-12.510	21.492	0.603
38 – Information and advice not available	-5.631	2.806	-11.157	-0.104	0.046
42 – Inconsistent information and advice	-6.916	3.376	-13.565	-0.267	0.042
13 – Informed of diagnosis unprofessionally	-6.623	2.860	-12.257	-0.989	0.021
Dietary advice	-5.448	2.547	-10.465	-0.430	0.033

R^2=0.241, Adjusted R^2=0.213, F(9,245) = 8.648, p<0.001

A lack of confidence in HCPs, and HCPs not listening prior to diagnosis were highly correlated, and in most cases, either variable could have been included in the final model.

9.4 Discussion

The aim of this chapter was to investigate the relationships between patients' experiences of health care services and HRQOL. Correlations and regression analyses were calculated to explore these relationships. The results indicate that patients' experience of health care services have a moderate to strong relationship with all aspects of HRQOL. These relationships persist when accounting for confounding factors, such as age, gender, and number of years since diagnosis.

Further analyses to explore which aspects of health care services are most strongly related to HRQOL found that problems with the provision of information and communication with HCPs were the key issues. Aspects of information provision were strongly related to all aspects of disease-specific HRQOL, with inconsistent information

and advice, poor access to information and advice, especially dietary advice, particular issues. One or more problems with communication, specifically HCPs not listening carefully prior to diagnosis and being informed of a CD diagnosis unprofessionally, were strongly related to the CDAQ overall index score, and the stigma, social isolation, and worries and concerns CDAQ dimensions.

The final regression models accounted for between 19.7 – 36.6% of the variability within the dependent variable (i.e. the CDAQ scores). The variability was the lowest for the dietary burden (19.7%) and worries and concerns (21.3%) domains, indicating that other aspects related to variation within these domains had not been captured by the model. This is common when investigating aspects of human behaviour.

The results of this analysis and recommendations arising from this research are discussed in depth in the concluding chapter.

CHAPTER 10:
Discussion and conclusions

10.1 Introduction

The aim of this thesis was to develop a PROM and patient experience questionnaire for adults with CD and use these to investigate the relationship between the HRQOL of adults with CD and their experiences of health care services. The questionnaires, named the Coeliac Disease Assessment Questionnaire (CDAQ) and the Coeliac Disease Patient Experience Questionnaire (CD-PEQ), were developed following an extensive process which included qualitative and cognitive interviews, input from experts, a translatability assessment, and a cross-sectional survey. The CDAQ and CD-PEQ were used in a second cross-sectional survey, the findings of which are discussed in this final chapter, along with the study's strengths and limitations, and suggestions for further research.

10.2 Discussion

The findings of the HRQOL questionnaires and the patient experience questionnaire will be discussed separately, prior to investigating the relationship between patients' experiences of health care services and HRQOL.

10.2.1 Health-related quality of life

General health-related quality of life

This study found psychological health (i.e. MCS score), vitality and general health, as measured by the SF-36v2, to be aspects of HRQOL that were most affected, with physical functioning the least affected. Other large cross-sectional studies, conducted in Germany

(Häuser, Gold, Stein et al., 2006) and Finland (Paavola et al., 2012), also found the vitality and general health domains to be the most reduced. Only one study (Barratt, Leeds and Sanders, 2011) within the UK has previously used the SF-36 in a large sample (i.e. n > 50) of adults with CD, recruiting 225 patients attending hospital follow-up, and presenting their HRQOL results by level of dietary adherence (i.e. full adherence / partial or no adherence). Comparing the results of the current study with that of Barratt et al., found that in those reporting full adherence, the MCS score was comparable (47.50 vs. 47.43), while the PCS score in the current study was slightly higher (49.32 vs. 47.34), indicating marginally better physical health. Barratt et al. found the vitality, general health, and social functioning domains to be the most impaired, with scores in the current study higher (VT: 50.63 vs. 43.0; GH: 58.40 vs. 43.0; SF: data not reported). The demographic characteristics of respondents in both studies were similar (in terms of gender, time since diagnosis, and proportion fully adherent), and therefore, it is possible that the difference in scores is due to the recruitment method. Those receiving hospital follow-up care may be experiencing worse health than those recruited through a support association.

The HRQOL of people in this study was found to be comparable to the general population, however, many aspects, particularly psychological health (MCS score) and vitality, were towards the lower bound of the normal range. These findings are consistent with previous research, which found aspects of mental health to be worse in people with CD, particularly anxiety and depression (Addolorato et al., 2008; Zingone, Siniscalchi et al., 2010; Zingone, Swift et al., 2015). With regards to vitality (i.e. feelings of fatigue), existing evidence shows that fatigue is a recognised symptom of CD (Zingone, Swift et al., 2015), however, there is mixed evidence regarding the persistence of fatigue

while following a GFD. Siniscalchi et al. (2005) found that people with CD had higher levels of fatigue than healthy controls both at diagnosis and in those following a GFD, while Pulido et al. (2013) found an improvement in fatigue over time in a large Canadian sample. A review (Zingone, Swift et al., 2015) of psychological morbidity in CD reports that there is a lack of evidence to conclude whether following a GFD alleviates fatigue. The current study found that levels of vitality were weakly correlated with length of time since diagnosis, with vitality improving as time since diagnosis increases. This provides some evidence to support the findings from Pulido et al.'s (2013) study.

When analysed by gender, the HRQOL of females with CD was significantly worse than the female general population, although the HRQOL of males with CD was comparable to males in the general population. These findings were expected, and are consistent with previous results (Hallert, Grännö, Grant et al., 1998; Tontini et al., 2010). Sverker et al. (2009) explored everyday dilemmas experienced by men and women with CD, and found that women experience greater cognitive burden around household work and food preparation, for which they were primarily responsible, which was further impacted by managing these burdens alongside other responsibilities, such as paid work. Reduced vitality in women with CD may also contribute towards these findings.

Disease-specific health-related quality of life

Dietary burden was found to have the greatest impact on disease-specific HRQOL, with annoyance about the cost of gluten-free substitute foods, frustrations about the choice of suitable food, and cravings for food and drinks containing gluten the most frequently occurring issues. This is not surprising, as Shah et al. (2014) found the burden of

following a GFD to be comparable with the treatment burden of end stage renal disease, and greater than that of other chronic conditions, such as hypertension.

This research found a significant relationship between dietary burden and adherence, suggesting that those experiencing greater dietary burden consume gluten on a more frequent basis (although cause and effect cannot be determined). Dietary burden was not significantly associated with any other aspect of HRQOL or overall HRQOL. These results are in line with the findings of a systematic review by Hall et al. (2009), the aim of which was to investigate factors associated with GFD adherence. Hall et al. conceded that while they found mixed evidence regarding the relationship between adherence and HRQOL, they conclude that overall the evidence suggests they are not related. The findings of this study suggest that further research exploring the relationship between dietary adherence and dietary burden is needed.

Social isolation had the least impact on HRQOL, with avoidance of social activities, daily activities being limited by CD, and feeling isolated from others the least frequently occurring issues. This is a surprising finding as participants in qualitative studies, including this research, frequently raise issues of this nature. For example, Sverker et al. (2005) asked participants to recall dilemmas they had faced in everyday life, and approximately 40% of the issues raised were about eating meals with others outside of the home. A possible explanation for this is the increase in awareness of the GFD and provision of gluten-free food in restaurants and supermarkets over recent years. This is partially as a result of an increased number of people choosing to follow a GFD, for example, as a lifestyle choice, with those on a GFD in the UK estimated to be

approximately 8.5 million (BBC, 2016). This increased awareness and provision is likely to make it easier for people with CD to participate in activities than it previously would have been.

Health-related quality of life and demographic factors

In this study, HRQOL was significantly worse in females, those belonging to BME groups, those who are older, have been diagnosed for longer, and who have more co-morbidities. The finding that HRQOL is worse in females is consistent with previous studies (Norström et al., 2011; Zarkadas et al., 2006). Reasons for this difference is unknown, but some have suggested that women perceive the burden of CD as greater than men and have more concerns about the impact of CD on socialising (Hallert, Grännö, Hultén et al., 2002).

While no literature could be found exploring the relationship between HRQOL and ethnicity, research by Butterworth et al. (2005) has explored clinical differences between White Caucasians and South Asians living in Britain. The research found South Asians were more likely to experience vitamin D and iron deficiency, and less likely to have symptoms of irritable bowel syndrome. Differences in HLA status were also found. It is possible that clinical differences are related to HRQOL. Research in India (Rajpoot and Makharia, 2013) has also identified barriers to following a GFD in Indian patients, commenting that girls can face adherence issues following marriage. The reasons for this are not stated, but it is possible that it is due to cultural issues, which may translate to Indians living in the UK. Further research is needed to explore the relationship between

ethnicity and HRQOL and determine the reasons for any differences in order to ensure that adequate support is provided.

10.2.2 Measuring health-related quality of life in coeliac disease

Measurement instruments available to assess HRQOL in CD were explored as part of this thesis. A systematic review identified two existing disease-specific measures of HRQOL in CD, the Celiac Disease Questionnaire (CDQ) (Häuser, Gold, Stallmach et al., 2007) and the Coeliac Disease Quality of Life Survey (CD-QOL) (Dorn et al., 2010). Limitations were identified in the development of both measures and therefore, a further aim of this thesis was to develop a new measure to assess the HRQOL of adults with CD. To achieve this, a new PROM, the Coeliac Disease Assessment Questionnaire (CDAQ), was developed in accordance with best practice guidelines, resulting in a 32-item questionnaire assessing the following five dimensions: stigma; dietary burden; symptoms; social isolation; and worries and concerns. As well as documenting the processes undertaken to develop the CDAQ, this thesis has also presented evidence supporting its reliability and validity.

The CDAQ has been developed in accordance with FDA guidelines, with candidate items drafted following qualitative interviews with people with CD. By including people with CD in the CDAQ's development, the measure includes issues of relevance to people living with the condition, resulting in a measure with good content validity. The process used to develop the CDAQ compares favourably with that of the CDQ, which did not utilise interviews or focus groups as part of its development, thus potentially limiting its content validity. While the CD-QOL utilised focus groups as part of its development, limited diversity in the demographics of the sample, together with item reduction performed by

experts, also potentially limit its content validity. Also, the CD-QOL does not contain any items about symptoms, which were identified by participants in this research as important.

While the CDAQ has good content validity, it was not possible to include some aspects of HRQOL in the final questionnaire. These items addressed events that typically occur less frequently, for example, holidays and medical tests. While these aspects were identified as issues of importance in the qualitative interviews, their inclusion in the CDAQ, which asks about experiences during the past four weeks, resulted in high ceiling effects and therefore, they were removed. Depending on the purpose of administering the CDAQ, these issues could be included as separate questions following the CDAQ. While the issues would not be captured in CDAQ scores, it would allow the information to be gathered, which may inform care on an individual level.

The CDAQ has good internal consistency, test-retest reliability, construct validity, and low levels of missing data. Further research to evaluate the CDAQ's responsiveness to change is currently underway.

The CDAQ has been made available for use by others[27] and can be used in research studies, including clinical trials, and there is potential for it to be used in clinical practice. One area where the CDAQ could prove very useful is in clinical trials which assess the effectiveness of new drug treatments for CD. There is increasing interest in the development of drugs to treat CD, with a number of different drugs currently in

[27] The CDAQ is managed by Oxford University Innovation Ltd.

development, with some having reached Phase 2 clinical trials (i.e. trials assessing the drug's effectiveness), including Alvine Pharmaceuticals' ALV003, Alba Therapeutics' AT-1001 and ImmusanT's Nexvax2 (Gottlieb et al., 2015). Some drug treatments are designed to be taken alongside a GFD to reduce the effect of inadvertent gluten consumption, for example, ALV003 is an enzyme which breaks down gluten to prevent intestinal damage (Gottlieb et al., 2015). Other treatments aim to allow people with CD to return to a gluten-containing diet, for example, Nexvax2 is a vaccine that aims to restore gluten tolerance (Gottlieb et al., 2015).

There is ongoing debate surrounding the best endpoints to assess the success of drug treatments in CD (Gottlieb et al., 2015). While an assessment of histology and serology (e.g. intestinal damage and biomarkers in the blood) is necessary, the FDA have recently highlighted the importance of assessing patient-reported outcomes, and in fact, state that demonstrating the effect of treatments on how patients 'feel, function, and survive' should be the main goal (Solis, 2015). The CDAQ measures the impact of CD on HRQOL, and therefore, it is well-placed for inclusion as an endpoint in clinical trials to assess the impact of drug treatments on patients' HRQOL. The results of this study further highlight the need to include measures of HRQOL in clinical trials, as the greatest impact on HRQOL was the burden of managing a GFD. Furthermore, as the CDAQ has been developed in accordance with FDA guidelines, evidence gathered regarding the impact of treatments can be used by companies as evidence towards labelling claims.

10.2.3 Patients' experiences of health care services

Aspects of health care services that were identified as the most problematic were generally focused on access to care, and knowledge of HCPs. With regards to follow-up care, the present study found that only 59.3% of respondents reported that they receive regular follow-up care, with a quarter of those not currently receiving care stating that they would like to do so. These findings are similar to previous research conducted in the UK (Bebb et al., 2006), which found 62% of people with CD received follow-up care, indicating that despite guidelines stating that all people with CD should be offered a review (PCSG, 2006; Ciclitira et al., 2010; NICE, 2015), in practice this is not occurring. The current study found most respondents' preference was follow-up with a hospital doctor or consultant, with few stating a preference to see a dietitian. This contrasts with previous findings where patients expressed a preference to see a dietitian with a doctor available (Bebb et al., 2006). The reason for this difference may be due to the current study asking respondents to select one HCP only. It is possible that respondents' preferences are associated with perceived knowledge of the HCP, as few perceived specialists to lack knowledge of CD, with more perceiving dietitians and GPs to lack this knowledge.

Of those receiving regular follow-up care, very few respondents (17.6%) reported that their appointment included an assessment of emotional well-being, despite evidence of higher levels of anxiety and depression in people with CD compared with the general population (Fera et al., 2003; Addolorato et al., 2001). The current study also found evidence of reduced psychological well-being, which, when analysed by gender, was outside the normal range for females only (i.e. females had worse psychological well-

being (as measured by the SF-36 MCS) than the general population). The importance of assessing emotional well-being should be stressed and could be included in the NICE guidelines as an aspect that should be reviewed as part of follow-up care. The Government's '*Five Year Forward View*' (National Health Service, 2014) has highlighted the need to integrate physical and mental health, something that is particularly important in helping people with long-term conditions to adapt and manage their health condition effectively (Naylor et al., 2016).

Poor follow-up may, to some extent, be due to a lack of guidance provided by relevant authorities. For example, the NICE guidance has only recently been extended to incorporate the management of CD (NICE, 2015), with the previous version (NICE, 2009) covering the diagnosis of CD only. There is also a discrepancy between the depth and clarity of information provided, with a clear pathway set out to diagnose CD, but somewhat vague guidance regarding how and when follow-up should occur. It is possible that as evidence regarding best practices around follow-up emerge, the clarity of guidance will improve, and improvements to services will follow.

A review of follow-up care within the UK (Kurien et al., 2016) also found significant variations in care provided and conclude that, at present, services do not have adequate funding to provide equitable care for everyone with CD. There is potential for the CDAQ to be used in clinical practice as a remote monitoring tool to assist in the identification of those struggling to manage their condition. This would enable those that may benefit from a review to be identified, while minimising the burden on the NHS and on people who do not require additional support.

Access to dietary advice and knowledge of HCPs were also found to be key aspects of health care services that require improvement, and are discussed in the next section of this chapter.

10.2.4 Relationship between health-related quality of life and experiences of health care services

This research has shown that patients' experiences of health care services have a moderate to strong correlation with HRQOL, with the relationship remaining after adjusting for confounding factors. While cause and effect cannot be determined, due to a cross-sectional study design, it can be speculated that the results mean that either poor experiences of services lead to poor HRQOL, or those with poorer HRQOL are not getting the support that they need and therefore report their experience of health care services as poor, or a combination of these factors. Either way, it would seem that improving health care services would result in an improvement in HRQOL.

Further in-depth analyses found that the aspects of patients' experience of health care most strongly related to HRQOL were: (1) the consistency and provision of information; (2) communication with HCPs; (3) difficulties obtaining prescriptions; and (4) perceived knowledge of GPs.

(1) The consistency and provision of information

The consistency and provision of information was strongly related to all aspects of disease-specific HRQOL and overall disease-specific HRQOL. Aspects of health care services that were most strongly related were regarding poor access to information and advice, particularly dietary advice, and inconsistent information and advice.

The current study found that a quarter of respondents felt that they did not receive enough information at the time of diagnosis, the majority (86.2%) of respondents had seen a dietitian following their diagnosis, with most (82.7%) finding the appointment helpful. Access to dietary advice has been explored in other studies outside the UK (Zarkadas et al., 2006; Ukkola et al., 2012; Mahadev et al., 2013), with access to dietary advice found to be slightly lower in these previous studies (76–79%). The Finnish study (Ukkola et al., 2012), asked respondents to rate the quality of information provided, with only 12% considering the information provided insufficient. This is consistent with the findings of the Canadian study (Zarkadas et al., 2006), which found that 76% rated the quality of information as good, very good, or excellent. In addition, Zarkadas et al. asked respondents what would contribute the most to improving the lives of people with CD, with 12.9% selecting better information about the diet.

While most respondents were able to see a dietitian following their diagnosis, something which was generally helpful to the respondent, the waiting time between diagnosis and the first dietetic appointment was perceived as too long by approximately a fifth of respondents. This issue was identified to a greater extent (49% compared with 21.6%) by Ukkola et al. (2012).

Consistent with the findings of this study are that of Häuser, Stallmach et al. (2007), who found that dissatisfaction with information provided by doctors was predictive of reduced HRQOL, as measured by the CDQ. In contrast to the findings of the current study, a USA survey (Mahadev et al., 2013) concluded that seeing a dietitian was not related to

HRQOL. While Mahadev et al. analysed their data according to whether or not patients had seen a dietitian, the current study also took in to account the patients' preference (i.e. whether or not they had seen a dietitian and whether or not they wanted to see a dietitian). For those already well versed in the GFD, because another family member has the condition for example, they may not feel it necessary to see a dietitian. This difference in analysis could explain the difference in findings. In addition, the current study used a composite score, which as well as access to a dietitian following diagnosis, also took into account the helpfulness and speed of access to appointments.

While most people are able to see a dietitian following diagnosis, and generally find this helpful, there are some who are not able to access the dietary advice they would like quickly enough, or at all. This group of people experience worse HRQOL. As CD is a chronic condition requiring significant dietary changes, it is important that patients receive enough information about the condition and the GFD at the point of diagnosis. In order to address this, provision needs to be increased and alternative ways of providing information explored.

Current service provision for dietetic services (i.e. the number of days dietitians allocate to people with CD) has been found to be insufficient (Nelson et al., 2007). In order for everyone requiring dietary advice to be offered that advice, and offered that advice more quickly following diagnosis, the provision of dietetic services for people with CD must be increased. One way in which this could be achieved is by offering CD clinics for groups of patients, which could provide information about CD and the GFD, while also providing individuals with an opportunity to meet other newly-diagnosed patients. Trott et al.

(2016) have trialled this approach, finding that it reduced the workload of dietitians, when compared with individual appointments, while achieving patient satisfaction. Further work is needed to fully evaluate this approach, including a health economic analysis (Trott et al., 2016).

(2) Communication with health care professionals

Communication with HCPs was significantly related to overall disease-specific HRQOL, and stigma, social isolation, and worries and concerns. Aspects of communication that were specifically related were respondents feeling that the HCP did not listen to them in consultations prior to their diagnosis, and being informed of the diagnosis in an unprofessional or inappropriate manner. In most cases (70.3%), the HCP spoken to the most often prior to diagnosis was a GP, with most respondents (82.8%) informed of their diagnosis by a hospital doctor or GP.

Few studies have explored communication between HCPs and people with CD. A Finnish study (Ukkola et al., 2012) found that patients regarding their diagnosis as 'a shock' had unsatisfactory communication with the doctor at the time of diagnosis, while also being provided with too little information about CD. Respondents may consider factors such as information provision and perceived knowledge of the HCP as aspects of communication.

(3) Difficulty obtaining prescriptions

Difficulty obtaining prescriptions was significantly related to overall disease-specific HRQOL, dietary burden and social isolation. In the current study, 70.1% had obtained gluten-free food on prescription in the last 12 months, although few reported receiving a review of their prescriptions as part of their follow-up care. This compares with another

UK survey (Bebb et al., 2006), which found that 89% (n=111) of respondents, recruited through a hospital database, were currently receiving prescriptions for gluten-free food. While a large proportion of people with CD receive prescriptions, evidence suggests limited information is available about prescriptions, with 30.2% of this sample reporting that they had not been given enough information about prescriptions. Furthermore, only 20% of participants in Bebb's study were receiving advice regarding the number of products required. In the current research, qualitative interview participants also raised various issues that they faced when trying to obtain gluten-free food on prescription (e.g. items not arriving on time, and receiving mouldy products).

Improving access to prescriptions may help improve HRQOL and reduce dietary burden and social isolation. In order to achieve this, it is recommended that alternative models of prescribing are considered. For example, Scotland have introduced a new initiative, the Scottish Gluten-Free Food Service, which allows users to place monthly orders for gluten-free food through a central online system, and collect the order from their nominated pharmacy, thus cutting out the GPs involvement. Patients are also likely to benefit from receiving information about prescriptions as part of their follow-up care.

(4) Perceived knowledge of GPs

The respondents' perception of GPs' knowledge was significantly related to dietary burden only. In addition, a lack of confidence in the HCP seen most often prior to diagnosis, most commonly a GP, was related to 'stigma'. It is likely that a lack of confidence in the GP, is in part a reflection of the respondents' confidence in their knowledge.

In this study, 66.4% of respondents felt that GPs lacked knowledge of CD, compared with just 7% in a study by Ukkola et al. (2012). Interestingly, despite a low proportion in Ukkola's study, when asked about future research in CD, patients requested that physicians' knowledge of CD was improved. The stark difference in results may be due to question wording, as it is not clear if respondents were able to select more than one reason for their dissatisfaction with physicians in Ukkola's study. Ukkola et al. also found that 59.0% of respondents were dissatisfied with dietary advice provided by physicians due to 'scant information'. The findings of a second study (Zarkadas et al., 2006), found a similar proportion (40.0%) rated the provision of information by doctors as poor or fair. In some cases, it may not be possible for patients to ascertain whether GPs lack knowledge of CD or simply are not effective in sharing their knowledge.

These are important findings because GPs are typically the primary point of contact for diagnosis, and therefore, lack of knowledge about CD could be a contributing factor to the lengthy duration to diagnosis (13.2 years) found in previous research (Gray and Papanicolas, 2010). GPs are also frequently consulted by patients about their CD following diagnosis (in this study, GPs were the most common HCP spoken to before diagnosis for 70.3% of respondents, and 41.0% of respondents had spoken to a GP about their CD in the past 12 months). In addition, the annual review process is increasingly managed in primary care, with guidelines (such as PCSG, 2006) recommending reviews are conducted in primary care if the patient is well.

To address this, initiatives aimed at increasing awareness and knowledge of CD among GPs and other HCPs are needed. This could perhaps take the form of specific training, or alternatively, software modules could be incorporated into current clinical practice systems, something that is already occurring in Wales (Preest, 2016). It follows that improvements in GPs' knowledge of CD is likely to reduce the delay to diagnosis that is so often experienced, as GPs will be aware of the condition and the ways in which it can present. It is possible that this is already happening (Gray and Papanicolas, 2010), with time to diagnosis in this study (mean 4 years) less than that reported previously (e.g. 13.2 years reported in Gray and Papanicolas, 2010). Furthermore, improving GPs' knowledge of CD and ability to provide their patients with sufficient information may reduce dietary burden and possibly stigma.

10.3 Key recommendations

Based on the findings of this study, it is recommended that health care providers focus on the following aspects of services, as improvements in these areas are most likely to improve the HRQOL of people with CD:

- Ensure timely access to dietary advice from a HCP with a specialist interest in CD for all patients following diagnosis;
- Develop initiatives to improve the knowledge of HCPs, in particular GPs and dietitians;
- Include an assessment of mental health at diagnosis and as part of the ongoing follow-up of people with CD, providing appropriate support where necessary; and
- Improve access to prescriptions.

10.4 Limitations and further research

The results of the study are based on a cross-sectional survey and therefore, causality cannot be determined. However, the study found significant associations between patients' experiences of health care services and HRQOL and therefore, focusing on improving health care services would be valuable. To overcome this limitation, a longitudinal study is needed.

Both cross-sectional surveys were distributed to members of Coeliac UK only. However, it is important to note that people with CD who were not members of Coeliac UK were involved in the development of the questionnaires following their recruitment through snowballing and online social networking groups. While there is no evidence to suggest members of Coeliac UK differ from the wider population of people with CD, it is possible that their membership is comprised of certain subgroups (e.g. those requiring additional support, or those who are particularly committed to managing their condition), while limited in others (e.g. those from Black and Minority Ethnic groups). Efforts were made during the development of the questionnaires in an attempt to capture issues of relevance to all people with CD. This was achieved in a number of ways, for example, a maximum variation sampling approach was taken for the qualitative interviews, a thorough development process following best practice guidelines was taken, and people with CD and a range of experts (including clinicians and translation specialists) were involved. As a result, it is unlikely that any major impacts of CD on HRQOL have been missed. Following the development of the surveys, a stratified sampling strategy was used in an attempt to ensure that certain groups, such as those from Black and Minority Ethnic groups) were represented.

It is possible that recruitment through a clinical setting would have identified other groups of people (e.g. those less committed to the management of their CD), which may have resulted in the development of additional questionnaire items. In order to investigate this further, interviews or focus groups with people with CD recruited through a clinical setting could be conducted to further assess the content validity of the CDAQ (i.e. whether all aspects of importance within this population group are covered by the CDAQ). In addition, further research should focus on assessing the reliability and validity of the CDAQ in samples recruited through other methods, in particular, a clinical sample.

Not all symptoms raised in the qualitative interviews and by experts could be captured in the final version of the CDAQ. Symptoms associated with CD can vary considerably (Green and Cellier, 2007) and therefore, it was not practical or appropriate to include all symptoms in the final measure. For example, an item about difficulties concentrating was removed due to a floor effect (the results of Survey 1 found 54.5% of respondents had 'never' experienced the symptom during the past 4 weeks). Other issues, such as skin rashes, resulting from the associated condition DH, would also most likely have been removed at this stage due to the low prevalence of the condition (0.03% in the UK (West et al., 2014)). While it is acknowledged that the CDAQ will not capture the presence of all symptoms associated with CD, it is highly likely that it will capture the impact of those symptoms on HRQOL. If the CDAQ is used in a study where it is necessary to capture broader CD symptomology, a coeliac-specific symptom measure, such as the Celiac Symptom Index (CSI) (Leffler, Dennis et al., 2009) could be administered alongside the CDAQ. On further investigation, if the CSI or similar measures were found to be

insufficient for this purpose, future research should focus on the development of a reliable, valid and responsive CD symptom scale.

Further research is needed to explore the reasons for differences in HRQOL between genders and ethnicities. Additional research is also needed to further explore the psychometric properties of the CDAQ and its potential uses. Responsiveness to change is an important property of PROMs, and as mentioned previously, work is underway to research this.

10.5 Contribution to the field

The main contributions that this thesis has made are as follows:

- Developed the Coeliac Disease Assessment Questionnaire (CDAQ), a reliable and valid disease-specific patient-reported outcome measure to assess health-related quality of life in people with CD;
- Developed the Coeliac Disease Patient Experience Questionnaire (CD-PEQ), a questionnaire that addresses experiences of health care services from pre- to post- diagnosis;
- Conducted the most extensive study of patients' experiences of health care services used to diagnose and manage CD within the UK, and to the authors' knowledge worldwide, to date;
- Identified a strong correlation between patients' experiences of health care services and HRQOL in people with CD; and
- Identified four key aspects of health care services that have a significant correlation with HRQOL, namely, (1) the consistency and provision of information,

(2) communication with health care professionals, (3) difficulty obtaining prescriptions, and (4) perceived knowledge of GPs.

10.6 Conclusions

The main aim of this study was to develop a CD-specific PROM and patient experience questionnaire and use these to assess the relationships between patients' experiences of health care services and HRQOL. The Coeliac Disease Assessment Questionnaire (CDAQ) and the Coeliac Disease Patient Experience Questionnaire (CD-PEQ) were developed and used in a cross-sectional survey. The survey was completed by 267 people with CD, and found the psychological health, vitality, general health, and dietary burden to have the greatest impact on HRQOL, with aspects of physical health and social isolation to be the least affected by CD. HRQOL was found to have a strong correlation with patients' experiences of health care services, with the provision of information, communication with HCPs, difficulty obtaining prescriptions, and knowledge of GPs found to be the most strongly related aspects. Improvements to these aspects of health care are likely to result in improvements to HRQOL. This study is the most comprehensive research to date that has investigated experiences of health care services and its relationship with HRQOL. Two questionnaires have been developed as part of this study and are available for use by others in future research and clinical practice. The development of the CDAQ, in particular, is a positive contribution to the field, as it is the first disease-specific PROM to assess HRQOL in CD that has been developed in accordance with best practice guidelines.

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APPENDICES

Appendix A. Scoping review – database search strategy

A scoping review to identify literature about patients' experiences of health care services in CD was conducted utilising the following search strategy:

("Celiac Disease"[Mesh] OR "Diet, Gluten-Free"[Mesh] OR "Coeliac disease" OR "Celiac disease" OR Gluten sensitiv* OR Gluten-sensitiv* OR Gluten enteropath* OR "celiac sprue" OR "coeliac sprue" OR "nontropical sprue" OR "non-tropical sprue" OR "gluten intolerance" OR "gluten induced enteropathy" OR "gluten-induced enteropathy" OR "gluten free diet" OR "gluten-free diet")

AND

("Healthcare Delivery"[Mesh] OR "Health Service"[Mesh] OR "diagnosis"[Mesh] OR "prescription" OR "Health Service" OR "diagnosis" OR "follow-up" OR "health care" OR "healthcare" OR "prescription" OR "patient experience" OR "patients' experience" OR "patient's experience" OR "dietitian" OR "dietetic")

Databases searched: PubMed; Google Scholar

Appendix B: Systematic review – database search strategies

Database search strategies for EMBASE, PsycINFO, CINAHL, and the BNI.

OVID search strategy (EMBASE, PsycINFO)

(celiac disease/ OR coeliac disease.tw. OR celiac disease.tw. OR gluten free diet/ OR Gluten sensitiv$.tw. OR Gluten-sensitiv$.tw. OR Gluten enteropath$.tw. OR celiac sprue.tw. OR coeliac sprue.tw. OR nontropical sprue.tw. OR non-tropical sprue.tw. OR gluten intolerance.tw. OR gluten induced enteropathy.tw. OR gluten-induced enteropathy.tw. OR gluten free diet.tw. OR gluten-free diet.tw.)
AND
(quality of life/ OR health status/ OR quality of life.tw. OR QOL.tw. OR HRQOL.tw. OR HR-QOL.tw. OR HRQL.tw. OR HR-PRO.tw. OR HRPRO.tw. OR PROM.tw. OR PROMs.tw. OR PROs.tw. OR health index.tw. OR health indices.tw. OR functional index.tw. OR functional indices.tw. OR health profile.tw. OR health status.tw. OR health state.tw. OR life quality.tw. OR wellbeing/ OR well being.tw. OR well-being.tw. OR wellbeing.tw. OR health level$.tw. OR level of health.tw. OR patient report$.tw. OR patient-report$.tw. OR patient rated.tw. OR patient-rated.tw. OR patient rating.tw. OR SF-36.tw. OR SF36.tw. OR SF-12.tw. OR SF12.tw. OR EQ-5D.tw. OR EQ5D.tw. OR GSRS.tw. OR PGWB.tw. OR HADS.tw. OR STAI.tw. OR BDI.tw. OR CDQ.tw. OR CD-QOL.tw. OR CDQOL.tw. OR GIQLI.tw. OR zung self-rating.tw. OR M-SDS.tw.)

EBSCOHost search strategy (CINAHL)

((MH "Celiac Disease") OR (MH "Diet, Gluten-Free") OR “Coeliac disease” OR “Celiac disease” OR Gluten sensitiv* OR Gluten-sensitiv* OR Gluten enteropath* OR “celiac sprue” OR “coeliac sprue” OR “nontropical sprue” OR “non-tropical sprue” OR “gluten intolerance” OR “gluten induced enteropathy” OR “gluten-induced enteropathy” OR “gluten free diet” OR “gluten-free diet”)
AND
((MH "Quality of Life") OR (MH "Health Status") OR (MH "Psychological Well-Being") OR “Quality of life” OR QOL OR HRQOL OR HR-QOL OR HRQL OR HR-PRO OR HRPRO OR PROM OR PROMs OR PROs OR "Health Index" OR “Health Indices” OR “Functional Index” OR “Functional Indices” OR “Health Profile” OR “Health Status” OR “Health State” OR “Life Quality” OR “Well Being” OR Well-being OR Wellbeing OR Health level* OR “Level of health” OR Patient report* OR Patient-report* OR “Patient Rated” OR “Patient-rated” OR “Patient Rating” OR SF-36 OR SF36 OR SF-12 OR SF12 OR EQ-5D OR EQ5D OR GSRS OR PGWB OR HADS OR STAI OR BDI OR CDQ OR CD-QOL OR CDQOL OR GIQLI OR “Zung self-rating” OR M-SDS)

Search not limited to title/abstract

ProQuest search strategy (BNI)

Search 1:

(subject("Coeliac Disease") OR “Coeliac disease” OR “Celiac disease” OR Gluten sensitiv* OR Gluten-sensitiv* OR Gluten enteropath* OR “celiac sprue” OR “coeliac sprue” OR “nontropical sprue” OR “non-tropical sprue” OR “gluten intolerance” OR “gluten induced enteropathy” OR “gluten-induced enteropathy” OR “gluten free diet” OR “gluten-free diet”)

Search 2:

(subject("Health and Quality of Life") OR “Quality of life” OR QOL OR HRQOL OR HR-QOL OR HRQL OR HR-PRO OR HRPRO OR PROM OR PROMs OR PROs OR "Health Index" OR “Health Indices” OR “Functional Index” OR “Functional Indices” OR “Health Profile” OR “Health Status” OR “Health State” OR “Life Quality” OR “Well Being” OR Well-being OR Wellbeing OR Health level* OR “Level of health” OR Patient report* OR Patient-report* OR “Patient Rated” OR “Patient-rated” OR “Patient Rating” OR SF-36 OR SF36 OR SF-12 OR SF12 OR EQ-5D OR EQ5D OR GSRS OR PGWB OR HADS OR STAI OR BDI OR CDQ OR CD-QOL OR CDQOL OR GIQLI OR “Zung self-rating” OR M-SDS)

Search 3:

(Search 1) AND (Search 2)

Search not limited to title/abstract

Appendix C: Qualitative interviews – letter of invitation

[Coeliac UK Letterhead here]

10 December 2012

[Member's Address]

Diagnosis and management of coeliac disease: Quality of life and patient's experiences of healthcare services

Dear [Title] [Surname],

I am writing to invite you to participate in a research study which is being undertaken by the Department of Public Health at the University of Oxford. The research aims to find out about people's experiences of using healthcare services to diagnose and manage coeliac disease, and how the condition impacts on their quality of life. We hope the research will help improve healthcare services for people living with the condition. We are writing to you because as a member of Coeliac UK you have agreed you may be contacted for research purposes.

Researchers want to interview you about your experiences of living with coeliac disease and using healthcare services to diagnose and manage your condition. The interview will last for around one hour. You do not have to have used healthcare services recently to take part. Further information about the study can be found in the enclosed information sheet.

Taking part in this study is voluntary and confidential. If you would like to take part, please complete the consent form and send it to the University of Oxford in the pre-paid envelope provided. A researcher will then contact you to arrange a suitable date and time for your interview. If you have any questions about the study, please contact Helen Boyce, the research contact at the University of Oxford, on 01865 289431 or email: Helen.Boyce@dph.ox.ac.uk.

Coeliac UK is a strong supporter of research into all aspects of coeliac disease and such research helps us get the evidence we need to improve services on your behalf. I do hope you will consider taking part in this project.

Thank you for taking the time to read this letter.

Yours sincerely,

Sarah Sleet
Chief Executive, Coeliac UK

Version 1.0, 14/03/2012, REC Ref No: MSD/IDREC/C1/2012/38

Appendix D: Qualitative interviews – participant information sheet

UNIVERSITY OF OXFORD

Health Services Research Unit
Department of Public Health

Rosemary Rue Building, Old Road Campus, Headington, Oxford OX3 7LF
Helen Boyce, Tel: +44 (0)1865 289431, Email: Helen.Boyce@dph.ox.ac.uk

Diagnosis and management of coeliac disease: Quality of life and patient's experiences of healthcare services

Information Sheet for Interview Participants

You are being invited to participate in this research study as you have been identified as having coeliac disease. This information sheet explains the study in detail to enable you to decide whether or not you would like to participate.

What is the purpose of this research?

In this study, we are interested in finding out about people's experiences of living with coeliac disease and their experiences of using healthcare services to diagnose and manage their condition. By talking to people with coeliac disease about their experiences, we hope to find out whether services are meeting the needs of patients and how they might be improved. We would also like to find out how coeliac disease affects the quality of life of those living with the condition.

Who is doing the research?

The research will be led by Helen Boyce, a researcher in the Department of Public Health at the University of Oxford, under the supervision of Professor Crispin Jenkinson and Dr Michele Peters. The research is funded by the Medical Research Council and is part of a doctoral research programme.

What will I have to do?

If you decide to participate in this research, you will be asked to take part in an interview which will last for approximately an hour and will be audio-recorded with your permission. During the interview, we will discuss your experiences of living with coeliac disease and your experiences of healthcare services used in relation to your coeliac disease. If at any point during the interview you decide that you do not want to continue, the interview will be stopped immediately. The interview will take place at a location, date and time at your convenience; this can be in your own home or at University premises in Oxford. You will be reimbursed for travel expenses where appropriate.

What will happen with the information that I provide?

The interview will be transcribed (written up) and you will be offered the opportunity to receive a written copy of your interview. Next, a questionnaire based on common aspects identified across all interviews will be developed to assess experiences of healthcare services and quality of life in coeliac disease. It is intended that the results of the questionnaire will be used to inform healthcare policy to improve the quality of healthcare for people with coeliac disease.

Who can take part?

Participants should be aged 18 years or over and have coeliac disease. In total, we are hoping to interview approximately 20 to 30 people.

Version 1.0, 14/03/2012, REC Ref No: MSD/IDREC/C1/2012/38

Director of HSRU
Professor Crispin Jenkinson DPhil

Head of Department
Professor Ray Fitzpatrick MA MSc PhD

Will participation be confidential?

Personal details and other data collected as part of this research will be accessible to the research team only and will **not** be passed on to your healthcare provider. Coeliac UK will not be informed of your decision of whether or not to participate and comments attributable to you will not be passed back to Coeliac UK. Paper documentation will be stored in locked filing cabinets and electronic files will be stored on a password protected computer. This is in accordance with the current Data Protection Act.

You will be assigned an identification number, and all documentation relating to the information that you provide (including audio recordings and transcripts of your interview) will be marked with this identification number and not your name.

Personal data (e.g. name and contact details) will not be kept beyond your involvement in the study. In accordance with guidelines produced by the Medical Research Council, anonymised interview transcripts and digital audio files will be kept for a period of twenty years to allow the research to be reviewed if necessary.

What will happen with the results of the study?

The University of Oxford is committed to the dissemination of its research for the benefit of society. Therefore, it is intended that the research will be written up as one or more papers to be submitted for publication in scientific journals, presented at conferences, and as a doctoral thesis. On successful submission of the thesis, it will be deposited in the University archives to facilitate its use in future research. The thesis will be available in print and online.

Identifiable data will not appear in written up reports. All identifying data will be anonymised; this means that participant names and other unique identifying information will not be used. All participants will be referred to by their assigned identification number, and therefore, it will not be possible to identify you or any other participant from the written up reports.

The results of the study will be made available on the Department of Public Health's website, which can be found at: http://www.publichealth.ox.ac.uk/research/hsru/coeliacdisease

How can I take part?

Participation in the study is entirely voluntary. If you decide that you would like to take part in the study, please complete the enclosed consent form and return it in the pre-paid envelope to: Helen Boyce, Department of Public Health, University of Oxford, Rosemary Rue Building, Old Road Campus, Oxford OX3 7LF. The researcher will then contact you to arrange a suitable location, date and time for the interview. If you have any questions that you would like to ask before deciding whether or not to take part, please contact Helen Boyce on 01865 289431 or email: Helen.Boyce@dph.ox.ac.uk. It is important to note that even if you decide to take part, you are free to withdraw from the study at any point in time without providing a reason.

Are there any risks involved in taking part?

Whilst we do not foresee any major risks involved in taking part in this study, you may find discussing your experiences of the condition upsetting. If participation in this research raises questions about the condition or living with the condition that you would like to discuss, you can contact Coeliac UK, a charity for people with coeliac disease, on the Helpline number 0845 305 2060. To find out more about Coeliac UK, you can visit their website: www.coeliac.org.uk.

Are there any benefits in taking part?

The information that you provide may help to inform healthcare policy and improve health services in the future. However, there are no direct benefits in taking part.

What can I do if I have any concerns about the research study?

This research has been reviewed by and received ethics clearance from the University of Oxford Central University Research Ethics Committee. If you have any concerns about the study, please contact the research team who will do their best to answer your query (Tel: 01865 289431, Email: Helen.Boyce@dph.ox.ac.uk). If the research team are unable to address your concerns and you would like to make a formal complaint about any aspect of the study, you may contact the Research Ethics Committee at the University of Oxford (email: ethics@medsci.ox.ac.uk; address: Medical Sciences Inter-Divisional Research Ethics Committee, Medical Sciences Divisional Office, Level 3 John Radcliffe Hospital, Oxford, OX3 9DU).

Appendix E: Qualitative interviews – participant consent form

Health Services Research Unit
Department of Public Health

Rosemary Rue Building, Old Road Campus, Headington, Oxford OX3 7LF
Helen Boyce, Tel: +44 (0)1865 289431, Email: Helen.Boyce@dph.ox.ac.uk

Diagnosis and management of coeliac disease: Quality of life and patient's experiences of healthcare services

Consent Form for Interview Participants

Please read and tick the following statements before signing your name below to consent to taking part in this research project.

		Please Tick
1.	I confirm that I have read and understood the information sheet for this research study, have had the opportunity to ask questions about the study and have had these answered satisfactorily.	☐
2.	I understand that personal data provided will be accessible to the research team only and will be stored and processed according to the Data Protection Act 1998	☐
3.	I understand that the research will be written up as a thesis and deposited in the University archives, published in academic journals, and presented at conferences. I understand that participant names and other unique identifying information will not appear in reports or publications.	☐
4.	I understand that this study has received ethics clearance from the University of Oxford Central University Research Ethics Committee	☐
5.	I confirm that I am aged 18 years or older and have coeliac disease	☐
6.	I agree to take part in this study	☐
7.	I permit the interview to be audio recorded	☐
8.	I understand that my participation is voluntary and I can withdraw from the study at any time without providing a reason	☐

Participant's Name (print): .....

Participant's Signature: ..... Date: .....

Researcher's Name (print): .....

Researcher's Signature: ..... Date: .....

Version 1.0, 14/03/2012, REC Ref No: MSD/IDREC/C1/2012/38

Director of HSRU
Professor Crispin Jenkinson DPhil

Head of Department
Professor Ray Fitzpatrick MA MSc PhD

Health Services Research Unit
Department of Public Health

Rosemary Rue Building, Old Road Campus, Headington, Oxford OX3 7LF
Helen Boyce, Tel: +44 (0)1865 289431, Email: Helen.Boyce@dph.ox.ac.uk

Diagnosis and management of coeliac disease: Quality of life and patient's experiences of healthcare services

Contact Details

Please provide your contact details below so that the researcher can contact you to arrange a suitable location, date and time for your interview.

Telephone No:	
Best time to phone:	
Email:	
Address:	

Please send this completed form to the University of Oxford in the enclosed pre-paid envelope.

Director of HSRU
Professor Crispin Jenkinson DPhil

Head of Department
Professor Ray Fitzpatrick MA MSc PhD

Appendix F. Qualitative interviews - recruitment search strategy

Search 1 – postcode areas

- **Yeovil area** (i.e. postcode areas within 20 miles of Yeovil): BA10, BA16, BA20, BA21, BA22, BA4, BA5, BA6, BA7, BA8, BA9, DT1, DT10, DT2, DT6, DT8, DT9, EX13, SP8, TA10, TA11, TA12, TA13, TA14, TA15, TA16, TA17, TA18, TA19, TA20, TA3, TA7
- **Oxford area** (i.e. postcode areas within 20 miles of Oxford): HP14, HP17, HP18, HP19, HP21, HP22, HP27, OX1, OX10, OX11, OX12, OX13, OX14, OX18, OX2, OX20, OX25, OX26, OX27, OX28, OX29, OX3, OX33, OX39, OX4, OX44, OX49, OX5, OX7, OX9, RG8, RG9, SN7
- **Birmingham** (i.e. postcode areas within 5 miles of Birmingham): B1, B10, B11, B12, B13, B14, B15, B16, B17, B18, B19, B2, B20, B21, B23, B24, B25, B26, B27, B28, B29, B3, B30, B33, B34, B35, B36, B4, B42, B43, B44, B5, B6, B66, B67, B68, B7, B71, B73, B8, B9.

Search 2

Coeliac UK ran the following search of their membership database to identify all members (approximately 50% men and 50% women) meeting the following criteria:

- Aged between 18 and 40 years old (ensuring a spread across this range),
- report that they have coeliac disease,
- have agreed to be contacted for research purposes,
- and live in the following geographical areas:
  - **Yeovil area** (i.e. postcode areas within 20 miles of Yeovil): postcodes as search 1
  - **Oxford area** (i.e. postcode areas within 20 miles of Oxford): postcodes as search 1
  - **Birmingham** (i.e. postcode areas within three miles of Birmingham): B1, B10, B11, B12, B15, B16, B18, B19, B2, B20, B21, B25, B3, B4, B5, B6, B7, B8, B9

While the same postcode areas were used for the Yeovil and Oxford areas, a reduced subset of postcode areas were used for Birmingham to try and identify members from a more urban area (i.e. radius reduced to three miles around Birmingham). For each of the three geographical areas, ten members identified from the above search were selected as follows:

- Four members diagnosed within the last two years;
- Three members belonging to an ethnic minority group;
- Three members from the remaining identified members.

As no members from black and minority ethnic groups resided in the Yeovil area, five members diagnosed within the last two years, and five members from the remaining members identified were selected. In the Oxford and Birmingham areas, there were fewer than three members from black and minority ethnic groups aged between 18 and 40. Therefore, some members were selected from outside of this age group (i.e. just over 40 years old).

In summary, of the 30 members invited, the majority were aged between 18 and 40, six belonged to black and minority ethnic groups, 13 had been diagnosed within the past two years, and ten resided in a central urban location. Note that any one member may belong to one or more of these groups (e.g. diagnosed for less than two years and lives in a central urban location).

Appendix G. Qualitative interviews - interview guide

Pre-diagnosis

Tell me about when you first suspected that something was wrong

- Did you experience any symptoms?
- What did you think might be wrong?
- What prompted you to seek advice? → From whom did you seek advice?
- How long was it between when you first suspected that something was wrong and seeking help?
- Is there a history of coeliac disease in your family?

Diagnosis

Can you tell me about the process that you went through to get your diagnosis? / What happened next?

- How long did it take to get a diagnosis (i.e. between first seeking help and being diagnosed)?
- Which health professionals did you see?
    - Tell me about your consultation with [the GP/gastroenterologist/dietitian].
- Which tests did you have?
- Did you have an endoscopy (endoscopic biopsy)? *If not, were you offered one?*
- How long have you been diagnosed?

Can you tell me about the moment that you were told that you have coeliac disease?

- How did you feel?
- How were you told?
    - Were you told in person, by letter?
    - Who told you?
- What did you know about coeliac disease at that time?
- What sort of information were you provided with?
- What were you told about how the condition is treated?

- What were you told would happen next?
- At the end of the consultation, how well informed did you feel about the condition and its treatment?

Initial treatment

Can you tell me what happened after you had received your diagnosis?

- Were you referred to any other health professionals? (e.g. dietitian, gastroenterologist)
    - Who advised you to start a gluten-free diet?
    - How did you find their advice?
    - How did you find the [GP/dietitian/gastroenterologist]?
- How did you feel about starting a gluten-free diet?
- What treatment advice were you given?
- Which tests did you receive? (e.g. bone scan, blood tests)
- How well informed did you feel [the GP/dietitian/gastroenterologist] was about your condition?

Follow-up care

I now want to move on from your diagnosis to discuss any on-going care that you receive.

Can you describe to me any on-going or follow-up care that you receive? (For example, some people see their doctor for an annual check-up whereas others do not receive any on-going care.)

A - *If **in receipt** of follow-up care*:

Can you tell me about your last follow-up appointment?

- What happened during the appointment?
- Who did you see?
- How often?

How is this care arranged?

- How is your follow-up care organised?

What are your thoughts about the follow-up care that you receive?

- How helpful are the appointments?
- Do you think it could be improved? If so, how?

Tell me about your relationship with the health professional.

- How do you feel health care professionals have treated you?
- How supportive have the health care professionals been?
- How easy is it to understand the health care professional's advice?
- How involved were you in decisions about your treatment?

B *- If patient* ***does not*** *receive follow-up care:*

Can you explain to me why you do not receive follow-up care?

- Have you been offered on-going care?
- What type of care were you offered?
- Why have you decided not to attend?

Do you think follow-up care would benefit you? If yes, how?

All:

Can you tell me about the last time that you needed to see a doctor (or another health professional) about your coeliac disease, other than a routine follow-up appointment?

- How was this appointment arranged?
- How easy or difficult was it to arrange the appointment?
- What happened during the appointment?
- How did you find the appointment?

- Did you feel that the health care professional listened to and understood your problem?
- How useful was the advice?

HRQOL

We've talked a bit about your experiences of health care. I would now like to move on to discuss how you feel your coeliac disease has impacted on your quality of life.

How does coeliac disease affect your quality of life?

- **Can you tell me about your life now compared with before you were diagnosed**
- Have you made any changes since finding out that you have coeliac disease? (e.g. work, social activities, leisure activities, relationships, travelling)
- Thinking about a typical day, what challenges do you face?

How have your friends and family handled your diagnosis?

- How supportive have friends and family members been? Examples? How did this make you feel?
- *[alternative] Has there been an occasion when they were [supportive / unsupportive]?*
- How important is it to you that friends and family understand your condition?

Some people with coeliac disease feel anxious or depressed at times, or have worries or concerns about their condition – can I ask whether you have ever experienced these feelings?

- [If yes], when you are feeling this way, how does it impact on your life?
- [If concerns], what are your worries or concerns – both now and for the future?

Some people with coeliac disease have found their condition can effect … *(see list below)* **have you ever had these problems?**

- *Fatigue; Anxiety and depression; Relationships; Eating out; Attending social events; Travelling and going on holiday; Purchasing food*

Gluten-free diet

I now want to move on to discuss your experiences of a gluten-free diet.

How do you find the gluten-free diet?

- *(How did you find adjusting to a gluten-free diet?)*
- Are there any particular occasions or situations that you find difficult? (e.g. eating out, travelling, socialising, supermarket shopping)
- Can you give me an example?
- How do you feel when confronted with a difficult situation?

How strict are you with the diet?

- Can you tell me what happens if you don't stick to the diet? *Short and long-term consequences?*
- Why do you choose to *strictly adhere/not adhere* to a gluten-free diet?
- How do you feel if, for some reason, you are unable to stick to the diet?

Can you describe to me what happens if you eat gluten, accidently or otherwise?

- How does it affect you? *Symptoms?*
- How do you handle it? *Do you seek medical advice?*

Do you receive any other treatments or therapies for your coeliac disease (e.g. supplements)?

- Who administers the treatment or therapy?

Information / support

How informed do you feel about your condition?

- What sort of information would you like to receive that you have not received?

Close

Finally, how would you describe what it is like to live with coeliac disease to somebody that has just been diagnosed?

Appendix H. Qualitative interviews - participant demographics form

UNIVERSITY OF OXFORD

Diagnosis and management of coeliac disease:
Quality of life and patient's experiences
of healthcare services

Please complete the following details about yourself. Your answers will be used to ensure that people with a range of experiences and backgrounds are included in the study.

Personal Details

Gender:	☐ Male ☐ Female
Age:	
What is your legal marital status or same-sex civil partnership status?	☐ Married / in a civil partnership ☐ Separated (but still legally married / in a civil partnership) ☐ Divorced / legally dissolved civil partnership ☐ Widowed / surviving partner from a civil partnership ☐ Single (never married and never formed a civil partnership)
What is your ethnic group?	Choose ONE section from A to E, and then tick the appropriate box to indicate your ethnic group. **A. White** ☐ English / Welsh / Scottish / Northern Irish / British ☐ Irish ☐ Gypsy or Irish Traveller ☐ Any other White background, please write in: _____ **B. Mixed / Multiple ethnic groups** ☐ White and Black Caribbean ☐ White and Black African ☐ White and Asian ☐ Any other Mixed / Multiple ethnic background, please write in: _____ **C. Asian / Asian British** ☐ Indian ☐ Pakistani ☐ Bangladeshi ☐ Chinese ☐ Any other Asian background, please write in: _____ **D. Black / African / Caribbean / Black British** ☐ African ☐ Caribbean ☐ Any other Black / African / Caribbean background, please write in: _____ **E. Other ethnic group** ☐ Arab ☐ Any other ethnic group, please write in: _____

Please turn over

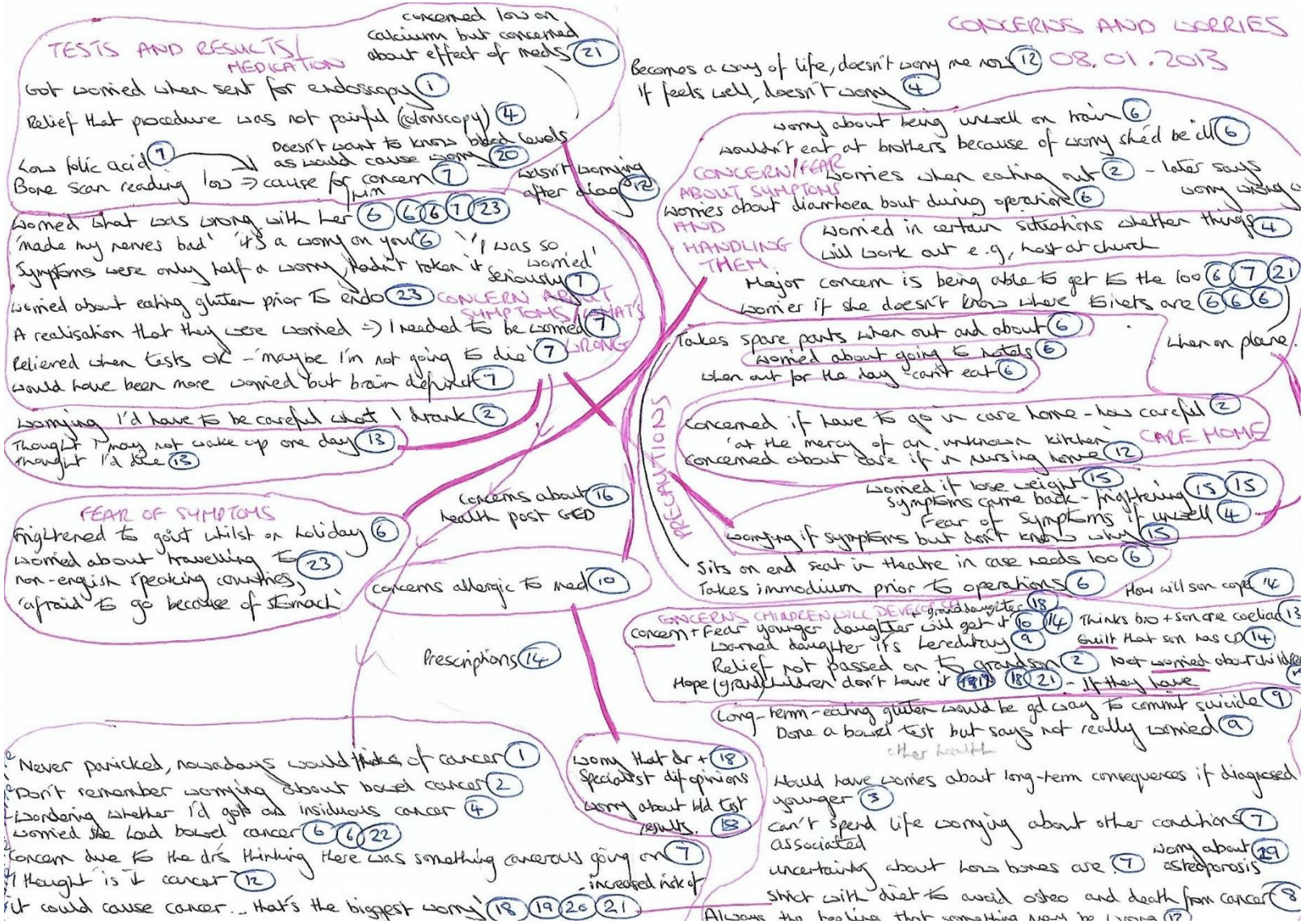
Which of these best describes what you are doing at present? *If more than one of these applies to you, please tick the main ONE only.*	☐ Full-time paid work (30 hours or more each week) ☐ Part-time paid work (under 30 hours each week) ☐ Full-time education at school, college or university ☐ Unemployed ☐ Permanently sick or disabled ☐ Fully retired from work ☐ Looking after the home ☐ Doing something else, please specify: _____
If you are employed, what is your occupation?	
Do you have any of the following conditions? *(please tick all that apply)*	☐ Coeliac Disease ☐ Dermatitis Herpetiformis (DH) ☐ Irritable Bowel Syndrome ☐ Type I Diabetes ☐ Type II Diabetes ☐ Depression ☐ Colitis ☐ Crohn's Disease ☐ Thyroid Disease ☐ Epilepsy ☐ Osteoporosis ☐ None of the above
Do you have any other health conditions?	☐ No ☐ Yes, please specify:
When were you diagnosed with coeliac disease?	Month _____ Year _____

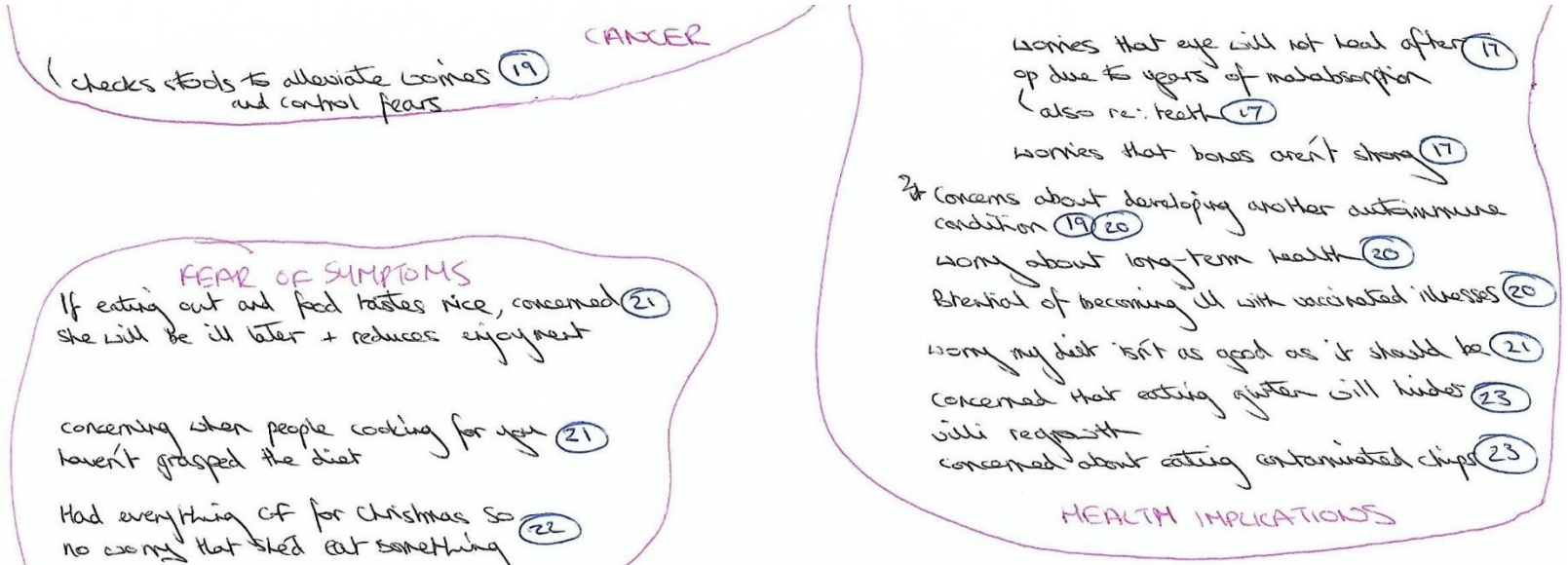
Appendix I. Qualitative interviews - final coding framework

Category	Code	Description
Gluten-free diet	Acceptability of gluten-free food	Palatability of gluten-free food (e.g. taste, texture); enjoyment of gluten-free food
	Cross-contamination	Measures taken to avoid cross-contamination; discussion of where cross-contamination can occur; attitude towards cross-contamination; concerns regarding cross-contamination
	Eating outside of the home	Managing the gluten-free diet when outside of the home; availability of gluten-free food when 'out and about' and on day trips (e.g. take-aways, cafes and restaurants); ease and arrangement of eating out in cafes, restaurants, and others' homes
	Food choice	Lack of choice of gluten-free food available; how food choice is affected by CD and its treatment
	Food shopping	Supermarket shopping; availability of gluten-free food products; the assessment of whether a food product is gluten-free. NOTE: this does not include difficulties in relation to eating out in cafes and restaurants.
	Risk	Discussion of risk (e.g. risk in relation to eating out)
Emotional health	Concerns and worries	Concerns and worries before and after diagnosis (e.g. concerns about symptoms pre-diagnosis; worry about situations; concerns about long-term health)
	Feelings	Feelings about being diagnosed with CD
	Isolation and exclusion	Feeling isolated or excluded as a result of CD and its treatment; exclusion from social events and experiences
	Unwanted visibility	The person dislikes drawing attention to themselves in relation to their condition and diet (e.g. embarrassment; 'sticking out'; being the centre of attention; don't want to be seen as 'making a fuss')
Impact on activities	Avoiding social activities	Avoidance of social events and activities due to CD and the gluten-free diet
	Holidays	Impact of CD and it's treatment on holidays; impact on holiday choice; problems faced; holiday planning; obtaining food on holiday; eating out on holiday
	Other social activities	Impact of CD and it's treatment on other social activities (e.g. weddings)
	Planning ahead	Planning ahead to manage the condition; actions taken ahead of time to ensure the availability of food
	Time	Time taken to prepare and purchase suitable food
	Travelling	Managing the condition and it's treatment whilst travelling; travelling to work; travelling to a holiday destination; planning and preparation prior to travelling

Category	Code	Description
	Work	Impact of CD and it's treatment on work activities and relationships; work attendance
Relationships	Lack of understanding	Comments or instances displaying a lack of understanding about the condition and it's treatment from others; unsupportive comments (e.g. fad diet, fussy eater)
	Support	Support received from outside of healthcare services (e.g. friends, family, partner)
	Trust	Discussion of trust (e.g. trust placed in others to provide uncontaminated gluten-free food)
Symptoms	Concentration	Difficulty concentrating on activities
	Energy	Fatigue; tiredness; lethargy
	Gastrointestinal	Consistency and frequency of bowel movements (e.g. diarrhoea); bloating; abdominal discomfort
	Pain	Pain
	Weight	Changes in body weight; impact of CD and it's treatment on weight
Financial issues	Impact on finances	Impact of condition on finances; cost of gluten-free food
Health care experience	Satisfaction with health care	Overall satisfaction with healthcare provision
	Diagnosis	The process of obtaining a diagnosis; consultations prior to diagnosis; diagnostic tests and investigations; time taken to diagnose CD
	Follow-up consultations	Medical care received after a diagnosis of CD had been made; arrangement and frequency of follow-up appointments; tests and investigations
	Access to services	Ease of accessing healthcare required; arrangement of appointments; acceptability of waiting times for appointments; acceptability of waiting times at appointments
	Prescriptions	Prescriptions in relation to CD; obtaining gluten-free food on prescription; cost of prescriptions; foods available on prescription
	Integrated care and continuity of care	Integration of care between health care providers (e.g. between the NHS and private care; between primary and secondary care); continuity of care; ease of seeing a certain health care professional (e.g. own doctor); seeing the same health care professional
	Relationship with health care professionals	The relationship between the health care professional (HCP) or health care provider and the person with CD; communication with HCP; manner of HCP; support from HCP; trust and confidence in HCP; felt listened to and understood by HCP; perception of HCP's knowledge
	Information provision	Information sought from and provided by health care professionals; quality of information provided; lack of information

Appendix J. Qualitative interviews – example 'OSOP' analysis




CANCER
checks foods to alleviate worries (19) and control fears
FEAR OF SYMPTOMS
If eating out and food tastes nice, concerned (21) she will be ill later + reduces enjoyment
concerning when people cooking for you (21) haven't grasped the diet
Had everything ok for Christmas so (22) no worry that shed eat something glutenous
worries that eye will not heal after (17) op due to years of malabsorption
(also re: teeth (17)
worries that bones aren't strong (17)
Concerns about developing another autoimmune condition (19) (20)
worry about long-term health (20)
Fearful of becoming ill with vaccinated illnesses (20)
worry my diet isn't as good as it should be (21)
concerned that eating gluten will hinder (23) milli regain
concerned about eating contaminated chips (23)
HEALTH IMPLICATIONS

Appendix K. CDAQ item tracking matrix

NB. Item numbers refer to candidate item numbers. ✓ indicates that an item has been amended, '-' indicates that an item is unchanged, # indicates that an item has been added, and × indicates that an item was deleted. The stages of development are as follows: (1) QAS-99; (2) Discussion with research team; (3) Expert opinions; (4) Cognitive interviews – Round one; (5) Cognitive interviews – Round two; (6) Translatability assessment; (7) Survey 1 – data distribution; (8) Factor analysis.

		Amendments made by stage of development[a]										
No	**Original item**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**Final item following amendments**	**In CDAQ?**	**Reason for deleting item**
1	…were you feeling down and/or in low spirits?	✓	✓	-	✓	-	-	×		have you felt depressed?	×	High inter-item correlation with item 65.
2	...were you worried that your children or grandchildren may develop coeliac disease?	✓	✓	-	-	-	-	-	-	have you felt worried that a family member may have or could develop coeliac disease?	✓	
3	...were you concerned about developing a health condition related to your coeliac disease?	-	✓	-	-	-	✓	-	-	have you felt concerned about developing a health problem related to your coeliac disease?	✓	
4	…did you worry that you would eat gluten by mistake?	✓	-	✓	-	-	✓	-	-	have you worried that you would accidentally eat or drink products that contain gluten?	✓	

		Amendments made by stage of development[a]										
No	**Original item**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**Final item following amendments**	**In CDAQ?**	**Reason for deleting item**
5	…did you worry that you would experience symptoms at an inconvenient time (e.g. travelling)?	✓	-	-	-	-	✓	-	×	have you worried that you would become ill at a difficult or inconvenient time (for example, while travelling or at a social event)?	×	Highly correlated with item 66 (r=0.706).
6	…did you feel isolated because of your coeliac disease?	✓	-	-	✓	-	✓	-	-	have you felt isolated from others because of your coeliac disease?	✓	
7	…did you feel that others excluded you [from activities] because of your coeliac disease?	✓	-	-	✓	-	✓	×		have you felt that others excluded you from attending social activities?	×	Floor effect > 50%
8	…did you feel like a nuisance to others?	✓	-	-	-	-	✓	-	-	have you felt you were a nuisance to other people?	✓	
9	…did you attract unwanted attention because of your condition or diet?	✓	✓	-	-	-	✓	-	-	have you received unwanted attention because of your coeliac disease or dietary needs?	✓	
10	…did you feel embarrassed or uncomfortable about discussing your dietary needs?	-	×							No amendments made to original item	×	Item deleted as similar to item 25.
11	…did you feel that you might appear that you were making a fuss [about your dietary needs]?	✓	-	-	-	-	✓	-	-	have you felt as though you might appear to be making a fuss about your dietary needs?	✓	
12	…did you feel guilty about refusing food from other people?	✓	✓	✓	-	-	✓	-	-	have you felt uncomfortable refusing unsuitable food or drink from other people?	✓	
13	…did you miss [not being able to eat] certain foods?	✓	✓	✓	-	-	✓	-	-	have you craved food or drinks that contain gluten?	✓	

		Amendments made by stage of development[a]										
No	**Original item**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**Final item following amendments**	**In CDAQ?**	**Reason for deleting item**
14	…were you concerned about the results of tests?	✓	✓	-	-	-	-	×		have you felt concerned about the results of medical tests?	×	Item not relevant to all respondents - missing data (including N/A) > 5%.
15	…were you frustrated by the choice of food available?	✓	✓	-	-	-	-	-	-	have you been frustrated by the choice of suitable food available (for example, in supermarkets, cafés or restaurants)?	✓	
16	…were you annoyed or frustrated by trying to find suitable food?	✓	-	-	-	-	✓	-	-	have you had difficulty finding suitable food?	✓	
17	…were you annoyed or frustrated by a product's ingredients changing, making it no longer gluten-free?	✓	×							…were you annoyed or frustrated by a product's ingredients changing, making it unsuitable?	×	Item really about difficulties finding suitable food, which is covered by item 16.
18	…were you disappointed with the taste or texture of gluten-free alternatives?	✓	✓	✓	-	-	-	-	-	have you been disappointed with the taste or texture of gluten-free substitutes?	✓	
19	…was your choice of food affected?	-	-	-	-	×				No amendments made to original item	×	Participants interpreted item in a different way to that intended.
20	…did you struggle to find something to eat when out and about?	✓	✓	-	✓	✓	✓	-	-	have you had difficulty finding something to eat when you were not at home?	✓	

		Amendments made by stage of development[a]										
No	**Original item**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**Final item following amendments**	**In CDAQ?**	**Reason for deleting item**
21	…did you find eating out difficult?	✓	×							…did you have problems with eating out, for example, at a restaurant, café, or friend's house?	×	Item is ambiguous 'problems with eating out' - what do we mean by problems? Issues covered by other items.
22	were you worried that you might be unwell after eating out (e.g. in a café, friend's house, or restaurant)?	✓	✓	✓	-	-	✓	-	-	have you worried that you might become ill after eating food prepared by others (for example, at other people's houses, restaurants, or cafés)?	✓	
23	…did you feel uncomfortable about other people having to cater for your diet?	✓	-	-	-	-	✓	-	×	have you felt uncomfortable about other people taking your dietary needs in to account when preparing food for you?	×	Highly correlated with item 8 (r=0.738)
24	…did you feel guilty about other people buying gluten-free foods especially for you?	✓	-	-	-	-	✓	-	-	have you felt guilty about other people buying gluten-free substitute foods for you?	✓	
25	..did you find it difficult to explain your dietary needs to others?	✓	✓	-	-	-	✓	-	×	have you felt embarrassed or uncomfortable discussing your coeliac disease or dietary needs?	×	Highly correlated with item 11 (r=0.718)
26	…did you alter your eating pattern (e.g. skipping lunch)?	✓	✓	-	-	-	-	-	×	have you had to miss meals or snacks because suitable food was unavailable?	×	Lowest loading item onto factor, item covered by items 16 and 40
27	…were you wary of eating something that you weren't sure was gluten-free?	-	×							No amendments made to original item	×	**Item deleted** as covered by '…did you worry that you

		Amendments made by stage of development[a]										
No	**Original item**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**Final item following amendments**	**In CDAQ?**	**Reason for deleting item**
												would eat gluten by mistake?'
28	…were you concerned or worried that your food had been contaminated with gluten?	✓	✓	-	-	-	✓	-	-	have you been concerned about cross-contamination (gluten-free food coming into contact with food that contains gluten)?	✓	
29	…were you disappointed with your gluten-free cooking and/or baking?	✓	✓	-	-	-	✓	×		have you had difficulties cooking or baking with gluten-free ingredients?	×	Item not relevant to all respondents - missing data (including N/A) > 5%.
30	…did you avoid social activities?	-	-	-	-	-	✓	-	-	have you avoided social activities?	✓	
31	…did you feel you were excluded from social activities?	×								No amendments made to original item	×	Item same as '…did you feel that others excluded you [from activities] because of your coeliac disease?'
32	…was your ability to travel affected (e.g. travelling to work, the shops, on holiday)?	✓	✓	-	-	-	✓	×		have you been unable to travel because you were ill (for example, going to work or the shops, or travelling on holiday)?	×	Floor effect > 50%
33	…did you have difficulty finding something to eat whilst travelling?	-	×							No amendments made to original item	×	Item deleted - Item covered by at least two other more generic items, item 16 and item 20

		Amendments made by stage of development[a]										
No	**Original item**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**Final item following amendments**	**In CDAQ?**	**Reason for deleting item**
34	…was your ability to go to work affected?	✓	×							...were you able to go to work?	×	Item already covered by '...were your usual [/daily/leisure] activities affected [by symptoms of coeliac disease]?', which is a more generic item as it refers to daily activities rather than work. Work activities may not apply to all.
35	…was you ability to undertake work activities affected?	✓	✓	-	-	-	✓	×		have your work activities been limited by your coeliac disease?	×	Item not relevant to all respondents - missing data (including N/A) > 5%, floor effect > 50%.
36	..were your work activities affected?	✓	-	-	-	-	✓	×		have you had difficulties carrying out work-related tasks?	×	Item not relevant to all respondents - missing data (including N/A) > 5%, floor effect > 50%.
37	…were your usual [/daily/leisure] activities affected [by symptoms of coeliac disease]?	-	✓	-	✓	-	✓	-	-	have your daily activities been limited by your coeliac disease?	✓	

		Amendments made by stage of development[a]										
No	**Original item**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**Final item following amendments**	**In CDAQ?**	**Reason for deleting item**
38	..were your holiday arrangements influenced by your condition?	✓	✓	-	-	-	✓	×		has your choice of holiday or holiday activities been limited by your coeliac disease?	×	Item not relevant to all respondents - missing data (including N/A) > 5%.
39	…were your holiday or leisure activities affected?	-	✓	✓	✓	-	✓	×		have your leisure activities been limited by your coeliac disease (for example, hobbies or sports)?	×	Floor effect > 50%
40	…did you feel frustrated by having to plan ahead? [did you feel it was a hassle to have to plan ahead? (e.g. taking food with you, researching restaurants)?	-	✓	✓	-	-	✓	-	-	have you felt frustrated by having to plan ahead (for example, taking food with you, or choosing restaurants)?	✓	
41	…were you frustrated by the time it took to find [or make] suitable food?	✓	✓	-	-	-	-	-	-	have you felt burdened by the time taken to find or make gluten-free food?	✓	
42	…were you wary of food prepared by others?	-	×							No amendments made to original item	×	**Item deleted** - The content of this item is better captured by a range of other items (4, 22, 28).
43	…did you feel guilty about the impact of your condition on other people?	✓	-	-	-	-	✓	-	-	have you felt guilty about the impact of your coeliac disease on friends and family?	✓	
44	…did you find it hard to correct people if they got it wrong?	-	✓	-	-	-	✓	-	-	have you found it difficult to let people know they have misunderstood your coeliac disease or dietary needs?	✓	

		Amendments made by stage of development[a]										
No	**Original item**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**Final item following amendments**	**In CDAQ?**	**Reason for deleting item**
45	…did you eat something that you were uncertain of because you didn't want to upset someone?	-	✓	✓	-	-	✓	-	×	have you eaten or drunk something that you were uncertain was gluten-free because you felt uncomfortable refusing?	×	Factor loadings < 0.5 on all factors, floor effect - 49.9%
46	…were you affected by the lack of support of friends or family members?	✓	-	-	-	-	✓	×		have you lacked the support of family or friends?	×	Floor effect > 50%
47	…did you feel guilty about the impact of your condition on friends or family members [/other people] (e.g. when choosing a restaurant, family meals)?	×								No amendments made to original item	×	**Item deleted** as similar to '...did you feel guilty about the impact of your condition on other people?'
48	…were you annoyed by others not [/lack of] understanding about your condition and/or dietary needs (e.g. dismissing it as a lifestyle choice or 'fad' diet; not understanding what a gluten-free diet entails)?	✓	✓	✓	-	-	✓	-	-	have you felt that people misunderstood your coeliac disease or dietary needs (for example, thinking you follow a gluten-free diet as a personal choice rather than for your coeliac disease)?	✓	
49	…were you affected by pain?	-	✓	-	-	-	✓	-	-	have you had pain that you think was caused by your coeliac disease?	✓	
50	…were you affected by tiredness or lack of energy?	-	✓	-	-	-	✓	-	-	have you had tiredness or a lack of energy that you think was caused by your coeliac disease?	✓	

		Amendments made by stage of development[a]										
No	**Original item**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**Final item following amendments**	**In CDAQ?**	**Reason for deleting item**
51	…did you need to rush to the toilet [because of diarrhoea / your bowels]?	×								No amendments made to original item	×	**Item deleted** as similar to '…were you affected by diarrhoea and/or loose bowel movements?'
52	…were you affected by diarrhoea and /or loose bowel movements?	✓	✓	✓	-	-	✓	-	-	have you been bothered by your bowel movements (for example, diarrhoea, loose stools, or constipation)?	✓	
53	…were you affected by bloating?	✓	✓	-	-	-	✓	-	-	have you had bloating in your abdomen?	✓	
54	…were you troubled by nausea and/or vomiting?	✓	✓	-	✓	✓	✓	-	-	have you had nausea or vomiting that you think was caused by your coeliac disease?	✓	
55	…were your daily/usual activities affected by diarrhoea and / or loose bowel movements?	×								No amendments made to original item	×	**Item deleted** as covered by '…were you affected by diarrhoea and/or loose bowel movements?' and '...were your usual [/daily/leisure] activities affected [by symptoms of coeliac disease]?'

		Amendments made by stage of development[a]										
No	**Original item**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**Final item following amendments**	**In CDAQ?**	**Reason for deleting item**
56	…was your concentration or ability to think clearly affected?	✓	-	-	✓	✓	✓	×		have you had difficulty concentrating or thinking clearly because of your coeliac disease?	×	Floor effect > 50%
57	…were you dissatisfied with your weight?	✓	✓	-	-	-	-	-	×	have you felt bothered by your weight?	×	Factor loadings < 0.5 on all factors
58	…were you annoyed or frustrated about the cost of gluten-free food?	✓	✓	-	-	-	-	-	-	have you felt annoyed or frustrated about the cost of gluten-free substitute foods?	✓	
59	…did you feel guilty about other people buying gluten-free foods for you?	×								No amendments made to original item	×	Item deleted as similar to '…did you feel guilty about other people buying gluten-free foods especially for you?'
60	…did you feel guilty about the impact of your condition on others?	✓	×							…did you feel guilty about the financial impact of your condition on family or friends?	×	Item deleted as it contains an assumption that there is a financial impact, which may not be the case. The item is better covered by items 62 and 24.
61	…were your work activities affected?	×								No amendments made to original item	×	**Item deleted** as covered by four other items

		Amendments made by stage of development[a]										
No	**Original item**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**Final item following amendments**	**In CDAQ?**	**Reason for deleting item**
62	…did the cost of buying gluten-free foods cause financial distress?	✓	✓	✓	✓	-	✓	-	×	have you had financial difficulties due to your coeliac disease (for example, due to the cost of following a gluten-free diet, or inability to work)?	×	Factor loadings < 0.5 on all factors
63	…did you stand out because of your condition or diet, when you did not want to?	×								No amendments made to original item	×	Item deleted as similar to '…did you attract unwanted attention because of your condition or diet?'
64	…were you tempted to eat something that contained gluten?	×								No amendments made to original item	×	**Item deleted** - more about adherence than QOL. Item content covered by '…did you miss [not being able to eat] certain foods?'
65	**New item added:** did you feel down or in low spirits?					#	✓	-	-	have you felt down or in low spirits?	✓	
66	**New item added:** did you worry that you would be unwell while out of the house?		#	✓	-	✓	✓	-	-	have you worried that you would become ill when you were not at home?	✓	
67	**New item added:** did you avoid eating out (for example, at a friend's house, restaurant, or café)?		#	✓	-	✓	✓	-	-	have you avoided going out to eat (for example, at a friend's house, restaurant, or café)?	✓	

		Amendments made by stage of development[a]										
No	**Original item**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**Final item following amendments**	**In CDAQ?**	**Reason for deleting item**
68	**New item added:** have you felt concerned that food prepared by others may contain gluten?				#	✓	✓	-	×	have you felt concerned that food prepared by others, and presented as gluten-free, may contain gluten?	×	Highly correlated with item 22 (r=0.685)

[a]Stage of development: (1) QAS-99; (2) Discussion with research team; (3) Expert opinions; (4) Cognitive interviews – Round one; (5) Cognitive interviews – Round two; (6) Translatability assessment; (7) Survey 1 – data distribution; (8) Factor analysis

Appendix L. CD-PEQ candidate items

List of candidate items for the CD-PEQ developed following qualitative interviews.

	Qualitative theme	Item
1	Access to services	How long did you have to wait for an endoscopy [after the blood test?]?
2	Access to services	How did you feel about the time that you had to wait for an endoscopy?
3	Access to services	If you have had questions about your coeliac disease [in the last 12 months], have you been able to speak to a healthcare professional?
4	Access to services	Are you getting the support that you need from healthcare services in order to manage your condition?
5	Diagnosis	For how long did you experience symptoms before seeking advice from a healthcare professional?
6	Diagnosis	How long was it between the onset of symptoms/first seeking advice and receiving a diagnosis?
7	Diagnosis	How do you feel about the length of time it took to diagnose your coeliac disease? / How quickly do you feel that you were diagnosed?
8	Diagnosis	How was your coeliac disease diagnosed?
9	Diagnosis	If you received a blood test only, were you offered an endoscopy?
10	Diagnosis	Did your diagnosis come about as a result of investigations because of another condition (e.g. anaemia, osteoporosis)?
11	Diagnosis	Who told you that you have been diagnosed with coeliac disease?
12	Diagnosis	Was your diagnosis communicated in a manner which you felt was appropriate?
13	Diagnosis	Were you provided with enough / any written information about your condition?
14	Diagnosis	Did healthcare professionals keep you informed throughout the diagnostic process?
15	Diagnosis	Did you receive a diagnosis of IBS prior to your diagnosis of coeliac disease?
16	Dietitian	Did anyone explain / who explained the gluten-free diet to you?
17	Dietitian	Were you provided with written information about the gluten-free diet?
18	Dietitian	Were you provided with enough information about the changes that you needed to make to your diet?
19	Dietitian	Did you see a dietitian [within x months of] receiving your

		diagnosis?
20	Dietitian	How helpful/useful did you find the dietitian/dietetic appointment?
21	Dietitian	How knowledgeable was the dietitian?
22	Dietitian	Have you seen a dietitian in the past 12 months?
23	Dietitian	How was the appointment with the dietitian arranged/who initiated the appointment request?
24	Follow-up consultations	Did you receive a second endoscopy after you had started a gluten-free diet?
25	Follow-up consultations	Have you received a bone scan since your diagnosis?
26	Follow-up consultations	Were you referred to see a dietitian after your diagnosis?
27	Follow-up consultations	Have you had a follow-up appointment for your coeliac disease in the past year?
28	Follow-up consultations	What happened at your last follow-up appointment?
29	Follow-up consultations	Did you have an opportunity to ask questions?
30	Follow-up consultations	Where was your follow-up appointment held?
31	Follow-up consultations	With whom was your follow-up appointment?
32	Follow-up consultations	How did you know your follow-up appointment was due?
33	Follow-up consultations	How was your follow-up appointment arranged?
34	Follow-up consultations	How satisfied are you with your follow-up care?
35	Follow-up consultations	How helpful was your last dietetic appointment?
36	Follow-up consultations	How clear are communications with healthcare services?
37	Follow-up consultations	Are you able to see a dietitian if you want to?
38	Follow-up consultations	Are you provided with enough information about medical test results?
39	Integrated care and continuity of care	Have you been provided with conflicting information in relation to your coeliac disease?
40	Integrated care and continuity of care	Did you see the same consultant / dietitian / doctor throughout?
41	Integrated care and continuity of care	How easy was it to obtain results of tests?
42	Knowledge of professionals	How knowledgeable were healthcare professionals about your symptoms / what could be wrong with you? OR How knowledgeable did you feel healthcare professionals were in the process of investigating your symptoms and diagnosing you with coeliac disease?
43	Knowledge of professionals	Do you feel that your doctor is knowledgeable about your condition?
44	Knowledge of professionals	Do you feel that your dietitian is knowledgeable about your condition?
45	Prescriptions	Which foods do you obtain on prescription? OR Do you have gluten-free food on prescription?

46	Prescriptions	Within the past year, were you allowed all of the items that you requested on prescription? OR Within the past year, were the items you requested on prescription ever queried?
47	Prescriptions	How easy do you think it is to obtain products on prescription? OR Do you understand the process by which to obtain gluten-free food? OR How straightforward do you think the process is to obtain gluten-free food on prescription?
48	Prescriptions	How knowledgeable have you found healthcare professionals to be with regards to the prescription process?
49	Prescriptions	Has a healthcare professional explained to you how to obtain gluten-free food on prescription?
50	Prescriptions	Have you been given information about which gluten-free foods are available on prescription?
51	Prescriptions	How reasonable do you find the cost of prescriptions?
52	Relationship with HCPs	Was your diagnosis communicated to you in an appropriate and sensitive manner?
53	Relationship with HCPs	How was your diagnosis communicated to you?
54	Relationship with HCPs	Were you provided with [enough] [written] information about coeliac disease at diagnosis?
55	Relationship with HCPs	How confident are you in your GP [/HCPs]? [at diagnosis or in general or within the last 12 months?]
56	Relationship with HCPs	Did your doctor / healthcare professional listen to your concerns and take them seriously?
57	Relationship with HCPs	How supportive and understanding was your doctor/HCP? [at last appointment; in general; at diagnosis?]

Appendix M. Question Appraisal System (QAS-99) coding form

QUESTION APPRAISAL SYSTEM (QAS-99):
CODING FORM

INSTRUCTIONS. Use one form for EACH question to be reviewed. In reviewing each question:

1) WRITE OR TYPE IN QUESTION NUMBER. ATTACH QUESTION.

Question number or question here:

2) Proceed through the form - Circle or highlight YES or NO for each Problem Type (1a... 8).

3) Whenever a YES is circled, write detailed notes on this form that describe the problem.

STEP 1 - READING: Determine if it is difficult for the interviewers to read the question uniformly to all respondents.	
1a. **WHAT TO READ**: Interviewer may have difficulty determining what *parts* of the question should be read.	YES NO
1b. **MISSING INFORMATION**: Information the interviewer needs to administer the question is *not* contained in the question.	YES NO
1c. **HOW TO READ**: Question is *not* fully scripted and therefore difficult to read.	YES NO
STEP 2 - INSTRUCTIONS: Look for problems with any introductions, instructions, or explanations from the *respondent's* point of view.	
2a. **CONFLICTING OR INACCURATE INSTRUCTIONS**, introductions, or explanations.	YES NO
2b. **COMPLICATED INSTRUCTIONS**, introductions, or explanations.	YES NO

Questionnaire Appraisal System
QAS-99
Research Triangle Institute

Taken from Willis and Lessler (1999)

STEP 3 - CLARITY: Identify problems related to communicating the *intent or meaning* of the question to the respondent.	
3a. **WORDING**: Question is lengthy, awkward, ungrammatical, or contains complicated syntax.	YES NO
3b. **TECHNICAL TERM(S)** are undefined, unclear, or complex.	YES NO
3c. **VAGUE:** There are multiple ways to interpret the question or to decide what is to be included or excluded.	YES NO
3d. **REFERENCE PERIODS** are missing, not well specified, or in conflict.	YES NO
STEP 4 - ASSUMPTIONS: Determine if there are problems with assumptions made or the underlying logic.	
4a. **INAPPROPRIATE ASSUMPTIONS** are made about the respondent or about his/her living situation.	YES NO
4b. **ASSUMES CONSTANT BEHAVIOR** or experience for situations that vary.	YES NO
4c. **DOUBLE-BARRELED**: Contains more than one implicit question.	YES NO

STEP 5 - KNOWLEDGE/MEMORY: Check whether respondents are likely to *not know* or have trouble *remembering* information.	
5a. **KNOWLEDGE** may not exist: Respondent is unlikely to *know* the answer to a factual question.	YES NO
5b. **ATTITUDE** may not exist: Respondent is unlikely to have formed the attitude being asked about.	YES NO
5c. **RECALL** failure: Respondent may not *remember* the information asked for.	YES NO
5d. **COMPUTATION** problem: The question requires a difficult mental calculation.	YES NO
STEP 6 - SENSITIVITY/BIAS: Assess questions for sensitive nature or wording, and for bias.	
6a. **SENSITIVE CONTENT** (general): The question asks about a topic that is embarrassing, very private, or that involves illegal behavior.	YES NO
6b. **SENSITIVE WORDING** (specific): Given that the general topic is sensitive, the wording should be improved to minimize sensitivity.	YES NO
6c. **SOCIALLY ACCEPTABLE** response is implied by the question.	YES NO

STEP 7 - RESPONSE CATEGORIES: Assess the adequacy of the range of responses to be recorded.	
7a. **OPEN-ENDED QUESTION** that is inappropriate or difficult.	YES NO
7b. **MISMATCH** between question and response categories.	YES NO
7c. **TECHNICAL TERM(S)** are undefined, unclear, or complex.	YES NO
7d. **VAGUE** response categories are subject to multiple interpretations.	YES NO
7e. **OVERLAPPING** response categories.	YES NO
7f. **MISSING** eligible responses in response categories.	YES NO
7g. **ILLOGICAL ORDER** of response categories.	YES NO
STEP 8 - OTHER PROBLEMS: Look for problems not identified in Steps 1 - 7.	
8. Other problems not previously identified.	YES NO

Appendix N. Expert opinions – letter of invitation

Dear [recipient name],

I am writing to invite you to participate as a member of an expert panel that we would like to form to discuss healthcare experiences and quality of life in coeliac disease. The expert panel is part of a research study being conducted at the University of Oxford.

Our research is exploring patients' experiences of healthcare services accessed to diagnose and manage coeliac disease. In addition, we are planning to identify how the condition impacts on health-related quality of life (HRQOL), and to explore relationships between patients' experiences and HRQOL.

As part of the study, a patient-reported outcome measure and patient experience questionnaire are being developed. The patient-reported outcome measure will assess quality of life in adults with coeliac disease, and the patient experience questionnaire will ask patients about their experiences of healthcare services. For your information about the study, the development of the measures, and the expert panels, please see the attached document.

The developed measures will be used to investigate the aims of this research. In addition, it is anticipated that the PROM will also go on to be used in future research studies and in clinical practice.

The expert panel will be asked to appraise these two questionnaires and discuss whether they are comprehensive. The panel will meet for two hours in [location] on [date]. The discussion will be audio-recorded to minimise note-taking.

I hope that you are interested in participating as your input would be valuable.

I look forward to hearing from you.

Kind Regards,
Helen Crocker

Appendix O. Expert opinions - information sheet

Health Services Research Unit
Department of Public Health

Rosemary Rue Building, Old Road Campus, Headington, Oxford OX3 7LF
Helen Crocker, Tel: +44 (0)1865 289431, Email: Helen.Crocker@dph.ox.ac.uk

RESEARCH STUDY

Diagnosis and management of coeliac disease: Quality of life and patients' experiences of healthcare services

Research Aims

This research study aims to explore patients' experiences of healthcare services utilised for the diagnosis and management of coeliac disease to determine whether services are meeting patients' needs. In addition, the impact of coeliac disease on health-related quality of life, and the relationship between patients' experiences and health-related quality of life will be explored.

This research is being led by Helen Crocker, a researcher in the Department of Public Health at the University of Oxford, under the supervision of Professor Crispin Jenkinson and Dr Michele Peters. The research is funded by the Medical Research Council and is part of a doctoral research programme.

Methods

This study will adopt a mixed-method approach, utilising both semi-structured interviews and a cross-sectional survey. Interview data and background literature have informed the development of two self-administered questionnaires: a patient-reported outcome measure (PROM), and a patient experience questionnaire. The PROM will assess quality of life in adults with coeliac disease, and the patient experience questionnaire will ask people with coeliac disease about their experiences of healthcare services from diagnosis through to current follow-up care.

Questionnaire Development

The questionnaires were developed after interviewing 23 adults with coeliac disease about their experiences of both living with the condition and using healthcare services in relation to their condition. Interview participants were recruited through Coeliac UK and snowball sampling. A variation was sought across participant demographic and disease characteristics, particularly gender, age, and duration since diagnosis. Data collected during the semi-structured interviews was audio-recorded with the participant's consent, transcribed verbatim, and analysed thematically in NVivo9 (a qualitative data analysis software package). The two questionnaires were developed based on this thematic analysis (i.e. common aspects identified across all interviews).

Expert Opinions

The next stage of this research involves asking a multi-disciplinary group of experts to review and comment on both the PROM and patient experience questionnaire. The primary purpose of obtaining experts' opinions is to ensure that the questionnaires adequately cover all aspects of quality of life and patients' experiences of healthcare respectively, and identify ways in which the questionnaires could be improved or made more useful.

Comments provided by experts will be reviewed and used to make amendments to the questionnaires. Following these amendments, a sample of people with coeliac disease will complete the questionnaires to

ensure they are performing as intended, prior to piloting the questionnaires to larger samples. The psychometric properties (e.g. reliability and validity) of the PROM will also be assessed.

Study Outcomes and Dissemination of Results

It is intended that the results of the study will be used to inform healthcare policy with the aim of improving the quality of healthcare for people with coeliac disease. More specifically, it is hoped that aspects of healthcare services requiring improvement will be identified. In addition, associations between quality of life and patients' experiences will be identified, providing additional evidence to inform guidance documentation produced by professional bodies about the diagnosis and management of coeliac disease (e.g. recommendations about whether and how patients should receive follow-up).

The University of Oxford is committed to the dissemination of its research for the benefit of society. Therefore, it is intended that the research will be written up as one or more papers to be submitted for publication in scientific journals, as a doctoral thesis, and presented at conferences.

Background Information

Patient-Reported Outcome Measures

Patient-Reported Outcome Measures (PROMs) are short questionnaires which measure health status from the patient's perspective. Measures are broadly classified as disease-specific or generic. Disease-specific measures are intended for use within a specific population (e.g. coeliac disease) and are therefore, able to assess aspects of health that are more relevant to patients. Generic measures can be administered to any population group and can therefore, be used to compare health across populations.

The UK Government are committed to extending the use of PROMs within the NHS to wherever practicable (see 'Equity and excellence: Liberating the NHS' (Department of Health, 2010)). Since 2009, in England, it has been mandatory for providers to invite patients undergoing one of four elective procedures (including hip or knee replacements) to complete PROMs.

This research involves the development of a disease-specific PROM to assess health-related quality of life in adults with coeliac disease. As well as being used in this study, it is anticipated that the measure could be used in other research studies, as an endpoint in clinical trials, to assist healthcare professionals in the provision of individual patient care, and to monitor quality of life over time.

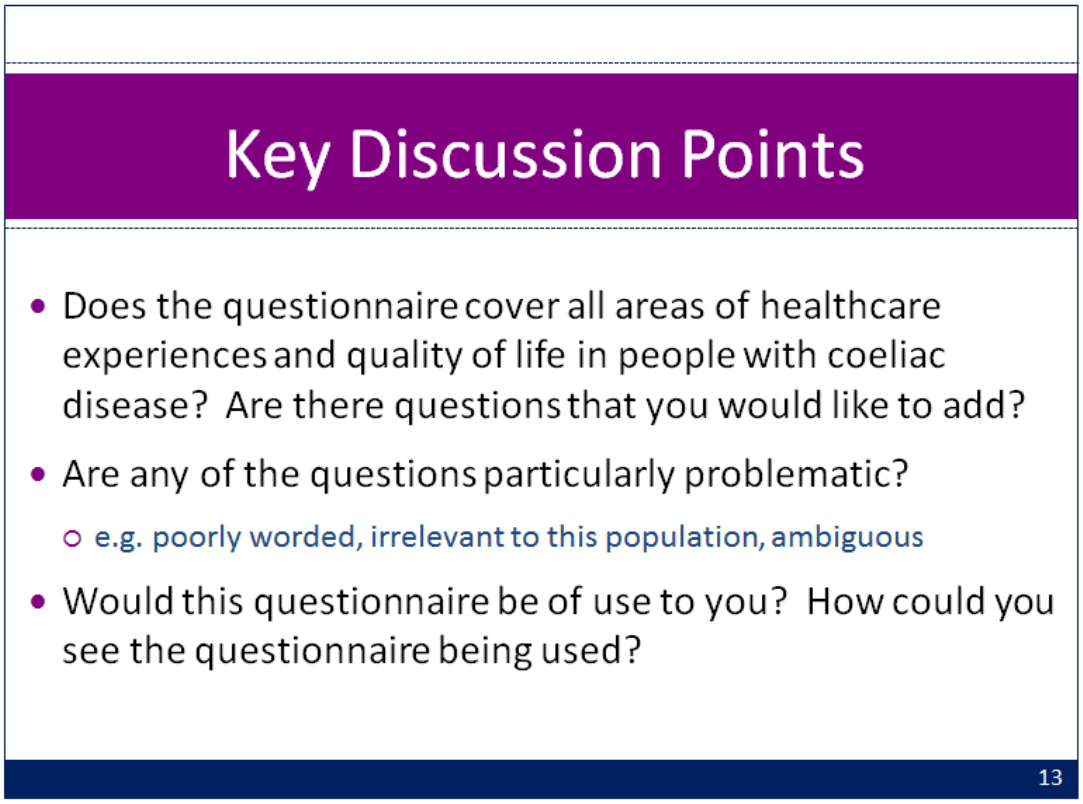
Measuring Patients' Experiences

There is increasing interest in asking patients about their experience of healthcare services as a method of gaining information to indirectly improve the quality of healthcare. In particular, the UK government has outlined, in the NHS Outcomes Framework, their commitment to ensuring patients have a positive experience of healthcare. Typically, patient experience questionnaires include dimensions such as access and waiting times, information provision, communication, physical environment, and co-ordination of care.

Coeliac Disease

Coeliac disease is a chronic autoimmune disease, which affects approximately one per cent of the UK population. Consumption of gluten, a protein found in wheat, barley, and rye, within this population group triggers an immune response which results in damage to the intestinal lining. The classic symptoms experienced by individuals prior to diagnosis include diarrhoea, abdominal discomfort, fatigue, and weight loss. However, symptoms vary widely. Serological testing is used to diagnose coeliac disease, but as false positives are possible, the diagnosis is typically confirmed by duodenal biopsy. At present, the only treatment for coeliac disease is a life-long gluten-free diet.

Appendix P. Expert opinions – discussion points handout



Evaluating the Questionnaire

Below are some additional questions that you might like to consider while reviewing the questionnaire:

1. Is the language of the question clear, direct and specific?
2. Is the question leading (i.e. asking for a 'desirable' response)?
3. Does the question contain words (e.g. professional jargon) that might be unfamiliar to all respondents?
4. Can the question be interpreted in more than one way?
5. Is the question likely to be endorsed by almost all respondents or by almost none?
6. Is the question consistent with the themes being measured?
7. Is the question likely to produce information of interest to you?
8. Do the response categories cover all possible answers?
9. Is the length of the questionnaire OK?
10. Are there any questions that could be deleted?
11. Are there any questions missing?

Appendix Q: Expert opinions – example comments and amendments

Examples of experts' comments are presented in the table below, together with the original item, and the amended item (if applicable). The table contains comments obtained in relation to ten patient experience items, and ten items from the CDAQ (i.e. the full table is not shown).

N.B. 'P1' refers to Expert Panel Meeting 1; 'P2' refers to Expert Panel Meeting 2; 'SC' is a Gastroenterologist; and 'MM' and 'RS' are GPs.

(a) Patient Experience Questionnaire

ID	Original question	Comments (source in brackets)	Notes and amendments	Amended
1	Which of the following symptoms did you have before you were diagnosed with coeliac disease?	(P1) It may be useful to distinguish between a short episode of a symptom and a longer period of it – may add 'ongoing', 'continuous' or 'persistant' in front of some of the symptoms, e.g. diarrhoea, tiredness, headache. (P1) Change 'anaemia' to 'unexplained anaemia'. (P1) The panel felt weight gain was an unusual symptom prior to diagnosis. As such, we may wish to separate 'weight loss' and 'weight gain' in to separate categories. (P1) 'Mouth ulcers' missing (P2) Some symptoms are missing, e.g. fertility problems, '*skin problems*' – not restricted to DH as people get other skin problems, neurological symptoms (e.g. numbness). (P1) Suggestion that we review the NICE guidelines to	**Amended response options:** **- Combine 'diarrhoea' and 'loose bowel movements' → 'Diarrhoea / loose bowel movements'** **- 'Pain' → 'Abdominal pain'** **- 'Bloating' → 'Abdominal bloating'** **- Amend 'Incomplete emptying' to 'Incomplete bowel movements'** **- 'Tiredness / lack of energy' → 'Chronic fatigue ('tired all the time')** **- 'Weight loss / gain' → 'Unexpected weight loss'** **- 'Rumbling in stomach' → 'Rumbling stomach'** **- Add 'Skin rash'** **- Add 'Anxiety / depression'?**	✓

ID	Original question	Comments (source in brackets)	Notes and amendments	Amended
		see their list of symptoms. (P2) Review the NICE guidelines for the top ten symptoms. (MM) 'Pain' response option quite general. (MM) 'Tiredness / lack of energy' could also be referred to as 'fatigue'. (MM) Could add 'skin rash' to cover people with Dermatitis Herpetiformis. (MM) Some people also present with depression.	Check understanding of 'nausea' in cognitive interviews.	
2	How long was it from when you first experienced symptoms to seeking medical advice?	(P1) Response options do not cover a wide enough range. Time periods could be much longer if the respondent first experienced symptoms as a child.	**Amended response categories:** **- 'Less than 3 months', '4-6 months', '7-12 months', '13-23 months', '24 months or more'**	✓
4	How would you rate the length of time it took to diagnose your coeliac disease?	(P1) The panel felt this needed clarification with regards to whether this was asking about the length of time since the onset of symptoms to diagnosis, or the length of time since seeking medical advice to diagnosis.	**Amended question:** **'How would you rate the length of time from when you first sought medical advice about your symptoms to receiving a definite diagnosis?'**	✓
5	Which health care professional did you speak to the most often before you received your diagnosis?	(P1) It would be useful to clarify that only one professional should be selected (tick one only). (P2) Embolden *before* to improve clarity (P1) The patient may have sought help from a nutritionist or other alternative therapist. This could be added as a response option, although the panel objected to a nutritionist being referred to as a health care professional. (P1) The patient may have spoken to a Pharmacist. (P1) The panel thought it is unlikely that the patient would have spoken to a Healthcare Assistant, and queried whether the patient would know the difference between a HCA and nurse.	**Amended question:** **- Embolden 'before'** **- Add '(Please tick one only)'** **Amended response options:** **- Add 'Pharmacist'** **- Remove 'Healthcare assistant'** **- Amend 'Hospital consultant, e.g. Gastroenterologist' to 'Hospital doctor'** Notes: - As Healthcare assistant is unlikely to be seen it will be removed from the	✓

ID	Original question	Comments (source in brackets)	Notes and amendments	Amended
		(P2) The respondent may not know what a *healthcare assistant* is. It was also thought that patients won't know the difference between a healthcare assistant and nurse. (P1) Hospital Consultant could refer to a range of different consultants, e.g. rheumatologist, gastroenterologist. (P2) *Clinic Doctor* may be a better term than Hospital Consultant as they won't always see a consultant.	response options. If a HCA was seen, it can be recorded in 'other'. - Check the understanding of 'Hospital doctor' with respondents in cognitive interviews. - Nutritionist not added as they are not a registered health care professional.	
6	Thinking about the health care professional that you spoke to the most often before you received your diagnosis, did this person…	(P2) Embolden *before* to improve clarity (P1) Leaf parts of question could be emboldened to make them stand out more. (P1) Reword to ask specifically about how they felt or their experience, e.g. 'did you feel this person'	**Amended question:** **-' Thinking about the health care professional that you spoke to the most often before you received your diagnosis, did you feel that this person…'** **- Embolden 'before'** **Amended response options:** **- '…listened carefully to you?** **- '…gave you confidence in them?'** **- '…took your symptoms seriously?'**	✓
7	Before your diagnosis of coeliac disease, did you receive an incorrect diagnosis (for example, Irritable Bowel Syndrome (IBS))?	(P1) The panel felt it was leading by giving one example of IBS. Coeliac disease could also be misdiagnosed as gastroenteritis. It is also misdiagnosed as a result of osteoporosis or anaemia not being followed-up, i.e. unexplained anaemia. (RS) When asked about other diagnoses which may have been provided initially, alternative routes were mentioned, i.e. patients presenting with anaemia and infertility. (RS) The wording 'incorrect' diagnosis could be a bit	**Amended question:** **'Before your diagnosis of coeliac disease, did you receive other diagnoses to explain your condition?'** **Amended response options:** **'Yes (what was the diagnosis/diagnoses? _____)'**	✓

ID	Original question	Comments (source in brackets)	Notes and amendments	Amended
		judgemental and felt that the word 'alternative' might be more appropriate.		
8	Did you receive enough information throughout the diagnostic process?	(P1) The panel felt it should ask whether they *feel or think* they received enough information. (P1) This question may be better placed at the end of the diagnosis section – after Q16.	**Amended question positioning:** **- Move to after question 11** Notes: It is implicit that the question is asking about their opinion. Question moved to a position in the questionnaire which better reflects the diagnostic pathway.	✓
9	Which tests did you have to diagnose your coeliac disease?	(P1) The definition of endoscopy could be amended to read 'in which a *fine* tube *with a camera* is passed *via* the *mouth* into the *gut*'. It was suggested that Coeliac UK's website is reviewed to see the wording they use. (P2) The definition of endoscopy should include a reference to a camera. (RS) Queried whether a diagnosis is ever made without the collection of a biopsy, and noted that the gold standard is to collect tissue. (P1) Gold standard is to take a biopsy as well – could say 'a sample of the gut would normally be taken'. (P1) It was raised that participants may not know which blood tests they have had. Therefore, maybe change question **a** to read 'blood test (antibody)' (P1) The terminology 'endoscopy (with biopsy)' was preferred for question **b**. (P1) It was also noted that those diagnosed longer periods of time ago may not have had these tests. They may instead have had a Crosby capsule (although it was felt that patients would not know	**Amended definition of endoscopy:** **'An endoscopy (sometimes called a gastroscopy) is a medical procedure in which a thin tube with a camera is passed via the mouth into the intestine in order to examine it. During the procedure, a sample (biopsy) of the intestine is normally taken for closer examination.'** **Amended question:** **Amend sub-section 'a' to read 'Blood test (antibody)'** **Amend sub-section 'b' to read 'Endoscopy (with biopsy)'.** **Added sub-section 'd' - 'Other, *please state* _ _ _ _ _ _ _ _ _ _'** Notes: Check respondents' understanding of intestine in the cognitive interviews –	✓

ID	Original question	Comments (source in brackets)	Notes and amendments	Amended
		what this is) or a gluten challenge. It was thought 'gluten challenge' could be added as some patients refuse more invasive tests, and this would also capture those who have come through the nutritionist route. (RS) When asked if the list of testing methods needs to be extended, he thought it would be sufficient to just put 'other' as he felt this will not relate to many.	would the term 'gut' be more understandable? The sub-section 'other' will allow for older methods of diagnosis to be captured, e.g. Crosby capsule, gluten challenge.	
10	Were you told to keep eating foods containing gluten until you received a definite diagnosis?	(P2) Preferred wording would be '…gluten while you were having your tests or investigations done?'	**Amended question:** **'Were you specifically told to eat foods containing gluten while your tests and investigations were being carried out?'** **Amended response options:** **- 'Yes, I was told to continue eating foods containing gluten'** **- 'Yes, I was told to re-introduce foods containing gluten'** **- 'No'** **- 'I can't remember'**	✓

(b) Patient-Reported Outcome Measure

ID	Original item	Comments (source in brackets)	Notes and amendments	Amended
1	Did you worry that you might be unwell after eating out (for example, at a friend's house, restaurant, or café)?	(P2) Eating out in restaurants may not occur in all cultures. Therefore, it is important to provide examples – eating in other people's houses, restaurants, or cafes. (P1) This is also about whether the patient has trust in	**Amended item:** **Amended item:** **'Did you worry that you might be unwell after eating food prepared by others (for example, at other people's houses,**	✓

ID	Original item	Comments (source in brackets)	Notes and amendments	Amended
		the establishment.	**restaurants or cafés)?'**	
4	Have you felt that people misunderstood your condition or dietary needs (for example, referring to your condition as a lifestyle choice)?	(P2) *Lifestyle choice* may be better phrased as *voluntary choice*, *personal choice* or *individual choice*. Helpful to include an example – choice rather than necessity.	**Amended item:** **'Have you felt that people misunderstood your condition or dietary needs (for example, referring to your gluten-free diet as a personal choice)?'** Notes: 'personal' is likely to better translate into other languages.	✓
6	Did you receive unwanted attention because of your condition or dietary needs?	(P2) The phrase *unwanted attention* was questioned, however, a more suitable phrase could not be identified. Concept trying to get at - being viewed as a disease rather than as a normal person. Suggestion – '*do you feel you need to talk about your condition too much?'*.	Notes: Explore this item further in cognitive interviews to ascertain how people with coeliac disease understand this question, particularly the phrase 'unwanted attention'.	✓
11	Have you been affected by diarrhoea or loose bowel movements?	(P2) The patient could also experience constipation. Therefore, it may be better phrased as '*have you been troubled or bothered by your bowel movements*' or '*have you had problems with your bowels (e.g. diarrhoea, or loose bowels, or constipation)*'. '*Troubled or bothered by*' might be better than '*affected*'. (P2) State that this is in relation to / caused by coeliac disease.	**Amended item:** **'Have you been troubled by your bowel movements (for example, diarrhoea, loose bowels, or constipation)?'** Notes: The instructions at the start of the questionnaire state that the questions are in relation to coeliac disease. To additionally state this in the item would make the item too long.	✓
12	Have you been affected by bloating in your abdomen?	(P2) State that this is in relation to / caused by coeliac disease.	Notes: The instructions at the start of the questionnaire state that the questions are in relation to coeliac disease. To additionally state this in the item would make the item too long.	✓

ID	Original item	Comments (source in brackets)	Notes and amendments	Amended
13	Have you been affected by nausea (feeling sick) or vomiting?	(P2) State that this is in relation to / caused by coeliac disease as opposed to another condition.	Notes: The instructions at the start of the questionnaire state that the questions are in relation to coeliac disease. To additionally state this in the item would make the item too long.	✓
18	Have your leisure activities been limited (for example, holidays, sports, or hobbies)?	(P2) Leisure activities may not transcend across countries/cultures	**Amended item:** **'Have your leisure activities been limited (for example, hobbies, sports, or holidays)?'** Notes: If there are issues regarding the translation of the concept 'leisure', this should be identified in the translatability assessment.	✓
19	Have your holiday or holiday activity choices been limited?	(P2) Holiday may not transcend across countries/cultures (some cultures may not understand the concept of a holiday) – may be better phrased as *going away from home*. Also, potentially covered in the planning question.	Notes: Leave item at present. It will probably be deleted in due course as it is unlikely that the issue will affect many. Expert opinions can lead to the addition of items, but should not result in items being deleted.	✓
20	Did you worry that you would be unwell while out of the house?	(P2) It was suggested that *'out of the house'* is reworded to '*away from your home*'. '*Out of the house*' could be taken too literally, e.g. when in the garden.	**Amended item:** **'Did you worry that you would be unwell while away from your home?'**	✓
24	Did you feel down or in low spirits?	(P1) Potential difficulties identifying the cause of depression, e.g. due to tiredness, or difficulties obtaining food.	Notes: This issue applies to various symptoms and is not something easily addressed.	✓

Appendix R. Cognitive interviews – information sheet

Health Services Research Unit
Nuffield Department of Population Health
Rosemary Rue Building, Old Road Campus, Headington, Oxford OX3 7LF

Research Contact: Helen Crocker, Postgraduate Research Student
Tel: +44 (0)1865 289431, Email: Helen.Crocker@dph.ox.ac.uk

Diagnosis and management of coeliac disease: Quality of life and patient's experiences of healthcare services

Information Sheet for Interview Participants

What is the purpose of this research?

The purpose of this research is to find out about people's experiences of living with coeliac disease and their experiences of using healthcare services to diagnose and manage their condition. In order to explore these issues, we have developed a questionnaire after conducting a number of interviews with people with coeliac disease. We would like to find out whether the questionnaire is easy to complete and how it can be improved before being used in a survey.

Who is doing the research?

The research is led by Helen Crocker, a researcher in the Nuffield Department of Population Health at the University of Oxford, under the supervision of Professor Crispin Jenkinson and Dr Michele Peters. The research is funded by the Medical Research Council and is part of a doctoral research programme. The research is being undertaken with the support of Coeliac UK.

What will I have to do?

If you decide to participate, you will be asked to take part in an interview which will last for approximately an hour. During the interview you will be asked to complete one section of the questionnaire, either about your experiences of living with coeliac disease, or about your experiences of healthcare services used in relation to your coeliac disease. As you complete the questionnaire, the researcher will ask you some questions about your experience of completing it (e.g. whether you thought any questions were ambiguous, difficult to understand or hard to answer). The primary purpose of the interview is to find out how the questionnaire can be improved rather than to find out about your personal experiences.

The interview will be conducted by telephone at your convenience, with the researcher calling you so that you do not incur call charges. The interview will be audio-recorded to minimise note-taking. If at any point during the interview you decide that you do not want to continue, the interview will be stopped.

What will happen with the information that I provide?

Your comments, along with comments provided by other people with coeliac disease, will be used to improve the questionnaire. The improved questionnaire will be used in a survey to assess experiences of healthcare services and quality of life in coeliac disease. It is intended that the results of this survey will be used to inform healthcare policy to improve the quality of healthcare for people with coeliac disease and find out how coeliac disease affects the quality of life of those living with the condition.

Version 1.2, 30/08/2013, REC Ref No: MSD-IDREC-C1-2013-142

Director of HSRU
Professor Crispin Jenkinson DPhil

Head of Department
Professor Sir Rory Collins FMed Sci FRCP

Who can take part?

Participants should be aged 18 years or over, live in England, and have coeliac disease. You will also need access to a telephone **or** Skype (software that allows voice calls over the Internet).

Will participation be confidential?

Personal details and other data collected as part of this research will be accessible to the research team only. Paper documentation will be stored in locked filing cabinets and electronic files will be stored on a password protected computer in accordance with the current Data Protection Act.

You will be assigned an identification number, and all documentation relating to the information that you provide will be marked with this identification number and not your name. Personal data (e.g. name and contact details) will not be kept beyond your involvement in the study. In accordance with guidelines produced by the Medical Research Council, anonymised digital audio files will be kept for a period of twenty years to allow the research to be reviewed if necessary.

What will happen with the results of the study?

The University of Oxford is committed to the dissemination of its research for the benefit of society. Therefore, it is intended that the research will be written up as one or more papers to be submitted for publication in scientific journals, presented at conferences, and as a doctoral thesis. On successful submission of the thesis, it will be deposited in the University archives to facilitate its use in future research. The thesis will be available in print and online. Identifiable data will not appear in presentations or any written materials.

How can I take part?

Participation in the study is entirely voluntary. If you have any questions that you would like to ask, please contact Helen Crocker on 01865 289431 or email: Helen.Crocker@dph.ox.ac.uk. If you decide that you would like to take part, please complete the enclosed consent form and return it to: Helen Crocker, Nuffield Department of Population Health, University of Oxford, Rosemary Rue Building, Old Road Campus, Oxford OX3 7LF or email Helen.Crocker@dph.ox.ac.uk. The researcher will then contact you to arrange a suitable date and time for the interview. You are free to withdraw from the study at any point in time without providing a reason and without penalty, and we will not contact you further.

Are there any risks involved in taking part?

We do not foresee any risks involved in taking part in this study. If participating in this research raises questions about the condition that you would like to discuss, you can contact Coeliac UK, a charity for people with coeliac disease, on their Helpline: 0845 305 2060 or visit their website: www.coeliac.org.uk.

Are there any benefits in taking part?

The information that you provide may help improve the questionnaire which will be used in a wider study intending to inform healthcare policy and improve health services in the future. There are no direct benefits in taking part.

What can I do if I have any concerns about the research study?

This research has been reviewed by and received ethics clearance from the University of Oxford Central University Research Ethics Committee. If you have any concerns about the study, please contact the research team (tel: 01865 289431, email: Helen.Crocker@dph.ox.ac.uk). If the research team are unable to address your concerns and you would like to make a formal complaint, you may contact the Research Ethics Committee at the University of Oxford (email: ethics@medsci.ox.ac.uk; address: Medical Sciences Inter-Divisional Research Ethics Committee, Medical Sciences Divisional Office, Level 3, John Radcliffe Hospital, Oxford, OX3 9DU).

Appendix S. Cognitive interviews - participant consent form

Health Services Research Unit
Nuffield Department of Population Health

Rosemary Rue Building, Old Road Campus, Headington, Oxford OX3 7LF

Research Contact: Helen Crocker, Postgraduate Research Student
Tel: +44 (0)1865 289431, Email: Helen.Crocker@dph.ox.ac.uk

Diagnosis and management of coeliac disease: Quality of life and patient's experiences of healthcare services

Consent Form for Interview Participants

The purpose of this research is to find out about people's experiences of living with coeliac disease and their experiences of using healthcare services to diagnose and manage their condition. Please read and tick the following statements and sign your name below to consent to taking part in this research project.

		Please Tick
1.	I confirm that I have read and understood the information sheet for this research study, have had the opportunity to ask questions about the study and have had these answered satisfactorily.	☐
2.	I understand that personal data provided will be accessible to the research team only. Paper documentation will be stored in locked filing cabinets within the department and electronic files stored on password protected computers. Personal data will not be kept beyond your involvement in the study and anonymised digital audio files will be kept for twenty years.	☐
3.	I understand that the research will be written up as a thesis and deposited in the University archives, published in academic journals, and presented at conferences. I understand that participant names and other unique identifying information will not appear in reports or publications.	☐
4.	I understand that this study has received ethics clearance from the University of Oxford Central University Research Ethics Committee.	☐
5.	I confirm that I am aged 18 years or older and have coeliac disease.	☐
6.	I agree to take part in this study.	☐
7.	I permit the interview to be audio recorded.	☐
8.	I understand that my participation is voluntary and I can withdraw from the study at any time without providing a reason and without penalty, and will not be contacted further.	☐
9.	I understand how to raise any concerns that I have about the study and how to make a formal complaint.	☐

Participant's Name (print): ……

Participant's Signature: …… Date: ……

Researcher's Name (print): ……

Researcher's Signature: …… Date: ……

Version 1.2, 30/08/2013, REC Ref No: MSD-IDREC-C1-2013-142

Director of HSRU
Professor Crispin Jenkinson DPhil

Head of Department
Professor Sir Rory Collins FMed Sci FRCP

Health Services Research Unit
Nuffield Department of Population Health

Rosemary Rue Building, Old Road Campus, Headington, Oxford OX3 7LF

Research Contact: Helen Crocker, Postgraduate Research Student
Tel: +44 (0)1865 289431, Email: Helen.Crocker@dph.ox.ac.uk

Diagnosis and management of coeliac disease: Quality of life and patient's experiences of healthcare services

Contact Details

Please provide your contact details below so that the researcher can contact you to arrange a suitable date and time for your interview.

Telephone No:	
Best time to phone:	
Email:	
Address *(needed to post questionnaire)*:	

Please send this completed form to the University of Oxford:

Either by post

Health Services Research Unit, Nuffield Department of Population Health, Rosemary Rue Building, Old Road Campus, Headington, Oxford, OX3 7LF

Or by email

Helen.Crocker@dph.ox.ac.uk

Appendix T. Cognitive interviews – letter of invitation

Health Services Research Unit
Nuffield Department of Population Health

Rosemary Rue Building, Old Road Campus, Headington, Oxford OX3 7LF

Research Contact: Helen Crocker, Postgraduate Research Student
Tel: +44 (0)1865 289431, Email: Helen.Crocker@dph.ox.ac.uk

[Date]

[Address]

Diagnosis and management of coeliac disease: Quality of life and patient's experiences of healthcare services

Dear [Title] [Surname],

Last year, you expressed an interest in participating in a research study conducted by the University of Oxford. As you may recall, the research aims to find out about people's experiences of using healthcare services to diagnose and manage coeliac disease and how the condition impacts on their quality of life. We hope the research will help improve healthcare services for people living with the condition.

As part of the ongoing research, we have developed a questionnaire asking about experiences of living with coeliac disease, and experiences of using healthcare services in relation to coeliac disease. We are writing to ask whether you would like to take part in an interview during which you will be asked to complete a questionnaire and answer some questions about your experiences of completing it. Interviews will be conducted via telephone and will last for around one hour. Further information can be found in the enclosed information sheet.

Taking part in this study is voluntary and confidential. If you would like to take part, please complete the consent form and send it to the University of Oxford in the pre-paid envelope provided. A researcher will then contact you to arrange a suitable date and time for your interview. If you have any questions about the study, please contact Helen Crocker on 01865 289431 or email: Helen.Crocker@dph.ox.ac.uk.

I do hope you will consider taking part in this project. You will not be contacted again in relation to this study, unless you decide to take part in an interview.

Yours sincerely,

Helen Crocker (nee Boyce)

Appendix U. Cognitive interviews - recruitment advert



Accompanying text: The University of Oxford is conducting a research study to find out about peoples' experiences of living with coeliac disease and using health care services to diagnose and manage the condition. To explore these issues, we have developed a questionnaire. We are now looking for volunteers willing to complete the questionnaire and answer some questions about it over the telephone (e.g. whether you thought any questions were ambiguous, difficult to understand or hard to answer). This will take around an hour. The questionnaire will be improved with your feedback and used in a survey to assess experiences of health care services and quality of life in coeliac disease.

Appendix V. Cognitive interviews – letter to accompany questionnaire

Health Services Research Unit
Nuffield Department of Population Health

Rosemary Rue Building, Old Road Campus, Headington, Oxford OX3 7LF

Research Contact: Helen Crocker, Postgraduate Research Student
Tel: +44 (0)1865 289431, Email: Helen.Crocker@dph.ox.ac.uk

Diagnosis and management of coeliac disease: Quality of life and patient's experiences of healthcare services

[Date]

[Participant's name]
[Participant's address]

Dear [participant's name],

Thank you for agreeing to take part in an interview as part of a research study exploring people's experiences of living with coeliac disease and their experiences of using healthcare services to diagnose and manage their condition.

As discussed, the interview will be carried out on [interview date] at [interview time]. The researcher will call you on the telephone number that you have provided. If this date and time are no longer convenient, please contact me to re-arrange your interview (contact details above).

Please find enclosed the questionnaire which you will be asked to complete one section of during the interview. Whilst completing the questionnaire, you will be asked some questions about your experience of completing it, e.g. whether you thought any questions were ambiguous, difficult to understand or hard to answer. There is no need to do any preparation for the interview. It is important that the questionnaire is completed during the interview and not before.

If you have any questions that you would like to ask before the interview, please do not hesitate to contact me by telephone: 01865 289431 or email: Helen.Crocker@dph.ox.ac.uk.

Yours sincerely,

Helen Crocker

REC Ref No: MSD-IDREC-C1-2013-142

Director of HSRU
Professor Crispin Jenkinson DPhil

Head of Department
Professor Sir Rory Collins FMed Sci FRCP

Appendix W: Concept elaboration document - CDAQ

Item No.	Item	Concept elaboration
1	did you worry that you might be unwell after eating food prepared by others (for example, at other people's houses, restaurants, or cafés)?	Concern or worry that the respondent would experience symptoms of CD (e.g. diarrhoea or abdominal bloating) after eating food that had been prepared by someone other than themselves.
2	did you feel embarrassed or uncomfortable discussing your condition or dietary needs?	Feeling embarrassed or uncomfortable in situations where the respondent has to disclose their CD (e.g. to obtain suitable food) or is asked to discuss their CD or gluten-free diet (e.g. an interested party asks questions about their condition).
3	did you feel as though you might appear to be making a fuss about your dietary needs?	The respondent felt or was made to feel by others that they were making a fuss about their condition or dietary needs.
4	have you felt that people misunderstood your condition or dietary needs (for example, referring to your gluten-free diet as a personal choice)?	The respondent felt that others misunderstood or did not completely understand the nature of their condition or its treatment. For example, thinking the individual follows a GFD as a lifestyle choice or personal preference.
5	did you find it difficult to let people know they have misunderstood your condition or dietary needs?	When the respondent came across people who misunderstood their condition or dietary needs, the respondent found it difficult to correct them or point out their misunderstanding.
6	did you receive unwanted attention because of your condition or dietary needs?	The respondent received unwanted attention or became the centre of attention when they did not want to be because of their condition and its treatment. For example, people asking lots of (unwanted) questions about the condition when at a dinner.
7	did you feel guilty about the impact of your condition on friends and family?	The respondent felt guilty about the impact that their condition or dietary needs has on their friends or family. For example, the ability to eat out, or restaurant selection.
8	have you felt worried that a family member may have or could develop coeliac disease?	The respondent felt worried or concerned that a family member may already have or may develop CD.
9	have you felt concerned about developing a health condition related to your coeliac disease?	The respondent felt worried or concerned that they may develop a health condition related to their CD in the future (e.g. bowel cancer or osteoporosis). Note that this is not intended to include concerns or worries about existing health conditions.

Item No.	Item	Concept elaboration
10	have you felt concerned about the results of medical tests?	The respondent felt worried or concerned about medical test results yet to be received or already received. These concerns could relate to recent medical tests (i.e. those conducted in the past 4 weeks) or they could be ongoing concerns about tests conducted in the more distant past.
11	have you been troubled by your bowel movements (for example, diarrhoea, loose bowels, or constipation)?	The respondent has experienced and been troubled by abnormal bowel movements (e.g. diarrhoea or loose bowel movements, or constipation) that are perceived to be related to their CD.
12	have you been affected by bloating in your abdomen?	The respondent has experience and been troubled or affected by abdominal bloating that is perceived to be related to their CD.
13	have you been affected by nausea (feeling sick) or vomiting?	The respondent has experienced and been troubled or affected by nausea (a feeling of sickness in the stomach or a feeling that one may vomit) or vomiting which is perceived to be related to their CD.
14	have you been affected by pain you think was caused by your coeliac disease?	The respondent has experienced and been troubled or affected by pain that they perceive to be related to their CD (e.g. abdominal pain).
15	have you been affected by tiredness or lack of energy you think was caused by your coeliac disease?	The respondent has experienced and been troubled or affected by (i.e. distressed by) feeling tired or a lack of energy that they perceive to be related to their CD.
16	have your daily activities been limited by symptoms of coeliac disease?	The respondent has not been able to perform their usual daily activities due to symptoms that they perceive to be related to their CD. The limitations experienced may range from not being able to perform the daily activities as fully as usual to not being able to perform the daily activities at all.
17	did you have difficulties with work-related tasks?	The respondent has not been able to perform tasks in the workplace as per usual due to their CD or symptoms experienced as part of their CD. The difficulties experienced performing work-related tasks may range from not being able to perform the tasks as fully as usual to not being able to perform the tasks at all.
18	have your leisure activities been limited (for example, hobbies, sports, or holidays)?	The respondent has had to limit their involvement in leisure activities due to their CD. Limitations may range from not participating as fully as usual to not being able to participate at all.

Item No.	Item	Concept elaboration
19	have your holiday or holiday activity choices been limited?	The respondent's choice of holiday or activities to participate in while on holiday has been limited due to coeliac disease (e.g. choice of holiday destination or accommodation type has been affected because of CD).
20	did you worry that you would be unwell while away from your home?	The respondent felt worried or concerned that they would experience symptoms of CD while they were away from their home and garden, e.g. while at work, travelling, on holiday or at the shops.
21	have you been unable to travel due to being unwell (for example, travelling to work, the shops, or on holiday)?	The respondent was unable to travel (i.e. leave their home and garden) due to symptoms experienced as a result of their CD.
22	did you feel isolated?	The respondent felt isolated or alone due to their condition or need to follow a gluten-free diet. For example, a person with CD may feel isolated if they are unable to join in eating a celebratory cake for a special occasion.
23	did you feel excluded from social activities?	The respondent felt excluded from social activities because of their CD or need to follow a gluten-free diet. The respondent may feel excluded due to the nature of the activity itself (e.g. bread tasting or baking event) or because of the actions of others (e.g. arranging an event that is unsuitable or doesn't consider their needs).
24	did you feel down or in low spirits?	The respondent felt down or in low spirits (i.e. experiencing depression or some aspects of depression). The respondent relates these feelings to their CD or its treatment.
25	did you have difficulty concentrating or thinking clearly?	The respondent had difficulty concentrating on things or thinking clearly as a result of their CD.
26	have you felt bothered by your weight?	The respondent is frustrated or bothered their weight, weight gain or weight loss that they perceive is related to their CD (e.g. weight gain after commencing treatment).
27	did you avoid social activities?	The respondent specifically did not attend certain social activities because of their CD or need to follow a gluten-free diet.
28	have your work activities been limited?	The respondent has been unable to perform some or all activities related to their work or the standard of the performance of these activities has been reduced.
29	did you avoid eating food prepared by others (for example, at a friend's house, restaurant, or café)?	The respondent avoided situations which would require them to eat food prepared by others (e.g. food prepared by a friend, at a restaurant or café, at work).

Item No.	Item	Concept elaboration
30	did you worry that you would accidentally eat or drink gluten?	The respondent felt worried or concerned that they may accidentally or unintentionally consume gluten. The concern could be due to a number of reasons, e.g. concerns about developing symptoms or long-term health problems as a result.
31	have you been concerned about cross-contamination (gluten-free food coming into contact with food containing gluten)?	The respondent felt worried or concerned that their gluten-free food would come into contact with food containing gluten. Note that this contact may not be direct, e.g. gluten-containing particles transferred via a wooden spoon to the gluten-free food.
32	did you feel awkward about refusing unsuitable food or drink from other people?	The respondent felt uncomfortable or rude refusing unsuitable food or drink (i.e. those containing gluten) that was offered to them.
33	did you eat or drink something that you were uncertain was gluten-free because it felt awkward to refuse?	The respondent ended up consuming food or drink that may contain gluten because they felt too uncomfortable or rude to refuse it.
34	did you worry that you would be unwell at an awkward or inconvenient time (for example, while travelling or at a social event)?	The respondent felt concerned or worried that they would develop symptoms of CD at a particularly inconvenient time (e.g. while away from the home or during in a meeting).
35	did you lack the support of family or friends?	The respondent felt that family and friends were not supportive of their condition or their need to follow a gluten-free diet.
36	did you feel you were a nuisance to other people?	The respondent felt that they were a nuisance or a bother to other people because of their coeliac disease or need to follow a gluten-free diet (e.g. due to others having to cater for them or when selecting a suitable restaurant when out with friends).
37	did you feel uncomfortable about other people catering for your dietary needs?	The respondent felt uncomfortable that other people had to cater specifically for their dietary needs (i.e. their need to follow a gluten-free diet).
38	did you feel guilty about other people buying gluten-free substitute foods for you?	The respondent felt guilty or sorry when other people purchased gluten-free substitute foods specifically for them. The guilt could be, for example, in relation to the cost of the substitute food or the inconvenience of having to buy something different specifically for them.
39	were your finances strained due to your coeliac disease (for example, due to the cost of following a gluten-free diet, or inability to work)?	The respondent's finances were strained due to their CD (e.g. due to the cost of needing to follow a gluten-free diet (typically gluten-free substitute foods are more expensive than their gluten-containing counterparts), or due to their inability to work as a result of their medical condition).

Item No.	Item	Concept elaboration
40	have you felt annoyed or frustrated about the cost of gluten-free substitute foods?	The respondent felt annoyed or frustrated by the cost of gluten-free substitute foods (typically gluten-free substitute foods are more expensive than their gluten-containing counterparts).
41	did you have difficulty trying to find suitable food?	The respondent had difficulty trying to find suitable food (i.e. gluten-free food). This could arise in a range of situations, for example: when the participant is out and about, on a day trip, on holiday, or at the supermarket.
42	have you had to miss meals or snacks because suitable food was unavailable?	The respondent had to go without food or drink at a meal or snack time because they were unable to find suitable food (i.e. gluten-free food).
43	was your choice of food affected?	The respondent's choice of food changed. This could be, for example, because they were unable to obtain what they wanted or they could not be certain that a dish was gluten-free and therefore chose a 'safe' option.
44	did you crave foods or drinks containing gluten?	The respondent intensely desired foods or drinks that contained gluten.
45	have you been disappointed with the taste or texture of gluten-free substitutes?	The respondent felt disappointed or discontent with the taste or texture (i.e. quality) of gluten-free substitutes (e.g. beer, bread, cake, biscuits).
46	did you have difficulties cooking or baking with gluten-free ingredients?	The respondent experienced difficulties cooking or baking with gluten-free substitute ingredients (e.g. gluten-free flour). Note: this item could be problematic if the respondent answers with regards to their cooking ability in general. Perhaps the following would be better: 'did you have difficulties cooking or baking gluten-free alternatives?' (could say 'never' because they don't bake/cook).
47	have you felt burdened by the time taken to find or make gluten-free food?	The respondent felt burdened by the time that it took to either find or make gluten-free food.
48	did you have difficulty finding something to eat while out and about?	The respondent had difficulty finding something suitable to eat while out and about (i.e. while away from their home).
49	have you been frustrated by the choice of suitable food available (for example, in supermarkets, cafés or restaurants)?	The respondent felt frustrated by the choice or range of gluten-free food available (e.g. in supermarkets, cafes or restaurants).
50	did you feel frustrated by having to plan ahead (for example, taking food with you, choosing restaurants)?	The respondent felt frustrated by having to plan ahead due to their CD or need to follow a gluten-free diet (e.g. when going on a day trip or holiday).

Appendix X. Cognitive interviews – CDAQ amendments

Amendments made to the CDAQ following two rounds of cognitive interviews. N.B. Response error categories: (1) participants answered items in general rather than in relation to their CD; (2) different interpretations of words or phrases between participants; and (3) items not interpreted as intended.

Q ID	Amendment Type	Response error category	Original wording	Reason for revision / participant comments (rounds 1 and 2)	Revised wording[a]
54	Item revised	1	…have you been affected by nausea (feeling sick) or vomiting?	Some participants considered their experience of nausea and vomiting in general rather than in relation to their coeliac disease. All participants understood the term 'nausea' as intended.	…have you been affected by nausea or vomiting that you think was caused by your coeliac disease?
56	Item revised	1	…did you have difficulty concentrating or thinking clearly?	Several participants answered the question in general rather than in relation to their coeliac disease. Clarification is needed.	…did you have difficulty concentrating or thinking clearly because of your coeliac disease?
-	Instructions revised	1	The following questions ask about how much your coeliac disease or gluten-free diet has affected you during the past 4 weeks.	Some participants reported having some difficulties determining whether certain items were asking about issues in general or in relation to coeliac disease. The questionnaire needs to set out more clearly that it is asking about the participant's quality of life in relation to their coeliac disease. This could be re-iterated throughout the questionnaire in a reminder at the top of each page.	Amend introduction: 'This questionnaire asks how you feel your coeliac disease has affected your life during the past 4 weeks.' Add the following to the top of each page: 'These questions relate to your coeliac disease'

Q ID	Amendment Type	Response error category	Original wording	Reason for revision / participant comments (rounds 1 and 2)	Revised wording[a]
-	Instruction revised	1	During the past 4 weeks, how often…	Some participants reported having some difficulties determining whether certain items were asking about issues in general or in relation to coeliac disease. The instructions were revised in order to clarify that all items should be answered in relation to coeliac disease.	Thinking about your coeliac disease, during the past 4 weeks, how often…
6	Item revised	1 and 2	…did you feel isolated?	Participants had difficulty understanding the term 'isolated'. Some interpreted it as asking about support and others as whether they felt part of the group. Furthermore, some participants were unsure whether the question was asking about isolation in general (i.e. whether the participant is generally alone or lonely) or in relation to their coeliac disease.	…did you feel isolated from others because of your coeliac disease?
1	Item added	1 and 2	…did you feel down or in low spirits?	Participants did not always or were unable to answer this specifically in relation to their coeliac disease. Participants appeared to comprehend the question well, although some felt that their answer would be different if asked whether they felt depressed. To explore whether an item directly asking about depression would be preferable, this item was revised. An additional item asking about 'feeling down or in low spirits' was added. Both items were included in Survey 1 prior to deciding which item to keep.	Additional item (65) added: …have you felt depressed?

Q ID	Amendment Type	Response error category	Original wording	Reason for revision / participant comments (rounds 1 and 2)	Revised wording[a]
7	Item revised	2	…did you feel excluded from social activities?	'Excluded' was interpreted by participants as either meaning partial exclusion (i.e. feeling like an outsider or 'not part of the group') or complete exclusion (i.e. not being able to attend). The latter interpretation is the intended concept and the item was revised to reflect this.	…did you feel excluded from attending social activities?
37	Item revised	2	…have your daily activities been limited by symptoms of coeliac disease?	Some participants answered this question in relation to whether their daily activities had been limited by their coeliac disease in general (e.g. not being able to find somewhere to eat at lunchtime). Whereas, some participants answered this question in relation to whether coeliac disease symptoms had limited their daily activities (e.g. one participant commented that attending meetings can be more difficult if symptoms are bad). This item was intended to ascertain whether symptoms limited the respondent's daily activities rather than coeliac disease in general. The item will not apply to all as not everybody experiences symptoms. As such, the respondent may select 'never' to indicate that they have not experienced symptoms, rather than their symptoms have not limited their daily activities. Therefore, it may be better to ask about limitations in general rather than specifically about symptoms.	…have your daily activities been limited?

Q ID	Amendment Type	Response error category	Original wording	Reason for revision / participant comments (rounds 1 and 2)	Revised wording[a]
20	Item revised	2	…did you have difficulty finding something to eat while out and about?	The phrase 'out and about' was interpreted differently by participants. One participant considered their local area only while another thought about finding food in strange cities. After round one, the phrase 'out and about' was changed to 'away from your home'. Following round two, the phrase was amended to 'when out of the house' for consistency with other items. Note that 'away from your home' was interpreted as holidaying rather than any instance of being away from the home.	…did you have difficulty finding something to eat when out of the house?
67	Item revised and item added	2	…did you avoid eating food prepared by others (for example, at a friend's house, restaurant, or café)?	Some participants interpreted the question as the avoidance of situations in which food was prepared by others (e.g. eating at a friend's house), whereas others talked about the avoidance of eating certain foods that have been prepared by others (e.g. wafer in an ice-cream). This item is intended to tap the wariness experienced by some when assessing the suitability of food prepared by others. Perhaps it would be best to ask about the respondent's underlying concerns rather than the actions that they have taken.	Item revised: …did you avoid eating out (for example, at a friend's house, restaurant, or café)? Additional item (51) added after round one: …have you felt concerned that food prepared by others may contain gluten? and amended after round two: …have you felt concerned that food prepared by others as gluten-free may contain gluten?

Q ID	Amendment Type	Response error category	Original wording	Reason for revision / participant comments (rounds 1 and 2)	Revised wording[a]
66	Item revised	3	…did you worry that you would be unwell while away from your home?	Many participants interpreted 'away from your home' as holidaying or being away for the weekend, rather than any instance of being away from their home as intended. In order to clarify the item's meaning, 'away from your home' was amended to 'out of the house'.	…did you worry that you would be unwell when out of the house?
62	Item revised	3	…were your finances strained due to your coeliac disease (for example, due to the cost of following a gluten-free diet, or inability to work)?	Several participants interpreted this question as asking whether they spend more on a GFD than they would on a gluten-containing diet, or whether gluten-free food is expensive. The intended meaning is whether CD has had a severe impact on the individual's finances. A subsequent item asks about the cost of gluten-free foods. Repositioning this to appear before this item may help people to interpret the item correctly as they would have already had a chance to express their feelings about the cost of gluten-free food.	…did you struggle financially due to your coeliac disease (for example, due to the cost of following a gluten-free diet, or inability to work)? Move this item to appear after the item '*have you felt annoyed or frustrated about the cost of gluten-free substitute foods?*'
19	Item deleted	3	…was your choice of food affected?	Many participants interpreted this question as asking whether their choice of food was affected by their CD, i.e. their need to select gluten-free food as opposed to gluten-containing. The intended meaning was whether choice was affected *within* their GFD, e.g. selecting naturally gluten-free food to minimise risk of gluten consumption. The item could not be reworded to reflect the intended meaning.	Delete item

[a]This is the final version of the revised item after both rounds of testing.

Appendix Y. Cognitive interviews – CD-PEQ amendments

Amendments made to the CD-PEQ following two rounds of cognitive interviews.

Item No.	Original item	Amendment (R1 / R2)	Amendment Type	Reason for revision / participant comments	Revised wording
2	Which of the following symptoms did you have before you were diagnosed with coeliac disease? (please tick all that apply)	Revised after R1	Response option added	If the participant was diagnosed with the condition as a child, they may not be able to answer the question.	'I can't remember' added as a response option
		Revised after R2	Two items added and response options added and amended	Items added to control questionnaire flow. Constipation, mouth ulcers, and brain fog were mentioned as symptoms not listed, and also mentioned in previous stages of development.	'How old were you when you were diagnosed with coeliac disease?' 'Have you been told by a doctor that you have coeliac disease?' Response options amended.
3	How long was it from when you first experienced symptoms to seeking medical advice?	Deleted after R1	Item deleted	Many participants had difficulty comprehending what this question was asking, and in addition, struggled to retrieve the relevant information. This question is not vital from a health services evaluation point of view.	-

Item No.	Original item	Amendment (R1 / R2)	Amendment Type	Reason for revision / participant comments	Revised wording
4	How long was it from when you first sought medical advice about your symptoms to receiving a definite diagnosis?	Revised after R2	Question amended and response option added	One participant provided 'time since diagnosis' rather than 'time to diagnose'. It is possible that participants may have had symptoms, but not sought advice.	Example added to make question clearer: 'How long was it from when you first sought medical advice (e.g. first spoke to your GP) to receiving a definite diagnosis?' Response option added: 'I did not seek medical advice'
5	How would you rate the length of time from when you first sought medical advice about your symptoms to receiving a definite diagnosis?	Revised after R1	Question and response options revised	Although participants appeared to have little problem with this question, one participant's answer was not in line with previous answers. Time-based response options were felt more appropriate.	How do you feel about how long it took to receive a definite diagnosis? Response options changed to 'very quick' to 'very slow'
		Revised after R2	Question revised	Many participants misinterpreted the question as asking about the time period to diagnose the condition once it was suspected, rather than in relation to the previous question.	How do you feel about the amount of time it took to receive a diagnosis?

Item No.	Original item	Amendment (R1 / R2)	Amendment Type	Reason for revision / participant comments	Revised wording
6	Which health care professional did you speak to the most often before you received your diagnosis?	Revised after R1	Response options revised	Many participants referred to hospital doctors as consultants.	Response options amended from 'Hospital doctor' to 'Hospital doctor / consultant'
		Revised after R2	Question revised	Not all participants understood the term 'health care professional' – revised.	Which health professional did you speak to the most often before you received your diagnosis?
7	Thinking about the health care professional that you spoke to the most often before you received your diagnosis, did you feel that this person…	Revised after R2	Question revised	Some participants thought about a group of individuals (e.g. all GPs that they had seen), which made the question more difficult to answer.	Thinking about the health professional you selected in question 4, did you feel that this person…
8	Before your diagnosis of coeliac disease, did you receive other diagnoses to explain your condition?	Deleted after R1	Item deleted	Some participants only recalled misdiagnoses during the discussion and some were unable to determine whether a condition constituted a misdiagnosis.	-
10	Which tests did you have to diagnose your coeliac disease?	Revised after R1	Response options revised	All participants were unfamiliar with the genetic test. It is uncommon for the test to be conducted.	Delete part '(c) Genetic test'

Item No.	Original item	Amendment (R1 / R2)	Amendment Type	Reason for revision / participant comments	Revised wording
11	Were you specifically told to eat foods containing gluten while your tests and investigations were being carried out?	Revised after R1	Question revised	Participants considered no information as being told to continue with a gluten-containing diet. Another referred to information read on the Internet. The question should specify who provided the information.	Did a health care professional specifically tell you to eat foods containing gluten while your tests and investigations were being carried out?
		Deleted after R2	Question deleted	A 'no' response could indicate that the respondent was unaware of what they were being tested for, but this communication is important in case they are already following a GFD.	-
12	How long did you have to wait for an endoscopy?	Revised after R1	Question and response options revised	None of the participants were certain of their answer. Therefore, asking about satisfaction with wait, rather than specific timescales, may be preferable.	How do you feel about how long you had to wait for an endoscopy? Response options amended to: 'very quick' → 'very slow'
		Revised after R2	Question revised	Periods of time considered are perhaps inconsistent due to different experiences of diagnosis.	How do you feel about the amount of time you had to wait for an endoscopy?
14	Who first informed you that you have been diagnosed with coeliac disease?	Revised after R1	Response option added	Based on responses and qualitative research, add 'receptionist' as an option.	Response option added: 'Receptionist'

Item No.	Original item	Amendment (R1 / R2)	Amendment Type	Reason for revision / participant comments	Revised wording
15	Were you informed of your diagnosis in both a professional and appropriate manner?	Revised after R2	Question revised	One participant was unsure whether communication of their diagnosis via a letter was appropriate or 'the norm'. Change wording to emphasise interest in their opinion.	Do you feel you were informed of your diagnosis in both a professional and appropriate manner?
16	At the time of your diagnosis, did you receive enough information about your coeliac disease from health care professionals?	Revised after R1	Question revised	Participants thought about information received in relation to their coeliac disease, including the gluten-free diet. Combine with question 17.	At the time of your diagnosis, did you receive enough information about coeliac disease and the gluten-free diet from health care professionals?
17	At the time of your diagnosis, did you receive enough information about the gluten-free diet from health care professionals?	Deleted after R1	Question merged with Q16	Merged with question 16	-
18	Following diagnosis, some people have some additional tests or vaccinations. Since your diagnosis of coeliac disease, have you had…	Revised after R1	Question part order revised	Re-order question parts in order of familiarity to participants.	Swap order of question parts (a) and (b)
		Revised after R2	Question revised	Many participants have not heard of the pneumococcal vaccine. However, people are likely to know what it is if they have received it.	Some people with coeliac disease have had additional tests or vaccinations. Have you

Item No.	Original item	Amendment (R1 / R2)	Amendment Type	Reason for revision / participant comments	Revised wording
				One participant has check-ups for another condition and therefore, had had some tests prior to diagnosis.	had…
19	Have you spoken to a dietitian about your coeliac disease?	Revised after R2	Question revised	Participants may have spoken to a dietitian prior to their diagnosis. If diagnosed at a young age, participant may not be able to answer this question.	After receiving a diagnosis, did you speak to a dietitian about your coeliac disease?
20	How long a gap was there between receiving a definite diagnosis and your appointment with a dietitian?	Revised after R1	Question and response options revised	Participants were uncertain of exact timescales, but could recall rough waiting times.	After receiving a definite diagnosis, how quickly did you have an appointment with a dietitian? Amend response options to 'very quick' to 'very slow'
		Revised after R2	Question and response options revised	Participant may have been seeing a dietitian prior to their diagnosis.	After receiving a diagnosis, how quickly did you have an appointment with a dietitian to discuss your coeliac disease? Remove option 'I have not been given a definite diagnosis of coeliac disease' as now asked at the beginning of the questionnaire.

Item No.	Original item	Amendment (R1 / R2)	Amendment Type	Reason for revision / participant comments	Revised wording
23	Were you offered a second appointment to speak to a dietitian within 6 months of your first appointment?	Revised after R1	Question revised	The timescale to which the question refers was disregarded in one instance.	Embolden 'within 6 months'
25	In the last 12 months, have you been able to speak to the following health care professionals about your coeliac disease when you needed?	Revised after R1	Question and response options revised	Participants were uncertain whether the question referred to speaking with a professional at an appointment or being able to ring up a professional for advice over the phone.	In the last 12 months, if you had a question or needed advice about your coeliac disease, have you been able to speak to a health care professional about it? Response options amended
		Revised after R2	Question and response options revised	In some instances, participants felt that it wasn't necessary to speak to a health care professional as they could get information from the Internet. Response option 'I sought advice elsewhere' could apply alongside other answers.	In the last 12 months, have you been able to get information and advice about your coeliac disease from a health professional when you wanted to do so? Response options amended.

Item No.	Original item	Amendment (R1 / R2)	Amendment Type	Reason for revision / participant comments	Revised wording
26	In the last 12 months, have you had enough information and advice from health care professionals about your coeliac disease and its treatment?	Deleted after R2	Question deleted	Participants may have sought advice elsewhere. Overlap with Q25.	-
28	Have you ever had a review appointment?	Revised after R1	Question and response options revised	As people have follow-up appointments for other conditions, it is worth clarifying that this question related to CD. Simplify response options to make selection easier.	Have you ever had a follow-up appointment for your coeliac disease? Response options amended.
		Revised after R2	Question revised	Participants' comments prompted the need to clarify that interest is in whether people are having regular follow-up appointments to manage their condition.	Do you have regular follow-up appointments for your coeliac disease?
29	When was your most recent review appointment for your coeliac disease?	Revised after R1	Instructions and response options revised	One participant did not consider their annual blood tests as follow-up. Another's follow-up was many years ago.	Instructions revised. Response options amended
		Revised after R2	Response options revised	Revised response options to reflect changes made to previous question. As interest is in regular follow-up appointments, it is expected that these will have occurred within the last couple of years.	Response options amended.

Item No.	Original item	Amendment (R1 / R2)	Amendment Type	Reason for revision / participant comments	Revised wording
30	Who was your most recent review appointment with?	Revised after R1	Response option amended	Hospital doctors also referred to as consultants.	Amend response option: 'Hospital doctor' to 'Hospital doctor / consultant'
31	Who would you prefer your review appointment to be with?	Revised after R1 and question added	Question revised and moved; question added	One participant commented that he doesn't want to see anybody as he does not need follow-up. This should be captured and therefore, an extra question was added. The word 'prefer' implies that alternative professional would be better or should be selected.	Re-word: 'Who would you like your follow-up appointments to be with?' Question added: 'Would you like to have follow-up appointments in the future?'
		Revised after R2	Question revised; question added	Some participants would like to see more than one type of health care professional. It would be useful to know how frequently people would like follow-up appointments.	'Who would you like follow-up appointments with? (please tick all that apply)' Question added: 'How often would you like to have follow-up appointments?'
32	Who initiated your most recent follow-up appointment?	Revised after R2	Response options revised	Two participants selected 'other' when 'I contacted the health care provider' was more appropriate.	Amend response options: 'Staff at the hospital'; 'Staff at the GP practice'; 'I contacted a health professional'; 'other'.

Item No.	Original item	Amendment (R1 / R2)	Amendment Type	Reason for revision / participant comments	Revised wording
33	Which of the following happened at your most recent follow-up appointment?	Revised after R2	Response options revised	One participant mentioned that she was weighed, but her BMI was not calculated. Revised response options as appropriate.	Response options amended: 'I was weighed'; 'My body mass index (BMI) was calculated'
35	At your most recent review appointment, when you had questions to ask, were you given helpful answers?	Revised after R1	Question revised	One participant commented that whether the answer was helpful would depend on the content of the answer.	At your most recent follow-up appointment, when you had questions to ask, were you given the information you needed?
		Revised after R2	Response options revised	No response option for participants who had the opportunity to ask questions, but who did not have any questions to ask.	Response options added: 'I did not have any questions'
36	Overall, how helpful was your most recent review appointment?	Revised after R1	Response options revised	Revise response options for consistency with other questions	Response options amended 'very helpful' to 'not very helpful'
37	Do you think you have received enough information from health care professionals about getting gluten-free food on prescription?	Revised after R2	Question revised	Some participants commented that they received this information from Coeliac UK rather than health professionals. It is more important to learn whether they received the information rather than who it was from.	Do you think you have received enough information about getting gluten-free food on prescription?

Item No.	Original item	Amendment (R1 / R2)	Amendment Type	Reason for revision / participant comments	Revised wording
38	How easy or difficult have you found getting gluten-free food on prescription?	Revised after R1	Question and response options revised	One participant answered in relation to gluten-free food in general, whereas another commented that the question could mean include all gluten-free foods.	How easy have you found it to obtain the gluten-free food products that are available on prescription?' Response categories amended 'very easy' to 'very difficult'
39	In the last 12 months, which gluten-free foods have you had on prescription?	Revised after R1	Question revised (formatting)	The researcher was surprised at the range of products participants received. Embolden 'on prescription' to ensure that respondents answer in relation to prescriptions.	Embolden 'on prescription'
40	Thinking about gluten-free foods, has anything you wanted on prescription been refused in the last 12 months?	Deleted after R2	Question deleted	It is possible that items aren't refused because people have learnt not to ask for it. Therefore, the information gathered from this question may not be very useful.	-
42	How reasonable do you find the cost of your prescriptions for your coeliac disease?	Revised after R1	Response option amended	Amend response option for consistency.	Response option amended from 'quite expensive' to 'fairly expensive'
		Revised after R2	Question revised	Delete 'reasonable'	How do you find the cost of your prescriptions for your coeliac disease?

Item No.	Original item	Amendment (R1 / R2)	Amendment Type	Reason for revision / participant comments	Revised wording
43	In general, have you received enough support from health care services to manage your coeliac disease?	Deleted after R1	Item deleted	Item similar to Q26.	-
45	In general, how often do the health care professionals you see about your coeliac disease appear informed about your and your medical history?	Revised after R1	Question revised	Participants were uncertain how to answer this question. The question implies seeing professionals when they may have spoken to them over the phone. It also implies the present.	In general, how often have the health care professionals that you have spoken to about your coeliac disease appeared informed about you and your medical history'
		Deleted after R2	Question deleted	Participants struggled to answer this question. In some cases, participants had not seen many health care professionals and therefore, were unable to formulate answers.	-
46	Thinking about your coeliac disease and the gluten-free diet, how often do health care professionals give you consistent information and advice?	Revised after R1	Question and response options revised	One participant selected the incorrect response category. The question is written in the present tense – amend to past tense to include things that have already happened. Response categories amended for consistency.	Thinking about your coeliac disease and the gluten-free diet, how often have health care professionals given you consistent information and advice? Response options revised
		Revised after R2	Question and response options revised	Not all participants answered this in relation to the consistency of	Thinking about your coeliac disease and the gluten-free

Item No.	Original item	Amendment (R1 / R2)	Amendment Type	Reason for revision / participant comments	Revised wording
				information and advice, but rather whether they had received information and advice.	diet, how consistent has information and advice from health professionals been? Embolden 'consistent'; response options amended.
47	From your experience, do you think the following health care professionals are knowledgeable about coeliac disease?	Revised after R1	Response options revised	Two participants answered part (d) as including GPs, perhaps because the statement includes the phrase 'GP surgeries'.	Amend part (d) to read 'Practice nurses / health care assistants' (also amend to other instances for consistency) Amend (b) to read 'Hospital doctors / consultants'
		Revised after R2	Response options revised	If participants have not seen the relevant health care professional they should be able to select 'not seen' or 'N/A'. Update list of health professionals for consistency.	Response options amended: 'I don't know / NA', 'specialist hospital doctors / gastroenterologists', 'other hospital doctors'
48	Overall, how would you rate the health care that you have received to help you manage your coeliac disease?	Revised after R1	Question revised	Some participants considered the whole process, from before diagnosis, through to diagnosis and management. Another only thought about management.	Overall, how would you rate the health care that you have received to help you manage your coeliac disease since diagnosis?

Appendix Z. Translatability assessment – summary of amendments to the CDAQ

The results of the translatability assessment are shown below in three tables. Table "A" shows amendments made to the CDAQ as recommended; Table "B" shows additional amendments made, which weren't specifically recommended; and Table "C" details the recommendations that were not followed.

(A) Amendments made as recommended by PharmaQuest

Q No	Original item (prior to conducting translatability assessment)	Revised item (item wording after considering results of the TA)	Translatability issue category	Reason for amendment
-	This questionnaire asks how you feel your **coeliac disease** has affected your life during the **past 4 weeks**.	This questionnaire asks how your **coeliac disease** has affected your life during the **past 4 weeks**.	1. Grammatical - structural	Removing the word 'feel' will make the sentence easier to translate. It is also probably unnecessary to include 'you feel' as part of the sentence and will be easier to read if removed.
-	Please tick **one** box for each question and answer **all** questions.	Please tick **one** box for **each** question.	1. Grammatical - structural	The original instruction could be misinterpreted in some languages as a request for the respondent to write answers down. Therefore, statement modified as suggested.
1	did you worry that you might be unwell after eating food prepared by others (for example, at other people's houses, restaurants, or cafés)?	have you worried that you might become ill after eating food prepared by others (for example, at other people's houses, restaurants, or cafés)?	1. Cross-cultural – vocabulary	The term 'unwell' was identified as difficult to translate into a number of languages. Therefore, it was replaced with 'become ill'.
			2. Grammatical - tenses	Changed tense for consistency.

Q No	Original item (prior to conducting translatability assessment)	Revised item (item wording after considering results of the TA)	Translatability issue category	Reason for amendment
2	did you feel embarrassed or uncomfortable discussing your condition or dietary needs?	have you felt embarrassed or uncomfortable discussing your coeliac disease or dietary needs?	1. Cross-cultural – vocabulary	'Condition' is a difficult word to translate and will be changed to 'coeliac disease'. This also makes the item more explicit and understandable.
			2. Grammatical – tenses	Changed tense for consistency.
3	did you feel as though you might appear to be making a fuss about your dietary needs?	have you felt as though you might appear to be making a fuss about your dietary needs?	1. Grammatical – tenses	Changed tense for consistency.
4	have you felt that people misunderstood your condition or dietary needs (for example, referring to your gluten-free diet as a personal choice)?	have you felt that people misunderstood your coeliac disease or dietary needs (for example, thinking you follow a gluten-free diet as a personal choice rather than for your coeliac disease)?	1. Cross-cultural – sociocultural differences	In many countries, the concept of following a gluten-free diet out of choice was not comprehended. As such, a clarifying statement needed to be added to the example.
			2. Cross-cultural – vocabulary	As above regarding 'condition'.
5	did you find it difficult to let people know they have misunderstood your condition or dietary needs?	have you found it difficult to let people know they have misunderstood your coeliac disease or dietary needs?	1. Cross-cultural – vocabulary	As above regarding 'condition'.
			2. Grammatical – tenses	Changed tense for consistency.
6	did you receive unwanted attention because of your condition or dietary needs?	have you received unwanted attention because of your coeliac disease or dietary needs?	1. Cross-cultural – vocabulary	As above regarding 'condition'.
			2. Grammatical – tenses	Changed tense for consistency.

Q No	Original item (prior to conducting translatability assessment)	Revised item (item wording after considering results of the TA)	Translatability issue category	Reason for amendment
7	did you feel guilty about the impact of your condition on friends and family?	have you felt guilty about the impact of your coeliac disease on friends and family?	1. Cross-cultural – vocabulary 2. Grammatical - tenses	As above regarding 'condition'. Changed tense for consistency.
9	have you felt concerned about developing a health condition related to your coeliac disease?	have you felt concerned about developing a health problem related to your coeliac disease?	1. Cross-cultural – vocabulary	'Health condition' changed to 'health problem' as condition not easily translatable.
11	have you been troubled by your bowel movements (for example, diarrhoea, loose bowels, or constipation)?	have you been bothered by your bowel movements (for example, diarrhoea, loose stools, or constipation)?	1. Cross-cultural - vocabulary 2. Cross-cultural - vocabulary	'Troubled' amended to 'bothered' to improve translatability. 'Loose bowels' is an English phrase that does not translate well. As such, amend 'loose bowels' to 'loose stools'.
12	have you been affected by bloating in your abdomen?	have you had bloating in your abdomen?	1. Cross-cultural – vocabulary	'Affected by' is a difficult term to translate and has therefore been amended to 'had'. This slightly changes the meaning of the item, but it is likely that respondents will interpret the item in the same way, i.e. whether or not they have had the symptom.
13	have you been affected by nausea or vomiting that you think was caused by your coeliac disease?	have you had nausea or vomiting that you think was caused by your coeliac disease?	1. Cross-cultural – vocabulary	'Affected by' amended to 'had' as in Q12.
14	have you been affected by pain you think was caused by your coeliac disease?	have you had pain you think was caused by your coeliac disease?	1. Cross-cultural – vocabulary	'Affected by' amended to 'had' as in Q12.

Q No	Original item (prior to conducting translatability assessment)	Revised item (item wording after considering results of the TA)	Translatability issue category	Reason for amendment
15	have you been affected by tiredness or lack of energy you think was caused by your coeliac disease?	have you had tiredness or a lack of energy that you think was caused by your coeliac disease?	1. Cross-cultural – vocabulary	'Affected by' amended to 'had' as in Q12.
17	did you have difficulties with work-related tasks?	have you had difficulties carrying out work-related tasks?	1. Grammatical – structural	The sentence lacked a verb making it difficult to translate. Therefore, 'carrying out' was added.
			2. Grammatical – tenses	Changed tense for consistency.
18	have your leisure activities been limited (for example, hobbies, sports, or holidays)?	have your leisure activities been limited by your coeliac disease (for example, hobbies or sports)?	1. Grammatical – wording-concept mismatch	'Holidays' removed as perhaps this is slightly different to 'leisure activities'.
19	have your holiday or holiday activity choices been limited?	has your choice of holiday or holiday activities been limited by your coeliac disease?	1. Grammatical – structural	Sentence restructured in order to make it clearer that choice relates to both the holiday and activities while on holiday.
20	did you worry that you would be unwell when out of the house?	have you worried that you would become ill when you were not at home?	1. Cross-cultural – vocabulary	'Unwell' does not translate well and has therefore been changed to 'become ill'.
			2. Cross-cultural - semantic	Some concerns were raised with the term 'house' and the phrase 'out of the house'. As such, this has been amended to 'when you were not at home'.
			3. Grammatical - tenses	Changed tense for consistency.

Q No	Original item (prior to conducting translatability assessment)	Revised item (item wording after considering results of the TA)	Translatability issue category	Reason for amendment
21	have you been unable to travel due to being unwell (for example, travelling to work, the shops, or on holiday)?	have you been unable to travel because you were ill (for example, going to work or the shops, or travelling on holiday)?	1. Cross-cultural – vocabulary	'Unwell' difficult to translate and therefore changed to 'ill'.
			2. Cross-cultural – semantic	'Travel' is often used to denote longer journeys in other languages and 'going' for smaller journeys. Therefore, different verbs have been added for different types of travel.
22	did you feel isolated from others because of your coeliac disease?	have you felt isolated from others because of your coeliac disease?	1. Grammatical - tenses	Changed tense for consistency.
23	did you feel excluded from attending social activities?	have you felt that others excluded you from attending social activities?	2. Grammatical - tenses	Changed tense for consistency
25	did you have difficulty concentrating or thinking clearly because of your coeliac disease?	have you had difficulty concentrating or thinking clearly because of your coeliac disease?	1. Grammatical – tenses	Changed tense for consistency.
27	did you avoid social activities?	have you avoided social activities?	1. Grammatical – tenses	Changed tense for consistency.
29	did you avoid eating out (for example, at a friend's house, restaurant, or café)?	have you avoided going out to eat (for example, at a friend's house, restaurant, or café)?	1. Grammatical – wording-concept mismatch	'Eating out' was considered complicated to translate as it does not tend to include eating at friend's houses, etc. 'Going out to eat' was considered a better alternative.
			2. Grammatical – tenses	Changed tense for consistency.

Q No	Original item (prior to conducting translatability assessment)	Revised item (item wording after considering results of the TA)	Translatability issue category	Reason for amendment
30	did you worry that you would accidentally eat or drink gluten?	have you worried that you would accidentally eat or drink products that contain gluten?	1. Grammatical – structural	Eating or drinking gluten was considered awkward to translate. As such, the item was re-worded to clarify that it is asking about the consumption of products containing gluten.
			2. Grammatical – tenses	Changed tense for consistency.
32	did you feel awkward about refusing unsuitable food or drink from other people?	have you felt uncomfortable refusing unsuitable food or drink from other people?	1. Cross-cultural – vocabulary	'Awkward' difficult to translate and therefore amended to 'uncomfortable'.
			2. Grammatical - tenses	Changed tense for consistency.
33	did you eat or drink something that you were uncertain was gluten-free because you felt awkward refusing?	have you eaten or drunk something that you were uncertain was gluten-free because you felt uncomfortable refusing?	1. Cross-cultural – vocabulary	'Awkward' difficult to translate and therefore amended to 'uncomfortable'.
			2. Grammatical - tenses	Changed tense for consistency.
34	did you worry that you would be unwell at an awkward or inconvenient time (for example, while travelling or at a social event)?	have you worried that you would become ill at a difficult or inconvenient time (for example, while travelling or at a social event)?	1. Cross-cultural – vocabulary	'Unwell' difficult to translate and therefore changed to 'ill'.
			2. Cross-cultural – vocabulary	'Awkward' difficult to translate and therefore amended to 'difficult'.
			3. Grammatical - tenses	Changed tense for consistency.
35	did you lack the support of family or friends?	have you lacked the support of family or friends?	1. Grammatical – tenses	Changed tense for consistency
36	did you feel down or in low spirits?	have you felt down or in low spirits?	1. Grammatical – tenses	Changed tense for consistency.

Q No	Original item (prior to conducting translatability assessment)	Revised item (item wording after considering results of the TA)	Translatability issue category	Reason for amendment
37	did you feel you were a nuisance to other people?	have you felt you were a nuisance to other people?	1. Grammatical – tenses	Changed tense for consistency
38	did you feel uncomfortable about other people catering for your dietary needs?	have you felt uncomfortable about other people taking your dietary needs in to account when preparing food for you?	1. Cross-cultural – vocabulary 2. Grammatical – tenses	The word 'catering' was identified as problematic with regards to translation and therefore, PQ recommended that more direct wording is used. Changed tense for consistency
39	did you feel guilty about other people buying gluten-free substitute foods for you?	have you felt guilty about other people buying gluten-free substitute foods for you?	2. Grammatical – tenses	Changed tense for consistency
41	did you struggle financially due to your coeliac disease (for example, due to the cost of following a gluten-free diet, or inability to work)?	have you had financial difficulties due to your coeliac disease (for example, due to the cost of following a gluten-free diet, or inability to work)?	1. Cross-cultural - semantic 2. Grammatical – tenses	To 'struggle financially' was deemed an English phrase and would be more translatable as 'having financial difficulties'. Changed tense for consistency.
42	did you have difficulty trying to find suitable food?	have you had difficulty finding suitable food?	1. Grammatical – structural 2. Grammatical – tenses	The word 'trying' is not necessary in this sentence and makes it harder to translate. Therefore, it has been removed. Changed tense for consistency.
44	did you crave food or drinks containing gluten?	have you craved food or drinks that contain gluten?	2. Grammatical – tenses	Changed tense for consistency

Q No	Original item (prior to conducting translatability assessment)	Revised item (item wording after considering results of the TA)	Translatability issue category	Reason for amendment
46	did you have difficulties cooking or baking with gluten-free ingredients?	have you had difficulties cooking or baking with gluten-free ingredients?	1. Grammatical - tenses	Changed tense for consistency
48	did you have difficulty finding something to eat when out of the house?	have you had difficulty finding something to eat when you were not at home?	1. Cross-cultural - semantic	'Out of the house' identified as a difficult phrase by the translators and could be perceived as referring to houses only (and not flats, etc.). Therefore, amended to 'when you were not at home'. [As question 20].
			2. Grammatical – tenses	Changed tense for consistency
50	did you feel frustrated by having to plan ahead (for example, taking food with you, choosing restaurants)?	have you felt frustrated by having to plan ahead (for example, taking food with you, choosing restaurants)?	1. Grammatical – tenses	Changed tense for consistency
51	have you felt concerned that food prepared by others as gluten-free may contain gluten?	have you felt concerned that food prepared by others, and presented as gluten-free, may contain gluten?	1. Grammatical - structural	To make the item easier to read and translate 'and presented' was added.

(b) Further amendments made in additional to those recommended

Q No	Original item (prior to conducting translatability assessment)	Revised item (item wording after considering results of the TA)	Translatability issue category	Reason for amendment
16	have your daily activities been limited?	have your daily activities been limited by your coeliac disease?	1. Grammatical – structural	Finnish translator recommended stating the reason for the limitation, therefore, 'by your coeliac disease' added. PharmaQuest did not support this as they felt it would limit the English version.
18	have your leisure activities been limited (for example, hobbies, sports, or holidays)?	have your leisure activities been limited by your coeliac disease (for example, hobbies or sports)?	1. Grammatical – structural	'By your coeliac disease' added to provide clarification of what the leisure activities may be limited by.
19	have your holiday or holiday activity choices been limited?	has your choice of holiday or holiday activities been limited by your coeliac disease?	1. Grammatical – structural	'By your coeliac disease' added to make the reasons for limitation clear.
23	did you feel excluded from attending social activities?	have you felt that others excluded you from attending social activities?	1. Grammatical – wording-concept mismatch	The meaning of exclusion is still a little unclear. Exclusion could mean that others excluded you or you felt unwelcome to attend. The item has been amended to reflect the first meaning. The second meaning is captured by item 22.
28	have your work activities been limited?	have your work activities been limited by your coeliac disease?	1. Grammatical – structural	Added 'by your coeliac disease' to ensure that the reason for the limitation is clear.
31	have you been concerned about cross-contamination (gluten-free food coming into contact with food containing gluten)?	have you been concerned about cross-contamination (gluten-free food coming into contact with food that contains gluten)?	1. Grammatical – structural	'Containing' amended to 'that contains' to improve readability.

Q No	Original item (prior to conducting translatability assessment)	Revised item (item wording after considering results of the TA)	Translatability issue category	Reason for amendment
44	did you crave food or drinks containing gluten?	have you craved food or drinks that contain gluten?	1. Grammatical - structural	'Containing' amended to 'that contain' to improve readability.

(c) Recommendations made by PharmaQuest but not followed

Q No	Original item (prior to conducting translatability assessment)	Translatability issue category	Reason for not amending
39	did you feel guilty about other people buying gluten-free substitute foods for you?	1. Cross-cultural - vocabulary	No changes PharmaQuest recommended adding an example of a substitute food in brackets. However, the cognitive interviews did not identify any problems understanding this term.
40	have you felt annoyed or frustrated about the cost of gluten-free substitute foods?	1. Cross-cultural - vocabulary	No changes PharmaQuest recommended adding an example of a substitute food in brackets. However, the cognitive interviews did not identify any problems understanding this term.

Appendix AA. Survey 1 – letter of invitation

[Coeliac UK Letterhead here]

[Date]

[Member's Address]

Diagnosis and management of coeliac disease: Quality of life and patient's experiences of healthcare services

Dear [Title] [Surname],

I am writing to make you aware of a research study which is being undertaken by the Nuffield Department of Population Health at the University of Oxford in collaboration with Coeliac UK. The research aims to develop a questionnaire that measures the impact of coeliac disease on quality of life. I am writing to you as a Member of Coeliac UK who has agreed you may be contacted for research purposes. Your name and contact details have not been made available to the University of Oxford.

If you would like to participate in the study, please complete the enclosed questionnaire and return it to the University of Oxford in the pre-paid envelope provided. The questionnaire asks you about your experiences of living with coeliac disease. Taking part in this study is voluntary and confidential.

Further information about the study can be found in the enclosed information sheet. If you have any questions about the study, please contact Helen Crocker, the research contact at the University of Oxford, by telephone: 01865 289431 or by email: Helen.Crocker@dph.ox.ac.uk.

Thank you for taking the time to read this letter.

Yours sincerely,

Heidi Urwin

Research Manager, Coeliac UK

Appendix BB. Survey 1 - participant information sheet

Health Services Research Unit
Nuffield Department of Population Health
Rosemary Rue Building, Old Road Campus, Headington, Oxford OX3 7LF

Research Contact: Helen Crocker, Postgraduate Research Student
Tel: +44 (0)1865 289431, Email: Helen.Crocker@dph.ox.ac.uk

Diagnosis and management of coeliac disease: Quality of life and patient's experiences of healthcare services

Information Sheet for Survey Participants

What is the purpose of this research?

The purpose of this research is to develop and validate a questionnaire that measures the impact of coeliac disease on quality of life. The questionnaire has been developed with input from people with coeliac disease, healthcare professionals, and researchers. In this survey, we would like to assess how well the questionnaire measures quality of life in people with coeliac disease and improve the questionnaire prior to its use in future research. This research study is part of a larger study which aims to explore experiences of living with coeliac disease and using healthcare services to diagnose and manage the condition.

Who is doing the research?

The research is led by Helen Crocker, a researcher in the Nuffield Department of Population Health at the University of Oxford, under the supervision of Professor Crispin Jenkinson and Dr Michele Peters. The research is funded by the Medical Research Council and is part of a doctoral research programme. The research is being undertaken with the support of Coeliac UK.

How can I take part?

Taking part in this study is voluntary and confidential. If you would like to take part, please complete the enclosed questionnaire and return it to the research team in the pre-paid envelope provided. The questionnaire asks about your experiences of living with coeliac disease. If you have any questions that you would like to ask, please contact Helen Crocker by telephone: 01865 289431 or by email: Helen.Crocker@dph.ox.ac.uk. Returning the completed questionnaire means that you understand the purpose of this study and are happy to take part. You are free to withdraw from the study at any point in time without providing a reason, without penalty, and you will not be contacted further.

What will happen with the information that I provide?

The results of this survey will be used to improve the questionnaire. The improved questionnaire will be used in a further survey to assess experiences of healthcare services and quality of life in coeliac disease. It is intended that the results of this second survey will inform healthcare policy to improve the quality of healthcare for people with coeliac disease and find out how coeliac disease affects the quality of life of those living with the condition. It is also intended that the improved questionnaire will be available for use in other research studies and clinical trials to measure quality of life in coeliac disease.

Version 1.1 (Survey 1), 04/08/2014, REC Ref No: MSD-IDREC-C1-2014-031

Director of HSRU
Professor Crispin Jenkinson DPhil

Head of Department
Professor Sir Rory Collins FMed Sci FRCP

Who can take part?

Participants should be aged 18 years or over, live in the UK, and have a medical diagnosis of coeliac disease. You have been made aware of this study as a Member of Coeliac UK who has agreed you may be contacted for research purposes. We are interested in all experiences of coeliac disease however well you manage your condition and whatever the extent of your symptoms.

Will participation be confidential?

Data collected as part of this research will be accessible to the research team only. Paper documentation will be stored in locked filing cabinets and electronic files will be stored on a password protected computer in accordance with the current Data Protection Act. In accordance with guidelines produced by the Medical Research Council, data will be kept for a period of ten years to allow the research to be reviewed if necessary.

Participation is anonymous. No personal data (e.g. name and contact details) has been made available to or will be collected by the research team.

What will happen with the results of the study?

The University of Oxford is committed to the dissemination of its research for the benefit of society. Therefore, it is intended that the research will be written up as one or more papers to be submitted for publication in scientific journals, presented at conferences, and as a doctoral thesis. On successful submission of the thesis, it will be deposited in the University archives to facilitate its use in future research. The thesis will be available in print and online.

Are there any risks involved in taking part?

We do not foresee any risks involved in taking part in this study. If participating in this research raises questions about the condition that you would like to discuss, you can contact Coeliac UK on their Helpline: 0845 305 2060 or visit their website: www.coeliac.org.uk.

Are there any benefits in taking part?

The information that you provide will help improve the questionnaire which will be used in a further study intending to inform healthcare policy and improve healthcare services in the future. There are no direct benefits in taking part.

What can I do if I have any concerns about the research study?

This study has been reviewed by, and received ethics clearance through, the University of Oxford Central University Research Ethics Committee. If you have a concern about any aspect of this project, please speak to the relevant researcher (Helen Crocker, tel: 01865 289431, email: Helen.Crocker@dph.ox.ac.uk) or her supervisor (Professor Crispin Jenkinson, tel: 01865 289441, email: Crispin.Jenkinson@dph.ox.ac.uk) who will do their best to answer your query. The researcher or supervisor should acknowledge your concern within 10 working days and give you an indication of how he/she intends to deal with it. If you remain unhappy or wish to make a formal complaint, please contact the chair of the Research Ethics Committee at the University of Oxford (Chair, Medical Sciences Inter-Divisional Research Ethics Committee; Email: ethics@medsci.ox.ac.uk; Address: Research Services, University of Oxford, Wellington Square, Oxford, OX1 2JD). The chair will seek to resolve the matter promptly.

Appendix CC. Survey 1 - questionnaire

Survey 1 commences on the following page

Coeliac Disease Questionnaire

What is the study about?
As part of our research, we are developing a questionnaire that measures the impact of coeliac disease on quality of life. The results of this survey will be used to improve the questionnaire. The improved questionnaire will be used in a further study to explore experiences of using healthcare services to diagnose and manage coeliac disease and the impact of the condition on quality of life.

Who can take part?
You can take part in this study if you are aged 18 years or over and have a medical diagnosis of coeliac disease. We are interested in all experiences of coeliac disease however well you manage your condition and whatever the extent of your symptoms. Participation in the study is voluntary.

How can I take part?
If you would like to take part in this study, please complete this questionnaire and return it in the pre-paid envelope provided. Please complete all questions. Tick one box for each question unless instructed otherwise.

Questions or help?
If you have any questions about the questionnaire, please contact Helen Crocker by telephone: 01865 289431 or by email: Helen.Crocker@dph.ox.ac.uk

REC Ref No: MSD-IDREC-C1-2014-031 (Survey 1)
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Coeliac Disease Assessment Questionnaire

This questionnaire asks how your **coeliac disease** has affected your life during the **past 4 weeks**.

Please tick **one** box for **each** question.

THESE QUESTIONS RELATE TO YOUR COELIAC DISEASE

During the past 4 weeks, how often…	Never	Rarely	Sometimes	Often	Always	N/A
1. have you worried that you might become ill after eating food prepared by others (for example, at other people's houses, restaurants, or cafés)?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
2. have you felt embarrassed or uncomfortable discussing your coeliac disease or dietary needs?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
3. have you felt as though you might appear to be making a fuss about your dietary needs?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
4. have you felt that people misunderstood your coeliac disease or dietary needs (for example, thinking you follow a gluten-free diet as a personal choice rather than for your coeliac disease)?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
5. have you found it difficult to let people know they have misunderstood your coeliac disease or dietary needs?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	

THESE QUESTIONS RELATE TO YOUR COELIAC DISEASE						
During the <u>past 4 weeks</u>, how often…	Never	Rarely	Sometimes	Often	Always	N/A
6. have you received unwanted attention because of your coeliac disease or dietary needs?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
7. have you felt guilty about the impact of your coeliac disease on friends and family?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
8. have you felt worried that a family member may have or could develop coeliac disease?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	☐
9. have you felt concerned about developing a health problem related to your coeliac disease?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
10. have you felt concerned about the results of medical tests?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	☐
11. have you been bothered by your bowel movements (for example, diarrhoea, loose stools, or constipation)?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
12. have you had bloating in your abdomen?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
13. have you had nausea or vomiting that you think was caused by your coeliac disease?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	

THESE QUESTIONS RELATE TO YOUR COELIAC DISEASE

During the <u>past 4 weeks</u>, how often…	Never	Rarely	Sometimes	Often	Always	N/A
14. have you had pain that you think was caused by your coeliac disease?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
15. have you had tiredness or a lack of energy that you think was caused by your coeliac disease?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
16. have your daily activities been limited by your coeliac disease?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
17. have you had difficulties carrying out work-related tasks?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	☐
18. have your leisure activities been limited by your coeliac disease (for example, hobbies or sports)?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
19. has your choice of holiday or holiday activities been limited by your coeliac disease?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	☐
20. have you worried that you would become ill when you were not at home?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
21. have you been unable to travel because you were ill (for example, going to work or the shops, or travelling on holiday)?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	

THESE QUESTIONS RELATE TO YOUR COELIAC DISEASE						
During the <u>past 4 weeks</u>, how often…	Never	Rarely	Sometimes	Often	Always	N/A
22. have you felt isolated from others because of your coeliac disease?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
23. have you felt that others excluded you from attending social activities?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
24. have you felt depressed?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
25. have you had difficulty concentrating or thinking clearly because of your coeliac disease?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
26. have you felt bothered by your weight?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
27. have you avoided social activities?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
28. have your work activities been limited by your coeliac disease?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	☐
29. have you avoided going out to eat (for example, at a friend's house, restaurant, or café)?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
30. have you worried that you would accidentally eat or drink products that contain gluten?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	

THESE QUESTIONS RELATE TO YOUR COELIAC DISEASE

During the <u>past 4 weeks</u>, how often…	Never	Rarely	Sometimes	Often	Always	N/A
31. have you been concerned about cross-contamination (gluten-free food coming into contact with food that contains gluten)?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
32. have you felt uncomfortable refusing unsuitable food or drink from other people?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
33. have you eaten or drunk something that you were uncertain was gluten-free because you felt uncomfortable refusing?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
34. have you worried that you would become ill at a difficult or inconvenient time (for example, while travelling or at a social event)?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
35. have you lacked the support of family or friends?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
36. have you felt down or in low spirits?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
37. have you felt you were a nuisance to other people?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
38. have you felt uncomfortable about other people taking your dietary needs in to account when preparing food for you?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	

THESE QUESTIONS RELATE TO YOUR COELIAC DISEASE

During the <u>past 4 weeks</u>, how often…	Never	Rarely	Sometimes	Often	Always	N/A
39. have you felt guilty about other people buying gluten-free substitute foods for you?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
40. have you felt annoyed or frustrated about the cost of gluten-free substitute foods?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
41. have you had financial difficulties due to your coeliac disease (for example, due to the cost of following a gluten-free diet, or inability to work)?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
42. have you had difficulty finding suitable food?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
43. have you had to miss meals or snacks because suitable food was unavailable?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
44. have you craved food or drinks that contain gluten?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
45. have you been disappointed with the taste or texture of gluten-free substitutes?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
46. have you had difficulties cooking or baking with gluten-free ingredients?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	☐
47. have you felt burdened by the time taken to find or make gluten-free food?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	

THESE QUESTIONS RELATE TO YOUR COELIAC DISEASE

During the <u>past 4 weeks</u>, how often…	Never	Rarely	Sometimes	Often	Always	N/A
48. have you had difficulty finding something to eat when you were not at home?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
49. have you been frustrated by the choice of suitable food available (for example, in supermarkets, cafés or restaurants)?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
50. have you felt frustrated by having to plan ahead (for example, taking food with you, or choosing restaurants)?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	
51. have you felt concerned that food prepared by others, and presented as gluten-free, may contain gluten?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	

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You and Your Health

The following questions ask for some basic information about you and your coeliac disease. This information will help us to see how quality of life varies between different population groups.

52. How long ago did you receive a diagnosis for your coeliac disease?

_____ Year(s) _____ Month(s)

53. Which tests did you have to diagnose your coeliac disease?

*Please tick **all** that apply*

1 ☐ Blood test (antibody)

2 ☐ Endoscopy (with biopsy)

3 ☐ Other, *please state* _

54. Thinking about your coeliac disease, how much does it impact on you and your health?

1 ☐ No impact

2 ☐ Mild impact

3 ☐ Moderate impact

4 ☐ Severe impact

5 ☐ Very severe impact

55. In the <u>last 12 months</u>, how often have you consumed food or drinks that contain gluten <u>on purpose</u>?

1 ☐ Never

2 ☐ Rarely

3 ☐ Sometimes

4 ☐ Often

5 ☐ Always

56. Which of the following medical conditions do you have?

*Please tick **all** that apply*

a ☐ Dermatitis Herpetiformis
b ☐ Irritable Bowel Syndrome
c ☐ Type 1 Diabetes
d ☐ Type 2 Diabetes
e ☐ Osteoporosis
f ☐ Autoimmune Thyroid Disease
g ☐ Autoimmune Liver Disease
h ☐ Depression
i ☐ Epilepsy
j ☐ Anaemia
k ☐ Lactose Intolerance
l ☐ Other, *please write in:*
_ _
m ☐ I do not have any of these conditions

57. Are you male or female?

1 ☐ Male
2 ☐ Female

58. What is your age?

_____ Years

59. What is the first part of your postcode? _ _ _ _

60. Which of these best describes what you are doing at present? *If more than one of these applies to you, please tick the main ONE only.*

1 ☐ Full-time paid work (30 hours or more each week)
2 ☐ Part-time paid work (under 30 hours each week)
3 ☐ Full-time education at school, college or university
4 ☐ Unemployed
5 ☐ Permanently sick or disabled
6 ☐ Fully retired from work
7 ☐ Looking after the home
8 ☐ Doing something else, *please write in*: _

61. What is your legal marital status or same-sex civil partnership status?

1 ☐ Single (never married and never formed a civil partnership)
2 ☐ Married / in a civil partnership
3 ☐ Separated (but still legally married / in a civil partnership)
4 ☐ Divorced / legally dissolved civil partnership
5 ☐ Widowed / surviving partner from a civil partnership

62. What is your ethnic group?

Choose ONE section from A to E, and then tick the appropriate box to indicate your ethnic group.

A. White

1 ☐ English / Welsh / Scottish / Northern Irish / British
2 ☐ Irish
3 ☐ Gypsy or Irish Traveller
4 ☐ Any other White background, please write in: _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _

B. Mixed / Multiple ethnic groups

5 ☐ White and Black Caribbean
6 ☐ White and Black African
7 ☐ White and Asian
8 ☐ Any other Mixed / Multiple ethnic background, please write in: _ _ _ _ _ _

C. Asian / Asian British

9 ☐ Indian
10 ☐ Pakistani
11 ☐ Bangladeshi
12 ☐ Chinese
13 ☐ Any other Asian background, please write in: _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _

D. Black / African / Caribbean / Black British

14 ☐ African
15 ☐ Caribbean
16 ☐ Any other Black / African / Caribbean background, please write in: _ _ _ _

E. Other ethnic group

17 ☐ Arab
18 ☐ Any other ethnic group, please write in: _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _

Any comments?

Please write any comments in the box below

Thank you for completing this questionnaire

Please return your completed questionnaire in the pre-paid envelope provided

Return address: Helen Crocker, Health Services Research Unit, Nuffield Department of Population Health, University of Oxford, Rosemary Rue Building, Old Road Campus, Oxford, OX3 7LF

Appendix DD. Survey 1 – reminder (Coeliac UK website)

Have you received a questionnaire about quality of life in coeliac disease?

Researchers at Oxford University are exploring adults' experiences of living with coeliac disease, and using healthcare services to diagnose and manage the condition. As part of the study, a questionnaire is being developed that will measure the impact of coeliac disease on quality of life.

A survey is currently underway to assess, and refine, the questionnaire. Eight hundred Members of Coeliac UK have been sent a copy to complete. If you have received one and would like to take part, please complete the questionnaire and return it to the research team in the pre-paid envelope provided.

If you have already returned the questionnaire, the research team would like to thank you for taking part. If you have lost the questionnaire and would like a replacement copy, or have any questions about the study, please contact Helen Crocker, the research contact at the University of Oxford (telephone: 01865 289431; email: Helen.Crocker@dph.ox.ac.uk).

Appendix EE: Survey 1 - distribution of responses and missing data for CDAQ items

		Missing data		Distribution of responses, n=411				
		No response	N/A	Never	Rarely	Sometimes	Often	Always
No	Item (abbreviated)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
1	Worried become ill	0	-	39 (9.5)	62 (15.1)	131 (31.9)	105 (25.5)	74 (18.0)
2	Embarrassed discussing CD	1 (0.2)	-	117 (28.5)	57 (13.9)	122 (29.7)	89 (21.7)	25 (6.1)
3	Appeared to make fuss	0	-	54 (13.1)	39 (9.5)	112 (27.3)	124 (30.2)	82 (20.0)
4	Others misunderstood CD	1 (0.2)	-	64 (15.6)	53 (12.9)	117 (28.5)	138 (33.6)	38 (9.2)
5	Difficult to mention misunderstanding	2 (0.5)	-	80 (19.5)	72 (17.5)	134 (32.6)	93 (22.6)	30 (7.3)
6	Received unwanted attention	0	-	134 (32.6)	119 (29.0)	105 (25.5)	46 (11.2)	7 (1.7)
7	Felt guilty about impact on friends and family	2 (0.5)	-	97 (23.6)	71 (17.3)	118 (28.7)	86 (20.9)	37 (9.0)
8	Worry about family member	1 (0.2)	4 (1.0)	83 (20.2)	59 (14.4)	126 (30.7)	82 (20.0)	56 (13.6)
9	Concern about developing problem	2 (0.5)	-	58 (14.1)	76 (18.5)	146 (35.5)	88 (21.4)	41 (10.0)
10	Concern about results of tests	**3 (0.7)**	**29 (7.1)**	101 (24.6)	96 (23.4)	106 (25.8)	48 (11.7)	28 (6.8)
11	Bothered by bowel movements	3 (0.7)	-	51 (12.4)	88 (21.4)	135 (32.8)	92 (22.4)	42 (10.2)
12	Had abdominal bloating	2 (0.5)	-	81 (19.7)	84 (20.4)	120 (29.2)	95 (23.1)	29 (7.1)
13	Had nausea or vomiting	2 (0.5)	-	**226 (55.0)**	89 (21.7)	63 (15.3)	25 (6.1)	6 (1.5)
14	Had pain	1 (0.2)	-	144 (35.0)	90 (21.9)	110 (26.8)	51 (12.4)	15 (3.6)
15	Tiredness or lack of energy	1 (0.2)	-	80 (19.5)	73 (17.8)	132 (32.1)	84 (20.4)	41 (10.0)
16	Daily activities limited	3 (0.7)	-	160 (38.9)	126 (30.7)	78 (19.0)	33 (8.0)	11 (2.7)
17	Difficulties work-related activities	**1 (0.2)**	**43 (10.5)**	**216 (52.6)**	85 (20.7)	45 (10.9)	16 (3.9)	5 (1.2)
18	Leisure activities limited	1 (0.2)	-	**209 (50.9)**	97 (23.6)	63 (15.3)	28 (6.8)	13 (3.2)
19	Limited holiday / holiday choices	**3 (0.7)**	**29 (7.1)**	124 (30.2)	54 (13.1)	87 (21.2)	55 (13.4)	59 (14.4)
20	Worried become ill not at home	1 (0.2)	-	103 (25.1)	79 (19.2)	99 (24.1)	80 (19.5)	49 (11.9)
21	Unable to travel due to being ill	1 (0.2)	-	**265 (64.5)**	80 (19.5)	46 (11.2)	13 (3.2)	6 (1.5)
22	Isolated from others	1 (0.2)	-	150 (36.5)	90 (21.9)	102 (24.8)	55 (13.4)	13 (3.2)
23	Excluded from attending activities	1 (0.2)	-	**259 (63.0)**	75 (18.2)	57 (13.9)	17 (4.1)	2 (0.5)
24	Felt depressed	2 (0.5)	-	162 (39.4)	80 (19.5)	100 (24.3)	56 (13.6)	11 (2.7)
25	Difficulty concentrating	2 (0.5)	-	**224 (54.5)**	80 (19.5)	71 (17.3)	24 (5.8)	10 (2.4)

No	Item (abbreviated)	Missing data		Distribution of responses, n=411				
		No response n (%)	N/A n (%)	Never n (%)	Rarely n (%)	Sometimes n (%)	Often n (%)	Always n (%)
26	Bothered by weight	0	-	98 (23.8)	76 (18.5)	104 (25.3)	83 (20.2)	50 (12.2)
27	Avoided social activities	1 (0.2)	-	173 (42.1)	79 (19.2)	115 (28.0)	37 (9.0)	6 (1.5)
28	Limited work activities	**1 (0.2)**	**63 (15.3)**	**218 (53.0)**	77 (18.7)	35 (8.5)	11 (2.7)	6 (1.5)
29	Avoided going out to eat	0	-	122 (29.7)	76 (18.5)	117 (28.5)	73 (17.8)	23 (5.6)
30	Worried accidentally consume	0	-	36 (8.8)	67 (16.3)	146 (35.5)	107 (26.0)	55 (13.4)
31	Concerned about cross-contamination	1 (0.2)	-	42 (10.2)	60 (14.6)	110 (26.8)	112 (27.3)	86 (20.9)
32	Felt uncomfortable refusing	1 (0.2)	-	116 (28.2)	61 (14.8)	120 (29.2)	75 (18.2)	38 (9.2)
33	Consumed as uncomfortable refusing	0	-	205 (49.9)	82 (20.0)	87 (21.2)	30 (7.3)	7 (1.7)
34	Worried ill at inconvenient time	0	-	119 (29.0)	91 (22.1)	112 (27.3)	61 (14.8)	28 (6.8)
35	Lacked support of family and friends	0	-	**306 (74.5)**	64 (15.6)	28 (6.8)	9 (2.2)	4 (1.0)
36	Felt down or in low spirits	0	-	112 (27.3)	96 (23.4)	137 (33.3)	58 (14.1)	8 (1.9)
37	Felt you were a nuisance	0	-	88 (21.4)	67 (16.3)	153 (37.2)	85 (20.7)	18 (4.4)
38	Felt uncomfortable others catering	0	-	76 (18.5)	64 (15.6)	139 (33.8)	98 (23.8)	34 (8.3)
39	Guilty about others buying food	4 (1.0)	-	89 (21.7)	49 (11.9)	114 (27.7)	100 (24.3)	55 (13.4)
40	Felt annoyed about the cost of GF food	0	-	13 (3.2)	19 (4.6)	40 (9.7)	107 (26.0)	**232 (56.4)**
41	Financial difficulties	2 (0.5)	-	192 (46.7)	73 (17.8)	59 (14.4)	45 (10.9)	40 (9.7)
42	Difficulty finding food	0	-	39 (9.5)	69 (16.8)	191 (46.5)	90 (21.9)	22 (5.4)
43	Missed meals or snacks	1 (0.2)	-	42 (10.2)	85 (20.7)	179 (43.6)	78 (19.0)	26 (6.3)
44	Craved food or drinks	0	-	75 (18.2)	74 (18.0)	99 (24.1)	83 (20.2)	80 (19.5)
45	Disappointed with taste or texture	3 (0.7)	-	7 (1.7)	33 (8.0)	187 (45.5)	139 (33.8)	42 (10.2)
46	Difficulties cooking or baking	**4 (1.0)**	**17 (4.1)**	57 (13.9)	87 (21.2)	165 (40.1)	62 (15.1)	19 (4.6)
47	Burdened by time to find or make	4 (1.0)	-	53 (12.9)	90 (21.9)	158 (38.4)	86 (20.9)	20 (4.9)
48	Difficulty finding food when out of house	4 (1.0)	-	12 (2.9)	32 (7.8)	130 (31.6)	179 (43.6)	54 (13.1)
49	Frustrated by choice of food	3 (0.7)	-	8 (1.9)	42 (10.2)	104 (25.3)	174 (42.3)	80 (19.5)
50	Frustrated by planning ahead	3 (0.7)	-	25 (6.1)	44 (10.7)	106 (25.8)	158 (38.4)	75 (18.2)
51	Concerned about food prepared by others	5 (1.2)	-	31 (7.5)	62 (15.1)	123 (29.9)	116 (28.2)	74 (18.0)

Figures emboldened where a floor/ceiling effect is present (i.e. >50%) or total missing data > 5%.

Appendix FF: Survey 1 – correlation matrix

Full correlation matrix showing correlations between each pair of items in the draft 51-item version of the CDAQ.

Item No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51
1	1	.51	.55	.54	.50	.37	.44	.35	.43	.37	.44	.42	.38	.44	.42	.40	.34	.36	.46	.58	.38	.38	.30	.39	.33	.35	.45	.31	.49	.64	.67	.50	.24	.49	.29	.37	.46	.47	.36	.33	.36	.36	.39	.21	.18	.19	.37	.44	.31	.47	.69
2	.51	1	**.72**	.48	.57	.50	.54	.26	.32	.26	.28	.31	.26	.32	.32	.28	.29	.27	.32	.43	.26	.43	.32	.36	.31	.30	.36	.26	.37	.46	.47	.55	.36	.32	.34	.35	.56	.59	.45	.26	.30	.28	.36	.12	.17	.18	.37	.43	.30	.42	.43
3	.55	**.72**	1	.55	.61	.47	.55	.28	.37	.26	.30	.30	.28	.36	.37	.32	.27	.28	.32	.42	.23	.42	.28	.35	.30	.29	.36	.23	.43	.52	.50	.59	.35	.38	.27	.36	.61	.64	.51	.29	.34	.33	.42	.20	.20	.22	.41	.46	.31	.47	.51
4	.54	.48	.55	1	.61	.35	.36	.27	.31	.26	.27	.28	.31	.36	.35	.36	.29	.31	.30	.40	.27	.32	.29	.28	.31	.27	.33	.24	.35	.41	.42	.42	.23	.42	.31	.30	.44	.43	.38	.31	.34	.33	.34	.17	.11	.10	.33	.39	.28	.40	.54
5	.50	.57	.61	.61	1	.47	.44	.28	.35	.30	.29	.33	.29	.37	.34	.26	.24	.22	.31	.43	.27	.42	.30	.33	.35	.26	.30	.16	.37	.42	.44	.53	.35	.41	.26	.35	.48	.47	.41	.25	.30	.29	.35	.16	.19	.18	.36	.40	.26	.40	.45
6	.37	.50	.47	.35	.47	1	.41	.25	.30	.25	.22	.25	.17	.28	.24	.26	.21	.23	.26	.32	.25	.30	.30	.22	.29	.19	.32	.23	.32	.30	.34	.38	.29	.29	.22	.28	.43	.43	.31	.17	.26	.21	.27	.14	.16	.15	.32	.31	.15	.26	.34
7	.44	.54	.55	.36	.44	.41	1	.36	.40	.42	.34	.36	.32	.36	.39	.38	.30	.36	.39	.39	.31	.48	.32	.38	.34	.31	.46	.28	.47	.48	.48	.48	.30	.34	.33	.38	.58	.56	.51	.33	.39	.27	.29	.26	.23	.24	.45	.40	.30	.47	.44
8	.35	.26	.28	.27	.28	.25	.36	1	.46	.42	.26	.18	.24	.25	.34	.25	.22	.26	.24	.34	.24	.33	.16	.26	.24	.23	.28	.15	.30	.35	.41	.31	.21	.25	.17	.23	.33	.36	.26	.27	.28	.18	.30	.16	.21	.17	.29	.25	.21	.30	.38
9	.43	.32	.37	.31	.35	.30	.40	.46	1	.66	.43	.38	.30	.37	.46	.40	.37	.39	.32	.42	.38	.39	.23	.35	.38	.34	.36	.33	.39	.45	.48	.37	.20	.41	.26	.37	.41	.39	.32	.33	.35	.29	.34	.20	.24	.26	.39	.34	.28	.35	.46
10	.37	.26	.26	.26	.30	.25	.42	.42	.66	1	.34	.32	.26	.28	.40	.36	.28	.30	.31	.34	.32	.34	.21	.34	.37	.28	.33	.29	.40	.42	.45	.39	.22	.30	.25	.36	.38	.36	.26	.23	.27	.21	.26	.20	.22	.27	.38	.30	.22	.32	.44
11	.44	.28	.30	.27	.29	.22	.34	.26	.43	.34	1	.57	.39	.51	.43	.39	.39	.37	.27	.45	.35	.20	.16	.36	.36	.35	.30	.38	.32	.38	.36	.33	.23	.47	.23	.36	.34	.30	.28	.24	.28	.24	.25	.18	.25	.24	.25	.23	.22	.31	.37
12	.42	.31	.30	.28	.33	.25	.36	.18	.38	.32	.57	1	.47	.55	.47	.39	.28	.27	.27	.37	.38	.26	.16	.36	.40	.36	.33	.26	.29	.31	.35	.36	.22	.39	.25	.38	.37	.32	.30	.25	.27	.24	.33	.16	.19	.21	.29	.30	.21	.24	.30
13	.38	.26	.28	.31	.29	.17	.32	.24	.30	.26	.39	.47	1	.52	.41	.33	.33	.28	.26	.32	.38	.22	.18	.27	.32	.27	.31	.22	.32	.34	.29	.32	.30	.34	.32	.29	.30	.29	.27	.19	.35	.24	.34	.18	.09	.10	.16	.33	.16	.25	.30
14	.44	.32	.36	.36	.37	.28	.36	.25	.37	.28	.51	.55	.52	1	.51	.41	.40	.35	.33	.44	.45	.26	.21	.35	.41	.33	.33	.38	.39	.38	.37	.38	.25	.44	.26	.36	.36	.32	.29	.25	.37	.27	.35	.19	.24	.20	.26	.31	.22	.27	.36
15	.42	.32	.37	.35	.34	.24	.39	.34	.46	.40	.43	.47	.41	.51	1	.58	.43	.43	.34	.43	.42	.33	.23	.48	.50	.38	.38	.37	.40	.37	.39	.39	.29	.39	.27	.50	.38	.35	.27	.29	.34	.34	.37	.27	.17	.20	.30	.34	.26	.32	.41
16	.40	.28	.32	.36	.26	.26	.38	.25	.40	.36	.39	.39	.33	.41	.58	1	.62	.66	.44	.45	.55	.39	.33	.45	.45	.27	.47	.59	.42	.35	.42	.36	.22	.49	.33	.42	.30	.30	.24	.21	.39	.32	.28	.17	.21	.20	.31	.30	.24	.29	.40
17	.34	.29	.27	.29	.24	.21	.30	.22	.37	.28	.39	.28	.33	.40	.43	.62	1	**.72**	.35	.39	.55	.33	.32	.44	.55	.31	.39	**.75**	.30	.29	.33	.35	.20	.42	.33	.41	.30	.31	.25	.14	.36	.18	.24	.16	.15	.13	.26	.20	.13	.26	.35
18	.36	.27	.28	.31	.22	.23	.36	.26	.39	.30	.37	.27	.28	.35	.43	.66	**.72**	1	.39	.45	.48	.37	.33	.40	.50	.25	.45	.66	.39	.33	.35	.32	.20	.46	.33	.39	.30	.27	.22	.15	.33	.20	.21	.15	.11	.13	.24	.20	.16	.24	.36
19	.46	.32	.32	.30	.31	.26	.39	.24	.32	.31	.27	.27	.26	.33	.34	.44	.35	.39	1	.63	.43	.42	.40	.34	.37	.22	.46	.37	.57	.44	.47	.35	.14	.50	.29	.31	.33	.33	.21	.23	.29	.27	.33	.11	.13	.17	.31	.35	.25	.34	.47
20	.58	.43	.42	.40	.43	.32	.39	.34	.42	.34	.45	.37	.32	.44	.43	.45	.39	.45	.63	1	.45	.44	.37	.38	.38	.32	.44	.37	.51	.57	.56	.47	.24	**.70**	.30	.33	.40	.34	.30	.30	.36	.33	.35	.18	.17	.15	.34	.42	.28	.41	.54
21	.38	.26	.23	.27	.27	.25	.31	.24	.38	.32	.35	.38	.38	.45	.42	.55	.55	.48	.43	.45	1	.40	.39	.39	.46	.25	.45	.54	.44	.31	.39	.31	.22	.52	.39	.37	.27	.26	.20	.18	.38	.22	.26	.11	.11	.14	.27	.25	.18	.22	.33
22	.38	.43	.42	.32	.42	.30	.48	.33	.39	.34	.20	.26	.22	.26	.33	.39	.33	.37	.42	.44	.40	1	.51	.52	.43	.32	.59	.35	.51	.38	.42	.44	.27	.39	.44	.46	.49	.44	.36	.24	.32	.24	.28	.23	.17	.14	.40	.32	.21	.35	.40
23	.30	.32	.28	.29	.30	.30	.32	.16	.23	.21	.16	.16	.18	.21	.23	.33	.32	.33	.40	.37	.39	.51	1	.40	.35	.17	.51	.46	.44	.29	.29	.38	.28	.31	.41	.34	.34	.29	.26	.13	.32	.23	.21	.14	.11	.10	.27	.24	.20	.25	.34

Item No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51
24	.39	.36	.35	.28	.33	.22	.38	.26	.35	.34	.36	.36	.27	.35	.48	.45	.44	.40	.34	.38	.39	.52	.40	1	.57	.39	.43	.42	.42	.35	.41	.37	.30	.35	.37	**.82**	.52	.42	.34	.20	.35	.27	.33	.32	.19	.14	.35	.33	.24	.36	.42
25	.33	.31	.30	.31	.35	.29	.34	.24	.38	.37	.36	.40	.32	.41	.50	.45	.55	.50	.37	.38	.46	.43	.35	.57	1	.41	.43	.53	.41	.29	.35	.35	.28	.39	.40	.52	.37	.31	.31	.16	.26	.16	.28	.23	.07	.11	.21	.23	.12	.18	.34
26	.35	.30	.29	.27	.26	.19	.31	.23	.34	.28	.35	.36	.27	.33	.38	.27	.31	.25	.22	.32	.25	.32	.17	.39	.41	1	.32	.28	.30	.31	.33	.35	.22	.29	.29	.42	.37	.30	.32	.28	.27	.25	.29	.21	.07	.13	.28	.26	.19	.26	.36
27	.45	.36	.36	.33	.30	.32	.46	.28	.36	.33	.30	.33	.31	.33	.38	.47	.39	.45	.46	.44	.45	.59	.51	.43	.43	.32	1	.51	.64	.44	.45	.44	.30	.41	.40	.43	.48	.43	.35	.19	.39	.28	.31	.22	.14	.10	.32	.34	.26	.31	.43
28	.31	.26	.23	.24	.16	.23	.28	.15	.33	.29	.38	.26	.22	.38	.37	.59	**.75**	.66	.37	.37	.54	.35	.46	.42	.53	.28	.51	1	.42	.31	.35	.34	.21	.37	.34	.38	.26	.25	.20	.12	.32	.18	.17	.14	.12	.13	.17	.12	.15	.19	.32
29	.49	.37	.43	.35	.37	.32	.47	.30	.39	.40	.32	.29	.32	.39	.40	.42	.30	.39	.57	.51	.44	.51	.44	.42	.41	.30	.64	.42	1	.51	.52	.48	.29	.49	.37	.43	.47	.46	.35	.30	.40	.36	.39	.24	.22	.24	.41	.48	.36	.46	.53
30	.64	.46	.52	.41	.42	.30	.48	.35	.45	.42	.38	.31	.34	.38	.37	.35	.29	.33	.44	.57	.31	.38	.29	.35	.29	.31	.44	.31	.51	1	**.76**	.48	.28	.52	.27	.34	.45	.50	.41	.34	.33	.34	.35	.21	.21	.25	.42	.46	.41	.54	.65
31	.67	.47	.50	.42	.44	.34	.48	.41	.48	.45	.36	.35	.29	.37	.39	.42	.33	.35	.47	.56	.39	.42	.29	.41	.35	.33	.45	.35	.52	**.76**	1	.50	.25	.49	.29	.38	.46	.47	.40	.37	.39	.33	.37	.14	.17	.21	.42	.44	.37	.51	.70
32	.50	.55	.59	.42	.53	.38	.48	.31	.37	.39	.33	.36	.32	.38	.39	.36	.35	.32	.35	.47	.31	.44	.38	.37	.35	.35	.44	.34	.48	.48	.50	1	.49	.46	.27	.38	.58	.59	.48	.26	.36	.32	.43	.21	.21	.22	.39	.39	.25	.41	.49
33	.24	.36	.35	.23	.35	.29	.30	.21	.20	.22	.23	.22	.30	.25	.29	.22	.20	.20	.14	.24	.22	.27	.28	.30	.28	.22	.30	.21	.29	.28	.25	.49	1	.32	.24	.28	.36	.35	.28	.17	.33	.26	.34	.30	.15	.15	.32	.32	.23	.32	.28
34	.49	.32	.38	.42	.41	.29	.34	.25	.41	.30	.47	.39	.34	.44	.39	.49	.42	.46	.50	**.70**	.52	.39	.31	.35	.39	.29	.41	.37	.49	.52	.49	.46	.32	1	.32	.35	.39	.34	.30	.27	.37	.26	.38	.18	.14	.16	.35	.38	.22	.39	.52
35	.29	.34	.27	.31	.26	.22	.33	.17	.26	.25	.23	.25	.32	.26	.27	.33	.33	.33	.29	.30	.39	.44	.41	.37	.40	.29	.40	.34	.37	.27	.29	.27	.24	.32	1	.38	.31	.32	.27	.12	.27	.23	.23	.16	.05	.12	.27	.26	.13	.27	.27
36	.37	.35	.36	.30	.35	.28	.38	.23	.37	.36	.36	.38	.29	.36	.50	.42	.41	.39	.31	.33	.37	.46	.34	**.82**	.52	.42	.43	.38	.43	.34	.38	.38	.28	.35	.38	1	.54	.46	.39	.25	.37	.28	.33	.33	.21	.21	.38	.33	.21	.31	.39
37	.46	.56	.61	.44	.48	.43	.58	.33	.41	.38	.34	.37	.30	.36	.38	.30	.30	.30	.33	.40	.27	.49	.34	.52	.37	.37	.48	.26	.47	.45	.46	.58	.36	.39	.31	.54	1	**.74**	.60	.35	.40	.32	.46	.27	.21	.27	.44	.45	.28	.44	.51
38	.47	.59	.64	.43	.47	.43	.56	.36	.39	.36	.30	.32	.29	.32	.35	.30	.31	.27	.33	.34	.26	.44	.29	.42	.31	.30	.43	.25	.46	.50	.47	.59	.35	.34	.32	.46	**.74**	1	.69	.35	.33	.30	.43	.24	.26	.30	.44	.46	.28	.48	.48
39	.36	.45	.51	.38	.41	.31	.51	.26	.32	.26	.28	.30	.27	.29	.27	.24	.25	.22	.21	.30	.20	.36	.26	.34	.31	.32	.35	.20	.35	.41	.40	.48	.28	.30	.27	.39	.60	.69	1	.38	.29	.28	.36	.22	.24	.28	.41	.37	.26	.42	.38
40	.33	.26	.29	.31	.25	.17	.33	.27	.33	.23	.24	.25	.19	.25	.29	.21	.14	.15	.23	.30	.18	.24	.13	.20	.16	.28	.19	.12	.30	.34	.37	.26	.17	.27	.12	.25	.35	.35	.38	1	.40	.36	.38	.29	.25	.26	.38	.44	.45	.42	.41
41	.36	.30	.34	.34	.30	.26	.39	.28	.35	.27	.28	.27	.35	.37	.34	.39	.36	.33	.29	.36	.38	.32	.32	.35	.26	.27	.39	.32	.40	.33	.39	.36	.33	.37	.27	.37	.40	.33	.29	.40	1	.43	.41	.28	.20	.20	.40	.40	.30	.32	.39
42	.36	.28	.33	.33	.29	.21	.27	.18	.29	.21	.24	.24	.24	.27	.34	.32	.18	.20	.27	.33	.22	.24	.23	.27	.16	.25	.28	.18	.36	.34	.33	.32	.26	.26	.23	.28	.32	.30	.28	.36	.43	1	.49	.30	.31	.30	.45	.54	.46	.40	.37
43	.39	.36	.42	.34	.35	.27	.29	.30	.34	.26	.25	.33	.34	.35	.37	.28	.24	.21	.33	.35	.26	.28	.21	.33	.28	.29	.31	.17	.39	.35	.37	.43	.34	.38	.23	.33	.46	.43	.36	.38	.41	.49	1	.30	.28	.30	.36	.54	.33	.41	.41
44	.21	.12	.20	.17	.16	.14	.26	.16	.20	.20	.18	.16	.18	.19	.27	.17	.16	.15	.11	.18	.11	.23	.14	.32	.23	.21	.22	.14	.24	.21	.14	.21	.30	.18	.16	.33	.27	.24	.22	.29	.28	.30	.30	1	.33	.20	.32	.30	.24	.30	.22
45	.18	.17	.20	.11	.19	.16	.23	.21	.24	.22	.25	.19	.09	.24	.17	.21	.15	.11	.13	.17	.11	.17	.11	.19	.07	.07	.14	.12	.22	.21	.17	.21	.15	.14	.05	.21	.21	.26	.24	.25	.20	.31	.28	.33	1	.44	.42	.32	.40	.28	.24
46	.19	.18	.22	.10	.18	.15	.24	.17	.26	.27	.24	.21	.10	.20	.20	.20	.13	.13	.17	.15	.14	.14	.10	.14	.11	.13	.10	.13	.24	.25	.21	.22	.15	.16	.12	.21	.27	.30	.28	.26	.20	.30	.30	.20	.44	1	.52	.33	.31	.31	.27
47	.37	.37	.41	.33	.36	.32	.45	.29	.39	.38	.25	.29	.16	.26	.30	.31	.26	.24	.31	.34	.27	.40	.27	.35	.21	.28	.32	.17	.41	.42	.42	.39	.32	.35	.27	.38	.44	.44	.41	.38	.40	.45	.36	.32	.42	.52	1	.54	.48	.55	.45
48	.44	.43	.46	.39	.40	.31	.40	.25	.34	.30	.23	.30	.33	.31	.34	.30	.20	.20	.35	.42	.25	.32	.24	.33	.23	.26	.34	.12	.48	.46	.44	.39	.32	.38	.26	.33	.45	.46	.37	.44	.40	.54	.54	.30	.32	.33	.54	1	.56	.63	.54
49	.31	.30	.31	.28	.26	.15	.30	.21	.28	.22	.22	.21	.16	.22	.26	.24	.13	.16	.25	.28	.18	.21	.20	.24	.12	.19	.26	.15	.36	.41	.37	.25	.23	.22	.13	.21	.28	.28	.26	.45	.30	.46	.33	.24	.40	.31	.48	.56	1	.61	.47
50	.47	.42	.47	.40	.40	.26	.47	.30	.35	.32	.31	.24	.25	.27	.32	.29	.26	.24	.34	.41	.22	.35	.25	.36	.18	.26	.31	.19	.46	.54	.51	.41	.32	.39	.27	.31	.44	.48	.42	.42	.32	.40	.41	.30	.28	.31	.55	.63	.61	1	.62
51	.69	.43	.51	.54	.45	.34	.44	.38	.46	.44	.37	.30	.30	.36	.41	.40	.35	.36	.47	.54	.33	.40	.34	.42	.34	.36	.43	.32	.53	.65	.70	.49	.28	.52	.27	.39	.51	.48	.38	.41	.39	.37	.41	.22	.24	.27	.45	.54	.47	.62	1

Values between 0.70 – 0.79 highlighted yellow and shown in bold; values ≥ 0.80 highlighted orange and shown in bold.

Appendix GG. Survey 2 – letter of invitation

[Coeliac UK Letterhead here]

[Date]

[Member's Address]

Diagnosis and management of coeliac disease: Quality of life and patient's experiences of healthcare services

Dear [Title] [Surname],

I am writing to make you aware of a research study which is being undertaken by the Nuffield Department of Population Health at the University of Oxford in collaboration with Coeliac UK. The research aims to find out about experiences of using healthcare services to diagnose and manage coeliac disease and how the condition impacts on quality of life. I am writing to you as a Member of Coeliac UK who has agreed you may be contacted for research purposes. Your name and contact details have not been made available to the University of Oxford.

If you would like to participate in the study, please complete the enclosed questionnaire and return it to the University of Oxford in the pre-paid envelope provided. The questionnaire asks you about your experiences of living with coeliac disease and using healthcare services to diagnose and manage your condition. You do not have to have used healthcare services recently to participate. Taking part in this study is voluntary and confidential.

Further information about the study can be found in the enclosed information sheet. If you have any questions about the study, please contact Helen Crocker, the research contact at the University of Oxford, by telephone: 01865 289431 or by email: Helen.Crocker@dph.ox.ac.uk.

Thank you for taking the time to read this letter.

Yours sincerely,

Heidi Urwin
Research Manager, Coeliac UK

Appendix HH. Survey 2 - participant information sheet

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Diagnosis and management of coeliac disease: Quality of life and patient's experiences of healthcare services

Information Sheet for Survey Participants

What is the purpose of this research?

The purpose of this research is to find out about experiences of living with coeliac disease and experiences of using healthcare services to diagnose and manage the condition. The study will also explore relationships between experiences of healthcare and quality of life. By asking people about their experiences, we hope to find out whether services are meeting the needs of patients and how they might be improved. We would also like to find out how coeliac disease affects the quality of life of those living with the condition. As part of the study, a questionnaire measuring the impact of coeliac disease on quality of life is being developed and validated.

Who is doing the research?

The research is led by Helen Crocker, a researcher in the Nuffield Department of Population Health at the University of Oxford, under the supervision of Professor Crispin Jenkinson and Dr Michele Peters. The research is funded by the Medical Research Council and is part of a doctoral research programme. The research is being undertaken with the support of Coeliac UK.

How can I take part?

Taking part in this study is voluntary and confidential. If you would like to take part, please complete the enclosed questionnaire and return it to the research team in the pre-paid envelope provided. The questionnaire asks about your experiences of living with coeliac disease and using healthcare services to diagnose and manage your condition.

The research team would like to send you Section 1 (pages 1-4) of the enclosed questionnaire again in two weeks' time. Completing these questions twice will allow us to see how well the questionnaire can measure quality of life in coeliac disease. If you are happy to receive a second questionnaire, please complete the name and address slip attached to the front of the questionnaire.

If you have any questions that you would like to ask, please contact Helen Crocker by telephone: 01865 289431 or by email: Helen.Crocker@dph.ox.ac.uk. Returning the completed questionnaires means that you understand the purpose of this study and are happy to take part. You are free to withdraw from the study at any point in time without providing a reason, without penalty, and you will not be contacted further.

What will happen with the information that I provide?

The results of this study will provide evidence of the impact coeliac disease has on quality of life, people's experiences of healthcare services in relation to their condition, and the relationships between experiences of care and quality of life. It is intended that the results will be used to inform healthcare policy to improve

the quality of healthcare for people with coeliac disease. It is also intended that the questionnaire developed to measure the impact of coeliac disease on quality of life will become available for use in other research studies and clinical trials.

Who can take part?

Participants should be aged 18 years or over, live in the UK, and have a medical diagnosis of coeliac disease. You have been made aware of this study as a Member of Coeliac UK who has agreed you may be contacted for research purposes. We are interested in all experiences of coeliac disease whatever the extent of your symptoms.

Will participation be confidential?

No personal data (e.g. name and contact details) has been made available to the research team. If you choose to provide your name and address, these details will be used to send you a second questionnaire only. You will be assigned an identification number, and both questionnaires will be marked with this identification number and not your name.

Personal details and other data collected as part of this research will be accessible to the research team only. Paper documentation will be stored in locked filing cabinets and electronic files will be stored on a password protected computer in accordance with the current Data Protection Act. Personal data (e.g. name and contact details) will not be kept beyond your involvement in the study. In accordance with guidelines produced by the Medical Research Council, anonymised data will be kept for a period of ten years to allow the research to be reviewed if necessary.

What will happen with the results of the study?

The University of Oxford is committed to the dissemination of its research for the benefit of society. Therefore, it is intended that the research will be written up as one or more papers to be submitted for publication in scientific journals, presented at conferences, and as a doctoral thesis. On successful submission of the thesis, it will be deposited in the University archives to facilitate its use in future research. The thesis will be available in print and online.

Are there any risks involved in taking part?

We do not foresee any risks involved in taking part in this study. If participating in this research raises questions about the condition that you would like to discuss, you can contact Coeliac UK on their Helpline: 0845 305 2060 or visit their website: www.coeliac.org.uk.

Are there any benefits in taking part?

The information that you provide may help to inform healthcare policy and improve healthcare services in the future. There are no direct benefits in taking part.

What can I do if I have any concerns about the research study?

This study has been reviewed by, and received ethics clearance through, the University of Oxford Central University Research Ethics Committee. If you have a concern about any aspect of this project, please speak to the relevant researcher (Helen Crocker, tel: 01865 289431, email: Helen.Crocker@dph.ox.ac.uk) or her supervisor (Professor Crispin Jenkinson, tel: 01865 289441, email: Crispin.Jenkinson@dph.ox.ac.uk) who will do their best to answer your query. The researcher or supervisor should acknowledge your concern within 10 working days and give you an indication of how he/she intends to deal with it. If you remain unhappy or wish to make a formal complaint, please contact the chair of the Research Ethics Committee at the University of Oxford (Chair, Medical Sciences Inter-Divisional Research Ethics Committee; Email: ethics@medsci.ox.ac.uk; Address: Research Services, University of Oxford, Wellington Square, Oxford, OX1 2JD). The chair will seek to resolve the matter promptly.

Appendix II. Survey 2 - questionnaire

Survey 2 commences on the following page

Coeliac Disease Questionnaire:
Quality of Life and Experiences of Healthcare

What is the study about?
The purpose of this research is to find out about people's experiences of living with coeliac disease and using healthcare services to diagnose and manage their condition. By asking people about their experiences, we hope to find out whether services are meeting the needs of patients and how they might be improved. We would also like to find out how coeliac disease affects quality of life, and identify any relationships between people's experiences of healthcare services and quality of life.

Who can take part?
You can take part in this study if you are aged 18 years or over and have coeliac disease. We are interested in all experiences of coeliac disease whatever the extent of your symptoms. Participation in the study is voluntary.

How can I take part?
If you would like to take part in the study, please complete this questionnaire and return it in the pre-paid envelope provided. The questionnaire is split into four sections: (1) Living with Coeliac Disease, (2) Your Health and Well-Being, (3) Experiences of Healthcare Services, and (4) About You. Please complete all questions. Tick one box for each question unless instructed otherwise.

Questions or help?
If you have any questions about the questionnaire, please contact Helen Crocker by telephone: 01865 289431 or by email: Helen.Crocker@dph.ox.ac.uk

REC Ref No: MSD-IDREC-C1-2014-031 (Survey 2)
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Section 1: Living with Coeliac Disease

This section of the questionnaire asks how your **coeliac disease** has affected your life during the **past 4 weeks**.

Please tick **one** box for **each** question.

THESE QUESTIONS RELATE TO YOUR COELIAC DISEASE						
During the past 4 weeks, how often…		Never	Rarely	Sometimes	Often	Always
1.	have you worried that you might become ill after eating food prepared by others (for example, at other people's houses, restaurants, or cafés)?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
2.	have you felt as though you might appear to be making a fuss about your dietary needs?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
3.	have you felt that people misunderstood your coeliac disease or dietary needs (for example, thinking you follow a gluten-free diet as a personal choice rather than for your coeliac disease)?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
4.	have you found it difficult to let people know they have misunderstood your coeliac disease or dietary needs?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
5.	have you received unwanted attention because of your coeliac disease or dietary needs?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
6.	have you felt guilty about the impact of your coeliac disease on friends and family?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
7.	have you felt worried that a family member may have or could develop coeliac disease?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

THESE QUESTIONS RELATE TO YOUR COELIAC DISEASE						
During the <u>past 4 weeks</u>, how often…		Never	Rarely	Sometimes	Often	Always
8.	have you felt concerned about developing a health problem related to your coeliac disease?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
9.	have you been bothered by your bowel movements (for example, diarrhoea, loose stools, or constipation)?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
10.	have you had bloating in your abdomen?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
11.	have you had nausea or vomiting that you think was caused by your coeliac disease?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
12.	have you had pain that you think was caused by your coeliac disease?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
13.	have you had tiredness or a lack of energy that you think was caused by your coeliac disease?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
14.	have your daily activities been limited by your coeliac disease?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
15.	have you worried that you would become ill when you were not at home?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
16.	have you felt isolated from others because of your coeliac disease?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
17.	have you avoided social activities?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
18.	have you avoided going out to eat (for example, at a friend's house, restaurant, or café)?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
19.	have you worried that you would accidentally eat or drink products that contain gluten?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

THESE QUESTIONS RELATE TO YOUR COELIAC DISEASE						
During the <u>past 4 weeks</u>, how often…		Never	Rarely	Sometimes	Often	Always
20.	have you been concerned about cross-contamination (gluten-free food coming into contact with food that contains gluten)?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
21.	have you felt uncomfortable refusing unsuitable food or drink from other people?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
22.	have you felt down or in low spirits?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
23.	have you felt you were a nuisance to other people?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
24.	have you felt guilty about other people buying gluten-free substitute foods for you?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
25.	have you felt annoyed or frustrated about the cost of gluten-free substitute foods?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
26.	have you had difficulty finding suitable food?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
27.	have you craved food or drinks that contain gluten?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
28.	have you been disappointed with the taste or texture of gluten-free substitutes?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
29.	have you felt burdened by the time taken to find or make gluten-free food?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
30.	have you had difficulty finding something to eat when you were not at home?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

THESE QUESTIONS RELATE TO YOUR COELIAC DISEASE						
During the <u>past 4 weeks</u>, how often…		Never	Rarely	Sometimes	Often	Always
31.	have you been frustrated by the choice of suitable food available (for example, in supermarkets, cafés or restaurants)?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
32.	have you felt frustrated by having to plan ahead (for example, taking food with you, or choosing restaurants)?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

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Section 2: Your Health and Well-Being

The SF-36v2 originally presented here cannot be made freely available via ORA because of copyright. A licence to use the SF-36v2 was obtained from OptumInsight Life Sciences Inc at: http://campaign.optum.com/optum-outcomes/what-we-do/health-surveys/sf-36v2-health-survey.html.

Section 3: Experiences of Healthcare Services

This section of the questionnaire asks about your experiences of using healthcare services to diagnose and manage your coeliac disease.

1. Have you been told by a doctor that you have coeliac disease?

1 ☐ Yes, I have been told that I have coeliac disease

2 ☐ No → **Go to Section 4, Question 1 (page 23)**

2. How long ago did you receive a diagnosis for your coeliac disease?

_____ Year(s) _____ Month(s)

3. How old were you when you were diagnosed with coeliac disease?

1 ☐ Less than 16 years old → **Go to Question 20 (page 16)**

2 ☐ 16 years old or over → **Go to Question 4**

Before Your Diagnosis

4. Which of the following symptoms did you have <u>before</u> you were diagnosed with coeliac disease? *(please tick <u>all</u> that apply)*

1 ☐ Diarrhoea / loose bowel movements

2 ☐ Constipation

3 ☐ Incomplete bowel movements

4 ☐ Abdominal pain

5 ☐ Abdominal bloating

6 ☐ Rumbling stomach

7 ☐ Nausea / vomiting

8 ☐ Skin rash

9 ☐ Mouth ulcers

10 ☐ Loss of appetite

11 ☐ Unexpected weight loss

12 ☐ Iron deficiency anaemia

13 ☐ Headache

14 ☐ 'Brain fog' / difficulty thinking

15 ☐ Chronic fatigue ('tired all the time')

16 ☐ Depression

17 ☐ Other, *please write in:* _

<u>OR</u>

18 ☐ I did not have any symptoms → **Go to Question 9 (page 13)**

19 ☐ I can't remember

5. How long was it from when you first sought medical advice about your symptoms (e.g. first spoke to your GP) to receiving a definite diagnosis?

_____ Year(s) _____ Month(s)

OR

1 ☐ I did not seek medical advice → **Go to Question 9 (page 13)**

2 ☐ I can't remember

6. How do you feel about the amount of time it took to receive a diagnosis?

1 ☐ It was *very* quick

2 ☐ It was *fairly* quick

3 ☐ It was *neither quick nor slow*

4 ☐ It was *fairly* slow

5 ☐ It was *very* slow

7. Which health professional did you speak to the most often <u>before</u> you received your diagnosis? *(please tick <u>one</u> only)*

1 ☐ Hospital doctor / consultant

2 ☐ GP

3 ☐ Dietitian

4 ☐ Hospital nurse

5 ☐ Practice nurse

6 ☐ Pharmacist

7 ☐ Other, *please write in:*

_ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _

8. Thinking about the health professional you selected in Question 7, did you feel that this person…

*Please tick **one** box on each row*

		Yes, definitely	Yes, to some extent	No	I can't remember
a)	listened carefully to you?	1 ☐	2 ☐	3 ☐	4 ☐
b)	gave you confidence in them?	1 ☐	2 ☐	3 ☐	4 ☐
c)	took your symptoms seriously?	1 ☐	2 ☐	3 ☐	4 ☐

Your Diagnosis

To diagnose coeliac disease, an endoscopy is often conducted. An **endoscopy** (sometimes called a gastroscopy) is a medical procedure in which a thin tube with a camera is passed via the mouth into the intestine in order to examine it. During the procedure, a sample (biopsy) of the intestine is normally taken for closer examination.

9. Which tests did you have to diagnose your coeliac disease?

*Please tick **one** box on each row*

	Yes	No, but I **was** offered one	No, I **was not** offered one	I don't know
a) Blood test (antibody)	1 ☐	2 ☐	3 ☐	4 ☐
b) Endoscopy (with biopsy)	1 ☐	2 ☐	3 ☐	4 ☐
c) Other, *please state* _ _ _

12. Who first informed you that you have been diagnosed with coeliac disease?

1 ☐ Hospital doctor / consultant
2 ☐ GP
3 ☐ Dietitian
4 ☐ Hospital nurse
5 ☐ Practice nurse
6 ☐ Receptionist
7 ☐ I can't remember
8 ☐ Other, *please write in:*
_ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _

13. Do you feel you were informed of your diagnosis in both a professional and appropriate manner?

1 ☐ Yes, definitely
2 ☐ Yes, to some extent
3 ☐ No

14. At the time of your diagnosis, did you receive enough information about coeliac disease and the gluten-free diet from <u>health professionals</u>?

1 ☐ Yes, I received enough information
2 ☐ No, I did not receive *enough* information
3 ☐ No, I did not receive *any* information
4 ☐ I did not want any information
5 ☐ I can't remember

Diet and Nutritional Advice

15. After receiving a diagnosis, did you speak to a dietitian about your coeliac disease? *A dietitian is an expert who provides advice about diet and nutrition.*

1 ☐ Yes
2 ☐ No, but I would have liked to → **Go to Question 20 (page 16)**
3 ☐ No, I did not need to → **Go to Question 20 (page 16)**
4 ☐ I can't remember → **Go to Question 20 (page 16)**

16. After receiving a diagnosis, how quickly did you have an appointment with a dietitian to discuss your coeliac disease?

1 ☐ It was *very* quick
2 ☐ It was *fairly* quick
3 ☐ It was *neither quick nor slow*
4 ☐ It was *fairly* slow
5 ☐ It was *very* slow
6 ☐ I can't remember

17. Thinking about your first appointment with a dietitian, which of the following were discussed? *(please tick <u>all</u> that apply)*

The dietitian…

1 ☐ explained the gluten-free diet
2 ☐ gave you written information about the gluten-free diet
3 ☐ explained the importance of a strict gluten-free diet
4 ☐ told you about where you could get gluten-free products
5 ☐ explained food labelling
6 ☐ told you about the prescription process and foods available on prescription
7 ☐ explained cross-contamination and how to avoid it
8 ☐ gave you tips about eating out
9 ☐ weighed you and calculated your body mass index (BMI)
10 ☐ discussed your calcium intake
11 ☐ discussed whether you can eat oats
12 ☐ told you about Coeliac UK

OR

13 ☐ None of the above
14 ☐ I can't remember

18. How helpful was your first appointment with a dietitian?

1 ☐ Very helpful
2 ☐ Fairly helpful
3 ☐ Not very helpful
4 ☐ Not at all helpful
5 ☐ I am not sure / I can't remember

19. Were you offered a second appointment to speak to a dietitian <u>within 6 months</u> of your first appointment?

1 ☐ Yes

2 ☐ No, but I would have liked one

3 ☐ No, but I did not want one

4 ☐ I can't remember

After Your Diagnosis

20. Some people with coeliac disease have had additional tests or vaccinations. Have you had …

*Please tick **one** box on each row*

		Yes	No, but I **was** offered one	No, I **was not** offered one	I don't know
a)	a repeat endoscopy (with biopsy)?	1 ☐	2 ☐	3 ☐	4 ☐
b)	a bone density scan (DEXA)?	1 ☐	2 ☐	3 ☐	4 ☐
c)	a pneumococcal vaccination (sometimes called the 'pneumo jab')?	1 ☐	2 ☐	3 ☐	4 ☐

Follow-up Appointments

Some people with coeliac disease have **follow-up appointments** to monitor their condition. Your follow-up appointment may involve having blood taken for testing and / or a discussion with a health professional **about your coeliac disease**. Appointments are usually carried out annually, but can be more or less frequent.

21. Do you have regular follow-up appointments for your coeliac disease?

1 ☐ Yes

2 ☐ No → **Go to Question 29 (page 18)**

3 ☐ I am not sure / I can't remember → **Go to Question 29 (page 18)**

22. When was your <u>most recent</u> follow-up appointment for your coeliac disease?

1 ☐ Less than 1 year ago
2 ☐ 1 - 2 years ago
3 ☐ More than 2 years ago

23. Who was your <u>most recent</u> follow-up appointment with?

1 ☐ Hospital doctor / consultant
2 ☐ GP
3 ☐ Dietitian
4 ☐ Hospital nurse
5 ☐ Practice nurse
6 ☐ I can't remember
7 ☐ Other, *please write in:*
_ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _

24. Who initiated your <u>most recent</u> follow-up appointment?

1 ☐ Staff at the hospital
2 ☐ Staff at the GP practice
3 ☐ I contacted a health professional
4 ☐ Other, *please write in:* _
5 ☐ I can't remember

25. Which of the following happened at your <u>most recent</u> follow-up appointment?
(please tick <u>all</u> that apply)

1 ☐ I was weighed
2 ☐ My body mass index (BMI) was calculated
3 ☐ Blood was taken for testing (this may have happened before or after your follow-up appointment)
4 ☐ My diet was assessed
5 ☐ Any difficulties I have adhering to the diet were discussed
6 ☐ My symptoms were discussed
7 ☐ My emotional well-being was assessed
8 ☐ My calcium intake was reviewed
9 ☐ My bone density was discussed
10 ☐ My prescription was reviewed / Access to prescriptions was discussed
11 ☐ My understanding of food labelling was discussed

<u>OR</u>

12 ☐ None of the above
13 ☐ I can't remember

26. At your <u>most recent</u> follow-up appointment, were you given the opportunity to ask your questions?

1 ☐ Yes
2 ☐ No → **Go to Question 28**
3 ☐ I did not have any questions → **Go to Question 28**
4 ☐ I can't remember → **Go to Question 28**

27. At your <u>most recent</u> follow-up appointment, when you had questions to ask, were you given the information you needed?

1 ☐ Yes, always
2 ☐ Sometimes
3 ☐ No, never
4 ☐ I can't remember
5 ☐ I did not have any questions

28. Overall, how helpful was your <u>most recent</u> follow-up appointment?

1 ☐ Very helpful
2 ☐ Fairly helpful
3 ☐ Not very helpful
4 ☐ Not at all helpful
5 ☐ I am not sure / I can't remember

29. Would you like to have follow-up appointments in the future?

1 ☐ Yes
2 ☐ No → **Go to Question 32 (page 19)**
3 ☐ I am not sure → **Go to Question 32 (page 19)**

30. Who would you like your follow-up appointments with? *(please tick <u>one</u> box only)*

1 ☐ Hospital doctor / consultant
2 ☐ GP
3 ☐ Dietitian
4 ☐ Hospital nurse
5 ☐ Practice nurse
6 ☐ I am not sure
7 ☐ Other, *please write in:*

_ _

31. How often would you like to have follow-up appointments?

1 ☐ Once a month
2 ☐ Once every six months
3 ☐ Once a year
4 ☐ Once every 2 years
5 ☐ Other, *please write in:* _
6 ☐ I am not sure

Prescriptions

32. Do you think you have received enough information about getting gluten-free food on prescription?

1 ☐ Yes, I have received enough information
2 ☐ No, I have not received *enough* information
3 ☐ No, I have not received *any* information
4 ☐ I do not need this information

33. How easy have you found it to obtain the gluten-free food products that are available <u>on prescription</u>?

1 ☐ Very easy
2 ☐ Fairly easy
3 ☐ Neither easy nor difficult
4 ☐ Fairly difficult
5 ☐ Very difficult
6 ☐ I have not tried to get gluten-free food on prescription

34. In the <u>last 12 months</u>, which gluten-free foods have you had <u>on prescription</u>? *(please tick <u>all</u> that apply)*

1 ☐ Bread / Rolls
2 ☐ Flour / Bread mixes
3 ☐ Crackers / Crispbreads
4 ☐ Breakfast cereals
5 ☐ Pasta
6 ☐ Pizza bases
7 ☐ Biscuits
8 ☐ Oats
9 ☐ Other, *please write in:*
_ _

<u>OR</u>

10 ☐ I have not had any gluten-free food on prescription in the last 12 months, because *(please say why)* _ → **Go to Question 37**

35. How do you pay for your prescriptions for your coeliac disease?

1 ☐ I pay for each prescription
2 ☐ I have a Prescription Pre-payment Certificate (PPC)
3 ☐ I do not pay for my prescriptions (I am entitled to free prescriptions) → **Go to Question 37**

36. How do you find the cost of your prescriptions for your coeliac disease?

1 ☐ Reasonable
2 ☐ Fairly expensive
3 ☐ Very expensive, but I can afford it
4 ☐ Very expensive, and I cannot afford it

Recent Healthcare

37. In the <u>last 12 months</u>, which health professionals have you spoken to specifically about your coeliac disease? *(please tick <u>all</u> that apply)*

1 ☐ Hospital doctor / consultant
2 ☐ GP
3 ☐ Dietitian
4 ☐ Hospital nurse
5 ☐ Practice nurse
6 ☐ Pharmacist
7 ☐ Other, *please write in:*
_ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _

<u>OR</u>

8 ☐ I have not spoken to a health professional specifically about my coeliac disease in the last 12 months

38. In the <u>last 12 months</u>, have you been able to get information and advice about your coeliac disease from a health professional when you wanted to do so?

1 ☐ Yes, always
2 ☐ Sometimes
3 ☐ No
4 ☐ I have not wanted to speak to a health professional

39. In the <u>last 12 months</u>, have you received enough information about the results of medical tests conducted in relation to your coeliac disease (e.g. blood tests, DEXA scan, endoscopy (with biopsy))?

1 ☐ Yes, I have received enough information
2 ☐ No, I have not received *enough* information
3 ☐ No, I have not received *any* information
4 ☐ I did not want any information
5 ☐ I can't remember
6 ☐ I have not had any tests

Overall Experience

40. Do you think the GP that you speak to the most often about your coeliac disease has a good understanding of the condition?

1 ☐ Yes, definitely
2 ☐ Yes, to some extent
3 ☐ No
4 ☐ I do not speak to the GP about my coeliac disease
5 ☐ I am not sure

41. From your experience, do you think the following health professionals are knowledgeable about coeliac disease?

*Please tick **one** box on each row*

		Yes	To some extent	No	I don't know / N/A
a)	Dietitians	1 ☐	2 ☐	3 ☐	4 ☐
b)	Specialist hospital doctors / Gastroenterologists	1 ☐	2 ☐	3 ☐	4 ☐
c)	Other hospital doctors	1 ☐	2 ☐	3 ☐	4 ☐
d)	GPs	1 ☐	2 ☐	3 ☐	4 ☐
e)	Practice nurses / healthcare assistants	1 ☐	2 ☐	3 ☐	4 ☐
f)	Pharmacists	1 ☐	2 ☐	3 ☐	4 ☐

42. Thinking about your coeliac disease and the gluten-free diet, how <u>consistent</u> has information and advice from health professionals been?

1 ☐ Very consistent
2 ☐ Fairly consistent
3 ☐ Not very consistent
4 ☐ Not at all consistent
5 ☐ I have not received any information or advice

43. Overall, how would you rate the healthcare that you have received to help you manage your coeliac disease <u>since diagnosis</u>?

1 ☐ Very good
2 ☐ Good
3 ☐ Fair
4 ☐ Poor
5 ☐ Very poor

<u>OR</u>

6 ☐ I have not received any healthcare since my diagnosis

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Section 4: About You

This section of the questionnaire asks for some basic information about you and your coeliac disease. This information will help us to see how healthcare experiences and quality of life varies between different population groups.

1. Thinking about your coeliac disease, how much does it impact on you and your health?

1 ☐ No impact
2 ☐ Mild impact
3 ☐ Moderate impact
4 ☐ Severe impact
5 ☐ Very severe impact

2. In the last 12 months, how often have you consumed food or drinks that contain gluten on purpose?

1 ☐ Never
2 ☐ Rarely
3 ☐ Sometimes
4 ☐ Often
5 ☐ Always

3. Are you a member of Coeliac UK?

1 ☐ Yes
2 ☐ No

4. From which of the following have you accessed information or support? *(please tick all that apply)*

1 ☐ Coeliac UK
2 ☐ Coeliac UK local group meetings
3 ☐ Friends or family with coeliac disease
4 ☐ Online forums / discussion groups (e.g. Facebook, Yahoo Groups)
5 ☐ The Internet
6 ☐ Other, *please write in*: _

5. Which of the following medical conditions do you have?

Please tick <u>all</u> that apply

1 ☐ Dermatitis herpetiformis
2 ☐ Irritable bowel syndrome
3 ☐ Microscopic colitis
4 ☐ Lymphoma
5 ☐ Type 1 Diabetes
6 ☐ Type 2 Diabetes
7 ☐ Autoimmune Thyroid Disease
8 ☐ Autoimmune Liver Disease
9 ☐ Sjögren's syndrome
10 ☐ Turner syndrome
11 ☐ Osteopenia
12 ☐ Osteoporosis
13 ☐ Iron deficiency anaemia
14 ☐ Vitamin B12 deficiency
15 ☐ Peripheral neuropathy
16 ☐ Epilepsy
17 ☐ Depression
18 ☐ Down's syndrome

19 ☐ Other, *please write in:* _

<u>OR</u>

20 ☐ I do not have any of these conditions

6. Are you male or female?

1 ☐ Male
2 ☐ Female

7. What is your age?

_____ Years

8. What is the first part of your postcode? _ _ _ _

9. Which of these best describes what you are doing at present? ***If more than one of these applies to you, please tick the main <u>one</u> only.***

1 ☐ Full-time paid work (30 hours or more each week)
2 ☐ Part-time paid work (under 30 hours each week)
3 ☐ Full-time education at school, college or university
4 ☐ Self-employed
5 ☐ Unemployed
6 ☐ Permanently sick or disabled
7 ☐ Fully retired from work
8 ☐ Looking after the home
9 ☐ Doing something else, *please write in*: _

10. What is your legal marital status or same-sex civil partnership status?

1 ☐ Single (never married and never formed a civil partnership)

2 ☐ Married / in a civil partnership

3 ☐ Separated (but still legally married / in a civil partnership)

4 ☐ Divorced / legally dissolved civil partnership

5 ☐ Widowed / surviving partner from a civil partnership

11. What is your ethnic group?

Choose ONE section from A to E, and then tick the appropriate box to indicate your ethnic group.

A. White

1 ☐ English / Welsh / Scottish / Northern Irish / British

2 ☐ Irish

3 ☐ Gypsy or Irish Traveller

4 ☐ Any other White background, please write in: _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _

B. Mixed / Multiple ethnic groups

5 ☐ White and Black Caribbean

6 ☐ White and Black African

7 ☐ White and Asian

8 ☐ Any other Mixed / Multiple ethnic background, please write in: _ _ _ _ _

C. Asian / Asian British

9 ☐ Indian

10 ☐ Pakistani

11 ☐ Bangladeshi

12 ☐ Chinese

13 ☐ Any other Asian background, please write in: _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _

D. Black / African / Caribbean / Black British

14 ☐ African

15 ☐ Caribbean

16 ☐ Any other Black / African / Caribbean background, please write in: _ _ _

E. Other ethnic group

17 ☐ Arab

18 ☐ Any other ethnic group, please write in: _

12. Today's date: _ _ _ _ _ _ _ _ _ _ _ _ _ _

Any comments?

If you have any comments about your coeliac disease, healthcare services, or this questionnaire, please write them in the box below.

Thank you for completing this questionnaire

Please return your completed questionnaire in the pre-paid envelope provided

Return address: Helen Crocker, Health Services Research Unit, Nuffield Department of Population Health, University of Oxford, New Richards Building c/o Richard Doll Building, Old Road Campus, Oxford, OX3 7LF

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Appendix JJ. Survey 2 – follow-up questionnaire

Survey 2 follow-up questionnaire commences on the following page

Living with Coeliac Disease

This questionnaire asks how your **coeliac disease** has affected your life during the **past 4 weeks**.

Please tick **one** box for **each** question.

THESE QUESTIONS RELATE TO YOUR COELIAC DISEASE

During the past 4 weeks, how often…		Never	Rarely	Sometimes	Often	Always
1.	have you worried that you might become ill after eating food prepared by others (for example, at other people's houses, restaurants, or cafés)?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
2.	have you felt as though you might appear to be making a fuss about your dietary needs?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
3.	have you felt that people misunderstood your coeliac disease or dietary needs (for example, thinking you follow a gluten-free diet as a personal choice rather than for your coeliac disease)?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
4.	have you found it difficult to let people know they have misunderstood your coeliac disease or dietary needs?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
5.	have you received unwanted attention because of your coeliac disease or dietary needs?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
6.	have you felt guilty about the impact of your coeliac disease on friends and family?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

THESE QUESTIONS RELATE TO YOUR COELIAC DISEASE						
During the <u>past 4 weeks</u>, how often…		Never	Rarely	Sometimes	Often	Always
7.	have you felt worried that a family member may have or could develop coeliac disease?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
8.	have you felt concerned about developing a health problem related to your coeliac disease?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
9.	have you been bothered by your bowel movements (for example, diarrhoea, loose stools, or constipation)?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
10.	have you had bloating in your abdomen?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
11.	have you had nausea or vomiting that you think was caused by your coeliac disease?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
12.	have you had pain that you think was caused by your coeliac disease?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
13.	have you had tiredness or a lack of energy that you think was caused by your coeliac disease?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
14.	have your daily activities been limited by your coeliac disease?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
15.	have you worried that you would become ill when you were not at home?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
16.	have you felt isolated from others because of your coeliac disease?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
17.	have you avoided social activities?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

THESE QUESTIONS RELATE TO YOUR COELIAC DISEASE					
During the <u>past 4 weeks</u>, how often…	Never	Rarely	Sometimes	Often	Always
18. have you avoided going out to eat (for example, at a friend's house, restaurant, or café)?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
19. have you worried that you would accidentally eat or drink products that contain gluten?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
20. have you been concerned about cross-contamination (gluten-free food coming into contact with food that contains gluten)?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
21. have you felt uncomfortable refusing unsuitable food or drink from other people?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
22. have you felt down or in low spirits?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
23. have you felt you were a nuisance to other people?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
24. have you felt guilty about other people buying gluten-free substitute foods for you?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
25. have you felt annoyed or frustrated about the cost of gluten-free substitute foods?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
26. have you had difficulty finding suitable food?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
27. have you craved food or drinks that contain gluten?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

THESE QUESTIONS RELATE TO YOUR COELIAC DISEASE

During the <u>past 4 weeks</u>, how often…	Never	Rarely	Sometimes	Often	Always
28. have you been disappointed with the taste or texture of gluten-free substitutes?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
29. have you felt burdened by the time taken to find or make gluten-free food?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
30. have you had difficulty finding something to eat when you were not at home?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
31. have you been frustrated by the choice of suitable food available (for example, in supermarkets, cafés or restaurants)?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
32. have you felt frustrated by having to plan ahead (for example, taking food with you, or choosing restaurants)?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

33. Compared with two weeks ago, how would you rate the impact of your coeliac disease on you and your health now?

1 ☐ Much better

2 ☐ A little better

3 ☐ About the same

4 ☐ A little worse

5 ☐ Much worse

34. Today's date: _ _ _ _ _ _ _ _ _ _ _ _ _ _

Thank you for completing this questionnaire

Please return your completed questionnaire in the pre-paid envelope provided

REC Ref No: MSD-IDREC-C1-2014-031 (Survey 2 TR)
©2015 HSRU, University of Oxford. Coeliac Disease Assessment Questionnaire (CDAQ)

Appendix KK. Survey 2 – letter accompanying follow-up questionnaire

Health Services Research Unit
Nuffield Department of Population Health
New Richards Building c/o Richard Doll Building, Old Road Campus, Headington, Oxford OX3 7LF

Researcher: Helen Crocker, Postgraduate Research Student
Tel: 01865 289431, Email: Helen.Crocker@dph.ox.ac.uk

«Title» «Forename» «Surname»
«Address_1»
«Address_2»
«Address_3»
«Town»
«County»
«Postcode»

«Q2_Date_to_Send»

Diagnosis and management of coeliac disease: Quality of life and patient's experiences of healthcare services

Dear «Title» «Surname»,

Thank you for completing a questionnaire asking you about your coeliac disease. You indicated that you would be willing to complete part of the questionnaire a second time. Completing this part of the questionnaire twice will allow us to see how well the questionnaire can measure quality of life in coeliac disease.

If you would like to participate, please complete the enclosed questionnaire and return it in the pre-paid envelope provided. Please complete all questions. Tick one box for each question unless instructed otherwise. We are interested in all experiences of coeliac disease whatever the extent of your symptoms. Taking part in this study is voluntary and confidential.

If you have any questions about the questionnaire, please contact Helen Crocker by telephone: 01865 289431 or by email: Helen.Crocker@dph.ox.ac.uk.

Yours sincerely,

Helen Crocker
Postgraduate Research Student

Version 1.0, 16/03/2015 (Survey 2 TR), REC Ref No: MSD-IDREC-C1-2014-031

Appendix LL. CDAQ scoring guide

The Coeliac Disease Assessment Questionnaire (CDAQ) consists of 32 questions addressing the following five dimensions: stigma; dietary burden; symptoms; social isolation; and worries and concerns. Each question is scored from 1 ('Never') to 5 ('Always'). Dimension scores are calculated by summing the scores of questions within each dimension and converting this score to a 0-100 metric, where 0 indicates poorest quality of life and 100 indicates highest quality of life as measured by the CDAQ.

The table below shows which questions belong to each dimension.

CDAQ dimensions

Dimension	No. of questions	Question numbers
Stigma	8	2, 3, 4, 5, 6, 21, 23, 24
Dietary burden	8	25, 26, 27, 28, 29, 30, 31, 32
Symptoms	5	9, 10, 11, 12, 13
Social isolation	5	14, 16, 17, 18, 22
Worries and concerns	6	1, 7, 8, 15, 19, 20

The calculation of scores

1. Score all questions

All questions are scored from 1 ('Never') to 5 ('Always') as set out in the table below, e.g. if the respondent has selected 'Sometimes', this is scored as a 3.

Scores for CDAQ questions

Response	Score
Never	1
Rarely	2
Sometimes	3
Often	4
Always	5

2. Invert question scores

Question scores are inverted. For example, questions coded as '1' are recoded to '5', questions coded as '2' are recoded to '4' and so on. The recoding system to invert scores is shown in the table below.

Original and inverted question scores

Response	Original score	Inverse score
Never	1	5
Rarely	2	4
Sometimes	3	3
Often	4	2
Always	5	1

3. Calculate dimension scores

Dimension scores are calculated using the formula below. Dimension scores range from 0 to 100, where 0 indicates poorest quality of life and 100 indicates highest quality of life.

Formula for scoring each dimension

DIMENSION SCORE = (((SUM OF SCORES FOR ALL QUESTIONS WITHIN THE DIMENSION) – LOWEST POSSIBLE DIMENSION SCORE) / DIMENSION SCORE RANGE) * 100

This is calculated as…

STIGMA = (((Q2 + Q3 + Q4 + Q5 + Q6 + Q21 + Q23 + Q24) – 8) / 32) * 100

DIETARY BURDEN = (((Q25 + Q26 + Q27 + Q28 + Q29 + Q30 + Q31 + Q32) - 8) / 32) *100

SYMPTOMS = (((Q9 + Q10 + Q11 + Q12 + Q13) – 5) / 20) * 100

SOCIAL ISOLATION = (((Q14 + Q16 + Q17 + Q18 + Q22) – 5) / 20) * 100

WORRIES AND CONCERNS = (((Q1 + Q7 + Q8 + Q15 + Q19 + Q20) – 6) / 24) * 100

4. **Calculating an overall index score**

An overall index score can be calculated. As per the dimension scores, the overall index score ranges from 0 to 100, where 0 indicates poorest quality of life and 100 indicates highest quality of life.

The formula for calculating the overall index score is:

OVERALL INDEX SCORE = (SUM OF DIMENSION SCORES) / 5

This is calculated as…

OVERALL INDEX SCORE = (STIGMA SCORE + DIETARY BURDEN SCORE + SYMPTOMS SCORE + SOCIAL ISOLATION SCORE + WORRIES AND CONCERNS SCORE) / 5

Missing data

If a respondent has not completed one or more questions, then the associated dimension score(s) and overall index score cannot be calculated.

Work regarding the best method of handling missing data is ongoing.

Appendix MM. Survey 2 - distribution of responses and missing data for CDAQ items

Item No[a]	Item (abbreviated)	Missing Data n (%)	Distribution of responses, n=268				
			Never n (%)	Rarely n (%)	Sometimes n (%)	Often n (%)	Always n (%)
1 (1)	Worried become ill	2 (0.7)	18 (6.7)	39 (14.6)	88 (32.8)	71 (26.5)	50 (18.7)
2 (3)	Appeared to make fuss	2 (0.7)	27 (10.1)	27 (10.1)	67 (25.0)	93 (34.7)	52 (19.4)
3 (4)	Others misunderstood CD	2 (0.7)	25 (9.3)	41 (15.3)	86 (32.1)	87 (32.5)	27 (10.1)
4 (5)	Difficult to mention misunderstanding	3 (1.1)	38 (14.2)	61 (22.8)	75 (28.0)	75 (28.0)	16 (6.0)
5 (6)	Received unwanted attention	3 (1.1)	90 (33.6)	63 (23.5)	70 (26.1)	32 (11.9)	10 (3.7)
6 (7)	Felt guilty about impact on friends and family	2 (0.7)	49 (18.3)	40 (14.9)	87 (32.5)	53 (19.8)	37 (13.8)
7 (8)	Worry about family member	2 (0.7)	77 (28.7)	35 (13.1)	88 (32.8)	43 (16.0)	23 (8.6)
8 (9)	Concern about developing problem	2 (0.7)	46 (17.2)	41 (15.3)	103 (38.4)	52 (19.4)	24 (9.0)
9 (11)	Bothered by bowel movements	2 (0.7)	31 (11.6)	47 (17.5)	92 (34.3)	66 (24.6)	30 (11.2)
10 (12)	Had abdominal bloating	3 (1.1)	57 (21.3)	43 (16.0)	70 (26.1)	74 (27.6)	21 (7.8)
11 (13)	Had nausea or vomiting	2 (0.7)	**139 (51.9)**	52 (19.4)	48 (17.9)	21 (7.8)	6 (2.2)
12 (14)	Had pain	3 (1.1)	71 (26.5)	58 (21.6)	86 (32.1)	36 (13.4)	14 (5.2)
13 (15)	Tiredness or lack of energy	2 (0.7)	59 (22.0)	47 (17.5)	68 (25.4)	61 (22.8)	31 (11.6)
14 (16)	Daily activities limited	3 (1.1)	98 (36.6)	80 (29.9)	52 (19.4)	26 (9.7)	9 (3.4)
15 (20)	Worried become ill not at home	3 (1.1)	61 (22.8)	62 (23.1)	81 (30.2)	47 (17.5)	14 (5.2)
16 (22)	Isolated from others	3 (1.1)	87 (32.5)	68 (25.4)	72 (26.9)	28 (10.4)	10 (3.7)
17 (27)	Avoided social activities	3 (1.1)	108 (40.3)	49 (18.3)	68 (25.4)	36 (13.4)	4 (1.5)
18 (29)	Avoided going out to eat	2 (0.7)	86 (32.1)	56 (20.9)	69 (25.7)	47 (17.5)	8 (3.0)
19 (30)	Worried accidentally consume	2 (0.7)	21 (7.8)	47 (17.5)	95 (35.4)	79 (29.5)	24 (9.0)
20 (31)	Concerned about cross-contamination	2 (0.7)	16 (6.0)	35 (13.1)	88 (32.8)	81 (30.2)	46 (17.2)
21 (32)	Felt uncomfortable refusing	2 (0.7)	59 (22.0)	59 (22.0)	74 (27.6)	51 (19.0)	23 (8.6)

Item No[a]	Item (abbreviated)	Missing Data n (%)	Distribution of responses, n=268				
			Never n (%)	Rarely n (%)	Sometimes n (%)	Often n (%)	Always n (%)
22 (36)	Felt down or in low spirits	3 (1.1)	59 (22.0)	65 (24.3)	82 (30.6)	47 (17.5)	12 (4.5)
23 (37)	Felt you were a nuisance	3 (1.1)	44 (16.4)	55 (20.5)	93 (34.7)	56 (20.9)	17 (6.3)
24 (39)	Guilty about others buying food	3 (1.1)	46 (17.2)	42 (15.7)	95 (35.4)	54 (20.1)	28 (10.4)
25 (40)	Felt annoyed about the cost of GF food	2 (0.7)	14 (5.2)	13 (4.9)	37 (13.8)	69 (25.7)	**133 (49.6)**
26 (42)	Difficulty finding food	2 (0.7)	22 (8.2)	44 (16.4)	124 (46.3)	60 (22.4)	16 (6.0)
27 (44)	Craved food or drinks	2 (0.7)	39 (14.6)	52 (19.4)	69 (25.7)	60 (22.4)	46 (17.2)
28 (45)	Disappointed with taste or texture	3 (1.1)	9 (3.4)	20 (7.5)	85 (31.7)	114 (42.5)	37 (13.8)
29 (47)	Burdened by time to find or make	2 (0.7)	34 (12.7)	57 (21.3)	95 (35.4)	64 (23.9)	16 (6.0)
30 (48)	Difficulty finding food when out of the house	3 (1.1)	10 (3.7)	25 (9.3)	89 (33.2)	96 (35.8)	45 (16.8)
31 (49)	Frustrated by choice of food	3 (1.1)	8 (3.0)	21 (7.8)	85 (31.7)	101 (37.7)	50 (18.7)
32 (50)	Frustrated by planning ahead	2 (0.7)	12 (4.5)	28 (10.4)	79 (29.5)	99 (36.9)	48 (17.9)

[a]Item number is in the format x(y), where x corresponds to the questionnaire numbers in the final version of the CDAQ (Survey 2, Appendix II), and y corresponds with the question numbers in the development version (Survey 1, Appendix CC).

Figures emboldened where a floor/ceiling effect is present (i.e. >50%) or missing data > 5%.

Appendix NN. CD-PEQ – recoding items as problem scores

Questions in grey boxes were not considered suitable for recoding as problem scores. Questions in white boxes have been recoded as dichotomous problem scores. Response options adjacent to a white box were coded as 0 ('no problem'), while response options adjacent to a black box were coded as 1 ('problem').

Introductory Questions

1. Have you been told by a doctor that you have coeliac disease? [Not coded]

1 ☐ Yes, I have been told that I have coeliac disease

2 ☐ No → **Go to Section 4, Question 1 (page 23)**

2. How long ago did you receive a diagnosis for your coeliac disease? [Not coded]

	Year(s)		Month(s)

3. How old were you when you were diagnosed with coeliac disease? [Not coded]

1 ☐ Less than 16 years old → **Go to Question 20 (page 16)**

2 ☐ 16 years old or over → **Go to Question 4**

'Before Your Diagnosis' Section

4. Which of the following symptoms did you have <u>before</u> you were diagnosed with coeliac disease? *(please tick <u>all</u> that apply)* [Not coded]

1 ☐ Diarrhoea / loose bowel movements

2 ☐ Constipation

3 ☐ Incomplete bowel movements

4 ☐ Abdominal pain

5 ☐ Abdominal bloating

6 ☐ Rumbling stomach

7 ☐ Nausea / vomiting

8 ☐ Skin rash

9 ☐ Mouth ulcers

10 ☐ Loss of appetite

11 ☐ Unexpected weight loss

12 ☐ Iron deficiency anaemia

13 ☐ Headache

14 ☐ 'Brain fog' / difficulty thinking

15 ☐ Chronic fatigue ('tired all the time')

16 ☐ Depression

17 ☐ Other, *please write in:* _

<u>OR</u>

18 ☐ I did not have any symptoms → **Go to Question 9 (page 13)**

19 ☐ I can't remember

5. **How long was it from when you first sought medical advice about your symptoms (e.g. first spoke to your GP) to receiving a definite diagnosis? [Not coded]**

_____ Year(s) _____ Month(s)

OR

1 ☐ I did not seek medical advice → **Go to Question 9 (page 13)**

2 ☐ I can't remember

6. **How do you feel about the amount of time it took to receive a diagnosis?**

1 ☐ It was *very* quick

2 ☐ It was *fairly* quick

3 ☐ It was *neither quick nor slow*

4 ☐ It was *fairly* slow

5 ☐ It was *very* slow

7. **Which health professional did you speak to the most often <u>before</u> you received your diagnosis? *(please tick <u>one</u> only)* [Not coded]**

1 ☐ Hospital doctor / consultant

2 ☐ GP

3 ☐ Dietitian

4 ☐ Hospital nurse

5 ☐ Practice nurse

6 ☐ Pharmacist

7 ☐ Other, *please write in:*

_ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _

8. **Thinking about the health professional you selected in Question 7, did you feel that this person…**

*Please tick **one** box on each row*

		Yes, definitely	Yes, to some extent	No	I can't remember
a)	listened carefully to you?	1 ☐	2 ☐	3 ☐	4 ☐
b)	gave you confidence in them?	1 ☐	2 ☐	3 ☐	4 ☐
c)	took your symptoms seriously?	1 ☐	2 ☐	3 ☐	4 ☐

'Your Diagnosis' Section

9. Which tests did you have to diagnose your coeliac disease?

*Please tick **one** box on each row*

	Yes	No, but I **was** offered one	No, I **was not** offered one	I don't know
a) Blood test (antibody)	1 ☐	2 ☐	3 ☒	4 ☐
b) Endoscopy (with biopsy)	1 ☐	2 ☐	3 ☒	4 ☐

c) Other, *please state* _

10. How do you feel about the amount of time you had to wait for an endoscopy?

1 ☐ It was *very* quick
2 ☐ It was *fairly* quick
3 ☐ It was *neither quick nor slow*
4 ☒ It was *fairly* slow
5 ☒ It was *very* slow
6 ☐ I can't remember the amount of time I had to wait
7 ☐ I have not had an endoscopy

11. Did you receive enough information throughout the diagnostic process?

1 ☐ Yes, I received enough information
2 ☒ No, I did not receive *enough* information
3 ☒ No, I did not receive *any* information
4 ☐ I did not want any information
5 ☐ I can't remember

12. Who first informed you that you have been diagnosed with coeliac disease? [Not coded]

1 ☐ Hospital doctor / consultant
2 ☐ GP
3 ☐ Dietitian
4 ☐ Hospital nurse
5 ☐ Practice nurse
6 ☐ Receptionist
7 ☐ I can't remember
8 ☐ Other, *please write in:* _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _

13. Do you feel you were informed of your diagnosis in both a professional and appropriate manner?

1 ☐ Yes, definitely
2 ■ Yes, to some extent
3 ■ No

14. At the time of your diagnosis, did you receive enough information about coeliac disease and the gluten-free diet from <u>health professionals</u>?

1 ☐ Yes, I received enough information
2 ■ No, I did not receive *enough* information
3 ■ No, I did not receive *any* information
4 ☐ I did not want any information
5 ☐ I can't remember

'Diet and Nutritional Advice' Section

15. After receiving a diagnosis, did you speak to a dietitian about your coeliac disease? *A dietitian is an expert who provides advice about diet and nutrition.*

1 ☐ Yes
2 ■ No, but I would have liked to → **Go to Question 20 (page 16)**
3 ☐ No, I did not need to → **Go to Question 20 (page 16)**
4 ☐ I can't remember → **Go to Question 20 (page 16)**

16. After receiving a diagnosis, how quickly did you have an appointment with a dietitian to discuss your coeliac disease?

1 ☐ It was *very* quick
2 ☐ It was *fairly* quick
3 ☐ It was *neither quick nor slow*
4 ■ It was *fairly* slow
5 ■ It was *very* slow
6 ☐ I can't remember

17. Thinking about your first appointment with a dietitian, which of the following were discussed? *(please tick <u>all</u> that apply)* [Not coded]

The dietitian…

1 ☐ explained the gluten-free diet
2 ☐ gave you written information about the gluten-free diet
3 ☐ explained the importance of a strict gluten-free diet
4 ☐ told you about where you could get gluten-free products
5 ☐ explained food labelling
6 ☐ told you about the prescription process and foods available on prescription
7 ☐ explained cross-contamination and how to avoid it
8 ☐ gave you tips about eating out
9 ☐ weighed you and calculated your body mass index (BMI)
10 ☐ discussed your calcium intake
11 ☐ discussed whether you can eat oats
12 ☐ told you about Coeliac UK

OR

13 ☐ None of the above
14 ☐ I can't remember

18. How helpful was your first appointment with a dietitian?

1 ☐ Very helpful
2 ☐ Fairly helpful
3 ☐ Not very helpful
4 ☐ Not at all helpful
5 ☐ I am not sure / I can't remember

19. Were you offered a second appointment to speak to a dietitian <u>within 6 months</u> of your first appointment?

1 ☐ Yes
2 ☐ No, but I would have liked one
3 ☐ No, but I did not want one
4 ☐ I can't remember

'After Your Diagnosis' Section

20. Some people with coeliac disease have had additional tests or vaccinations. Have you had …

*Please tick **one** box on each row*

		Yes	No, but I **was** offered one	No, I **was not** offered one	I don't know
a)	a repeat endoscopy (with biopsy)?	1 ☐	2 ☐	3 ☐	4 ☐
b)	a bone density scan (DEXA)?	1 ☐	2 ☐	3 ☐	4 ☐
c)	a pneumococcal vaccination (sometimes called the 'pneumo jab')?	1 ☐	2 ☐	3 ■	4 ☐

Note: questions 20a (…a repeat endoscopy?) and 20b (…a bone density scan?) were excluded as these tests are not required for all according to guidelines.

Follow-up Appointments

If Q21 = 'No' and Q29 = 'Yes' then mark as a problem

21. Do you have regular follow-up appointments for your coeliac disease?

1 ☐ Yes
2 ■ No → **Go to Question 29 (page 18)**
3 ☐ I am not sure / I can't remember → **Go to Question 29 (page 18)**

Combined with

29. Would you like to have follow-up appointments in the future?

1 ■ Yes
2 ☐ No → **Go to Question 32 (page 19)**
3 ☐ I am not sure → **Go to Question 32 (page 19)**

22. When was your <u>most recent</u> follow-up appointment for your coeliac disease?

1 ☐ Less than 1 year ago
2 ☐ 1 - 2 years ago
3 ■ More than 2 years ago

23. Who was your <u>most recent</u> follow-up appointment with? [Not coded]

1 ☐ Hospital doctor / consultant
2 ☐ GP
3 ☐ Dietitian
4 ☐ Hospital nurse
5 ☐ Practice nurse
6 ☐ I can't remember
7 ☐ Other, *please write in:*
_ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _

24. Who initiated your <u>most recent</u> follow-up appointment? [Not coded]

1 ☐ Staff at the hospital
2 ☐ Staff at the GP practice
3 ☐ I contacted a health professional
4 ☐ Other, *please write in:* _
5 ☐ I can't remember

25. Which of the following happened at your <u>most recent</u> follow-up appointment? *(please tick <u>all</u> that apply)* [Not coded]

1 ☐ I was weighed
2 ☐ My body mass index (BMI) was calculated
3 ☐ Blood was taken for testing (this may have happened before or after your follow-up appointment)
4 ☐ My diet was assessed
5 ☐ Any difficulties I have adhering to the diet were discussed
6 ☐ My symptoms were discussed
7 ☐ My emotional well-being was assessed
8 ☐ My calcium intake was reviewed
9 ☐ My bone density was discussed
10 ☐ My prescription was reviewed / Access to prescriptions was discussed
11 ☐ My understanding of food labelling was discussed

<u>OR</u>

12 ☐ None of the above
13 ☐ I can't remember

26. At your <u>most recent</u> follow-up appointment, were you given the opportunity to ask your questions?

1 ☐ Yes
2 ■ No → **Go to Question 28**
3 ☐ I did not have any questions → **Go to Question 28**
4 ☐ I can't remember → **Go to Question 28**

27. At your <u>most recent</u> follow-up appointment, when you had questions to ask, were you given the information you needed?

1 ☐ Yes, always
2 ■ Sometimes
3 ■ No, never
4 ☐ I can't remember
5 ☐ I did not have any questions

28. Overall, how helpful was your <u>most recent</u> follow-up appointment?

1 ☐ Very helpful
2 ☐ Fairly helpful
3 ☐ Not very helpful
4 ☐ Not at all helpful
5 ☐ I am not sure / I can't remember

30. Who would you like your follow-up appointments with? *(please tick <u>one</u> box only)* [Not coded]

1 ☐ Hospital doctor / consultant
2 ☐ GP
3 ☐ Dietitian
4 ☐ Hospital nurse
5 ☐ Practice nurse
6 ☐ I am not sure
7 ☐ Other, *please write in:* _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _

31. How often would you like to have follow-up appointments? [Not coded]

1 ☐ Once a month
2 ☐ Once every six months
3 ☐ Once a year
4 ☐ Once every 2 years
5 ☐ Other, *please write in:* _
6 ☐ I am not sure

'Prescriptions' Section

32. Do you think you have received enough information about getting gluten-free food on prescription?

1 ☐ Yes, I have received enough information
2 ☐ No, I have not received *enough* information
3 ☐ No, I have not received *any* information
4 ☐ I do not need this information

33. How easy have you found it to obtain the gluten-free food products that are available <u>on prescription</u>?

1 ☐ Very easy
2 ☐ Fairly easy
3 ☐ Neither easy nor difficult
4 ☐ Fairly difficult
5 ☐ Very difficult
6 ☐ I have not tried to get gluten-free food on prescription

34. **In the last 12 months, which gluten-free foods have you had on prescription? *(please tick all that apply)* [Not coded]**

1 ☐ Bread / Rolls
2 ☐ Flour / Bread mixes
3 ☐ Crackers / Crispbreads
4 ☐ Breakfast cereals
5 ☐ Pasta
6 ☐ Pizza bases
7 ☐ Biscuits
8 ☐ Oats
9 ☐ Other, *please write in:* _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _

OR

10 ☐ I have not had any gluten-free food on prescription in the last 12 months, because *(please say why)* _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _

38. **In the <u>last 12 months</u>, have you been able to get information and advice about your coeliac disease from a health professional when you wanted to do so?**

1 ☐ Yes, always
2 ☐ Sometimes
3 ☐ No
4 ☐ I have not wanted to speak to a health professional

39. **In the <u>last 12 months</u>, have you received enough information about the results of medical tests conducted in relation to your coeliac disease (e.g. blood tests, DEXA scan, endoscopy (with biopsy))?**

1 ☐ Yes, I have received enough information
2 ☐ No, I have not received *enough* information
3 ☐ No, I have not received *any* information
4 ☐ I did not want any information
5 ☐ I can't remember
6 ☐ I have not had any tests

'Overall Experience' Section

40. **Do you think the GP that you speak to the most often about your coeliac disease has a good understanding of the condition?**

1 ☐ Yes, definitely
2 ☐ Yes, to some extent
3 ☐ No
4 ☐ I do not speak to the GP about my coeliac disease
5 ☐ I am not sure

41. **From your experience, do you think the following health professionals are knowledgeable about coeliac disease?**

*Please tick **one** box on each row*

		Yes	To some extent	No	I don't know / N/A
a)	Dietitians	1 ☐	2 ☐	3 ☐	4 ☐
b)	Specialist hospital doctors / Gastroenterologists	1 ☐	2 ☐	3 ☐	4 ☐
c)	Other hospital doctors	1 ☐	2 ☐	3 ☐	4 ☐
d)	GPs	1 ☐	2 ☐	3 ☐	4 ☐
e)	Practice nurses / healthcare assistants	1 ☐	2 ☐	3 ☐	4 ☐
f)	Pharmacists	1 ☐	2 ☐	3 ☐	4 ☐

42. Thinking about your coeliac disease and the gluten-free diet, how <u>consistent</u> has information and advice from health professionals been?

1 ☐ Very consistent
2 ☐ Fairly consistent
3 ■ Not very consistent
4 ■ Not at all consistent
5 ☐ I have not received any information or advice

43. Overall, how would you rate the health care that you have received to help you manage your coeliac disease <u>since diagnosis</u>?

1 ☐ Very good
2 ☐ Good
3 ☐ Fair
4 ■ Poor
5 ■ Very poor

<u>OR</u>

6 ☐ I have not received any health care since my diagnosis

Appendix OO. Survey 2 – CD-PEQ results: frequency data

NB. 'n' in brackets following each table caption indicates the number of people eligible to complete the question.

Q2 – How long ago did you receive a diagnosis for your coeliac disease? (n=268)

Years	n	%
<1	28	10.4
1-4	113	42.2
5-9	40	14.9
10-14	40	14.9
15-19	15	5.6
20-24	4	1.5
≥25	16	6.0

Missing = 12

The mean length of time since diagnosis (in years) was 7.80 ± 9.59 (range 3 months-50 years) (n=256).

Q3 – Age at diagnosis (with calculated values) (n=268)

Years	n	%
<16	11	4.1
≥16	250	93.3

Missing = 7

Where data for the above item was missing, it was calculated where possible as 'current age' – 'time since diagnosis'. Only those aged 16 or over at the time of diagnosis were included in the analysis of questions 4-19 (inclusive).

Q4 – Which of the following symptoms did you have before you were diagnosed with coeliac disease? (n=250)

	Yes	
	n	%
Abdominal bloating	171	68.4
Diarrhoea / loose bowel movements	167	66.8
Abdominal pain	153	61.2
Chronic fatigue ('tired all the time')	138	55.2
Iron deficiency anaemia	133	53.2
Unexpected weight loss	107	42.8
Rumbling stomach	94	37.6
Headache	83	33.2
'Brain fog' / difficulty thinking	82	32.8
Mouth ulcers	80	32.0
Nausea / vomiting	78	31.2
Incomplete bowel movements	75	30.0
Constipation	75	30.0
Depression	60	24.0
Other	54	21.6
Loss of appetite	49	19.6
Skin rash	48	19.2
No symptoms	6	2.4
Can't remember	1	0.4

Missing = 0

Q5 – How long was it from when you first sought medical advice about your symptoms (e.g. first spoke to your GP) to receiving a definite diagnosis? (n=244)

	n	%
<1	94	38.5
1-4	50	20.5
5-9	19	7.8
10-14	12	4.9
15-19	2	0.8
20-24	4	1.6
≥25	7	2.9
I did not seek medical advice	15	6.1
I can't remember	32	13.1

Missing = 9

The mean length of time to diagnose coeliac disease (in years) was 4.00 ± 7.97 (range 1 month – 50 years) (n=188).

Q6 – How do you feel about the amount of time it took to receive a diagnosis? (n=229)

	n	%
It was very quick	44	19.2
It was fairly quick	57	24.9
It was neither quick nor slow	15	6.6
It was fairly slow	39	17.0
It was very slow	71	31.0

Missing = 3

Q7 – Which health professional did you speak to the most often before you received your diagnosis? (n=229)

	n	%
GP	161	70.3
Hospital doctor / consultant	50	21.8
Other	4	1.7

Missing/multiple = 14

Q8 – Thinking about the health professional you selected in Question 7, did you feel that this person…? (n=229)

	… listened carefully to you?		… gave you confidence in them?		… took your symptoms seriously?	
	n	%	n	%	n	%
Yes, definitely	121	52.8	112	48.9	127	55.5
Yes, to some extent	61	26.6	55	24.0	47	20.5
No	37	16.2	50	21.8	47	20.5
I can't remember	4	1.7	4	1.7	3	1.3
Missing / multiple	6	2.6	8	3.5	5	2.1

Q9 – Which tests did you have to diagnose your coeliac disease? (n=250)

	Blood test (antibody)		Endoscopy (with biopsy)	
	n	%	n	%
Yes	201	80.4	235	94.0
No, but I was offered one	0	0	3	1.2
No, I was not offered one	8	3.2	4	1.6
I don't know	3	1.2	0	0
Missing	38	15.2	8	3.2

Q10 – How do you feel about the amount of time you had to wait for an endoscopy? (n=250)

	n	%
It was very quick	67	26.8
It was fairly quick	107	42.8
It was neither quick nor slow	22	8.8
It was fairly slow	19	7.6
It was very slow	13	5.2
I can't remember	9	3.6
I have not had an endoscopy	6	2.4

Missing / multiple, n=7

Q11 – Did you receive enough information throughout the diagnostic process? (n=250)

	n	%
Yes, I received enough information	187	74.8
No, I did not receive enough information	36	14.4
No, I did not receive any information	14	5.6
I did not want any information	2	0.8
I can't remember	8	3.2

Missing, n=3

Q12 – Who first informed you that you have been diagnosed with coeliac disease? (n=250)

	n	%
Hospital doctor / consultant	130	52.0
GP	92	36.8
Hospital nurse	4	1.6
I can't remember	4	1.6
Dietitian	2	0.8
Receptionist	2	0.8
Practice nurse	1	0.4
Other	7	2.8

Missing / multiple, n=8

Q13 – Do you feel you were informed of your diagnosis in both a professional and appropriate manner? (n=250)

	n	%
Yes, definitely	181	72.4
Yes, to some extent	48	19.2
No	18	7.2

Missing, n=3

Q14 – At the time of your diagnosis, did you receive enough information about coeliac disease and the gluten-free diet from health professionals? (n=250)

	n	%
Yes, I received enough information	173	69.2
No, I did not receive enough information	52	20.8
No, I did not receive any information	17	6.8
I did not want any information	1	0.4
I can't remember	4	1.6

Missing, n=3

Q15 – After receiving a diagnosis, did you speak to a dietitian about your coeliac disease? (n=250)

	n	%
Yes	231	92.4
No, but I would have liked to	9	3.6
No, I did not need to	6	2.4
I can't remember	1	0.4

Missing, n=3

Q16 – After receiving a diagnosis, how quickly did you have an appointment with a dietitian to discuss your coeliac disease? (n=231)

	n	%
It was very quick	57	24.7
It was fairly quick	91	39.4
It was neither quick nor slow	18	7.8
It was fairly slow	34	14.7
It was very slow	16	6.9
I can't remember	14	6.1

Missing, n=1

Q17 – Thinking about your first appointment with a dietitian, which of the following were discussed? (please tick all that apply) (n=231)

The dietitian…	Yes n	%
explained the gluten-free diet	208	90.0
gave you written information about the gluten-free diet	192	83.1
explained the importance of a strict gluten-free diet	184	79.7
told you about Coeliac UK	182	78.8
told you about the prescription process and foods available on prescription	167	72.3
told you about where you could get gluten-free products	165	71.4
explained cross-contamination and how to avoid it	152	65.8
discussed your calcium intake	122	52.8
explained food labelling	121	52.4
weighed you and calculated your body mass index (BMI)	119	51.5
discussed whether you can eat oats	107	46.3
gave you tips about eating out	86	37.2
None of the above	5	2.2
I can't remember	5	2.2

Missing, n=1

Q18 – How helpful was your first appointment with a dietitian? (n=231)

	n	%
Very helpful	116	50.2
Fairly helpful	75	32.5
Not very helpful	23	10.0
Not at all helpful	13	5.6
I am not sure / I can't remember	3	1.3

Missing, n=1

Q19 – Were you offered a second appointment to speak to a dietitian within 6 months of your first appointment? (n=231)

	n	%
Yes	138	59.7
No, but I would have liked one	40	17.3
No, but I did not want one	28	12.1
I can't remember	22	9.5

Missing, n=3

Q20 – Some people with coeliac disease have had additional tests or vaccinations. Have you had…? (n=268)

	… a repeat endoscopy (with biopsy)?		… a bone density scan (DEXA)?		… a pneumococcal vaccination?	
	n	**%**	**n**	**%**	**n**	**%**
Yes	71	26.5	200	74.6	64	23.9
No, but I was offered one	12	4.5	5	1.9	9	3.4
No, I was not offered one	159	59.3	51	19.0	141	52.6
I don't know	5	1.9	3	1.1	27	10.1
Missing	21	7.8	9	3.4	27	10.1

Q21 – Do you have regular follow-up appointments for your coeliac disease? (n=268)

	n	**%**
Yes	159	59.3
No	93	34.7
I am not sure / I can't remember	10	3.7

Missing, n=6

Q22 – When was your <u>most recent</u> follow-up appointment for your coeliac disease? (n=159)

	n	**%**
Less than 1 year ago	119	74.8
1 – 2 years ago	31	19.5
More than 2 years ago	8	5.0

Missing, n=1

Q23 – Who was your <u>most recent</u> follow-up appointment with? (n=159)

	n	**%**
Hospital doctor / consultant	74	46.5
GP	33	20.8
Dietitian	30	18.9
Hospital nurse	5	3.1
Practice nurse	6	3.8
Other	1	0.6

Missing, n=0; Multiple responses, n=10

Q24 – Who initiated your <u>most recent</u> follow-up appointment? (n=159)

	n	**%**
Staff at the hospital	100	62.9
Staff at the GP practice	21	13.2
I contacted a health professional	27	17.0
Other	5	3.1
I can't remember	6	3.8

Missing, n=0

Q25 – Which of the following happened at your most recent follow-up appointment? (please tick all that apply) (n=159)

	Yes	
	n	%
Blood was taken for testing	124	78.0
I was weighed	111	69.8
My symptoms were discussed	88	55.3
Any difficulties I have adhering to the diet were discussed	74	46.5
My diet was assessed	73	45.9
My bone density was discussed	62	39.0
My calcium intake was reviewed	59	37.1
My body mass index (BMI) was calculated	45	28.3
My prescription was reviewed / Access to prescriptions was discussed	34	21.4
My emotional well-being was assessed	28	17.6
My understanding of food labelling was discussed	18	11.3
None of the above	2	1.3
I can't remember	2	1.3

Missing, n=0

Q26 – At your most recent follow-up appointment, were you given the opportunity to ask your questions? (n=159)

	n	%
Yes	137	86.2
No	5	3.1
I did not have any questions	12	7.5
I can't remember	5	3.1

Missing, n=0

Q27 – At your most recent follow-up appointment, when you had questions to ask, were you given the information you needed? (n=137)

	n	%
Yes, always	100	73.0
Sometimes	27	19.7
No, never	4	2.9
I can't remember	1	0.7
I did not have any questions	4	2.9

Missing, n=1

Q28 – Overall, how helpful was your most recent follow-up appointment? (n=159)

	n	%
Very helpful	85	53.5
Fairly helpful	49	30.8
Not very helpful	18	11.3
Not at all helpful	5	3.1
I am not sure / I can't remember	2	1.3

Missing, n=0

Q29 – Would you like to have follow-up appointments in the future? (n=268)

	n	%
Yes	225	84.0
No	25	9.3
I am not sure	14	5.2

Missing, n=4

Q30 – Who would you like your follow-up appointments with? (n=225)

	n	%
Hospital doctor / consultant	109	48.4
GP	42	18.7
Dietitian	24	10.7
Hospital nurse	8	3.6
Practice nurse	7	3.1
I am not sure	11	4.9
Other	3	1.3

Missing, n=1; Multiple, n=20

Q31 – How often would you like to have follow-up appointments? (n=225)

	n	%
Once every six months	50	22.2
Once a year	136	60.4
Once every 2 years	29	12.9
Other	8	3.6
I am not sure	1	0.4

Missing, n=0; Multiple, n=1

Q32 – Do you think you have received enough information about getting gluten-free food on prescription? (n=268)

	n	%
Yes, I have received enough information	174	64.9
No, I have not received enough information	63	23.5
No, I have not received any information	18	6.7
I do not need this information	9	3.4

Missing, n=4

Q33 – How easy have you found it to obtain gluten-free food products that are available on prescription? (n=268)

	n	%
Very easy	71	26.5
Fairly easy	70	26.1
Neither easy nor difficult	20	7.5
Fairly difficult	36	13.4
Very difficult	18	6.7
I have not tried to get gluten-free food on prescription	49	18.3

Missing, n=4

Q34 – In the last 12 months, which gluten-free foods have you had on prescription? (please tick all that apply) (n=268)

	Yes	
	n	%
Bread / Rolls	165	61.6
Flour / Bread mixes	111	41.4
Crackers / Crispbreads	74	27.6
Breakfast cereals	62	23.1
Pasta	115	42.9
Pizza bases	77	28.7
Biscuits	39	14.6
Oats	34	12.7
Other	2	0.7
I have not had any GFF prescriptions in the last 12 months	75	28.0

Missing, n=5

Other = pizza, xanthan gum

No of people having food on prescription, n=188 (70.1%)

Q35 – How do you pay for your prescriptions for your coeliac disease? (n=188)

	n	%
I pay for each prescription	5	2.7
I have a Prescription Pre-payment Certificate	60	31.9
I do not pay for my prescriptions (entitled to free prescriptions)	123	65.4

Missing, n=0

Q36 – How do you find the cost of your prescriptions for your coeliac disease? (n=65)

	n	%
Reasonable	32	49.2
Fairly expensive	16	24.6
Very expensive, but I can afford it	10	15.4
Very expensive, and I cannot afford it	5	7.7

Missing, n=2

Q37 – In the last 12 months, which health professionals have you spoken to specifically about your coeliac disease? (please tick all that apply) (n=268)

	n	%
Hospital doctor / consultant	103	38.4
GP	110	41.0
Dietitian	78	29.1
Hospital nurse	12	4.5
Practice nurse	15	5.6
Pharmacist	26	9.7
Other	5	1.9
I have not spoken to a HCP in the last 12 months about CD	83	31.0

Missing, n=4

Spoken to HCP in the last 12 months about CD, n=181 (67.5%)

Q38 – In the last 12 months, have you been able to get information and advice about your coeliac disease from a health professional when you wanted to do so? (n=268)

	n	%
Yes, always	93	34.7
Sometimes	52	19.4
No	30	11.2
I have not wanted to speak to a HCP	83	31.0

Missing / multiple, n=10

Q39 – In the last 12 months, have you received enough information about the results of medical tests conducted in relation to your coeliac disease? (n=268)

	n	%
Yes, I have received enough information	108	40.3
No, I have not received enough information	53	19.8
No, I have not received any information	25	9.3
I did not want any information	1	0.4
I can't remember	2	0.7
I have not had any tests	73	27.2

Missing / multiple, n=6

Q40– Do you think the GP that you speak to the most often about your coeliac disease has a good understanding of the condition? (n=268)

	n	%
Yes, definitely	88	32.8
Yes, to some extent	82	30.6
No	32	11.9
I do not speak to the GP about my coeliac disease	53	19.8
I am not sure	9	3.4

Missing / multiple, n=4

Q41 – From your experience, do you think the following health professionals are knowledgeable about coeliac disease? (n=268)

	Yes		To some extent		No		I don't know / NA		Missing
	n	%	n	%	n	%	n	%	
Specialist hospital doctors	210	78.4	27	10.1	2	0.7	23	8.6	6
Dietitians	196	73.1	42	15.7	9	3.4	16	6.0	5
GPs	67	25.0	141	52.6	37	13.8	17	6.3	6
Pharmacists	67	25.0	100	37.3	26	9.7	66	24.6	9
Practice nurses / HCAs	30	11.2	86	32.1	50	18.7	85	31.7	17
Other hospital doctors	19	7.1	77	28.7	35	13.1	112	41.8	25

Q42 – Thinking about your coeliac disease and the gluten-free diet, how consistent has information and advice from health professionals been? (n=268)

	n	%
Very consistent	79	29.5
Fairly consistent	117	43.7
Not very consistent	30	11.2
Not at all consistent	14	5.2
I have not received any information and advice	24	9.0

Missing / multiple, n=4

Q43 – Overall, how would you rate the healthcare that you have received to help you manage your coeliac disease since diagnosis? (n=268)

	n	%
Very good	80	29.9
Good	78	29.1
Fair	64	23.9
Poor	17	6.3
Very poor	4	1.5
I have not received any healthcare since diagnosis	20	7.5

Missing / multiple, n=5

Appendix PP. Survey 2 - SF-36v2 scores (0-100)

Quality of life in coeliac disease (n=267)

		Scores (0-100)		
	n	***Mean***	***SD***	***Range***
SF-36v2 scores				
Physical Functioning (PF)	267	82.48	24.29	0 - 100
Role-Physical (RP)	266	77.00	27.39	0 - 100
Bodily Pain (BP)	265	66.82	25.58	0 - 100
General Health (GH)	267	57.76	24.47	0 - 100
Vitality (VT)	266	50.78	22.83	0 - 100
Social Functioning (SF)	266	77.21	25.50	0 - 100
Role-Emotional (RE)	265	80.63	25.30	0 - 100
Mental Health (MH)	266	69.16	19.51	5 - 100

Appendix QQ. Multiple regression analysis – initial models

The first model for two regression analyses (where the dependent variable is the CDAQ overall index score) are shown below, and include all variables prior to any being deleted.

Association between HRQOL and 'overall experiences problem score'

Dependent variable: CDAQ overall index score

Variable	B	SE_B	95% Confidence Interval (CI)		p
Intercept	58.641	3.823	51.107	66.176	<0.001
Age	0.128	0.070	-0.010	0.267	0.069
Gender (male)	7.243	2.051	3.202	11.285	0.001
No of comorbidities	-3.054	0.711	-4.455	-1.652	<0.001
Ethnicity (BME)	-5.924	3.059	-11.953	0.105	0.054
Years since diagnosis	0.223	0.110	0.006	0.439	0.044
Marital status – married	-0.038	2.508	-4.980	4.905	0.988
Marital status – separated or divorced	-6.647	4.363	-15.246	1.951	0.129
Marital status – widowed	1.434	5.463	-9.330	12.199	0.793
Gluten consumption - rarely	1.141	2.648	-4.077	6.359	0.667
Gluten consumption – sometimes	-3.191	3.274	-9.643	3.261	0.331
Gluten consumption – often or always	-1.330	6.826	-14.783	12.122	0.846
Overall experiences problem score	-1.508	0.231	-1.963	-1.052	<0.001

R2=0.405, Adjusted R2=0.373

Association between HRQOL and individual patient experience items

Dependent variable: CDAQ overall index score

Variable	B	SE_B	95% CI		p
Intercept	58.516	4.649	49.350	67.681	**<0.001**
Age	0.107	0.078	-0.048	0.261	0.175
Gender (male)	7.882	2.205	3.535	12.229	**<0.001**
Ethnicity (BME)	-6.425	3.277	-12.887	0.036	0.051
No of comorbidities	-2.803	0.762	-4.305	-1.301	**<0.001**
Years since diagnosis	0.256	0.117	-0.025	0.488	**0.030**
Marital status – married	-0.125	2.639	-5.329	5.079	0.962
Marital status – separate or divorced	-6.723	4.568	-15.729	2.282	0.143
Marital status - widowed	4.743	5.990	-7.069	16.554	0.429
Gluten consumption – rarely	0.482	2.826	-5.090	6.053	0.865
Gluten consumption – sometimes	-3.004	3.609	-10.119	4.112	0.406
Gluten consumption – often or always	0.982	7.217	-13.248	15.213	0.892
6. Felt their diagnosis of CD was slow	-0.698	2.750	-6.119	4.723	0.800
8a. HCP didn't always listen carefully	-3.092	4.083	-11.141	4.957	0.450
8b. HCP didn't always inspire confidence	-6.549	4.056	-14.546	1.448	0.108
8c. HCP didn't always take symptoms seriously	4.072	4.529	-4.857	13.002	0.370
9b. Not offered endoscopy to diagnose	1.854	11.508	-20.835	24.543	0.872
10. Slow wait to receive an endoscopy	-0.264	3.243	-6.658	6.131	0.935
11. Not enough information throughout diagnosis	-1.384	3.259	-7.809	5.041	0.671
13. Informed of diagnosis unprofessionally	-3.375	2.508	-8.319	1.570	0.180
14. Not enough information at time of diagnosis	-0.745	2.990	-6.640	5.149	0.803
20c. Pneumococcal vaccination not offered	0.389	2.166	-3.883	4.660	0.858
32. Not given enough information about prescriptions	-3.635	2.425	-8.415	1.146	0.135
33. Difficulties obtaining prescriptions	-3.830	2.707	-9.168	1.508	0.159
38. Information and advice not always available from HCPs	-4.035	2.467	-8.900	0.829	0.103
39. Not enough information about medical test results	-2.682	2.560	-7.730	2.366	0.296
40. GP didn't always have good understanding of CD	4.633	2.501	-0.297	9.564	0.065
41a. Felt dietitians lacked knowledge about CD	-2.041	2.875	-7.710	3.629	0.479
41b. Specialist doctors lacked knowledge about CD	3.098	3.349	-3.504	9.701	0.356
41d. Felt GPs weren't always knowledgeable about CD	-2.778	2.773	-8.245	2.689	0.318
42. HCPs provided inconsistent information and advice	-5.208	3.010	-11.142	0.726	0.085
Dietary advice summary score	-2.576	2.586	-7.673	2.522	0.320
Follow-up summary score	0.393	2.201	-3.946	4.732	0.858

R^2=0.448, Adjusted R^2=0.362