Psychiatric Illnesses in General Hospital Inpatients

Maike van Niekerk

St. John's College

University of Oxford

Supervised by

Professor Michael Sharpe and Dr Jane Walker

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This thesis is submitted to the Department of Psychiatry, University of Oxford, in partial fulfilment of the requirements for the degree of

Doctor of Philosophy in Psychiatry

Declaration Statement

I declare that this thesis is my own work, unless explicitly stated otherwise. I have not submitted this work, in whole or in part, for any other degree or professional qualification.

Maike van Niekerk

St. John’s College

University of Oxford

Declaration

Supervisors

I was supervised by Professor Michael Sharpe (Professor of Psychological Medicine, University of Oxford) and Dr Jane Walker (Senior Clinical Researcher and Consultant Psychiatrist in Psychological Medicine, University of Oxford).

I also received statistical guidance from Professor Chris Frost (Professor of Medical Statistics, London School of Hygiene and Tropical Medicine).

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I was supported by the Rhodes Trust.

In this thesis, I used data collected from patients who had agreed to participate in The HOME Study, which was funded by the National Institute for Health Research (NIHR) Health Services and Delivery Research Programme.

Thesis

There are three major studies in my thesis: (1) a meta-review, (2) a systematic review and (3) a cross-sectional study. Below, I outline my contribution to each of these studies as well as the assistance I received from others.

Meta-review and systematic review

Personal contribution to the work

I was responsible for conducting the meta-review and the systematic review, which included: (1) designing the reviews; (2) developing the search strategy for each review; (3) selecting articles to include in each review (with a second independent researcher); (4) extracting data from relevant articles included in each review (with a second independent researcher); (5) interpreting the results of each review; and (6) writing the associated thesis chapters.

Assistance received

I received the following assistance:

Ms Elinor Harriss assisted with the development of search strategies for the meta-review and the systematic review. Dr Jane Walker, Dr Mark Toynbee, Mr Ben Steward, Mr Elliot Hampsey, Dr Rhian Bold and Ms Harriet Hobbs assisted with selection of articles and data extraction. Dr Nicholas Magill conducted the statistical analyses.

Cross-sectional study

I used data collected from patients who had agreed to participate in a large randomised controlled trial, The HOME Study, for the cross-sectional study.

Personal contribution to the work

I was responsible for: (1) designing the cross-sectional study; (2) assisting in recruitment and data collection for The HOME Study, which included identifying potential participants, obtaining informed consent or consultee agreement for study participation, collecting data from participants and randomising participants; (3) co-training and co-assessing HOME Study team members involved in recruitment and data collection; (4) assisting in data cleaning; (5) planning the cross-sectional study's analyses; (6) interpreting the results of the analyses; and (7) writing the associated thesis chapters.

Assistance received

The following HOME Study team members were involved in collecting or cleaning the data used in the cross-sectional study: Ms Anna Scholcz, Mr Ben Steward, Ms Chloë Stokes, Ms Eleanor Macey, Mr Elliot Hampsey, Mr George Kitchen, Ms Georgiana Jennings, Ms Hannah Chaitow, Ms Harriet Hobbs, Ms Iona Cairns, Ms Isabelle Rocroi, Ms Jennifer Mbanu, Ms Julie Philps, Ms Katie Keating-Fedders, Ms Laura Hollands, Ms Louise Pollard, Ms Lucy McIvor, Dr Mark Toynbee, Mr Michael Daly, Ms Naomi Hannaway, Ms Nicola Walker, Ms Rhian Kant, Dr Ruth Harman, Ms Shelley Campbell, Ms Sophie Howitt, Ms Stacey Horne, Ms Tanja Christensen, Mr Timur Ohloff and Mr William Turner. Dr Nicholas Magill conducted the statistical analyses.

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Dedication

I dedicate this thesis to my mother, Katrin Köhler. It is in her loving memory that I aspire to improve the psychiatric care provided to others who are medically ill.

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List of Abbreviations

Abbreviation	Explanation
A&E	Accident & Emergency
ACP	American College of Physicians
AMI	Acute Myocardial Infarction
AMSTAR	A MeaSurement Tool to Assess systematic Reviews
AMSTAR 2	A MeaSurement Tool to Assess systematic Reviews 2
AMTS	Abbreviated Mental Test Score
Barthel ADL Index	Barthel Activities of Daily Living Index
BDI	Beck Depression Inventory
BDI-SF	Beck Depression Inventory-Short Form
BIOSIS	BioSciences Information Service of Biological Abstracts
BPRS	Brief Psychiatric Rating Scale
CAM	Confusion Assessment Method
CAMCOG	Cognitive section of CAMDEX (see below for CAMDEX)
CAMDEX	Cambridge Mental Disorders of the Elderly Examination
CAPE	Clifton Assessment Procedure for the Elderly
CCTR	Cochrane Controlled Trials Register
CDR Scale	Clinical Dementia Rating Scale
CDSR	Cochrane Database of Systematic Reviews
CES-D	Center for Epidemiologic Studies Depression Scale
CHD	Coronary Heart Disease
CI	Confidence Interval
CIDI	Composite International Diagnostic Interview
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CIS	Clinical Interview Schedule
CNKI	China National Knowledge Infrastructure
COPD	Chronic Obstructive Pulmonary Disease
CPRS	Comprehensive Psychiatric Rating Scale
CSHA	Canadian Study of Health and Aging protocol

Abbreviation	Explanation
DAS	Delirium Assessment Scale
DCR	Diagnostic Criteria for Research
DIS	Diagnostic Interview Schedule
DISH	Depression Interview and Structured Hamilton
DSM	Diagnostic and Statistical Manual of Mental Disorders
EMBASE	Excerpta Medica dataBASE
ENT	Ears, Nose and Throat
GAD	Generalised Anxiety Disorder
GAD-2	Generalized Anxiety Disorder 2-item scale
GAD-7	Generalized Anxiety Disorder 7-item scale
GDS	Geriatric Depression Scale
GMS	Geriatric Mental State / Geriatric Mental State Schedule
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HAD-D	Hospital Anxiety and Depression scale, Depression subscale
HADS	Hospital Anxiety and Depression Scale
HAM-D / HAMD / HDRS / HDS	Hamilton Rating Scale for Depression / Hamilton Depression Rating Scale / Hamilton Depression Scale
ICD	International Classification of Diseases
ICU	Intensive Care Unit
IQCODE	Informant Questionnaire on Cognitive Decline in the Elderly
IQR	Inter-Quartile Range
LILACS	Latin American and Caribbean Health Sciences Literature
MADRS	Montgomery-Asberg Depression Rating Scale
MCI	Mild Cognitive Impairment
MEDLARS	MEDical Literature Analysis and Retrieval System
MEDLINE	Online counterpart to MEDLARS (see above for MEDLARS)
MINI	Mini-International Neuropsychiatric Interview
MMMS Examination	Modified Mini-Mental State Examination
MMSE	Mini-Mental State Examination
MoCA	Montreal Cognitive Assessment

Abbreviation	Explanation
MOOSE	Meta-analysis Of Observational Studies in Epidemiology
MSQ	Mental Status Questionnaire
NA	Not Available
NRSI	Non-Randomised Studies of Healthcare Interventions
OBS Scale	Organic Brain Syndrome Scale
OQAQ	Overview Quality Assessment Questionnaire
OR	Odds Ratio
PHQ-2	Patient Health Questionnaire 2-item scale
PHQ-9	Patient Health Questionnaire 9-item scale
PI	Prediction Interval
PICO	Population, Intervention, Comparator group, Outcome
PRISMA checklist	Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist
PROSPERO	International Prospective Register of Systematic Reviews
PSE	Present State Examination
PsycINFO	Psychological Information Database
R-AMSTAR	Revised-A MeaSurement Tool to Assess systematic Reviews
RCT	Randomised Controlled Trial
RDC	Research Diagnostic Criteria
RoB	Risk of Bias
ROBIS	Risk of Bias in Systematic Reviews
RR	Relative Risk
SADS	Schedule for Affective Disorders and Schizophrenia
SCAN	Schedules for Clinical Assessment in Neuropsychiatry
SCID	Structured Clinical Interview for DSM (see above for DSM)
SciELO	Scientific Electronic Library Online
SD	Standard Deviation
SDS	Zung Self-Rating Depression Scale (see ZDS)
SE	Standard Error
SF-12	12-Item Short Form Health Survey
SPMSQ	Short Portable Mental Status Questionnaire

Abbreviation	Explanation
SRQ-24	Self-Reporting Questionnaire (24 item)
STAI	State-Trait Anxiety Inventory
STROBE	STrengthening the Reporting of OBservational studies in Epidemiology
T-MoCA	Telephone Montreal Cognitive Assessment
WAIS	Wechsler Adult Intelligence Scale
WANFANG	Wanfang Data
WBI-5	World Health Organization Five-Item Well-Being Index
WOS	Web of Science
ZDS	Zung Depression Scale (see SDS)
There are multiple abbreviations for some psychiatric measures because abbreviations for measures were extracted directly from the studies cited in the thesis.	

Abstract

Psychiatric Illnesses in General Hospital Inpatients

Maike van Niekerk, St. John's College
Doctor of Philosophy in Psychiatry
Submitted: Michaelmas Term 2020

Background

Psychiatric illnesses are problematic in the medically ill, particularly amongst those admitted to general hospitals. An admission to a general hospital provides the opportunity to identify and, where appropriate, treat these conditions. To achieve this by better psychiatric service provision, we first need to know how common psychiatric illnesses are in general hospital inpatients.

Research aim

The overall aim of this thesis was therefore to determine the prevalence of psychiatric illnesses in general hospital inpatients.

Methods

I conducted: (1) a **meta-review** of the prevalence of psychiatric illnesses in general hospital inpatients; (2) a **systematic review** of the prevalence of anxiety disorders in general hospital inpatients; and (3) a **cross-sectional study** of the prevalence and associations of clinically significant anxiety, depression and cognitive impairment in older general hospital inpatients.

Results

The main findings of this thesis are as follows:

Meta-review

The prevalence of diagnosed: **depression** ranged from 2% to 56% in general hospital inpatients (mean prevalence of 12%); **delirium** ranged from 10% to 31% in medical inpatients at admission to hospital; and **dementia** ranged from 2.8% to 63.0% in older general hospital inpatients. I did not find a systematic review of the prevalence of anxiety in the whole population of general hospital inpatients; therefore, I systematically reviewed this literature.

Systematic review

The mean prevalence of **panic disorder** was 2% and **generalised anxiety disorder** was 7% in general medical and surgical inpatients.

Cross-sectional study

The prevalence of **clinically significant anxiety**, **depression** and **cognitive impairment** was 41.8%, 43.6% and 64.1% respectively in older general hospital inpatients. I found evidence to suggest psychiatric illnesses were especially common in the “sickest” patients and those without a spouse or partner. Patients with clinically significant anxiety or depression also appeared to be more likely to experience symptoms of other psychiatric illnesses.

Conclusion

The finding that psychiatric illnesses are highly prevalent in general hospital inpatients has important implications for clinical care and healthcare policy. In particular, it suggests that general hospital services must address the needs of patients suffering from both medical *and* psychiatric illnesses. Better psychiatric care provision in general hospitals has the potential to improve outcomes for these patients.

Chapter 1
Introduction

1.1 Background

Comorbid psychiatric illnesses are problematic in the medically ill. They are associated with distress, poorer self-care, greater medical symptom burden, worse functional impairment and poorer quality of life.[1-9] They are especially problematic for patients admitted to general hospitals, where they are associated with longer hospital stays, higher rates of hospital readmission, more in-hospital adverse events and greater healthcare costs.[1,10-12] Despite their importance, comorbid psychiatric illnesses are often not recognised and treated in people with medical illnesses, including during admission to hospital.[13-17]

An admission to a general hospital for a medical illness offers an opportunity for the identification and, where appropriate, treatment of psychiatric illnesses. But to achieve this by better psychiatric service provision, we first need to know how common psychiatric illnesses are in general hospital inpatients. The overall aim of this thesis was therefore to determine the *prevalence* of *psychiatric illnesses* in general hospital inpatients.

1.2 Key concepts

1.2.1 Prevalence

Prevalence refers to the proportion of people in a group who *have* a condition, or *are* a “case”, at a given time.[18] Prevalence is calculated by dividing the number of people who have a condition in a group by the total number of people in that group at a given time.[18]

There are two main types of prevalence: *point prevalence* and *period prevalence*.[19] *Point prevalence* refers to the proportion of people in a group who have a condition at a given *point* in time.[19] In other words, people are assessed for a condition *once* and are included in the point prevalence estimate if they have the condition at their assessment. *Period prevalence* refers to the proportion of people in a group who have a condition during a given *period* of time.[19] In other words, people are assessed for a condition *multiple times* over a specific *interval of time* and are included in the period prevalence estimate if they have the condition on at least one of their assessments. Unlike point prevalence, period prevalence can capture people who did not have a condition at one time point, but developed it at a later time point.

The term *prevalence* differs from the term *incidence. Incidence* refers to the proportion of people in a group who *develop* a condition, or *become* a “case”, during a specific period of time.[18] It is calculated by dividing the number of people who *developed* a condition (i.e. did not previously have it) in a group by the total number of people in that group at risk of developing the condition.[18]

In this thesis, I aimed to determine the *prevalence* of people with psychiatric illnesses (“cases”) in general hospital inpatient wards, which is important for guiding psychiatric service provision.

1.2.2 Psychiatric illnesses

1.2.2.1 Introduction

Psychiatric symptoms (e.g. feeling down, nervous and worried) are a part of people's everyday life. Some individuals, however, experience symptoms that persist and cause them significant distress or impairment in their daily functioning; such symptoms may be considered clinically significant. There are two ways of defining when psychiatric symptoms are clinically significant. The first is to apply a cut-off (or "threshold") score on a rating scale and the second is to use diagnostic criteria in a clinical interview. I explain the difference between these two ways of defining clinical significance, using clinically significant depression as an example.

1.2.2.2 Psychiatric illnesses defined using cut-off scores

Clinically significant depression can be defined using a cut-off score on a depression rating scale. A cut-off score represents the boundary between "normal" and "abnormal" on a rating scale.[20] Only those individuals whose scores equal or exceed a cut-off score are considered to have clinically significant depression.[20] There are different methods used to determine cut-off scores, including choosing a score based on its ability to differentiate between individuals with and without a diagnosed depressive disorder or its agreement with established cut-off scores on other existing depression rating scales.[21]

1.2.2.3 Psychiatric illnesses defined using diagnostic criteria

Clinically significant depression can also be defined using diagnostic criteria in a clinical interview. Diagnostic criteria are more stringent in their definition of clinically significant depression than cut-off scores. Diagnostic criteria are essentially "guidelines" for making medical and psychiatric diagnoses (e.g. Diagnostic and Statistical Manual of Mental Disorders [DSM] criteria[22] and International Classification of Diseases [ICD] criteria[23]). Diagnostic criteria define clinically significant depression based on a specific *pattern* and *severity* of depressive symptoms that must be present for a *specific duration of time*.[22] These criteria also specify things that must be ruled out in order for clinically significant depression to be present (e.g. depressive symptoms cannot be due to a substance, medication or other medical condition).[22] Diagnostic criteria, unlike cut-off scores, can be used to diagnose individuals with a depressive disorder.

1.2.2.4 Operationalising the term "psychiatric illness"

In this thesis, I aimed to determine the prevalence of cases of *psychiatric illnesses* in general hospital inpatients. I use the term *psychiatric illness* to broadly encompass those psychiatric symptoms defined as clinically significant according to either (1) a cut-off score on a rating scale or (2) diagnostic criteria in a clinical interview.

1.3 Thesis outline

Chapter 1 is a brief introduction to this thesis.

Chapter 2 is an outline of the research aims of this thesis.

Chapter 3 is a description of different types of literature reviews, which provides background information for the two literature reviews in this thesis in **Chapters 4** and **5**.

Chapter 4 is a meta-review of the prevalence of psychiatric illnesses in general hospital inpatients.

Chapter 5 is a systematic review of the prevalence of anxiety disorders in general hospital inpatients.

Chapter 6 is a background description of my cross-sectional study of the prevalence and associations of clinically significant anxiety, depression and cognitive impairment in older (aged ≥ 65 years) general hospital inpatients. This cross-sectional study is broken down into three substudies:

(1) **Chapter 7** is the substudy on clinically significant anxiety;

(2) **Chapter 8** is the substudy on clinically significant depression; and

(3) **Chapter 9** is the substudy on clinically significant cognitive impairment.

Chapter 10 is a summary of the findings of my meta-review, systematic review and cross-sectional study.

Chapter 11 is a discussion of the implications of the findings of this thesis.

Chapter 12 is a brief conclusion to this thesis.

Chapter 2
Research aims

The overall aim of this thesis was to determine the prevalence of psychiatric illnesses in general hospital inpatients.

2.1 Aim one

I aimed to summarise literature on the prevalence of psychiatric illnesses in general hospital inpatients, using a meta-review.

2.2 Aim two

In conducting my meta-review, I found that there were no systematic reviews of the prevalence of anxiety in the whole population of adult general hospital inpatients. I therefore aimed to summarise literature on the prevalence of anxiety disorders in general hospital inpatients, using a systematic review.

2.3 Aim three

I aimed to determine the prevalence of clinically significant anxiety, depression and cognitive impairment in older (aged ≥ 65 years) general hospital inpatients, and the associations of these, using a cross-sectional study.

Chapter 3
Background to literature reviews

3.1 Introduction

I conducted two literature reviews in this thesis: (1) a *meta-review* summarising literature on the prevalence of psychiatric illnesses in general hospital inpatients (**Chapter 4**) and (2) a *systematic review* summarising literature on the prevalence of anxiety disorders in general hospital inpatients (**Chapter 5**), having found one was lacking when conducting my meta-review. In this chapter, I explain the difference between some of the most common types of literature reviews.

3.2 Type of literature reviews

Scientific journals often publish reviews that provide a summary of the literature on a particular topic.[24] Reviews (also known as *literature reviews*) help people stay up to date with literature that is accumulating in their field of interest.[24] There are many different types of reviews.[25] Three of the most common types of reviews are *narrative reviews*, *systematic reviews* and *meta-reviews*.[25]

3.2.1 Narrative reviews

One of the most common types of reviews is a *narrative* (or *non-systematic) review*.[24,25] The purpose of a narrative review is to provide a summary of relevant literature on a topic.[25] Narrative reviews do not specifically aim to summarise all of the available literature on their topic of interest.[25] Rather,

researchers conducting this type of review may choose to include literature that supports or refutes a certain viewpoint.[24,25] This means narrative reviews can be useful for obtaining a broad understanding of a topic or presenting a specific argument. However, due to their subjective nature, narrative reviews are less appropriate for providing a comprehensive summary of the literature on a particular topic.[24,25]

3.2.2 Systematic reviews

Systematic reviews attempt to draw together *all* of the available literature that address a particular research question.[18,25] In contrast with other forms of reviewing literature, systematic reviews are characterised by their predefined, clear, reproducible and comprehensive methods of identifying and selecting all relevant literature.[18] Systematic reviews are generally more focussed than other types of reviews, and they aim to answer a *clear* and *specific* research question.[18] Systematic reviews often include quality appraisals of their included literature,[26] which can help to determine the strength of the evidence in a particular field. Because of their comprehensive approach, systematic reviews can be time-intensive and demanding to conduct.[26]

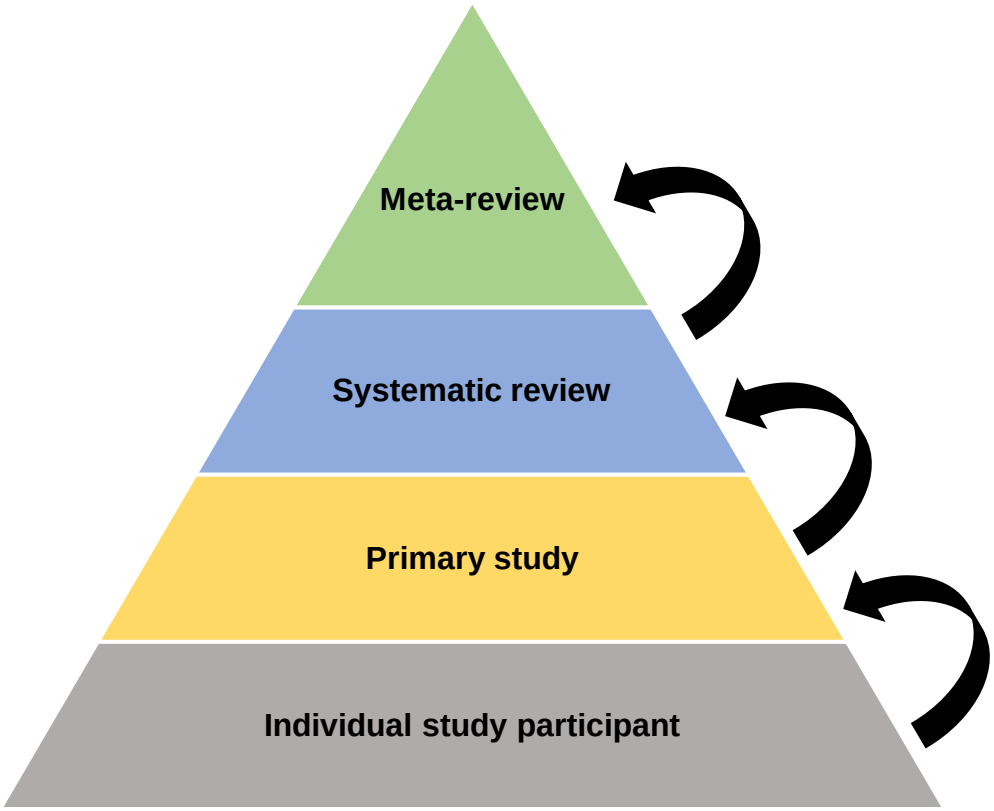
3.2.3 Meta-reviews

When multiple systematic reviews have been conducted on a topic, researchers may choose to consolidate the findings of these reviews in the form of a *meta-review*.[26,27] A meta-review (also known as an *umbrella review*, an *overview of reviews* and a *review of reviews*) is a systematic review of systematic

reviews.[26,27] While most types of reviews collate findings from multiple primary studies, meta-reviews collate findings from multiple systematic reviews (see **Figure 1**).[26,27] The aim of a meta-review is to summarise systematic reviews, rather than to re-synthesize their findings.[28] Meta-reviews offer a “wide picture” of the evidence on a particular topic, which can make them useful for identifying consistencies and differences within this evidence base.[28]

The terms *meta-review* and *systematic review* are sometimes confused with the term *meta-analysis*. The terms are different: meta-reviews and systematic reviews are types of reviews, while a meta-analysis is an analytical technique.[26] A *meta-analysis* is a statistical analysis that combines the results of several independent quantitative studies into a single result.[18] When the primary studies included in a literature review are sufficiently similar to each other, it may be appropriate to combine their results by conducting a meta-analysis.[24]

Figure 1. Diagram depicting a meta-review



Chapter 4
Prevalence of psychiatric illnesses in general hospital inpatients: A meta-review

4.1 Background

Psychiatric illnesses are clinically important in general hospital inpatients. Not only are these illnesses associated with poorer outcomes for patients (e.g. worse functional impairment), they are also associated with longer hospital stays, greater need for nursing care, higher rates of hospital readmissions and higher healthcare costs.[1,5,10-12] Despite their importance, we lack summary information on the prevalence of psychiatric illnesses in the general hospital setting.

4.2 Research aim

I therefore aimed to summarise literature on the prevalence of psychiatric illnesses in general hospital inpatients.

4.3 Research question

What is the prevalence of psychiatric illnesses in general hospital inpatients? Specifically, what is the prevalence of anxiety, depression, delirium, dementia and substance abuse in general hospital inpatients?

4.4 Methods

4.4.1 Study design

When I performed a preliminary search of the literature on the prevalence of psychiatric illnesses in general hospital inpatients, I found a small number of relevant systematic reviews on this topic. I could not find, however, a comprehensive overview of the literature in this field. I therefore chose to conduct a *meta-review* (a systematic review of systematic reviews, see **Chapter 3**) of the prevalence of psychiatric illnesses in general hospital inpatients. It was important for my meta-review to be clinically useful,[26] so I focussed on the psychiatric illnesses that clinicians consider to be common and burdensome in general hospital wards: anxiety, depression, delirium, dementia and substance abuse (see **Figure 2**).

Figure 2. Brief descriptions of psychiatric illnesses of interest in the meta-review

Psychiatric illness	**Features**[29-32]
Anxiety	Excessive fear or worrying (apprehension); physical symptoms (e.g. trembling and increased heart rate); avoidance behaviours resulting in distress and/or impairment.
Depression	Low mood; loss of interest or pleasure; feelings of worthlessness or inappropriate guilt; recurrent thoughts of death; suicidal ideation; weight changes; sleep disturbance; fatigue; impaired concentration; psychomotor disturbance.
Delirium	Acute, often fluctuating, cognitive disturbance; inattention (including distractibility, reduced vigilance or concentration) is a cardinal feature; usually reversible.
Dementia	Insidious, often progressive, cognitive decline that causes functional impairment; memory deficit is a cardinal feature; not usually reversible.
Substance abuse	Excessive and maladaptive use of a substance, such as alcohol.

4.4.2 Protocol

I wrote a *protocol* (i.e. a detailed predefined plan) for my meta-review to minimise the potential for bias during the review process.[26] I registered my meta-review and its protocol on the International Prospective Register of Systematic Reviews (PROSPERO), number CRD42019125574.

4.4.3 Selection criteria

I included studies if they met the following selection criteria: (1) the study was a systematic review; (2) the systematic review aimed to estimate the prevalence of anxiety, depression, delirium, dementia or substance abuse (defined using diagnostic criteria in clinical interviews or cut-off scores on rating scales); and (3) the primary studies included in the systematic review (or a clear subgroup) were of adult (aged ≥ 16 years) general hospital inpatients. I elaborate on these criteria below. I also only included studies for which I could obtain the full paper to allow *data extraction* (i.e. the process of retrieving data from systematic reviews). I did not apply any language restrictions.

4.4.3.1 Criterion 1

I only included systematic reviews. Informed by existing literature,[26] my supervisors and I defined a "*systematic review*" as a literature review with clear objectives, predefined selection criteria, a systematic search strategy, reproducible methods and a systematic presentation of findings.

4.4.3.2 Criterion 2

I only included systematic reviews that aimed to estimate the prevalence of anxiety, depression, delirium, dementia or substance abuse, defined using diagnostic criteria in clinical interviews or cut-off scores on rating scales. I therefore did not include: (1) reviews designed to address a different research question that happened to include prevalence studies, because their authors may not have systematically searched for all of the available literature on prevalence – this would mean that the prevalence estimates reported in these reviews might not accurately summarise the literature; (2) reviews that aimed to estimate the *incidence* of anxiety, depression, delirium, dementia or substance abuse (see **Chapter 1** for definition of incidence); (3) reviews that aimed to estimate the combined prevalence of multiple psychiatric illnesses (e.g. combined prevalence of anxiety and depression); and (4) reviews that included primary studies which did not assess for psychiatric illnesses using clinical interviews or rating scales (e.g. used medical records).

4.4.3.3 Criterion 3

I included systematic reviews with primary studies (or a clear subgroup) of adult (aged ≥ 16 years) general hospital inpatients admitted to *any* general hospital ward or diagnosed with *any* medical illness. This meant that I did not include reviews of studies conducted in rehabilitation centres, psychiatric hospitals (or patients referred to psychiatry services in general hospitals), hospice settings, and accident & emergency (A&E) departments. I only included a review if it reported a prevalence estimate specifically for the population of interest (that is,

adult general hospital inpatients). This meant that I did not include reviews where only some of the studies contributing to the prevalence estimate were of adult general hospital inpatients. I did not include these reviews because it was not possible, without examining the primary studies in detail (in particular their sample sizes), to determine the degree to which the prevalence estimate was affected by the studies of other samples.

4.4.4 Search strategy

In accordance with recommendations,[26] I developed a search strategy by combining the main concepts from my research question: (1) prevalence, (2) psychiatric illnesses (i.e. anxiety, depression, delirium, dementia and substance abuse), (3) general hospital inpatients and (4) systematic reviews (as I was conducting a meta-review).

I identified relevant reviews by searching OVID MEDLINE, OVID EMBASE, OVID PsycINFO, EBSCO Host Cumulative Index to Nursing and Allied Health Literature (CINAHL), and Scopus from database inception to April 2020. Searches were run for the combination of “prevalence”, “anxiety, depression, delirium, dementia or substance abuse”, “general hospital inpatient” and “systematic review or meta-analysis” using standardised subject terms and free-text terms, including synonyms and alternative spellings (see **Appendix 1** for search strategies). I searched multiple health-related bibliographic databases in order to (1) identify as much relevant literature as possible and (2) reduce the risk of reporting bias.[26] I contacted the authors of relevant conference abstracts found through my electronic database search to obtain any associated publications. I also conducted both manual reference list searches and forward-citation searches for the articles that I included. I worked closely with my supervisors (both experienced psychiatrists in the field of my meta-review) and an information specialist to develop my search strategy and chose appropriate electronic databases to search, in order to maximise the quality of my search.[26,33] Information specialists are methodologists with expertise in

identifying literature; they often advise researchers on methods for conducting systematic reviews (e.g. choosing appropriate databases for conducting literature searches, designing search strategies and running searches).[26,34]

4.4.5 Data collection

I imported all articles identified through the electronic database search into EndNote. I screened all articles' titles and abstracts to determine whether each might meet my selection criteria. I then reviewed the full text of relevant articles, with the help of a translator where necessary.

I extracted data from all eligible systematic reviews using a specially designed, standardised data extraction form that I developed. As recommended,[26] my supervisor and I piloted this data extraction form before extracting data to ensure it was useable and it extracted all of the necessary information. I extracted the following data: authors; aim(s); criteria for including primary studies; databases searched; risk of bias and/or quality assessment(s); heterogeneity; method(s) of synthesis/analysis; population of interest; number of relevant primary studies included as well as their publication dates and sample sizes; and finding(s). I chose only to extract data that were presented in the systematic reviews themselves. I did not conduct primary study level data extraction because the "unit of analysis" in a meta-review is systematic reviews *not* primary studies. This decision is in accordance with recommendations for conducting meta-reviews.[28]

A second researcher independently conducted each of the aforementioned data collection steps, which minimised the chance of errors occurring.[26] I consulted a third independent researcher (consultant psychiatrist and senior clinical researcher) to resolve any disagreements about the data that we extracted.

4.4.6 Quality assessments

Systematic reviews can be assessed in terms of their *methodological quality* and *reporting quality.*[35,36] *Methodological quality* considers how well a systematic review was conducted, while *reporting quality* considers how well a systematic review was reported.[35,36] I chose to assess both the methodological quality and reporting quality of each systematic review, because it is possible for a systematic review to have poor methodological quality but good reporting quality (or vice versa).[36]

There is no universally accepted and recommended quality assessment measure for meta-reviews.[26,28,37] I chose to use an adapted form of "A MeaSurement Tool to Assess systematic Reviews 2" (AMSTAR 2)[38] to assess methodological quality and the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA) checklist[39] to assess reporting quality. In **Table 1**, I describe common quality assessment measures used in meta-reviews, as well as my rationale for choosing AMSTAR 2 and the PRISMA checklist. I chose not to repeat or update the quality assessments done by the authors of the systematic reviews, because the aim of a meta-review is to summarise and present data from systematic reviews – it is *not* to re-synthesize their results.[28]

To minimise the risk of potential errors,[26] a second researcher (psychiatry trainee and academic clinical fellow) independently conducted quality assessments. We resolved any disagreements by consulting a third independent researcher (consultant psychiatrist and senior clinical researcher).

4.4.6.1 AMSTAR 2

AMSTAR 2 is a checklist with 16 domains which assesses the methodological quality of systematic reviews.[38] This checklist is commonly used in meta-reviews to appraise systematic reviews of randomised and non-randomised studies of healthcare interventions. It assesses (among other things) the quality of a systematic review's literature search, study selection, data extraction, reporting and risk of bias assessment.[38] It also assesses if a review accounted for risk of bias and heterogeneity in interpreting its results, and if it conducted its meta-analysis appropriately (when applicable).[38]

Since AMSTAR 2 was made specifically to appraise systematic reviews of interventional studies, I worked with my supervisors to adapt some domains so that they were applicable to systematic reviews of observational studies relevant to this meta-review (see **Appendix 2** for adaptations). The developers of AMSTAR 2 strongly discourage ascribing quality rating scores to systematic reviews, because these scores may be misleading, potentially concealing critical weaknesses in reviews.[38] I therefore did not assign quality scores to any of the included systematic reviews.

4.4.6.2 PRISMA checklist

The PRISMA checklist is a 27-item checklist which assesses the reporting quality of systematic reviews.[39] It assesses the content and reporting of a systematic review's title, abstract, introduction, methods, results, discussion and funding.[39] The PRISMA checklist guidelines do not state that one should combine the individual items on the PRISMA checklist to derive a composite score, so I did not ascribe quality scores to included systematic reviews.[40]

Table 1. Quality assessment measures for assessing systematic reviews

Measure	Description of measure	Measure chosen
Methodological quality assessment measures[a]		
Overview Quality Assessment Questionnaire (OQAQ)[41]	OQAQ is a 10-item measure that was designed to assess the methodological quality of systematic reviews.[41] It is the most frequently used instrument for measuring the methodological quality of systematic reviews.[27,42] It is valid (accurate) and reliable (consistent).[41,42] It has been critiqued because users have had to develop their own rules to operationalise its items and because it does not assess for some important sources of bias.[36]	I chose to assess the systematic reviews in my meta-review using AMSTAR 2 because it is valid, reliable, clear and simple. It includes all of the key components of OQAQ and AMSTAR, and is more practical to use than ROBIS. It also has a guidance document which helps ensure that quality assessments are done consistently between reviewers.
A MeaSurement Tool to Assess systematic Reviews (AMSTAR)[43]	AMSTAR is an 11-domain measure that was designed to assess the methodological quality of systematic reviews of randomised controlled trials.[43] It is commonly used[27,41] and is the most frequently recommended quality assessment measure for appraising systematic reviews.[37] It was developed by combining the enhanced OQAQ[44] and a checklist created by Sacks et al.[45].[43] It is valid, reliable and easy to use.[36,42,43,46-48] It has been critiqued because[49-51]: it focuses solely on systematic reviews of randomised controlled trials; some of its items assess reporting quality more than methodological quality; it does not have detailed instructions for evaluating items; some of its items are unclear; and it does not sufficiently assess for or account for risk of bias.	
A MeaSurement Tool to Assess systematic Reviews 2 (AMSTAR 2)[38]	AMSTAR 2 is an updated version of AMSTAR. It consists of 16 domains, 10 of which are from the original AMSTAR.[38] AMSTAR 2 expanded its focus to assess the methodological quality of systematic reviews of randomised *and non-randomised* studies of healthcare interventions.[38] Its items are more simple, clear and specific than the original AMSTAR, and there is a comprehensive user guide available for use.[38] It also includes a more detailed analysis of risk of bias and how risk of bias is handled in a review's results than the original AMSTAR.[38] AMSTAR 2 has good validity and fair reliability.[52] Its developers did not perform an extensive validation of AMSTAR 2, because it retains most of the domains of the original, validated measure with some changes in wording and elaboration of content.[38] Since AMSTAR 2 is an updated version of AMSTAR, it has been suggested that this measure may be preferred.[26]	
Revised-A MeaSurement Tool to Assess systematic Reviews (R-AMSTAR)[53]	R-AMSTAR is a revised version of AMSTAR.[53] It includes all of the items from the original AMSTAR, however it is designed to provide a composite quality rating score.[53] The developers of the original AMSTAR do not recommend assigning overall quality rating scores to systematic reviews, because they may conceal critical weaknesses in the reviews.[38] It has been suggested that R-AMSTAR's measurement properties must be investigated further.[48]	

Risk of Bias in Systematic Reviews (ROBIS)[54]	ROBIS is a measure designed to assess risk of bias in systematic reviews.[54] It includes three phases: (1) assessing relevance (optional); (2) identifying concerns with the systematic review process; and (3) judging overall risk of bias for the systematic review.[54] It differs from OQAQ, AMSTAR, AMSTAR 2 and R-AMSTAR because it specifically assesses risk of bias, while the other measures have broader objectives of critical appraisal. ROBIS is more difficult to use than other assessment measures and requires users to have sufficient expertise in the subject matter.[52,55] While AMSTAR and AMSTAR 2 focus on reviews of healthcare interventions, ROBIS has a wider application (reviews of interventions, diagnostic test accuracy, prognosis and aetiology).[54] ROBIS exhibits good validity and fair reliability,[55] however it achieved lower inter-rater reliability (consistency between users) than AMSTAR[56,57] and AMSTAR 2.[52] ROBIS is more time-intensive than AMSTAR.[55,57]	
Reporting quality assessment measures		
Meta-analysis Of Observational Studies in Epidemiology (MOOSE)[58]	MOOSE is a 35-item checklist that was designed to assess the reporting quality of meta-analyses of observational studies in epidemiology.[58] It cannot be used to gauge the methodological quality of a meta-analysis.[58]	I chose to assess the systematic reviews in my meta-review using the PRISMA checklist because it is widely used in published reviews. It also has a guidance document which helps ensure that quality assessments are done consistently between reviewers.
Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist[39]	The PRISMA checklist is a 27-item checklist that was designed to assess the reporting quality of systematic reviews.[39] It was made primarily to assess reviews of randomised trials, but is commonly applied to other research designs. It cannot be used to gauge the methodological quality of a systematic review.[39]	

AMSTAR = A MeaSurement Tool to Assess systematic Reviews; AMSTAR 2 = A MeaSurement Tool to Assess systematic Reviews 2; MOOSE = Meta-analysis Of Observational Studies in Epidemiology; OQAQ = Overview Quality Assessment Questionnaire; PRISMA checklist = Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist; R-AMSTAR = Revised-A MeaSurement Tool to Assess systematic Reviews; ROBIS = Risk of Bias in Systematic Reviews.

[a]**Table 1** is not entirely in alphabetical order (OQAQ is described before AMSTAR) to improve readability, as AMSTAR was developed based on the enhanced OQAQ.

4.4.7 Analyses

I present the findings of this meta-review using *narrative syntheses*. *Synthesis* is the process of bringing together data from a set of studies included in a review, for the purpose of drawing conclusions about that body of evidence.[26] *Narrative synthesis* is a type of synthesis that uses primarily words and text to bring together data.[59] This contrasts with *meta-analysis* (defined in **Chapter 3**) which uses statistical approaches to bring together data.[26] It was not appropriate to do a meta-analysis, because the systematic reviews that I included had substantial clinical heterogeneity and some of the reviews included the same primary studies.

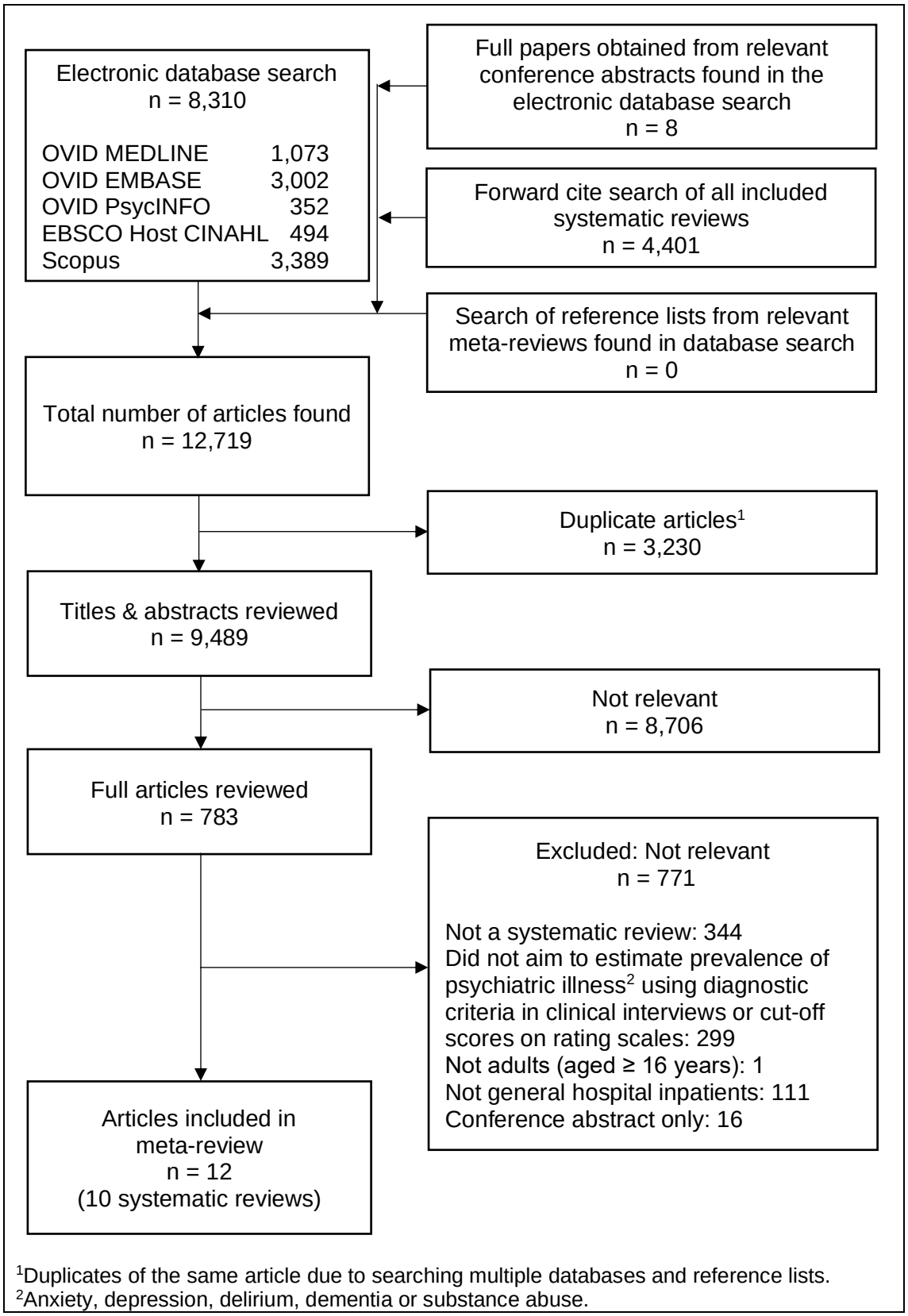
4.5 Results

4.5.1 Overview

My initial screening of 9,489 titles and abstracts yielded 783 articles for full review, seven of which required the help of a translator. A second researcher and I found 10 systematic reviews (described in 12 articles) that met selection criteria (see **Figure 3** for flowchart).[11,60-70] The number of relevant primary studies included in each review ranged from two to 60 (total sample sizes ranged from 299 to 14,326).

The prevalence of anxiety was summarised in one review,[63] depression in eight,[60-64,66-70] delirium in one,[65] and dementia in one.[11] I summarise the findings of these reviews in **Table 2**, **Table 3** and **Table 4**. I did not find any reviews summarising literature on the prevalence of substance abuse in adult general hospital inpatients. The majority of reviews focussed on inpatients with specific medical illnesses (e.g. cardiovascular disease and cancer), rather than the whole population of general hospital inpatients.

Figure 3. Prevalence of psychiatric illnesses in general hospital inpatients: A meta-review flowchart



[1]Duplicates of the same article due to searching multiple databases and reference lists.
[2]Anxiety, depression, delirium, dementia or substance abuse.

Table 2. Systematic reviews of the prevalence of psychiatric illnesses in general hospital inpatients included in the meta-review

Psychiatric Illness	Review	Population of interest	Primary studies			Finding(s)
			Number	Dates published	Total of sample sizes	
Anxiety	Mitchell et al. (2017)[63]	Inpatients who had experienced a stroke	NA	NA	NA	*Any anxiety disorder diagnosis* Pooled: 10.7% (95% CI, 3.8% to 20.4%)
Depression	Castro-de-Araújo et al. (2013, 2015)[60,61]	Elderly inpatients (Brazil)	4	2002 – 2008	299	*Significant symptoms* Range: 20% to 57%; Combined estimate: 45% (95% CI, 31% to 60%)
	Mitchell et al. (2011)[62]	Inpatients with cancer	8	1984 – 2004	933	*Any depression diagnosis* Pooled: 12.3% (95% CI, 6.6% to 19.4%)
	Mitchell et al. (2017)[63]	Inpatients who had experienced a stroke	NA	NA	NA	*Major depression*[a] Pooled: 18.1% (95% CI, 14.4% to 22.1%) *Any depression diagnosis* Pooled: 33.9% (95% CI, 29.0% to 39.0%)
	Ren et al. (2014)[64]	Inpatients with coronary heart disease (China)	23	2000 – 2013	5,236	*Significant symptoms* Range: 22.8% to 84.0%; Meta-analytical prevalence: 51% (95% CI, 43% to 58%)
	Thombs et al. (2006a)[66] Bush et al. (2005)[67]	Inpatients hospitalised for acute myocardial infarction	24	1986 – 2004	14,326	*Any depression diagnosis*[b] Range: 16% to 45%; Weighted prevalence: 20.5% (95% CI, 19.8% to 21.3%) *Significant symptoms*[c] Range: 10% to 47%
	Thombs et al. (2006b)[68]	Inpatients with burn injuries	5	1983 – 2002	400	*Major depression*[d] 4%; *Dysthymia*[d] 4% *Significant symptoms*[e] Range: 30% to 35%
	Walker et al. (2013)[69]	Inpatients with cancer	2	NA	NA	*Major depression* Range: 4% to 14%
	Walker et al. (2018)[70]	General hospital inpatients	60	1985 – 2015	12,540	*Depression diagnosis* Range: 2% to 56% (medical/surgical inpatients only[f] 2.7% to 33.6%) Mean (medical/ surgical inpatients only[f]): 12% (95% CI, 10% to 15%)
Delirium	Siddiqi et al. (2006)[65]	Medical inpatients at time of admission	8	1982 – 2005	3,558	Range: 10% to 31%
Dementia	Mukadam & Sampson (2011)[11]	Older general hospital inpatients	14	1986 – 2008	4,989	Range: 2.8% to 63.0%

Note: Dates published and total of sample sizes taken from the systematic reviews' tables, where not available in the text.
CI = Confidence Interval; NA = Not Available. [a]32 analyses; [b]8 studies; [c]17 studies; [d]2 studies; [e]3 studies; [f]31 studies.

4.5.2 Anxiety

I did not find any reviews that summarised the prevalence of anxiety in the whole population of adult general hospital inpatients. However, I found one relevant review of patients who had experienced a stroke.[63] It summarised studies of the prevalence of anxiety disorders (generalised anxiety disorder, panic disorder, agoraphobia, social phobia and obsessive-compulsive disorder) diagnosed using clinical interviews.[63] In the subgroup of studies conducted in the acute hospital setting, it estimated that the pooled prevalence of anxiety disorders was 10.7%.[63] Although the reviewers reported high heterogeneity between the studies included in their analysis (I^2 = 90.7%),[63] they did not discuss this further in their review. Since this review focussed on only one medical illness (stroke), it does not provide a good indication of the prevalence of anxiety in general hospital inpatients more broadly.

4.5.3 Depression

I found eight reviews that summarised the prevalence of depression in general hospital inpatients, defined either using diagnostic criteria in a clinical interview or a cut-off on a depression rating scale.[60-64,66-70] Two of the reviews focussed on the whole population of general hospital inpatients,[60,61,70] while the remaining focussed on general hospital inpatients with specific medical illnesses.[62-64,66-69]

4.5.3.1 Whole population of general hospital inpatients

One review focussed on inpatients admitted to any general hospital ward.[70] It reported prevalence estimates of diagnosed depression ranging from 2% to 56%.[70] This review included 31 studies of general medical and/or surgical inpatients, and 29 studies of inpatients with very specific clinical characteristics.[70] The reviewers calculated the mean prevalence of diagnosed depression (in general medical and surgical inpatients) and estimated it to be 12% (prevalence estimates ranged from 2.7%[a] to 33.6%).[70] The reviewers restricted this analysis to general medical and surgical inpatients because they stated that the other inpatient samples were not representative of the general hospital inpatient population.[70] The reviewers noted that, despite restricting their analysis to general medical and surgical inpatients only, there was still high heterogeneity observed between the studies' prevalence estimates (I^2 = 91%).[70] They performed a number of investigations to assess for potential sources of this heterogeneity; however, their analyses were unable to adequately explain

[a]Reported 2.7% as lowest prevalence estimate in table of review, but 5% in abstract and text of review.

it.[70] The reviewers stated that the heterogeneity between studies was likely due to population, healthcare system and patient differences as well as methodological ones.[70]

One review summarised studies of older (aged ≥ 60 years) general hospital inpatients in Brazil.[60,61] This review reported a higher combined prevalence of depression (45%) than the previous review.[60,61] The combined prevalence (45%) was calculated from studies that had used cut-off scores on depression rating scales, rather than studies that used diagnostic criteria in clinical interviews (as was the case in the previous review).[60,61] The reviewers noted that most of the studies in their review used the same rating scale (15-item Geriatric Depression Scale).[60,61] Still, the reviewers found high heterogeneity between the studies (I^2 = 80.6% in studies of hospitalised patients).[60,61] The reviewers hypothesised that this heterogeneity was likely due to differences in how the primary studies selected their study samples.[60,61] However, the reviewers were not able to formally investigate this as many of the primary studies did not adequately describe their methods of selecting participants.[60,61]

4.5.3.2 General hospital inpatients with specific medical illnesses

The remaining six reviews summarised studies of the prevalence of depression in patients with specific medical illnesses.[62-64,66-69] One review focussed on inpatients who had experienced a stroke,[63] two focussed on inpatients with cancer,[62,69] two focussed on inpatients with heart disease[a],[64,66,67] and one focussed on inpatients with burn injuries.[68]

One review estimated that 18.1% of inpatients who had experienced a stroke had major depression and that 33.9% had any depression diagnosis (major depression, minor depression or dysthymia).[63] The reviewers reported considerable heterogeneity between the studies included in both aforementioned analyses (I^2 = 89.1% and I^2 = 88.6% respectively).[63] The reviewers noted that one major difference between the studies included in their review was how they "handled" patients with aphasia.[63] However, in subgroup analyses, reviewers found that the pooled prevalence of major depression was not statistically different in studies that included or excluded patients with aphasia.[63]

The estimates from this review were higher than those reported in the two reviews that focussed on patients with cancer. One of these reviews reported that the prevalence of major depression in inpatients with cancer ranged from 4% to 14%,[69] while the other reported a pooled prevalence of 12.3% for any depression diagnosis.[62] This pooled prevalence estimate of depression is

[a]One review focussed on inpatients hospitalised for an *acute myocardial infarction*[66,67] and one focussed on inpatients with *coronary heart disease*.[64]

similar to the mean prevalence found in general medical and surgical inpatients (12%).[70]

Two reviews focussed on patients with heart disease.[64,66,67] One review estimated that 20.5% of patients hospitalised for an acute myocardial infarction had a depression diagnosis (major depression, minor depression or dysthymia),[66,67] whilst the other estimated that 51% of inpatients with coronary heart disease had clinically significant depressive symptoms.[64] The latter review found substantial heterogeneity between primary studies included (I^2 = 97%).[64] The reviewers noted this might have been from differences in assessment measures used and variations in diagnostic criteria for coronary heart disease.[64] However, the reviewers were not able to investigate the effect of these variations due to insufficient reporting within the primary studies included.[64]

The final review summarised studies of inpatients with burn injuries.[68] It found two studies that reported the prevalence of major depression, both of which estimated it to be 4%.[68] The reviewers remarked that the prevalence of major depression was much lower than estimates found in other patient populations, including patients who had experienced a stroke and patients hospitalised for an acute myocardial infarction.[68] The reviewers asserted that the low prevalence of major depression might be inaccurate because (1) the studies included were of low quality and (2) there are numerous challenges associated with evaluating depression in patients with burn injuries, including the potential overlap between somatic symptoms used to diagnose depression and symptoms related to burn injuries and their treatment.[68]

4.5.4 Delirium

I found one review that summarised the prevalence of delirium diagnoses in general hospital inpatients.[65] It summarised studies of inpatients (mean age > 75 years[a]) admitted to a variety of general medical and elderly care wards.[65] This review only included studies that met predefined quality criteria (see **Table 3**).[65] It reported prevalence estimates ranging from 10% to 31% in primary studies where patients were examined within 24 hours of admission into hospital.[65]

The reviewers noted that their findings were likely an underestimate of the prevalence of delirium.[65] This is because (1) the review excluded primary studies of delirium tremens and (2) many of the primary studies in the review excluded patients who were unable to consent for themselves, had communication difficulties or had difficulties completing interviews.[65] Delirium can affect a person's ability to consent, communicate and concentrate, which means the aforementioned criteria likely differentially excluded those with delirium.[65]

The reviewers reported that they were unable to combine results from the primary studies because of the methodological differences between the studies.[65] One of the differences noted between studies was the delirium assessment measures used and professional backgrounds of the assessors.[65]

[a]One of the eight relevant studies did not report mean age of participants.

4.5.5 Dementia

I found one review that summarised the prevalence of dementia diagnoses in general hospital inpatients.[11] It summarised studies on older (aged > 55 years) inpatients admitted to a variety of general hospital wards for reasons other than hip fracture (e.g. medical, surgical, gynaecological, trauma, orthopaedic and geriatric wards).[11]

It reported prevalence estimates that ranged widely, from 2.8% to 63.0%.[11] The reviewers attributed this wide prevalence range, in part, due to the clinical heterogeneity noted in the study populations.[11] For example, the lowest prevalence estimate was reported in a study of relatively young inpatients (mean age of 69.9 years) admitted to medical, surgical and gynaecological wards.[11] By contrast, the highest prevalence estimate came from a study of older inpatients (mean age of 82.0 years) admitted to a geriatric unit. Due to the considerable differences in study populations (see **Table 3** for I^2 values), the reviewers reported that it was not possible to combine results from studies.[11]

The reviewers reported that the quality of the studies included varied widely, with many studies not explicitly stating their selection criteria or response rates.[11]

4.5.6 Substance abuse

I did not find any reviews that summarised studies of the prevalence of substance abuse in adult general hospital inpatients.

Table 3. Additional details on the systematic reviews of the prevalence of psychiatric illnesses in general hospital inpatients included in the meta-review

Review	Aim(s)	Summary of criteria for including primary studies	Databases searched	Studies in review that were of the prevalence of psychiatric illnesses in adult general hospital inpatients			
				Number of studies	Risk of bias and/or quality assessment(s)	Heterogeneity	Method(s) of synthesis/ analysis
Castro-de-Araújo et al. (2013, 2015)[60,61]	To investigate studies published between 1991 and 2010 on the prevalence of depressive morbidity among elderly Brazilians assisted at healthcare facilities; to establish the prevalence of depression and identify its related factors; and to conduct a meta-analysis to assess the prevalence of depressive syndrome among elderly individuals assisted or hospitalised at healthcare facilities.	Participants aged ≥ 60 years; major depressive disorder, dysthymia or clinically significant depressive symptoms defined according to standard diagnostic criteria or structured questionnaires; population-based study; publication in Portuguese, English or Spanish.	LILACS, MEDLINE and SciELO from January 1991 to June 2010.	Subgroup (4 of 15)	No risk of bias or quality assessment conducted.	I^2 = 80.6%, τ^2 = 0.074, p = 0.0014.	Narrative synthesis. Meta-analysis using random-effects model.
Mitchell et al. (2011)[62]	To quantitatively summarise the prevalence of robustly defined depression, anxiety and adjustment disorders in patients with cancer	Participants aged ≥ 18 years with cancer in hospital setting; caseness determined using psychiatric interviews; depression not	EMBASE, MEDLINE, PsycINFO and Web of Knowledge[a] from inception	Subgroup (8 of 94)	5-point bias risk scale (0=no appreciable bias risk to 4=high bias risk). 4-point	–	Meta-analysis using random-effects model.

	in oncological, haematological and palliative-care settings; and to examine the main correlates of depression in these settings.	reported before diagnosis of cancer; not epidemiologically selective sample or community survey.	to November 2010.		quality rating scale (1=low quality to 4=high quality). Mean bias risk 2 (range 1 to 3); Mean quality score 2 (range 1 to 3)*.		
Mitchell et al. (2017)[63]	To ascertain the prevalence and predictors of mood disorders, determined by structured clinical interviews (ICD or DSM criteria) in people after stroke.	Participants were adults who had experienced a stroke; depression, anxiety or mood disorder determined using robust interview by trained professional (not 2-stage procedure, not lifetime) in acute hospital, rehabilitation or community setting.	MEDLINE (PubMed), PsycINFO and Web of Knowledge from inception to June 2016.	Subgroup (33[b] of 108)	5-point bias risk scale (0=no appreciable bias risk to 4=high bias risk). 4-point quality rating scale (1=low quality to 4=high quality). Mean bias risk 1 (range 1 to 3); Mean quality score 3 (range 2 to 4)*.	Any anxiety disorder diagnosis: I^2 = 90.7% (95% CI, 70.8% to 95.2%); Major depression: I^2 = 89.1% (95% CI, 86.1% to 91.2%); Any depression diagnosis: I^2 = 88.6% (95% CI, 84.9% to 91.1%).	Meta-analyses using random-effects model.
Mukadam & Sampson (2011)[11]	To review systematically the prevalence, associations and outcomes of dementia in older people	Participants aged > 55 years in general hospital (not hip fractures); caseness defined using validated diagnostic	EMBASE, MEDLINE, PsycINFO and PubMed (from 1974, 1950, 1806 and	All (14)	10-item quality rating scale (higher scores better).	Studies using DSM-III/III-R criteria: I^2 = 98% (95% CI, 97% to 99%);	Narrative synthesis. Did not conduct meta-analysis due to

	admitted to general hospitals; to examine the range of diagnostic tools used; and to highlight gaps in the literature.	criteria; publication in English.	1950 respectively) to March 2008.		Mean quality score 7 (range 4 to 9)*.	Studies using DSM-IV criteria: I^2 = 87% (95% CI, 64% to 96%).	considerable heterogeneity in study populations.
Ren et al. (2014)[64]	To estimate the pooled prevalence of depression comorbid with coronary heart disease (CHD) in China with meta-analysis.	Participants were adults with established CHD.	CNKI, EMBASE, Ovid MEDLINE and WANFANG from inception to September 2013.	Subgroup (23 of 27)	Study-specific assessment measure based on STROBE statement. 8 studies had low bias risk.	I^2 = 97%, p = 0.000.	Narrative synthesis. Meta-analysis using random-effects model.
Siddiqi et al. (2006)[65]	To determine occurrence (prevalence, incidence and occurrence) and outcomes of delirium in medical inpatients, through a systematic review of the literature.	Participants were general medical inpatients or similar (not delirium tremens, psychiatric unit, surgical unit, accident and emergency, hospice, intensive care unit, or patients referred to liaison psychiatry); caseness determined using current consensus criteria.	ACP Journal Club, CCTR, CDSR, CINAHL, EMBASE, MEDLINE and PsycINFO between 1980 and July 2005. Handsearched Consultation-Liaison Literature Database.	Subgroup (8 of 40)	Only included studies that met quality criteria adapted from Evidence-Based Mental Health "Guidelines for Evaluating Prevalence Studies" and American Medical Association "Users Guide to Evidence-Based Medicine".	–	Narrative synthesis. Did not conduct meta-analysis due to considerable methodological heterogeneity in studies.

Thombs et al. (2006a)[66] **Bush et al. (2005)**[67]	To assess the prevalence and persistence of depression in adult patients with acute myocardial infarction (AMI), and the relationship between assessment modality and prevalence.	Participants with AMI; timing of depression assessment relative to AMI reported; depressive caseness determined using standardised interview or validated questionnaire; publication since 1980 and in English.	CINAHL, Cochrane, EMBASE, MEDLINE and PsycINFO between 1980 and March 2004.	Subgroup (24 of 33)	Quality criteria of International GRADE Working Group. Study-specific methodological quality assessment measure. Overall quality of studies was medium.	–	Narrative synthesis. Meta-analyses estimating weighted prevalences.
Thombs et al. (2006b)[68]	To systematically review the prevalence, persistence and risk factors for depression in patients post-burn injury.	Participants with burn injuries (not self-inflicted); standardised depression interview or validated questionnaire; published in English.	CINAHL, MEDLINE and PsycINFO (search conducted in June 2006).	Subgroup (5 of 18)	4-tiered bias rating system based on American Academy of Neurology guidelines (level 1=low bias to level 4=very high bias). All studies scored level 4.	–	Narrative synthesis.
Walker et al. (2013)[69]	To obtain the best estimate of the prevalence of depression in clinically meaningful subgroups of cancer patients (inpatient, outpatient,	Participants aged ≥ 18 years with definite cancer diagnosis; depression caseness determined using diagnostic interviews.	EMBASE Classic+ EMBASE, MEDLINE, PsycINFO (from 1947, 1950 and 1806	Subgroup (2 of 15)	Only included studies that used random or consecutive sampling, had ≥ 70% response rate, had a clear	–	Narrative synthesis.

	mixed and palliative care).		respectively), BIOSIS and WOS to January 2012.		definition of depression caseness (using standard diagnostic criteria) and sample size ≥ 100.		
Walker et al. (2018)[70]	To conduct a systematic review of studies of the prevalence of depression in general hospital inpatients.	Participants aged ≥ 16 years in general hospital; depression caseness determined using diagnostic interviews.	EMBASE, MEDLINE and PsycINFO (from 1974, 1946 and 1976 respectively) to December 2015.	All (60)	Only included studies that used random or consecutive sampling, had ≥ 70% response rate and had a clear definition of depression caseness (using standard diagnostic criteria).	Studies of general medical or surgical inpatients (31 of 60): I^2 = 91%.	Narrative synthesis. Meta-analysis using random-effects model.

ACP = American College of Physicians; AMI = Acute Myocardial Infarction; BIOSIS = BioSciences Information Service of Biological Abstracts; CCTR = Cochrane Controlled Trials Register; CDSR = Cochrane Database of Systematic Reviews; CHD = Coronary Heart Disease; CI = Confidence Interval; CINAHL = Cumulative Index to Nursing and Allied Health Literature; CNKI = China National Knowledge Infrastructure; DSM = Diagnostic and Statistical Manual of Mental Disorders; EMBASE = Excerpta Medica dataBASE; GRADE = Grading of Recommendations Assessment, Development and Evaluation; ICD = International Classification of Diseases; LILACS = Latin American and Caribbean Health Sciences Literature; MEDLINE = Online counterpart to MEDLARS (MEDical Literature Analysis and Retrieval System); PsycINFO = Psychological Information Database; SciELO = Scientific Electronic Library Online; STROBE = STrengthening the Reporting of OBservational studies in Epidemiology; WANFANG = Wanfang Data; WOS = Web of Science.

[a]Authors reported searching Web of Knowledge in abstract of review, but not in text of review.

[b]Review included 147 analyses (in 108 publications), 33 of which took place in an acute hospital setting.

*Calculated using data reported in review.

Table 4. Psychiatric assessment measures and caseness definitions reported in the systematic reviews of the prevalence of psychiatric illnesses in general hospital inpatients included in the meta-review

Psychiatric Illness	Review	Assessment measure(s)	Caseness definition(s)
Anxiety	Mitchell et al. (2017)[63]	Clinical interviews.	DSM or ICD criteria.
Depression	Castro-de-Araújo et al. (2013, 2015)[60,61]	GDS (1 study); GDS-15 (2 studies); HAM-D (1 study).	NA (4 studies).
	Mitchell et al. (2011)[62]	Clinical interview (2 studies); SCID (3 studies); NA (3 studies).	DSM-III (2 studies); DSM-III-R (3 studies); DSM-IV (2 studies); ICD-10 (1 study).
	Mitchell et al. (2017)[63]	*Major depression:* CIDI (2 studies); CPRS, HDRS (1 study); MINI (1 study); PSE (10 studies); RDC (1 study); SADS interview (3 studies); SCID (9 studies); Unstructured clinical interview (4 studies). *Any depression diagnosis:* Clinical interviews.	*Major depression:* DSM-III (7 studies); DSM-III-R (6 studies); DSM-IV (14 studies); DSM-IV-R (1 study); DSM-IV-TR (2 studies); RDC (1 study). *Any depression diagnosis:* DSM or ICD criteria.
	Ren et al. (2014)[64]	BDI (1 study); GDS (1 study); HADS (2 studies); HAMD (5 studies); HAMD & HADS (2 studies); HAMD & SDS (2 studies); SDS (10 studies).	NA (23 studies).
	Thombs et al. (2006a)[66,a] Bush et al. (2005)[67]	BDI (7 studies); BDI & HAM-D (1 study); BDI-II (1 study); DIS (4 studies); DISH (1 study); HADS (5 studies); HAM-D (1 study); Holland Sgroi Anxiety Depression Scale (1 study); Montgomery-Asberg (1 study); PSE (1 study); RDC (1 study); SCID (1 study).	BDI ≥ 10 (5 studies); BDI ≥ 10, HAM-D caseness NA (1 study); BDI ≥ 13 (1 study); BDI ≥ 16 (1 study); BDI-II ≥ 12 (1 study); Clinical interview (8 studies); HADS ≥ 8 (1 study); HADS ≥ 11 (1 study); HADS ≥ 8, ≥ 11 (3 studies); NA (3 studies).
	Thombs et al. 2006b)[68]	BDI (1 study); BDI-SF (1 study); SCID-III-R (2 studies); ZDS (1 study).	BDI ≥ 8 (1 study); BDI-SF ≥ 8 (1 study); DSM-III-R (2 studies); NA (1 study).
	Walker et al. (2013)[69]	SCID (2 studies).	DSM (2 studies).

Psychiatric Illness	Review	Assessment measure(s)	Caseness definition(s)
	Walker et al. (2018)[70,b]	CIDI (2 studies); CIS (2 studies); CIS + clinical interview if psychiatric diagnosis or MMSE < 23 (1 study); Clinical interview (3 studies); DIS (3 studies); GMS (2 studies); Interview based on the DIS (1 study); MINI (3 studies); MINI-Plus (1 study); PSE (2 studies); SCAN (2 studies); SCID-III-R (1 study); SCID-IV (4 studies); Semi-Structured Interview (2 studies); Standardised Psychiatric Interview Modified Version (1 study); Structured Diagnostic Assessment Questionnaire (1 study).	CATEGO computer programme, inclusive approach (1 study); DSM-III (3 studies); DSM-III, actuarial approach (1 study); DSM-III-R (6 studies); DSM-III-R, aetiologic approach (1 study); DSM-III-R, inclusive approach (1 study); DSM-IV (10 studies); DSM-IV, etiologic approach (1 study); ICD-9 (3 studies); ICD-10 (2 studies); ICD-10 Diagnostic Criteria for Research (1 study); SCAN (1 study).
Delirium	Siddiqi et al. (2006)[65]	CAM & clinical data (1 study); Clinical judgement (Folstein & McHugh method) (1 study); DAS & MMSE (1 study); MMSE, BPRS & clinical examination (1 study); MSQ, MMSE & clinical examination (1 study); OBS Scale (1 study); SPMSQ & CAM (2 studies).	CAM (1 study); DSM-III (4 studies); DSM-III-R (2 studies); DSM-IV (1 study).
Dementia	Mukadam & Sampson (2011)[11]	AMTS (1 study); CAMDEX & MMSE (1 study); CAPE (1 study); CIS & Global Severity Scale (1 study); Clinical examination (1 study); MMSE (1 study); MMSE & CAMCOG (1 study); MMSE & IQCODE (1 study); MMSE, Digit Span & WAIS (1 study); MMSE & Short Cognitive Evaluation (1 study); MSQ & MMSE (1 study); SPMSQ & clinical examination (2 studies); SRQ-24, GMS & MMSE (1 study).	CSHA (1 study); DSM-III (2 studies); DSM-III-R (6 studies); DSM-IV (2 studies); DSM-IV-TR (1 study); ICD-10 (2 studies).

Note: Assessment measures and caseness definitions taken from the systematic reviews' tables, where not available in the text.
AMTS = Abbreviated Mental Test Score; BDI = Beck Depression Inventory; BDI-SF = Beck Depression Inventory-Short Form; BPRS = Brief Psychiatric Rating Scale; CAM = Confusion Assessment Method; CAMCOG = Cognitive section of CAMDEX; CAMDEX = Cambridge Mental Disorders of the Elderly Examination; CAPE = Clifton Assessment Procedure for the Elderly; CIDI = Composite International Diagnostic Interview; CIS = Clinical Interview Schedule; CPRS = Comprehensive Psychiatric Rating Scale; CSHA = Canadian Study of Health and Aging protocol; DAS = Delirium Assessment Scale; DIS = Diagnostic Interview Schedule; DISH = Depression Interview and Structured Hamilton; DSM = Diagnostic and Statistical Manual of Mental Disorders; GDS = Geriatric Depression Scale; GMS = Geriatric Mental State / Geriatric Mental State Schedule; HADS = Hospital Anxiety and Depression Scale; HAM-D / HAMD / HDRS = Hamilton Rating Scale for Depression / Hamilton Depression Scale / Hamilton Depression Rating Scale; ICD = International Classification of Diseases; IQCODE = Informant Questionnaire on Cognitive Decline in the Elderly; MINI = Mini-International Neuropsychiatric Interview; MMSE = Mini-Mental State Examination; MSQ = Mental Status Questionnaire; NA = Not Available; OBS Scale = Organic Brain Syndrome Scale; PSE = Present State Examination; RDC = Research Diagnostic Criteria; SADS = Schedule for Affective Disorders and Schizophrenia; SCAN = Schedules for Clinical Assessment in Neuropsychiatry; SCID = Structured Clinical Interview for DSM; SDS = Zung Self-

Rating Depression Scale; SPMSQ = Short Portable Mental Status Questionnaire; SRQ-24 = Self-Reporting Questionnaire (24 item); WAIS = Wechsler Adult Intelligence Scale; ZDS = Zung Depression Scale.
[a]One study was included twice because it reported two prevalence estimates (one using clinical interview, one using rating scale).
[b]Subset of studies (31 of 60) of general medical and/or surgical inpatients.

4.5.7 Quality assessments

I summarise results of the AMSTAR 2 and PRISMA checklist assessments in **Table 5** and **Table 6** respectively**.** I found the quality of most systematic reviews to be low. Reasons for low-quality included: (1) not having a registered and accessible protocol; (2) applying strict language restrictions when selecting studies; (3) incomplete reporting on characteristics of studies included; and (4) lack of explicit clinical and statistical justifications for conducting meta-analyses. Most systematic reviews also did not report their studies' funding sources or assess for publication bias; however, these quality measures are less relevant to prevalence studies than other study designs (e.g. trials).

Although the overall quality of most of the systematic reviews was poor, there were some aspects of good quality, including: (1) selecting studies and extracting data in duplicate; (2) including studies with appropriate designs for estimating prevalence; (3) assessing studies for sample representativeness; and (4) discussing heterogeneity observed in their results.

Table 5. AMSTAR 2 quality assessments of the systematic reviews in the meta-review of the prevalence of psychiatric illnesses in general hospital inpatients

AMSTAR 2 Domain	Castro-de- Araújo et al. (2013, 2015)[60,61]	Mitchell et al. (2011)[62]	Mitchell et al. (2017)[63]	Mukadam & Sampson (2011)[11]	Ren et al. (2014)[64]	Siddiqi et al. (2006)[65]	Thombs et al. (2006a)[66] Bush et al. (2005)[67]	Thombs et al. (2006b)[68]	Walker et al. (2013)[69]	Walker et al. (2018)[70]
1[a]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
2	N	N	N	N	N	N	N	N	N	N
3[a]	Y	Y	Y	Y	N**	Y	N	Y	Y	Y
4[a]	N	Y	Y	N	N	N	N	N	PY	PY
5	N	N**	Y	N	Y	N	Y	Y	Y	Y
6	N	Y	Y	N**	Y	N**	Y	Y	Y	Y
7	N	N	N	N	N	Y	Y	N	Y	Y
8[a]	N	N	N	N	N	Y	Y	N	N	N
9[a]	N	Y	Y	Y	N	Y	Y	Y	Y	Y
10	N	N	N	N	N	N	N	N	N	N
11[a]	N	N	N	N*	N	N*	N	N*	N*	Y
12	N	Y	Y	N*	N	N*	N	N*	N*	Y
13	N	Y	Y	Y	N	Y	Y	Y	Y	Y
14	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
15	N	Y	Y	N*	N	N*	N	N*	N*	N
16	Y	Y	Y	Y	N	Y	Y	Y	Y	Y

AMSTAR 2 = A MeaSurement Tool to Assess systematic Reviews 2.
Legend: “Y” = Yes; “PY” = Partial Yes; “N” = No; “N*” = No because no meta-analysis; “N**” = “No because unclear”.
[a]Indicates domain has been adapted (see **Appendix 2** for adaptations).
1. Research question and inclusion criteria included necessary components; 2. Review contained explicit statement of methods established prior to conduct of review and reported any significant deviations from protocol; 3. Selected appropriate study designs for inclusion; 4. Used comprehensive search strategy; 5. Performed study selection in duplicate; 6. Performed data extraction in duplicate; 7. Provided list of excluded studies and justification for exclusion; 8. Described included studies in adequate detail; 9. Used satisfactory technique for assessing the risk of bias in individual studies included in review; 10. Reported sources of funding for studies included in review; 11. If meta-analysis performed, used appropriate methods for statistical combination of results; 12. If meta-analysis performed, assessed impact of risk of bias in individual studies on results; 13. Accounted for risk of bias in individual studies when interpreting/ discussing results; 14. Provided satisfactory explanation for, and discussion of, any heterogeneity observed in results; 15. Carried out an adequate investigation of publication bias and discussed likely impact on results; and 16. Reported any potential sources of conflict of interest (including funding and role of funders).[38]

Table 6. PRISMA checklist quality assessments of the systematic reviews in the meta-review of the prevalence of psychiatric illnesses in general hospital inpatients

PRISMA Checklist Item	Castro-de- Araújo et al. (2013, 2015)[60,61]	Mitchell et al. (2011)[62]	Mitchell et al. (2017)[63]	Mukadam & Sampson (2011)[11]	Ren et al. (2014)[64]	Siddiqi et al. (2006)[65]	Thombs et al. (2006a)[66] Bush et al. (2005)[67]	Thombs et al. (2006b)[68]	Walker et al. (2013)[69]	Walker et al. (2018)[70]
1	Y	Y	Y	Y	Y	Y	N	Y	Y	Y
2	N	Y	Y	Y	N	N	N	N	N	N
3	Y	Y	N	Y	Y	Y	Y	Y	Y	Y
4	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
5	N	N	N	N	N	N	N	N	N	N
6	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
7	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
8	Y	Y	Y	Y	N	N	Y	Y	Y	Y
9	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
10	Y	Y	Y	N	Y	N	Y	Y	Y	Y
11	Y	N	Y	Y	Y	N	Y	N	Y	Y
12	N	Y	Y	Y	Y	Y	Y	Y	Y	Y
13	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
14	Y	Y	Y	N	Y	N	N	N	N	Y
15	N	Y	Y	N	N	N	N	N	N	N
16	N	Y	Y	N	N	N	N	N	N	Y

PRISMA Checklist Item	Castro-de- Araújo et al. (2013, 2015)[60,61]	Mitchell et al. (2011)[62]	Mitchell et al. (2017)[63]	Mukadam & Sampson (2011)[11]	Ren et al. (2014)[64]	Siddiqi et al. (2006)[65]	Thombs et al. (2006a)[66] Bush et al. (2005)[67]	Thombs et al. (2006b)[68]	Walker et al. (2013)[69]	Walker et al. (2018)[70]
17	Y	Y	Y	N	Y	Y	Y	N	Y	Y
18	Y	Y	Y	Y	Y	Y	Y	Y	N	Y
19	N	Y	Y	Y	N	N	Y	Y	Y	Y
20	Y	N	N[a]	Y	Y	Y	Y	Y	Y	Y
21	Y	Y	Y	N	Y	N	N	N	N	Y
22	N	Y	Y	N	N	N	N	N	N	N
23	N	Y	Y	N	N	N	N	N	N	Y
24	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
25	Y	Y	Y	Y	N	Y	Y	Y	Y	Y
26	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
27	Y	Y	Y	N	N	Y	Y	Y	Y	Y

PRISMA checklist = Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist.
Legend: “Y” = Yes & “N” = No.
[a]Authors reported the results of the primary studies of the prevalence of major depression in acute settings but not remainder of primary studies.
1. Title: Identified as a systematic review, meta-analysis or both; 2. Structured summary; 3. Rationale; 4. Objectives: Provided an explicit statement of questions being addressed; 5. Protocol and registration details; 6. Eligibility criteria; 7. Information sources: Described all information sources in the search and date last searched; 8. Search: Presented full electronic search strategy for at least one database; 9. Study selection: Stated process for selecting studies; 10. Data collection process: Described method of extracting data; 11. Data items: Listed and defined all variables for which data were sought; 12. Risk of bias in individual studies: Described methods used for assessing risk of bias; 13. Summary measures: Stated principal summary measures; 14. Synthesis of results: Described methods of handling data and combining results of studies (including heterogeneity); 15. Risk of bias

across studies: Specified any assessment of risk of bias that may affect cumulative evidence; 16. Additional analyses: Described methods of additional analyses; 17. Study selection: Gave numbers of studies screened, assessed for eligibility and included in review, with reasons for exclusions at each stage; 18. Study characteristics: For each study, presented characteristics for which data were extracted; 19. Risk of bias within studies: Presented data on risk of bias of each study; 20. Results of individual studies: Provided summary data for each study and confidence intervals; 21. Synthesis of results: Presented results of each meta-analysis done (including heterogeneity); 22. Risk of bias across studies: Presented results of any assessment; 23. Additional analysis: Gave results of any additional analysis, if done; 24. Summary of evidence: Summarised main findings and considered relevance of findings to key groups; 25. Limitations: Discussed limitations at the study, outcome and review-level; 26. Conclusions: Provided an interpretation of results; and 27. Funding: Described sources of funding and role of funders.[39]

4.6 Discussion

4.6.1 Main findings

To my knowledge, this is the first meta-review of the prevalence of psychiatric illnesses in general hospital inpatients. Ten systematic reviews met selection criteria.[11,60-70] The prevalence of anxiety was summarised in only one review of limited relevance,[63] depression in eight,[60-64,66-70] delirium in only one,[65] dementia in only one,[11] and substance abuse in none. The reviews reported a wide range of prevalence estimates and focussed on different patient populations.

In the reviews of the whole population of general hospital inpatients (i.e. not inpatients with specific medical illnesses), the prevalence of diagnosed:

(1) **depression** ranged from 2% to 56% (mean prevalence of 12%[a]),[70]

(2) **delirium** ranged from 10% to 31% at admission,[65] and

(3) **dementia** ranged from 2.8% to 63.0%.[11,b]

There were **no reviews** of the prevalence of **anxiety** or **substance abuse** in the whole population of adult general hospital inpatients.

[a]Subsample of studies of general medical and surgical inpatients (prevalence estimates ranged from 2.7% to 33.6%).
[b]Studies of older general hospital inpatients.

4.6.2 Heterogeneity of systematic reviews

There was clear heterogeneity in the systematic reviews included in my meta-review, both *within* the reviews themselves as well as *between* reviews.

4.6.2.1 Heterogeneity within systematic reviews

In all five systematic reviews which assessed for heterogeneity between the primary studies they included, high heterogeneity was observed ($I^2 \geq 80\%$).[11,60,61,63,64,70] Some reviews attempted to account for the heterogeneity observed between their included studies when conducting their analyses: one review, for example, focussed its meta-analysis on studies of patients admitted to similar general hospital wards,[70] while two reviews did not conduct a meta-analysis because of the heterogeneity observed.[11,65] However, the majority of reviews conducted meta-analyses without providing explicit clinical and/or statistical justifications for doing so; this was highlighted in their AMSTAR 2 assessment (see **Section 4.5.7 Quality assessments** and **Table 5**).

4.6.2.2 Heterogeneity between systematic reviews

4.6.2.2.1 Population of interest

There were differences in the systematic reviews' population of interest. Some reviews defined their population of interest primarily by *setting.* Four reviews, for example, summarised studies of the whole population of patients admitted to general hospitals.[11,60,61,65,70] Therefore, their primary focus was the *general hospital setting*. This contrasted with other reviews which defined their population of interest primarily by a particular *medical illness* (e.g. cancer).[62-64,66-69] Amongst these reviews, there was also considerable differences in the types of medical illnesses they focussed on (e.g. cardiovascular disease, cancer and burn injuries). This fundamental difference between reviews makes it difficult to discuss how their findings relate to one another.

4.6.2.2.2 Assessment measures and caseness definitions

There was also a wide range of assessment measures and caseness definitions used to measure psychiatric illnesses between systematic reviews. This was apparent in the reviews which focussed on depression. Four reviews included studies that used diagnostic criteria in clinical interviews,[62,63,69,70] two included studies which used cut-off scores on rating scales,[60,61,64] and two included studies that used diagnostic criteria in clinical interviews and studies that used cut-off scores on rating scales.[66-68] Perhaps unsurprisingly, the reviews which combined results of studies that used cut-off scores on rating scales ("clinically significant depressive symptoms") reported larger prevalence estimates than

those that only included studies that used diagnostic criteria in clinical interviews ("depression diagnosis"). There are two notable examples of this:

(1) First – in reviews of the whole population[a] of general hospital inpatients – the estimated prevalence of diagnosed depression was 12% in one review[70] and clinically significant depressive symptoms was 45% in another review.[60,61]

(2) Second – in reviews of inpatients with heart diseases[b] – the estimated prevalence of diagnosed depression was 20.5% in one review[66,67] and clinically significant depressive symptoms was 51% in another review.[64]

The differences in assessment measures and caseness definitions *within* reviews and *between* reviews add to the complexity of concluding how common psychiatric illnesses are in general hospital inpatients.

[a]One review focussed on *adult* inpatients[70] and one review focussed on *older* inpatients.[60,61]
[b]One review focussed on inpatients hospitalised for an *acute myocardial infarction*[66,67] and one focussed on inpatients with *coronary heart disease*.[64]

4.6.3 Relevant systematic reviews not included in meta-review

There are a number of relevant systematic reviews that I found while conducting my meta-review, which aimed to summarise literature on psychiatric illness prevalence in general hospital inpatients but did not meet my strict selection criteria. I summarise the results of these reviews briefly in **Table 7**.

Amongst these systematic reviews, I found one rigorous review on the prevalence of substance abuse in general hospital inpatients.[71] This review summarised studies of the prevalence of alcohol-related conditions (defined using ICD-10 diagnostic criteria) in general hospital inpatients in the United Kingdom.[71] However, I did not include this review in my meta-review because it did not focus solely on studies of adult (aged ≥ 16 years) inpatients or provide a prevalence estimate for this subgroup. The review estimated that 16.10% of general medical and surgical inpatients and 17.07% of inpatients in intensive care units (ICUs) had a diagnosis of harmful use of alcohol.[71] It also estimated that 6.21% of inpatients on general medical and surgical wards and 17.41% of inpatients in ICUs had an alcohol dependence diagnosis.[71] It was not possible for me to determine how much these estimates were influenced by the inclusion of individuals aged less than 16 years in the studies without examining the primary studies included in this review.

I also found two reviews of interest that aimed to estimate the overall burden of psychiatric illnesses in general hospital inpatients. One of these reviews estimated that 32% of inpatients with cancer in acute care had a mental disorder diagnosis.[72] The second review summarised studies of the prevalence

of mental disorders in inpatients with chronic physical diseases, calculating a pooled prevalence of 39.2% in studies that used clinical interviews or rating scales.[73] These reviews shed light on how common psychiatric illnesses, as a whole, are in inpatient populations.

4.6.4 Recommendation for future systematic review

I found limited literature on the prevalence of anxiety in general hospital inpatients and only a review of the prevalence of anxiety disorders in inpatients who had experienced a stroke.[63] I found no reviews of the *whole population* of general hospital inpatients. My findings are consistent with those of a recent meta-review of the prevalence of anxiety in adult populations – this meta-review also did not report finding any reviews of anxiety in the general hospital setting.[74] Anxiety disorders are thought to be common and distressing in the medically ill,[4,74,75] and therefore potentially problematic for patients admitted to general hospitals. Consequently, there is an urgent need for a systematic review summarising literature on the prevalence of anxiety in the whole population of general hospital inpatients. I therefore conducted such a review in **Chapter 5**.

4.6.5 Strengths

My meta-review has several strengths. First, I worked alongside an information specialist to develop a systematic search strategy to find all relevant published reviews. Second, I applied strict inclusion criteria to minimise selection bias. Third, I did not apply any restrictions on language or publication date. Fourth, I conducted rigorous methodological and reporting quality assessments for all included reviews. Fifth, I included a wide range of psychiatric illnesses, which contrasts with previous reviews which have focussed on a single illness.

4.6.6 Limitations

My meta-review also has several limitations. First, meta-reviews are limited by the methods and reporting of the systematic reviews that they include; the quality of the systematic reviews in this meta-review was generally poor. Second, a meta-review can only report on the results of primary studies that have already been included in a published systematic review. Because of this, relevant literature conducted on the prevalence of psychiatric illnesses in general hospital inpatients has likely been overlooked and not included in this meta-review. Third, I could not provide an overall estimate of the prevalence of specific psychiatric illnesses, because the reviews had substantial clinical heterogeneity and included some of the same primary studies. Fourth, I did not attempt to include grey literature (i.e. literature that is not formally published in sources such as books or journal articles[76]). However, I did make efforts to find all of the relevant literature through my inclusive search strategies (e.g. searching multiple databases, contacting authors of relevant conference abstracts for associated publications and forward-citation searches of included reviews).

4.6.7 Implications and conclusions

My meta-review offers an overview of how common specific psychiatric illnesses are in the general hospital setting. This information may be helpful for busy healthcare professionals working in general hospitals who require a summary of how common psychiatric illnesses are in their patients and hospital managers who require information for planning the provision of psychiatric care in general hospitals.

Findings from my meta-review underscore that research on psychiatric illnesses in general hospital inpatients is still limited. Some psychiatric illnesses had no systematic reviews reporting on their prevalence in the whole population of adult general hospital inpatients. Furthermore, my quality assessments indicate that the relevant systematic reviews that have been done are generally poor quality. Consequently, there is a need for more high-quality research on the prevalence of psychiatric illnesses in general hospital settings.

Despite the limitations of the systematic reviews included in my meta-review, they offer reasonable evidence to conclude that psychiatric illnesses are common enough in general hospital inpatients to suggest their management is important.

Table 7. Relevant systematic reviews of the prevalence of psychiatric illnesses that were excluded from the meta-review

Psychiatric Illness	Review	Relevant patient population	Number of relevant primary studies	Finding(s)
Anxiety	Tully et al. (2014)[77]	Inpatients with coronary heart disease[a]	NA[e]	*Any anxiety disorder diagnosis* Pooled: 17.09% (95% CI, 8.27% to 32.03%)
Depression	Buckland et al. (2019)[78]	Female inpatients with coronary heart disease[b]	8	*Significant symptoms* Range: 27.9% to 40.3%; calculated average: 35.75%
	Lecheler et al. (2017)[79]	Patients hospitalised due to exacerbation of chronic obstructive pulmonary disease[b]	15	*Significant symptoms* Range: 9.5%[f] to 85.6%
	Rutledge et al. (2006)[80]	Inpatients with heart failure[b]	10	*Depression* Weighted "conservative" prevalence: 16% (SD = 9%)[g] Weighted "liberal" prevalence: 38% (SD = 13%)[h]
Delirium	Hosie et al. (2013)[81]	Inpatients in palliative care settings[a]	7	Range: 13.3% to 42.3% (at admission)[i] Range: 26% to 62% (during admission)[j]
	Khalighi et al. (2019)[82]	General hospital inpatients (Iran)[a]	23	Pooled: 21.8% (95% CI, 17.5% to 27.5%) (overall) Pooled: 24.7% (95% CI, 18.1% to 32.7%) (critical care only)[k] Pooled: 17.5% (95% CI, 13.6% to 22.3%) (general wards only)[l]
	Koirala et al. (2020)[83]	General hospital inpatients[a]	9	Range: 9% to 32%[m] Meta-analysis estimate: 22.3% (95% PI, 17.8% to 27.7%)
	Krewulak et al. (2018)[84]	Inpatients in intensive care units[b]	31	Pooled: 31% (95% CI, 24% to 41%)
	Watt et al. (2019)[85]	Inpatients in palliative care settings[a]	23	Range: 6.6% to 73% (median: 32%) (at admission)[n] Range: 19% to 88% (median: 60%) (during admission)[o]
Substance abuse	Roberts et al. (2019)[71]	General hospital inpatients (United Kingdom)[c]	NA[e]	*Harmful use of alcohol diagnosis (F10.1, ICD-10 DRC)* Pooled: 16.10% (95% CI, 13.87% to 18.45%) (medical/surgical) Pooled: 17.07% (95% CI, 14.23% to 20.35%) (ICU) *Alcohol dependence diagnosis (F10.2, ICD-10 DRC)* Pooled: 6.21% (95% CI, 3.57% to 9.48%) (medical/surgical) Pooled: 17.41% (95% CI, 14.54% to 20.71%) (ICU)

Psychiatric Illness	Review	Relevant patient population	Number of relevant primary studies	Finding(s)
Multiple psychiatric illnesses	Daré et al. (2019)[73]	Inpatients with chronic physical diseases (developing and emerging countries)[d]	13	*Mental disorder (symptoms and diagnosis)* Pooled: 39.2% (95% CI, 31.1% to 47.9%)
	Singer et al. (2010)[72]	Inpatients with cancer[d]	8	*Mental disorder diagnosis* Range: 23% to 53% Combined estimate: 32% (95% CI, 27% to 37%)
	Suwanpasu & Sattayasomboon (2015)[86]	Older medical inpatients hospitalised with a hip fracture[d]	15	*Delirium superimposed on dementia* Estimated prevalence: 69.7% (95% CI, 60.4% to 77.7%)

CI = Confidence Interval; DCR = Diagnostic Criteria for Research; ICD = International Classification of Diseases; ICU = Intensive Care Unit; NA = Not Available; PI = Prediction Interval; SD = Standard Deviation.

Excluded from meta-review because: [a]Not general hospital inpatients according to meta-review's definition; [b]Did not aim to estimate psychiatric illness prevalence using diagnostic criteria in clinical interviews or cut-off scores on rating scales (e.g. used medical records); [c]Not adults (aged ≥ 16 years); [d]Aimed to estimate the combined prevalence of multiple psychiatric illnesses, rather than a single psychiatric illness.

[e]In supplementary documents, reviewers reported the number of studies on inpatients, however did not specify the number included in their pooled prevalence analyses.

[f]Study that reported lowest prevalence assessed depression one year prior to admission.

[g]8 studies; [h]7 studies; [i]5 studies; [j]4 studies; [k]15 studies; [l]8 studies; [m]Reported 32% and 34% as highest prevalence in text; [n]18 studies; [o]11 studies.

Chapter 5
Prevalence of anxiety disorders in general hospital inpatients: A systematic review

5.1 Background

Anxiety disorders are characterised by excessive fear and worrying which cause individuals significant distress or functional impairment.[22] These psychiatric disorders are important in the medically ill because they are associated with greater symptom burden, lower quality of life and greater functional impairment.[4,75,87] While there are a number of systematic reviews of the prevalence of anxiety disorders in the medically ill, most of these focus on patient populations with specific medical illnesses (e.g. cardiovascular disease), rather than on patient populations in specific clinical settings.[74] My meta-review of the prevalence of psychiatric illnesses in general hospital inpatients (**Chapter 4**) highlighted that there are no systematic reviews of the prevalence of anxiety in the whole population of adult general hospital inpatients.

5.2 Research aim

I therefore aimed to summarise literature on the prevalence of anxiety disorders in general hospital inpatients.

5.3 Research question

What is the prevalence of anxiety disorders in general hospital inpatients? Specifically, what is the prevalence of panic disorder, generalised anxiety disorder and phobias in general hospital inpatients?

5.4 Methods

5.4.1 Study design

I conducted a *systematic review* of studies of the prevalence of anxiety disorders in adult general hospital inpatients (see **Chapter 3** for an explanation of a systematic review). I focussed on panic disorder, generalised anxiety disorder (GAD) and phobias.

(1) **Panic disorder** is characterised by *recurrent*, *unexpected* episodes of extreme anxiety ("panic attacks") which usually last for several minutes.[88] Symptoms of panic attacks include (but are not limited to) palpitations, increased heart rate, sweating, trembling and shortness of breath.[88]

(2) **GAD** is characterised by *persistent*, *excessive* anxiety and worry that is typically focussed on minor or everyday matters.[89] GAD is also marked by a variety of other symptoms, including restlessness, muscle tension, irritability and trouble concentrating.[89]

(3) **Phobias** are a group of anxiety disorders characterised by *excessive* fear that arises from a *specific object* or *situation*.[90] The phobic object or situation is usually avoided.[90]

5.4.2 Protocol

I registered my systematic review and its protocol on PROSPERO, number CRD42020189722. Similar to my meta-review, I wrote a protocol for this review to minimise the potential for bias during the review process.[26]

5.4.3 Selection criteria

I included studies if they met the following selection criteria: (1) the study clearly aimed to estimate the current prevalence of panic disorder, GAD or phobias (i.e. studies that were designed to address a different research question, but happened to include prevalence studies were excluded; studies that only reported the *combined* prevalence of *multiple* anxiety disorders were excluded); (2) anxiety caseness was determined using a clinical interview; (3) study participants (or a clear subgroup) were general hospital inpatients at the time of anxiety assessment; (4) study participants (or a clear subgroup) were adults (aged ≥ 16 years); (5) the publication was a primary study (i.e. not a review); (6) the publication was not a conference abstract only; and (7) the full publication was obtainable to allow for data extraction. I did not apply any language restrictions.

I applied three quality criteria to determine if studies met basic methodological standards. These three criteria formed a checklist.[69,70,91] I chose to use a "checklist approach" so that my quality assessments were consistent, systematic and reproducible. The three quality criteria were:

(1) the study sample was obtained using a random or consecutive sampling method;

(2) study data were available for analysis on at least 70% of the eligible patients; and

(3) anxiety caseness was clearly defined using standard diagnostic criteria (i.e. DSM[22], ICD[23] or similar).

I applied the first two criteria to ensure the study's sample was representative of the target population, thereby minimising selection bias. I applied the third criterion so that studies would be similar enough to compare their prevalence estimates. For each of the three criteria, every study was rated as "yes", "no" or "unknown". I did this, rather than calculate an overall quality score, because (1) it ensured that all key aspects of methodological quality were met and (2) it avoided making assumptions about the relative importance of each quality criterion item.[92]

5.4.4 Search strategy

As recommended,[26] I developed a search strategy by combining the main concepts from my research question: (1) prevalence, (2) anxiety disorders and (3) general hospital inpatients. Similar to my meta-review, I developed this search strategy with guidance from my supervisors and an information specialist, in an attempt to maximise its quality (see **Appendix 3** for search strategies).[26,33] I identified relevant studies by searching OVID MEDLINE, OVID EMBASE and OVID PsycINFO from database inception to August 2019. In my meta-review, I searched an additional two databases: EBSCO Host CINAHL and Scopus. I made the decision not to search these databases for my systematic review, because none of the relevant reviews included in my meta-review were uniquely found in either of these databases. When conducting reviews, it is important to balance the thoroughness of a search with the efficient and pragmatic use of time.[26] I ran searches for the combination of "prevalence", "anxiety" and "general hospital inpatient" using standardised subject terms and free-text terms, including synonyms and alternative spellings. I also contacted the authors of relevant conference abstracts found through my electronic database search to obtain any associated publications. Finally, I searched through relevant systematic reviews to identify potentially relevant studies.

5.4.5 Data collection

I imported all articles identified through the electronic database search into EndNote. I screened all articles' titles and abstracts to determine whether each might meet my selection criteria. I then reviewed the full text of relevant articles, with the help of a translator where necessary.

I extracted data from all articles included in the review using a specially designed, standardised data extraction form. I extracted the following data: authors; setting (e.g. ward type, hospital type and country in which study took place); inclusion criteria; sample size; participants' ages; percentage of female participants; type of anxiety interview used; profession of the interviewer; anxiety caseness definition applied; and prevalence of anxiety in sample (for cohort studies, I extracted the prevalence of anxiety at the first time point only).

Each of the aforementioned steps were also completed by a second independent researcher to minimise the possibility of bias.[26] A third independent researcher (consultant psychiatrist and senior clinical researcher) also conducted quality criteria assessments to reduce any possibility of excluding relevant articles. This third independent researcher also resolved any disagreements between myself and the second independent researcher.

5.4.6 Analyses

5.4.6.1 Clinical analyses

I reviewed the data extracted from each of the eligible studies with my supervisors to determine whether or not it was appropriate to conduct meta-analyses. We found that there was a high degree of heterogeneity in the participants' clinical characteristics. While some studies focussed on general medical and/or surgical inpatients, for instance, others focussed on inpatients with very specific clinical characteristics (e.g. diagnosis of hyperemesis gravidarum) or on inpatients admitted to specialist wards (e.g. stem cell transplant units). The studies of inpatients with very specific clinical characteristics (or on specialist wards) were not representative of the broader population of general hospital inpatients.

In order to deal with this clinical heterogeneity, I chose to restrict statistical analyses to studies of general medical and/or surgical inpatients (I summarise the results of the remaining studies in table form). I also restricted the statistical analyses to studies that used DSM diagnostic criteria[22] (all but one study of general medical and/or surgical inpatients) to further reduce clinical heterogeneity.

5.4.6.2 Statistical analyses

I planned the statistical analyses and interpreted the findings. A professional statistician conducted the statistical analyses. Analyses were conducted for panic disorder and GAD, but not for phobias, because there was an insufficient number of studies of the prevalence of phobias.

Forest plots were used to display the proportion of patients diagnosed with panic disorder and the proportion diagnosed with GAD in each study. I^2 statistics were calculated to assess statistical heterogeneity, as they describe the total proportion of observed variation across studies that is due to between-study heterogeneity.[93] Larger I^2 values indicate greater between-study heterogeneity.[93]

Meta-analyses were conducted using random-effects models due to the considerable statistical heterogeneity found between included studies.[94] The prevalence estimates for panic disorder and for GAD were expressed as log-odds. The random-effects models assumed that these estimates followed normal distributions.[94] The inverse variance method was used in the meta-analyses. This means that larger studies with smaller standard errors (and therefore lower variance) were given greater weight.[26,94]

I report the mean of each distribution, which can be thought of as a “typical” prevalence of panic disorder and a “typical” prevalence of GAD. I also report the confidence intervals (CIs) associated with these means, to quantify the precision of the mean of the study-specific prevalences. I also report the 95% prediction intervals for panic disorder and for GAD to describe the between-

study variability of prevalence estimates. The 95% prediction intervals are the intervals within which 95% of the underlying study-specific prevalences of panic disorder and GAD are predicted to lie.[26,70]

5.5 Results

5.5.1 Overview

My initial screening of 17,755 titles and abstracts yielded 4,538 articles for full review. A second researcher and I considered 49 articles (of 48 separate studies) to be relevant. Of these, 27 articles (of 26 separate studies) met my quality criteria (see **Figure 4** for flowchart and **Table 8** for quality assessments).[95-121]

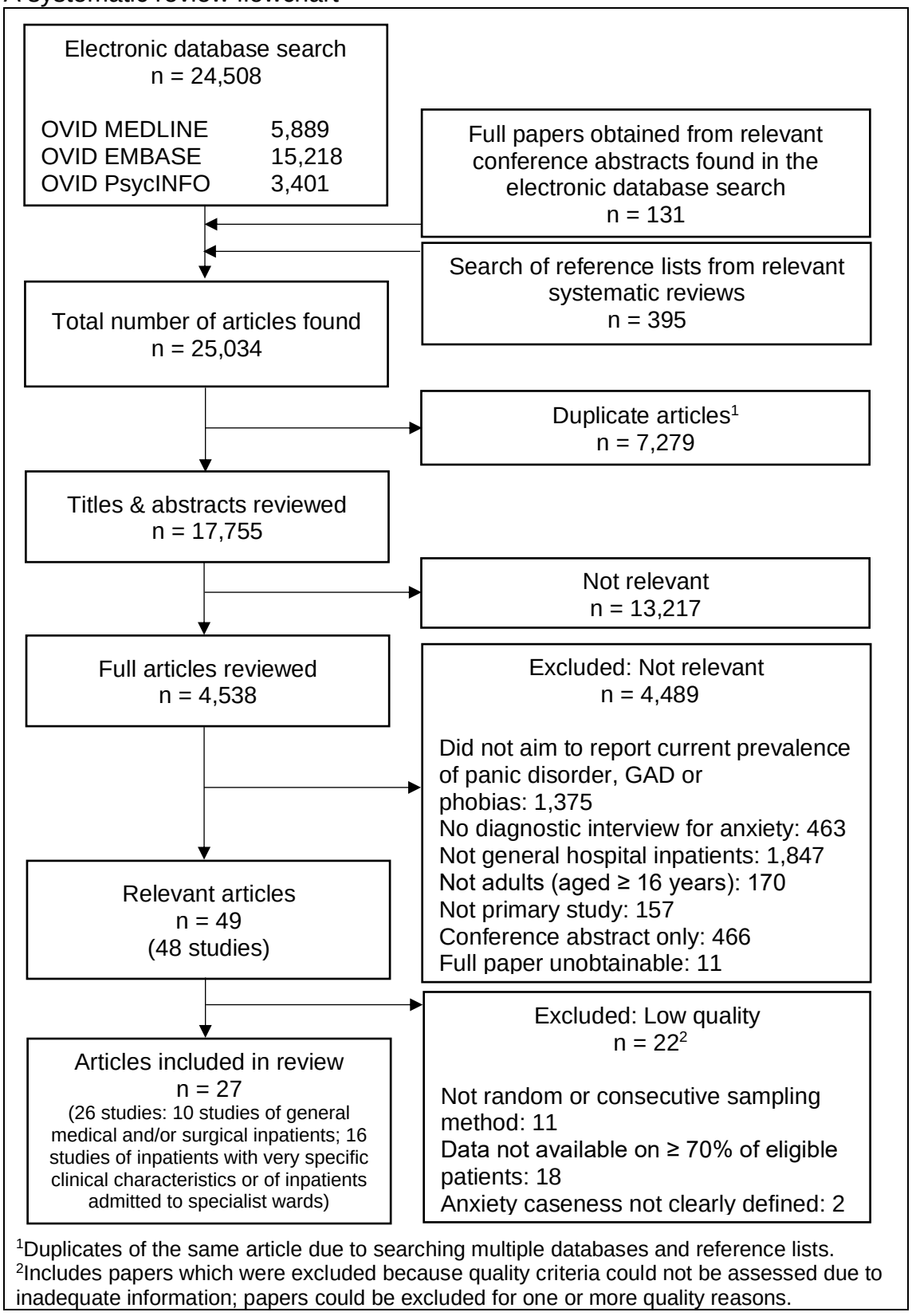
These 26 studies were conducted in 17 countries (Australia, Brazil, Finland, France, Germany, Greece, India, Italy, Japan, Nigeria, Pakistan, South Africa, Spain, Sweden, Turkey, the United Kingdom and the United States). They included a total of 4,737 participants (median sample size of 107, range from 31 to 719).

The prevalence of panic disorder was reported in 17 studies,[95-99,101,106-108,110,112,113,116-121] GAD in 22 studies,[95-99,101-105,107-109,111,113-121] and phobias in eight studies.[100,108,112-114,116-118,120] A variety of diagnostic interviews and associated criteria were used. The most commonly used diagnostic interview was the Structured Clinical Interview for DSM (SCID).[122] The vast majority of studies used DSM diagnostic criteria, and had a psychiatrist and/or psychologist conduct the diagnostic interviews.

10 studies were of general medical and/or surgical inpatients (see **Table 9**).[95-104] The remaining 16 studies were of inpatients with very specific clinical characteristics or of inpatients admitted to specialist wards, which meant their

samples were less representative of the target population of general hospital inpatients (see **Table 10**).[105-121]

Figure 4. Prevalence of anxiety disorders in general hospital inpatients: A systematic review flowchart



[1]Duplicates of the same article due to searching multiple databases and reference lists.
[2]Includes papers which were excluded because quality criteria could not be assessed due to inadequate information; papers could be excluded for one or more quality reasons.

Table 8. Quality assessments of the relevant studies in the systematic review of the prevalence of anxiety disorders in general hospital inpatients

Study	Random or consecutive sampling method	Data available on ≥ 70% of eligible patients	Anxiety caseness was clearly defined	Passes quality assessment
Aghanwa & Ndububa (2002)[105]	Yes	Yes	Yes	Yes
Alexander et al. (1993)[106]	Yes	Yes	Yes	Yes
Alexander et al. (1994)[107]	Yes	Yes	Yes	Yes
Ames et al. (1994)[123]	No	Unknown	Unknown	No
Annagür et al. (2013)[108]	Yes	Yes	Yes	Yes
Ateşci et al. (2004)[109]	Yes	Yes	Yes	Yes
Booth et al. (1998)[124]	Yes	Unknown	Yes	No
Bryant et al. (2009)[125]	Yes	Yes	Unknown	No
Bunevicius et al. (2005)[126]	Unknown	Unknown	Yes	No
Carter et al. (1992)[110]	Yes	Yes	Yes	Yes
Celano et al. (2013)[127]	Yes	No	Yes	No
Dicker et al. (2011)[128]	Unknown	No	Yes	No
Dogar et al. (2008)[111]	Yes	Yes	Yes	Yes
Dyster-Aas et al. (2008)[112]	Yes	Yes	Yes	Yes
Fava et al. (1984)[129]	Yes	Unknown	Yes	No
Hansen et al. (2001)[130]	Yes	No	Yes	No
Jenkins et al. (1994)[95]	Yes	Yes	Yes	Yes
John (2013)[131]	Unknown	Unknown	Yes	No
Jorge et al. (1993)[132]	Yes	Unknown	Yes	No
Kathol & Wenzel (1992)[96]	Yes	Yes	Yes	Yes
Kayhan et al. (2013)[97]	Yes	Yes	Yes	Yes
Köroğlu & Tural (2010)[98]	Yes	Yes	Yes	Yes
Kulkarni et al. (2013)[133]	Yes	Unknown	Yes	No
Lykouras et al. (1996)[113]	Yes	Yes	Yes	Yes
Madianos et al. (2001)[114]	Yes	Yes	Yes	Yes
Marchesi et al. (2001)[134]	Unknown	Yes	Yes	No
Marchesi et al. (2004)[99]	Yes	Yes	Yes	Yes
Martucci et al. (1999)[135]	No	No	Yes	No
Minagawa et al. (1996)[115]	Yes	Yes	Yes	Yes
Nair & Pillay (1997)[100]	Yes	Yes	Yes	Yes
Niecke et al. (2019)[136]	Unknown	No	Yes	No
Palmu et al. (2010, 2011)[116,117]	Yes	Yes	Yes	Yes
Petrak et al. (2003)[118]	Yes	Yes	Yes	Yes

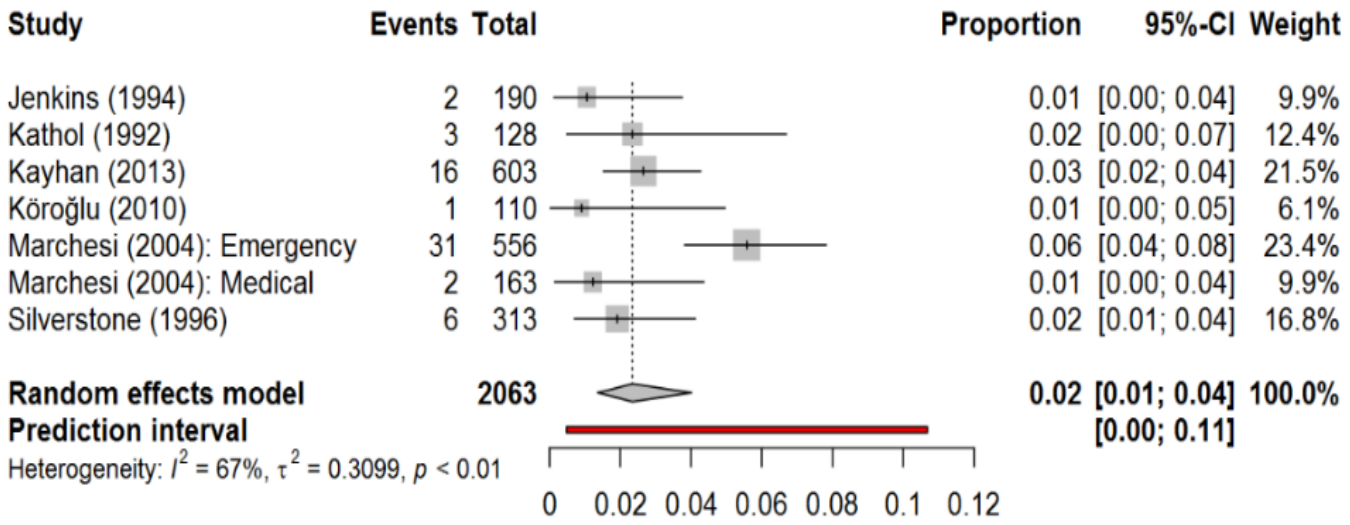
Study	Random or consecutive sampling method	Data available on ≥ 70% of eligible patients	Anxiety caseness was clearly defined	Passes quality assessment
Placidi et al. (1998)[137]	Yes	Unknown	Yes	No
Potoczek et al. (2006)[138]	Unknown	Yes	Yes	No
Potoczek et al. (2008)[139]	Unknown	Yes	Yes	No
Prieto et al. (2002)[119]	Yes	Yes	Yes	Yes
Radat et al. (1999)[140]	Yes	Unknown	Yes	No
Silverstone (1996)[101]	Yes	Yes	Yes	Yes
Singer et al. (2013)[120]	Yes	Yes	Yes	Yes
Singh et al. (2015)[141]	Unknown	Unknown	Yes	No
Soeiro et al. (2008)[102]	Yes	Yes	Yes	Yes
Tan et al. (2014)[142]	Yes	Unknown	Yes	No
Thalassinos et al. (1992)[103]	Yes	Yes	Yes	Yes
Uwakwe (2000)[104]	Yes	Yes	Yes	Yes
Vögele & von Leupoldt (2008)[143]	Yes	Unknown	Yes	No
Weiss & Rosenberg (1985)[144]	Unknown	Unknown	Yes	No
Yellowlees et al. (1987)[121]	Yes	Yes	Yes	Yes

5.5.2 Studies of general medical and/or surgical inpatients

5.5.2.1 Panic disorder

Six studies estimated the prevalence of panic disorder in general medical and/or surgical inpatients.[95-99,101] These included a total of 2,063 participants (median sample size of 251.5, range from 110 to 719). The studies all used DSM diagnostic criteria to define panic disorder caseness. There was moderate heterogeneity observed between study findings (I^2 = 67%).[93] The reported prevalence estimates ranged from 0.9% to 5.6%. The mean prevalence was 2% (95% CI, 1% to 4%) and the 95% prediction interval was 0% to 11% (see **Figure 5**).

Figure 5. Prevalence of panic disorder in studies of general medical and surgical inpatients included in the systematic review



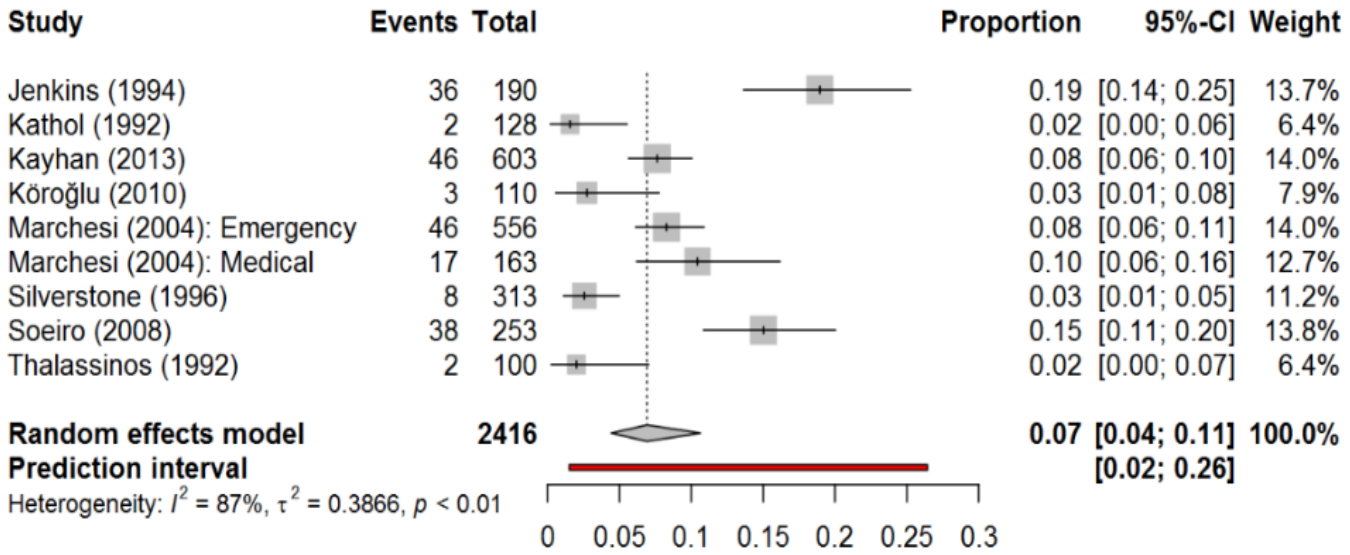
CI = Confidence Interval.

5.5.2.2 Generalised anxiety disorder (GAD)

Nine studies estimated the prevalence of GAD in general medical and/or surgical inpatients.[95-99,101-104] These included a total of 2,522 participants (median sample size of 190, range from 100 to 719). The reported prevalence estimates for GAD ranged from 0.9% to 18.9%.

Eight of the nine studies used DSM diagnostic criteria (total of 2,416 participants, median sample size of 221.5, range from 100 to 719).[95-99,101-103] There was high heterogeneity observed between study findings (I^2 = 87%).[93] The reported prevalence estimates ranged from 1.6% to 18.9%. The mean prevalence was 7% (95% CI, 4% to 11%) and the 95% prediction interval was 2% to 26% (see **Figure 6**).

Figure 6. Prevalence of generalised anxiety disorder in studies of general medical and surgical inpatients included in the systematic review



CI = Confidence Interval.

5.5.2.3 Phobias

There was limited information on the prevalence of phobias in general medical and surgical inpatients. Only one study reported the prevalence of simple phobia (also known as specific phobia[22]), with an estimate of 0.4%.[100]

5.5.3 Studies of inpatients with specific clinical characteristics or of inpatients admitted to specialist wards

17 articles (of 16 separate studies) were of inpatients with specific clinical characteristics or of inpatients admitted to specialist wards.[105-121] I summarise the results of these studies in **Table 10**. In brief, the prevalence of panic disorder was reported in 11 studies,[106-108,110,112,113,116-121] GAD in 13 studies,[105,107-109,111,113-121] and phobias in seven studies.[108,112-114,116-118,120] Studies included a total of 1,985 participants (median sample size of 83, range from 31 to 502).

Table 9. Studies of the prevalence of anxiety disorders in general medical and/or surgical inpatients included in the systematic review

Study	Setting	Inclusion criteria	Sample size	Age	% female	Anxiety interview (interviewer)	Diagnostic criteria	Anxiety prevalence (%)
Jenkins et al. (1994)[95]	General surgical wards in a university hospital (United Kingdom).	Aged 16 to 80 years; elective or emergency admission; pre-surgery; well enough to participate; able to read and speak English.	190	Not stated	Not stated	Stage 1: General Health Questionnaire (cut-off ≥ 12) Stage 2: Composite International Diagnostic Interview (psychiatrist)	DSM-III	Panic disorder: 1.1* GAD: 18.9*
Kathol & Wenzel (1992)[96]	Medical wards & medical subspecialty units in a Veterans Administration hospital and a university hospital (United States).	Likely to stay in hospital ≥ 3 days; no obvious memory difficulties; not requiring intensive care unit treatment; able to speak English.	128	Age (mean): 56	21%*	Stage 1: Hamilton Anxiety Scale and Hamilton Depression Rating Scale (cut-off ≥ 6 on either) Stage 2: Structured Diagnostic Assessment Questionnaire (trained interviewer)	DSM-III	Panic disorder: 2.3* GAD: 1.6*

Study	Setting	Inclusion criteria	Sample size	Age	% female	Anxiety interview (interviewer)	Diagnostic criteria	Anxiety prevalence (%)
Kayhan et al. (2013)[97]	General and subspecialty medical and surgical wards in a tertiary university hospital (Turkey).	Aged ≥ 18 years; hospitalised for ≥ 2 days; well enough to participate; no mental retardation, psychotic disorder or delirium; not in perinatal period.	603	Age (mean, SD): 51.07, 15.72	49.6%	Structured Clinical Interview for DSM-IV (psychiatrist)	DSM-IV	Panic disorder: 2.7 GAD: 7.6
Köroğlu & Tural (2010)[98]	Internal medicine wards in a university hospital (Turkey).	Aged 18 to 75 years; no delirium; not suffering from terminal-stage cancer.	110	Age (mean, SD): 47.2, 15.0	53.6%	Structured Clinical Interview for DSM-IV (not stated)	DSM-IV	Panic disorder: 0.9* GAD: 2.7*
Marchesi et al. (2004)[99]	Emergency ward (acute medical) & medical departments in a general hospital (Italy).	Aged 18 to 65 years; mentally and physically able to participate; Italian speaker.	719 (556 emergency, 163 medical)	Age (mean, SD): 41.8, 14.1 Emergency: 39.7, 13.7 Medical: 49.1, 12.8	Overall: 52.2% Emergency: 53.4% Medical: 47.9%	Stage 1: General Health Questionnaire-30 (cut-off > 4) Stage 2: Mini International Neuropsychiatric Interview (psychiatrist)	DSM-IV	*Emergency* Panic disorder: 5.6 GAD: 8.2 *Medical* Panic disorder: 1.2 GAD: 10.4

Study	Setting	Inclusion criteria	Sample size	Age	% female	Anxiety interview (interviewer)	Diagnostic criteria	Anxiety prevalence (%)
Nair & Pillay (1997)[100]	General medical, general surgical & gynaecological wards in an academic general hospital (South Africa).	Aged ≥ 18 years; well enough to participate.	230	Age (mean, range): 40, 18 to 82	57%	Stage 1: General Health Questionnaire-30 (cut-off ≥ 12), screening for abnormal mental state, past psychiatric history, substance abuse Stage 2: Structured Clinical Interview for DSM-III-R (psychiatrist)	DSM-III-R	Simple phobia: 0.4*
Silverstone (1996)[101]	Medical wards in a university hospital (United Kingdom).	Emergency admission; hospitalised for ≥ 7 days; able to communicate well enough for interview; score ≥ 22 on MMSE.	313	Age (mean, SE): DSM-IV diagnosis: 65.4, 1.6 No DSM-IV diagnosis: 71.9, 0.9	49%*	Schedule for Clinical Assessment in Neuropsychiatry (not stated)	DSM-IV	Panic disorder: 1.9* GAD: 2.6*
Soeiro et al. (2008)[102]	Medical & surgical wards in a tertiary university hospital	Aged ≥ 18 years; hospitalised for ≥ 2 days; not	253	Age (mean, SD, range): 47.1, 19.0, 18 to 85	43.1%	Mini International Neuropsychiatric Interview-Plus (trained interviewer)	DSM-IV	GAD: 15.0

Study	Setting	Inclusion criteria	Sample size	Age	% female	Anxiety interview (interviewer)	Diagnostic criteria	Anxiety prevalence (%)
	(Brazil).	disorientated or confused.						
Thalassinos et al. (1992)[103]	Internal medicine department of a university hospital (France).	Aged > 65 years; well enough to participate.	100	Age (mean, SD): Females: 80, 7 Males: 77, 7	71%	Diagnostic Interview Schedule (author)	DSM-III	GAD: 2.0
Uwakwe (2000)[104]	Medical, surgical & gynaecological wards in a university teaching hospital (Nigeria).	Aged ≥ 60 years; well enough to participate.	106	Age (mean, SD): 69.9, 8.4	38.7%	Geriatric Mental State Schedule (psychiatrist)	ICD-10 DCR	GAD: 0.9

DCR = Diagnostic Criteria for Research; DSM = Diagnostic and Statistical Manual of Mental Disorders; GAD = Generalised Anxiety Disorder; ICD = International Classification of Diseases; MMSE = Mini-Mental State Examination; SD = Standard Deviation; SE = Standard Error.
*Calculated using data from paper.

Table 10. Studies of the prevalence of anxiety disorders in specific inpatient groups[a] included in the systematic review

Study	Setting	Inclusion criteria	Sample size	Age	% female	Anxiety interview (interviewer)	Diagnostic criteria	Anxiety prevalence (%)
Aghanwa & Ndububa (2002)[105]	Gastroenterology unit in a university teaching hospital (Nigeria).	Diagnosis of liver cirrhosis; no history of psychiatric illness; no physical comorbidity; well enough to participate.	31	Age (mean, SD): 44.3, 13.1	38.7%*	Present State Examination (not stated)	ICD-10	GAD: 12.9
Alexander et al. (1993)[106]	Oncology unit of a medical college hospital (India).	Primary diagnosis of cancer; well enough for interview.	60	Age (mean, SD): 53.2, 13.9	40%*	Clinical interview (psychiatrist)	DSM-III-R	Panic disorder: 3
Alexander et al. (1994)[107]	Cardiology ward of a medical college hospital (India).	Chest pain; no evidence of rheumatic heart disease, non-ischaemic cardiomyopathy or congenital heart disease.	58 (28 non-cardiac chest pain, 30 ischemic heart disease)	Age (mean, SD): Non-cardiac chest pain: 41, 13 Ischemic heart disease: 56, 9	0%	Schedule for Affective Disorders and Schizophrenia (psychiatrist)	DSM-III-R	*Non-cardiac chest pain* Panic disorder: 50 GAD: 3.6 *Ischemic heart disease* Panic disorder: 10 GAD: 3.3
Annagür et al. (2013)[108]	Obstetric inpatient clinic of a university hospital (Turkey).	Diagnosis of hyperemesis gravidarum; aged 20 to 40 years; able to communicate in Turkish; no	47	Age (mean, SD): 27.38, 5.27	100%	Structured Clinical Interview for DSM-IV (psychiatrist)	DSM-IV	Panic disorder: 8.5 GAD: 12.8 Specific phobia: 4.3 Social phobia: 2.1

Study	Setting	Inclusion criteria	Sample size	Age	% female	Anxiety interview (interviewer)	Diagnostic criteria	Anxiety prevalence (%)
		severe medical illnesses or gestational problems; no cognitive impairment or psychosis.						
Ateşci et al. (2004)[109]	Gynaecology, obstetrics, oncology, medical and general surgical wards in a university hospital (Turkey).	Diagnosis of cancer; post-chemotherapy; literate; not terminally ill; no cognitive impairment.	117	Age (mean, SD): 53.7, 14.2	51.3%	Structured Clinical Interview for DSM-IV (psychiatrist)	DSM-IV	GAD: 0.9*
Carter et al. (1992)[110]	Coronary intensive care unit in a university hospital (United States).	Acute chest pain; able to give a reliable history.	62	Age (mean, SD): Panic disorder: 52.2, 11.3 No panic disorder: 65.0, 9.9	25.8%*	Structured Clinical Interview for DSM-III-R (psychiatrist, clinical psychologist)	DSM-III-R	Panic disorder: 30.6
Dogar et al. (2008)[111]	Cardiac unit in a tertiary care hospital (Pakistan).	Not specified.	100	Age (mean, SD): 52.2, 11.12	40%*	Clinical interview (not stated)	DSM-IV	GAD: 21*

Study	Setting	Inclusion criteria	Sample size	Age	% female	Anxiety interview (interviewer)	Diagnostic criteria	Anxiety prevalence (%)
Dyster-Aas et al. (2008)[112]	National burns unit in a university hospital (Sweden).	≥ 5% burns or hospitalised for > 1 day; aged ≥ 18 years; Swedish speaker; no documented cognitive impairment.	73	Age (mean, SD, range): 43.4, 15.6, 19 to 89	27.4%*	Structured Clinical Interview for DSM-IV (psychiatrist or trained interviewer)	DSM-IV	Panic disorder: 3 Simple phobia: 16 Social phobia: 6
Lykouras et al. (1996)[113]	Neurology department in a university hospital (Greece).	Able to communicate and read.	107	Age (mean, range): 43.7, 16 to 78	53.3%*	Structured Clinical Interview for DSM-III-R (psychiatrist)	DSM-III-R	Panic disorder 0.9* GAD: 14.0* Simple phobia: 0.9*
Madianos et al. (2001)[114]	Burns unit in a general hospital (Greece).	Able to communicate well enough for interview.	45	Age (mean, SD): Females: 52.6, 20.9 Males: 40.1, 13.5	44.4%*	Structured Clinical Interview for DSM-III-R (psychiatrist)	DSM-III-R	GAD: 2.2 Simple phobia: 6.7
Minagawa et al. (1996)[115]	Palliative care unit of a cancer hospital (Japan).	Incurable cancer; died within 6 months of hospital admission.	93	Age (mean, SD): 67.2, 11.9	41%	Stage 1: Mini-Mental State Examination (MMSE) Stage 2: Psychiatric interview with patient and relatives if	DSM-III-R	GAD: 1.1

Study	Setting	Inclusion criteria	Sample size	Age	% female	Anxiety interview (interviewer)	Diagnostic criteria	Anxiety prevalence (%)
						MMSE score < 24, Structured Clinical Interview for DSM-III-R if score ≥ 24 (psychiatrist)		
Palmu et al. (2010, 2011)[116,117]	National burns unit in a university hospital (Finland).	Aged ≥ 18 years; Finnish speaker; no cognitive or communication problems.	107	Age (mean, SD): 45.4, 16.4	29.9%	Structured Clinical Interview for DSM-IV-TR (psychiatrist)	DSM-IV-TR	Panic disorder: 5.6 GAD: 0 Simple phobia: 5.6 Social phobia: 0
Petrak et al. (2003)[118]	12 general hospitals, inpatient rehabilitation clinics and inpatient university clinics (Germany).	Recent diagnosis of type 1 diabetes; aged 17 to 40 years; able to understand German.	313	Age (mean, SD): 28.2, 6.3	37.7%	Diagnostic Interview for Mental Disorders short version (psychologist)	DSM-IV	Panic disorder: 1.0 GAD: 1.0 Simple phobia: 2.9 Social phobia: 2.2
Prieto et al. (2002)[119]	Stem cell transplant unit of a university hospital (Spain).	Diagnosis of haematological cancer; hospitalised for first stem cell transplant; aged ≥ 16 years.	220	Age (mean, range): 38.4, 16 to 65	41.4%*	Structured psychiatric interview (psychiatrist)	DSM-IV	Panic disorder: 1.4 GAD: 1.8

Study	Setting	Inclusion criteria	Sample size	Age	% female	Anxiety interview (interviewer)	Diagnostic criteria	Anxiety prevalence (%)
Singer et al. (2013)[120]	16 inpatient clinics (Germany).	Diagnosis of cancer; no recurrent disease or distant metastasis; treated with curative intent; aged ≤ 55 years; adequate proficiency in German.	502	33.9% aged < 45 66.1% aged 44 to 55	46.6%	Structured Clinical Interview for DSM-IV (trained interviewer)	DSM-IV	Panic disorder: 3.4 GAD: 2.6 Specific phobia: 4.0 Social phobia: 0.2
Yellowlees et al. (1987)[121]	Respiratory unit in a teaching hospital (Australia).	Chronic airflow obstruction (due to chronic bronchitis, emphysema or chronic asthma with a significant irreversible obstructive component); aged ≥ 40 years; ≥ 1 previous hospital admission caused by respiratory	50	Age (mean, SD, range): 65, 9.9, 40 to 81	36%*	Clinical interview (psychiatrist)	DSM-III	Panic disorder: 24 GAD: 10

Study	Setting	Inclusion criteria	Sample size	Age	% female	Anxiety interview (interviewer)	Diagnostic criteria	Anxiety prevalence (%)
		disease; not suffering from malignant disease.						

Note: Specific phobia and simple phobia are the same disorder.
DSM = Diagnostic and Statistical Manual of Mental Disorders; GAD = Generalised Anxiety Disorder; ICD = International Classification of Diseases; MMSE = Mini-Mental State Examination; SD = Standard Deviation.
[a]Inpatients with specific clinical characteristics or inpatients admitted to specialist wards.
*Calculated using data from paper.

5.6 Discussion

5.6.1 Main findings

To my knowledge, this is the first systematic review of the prevalence of anxiety disorders in the whole population of adult general hospital inpatients. The 27 articles (of 26 separate studies) included in this review were published between 1987 and 2013, were conducted in 17 countries, and included a total of 4,737 participants.[95-121] I found that studies reported a wide range of prevalence estimates for panic disorder, GAD and phobias. In studies of general medical and surgical inpatients which used DSM diagnostic criteria, I found that the mean prevalence of **panic disorder** was **2%** and **GAD** was **7%**. I also found that studies did not adequately address phobic anxiety – particularly agoraphobia and fear of falling – which is perhaps surprising given that this type of anxiety would likely have important implications for patient outcomes (e.g. the association between fear of falling and adverse rehabilitation outcomes in older adults, including greater functional decline and activity restriction[145]).

5.6.2 Interpretation of main findings

The mean prevalence of panic disorder and GAD in general medical and surgical inpatients may appear to be low, however these prevalence estimates are substantially greater than those which have been reported in the general population.[146,147] One systematic review estimated the current prevalence of panic disorder and GAD to be 0.88% and 2.30% respectively in older adults in Western countries.[146] Another review estimated the 12-month prevalence to be 0.99% and 2.6% in working age adults.[147]

It is perhaps not surprising that the prevalence of panic disorder and GAD is much higher in general medical and surgical inpatients than in the general population. Several other systematic reviews have also found anxiety disorders to be relatively common in the medically ill.[74,a] A review of adults with coronary heart disease and end-stage heart failure, for example, estimated 10.94% to have GAD,[148] and a review of adults with type 1 and type 2 diabetes estimated 1.3% to have panic disorder and 13.5% to have GAD.[149] Both reviews, like mine, reported prevalence estimates for anxiety disorders that were higher than those reported in the general population – especially for GAD.

There are a number of possible explanations for why panic disorder and GAD are more common in patients with medical illnesses (e.g. general medical and surgical inpatients) than the general population. Evidence suggests that the

[a]It is challenging to directly compare findings of this systematic review with most previous reviews of the prevalence of anxiety for two main reasons. First, reviews have often included studies that assessed for anxiety using rating scales (i.e. have not focussed solely on studies that used clinical interviews).[74] Second, reviews have often reported the prevalence of "any anxiety disorder", rather than the prevalence of different anxiety disorders separately.[74]

relationship between anxiety disorders and medical illnesses is likely bidirectional.[150] On the one hand, it is possible that anxiety disorders increase the risk for certain medical illnesses – either directly (e.g. due to the effects of ongoing psychological stress) or indirectly (e.g. due to poor health-related behaviours associated with anxiety disorders).[150] On the other hand, it could be that the stress of being medically ill places individuals at an increased risk for developing anxiety disorders (e.g. coping with distressing symptoms and dealing with uncertainties about one's health). It could also be that certain individuals are vulnerable to *both* anxiety disorders *and* medical illnesses (i.e. anxiety disorders and medical illnesses have a common vulnerability). There is evidence, for example, to suggest that anxiety disorders and numerous medical illnesses are more common in people living in deprived areas.[151,152] Another possibility may be that some individuals with medical illnesses are misdiagnosed with an anxiety disorder because they have somatic symptoms that mimic anxiety. Consequently, "falsely high" prevalence estimates for anxiety disorders may be obtained.

5.6.3 Strengths

My systematic review has several strengths. First, I obtained guidance from an information specialist to develop a systematic search strategy to find all relevant published studies. Second, I supplemented my electronic database search by rigorously searching the references of relevant systematic reviews. By doing this, I obtained several additional eligible studies. Third, I did not apply language restrictions, which helped improve the generalisability of my review's results. Fourth, I applied basic quality criteria for inclusion, thereby excluding studies that had fundamental flaws in their study methods. Fifth, I focussed on studies where the diagnosis of anxiety was made using a diagnostic interview, thereby only reporting on definite cases of anxiety.

5.6.4 Limitations

My systematic review also has limitations. First, I depended on published literature on the prevalence of anxiety disorders, of which there was surprisingly little. This meant my meta-analyses and associated mean prevalence estimates were based on a small number of studies. Second, I relied on the reporting of primary studies themselves to assess their relevance and quality. I could have therefore excluded potentially relevant studies which were well conducted but poorly reported. Third, the majority of studies (nearly two-thirds) focussed on inpatients with *specific* clinical characteristics which are unlikely to generalise more broadly to patients in the general hospital setting. Moreover, even after focussing my analyses on studies of general medical and surgical inpatients, there was considerable statistical heterogeneity between these studies. Because of this heterogeneity, there may be problems generalising results from these studies as well. Fourth, I did not include primary studies that estimated the prevalence of “any anxiety disorder”. I did not include these studies because they define “any anxiety disorder” in different ways, which makes it difficult to draw comparisons between them (e.g. some studies include post-traumatic stress disorder and obsessive-compulsive disorder, while others exclude it). Other systematic reviews of the prevalence of anxiety disorders have similarly highlighted limitations in interpreting the results of studies where multiple anxiety disorders have been “collapsed together”.[148,153]

5.6.5 Implications and conclusions

I found little literature on the prevalence of anxiety disorders in general hospital inpatients, despite its well-documented adverse effects on individuals with medical illnesses. Moreover, most relevant literature focussed on inpatients with specific clinical characteristics (e.g. inpatients with burn injuries), which is unlikely to be generalisable to general hospital inpatients more broadly.

It is notable that of the 49 relevant articles, 22 were excluded from this review because they did not meet basic methodological standards. Even amongst the higher quality studies, their reporting quality was often poor and their sample sizes were generally small which could lead to inaccurate results. There is therefore an ongoing need for better quality studies of the prevalence of anxiety disorders in general hospital inpatients, particularly in general medical and surgical inpatients (rather than inpatients with specific clinical characteristics). I outline recommendations to improve the quality of future studies in **Chapter 11**. I would also recommend that future studies report the prevalence of individual anxiety disorders (or, if reporting the combined prevalence of "any anxiety disorder", clearly state which disorders are included in their estimate).

In conducting this systematic review, I found that the mean reported prevalences of panic disorder and GAD in general medical and surgical inpatients appeared to be greater than the estimated prevalence of these disorders in the general population. However, I was not able to account for potential confounding variables that might explain this finding due to the limitations of the available data. The findings of this review therefore tentatively

suggest that general hospital inpatients have higher rates of anxiety disorders relative to the general population.

Chapter 6
Background to cross-sectional study

6.1 Introduction

Older adults (aged ≥ 65 years) are an extremely important patient population in general hospitals. There are several reasons for this. First, older adults make up the majority of unplanned admissions.[154] Second, once admitted, older adults remain in hospital for much longer than younger patients.[154,155] Third, older adults are a rapidly increasing population[156,157] – this means general hospitals will have to continue to care for increasing numbers of older adults.

Psychiatric illnesses are problematic for this important patient population: they are associated with longer hospital stays, higher rates of rehospitalisation, and greater in-hospital adverse events and mortality.[1,11,158-161] Despite their importance, they are often undetected (and therefore untreated) in these patients.[14,17,162-165] If we want to improve management of psychiatric illnesses in this patient population, accurate information on their prevalence and associations is necessary.

Systematic reviews of the prevalence of psychiatric illnesses in older general hospital inpatients have (1) found existing literature is often limited and (2) reported concerns with the quality of existing literature (see meta-review, **Chapter 4**).[11,60,61,65] My systematic review (**Chapter 5**) also highlighted the paucity of studies focussed on this patient population. High-quality research on the prevalence and associations of psychiatric illnesses in older general hospital inpatients is therefore needed to inform care.

6.1.1 Cross-sectional study

I therefore did a *cross-sectional study* to determine the prevalence and associations of clinically significant anxiety, depression and cognitive impairment in older (aged ≥ 65 years) general hospital inpatients.

The data I used for this study were collected (pre-randomisation) from patients who had agreed to participate in a large randomised controlled trial, The HOME Study.[166] The HOME Study is a multicentre randomised controlled trial comparing the effect of adding Proactive Integrated Psychological Medicine to usual care, with usual care alone, on the time older (aged ≥ 65 years) general hospital inpatients spend in hospital.[166-168] The trial is registered with Current Controlled Trials, number ISRCTN86120296.

I was a member of The HOME Study team before the trial commenced up until trial recruitment finished. This meant that I had the unique opportunity to work closely with my supervisors to ensure that all of the procedures used in the trial (see **Section 6.6 Procedures**) would also be useful for my cross-sectional study.

In this chapter, I provide a broad overview of the cross-sectional study. In subsequent chapters, I divide this cross-sectional study into three substudies on clinically significant anxiety (**Chapter 7**), depression (**Chapter 8**) and cognitive impairment (**Chapter 9**).

6.2 Research questions

6.2.1 Substudy 1: Chapter 7

(1) What is the point prevalence of clinically significant anxiety in older general hospital inpatients?

(2) What demographic and clinical characteristics are associated with clinically significant anxiety in older general hospital inpatients?

6.2.2 Substudy 2: Chapter 8

(1) What is the point prevalence of clinically significant depression in older general hospital inpatients?

(2) What demographic and clinical characteristics are associated with clinically significant depression in older general hospital inpatients?

6.2.3 Substudy 3: Chapter 9

(1) What is the point prevalence of clinically significant cognitive impairment in older general hospital inpatients?

(2) What demographic and clinical characteristics are associated with clinically significant cognitive impairment in older general hospital inpatients?

6.3 Key concepts

6.3.1 Point prevalence

In my study, I aimed to determine the *point prevalence* of clinically significant anxiety, depression and cognitive impairment in older general hospital inpatients; I defined *point prevalence* in **Chapter 1**. The “point” at which older general hospital inpatients were assessed for this study was soon after their admission to hospital (i.e. within one week).

6.3.2 Associations

Clinical research often involves studying relationships between *variables*. *Variables* are “things” that can have different values (e.g. sex is a variable).[18]

It is important to distinguish between *association* and *causation. Association* is the measurable relationship between two variables.[18] It does not imply that one variable gives rise to another.[18] *Causation*, in epidemiology, can be described as a relationship where an exposure to something (e.g. an infection) is responsible for producing, or increasing the likelihood of, an outcome (e.g. an illness).[18] Causation is extremely difficult to ascertain. Researchers often use the Bradford Hill Criteria – a group of nine principles – to help them to determine if an association is causal (e.g. one of the nine principles is “consistency”, meaning if different people repeatedly observe an association in different places, circumstances and times, it strengthens the likelihood that that association is causal).[169]

I aimed to examine the *association* of clinically significant anxiety, depression and cognitive impairment with several demographic and clinical characteristics (or *variables*) in older general hospital inpatients. The method I used, a cross-sectional survey, did not allow me to conclude if any associations I found were causal. I describe the statistical methods used to examine these associations in detail later in this chapter (see **Section 6.7.3 Statistical analyses**).

6.3.3 Cross-sectional study

In order to answer a research question, it is important to choose an appropriate *study design*.[18] *Study designs* are "frameworks" used for collecting, measuring and analysing data for a research study.[170]

In clinical research, two of the most common types of study designs are *experimental* (or *interventional*) *study designs* and *observational study designs*.[170,171] In *experimental studies,* researchers aim to study the effects of an intervention on study participants (e.g. The HOME Study[166]).[167,168] In *observational studies,* researchers simply observe study participants without introducing any interventions.[167,168] Observational studies are useful for describing the characteristics of a group; they can be *descriptive* (i.e. studies that simply measure and describe study variables) *or analytical* (i.e. studies that measure study variables and look for *relationships* between them).[167,168]

One of the main types of observational studies is a *cross-sectional study.*[18] *Cross-sectional studies* measure variables of interest in a group of participants at a single time or within a short period of time.[18] The data they produce can be used to describe the prevalence of an illness and to analyse its associations.[18]

I aimed to measure the point prevalence and to determine the associations of clinically significant anxiety, depression and cognitive impairment in older general hospital inpatients using a *cross-sectional study design*.

6.4 Samples

6.4.1 Overview

The sample for my cross-sectional study was HOME Study participants who had completed relevant measures.[166] Specifically, it comprised of patients aged 65 years or older who had[166]:

(1) been admitted non-electively to the John Radcliffe Hospital (Oxford, United Kingdom), the Royal Devon and Exeter Hospital (Exeter, United Kingdom) or the Addenbrooke's Hospital (Cambridge, United Kingdom) between 2nd May 2018 and 5th March 2020;

(2) been an inpatient on an acute ward where trial recruitment was taking place;

(3) been an inpatient for less than one week (i.e. recently admitted) at the time of trial enrolment;

(4) been expected (by their clinical team) to remain an inpatient for at least two days from the time of trial enrolment;

(5) been expected (by their clinical team) to survive the hospital admission;

(6) been able to read or speak English (for practical reasons);

(7) not been referred to the usual care liaison psychiatry team at the time of trial enrolment;

(8) not been considered ineligible to participate in the trial due to other practical or clinical reasons (e.g. not being from the local area served by the hospital);

(9) given informed consent or, if unable to give consent, a consultee (i.e. a person who knew the patient well, such as a family member, friend or healthcare professional caring for them) had advised that their trial participation was appropriate; and

(10) completed the relevant measures for each of my substudies (see **below** and **Section 6.5 Measures** for description of measures).

6.4.2 Sample in substudies 1 and 2

The substudies on the prevalence and associations of clinically significant anxiety (**substudy 1, Chapter 7**) and depression (**substudy 2, Chapter 8**) use the same sample of HOME Study participants. This sample comprised of participants for whom all items of the following measures were obtained:

(1) Generalized Anxiety Disorder 2-item scale (GAD-2),[75]

(2) Patient Health Questionnaire 2-item scale (PHQ-2),[172] and

(3) Barthel Activities of Daily Living (ADL) Index.[173-175]

In The HOME Study, some responses to these measures were provided by proxies (e.g. for participants with severe cognitive impairment).[166] Based on existing evidence,[176-181] I judged that responses provided by proxies may differ from responses provided by patients. I therefore chose to confine my analyses to the subsample of participants who answered all items of these three measures entirely themselves (i.e. had no proxy-reported responses).

For analyses of the association of clinically significant anxiety and depression with cognitive impairment, I only included those who also had a cognitive function (Telephone Montreal Cognitive Assessment [T-MoCA][182,183]) assessment (defined as at least 80% of T-MoCA items completed[a]).

I describe these samples in greater detail in **Chapters 7** and **8.**

[a]There are 16 items on the T-MoCA that are scored. Therefore, participants had to have data on at least 13 of the 16 items to be included in analyses of the association of clinically significant anxiety (Chapter 7) and depression (Chapter 8) with cognitive impairment.

6.4.3 Sample in substudy 3

The sample I used in the substudy on the prevalence and associations of clinically significant cognitive impairment (**substudy 3, Chapter 9**) was different than the one used in substudies 1 and 2 (outlined above).

In this substudy, the sample comprised of all HOME Study participants who had a cognitive function (T-MoCA[182,183]) assessment (defined as at least 80% of T-MoCA items completed[a]). This is a larger sample than that of participants who completed all items of the GAD-2,[75] PHQ-2[172] and Barthel ADL Index.[173-175]

I describe this sample in greater detail in **Chapter 9**.

[a]There are 16 items on the T-MoCA that are scored. Therefore, participants had to have data on at least 13 of the 16 items to be included in this substudy.

6.5 Measures

6.5.1 Demographic characteristics

The following demographic characteristics were collected from participants' medical records: date of birth; sex (female or male); relationship status (spouse/partner or no spouse/partner); employment status (working or retired/not working); and postcode (to determine whether participants lived in an urban or rural setting and to calculate their socioeconomic deprivation index).

6.5.2 Clinical characteristics

Reasons for hospital admission, collected from participants' medical records, were categorised according to ICD-10 "symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified*"* codes.[23] Each participant was coded as having one primary reason for hospital admission.

Diagnoses (medical and psychiatric) recorded on admission to hospital in participants' medical records were grouped by the body system that they affected, according to the following ICD-10 codes: (1) certain infectious and parasitic diseases; (2) neoplasms; (3) diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism; (4) endocrine, nutritional and metabolic diseases; (5) mental and behavioural disorders; (6) diseases of the nervous system; (7) diseases of the eye and adnexa; (8) diseases of the ear and mastoid process; (9) diseases of the circulatory system; (10) diseases of the respiratory system; (11) diseases of the digestive system; (12) diseases of the skin and subcutaneous tissue; (13) diseases of the musculoskeletal system and connective tissue; (14) diseases of the genitourinary system; (15) congenital malformations, deformations and chromosomal abnormalities; and (16) injury, poisoning and certain other consequences of external causes.[23] I used these data to assign each participant a multimorbidity score, defined as the number of body systems with a diagnosis on admission (i.e. a count between zero and 16).

Independent functioning was measured using the Barthel ADL Index.[173-175] Although this measure is traditionally administered by directly observing patients,[173] here it was administered using a brief interview with participants.[166]

This measure consists of 10 items that assess the following activities of daily living: (1) mobilising; (2) ascending and descending stairs; (3) transferring; (4) eating; (5) dressing; (6) bathing; (7) grooming; (8) toileting; (9) controlling bladder; and (10) controlling bowels.[173,175] Scores on the Barthel ADL Index range from zero to 20, with lower scores indicating worse independent functioning.[174,175]

Anxiety was measured using the GAD-2 in a brief interview with participants.[75] I discuss the GAD-2 in greater detail in **Chapter 7**.

Depression was measured using the PHQ-2 in a brief interview with participants.[172] I discuss the PHQ-2 in greater detail in **Chapter 8**.

Cognitive impairment was measured using the T-MoCA in a brief assessment of participants.[182,183] I discuss the T-MoCA in greater detail in **Chapter 9**.

As previously stated, if a participant was not able to answer the Barthel ADL Index, GAD-2 or PHQ-2 themselves (e.g. due to severe cognitive impairment), a proxy who knew them well (e.g. family member, carer or ward staff) was asked to provide answers on their behalf.[166]

6.6 Procedures

6.6.1 Overview

I worked as a member of The HOME Study team between 2nd May 2018 and 5th March 2020. I personally recruited and collected data from participants in Oxford. I also helped to support the research teams at the other two sites (Exeter and Cambridge) by visits and regular teleconference calls.

6.6.2 Identification of potential participants

Potential participants were identified using a systematic screening process. This meant all patients admitted to an acute medical ward where recruitment was taking place were "screened" to determine if they met selection criteria.[166] This process was done by accessing patients' medical records and, where necessary, speaking with patients' medical teams.[166] It was beneficial to use a systematic screening process to identify potential participants because (1) it gave all potentially eligible patients the opportunity to participate and (2) it helped ensure the study sample was as representative as possible of older general hospital inpatients.[166]

6.6.3 Informed consent or consultee agreement

It is an ethical requirement in research to obtain informed and voluntary consent from individuals before they take part in a study.[184]

Patients who met all of the selection criteria were approached to take part in The HOME Study.[166] They were offered verbal and written information about the research, and they had their questions and concerns answered.[166] The information provided was free of technical jargon and complicated sentences to ensure it was readily understandable. If a patient understood the research and agreed to participate, their written informed consent was obtained.[166]

Patients were presumed to have the ability to make a decision about taking part in this research. However, if there was evidence that a patient was not able to make an informed decision about trial participation, a brief capacity assessment was done. If a patient lacked capacity, a consultee was identified and asked to advise on the patient's likely thoughts and feelings about the research and, if appropriate, their written or verbal agreement was obtained.[166] These procedures are in accordance with the Mental Capacity Act 2005.[166,185]

6.6.4 Implementation of quality measures

Research quality refers to a variety of factors including the validity (accuracy) and reliability (consistency) of data collected. Many techniques can be used to ensure the quality of research procedures, including: writing standard operating procedures; piloting data collection forms; training and certifying researchers; facilitating operational meetings; and conducting quality assessments.[18] I had the opportunity to work with my supervisors to develop and implement these aforementioned measures in the context of The HOME Study, which also ensured high-quality data were collected for my cross-sectional study.

6.6.4.1 Writing standard operating procedures

Standard operating procedures (or *study procedures*) are an important aspect of quality control. This is because they provide guidelines to ensure study procedures are done uniformly and to a high standard throughout a study.[18]

I co-wrote and helped maintain standard operating procedures for collection of trial baseline data used in my cross-sectional study. This included instructions for: identifying potential participants; giving study information; obtaining informed consent or consultee agreement; and collecting data. I did this to ensure procedures for collecting data were clear and straightforward, and to ensure data were collected in a rigorous and systematic manner. To make sure the procedures were consistently followed, I also helped train researchers in the use of the standard operating procedures which were relevant to their roles.

6.6.4.2 Piloting data collection forms

The design of data collection forms has an important influence on the quality of data that is collected.[18] Because of this, it has been recommended that data collection forms are pre-tested before study commencement.[18] I piloted all of the data collection forms relevant to my cross-sectional study before the trial commenced. I did this to make sure that the data collection forms were user-friendly. This was important to minimise the chance of errors occurring during data collection. I practised collecting information from patients' medical records using the data collection forms. Based on my findings, I worked with my supervisors to refine the data collection forms to improve their usability.

6.6.4.3 Training and certifying researchers

Standardised training of research study staff is fundamental for conducting high-quality research.[18] It has been recommended that researchers working on a study be: trained in performing study procedures before study commencement; formally tested on their competencies; and certified when they achieve the prescribed level of performance.[18]

I co-developed a rigorous training programme for all researchers responsible for recruiting and collecting data from participants in The HOME Study. I also co-trained and evaluated all of these researchers, of which there were 21 in total. Training researchers to collect data systematically helped to reduce the likelihood of errors occurring in data collection. The training programme included a combination of didactic teaching sessions, pre-recorded educational videos, supervised shadowing and facilitated role-play scenarios. The purpose

of the training was to ensure researchers: (1) understood, observed and practised study procedures; (2) received feedback on their training progress; and (3) developed skills to meet workplace standards. When researchers completed their training, their competencies were evaluated in role-play scenarios with actors using standardised assessment sheets, which I helped to develop. These forms were used to ensure that all researchers were assessed uniformly. After each assessment, researchers received individualised feedback on their performance.

6.6.4.4 Facilitating operational meetings

It has been suggested that holding regular meetings for research teams can improve the quality of a research study by acting as a source of on-the-job training and morale.[18] I chaired weekly operational meetings for all of the researchers responsible for recruiting participants and collecting data which I used in my cross-sectional study. These meetings were beneficial for a number of reasons. First, I was able to monitor the conduct of data collection across all study sites and regularly check if researchers were adhering to study procedures. Second, I was able to readily resolve data collection queries (e.g. picking the correct questionnaire responses). Third, I was able to support researchers through challenging recruitment and data collection experiences, and I could work with them to develop strategies to handle similar scenarios in the future.

6.6.4.5 Conducting quality assessments

Periodic reviews of researchers' performance are vital for sustaining research quality.[18] I worked alongside my supervisor to conduct regular, in-person quality assessments of all researchers responsible for recruiting participants and collecting data. We did this to ensure: (1) study procedures were being adhered to throughout the duration of the study; (2) if errors were identified, we could work with researchers to correct these errors and prevent them from happening again in the future; and (3) excellent quality data were being collected for the trial and for my cross-sectional study.

Researchers were assessed while they recruited participants and collected data using the same standardised rating sheets that were used to certify them. This was done to ensure a consistent metric of performance was being applied throughout the duration of the study. After each assessment, researchers received individualised feedback on their performance and (where necessary) a plan was developed to prevent identified errors from occurring again in the future. All of these assessments were maintained in a file in order to track researchers' ongoing performance. The aforementioned procedures are in accordance with recommendations for quality control in clinical research.[18]

6.7 Analyses

6.7.1 Overview

I planned the analyses for my three substudies which were conducted by a professional statistician. I describe these analyses below and their findings in **Chapters 7, 8** and **9.**

6.7.2 Sample description

For each substudy, I describe the characteristics of the participants included in the analyses using descriptive statistics.

6.7.3 Statistical analyses

6.7.3.1 Distribution of psychiatric symptom scores

I describe the distribution of anxiety (**Chapter 7**), depression (**Chapter 8**) and cognitive function (**Chapter 9**) scores of the participants included in the analyses in each substudy, using the measures previously described (GAD-2, PHQ-2 and T-MoCA respectively). I do this by reporting descriptive statistics (i.e. means, standard deviations [SDs], ranges, medians, inter-quartile ranges [IQRs] and frequency tables) and histograms for each substudy.

6.7.3.2 Prevalence of psychiatric illnesses

I estimated the prevalence of clinically significant anxiety (**Chapter 7**), depression (**Chapter 8**) and cognitive impairment (**Chapter 9**) in the participants included in the analyses in each substudy. I did this using the measures of anxiety (GAD-2), depression (PHQ-2) and cognitive impairment (T-MoCA) in combination with recommended cut-off scores for clinical significance on these measures (details of which can be found in **Chapters 7**, **8** and **9**).

6.7.3.3 Associations of psychiatric illnesses

6.7.3.3.1 Logistic regressions (main analyses)

I used *univariable* and *multivariable logistic regressions* to assess the associations of clinically significant anxiety (**Chapter 7**), depression (**Chapter 8**) and cognitive impairment (**Chapter 9**) with participants' demographic and clinical characteristics.

Logistic regressions were used because the "outcome" variable of interest in each substudy was binary (e.g. having clinically significant anxiety or not having clinically significant anxiety).[19] *Univariable* logistic regression involves estimating the association between two variables (an "outcome" variable and a "predictor" variable[a]).[94] *Multivariable* logistic regression involves estimating the association between two variables (an "outcome" variable and a "predictor" variable), while "adjusting" or "controlling" for other variables (some of which may be *confounders*).[94] When an association between two variables is due (or partly due) to a third variable, this third variable is called a *confounder*.[94] If this third variable (or confounder) is not "adjusted" or "controlled" for, it will bias the association between the two other variables.[94] I adjusted for age and sex in the multivariable logistic regression analyses in **Chapters 7**, **8** and **9**.

[a]The "outcome" variable is sometimes called the dependent or response variable.[19] In my substudies, the "outcome" variables were clinically significant anxiety in Chapter 7, depression in Chapter 8 and cognitive impairment in Chapter 9. The "predictor" variable is sometimes called the independent or explanatory variable.[19] In my substudies, the "predictor" variables were participants' demographic and clinical characteristics (such as age, sex and multimorbidity score).

In these logistic regression analyses, the strengths of the associations were described using odds ratios (ORs). The interpretation of an OR in a logistic regression analysis is as follows:

(1) For binary “predictor” variables: The OR is the odds of an outcome (e.g. clinically significant anxiety) happening in one group (e.g. females), divided by the odds of it happening in another group (e.g. males).[19]

(2) For continuous “predictor” variables: The OR is the change in the odds of an outcome (e.g. clinically significant anxiety) for a one-unit change in the continuous “predictor” variable (e.g. increase in one year of age).[19]

I report the 95% confidence interval (CI) for each OR. CIs are a statistical measure of precision. In this case, the CI for an OR is the range of values that we can be 95% certain contains the OR in the “true” population (i.e. the OR that would be obtained if data had been collected from the whole population).[19]

I also report a *p*-value for each OR. The *p*-value indicates the probability of having observed the association by chance assuming that there is no association between the variables.[19] Since a *p*-value is a probability, its value can range from zero and one – the smaller the *p*-value, the lower the probability.[19] By convention, a CI for an OR that does not contain the number one and, linked to this, a *p*-value less than 0.05 are used to denote statistical significance.[19]

6.7.3.3.2 Linear regressions (supplementary analyses)

I also did supplementary analyses using *univariable* and *multivariable linear regressions* to assess the associations of greater anxiety scores (**Chapter 7**), greater depression scores (**Chapter 8**) and worse cognitive impairment scores (**Chapter 9**) with participants' demographic and clinical characteristics. I did these supplementary analyses in order to examine the associations of psychiatric symptoms in finer detail. These analyses also had greater statistical power than the logistic regression analyses because the "outcome" variables of interest were continuous (e.g. greater anxiety scores), rather than binary (e.g. having clinically significant anxiety or not having clinically significant anxiety).

Since the "outcome" variables of interest in these analyses were continuous, *linear regressions* were used.[19] *Univariable* linear regression involves estimating the association between two variables (an "outcome" variable and a "predictor" variable[a]).[94] *Multivariable* linear regression involves estimating the association between two variables (an "outcome" variable and a "predictor" variable), while adjusting for other variables (including possible confounders).[94] I adjusted for age and sex in the multivariable linear regression analyses in **Chapters 7, 8** and **9.**

In these linear regressions, the strengths of the associations were described using regression coefficients.[94] A regression coefficient gives the predicted change in an "outcome" variable (e.g. anxiety scores) for a one-unit change in a

[a]The "outcome" variables in my substudies were greater anxiety scores in Chapter 7, greater depression scores in Chapter 8 and worse cognitive impairment scores in Chapter 9. The "predictor" variables in my substudies were participants' demographic and clinical characteristics (such as age, sex and multimorbidity score).

“predictor” variable (e.g. increase in one year of age).[19] A positive regression coefficient suggests that as one variable increases, the other variable increases as well, while a negative regression coefficient suggests that as one variable increases, the other variable decreases.[19]

For each regression coefficient, I obtained a CI and *p*-value. If the CI for a regression coefficient did not contain zero, it implied the relationship between the two variables was statistically significant.[19] As noted above, an associated *p*-value of less than 0.05 was also used to denote statistical significance.[19]

6.7.3.4 Handling missing data

Participants had to have at least 80% of the items of a T-MoCA completed to be included in: (1) the analyses of the associations of clinically significant anxiety (**Chapter 7**) and depression (**Chapter 8**) with cognitive impairment; and (2) the substudy of the prevalence and associations of clinically significant cognitive impairment (**Chapter 9**).

For the participants with up to 20% of missing T-MoCA items, scores for missing items were imputed using *individual mean imputation*. *Individual mean imputation* is a simple form of imputation that involves: (1) calculating the mean of a participant's non-missing item scores and (2) using this mean to replace each of the participant's missing item scores.[186] The imputation used a mean that was weighted according to the maximum value of each of the T-MoCA items (i.e. one, three or five points, see **Table 25** in **Chapter 9** for the maximum value of each T-MoCA item). This method of handling missing data assumes that the missing item scores are similar to the non-missing item scores (i.e. they have the same mean value).[186] Although literature on handling missing items on cognitive function assessments is limited, relevant studies of older general hospital inpatients have used similar approaches to handle missing data (i.e. effectively mean imputation).[187,188]

Individual mean imputation was used to impute data for approximately 4% of the study sample in **Chapters 7**, **8** and **9**. Any bias caused by the use of individual mean imputation was limited by the fact that it was used only for participants who were missing three or fewer items on the T-MoCA.

Chapter 7
Substudy 1: Prevalence and associations of clinically significant anxiety in older general hospital inpatients

7.1 Research aim

I aimed to determine the prevalence and associations of clinically significant anxiety (defined as a GAD-2 score ≥ 3) in older (aged ≥ 65 years) general hospital inpatients.

7.2 Hypotheses

I hypothesised that the following demographic and clinical characteristics would be associated with clinically significant anxiety in older general hospital inpatients:

(1) younger age;

(2) female sex;

(3) not having a spouse or partner;

(4) greater multimorbidity score;

(5) worse independent functioning;

(6) greater depression severity; and

(7) worse cognitive impairment.

I made these hypotheses based on my own experience of working with older general hospital inpatients and on other existing literature on anxiety in older adults.[189,190]

7.3 Methods

7.3.1 Sample

As outlined in **Chapter 6**, I included a patient's data in this substudy if they participated in The HOME Study[166] and completed all items of the following measures: the GAD-2,[75] the PHQ-2[172] and the Barthel ADL Index.[173-175] Some participants in The HOME Study did not complete all items of the aforementioned measures because they: (1) refused, (2) were too cognitively impaired or (3) were physically unable (e.g. patients with severe communication difficulties). For analyses of the association of clinically significant anxiety and cognitive impairment, I only included those who also had at least 80% of the items of a cognitive function (T-MoCA[182,183]) assessment completed.[a] This excluded participants for whom assessors administering the T-MoCA were not able to score at least 80% of items because the participant: (1) refused to be assessed or (2) could not be assessed due to having a severe communication impairment (e.g. deafness or dysphasia).

[a]There are 16 items on the T-MoCA that are scored. Therefore, participants had to have data on at least 13 of the 16 items to be included in analyses of the association of clinically significant anxiety and cognitive impairment.

7.3.2 Anxiety measure

7.3.2.1 Generalized Anxiety Disorder 2-item scale (GAD-2)

The GAD-2 is made up of two items that assess key anxiety symptoms in the preceding two weeks: (1) feeling nervous, anxious or on edge and (2) not being able to stop or control worrying (see **Figure 7**).[75] For each of the items, the response options are “not at all”, “several days”, “more than half the days” and “nearly every day” , which are scored as zero, one, two and three, respectively.[75] Scores on the GAD-2 range from zero to six, with higher scores indicating greater anxiety severity.[75]

The GAD-2 was developed from the Generalized Anxiety Disorder 7-item scale (GAD-7).[75,191] The GAD-7 comprises seven items which are partially linked to the DSM-IV diagnostic criteria for GAD.[191] The first two items of the GAD-7 make up the GAD-2.[75] The GAD-7 was initially developed as a short screening measure for identifying probable cases of GAD.[191] Although originally developed to screen for GAD, both the GAD-7 and GAD-2 have also been found to have good sensitivity and specificity for detecting probable cases of panic disorder and social anxiety disorder.[75] When applying a cut-off score of three or greater, the sensitivity and specificity of the GAD-2 for detecting GAD are 86% and 83% respectively; panic disorder are 76% and 81%; and social anxiety disorder are 70% and 81%.[75] In other words, the GAD-2 is good at correctly detecting those with anxiety disorders (“true positives”) as well as those without anxiety disorders (“true negatives”).

Figure 7. Generalized Anxiety Disorder 2-item scale (GAD-2)[75]

Item	Response options	Score
Over the last two weeks, how often have you been bothered by feeling nervous, anxious or on edge?	Not at all	0 points
	Several days	1 point
	More than half the days	2 points
	Nearly every day	3 points
Over the last two weeks, how often have you been bothered by not being able to stop or control worrying?	Not at all	0 points
	Several days	1 point
	More than half the days	2 points
	Nearly every day	3 points

7.3.2.2 Cut-off score on the GAD-2

In this substudy, the GAD-2 was used to measure anxiety symptoms, rather than as a screening measure to detect anxiety disorders. I defined clinically significant anxiety as a GAD-2 score of three or greater, as recommended by the developers of the scale.[75,192] Previous studies which have used the GAD-2 to determine the prevalence of clinically significant anxiety have similarly chosen a cut-off score of three or greater, using its validation against anxiety disorders to define the threshold for clinically significant anxiety.

7.3.2.3 Advantages of the GAD-2

The GAD-2 is a suitable anxiety measure for acutely unwell, older general hospital inpatients for three main reasons.

First, the GAD-2 is brief. It takes approximately one minute to complete, making it one of the briefest anxiety measures available.[193] Older general hospital inpatients are generally extremely unwell which can make it difficult and tiring for these patients to answer questions. The brevity of the GAD-2 therefore minimises the chance of overburdening these acutely ill patients, which increases the likelihood of them completing the anxiety measure.

Second, the GAD-2 measures common cognitive symptoms of anxiety (nervousness and uncontrollable worrying) and does not include somatic symptoms of anxiety (e.g. heart racing and dizziness[22]). Anxiety measures that assess for somatic symptoms may overestimate anxiety in medical settings because somatic symptoms may arise from other medical illnesses.[193] Therefore, the GAD-2's focus on cognitive symptoms of anxiety makes it suitable to use in medically ill general hospital inpatients.

Third, the GAD-2 has excellent psychometric properties. It has good *validity* (*convergent validity*, *divergent validity* and *construct validity*) and *reliability* (*internal reliability* and *test-retest reliability*):

(1) *Validity* refers to the accuracy of a measure.[18] The developers of the GAD-2 assessed its validity by examining correlations between symptom severity on the GAD-2 and another patient-reported health survey, which included subscales on mental health, role functioning, bodily pain and

physical functioning.[194,195] The GAD-2 and the mental health subscale were strongly correlated (correlation = 0.72),[194] which demonstrates the GAD-2 has good *convergent validity*. One would expect the two scales to be strongly correlated because they assess similar constructs. Conversely, the GAD-2 had weaker correlations with the role functioning, bodily pain and physical functioning subscales (correlations ranged from 0.28 to 0.32),[194] which demonstrates the GAD-2 has good *divergent validity.* One would expect the aforementioned subscales to be more weakly correlated than the mental health subscale because anxiety is a different construct from role functioning, bodily pain and physical functioning. Having said that, one would expect the GAD-2 to have *some* association with these subscales, since anxiety disorders are associated with worse role functioning, bodily pain and physical functioning.[75] Based on findings from this study, it appears the GAD-2 demonstrates good *construct validity* (i.e. it measures what it is intending to measure[18]).

(2) *Reliability* refers to the consistency of a measure.[18] The GAD-2 has excellent *internal reliability*, because its two items are closely related to each other, with an estimated Cronbach alpha of 0.82.[194] It also has good *test-retest reliability*, because it consistently measures anxiety over time, with an estimated intraclass correlation coefficient of 0.81.[196]

7.3.2.4 Disadvantages of the GAD-2

There are three main disadvantages of the GAD-2.

First, the GAD-2 cannot be used to diagnose an anxiety disorder.[75] The GAD-2 can only be used to measure anxiety symptoms in patients, to identify patients with clinically significant anxiety by applying a cut-off score or to identify patients likely to have an anxiety disorder. The actual diagnosis of an anxiety disorder and the initiation of appropriate treatment for it requires a much more comprehensive clinical assessment. This assessment would usually include a diagnostic interview including history-taking, and often third-party information.

Second, the GAD-2 does not assess the "severity" of the anxiety symptoms it measures. Although the GAD-2 assesses how *often* individuals have been "bothered" by anxiety symptoms in the preceding two weeks (i.e. "not at all", "several days", "more than half the days" or "nearly every day"),[75] it does not assess the *degree* to which individuals have been bothered by these symptoms. A clinical interview, by contrast, would obtain a more accurate understanding of the "severity" of anxiety symptoms.

Third, the GAD-2 does not measure the whole range of anxiety symptoms; it focusses on only two core anxiety symptoms.[75] Consequently, some patients with anxiety symptoms may not get a high score on the GAD-2, for example those with predominately somatic symptoms.

7.3.3 Statistical analyses

As described in **Chapter 6**, I report the distribution of anxiety (GAD-2) scores and point prevalence of clinically significant anxiety (defined as a GAD-2 score ≥ 3) in study participants. I also describe the associations of clinically significant anxiety (defined as a GAD-2 score ≥ 3) with the following demographic and clinical characteristics: age, sex, relationship status, multimorbidity score, independent functioning, depression severity and cognitive impairment. I used univariable and multivariable logistic regressions to assess the associations of clinically significant anxiety with participants' demographic and clinical characteristics (listed above), adjusting for age and sex in the multivariable analyses. To supplement these analyses, I used univariable and multivariable linear regressions to assess the associations of greater anxiety (GAD-2) scores with participants' demographic and clinical characteristics (listed above), adjusting for age and sex in the multivariable analyses. In analyses of the association of clinically significant anxiety and cognitive impairment, participants with up to 20% of missing T-MoCA items had scores imputed for these items using individual mean imputation (see **Chapter 6 Section 6.7.3.4** for more detail).

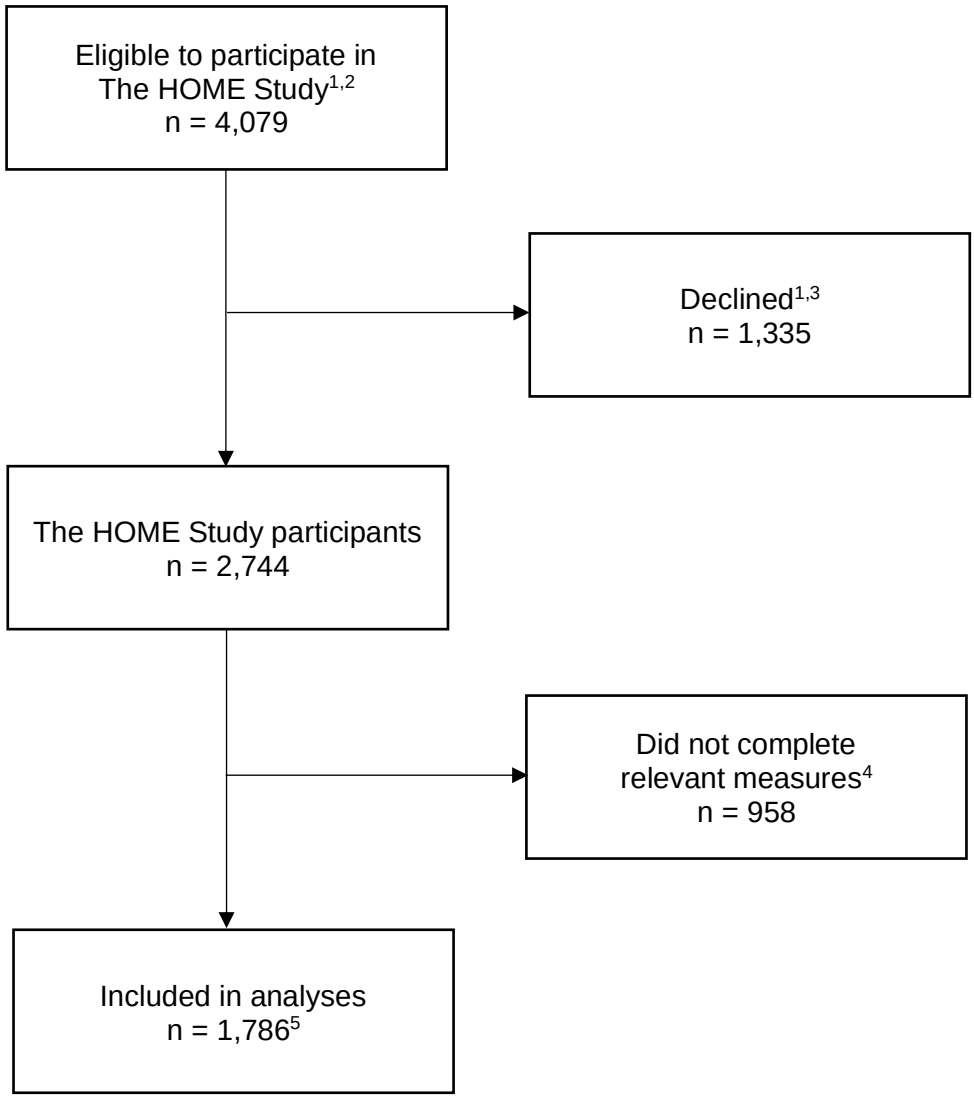
7.4 Results

7.4.1 Sample description

4,079 patients[a] were eligible to take part in The HOME Study. Of these, 2,744 participated. Data on 1,786 participants were analysed; 958 were excluded from the analyses because they did not complete all items of the relevant measures (GAD-2, PHQ-2 or Barthel ADL Index) (see **Figure 8**).

[a]Patients could be counted more than once (i.e. units are “hospital admissions”, rather than individual patients).

Figure 8. Prevalence and associations of clinically significant anxiety in older general hospital inpatients flowchart



[1]The units are "hospital admissions", rather than individual patients.
[2] The main reasons for ineligibility were (1) being under 65 years of age and (2) planned discharge from hospital within two days.
[3]The main reasons for refusal were (1) not being interested in taking part in research and (2) feeling that there was already too much going on.
[4]Participant either refused, was too cognitively impaired or was physically unable (e.g. had severe communication difficulties) to complete all items of relevant measures (GAD-2, PHQ-2 and Barthel ADL Index). Of the 958 participants excluded, 92 were excluded for having ≥ one item missing on the relevant measures and 866 were excluded for having data provided by a proxy for ≥ one item on the relevant measures.
[5]1,719 of these participants (96%) had at least 80% of the items of a T-MoCA completed and were therefore included in analyses of the association of clinically significant anxiety and cognitive impairment. Most of these participants had a full T-MoCA completed (1,645 participants, 96%), with only a small proportion requiring scores to be imputed for 20% or less of missing T-MoCA items. 65 participants had scores imputed for one missing item, five had scores imputed for two missing items and four had scores imputed for three missing items.

7.4.1.1 Demographic characteristics of participants in analyses

Participants included in this substudy were old, with a mean age of over 80 years (see **Table 11**). There was a similar proportion of female and male participants. There were also similar proportions of participants with and without a spouse or partner, and living in urban and rural settings. The majority of participants were retired or not working, which is unsurprising given the mean age of participants. While there was a spread in participants' socioeconomic deprivation index scores, few fell into the most deprived category.

Table 11. Prevalence and associations of clinically significant anxiety in older general hospital inpatients: Demographic characteristics of participants in analyses

	Sample (n = 1,786)
Age (years)	
Mean (SD)	80.84 (8.15)
Range	65.03 to 100.30
65 to 74 years	503 (28.16%)
75 to 84 years	675 (37.79%)
≥ 85 years	608 (34.04%)
Sex	
Female	874 (48.94%)
Male	912 (51.06%)
Relationship status	
Spouse or partner	825 (46.19%)
No spouse or partner	961 (53.81%)
Employment status	
Working	49 (2.74%)
Retired or not working	1,737 (97.26%)
Residence area	
Urban setting	987 (55.26%)
Rural setting	799 (44.74%)
Socioeconomic deprivation index[a]	
0	40 (2.24%)
1	218 (12.21%)
2	421 (23.57%)
3	496 (27.77%)
4	611 (34.21%)

Data are number (%) unless otherwise indicated.
SD = Standard Deviation.
[a]0 = most deprived, 4 = least deprived.

7.4.1.2 Clinical characteristics of participants in analyses

The most common reasons for participants' admission to hospital were having (1) symptoms and signs involving the circulatory and respiratory systems (e.g. chest pain and shortness of breath) and (2) general symptoms and signs (e.g. fever and fatigue) (see **Table 12**).

Participants had high multimorbidity. On average, they had three body systems with at least one diagnosis charted in their medical records on admission. Over 70% of participants had at least one diagnosis affecting their circulatory system (e.g. ischemic heart disease and hypertension) and over 40% had an endocrine, nutritional or metabolic disease (e.g. diabetes). Participants were prescribed an average of 12 medications.

Generally, participants were also physically and cognitively unwell. On average, participants had severe functional impairment (as measured by the Barthel ADL Index)[173-175,197] and moderate cognitive impairment (as measured by the T-MoCA).[182,183,198]

Table 12. Prevalence and associations of clinically significant anxiety in older general hospital inpatients: Clinical characteristics of participants in analyses

	Sample (n = 1,786)
Reason for hospital admission	
Symptoms and signs involving the circulatory and respiratory systems	523 (29.28%)
General symptoms and signs	410 (22.96%)
Symptoms and signs involving the digestive system and abdomen	262 (14.67%)
Falls and injuries	230 (12.88%)
Symptoms and signs involving the skin and subcutaneous tissue	111 (6.22%)
Symptoms and signs involving cognition, perception, emotional state and behaviour	103 (5.77%)
Symptoms and signs involving the urinary system	93 (5.21%)
Abnormal investigation findings	28 (1.57%)
Symptoms and signs involving the nervous and musculoskeletal systems	26 (1.46%)
Multimorbidity (presence of a diagnosis in each body system on admission)	
Diseases of the circulatory system	1,284 (71.89%)
Endocrine, nutritional and metabolic diseases	722 (40.43%)
Diseases of the musculoskeletal system and connective tissue	585 (32.75%)
Diseases of the respiratory system	574 (32.14%)
Diseases of the genitourinary system	500 (28.00%)
Diseases of the digestive system	448 (25.08%)
Neoplasms	408 (22.84%)
Diseases of the nervous system	283 (15.85%)
Mental and behavioural disorders	271 (15.17%)
Diseases of the eye and adnexa	185 (10.36%)
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	162 (9.07%)
Diseases of the skin and subcutaneous tissue	119 (6.66%)
Certain infectious and parasitic diseases	91 (5.10%)
Injury, poisoning and certain other consequences of external causes	65 (3.64%)
Diseases of the ear and mastoid process	46 (2.58%)
Congenital malformations, deformations and chromosomal abnormalities	9 (0.50%)

Multimorbidity score (number of body systems with a diagnosis on admission, 0 to 16)	
Mean (SD)	3.22 (1.68)
Number of medications	
Mean (SD)	11.76 (5.44)
Independent functioning (Barthel ADL Index, 0 to 20)[a]	
Mean (SD)	11.02 (5.46)
Depression (PHQ-2, 0 to 6)[b]	
Mean (SD)	2.37 (2.06)
Cognitive impairment (T-MoCA, 0 to 30)[c,d]	
Mean (SD)	16.84 (6.42)

Data are number (%) unless otherwise indicated.
Barthel ADL Index = Barthel Activities of Daily Living Index; PHQ-2 = Patient Health Questionnaire 2-item scale; SD = Standard Deviation; T-MoCA = Telephone Montreal Cognitive Assessment.
[a]Lower scores indicate worse independent functioning.
[b]Higher scores indicate greater depression severity.
[c]Lower scores indicate worse cognitive impairment.
[d]Data available for 1,719 participants who had at least 80% of the items of a T-MoCA completed.

7.4.2 Distribution of anxiety scores

7.4.2.1 Total GAD-2 score

Participants had a mean total anxiety (GAD-2) score of 2.4 (SD of 2.1), with scores ranging from zero to six (see **Table 13**). The distribution of participants' total anxiety scores can be seen in **Figure 9.** The most frequent GAD-2 score was zero (i.e. the minimum score).

7.4.2.2 Individual GAD-2 item scores

As previously outlined, the GAD-2 comprises two items: the first focusses on nervousness and the second on uncontrollable worrying. A greater proportion of participants reported feeling nervous, anxious or on edge for at least several days in the preceding two weeks (item 1, 66.3%) than not being able to stop or control worrying (item 2, 56.0%).

7.4.3 Prevalence of clinically significant anxiety

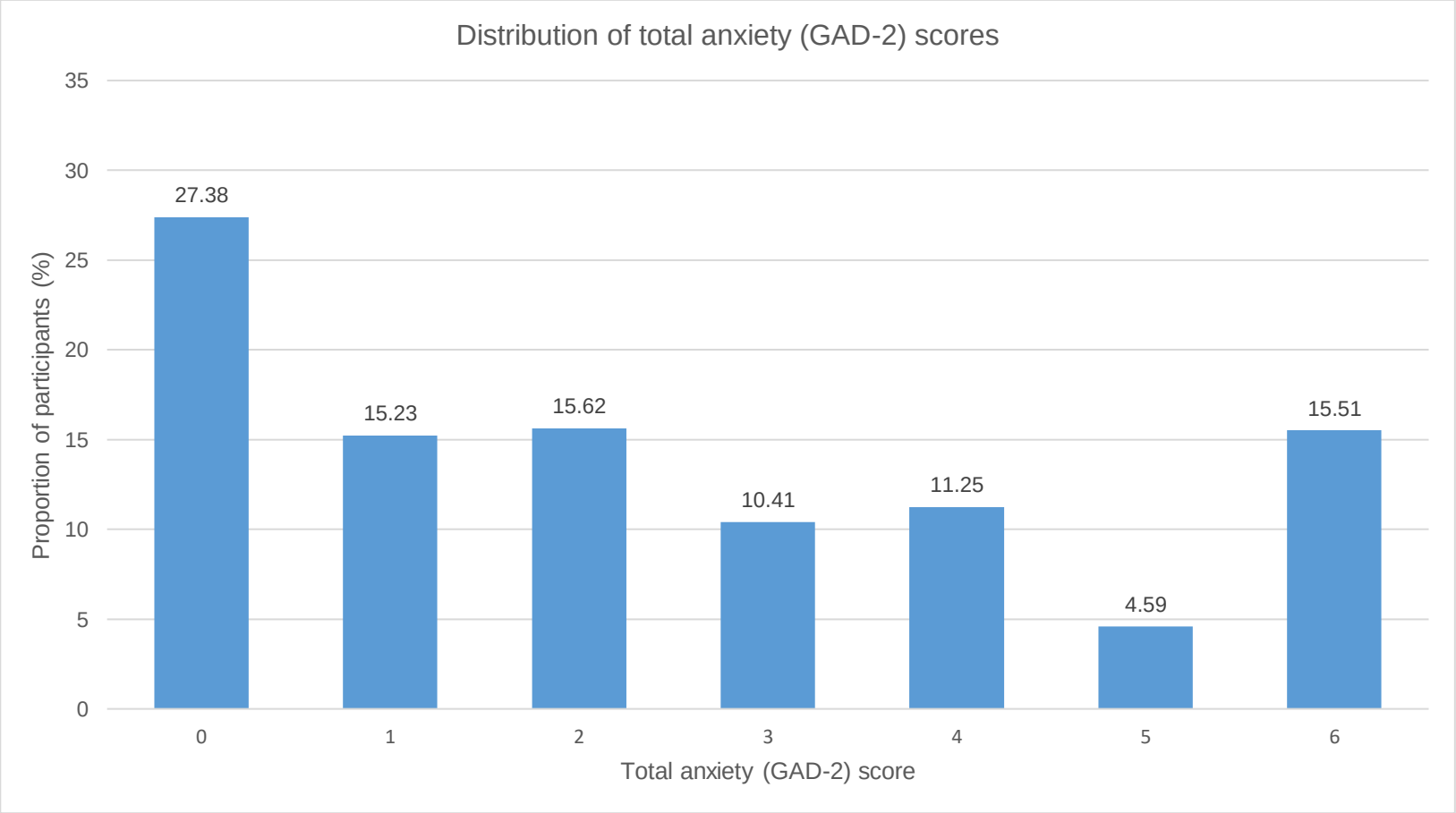
41.8% of participants had clinically significant anxiety, defined as a GAD-2 score of three or greater.

Table 13. Prevalence and associations of clinically significant anxiety in older general hospital inpatients: Distribution of anxiety (GAD-2) scores of participants in analyses

	Sample (n = 1,786)
GAD-2	
Mean (SD)	2.39 (2.13)
Median (IQR)	2 (0 to 4)
Range	0 to 6
Total score of 0	489 (27.38%)
Total score of 1	272 (15.23%)
Total score of 2	279 (15.62%)
Total score of 3	186 (10.41%)
Total score of 4	201 (11.25%)
Total score of 5	82 (4.59%)
Total score of 6	277 (15.51%)
Total score of 3 or greater	746 (41.77%)
GAD-2 Item 1 (Feeling nervous, anxious or on edge)	
Not at all	602 (33.71%)
Several days	518 (29.00%)
More than half the days	223 (12.49%)
Nearly every day	443 (24.80%)
GAD-2 Item 2 (Not being able to stop or control worrying)	
Not at all	786 (44.01%)
Several days	417 (23.35%)
More than half the days	195 (10.92%)
Nearly every day	388 (21.72%)

Data are number (%) unless otherwise indicated.
GAD-2 = Generalized Anxiety Disorder 2-item scale; IQR = Inter-Quartile Range; SD = Standard Deviation.

Figure 9. Histogram of the distribution of total anxiety (GAD-2) scores of participants in analyses



GAD-2 = Generalized Anxiety Disorder 2-item scale.

7.4.4 Associations of clinically significant anxiety

Table 14 and **Table 15** present the results of the univariable and multivariable analyses of associations of clinically significant anxiety (defined as a GAD-2 score ≥ 3) with participants' demographic and clinical characteristics.

Age. There was no evidence of an association between clinically significant anxiety and age in the univariable analysis or the multivariable analysis (where sex was adjusted for).

Sex. Clinically significant anxiety was associated with sex in the univariable analysis – the odds of clinically significant anxiety were found to be greater among females (OR = 0.80, 95% CI, 0.66 to 0.97, i.e. the odds of clinically significant anxiety were estimated to be 20% lower in males than females). These findings remained after adjusting for age in the multivariable analysis (adjusted OR = 0.81, 95% CI, 0.67 to 0.97).

Relationship status. Clinically significant anxiety was associated with relationship status, with the odds estimated to be higher among those without a spouse or partner. The association was moderately strong (OR = 1.33, 95% CI, 1.10 to 1.61) and persisted after adjusting for age and sex in the multivariable analysis (adjusted OR = 1.27, 95% CI, 1.04 to 1.55). In other words, I found those without a spouse or partner were estimated to have a 33% increase in odds of clinically significant anxiety when compared to those with a spouse or partner (27% after adjusting for age and sex).

Multimorbidity score. Clinically significant anxiety was associated with a greater multimorbidity score in the univariable analysis. The association was

moderately strong (OR = 1.12, 95% CI, 1.06 to 1.19) and was unchanged after adjusting for age and sex in the multivariable analysis (adjusted OR = 1.12, 95% CI, 1.06 to 1.19, i.e. a one-unit increase in multimorbidity score was associated with a 12% increase in odds of clinically significant anxiety).

Independent functioning. Clinically significant anxiety had a moderately strong association with worse independent functioning in the univariable analysis (OR = 0.93, 95% CI, 0.91 to 0.94) and did not change after adjusting for age and sex in the multivariable analysis (adjusted OR = 0.93, 95% CI, 0.91 to 0.94). That is to say, the odds of clinically significant anxiety were estimated to decrease by 7% for a one-unit increase in independent functioning (Barthel ADL Index) score (where lower scores indicate worse independent functioning).

Depression. Clinically significant anxiety was **strongly** associated with greater depression severity in the univariable analysis (OR = 2.01, 95% CI, 1.89 to 2.15, i.e. the odds of clinically significant anxiety were estimated to **double** for every one-unit increase in depression [PHQ-2] score, where higher scores indicate greater depression severity). This association remained after adjusting for age and sex in the multivariable analysis (adjusted OR = 2.03, 95% CI, 1.90 to 2.17).

Cognitive impairment. Clinically significant anxiety had a moderately strong association with worse cognitive impairment in the univariable analysis (OR = 0.95, 95% CI, 0.93 to 0.96, i.e. the odds of clinically significant anxiety were estimated to decrease by 5% for a one-unit increase in cognitive function [T-MoCA] score, where lower scores indicate worse cognitive function). This

association remained after adjusting for age and sex in the multivariable analysis (adjusted OR = 0.94, 95% CI, 0.93 to 0.96).

Supplementary analyses. All previous analyses were repeated with anxiety being treated as a continuous variable (i.e. greater anxiety scores), rather than a binary variable (i.e. having clinically significant anxiety or not having clinically significant anxiety). These analyses yielded similar results. There was, however, one difference: greater anxiety scores were *not* associated with not having a spouse or partner (when age and sex were adjusted for) whereas there was an association for clinically significant anxiety.

Table 14. Univariable analyses of associations of demographic and clinical characteristics and clinically significant anxiety (defined as a GAD-2 score ≥ 3)

	Unadjusted odds ratio (95% CI)	***p*-value**
Age	1.01 (0.99 to 1.02)	0.32
Sex		
Female	1	
Male	0.80 (0.66 to 0.97)	0.02
Relationship status		
Spouse or partner	1	
No spouse or partner	1.33 (1.10 to 1.61)	0.003
Multimorbidity score[a]	1.12 (1.06 to 1.19)	< 0.001
Independent functioning (Barthel ADL Index score)[b]	0.93 (0.91 to 0.94)	< 0.001
Depression (PHQ-2 score)[c]	2.01 (1.89 to 2.15)	< 0.001
Cognitive impairment (T-MoCA score)[d,e]	0.95 (0.93 to 0.96)	< 0.001

Barthel ADL Index = Barthel Activities of Daily Living Index; CI = Confidence Interval; PHQ-2 = Patient Health Questionnaire 2-item scale; T-MoCA = Telephone Montreal Cognitive Assessment.
[a]Number of body systems with a diagnosis on admission (scores range from 0 to 16).
[b]Lower scores indicate worse independent functioning (scores range from 0 to 20).
[c]Higher scores indicate greater depression severity (scores range from 0 to 6).
[d]Lower scores indicate worse cognitive impairment (scores range from 0 to 30).
[e]Univariable analysis of 1,719 participants who had at least 80% of the items of a T-MoCA completed.

Table 15. Multivariable analyses of associations of demographic and clinical characteristics and clinically significant anxiety (defined as a GAD-2 score ≥ 3) adjusted for age and sex

	Adjusted odds ratio (95% CI)	***p*-value**
Age[a]	1.01 (0.99 to 1.02)	0.39
Sex[b]		
Female	1	
Male	0.81 (0.67 to 0.97)	0.03
Relationship status[c]		
Spouse or partner	1	
No spouse or partner	1.27 (1.04 to 1.55)	0.02
Multimorbidity score[c,d]	1.12 (1.06 to 1.19)	< 0.001
Independent functioning (Barthel ADL Index score)[c,e]	0.93 (0.91 to 0.94)	< 0.001
Depression (PHQ-2 score)[c,f]	2.03 (1.90 to 2.17)	< 0.001
Cognitive impairment (T-MoCA score)[c,g,h]	0.94 (0.93 to 0.96)	< 0.001

Barthel ADL Index = Barthel Activities of Daily Living Index; CI = Confidence Interval; PHQ-2 = Patient Health Questionnaire 2-item scale; T-MoCA = Telephone Montreal Cognitive Assessment.
[a]Analysis adjusted for sex.
[b]Analysis adjusted for age.
[c]Analysis adjusted for age and sex.
[d]Number of body systems with a diagnosis on admission (scores range from 0 to 16).
[e]Lower scores indicate worse independent functioning (scores range from 0 to 20).
[f]Higher scores indicate greater depression severity (scores range from 0 to 6).
[g]Lower scores indicate worse cognitive impairment (scores range from 0 to 30).
[h]Multivariable analysis of 1,719 participants who had at least 80% of the items of a T-MoCA completed.

7.5 Discussion

7.5.1 Main findings

I found that clinically significant anxiety was common in older general hospital inpatients, occurring in more than 40 percent. It was strongly associated with being “sicker” (i.e. greater multimorbidity score, worse independent functioning, greater depression severity and worse cognitive impairment). It was also associated with female sex and not having a spouse or partner. The aforementioned findings all remained after adjusting for age and sex. I did not find evidence of an association between clinically significant anxiety and age.

7.5.2 Prevalence of clinically significant anxiety

7.5.2.1 Overview of results

The high prevalence of clinically significant anxiety did not surprise me, based on my experience working with the older general hospital inpatients included in this study. The patients were extremely sick. In conversations with them, many told me that their poor health made them feel both nervous and worried: the two anxiety symptoms measured in this substudy. Many worried about falling, being unable to manage at home, being dependent on (and a burden to) their families and dying soon. Several also found the hospital experience to be anxiety-provoking (e.g. the noisiness of the ward). I also spoke with patients early in their admission, when few had a clear medical and discharge plan in place: this uncertainty worried many.

7.5.2.2 Relevant studies of the prevalence of clinically significant anxiety in older general hospital inpatients

7.5.2.2.1 Clinically significant anxiety defined using a cut-off score

Previous studies of older general hospital inpatients that also used a cut-off score to define clinically significant anxiety have reported similarly high prevalence estimates (see **Table 16**).[199,200] It is difficult to make direct comparisons between these studies and mine because they (1) used different anxiety measures and (2) were conducted in different settings (e.g. different countries and different types of hospital wards). It is notable, however, that each of these studies assessed fewer than 100 participants.[199,200]

Al Aqqad et al. (2017) studied older adults in Malaysia who had been admitted to respiratory wards with an acute exacerbation of chronic obstructive pulmonary disease (COPD).[199] This study estimated a slightly lower prevalence of clinically significant anxiety (34.57%) than my substudy and assessed patients on discharge from hospital.[199] Participants in this study had high multimorbidity, however differed from participants in my study in that they were younger, predominately male and functionally independent.[199] It is possible these differences contributed to their lower prevalence estimate because I found female sex and worse independent functioning to be associated with clinically significant anxiety.

Kvaal et al. (2001) examined the prevalence of clinically significant anxiety in older general hospital inpatients in Norway.[200] It used a measure that assessed for “state” anxiety (i.e. anxiety in the preceding three days).[200] This study found a markedly similar prevalence (43%) to my substudy.[200] Participants in this

study, like mine, were older adults who were expected to survive their hospital admission.[200] Participants in this study were also very old, with a mean age over 80 years.[200] Unlike my substudy, this study excluded patients with known post-traumatic stress disorder, psychosis and alcoholism, and who recently suffered from a stroke.[200]

7.5.2.2.2 Clinically significant anxiety defined using diagnostic criteria

In my systematic review (**Chapter 5**), I only included two studies that estimated the prevalence of clinically significant anxiety (defined using diagnostic criteria) in older general hospital inpatients.[103,104] It is notable that these studies, similar to those previously described, assessed a small number of participants (100 and 106).[103,104] Both studies estimated the prevalence of GAD, reporting prevalence estimates of 0.9% and 2.0%.[103,104] The characteristics of these studies are summarised in **Table 17**. It is not surprising that these studies estimated prevalences of anxiety disorders much lower than that of clinically significant anxiety which I found. This is because, unlike cut-off scores on anxiety measures, diagnostic criteria specify strict criteria for symptom severity, pattern and duration.

Table 16. Studies of the prevalence of clinically significant anxiety (defined using a cut-off score) in older general hospital inpatients[a]

Study	Setting	Selection criteria	Sample characteristics	Anxiety measure	Cut-off score	Finding(s)
Al Aqqad et al. (2017)[199]	Respiratory wards in four major hospitals (Malaysia).	Aged ≥ 60 years; hospitalised with primary diagnosis of acute exacerbation of COPD; no coexisting active pulmonary tuberculosis; cognitively able to complete questionnaires. Excluded patients who died during hospitalisation; were transferred to or from another hospital; and did not complete questionnaires.	Sample size = 81 Age (median, IQR) = 72, 66.4 to 78.0 % female = 2.47%	GAD-7	Anxiety (scores ≥ 5)	Prevalence: 34.57% (assessed on discharge). Associations: Anxiety scores were significantly higher among patients with severe dyspnoea. No statistically significant difference in rates of anxiety between ethnic groups. Anxiety was not associated with short-term hospital readmission or disease severity.
Kvaal et al. (2001)[200]	Department of geriatric medicine in a university hospital (Norway).	Aged ≥ 70 years; ≥ 1 chronic somatic disease(s); able to hear and write; no cognitive impairment (sumscore 10-12 points on MMSE short version), psychosis, alcoholism or recent stroke (last 12 months); not in a "terminal state" or expected to die during hospital admission; no severe life events (e.g. loss of spouse or children) during the last 6 months; no known post-traumatic stress disorder.	Sample size = 98[b] Age (mean, range) = 81.8, 70 to 96 % female = 67%	STAI, state subscale (Norwegian version)	Clinically significant anxiety (cut-off of 39/40)	Prevalence: 43%, 41% of females & 47% of males (assessment time point not stated). Associations: No statistically significant difference in STAI score by gender, age, marital status, living arrangement, education, former occupation, or number of drugs in regular use (after adjusting for COPD diagnosis). STAI scores were "marginally significantly higher" (p = 0.05) in patients with COPD compared to the other diagnostic groups.

COPD = Chronic Obstructive Pulmonary Disease; GAD-7 = Generalized Anxiety Disorder 7-item scale; IQR = Inter-Quartile Range; MMSE = Mini-Mental State Examination; STAI = State-Trait Anxiety Inventory. [a]I searched MEDLINE from database inception to July 2020 for relevant studies that included prevalence, anxiety and general hospital inpatient (as well as synonyms and alternative spellings) in their titles. **Table 16** summarises the results of the relevant studies. [b]Two patients had one missing STAI item; authors did not report how missing data were handled.

Table 17. Studies of the prevalence of clinically significant anxiety (defined using diagnostic criteria) in older general hospital inpatients[a]

Study	Setting	Selection criteria	Sample characteristics	Anxiety measure	Caseness definition	Finding(s)
Thalassinos et al. (1992)[103]	Internal medicine department of a university hospital (France).	Aged > 65 years; well enough to participate.	Sample size = 100 Age (mean, SD) = Females: 80, 7 Males: 77, 7 % female = 71%	Diagnostic Interview Schedule	GAD (DSM-III)	Prevalence: 2.0% Associations: No associations of GAD reported.
Uwakwe (2000)[104]	Medical, surgical & gynaecological wards in a university teaching hospital (Nigeria).	Aged ≥ 60 years; well enough to participate.	Sample size = 106 Age (mean, SD) = 69.9, 8.4 % female = 38.7%	Geriatric Mental State Schedule	GAD (ICD-10 DCR)	Prevalence: 0.9% Associations: No associations of GAD reported.

DCR = Diagnostic Criteria for Research; DSM = Diagnostic and Statistical Manual of Mental Disorders; GAD = Generalised Anxiety Disorder; ICD = International Classification of Diseases; SD = Standard Deviation.

[a]I summarised relevant studies included in my systematic review of the prevalence of anxiety disorders in general hospital inpatients (see **Chapter 5**).

7.5.2.3 Relevant studies of the prevalence of clinically significant anxiety in older adults in community settings

Most research on the prevalence of clinically significant anxiety in older adults has been conducted in community settings, rather than general hospital settings. Prevalence estimates of clinically significant anxiety in community-dwelling older adults vary widely (see **Table 18**).[201-203] One review of studies of the prevalence of "anxiety symptoms" in older adults in community settings reported estimates that ranged from 15% to 52.3%.[201] My findings are most comparable to the "upper" prevalence estimates of "anxiety symptoms" in older adults in community settings. As one would expect, studies that examined the prevalence of anxiety disorders in older adults in community settings consistently reported much lower prevalence estimates than I obtained in my substudy (see **Table 18**).[146,201-203]

Table 18. Relevant systematic reviews of the prevalence of anxiety in older adults in community settings[a]

Systematic review	Reviewers' findings
Bryant et al. (2008) *The prevalence of anxiety in older adults: Methodological issues and a review of the literature*[201]	Review focussed on older adults (aged > 60 years) in community and clinical settings. In community settings, it reported that the prevalence of "anxiety disorders" and "anxiety symptoms" ranged from 1.2% to 15% and 15% to 52.3% respectively.
Cheng et al. (2019) *The prevalence and predictors of anxiety and depression in near-centenarians and centenarians: A systematic review*[202]	Review focussed on older adults (aged ≥ 95 years) in community settings. It reported prevalence estimates for "anxiety disorders" and "anxiety symptoms" that ranged from 3.3% to 5.9% and 9.5% to 45.4% respectively.
Creighton et al. (2016) *The prevalence of anxiety among older adults in nursing homes and other residential aged care facilities: A systematic review*[203]	Review focussed on older adults (aged ≥ 50 years) in residential aged care facilities. It reported that the prevalence of "anxiety disorders" and "clinically significant anxiety symptoms" ranged from 3.2% to 20% and 6.5% to 58.4% respectively.
Volkert et al. (2013) *The prevalence of mental disorders in older people in Western countries: A meta-analysis*[146]	Review focussed on older adults (aged ≥ 50 years) in community settings in Europe and North America. It reported the overall random-effects estimate for: (1) current and lifetime panic disorder was 0.88% (95% CI, 0.76% to 0.99%) and 2.63% (95% CI, 2.43% to 2.84%) respectively; (2) current and lifetime GAD was 2.30% (95% CI, 2.03% to 2.57%) and 6.36% (95% CI, 5.57% to 7.14%) respectively; and (3) current and lifetime specific phobia was 4.52% (95% CI, 4.15% to 4.89%) and 6.66% (95% CI, 6.17% to 7.15%) respectively.

CI = Confidence Interval; GAD = Generalised Anxiety Disorder.
[a]Reviews included primary studies that used a number of different types of anxiety assessment measures and definitions to define clinically significant anxiety.

7.5.3 Associations of clinically significant anxiety

7.5.3.1 Overview of results

Age. I hypothesised that clinically significant anxiety would be associated with younger age. I observed that very old patients (such as those aged 80 years and older) were often very stoic and reserved. Therefore, I thought these very old patients would be less likely to disclose anxiety symptoms. However, I did not find evidence of an association between clinically significant anxiety and age, even after sex was adjusted for. It is possible that any association might have been missed because of the small range of ages in my sample.

Sex. In accordance with my hypothesis, I found that clinically significant anxiety was associated with female sex, even after adjusting for age. There could be several reasons for this finding. One reason may be that females experience more anxiety symptoms than males. Another possible reason may be that females feel more comfortable discussing their feelings and reporting anxiety symptoms than males – I found this to be the case in my personal experience of collecting data for this substudy.

Relationship status. I found that clinically significant anxiety was associated with not having a spouse or partner, even after adjusting for age and sex. This finding is consistent with my hypothesis. When collecting data, I often interacted with spouses and partners of participants. I saw how spouses and partners often offered participants emotional support (e.g. reassurance) and practical help (e.g. coordinating care). It seems plausible that these factors may help

older general hospital inpatients to experience fewer anxiety symptoms in the face of stressors, such as being medically ill and hospitalised.

Multimorbidity score. As hypothesised, I found clinically significant anxiety was associated with a greater multimorbidity score, even after adjusting for age and sex. I observed that older general hospital inpatients with multiple illnesses were frequently burdened by the negative consequences of each of their illnesses and that their complex care needs were often unmet. In light of this, it is understandable that having more medical illnesses (i.e. a greater multimorbidity score) would be associated with clinically significant anxiety.

Independent functioning. I found that clinically significant anxiety was associated with worse independent functioning, even after adjusting for age and sex, which is consistent with my hypothesis. Several factors could explain this finding. It could be that losing one's functional abilities – and becoming increasingly dependent on others – is anxiety-provoking. It could also be that older general hospital inpatients who are nervous and worried are less likely to engage in forms of physical activity (e.g. walking and getting out of bed) because they are scared of hurting themselves. This, in turn, could result in worse functional impairment.

Depression. As hypothesised, I found clinically significant anxiety was strongly associated with greater depression severity, even after adjusting for age and sex. This was the strongest association that I found in my analyses. One would likely expect this finding, considering the well-documented co-occurrence of anxiety and depression in older adults.[204] Patients that I spoke to who were nervous and worried (anxiety symptoms) often told me they also felt down and

had little interest in doing things (depressive symptoms). For example, several older adults told me they had *little interest* in doing things they normally would because they were constantly *worried* that they would hurt themselves trying to do those things. For many, not doing these activities also made them *feel down*.

Cognitive impairment. In accordance with my hypothesis, I found that clinically significant anxiety was associated with worse cognitive impairment, even after adjusting for age and sex. Numerous factors could contribute to this association. Many patients that I spoke to who recognised that their cognitive functioning was worsening told me that it made them feel nervous and/or worried. Moreover, my experience working on acute medical wards showed me that these environments were disorientating – especially for older adults that were cognitively impaired. They were constantly noisy, had a frequent turnover of staff and had routines that differed significantly from what patients were used to. It seems reasonable to expect that someone who is already confused would find these environments to be particularly distressing.

7.5.3.2 Relevant studies of the associations of clinically significant anxiety in older general hospital inpatients

Studies of older general hospital inpatients summarised in **Section 7.5.2.2** examined very few associations of anxiety (see **Table 16** and **Table 17**).[103,104,199,200] The limited data can be summarised as follows. Al Aqqad et al. (2017) reported that anxiety scores were significantly higher in participants with severe dyspnoea,[199] and Kvaal et al. (2001) reported that anxiety scores were "marginally significantly higher" ($p = 0.05$) in participants with COPD.[200] Kvaal et al. (2001) also reported that there were no significant differences in anxiety scores between groups of participants dichotomised by gender, age, marital status, living arrangement, education, former occupation, or number of drugs in regular use (after adjusting for COPD diagnosis).[200] Although Kvaal et al. (2001) examined associations of gender, age and marital status,[200] it is challenging to directly compare their results with mine because I examined associations of "clinically significant anxiety" (defined as a GAD-2 score ≥ 3) whilst they compared median anxiety scores between groups of participants.

7.5.3.3 Relevant studies of the associations of clinically significant anxiety in older adults in community settings

Two reviews have summarised studies of associations of anxiety in older adults in community settings,[205,206] one of which focussed specifically on residential aged care facilities.[206] These reviews found inconsistent evidence on the association between anxiety and age – most studies found no evidence of an association (consistent with my findings), but several reported younger age to be associated with anxiety.[205,206] Female gender was associated with anxiety in several studies as it was in mine,[205,206] although this association was reported less consistently in literature focussed on residential aged care facilities.[206] Neither review found evidence of an association between marital status and anxiety,[205,206] which contrasts with my findings. It could be that spouses and partners offer support that is particularly helpful in reducing anxiety symptoms in older adults who are medically ill and hospitalised. Older adults in the community may not require this type of support as they are typically less acutely unwell when compared to those in general hospitals.

I found that clinically significant anxiety was associated with a greater multimorbidity score and worse independent functioning – several (but not all) studies of older adults in community settings have reported similar findings.[205,206] One review found, as I did, that there is strong evidence to

[205]Review's inclusion criteria: Participants aged ≥ 50 years; conducted in community or primary care setting in a Western country; examined ≥ one risk factor for anxiety or depression; cross-sectional or longitudinal study design; written in English; and published between 1995 and 2005.

[206]Review's inclusion criteria: Participants were residential aged care facility residents aged ≥ 50 years; examined ≥ one association(s) of anxiety (included studies that used anxiety as dependent or independent variable); cross-sectional or longitudinal study design; and written in English. Excluded case reports, qualitative studies, reviews, dissertations and abstracts.

suggest that an association between anxiety and depression exists.[206] In contrast with my findings, the review of older adults in residential aged care facilities reported some evidence that higher cognitive functioning, not reduced functioning, was associated with anxiety.[206] I did not include patients with severe cognitive impairment – it is possible if I included these patients that I could have obtained different results.

7.5.4 Strengths

My cross-sectional substudy has several strengths.

First, it has a large sample size. It is important for the sample size of a study to be sufficiently large in order to obtain accurate findings.[19]

Second, anxiety was measured at a consistent time frame in participants' admission to hospital (i.e. within one week of admission). Measuring anxiety at approximately the same time in patients' admission to hospital helps provide a more homogenous study sample.

Third, I examined associations of clinically significant anxiety in older general hospital inpatients as well as its prevalence.

Fourth, this substudy included severely ill patients. Their inclusion increases the ability to generalise results from this substudy because older general hospital inpatients are often frail and acutely unwell, with high rates of multimorbidity.[207]

Fifth, the researchers who collected data used in this substudy underwent rigorous training and monitoring to ensure study quality.

7.5.5 Limitations

My cross-sectional substudy also has several limitations.

The most important limitation is that its sample was drawn from a sample of people who agreed to participate in a clinical trial. This may reduce the generalisability of the findings in a number of ways. For instance, the trial had selection criteria which excluded patients: (1) who had already been referred to the usual care liaison psychiatry team during their admission; (2) who did not read or speak English; and (3) for whom trial participation was considered practically or clinically inappropriate (e.g. patients who were not from the local area that the hospital served). The exclusion of older general hospital inpatients already referred to liaison psychiatry is potentially of particular importance, given they are likely to have high rates of psychiatric symptoms and illnesses. However, only a relatively small proportion of patients (around 3.5%[a]) were excluded from the trial based on these three aforementioned criteria.

Moreover, the findings may not be generalisable to other populations of older general hospital inpatients (e.g. older adults who are terminally ill and those who have been in hospital for a while). In particular, the findings might not generalise to those with severe cognitive impairment, since this study focussed on patients able to complete all items of the GAD-2, PHQ-2 and Barthel ADL Index. It should also be noted that all participants included in this sample attended teaching hospitals in the United Kingdom and the findings might not

[a]Patients could be counted more than once (i.e. units are “hospital admissions”, rather than individual patients).

generalise to older adults admitted to other types of general hospitals or other clinical settings.

It is also important to note that around one-third of eligible older general hospital inpatients declined to take part in the clinical trial that this sample was drawn from. This refusal rate may reduce the generalisability of the findings. However, the people who refused to take part in The HOME Study were similar to the people who participated in terms of age and sex (i.e. percentage of females and males).[a]

There were also limitations in the way in which some data were collected for this substudy. As previously discussed, there are shortcomings of using the GAD-2 to measure anxiety, including that it cannot be used to diagnose an anxiety disorder.[75] Moreover, several demographic and clinical characteristics were collected from medical records, which are prone to inaccuracies. Multimorbidity score, for example, was measured based on diagnoses charted in participants' medical records when they were admitted into hospital. This offers a relatively "crude" measure of multimorbidity.

Another limitation is that I was only able to examine associations of clinically significant anxiety with the limited number of demographic and clinical characteristics that I had data on. Because of this, there are numerous associations that I was not able to study. Additionally, for analyses of the association between clinically significant anxiety and cognitive impairment, T-

[a]The HOME Study researchers had approval to collect information on age and sex only for the patients who declined participation.

MoCA scores were imputed for 20% or less of missing items in a small proportion of participants (4%).

Lastly, I was not able to conclude if any of the associations I found between clinically significant anxiety and participants' demographic and clinical characteristics were causal, because of the cross-sectional study design used.

7.5.6 Implications and conclusions

To my knowledge, this is the largest study to examine the prevalence and associations of clinically significant anxiety in older general hospital inpatients. Its findings suggest that clinically significant anxiety is common in this patient population, occurring in over 40 percent. It also offers information on which older inpatients are most likely to have it: females, those without a spouse or partner, and those who are “sicker” (i.e. those with greater multimorbidity, worse independent functioning, greater depression severity and worse cognitive impairment).

There remains a need for more high-quality studies of anxiety in older general hospital inpatients. While this study provides information on the prevalence of clinically significant anxiety defined using a cut-off score, it does not offer information on the prevalence of anxiety disorders. In my systematic review (**Chapter 5**) I found only two studies of the prevalence of anxiety disorders in this patient population, both of which had small sample sizes. Therefore, additional research on this topic is required.

There are also a number of associations of clinically significant anxiety that have not yet been examined which could be important to these patients. Research on modifiable factors (e.g. pain severity) might be particularly useful, because addressing these may provide the opportunity to reduce anxiety in older general hospital inpatients.

Better information on anxiety in older general hospital inpatients is needed to inform psychiatric care for this patient population.

Chapter 8
Substudy 2: Prevalence and associations of clinically significant depression in older general hospital inpatients

8.1 Research aim

I aimed to determine the prevalence and associations of clinically significant depression (defined as a PHQ-2 score ≥ 3) in older (aged ≥ 65 years) general hospital inpatients.

8.2 Hypotheses

I hypothesised that the following demographic and clinical characteristics would be associated with clinically significant depression in older general hospital inpatients:

(1) younger age;

(2) female sex;

(3) not having a spouse or partner;

(4) greater multimorbidity score;

(5) worse independent functioning;

(6) greater anxiety severity; and

(7) worse cognitive impairment.

I made these hypotheses based on my own experience working with older general hospital inpatients and on studies of other populations of older adults.[208-211]

8.3 Methods

8.3.1 Sample

As outlined in **Chapter 6**, this substudy included the same sample of participants as my substudy on the prevalence and associations of clinically significant anxiety in older general hospital inpatients (**Chapter 7**). I described this sample in detail on **page 149**.

8.3.2 Depression measure

8.3.2.1 Patient Health Questionnaire 2-item scale (PHQ-2)

The PHQ-2 comprises two items that assess key symptoms of depression in the preceding two weeks: (1) having little interest or pleasure in doing things and (2) feeling down, depressed or hopeless (see **Figure 10**).[172] For each of the items, the response options are “not at all”, “several days”, “more than half the days” and “nearly every day”, which are scored as zero, one, two and three, respectively.[172] Scores on the PHQ-2 range from zero to six, with higher scores indicating greater depression severity.[172]

The PHQ-2 was developed from the Patient Health Questionnaire 9-item scale (PHQ-9).[172,212] The PHQ-9 comprises nine items which are linked to the DSM-IV diagnostic criteria for major depression. The first two items of the PHQ-9 make up the PHQ-2.[172] The PHQ-9 was initially developed as a questionnaire to help clinicians to diagnose depressive disorders and to measure depression severity, and the PHQ-2 was subsequently developed as a brief depression screening measure.[172,212] The PHQ-9 and PHQ-2 have been found to have good sensitivity and specificity for detecting probable cases of major depression.[172,212] When applying a cut-off score of three or greater, the sensitivity and specificity of the PHQ-2 for detecting major depression are 83%-87% and 78%-90[a]% respectively.[21,172] In other words, the PHQ-2 is good at correctly detecting those with major depression (“true positives”) as well as those without major depression (“true negatives”).

[a]Authors reported specificity of 90% in table and text of paper, but 92% in abstract of paper.[172]

Figure 10. Patient Health Questionnaire 2-item scale (PHQ-2)[172]

Item	Response options	Score
Over the last two weeks, how often have you been bothered by little interest or pleasure in doing things?	Not at all	0 points
	Several days	1 point
	More than half the days	2 points
	Nearly every day	3 points
Over the last two weeks, how often have you been bothered by feeling down, depressed or hopeless?	Not at all	0 points
	Several days	1 point
	More than half the days	2 points
	Nearly every day	3 points

8.3.2.2 Cut-off score on the PHQ-2

In this substudy, the PHQ-2 was used to measure symptoms of depression, rather than as a screening measure for major depression. I defined clinically significant depression as a PHQ-2 score of three or greater, as recommended by the developers of the scale.[172,192] Validation studies of the PHQ-2 have recommended using a cut-off score of three or greater to define clinically significant depression because this cut-off has optimal sensitivity and specificity for detecting probable cases of major depression.[21,172]

8.3.2.3 Advantages of the PHQ-2

The PHQ-2 is a suitable depression measure for acutely unwell, older general hospital inpatients for three main reasons.

First, the PHQ-2 is brief. Older general hospital inpatients are usually severely unwell which can make it challenging for them to complete questionnaires. The brevity and simplicity of the PHQ-2 minimises the burden placed on these ill patients when they complete it. Using depression measures that are minimally burdensome also increases the likelihood of collecting data from patients.

Second, the PHQ-2 does not measure somatic symptoms of depression (e.g. fatigue and loss of energy[22]). The PHQ-2's lack of focus on somatic symptoms makes it particularly useful for assessing medically ill patients (e.g. older general hospital inpatients). Somatic symptoms of depression can be very similar to somatic symptoms that result from medical illnesses. Because of this, depression measures that assess for somatic symptoms may misattribute medically related somatic symptoms to depression and estimate a "falsely high" depression prevalence.

Third, the PHQ-2 demonstrates good psychometric properties. The PHQ-2 has excellent validity (convergent validity, divergent validity and construct validity) and reliability (internal reliability and test-retest reliability):

(1) Convergent validity: The PHQ-2's convergent validity was assessed by measuring its association with three other depression-related measures: (1) Hospital Anxiety and Depression Scale (HADS), (2) World Health Organization Five-Item Well-Being Index (WBI-5) and (3) 12-Item Short

Form Health Survey (SF-12) mental health subscale.[21] The PHQ-2 was strongly associated with the HADS (correlation coefficient = 0.67), WBI-5 (correlation coefficient = –0.69) and SF-12 mental health subscale (correlation coefficient = –0.71), which demonstrates it has good convergent validity.[21] One would expect the PHQ-2 to be strongly associated with all three measures because it intends to measure a similar construct as them. Other validation studies have obtained similar findings.[172,194]

(2) Divergent validity: The PHQ-2's divergent validity was assessed by measuring its association with a physical functioning measure (SF-12 physical functioning subscale).[21] The PHQ-2 demonstrated good divergent validity because it was weakly associated with the SF-12 physical functioning subscale (correlation coefficient = –0.23).[21] One would expect the two measures to be weakly associated because depression and physical functioning are different constructs. Other validation studies have reported comparable results.[172,194]

(3) Construct validity: Since the PHQ-2 demonstrated acceptable convergent validity and divergent validity, researchers concluded the PHQ-2 measures the construct it is intending to measure (i.e. depression) and therefore has good construct validity.[21]

(4) Internal reliability: The PHQ-2 has good internal reliability, with a Cronbach alpha of 0.81 to 0.83.[21,194] In other words, its two items consistently measure the same construct.

(5) Test-retest reliability: The PHQ-2 was found to consistently measure depression over time, with an estimated intraclass correlation coefficient of 0.79.[196]

8.3.2.4 Disadvantages of the PHQ-2

There are three main disadvantages of the PHQ-2.

First, the PHQ-2 cannot be used to diagnose a depressive disorder.[172] It can be used to measure symptoms of depression, to identify clinically significant depression by applying a cut-off score and to identify patients likely to have a depressive disorder. A comprehensive clinical assessment would be required to obtain enough information and context to diagnose an individual with a depressive disorder and to determine whether or not to initiate treatment.

Second, the PHQ-2 does not measure the "severity" of the symptoms of depression it measures. The PHQ-2 measures how *often* individuals have been bothered by two symptoms of depression,[172] however it does not assess *how much* individuals have been bothered by these symptoms. Comprehensive depression measures (e.g. clinical interviews) can obtain more accurate measurements of the "severity" of patients' symptoms of depression.

Third, the PHQ-2 does not assess for all of the different symptoms of depression; instead, it measures two core symptoms.[172] As a result, it is possible that some patients who have depressive symptoms will not score highly on the PHQ-2 (e.g. patients with mainly somatic symptoms of depression).

8.3.3 Statistical analyses

As described in **Chapter 6**, I report the distribution of depression (PHQ-2) scores and point prevalence of clinically significant depression (defined as a PHQ-2 score ≥ 3) in study participants. I also describe the associations of clinically significant depression (defined as a PHQ-2 score ≥ 3) with the following demographic and clinical characteristics: age, sex, relationship status, multimorbidity score, independent functioning, anxiety severity and cognitive impairment. I used univariable and multivariable logistic regressions to assess the associations of clinically significant depression with participants' demographic and clinical characteristics (listed above), adjusting for age and sex in the multivariable analyses. To supplement these analyses, I used univariable and multivariable linear regressions to assess the associations of greater depression (PHQ-2) scores with participants' demographic and clinical characteristics (listed above), adjusting for age and sex in the multivariable analyses. In analyses of the association of clinically significant depression and cognitive impairment, participants with up to 20% of missing T-MoCA items had scores imputed for these items using individual mean imputation (see **Chapter 6 Section 6.7.3.4** for more detail).

8.4 Results

8.4.1 Sample description

As previously stated, this substudy included the same sample of 1,786 participants as my substudy on the prevalence and associations of clinically significant anxiety in older general hospital inpatients (**Chapter 7**). I described this sample in detail on **pages 156 to 162**.

8.4.2 Distribution of depression scores

8.4.2.1 Total PHQ-2 score

Participants had a mean total depression (PHQ-2) score of 2.4 (SD of 2.1), with scores ranging from zero to six (see **Table 19**). The distribution of participants' total depression scores are depicted in **Figure 11.** The most common PHQ-2 score was zero (i.e. the minimum PHQ-2 score).

8.4.2.2 Individual PHQ-2 item scores

The PHQ-2 is made up of two items: the first focusses on having little interest or pleasure and the second on feeling down. Similar proportions of participants reported little interest or pleasure for at least several days in the preceding two weeks (item 1, 57.1%) and feeling down, depressed or hopeless (item 2, 62.8%).

8.4.3 Prevalence of clinically significant depression

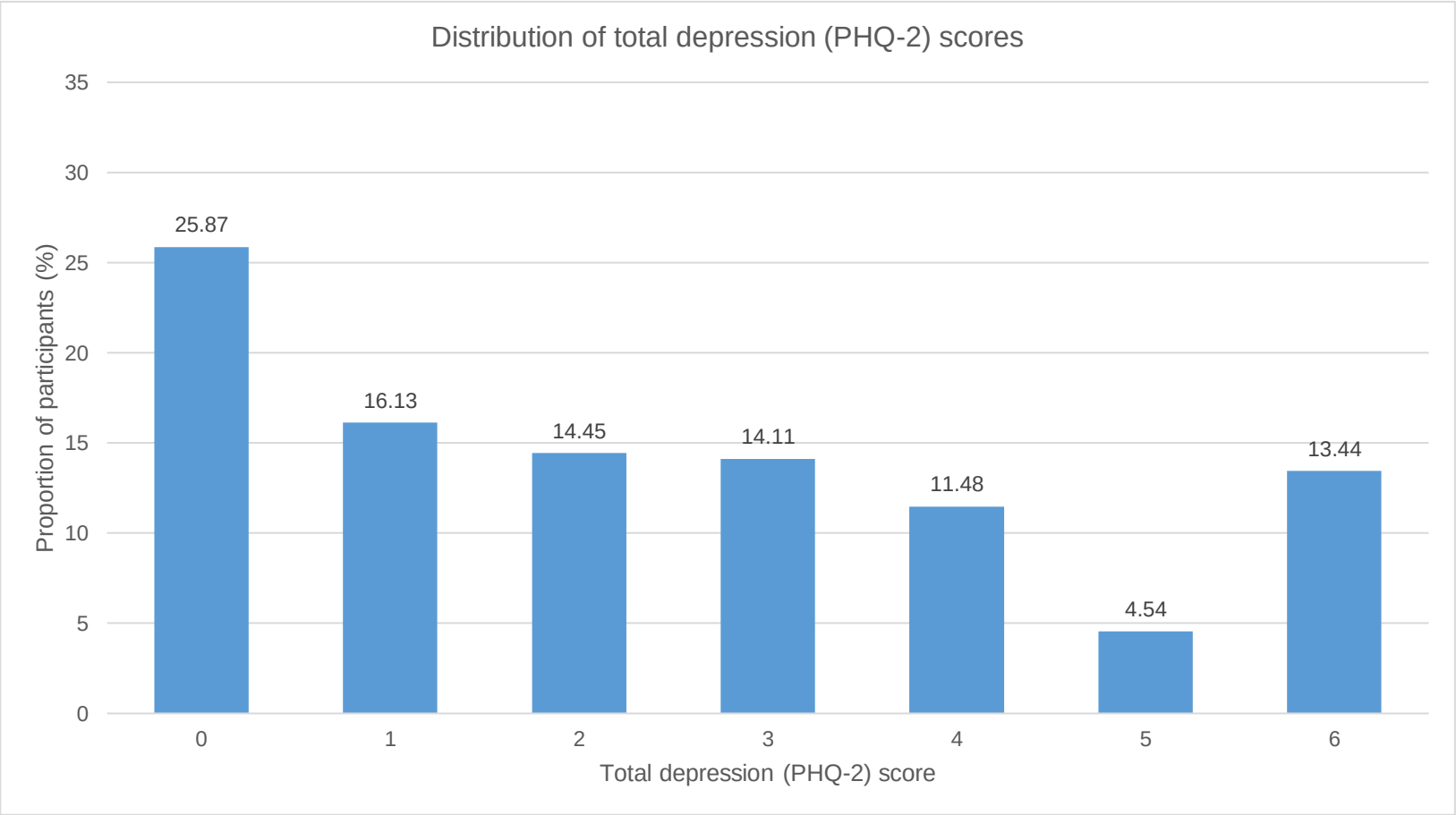
43.6% of participants had clinically significant depression, defined as a PHQ-2 score of three or greater.

Table 19. Prevalence and associations of clinically significant depression in older general hospital inpatients: Distribution of depression (PHQ-2) scores of participants in analyses

	Sample (n = 1,786)
PHQ-2	
Mean (SD)	2.37 (2.06)
Median (IQR)	2 (0 to 4)
Range	0 to 6
Total score of 0	462 (25.87%)
Total score of 1	288 (16.13%)
Total score of 2	258 (14.45%)
Total score of 3	252 (14.11%)
Total score of 4	205 (11.48%)
Total score of 5	81 (4.54%)
Total score of 6	240 (13.44%)
Total score of 3 or greater	778 (43.56%)
PHQ-2 Item 1 (Little interest or pleasure in doing things)	
Not at all	767 (42.95%)
Several days	381 (21.33%)
More than half the days	195 (10.92%)
Nearly every day	443 (24.80%)
PHQ-2 Item 2 (Feeling down, depressed or hopeless)	
Not at all	664 (37.18%)
Several days	517 (28.95%)
More than half the days	207 (11.59%)
Nearly every day	398 (22.28%)

Data are number (%) unless otherwise indicated.
IQR = Inter-Quartile Range; PHQ-2 = Patient Health Questionnaire 2-item scale; SD = Standard Deviation.

Figure 11. Histogram of the distribution of total depression (PHQ-2) scores of participants in analyses



PHQ-2 = Patient Health Questionnaire 2-item scale.

8.4.4 Associations of clinically significant depression

I present the results of the univariable and multivariable analyses of associations of clinically significant depression (defined as a PHQ-2 score ≥ 3) with participants' demographic and clinical characteristics in **Table 20** and **Table 21**.

Age, sex and relationship status. There was no evidence of an association between clinically significant depression and age, sex or relationship status in the univariable analyses or in the multivariable analyses (where age and sex were adjusted for).

Multimorbidity score. Clinically significant depression was associated with a greater multimorbidity score in the univariable analysis. The association was moderately strong (OR = 1.08, 95% CI, 1.02 to 1.14, i.e. a one-unit increase in multimorbidity score was associated with an 8% increase in odds of clinically significant depression). These findings did not change after adjusting for age and sex in the multivariable analysis (adjusted OR = 1.08, 95% CI, 1.02 to 1.14).

Independent functioning. Clinically significant depression had a moderately strong association with worse independent functioning in the univariable analysis (OR = 0.93, 95% CI, 0.91 to 0.94, i.e. the odds of clinically significant depression were estimated to decrease by 7% for a one-unit increase in independent functioning [Barthel ADL Index] score, where lower scores indicate worse independent functioning). These findings remained after adjusting for age

and sex in the multivariable analysis (adjusted OR = 0.92, 95% CI, 0.90 to 0.94).

Anxiety. Clinically significant depression was **strongly** associated with greater anxiety severity in the univariable analysis (OR = 1.95, 95% CI, 1.83 to 2.08). In other words, the odds of clinically significant depression were estimated to nearly **double** for every one-unit increase in anxiety (GAD-2) score, where higher scores indicate greater anxiety severity. These findings remained after adjusting for age and sex in the multivariable analysis, with an association similar in strength (adjusted OR = 1.96, 95% CI, 1.84 to 2.08).

Cognitive impairment. Clinically significant depression was associated with worse cognitive impairment in the univariable analysis. The association was moderately strong (OR = 0.96, 95% CI, 0.94 to 0.97, i.e. the odds of clinically significant depression were estimated to decrease by 4% for a one-unit increase in cognitive function [T-MoCA] score, where lower scores indicate worse cognitive function). These findings persisted after adjusting for age and sex in the multivariable analysis (adjusted OR = 0.95, 95% CI, 0.93 to 0.96).

Supplementary analyses. All previous analyses were repeated with depression being treated as a continuous variable (i.e. greater depression scores), rather than a binary variable (i.e. having clinically significant depression or not having clinically significant depression). These analyses yielded the same results.

Table 20. Univariable analyses of associations of demographic and clinical characteristics and clinically significant depression (defined as a PHQ-2 score ≥ 3)

	Unadjusted odds ratio (95% CI)	***p*-value**
Age	1.00 (0.98 to 1.01)	0.41
Sex		
Female	1	
Male	0.96 (0.80 to 1.16)	0.68
Relationship status		
Spouse or partner	1	
No spouse or partner	1.07 (0.89 to 1.29)	0.48
Multimorbidity score[a]	1.08 (1.02 to 1.14)	0.01
Independent functioning (Barthel ADL Index score)[b]	0.93 (0.91 to 0.94)	< 0.001
Anxiety (GAD-2 score)[c]	1.95 (1.83 to 2.08)	< 0.001
Cognitive impairment (T-MoCA score)[d,e]	0.96 (0.94 to 0.97)	< 0.001

Barthel ADL Index = Barthel Activities of Daily Living Index; CI = Confidence Interval; GAD-2 = Generalized Anxiety Disorder 2-item scale; T-MoCA = Telephone Montreal Cognitive Assessment.
[a]Number of body systems with a diagnosis on admission (scores range from 0 to 16).
[b]Lower scores indicate worse independent functioning (scores range from 0 to 20).
[c]Higher scores indicate greater anxiety severity (scores range from 0 to 6).
[d]Lower scores indicate worse cognitive impairment (scores range from 0 to 30).
[e]Univariable analysis of 1,719 participants who had at least 80% of the items of a T-MoCA completed.

Table 21. Multivariable analyses of associations of demographic and clinical characteristics and clinically significant depression (defined as a PHQ-2 score ≥ 3) adjusted for age and sex

	Adjusted odds ratio (95% CI)	***p*-value**
Age[a]	1.00 (0.98 to 1.01)	0.40
Sex[b]		
Female	1	
Male	0.96 (0.79 to 1.15)	0.65
Relationship status[c]		
Spouse or partner	1	
No spouse or partner	1.09 (0.89 to 1.33)	0.40
Multimorbidity score[c,d]	1.08 (1.02 to 1.14)	0.01
Independent functioning (Barthel ADL Index score)[c,e]	0.92 (0.90 to 0.94)	< 0.001
Anxiety (GAD-2 score)[c,f]	1.96 (1.84 to 2.08)	< 0.001
Cognitive impairment (T-MoCA score)[c,g,h]	0.95 (0.93 to 0.96)	< 0.001

Barthel ADL Index = Barthel Activities of Daily Living Index; CI = Confidence Interval; GAD-2 = Generalized Anxiety Disorder 2-item scale; T-MoCA = Telephone Montreal Cognitive Assessment.
[a]Analysis adjusted for sex.
[b]Analysis adjusted for age.
[c]Analysis adjusted for age and sex.
[d]Number of body systems with a diagnosis on admission (scores range from 0 to 16).
[e]Lower scores indicate worse independent functioning (scores range from 0 to 20).
[f]Higher scores indicate greater anxiety severity (scores range from 0 to 6).
[g]Lower scores indicate worse cognitive impairment (scores range from 0 to 30).
[h]Multivariable analysis of 1,719 participants who had at least 80% of the items of a T-MoCA completed.

8.5 Discussion

8.5.1 Main findings

Clinically significant depression occurred frequently in older general hospital inpatients, affecting approximately 40 percent. It was strongly associated with being “sicker” (i.e. greater multimorbidity score, worse independent functioning, greater anxiety severity and worse cognitive impairment). These findings all remained after adjusting for age and sex. I did not find evidence of an association between clinically significant depression and age, sex or relationship status.

8.5.2 Prevalence of clinically significant depression

8.5.2.1 Overview of results

I expected that a large proportion of older general hospital inpatients would have clinically significant depression, based on my experience working with the patients who took part in this substudy. Patients often told me about losses that they were experiencing which made them feel down – these included losing their independence, good health and careers, as well as those who were close to them (e.g. their spouse and friends). The prospect that these things were unlikely to get better with time (e.g. their health was likely to continue to worsen) made many feel hopeless. Related to this, patients frequently said that they were no longer interested in doing things that they usually would because their diminishing health made it difficult (if not impossible) to do these activities. Patients often added they no longer had a social circle to enjoy doing these activities with and they felt too down to engage in these activities. Interestingly, older general hospital inpatients involved in another study of the prevalence and associations of clinically significant depression expressed remarkably similar circumstances that caused them to experience symptoms of depression.[188]

8.5.2.2 Relevant studies of the prevalence of clinically significant depression in older general hospital inpatients

8.5.2.2.1 Clinically significant depression defined using a cut-off score

Several previous studies have estimated the prevalence of clinically significant depression – defined using a cut-off score – in older general hospital inpatients (see **Table 22**).[188,199,213-224]

These studies were conducted in a number of countries (Brazil, China, Hungary, Ireland, Malaysia, the Netherlands, Norway, Spain, Switzerland, the United Kingdom and the United States). They included older adults admitted to a variety of general hospital wards, including general medical, surgical, geriatric, respiratory, neurology and cardiology wards. The majority recruited small sample sizes of fewer than 200 participants.[188,199,213,217,218,220-222] Studies used a variety of depression measures (primarily the Geriatric Depression Scale[225]) – although most used self-rated measures,[188,199,213-219,221-224] some used observer-rated measures.[216,217,220]

These studies reported prevalence estimates for clinically significant depression that ranged widely, from 10.3% to 73%. Most studies, however, reported a prevalence estimate between around 20% and 50%.[199,213-215,217-219,222-224]

The lowest prevalence estimate (10.3%) was reported in a study of old inpatients (mean age of 80.7 years) admitted to the internal medicine service of a general community hospital.[216] This study explicitly excluded those with poor physical functioning and severe cognitive impairment,[216] and its participants (on average) had relatively good functional independence and low levels of clinically significant anxiety. These characteristics could have contributed to its low

prevalence estimate because I found that worse cognitive impairment, worse independent functioning and greater anxiety severity were associated with clinically significant depression. The authors explained they may have obtained a low prevalence estimate because their study was conducted in a rural setting; they speculated that social and cultural factors related to living in rural areas (e.g. nearness to nature and local sense of belonging) might improve older medically ill individuals' well-being.[216] They also speculated if they had included severely ill patients (i.e. those with poor physical functioning and severe cognitive impairment) they may have obtained a higher prevalence estimate.[216]

The highest prevalence estimate (73%) was reported in a study of relatively young inpatients (median age of 73 years) admitted to an internal medicine department of a general hospital.[220] It is perhaps not surprising that this study obtained such a high prevalence given that it used the Hamilton Rating Scale for Depression which has items that assess for somatic symptoms of depression (e.g. insomnia, bodily aches and heaviness, and loss of appetite).[226,227] Older general hospital inpatients are likely to experience many somatic symptoms related to their medical illnesses. Therefore, depression measures that include somatic symptoms are likely to find higher prevalences of depression than depression measures that do not.

It is challenging to directly compare the findings of these studies with mine because they studied different populations (e.g. many studies included much younger participants[188,199,213,217,218,220,221]) using different depression measures (none used the PHQ-2). However, it is notable that the one other study

conducted in the United Kingdom reported the same prevalence as my substudy.[215]

8.5.2.2.2 Clinically significant depression defined using diagnostic criteria

In my meta-review (**Chapter 4**), I included a systematic review which summarised studies of the prevalence of depression in general hospital inpatients, where depression was defined using diagnostic criteria.[70] 14 articles (of 12 separate studies) included in this review focussed on older general hospital inpatients (summarised in **Table 23**).[70] These studies reported prevalence estimates for diagnosed depression that ranged from 2.7% to 27.4%,[70] which is lower than the prevalence of clinically significant depression that I found. As discussed in **Chapter 7**, studies that use diagnostic criteria tend to report lower prevalences than those that use cut-off scores because diagnostic criteria specify strict criteria for symptom severity, pattern and duration. In comparison to my substudy, the studies of older adults included in this systematic review had much smaller sample sizes (median sample size of 114).

Table 22. Studies of the prevalence of clinically significant depression (defined using a cut-off score) in older general hospital inpatients

Study	Setting	Selection criteria	Sample characteristics	Depression measure	Cut-off score	Prevalence
Al Aqqad et al. (2017)[199,a]	Respiratory wards in four major hospitals (Malaysia).	Aged ≥ 60 years; hospitalised with primary diagnosis of acute exacerbation of COPD; no coexisting active pulmonary tuberculosis; cognitively able to complete questionnaires. Excluded those who died during hospitalisation; were transferred to or from another hospital; and did not complete questionnaires.	Sample size = 81 Age (median, IQR) = 72, 66.4 to 78.0 % female = 2.47%	GDS-15	Depression (scores ≥ 6)	38.27 % (assessed on discharge).
Conde Martel et al. (2013)[213,a]	Internal medicine service in a hospital (Spain).	Aged > 64 years; no aphasia, coma, unstable condition or advanced dementia preventing adequate communication; no depression that required psychiatric evaluation.	Sample size = 115 Age (mean) = 70.5 % female = 61.7%	GDS-15 (Spanish version)	Depressive symptoms (scores ≥ 6)	40% (assessed within 48 hours of admission).
Covinsky et al. (1999)[214,b]	General medicine service in a teaching hospital (United States).	Aged ≥ 70 years; not too ill or confused to participate; not admitted from a nursing home.	Sample size = 573 Age (mean) = 79.9 % female = 67.8%	GDS-15	Depressive symptoms (scores ≥ 6)	34% (assessed within 48 hours of admission).
Cullum et al. (2006)[215,b]	Acute wards of a district general hospital (United Kingdom).	Aged ≥ 65 years; hospitalised for 3 to 6 days at time of screening; no severe dysphasia, deafness or diagnosis of alcohol dependency; not too physically unwell or confused to participate; current residence within area covered by West Suffolk Primary Care Trust.	Sample size = 618 Age (mean, SD) = 80.2, 7.48 % female = 59%	GDS-15	Screening for probable depressive disorder (scores ≥ 5)	44%

Study	Setting	Selection criteria	Sample characteristics	Depression measure	Cut-off score	Prevalence
Helvik et al. (2010)[216,a]	Internal medicine service in a general community hospital in a rural area (Norway).	Aged ≥ 65 years; ≥ 2 days in hospital; non-elective admission; belonged to region; not involved in other research projects; no severe cognitive impairment or communication difficulties; no "terminal state"; no poor physical functioning.	Sample size = 484 Age (mean, SD, range) = 80.7, 7.4, 65 to 101 % female = 50.2%	HAD-D	Depression (scores ≥ 8)	10.3%
				MADRS[c]	Clinically significant depression symptoms (scores ≥ 10)	13.4%
Koenig et al. (1988)[217,b]	Medical and neurologic services of a Veterans Affairs medical centre (United States).	Aged ≥ 70 years; not transferred from other units in hospital; not readmitted during period of observation; no cognitive impairment, communication problems or severe neurologic illness that precluded assessment.	Sample size = 130 Age (mean) = 73.6 % female = 0%	GDS-30[d]	Depressive symptoms (scores ≥ 11)	19.5% (assessed approximately 24 to 48 hours after admission).
Koenig et al. (1993)[188,b]	General medicine and cardiology services in a private teaching hospital (United States).	Aged ≥ 60 years; hospitalised for ≥ 48 to 72 hours; not too sedated or cognitively impaired to preclude a diagnostic interview.	Sample size = 76 Age (mean, range) = 70, 60 to 89 % female = 46% (70% general medicine & 37.5% cardiology)	CES-D	Depressive symptoms (scores > 15)	60% of general medicine inpatients and 26.8% of cardiology inpatients (assessed within 48 to 96 hours of admission).
Kok et al. (1995)[218,a]	General medical and surgical wards in a	Aged ≥ 65 years; hospitalised for ≥ 2 days; no physical or communication problems that precluded psychological testing.	Sample size = 198 Age (mean, SD) = 74, 6.0 % female = 41.9%*	BDI	Probable case of depression (scores ≥ 13)	19.2% (assessed within 5 days of admission).

Study	Setting	Selection criteria	Sample characteristics	Depression measure	Cut-off score	Prevalence
	university hospital (Netherlands).			GDS-30	Probable case of depression (scores ≥ 11)	19.7% (assessed within 5 days of admission).
Li et al. (2016)[219,a]	General wards, internal wards and surgical wards in general hospitals (China).	Aged ≥ 60 years; stabilised medical condition; no severe cardiopulmonary disease, crucial organic failure or severe cognitive impairment.	Sample size = 2,373 Age = 28% (60 to 69 years), 36.5% (70 to 79 years), 35.5% (≥ 80 years) % female = 33.5%	GDS-30	Depression (scores ≥ 11)	18.1%
Linka et al. (2000)[220,b]	Internal medicine department of a general hospital (Hungary).	Aged ≥ 65 years; ability to cooperate.	Sample size = 100 Age (median, IQR) = 73, 70 to 77.5 % female = 64%	HDS 17-item[c]	Mild depressive symptoms (scores 8 to 15) Severe depressive symptoms (scores ≥ 16)	73% total: 46% had mild depressive symptoms, 27% had severe depressive symptoms (assessed “some days” before discharge).
Mendes-Chiloff et al. (2008)[221,a]	University hospital (Brazil).	Aged ≥ 60 years; no severe pain at time of interview; no communication difficulties or hearing problems; no severe cognitive impairment or delirium; not on mechanical ventilation.	Sample size = 189 Age (mean, SD, range) = 70, 7.08, 60 to 92 % female = 55%	GDS-15	Mild depressive symptoms (scores 6 to 10) Severe depressive symptoms (scores ≥ 11)	56.1% total: 51.8% had mild depressive symptoms, 4.3% had severe depressive symptoms (majority of interviews conducted 7 to 10 days after admission).
O’Riordan et al. (1989)[222,b]	Acute geriatric medical unit	No dysphasia, coma, severe sensory impairment or confusion; not critically ill.	Sample size = 111 Age (mean, range) =	GDS-30	Possible depression (scores ≥ 11)	28.8% (assessed within 3 to 7 days of admission).

Study	Setting	Selection criteria	Sample characteristics	Depression measure	Cut-off score	Prevalence
	in a teaching hospital (Ireland).		80, 66 to 98 % female = 66.6%			
Pouget et al. (2000)[223,a]	Internal medicine service in a tertiary academic medical centre (Switzerland).	Aged ≥ 75 years; hospitalised for ≥ 48 hours; non-elective admission; no severe cognitive impairment, communication difficulties or unstable medical conditions that precluded assessment; not living in a nursing home; no private insurance.	Sample size = 401 Age (mean) = 82.4 % female = 60.9%	GDS-15	Depressed mood (scores ≥ 6)	22.4% (assessed within 48 hours of admission).
Zou et al. (2018)[224,a]	Geriatric wards in a tertiary hospital (China).	Aged ≥ 60 years; no severe cognitive dysfunction, hearing impairment, severe cardiopulmonary disease, reduced level of consciousness, crucial organ failure or unstable medical illnesses.	Sample size = 411 Age (mean, SD, range) = 75.9, 8.1, 60 to 97 % female = 35.5%	GDS-15	Depressive symptoms (scores ≥ 6)	32.8% (assessed within 48 hours of admission).

BDI = Beck Depression Inventory; CES-D = Center for Epidemiologic Studies Depression Scale; COPD = Chronic Obstructive Pulmonary Disease; GDS = Geriatric Depression Scale; HAD-D = Hospital Anxiety and Depression scale, Depression subscale; HDS = Hamilton Rating Scale for Depression; IQR = Inter-Quartile Range; MADRS = Montgomery-Asberg Depression Rating Scale; SD = Standard Deviation.

[a]I searched MEDLINE from database inception to July 2020 for relevant studies that included prevalence, depression and general hospital inpatient (as well as synonyms and alternative spellings) in their titles. **Table 22** summarises the results of the relevant studies for which I could obtain a full paper.

[b]I extracted some relevant studies from Helvik et al. (2010)'s table of studies of the prevalence of depression in elderly medical inpatients.[216]

[c]Observer-rated depression measure.

[d]Paper also reported several adjusted and unadjusted prevalence estimates using the Hamilton Depression Scale and Montgomery-Asberg Depression Rating Scale, both of which are observer-rated depression measures.

*Calculated using data from paper.

Table 23. Studies of the prevalence of clinically significant depression (defined using diagnostic criteria) in older general hospital inpatients[a]

Study, Year, Country	Sample size	Depression measure	Caseness definition	Prevalence
Fenton et al. (1994)[228] (Canada)	215	DIS	Major depression (DSM-III, actuarial approach)	27.4%
Koenig et al. (1991)[229] (United States)	332	DIS	Major depression (DSM-III-R, aetiologic approach)	13.3%
Koenig et al. (1993)[188] (United States)	76	Clinical interview	Major depression (DSM-III-R, inclusive approach)	13.1%
Koenig et al. (1997)[230] (United States)	460	Interview based on the DIS	Major depression (DSM-IV, etiologic approach)	16.5%
Kok et al. (1992, 1995)[218,231] (Netherlands)	188	Stage 1: BDI ≥ 13, GDS ≥ 11, MMSE < 24 Stage 2: GMS	Major depression (DSM-III-R)	2.7%
Kumar et al. (2012)[232] (India)	120	Semi-structured interview	Depression (ICD-10)	25%
Lázaro et al. (1991)[233] (Spain)	95	CIS + clinical interview if psychiatric diagnosis or MMSE < 23	Major depression (DSM-III-R)	10%
Lázaro et al. (1995)[234] (Spain)	108	Clinical interview	Major depression (DSM-III-R)	4.6%
Linka et al. (1999, 2000)[220,235] (Hungary)	100	Semi-structured interview based on DSM-IV criteria	Major depression (DSM-IV)	11.0%
Thalassinos et al. (1992)[103] (France)	100	DIS	Major depression (DSM-III)	5%

Study, Year, Country	Sample size	Depression measure	Caseness definition	Prevalence
Wancata et al. (2000)[236] (Austria)	244	CIS	Major depression (DSM-III-R and score of ≥ 2 on a 5-point severity scale)	2.9%
Uwakwe (2000)[104] (Nigeria)	106	GMS	Depression (ICD-10)	22.6%

BDI = Beck Depression Inventory; CIS = Clinical Interview Schedule; DIS = Diagnostic Interview Schedule; DSM = Diagnostic and Statistical Manual of Mental Disorders; GDS = Geriatric Depression Scale; GMS = Geriatric Mental State Schedule; ICD = International Classification of Diseases; MMSE = Mini-Mental State Examination.

[a]Data extracted from Walker et al. (2018) The prevalence of depression in general hospital inpatients: A systematic review and meta-analysis of interview-based studies.[70] Studies were all conducted on general medical and/or surgical wards.[70]

8.5.2.3 Relevant studies of the prevalence of clinically significant depression in older adults in community settings

There are several reviews summarising studies of the prevalence of depression in older adults in community settings (see **Table 24**). As depicted in **Table 24**, studies of older adults in community settings report a wide range of prevalence estimates for clinically significant depression. Findings from this substudy correspond most closely to the "upper" prevalence estimates of "depressive symptoms" in older adults in community settings.[202,237] I consistently estimated a higher prevalence of clinically significant depression than those studies that estimated the prevalence of major depression in older adults in community settings.[146,237,238] As previously described, this is because diagnostic criteria for major depression is much more stringent than a cut-off score on a depression measure.

Table 24. Relevant systematic reviews of the prevalence of depression in older adults in community settings[a]

Systematic review	Reviewers' findings
Cheng et al. (2019) *The prevalence and predictors of anxiety and depression in near-centenarians and centenarians: A systematic review*[202]	Review focussed on older adults (aged ≥ 95 years) in community settings. It reported prevalence estimates for "depressive symptoms" that ranged from 0% to 65%.
Djernes (2006) *Prevalence and predictors of depression in populations of elderly: A review*[237]	Review focussed on Caucasian older adults (age not specified) in community and institutional settings. It reported that the prevalence of major depression and "clinically relevant depressive symptom cases" ranged from 0.9% to 42% and 7.2% to 49% respectively.
Luppa et al. (2012) *Age- and gender-specific prevalence of depression in latest-life: Systematic review and meta-analysis*[238]	Review focussed on older adults (aged ≥ 75 years) in community settings. It reported that the prevalence of current and lifetime major depression ranged from 4.6% to 9.3% and 3.7% to 28.0% respectively. It estimated the pooled prevalence of current major depression to be 7.2% (95% CI, 4.4% to 10.6%).
Volkert et al. (2013) *The prevalence of mental disorders in older people in Western countries: A meta-analysis*[146]	Review focussed on older adults (aged ≥ 50 years) in community settings in Europe and North America. It reported the overall random-effects estimate for current and lifetime major depression was 3.29% (95% CI, 3.07% to 3.51%) and 16.52% (95% CI, 15.50% to 17.54%) respectively.

CI = Confidence Interval.

[a]Reviews included primary studies that used a number of different types of depression assessment measures and definitions to define clinically significant depression.

8.5.3 Associations of clinically significant depression

8.5.3.1 Overview of results

Age. I hypothesised that clinically significant depression would be associated with younger age in older general hospital inpatients. When conducting research with this patient population, I observed that very old patients (such as those aged 80 years and older) were often hesitant to share their feelings. Many also told me that there was no point in feeling down because one had to "get on with things". In contrast with my hypothesis, I did not find evidence of an association between clinically significant depression and age, even after adjusting for sex. Several relevant studies of older general hospital inpatients (discussed below) have also reported this finding, which indicates this association may not exist.

Sex. I hypothesised that clinically significant depression would be associated with female sex because I noticed female inpatients were often more willing to speak about their emotions than male inpatients. Despite this, I did not find evidence of an association between clinically significant depression and sex, even after adjusting for age. There could be several reasons for this. First, it could be that, although depression is generally more common in females than males[22], certain age- and illness-related risk factors increased depression in male older general hospital inpatients, essentially causing them to "catch up" to females (e.g. vascular diseases associated with depression[239]). Second, it is possible that being medically unwell and hospitalised substantially increases depression irrespective of sex, to an extent that overrides the association between depression and sex in the general population.[221,224] Third, the PHQ-2

may be measuring something other than “true depression” (e.g. frailty or adjustment to being in hospital).

Relationship status. I was surprised that – contrary to my hypothesis – I did not find evidence of an association between clinically significant depression and not having a spouse or partner, even after adjusting for age and sex. I initially thought that having the support and company of a spouse or partner would help older inpatients to experience fewer symptoms of depression. However, upon reflection, I am less surprised that I did not find evidence of an association. Nearly every participant who told me that they had little interest in doing things said it was because of their poor health. Many also said their poor health was why they felt down. In light of this, having a spouse or partner would not necessarily address the issue (i.e. poor health status) that was causing many to experience symptoms of depression.

Multimorbidity score. As hypothesised, I found clinically significant depression was associated with a greater multimorbidity score, even after adjusting for age and sex. Older inpatients involved in this study frequently told me that having multiple medical illnesses caused them to have to adjust to a more limited and less fulfilling lifestyle. It therefore seems understandable that having more medical illnesses (i.e. a greater multimorbidity score) would be associated with clinically significant depression.

Independent functioning. I found that clinically significant depression was associated with worse independent functioning, even after adjusting for age and sex. This finding is consistent with my hypothesis. As previously described, older general hospital inpatients often told me that losing their independence

made them feel down, particularly because it made it difficult (if not impossible) for them to do activities that once brought them meaning. I also noticed that many older inpatients who reported having symptoms of depression did not engage in physical therapy, which likely worsened their functioning. Other relevant studies have similarly hypothesised that the association is likely bidirectional.[188,213]

Anxiety. In accordance with my hypothesis, I found that clinically significant depression was associated with greater anxiety severity, even after adjusting for age and sex. This was the strongest association I found in my analyses. As described in **Chapter 7**, many older inpatients who told me they felt down and had little interest in doing things (depressive symptoms) also reported feeling worried and nervous (anxiety symptoms).

Cognitive impairment. As hypothesised, I found clinically significant depression was associated with worse cognitive impairment, even after adjusting for age and sex. It was very common for patients who recognised their cognitive function was worsening to tell me it made them down. Some of these patients also remarked that their family was distressed that their cognitive function was worsening, which in turn made the patients feel sad.

8.5.3.2 Relevant studies of the associations of clinically significant depression in older general hospital inpatients[a]

Age. The literature on the association between clinically significant depression and age in older general hospital inpatients is inconsistent, an observation made in several other studies.[217,221]

(1) **No association with age:** Most studies have not found evidence of an association between clinically significant depression and age, consistent with my results.[188,213,214,217,221,223,224,234,b,c]

(2) **Association with older age:** There are a small number of studies that have reported an association between clinically significant depression and older age.[216,217,d] It is notable that the only studies that have reported this association were of samples of exclusively male patients.[216,217] One of these studies explained that men (at least in rural areas) often do activities related to their previous work (e.g. in the primary sector) and may have fewer opportunities to do these meaningful activities as they get older and more disabled, resulting in greater depression.[216] Another proposed rationale for this association is that as people age, they experience more risk factors for depression (e.g. losses, health problems and reduced social support).[221]

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[a]Studies used a variety of statistical analyses to evaluate associations, including logistic regressions, *t*-tests and chi-squared tests.
[b]Two of these studies found an association with older age which disappeared after adjusting for other variables (e.g. multimorbidity and independent functioning).
[c]Two of these studies examined associations of greater depression severity (i.e. depression treated as a continuous variable), therefore did not technically report associations of "clinically significant depression".
[d]One of these studies reported older age was associated with major depression (defined using diagnostic criteria), but was not associated with frequency of depressive symptoms.

(3) **Association with younger age**: There are also a small number of studies that have reported an association between clinically significant depression and younger age.[199,216] Interestingly, one of the studies that found an association with older age in male patients (described above) found the opposite association in female patients (i.e. an association with younger age).[216] It stated that other studies have not similarly found an interaction effect between age and gender on the prevalence of depression.[216] Only one other study has reported an association with younger age; its authors explained this association may have occurred because (1) older patients in their study had "less disease and dyspnoea severity" than younger patients and (2) older patients might accept their symptoms as part of normal aging, while younger patients may struggle more to cope with lifestyle changes caused by their medical illnesses.[199]

Sex. The majority of studies, similar to mine, have not found evidence of an association between clinically significant depression and sex.[188,213,214,221,223,224,a] Only a small number of studies found evidence of an association with female sex,[228,234,b] none of which adjusted for potential confounding variables in their analyses. It is possible if they did, they would not have found an association with female sex. For example, Koenig et al. (1993) reported a "trend" for depression being more common in women than men which weakened to non-significance after adjusting for health and insurance status.[188] The authors

[a]One of these studies found an association with female sex which disappeared after adjusting for other variables (e.g. multimorbidity and independent functioning).
[b]One of these studies compared mean depression scores between women and men, therefore did not technically report associations of "clinically significant depression".

explained that women were more likely than men to be sick and have a lower socioeconomic status which increased their risk for depression (rather than their sex in and of itself).[188]

Relationship status. There is scant evidence on the association between clinically significant depression and relationship status, with existing literature presenting conflicting results.[217,221,234,a]

Multimorbidity and independent functioning. The majority of the literature, consistent with my findings, has reported an association between clinically significant depression and (1) greater multimorbidity[213,214,223] and (2) worse independent functioning.[188,213,214,216,217,221,228,229]

Only a small number of studies have found these associations to disappear after adjusting for other variables. The results of these studies are perhaps unsurprising given they adjusted for variables strongly associated with multimorbidity[224,b] and independent functioning.[223,224,c]

Anxiety. Although the literature on the association between clinically significant depression and anxiety is limited, it suggests a strong association, which is in accordance with my results.[216]

Cognitive impairment. As several other studies have noted,[220,223] evidence on the association between clinically significant depression and cognitive impairment is inconsistent. Some literature, similar to mine, found evidence that

[a]One of these studies compared mean depression scores by marital status, therefore did not technically report associations of "clinically significant depression".
[b]Study adjusted for frailty (one of the five items on frailty measure assessed for multimorbidity).
[c]One study adjusted for "admission" functional status when examining associations of "pre-admission" functional status; one study adjusted for frailty (two of the five items on frailty measure assessed for functional ability).

clinically significant depression was associated with worse cognitive impairment.[213,223,224] However, other literature has not found evidence of an association.[188,214,216,217,220,221,a,b,c] I found this association was only moderately strong which may explain some inconsistencies in the evidence base. It is also notable that a systematic review found that increased depression severity was associated with reduced cognitive performance in some cognitive domains (episodic memory, executive function and processing speed) but not others (visuospatial memory and semantic memory).[240] Although this review did not focus on older general hospital inpatients, its findings illustrate that some of the inconsistencies in the evidence base reported above may be due, in part, to associations of depression varying across different cognitive domains.

[a]Two of these studies found an association with worse cognitive impairment which disappeared after adjusting for other variables (e.g. age and years of education).
[b]One of these studies reported patients with clinically significant depression had significantly worse cognitive impairment than patients without it in text of paper, however table of paper indicated non-significant difference in cognitive function scores ($p = 0.15$).
[c]One of these studies examined associations of greater depression severity (i.e. depression treated as a continuous variable), therefore did not technically report associations of "clinically significant depression".

8.5.3.3 Relevant studies of the associations of clinically significant depression in older adults in community settings

Three reviews have summarised studies of associations of depression in older adults in community settings.[205,237,241] Reviews reported inconsistencies in the evidence base on the association between depression and age – while the majority of studies have not found evidence of an association (similar to my findings), others have reported an association with older or younger age.[205,237,241]

In contrast with my findings, there is some evidence to suggest female gender is associated with depression in older adults in community settings (although this association has not been consistently reported across studies).[205,237,241] There could be several explanations for why I did not find evidence of this association in older general hospital inpatients, some of which I outlined on **page 222**.

While there are mixed results on the association between depression and marital status,[205,237,241] one review concluded (based on its meta-analysis) being unmarried did not appear to be a risk factor for depression.[241] The results of this review are consistent with my findings.

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[205]Review's inclusion criteria: Participants aged ≥ 50 years; conducted in community or primary care setting in a Western country; examined ≥ one risk factor for anxiety or depression; cross-sectional or longitudinal study design; written in English; and published between 1995 and 2005.

[237]Review's inclusion criteria: Participants were Caucasian, elderly people living in private households or institutions; conducted in community or institutional setting; examined prevalence or risk factors of depression (determined using diagnostic interviews or rating scales); written in English, German, French or Scandinavian language; and published between 1993 and 2004.

[241]Review's inclusion criteria: Participants aged ≥ 50 years and community residents; examined ≥ one risk factor for depression; used an acceptable definition of depression (diagnostic criteria or cut-off on rating scale); prospective study design that excluded subjects with depression at baseline (or controlled for baseline depression in analysis); and written in English or French.

In accordance with my findings, reviews have found substantial evidence for an association between depression and (1) greater number of chronic diseases (i.e. greater multimorbidity)[205,237] and (2) worse functional impairment or disability.[205,237,241] Several studies have also reported an association between depression and anxiety.[237]

Literature on the association between depression and cognitive impairment in older adults in community settings appears to be inconsistent. Although several studies (similar to mine) have found evidence of an association with worse cognitive impairment,[205,237,241] one review concluded (based on its meta-analysis) cognitive impairment was an “uncertain” risk factor for depression.[241]

8.5.4 Strengths

My cross-sectional substudy has several strengths (similar to those outlined in **Chapter 7**). First, it has a large sample size, which helps improve its accuracy.[19] Second, depression was measured at a consistent time frame in participants' admission to hospital (i.e. within one week of admission), which helped to provide a more homogenous study sample. Third, it included severely ill patients. Since older general hospital inpatients are usually extremely unwell, including severely ill patients increases the generalisability of its findings. Fourth, the researchers who collected data used in this substudy were rigorously trained and monitored to ensure study procedures were done consistently and to a high standard.

8.5.5 Limitations

My cross-sectional substudy also has several limitations. The limitations of this substudy mirror those outlined in my substudy on the prevalence and associations of clinically significant anxiety in older general hospital inpatients (see **Chapter 7, pages 187 to 189).**

Briefly, the main limitations of the substudy are:

(1) its sample was drawn from a trial which likely reduces the generalisability of its findings;

(2) it focussed on a specific subpopulation of older general hospital inpatients (recently admitted to hospital, not terminally ill and cognitively well enough to answer relevant measures) in the United Kingdom and its findings may not generalise to other populations of older general hospital inpatients;

(3) the measure used to assess for clinically significant depression (PHQ-2) cannot be used to diagnose depressive disorders;

(4) some data on participants' demographic and clinical characteristics were collected from medical records which are prone to inaccuracies;

(5) its analyses of the associations of clinically significant depression were limited to the demographic and clinical characteristics for which data were available;

(6) T-MoCA scores were imputed for 20% or less of missing items in a small proportion of participants (4%); and

(7) its cross-sectional study design did not allow me to determine causal relationships between clinically significant depression and participants' demographic and clinical characteristics.

8.5.6 Implications and conclusions

I found that clinically significant depression was common in older general hospital inpatients, occurring in over 40 percent. It was particularly common amongst those with greater anxiety severity. Despite it being highly prevalent in this patient population, it remains largely undetected and undertreated. Further research is required to evaluate approaches to identify and, where appropriate, manage depression in older general hospital inpatients. Findings from this study offer useful information to guide these approaches as they highlight which older inpatients are most likely to have clinically significant depression. Specifically, they suggest that clinically significant depression occurs most frequently in the "sickest" older adults (those with greater multimorbidity, worse independent functioning, greater anxiety severity and worse cognitive impairment).

Chapter 9
Substudy 3: Prevalence and associations of clinically significant cognitive impairment in older general hospital inpatients

9.1 Research aim

I aimed to determine the prevalence and associations of clinically significant cognitive impairment (defined as a T-MoCA score ≤ 17 out of 30) in older (aged ≥ 65 years) general hospital inpatients.

9.2 Hypotheses

I hypothesised that the following demographic and clinical characteristics would be associated with clinically significant cognitive impairment in older general hospital inpatients:

(1) older age;

(2) female sex;

(3) not having a spouse or partner; and

(4) greater multimorbidity score.

I made these hypotheses based on my own experience working with older general hospital inpatients and on existing literature on cognitive impairment in older adults.[158,242-245]

9.3 Methods

9.3.1 Sample

As outlined in **Chapter 6**, I included a patient's data in this substudy if they participated in The HOME Study[166] and had at least 80% of the items of a cognitive function (T-MoCA[182,183]) assessment completed.[a] This excluded participants for whom assessors administering the T-MoCA were not able to score at least 80% of items because the participant: (1) refused to be assessed or (2) could not be assessed due to having a severe communication impairment (e.g. deafness or dysphasia). As stated in **Chapter 6**, the sample used in this substudy is different from the one used in **Chapters 7** and **8** on the prevalence and associations of clinically significant anxiety and depression.

[a]There are 16 items on the T-MoCA that are scored. Therefore, participants had to have data on at least 13 of the 16 items to be included in this substudy.

9.3.2 Cognitive impairment measure

9.3.2.1 Telephone Montreal Cognitive Assessment (T-MoCA)

The Montreal Cognitive Assessment (MoCA) is a commonly used screening measure for cognitive impairment.[182] It was developed to help clinicians identify patients with mild cognitive impairment, which is often missed by less sensitive measures of cognitive function.[182] The MoCA includes items that assess visuospatial abilities, executive functions, naming, attention, language, abstraction, delayed recall and orientation (see **Table 25**).[182,246] Scores range from zero to 30, with lower scores indicating worse cognitive function.[182]

The T-MoCA is a version of the MoCA, adapted for use over the telephone.[183] It therefore includes all the sections of the MoCA that do not require the use of a pencil and paper or a visual stimulus (see **Table 25** and **Figure 12**).[183] The T-MoCA is identical to the MoCA-BLIND, which was developed for patients with visual impairment.[247-249] T-MoCA raw scores range from zero to 22.[183,248,249] These are converted to scores ranging from zero to 30 (T-MoCA raw score x 30 / 22) to allow comparison with MoCA scores.[198]

The T-MoCA has excellent sensitivity and reasonable specificity for detecting mild cognitive impairment. Using a raw cut-off score of 18 or less out of 22 (equivalent to 25 or less out of 30 on the MoCA), the sensitivity and specificity of the T-MoCA for detecting any mild cognitive impairment are 81%-89% and 46%-73% respectively.[183,250]

9.3.2.2 Cut-off scores on the T-MoCA

I converted T-MoCA raw scores to scores out of 30 (T-MoCA raw score x 30 / 22) as recommended, and the following recommended categories of cognitive function were applied: scores 26 to 30 = normal cognitive function; scores 18 to 25 = mild cognitive impairment; scores 10 to 17 = moderate cognitive impairment; and scores zero to nine = severe cognitive impairment.[198] I defined clinically significant cognitive impairment as a score of 17 or less, thereby including those with moderate to severe cognitive impairment.

Table 25. Montreal Cognitive Assessment (MoCA) versus Telephone Montreal Cognitive Assessment (T-MoCA)

Domain of cognitive functioning	Assessment item	Maximum score for assessment item	MoCA[246,251]	T-MoCA[183,248,249]
Visuospatial abilities / Executive functions	Alternating trail making task	1 point	✓	X
	Three-dimensional cube copy task	1 point	✓	X
	Clock-drawing task	3 points	✓	X
Naming	Naming low-familiarity animals task (3 animals)	3 points (1 point per animal)	✓	X
Attention	Forward digit span repetition task	1 point	✓	✓
	Backward digit span repetition task	1 point	✓	✓
	Sustained attention task (target detection using tapping)	1 point	✓	✓
	Serial sevens subtraction task	3 points	✓	✓
Language	Repetition of syntactically complex sentence task (first sentence)	1 point	✓	✓
	Repetition of syntactically complex sentence task (second sentence)	1 point	✓	✓
	Verbal fluency task	1 point	✓	✓
Abstraction	Description of similarities between two nouns task (first noun set)	1 point	✓	✓
	Description of similarities between two nouns task (second noun set)	1 point	✓	✓
Delayed recall	Delayed recall of nouns task (5 nouns)	5 points (1 point per noun)	✓	✓
Orientation	Orientation to date task	1 point	✓	✓
	Orientation to month task	1 point	✓	✓
	Orientation to year task	1 point	✓	✓
	Orientation to day task	1 point	✓	✓
	Orientation to place task	1 point	✓	✓
	Orientation to nearest city task	1 point	✓	✓
Total maximum score			30	22[a]

MoCA = Montreal Cognitive Assessment; T-MoCA = Telephone Montreal Cognitive Assessment.

[a]T-MoCA raw scores range from zero to 22; however, raw scores are converted to scores ranging from zero to 30 (T-MoCA raw score x 30 / 22) to allow comparison with MoCA scores.[198]

Figure 12. Telephone Montreal Cognitive Assessment (T-MoCA)[183,248,249]

Assessment item question	Scoring system		Score
Items that are not scored			
I'm going to read a list of words that I'd like you to remember now and later on. When I've finished, tell me as many words as you can remember. It doesn't matter what order you say them in: *Face, Velvet, Church, Daisy, Red*	Not scored		Not scored
I'm going to read the same list for a second time. Again, when I've finished, tell me as many words as you can, including the ones you said the first time: *Face, Velvet, Church, Daisy, Red*	Not scored		Not scored
Items that are scored			
Now I'm going to say some numbers and when I'm finished, please repeat them exactly as I said them: *21854*	Repeated accurately?	Yes	1 point
		No	0 points
Now I'm going to say some more numbers, but this time I want you to repeat them in the backwards order: *742*	Repeated accurately?	Yes	1 point
		No	0 points
Now I'm going to read a sequence of letters. Every time I say the letter A, tap your hand once. If I say a different letter, don't tap your hand: *F B A C M N A A J K L B A F A K D E A A A J A M O F A A B*	Number of errors?	0 errors	1 point
		1 error	1 point
		≥ 2 errors	0 points
Now I will ask you to count by subtracting 7 from 100 and then keep subtracting 7 from your answer until I tell you to stop.	Number of correct numbers?	4 or 5 numbers	3 points
		2 or 3 numbers	2 points
		1 number	1 point
		0 numbers	0 points
I'm going to read you a sentence. Repeat it after me, exactly as I say it: *I only know that John is the one to help today.*	Repeated accurately?	Yes	1 point
		No	0 points
Now I'm going to read another sentence. Again, please repeat it after me, exactly as I say it: *The cat always hid under the couch when dogs were in the room.*	Repeated accurately?	Yes	1 point
		No	0 points

Assessment item question	Scoring system		Score
This time I am going to ask you to tell me as many words as you can think of that begin with a certain letter of the alphabet that I will tell you in a moment. You can say any kind of word you want, except for proper nouns (like Bob or Birmingham), numbers, or words that begin with the same sound but have a different ending, for example, love, lover, loving. I will tell you to stop after one minute. Are you ready? Now, tell me as many words as you can think of that begin with the letter F. *(time for 60 seconds)*	Number of words repeated?	≥ 11 words	1 point
		< 11 words	0 points
Now, can you tell me how a train and a bicycle are alike?	Correct?	Yes	1 point
		No	0 points
And can you tell me how a watch and a ruler are alike?	Correct?	Yes	1 point
		No	0 points
I read some words to you earlier, which I asked you to remember. Can you tell me as many of those words as you can remember?	Number of words recalled correctly?	5 words	5 points
		4 words	4 points
		3 words	3 points
		2 words	2 points
		1 word	1 point
		0 words	0 points
Please could you tell me what day of the week it is today?	Correct?	Yes	1 point
		No	0 points
And what's the date?	Correct?	Yes	1 point
		No	0 points
What month is it?	Correct?	Yes	1 point
		No	0 points
And what year is it?	Correct?	Yes	1 point
		No	0 points
And what is the name of the place you are in at the moment?	Correct?	Yes	1 point
		No	0 points
And finally, what is your nearest city?	Correct?	Yes	1 point
		No	0 points

9.3.2.3 Advantages of the T-MoCA

The T-MoCA is a suitable cognitive impairment measure for acutely unwell, older general hospital inpatients for several reasons.

First, the T-MoCA is brief and relatively straightforward to administer. It also has clear guidance documents available for use.[249] Researchers can therefore be trained to administer it. Proper cognitive testing, by contrast, takes a long time to complete and must be conducted by experts (e.g. clinicians). The T-MoCA's brevity is also beneficial for assessing older general hospital inpatients because these patients are usually extremely unwell, making lengthy assessment measures exhausting and distressing for some to complete.

Second, the T-MoCA assesses multiple cognitive domains.[249] Unlike many cognitive impairment measures which assess one or two cognitive domains (e.g. verbal recall),[252] the T-MoCA assesses several.[249] It also includes domains that might be affected by (1) longer-term cognitive problems (e.g. dementia) and (2) shorter-term cognitive problems (e.g. delirium). The T-MoCA may therefore identify individuals with cognitive impairment that other cognitive impairment measures would not.

Third, the T-MoCA can be used to assess for cognitive impairment in individuals with visual and physical impairments because it does not involve the use of a pencil and paper or visual stimulus.[183] Older general hospital inpatients often suffer from ailments that affect their ability to see and/or write, making the T-MoCA suitable for this patient population.

Fourth, the T-MoCA is a very sensitive cognitive impairment measure.[183,250] Although there is limited evidence on its other psychometric properties, research on the psychometric properties of the original MoCA demonstrate it likely has good validity and reliability:

(1) Validity: The MoCA has good convergent validity, as demonstrated by its strong correlation with the Mini-Mental State Examination (MMSE) (correlation coefficient = 0.87).[182] One would expect the two measures to be strongly correlated because they both measure cognitive impairment. The MoCA developers stated this strong correlation demonstrates the MoCA has excellent *content validity* because the MMSE is known to comprehensively assess cognitive functioning.[182]

(2) Reliability: The MoCA has excellent internal reliability, with a Cronbach alpha of 0.83.[182] It also has good test-retest reliability, with an estimated correlation coefficient of 0.92.[182]

9.3.2.4 Disadvantages of the T-MoCA

The T-MoCA also has several disadvantages.

First, there is no research reporting validated cut-off scores to differentiate between mild, moderate and severe cognitive impairment on the T-MoCA. Although I was able to use the categories of cognitive function which have been recommended for the MoCA, there are no studies that have validated these categories.[198] Additionally, the recommended conversion equation that I used to convert T-MoCA scores out of 30 (rather than 22) has not been validated.[198]

Second, the T-MoCA is heavily language-dependent, which makes it challenging to use in individuals with severe communication difficulties (e.g. those with hearing problems or dysphasia). Some patients in general hospitals suffer from medical illnesses that affect their ability to verbally communicate, making the T-MoCA potentially problematic to use in general hospital settings.

Third, the T-MoCA does not assess visuospatial functioning,[183] which makes it less comprehensive than the MoCA.

Fourth, the T-MoCA cannot be used to diagnose a cognitive disorder. Although the T-MoCA can measure cognitive impairment, identify those with clinically significant cognitive impairment by applying a cut-off score and screen for cognitive disorders, it cannot diagnose a cognitive disorder. Diagnosing an individual with a cognitive disorder and determining an appropriate treatment plan for that individual would require a much more comprehensive evaluation.

Fifth, although the T-MoCA was administered by trained researchers, they were not clinicians or trained neurocognitive testers.

9.3.3 Statistical analyses

As described in **Chapter 6**, I report: (1) the distribution of cognitive function (T-MoCA) scores; (2) the proportion of study participants with normal cognitive function, mild cognitive impairment, moderate cognitive impairment and severe cognitive impairment; and (3) the point prevalence of clinically significant cognitive impairment (defined as a T-MoCA score ≤ 17). I also describe the associations of clinically significant cognitive impairment (defined as a T-MoCA score ≤ 17) with the following demographic and clinical characteristics: age, sex, relationship status and multimorbidity score. I used univariable and multivariable logistic regressions to assess the associations of clinically significant cognitive impairment with participants' demographic and clinical characteristics (listed above), adjusting for age and sex in the multivariable analyses. To supplement these analyses, I used univariable and multivariable linear regressions to assess the associations of worse cognitive impairment (T-MoCA) scores with participants' demographic and clinical characteristics (listed above), adjusting for age and sex in the multivariable analyses. For participants with up to 20% of missing T-MoCA items, scores were imputed for these items using individual mean imputation (see **Chapter 6 Section 6.7.3.4** for more detail).

Unlike **Chapters 7** and **8**, I did not examine associations of clinically significant cognitive impairment with independent functioning, anxiety or depression. This is because, for participants with severe cognitive impairment, these clinical characteristics were participant- or proxy-reported. I considered it statistically and clinically inappropriate to examine associations with the aforementioned

clinical characteristics because findings from previous studies suggest that self- and proxy-reported responses are often not sufficiently similar to each other.[176-181]

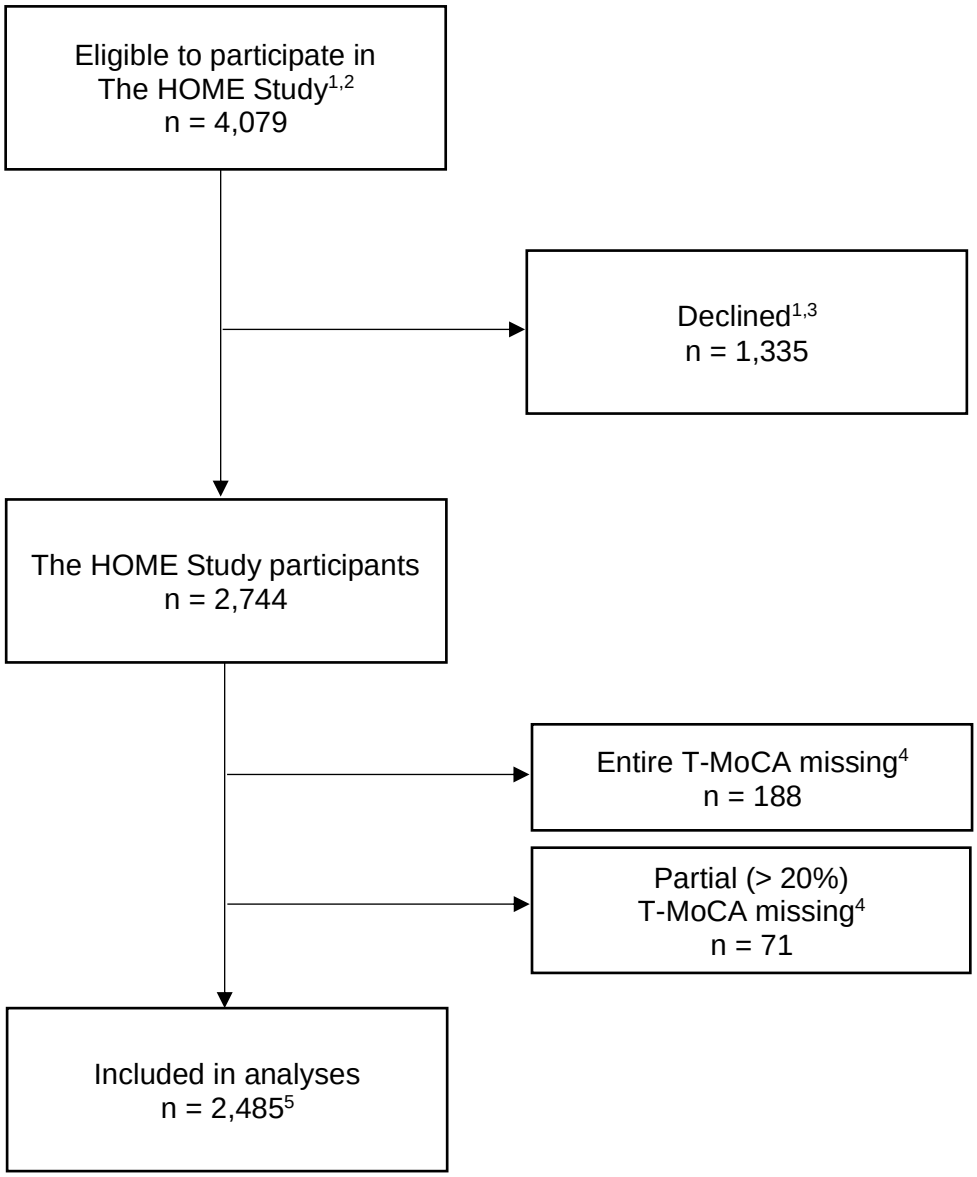
9.4 Results

9.4.1 Sample description

4,079 patients[a] were eligible to take part in The HOME Study. Of these, 2,744 participated. Data on 2,485 participants were analysed; 259 participants were excluded from the analyses because they did not have at least 80% of the items of a T-MoCA completed (see **Figure 13**). The majority of participants had a full T-MoCA completed (2,385 participants, 96%), with only a small proportion requiring scores to be imputed for 20% or less of missing T-MoCA items. 87 participants had scores imputed for one missing item, seven had scores imputed for two missing items and six had scores imputed for three missing items.

[a]Patients could be counted more than once (i.e. units are “hospital admissions”, rather than individual patients).

Figure 13. Prevalence and associations of clinically significant cognitive impairment in older general hospital inpatients flowchart



[1]The units are "hospital admissions", rather than individual patients.
[2] The main reasons for ineligibility were (1) being under 65 years of age and (2) planned discharge from hospital within two days.
[3]The main reasons for refusal were (1) not being interested in taking part in research and (2) feeling that there was already too much going on.
[4]Participant refused to be assessed or could not be assessed due to having a severe communication impairment (e.g. deafness or dysphasia).
[5]The majority of participants had a full T-MoCA (2,385 participants, 96%), with only a small proportion requiring 20% or less of their scores to be imputed.

9.4.1.1 Demographic characteristics of participants in analyses

Participants included in this substudy were old, with a mean age of 82 years (see **Table 26**). It can be seen in **Table 26** that the greatest proportion of participants were in the oldest age bracket of 85 years and older (over 40%). There was a similar proportion of female and male participants. There was a slightly greater proportion of participants without a spouse or partner than with a spouse or partner, and living in urban settings than rural settings. Nearly all participants were retired or not working, which one would expect given the mean age of participants. Although there was a spread in participants' socioeconomic deprivation index scores, there were very few participants in the most deprived category.

Table 26. Prevalence and associations of clinically significant cognitive impairment in older general hospital inpatients: Demographic characteristics of participants in analyses

	Sample (n = 2,485)
Age (years)	
Mean (SD)	82.16 (8.15)
Range	65.03 to 102.99
65 to 74 years	565 (22.74%)
75 to 84 years	891 (35.86%)
≥ 85 years	1,029 (41.41%)
Sex	
Female	1,215 (48.89%)
Male	1,270 (51.11%)
Relationship status	
Spouse or partner	1,119 (45.03%)
No spouse or partner	1,366 (54.97%)
Employment status	
Working	55 (2.21%)
Retired or not working	2,430 (97.79%)
Residence area	
Urban setting	1,425 (57.34%)
Rural setting	1,060 (42.66%)
Socioeconomic deprivation index[a]	
0	66 (2.66%)
1	295 (11.87%)
2	557 (22.41%)
3	701 (28.21%)
4	866 (34.85%)

Data are number (%) unless otherwise indicated.
SD = Standard Deviation.
[a]0 = most deprived, 4 = least deprived.

9.4.1.2 Clinical characteristics of participants in analyses

The most common reasons that participants were admitted to hospital were having (1) symptoms and signs involving the circulatory and respiratory systems (e.g. chest pain and shortness of breath) and (2) general symptoms and signs (e.g. fever and fatigue) (see **Table 27**).

Generally, participants had high multimorbidity. Participants had an average of three body systems with at least one diagnosis charted in their medical records on admission and an average of 11 medications prescribed. Over 70% of participants had at least one diagnosis affecting their circulatory system (e.g. ischemic heart disease and hypertension). Around 25% of participants had at least one mental or behavioural disorder charted in their medical records on admission.

On average, participants had severe functional impairment (as measured by the Barthel ADL Index)[170-172,194] and had high rates of clinically significant anxiety and depression (as measured by the GAD-2 and PHQ-2 respectively).[75,172,192]

Table 27. Prevalence and associations of clinically significant cognitive impairment in older general hospital inpatients: Clinical characteristics of participants in analyses

	Sample (n = 2,485)
Reason for hospital admission	
Symptoms and signs involving the circulatory and respiratory systems	668 (26.88%)
General symptoms and signs	572 (23.02%)
Falls and injuries	345 (13.88%)
Symptoms and signs involving the digestive system and abdomen	299 (12.03%)
Symptoms and signs involving cognition, perception, emotional state and behaviour	243 (9.78%)
Symptoms and signs involving the urinary system	154 (6.20%)
Symptoms and signs involving the skin and subcutaneous tissue	131 (5.27%)
Symptoms and signs involving the nervous and musculoskeletal systems	39 (1.57%)
Abnormal investigation findings	34 (1.37%)
Multimorbidity (presence of a diagnosis in each body system on admission)	
Diseases of the circulatory system	1,796 (72.27%)
Endocrine, nutritional and metabolic diseases	976 (39.28%)
Diseases of the musculoskeletal system and connective tissue	773 (31.11%)
Diseases of the respiratory system	740 (29.78%)
Diseases of the genitourinary system	721 (29.01%)
Mental and behavioural disorders	639 (25.71%)
Diseases of the digestive system	576 (23.18%)
Neoplasms	568 (22.86%)
Diseases of the nervous system	431 (17.34%)
Diseases of the eye and adnexa	277 (11.15%)
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	218 (8.77%)
Diseases of the skin and subcutaneous tissue	144 (5.79%)
Certain infectious and parasitic diseases	108 (4.35%)
Injury, poisoning and certain other consequences of external causes	98 (3.94%)
Diseases of the ear and mastoid process	64 (2.58%)

Congenital malformations, deformations and chromosomal abnormalities	13 (0.52%)
Multimorbidity score (number of body systems with a diagnosis on admission, 0 to 16)	
Mean (SD)	3.28 (1.66)
Number of medications	
Mean (SD)	11.42 (5.23)
Independent functioning (Barthel ADL Index, 0 to 20)[a,b,c]	
Mean (SD)	9.38 (5.81)
Anxiety (GAD-2, 0 to 6)[a,d,e]	
Mean (SD)	2.50 (2.15)
Clinically significant anxiety (GAD-2 score ≥ 3)[75,192]	1,073 (44.10%)
Depression (PHQ-2, 0 to 6)[a,f,g]	
Mean (SD)	2.54 (2.09)
Clinically significant depression (PHQ-2 score ≥ 3)[172,192]	1,147 (47.28%)

Data are number (%) unless otherwise indicated.
Barthel ADL Index = Barthel Activities of Daily Living Index; GAD-2 = Generalized Anxiety Disorder 2-item scale; PHQ-2 = Patient Health Questionnaire 2-item scale; SD = Standard Deviation.
[a]Measure answered by participants themselves or (where necessary) proxies who knew them well.
[b]Lower scores indicate worse independent functioning.
[c]Data available for 2,484 participants.
[d]Higher scores indicate greater anxiety severity.
[e]Data available for 2,433 participants.
[f]Higher scores indicate greater depression severity.
[g]Data available for 2,426 participants.

9.4.2 Distribution of cognitive function scores

Participants had a mean T-MoCA score of 13.0 (SD of 8.5), with scores ranging from zero to 30 (see **Table 28**). The distribution of participants' cognitive function (T-MoCA) scores can be seen in **Figure 14.** As can be seen in **Figure 14**, the most common score was zero (i.e. the lowest T-MoCA score). Participants with a score of zero either (1) answered all T-MoCA items incorrectly or (2) were unable to answer any T-MoCA items, usually because they had impaired consciousness.

Similar proportions of participants (around 30%) had mild, moderate and severe cognitive impairment (see **Table 28** and **Figure 15**). Only a very small proportion of participants (around 7.0%) had normal cognitive function.

9.4.3 Prevalence of clinically significant cognitive impairment

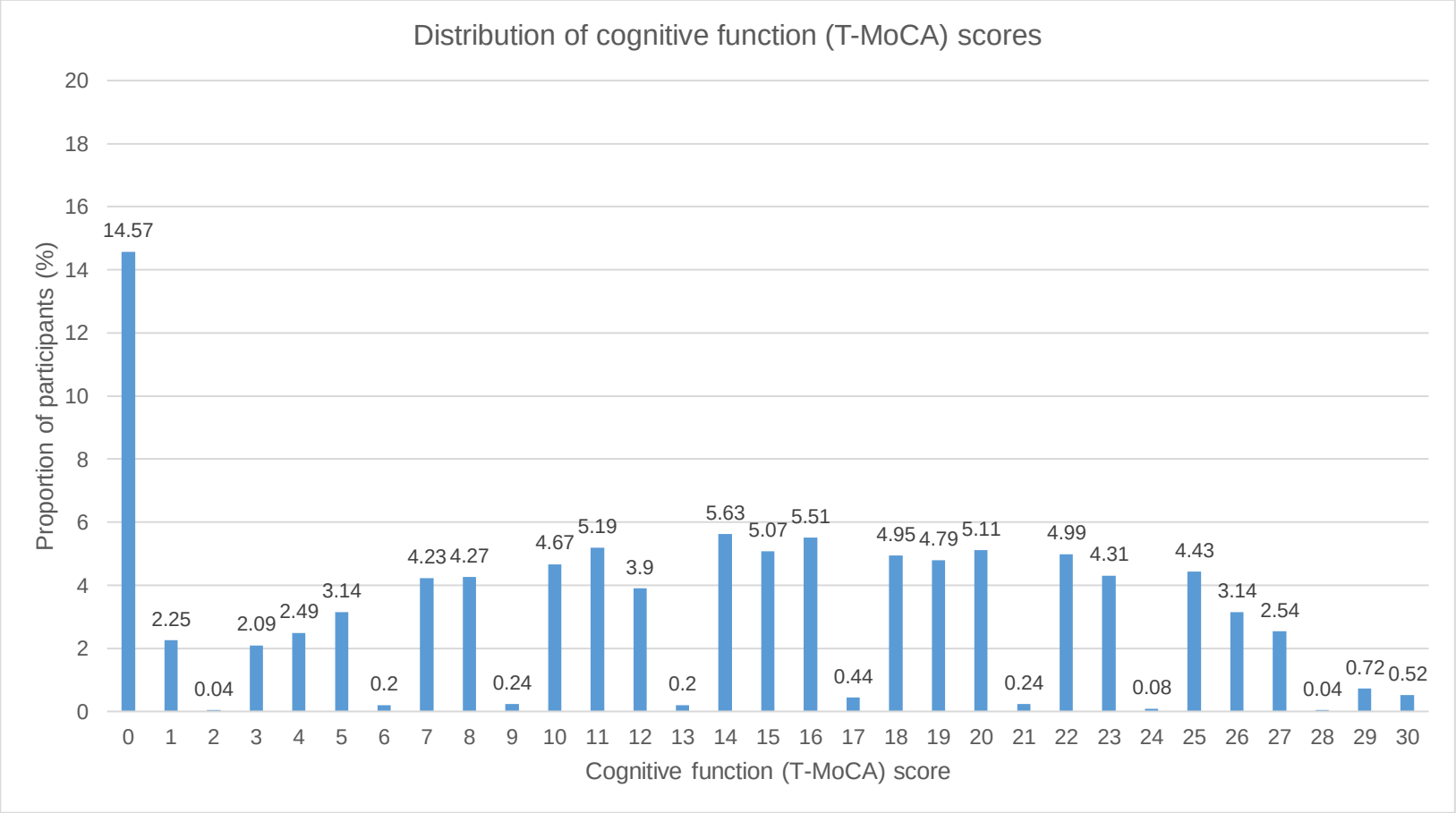
64.1% of participants had clinically significant cognitive impairment, defined as a T-MoCA score of 17 or less.

Table 28. Prevalence and associations of clinically significant cognitive impairment in older general hospital inpatients: Distribution of cognitive function (T-MoCA) scores of participants in analyses

	Sample (n = 2,485)
T-MoCA	
Mean (SD)	13.02 (8.49)
Median (IQR)	13.64 (6.82 to 20.45)
Range	0 to 30
Normal cognitive function (score 26 to 30)	173 (6.96%)
Mild cognitive impairment (score 18 to 25)	718 (28.89%)
Moderate cognitive impairment (score 10 to 17)	761 (30.62%)
Severe cognitive impairment (score 0 to 9)	833 (33.52%)

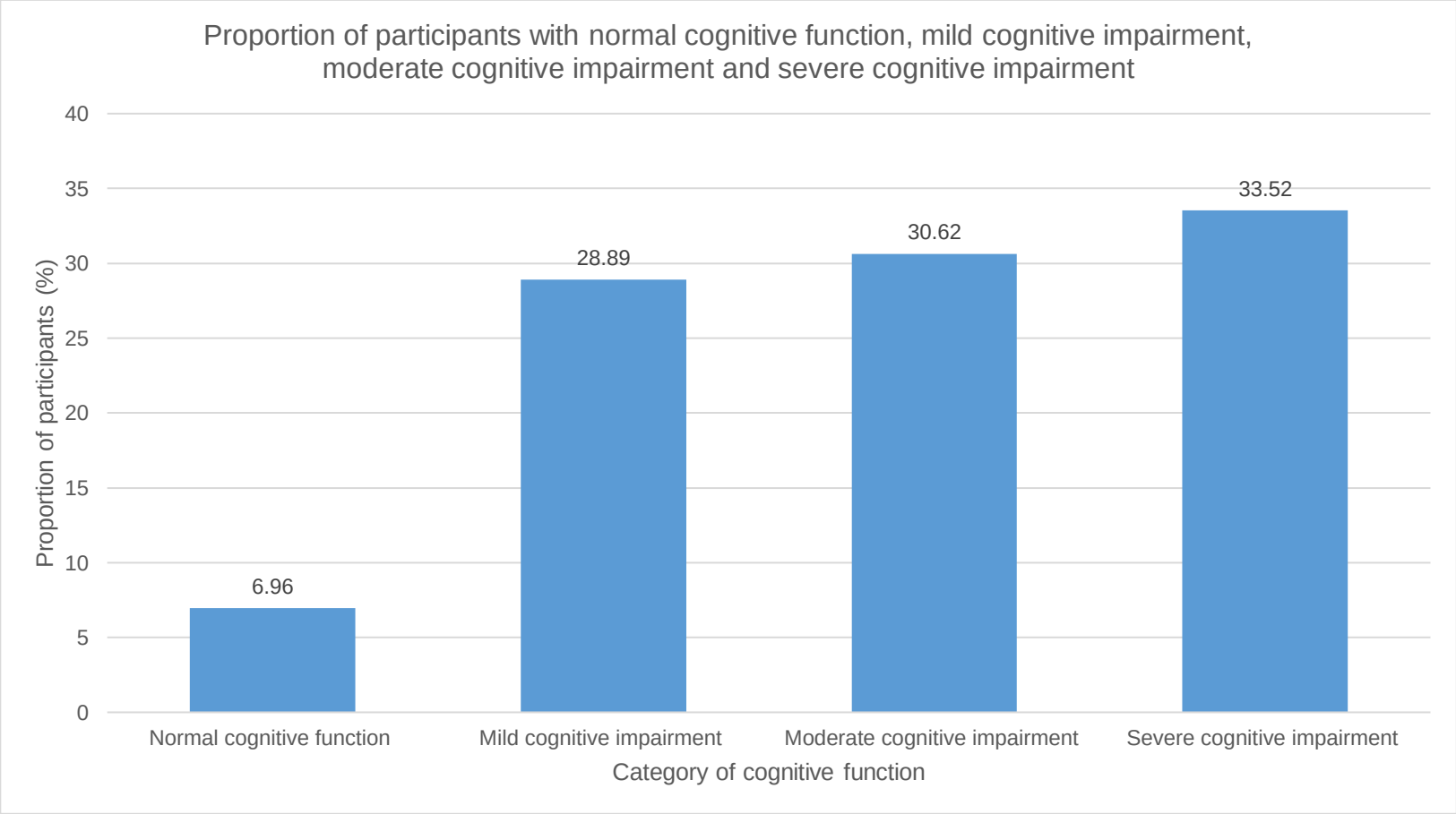
Data are number (%) unless otherwise indicated.
IQR = Inter-Quartile Range; SD = Standard Deviation; T-MoCA = Telephone Montreal Cognitive Assessment.

Figure 14. Histogram of the distribution of cognitive function (T-MoCA) scores of participants in analyses



T-MoCA = Telephone Montreal Cognitive Assessment.

Figure 15. Histogram of the proportion of participants with normal cognitive function, mild cognitive impairment, moderate cognitive impairment and severe cognitive impairment



9.4.4 Associations of clinically significant cognitive impairment

Table 29 and **Table 30** present the results of the univariable and multivariable analyses of associations of clinically significant cognitive impairment (defined as a T-MoCA score ≤ 17) with participants' demographic and clinical characteristics.

Age. Clinically significant cognitive impairment had a strong association with older age in the univariable analysis, with the odds estimated to double every eight years (OR = 1.09, 95% CI, 1.08 to 1.10, i.e. every increase in one year of age was associated with a 9% increase in odds of clinically significant cognitive impairment). These findings did not change after adjusting for sex in the multivariable analysis (adjusted OR = 1.09, 95% CI, 1.08 to 1.10).

Sex. There was no evidence of an association between clinically significant cognitive impairment and sex in the univariable analysis or in the multivariable analysis (where age was adjusted for).

Relationship status. Clinically significant cognitive impairment was associated with relationship status – the odds of clinically significant cognitive impairment were estimated to be higher among those without a spouse or partner. This association was quite strong (OR = 1.64, 95% CI, 1.39 to 1.93, i.e. the odds of clinically significant cognitive impairment were estimated to be 64% higher in those without a spouse or partner when compared to those with one). Although these findings remained after adjusting for age and sex in the multivariable analysis, the association became weaker (adjusted OR = 1.23, 95% CI, 1.02 to 1.47) which suggests there may be some confounding.

Multimorbidity score. There was no evidence of an association between clinically significant cognitive impairment and multimorbidity score in the univariable analysis or in the multivariable analysis (where age and sex were adjusted for).

Supplementary analyses. All previous analyses were repeated with cognitive impairment being treated as a continuous variable (i.e. worse cognitive impairment scores), rather than a binary variable (i.e. having clinically significant cognitive impairment or not having clinically significant cognitive impairment). Most findings remained constant. There was, however, one difference in findings: worse cognitive impairment scores were associated with greater multimorbidity scores, even after adjusting for age and sex. The T-MoCA was estimated to be 0.31 points lower (95% CI, –0.51 to –0.11) for every one-point increase in multimorbidity score[a] (0.27 points lower after adjusting for age and sex [95% CI, –0.46 to –0.08]). This contrasts with my finding that clinically significant cognitive impairment (defined as a T-MoCA score ≤ 17) was not associated with multimorbidity scores.

[a]A one-point increase in multimorbidity score equates to an increase in one body system with a diagnosis on admission to hospital.

Table 29. Univariable analyses of associations of demographic and clinical characteristics and clinically significant cognitive impairment (defined as a T-MoCA score ≤ 17)

	Unadjusted odds ratio (95% CI)	***p*-value**
Age	1.09 (1.08 to 1.10)	< 0.001
Sex		
Female	1	
Male	0.90 (0.76 to 1.06)	0.19
Relationship status		
Spouse or partner	1	
No spouse or partner	1.64 (1.39 to 1.93)	< 0.001
Multimorbidity score[a]	1.03 (0.98 to 1.09)	0.20

CI = Confidence Interval.
[a]Number of body systems with a diagnosis on admission (scores range from 0 to 16).

Table 30. Multivariable analyses of associations of demographic and clinical characteristics and clinically significant cognitive impairment (defined as a T-MoCA score ≤ 17) adjusted for age and sex

	Adjusted odds ratio (95% CI)	***p*-value**
Age[a]	1.09 (1.08 to 1.10)	< 0.001
Sex[b]		
Female	1	
Male	0.98 (0.83 to 1.17)	0.85
Relationship status[c]		
Spouse or partner	1	
No spouse or partner	1.23 (1.02 to 1.47)	0.03
Multimorbidity score[c,d]	1.02 (0.97 to 1.08)	0.39

CI = Confidence Interval.
[a]Analysis adjusted for sex.
[b]Analysis adjusted for age.
[c]Analysis adjusted for age and sex.
[d]Number of body systems with a diagnosis on admission (scores range from 0 to 16).

9.5 Discussion

9.5.1 Main findings

Clinically significant cognitive impairment (defined as a T-MoCA score ≤ 17) was highly prevalent in older general hospital inpatients, occurring in over 60 percent. I also found that clinically significant cognitive impairment was associated with older age and with not having a spouse or partner. These findings remained after adjusting for age and sex. I did not find evidence of an association between clinically significant cognitive impairment and sex or multimorbidity score.

9.5.2 Prevalence of clinically significant cognitive impairment

9.5.2.1 Overview of results

I was not surprised to find such a high prevalence of clinically significant cognitive impairment in older general hospital inpatients, based on my experience doing research with the patients included in this substudy. When I administered the T-MoCA, most patients struggled to answer the assessment items. In the first few weeks of working with these patients, I was surprised by the sheer number of patients who struggled to answer even the most "basic" assessment items (e.g. orientation to place). Patients' family members – who were frequently present while I administered the T-MoCA – often told me that patients' cognition was chronically poor (e.g. history of dementia) and/or was noticeably worse during their hospital admission (e.g. acute confusion due to an infection).

However, it is important to note that patients were deemed as having clinically significant cognitive impairment based solely on a cut-off score on a single measure of cognitive impairment. This cut-off score provides no information on the likely cause of the cognitive impairment, nor does it provide sufficient evidence to diagnose an individual with a cognitive disorder. In this substudy, patients' cognitive impairment was likely caused by many factors, such as dementia, delirium, fatigue, severe pain, feeling unwell and sensory disturbances (e.g. hearing deficits). It is also likely that at least some patients found to have clinically significant cognitive impairment in this substudy improved later in their admission or after being discharged from hospital (i.e. they had only a transitory cognitive impairment).

9.5.2.2 Relevant studies of the prevalence of clinically significant cognitive impairment in older general hospital inpatients

9.5.2.2.1 Clinically significant cognitive impairment defined using a cut-off score

Several previous studies have estimated the prevalence of clinically significant cognitive impairment – defined using a cut-off score – in older general hospital inpatients (see **Table 31**).[187,220,253-257]

These studies were conducted in several countries (Brazil, Germany, Hungary, Ireland and the United Kingdom) on a variety of general hospital wards, including acute medical and surgical wards. Most studies recruited small samples of participants, with a relatively equal proportion of female and male patients.

Methods of obtaining consent for study participation were variable, with only a small number including the use of proxies.[187,253] Most studies used either the MMSE or the MoCA to assess patients' cognitive function.[187,220,254-257] The cut-off scores used to define clinically significant cognitive impairment varied across studies.

Studies reported prevalence estimates for clinically significant cognitive impairment that ranged from 22.3% to 92%. The majority of studies, however, reported estimates between 40% and 70%.[187,220,253,254,257] Studies that used the MoCA consistently reported higher prevalence estimates when compared to those that used the MMSE.

The lowest prevalence estimate (22.3%) was reported in a study of relatively young inpatients (mean age of 74.7 years) admitted to acute medical and

surgical wards in a district general hospital.[255] This study aimed to determine the proportion of patients with “dementing disorders”, defined as “significant cognitive impairment” (MMSE score ≤ 23).[255] Because the focus of this study was on “dementing disorders”, the authors undertook several measures to avoid including cognitive impairment that was attributable to an acute illness (see **Table 31**).[255] Prevalence estimates reported by other studies included patients whose cognitive impairment could have likely been attributed to an acute illness. Therefore, it is perhaps unsurprising that these studies reported a much higher prevalence. Only one other study reported a similarly low prevalence, which one might expect considering (1) it excluded some patients with severe cognitive impairment or delirium and (2) its participants were relatively young and had to be able to provide informed consent to participate.[256]

The highest prevalence estimate was reported in an audit of consecutive acute general medicine patients (aged ≥ 75 years) admitted to the John Radcliffe Hospital (one of the three study sites where data were collected for this substudy).[257] It found that 92% of inpatients had at least mild cognitive impairment (defined as a MoCA score ≤ 25).[257] It is notable that I found a nearly identical proportion of patients (93%) who scored 25 or less on the T-MoCA. The other study that reported a relatively high prevalence of clinically significant cognitive impairment also used the MoCA.[254] It found that 66.9% of patients had cognitive impairment (defined as a MoCA score ≤ 25).[254] However – after taking into account patients who were unable to attempt (or complete) the MoCA (see **Table 31**) – it estimated that nearly 85% of patients had impaired cognition.[254]

9.5.2.2.2 Clinically significant cognitive impairment defined using diagnostic criteria

Several studies have estimated the prevalence of clinically significant cognitive impairment – defined using diagnostic criteria – in older general hospital inpatients. In my meta-review, I found two relevant systematic reviews summarising this literature (see **Chapter 4**).[11,65] One of these reviews summarised studies of the prevalence of delirium and reported estimates that ranged from 10% to 31% at admission to hospital.[65,a] The other review summarised studies of the prevalence of dementia in older (aged > 55 years) general hospital inpatients.[11] It reported estimates that ranged from 2.8% to 63.0%.[11] It is not surprising that I found a higher prevalence of clinically significant cognitive impairment than studies included in these reviews because I used a cut-off score on a cognitive impairment measure, which is much less stringent than diagnostic criteria for *specific* cognitive disorders.

[a]Mean age of participants in seven of the eight relevant studies included in this review was greater than 75 years. One of the eight relevant studies did not report the mean age of its participants.

Table 31. Studies of the prevalence of clinically significant cognitive impairment (defined using a cut-off score) in older general hospital inpatients

Study	Setting	Selection criteria	Sample characteristics	Cognitive impairment measure	Cut-off score	Prevalence
Bickel et al. (2018)[253,a]	172 inpatient wards of 33 randomly selected general hospitals (excluded: hospitals with < 150 inpatient beds; private and specialty hospitals; rehabilitation clinics; and day clinics & night clinics) (Germany).	Aged ≥ 65 years; spoke German; not moribund or in a critical condition; not on intensive care unit or isolation unit; not on specialised ward for psychiatry, neurology or geriatric medicine.	Sample size = 1,469 Age (mean, SD, range) = 78.6, 7.4, 65 to 105 % female = 53.8% Wards = Medical wards, trauma surgery, general surgery and other specialities (e.g. orthopaedics, urology, gynaecology, ENT).	5-point CDR Scale	Mild cognitive impairment (CDR = 0.5) Severe cognitive impairment (CDR ≥ 1)	40% (95% CI, 36.2% to 43.7%) had mild or severe cognitive impairment (median length of inpatient stay prior to survey was 5 days).
Hewitt et al. (2014)[254,a]	Acute general surgical admission and assessment units in two teaching hospitals and one district general hospital (England, Scotland and Wales – United Kingdom).	Aged > 65 years.	Sample size = 245 Age (mean, SD) = 76.9, 8.1 % female = 55.5%	MoCA	Cognitive impairment (or "failed" the MoCA) (scores ≤ 25)	66.9% had cognitive impairment; 18% were unable to complete MoCA; and 15.1% had normal cognitive function (reasons for incompletion: known dementia, too unwell, too tired, physical/visual impairment, asleep, reduced Glasgow Coma Scale, unable to finish, unavailable, refused).
Hickey et al. (1997)[255,a]	Acute medical and surgical wards in a district general hospital (excluded	Aged ≥ 65 years.	Sample size = 112 Age (mean) = 74.7 % female = 43.8%*	MMSE (minor adaption to be applicable for Ireland) &	Significant cognitive impairment (scores ≤ 23)	22.3% had significant cognitive impairment (assessed at least 48 hours after admission &

Study	Setting	Selection criteria	Sample characteristics	Cognitive impairment measure	Cut-off score	Prevalence
	intensive care, coronary care and psychiatric units) (Ireland).			corroborative evidence of cognitive decline	<u>Severity levels</u> Mild to moderate cognitive impairment (scores 17 to 23) Severe cognitive impairment (scores ≤ 16)	reassessed to avoid inclusion of those who were confused due to acute illness; patients who were persistently clinically unwell were not included). *Acute medical wards*: 31% had significant cognitive impairment (21.1% mild to moderate & 9.9% severe). *Surgical wards*: 7.3% had significant cognitive impairment (4.9% mild to moderate & 2.4% severe).
Linka et al. (2000)[220,b]	Internal medicine department of a general hospital (Hungary).	Aged ≥ 65 years; ability to cooperate.	Sample size = 100 Age (median, IQR) = 73, 70 to 77.5 % female = 64%	MMMS Examination (Hungarian adaptation)	Cognitive dysfunction (scores < 85) <u>Severity levels</u> Mild cognitive impairment (scores 75 to 84) Moderate cognitive impairment (scores 60 to 74) Severe cognitive impairment (scores ≤ 59)	66% had cognitive dysfunction: 30% mild, 19% moderate and 17% severe cognitive impairment (assessed "some days" before discharge).
Mendes-Chiloff et al. (2009)[256,a]	University hospital (Brazil).	Aged ≥ 60 years; not in immediate	Sample size = 200 Age (mean, SD, range) =	MMSE (version that was adapted	Cognitive impairment (cut off score of 13 for	29% had cognitive impairment (majority of

Study	Setting	Selection criteria	Sample characteristics	Cognitive impairment measure	Cut-off score	Prevalence
		postsurgical period (some excluded for: severe pain at time of interview; communication difficulties or hearing problems; severe cognitive impairment; delirium; being on mechanical ventilation).	70, 7.1, 60 to 92 % female = 56%	and validated in Brazil)	individuals who were illiterate, 18 for individuals with low/medium educational level and 26 for individuals with a higher educational level)	interviews conducted 7 to 10 days after admission).
Pendlebury et al. (2015)[257,b]	Acute medical ward in a teaching hospital (United Kingdom).	Audit of patients aged ≥ 75 years.	Sample size = 264 Age (mean, SD, range) = 84.3, 5.6, 75 to 101 % female: 56% *Initial assessment on admission: 228 had an AMTS (reason for not having an AMTS, i.e. "untestability": unwell, dysphasic, reduced consciousness/ drowsiness, severe confusion/agitation,*	AMTS	Cognitive impairment (scores < 9)	1st AMTS: 56% had cognitive impairment (assessed on admission). 2nd AMTS: 60% had cognitive impairment (reassessed ≥ 72 hours after admission).
				MoCA	Mild cognitive impairment (scores < 26) Moderate to severe cognitive impairment (scores < 20)	92% had mild cognitive impairment & 65% had moderate to severe cognitive impairment (could be included in both estimates; assessed ≥ 72 hours after admission).

Study	Setting	Selection criteria	Sample characteristics	Cognitive impairment measure	Cut-off score	Prevalence
			fatigue, lack of English). *Follow-up assessment ≥ 72 hours after admission: 100 had a repeat AMTS; 91 had a MoCA.*			
Sampson et al. (2009)[187,a]	Medical acute admissions unit in a general hospital (United Kingdom).	Aged > 70 years; unplanned acute admission; admitted for > 48 hours; sufficient English; no persistent delirium (assessed using CAM); not moribund or unconscious.	Sample size = 617 Age (mean, range) = 83, 70 to 101 % female = 59%	MMSE[c]	Moderate cognitive impairment (scores 16 to 23) Severe cognitive impairment (scores 0 to 15)	47.9% had cognitive impairment: 22.8% moderate cognitive impairment & 25.1% severe cognitive impairment (assessed within 72 hours of admission).

AMTS = Abbreviated Mental Test Score; CAM = Confusion Assessment Method; CDR Scale = Clinical Dementia Rating Scale; CI = Confidence Interval; ENT = Ears, Nose and Throat; IQR = Inter-Quartile Range; MMMS Examination = Modified Mini-Mental State Examination; MMSE = Mini-Mental State Examination; MoCA = Montreal Cognitive Assessment; SD = Standard Deviation.

[a]I searched MEDLINE from database inception to July 2020 for relevant studies that included prevalence, cognitive impairment and general hospital inpatient (as well as synonyms and alternative spellings) in their titles. **Table 31** summarises the results of the relevant studies. I summarised studies that reported the prevalence of cognitive impairment broadly (not specifically delirium or dementia).

[b]Not obtained in MEDLINE search; found in supplementary search.

[c]If participant was unable to complete particular item(s) of the MMSE (e.g. due to hearing or visual impairment) scores were adjusted taking into account the change in denominator. *Calculated using data from paper.

9.5.2.3 Relevant studies of the prevalence of clinically significant cognitive impairment in older adults in community settings

The prevalence of cognitive impairment is lower in community settings than it is in general hospital settings. I found three relevant reviews summarising literature of the prevalence of cognitive impairment in older adults in community settings (see **Table 32**).[158,258,259] These reviews reported that the prevalence of delirium ranged from 1% to 2%,[158] dementia ranged from 2% to 8.5%,[258] and mild cognitive impairment ranged from 3% to 42%.[259] Most of these prevalence estimates are lower than those reported in the systematic reviews of older adults in the general hospital setting (described above) and are consistently lower than the prevalence of clinically significant cognitive impairment I found in my substudy.

Table 32. Relevant reviews of the prevalence of cognitive impairment in older adults in community settings

Review	Reviewers' findings
Inouye et al. (2014) *Delirium in elderly people*[158]	Narrative review summarising literature on delirium in elderly people (aged ≥ 65 years). It included literature that measured delirium using a validated delirium instrument. It reported the prevalence of delirium in the community ranged from 1% to 2%.
Prince et al. (2013) *The global prevalence of dementia: A systematic review and metaanalysis*[258]	Systematic review summarising population-based studies of the prevalence of dementia (defined using standard diagnostic criteria) in older adults (aged ≥ 60 years) in 21 Global Burden of Disease regions. It reported age-standardised estimates that ranged from 2.07% to 8.50%. It noted estimates in most world regions ranged from 5% to 7%.
Ward et al. (2012) *Mild cognitive impairment: Disparity of incidence and prevalence estimates*[259]	Systematic review summarising population-based studies of the prevalence or incidence of diagnosed mild cognitive impairment (MCI) and related terms. Prevalence estimates varied according to the terminology used for MCI (e.g. "MCI", age-associated memory impairment and cognitive impairment no dementia). Studies that used the term "MCI" reported prevalence estimates that ranged from 3% to 42%; these studies all focussed on older adults.

MCI = Mild Cognitive Impairment.

9.5.3 Associations of clinically significant cognitive impairment

9.5.3.1 Overview of results

Age. As hypothesised, I found clinically significant cognitive impairment and older age were associated, even after adjusting for sex. The association between clinically significant cognitive impairment and older age has been consistently documented in the literature, which I describe in the next section.

Sex. I hypothesised that female sex would be associated with clinically significant cognitive impairment. I made this hypothesis because numerous cross-sectional and longitudinal studies have found a higher prevalence of clinically significant cognitive impairment in women than men.[11,260] It is possible these studies obtained these findings because female sex is a risk factor for clinically significant cognitive impairment, or it may be that women tend to live longer than men and are therefore at higher risk for it.[261] I did not find evidence of an association between clinically significant cognitive impairment and sex (before or after adjusting for age).

Relationship status. Consistent with my hypothesis, I found that clinically significant cognitive impairment was associated with not having a spouse or partner, even after adjusting for age and sex. While collecting data for this substudy, I often saw older inpatients' spouse or partner help them manage their medical illnesses (e.g. help them follow treatment regimens; remind them to eat, drink and mobilise; and notify healthcare professionals if their health status changed). Spouses and partners providing this type of help may be protective against cognitive impairment, especially acute confusion which is

caused by medical-related problems. The frequent social contact offered by a spouse or partner has also been suggested to protect against cognitive impairment.[244,260]

Multimorbidity score. I hypothesised clinically significant cognitive impairment and a greater multimorbidity score would be associated. I thought older adults with greater multimorbidity would be more likely to (1) experience medical problems (e.g. infections) that could cause acute confusion; (2) take medications that could impair cognitive function; and (3) have illnesses that are associated with cognitive impairment which, in combination with others, would be even more strongly associated. However, I did not find evidence that clinically significant cognitive impairment was associated with a greater multimorbidity score, although the measure of multimorbidity I used was crude.

9.5.3.2 Relevant studies of the associations of clinically significant cognitive impairment in older general hospital inpatients[a]

Age. In accordance with my results, there is substantial evidence to indicate that clinically significant cognitive impairment is associated with older age.[11,158,187,253,256,262-270] Several studies have found this association to persist even after adjusting for other patient characteristics, such as sex and independent functioning.[253,256,262-265] This finding is important as it indicates that we can be reasonably confident that another variable is not accounting for the association.

Sex. The literature on the association between clinically significant cognitive impairment and sex is inconsistent.

(1) **No association with sex:** Most studies have not found evidence of an association between clinically significant cognitive impairment and sex, an observation consistent with my findings.[253,256,262,264-268,271] Several studies that adjusted for patient characteristics (such as age) also did not find evidence of an association.[253,256,264,266]

(2) **Association with male sex:** There is some evidence of an association between male gender and delirium.[269] Notably, however, a systematic review concluded (based on its meta-analysis) that male sex is *not* a risk factor for developing delirium in older medical inpatients (pooled OR = 0.86, 95% CI, 0.65 to 1.14).[268]

[a]Studies used a variety of statistical analyses to evaluate associations, including logistic regressions, *t*-tests and chi-squared tests.

(3) **Association with female sex:** A review of dementia in older general hospital inpatients found several studies that reported a higher prevalence of dementia in females than males.[11] However, it noted studies did not report if these differences were significant.[11] I found only one study that reported a significant association with female sex – it is also the only study focussing on mild cognitive impairment (defined using diagnostic criteria[a]).[263] Because of this, it is difficult to directly compare its results with existing literature. It is notable, however, that the authors of this study stated their findings contradicted those of other studies (conducted in community settings) which found only slight sex-related differences in the prevalence of mild cognitive impairment.[263]

Relationship status. There is very little evidence on the association between clinically significant cognitive impairment and relationship status. Although a small number of studies have reported an association,[253,256,265] they found it disappeared in analyses that adjusted for other patient characteristics.[253,256,b] I also found that the association between clinically significant cognitive impairment and not having a spouse or partner became much weaker after adjusting for age and sex (although it remained significant).

It seems that while an association between clinically significant cognitive impairment and relationship status may exist, much of this association can be

[a]Consensus criteria proposed by the International Working Group on Mild Cognitive Impairment.
[b]One of these studies assessed associations using multivariable logistic regression analyses (adjusting for age and sex). The other conducted forward stepwise multivariate logistic regression analyses (variables included in the model: marital status, age, sex, educational level, occupational qualification, family arrangements, number of previous hospitalisations, ward type, depressive symptoms and functional dependence).

explained by other confounding variables. Age appears to be one of these variables, in that some of the apparent association between clinically significant cognitive impairment and not having a spouse or partner is likely explained by the fact that people without a spouse or partner are *older* than those with one. In other words, older age acts as a "confounding variable" because it is associated with (1) not having a spouse or partner (e.g. spouse or partner dying) and (2) clinically significant cognitive impairment (as described above).

Multimorbidity. The literature on the association between clinically significant cognitive impairment and multimorbidity is inconsistent. While some studies have found an association with greater multimorbidity,[265,270,272,273] others have not found evidence of an association.[187,262,263,267,271,274-276,a]

The inconsistent findings in the evidence base may have to do, at least in part, with the various (often crude) ways in which studies have measured multimorbidity. For instance, studies have measured multimorbidity using the Charlson Comorbidity Index,[187,262,263,267,271,273,275] the Cumulative Illness Rating Scale,[265,272,276] and the number of medical diagnoses patients have.[270,274] Amongst those studies using the same measure, they have also often defined multimorbidity differently. In light of this, it is perhaps unsurprising that studies have reported conflicting results. It is notable, however, that most studies that used the Charlson Comorbidity Index[277] have not found evidence of an association.[187,262,263,267,271,275,b]

[a]Two of these studies did not find evidence of an association in their logistic regression analyses, however found those with delirium had significantly higher mean multimorbidity scores.
[b]One of these studies did not find evidence of an association in their logistic regression analysis, however found those with delirium had significantly higher mean multimorbidity scores.

I did not find evidence of an association between clinically significant cognitive impairment and multimorbidity score. Yet, it is interesting that I found an association with greater multimorbidity in analyses where cognitive impairment was treated continuously (i.e. worse cognitive impairment scores).

9.5.3.3 Relevant studies of the associations of clinically significant cognitive impairment in older adults in community settings

There is a considerable amount of evidence indicating clinically significant cognitive impairment and older age are associated.[260,261,278,279] There are inconsistent findings in the evidence base on the association between clinically significant cognitive impairment and sex, with the majority of literature reporting either no evidence of an association or an association with female sex.[260,261,278,279]

A recent review of community-dwelling older adults[a] concluded that people who were lifelong single or widowed were at an increased risk of dementia when compared to those who were married (relative risk [RR] = 1.42, 95% CI, 1.07 to 1.90 and RR = 1.20, 95% CI, 1.02 to 1.41 respectively).[243,b] This review only included studies that adjusted for age and sex in their analyses.[243] It is notable that the review reported that the associations previously described were attenuated after adjustment for education and physical health.[243] This finding suggests potential confounding, which mirrors the results obtained in studies of older general hospital inpatients.

The literature on the association between clinically significant cognitive impairment and multimorbidity is conflicting. Similar to studies conducted in the general hospital setting, those in community settings have reported an association with greater multimorbidity[242,280] or no association.[281]

[a]Review included studies if sample consisted of ≥ 50% of individuals aged ≥ 65 years at the time of dementia ascertainment or clear subgroup of individuals aged ≥ 65 years.
[b]Review did not find evidence of an association in divorced people.

9.5.4 Strengths

My cross-sectional substudy has several strengths (similar to those outlined in **Chapters 7** and **8**). First, it has a large sample size, which helps improve its accuracy.[19] Second, cognitive function was assessed at a consistent time frame in participants' admission to hospital (i.e. within one week of admission), which helped to provide a more homogenous study sample. Third, it included patients who did not have the capacity to provide informed consent, but a proxy advised study participation was appropriate. Cognitive impairment may affect a person's ability to consent, therefore the inclusion of those lacking capacity improves the generalisability of study results. Fourth, it included severely ill patients. Since older general hospital inpatients are usually extremely unwell, including severely ill patients increases the generalisability of its findings. Fifth, the researchers who collected data used in this substudy underwent rigorous training and monitoring to ensure high-quality data were collected.

9.5.5 Limitations

My cross-sectional substudy also has several limitations. The limitations of this substudy mirror *most* of those outlined in my substudy on the prevalence and associations of clinically significant anxiety and depression in older general hospital inpatients (see **Chapter 7, pages 187 to 189** and **Chapter 8, pages 232 to 233)**.

Briefly, the main limitations of the substudy are:

(1) its sample was drawn from a trial which likely reduces the generalisability of its findings;

(2) it focussed on a specific subpopulation of older general hospital inpatients (recently admitted to hospital and not terminally ill) in the United Kingdom and its findings may not generalise to other populations of older general hospital inpatients;

(3) the measure used to assess for clinically significant cognitive impairment (T-MoCA) cannot be used to diagnose cognitive disorders;

(4) the T-MoCA was not administered by clinicians or trained neurocognitive testers (instead, it was administered by trained researchers);

(5) T-MoCA scores were imputed for 20% or less of missing items in a small proportion of participants (4%);

(6) data on participants' demographic and clinical characteristics were collected from medical records which are prone to inaccuracies;

(7) its analyses of the associations of clinically significant cognitive impairment were limited to the demographic and clinical characteristics for which data were available; and

(8) its cross-sectional study design did not allow me to determine causal relationships between clinically significant cognitive impairment and participants' demographic and clinical characteristics.

9.5.6 Implications and conclusions

I found that clinically significant cognitive impairment was common in older general hospital inpatients, occurring in over 60 percent. Since older general hospital inpatients are estimated to make up two-thirds of admissions into general hospitals in the United Kingdom,[154] we can expect around 40 percent of patients admitted to general hospitals to have clinically significant cognitive impairment. This is important, considering the detrimental effects cognitive impairment has on patients and the challenges posed for the healthcare services that they use. Future research should examine ways of more systematically identifying and, where necessary, specifically managing those with clinically significant cognitive impairment. This study suggests which older general hospital inpatients are most likely to have clinically significant cognitive impairment – those who are older and without a spouse or partner.

Chapter 10
Summary of findings

10.1 Aim one

I aimed to summarise literature on the prevalence of psychiatric illnesses in general hospital inpatients, using a meta-review. I found:

(1) **Anxiety.** There were no systematic reviews of the prevalence of anxiety in the whole population of adult general hospital inpatients.

(2) **Depression.** The prevalence of depression (defined using diagnostic criteria) ranged from **2%** to **56%** in adult general hospital inpatients. In studies of adult general medical and surgical inpatients, the mean prevalence was **12%** (prevalence estimates ranged from **2.7%** to **33.6%**).

(3) **Delirium.** The prevalence of delirium (defined using diagnostic criteria) ranged from **10%** to **31%** in adult medical inpatients at admission to hospital.

(4) **Dementia.** The prevalence of dementia (defined using diagnostic criteria) ranged from **2.8%** to **63.0%** in older general hospital inpatients.

(5) **Substance abuse.** There were no systematic reviews of the prevalence of substance abuse in the whole population of adult general hospital inpatients. However, a relevant review estimated the prevalence of harmful use of alcohol and alcohol dependence (defined using diagnostic criteria) in general medical and surgical inpatients in the United Kingdom to be **16.10%** and **6.21%** respectively. This review was not included in my meta-review because it did not focus solely on adult (aged ≥ 16 years) inpatients.

10.2 Aim two

Having found that there was no systematic review of the prevalence of anxiety in the whole population of adult general hospital inpatients, I aimed to systematically review this literature. I found:

(1) **Panic disorder.** The prevalence of panic disorder (defined using diagnostic criteria) ranged from **0.9%** to **5.6%** in adult general medical and surgical inpatients. In studies that used DSM diagnostic criteria, the mean prevalence was **2%**.

(2) **Generalised anxiety disorder.** The prevalence of generalised anxiety disorder (defined using diagnostic criteria) ranged from **0.9%** to **18.9%** in adult general medical and surgical inpatients. In studies that used DSM diagnostic criteria, the mean prevalence was **7%**.

(3) **Phobias.** There was limited information on the prevalence of phobias (defined using diagnostic criteria) in adult general medical and surgical inpatients.

10.3 Aim three

I aimed to determine the prevalence of clinically significant anxiety, depression and cognitive impairment in older (aged ≥ 65 years) general hospital inpatients, using a cross-sectional study. In order to find out which patients were most likely to have these psychiatric illnesses, I also aimed to determine the patient characteristics associated with these conditions. I found:

(1) **Clinically significant anxiety.** The prevalence of clinically significant anxiety (defined as a GAD-2 score ≥ 3) was **41.8%**. It was associated with female sex, not having a spouse or partner, and being “sicker” (i.e. greater multimorbidity score, worse independent functioning, greater depression severity and worse cognitive impairment). Its strongest association was with greater depression severity. I did not find evidence of an association between clinically significant anxiety and age.

(2) **Clinically significant depression.** The prevalence of clinically significant depression (defined as a PHQ-2 score ≥ 3) was **43.6%**. It was associated with being “sicker” (i.e. greater multimorbidity score, worse independent functioning, greater anxiety severity and worse cognitive impairment). Its strongest association was with greater anxiety severity. I did not find evidence of an association with age, sex or relationship status.

(3) **Clinically significant cognitive impairment.** The prevalence of clinically significant cognitive impairment (defined as a T-MoCA score ≤ 17 out of 30) was **64.1%**. It was associated with older age and not having

a spouse or partner. I did not find evidence of an association between clinically significant cognitive impairment and sex or multimorbidity score. It is important to note that in the cross-sectional study, clinically significant anxiety, depression and cognitive impairment were determined using only cut-off scores on rating scales. These findings cannot therefore be interpreted as psychiatric diagnoses.

Chapter 11
Implications of findings

The main finding of this thesis is that psychiatric illnesses are highly prevalent in adult and older general hospital inpatients.

In older general hospital inpatients, I found evidence to suggest that psychiatric illnesses are especially common in the "sickest" patients (such as those with high multimorbidity and poor independent functioning) and those who do not have a spouse or partner.[a] Patients with clinically significant anxiety also appear to be more likely to have symptoms of other psychiatric illnesses (such as greater depression severity and worse cognitive impairment). Those with clinically significant depression similarly experience worse psychiatric symptoms (such as greater anxiety severity and worse cognitive impairment).

These findings have important implications for clinical care and healthcare policy.

[a]I found (1) clinically significant anxiety and depression were more common in patients who were "sicker" (e.g. those with high multimorbidity and poor independent functioning) and (2) clinically significant anxiety and cognitive impairment were more common in those without a spouse or partner.

11.1 Psychiatric care

Psychiatric illnesses are arguably sufficiently common in general hospital inpatients to make it worthwhile for healthcare professionals with psychiatric expertise to be *proactively* involved in patients' care and be *integrated* members of medical ward teams.

As a part of my doctoral studies, I had the unique opportunity to be a part of a randomised controlled trial (The HOME Study) which tested a new proactive and integrated way of delivering psychiatric care to patients in general hospitals.[166-168] In the new service model being tested, psychiatrists (and assistants with psychiatric expertise)[166,168]: proactively reviewed ward admissions; assessed patients as soon as possible after their admission, using a comprehensive biopsychosocial approach; and worked as integrated members of the medical ward team with shared patient responsibility. This "proactive" and "integrated" way of working has the potential to overcome the barriers to caring for patients with medical-psychiatric comorbidity faced by more traditional ways of delivering psychiatric care (e.g. reliance on medical ward teams to refer patients to psychiatry and implement treatment recommendations made by psychiatry). It seems unlikely that traditional ways of delivering psychiatric care could be sufficient for the high prevalence of need I report in this thesis because (1) psychiatry only see the small percentage of patients who are referred to them (despite the high prevalence of psychiatric illnesses) and (2) recommendations made by psychiatry are frequently not implemented by ward teams.[282,283]

More research is needed to evaluate innovative models of delivering psychiatric care in general hospitals – The HOME Study is the first randomised controlled trial to test a new service model for inpatient psychiatry in over a decade and its results are ongoing.[166-168]

11.2 Medical ward teams and senior management

It is essential for medical ward teams and senior management in general hospitals to be aware that many of the patients they care for have psychiatric illnesses. Medical ward teams and hospital managers also need to be aware of the potential benefit of providing both medical *and* psychiatric care to general hospital inpatients, and be motivated to integrate psychiatric care into clinical care.[284,285]

In order for medical ward teams to care for those with medical-psychiatric multimorbidity, they need to be competent in identifying common psychiatric illnesses.[284] To be able to do this, medical ward teams will likely require comprehensive education and training.[284] Research on the patient factors associated with psychiatric illnesses, such as those examined in this thesis, should be a part of this education. For example, medical ward teams caring for older general hospital inpatients should be aware that clinically significant anxiety and depression are particularly common in patients with high multimorbidity, poor independent functioning and impaired cognitive function, and that patients with clinically significant anxiety are more likely to have greater depression severity (and vice versa). It would also be beneficial for medical ward teams to know that some psychiatric illnesses (such as clinically significant anxiety and cognitive impairment) appear to occur more frequently in patients who do not have a spouse or partner. Medical ward teams can then use this information to identify patients who are most likely to have psychiatric illnesses and provide these patients with appropriate medical *and* psychiatric care.

11.3 Commissioners

Commissioners of general medical services can also play a crucial role in improving psychiatric care for general hospital inpatients.[284,286] Commissioning is the process of procuring health services, which involves (1) assessing health needs, (2) planning and purchasing services to meet those needs, and (3) monitoring the quality of those services.[287] Results from this thesis clearly show the need to provide psychiatric services to general hospital inpatients with sustainable sources of funding.

11.4 Researchers

I found that much of the research examining the prevalence of psychiatric illnesses in the medically ill focussed on patients with specific medical illnesses, rather than on patients in specific clinical settings (such as general hospital settings). It is concerning that high-quality research on the prevalence and associations of psychiatric illnesses in general hospital inpatients is so sparse, given the important negative consequences of these conditions.

The literature on anxiety was particularly limited. I therefore conducted a systematic review of the prevalence of anxiety disorders in general hospital inpatients (**Chapter 5**) and a cross-sectional study of the prevalence and associations of clinically significant anxiety in older general hospital inpatients (**Chapter 7**). There are still gaps however – for example, little is known about anxiety in patients with impaired cognition. Given the difficulties of doing research in patients with cognitive impairment, it is perhaps understandable that studies have often excluded these patients, but it means that important questions remain unanswered. There is also little evidence on the associations of anxiety in this population. I was able to examine only the small number of associations for which I had data and future research could examine others. The literature on substance abuse in general hospital inpatients also appears to be limited, indicating an important area for future research.

I also found that in general the quality of studies in this field was poor, an observation also noted by several systematic reviewers (see **Chapters 4** and **5**). In order to improve the methodological quality of future research studies, I

would recommend that researchers: obtain a large enough sample to accurately estimate the prevalence of psychiatric illnesses based on a sample size calculation; use random or consecutive sampling; and use standard diagnostic criteria to determine psychiatric disorder caseness or (at minimum) a validated cut-off score on a rating scale that has good psychometric properties.

It is also important that future research studies are reported clearly. Therefore, I would recommend that researchers provide a clear description of: their sampling method; the setting in which their study took place; their inclusion and exclusion criteria; the number of patients who agreed and declined to take part (i.e. response rate); participants' demographic and clinical characteristics; the psychiatric assessment method and caseness definition used; and their study's strengths and limitations.

Chapter 12
Conclusion

In this thesis, I present evidence that psychiatric illnesses are highly prevalent in adult and older general hospital inpatients. In older general hospital inpatients, these illnesses seem to occur most commonly in the “sickest” patients (such as those with high multimorbidity and poor independent functioning) and those without a spouse or partner. Those patients with clinically significant anxiety also appear to be more likely to experience symptoms of other psychiatric illnesses (such as greater depression severity and worse cognitive impairment); this finding was similar for those with clinically significant depression. These findings have important implications for clinical care and healthcare policy. In particular, they suggest that general hospital service models, which are largely oriented around solely providing medical care, need to ensure that they address the needs of patients suffering from both medical *and* psychiatric illnesses. Better psychiatric care provision in general hospitals has the potential to improve outcomes for these patients.

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Appendix 1
Search strategies used in meta-review

OVID MEDLINE (1948 to April 2020)

1	prevalence/
2	incidence/
3	prevalen*.ti,ab.
4	inciden*.ti,ab.
5	frequen*.ti,ab.
6	rate*.ti,ab.
7	occurr*.ti,ab.
8	1 or 2 or 3 or 4 or 5 or 6 or 7
9	Hospitals, District/
10	Hospitals, General/
11	Tertiary Care Centers/
12	exp Hospitals, Teaching/
13	"district hospital*".ti,ab.
14	"general hospital*".ti,ab.
15	"tertiary hospital*".ti,ab.
16	"teaching hospital*".ti,ab.
17	"medical centre*".ti,ab.
18	"medical center*".ti,ab.
19	"general medical".ti,ab.
20	(ward* adj4 patient*).ti,ab.
21	(hospital* adj4 patient*).ti,ab.
22	Inpatients/
23	in$patient*.ti,ab.
24	Hospitalization/
25	Hospital Units/
26	Patient Admission/
27	9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 36
28	exp Dementia/
29	exp Neurocognitive Disorders/
30	exp Cognition Disorders/
31	exp Neurobehavioral Manifestations/
32	"organic brain disease*".ti,ab.
33	"organic brain syndrome*".ti,ab.
34	dement*.ti,ab.
35	alzheimer*.ti,ab.
36	(lewy* adj2 bod*).mp.
37	Delirium/
38	deliri*.mp.
39	"acute confus*".ti,ab.
40	"acute organic psychosyndrome".ti,ab.
41	"acute brain syndrome".ti,ab.
42	"metabolic encephalopathy".ti,ab.
43	"acute psycho-organic syndrome".ti,ab.
44	"clouded state".ti,ab.

45 "clouding of consciousness".ti,ab.
46 "exogenous psychosis".ti,ab.
47 "toxic psychosis".ti,ab.
48 "toxic confusion".ti,ab.
49 exp Substance-Related Disorders/
50 abstin*.ti,ab.
51 abstain*.ti,ab.
52 abuse*.ti,ab.
53 addict*.ti,ab.
54 dependen*.ti,ab.
55 misuse.ti,ab.
56 overdose.ti,ab.
57 withdrawal.ti,ab.
58 Depression/
59 exp Depressive Disorder/
60 depression.ti,ab.
61 (depress$3 and (symptom$ or mood)).ti,ab.
62 Depression, Postpartum/
63 (depressi* adj3 disorder*).tw.
64 (depressi* adj3 symptom*).tw.
65 exp Anxiety/
66 Panic/
67 neurotic*.ti,ab.
68 neurosis*.ti,ab.
69 anxiety.ti,ab.
70 panic.ti,ab.
71 agoraphobi*.ti,ab.
72 obsess*.ti,ab.
73 compulsi*.ti,ab.
74 phobi*.ti,ab.
75 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 (2799615)
76 (((comprehensive* or integrative or systematic*) adj3 (bibliographic* or review* or literature)) or (meta-analy* or metaanaly* or "research synthesis" or ((information or data) adj3 synthesis) or (data adj2 extract*))).ti,ab. or (cinahl or (cochrane adj3 trial*) or embase or MedLine or psyclit or (psycinfo not "psycinfo database") or pubmed or scopus or "sociological abstracts" or "web of science").ab. or ("cochrane database of systematic reviews" or evidence report technology assessment or evidence report technology assessment summary).jn. or Evidence Report: Technology Assessmcent*.jn. or ((review adj5 (rationale or evidence)).ti,ab. and review.pt.) or meta-analysis as topic/ or Meta-Analysis.pt.
77 "literature review".ti,ab.
78 76 or 77
79 8 and 27 and 75 and 78

OVID EMBASE (1947 to April 2020)

1 prevalence/
2 incidence/
3 prevalen*.ti,ab.
4 inciden*.ti,ab.
5 frequen*.ti,ab.
6 rate*.ti,ab.
7 occurr*.ti,ab.
8 1 or 2 or 3 or 4 or 5 or 6 or 7
9 public hospital/
10 general hospital/
11 tertiary care center/
12 exp teaching hospital/
13 "district hospital*".ti,ab.
14 "general hospital*".ti,ab.
15 "tertiary hospital*".ti,ab.
16 "teaching hospital*".ti,ab.
17 "medical centre*".ti,ab.
18 "medical center*".ti,ab.
19 "general medical".ti,ab.
20 (ward* adj4 patient*).ti,ab.
21 (hospital* adj4 patient*).ti,ab.
22 hospital patient/
23 in$patient*.ti,ab.
24 hospitalization/
25 "hospital subdivisions and components"/
26 hospital admission/
27 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26
28 exp Dementia/
29 exp Neurocognitive Disorders/
30 exp Cognition Disorders/
31 exp Neurobehavioral Manifestations/
32 "organic brain disease*".ti,ab.
33 "organic brain syndrome*".ti,ab.
34 dement*.ti,ab.
35 alzheimer*.ti,ab.
36 (lewy* adj2 bod*).mp.
37 Delirium/
38 deliri*.mp.
39 "acute confus*".ti,ab.
40 "acute organic psychosyndrome".ti,ab.
41 "acute brain syndrome".ti,ab.
42 "metabolic encephalopathy".ti,ab.
43 "acute psycho-organic syndrome".ti,ab.
44 "clouded state".ti,ab.
45 "clouding of consciousness".ti,ab.
46 "exogenous psychosis".ti,ab.
47 "toxic psychosis".ti,ab.
48 "toxic confusion".ti,ab.
49 exp Substance-Related Disorders/

50 abstin*.ti,ab.
51 abstain*.ti,ab.
52 abuse*.ti,ab.
53 addict*.ti,ab.
54 dependen*.ti,ab.
55 misuse.ti,ab.
56 overdose.ti,ab.
57 withdrawal.ti,ab.
58 Depression/
59 exp Depressive Disorder/
60 depression.ti,ab.
61 (depress$3 and (symptom$ or mood)).ti,ab.
62 Depression, Postpartum/
63 (depressi* adj3 disorder*).tw.
64 (depressi* adj3 symptom*).tw.
65 exp Anxiety/
66 Panic/
67 neurotic*.ti,ab.
68 neurosis*.ti,ab.
69 anxiety.ti,ab.
70 panic.ti,ab.
71 agoraphobi*.ti,ab.
72 obsess*.ti,ab.
73 compulsi*.ti,ab.
74 phobi*.ti,ab.
75 28 or 29 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74
76 (((comprehensive* or integrative or systematic*) adj3 (bibliographic* or review* or literature)) or (meta-analy* or metaanaly* or "research synthesis" or ((information or data) adj3 synthesis) or (data adj2 extract*))).ti,ab. or (cinahl or (cochrane adj3 trial*) or embase or MedLine or psyclit or (psycinfo not "psycinfo database") or pubmed or scopus or "sociological abstracts" or "web of science").ab. or ("cochrane database of systematic reviews" or evidence report technology assessment or evidence report technology assessment summary).jn. or Evidence Report: Technology Assessment*.jn. or ((review adj5 (rationale or evidence)).ti,ab. and review.pt.) or meta-analysis as topic/
77 meta analysis/
78 "systematic review"/
79 "literature review".ti,ab.
80 76 or 77 or 78 or 79
81 8 and 27 and 77 and 80

OVID PsycINFO (1806 to April 2020)

1 epidemiology/
2 prevalen*.ti,ab.
3 inciden*.ti,ab.
4 frequen*.ti,ab.
5 rate*.ti,ab.
6 occurr*.ti,ab.
7 1 or 2 or 3 or 4 or 5 or 6
8 "district hospital*".ti,ab.
9 "general hospital*".ti,ab.
10 "tertiary hospital*".ti,ab.
11 "teaching hospital*".ti,ab.
12 "medical centre*".ti,ab.
13 "medical center*".ti,ab.
14 "general medical".ti,ab.
15 (ward* adj4 patient*).ti,ab.
16 (hospital* adj4 patient*).ti,ab.
17 exp Hospitalized Patients/
18 in$patient*.ti,ab.
19 Hospitalization/
20 hospital admission/
21 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 (90329)
22 exp Dementia/
23 exp cognitive impairment/
24 neurodegenerative diseases/ or exp alzheimer's disease/
25 "organic brain disease*".ti,ab.
26 "organic brain syndrome*".ti,ab.
27 dement*.ti,ab.
28 alzheimer*.ti,ab.
29 (lewy* adj2 bod*).mp.
30 Delirium/
31 deliri*.mp.
32 "acute confus*".ti,ab.
33 "acute organic psychosyndrome".ti,ab.
34 "acute brain syndrome".ti,ab.
35 "metabolic encephalopathy".ti,ab.
36 "acute psycho-organic syndrome".ti,ab.
37 "clouded state".ti,ab.
38 "clouding of consciousness".ti,ab.
39 "exogenous psychosis".ti,ab.
40 "toxic psychosis".ti,ab.
41 "toxic confusion".ti,ab.
42 exp Drug Dependency/ or exp Drug Abuse/ or exp Drug Addiction/ or exp Alcoholism/
43 abstin*.ti,ab.
44 abstain*.ti,ab.
45 abuse*.ti,ab.
46 addict*.ti,ab.
47 dependen*.ti,ab.
48 misuse.ti,ab.
49 overdose.ti,ab.

50 withdrawal.ti,ab.
51 Depression/
52 exp major depression/
53 depression.ti,ab.
54 (depress$3 and (symptom$ or mood)).ti,ab.
55 (depressi* adj3 disorder*).tw.
56 (depressi* adj3 symptom*).tw.
57 exp Anxiety/
58 Panic/
59 neurotic*.ti,ab.
60 neurosis*.ti,ab.
61 anxiety.ti,ab.
62 panic.ti,ab.
63 agoraphobi*.ti,ab.
64 obsess*.ti,ab.
65 compulsi*.ti,ab.
66 phobi*.ti,ab.
67 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66
68 (((comprehensive* or integrative or systematic*) adj3 (bibliographic* or review* or literature)) or (meta-analy* or metaanaly* or "research synthesis" or ((information or data) adj3 synthesis) or (data adj2 extract*))).ti,ab,id. or ((review adj5 (rationale or evidence)).ti,ab,id. and "Literature Review".md.) or (cinahl or (cochrane adj3 trial*) or embase or MedLine or psyclit or pubmed or scopus or "sociological abstracts" or "web of science").ab. or ("systematic review" or "meta analysis").md.
69 "literature review".ti,ab.
70 68 or 69
71 7 and 21 and 67 and 70

EBSCO Host CINAHL (1937 to April 2020)

S1	JN “Cochrane Database of Systematic Reviews”
S2	TI ((MedLine or pubmed or psyclit or cinahl or (psycinfo not “psycinfo database”) or “web of science” or scopus or embase)) OR AB ((MedLine or pubmed or psyclit or cinahl or (psycinfo not “psycinfo database”) or “web of science” or scopus or embase))
S3	TI ((systematic* n3 review*) OR (systematic* n3 bibliographic*) OR (systematic* n3 literature) OR (comprehensive* n3 literature) OR (comprehensive* n3 bibliographic*) OR (integrative n3 review)) OR AB ((systematic* n3 review*) OR (systematic* n3 bibliographic*) OR (systematic* n3 literature) OR (comprehensive* n3 literature) OR (comprehensive* n3 bibliographic*) OR (integrative n3 review))
S4	TI ((information n2 synthesis) OR (data n2 synthesis) OR (data n2 extract*)) OR AB ((information n2 synthesis) OR (data n2 synthesis) OR (data n2 extract*))
S5	(MH "Prevalence")
S6	(MH "Incidence")
S7	TI (prevalen* OR inciden* OR frequen* OR rate* OR occurr*) OR AB (prevalen* OR inciden* OR frequen* OR rate* OR occurr*)
S8	S1 OR S2 OR S3 OR S4
S9	S5 OR S6 OR S7
S10	(MH "Hospitals, Public+")
S11	(MH "Hospitals, Community")
S12	TI ("district hospital*" OR "general hospital*" OR "tertiary hospital*" OR "teaching hospital*" OR "medical centre*" OR "medical center*" OR "general medical" OR inpatient*) OR AB ("district hospital*" OR "general hospital*" OR "tertiary hospital*" OR "teaching hospital*" OR "medical centre*" OR "medical center*" OR "general medical" OR inpatient*)
S13	(MH "Inpatients")
S14	(MH "Hospitalization+")
S15	S10 OR S11 OR S12 OR S13 OR S14
S16	(MH "Dementia+")
S17	(MH "Cognition Disorders+")
S18	(MH "Neurobehavioral Manifestations+")
S19	TI ("organic brain disease*" OR "organic brain syndrome*" OR dement* OR alzheimer* OR (lewy n2 bod*)) OR AB ("organic brain disease*" OR "organic brain syndrome*" OR dement* OR alzheimer* OR (lewy n2 bod*))
S20	(MH "Delirium")
S21	TI (deliri* OR "acute confus*" OR "acute organic psychosyndrome" OR "acute brain syndrome" OR "metabolic encephalopathy") OR AB (deliri* OR "acute

	confus*" OR "acute organic psychosyndrome" OR "acute brain syndrome" OR "metabolic encephalopathy")
S22	(MH "Substance Abuse+")
S23	TI ("acute psycho-organic syndrome" OR "clouded state" OR "clouding of consciousness" OR "exogenous psychosis" OR "toxic psychosis" OR "toxic confusion")) OR AB ("acute psycho-organic syndrome" OR "clouded state" OR "clouding of consciousness" OR "exogenous psychosis" OR "toxic psychosis" OR "toxic confusion"))
S24	TI (abstin* OR abstain* OR abuse* OR addict* OR dependen* OR misuse OR overdose OR withdrawal) OR AB (abstin* OR abstain* OR abuse* OR addict* OR dependen* OR misuse OR overdose OR withdrawal)
S25	(MH "Depression+") OR (MH "Depression, Postpartum")
S26	TI (depression OR (depress* n2 (symptom* OR mood)) OR (depressi* n3 disorder*)) OR AB (depression OR (depress* n2 (symptom* OR mood)) OR (depressi* n3 disorder*))
S27	TI depressi* n3 symptom* OR AB depressi* n3 symptom*
S28	(MH "Anxiety+")
S29	(MH "Panic Disorder")
S30	(MH "Phobic Disorders+")
S31	TI (neurotic* OR neurosis* OR anxiety OR panic OR agoraphobi* OR obsess* OR compulsi* OR phobi*) OR AB (neurotic* OR neurosis* OR anxiety OR panic OR agoraphobi* OR obsess* OR compulsi* OR phobi*)
S32	S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31
S33	S8 AND S9 AND S15 AND S32

Scopus (2004 to April 2020)

(TITLE-ABS-KEY (prevalen* OR inciden* OR frequen* OR rate* OR occurr*))

AND

((TITLE-ABS-KEY ("district hospital*" OR "general hospital*" OR "tertiary hospital*" OR "teaching hospital*" OR "medical centre*" OR "medical center*" OR "general medical")) OR (TITLE-ABS-KEY (ward* W/4 patient*)) OR (TITLE-ABS-KEY (hospital* W/4 patient*)) OR (TITLE-ABS-KEY (inpatient*)) OR (TITLE-ABS-KEY (hospitalisation OR hospitalization)) OR (TITLE-ABS-KEY ("hospital unit*")) OR (TITLE-ABS-KEY ((patient* OR hospital*) W/2 (admission OR admit*))))

AND

((TITLE-ABS-KEY ("organic brain disease*" OR "organic brain syndrome*" OR dement* OR alzheimer* OR (lewy* W/2 bod*))) OR (TITLE-ABS-KEY (deliri* OR "acute confus*" OR "acute organic psychosyndrome" OR "acute brain syndrome" OR "metabolic encephalopathy")) OR (TITLE-ABS-KEY ("acute psycho-organic syndrome" OR "clouded state" OR "clouding of consciousness" OR "exogenous psychosis" OR "toxic psychosis" OR "toxic confusion")) OR (TITLE-ABS-KEY (abstin* OR abstain* OR abuse* OR addict* OR dependen* OR misuse OR overdose OR withdrawal)) OR (TITLE-ABS-KEY (depression OR (depress* W/2 (symptom* OR mood)) OR (depressi* W/3 disorder*))) OR (TITLE-ABS-KEY (depressi* W/3 symptom*)) OR (TITLE-ABS-KEY (neurotic* OR neurosis* OR anxiety OR panic OR agoraphobi* OR obsess* OR compulsi* OR phobi*)))

AND

((TITLE-ABS-KEY ((comprehensive* OR integrative OR systematic*) W/3 (bibliographic* OR review* OR literature))) OR (TITLE-ABS-KEY (meta-analy* OR metaanaly* OR "research synthesis" OR ((information OR data) W/3 synthesis) OR (data W/2 extract*))) OR (ABS (cinahl OR (cochrane W/3 trial*) OR embase OR MedLine OR psyclit OR (psycinfo AND not "psycinfo database") OR pubmed OR scopus OR "sociological abstracts" OR "web of science")) OR (TITLE-ABS-KEY (review W/5 (rationale OR evidence))) OR (TITLE-ABS-KEY ("literature review")

Appendix 2
Adaptations to AMSTAR 2

Domain	Original AMSTAR 2 domain	Adapted AMSTAR 2 domain for meta-review	Rationale for adaptation of AMSTAR 2 domain for meta-review
1	**Did the research questions and inclusion criteria for the review include the components of PICO?**		
	For Yes: ☐ Population ☐ Intervention ☐ Comparator group ☐ Outcome **Optional (recommended)** ☐ Timeframe for follow-up	**Adaptation made** **For Yes:** ☐ Patient population ☐ Psychiatric illness of interest ☐ Outcome (prevalence)	I adapted this domain to be relevant for reviews of prevalence studies. PICO is commonly used to describe interventional studies, however is less appropriate for describing prevalence studies (i.e. cross-sectional studies and cohort studies). I adapted this domain to include the following essential components: patient population, psychiatric illness of interest and outcome (prevalence).
2	**Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?**		
	For Partial Yes, the authors state that they have a written protocol or guide that included ALL of the following: ☐ Review question(s) ☐ A search strategy ☐ Inclusion/ exclusion criteria ☐ A risk of bias assessment **For Yes, must satisfy partial yes criteria, plus the protocol should be registered and**	No adaptations made.	Not applicable.

	should also have specified: ☐ A meta-analysis/synthesis plan if appropriate, *and* ☐ A plan for investigating causes of heterogeneity ☐ Justification for any deviations from the protocol		
3	**Did the review authors explain their selection of the study designs for inclusion in the review?**		
	For Yes, must satisfy ONE of the following: ☐ Explanation for including only RCTs ☐ OR Explanation for including only NRSI ☐ OR Explanation for including both RCTs and NRSIs	**Adaptation made** **For Yes, the review must satisfy the following:** ☐ Include only cross-sectional studies and cohort studies	I adapted this domain to be relevant for reviews of prevalence studies. Cross-sectional studies and cohort studies are appropriate study designs for measuring prevalence because they measure the proportion of people in a group who have a medical illness at a given time.
4	**Did the review authors use a comprehensive literature search strategy?**		
	For Partial Yes, must include ALL of the following: ☐ Searched at least 2 databases (relevant to research question) ☐ Provided key word and/or search strategy ☐ Justified publication restrictions (e.g. language) **For Yes, must also have ALL of the following:** ☐ Searched the reference lists/	**Adaptation made** **For Yes, removed:** ☐ Searched trial/study registries	I removed "searched trial/study registries" because this item is not necessary for reviews of prevalence studies (i.e. reviews of cross-sectional and cohort studies).

	bibliographies of included studies ☐ Searched trial/study registries ☐ Included/ consulted content experts in the field ☐ Where relevant, searched for grey literature ☐ Conducted search within 24 months of completion of the review		
5	**Did the review authors perform study selection in duplicate?**		
	For Yes, must include ONE of the following: ☐ At least two reviewers independently agreed on selection of eligible studies and achieved consensus on which studies to include ☐ OR two reviewers selected a sample of eligible studies and achieved good agreement (at least 80 percent), with the remainder selected by one reviewer	No adaptations made.	Not applicable.
6	**Did the review authors perform data extraction in duplicate?**		
	For Yes, must include ONE of the following: ☐ At least two reviewers achieved consensus on which data to extract from included studies ☐ OR two reviewers extracted data from a sample	No adaptations made.	Not applicable.

	of eligible studies and achieved good agreement (at least 80 percent), with the remainder extracted by one reviewer		
7	**Did the review authors provide a list of excluded studies and justify the exclusions?**		
	For Partial Yes: ☐ Provided a list of all potentially relevant studies that were read in full-text form but excluded from the review **For Yes, must also have:** ☐ Justified the exclusion from the review of each potentially relevant study	No adaptations made.	Not applicable.
8	**Did the review authors describe the included studies in adequate detail?**		
	For Partial Yes, must include ALL of the following: ☐ Described populations ☐ Described interventions ☐ Described comparators ☐ Described outcomes ☐ Described research designs **For Yes, must also have ALL the following:** ☐ Described population in detail ☐ Described intervention in detail (including	**Adaptation made** **For Yes, must have described ALL of the following:** ☐ Study design ☐ Inclusion criteria ☐ Study setting ☐ Sample demographics ☐ Psychiatric illness assessment measure(s) ☐ Psychiatric illness caseness definition(s) ☐ Prevalence estimates **No "Partial Yes" score**	I adapted this domain to be relevant for reviews of prevalence studies. PICO is commonly used to describe interventional studies, however is less appropriate for describing prevalence studies (i.e. cross-sectional studies and cohort studies). I adapted this domain to include the following essential components: study design, inclusion criteria, study setting, sample demographics, psychiatric illness assessment measure(s), psychiatric illness caseness definition(s) and prevalence estimates**.**

	doses where relevant) ☐ Described comparator in detail (including doses where relevant) ☐ Described study's setting ☐ Timeframe for follow-up		
9	**Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?**		
	For Partial Yes, must have assessed RoB: ☐ From confounding, and ☐ From selection bias **For Yes, must also have assessed RoB:** ☐ Methods used to ascertain exposures and outcomes, and ☐ Selection of the reported result from among multiple measurements or analyses of a specified outcome	**For Yes, must have assessed RoB:** ☐ From unrepresentative samples	I adapted this domain to be relevant for reviews of prevalence studies. When examining risk of bias in prevalence studies, the most important thing to assess for is the representativeness of their study samples.
10	**Did the review authors report on the sources of funding for the studies included in the review?**		
	For Yes: ☐ Must have reported on the sources of funding for individual studies included in the review. Note: Reporting that the reviewers looked for this information but it was not reported by study authors also qualifies	No adaptations made.	Not applicable.

11	**If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?**		
	For Yes, must include all of the following: ☐ The authors justified combining the data in a meta-analysis ☐ AND they used an appropriate weighted technique to combine study results, adjusting for heterogeneity if present ☐ AND they statistically combined effect estimates from NRSI that were adjusted for confounding, rather than combining raw data, or justified combining raw data when adjusted effect estimates were not available ☐ AND they reported separate summary estimates for RCTs and NRSI separately when both were included in the review	**For Yes, must include all of the following:** ☐ The authors justified combining the data in a meta-analysis ☐ AND they used an appropriate weighted technique to combine study results, adjusting for heterogeneity if present	I removed the last two items from this domain which focus on NRSI and RCTs, because they are not applicable to prevalence studies.
12	**If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?**		
	For Yes, must include either of the following: □ Included only low risk of bias RCTs □ OR, if the pooled estimate was based on RCTs and/or NRSI at variable RoB, the authors performed analyses to investigate	**For Yes, must include either of the following:** □ Included only low risk of bias studies □ OR, if the pooled estimate was based on studies of variable RoB, the authors performed analyses to investigate possible impact of	I did not adapt this domain – I simply replaced the words “RCTs” and “NRSI” with “studies” and removed the word “effect”.

	possible impact of RoB on summary estimates of effect	RoB on summary estimates	
13	**Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?**		
	For Yes, must include one of the following: □ included only low risk of bias RCTs □ OR, if RCTs with moderate or high RoB, or if NRSI were included the review provided a discussion of the likely impact of RoB on the results	**For Yes, must include one of the following**: □ included only low risk of bias studies □ OR, if studies with moderate or high RoB were included the review, provided a discussion of the likely impact of RoB on the results	I did not adapt this domain – I simply replaced the words “RCTs” and “NRSI” with “studies”.
14	**Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?**		
	For Yes, must include one of the following: □ There was no significant heterogeneity in the results □ OR if heterogeneity was present the authors performed an investigation of sources of any heterogeneity in the results and discussed the impact of this on the results of the review	No adaptations made.	Not applicable.
15	**If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?**		
	For Yes: □ Performed graphical or statistical tests for publication bias and discussed the likelihood and magnitude of	No adaptations made.	Not applicable.

	impact of publication bias		
16	**Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?**		
	For Yes, must include either of the following: □ The authors reported no competing interests □ OR the authors described their funding sources and how they managed potential conflicts of interest	No adaptations made.	Not applicable.

AMSTAR 2 = A MeaSurement Tool to Assess systematic Reviews 2; NRSI = Non-Randomised Studies of Healthcare Interventions; PICO = Population, Intervention, Comparator group, Outcome; RCT = Randomised Controlled Trial; RoB = Risk of Bias.

Original AMSTAR 2 Publication

Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: A critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *British Medical Journal* 2017; **358**: j4008. https://amstar.ca/docs/AMSTAR-2.pdf

Appendix 3
Search strategies used in systematic review

OVID MEDLINE (1948 to August 2019)

1 Prevalence/
2 Incidence/
3 prevalen*.ti,ab.
4 inciden*.ti,ab.
5 frequen*.ti,ab.
6 rate*.ti,ab.
7 occurr*.ti,ab.
8 Hospitals, General/
9 Hospitals, District/
10 Tertiary Care Centers/
11 exp Hospitals, Teaching/
12 "district hospital*".ti,ab.
13 "tertiary hospital*".ti,ab.
14 "teaching hospital*".ti,ab.
15 "medical centre*".ti,ab.
16 "medical center*".ti,ab.
17 "general medical".ti,ab.
18 (ward* adj4 patient*).ti,ab.
19 (hospital* adj4 patient*).ti,ab.
20 Inpatients/
21 in$patient*.ti,ab.
22 Hospitalization/
23 hospitali*.ti,ab.
24 Hospital Units/
25 exp Hospital Units/
26 Patient Admission/
27 exp Anxiety/
28 Panic/
29 neurotic*.ti,ab.
30 (neurosis or neuroses).ti,ab.
31 anxiety.ti,ab.
32 panic.ti,ab.
33 agoraphobi*.ti,ab.
34 phobi*.ti,ab.
35 1 or 2 or 3 or 4 or 5 or 6 or 7
36 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26
37 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34
38 35 and 36 and 37

OVID EMBASE (1947 to August 2019)

1 Prevalence/
2 Incidence/
3 prevalen*.ti,ab.
4 inciden*.ti,ab.
5 frequen*.ti,ab.
6 rate*.ti,ab.
7 occurr*.ti,ab.
8 Hospitals, General/
9 Hospitals, District/
10 Tertiary Care Centers/
11 exp Hospitals, Teaching/
12 "district hospital*".ti,ab.
13 "tertiary hospital*".ti,ab.
14 "teaching hospital*".ti,ab.
15 "medical centre*".ti,ab.
16 "medical center*".ti,ab.
17 "general medical".ti,ab.
18 (ward* adj4 patient*).ti,ab.
19 (hospital* adj4 patient*).ti,ab.
20 Inpatients/
21 in$patient*.ti,ab.
22 Hospitalization/
23 hospitali*.ti,ab.
24 Hospital Units/
25 exp Hospital Units/
26 Patient Admission/
27 exp Anxiety/
28 Panic/
29 neurotic*.ti,ab.
30 (neurosis or neuroses).ti,ab.
31 anxiety.ti,ab.
32 panic.ti,ab.
33 agoraphobi*.ti,ab.
34 phobi*.ti,ab.
35 1 or 2 or 3 or 4 or 5 or 6 or 7
36 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26
37 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34
38 35 and 36 and 37

OVID PsycINFO (1806 to August 2019)

1	Epidemiology/
2	prevalen*.ti,ab.
3	inciden*.ti,ab.
4	frequen*.ti,ab.
5	rate*.ti,ab.
6	occurr*.ti,ab.
7	"district hospital*".ti,ab.
8	"tertiary hospital*".ti,ab.
9	"teaching hospital*".ti,ab.
10	"medical centre*".ti,ab.
11	"medical center*".ti,ab.
12	"general medical".ti,ab.
13	(ward* adj4 patient*).ti,ab.
14	(hospital* adj4 patient*).ti,ab.
15	exp Hospitalized Patients/
16	in$patient*.ti,ab.
17	Hospitalization/
18	hospitali*.ti,ab.
19	Hospital admission/
20	exp Anxiety/
21	Panic/
22	neurotic*.ti,ab.
23	(neurosis or neuroses).ti,ab.
24	anxiety.ti,ab.
25	panic.ti,ab.
26	agoraphobi*.ti,ab.
27	phobi*.ti,ab.
28	1 or 2 or 3 or 4 or 5 or 6
29	7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19
30	20 or 21 or 22 or 23 or 24 or 25 or 26 or 27
31	28 and 29 and 30

Appendix 4
Relevant publications

The HOME Study Protocol

Walker J, Burke K, Toynbee, M, **van Niekerk M**, Frost C, Magill N, Walker S, Sculpher M, White IR, Sharpe M. The HOME Study: Study protocol for a randomised controlled trial comparing the addition of Proactive Psychological Medicine to usual care, with usual care alone, on the time spent in hospital by older acute hospital inpatients. *Trials* 2019; **20**: 483.

The HOME Study Statistical and Economic Analysis Plan

Magill N, White IR, Walker J, Burke K, Toynbee M, **van Niekerk M**, Yang F, Walker S, Sculpher M, Sharpe M & Frost C. The HOME Study: Statistical and economic analysis plan for a randomised controlled trial comparing the addition of Proactive Psychological Medicine to usual care, with usual care alone, on the time spent in hospital by older acute hospital inpatients. *Trials* 2020; **21**: 373.