

A comparison of primary care doctors and dentists in the referral of oral cancer: a systematic literature review

Langton S, Cousin GCS, Bankhead CR and Plüddemann A

Mr Steve Langton MSc (Oxon), FDSRCS, FDSRCPS, FRCS*
DPhil student, University of Oxford, UK and Retired Consultant Maxillofacial Surgeon
stephen.langton@kellogg.ox.ac.uk

Mr Gary Cousin MB,ChB(Hons) BDS FDSRCS FDSRCPS FRCS FRCS(OMFS)
Consultant Maxillofacial Surgeon, Royal Blackburn Hospital, Blackburn, UK
gary.cousin@hotmail.co.uk

Professor Clare Bankhead, BSc, MSc, DPhil (Oxon)
Associate Professor, Nuffield Department of Primary Care Health Sciences, University of Oxford, UK
clare.bankhead@phc.ox.ac.uk

Dr Annette Plüddemann BSc, MSc, PhD
Nuffield Department of Primary Care Health Sciences, University of Oxford, UK
annette.plueddemann@phc.ox.ac.uk

*Corresponding author

Address for correspondence: Steve Langton 2 Ravensdale Road, Bolton, Lancashire, BL1 5DN
stephen.langton@kellogg.ox.ac.uk

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ABSTRACT

Background: Oral cancer is referred to specialists by both GPs and dentists, with varying proportions reported in different studies. However, some have also noted that dentists more frequently refer oral cancer in the absence of patient-perceived symptoms and may refer oral cancers at an earlier stage. Unfortunately, approximately half the UK adult population do not receive regular dental care.

Objectives: Conduct a systematic review on studies that compare GPs and dentists in the referral of oral cancer focusing on three aspects: (1) proportion of diagnosed oral cancers (2) stage on presentation (3) delay.

Methods: *Electronic searches:* Medline, Embase, Scopus, Google Scholar, Web of Science, CINAHL. *Additional searches:* reference lists, authors and conference proceedings.

Results: 22 studies from 10 countries were included, a total of 4953 oral cancers. The percentage of medical referrals ranged from 13% to 86%, the percentage of dental referrals from 15% to 80%. Random-effects meta-analysis indicated a combined relative risk of medical/dental referral of 1.36 (95%CI 0.99 to 1.86). For UK-based studies, the relative risk was also 1.36 (95% CI 1.05 to 1.76). There was considerable heterogeneity for all studies and for a sub-group of UK studies: I^2 96.4% (95% CI 95.4 to 97.1) and 81.0% (95% CI 63.3 to 90.1) respectively. Several studies showed a lower stage for dentally-referred cancers; the combined risk of dentists/GPs referring early (stage 1 and 2) disease was 1.37 (95% CI 1.17 to 1.60) and one cause may be the much higher number of cases referred by dentists in the absence of symptoms. No studies demonstrated a statistically significant difference in delay.

Authors' conclusions: Oral cancer is referred by both GPs and dentists, typically about 50% and 40% respectively although there is a wide range, probably depending on local circumstances. Both groups require skills in oral examination and lesion recognition and risk factor knowledge. Effectively, regular dental attenders are a select population gaining a regular screen for oral cancer, yet it is likely that this is not delivered to those with the highest risk. It is suggested that further work is required on accessing high-risk individuals, both for possible screening and preventive interventions.

INTRODUCTION

Oral cancer is the sixth most common cancer in the world¹ and approximately 6500 cases are diagnosed per year in the UK.² The incidence of oral cancer is projected to rise by 33% in the UK from 2014 to 2035, with 20 cases per 100,000 people in 2035.³

Disease stage at presentation has a major influence on survival^{4,5} and cancers that are larger and have spread to the lymph nodes have a much poorer prognosis. Two-year crude survival for stage 1 (early) disease is approximately 90% whilst for stage 4 (advanced) disease the rate is less than 50%⁶ and clearly early diagnosis is very important. Unfortunately, approximately 50% of oral cancers present at advanced stage 3 or 4, despite the accessibility of the mouth to relatively easy examination.⁷

Oral cancer is unique amongst malignancies in that it is referred to specialist care by both primary care doctors and dentists, which is unlikely for other types of cancer.⁸ Proportions referred by each group vary across studies. A study of 200 oral cancer patients in the UK² reported that 57% were referred from their GP, 32% by their dentist, 2% via a hospital emergency department and 9% unknown, whilst in a Canadian series 65% of oral cancers were referred from a dentist.⁹ In the UK, both medical and dental primary care practitioners are provided with a list of 'guideline' symptoms and signs to assist in the referral of oral cancer.^{10,11} Several authors note the importance of utilising these guidelines in conjunction with thorough history and examination – '*the principles of good medical practice are paramount*'.¹⁰ However, one study¹³ found that only 18% of family physicians carried out an examination of the mouth on half their patients.

Further differences between the referrals from each group of practitioners have been reported. An American study⁹ reported that 47% of dentist-diagnosed oral cancers were identified during a non-symptom driven visit whilst all medical referrals were symptom-driven. In the same study, the non-symptom diagnoses were at a statistically significant lower average clinical and pathological stage (1.7 and 1.6 respectively) than lesions detected during a symptom-directed examination (2.6 and 2.5 respectively). It would seem, therefore, that 'routine examination' of the oral soft tissues at a dental check-up has importance in the early diagnosis of oral cancer and dental practitioners are in a good position to carry out routine soft tissue examination of the oral cavity.¹⁴ However, English NHS data for 2017-18 indicated that only 50.9% of adults had visited an NHS dentist in the previous 2 years¹⁵ and it is probable that those at highest risk of oral cancer are least likely to attend regular dental consultations.¹⁶

The overall aim of this systematic review is to compare primary care doctors and dentists in the referral of oral cancer, focusing on three main objectives: (1) the proportion of diagnosed cancers that were referred by each profession (2) differences in stage on presentation for referrals from each profession (3) differences in delay.

METHODS

Types of Studies

Studies that examined the referral of oral cancer and compared GPs and dentists, i.e. the study included data for both professions, were considered for this review. They were required to include one or more of the following outcomes:

- (1) Proportion/percentage of diagnosed cancers referred by each profession
- (2) Stage on presentation for each profession
- (3) Presentation delay in relation to each profession

Studies were required to report on diagnosed oral cancers, rather than suspected cancer referrals. Scoping indicated that most studies were likely to be case series but other designs were acceptable, provided that they reported one or more of the required outcomes. Case reports, economic studies and qualitative studies were excluded. Rare types of intra-oral malignancy (such as lymphoma) were excluded.

Search Methods

The following electronic resources were searched: MEDLINE, EMBASE, Scopus, Google Scholar, Web of Science, CINAHL to May 2019. Further resources included: browsing the reference lists in initially-identified studies, author searching (in relation to initially-identified studies), citation index search, browsing the 'find similar' sections of many electronic databases. In an attempt to identify on-going studies the Research Registry (<https://www.researchregistry.com>) and database of theses (EThOS - Electronic Theses Online Service) were examined. Search terms included: mouth neoplasms, oral cancer and mouth cancer in combination with primary health care, primary care, general practitioner, GP, physicians, dentist, general dental practitioner and GDP.

Selection of studies

Following elimination of duplicates, abstracts were assessed to identify papers that included a comparison of primary care doctors and dentists in the referral of oral cancer by a single reviewer (SL). Abstracts indicating that the study did not fulfil the inclusion criteria - for example, qualitative studies or commentaries - were excluded at this stage. For the remaining studies, copies of the full papers were obtained and assessed by two reviewers for inclusion in the systematic review according to the pre-defined criteria.

Data extraction

Data were extracted by three independent reviewers (SL, CB and GCSC). This was followed by a discussion to cross-check the data and to resolve any discrepancies by jointly re-examining the relevant paper and arriving at an agreement.

Basic extracted data included first author, publication year, study setting, country of origin, study size and study type. Percentages of dental and medical referrals were extracted, together with stage data and data on delay. The authors' main conclusions were noted.

Assessment of study quality

For the assessment of study quality, the 'MINORS' index¹⁷ was used, evaluated by a single author. MINORS is a 12-item checklist, 8 items are for non-comparative studies and 4 additional items for comparative studies. Items are 'scored' 2 (reported and adequate), 1 (reported but inadequate) and 0 (not reported). The scale has been used to give an assessment of study quality in a number of systematic reviews to evaluate approximate study quality (0-5 = 'poor', 6-10 = 'fair', 11-16 'good').^{18,19} However, the use of numerical scales for study quality is often discouraged²⁰ and therefore the results are presented as a table to give a general view of quality.

Missing data

Attempting to obtain missing and/or unclear data, several authors were contacted by email. However, in several instances this was not possible because the required outcome had not been measured or the authors could not respond. Therefore, it was decided to analyse only the available data for each outcome.

Synthesis and analysis of data

Data synthesis and analysis was carried out with MedCalc© software version 19.1. Forest plots were generated for relative risk of dental and medical referral. DerSimonian-Laird meta-analysis was

undertaken, random-effects if I^2 was over 60%, fixed effects if less. For stage data, due to the differences in the way results were reported, meta-analysis was carried out for 4 studies, the other results were reported as table and narrative. Delay data were reported as a table and narrative.

Heterogeneity

There are several potential sources of clinical and methodological heterogeneity in this review including oral cancer rates, access to health professionals and willingness to consult a health professional. Different types of primary to specialist referral systems may be in place and referral patterns may, of course, have changed over the years.

Heterogeneity was estimated by: (1) generation of forest plots and inspection of the 95% confidence intervals (2) calculation of I^2 and associated confidence intervals, estimating the percentage of variation caused by heterogeneity.

Subgroups

Analysis of subgroups of studies undertaken in the UK was planned for each outcome, if data were available, to identify the effect of studies carried out within the same system of medical care.

RESULTS

Search outcome

895 papers were identified by electronic searches, 9 from other sources. Scrutiny of abstracts revealed 32 studies on referral of oral cancer from primary to secondary care. Of these, 22 included data on the referral of oral cancer by primary care doctors and dentists (*figure1*).

Description of included studies

22 studies were included in the review^{9,21-32, 33-38,29,2,40} (*table 1*). All 22 studies included data on proportion (percentage) of diagnosed oral cancers that were referred by primary care doctors (possibly referred to as 'general practitioner', 'GP' or 'primary care physician') and dentists. 8 studies compared medical and dental oral cancer referrals in relation to stage on presentation (or an aspect of 'stage' such as primary cancer size). 9 studies included comparative data on delay. 8 studies originated from the UK, 2 from each of USA, Australia and Denmark and 1 from each of Ireland, Canada, Netherlands, Finland, Thailand, Israel, Japan and Argentina. 15 studies were retrospective case series, 1 a prospective case series, 3 were questionnaires, 2 used a combination of case series

analysis and patients interviews and 1 patient interviews alone. Overall, 4953 oral cancers were included and the number of oral cancers in each study ranged from 20 to 1841

Description of excluded studies

10 studies were excluded at the 'eligibility' stage⁴¹⁻⁵⁰ (*figure 1, supplementary table i*). Of these, 6 studies focused on oral cancer knowledge or diagnostic skills of the dental and medical practitioners, 2 studies included suspected oral cancer referrals, rather than diagnosed cancers, in 1 paper the referral sources were unclear and 1 paper reported stage in relation to regularity of dental care, rather than comparing primary care doctors and dentists.

On-going studies

No on-going studies were identified.

Study quality

Most studies in this review are retrospective cohort studies, although three studies derived data from questionnaires^{2,26,30} and one from patient interviews³⁵. Retrospective cohort studies rely on previously-collected information, in this case from case records and therefore depend on accuracy of collection and recording and therefore are prone to information bias, although this is difficult to quantify in most of the studies in this review. Selection bias may also be a factor – for example in the type of unit collecting the information. One further bias in relation to delay is recall bias; this is particularly the case for patients, for example remembering when symptoms first became evident.

A pragmatic approach was adopted in relation to study quality. Of the included studies, 3 focused specifically on dental/medical referral of oral cancer^{9,21,32}. However, most other studies examined oral cancer referral or early diagnosis in relation to a broader range of factors, in which the required outcomes for this review were variables included in the study. Furthermore, studies ranged from 10-year population-based studies including almost 2000 patients³⁸ to small, audit-type studies³⁹.

'MINORS' scores are given in supplementary table ii. Studies scoring over 11 are generally considered to be of 'good' quality.

Effects of the intervention

Percentages of cases referred by primary care medical and dental practitioners

There was a wide range of percentages of cases referred by each profession across 22 studies (*table 2*). Medical referrals ranged from 13%²⁸ to 83%³⁰, dental referrals ranged from 15%^{30,32} to 80%²⁸.

Most oral cancers were referred by primary care doctors and dentists – the mean percentage

referred by combined 'other' mechanisms (not usually specified but likely to include emergency hospital presentations and referrals from other hospital departments) was 12.2%, range 0 to 31%.

Meta-analysis: relative risk of dental or medical referral

Meta-analysis was undertaken for the relative risk of medical and dental referral for all studies (*figure 2*) and UK studies (*figure 3*). Considerable heterogeneity was evident in all studies ($I^2 = 96.4\%$, 95% CI 95.4 to 97.1), slightly less for studies carried out in the UK ($I^2 = 81.0\%$, 95% CI 63.3 to 90.1).

The overall pooled (random effects) risk ratio for medical compared to dental referral was 1.36 (95%CI 0.99 to 1.86); for UK studies the pooled risk ratio was almost identical, 1.36 (95% CI 1.05 to 1.76).

Stage of oral cancer on referral - comparison between referrals from primary care doctors and dentists

8 studies compared oral cancer referrals from primary care doctors and dentists in relation to stage on referral^{9, 21-23,25,27 29, 35}(*table 3*). Stage data were reported in several different ways including comparing primary tumour (T) stage, specific groupings of T stage, overall stage and nodal involvement, which precluded formal meta-analysis of all studies. However, 5 studies did show a statistically significant difference in relation to stage on presentation, all demonstrating a greater proportion of late disease being referred by doctors^{9,21, 22,25,27}. Furthermore, one study⁹ showed an increased proportion of patients with metastatic node disease for cancers referred by primary care doctors. 3 studies showed no statistically significant difference between doctors and dentists in relation to stage on referral^{24, 29, 35}. Meta-analysis (fixed effects) was undertaken for 4 studies^{9,21,22,35} reporting data similarly. The combined risk of dentists/GPs referring early (stage 1 and 2) disease was 1.37 (95% CI 1.17 to 1.60), I^2 0.0% (95% CI 0.0 to 78.3) - *figure 4*.

Delay on presentation

8 papers compared delay for referrals from primary care doctors and dentists^{21,22,23,28,29,33,34,37}(*table 4*). 'Professional' delay was assessed in 5 studies, 'appraisal period' (patient delay) was measured in 2 studies and the type of delay was not specified in 1 further study. There was no consistency in the method of assessment of delay across studies and formal meta-analysis was not possible. Overall, 2 studies^{23,37} reported no difference in delay whilst 6 reported slightly increased delay for dentists' referrals^{21,22,29,33,34,37}. No studies reported a difference of statistical significance.

Other reported findings

Several studies reported on the number/proportion of oral cancer cases referred following 'incidental' or 'symptomless' identification at routine examination. In one Dutch study,²⁴ 7 (14%) of a series of 50 cancers were diagnosed at routine dental examination. An Australian study of 51 oral cancers²⁵ noted that 11 cases (22%) were identified as 'incidental' findings. A further study⁹ found that of 51 oral cancers, 18 (35%) of cases were referred on a non-symptomatic basis. Non-symptomatic cases were associated with a significantly smaller lesion ($p = 0.03$) and cancer stage ($p = 0.007$). A UK study³⁵ found that oral cancer identified at 'a routine check-up' was more likely to be at early stage (stage 1 & 2) than oral cancer referred following symptomatic presentation. Canadian research³⁸ found that dentists were more likely to detect asymptomatic cases than primary care doctors (15% vs 1.4%, $p < 0.0001$).

DISCUSSION

GP and dentist referrals

This review confirms that both primary care doctors and dentists have an important role in the referral of oral cancer to specialist services. Meta-analysis of GP/dentist referral risk ratio indicated that approximately 14 oral cancers are referred from GPs for every 10 from a dentist although there was considerable variation between studies undertaken in different countries – and indeed between studies in the same country. Subgroup analysis of UK studies similarly demonstrated varying proportions of dental and medical referrals, albeit with a smaller range.

The results of these meta-analyses do, of course, need to be interpreted in the light of the considerable heterogeneity that exists between studies undertaken in different countries with varying medical, dental and secondary care systems. The context of the study is also an important consideration. For example, one study in this review⁹, which had a notably high proportion of dentally-referred cancers, included referrals from two dental practitioners with a background of training in maxillofacial surgery. Another study²², again reporting a high proportion of dentally-referred cancers, originated from an academic oral medicine department, which may have a different referral 'profile' to a typical oral and maxillofacial or head and neck unit.

Why might patients present initially to one profession or the other? Studies analysing the presentation of lesions in different parts of the mouth have reported that a dentist was more likely to refer an oral cancer in relation to the areas related to the dentition or dentures^{23,24,30}.

Alternatively, an Australian study⁴⁰ has suggested that the fact that GP consultations attract a

financial insurance rebate whilst dental consultations do not was a reason why there had been a shift towards initial oral cancer presentations to GPs. A UK study examining the role of general medical practice in the diagnosis of oral cancer² suggested that *'evidence is emerging that patients with oral symptoms would rather see their GP than their dentist'*. This view was supported in a further study on early oral cancer detection in which over 70% of respondents considered it likely that they would consult a GP compared to 29% - 45% who would consult a dentist with symptoms of potential oral cancer⁵¹. However, patients attending GPs with 'routine' dental problems is a common occurrence and, furthermore, socio-economically deprived patients, the social group more likely to present with oral cancer, are particularly prone to do this.⁵²

Although studies have shown that patients do have variable views on whether they would first attend a primary medical or dental practitioner with a variety of oral-facial problems,⁵³ one reason probably influencing the choice of practitioner first seen in relation to oral cancer – and possibly the 'elephant in the room' in relation to this issue – is access to dental services. In the UK, for the 2-year period to March 2018, 49.1% of adults had not seen an NHS dentist.¹⁵ This phenomenon is by no means restricted to the UK and typically impacts on people who have low income, are unemployed and lacking health insurance,⁵⁴ factors also having established associations with oral cancer.^{55,56}

Stage on presentation

As primary care doctors and dentists refer nearly all oral cancer, the question arises whether referrals from each group have different characteristics that may, potentially, translate into different outcomes.

Overall, studies in this review did not provide data on stage in a consistent format which made full statistical meta-analysis inappropriate. For example, one study grouped T₂ and T₃ cancers together as an 'intermediate' group, one study reported average clinical and pathological stage and another the median size of the referred cancer. However, the overall pattern was for either a report of 'no statistical difference' or an earlier stage for dentally-referred cancers.

Several factors may account for the differences in stage on presentation between oral cancers referred by primary care doctors and dentists. One reason may be the proportion of oral cancers identified in the absence of symptoms, as 'incidental' findings. Such diagnoses are made much more frequently by dentists, being very rare in primary care medical practice³⁸ and evidence exists that an earlier stage on diagnosis is present with individuals who receive regular dental care⁴¹. In the studies in this review, asymptomatic oral cancer diagnoses were reported in 5 studies^{9,24,25,33,38}, comprising between 14% and 35% of cases. In these studies, all except one study reported all asymptomatic

referrals being from dentists. In one study³⁸ 15% of dental referrals were asymptomatic compared to 1.4% of GP referrals.

Studies comparing GPs and dentists in knowledge of oral cancer, pre-malignant lesions, risk factors and oral examination skills and habits indicate dentists are more likely to examine the oral cavity routinely although in one study 94% of GPs did in response to oral soreness.^{44,45} On the other hand, some argue⁵⁷ that *'the medical practitioner is the most likely resource'* for oral cancer screening as doctors are more likely to encounter at-risk patients because of co-existing medical conditions.

This review shows that in a range of different health systems a proportion of oral cancers are, effectively, diagnosed by an 'informal screening procedure' – usually a visit to a dental surgeon – and this, of course links to the rather broader and certainly more complicated question of whether a more systematic, evidence-based approach to screening would be effective. A Cochrane systematic review⁵⁸ provided evidence of reduced mortality, a stage-shift towards earlier diagnosis and reduced costs. However, the reviewers considered that there was insufficient evidence to recommend population-based screening. The Global Oral Cancer Forum⁵⁹ explored the question of screening for oral cancer in considerable detail and reported that accumulated evidence suggested that opportunistic screening of high-risk groups was cost effective but not practical in dental practice as few of the high-risk individuals attended regularly. To date, no screening program for oral cancer has been introduced into the UK.⁶⁰

Differences in delay between medical and dental referrals

9 studies in this review reported on either 'patient delay' (sometimes referred to as 'appraisal period' delay) or 'professional delay' (practitioner delay). In common with stage of presentation data, there was inconsistency in the method of reporting. For example, studies reported 'mean duration of symptoms', 'mean professional delay', 'median delay' and 'duration of cancer'. Definitions of what period exactly represented delay also varied. For example, one study³³ defined 'practitioner delay' as being over 6 days delay, whilst other studies³⁴ defined 'practitioner delay' as over 2 weeks and this inconsistency made statistical meta-analysis impossible. The overall pattern was one of slightly greater delay for dental referrals, although in no studies was a difference between medical and dental referrals of statistical significance reported. A slightly longer delay in dental referrals has been observed in previous work⁶¹. Several authors consider one explanation of the difference in delay is that dentists more commonly initiate a 'treatment trial', such as altering dentures prior to referring for secondary care opinion.^{40, 61} However, inappropriate initial treatment is not confined to dentists. A study of 779 patients with oral cancer⁶² found 14.8% had initially

received inappropriate management, with medical practitioners most often prescribing antibiotics and dentists extracting teeth or adjusting dentures.²²

Furthermore, the link between diagnostic delay and stage on diagnosis for oral cancer is not clear. It would seem intuitive that delay in diagnosis results in larger cancers and a reduction in survival. However, studies do not point towards a consistent relationship between delay, cancer stage and survival. One study³⁵ found no correlation between delay and stage and suggests that ‘the error is to assume that symptoms are related to the size a tumour’ – in other words, large oral cancers may remain asymptomatic and unnoticed by the patient. However, other work has reported that delayed referral correlated with both more advanced stage at presentation and poorer survival⁶³. A meta-analysis found that diagnostic delay was a ‘moderate’ factor in stage on presentation⁶⁴ although studies on the relationship between delay and stage for oral cancer are not common.⁶⁵

Implications for practice and research

The findings of our study confirm the important role that both primary care doctors and dentists have in the referral of oral cancer. Guidelines for GPs and dentists in oral cancer diagnosis in the UK are issued by the National Institute of Health and Care Excellence (NICE). The most recent guidelines¹¹ advise that lip lumps, erythroplakia or leuko-erythroplakia are referred initially by GPs to a dentist for evaluation. Whilst some work suggests² that increased GP-dentist collaboration is desirable, others consider that such an approach, whilst potentially reducing the secondary care workload, may result in diagnostic delay. This may be worsened by a lack of formal GP-dentist referral systems and insufficient access to dental care for many patients⁶⁶.

The earlier stage of diagnosis by dentists in several studies in this review emphasises the important role of dentists and, potentially, regular dental check-ups in the early diagnosis of oral cancer. However, it is evident that a large section of the population in the UK and elsewhere do not benefit from regular dental care and are often the ones most at risk of oral cancer – the so-called ‘inverse screening law’⁶⁷.

The lack of an oral cancer screening program in the UK continues to be subject of interesting debate. It has been pointed out that the mouth is accessible to simple examination and lesions are relatively easy to detect⁶⁸. Therefore, one might reasonably assume that an oral cancer screening program would be straightforward to put into effect. A systematic review⁷⁹ found ‘conventional oral examination’ (COE), across 10 studies, gave varying diagnostic accuracy, although sensitivity was at least 0.7 and specificity at least 0.9 in all studies, values of the order delivered by cervical cancer and breast cancer screening programmes. In the only RCT (to date) on oral cancer screening, a large 15 -

year study carried out in India⁷⁰, a 24% mortality reduction for high risk individuals was demonstrable. Interestingly, screening was carried out by trained, non-medical, graduates.

It is suggested that further work is required in the identification of high-risk individuals, methods of accessing such people, both for possible screening and preventive interventions, cost-benefit studies and assessment of the use of 'allied healthcare professionals' for oral cancer/pre-cancer screening examinations.

Strengths and weaknesses

This review provides insight into the referral of oral cancer to specialist care by primary care doctors and dentists, focusing on the proportions referred by each specialty, the differences in stage on presentation and difference in delay, across 22 studies from 12 countries.

However, the included studies did not present data – such as stage – in a consistent format, making formal meta-analysis of some outcomes inappropriate. The long-standing problem of different definitions and methods in studies on early cancer diagnosis research has been addressed by the Aarhus statement⁷¹ although this review includes studies undertaken up to 30 years before the Aarhus guidelines were produced. Studies from different countries, and even within the same country, will be influenced by the local systems for referral and organisation of both primary and secondary services. Such differences, together with changes in systems over time, have almost certainly been sources of considerable heterogeneity. The wide range of countries involved does, of course, mean that transferability needs to be interpreted with caution.

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