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ASTRACT

Background The burden of cancer falls predominantly on older adults. Prompt presentation to primary care with cancer symptoms could result in an earlier diagnosis. However patient symptom appraisal and help seeking decisions involving cancer symptoms are complex and may be further complicated in older adults.

Aim To explore the effect of older age on patients' appraisal of symptoms that may indicate cancer and their decision to seek help for these symptoms.

Design Mixed methods systematic review

Method Medline, Embase, CINAHL, PsycInfo, Cochrane Library, Web of Science Core Collection, ASSIA, ISRCTN registry and NICE were searched for studies on the symptom appraisal and help seeking decisions relating to cancer symptoms by adults aged 65 and over. Studies were analysed using thematic synthesis and according to the Synthesis Without Meta-Analysis (SWiM) guidelines

Results Eighty studies were included in the review with a total of 324,995 participants. The studies suggested a possible association between increasing age and a prolonged symptom appraisal interval. Factors such as reduced knowledge of cancer symptoms and differences in symptom interpretation may contribute to this prolonged interval. In contrast, we found a possible association between increasing age and prompt help-seeking. Themes affecting help seeking in older adults included the influence of family and carers, competing priorities, fear, embarrassment, fatalism, co-morbidities, a desire to avoid doctors, a perceived need to not waste doctor's time and patient self-management of symptoms.

Conclusions This review suggests that increasing age is associated with delayed cancer symptom appraisal. When symptoms are recognised as potentially serious, increasing age was associated with prompt help seeking although factors such as fear of wasting a doctor's time could prolong this. As a result of this review, policy makers, charities and information from GPs should aim to ensure older adults are able to recognise potential symptoms of cancer and can seek help promptly.

BACKGROUND

Worldwide, the population of adults aged over 65 is growing faster than any other age group (1). The burden of cancer falls predominantly on older patients with half of all new diagnoses occurring in people aged over 70 and incidence rates for all cancers increasing most rapidly in the over 75 age group (1, 2).

Shorter times to diagnosis result in more favourable cancer outcomes and patient experience (3, 4). As a result, cancer strategies prioritise prompt presentation by patients with symptoms which could be caused by cancer. However, previous qualitative research has highlighted the complexity of patient appraisal and help seeking decisions involving cancer 'alarm symptoms'. This complexity includes a lack of awareness of cancer symptoms as well as concerns about wasting doctors' time and fears around facing a diagnosis of cancer, all of which may delay presentation to primary care (5,

6). In older adults, the recognition of cancer symptoms could be further complicated by the presence of chronic diseases, and cognitive impairment which may affect the ability to recognise new symptoms (7, 8). In addition to this, symptoms may be dismissed as part of the aging process and social isolation may result in the absence of a person to prompt presentation.

The aim of this review is to explore the effect of older age on the appraisal of symptoms that could indicate cancer in older adults and the decision to seek help in primary care for these symptoms.

METHOD

Protocol

Prior to commencing this review, a study protocol was registered with PROSPERO (reference number: CRD42020180656). The review has been conducted and reported according to the Cochrane Handbook for Systematic Reviews and the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement (9).

Definition of older adults

There is no universally accepted age threshold for defining old age. We adopted the World Health Organization's definition of 'older people' as those aged 65 and over (10).

Theoretical model

The model of pathways to treatment was used to provide a theoretical underpinning for the analysis of patient appraisal and help seeking (11). The model is recommended for mapping and examining pathways to cancer diagnosis. The model defines the appraisal interval as the time between detecting a bodily change and perceiving a reason to discuss this bodily change with a health care professional (HCP). The help seeking interval is defined as the time between perceiving a need to seek medical help and arranging and attending an appointment with a HCP. The patient interval encompasses both the appraisal and help seeking interval and is defined as the time from first noticing a symptom to presenting to a HCP.

Eligibility criteria

We included studies of patients aged 65 or over, or with a subgroup of patients aged 65 or over, with symptoms and signs that warrant investigation and referral for suspected cancer (12) presenting to primary care before diagnosis. Editorials, case studies, reviews, expert opinion papers and studies that were published as abstracts only were excluded from the review. Systematic reviews, published thesis and dissertations were not included but when these were identified reference lists were screened for relevant studies.

Search strategy

We searched Ovid MEDLINE(R) ALL 1946 to July 28, 2021, Embase (Ovid) 1947 to 2021 July 28, CINAHL (EBSCOhost), APA PsycInfo (Ovid) 1806 to July Week 3 2021, Cochrane Central Register of Controlled Trials (Wiley) Issue 7 of 12, July 2021 , Cochrane Database of Systematic Reviews (Wiley) Issue 7 of 12, July 2021, Web of Science Core Collection (individual databases listed in appendix X), Applied Social Sciences Index and Abstracts (ProQuest), ISRCTN registry, ClinicalTrials.gov and National Institute of health and Clinical Excellence (NICE) Evidence Search for published and unpublished studies of cancer-related shared decision making for older adults in primary care. The

search was originally conducted in April 2020 and updated on 29th July 2021 by re-running all searches without date limits and removing duplicates from the original searches using EndNote.

Subject headings and free text words were identified for use in the search concepts by DJ and JW and was based on a search strategy published in a similar review (13). No language, data or study design limits were used. Full search strategies are available in the appendix.

Further relevant studies were sought by reviewing reference lists of the included studies, and manually searching conference abstracts using the conference handbooks from events organised by; the cancer and primary care research international network (Ca-PRI) (14) the National Cancer Research Institute (NCRI)(15), Macmillan Cancer Support (16) and Cancer Research UK (17).

Search results were managed in an EndNote library where duplicates were removed automatically and manually using University of Leeds AUHE guidance.

Data collection

All titles and abstracts were independently reviewed by two researchers (DJ and EdM) using the review software Rayyan. Any disagreements were resolved through discussion or through adjudication by a third reviewer (RN) if required. All reasons for exclusion were recorded. Data extraction was undertaken using a data extraction template.

Risk of bias of included studies

The mixed methods appraisal tool (MMAT) was used to appraise the methodological quality of the included studies (18). The tool allows the appraisal of randomised, non-randomised, quantitative descriptive, qualitative, and mixed-methods studies. The tool provides five methodological quality criteria which vary for each type of study (19). The reviewers' reasons for ratings, including strengths and weaknesses of studies were recorded independently by two reviewers (DJ and EdM). Any disagreements were resolved through discussion.

Synthesis of results

Qualitative studies were analysed using thematic synthesis described by Thomas & Harden (20). Thematic synthesis includes line by line coding of all results, the organisation of the codes into themes and finally further interpretation to develop analytical themes which aim to offer a new interpretation of the study findings. This was undertaken independently by two reviewers (DJ and SH). We followed the ENTREQ guidelines for reporting the synthesis of qualitative research (21).

Quantitative studies did not provide data suitable for meta-analysis due to heterogeneous effect measures and clinical and methodological diversity. As a result, we undertook the analysis reporting using the SWiM (Synthesis Without Meta-Analysis) reporting guidelines and checklist (22).

Following the separate analysis of qualitative and quantitative data, the findings were combined by considering the barriers and facilitators to appraisal and help seeking. This method was based on previous published guidance on integrating qualitative research in systematic reviews (23).

RESULTS

The database searches identified 5972 studies which reduced to 3934 when duplicates were removed. After title and abstract screening and full text review, 80 papers were included in this

review including 324995 participants (figure 1). Studies ranged in size from 10 to 65192 participants. Forty-six papers included quantitative data (24-69) and 31 provided qualitative data (70-100), three were mixed methods studies and provided both qualitative and quantitative data (101-103). Study settings were UK, Australia, Denmark, Estonia, France, Germany, Holland, Malaysia, South Africa, Spain, Sweden, Trinidad and Tobago and USA. There were no clear differences in the appraisal or help seeking of older adults by country and whilst most of the included countries have a GP gatekeeper health care system, no system factors were highlighted in the studies. A variety of cancers were studied including "any cancer", colorectal, brain, breast, lung, prostate, lymphoma, ovarian, upper gastrointestinal, bladder, cervical, leukaemia, gastric, myeloma, head and neck, melanoma, pancreatic and penile. Overall, the quality of studies was judged to be high with an average MMAT across the 80 included studies of 4.6 out of a maximum possible score of 5.0. See figure 2 for a summary of the results and supplementary tables 1-3 for details on the included studies.

Appraisal interval

This review included 45 studies which considered the association between age, the appraisal of cancer symptoms and the length of the appraisal interval, as defined by the model of pathways to treatment. Seventeen studies provided quantitative data. Nine studies found that increasing age was associated with prolonged symptom appraisal (24, 26, 28, 33, 40, 45, 48, 64, 102), four studies found no association between age and symptom appraisal (27, 41, 43, 46) and only two found that increasing age was associated with shorter symptom appraisal (29, 35). Two studies had mixed findings, highlighting factors which both shortened and prolonged the appraisal interval (38, 39). These data are summarised in supplementary table 1.

Analysis of the 28 qualitative studies (70-94, 99, 101, 102) highlighted three themes affecting patients' appraisal of possible cancer symptoms:

- symptom awareness,
- symptoms interpreted as old age,
- symptoms interpreted as being caused by co-morbidities.

The studies suggested that older adults were less aware of potential cancer symptoms resulting in patients not perceiving a need to present to a HCP. When a bodily change was detected, there were examples of patients explaining symptoms as part of the ageing process and as such did not perceive the bodily change as a reason to visit a HCP. Similarly, older adults with existing comorbidities tended to explain new bodily changes as being part of their existing medical problems, or as side effects of medication. This interpretation or normalisation of cancer symptoms resulted in patients not perceiving a need to consult with a HCP, and delaying diagnosis. Table 1 shows the themes from the qualitative analysis and illustrative quotes supporting these findings.

Help seeking interval

This review included 48 studies which considered the association between age and help seeking for cancer symptoms. Eighteen studies provided quantitative data. The majority of these studies suggest an association between increasing age and a shorter help seeking interval. Ten studies found that increasing age was associated with shorter help seeking interval (43, 48, 52, 56, 60, 62, 67-69, 103), five studies found no association between age and help seeking (50, 51, 55, 66, 101) and only one found that increasing age was associated with a prolonged help seeking interval (59). Two studies had mixed findings highlighting multiple factors which could both shorten and prolong the help seeking interval. For example one study found older adults were statistically less likely to want to know they had cancer (which may delay help-seeking), but were also less likely to be 'put off' by perceived barriers to help-seeking (which may shorten help-seeking). (58, 64). These data are summarised in supplementary table 2.

Four quantitative studies (59, 60, 62, 64) and 30 qualitative studies (70-91, 95-101, 103) considered barriers to help seeking for cancer symptoms among older adults. The studies highlighted and investigated several barriers to help seeking which are listed below;

- the influence of family, carers and friends, e.g. older adults being encouraged to seek help by family or carers.
- competing priorities (e.g. caring for unwell or frail spouses ,
- fear (e.g. fear of a cancer diagnosis or of investigations),
- embarrassment (e.g. intimate examinations with doctors who are likely to be younger than them),
- fatalism (a believe that life's events are predetermined),
- co-morbidities (co-morbidities which tend to increase with advancing age),
- a desire to avoid doctors,
- a perceived need to not waste doctors time,
- self-management of symptoms (e.g. trying 'over the counter' or alternative treatments prior to visiting the GP).

These themes and supporting illustrative quotes are presented in table 2.

The patient interval

A further 16 studies considered the association between increasing age and both appraisal and help seeking intervals combined, this is known as the patient interval. These studies do not suggest an association between increasing age and the patient interval. Seven studies found that increasing age was associated with a shorter patient interval (32, 36, 37, 42, 44, 63, 90), five found increasing age had no effect on the patient interval (25, 30, 31, 47, 49) and four studies suggested patient age was associated with a longer patient interval (26, 34, 54, 61). These data are summarised in supplementary table 3.

DISCUSSION

Summary

Cancer is a disease of older adults with over half of new cancer diagnoses occurring in those over 70. Decisions on the recognition and referral of cancer in older adults are difficult, with factors such as frailty and co-morbidities meaning that management options are often limited. However, delayed presentation to primary care is likely to reduce the chance of curative treatment still further. If cancer symptoms are not recognised and help not sought, we will increasingly miss a large burden of potentially curable disease. As a result this review has considered the effect of age on the presentation to primary care and the factors which affect this. It is the first systematic review to investigate the association between increasing age and the appraisal and help seeking of cancer symptoms. The findings of the review suggest an association between increasing age and a prolonged appraisal interval. As a result, the time from first noticing a bodily change to perceiving a need to seek help may be longer in older adults. In contrast, the review suggests an association between increasing age and a shortened help seeking interval, with most studies suggesting older adults were more likely to seek help promptly when they detected symptoms which they perceived could be cancer. Despite this, the evidence highlighted several factors specific to older adults which could potentially delay help-seeking. Overall increasing age showed no association with the length of the patient interval.

Strengths and limitations

This systematic review includes 80 studies of good methodological quality and has been conducted in accordance with best practice guidelines. Studies were included from a variety of countries and investigated a wide range of cancer types using both qualitative and quantitative methods.

However, this study has some limitations. Firstly, the heterogeneity of included studies precluded meta-analysis of quantitative data. Secondly, due to the observational nature of some of the included studies, it is unclear whether there is a causative link between older age and the factors highlighted. Finally, whilst all that data analysed was from those aged 65 and over, there was little comparison between younger and older adults. As a result, some of the factors identified may not be specific to older adults and may be equally relevant to a younger patient group. All patients may, for example, have competing priorities and may suffer from emotions such as fear and embarrassment. It is possible that there are differences in the competing priorities and emotions of older adults such as perhaps being more likely to have dependant partners. These differences would not be possible to identify without further work to compare findings in older and younger adults.

Whilst many of the included studies were clearly investigating appraisal or help-seeking intervals, there were studies in which it was more difficult to disentangle the two intervals. This is challenging and a recognised methodological issue when exploring the pathway to cancer diagnosis.

Comparison with literature

This review suggests an association between increasing age and prolonged symptom appraisal. The qualitative studies in this review suggested that a lack of cancer knowledge and normalising symptoms may contribute to this. Earlier studies support this finding, suggesting that older adults have lower cancer awareness measure scores (104) and lower health literacy (105).

Factors affecting help seeking in this review were also highlighted in other studies. In one review older adults cited family and carer difficulties (106) as a barrier to seeking help for symptoms of dementia. A review on the impact of co-morbidities on cancer diagnosis found that co-morbidities could be associated with both prolonged and shortened time to diagnosis (107), supporting the finding of this review. Fear was a prominent theme in a review considering help seeking for cancer symptoms in all age groups (108). A systematic review considering the risk factors for delayed presentation of cancers found evidence of delay in older patients with breast cancer and reported that fear of cancer contributed to this delayed presentation (5).

Studies have considered factors affecting appraisal and help seeking in the general population. One study found that symptom knowledge and correct symptom interpretation improved the appraisal interval in the general population, supporting the findings of this study (109). Whitaker et al reported similar factors to this review, in their study on adults aged fifty and over but also report others such as lack of confidence in the health care system and the importance of 'instinct' or gut feeling which we did not find in this review (6).

Implications for policy and practice

This review suggests that increasing age is associated with prolonged appraisal of cancer symptoms and a shortened time to seek help. Symptom appraisal in older adults is complex, with multiple issues such as a possible lack of awareness of cancer symptoms, the attribution of symptoms to ageing, and the presence of other co-morbidities. Further research needs to investigate the best approaches to improve symptom appraisal in older adults. It is possible, that cancer awareness

campaigns, such as the UK's "Be Clear on Cancer" (110) and the US Centre for Disease Control's "Inside Knowledge" (111), may improve awareness, however subsequent cancer awareness campaigns should be designed to ensure they reach an older population, through more targeted advertising or through other means such as cancer champions in elderly care day centres or care homes. The challenge of distinguishing symptoms which may be due to cancer from normal signs of ageing and symptoms of co-morbidities is complex and difficult. In primary care, older adults are more likely to have contact with primary care due to the higher burden of co-morbidities in this population. It is possible that annual reviews of other chronic conditions may allow an opportunity for HCPs and patients to recognise and discuss cancer symptoms. Posters or literature in waiting rooms could also support older adults to recognise cancer symptoms. When patients are diagnosed with chronic conditions there is an opportunity to discuss and advise patients about expected symptoms and their duration and symptoms which should prompt concern."

Whilst increasing age was possibly associated with a shortened help seeking interval, this review highlighted potential barriers to help seeking in older adults. Future research could be targeted at interventions to reduce the impact of these barriers. Healthcare practitioners and policy makers may be able to implement changes to encourage patients with cancer symptoms to present promptly. For example, this review found that a dislike of visiting GPs and a fear of wasting doctors' time may delay help seeking. Local or national campaigns could seek to legitimise help seeking in older adults. This may include public health information that symptoms should not be normalised or attributed to age, on the expected time course or length of symptoms and the need to return if symptoms persist. In light of the COVID-19 pandemic and the changes this has made to general practice, public information targeted to older adults on the safety of attending general practice, the availability of GPs and how best to access care may be helpful. The management of fatalistic attitudes is difficult, but incorporating information about the curability of early-stage cancers in public education campaigns may improve help seeking (59)**.** Whilst self-management is encouraged by policy makers, the review suggested an unintended consequence of this self-management may be delayed presentation with symptoms. Pharmacists and dispensaries could be well placed to recognise potentially harmful self-management of certain red flag symptoms (such as the use of antacid medication for dyspepsia) and are encouraged to promote help seeking, however there are no formal referral pathways for community pharmacists to refer patients to primary care or any mechanism for them to ensure help seeking has taken place (112). Further research is needed and future public health self-management messages may need to take this into account, especially in older adults with potentially red flag symptoms. Finally, the role of family and carers was highlighted in this review, increasing social isolation in the elderly is well documented, but the effect of this on cancer diagnosis is unknown and is a key area of future research.

With increasing age comes an increasing risk of other factors such as frailty syndromes, co-morbidities and cognitive impairment which may confound the results of this review. It is possible that these factors may play a significant role in the appraisal and help seeking of cancer symptoms and are as, or more important than age alone. Future research should try to disentangle this, and explore the effect that co-morbidities, frailty and cognitive impairment have on cancer diagnosis.

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Ethical approval

Not applicable.

Data

The full search strategy and all data are available in the supplementary material.

Provenance

Freely submitted; externally peer reviewed.

Competing interests

The authors have declared no competing interests.

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Table 1: Themes and illustrative quotes demonstrating the impact of age on the appraisal of symptoms, highlighting symptom awareness and interpretation

Theme	Sub theme	Illustrative quotes
Symptom awareness	Studies suggested older adults are less aware of potential cancer symptoms	A 65-69 year old man with a delayed diagnosis of colorectal cancer stated: *"I wasn't thinking of cancer, I'd never associated that sort of symptom with cancer"* (79). A 75 year old man with prostate cancer who delayed help seeking for six months stated: *"I would never have thought there's something wrong with the prostate, I didn't even know what the prostate was"* (82). A 68 year old man with persistent chest pain stated: *"I'd never heard anything about checking for lung cancer or that type of thing"* (83).
Symptoms interpreted as 'old age'	Older adults tended to explain new symptoms as part of the ageing process	On discussing worsening breathlessness a patient stated *"I was not able to walk as fast as I used to be able to, but I didn't think much about it. I am 72 I am going to begin to slow down".* (77) Another patient noticed a breast change and stated *"I thought it was my age, sagging, shrinkage, you know, everything going south, as it were"* (101) A patient eventually diagnosed with myeloma attributed multiple symptoms to the ageing process *"It was a gradual process which I put down to old age, I had a bad back, but I was willing to accept that my back hurt a bit"* (90)
Symptoms interpreted as being caused by co-morbidities	Older adults tended to explain new symptoms as being a result of an existing co-morbidity	A 69 year old patient diagnosed with lung cancer states *"yeah, well I'm asthmatic, you have a tendency to cough more". (76).* A 73 year old women with colorectal cancer blamed her change in bowel habit on new cholesterol medication *"she [GP] changed me to simvastatin and it was a while after I got these sensations, I thought is it because I am taking these statins?" (76).* As co-morbidities and as a result, medications increase with increasing age, this is more likely to affect older adults. A qualitative study of GP case reports of patients with lung cancer found a number of examples of co-morbidities delaying diagnosis in older adults. Including persistent coughing thought to be due to blood pressure medication and increased breathlessness thought to be due to heart failure (96).

Table 2: Themes and illustrative quotes demonstrating the impact of age on patient help seeking

Theme	Sub theme	Illustrative quotes
The influence of family and carers	Family and carers encouraged older patients to seek help	A 75-79 year old ex-smoker with a persistent cough stated *"My wife persuaded me to go to the doctor about it. I wasn't too worried about it."* (77) Finally 65-69 year old with symptoms suggested of colorectal cancer reported that her daughter was *"on the bossy side"* and had said to her *"don't leave it mam, go." (79)*
Competing priorities	Older adults reported delaying help seeking as a result of competing priorities such as caregiving roles, or other life events.	An older adult reported finding found a breast lump but delayed seeking help due to her husband. She stated *"my husband went in to hospital for a hip operation. I thought I'd will until he came home"*. (101) A 69 year old male with symptoms of lung cancer was due to go on holiday and as a result did not report his symptoms so as to not *"spoil the vacation". (75)*
Fear	Older adults reported that fear and embarrassment resulted in a delay in help seeking for cancer symptoms	A 71 patient described deferring help seeking due to 'fear': *"I suppose deep down I didn't want to know anything else, you know, we're back to this thing that you know I think we are frightened, we do get frightened occasionally that. . . there is something more serious and so if you can sort of, pretend that it's just a bad back, you're quite happy to just accept that" (90)* A 65-69 year old patient reported the embarrassment of an intimate examination: *"it was just the embarrassment of knowing that I might have to have somebody's finger pushed up your bum for an examination ... that was probably the thing that put me off going more than anything in the first instance was the embarrassment of that sort of thing"* (79)

The perceived role of the doctor in help seeking	Older adults perceived 'the doctor' in a way which delayed help seeking	An older patient reported: *I'm not someone who goes to the doctor. I never used to trouble. If I had a cold I'd see to it myself. I didn't like the idea of going to be honest and I didn't want to go. When I did go she said 'Oh you've not been here for so many years!''* (8) An older adult reported being embarrassed by seeing younger doctors: *'I was beginning to come to my senses and thought I'd better go the doctors, but I'm an embarrassed person, you know, showing yourself like that . . .he's a young, good-looking doctor'* (101)
Co-morbidities	As a result of co-morbidities, patients expect new symptoms and do not seek help	A 67 year old woman with unexplained weight loss also had comorbidities which resulted in a frequent 'aches and pains'. Due to this she reported only attending the doctor with serious symptoms: *'I have the arthritis, and I have so many aches here, there, and everywhere. And the GP, there's nothing he can do. I am already taking medications for that through the hospital, you know. So I don't bother the GP with all my symptoms every time, just what I think is pertinent.'* (100)
Self management	Older adults described a preference for 'watchful waiting' or self-management which delayed help seeking	A 75-79 year old man described trying medication they could buy before seeking help: "*You do the usual, you take your Lemsip's and your Beechams Powders and when it doesn't clear up after a week you think well you need some antibiotics or something slightly stronger. So that was when I went to the doctors. (77)* A 71 year old man with cancer symptoms stated: *"I believed that this sickness was a sign for me to get right with God. I put off my baptism for a long time now and I realized that was what I needed to do. So I went and get baptized."* (93)

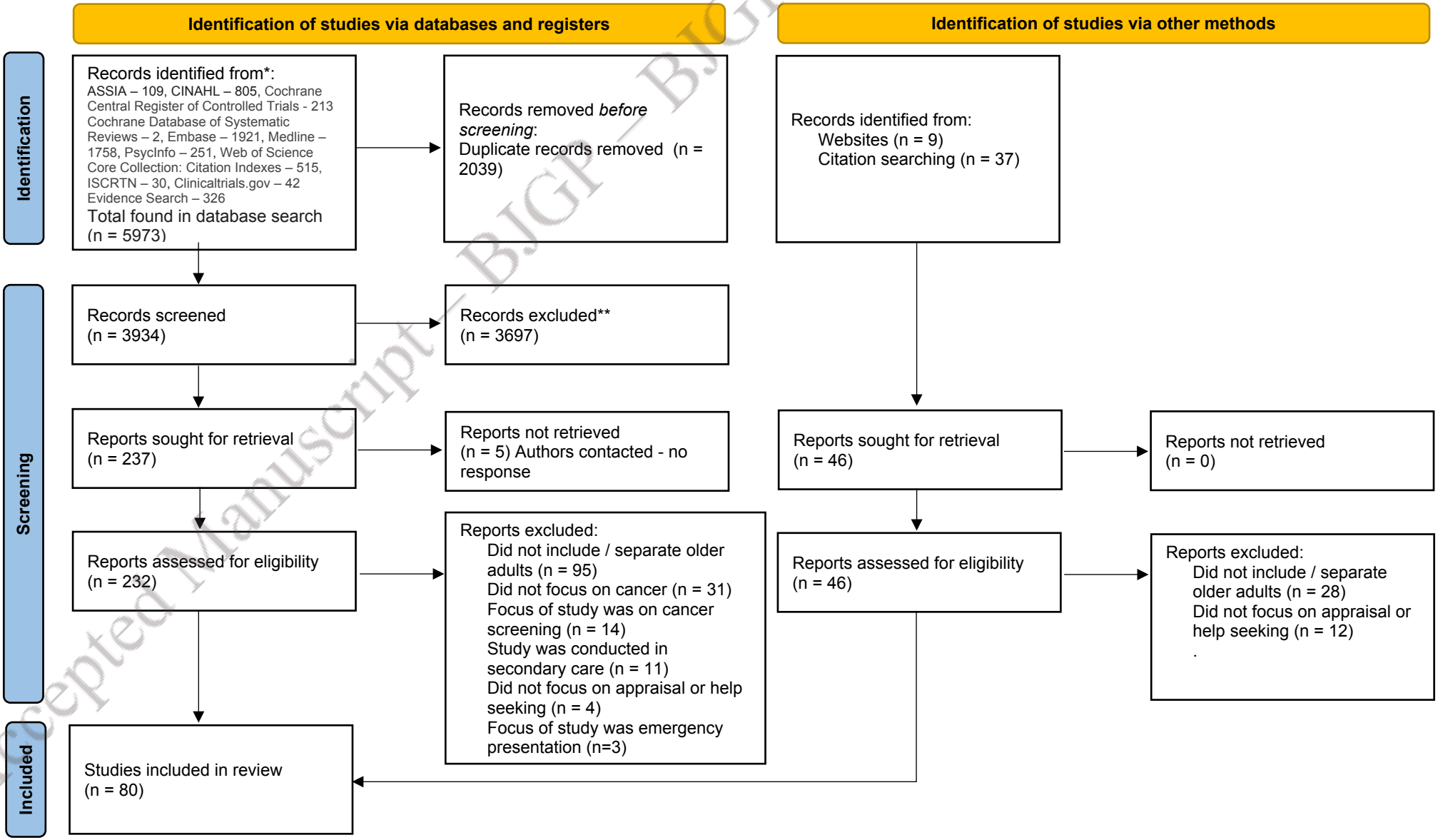

Figure 1: PRISMA flow diagram

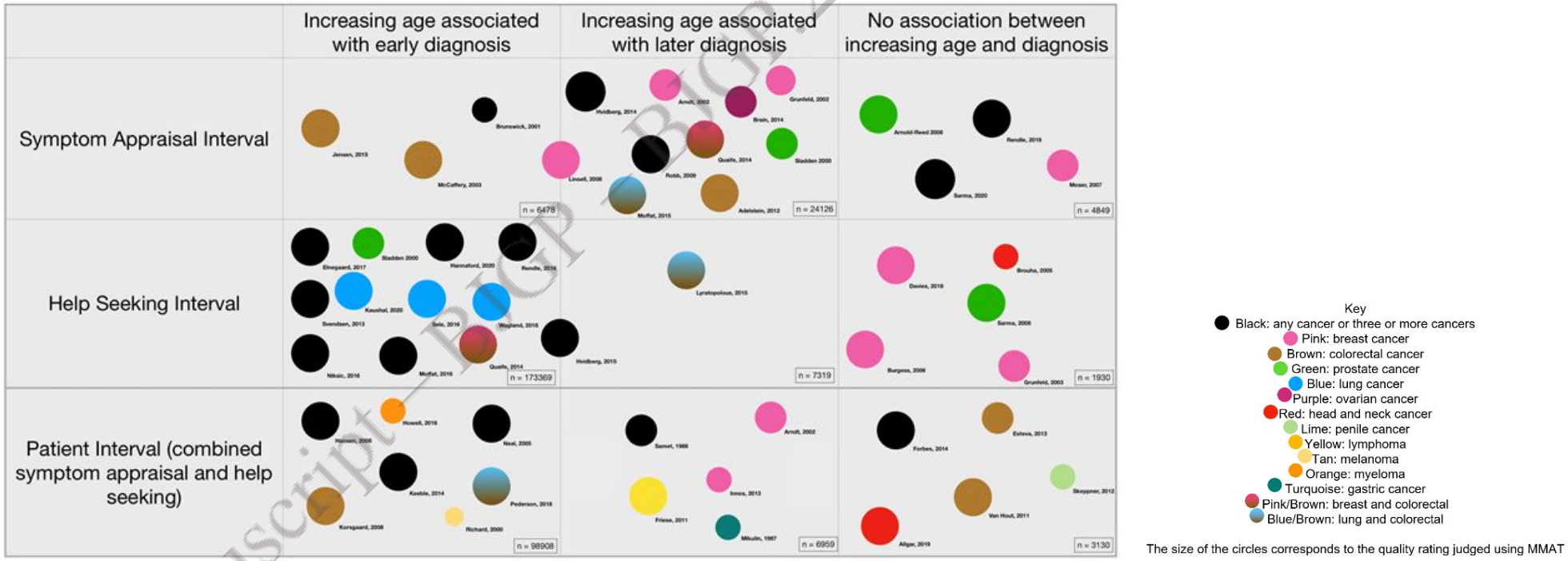

Figure 2 - Diagram to show the number of quantitative studies, the association with appraisal and help seeking, the cancer investigated, and the quality assessment. Size of circle corresponds to the quality rating judged using MMAT.

MMAT = mixed-methods appraisal tool.