

Title: The Prevalence of Anxiety in General Hospital Inpatients: A Systematic Review and Meta-Analysis

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ABSTRACT

Objective

To determine the prevalence of anxiety in general hospital inpatients by conducting a systematic review and meta-analysis of all relevant published studies.

Method

We searched Ovid Medline, Ovid Embase and Ovid PsycINFO from inception to December 2020. We included studies of the prevalence of anxiety symptoms of clinically significant severity (using cut-off scores on rating scales) and of the prevalence of anxiety disorders (using diagnostic interviews) in general hospital inpatients. Two independent reviewers assessed articles and extracted data. The review is registered with PROSPERO, number CRD42020189722.

Results

We included 32 studies. Pooled prevalence estimates in random-effects meta-analyses were: anxiety symptoms 28% (95% CI 19% to 38%, 95% prediction interval 5% to 72%), any anxiety disorder 8% (95% CI 5% to 12%, 95% prediction interval 2% to 33%), panic disorder 3% (95% CI 2% to 4%, 95% prediction interval 1% to 8%), generalized anxiety disorder 5% (95% CI 3% to 8%, 95% prediction interval 1% to 23%). There was high heterogeneity in prevalence, little of which was explained in exploratory analyses of a limited number of potential determinants.

Conclusion

Anxiety symptoms of clinically significant severity affect more than one in four inpatients and anxiety disorders affect nearly one in ten.

KEYWORDS:

Anxiety; Prevalence, General hospital inpatient; Systematic review; Meta-analysis

1. Introduction

Psychiatric comorbidities complicate the medical care of general hospital inpatients [1, 2].

Anxiety is one such comorbidity. The presence of comorbid anxiety not only indicates distress, but is also associated with increased use of healthcare resources and poorer outcomes [3].

In order to better understand and manage comorbid anxiety in general hospital inpatients, and to plan Consultation-Liaison Psychiatry provision, we need to know its prevalence in that population. Whilst there are systematic reviews of the prevalence of anxiety in populations with specific medical diagnoses [4], we are not aware of any reviews of its prevalence in the inpatient population.

We therefore aimed to determine the prevalence of anxiety in general hospital inpatients by conducting a systematic review of all the relevant published studies. We included studies that aimed to estimate either: (a) the prevalence of anxiety symptoms, in which the presence of anxiety symptoms of clinically significant severity was determined using cut-off scores on symptom rating scales; or (b) the prevalence of anxiety disorders, in which the presence of any anxiety disorder or of specific anxiety disorders was determined using diagnostic interviews.

2. Method

2.1 Design

We conducted a systematic review and meta-analysis, using procedures that accorded with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [5, 6]. We registered the study protocol with PROSPERO (number CRD42020189722).

2.2 Search strategy

We identified studies by searching Ovid Medline, Ovid Embase and Ovid PsycINFO (from 1946, 1974 and 1806 respectively) to December 2020. Searches were run for the combination of 'prevalence', 'general hospital inpatient' and 'anxiety' using both standardized subject terms and free text terms, including synonyms and alternative spellings. All references were exported (to Endnote X9, Thomson Reuters, New York, NY) and duplicates were removed following the method described by Falconer [7]. We provide full details of the searches used in the Appendix. We also manually searched the reference lists of review articles obtained through the electronic searches.

2.3 Selection criteria – relevance

We included studies (in any language) if they met all of the following criteria: (1) the study clearly aimed to estimate the prevalence of current anxiety in the inpatients of a whole general hospital or specified units within the hospital; (2) all study participants (or a clear subgroup) were adults aged 16 or older; (3) the prevalence of either anxiety symptoms (determined using a standard and widely used rating scale) or anxiety disorders (determined using a diagnostic interview) was reported or could be calculated using data from the paper.

We excluded studies if they only included patients with specific medical diagnoses or specific demographic characteristics.

2.4 Selection criteria – methodological quality

We only included studies that met all of the following basic methodological quality criteria:

(1) the study sample was obtained using a random or consecutive sampling method (to minimize participant selection bias); (2) data were available for analysis on at least 70% of the eligible patients (also to minimize participant selection bias); (3) the study clearly defined ‘anxiety’ by using either a specified cut-off score or standard diagnostic criteria (to allow the summary and synthesis of findings) [8, 9]. We only included studies that met these criteria because meta-analyses of low quality studies may yield misleading results [10]. We used quality criteria rather than a quality scale score because a study could potentially achieve a high score on a quality scale but still have a high risk of bias from one aspect of its methods [11].

2.5 Data extraction

Two researchers independently screened the titles and abstracts of all articles identified by the searches, using Endnote and Excel, to determine whether each might meet our selection criteria. If an article was considered to be potentially relevant, two researchers reviewed the full text, with the help of a translator where necessary. Any disagreements about whether to include an article were resolved by discussion with a third researcher. For each included study the following data were independently extracted using a specially designed, standardized data extraction form: country in which the study took place; hospital units

from which participants were recruited; participant inclusion criteria; sample size; age and sex of participants; rating scale and cut-off score used to define the presence of anxiety symptoms; interview and diagnostic criteria used to determine the presence of anxiety disorders as well as whether a hierarchical approach was taken; timing of the anxiety assessment after admission to hospital; prevalence of anxiety symptoms or anxiety disorders in the study sample (for cohort studies, we extracted the prevalence of anxiety at the first time point only).

2.6 Data synthesis and analysis

We were able to synthesize data on the prevalence of anxiety symptoms, any anxiety disorder, and the specific anxiety disorders panic disorder and generalized anxiety disorder. There were insufficient data on other specific anxiety disorders (for example, phobias) for us to produce meaningful summaries.

We used forest plots to display the study-specific prevalences (proportions with exact binomial 95% confidence intervals) of anxiety symptoms and anxiety disorders (any anxiety disorder, panic disorder and generalized anxiety disorder) in each study. We used the logit transformation to express each of the prevalence estimates as a log-odds and conducted meta-analyses using random-effects models. We used random-effects models because underlying prevalences (i.e. the prevalences if each study was of infinite size) are likely to vary from study to study according to factors, both measured and unmeasured, that differ between them [12]. The random-effects model assumes that underlying study-specific prevalences (when expressed as log odds) follow a normal distribution characterized by a mean and standard deviation, rather than taking a single value. For each meta-analysis we

report the (back-transformed) mean, which may be considered to be the ‘typical prevalence’, with a 95% confidence interval to quantify its precision. We also report the 95% prediction interval, which is the interval within which 95% of underlying study-specific prevalence estimates are predicted to lie.

We assessed heterogeneity using Cochran’s Q tests and I^2 statistics. We also conducted exploratory analyses to investigate the following potential sources of heterogeneity in the prevalences of anxiety symptoms and of any anxiety disorder: mean (or median where mean was not available) age of study participants; percentage of female participants; year of study publication; and the use of DSM or ICD diagnostic criteria (for any anxiety disorder only). We plotted (using bubble plots) prevalences against each potential source of heterogeneity and used meta-regression to estimate associations with the prevalences on the log odds scale.

We conducted the statistical analysis in R v3.5.2 using the “meta” package v4.18-0 and the “metafor” v2.4-0 package [13-15].

3. Results

3.1 Literature overview

Our initial screening of 20 416 titles and associated abstracts yielded 4927 articles for full paper review. We considered 96 of these to be relevant. Of these 96 articles, 33 (34%), describing 32 separate studies, met our quality criteria (see Figure 1 and Appendix) [16-48].

[Figure 1 about here]

The studies were mostly small in size (sample sizes ranged from 45 to 2009, median 210) and were conducted in a variety of hospital units (there were no studies of the prevalence of anxiety in the inpatients of a whole general hospital). The samples commonly excluded certain categories of patients, such as those with cognitive impairment and those who were very physically unwell. Some studies excluded patients if they had been admitted following a suicide attempt or had known psychiatric disorders. Study reports often lacked information on when during the admission the anxiety assessments were conducted; in those that did include this information the timing ranged from the first day to the third week of hospital admission (see Tables 1 and 2).

3.2 Prevalence of anxiety symptoms (rating scale studies)

12 of the 32 studies (total 6234 participants) used rating scales to determine the prevalence of clinically significant anxiety symptoms (see Table 1). Six studies used the anxiety subscale of the Hospital Anxiety and Depression Scale, two used the Generalized Anxiety Disorder-7 scale, two used the Zung Self-Rating Anxiety Scale and two used the State-Trait Anxiety Inventory.

[Table 1 about here]

The prevalence of clinically significant anxiety symptoms ranged from 11% to 62% (see Figure 2). The pooled prevalence was 28% (95% CI 19% to 38%, 95% prediction interval 5% to 72%). There was considerable statistical heterogeneity ($I^2=98\%$); that is, there was large variation between the studies' prevalence estimates that was unlikely to have occurred by chance.

[Figure 2 about here]

3.3 Prevalence of anxiety disorders (diagnostic interview studies)

The remaining 20 studies (total 4294 participants) used diagnostic interviews to determine the presence of anxiety disorders (see Table 2). Ten studies used diagnostic criteria from the Diagnostic and Statistical Manual of Mental Disorders (DSM), four used criteria from the International Classification of Diseases (ICD), one used the Automated Geriatric Examination for Computer Assisted Taxonomy (AGECAT) and one used the CATEGO system. A summary of the DSM and ICD diagnostic criteria (which differ between these two main systems and between the different versions of the systems) is provided in the Appendix.

Some studies explicitly used a hierarchical approach to diagnosis (for example, only diagnosing anxiety if depression was not also present), some clearly did not (that is, they allowed participants to receive multiple diagnoses where appropriate) and others were unclear about how they had addressed this issue (see Table 2).

[Table 2 about here]

16 studies (total 3982 participants) reported on the prevalence of any anxiety disorder. The specific disorders included within any anxiety disorder differed between studies, but in most cases included both panic disorder and generalized anxiety disorder (see Table 2).

Prevalence estimates for any anxiety disorder ranged from 2% to 29% (see Figure 3). The pooled prevalence of any anxiety disorder was 8% (95% CI 5% to 12%, 95% prediction interval 2% to 33%, $I^2=92\%$).

[Figure 3 about here]

The prevalence of panic disorder (10 studies, total 2530 participants) ranged from 0% to 6% (see Figure 4). The pooled prevalence was 3% (95% CI 2% to 4%, 95% prediction interval 1% to 8%, $I^2=48\%$).

[Figure 4 about here]

The prevalence of generalized anxiety disorder (11 studies, total 2649 participants) ranged from 0% to 21% (see Figure 5). The pooled prevalence was 5% (95% CI 3% to 8%, 95% prediction interval 1% to 23%, $I^2=86\%$).

[Figure 5 about here]

3.4 Exploration of heterogeneity

The bubble plots of the prevalence of anxiety symptoms and the prevalence of any anxiety disorder against mean (or median where mean was not available) age of study participants, percentage of female participants, year of study publication and use of DSM or ICD diagnostic criteria are shown in the Appendix Figures 1-7. For the studies of anxiety symptoms, there was no statistical evidence that age ($p=0.715$), percentage of female participants ($p=0.247$) or year of publication ($p=0.532$) explained the between-study variability in prevalence. For the studies of any anxiety disorder, there was no statistical evidence that either age ($p=0.257$) or percentage of female participants ($p=0.500$) were associated with prevalence. More recent publication year was associated with a higher prevalence of any anxiety disorder (odds ratio 1.06 per year increase, 95% CI 1.02 to 1.10, $p=0.004$), although there was still substantial residual heterogeneity ($I^2=85\%$). Studies that used ICD criteria reported a lower prevalence than those that used DSM criteria (odds ratio 0.30, 95% CI 0.13 to 0.71, $p=0.006$), again with high residual heterogeneity ($I^2=89\%$).

4. Discussion

4.1 Main findings

To the best of our knowledge, this is the first systematic review of the prevalence of anxiety in the general hospital inpatient population. We included 32 studies conducted in a variety of general hospital units; 12 studies of the prevalence of anxiety symptoms using cut-off scores on symptom rating scales and 20 studies of the prevalence of anxiety disorders using diagnostic interviews. The pooled prevalence of anxiety symptoms was 28% and the pooled prevalence of any anxiety disorder was 8%. For specific anxiety disorders, the pooled prevalence of panic disorder was 3% and the pooled prevalence of generalized anxiety disorder was 5%.

4.2 Discussion of findings

Perhaps not surprisingly, our estimate of the pooled prevalence of anxiety symptoms in general hospital inpatients (28%) is much higher than reported in studies of the general population. For example, large community studies have reported prevalence estimates of approximately 14% using the anxiety subscale of the Hospital Anxiety and Depression Scale (cut-off ≥ 8) and 9% using the Generalized Anxiety Disorder-7 scale (cut-off ≥ 8) [49, 50].

Our estimate of the pooled prevalence of any anxiety disorder, whilst also fairly high (8%), may not in fact be much higher than that found in the general population. For example, a systematic review of the global literature reported an average prevalence in the general population of approximately 7% [51]. Similarly, our pooled prevalence estimates of 3% and

5% for panic disorder and generalized anxiety disorder respectively are only modestly higher than 1-2% one-year general population prevalences [52].

Why might it be that general hospital inpatients have a much higher prevalence of anxiety symptoms than the general population, but not a much higher prevalence of anxiety disorders? We suggest three potential reasons: First, anxiety symptoms caused by acute illness and hospital admission are unlikely to meet the stringent diagnostic criteria for anxiety disorders, especially those criteria pertaining to duration. For example, the DSM-III-R and DSM-IV criteria for generalized anxiety disorder require symptoms to have been present for at least six months and the DSM-III-R and DSM-IV criteria for panic disorder require that the patient not only has recurrent panic attacks, but also at least one month of persistent concern about future panic attacks. Second, diagnostic criteria often require that anxiety is deemed by the interviewer to be 'unrealistic' or 'excessive'. Hence people who are medically ill and have been admitted to hospital may be considered by the interviewer to have 'understandable' anxiety and consequently given a diagnosis of adjustment disorder, rather than of anxiety disorder. Third, most of the diagnostic criteria for anxiety disorders require the interviewer to judge that the patient's symptoms are 'not due to a general medical disorder'. Such judgements are difficult to make and may potentially lead to undercounting of physical symptoms toward the presence of an anxiety disorder.

4.3 Reasons for heterogeneity in prevalences

We found substantial statistical heterogeneity in the study-specific prevalences, with large I^2 and wide prediction intervals. We were only able to investigate a small number of the potential sources of this heterogeneity, as explained below. In the exploratory analyses that

we did conduct, we were unable to identify factors that explained the heterogeneity in the prevalences of anxiety symptoms. We did find that more recent publication year was associated with a modestly higher reported prevalence of any anxiety disorder, perhaps reflecting a greater interest in anxiety disorders in recent years rather than an increasing population prevalence [52]. We also found that studies which used ICD diagnostic criteria reported a lower prevalence of any anxiety disorder than those that used DSM criteria, which may be related to the use of more systematic interviews to identify DSM disorders. However, the residual heterogeneity remained high in all our investigations, indicating that neither of these factors explained a material amount of the heterogeneity in the prevalences of any anxiety disorder.

Our findings from these explorations of the potential sources of heterogeneity should be interpreted with considerable caution, due to the inherent limitations of such analyses [10]. Furthermore, there are a number of other potential sources of heterogeneity that we were unable to investigate. These include: the country in which the study was conducted; the type of hospital unit from which participants were recruited; the choice of rating scale and cut-off in studies of anxiety symptoms; whether a hierarchical approach to diagnosis was used in interview studies (which may lead to a diagnosis of depression overshadowing a diagnosis of anxiety disorder) [53]; and the timing of the assessment of anxiety after admission to hospital [37]. We were unable to analyze these variables because either: (a) the categories of studies derived for analysis were too small (for example, the majority of countries were represented by only a single study) or (b) there were too many missing data (for example, the majority of studies did not report the timing of the anxiety assessment).

4.4 Methodological quality including risk of bias

Despite meeting our basic quality criteria, many of the studies we included still had methodological shortcomings. In particular, many of the samples studied were potentially biased by the exclusion of certain categories of patients, such as those who were very physically unwell and those who had known psychiatric disorders. Furthermore, the reporting of study methods was often unclear and important aspects of study design, such as when during the admission the anxiety assessments were conducted and whether a diagnostic hierarchy was employed, were frequently missing.

4.5 The challenges of systematically reviewing studies of anxiety prevalence in general hospital inpatients.

We encountered a number of challenges in doing this review. The way that articles are indexed in publication databases, and the inconsistent use of language within the titles and abstracts of the articles, made it exceptionally difficult to search for relevant studies. Whilst there are commonly used standardized subject terms and obvious free text search terms for 'anxiety', searching for 'general hospital inpatients' and 'prevalence' is more difficult. To find studies of inpatients, we needed to use multiple additional search terms such as 'hospital' and 'medical center' because many studies are not indexed using the term 'inpatient'. Similarly, authors have sometimes used words such as 'incidence' or 'occurrence' to mean 'prevalence' so we also needed to add these search terms.

The use of a number of different rating scales and diagnostic criteria also made it difficult to compare and summarize studies. The studies of the prevalence of anxiety symptoms used a variety of scales, which differ in the aspects of anxiety that they measure. For example,

some scales (such as the Zung Self-Rating Anxiety Scale) include a number of physical symptoms, whereas others (such as the anxiety subscale of the Hospital Anxiety and Depression Scale) do not. The studies of the prevalence of anxiety disorders mostly used the ICD and DSM classification systems. However, whilst these diagnostic systems are comparable for many psychiatric disorders, they differ both between each other and over time in their approach to anxiety disorders [54]. For example, they have included different specific disorders within the overall category of anxiety disorders and have had different approaches to the diagnosis of panic disorder (for details see Appendix).

4.6 Strengths and limitations of this review

The strengths of this review include: (a) a comprehensive, sensitive search of the published literature with no restriction on language; (b) clearly defined inclusion and exclusion criteria for studies in order to minimize bias in study selection; (c) the inclusion of only studies that met basic quality criteria.

The main limitations are: (a) the likely inability to find all potentially relevant studies due to limitations in article titles, abstracts and indexing; (b) the exclusion of studies that were designed to address a different research question but happened to include a prevalence estimate (for example, clinical trials and questionnaire validation studies) (c) a reliance on the published reports to assess studies' relevance and quality, which may potentially have led to us excluding studies that were in fact well conducted, but only poorly reported; (d) the absence of data on several of the more specific anxiety disorders such as phobias; (e) the limited ability to statistically investigate many potential sources of heterogeneity.

4.7 Other literature

We are not aware of any previous systematic review of the prevalence of anxiety in the general hospital inpatient population. However, we did find a meta-review of systematic reviews which summarized the findings of systematic reviews of the prevalence of anxiety in patients with diagnoses of multiple sclerosis, cardiovascular disease, cancer, respiratory disease, diabetes and other chronic illnesses [4]. The authors of this meta-review concluded that anxiety is more prevalent in populations with chronic physical illnesses than in healthy populations which is consistent with our finding of a higher prevalence of anxiety in the general hospital inpatient setting.

4.8 Implications for clinical practice

The finding that more than a quarter of general hospital inpatients have anxiety symptoms is important, as it may be a marker of patients' unaddressed fears and concerns. Whilst anxiety disorders, as defined by diagnostic criteria, are less prevalent than anxiety symptoms, they still affect nearly one in ten inpatients. There is an argument therefore for the better identification of patients with anxiety by systematic screening, and review of the need for treatment, either during the hospital stay or after discharge.

4.9 Implications for future research

Although we found a number of studies of the prevalence of anxiety in general hospital inpatients, the usefulness of the data they provided was limited by their methodological shortcomings. There is consequently a need for better study design and reporting. A particularly important issue is the need for greater clarity and consistency in the criteria used to determine if symptoms are attributed to a diagnosis of anxiety disorder, to the

patient's medical condition or to their adjustment to stressors. The high heterogeneity observed between the studies could not be adequately explained by the available data and provides a topic for future research. We also need more studies of patient populations defined by clinical setting rather than by medical diagnosis, in order to inform the planning of Consultation-Liaison Psychiatry services.

4.10 Conclusions

Anxiety is common in general hospital inpatients. Anxiety symptoms of clinically significant severity affect more than one in four inpatients and anxiety disorders affect nearly one in ten. These estimates suggest both considerable patient suffering and the potential complication of medical care. We conclude that anxiety in general hospital inpatients deserves greater attention from both clinicians and researchers.

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Disclosures

None.

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Table 1: Studies of the prevalence of clinically significant anxiety symptoms in general hospital inpatients

Study	Hospital unit(s)	Inclusion criteria	Sample size	Age	% female	Anxiety rating-scale	Cut-off score used	Timing of assessment after admission	Prevalence of clinically significant anxiety symptoms (%)
Cardoso 2010 (Portugal)	Gastroenterology intensive care	Aged ≥ 18 ; intensive care unit stay ≥ 24 hours; cognitively able to complete assessment.	65	Mean 57.2, SD 15.8	41.5	Hospital Anxiety and Depression Scale, Anxiety Subscale	≥ 8	Within 72 hours	29
Esteghamat 2014 (Iran)	Internal medicine & general surgery	Aged ≥ 18 ; hospitalized for ≤ 24 hours; no psychological or mental disabilities, decreased consciousness or cognitive impairment.	359	Mean 49.18, SD 19.49	56.3	Hospital Anxiety and Depression Scale, Anxiety Subscale	≥ 11	Within 24 hours	39
Gorini 2020 (Italy)	Cardiology	All patients included.	2009	Mean 64.0, SD 14.6 ^a	29.02 ^a	Generalized Anxiety Disorder-7	≥ 8	Not reported	16
Huang 2019 (China)	Medical & surgical sub-specialties ^b	Physically and mentally able to complete self-report questionnaire; not being discharged on survey day.	1329	Mean 52.7, SD 16.5	41.9	Generalized Anxiety Disorder-7 (Chinese version)	≥ 10	Not reported	15

Koc 2017 (Turkey)	Oncology	Aged ≥ 18 ; literate; physically and mentally able to take part.	356	Mean 54.6, SD 16.7	42.7	Hospital Anxiety and Depression Scale, Anxiety Subscale	≥ 11	Not reported	62
Li 2018 (China)	Head and neck surgical oncology	Aged ≥ 18 ; awaiting surgery; no heart disease, diabetes, kidney disease or psychiatric illness; no family history of psychiatric illness.	228	Mean 48.5, SD 11.6	71.1	Zung Self-Rating Anxiety Scale	$\geq 50^c$	Not reported	36
Mazeraud 2020 (France)	Medical-surgical intensive care	Breathing spontaneously; not admitted for suicide attempt; no delirium or impaired consciousness; no history of altered neuro-cognition; French speaking.	391	Median 63, Range 49-74	40.7	State-Trait Anxiety Inventory	≥ 40	Within 12 hours	52
Meyer 2002 (Germany)	Internal medicine	Sufficient knowledge of German; no severe cognitive impairment.	575	Mean 58.7, SD 15.1	42.8	Hospital Anxiety and Depression Scale, Anxiety Subscale	≥ 11	Not reported	18
Rincon 2001 (Colombia)	Medical, surgical & coronary critical care	Verbal communication not impaired by structural cerebral damage or excessive sedation.	95	Mean 61, SD 14.3 ^d	38.5 ^{d*}	Hospital Anxiety and Depression Scale, Anxiety Subscale	≥ 10	First day of admission	24
Şahan 2021 (Turkey)	Coronavirus-19	No Alzheimer's disease or psychosis; no hearing disability; Turkish speaking.	281	Mean 55.0, SD 14.9	49.1	Hospital Anxiety and Depression Scale, Anxiety Subscale	≥ 10	Not reported	35

Tecchio 2013 (Italy)	Bone marrow transplant	Aged ≥ 16 ; undergoing first autologous or allogenic hematopoietic stem cell transplant; no major psychiatric disorder or mental retardation; full understanding of spoken & written Italian.	107	Median 51, Range 16-70	38.3	State-Trait Anxiety Inventory	Male ≥ 55 , Female ≥ 61 (scores in 95 th percentile of normative sample)	Not reported	11
Tian 2019 (China)	Ear Nose & Throat	Aged ≥ 18 ; not an emergency admission; no cognitive impairment, coma, severe depression, drug addiction or mental disturbance; medically stable.	439	Department 1: Mean 41.7, SD 13.2 Department 2: Mean 49.7, SD 17.1 Department 3: Mean 42.2, SD 13.8	43.3*	Zung Self-Rating Anxiety Scale	$\geq 50^c$	Within 1-2 days	16

^a Demographic data for 2006 participants; ^b Oncology, cardiology, respiratory medicine, rehabilitation, geriatrics & gerontology, general practice, pain management, rheumatology, hepatic surgery, thyroid & breast surgery; ^c Cut-off relates to index score; ^d Demographic data for 96 participants (only 95 completed anxiety assessment). SD = Standard Deviation. * Calculated using data from paper. If a study reported the prevalence of anxiety symptoms using more than one cut-off, we used the prevalence related to the recommended cut-off.

Table 2: Studies of the prevalence of anxiety disorders in general hospital inpatients

Study	Hospital unit(s)	Inclusion criteria	Sample size	Age	% female	Anxiety interview (interviewer)	Diagnostic criteria	Hierarchy used	Timing of assessment after admission	Prevalence of anxiety disorders (%)		
										Any	Panic disorder	GAD
Abiodun 1990 (Nigeria)	Medicine & surgery	Aged ≥ 16 ; well enough to participate; English or Yoruba speaker.	275	Medicine: Mean 40 Surgery: Mean 38.9	44*	Psychiatric interview including Present State Examination (psychiatrist)	ICD-9	Unclear	Not reported	7 ^{a*}	-	-
Alexander 1993 (India)	Oncology	Well enough for interview.	60	Mean 53.2, SD 13.9	40*	Clinical interview (psychiatrist)	DSM-III-R	Unclear	Within 3-7 days	-	3	-
Arolt 1997 (Germany)	Internal medicine & surgery	Well enough to participate; not suffering from severe psycho-organic syndromes.	400	Medicine: Mean 62.5, SD 17.9 Surgery: Mean 59.7, SD 20.0	Medicine : 50.5 Surgery: 53.0	Clinical interview including Composite International Diagnostic Interview (psychiatrist) ^b	ICD-10	Yes	Not reported	2 ^c	-	-
Burn 1993 (UK)	Acute geriatric medicine	Aged > 65; no speech disorder or severe deafness.	100	Mean 82, Range 69-99	64*	Geriatric Mental State (trained interviewer)	AGECAT	Yes	Not reported	7 ^d	-	-
Dogar 2008 (Pakistan)	Cardiology	Not specified.	100	Mean 52.2, SD 11.12	40*	Clinical interview (not stated)	DSM-IV	No	Not reported	-	-	21*

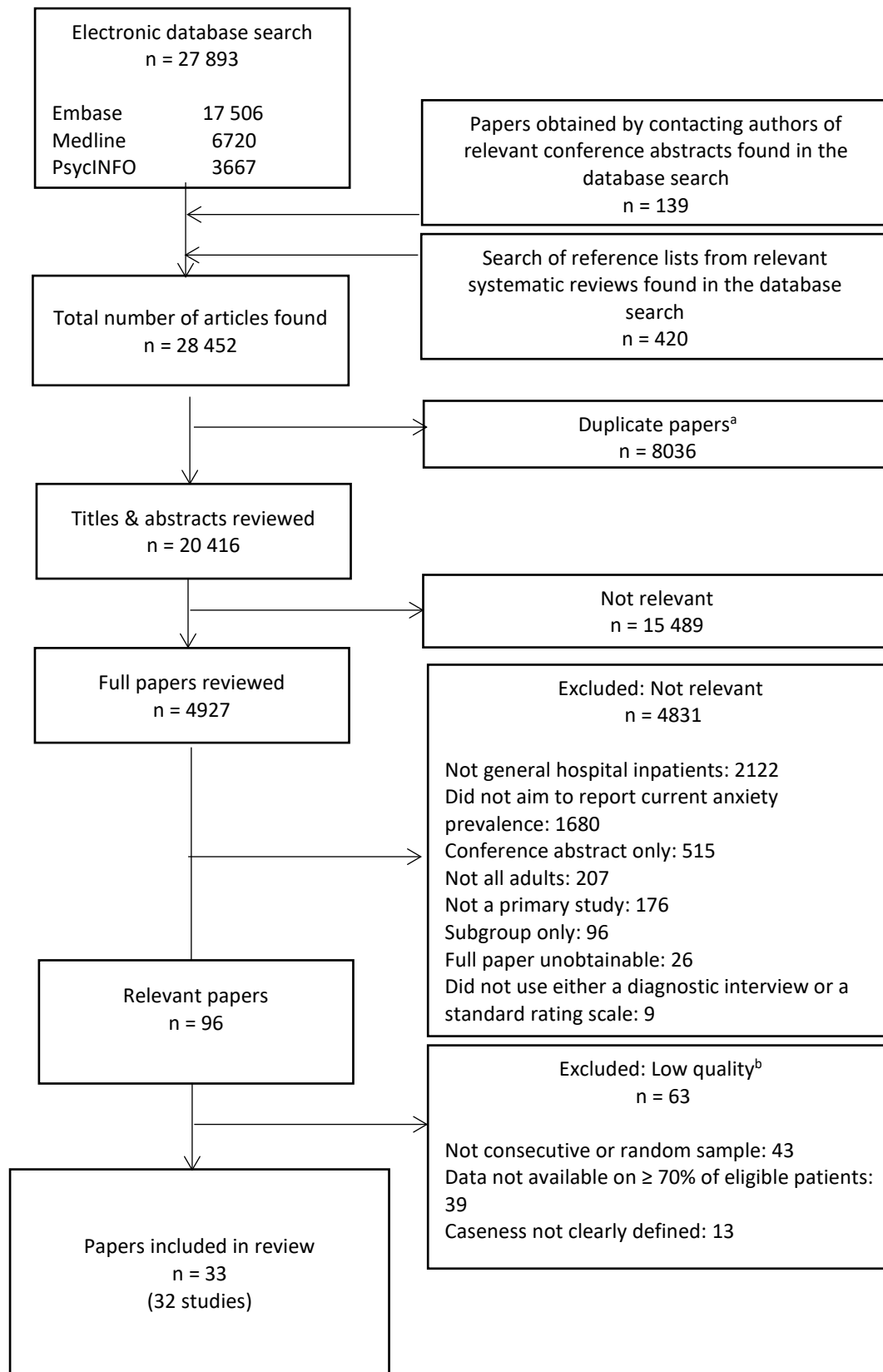
Dyster-Aas 2008 (Sweden)	Burns	Aged ≥ 18 ; $\geq 5\%$ burns or hospitalized for > 1 day; Swedish speaker; no documented cognitive impairment.	73	Mean 43.4, SD 15.6	27.4*	Structured Clinical Interview for DSM-IV (psychiatrist or trained interviewer)	DSM-IV	No	Not reported	29 ^e	3	-
Feldman 1987 (UK)	General medicine	Aged ≥ 18 ; hospitalized for ≥ 24 hours; not admitted due to suicide attempt; well enough to participate.	382	Not reported	Not reported	Stage 1: General Health Questionnaire 30 (cut-off ≥ 5) & 2 additional questions Stage 2: Present State Examination (not stated)	CATEGO ^f	Unclear	Not reported	7 ^{g*}	-	-
Fritzsche 2001 (Germany)	Dermatology	Aged ≥ 16 ; hospitalized for ≥ 48 hours; cognitively & physically able to participate; adequate German.	77	Mean 51.6, SD 17.96 ^h	59	Structured Diagnostic Interview for Mental Illness (research assistant)	ICD-10	Unclear	Not reported	3 ^c	-	-
Jenkins 1994 (UK)	General surgery	Aged 16-80; elective or emergency admission; pre-surgery; well enough to participate; able to read & speak English.	197	Not reported	Not reported	Stage 1: General Health Questionnaire (cut-off ≥ 12) Stage 2: Semi-structured Interview (psychiatrist) ^b	DSM-III	No	Within 24 hours	16 ⁱ	0*	2*
Kathol 1992 (USA)	Medicine & medical subspecialties	Likely to stay in hospital ≥ 3 days; no obvious memory difficulties; not requiring intensive care unit treatment; able to speak English.	128	Mean 56	21*	Stage 1: Hamilton Anxiety Scale & Hamilton Depression Rating Scale	DSM-III	No	Within 24 hours	4 ^j	2*	2*

						(cut-off ≥ 6 on either) Stage 2: Structured Diagnostic Assessment Questionnaire (trained interviewer)						
Kayhan 2013 (Turkey)	General & subspecialty medicine & surgery	Aged ≥ 18 ; hospitalized for ≥ 2 days; well enough to participate; no mental retardation, psychotic disorder or delirium; not in perinatal period.	603	Mean 51.07, SD 15.72	49.6	Structured Clinical Interview for DSM-IV (psychiatrist)	DSM-IV	No	Not reported	24 ^e	3	8
Keller 2004 (Germany)	Surgical oncology	Aged ≥ 18 ; physically and mentally able to participate.	78	≤ 30 : 1.3% 31-50: 26.9% 51-70: 61.5% > 70: 10.3%	38.5	Structured Clinical Interview for DSM-IV (clinical psychologist)	DSM-IV	No	Not reported	3 ^e	-	-
Kigamwa 1991 (Kenya)	Medicine	Well enough to participate; not admitted after taking an overdose; fluent in English or Kiswahili.	200	Not reported	Not reported	Stage 1: Self Reporting Questionnaire (cut-off > 8) Stage 2: Standardized Psychiatric Interview (not stated)	ICD-9	Unclear	Not reported	4 ^k	-	-
Köroğlu 2010 (Turkey)	Internal medicine	Aged 18-75; no delirium; not suffering from terminal-stage cancer.	110	Mean 47.2, SD 15.0	53.6	Structured Clinical Interview for DSM-IV (not stated)	DSM-IV	No	Not reported	9 ^{l*}	1 [*]	3 [*]

Lykouras 1996 (Greece)	Neurology	Able to communicate & read.	107	Mean 43.7, Range 16-78	53.3*	Structured Clinical Interview for DSM-III-R (psychiatrist)	DSM-III-R	Unclear	Third, fourth or fifth day ^m	-	-	14*
Madianos 2001 (Greece)	Burns	Able to communicate well enough for interview.	45	Male: Mean 40.1, SD 13.5 Female: Mean 52.6, SD 20.9	44.4*	Structured Clinical Interview for DSM-III-R (psychiatrist)	DSM-III-R	Unclear	During third week	-	-	2
Marchesi 2004 (Italy)	Emergency medicine & medicine	Aged 18-65; mentally & physically able to participate; Italian speaker.	719	Emergency medicine: Mean 39.7, SD 13.7 Medicine: Mean 49.1, SD 12.8	Emergency medicine : 53.4 Medicine : 47.9	Stage 1: General Health Questionnaire-30 (cut-off > 4) Stage 2: Mini International Neuropsychiatric Interview (psychiatrist)	DSM-IV	Unclear	Not reported	17 ^{n*}	5*	9*
Palmu 2010, 2011 (Finland)	Burns	Aged ≥ 18; Finnish speaker; no cognitive or communication problems.	107	Mean 45.4, SD 16.4	29.9	Structured Clinical Interview for DSM-IV-TR (psychiatrist)	DSM-IV-TR	No	Not reported	16 ^e	6	0
Prieto 2002 (Spain)	Stem cell transplant	Aged ≥ 16; hospitalized for first stem cell transplant.	220	Mean 38.4, Range 16-65	41.4*	Structured psychiatric interview (psychiatrist)	DSM-IV	No	Within 48 hours	3 ^e	0	2
Silverstone 1996 (UK)	Medicine	Emergency admission; hospitalized for ≥ 7 days; able to communicate well enough for interview; MMSE score ≥ 22.	313	DSM-IV diagnosis: Mean 65.4, SE 1.6 No DSM-IV diagnosis: Mean 71.9, SE 0.9	49.2*	Schedule for Clinical Assessment in Neuropsychiatry (not stated)	DSM-IV	No	Seventh day	7 ^o	2*	3*

^a Anxiety states & Phobic state; ^b Different prevalence estimates were obtained using computer-generated diagnoses; ^c Anxiety disorders; ^d Anxiety diagnostic syndrome; ^e Any anxiety disorder; ^f Modified rules were used to include all symptoms rather than excluding those considered to be understandable; ^g Anxiety diagnosis; ^h Demographic data for 86 participants (only 77 completed anxiety assessment); ⁱ Panic disorder, Generalized anxiety disorder & Current anxiety; ^j Panic disorder & Generalized anxiety disorder; ^k Anxiety states; ^l Panic disorder, Generalized anxiety disorder & Anxiety disorder not otherwise specified; ^m GHQ-28 completed two to three days after admission and Structured Clinical Interview completed within two days of GHQ-28; ⁿ Panic disorder, Generalized anxiety disorder, Mixed anxiety-depressive disorder & Other anxiety disorders; ^o Panic disorder, Generalized anxiety disorder & Anxiety disorder due to medical disorder. AGE CAT = Automated Geriatric Examination for Computer Assisted Taxonomy, DSM = Diagnostic and Statistical Manual of Mental Disorders, GAD = Generalized anxiety disorder, ICD = International Classification of Diseases, MMSE = Mini-Mental State Examination, SD = Standard Deviation, SE = Standard Error. * Calculated using data from paper.

Figure 1: The prevalence of anxiety in general hospital inpatients: systematic review flowchart



^a Duplicates of the same paper due to searching multiple databases and reference lists.

^b Papers could be excluded for one or more quality reason.

Figure 2: Prevalence of clinically significant anxiety symptoms in general hospital inpatients

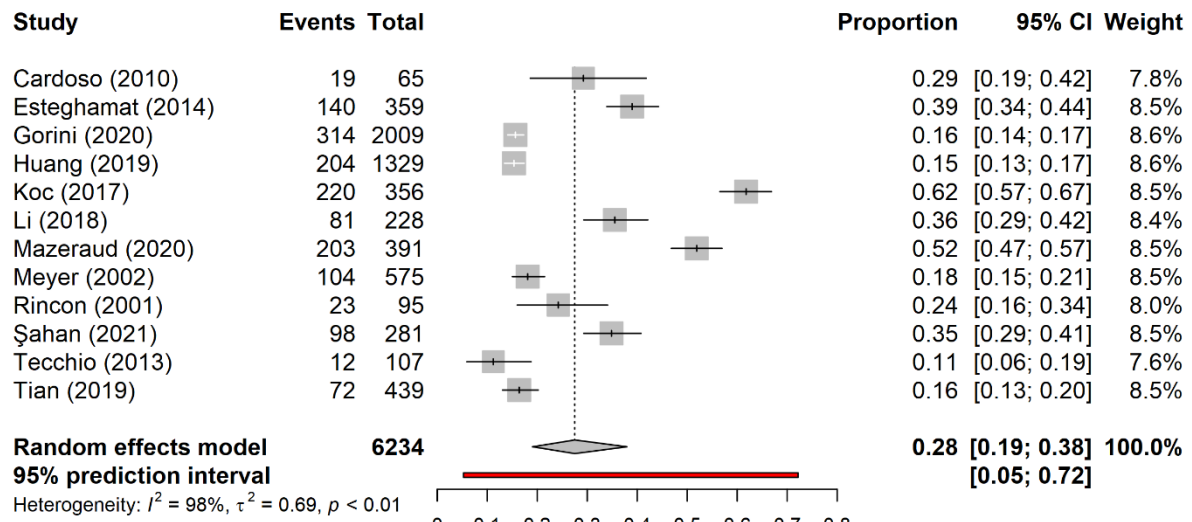


Figure 3: Prevalence of any anxiety disorder in general hospital inpatients

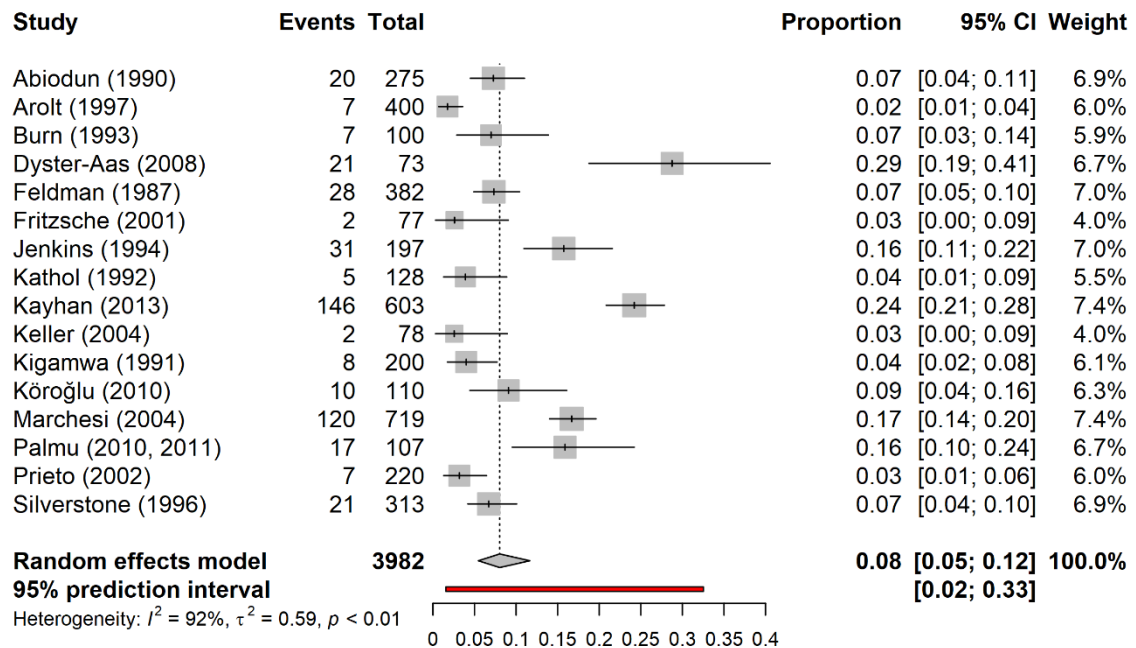


Figure 4: Prevalence of panic disorder in general hospital inpatients

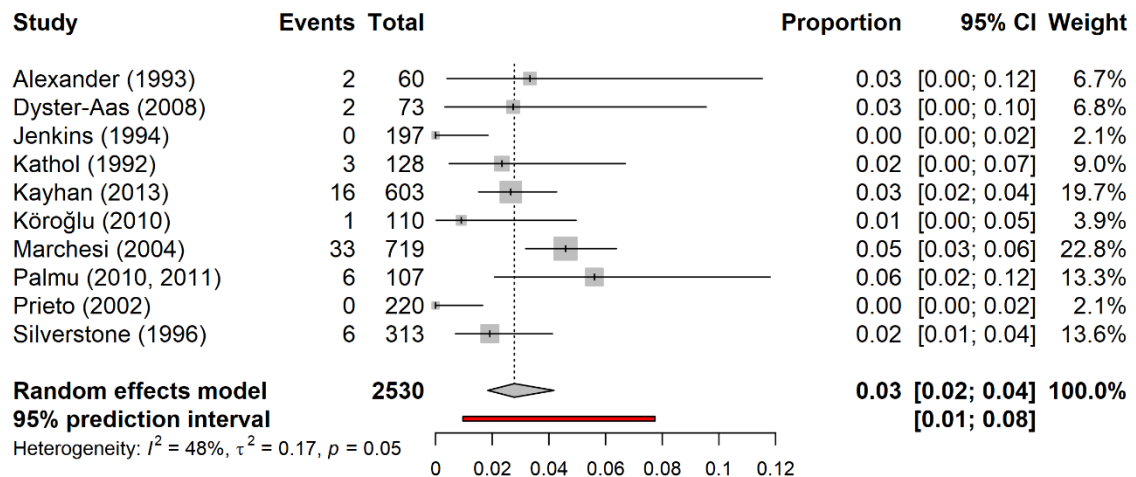
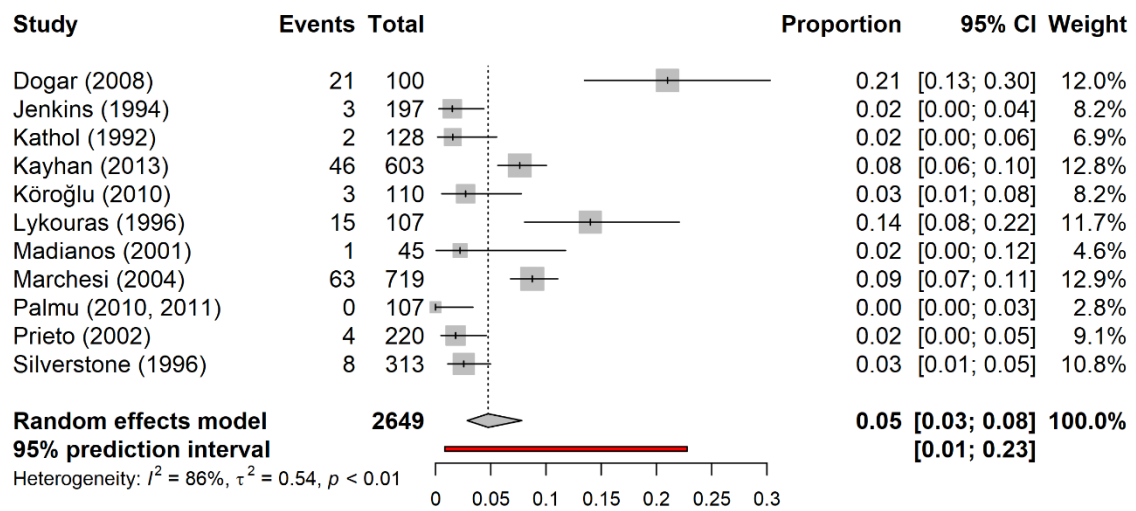


Figure 5: Prevalence of generalized anxiety disorder in general hospital inpatients



Online Appendix

Supplement to: The Prevalence of Anxiety in General Hospital Inpatients: A Systematic Review and Meta-Analysis

This appendix has been provided by the authors to give readers additional information about their work.

Search strategies

We ran searches in August 2019. We updated them in December 2020.

Ovid Medline (1946 to 2020)

- 1 Prevalence/
- 2 Incidence/
- 3 prevalen*.ti,ab.
- 4 inciden*.ti,ab.
- 5 frequen*.ti,ab.
- 6 rate*.ti,ab.
- 7 occur*.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 (1974 to 2020)

- 1 Prevalence/
- 2 Incidence/
- 3 prevalen*.ti,ab.
- 4 inciden*.ti,ab.
- 5 frequen*.ti,ab.
- 6 rate*.ti,ab.
- 7 occur*.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 2020)

- 1 Epidemiology/
- 2 prevalen*.ti,ab.
- 3 inciden*.ti,ab.
- 4 frequen*.ti,ab.
- 5 rate*.ti,ab.
- 6 occur*.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

Summary of the DSM and ICD diagnostic criteria for anxiety disorders

Diagnostic system	Classification of Anxiety disorders	Diagnostic criteria for Panic disorder	Diagnostic criteria for Generalized anxiety disorder
DSM-III	<p>Phobic disorders</p> <ul style="list-style-type: none"> - Agoraphobia with panic attacks - Agoraphobia without panic attacks - Social phobia - Simple phobia <p>Anxiety states</p> <ul style="list-style-type: none"> - Panic disorder - Generalised Anxiety Disorder - Obsessive Compulsive Disorder - Post-traumatic Stress Disorder, Acute - Post-traumatic Stress Disorder, Chronic or Delayed - Atypical anxiety disorder 	<p>≥ 3 panic attacks within a 3-week period, not precipitated by exposure to a circumscribed phobic stimulus.</p> <p>Not due to a physical disorder or another mental disorder.</p> <p>Not associated with agoraphobia.</p>	<p>Generalised, persistent anxiety with symptoms from ≥ 3 of: motor tension, autonomic hyperactivity, apprehensive expectation, vigilance and scanning.</p> <p>Continuous for ≥ 1 month.</p> <p>Not due to another mental disorder.</p>
DSM-III-R	<p>Panic disorder with agoraphobia</p> <p>Panic disorder without agoraphobia</p> <p>Agoraphobia without history of panic disorder</p> <p>Social phobia</p> <p>Simple phobia</p> <p>Obsessive-compulsive disorder</p> <p>Post-traumatic stress disorder</p> <p>Generalised Anxiety Disorder</p> <p>Anxiety disorder not otherwise specified</p>	<p>≥ 1 panic attack that were unexpected and not triggered by situations in which the person was the focus of others' attention.</p> <p>Either 4 attacks within a 4-week period or ≥ 1 attack have been followed by at least 1 month of persistent fear of having another attack.</p> <p>During at least some of the attacks, ≥ 4 symptoms developed suddenly and increased in intensity within 10 minutes of the beginning of the first symptom noticed in the attack.</p>	<p>Unrealistic or excessive anxiety and worry about ≥ 2 life circumstances for ≥ 6 months, during which the person has been bothered more days than not by these concerns.</p> <p>If another Axis I disorder is present, the focus of the anxiety and worry is unrelated to it.</p> <p>The disturbance does not occur only during the course of a mood disorder or psychotic disorder.</p>

		It cannot be established that an organic factor initiated and maintained the disturbance.	<p>≥ 6 are often present from: trembling, twitching or feeling shaky; muscle tension, aches or soreness; restlessness; easy fatigability; shortness of breath or smothering sensations; palpitations or accelerated heart rate; sweating or cold clammy hands; dry mouth; dizziness or lightheadedness; nausea, diarrhea or other abdominal distress; flushes or chills; frequent urination; trouble swallowing or 'lump in throat'; feeling keyed up or on edge; exaggerated startle response; difficulty concentrating or 'mind going blank' because of anxiety; trouble falling or staying asleep; irritability.</p> <p>It cannot be established that an organic factor initiated and maintained the disturbance.</p>
DSM-IV	Panic disorder without agoraphobia Panic disorder with agoraphobia Agoraphobia without history of panic disorder Specific phobia Social phobia Obsessive-compulsive disorder Posttraumatic stress disorder Acute stress disorder Generalised anxiety disorder Anxiety disorder due to a general medical condition	<p>Recurrent unexpected panic attacks.</p> <p>≥ 1 attack has been followed by ≥ 1 month of: persistent concern about having additional attacks, worry about implications or consequence of attack, or significant change in behaviour related to attacks.</p> <p>Attacks are not due to the direct physiological effects of a substance or general medical condition.</p>	<p>Excessive anxiety and worry more days than not for ≥ 6 months about a number of events or activities.</p> <p>The person finds it difficult to control the worry.</p> <p>≥ 3 present (at least some on most days for ≥ 6 months) from: restlessness or feeling keyed up or on edge; being easily fatigued; difficulty concentrating or mind going</p>

	<p>Substance-induced anxiety disorder</p> <p>Anxiety disorder not otherwise specified</p>	<p>Attacks are not better accounted for by another mental disorder.</p>	<p>blank; irritability; muscle tension; sleep disturbance.</p> <p>The focus of anxiety is not confined to features of an Axis I disorder (e.g. to panic attacks in Panic disorder).</p> <p>The anxiety, worry or physical symptoms cause clinically significant distress or impairment in functioning.</p> <p>The disturbance is not due to the direct physiological effects of a substance or general medical condition.</p>
ICD-9	<p>Anxiety states</p> <ul style="list-style-type: none"> - Anxiety neurosis - Anxiety reaction - Anxiety state - Panic attack - Panic disorder - Panic state <p>Phobic state</p> <ul style="list-style-type: none"> - Agoraphobia - Animal phobias - Anxiety-hysteria - Claustrophobia - Phobia not otherwise specified 	<p>No specific criteria described.</p> <p>Anxiety states are described as combinations of physical and mental manifestations of anxiety, not attributable to real danger and occurring in attacks or as a persisting state.</p>	<p>No specific criteria described.</p> <p>Anxiety states are described as combinations of physical and mental manifestations of anxiety, not attributable to real danger and occurring in attacks or as a persisting state.</p>

ICD-10	<p>Phobic anxiety disorders</p> <ul style="list-style-type: none"> - Agoraphobia without panic disorder - Agoraphobia with panic disorder - Social phobias - Specific (isolated) phobias - Other phobic anxiety disorders - Phobic anxiety disorder, unspecified <p>Other anxiety disorders</p> <ul style="list-style-type: none"> - Panic disorder (episodic paroxysmal anxiety) - Generalised Anxiety Disorder - Mixed anxiety and depressive disorder - Other mixed anxiety disorders - Other specified anxiety disorders - Anxiety disorder, unspecified 	<p>Several attacks of autonomic anxiety within a period of about 1 month in circumstances where there is no objective danger, without being confined to known or predictable situations, and with comparative freedom from anxiety symptoms between attacks.</p> <p>Only diagnosed in the absence of any of the phobias.</p>	<p>Primary symptoms of anxiety most days for at least several weeks at a time and usually for several months.</p> <p>Symptoms should usually involve elements of: apprehension, motor tension and autonomic overactivity.</p> <p>Must not meet the full criteria for depressive episode, phobic anxiety disorder, panic disorder or obsessive-compulsive disorder.</p>
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N.B. Symptoms required to diagnose a panic attack are described separately

Methodological quality assessment of relevant studies

Study	Consecutive or random sample	Caseness clearly defined	Data available on $\geq 70\%$ eligible patients
Abiodun 1990	Yes	Yes	Yes
Akinsulore 2015	No	Yes	Unknown
Al-Atram 2018	No	Yes	Unknown
Alexander 1993	Yes	Yes	Yes
Ames 1994	No	Unknown	Unknown
Arolt 1997	Yes	Yes	Yes
Arora 2019	Unknown	Yes	Unknown
Austin 2011	Unknown	Yes	Yes
Beausang 1998	Yes	No	Yes
Boizonave 2003	Unknown	No	Unknown
Booth 1998	Yes	Yes	Unknown
Burn 1993	Yes	Yes	Yes
Buzgova 2014	Unknown	Yes	Unknown
Buzgova 2015	Unknown	Yes	Yes
Capocaccia 1993	Unknown	No	Unknown
Cardoso 2010	Yes	Yes	Yes
Castro-Camacho 2012	Yes	No	Unknown
Celano 2013	Yes	Yes	No
Chaturvedi 1994	Yes	No	Unknown
De Fazio 2017	Yes	Yes	Unknown
de Moraes 2010	Unknown	Yes	Yes
Dicker 2011	Unknown	Yes	No
Dogar 2008	Yes	Yes	Yes
Dyster-Aas 2008	Yes	Yes	Yes
Esteghamat 2014	Yes	Yes	Yes
Feldman 1987	Yes	Yes	Yes
Fritzsche 2001	Yes	Yes	Yes
Gascon 2012	Unknown	No	Unknown
Giles Gordon 1992	Yes	No	Yes
Gopalan 2016	Yes	Yes	Unknown
Gorini 2020	Yes	Yes	Yes
Grassi 1996	Unknown	No	Yes
Gulich 2013	Unknown	Yes	Yes
Gurr 2012	Unknown	Yes	Yes
Hadi 2010	Yes	Yes	Unknown
Hansen 2001	Yes	Yes	No
Hardman 1989	Yes	Yes	Unknown
Harter 2000	Unknown	Yes	Yes

Hernandez-Palazon 2015	No	Yes	Unknown
Hosaka 1994	Unknown	Yes	Unknown
Hosaka 1996	Unknown	Yes	Unknown
Huang 2019	Yes	Yes	Yes
Jafar 2009	No	Yes	Unknown
Jenkins 1994	Yes	Yes	Yes
Kathol 1992	Yes	Yes	Yes
Kayhan 2013	Yes	Yes	Yes
Kelleci 2009	Unknown	Yes	Unknown
Keller 2004	Yes	Yes	Yes
Kigamwa 1991	Yes	Yes	Yes
Koc 2017	Yes	Yes	Yes
Köroğlu 2010	Yes	Yes	Yes
Kvaal 2001	Unknown	Yes	Yes
Latif 2017	No	Yes	Unknown
Lepine 1986	Yes	Yes	Unknown
Li 2018	Yes	Yes	Yes
Liu 2017	No	Yes	Unknown
Lykouras 1996	Yes	Yes	Yes
Madianos 2001	Yes	Yes	Yes
Marchesi 2001	Unknown	Yes	Yes
Marchesi 2004	Yes	Yes	Yes
Marco Sanjuan 1999	Unknown	No	Yes
Marcolino 2007	Unknown	Yes	Yes
Marcolino 2007	Unknown	Yes	Yes
Martucci 1999	No	Yes	No
Mazeraud 2020	Yes	Yes	Yes
Meyer 2002	Yes	Yes	Yes
Mina 2012	Yes	Yes	Unknown
Minagawa 1996	No	Yes	Yes
Mirani 2019	Unknown	Yes	Unknown
Mohammed 2014	No	Yes	Unknown
Mulugeta 2018	No	Yes	Yes
Nagle-Yang 2019	Unknown	Yes	No
Ni Mhaolain 2008	Yes	Yes	Unknown
Niecke 2019	Unknown	Yes	No
Nigussie 2014	No	Yes	Yes
Palmu 2010, 2011	Yes	Yes	Yes
Paul 2013	No	Yes	Unknown
Phillips 1996	Yes	No	No
Prieto 2002	Yes	Yes	Yes
Rincon 2001	Yes	Yes	Yes

Şahan 2021	Yes	Yes	Yes
Sanson 2018	Yes	No	Yes
Shdaifat 2020	No	Yes	Unknown
Shoar 2016	Yes	Yes	Unknown
Silverstone 1996	Yes	Yes	Yes
Soeiro 2008	Yes	Unknown	Yes
Tan 2014	Yes	Yes	Unknown
Tecchio 2013	Yes	Yes	Yes
Teunissen 2007	Yes	Yes	No
Thew 2016	Unknown	Yes	Yes
Tian 2019	Yes	Yes	Yes
Wang 2019	No	Yes	Yes
Wang 2020	No	Yes	Yes
Yildirim 2010	Unknown	Yes	Yes
Zhao 2020	Unknown	Yes	Yes

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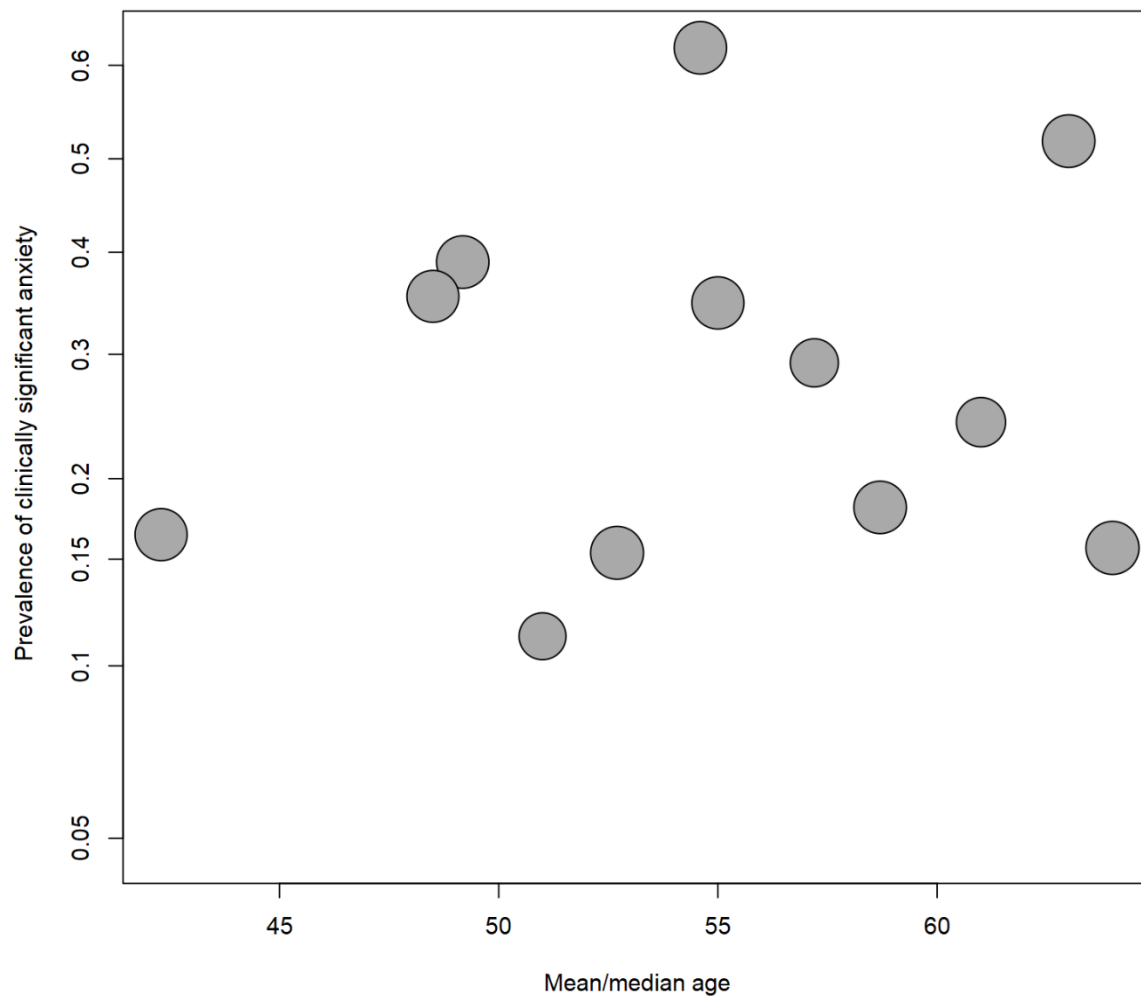
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Explorations of heterogeneity in studies included in the review

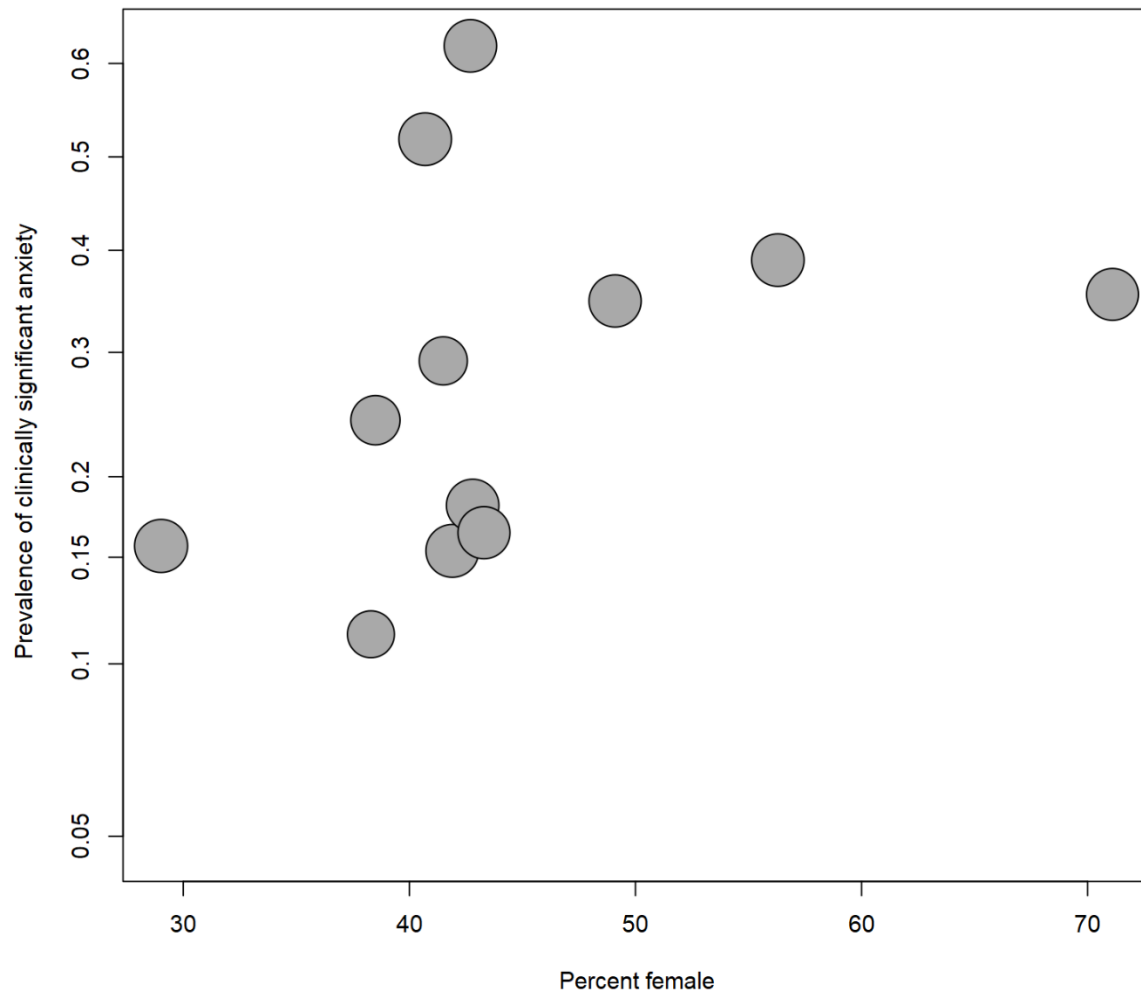
Figure A1: Bubble plot of the prevalence of clinically significant anxiety symptoms in each study against mean or median age.



There was no statistical evidence of an association between odds of anxiety symptoms and mean or median age ($p=0.715$). Each one year increase was associated with 1.02 (95% CI 0.93 to 1.10) times the odds of anxiety symptoms.

This analysis included data on 12 studies: Cardoso, 2010; Esteghamat, 2014; Gorini, 2020; Huang, 2019; Koc, 2017; Li, 2018; Mazeraud, 2020; Meyer, 2002; Rincon, 2001; Şahan, 2021; Tecchio, 2013; Tian, 2019.

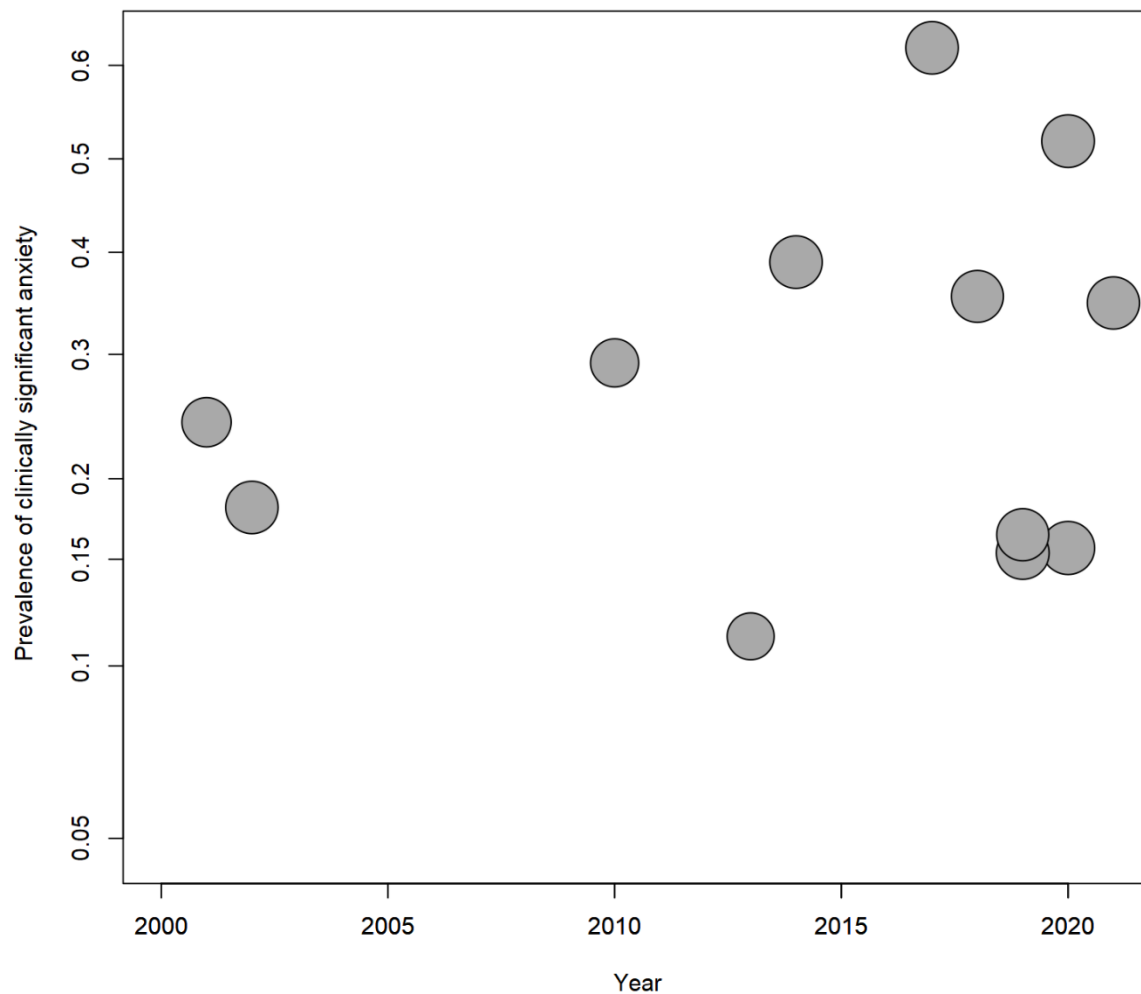
Figure A2: Bubble plot of the prevalence of clinically significant anxiety symptoms in each study against percentage of female participants.



There was no statistical evidence of an association between odds of anxiety symptoms and percentage of female participants ($p=0.247$). Each percentage point increase was associated with 1.03 (95% CI 0.98 to 1.08) times the odds of anxiety symptoms.

This analysis included data on 12 studies: Cardoso, 2010; Esteghamat, 2014; Gorini, 2020; Huang, 2019; Koc, 2017; Li, 2018; Mazeraud, 2020; Meyer, 2002; Rincon, 2001; Şahan, 2021; Tecchio, 2013; Tian, 2019.

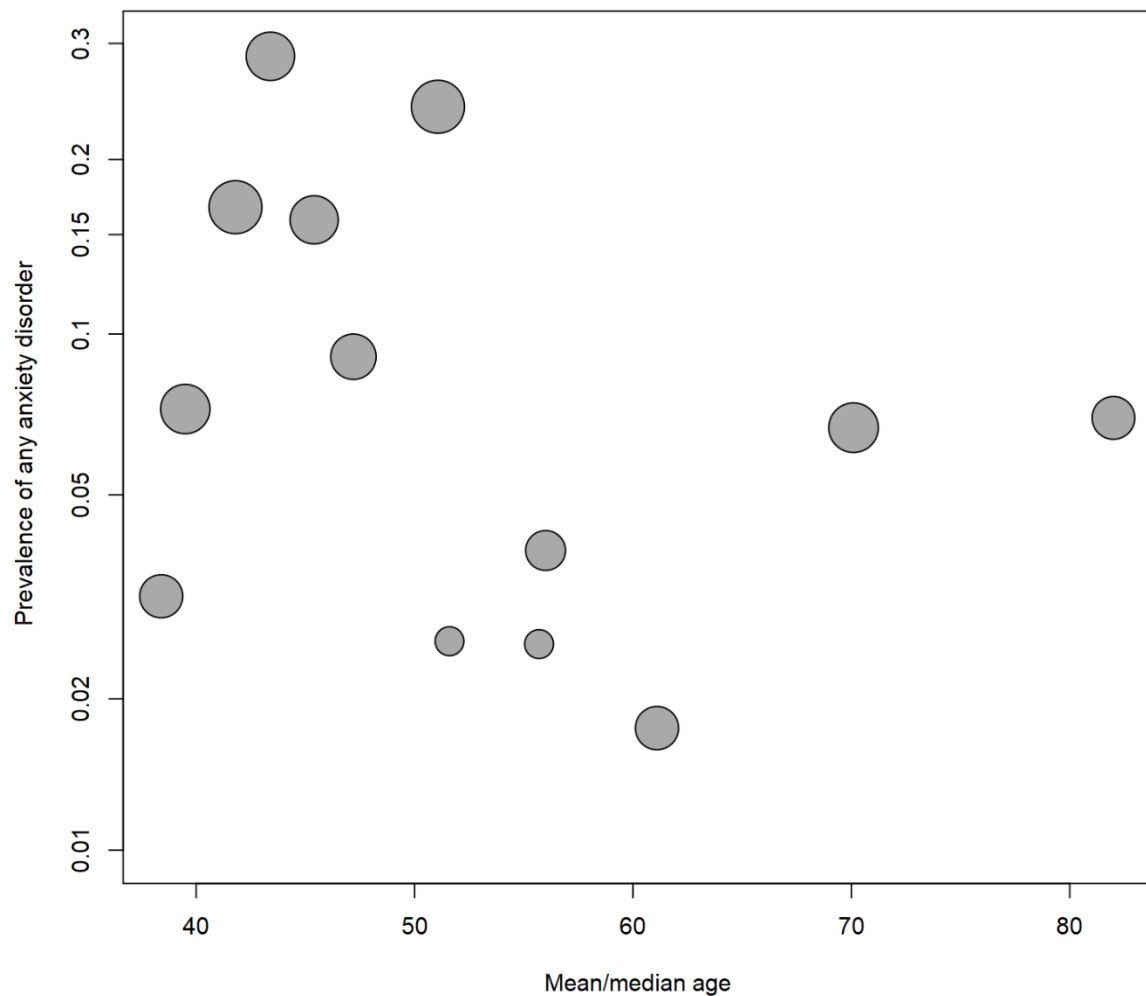
Figure A3: Bubble plot of the prevalence of clinically significant anxiety symptoms in each study against year of publication.



There was no statistical evidence of an association between odds of anxiety symptoms and year of publication ($p=0.532$). Each one year increase was associated with 1.02 (95% CI 0.95 to 1.11) times the odds of anxiety symptoms.

This analysis included data on 12 studies: Cardoso, 2010; Esteghamat, 2014; Gorini, 2020; Huang, 2019; Koc, 2017; Li, 2018; Mazeraud, 2020; Meyer, 2002; Rincon, 2001; Şahan, 2021; Tecchio, 2013; Tian, 2019.

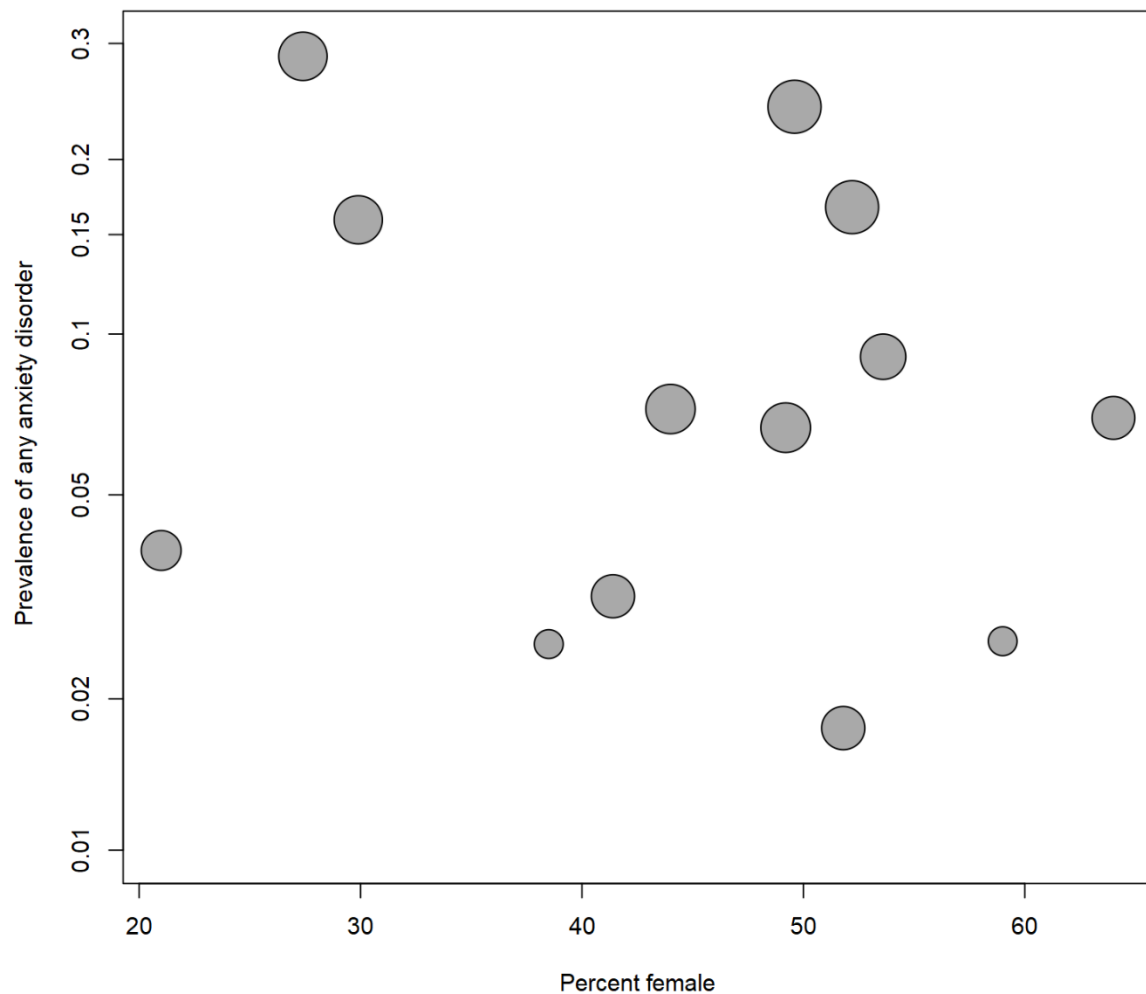
Figure A4: Bubble plot of the prevalence of any anxiety disorder in each study against mean or median age



There was no statistical evidence of an association between odds of any anxiety disorder and mean or median age ($p=0.257$). Each one year increase was associated with 0.98 (95% CI 0.94 to 1.02) times the odds of any anxiety disorder.

This analysis included data on 13 studies: Abiodun, 1990; Arolt, 1997; Burn, 1993; Dyster-Aas, 2008; Fritzsche, 2001; Kathol, 1992; Kayhan, 2013; Keller, 2004; Köroğlu, 2010; Marchesi, 2004; Palmu, 2010, 2011; Prieto, 2002; Silverstone, 1996.

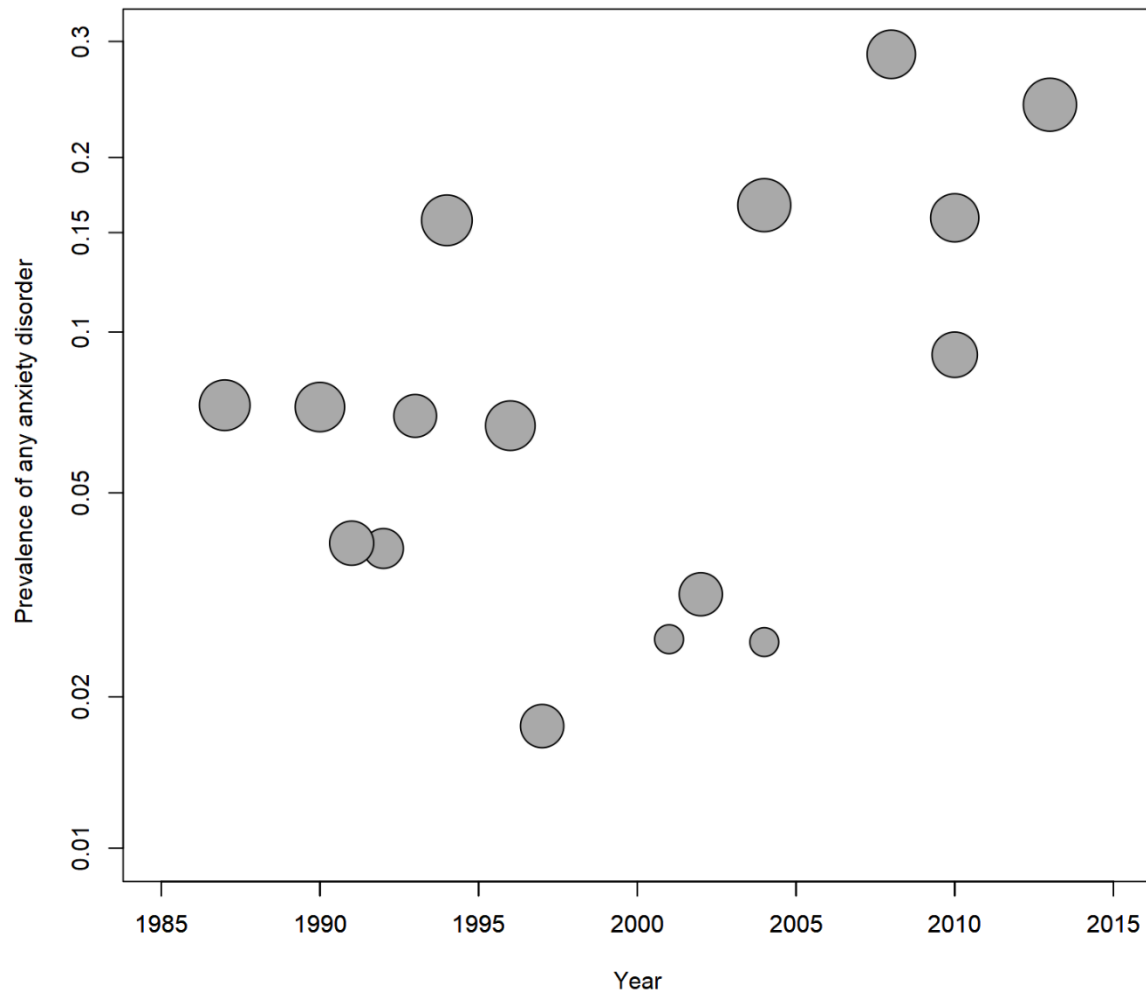
Figure A5: Bubble plot of the prevalence of any anxiety disorder in each study against percentage of female participants



There was no statistical evidence of an association between odds of any anxiety disorder and percentage of female participants ($p=0.500$). Each percentage point increase was associated with 0.99 (95% CI 0.95 to 1.03) times the odds of any anxiety disorder.

This analysis included data on 13 studies: Abiodun, 1990; Arolt, 1997; Burn, 1993; Dyster-Aas, 2008; Fritzsche, 2001; Kathol, 1992; Kayhan, 2013; Keller, 2004; Köroğlu, 2010; Marchesi, 2004; Palmu, 2010, 2011; Prieto, 2002; Silverstone, 1996.

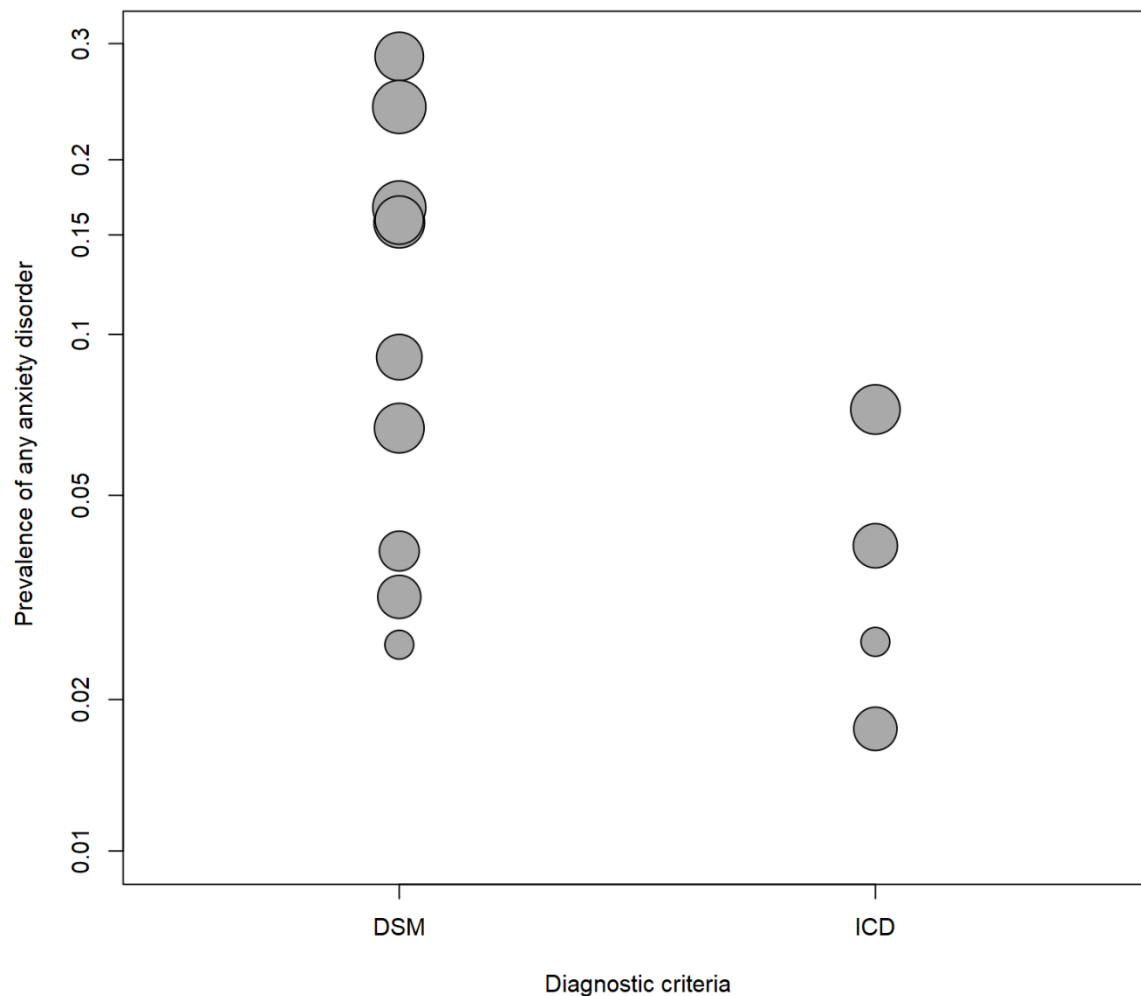
Figure A6: Bubble plot of prevalence of any anxiety disorder in each study against year of publication



There was statistically significant evidence of an association between odds of any anxiety disorder and year of publication ($p=0.004$). Each one year increase was associated with 1.06 (95% CI 1.02 to 1.10) times the odds of any anxiety disorder. Between 1990-95, the fitted prevalence of any anxiety disorder increased from 5% to 7%, and between 2005-10 it increased from 11% to 14%.

This analysis included data on 16 studies: Abiodun, 1990; Arolt, 1997; Burn, 1993; Dyster-Aas, 2008; Feldman, 1987; Fritzsche, 2001; Jenkins, 1994; Kathol, 1992; Kayhan, 2013; Keller, 2004; Kigamwa, 1991; Köroğlu, 2010; Marchesi, 2004; Palmu, 2010, 2011; Prieto, 2002; Silverstone, 1996.

Figure A7: Bubble plot of prevalence of any anxiety disorder in each study against DSM or ICD diagnostic criteria



There was statistically significant evidence of an association between odds of any anxiety disorder and diagnostic criteria ($p=0.006$). The odds of any anxiety disorder for studies that used the ICD criteria were 0.30 (95% CI 0.13 to 0.71) times the odds for studies that used the DSM criteria. The fitted prevalence of any anxiety disorder was 4% for studies that used ICD criteria and 11% for studies that used DSM criteria.

This analysis included data on 14 studies: Abiodun, 1990; Arolt, 1997; Dyster-Aas, 2008; Fritzsche, 2001; Jenkins, 1994; Kathol, 1992; Kayhan, 2013; Keller, 2004; Kigamwa, 1991; Köroğlu, 2010; Marchesi, 2004; Palmu, 2010, 2011; Prieto, 2002; Silverstone, 1996.

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 4
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Pages 5-7
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 5
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Appendix
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Pages 6-7
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Pages 6-7
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Pages 6-7
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Pages 6-7
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 6
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Pages 7-8
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	N/A
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Pages 7-8
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Pages 7-8
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Pages 7-8
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Pages 7-8

Section and Topic	Item #	Checklist item	Location where item is reported
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Pages 7-8
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 9, Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Figure 1, Appendix
Study characteristics	17	Cite each included study and present its characteristics.	Tables 1 & 2
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Appendix
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Tables 1 & 2, Figures 2-5
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Tables 1 & 2, Appendix
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Figures 2-5 Pages 10-11
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Page 12, Appendix
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Figures 2-5 Pages 10-11
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Pages 13-14
	23b	Discuss any limitations of the evidence included in the review.	Page 17
	23c	Discuss any limitations of the review processes used.	Page 17
	23d	Discuss implications of the results for practice, policy, and future research.	Pages 18-19
OTHER INFORMATION			

Section and Topic	Item #	Checklist item	Location where item is reported
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 2, page 5
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 5
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	All updates on Prospero via registration number Page 5
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 20
Competing interests	26	Declare any competing interests of review authors.	Page 20
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Data extracted and used in Tables 1 & 2; full search strategies in Appendix

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

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