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Prevalence of anxiety and depression in adults who are high users of healthcare services and magnitude of associated costs: a systematic review

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ABSTRACT

Objectives Anxiety and depression are common and associated with higher use of general healthcare services. The aims of this systematic review were to (1) estimate the prevalence of anxiety and depression in adults who are high or costly users of general healthcare services in comparison to routine users and (2) estimate the magnitude of healthcare costs associated with the presence of anxiety and depression.

Design Systematic review of the available literature.

Data sources MEDLINE, PsycINFO, EMBASE, CINAHL, PROSPERO and Cochrane Library were systematically searched without language restriction from inception to 1 April 2019 and updated on 25 October 2022, 16 October 2024 and 18 February 2026.

Eligibility criteria Eligible studies described adults aged ≥18 years who were defined as high or costly general healthcare users and where the prevalence and/or associated costs of anxiety and/or depression were quantified.

Data extraction and synthesis Three reviewers independently extracted information on study characteristics, exposure and outcomes.

Results From the 38 412 identified articles, 27 studies from 10 countries (in Europe, North America and Asia) involving 6 145 907 participants met eligibility criteria and were included. There were wide variations in the estimated prevalence of anxiety (3.8–67.2%) and depression (4.7–77.9%) among high healthcare users. The prevalence of both disorders was higher among high healthcare users than routine users in all studies with non-high user comparator groups. Only four studies investigated healthcare costs associated with depression. These uniformly reported that general healthcare costs are higher for those with depression than those without. No studies investigated costs associated with anxiety.

Conclusions Anxiety and depression are over-represented among high or costly healthcare users, although accurate quantification of the magnitude of difference is precluded by significant methodological heterogeneity and variability in definitions used. Improved identification of covert mental health problems is essential for the provision of effective interventions for patients and healthcare expenditure reduction. Future research should prioritise a standardised approach, with agreed definitions for high and/or costly healthcare use in different contexts.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This review used a comprehensive, multi-database search strategy covering a broad range of sources.
- ⇒ No language or date restrictions were applied during study selection.
- ⇒ Searches were updated at multiple time points, including during revision.
- ⇒ Independent screening, data extraction and quality appraisal were undertaken by multiple reviewers.
- ⇒ High methodological heterogeneity across included studies precluded the planned meta-analysis.

PROSPERO registration number CRD42018102628.

BACKGROUND

Across the world, a large proportion of healthcare use is incurred by a small proportion of patients.[1–4] This has been observed consistently across a range of healthcare settings, including general practice (GP),[5 6] emergency departments (ED),[7–9] hospitals[10 11] and outpatient clinics.[12] In the UK, 'frequent attenders', defined as the top 10% of all consulters, account for 43% of face-to-face consultations in primary care.[6] This population is therefore associated with disproportionately high healthcare costs. Approximately 5% of patients in the USA account for around 50% of all national healthcare expenditure.[13] It is estimated that high use of Accident and EDs, defined as five or more attendances per year, incurs a cost of at least £2.5 billion per year to the UK's National Health Service.[14]

Numerous factors contribute to the frequent use of healthcare services, one of which can be psychological distress[15]; Katon used the term 'distressed users' to describe a population of high users of primary and secondary healthcare services with significant mental health problems,[16] although distress is not always present among high healthcare

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users. Mood and anxiety disorders,[17–19] somatoform disorders,[17 18] substance use disorders[18–20] and a history of childhood abuse or neglect[21] are all associated with higher healthcare service use. A recent systematic review found that patients with severe mental illness use inpatient, emergency and primary care services for non-psychiatric medical disorders significantly more than those without.[22]

In recent years, efforts have been made to improve the care of high or costly healthcare users with variable success.[23–25] The effectiveness of care can be optimised by targeting the interventions specifically to those most likely to benefit.[26] Anxiety and depression are the most common forms of mental disorder, and specific, effective interventions to treat them in people with co-morbid physical health needs already exist.[27 28] These interventions could be adapted to target a subgroup of high or costly healthcare users, with a view to improve their health while reducing healthcare expenditure.

No published literature review has quantified the association of depression and/or anxiety with high or costly general healthcare use and the associated healthcare costs. An improved understanding of this association will highlight the need for existing treatments to be evaluated in this subgroup. This aligns with recent calls for better integration of physical and mental health services, while acknowledging the bidirectional relation between mental and physical problems.[29]

Understanding the extent to which anxiety and depression are over-represented among high users of healthcare services also has important implications for health service planning and delivery. If a substantial proportion of high-cost utilisation is associated with potentially treatable mental health conditions, this may represent an opportunity to improve patient outcomes while reducing avoidable healthcare use. This evidence is particularly relevant for policymakers and service designers seeking to develop targeted, cost-effective interventions for high-need populations. A clearer synthesis of this association may therefore inform both clinical practice and resource allocation decisions across healthcare systems. It may help prioritise early mental health intervention within high-cost populations, where the potential return on investment is greatest.

AIMS

This systematic review addresses the questions:

1. What is the prevalence of anxiety and depression in adults aged ≥18 years, who are defined as high users of healthcare or who accrue high healthcare costs, in comparison with routine healthcare users?
2. What is the magnitude of healthcare costs associated with the presence of anxiety and depression among adults who are high or costly healthcare users?

METHODS

This review was conducted according to the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) statement guidelines[30] (PRISMA checklist can be found in online supplemental file 1) to enhance the transparency and reproducibility of the review process. The protocol is registered in the PROSPERO database and has been published in *BMJ Open*.[31]

Eligibility criteria

This review included studies where cases were adults aged ≥18 years defined as high or costly users of healthcare services, and who had an anxiety and/or depressive disorder that met established diagnostic thresholds, as outlined by the authors. International, full-text peer-reviewed studies published in any language were considered for inclusion.

It is important to distinguish between the emotions of anxiety and depression, which are common and transient responses to stress, and anxiety and depressive disorders, which involve persistent and impairing symptoms that meet diagnostic criteria. Definitions of anxiety and depression can vary, encompassing both patient-reported experiences and clinician-assessed diagnoses. For the purposes of this manuscript, the terms ‘anxiety’ and ‘depression’ will be used to refer to clinically significant disorders unless otherwise specified.

Only general anxiety disorders were included in this review to maximise clinical applicability; GPs and hospital physicians are more likely to be able to identify covert general anxiety, and more established treatment pathways exist for these conditions. Specific anxiety disorders such as obsessive-compulsive disorder and post-traumatic stress disorder were considered more specialist and were therefore excluded from this review.

We included studies that described ‘high-cost patients’, ‘patients who accrue high healthcare costs’, ‘high users’, ‘distressed high users or utilisers of care’ and ‘frequent attenders’. In all studies, a validated measure of the presence of anxiety and/or depression was required, such as the application of a standardised research interview to generate a diagnosis according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-V)[32] or the International Classification of Diseases (ICD-10).[33] Studies examining general physical healthcare use in primary and secondary care were included. Studies focusing on use of mental health services or specific medical sub-specialties such as oncology were excluded. Observational studies, including retrospective and prospective cohort studies, case-control and cross-sectional studies, were considered. Case studies and series and interventional studies were excluded.

Search strategy

A comprehensive search strategy was developed in collaboration with content experts and information specialists at the Universities of Birmingham and Manchester to retrieve articles relevant to the aims of the review. The following electronic databases were searched systematically without language restriction from inception to 1 April 2019 and updated on 25 October 2022, 16 October 2024

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Table 1 Inclusion criteria checklist based on the PRISMA guidelines

Study design	Cohort studies (retrospective and prospective) Case–control and nested case–control studies Cross-sectional studies
Participants	Adults aged ≥18 years High healthcare users and/or accruing high healthcare costs Presence of anxiety and/or depression that meets established diagnostic criteria
Comparator	Routine healthcare users Frequent/high-cost users without anxiety/depression
Outcome	Prevalence of anxiety and/or depression in high users of healthcare and/or high-cost patients Magnitude of cost or use of healthcare associated with the presence of anxiety and/or depression

and 18 February 2026: MEDLINE, PsycINFO, EMBASE, CINAHL, PROSPERO and the Cochrane Library. The updated searches did not identify any additional eligible studies published since the original search. The reference lists of all articles returned by the database searches were hand-searched to maximise the likelihood of identifying all relevant studies. Search strategies for each database are shown in online supplemental file 2).

Study selection

The records retrieved by the searches were imported into Clarivate EndNote software (X9, Clarivate Analytics, Philadelphia, PA)[34] to facilitate reference management. The 'Find Duplications' EndNote function was used to identify duplicate records (based on authors, year and title); duplicate entries were manually removed and only the most complete record was retained. Two reviewers (FJ and OCL) then independently reviewed the titles and abstracts to ascertain eligibility for full-text screening and labelling; excluded records were labelled with the rationale for their exclusion. Three reviewers (DR, FJ, AKT) then independently reviewed full-text versions to determine suitability for inclusion. This was achieved by referring to an inclusion criteria checklist, shown in table 1, determined a priori to ensure consistency with the review process and adherence to the PRISMA guidelines.[30] Excluded records were labelled with the rationale for their exclusion. Any disagreement during this stage was resolved by discussion and involvement of a third or fourth reviewer (EG and AB).

Data extraction

A standardised data extraction form was developed a priori based on the framework by Hayden and colleagues[35] (see online supplemental file 3). The form was developed iteratively, focusing on population, comparator, outcome and study design, before being independently piloted by two reviewers (FJ, OCL) on existing papers. Following initial familiarisation with the studies eligible for full-text inclusion, three reviewers (DR, FJ, AKT) extracted the following information using the form: study design, study details (author(s), publication year, country, language of publication), recruitment setting, sample size, demographic information (sex, ethnicity), criteria used to define high use or high costs, method(s) used to record anxiety/depression (self-report measure, validated or non-validated, clinical interview), prevalence of depression and anxiety, healthcare use, costs and associated ranges and the methods used to evaluate this. Authors were contacted directly in the case of missing data. Data extraction was verified by two other reviewers (AB, EG) to ensure consistency across the data extracted. Any discrepancies or disagreements were resolved by discussion and re-visiting the relevant article together. Extracted data were also compiled in a Microsoft Excel spreadsheet to ensure consistency in the review process.

Quality assessment

Three reviewers (DR, FJ, AKT) assessed the quality of each included article to minimise bias. This was achieved by completing a modified form of the Ottawa-Newcastle Scale[36] assessing the quality of cohort, case-control and cross-sectional studies. The form was first piloted by two researchers (FJ, OCL) to ensure feasibility and suitability. Quality assessment included consideration of sampling strategy, methods used to establish exposure and outcome, and analytic method employed. In articles with multiple outcomes of interest, assessment of the method used to establish each outcome was undertaken separately, and consideration and adjustment for confounders were assessed in relation to the outcome of interest (prevalence and/or associated cost). The stages and domains of this tool are shown in online supplemental file 4). The quality assessment process was then independently verified by two other reviewers (AB, EG) to minimise the contribution of personal judgments and subjectivity to the assessment. Differences in opinion were resolved by consensus and discussion among the reviewers. Risk of bias was presented in accordance with recommendations from the Cochrane Collaboration[37 38]; instead of a composite score, risk was categorised as 'high risk', 'low risk' or 'unclear' for each domain.

Statistical analysis

Prevalence estimates were extracted or calculated from the data available, and considered separately for age, gender, ethnicity and definition of caseness, where applicable. They were reported as frequency (%) or OR with 95% CIs between groups. The level of heterogeneity between study data was explored. We planned to quantify

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heterogeneity using the I^2-statistical test with 95% CI, if appropriate.

The magnitude of healthcare utilisation and costs associated with high or costly users were extracted for each study, where applicable. Where reported, differences between the cost or healthcare use associated with the presence of anxiety and/or depression were recorded. Standardised mean differences with accompanying 95% CI and median OR of costs of healthcare utilisation were extracted. We did not plan to pool or calculate costs or health use across studies. In cases of insufficient data, authors were contacted twice by email; once initially, with one reminder sent if no response was received.

Due to substantial heterogeneity in study design, populations and outcome definitions, quantitative pooling was not considered appropriate and a narrative synthesis approach was adopted. Studies were grouped according to key themes, including (1) prevalence of anxiety, (2) prevalence of depression and (3) magnitude of associated healthcare costs. Within these groupings, findings were examined by clinical setting (primary vs secondary care), diagnostic approach (eg, structured interview, self-report and administrative data) and presence of comparator groups. Patterns in prevalence estimates, relative effect measures (eg, ORs) and cost differences were assessed, alongside the consistency and direction of effects. Findings were interpreted in light of study quality and risk of bias.

Patient and public involvement statement

Patients and the public were not involved in the design and conduct of this systematic review. The research question was informed by the lack of existing literature examining the outcomes of interest: prevalence of anxiety and/or depressive disorders in high healthcare users or those who accrue high healthcare costs and the magnitude of healthcare use associated with anxiety and/or depression across adult populations in any general healthcare setting.

RESULTS

Literature search

The search strategy yielded 38 412 articles (MEDLINE: n=23 613; PsycINFO: n=768; EMBASE: n=13 933; CINAHL: n=98; PROSPERO: n=0; the Cochrane Library: n=0). Additional reference searches found no further studies. After excluding 618 duplicates, the titles and abstracts of 37 794 articles were screened for relevance. Title and abstract screening resulted in the exclusion of 37 706 articles, mainly because they did not provide information on healthcare use or the presence of anxiety and/or depression. Of the 88 reports sought for retrieval, 59 were excluded at full-text review. A further two studies were excluded because the full-text articles could not be retrieved. The details of the 61 studies excluded at the final stage can be found in online supplemental file 5). 27 articles[16 17 39–63] were included in the final analysis. A flow diagram of the study identification process, including reasons for exclusion at each stage, is presented as a PRISMA flow diagram[30] in figure 1.

Study characteristics

27 studies involving 290 844 high healthcare users, 5 851 248 comparators and 3815 individuals from one study[53] who were not divided into high or regular healthcare users were included in the final analysis. Variation was detected between studies regarding study design and setting, data source and collection, definitions of high healthcare use, anxiety and depression, and reported prevalence rates. Included studies were from 10 countries, with most being performed in the USA (n=9), followed by the Netherlands (n=3), the UK (n=3) and Spain (n=3). Most studies took place in primary care or used primary care data (n=17), followed by secondary care (n=9), and one study looked at the number of referrals from primary care to secondary care.[62]

14 studies included a non-high healthcare user comparator group and 13 focused on describing the characteristics of high healthcare users without comparators. 17 studies had a cross-sectional design, six were cohort studies and four were case-control studies. Age and sex were inconsistently reported across studies. The mean age of participants ranged from 37 to 82.8 years in the high healthcare user group and from 38.8 to 72.4 years in the comparator group. The percentage of female participants ranged from 5.0 to 77.5 in the high user group and from 50.3 to 77.5 in the comparator group. Only five studies reported the ethnicity of participants[16 45 48 59 60] and the proportion who were White ranged from 14.4–92.3%. An overview of study characteristics, including study design and the presence of a comparator, can be found in table 2.

Study quality

None of the included studies had a low risk of bias in all domains, according to the adapted checklist of the Ottawa-Newcastle Scale.[36] 26 of the 27 studies clearly defined the process of selecting participants (low risk of bias), and 23 adequately described the study population. Exposure and outcome were almost universally well-described; all 27 studies presented valid measures for ascertaining high or costly service use (the exposure of interest), and 23 used appropriate outcome measures (prevalence of anxiety and/or depression and/or associated costs). For all studies, the analytic approach utilised was appropriate, and 17 studies had a low risk of bias of analysis and methods to control for confounders. No studies had a low risk of bias relating to sample size, due to either an absence (n=25) or poor description (n=2) of the sample size calculation. Table 3 displays the review quality scores per item based on the adapted Ottawa-Newcastle scale.[36]

Diagnostic tools/measures used

13 of the 27 included studies measured the presence of anxiety[16 17 39 42 45 46 52 53 56 59–61 63]; these are listed in online

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supplemental file 6). Significant diversity in the measures used to ascertain the presence of anxiety was noted: diagnostic instruments with structured interviews were used in eight studies,[16 17 46 52 53 56 59 61] self-reported symptom checklists were used in two studies[39 63] and diagnoses were extracted from medical records in two studies.[42 45] In one study, the presence of anxiety was ascertained by identifying diagnostic codes in administrative healthcare claims for patients from a commercially insured population in the USA.[60]

The presence of depression was measured in 25 of the included studies[16 17 39–51 53–59 61–63]; these are listed in table 3. Like for anxiety, a variety of diagnostic tools were used to ascertain the presence of depression; 11 studies used structured interviews,[16 17 44 46 53–57 59 61] 10 studies used self-reported symptom checklists,[39 41 43 47 49–51 58 62 63] and 3 studies used diagnoses documented in medical records.[42 45 48] In one study, the presence of depression was ascertained by identifying diagnostic codes in inpatient and outpatient claims from a private healthcare database.[40]

There were a variety of definitions and thresholds used to identify populations of high or costly users of healthcare. The most common approach was to classify high or costly users as those who exceeded a threshold number of contacts with healthcare providers per unit time; this was utilised in 15 of the included studies.[17 39 41 42 45 46 51 52 54 56–59 61 62] However, there was considerable diversity in the cut-off chosen, and this ranged from three or more referrals in a 5-year period[62] to five or more visits to the primary care practitioner

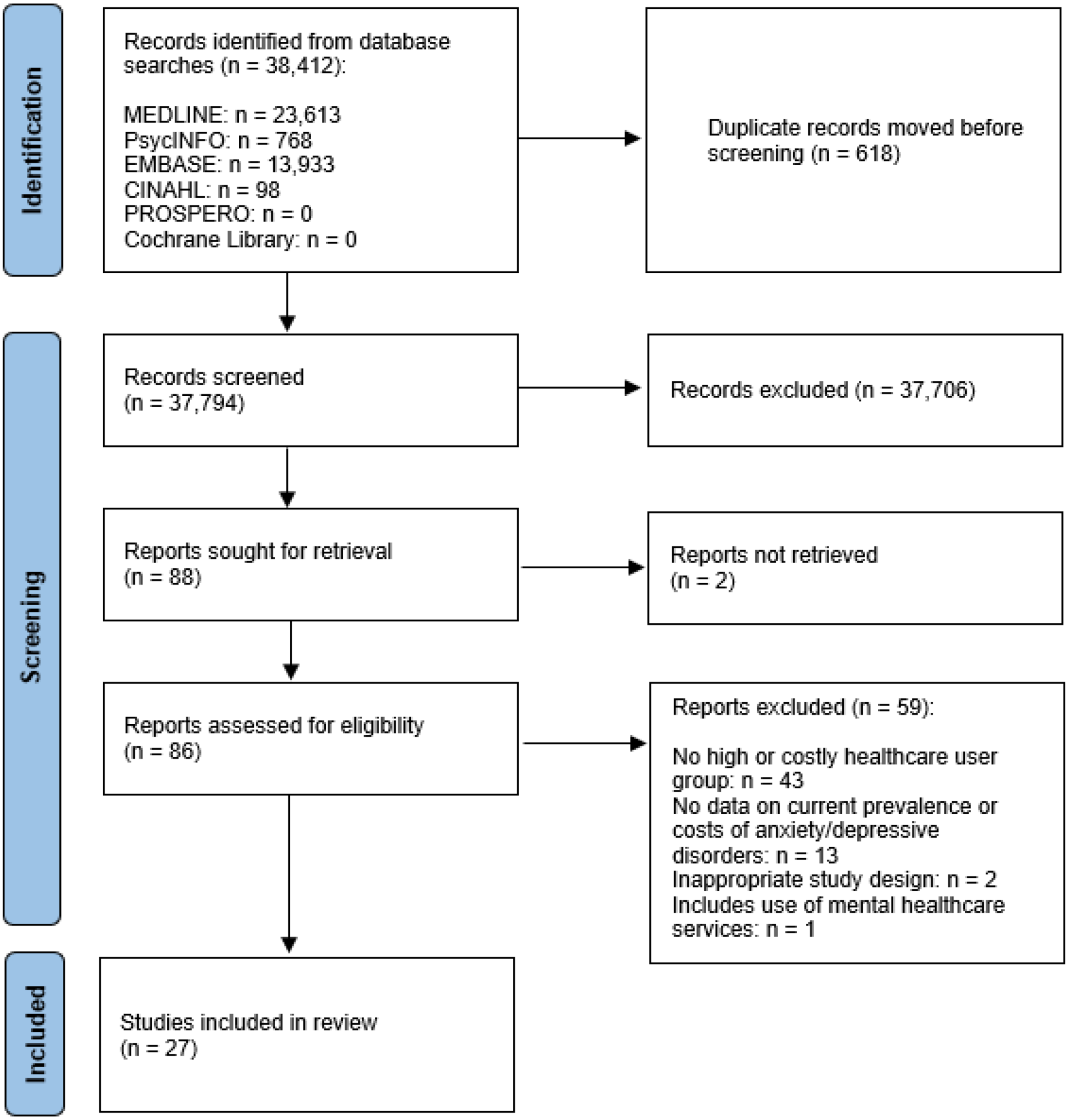

Figure 1 Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) flow diagram of the study selection process.

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Table 2 Characteristics of included studies

Study characteristics					High users				Comparators			
Study	**Year**	**Origin**	**Setting**	**Study design**	**Number of participants**	**Mean age in years (SD)**	**Sex (% female)**	**Ethnicity (% white)**	**Number of participants**	**Mean age in years (SD)**	**Gender (% female)**	**Ethnicity (% white)**
Agarwal *et al*[39]	2019	Canada	Secondary care	Cross-sectional	67	Not reported	50.7	Not reported	No comparator group			
Ash *et al*[40]	2001	USA	Secondary care	Cohort	13 328	Not reported	Not reported	Not reported	No comparator group			
Berghofer *et al*[41]	2014	Germany	Primary care	Cross-sectional	507	Not reported	Not reported	Not reported	753	Not reported	Not reported	Not reported
Demers[42]	1995	Canada	Secondary care	Cohort	3639	Not reported	58.0	Not reported	5 842 471	Not reported	Not reported	Not reported
Dowrick *et al*[43]	2000	UK, Spain	Primary care	Case-control	127	*46.1	73.2	Not reported	175	*45.1	50.3	Not reported
Ferrari *et al*[44]	2008	Italy	Primary care	Case-control	50	50.7 (12.9)	76.0	Not reported	50	38.8 (14.8)	56.0	Not reported
Ford *et al*[45]	2004	USA	Primary care	Case-control	250	54.0 (19.4)	50.0	88.0	250	69.0 (17.6)	Not reported	94.5
Gili *et al*[46]	2011	Spain	Primary care	Cohort	318	53.3 (13.9)	67.6	Not reported	203	46.7 (14.3)	62.1	Not reported
Henk *et al*[47]	1996	USA	Primary care	Cohort	786	Not reported	Not reported	Not reported	No comparator group			
Hunter *et al*[48]	2015	USA	Secondary care	Cross-sectional	261 515	*63.4	5.0	69.5	No comparator group			
Jakobsson *et al*[49]	2011	Sweden	Secondary care	Cohort	13	82.8 (6.3)	46.2	Not reported	50	*83.9	*74.0	Not reported
Katon *et al*[16]	1990	USA	Primary care	Cross-sectional	119	45.1 (12.6)	62.1	77.2	No comparator group			
Katzelnick *et al*[50]	1997	USA	Secondary care	Cross-sectional	512	53.2 (14.4)	66.6	Not reported	482	50.1 (16.9)	59.5	Not reported
Koskela *et al*[51]	2010	Finland	Primary care	Cohort	85	52.7 (95% CI 50.3 to 55.2)	69.4	Not reported	No comparator group			
Kujanpaa *et al*[52]	2014	Finland	Primary care	Cross-sectional	150	62.7 (13.0)	69.3	Not reported	No comparator group			
Luciano *et al*[53]	2010	Spain	Primary care	Cross-sectional	Demographic data only reported for entire sample 3815 participants, mean age 54.3 years (SD 17.31), 63% female, ethnicity not reported							
Menchetti *et al*[54]	2006	Italy	Primary care	Cross-sectional	262	Not reported	*66.0	Not reported	1592	Not reported	*65.5	Not reported
Patel *et al*[17]	2015	UK	Primary care	Case-control	71	57.0 (19.0)	77.5	Not reported	71	56.0 (18.0)	77.5	Not reported
Pearson *et al*[55]	1999	USA	Primary care	Cross-sectional	7203	*47.5	*69.1	Not reported	No comparator group			
Portegijs *et al*[56]	1996	Netherlands	Primary care	Cross-sectional	106	Not reported	61.3	Not reported	No comparator group			
Portegijs *et al*[57]	1996	Netherlands	Primary care	Cross-sectional	80	37 (not specified further)	56.3	Not reported	No comparator group			
Press *et al*[58]	2012	Israel	Primary care	Cross-sectional	94	74.6 (5.5)	60.6	Not reported	86	72.4 (5.5)	57.0	Not reported
Rentas *et al*[59]	2019	USA	Secondary care	Cross-sectional	195	Not reported	50.3	14.4	No comparator group			
Robinson *et al*[60]	2016	USA	Secondary care	Cross-sectional	193	49.3 (11.0)	77.2	92.3	1728	46.2 (11.7)	77.1	90.8
Schmitz *et al*[61]	2002	Germany	Secondary care	Cross-sectional	389	45.4 (13.1)	63.7	Not reported	3337	40.8 (13.1)	51.8	Not reported

Continued

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Table 2 Continued

Study characteristics					High users			Comparators	
Sharpe *et al*[62]	2012	UK	Referrals from primary to secondary care	Cross-sectional	162	50.8 (10.3)	59.3	Not reported	No comparator group
Smits *et al*[63]	2014	Netherlands	Primary care	Cross-sectional	623	52 (not specified further)	52.7	Not reported	No comparator group

*Not reported but calculated manually by the reviewers.

in a 3-month period.[41] Another definition used in nine studies[16 40 47 48 50 53 55 60 63] involved a top percentage of healthcare users, ranging from the top 25%[53] to the top 0.5%.[40] The remaining studies had unique definitions of high or costly users. Ferrari and colleagues generated a list of individuals with the highest number of primary care contacts and worked down this list until fifty participants were recruited,[44] and Jakobsson and colleagues used hierarchical clustering analysis to define high users.[49] Dowrick and colleagues defined high users as those whose annual rate of consultation was at least twice as high as the primary care practice's sex- and age-related mean.[43]

In view of the large methodological heterogeneity between the studies included in the review, and wide variations in the definitions used to identify high or costly healthcare users and the presence of anxiety and depression, we decided that a meta-analysis would not provide a meaningful summary and instead decided to describe the main findings narratively.

Prevalence estimates for anxiety

13 studies measured the presence of anxiety in high or costly users [16 17 39 42 45 52 56 59–61 63] and prevalence estimates ranged from 3.8%[56] to 67.2%.[39] Five studies[17 45 46 60 61] reported the prevalence of anxiety among a non-high user comparator group; this prevalence rate ranged from 2.0%[45] to 39.3%.[60] In all five studies, the prevalence of anxiety was higher among high healthcare users than among comparators. No studies reported prevalence data by age group or gender.

Four studies[17 45 46 53] reported ORs instead of, or in addition to, prevalence estimates, to summarise the difference in the presence of anxiety between the two groups. The ratios reported in the included studies ranged from 0.50 (95% CI 0.2 to 1.9)[46] to 20.0 (95% CI 3.2 to 829.0).[17] Two studies[17 45] reported an OR of greater than one (ie, greater odds of an anxiety disorder in high user group compared with comparator). Both were statistically significant; OR 4.3 (95% CI 1.6 to 11.5)[45] and OR 20.0 (95% CI 3.2 to 829.0).[17] The other two studies[46 53] reported an OR of less than one (ie, greater odds of anxiety in comparator group compared with high users). Of these two, only the OR reported by Luciano and colleagues was statistically significant (OR 0.58, 95% CI 0.34 to 0.98), and this was when high healthcare users were defined as the top 25% consulting patients in a 1-year period, stratified by the presence of physical and mental conditions.[53]

For the reader's interest, we calculated unadjusted ORs and 95% CIs for studies where these were not reported, using the number of events in the high user and non-high user groups where possible. These calculations were conducted for two studies.[60 61] In both cases, the ORs were greater than one; OR 1.4 (95% CI 1.1 to 1.9)[60] and OR 1.5 (95% CI 1.0 to 2.2).[61] These suggest that anxiety is more prevalent among high healthcare users than in routine use comparators. The prevalence rates and ORs of anxiety in the included studies, including those

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Table 3 Quality assessment of included studies

Reference	Selection of participants	Adequate description of study population	Validated method for ascertaining exposure	Validated method to confirm outcome	Analysis and controls for confounders	Sample size calculation	Analytical methods appropriate
Agarwal *et al*[39]	Low risk	Low risk	Low risk	Low risk	N/A*	Not reported†	Low risk
Ash *et al*[40]	Low risk	Low risk	Low risk	Unclear	N/A*	High risk	Low risk
Berghofer *et al*[41]	High risk	Unclear	Low risk	Low risk	High risk	Not reported†	Low risk
Demers[42]	Low risk	Unclear	Low risk	High risk	N/A*	Not reported†	Low risk
Dowrick *et al*[43]	Low risk	Low risk	Low risk	Low risk	Low risk	Not reported†	Low risk
Ferrari *et al*[44]	Low risk	Low risk	Low risk	Low risk	High risk	Not reported†	Low risk
Ford *et al*[45]	Low risk	Low risk	Low risk	High risk	Low risk	Not reported†	Low risk
Gili *et al*[46]	Low risk	Low risk	Low risk	Low risk	Low risk	High risk	Low risk
Henk *et al*[47]	Low risk	High risk	Low risk	Low risk	Low risk	Not reported†	Low risk
Hunter *et al*[48]	Low risk	Low risk	Low risk	High risk (prevalence) Low risk (costs)	Low risk	Not reported†	Low risk
Jakobsson *et al*[49]	Low risk	Low risk	Low risk	Low risk	High risk	Not reported†	Low risk
Katon *et al*[16]	Low risk	Low risk	Low risk	Low risk	N/A*	Not reported†	Low risk
Katzelnick *et al*[50]	Low risk	Low risk	Low risk	Low risk	High risk	Not reported†	Low risk
Koskela *et al*[51]	Low risk	Low risk	Low risk	Low risk	Low risk	Not reported†	Low risk
Kujanpaa *et al*[52]	Low risk	Low risk	Low risk	Low risk	N/A*	Not reported†	Low risk
Luciano *et al*[53]	Low risk	Low risk	Low risk	Low risk	Low risk	Not reported†	Low risk
Menchetti *et al*[54]	Low risk	Low risk	Low risk	Low risk	Low risk	Not reported†	Low risk
Patel *et al*[17]	Low risk	Low risk	Low risk	Low risk	Low risk	Not reported†	Low risk
Pearson *et al*[55]	Low risk	High risk	Low risk	Low risk	N/A*	Not reported†	Low risk
Portegijs *et al*[56]	Low risk	Low risk	Low risk	Low risk	Low risk	Not reported†	Low risk
Portegijs *et al*[57]	Low risk	Low risk	Low risk	Low risk	Low risk	Not reported†	Low risk
Press *et al*[58]	Low risk	Low risk	Low risk	Low risk	Low risk	Not reported†	Low risk
Rentas *et al*[59]	Low risk	Low risk	Low risk	Low risk	Low risk	Not reported†	Low risk
Robinson *et al*[60]	Low risk	Low risk	Low risk	Low risk	Low risk	Not reported†	Low risk
Schmitz *et al*[61]	Low risk	Low risk	Low risk	Low risk	Low risk	Not reported†	Low risk
Sharpe *et al*[62]	Low risk	Low risk	Low risk	Low risk	Low risk	Not reported†	Low risk
Smits *et al*[63]	Low risk	Low risk	Low risk	Low risk	Low risk	Not reported†	Low risk

Low risk’ indicates low risk of bias in that domain; ‘high risk’” indicates high risk of bias; ‘unclear’ indicates where risk of bias was unclear.
*‘N/A’ indicates that this criterion was not applicable as only descriptive data were presented and/or groups were not compared.
†‘Not reported’ indicates that a sample size calculation was not provided, precluding commentary on bias for this criterion.

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calculated manually by the reviewers, are summarised in online supplemental table 1).

Prevalence estimates for anxiety according to diagnostic criteria

Diverse methods and criteria were used in the included studies to ascertain the presence of anxiety. Two studies reported prevalence estimates according to self-completed questionnaires; Agarwal and colleagues administered the EQ-5D-3L[39] and Smits and colleagues administered the Patient Health Questionnaire (PHQ)[63]. The prevalence of anxiety ranged from 7%[63] to 67.2%[39] among high healthcare users; neither reported prevalence estimates among non-high user comparators. Three studies[42 45 60] reported prevalence estimates of anxiety according to ICD criteria—either ICD-9[42 60] or unspecified[45]—derived from participant records, although two used medical records[42 45] and one used administrative claim records.[60] The rates ranged from 8.0%[45] to 48.2%[60] among high healthcare users, and 2.0%[45] to 39.3%[60] among comparators. The only included study to use the SCAN interview to diagnose anxiety according to ICD-10 criteria was by Gili and colleagues.[46]

The remaining seven studies[16 17 52 53 56 59 61] used differing structured interviews to estimate the prevalence of anxiety according to DSM criteria, although the version of DSM used also differed between them. Five studies used DSM-IV criteria[17 52 53 59 61] and two used DSM-III-R criteria.[16 56] The prevalence of anxiety according to DSM-IV criteria ranged from 4.0%[52] to 32.4%[17] among high users and 4.4%[17] to 5.4%[61] among comparators. The prevalence of anxiety among high users according to DSM-III-R criteria ranged from 3.8%[56] to 21.8%[16]; neither of these two studies had a comparator group. There was great variation in the interview schedules used; two studies used Structured Clinical Interview for DSM Disorders (SCID)[17 53], one used Diagnostic Interview Schedule (DIS)[16], one used Mini International Neuropsychiatric Interview (MINI)[52], one used the Composite International Diagnostic Interview (M-CIDI)[61], one used a comprehensive behavioural health assessment[59] and one used a specifically designed questionnaire.[56] The wide breadth of tools used precludes summary of prevalence ranges according to interview schedule; prevalence estimates from each included article can be found in online supplemental table 1).

Prevalence estimates for anxiety according to clinical setting

Of the 12 included studies that reported prevalence estimates for anxiety, seven took place in a primary care setting.[16 17 45 46 52 56 63] In primary care, prevalence estimates for anxiety ranged from 3.8%[56] to 32.4%[17] among high healthcare users, and from 2.0%[45] to 4.4%[17] among non-high user comparators. The remaining five studies[39 42 59–61] took place in the secondary care setting, and the prevalence of anxiety varied from 7.7%[61] to 67.2%[39] among high users and from 5.4%[61] to 39.3%[60] among comparators.

Prevalence estimates for depression

21 studies reported the prevalence of depression among high or costly healthcare users.[16 17 39–46 48–51 55 56 58 59 61–63] We also calculated the prevalence of depression among high users using raw data where possible; this was calculated for two further studies.[54 57] Prevalence estimates for depression among high users ranged from 4.7%[56] to 77.9%.[58] Nine studies reported the prevalence of depression among non-high user comparators,[17 41 43–46 50 58 61] and we manually calculated the prevalence of depression among comparators for the two studies where this was possible.[49 54] The reported prevalence among comparators ranged from 3.8%[61] to 53.5%.[49] In all 11 studies with prevalence rates available for the two groups, the prevalence of depression was higher among high healthcare users than among comparators. No studies reported prevalence data by age group or gender.

Six studies[17 43 45 46 53 58] reported ORs instead of, or in addition to, prevalence estimates, to summarise the difference in the presence of depression between the two groups. The ratios reported in the included studies ranged from 1.0 (95% CI 0.75 to 1.34)[53] to 26.6 (95% CI 12.4 to 56.8).[43] Of these six studies, five[17 43 45 46 58] reported a statistically significant OR greater than one (ie, in favour of a greater odds of depression in high users vs comparators). The other study[53] provided six different ORs, each for a different definition of high users. Of these ORs, two were statistically insignificant, and four were significantly greater than one, suggesting that depression is more common among high users than in non-high user comparators.

We manually calculated unadjusted ORs and 95% CIs for studies where these were not reported, using the raw data provided. These calculations were conducted for six studies.[41 44 49 50 54 61] These ORs ranged from 1.7 (95% CI 1.1 to 2.6)[61] to 14.7 (95% CI 3.2 to 67.6).[44] In all cases, the ORs were greater than one and statistically significant, suggesting that depression is more prevalent among high healthcare users. The prevalence rates and ORs of depression in the included studies, including those calculated manually by the reviewers, are summarised in online supplemental file 6).

Prevalence estimates for depression according to diagnostic criteria

A wide variety of tools and diagnostic criteria were used to ascertain the presence of depression and to estimate its prevalence among high healthcare users and routine user comparator groups.

Nine studies[39 41 43 49–51 58 62 63] used self-completed questionnaire items to ascertain depression among participants. Tools used included variations of the PHQ[41 62 63], Beck Depression Inventory (BDI)[43 51], Geriatric Depression Scale (GDS)[49 58], EQ-5D-3L[39] and the Medical Outcomes Study (MOS) depression screen.[50] The estimated

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prevalence of depression among high healthcare users according to these self-reported measures ranged from 5%[63] to 77.9%,[58] and prevalence estimates among routine user comparators ranged from 5.1%[43] to 53.5%.[49]

Four studies[40 42 45 48] reported prevalence estimates for depression according to ICD criteria—either ICD-9[40 42 48] or unspecified[42]—derived from participant records. Three of these studies used medical records,[42 45 48] and one used inpatient and outpatient medical claim records.[40] Estimates for the prevalence of depression according to participant records among high healthcare users were varied, ranging from 4.8%[40] to 29%.[48] Only one of these studies included a comparator group, and the prevalence of depression among routine healthcare users was 7%.[45]

The remaining 10 studies[16 17 44 46 54–57 59 61] used structured interviews with participants to identify the presence of depression according to established criteria. Two studies[46 54] used ICD-10 criteria and found the prevalence of depression ranged from 16.0%[54] to 19.8%[46] among high users and from 5.4%[46] to 16.0%[54] among comparators. Three studies[16 56 57] used the DIS to identify depression according to DSM-III-R criteria. None of these three studies included a comparator group, but the prevalence of depression among high users according to DSM-III-R was reported to be from 4.7%[56] to 23.5%.[16] Five studies[17 44 55 59 61] used interviews to identify depression according to DSM-IV criteria. The prevalence estimates among high users were 6.2%[61] to 45.6%,[17] and among routine users the estimates were 3.8%[61] to 20.6%.[17]

Prevalence estimates for depression according to clinical setting

Of the 23 studies that either reported prevalence estimates for depression or, where it was possible for the reviewers to manually calculate the estimates, 14 took place in the primary care setting.[16 17 41 43–46 51 54–58 63] In primary care, estimates for the prevalence of depression among high healthcare users ranged from 4.7%[56] to 77.9%,[58] and the estimates among non-high user comparators ranged from 4.0%[44] to 20.6%.[17] Eight studies took place in a secondary care setting.[39 40 42 48–50 59 61] In secondary care, estimates for the prevalence of depression ranged from 4.8%[40] to 67.2%[39] among high users, and from 3.8%[61] to 53.5%[49] among comparators. The remaining study[62] used the number of referrals from primary care to specialist services to identify high healthcare users; its findings were therefore not included in either primary or secondary care estimates.

Magnitude of associated costs

Only four studies included in the review investigated the magnitude of healthcare costs associated with the presence of depression in high users of healthcare,[40 47 48 60] and no studies investigated costs associated with anxiety. Although all four studies originated from the USA, the variety of definitions used to define high healthcare use (as summarised in online supplemental table 1) precluded the pooling of healthcare estimates. Therefore, we have summarised the main findings narratively. Cost estimates across studies are derived from figures from different healthcare systems, time periods, costing methodologies, type of costs included (eg, direct medical, non-medical, indirect) and cost perspectives (healthcare vs societal). Moreover, they are reported in different currencies, without conversions, standardisation for inflation or purchasing power parity. As such, direct comparisons of these cost estimates should be interpreted with caution. Here, we present these descriptively with indicative, rather than definitive, interpretations.

Ash and colleagues analysed the Medstat's MarketScan Research Database which consisted of inpatient and ambulatory healthcare records of individuals covered by employee-sponsored benefit plans during 1997 and 1998.[40] The Diagnostic Cost Group hierarchical condition category prospective model was used to identify the higher cost patient tier of having 10 or more comorbidities identified in the notes. Individuals with depression incurred 2.3 times higher healthcare costs than their disease cohort average ($1651).

Henk and colleagues[47] examined a sample of high utiliser patients enrolled with a prepaid health maintenance organisation in Madison, Wisconsin to determine whether high healthcare users with depression incur higher medical costs compared with high users without depression in the next year. The total average medical and pharmaceutical costs associated with high utilisers with depression were $239.05 (SD±601.76) and $279.62 (SD±428.23) respectively, with average annual costs of $5509.50 (SD±5426.70), $6681.60 (SD±8091.30) and $5764.30 (±7260.10) for years 1, 2 and 3 respectively. In contrast, the total average medical and pharmaceutical costs for high utilisers without depression were lower at $24.98 (SD±136.78) and $50.85 (SD±202.29), with average annual costs of $5359.50 (SD±5783.30), $6540.00 (SD±7568.80) and $4227.00 (SD±5483.10) for years 1, 2 and 3. Following regression analyses adjusting for age, gender, benefit package and co-morbidity, depressed high utilisers incurred 26% (range 20–33%; p<0.01) higher expenditure than high utilisers without depression.

Hunter and colleagues investigated use and associated costs of mental and medical-surgical care among the costliest 5% of veteran affairs (VA) patients with and without a diagnosis of mental health and across various groups of high-cost patients with mental health conditions.[48] They used VA administrative records from October 2009 to September 2010 to identify eligible patients. Among patients receiving treatment for depression, the total cost for the fiscal year 2010 was $65 643 and the total mental health cost for the same year was $7407. Therefore, cost associated with general services equates to $58 236 per year.

Finally, Robinson and colleagues compared high users with a history of depression (HUDs) with a comparator group of non-high users with depression (non-HUDs) using administrative data derived from the HealthCore Integrated Research Database.[60] This database stores

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data regarding medical and pharmacy costs from across 14 geographically diverse US health plans. HUDs were in the top 10% of total all-cause costs in the preceding 12 months. Mean annual healthcare costs were eight times higher in HUDs ($56 145) compared with non-HUDs ($6954). The all-cause physician office mean costs, all-cause outpatient costs, mental health-related outpatient costs, all-cause ED costs and mental health-related ED costs for HUDs were $4574 (SD $5900), $19 603 (SD $31 033), $3177 (SD $11 434), $1856 (SD±$7237) and $511 (SD±$2216), respectively. These costs were greater than the following respective costs for the non-HUD group: $898 (SD $1328); $2013 (SD $2983); $205 (SD $818); $307 (SD $1085); and $65 (SD±$430).

DISCUSSION

Summary of evidence

There is a body of evidence summarising the prevalence and costs of anxiety and depression, but no study, to our knowledge, has systematically reviewed this topic among high users of healthcare services or those who incur high healthcare costs. This systematic review sought to answer the following questions: (1) What is the prevalence of anxiety and depression in adults aged ≥18 years, defined as high users of healthcare or who accrue high healthcare costs, in comparison with routine healthcare users? and (2) What is the magnitude of healthcare costs associated with the presence of anxiety and depression among adults who are high or costly healthcare users? We identified twenty-seven relevant articles with considerable variation in study design, definitions and methods of identifying ‘high user’ or ‘high cost’ populations, definitions and methods used to identify the presence of anxiety and depression, the presence and definition of comparator groups, country, type of health service and clinical setting. The quality of the included studies varied, and no study received a ‘low bias’ score in all assessed domains.

The prevalence of anxiety was greater among high healthcare users than non-high user comparators in all five studies that included a routine user comparator group.[17 45 46 60 61] However, the estimated prevalence among high users varied considerably, ranging from 3.8%[56] to 67.2%,[39] reflecting the high methodological heterogeneity. No studies reported prevalence estimates for anxiety by age group or gender, precluding analysis according to these variables. ORs were reported in four studies[17 45 46 53] and calculated manually by the reviewers using reported data for two additional studies.[60 61] Of these six, four reported an OR of significantly greater than one,[17 45 60 61] further suggesting that anxiety is more likely among high healthcare user populations than routine healthcare users. Only one OR was significantly below one,[53] although this anomalous finding may be explained by the broader definition of high users as the top 25% consulting patients in a 1-year period.

In all 11 studies investigating the prevalence of depression among high user and routine user groups, the prevalence of depression was higher among high users of general healthcare services.[17 41 43–46 49 50 54 58 61] Like anxiety, there was wide variation in the prevalence estimates for depression, ranging from 4.7%[56] to 77.9%,[58] and no studies reported prevalence rates according to age group or gender. Of the 12 studies where ORs were reported or could be calculated, 11[17 41 43–46 49 50 54 58 61] provided an OR of significantly greater than one. The other study[53] provided six different ORs, each with different definitions of high users. Of these, two ORs were not statistically significant, and four were significantly greater than one, further suggesting that depression is more common among high users than in non-high user comparators.

The magnitude of costs associated with depression in high or costly healthcare users was reported in only four studies,[40 47 48 60] and no articles reported cost estimates for anxiety. No two studies defined high healthcare users in the same way, and results were therefore presented narratively. Only two studies[40 47] compared high healthcare users with a routine user comparator group, and both identified that depression was associated with a significantly higher healthcare cost. This is consistent with the finding that depression is over-represented in high healthcare user groups, with a correspondingly raised associated financial burden.

The key take-home message from this review is that anxiety and depression are over-represented among high and/or costly healthcare users. This is likely a result of a complex interplay of diverse factors, such as multimorbidity, age, recent diagnosis and/or relapse of anxiety and/or depression, appropriate healthcare use among those with common mental disorders (eg, primary care-based counselling and therapy services), and psychosomatic symptoms. Use of healthcare services is partly influenced by the local healthcare system and associated infrastructure, and as such pooling of results from different countries across time without appropriate standardisation cannot produce meaningful interpretations.

Strengths and limitations

This is the first systematic review to identify and present an in-depth synthesis of the best available evidence describing the prevalence of anxiety and depressive disorders among high or costly users of general healthcare services, and the magnitude of associated costs. One of the key strengths is its comprehensiveness and the rigorous methodological approach used[35 36] in accordance with PRISMA guidance.[30] Three reviewers screened the articles returned against agreed eligibility criteria, extracted the data and assessed the quality of the studies, and this was verified by two further reviewers. The entire team was involved and consulted in cases of opinion discrepancy. A comprehensive search strategy was developed and used to maximise the likelihood of capturing all relevant studies. This included searches of the grey literature and reviews of reference lists, and the search was repeated during manuscript preparation to capture more recent publications.

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The review was limited by the variable quality of the included studies and the possibility of bias across numerous methodological domains. Many studies lacked essential information (despite reaching out to original authors), such as descriptive data of the included population, precluding commentary on the measurement of the effect of these variables. The high methodological heterogeneity precluded meaningful meta-analysis, and a narrative summary is thus presented. Furthermore, the findings of this study have limited generalisability in view of the unique study design settings and variable definitions of high and/or costly healthcare use.

An additional limitation relates to the comparability of studies conducted across different healthcare systems. There was substantial variation in how high or costly healthcare users were defined, as well as differences in healthcare delivery models, funding structures and access to services across countries. These structural and contextual factors are likely to influence healthcare utilisation patterns and associated costs independently of patient characteristics, thereby limiting direct comparability. As a result, findings should be interpreted as indicative of broader patterns rather than precise cross-country estimates, and caution is warranted when generalising conclusions across settings.

Implications of results

The findings of this review suggest that people with anxiety and/or depression account for a disproportionate amount of general healthcare use and resources in primary and secondary care settings. This is consistent with existing literature reporting higher rates of mental disorders in high healthcare users.[64 65] It is important to consider the motives for health-seeking behaviour to identify clinically beneficial and cost-effective strategies for this group. Anxiety and depression may affect an individual's perceived health, subsequently driving contact with healthcare services for reassurance,[66] and health anxiety is associated with increased use of primary, somatic specialist and mental specialist healthcare in the general adult population.[67] This may act as one of various mechanisms behind the findings of this review, although frequency of healthcare use may also be explained by age, multimorbidity and routine use for certain conditions according to best practice guidelines, alongside other confounding factors.

Given the disproportionate use of general healthcare services by people living with anxiety and depression, improved identification of covert mental health problems is essential for the provision of effective interventions for patients and the reduction of healthcare expenditure. This is challenging for clinicians when anxiety and depression are not the primary reasons for seeking care but are concomitant and potential determinants of acute and chronic physical co-morbidity. Peters and colleagues found that many patients do not present the emotional aspects of their problems due to a lack of trust, and they argue that clinicians should improve their awareness of patients' past and present help-seeking and self-management strategies.[68] Clinicians have many opportunities to pick up on undiagnosed mental health conditions and increased awareness of these conditions through appropriate training and efforts to identify them are likely to be beneficial for both patients and healthcare systems.[69]

Anxiety and depression are common mental disorders, for which there are effective interventions such as, but not limited to, psychotherapies and antidepressant medications. In view of the findings of this review, there is a rationale to develop specialist psychological interventions for high or costly healthcare users with anxiety and/or depression. These interventions have already been successfully adapted for individuals with co-morbid physical illness.[70 71] In recent years, evidence-based interventions have been developed for high need, high-cost patients, including problem-solving therapy, and models of care such as problem adoption therapy and care, and case management and disease management.[72] Berkman and colleagues argue that individualised patient engagement strategies are essential to the success of interventions for this group, and they describe strategies to optimise the relationship between patients and healthcare providers, including emotional support, self-management skills building and acknowledgment of patient disorders[25]. It is essential to understand the nature and extent of mental disorders among this population to plan effective interventions.

In terms of future research, the heterogeneity of our findings demonstrates a need for a standardised approach to defining and understanding high and costly healthcare users. An agreed definition of high and/or costly healthcare use in different contexts would be helpful to integrate the estimates of socioeconomic and clinical characteristics of this high-need group, and to enable the conduct of cost-effectiveness studies in this area. The Royal College of Emergency Medicine defines frequent use of EDs as five attendances or more per year,[73] and a similar, universal definition is indicated for the primary care and secondary care outpatient settings.

CONCLUSIONS

Anxiety and depression are over-represented among high and/or costly general healthcare users but are often under-identified and under-addressed. This review quantifies the prevalence of anxiety and depression within this population, describes associated costs, and explores reasons underlying this association, which include age, multimorbidity, routine use of services for certain conditions (eg, psychological interventions in primary care), health anxiety and somatisation. This group incurs disproportionate healthcare costs and resources compared with the general population, which should be considered by stakeholders, policymakers, clinicians and researchers. Evidence-based interventions to treat anxiety and depression among those with medical co-morbidities exist, and these could be adapted to address the needs of this population. Future research should consider a unified

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approach to the definition of high healthcare use and the identification of anxiety and depression.

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