

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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18 **ABSTRACT**

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

22 **Design.** Systematic review of the available literature.

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

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

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

28 **Results.** From the 38,412 identified articles, 27 studies from 10 countries (in Europe, North America and Asia) involving 6,145,907 participants
29 met eligibility criteria and were included. There were wide variations in the estimated prevalence of anxiety (3.8-67.2%) and depression (4.7-
30 77.9%) among high healthcare users. The prevalence of both disorders was higher among high healthcare users than routine users in all
31 studies with non-high user comparator groups. Only four studies investigated healthcare costs associated with depression. These uniformly
32 reported that general healthcare costs are higher for those with depression than those without. No studies investigated costs associated with
33 anxiety.

34 **Conclusions.** Anxiety and depression are over-represented among high or costly healthcare users, although accurate quantification of the
35 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.

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Keywords: depression, anxiety, healthcare utilisation, high cost, high healthcare cost, frequent attenders, prevalence, primary care, secondary care, health economics

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 by multiple reviews
- High methodological heterogeneity across included studies precluded the planned meta-analysis

BACKGROUND

Across the world, a large proportion of healthcare use is incurred by a small proportion of patients^{1,2,3,4}. This has been observed consistently across a range of healthcare settings, including general practice (GP)^{5,6}, emergency departments (ED)^{7,8,9}, hospitals^{10,11} and outpatient clinics¹². In the UK, ‘frequent attenders’, defined as the top 10% of all consultants, account for 43% of face-to-face consultations in

54 primary care⁶. This population is therefore associated with disproportionately high healthcare costs. Approximately 5% of patients in the USA
55 account for around 50% of all national healthcare expenditure¹³. It is estimated that high use of Accident and Emergency departments, defined
56 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 (NHS)¹⁴.

57 Numerous factors contribute to the frequent use of healthcare services, one of which can be psychological distress¹⁵; Katon used the
58 term 'distressed users' to describe a population of high users of primary and secondary healthcare services with significant mental health
59 problems¹⁶, although distress is not always present among high healthcare users. Mood and anxiety disorders^{17,18,19}, somatoform disorders^{17,18},
60 substance use disorders^{18,19,20} and a history of childhood abuse or neglect²¹ are all associated with higher healthcare service use. A recent
61 systematic review found that patients with severe mental illness use inpatient, emergency, and primary care services for non-psychiatric
62 medical disorders significantly more than those without²².

63 In recent years, efforts have been made to improve the care of high or costly healthcare users with variable success^{23,24,25}. The
64 effectiveness of care can be optimised by targeting the interventions specifically to those most likely to benefit²⁶. Anxiety and depression are
65 the most common forms of mental disorder, and specific, effective interventions to treat them in people with co-morbid physical health needs
66 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
67 health while reducing healthcare expenditure.

68 No published literature review has quantified the association of depression and/or anxiety with high or costly general healthcare use
69 and the associated healthcare costs. An improved understanding of this association will highlight the need for existing treatments to be
70 evaluated in this subgroup. This aligns with recent calls for better integration of physical and mental health services, while acknowledging the
71 bidirectional relation between mental and physical problems²⁹.

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

79

80 **AIMS**

81 This systematic review addresses the questions:

- 82 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
83 high healthcare costs, in comparison with routine healthcare users?
- 84 2. What is the magnitude of healthcare costs associated with the presence of anxiety and depression among adults who are high or costly
85 healthcare users?

86

87 **METHODS**

This review was conducted according to the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) statement guidelines³⁰ (PRISMA checklist can be found in Supplementary 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; General Practitioners (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 (OCD) and post-traumatic stress disorder (PTSD) 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,

106 such as the application of a standardised research interview to generate a diagnosis according to the Diagnostic and Statistical Manual of
107 Mental Disorders (DSM-V)³² or the International Classification of Diseases (ICD-10)³³. Studies examining general physical healthcare use in
108 primary and secondary care were included. Studies focusing on use of mental health services, or specific medical sub-specialties such as
109 oncology, were excluded. Observational studies, including retrospective and prospective cohort studies, case-control and cross-sectional
110 studies were considered. Case studies and series and interventional studies were excluded.

111

112 **Search strategy**

113 A comprehensive search strategy was developed in collaboration with content experts and information specialists at the Universities of
114 Birmingham and Manchester to retrieve articles relevant to the aims of the review. The following electronic databases were searched
115 systematically without language restriction from inception to 1 April 2019 and updated on 25 October 2022, 16 October 2024 and 18 February
116 2026: MEDLINE, PsycINFO, EMBASE, CINAHL, PROSPERO and the Cochrane Library. The updated searches did not identify any additional
117 eligible studies published since the original search. The reference lists of all articles returned by the database searches were hand-searched to
118 maximise the likelihood of identifying all relevant studies. Search strategies for each database are shown in Supplementary file 2.

119

120 **Study selection**

121 The records retrieved by the searches were imported into Clarivate EndNote software (X9, Clarivate Analytics, Philadelphia, PA)³⁴ to
122 facilitate reference management. The “Find Duplications” EndNote function was used to identify duplicate records (based on authors, year and
123 title); duplicate entries were manually removed and only the most complete record was retained. Two reviewers (FJ and OL) then

124 independently reviewed the titles and abstracts to ascertain eligibility for full-text screening and labelling; excluded records were labelled with
 125 the rationale for their exclusion. Three reviewers (DR, FJ, AKT) then independently reviewed full-text versions to determine suitability for
 126 inclusion. This was achieved by referring to an inclusion criteria checklist, shown in Table 1, determined a priori to ensure consistency with the
 127 review process and adherence to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines³⁰. Excluded
 128 records were labelled with the rationale for their exclusion. Any disagreement during this stage were resolved by discussion and involvement of
 129 a third or fourth reviewer (EG and AB).

130

131 **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	Adult aged ≥18 years High healthcare users and/or accrue 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

132

133 **Data extraction**

134 A standardised data extraction form was developed a priori based on the framework by Hayden and colleagues³⁵ (see Supplementary
135 file 3). The form was developed iteratively, focusing on population, comparator, outcome, and study design, before being independently piloted
136 by two reviewers (FJ, OL) on existing papers. Following initial familiarisation with the studies eligible for full-text inclusion, three reviewers (DR,
137 FJ, AKT) extracted the following information using the form: study design, study details (author(s), publication year, country, language of
138 publication), recruitment setting, sample size, demographic information (sex, ethnicity), criteria used to define high use or high costs, method(s)
139 used to record anxiety/depression (self-report measure, validated or non-validated, clinical interview), prevalence of depression and anxiety,
140 healthcare use, costs and associated ranges and the methods used to evaluate this. Authors were contacted directly in the case of missing
141 data. Data extraction was verified by two other reviewers (AB, EG) to ensure consistency across the data extracted. Any discrepancies or
142 disagreements were resolved by discussion and re-visiting the relevant article together. Extracted data were also compiled in a Microsoft Excel
143 spreadsheet to ensure consistency in the review process.

144

145 **Quality assessment**

146 Three reviewers (DR, FJ, AKT) assessed the quality of each included article to minimise bias. This was achieved by completing a
147 modified form of the Ottawa-Newcastle Scale³⁶ assessing the quality of cohort, case-control and cross-sectional studies. The form was first
148 piloted by two researchers (FJ, OL) to ensure feasibility and suitability. Quality assessment included consideration of sampling strategy,
149 methods used to establish exposure and outcome, and analytic method employed. In articles with multiple outcomes of interest, assessment of
150 the method used to establish each outcome was undertaken separately, and consideration and adjustment for confounders were assessed in

151 relation to the outcome of interest (prevalence and/or associated cost). The stages and domains of this tool are shown in Supplementary file 4.
152 The quality assessment process was then independently verified by two other reviewers (AB, EG) to minimise the contribution of personal
153 judgments and subjectivity to the assessment. Differences in opinion were resolved by consensus and discussion among the reviewers. Risk of
154 bias was presented in accordance with recommendations from the Cochrane Collaboration^{37,38}; instead of a composite score, risk was
155 categorised as “high risk”, “low risk”, or “unclear” for each domain.

156

157 **Statistical analysis**

158 Prevalence estimates were extracted or calculated from the data available, and considered separately for age, gender, ethnicity and
159 definition of caseness, where applicable. They were reported as frequency (%) or odds ratio (OR) with 95% confidence intervals (CI) between
160 groups. The level of heterogeneity between study data was explored. We planned to quantify heterogeneity using the I²-statistical test with 95%
161 CI, if appropriate.

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

167 Due to substantial heterogeneity in study design, populations, and outcome definitions, quantitative pooling was not considered
168 appropriate and a narrative synthesis approach was adopted. Studies were grouped according to key themes, including (1) prevalence of

169 anxiety, (2) prevalence of depression, and (3) magnitude of associated healthcare costs. Within these groupings, findings were examined by
170 clinical setting (primary vs secondary care), diagnostic approach (e.g. structured interview, self-report, administrative data), and presence of
171 comparator groups. Patterns in prevalence estimates, relative effect measures (e.g., odds ratios), and cost differences were assessed,
172 alongside the consistency and direction of effects. Findings were interpreted in light of study quality and risk of bias.

173

174 **Patient and public involvement statement**

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

179

180 **RESULTS**

181 **Literature search**

182 The search strategy yielded 38,412 articles (MEDLINE: n=23,613; PsycINFO: n=768; EMBASE: n=13,933; CINAHL: n=98;
183 PROSPERO: n=0; the Cochrane Library: n=0). Additional reference searches found no further studies. After excluding 618 duplicates, the titles
184 and abstracts of 37,794 articles were screened for relevance. Title and abstract screening resulted in the exclusion of 37,706 articles, mainly
185 because they did not provide information on healthcare use or the presence of anxiety and/or depression. Of the 88 reports sought for retrieval,
186 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

187 61 studies excluded at the final stage can be found in Supplementary file 5. 27 articles^{16,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64}
188 were included in the final analysis. A flow diagram of the study identification process, including reasons for exclusion at each stage, is
189 presented as a PRISMA flow diagram³⁰ in Figure 1.

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

193 **Study characteristics**

194 Twenty-seven studies involving 290,844 high healthcare users, 5,851,248 comparators and 3,815 individuals from one study⁵³ who
195 were not divided into high or regular healthcare users were included in the final analysis. Variation was detected between studies regarding
196 study design and setting, data source and collection, definitions of high healthcare use, anxiety, and depression, and reported prevalence
197 rates. Included studies were from 10 countries, with most being performed in the USA (n=9), followed by the Netherlands (n=3), the United
198 Kingdom (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),
199 and one study looked at the number of referrals from primary care to secondary care⁶³.

200 14 studies included a non-high healthcare user comparator group and thirteen focused on describing the characteristics of high healthcare
201 users without comparators. 17 studies had a cross-sectional design, six were cohort studies and four were case-control studies. Age and sex
202 were inconsistently reported across studies. The mean age of participants ranged from 37-82.8 years in the high healthcare user group, and
203 from 38.8-72.4 years in the comparator group. The percentage of female participants ranged from 5.0-77.5 in the high user group and from

50.3-77.5 in the comparator group. Only five studies reported the ethnicity of participants^{16,45,48,60,61} 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.

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	13328	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	261515	*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 50.3-55.2)	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 ⁵⁵	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 ⁵⁶	1999	USA	Primary care	Cross-sectional	7203	*47.5	*69.1	Not reported	No comparator group			
Portegijs et al ⁵⁷	1996	Netherlands	Primary care	Cross-sectional	106	Not reported	61.3	Not reported	No comparator group			
Portegijs et al ⁵⁸	1996	Netherlands	Primary care	Cross-sectional	80	37 (not specified further)	56.3	Not reported	No comparator group			
Press et al ⁵⁹	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 ⁶⁰	2019	USA	Secondary care	Cross-sectional	195	Not reported	50.3	14.4	No comparator group			
Robinson et al ⁶¹	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 ⁶²	2002	Germany	Secondary care	Cross-sectional	389	45.4 (13.1)	63.7	Not reported	3337	40.8 (13.1)	51.8	Not reported
Sharpe et al ⁶³	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 ⁶⁴	2014	Netherlands	Primary care	Cross-sectional	623	52 (not specified further)	52.7	Not reported	No comparator group			

208 *Not reported but calculated manually by the reviewers.

209

210 **Study quality**

211 None of the included studies had a low risk of bias in all domains, according to the adapted checklist of the Ottawa-Newcastle Scale³⁶.

212 26 of the 27 studies clearly defined the process of selecting participants (low risk of bias), and 23 adequately described the study population.

213 Exposure and outcome were almost universally well-described; all 27 studies presented valid measures for ascertaining high or costly service

214 use (the exposure of interest), and 23 used appropriate outcome measures (prevalence of anxiety and/or depression and/or associated costs).

215 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

216 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

217 size calculation. Table 3 displays the review quality scores per item based on the adapted Ottawa-Newcastle scale³⁶.

218

219 **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 ⁵⁵	Low risk	Low risk	Low risk	Low risk	Low risk	Not reported**	Low risk
Pearson et al ⁵⁶	Low risk	High risk	Low risk	Low risk	N/A*	Not reported**	Low risk

Portegijs et al ⁵⁷	Low risk	Low risk	Low risk	Low risk	Low risk	Not reported**	Low risk
Portegijs et al ⁵⁸	Low risk	Low risk	Low risk	Low risk	Low risk	Not reported**	Low risk
Press et al ⁵⁹	Low risk	Low risk	Low risk	Low risk	Low risk	Not reported**	Low risk
Rentas et al ⁶⁰	Low risk	Low risk	Low risk	Low risk	Low risk	Not reported**	Low risk
Robinson et al ⁶¹	Low risk	Low risk	Low risk	Low risk	Low risk	Not reported**	Low risk
Schmitz et al ⁶²	Low risk	Low risk	Low risk	Low risk	Low risk	Not reported**	Low risk
Sharpe et al ⁶³	Low risk	Low risk	Low risk	Low risk	Low risk	Not reported**	Low risk
Smits et al ⁶⁴	Low risk	Low risk	Low risk	Low risk	Low risk	Not reported**	Low risk

220 “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. *

221 “N/A” indicates that this criterion was not applicable as only descriptive data were presented and/or groups were not compared. ** “Not

222 reported” indicates that a sample size calculation was not provided, precluding commentary on bias for this criterion.

223

224 **Diagnostic tools/measures used**

225 13 of the 27 included studies measured the presence of anxiety^{16,39,42,45,46,52,53,55,57,60,61,62,64}; these are listed in Supplementary table 1.

226 Significant diversity in the measures used to ascertain the presence of anxiety was noted: diagnostic instruments with structured interviews

227 were used in eight studies^{16,46,52,53,55,57,60,62}, self-reported symptom checklists were used in two studies^{39,64} and diagnoses were extracted from

228 medical records in two studies^{42,45}. In one study, the presence of anxiety was ascertained by identifying diagnostic codes in administrative

229 healthcare claims for patients from a commercially insured population in the USA⁶¹.

230 The presence of depression was measured in 25 of the included studies^{16,39,40,41,42,43,44,45,46,47,48,49,50,51,53,54,55,56,57,58,59,60,62,63,64}; these are

231 listed in Table 3. Like for anxiety, a variety of diagnostic tools were used to ascertain the presence of depression; eleven studies used

232 structured interviews^{16,44,46,53,54,55,56,57,58,60,62}, ten studies used self-reported symptom checklists^{39,41,43,47,49,50,51,59,63,64}, and three studies used
233 diagnoses documented in medical records^{42,45,48}. In one study, the presence of depression was ascertained by identifying diagnostic codes in
234 inpatient and outpatient claims from a private healthcare database⁴⁰.

235 There were a variety of definitions and thresholds used to identify populations of high or costly users of healthcare. The most common
236 approach was to classify high or costly users as those who exceeded a threshold number of contacts with healthcare providers per unit time;
237 this was utilised in 15 of the included studies^{39,41,42,45,46,51,52,54,55,57,58,59,60,62,63}. However, there was considerable diversity in the cut-off chosen,
238 and this ranged from three or more referrals in a five-year period⁶³ to five or more visits to the primary care practitioner in a three-month
239 period⁴¹. Another definition used in nine studies^{16,40,47,48,50,53,56,61,64} involved a top percentage of healthcare users, ranging from the top 25%⁵³ to
240 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
241 the highest number of primary care contacts and worked down this list until fifty participants were recruited⁴⁴, and Jakobsson and colleagues
242 used hierarchical clustering analysis to define high users⁴⁹. Dowrick and colleagues defined high users as those whose annual rate of
243 consultation was at least twice as high as the primary care practice's sex- and age-related mean⁴³.

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

247

248 **Prevalence estimates for anxiety**

249 13 studies measured the presence of anxiety in high or costly users^{16,39,42,45,46,52,55,57,60,61,62,64} and prevalence estimates ranged from
250 3.8%⁵⁷ to 67.2%³⁹. Five studies^{45,46,55,61,62} reported the prevalence of anxiety among a non-high user comparator group; this prevalence rate
251 ranged from 2.0%⁴⁵ to 39.3%⁶¹. In all five studies, the prevalence of anxiety was higher among high healthcare users than among comparators.
252 No studies reported prevalence data by age group or gender.

253 Four studies^{45,46,53,55} reported odds ratios instead of, or in addition to prevalence estimates, to summarise the difference in the presence
254 of anxiety between the two groups. The ratios reported in the included studies ranged from 0.50 (95% CI 0.2-1.9)⁴⁶ to 20.0 (95% CI 3.2-
255 829.0)⁵⁵. Two studies^{45,55} reported an odds ratio of greater than one (i.e. greater odds of an anxiety disorder in high user group compared with
256 comparator). Both were statistically significant; OR 4.3 (95% CI 1.6-11.5)⁴⁵ and OR 20.0 (95% CI 3.2-829.0)⁵⁵. The other two studies^{46,53}
257 reported an odds ratio of less than one (i.e. greater odds of anxiety in comparator group compared with high users). Of these two, only the
258 odds ratio reported by Luciano and colleagues was statistically significant (OR 0.58, 95% CI 0.34-0.98), and this was when high healthcare
259 users were defined as the top 25% consulting patients in a 1-year period, stratified by the presence of physical and mental conditions⁵³.

260 For the reader's interest, we calculated unadjusted odds ratios and 95% confidence intervals for studies where these were not reported,
261 using the number of events in the high user and non-high user groups where possible. These calculations were conducted for two studies^{61,62}.
262 In both cases, the odds ratios were greater than one; OR 1.4 (95% CI 1.1-1.9)⁶¹ and OR 1.5 (95% CI 1.0-2.2)⁶². These suggest that anxiety is
263 more prevalent among high healthcare users than in routine use comparators. The prevalence rates and odds ratios of anxiety in the included
264 studies, including those calculated manually by the reviewers, are summarised in Supplementary table 1.

265

266 **Supplementary table 1.** Estimated prevalence rates of anxiety and depression in high healthcare users.

267

268 **Prevalence estimates for anxiety according to diagnostic criteria**

269 Diverse methods and criteria were used in the included studies to ascertain the presence of anxiety. Two studies reported prevalence
270 estimates according to self-completed questionnaires; Agarwal and colleagues administered the EQ-5D-3L³⁹ and Smits and colleagues
271 administered the PHQ⁶⁴. The prevalence of anxiety ranged from 7%⁶⁴ to 67.2%³⁹ among high healthcare users; neither reported prevalence
272 estimates among non-high user comparators. Three studies^{42,45,61} reported prevalence estimates of anxiety according to ICD criteria – either
273 ICD-9^{42,61} or unspecified⁴⁵ – derived from participant records, although two used medical records^{42,45} and one used administrative claim
274 records⁶¹. The rates ranged from 8.0%⁴⁵ to 48.2%⁶¹ among high healthcare users, and 2.0%⁴⁵ to 39.3%⁶¹ among comparators. The only
275 included study to use the SCAN interview to diagnose anxiety according to ICD-10 criteria was by Gili and colleagues⁴⁶.

276 The remaining seven studies^{16,52,53,55,57,60,62} used differing structured interviews to estimate the prevalence of anxiety according to DSM
277 criteria, although the version of DSM used also differed between them. Five studies used DSM-IV criteria^{52,53,55,60,62} and two used DSM-III-R
278 criteria^{16,57}. The prevalence of anxiety according to DSM-IV criteria ranged from 4.0%⁵² to 32.4%⁵⁵ among high users and 4.4%⁵⁵ to 5.4%⁶²
279 among comparators. The prevalence of anxiety among high users according to DSM-III-R criteria ranged from 3.8%⁵⁷ to 21.8%¹⁶; neither of
280 these two studies had a comparator group. There was great variation in the interview schedules used; two studies used SCID^{53,55}, one used
281 DIS¹⁶, one used MINI⁵², one used M-CIDI⁶², one used a comprehensive behavioural health assessment⁶⁰ and one used a specifically designed
282 questionnaire⁵⁷. The wide breadth of tools used precludes summary of prevalence ranges according to interview schedule; prevalence
283 estimates from each included article can be found in Supplementary table 1.

284

285 **Prevalence estimates for anxiety according to clinical setting**

286 Of the 12 included studies that reported prevalence estimates for anxiety, seven took place in a primary care setting^{16,45,46,52,55,57,64}. In
287 primary care, prevalence estimates for anxiety ranged from 3.8%⁵⁷ to 32.4%⁵⁵ among high healthcare users, and from 2.0%⁴⁵ to 4.4%⁵⁵ among
288 non-high user comparators. The remaining five studies^{39,42,60,61,62} took place in the secondary care setting, and the prevalence of anxiety varied
289 from 7.7%⁶² to 67.2%³⁹ among high users and from 5.4%⁶² to 39.3%⁶¹ among comparators.

291 **Prevalence estimates for depression**

292 21 studies reported the prevalence of depression among high or costly healthcare users^{16,39,40,41,42,43,44,45,46,48,49,50,51,55,56,57,59,60,62,63,64}. We
293 also calculated the prevalence of depression among high users using raw data where possible; this was calculated for two further studies^{54,58}.
294 Prevalence estimates for depression among high users ranged from 4.7%⁵⁷ to 77.9%⁵⁹. Nine studies reported the prevalence of depression
295 among non-high user comparators^{41,43,44,45,46,50,55,59,62}, and we manually calculated the prevalence of depression among comparators for the two
296 studies where this was possible^{49,54}. The reported prevalence among comparators ranged from 3.8%⁶² to 53.5%⁴⁹. In all 11 studies with
297 prevalence rates available for the two groups, the prevalence of depression was higher among high healthcare users than among comparators.
298 No studies reported prevalence data by age group or gender.

299 Six studies^{43,45,46,53,55,59} reported odds ratios instead of, or in addition to, prevalence estimates, to summarise the difference in the
300 presence of depression between the two groups. The ratios reported in the included studies ranged from 1.0 (95% CI 0.75-1.34)⁵³ to 26.6 (95%
301 CI 12.4-56.8)⁴³. Of these six studies, five^{43,45,46,55,59} reported a statistically significant odds ratio greater than one (i.e. in favour of a greater odds
302 of depression in high users versus comparators). The other study⁵³ provided six different odds ratios, each for a different definition of high

303 users. Of these odds ratios, two were statistically insignificant, and four were significantly greater than one, suggesting that depression is more
304 common among high users than in non-high user comparators.

305 We manually calculated unadjusted odds ratios and 95% confidence intervals for studies where these were not reported, using the raw
306 data provided. These calculations were conducted for six studies^{41,44,49,50,54,62}. These odds ratios ranged from 1.7 (95% CI 1.1-2.6)⁶² to 14.7
307 (95% CI 3.2-67.6)⁴⁴. In all cases, the odds ratios were greater than one and statistically significant, suggesting that depression is more
308 prevalent among high healthcare users. The prevalence rates and odds ratios of depression in the included studies, including those calculated
309 manually by the reviewers, are summarised in Supplementary table 1.

310

311 **Prevalence estimates for depression according to diagnostic criteria**

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

314 Nine studies^{39,41,43,49,50,51,59,63,64} used self-completed questionnaire items to ascertain depression among participants. Tools used
315 included variations of the PHQ^{41,63,64}, BDI^{43,51}, GDS^{49,59}, EQ-5D-3L³⁹ and the MOS depression screen⁵⁰. The estimated prevalence of
316 depression among high healthcare users according to these self-reported measures ranged from 5%⁶⁴ to 77.9%⁵⁹, and prevalence estimates
317 among routine user comparators ranged from 5.1%⁴³ to 53.5%⁴⁹.

318 Four studies^{40,42,45,48} reported prevalence estimates for depression according to ICD criteria – either ICD-9^{40,42,48} or unspecified⁴² –
319 derived from participant records. Three of these studies used medical records^{42,45,48}, and one used inpatient and outpatient medical claim
320 records⁴⁰. Estimates for the prevalence of depression according to participant records among high healthcare users were varied, ranging from

321 4.8%⁴⁰ to 29%⁴⁸. Only one of these studies included a comparator group, and the prevalence of depression among routine healthcare users
322 was 7%⁴⁵.

323 The remaining 10 studies^{16,44,46,54,55,56,57,58,60,62} used structured interviews with participants to identify the presence of depression
324 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
325 among high users and from 5.4%⁴⁶ to 16.0%⁵⁴ among comparators. Three studies^{16,57,58} used the DIS to identify depression according to DSM-
326 III-R criteria. None of these three studies included a comparator group, but the prevalence of depression among high users according to DSM-
327 III-R was reported to be from 4.7%⁵⁷ to 23.5%¹⁶. Five studies^{44,55,56,60,62} used interviews to identify depression according to DSM-IV criteria. The
328 prevalence estimates among high users were 6.2%⁶² to 45.6%⁵⁵, and among routine users the estimates were 3.8%⁶² to 20.6%⁵⁵.

329

330 **Prevalence estimates for depression according to clinical setting**

331 Of the 23 studies that either reported prevalence estimates for depression or, where it was possible for the reviewers to manually
332 calculate the estimates, 14 took place in the primary care setting^{16,41,43,44,45,46,51,54,55,56,57,58,59,64}. In primary care, estimates for the prevalence of
333 depression among high healthcare users ranged from 4.7%⁵⁷ to 77.9%⁵⁹, and the estimates among non-high user comparators ranged from
334 4.0%⁴⁴ to 20.6%⁵⁵. Eight studies took place in a secondary care setting^{39,40,42,48,49,50,60,62}. In secondary care, estimates for the prevalence of
335 depression ranged from 4.8%⁴⁰ to 67.2%³⁹ among high users, and from 3.8%⁶² to 53.5%⁴⁹ among comparators. The remaining study⁶³ used the
336 number of referrals from primary care to specialist services to identify high healthcare users; its findings were therefore not included in either
337 primary or secondary care estimates.

338

339 **Magnitude of associated costs**

340 Only four studies included in the review investigated the magnitude of healthcare costs associated with the presence of depression in
341 high users of healthcare^{40,47,48,61}, and no studies investigated costs associated with anxiety. Although all four studies originated from the USA,
342 the variety of definitions used to define high healthcare use (as summarised in Supplementary table 1) precluded the pooling of healthcare
343 estimates. Therefore, we have summarised the main findings narratively. Cost estimates across studies are derived from figures from different
344 healthcare systems, time periods, costing methodologies, type of costs included (e.g. direct medical, non-medical, indirect), and cost
345 perspectives (healthcare vs societal). Moreover, they are reported in different currencies, without conversions, standardisation for inflation or
346 purchasing power parity. As such, direct comparisons of these cost estimates should be interpreted with caution. Here, we present these
347 descriptively with indicative, rather than definitive, interpretations.

348 Ash and colleagues analysed the Medstat's MarketScan Research Database which consisted of inpatient and ambulatory healthcare
349 records of individuals covered by employee-sponsored benefit plans during 1997 and 1998⁴⁰. The Diagnostic Cost Group (DCG) hierarchical
350 condition category (HCC) prospective model was used to identify the higher cost patient tier of having ten or comorbidities identified in the
351 notes. Individuals with depression incurred 2.3 times higher healthcare costs than their disease cohort average (\$1,651).

352 Henk and colleagues⁴⁷ examined a sample of high utiliser patients enrolled with a prepaid health maintenance organisation (HMO) in
353 Madison, Wisconsin to determine whether high healthcare users with depression incur higher medical costs compared to high users without
354 depression in the next year. The total average medical and pharmaceutical costs associated with high utilisers with depression were \$239.05

355 (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
356 \$5764.30 (+/-7260.10) for years 1, 2 and 3 respectively. In contrast, the total average medical and pharmaceutical costs for high utilisers
357 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),
358 \$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
359 package and co-morbidity, depressed high utilisers incurred 26% (range 20-33%; $p<0.01$) higher expenditure than high utilisers without
360 depression.

361 Hunter and colleagues investigated use and associated costs of mental and medical-surgical care among the costliest 5% of veteran
362 affairs (VA) patients with and without a diagnosis of mental health and across various groups of high-cost patients with mental health
363 conditions⁴⁸. They used VA administrative records from October 2009 to September 2010 to identify eligible patients. Among patients receiving
364 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 \$7,407.
365 Therefore, cost associated with general services equates to \$58,236 per year.

366 Finally, Robinson and colleagues compared high users with a history of depression (HUDs) with a comparator group of non-high users
367 with depression (non-HUDs) using administrative data derived from the HealthCore Integrated Research Database (HIRD)⁶¹. This database
368 stores data regarding medical and pharmacy costs from across 14 geographically diverse US health plans. HUDs were in the top 10% of total
369 all-cause costs in the preceding 12 months. Mean annual healthcare costs were eight times higher in HUDs (\$56,145) compared with non-
370 HUDs (\$6,954). The all-cause physician office mean costs, all-cause outpatient costs, mental health-related outpatient costs, all-cause
371 emergency department (ED) costs and mental health-related ED costs for HUDs were \$4574 (SD \$5900), \$19,603 (SD \$31,033), \$3177 (SD

372 \$11,434), \$1856(SD+-7237) and \$511 (SD+-2216), respectively. These costs were greater than the following respective costs for the non-HUD
373 group: \$898 (SD \$1328); \$2013 (SD \$2983); \$205 (SD \$818); \$307 (SD 1085); and \$65 (SD+-\$430).

374

375 **DISCUSSION**

376

377 **Summary of evidence**

378 There is a body of evidence summarising the prevalence and costs of anxiety and depression, but no study, to our knowledge, has
379 systematically reviewed this topic among high users of healthcare services or those who incur high healthcare costs. This systematic review
380 sought to answer the following questions: (1) What is the prevalence of anxiety and depression in adults aged ≥ 18 years, defined as high users
381 of healthcare or who accrue high healthcare costs, in comparison with routine healthcare users? and (2) What is the magnitude of healthcare
382 costs associated with the presence of anxiety and depression among adults who are high or costly healthcare users? We identified twenty-
383 seven relevant articles with considerable variation in study design, definitions and methods of identifying 'high user' or 'high cost' populations,
384 definitions and methods used to identify the presence of anxiety and depression, the presence and definition of comparator groups, country,
385 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
386 domains.

387 The prevalence of anxiety was greater among high healthcare users than non-high user comparators in all five studies that included a
388 routine user comparator group^{45,46,55,61,62}. However, the estimated prevalence among high users varied considerably, ranging from 3.8%⁵⁷ to
389 67.2%³⁹, reflecting the high methodological heterogeneity. No studies reported prevalence estimates for anxiety by age group or gender,

390 precluding analysis according to these variables. Odds ratios were reported in four studies^{45,46,53,55} and calculated manually by the reviewers
391 using reported data for two additional studies^{61,62}. Of these six, four reported an odds ratio of significantly greater than one^{45,55,61,62}, further
392 suggesting that anxiety is more likely among high healthcare user populations than routine healthcare users. Only one odds ratio was
393 significantly below one⁵³, although this anomalous finding may be explained by the broader definition of high users as the top 25% consulting
394 patients in a one-year period.

395 In all 11 studies investigating the prevalence of depression among high user and routine user groups, the prevalence of depression was
396 higher among high users of general healthcare services^{41,43,44,45,46,49,50,54,55,59,62}. Like anxiety, there was wide variation in the prevalence
397 estimates for depression, ranging from 4.7%⁵⁷ to 77.9%⁵⁹, and no studies reported prevalence rates according to age group or gender. Of the
398 12 studies where odds ratios were reported or could be calculated, 11^{41,43,44,45,46,49,50,54,55,59,62} provided an odds ratio of significantly greater than
399 one. The other study⁵³ provided six different odds ratios, each with different definitions of high users. Of these, two odds ratios were not
400 statistically significant, and four were significantly greater than one, further suggesting that depression is more common among high users than
401 in non-high user comparators.

402 The magnitude of costs associated with depression in high or costly healthcare users was reported in only four studies^{40,47,48,61}, and no
403 articles reported cost estimates for anxiety. No two studies defined high healthcare users in the same way, and results were therefore
404 presented narratively. Only two studies^{40,47} compared high healthcare users with a routine user comparator group, and both identified that
405 depression was associated with a significantly higher healthcare cost. This is consistent with the finding that depression is over-represented in
406 high healthcare user groups, with a correspondingly raised associated financial burden.

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

413

414 **Strengths and limitations**

415 This is the first systematic review to identify and present an in-depth synthesis of the best available evidence describing the prevalence
416 of anxiety and depressive disorders among high or costly users of general healthcare services, and the magnitude of associated costs. One of
417 the key strengths is its comprehensiveness and the rigorous methodological approach used^{35,36} in accordance with PRISMA guidance³⁰. Three
418 reviewers screened the articles returned against agreed eligibility criteria, extracted the data and assessed the quality of the studies, and this
419 was verified by two further reviewers. The entire team was involved and consulted in cases of opinion discrepancy. A comprehensive search
420 strategy was developed and used to maximise the likelihood of capturing all relevant studies. This included searches of the grey literature and
421 reviews of reference lists, and the search was repeated during manuscript preparation to capture more recent publications.

422 The review was limited by the variable quality of the included studies and the possibility of bias across numerous methodological
423 domains. Many studies lacked essential information (despite reaching out to original authors), such as descriptive data of the included
424 population, precluding commentary on the measurement of the effect of these variables. The high methodological heterogeneity precluded

425 meaningful meta-analysis, and a narrative summary is thus presented. Furthermore, the findings of this study have limited generalisability in
426 view of the unique study design settings and variable definitions of high and/or costly healthcare use.

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

433

434 **Implications of results**

435 The findings of this review suggest that people with anxiety and/or depression account for a disproportionate amount of general
436 healthcare use and resources in primary and secondary care settings. This is consistent with existing literature reporting higher rates of mental
437 disorders in high healthcare users^{65,66}. It is important to consider the motives for health-seeking behaviour to identify clinically beneficial and
438 cost-effective strategies for this group. Anxiety and depression may affect an individual's perceived health, subsequently driving contact with
439 healthcare services for reassurance⁶⁷, and health anxiety is associated with increased use of primary, somatic specialist and mental specialist
440 healthcare in the general adult population⁶⁸. This may act as one of various mechanisms behind the findings of this review, although frequency
441 of healthcare use may also be explained by age, multimorbidity and routine use for certain conditions according to best practice guidelines,
442 alongside other confounding factors.

443 Given the disproportionate use of general healthcare services by people living with anxiety and depression, improved identification of
444 covert mental health problems is essential for the provision of effective interventions for patients and the reduction of healthcare expenditure.
445 This is challenging for clinicians when anxiety and depression are not the primary reasons for seeking care but are concomitant and potential
446 determinants of acute and chronic physical co-morbidity. Peters and colleagues found that many patients do not present the emotional aspects
447 of their problems due to a lack of trust, and they argue that clinicians should improve their awareness of patients' past and present help-
448 seeking and self-management strategies⁶⁹. Clinicians have many opportunities to pick up on undiagnosed mental health conditions and
449 increased awareness of these conditions through appropriate training and efforts to identify them are likely to be beneficial for both patients and
450 healthcare systems⁷⁰.

451 Anxiety and depression are common mental disorders, for which there are effective interventions such as, but not limited to,
452 psychotherapies and antidepressant medications. In view of the findings of this review, there is a rationale to develop specialist psychological
453 interventions for high or costly healthcare users with anxiety and/or depression. These interventions have already been successfully adapted
454 for individuals with co-morbid physical illness^{71,72}. In recent years, evidence-based interventions have been developed for high need, high-cost
455 patients, including problem-solving therapy, and models of care such as problem adoption therapy and care, and case management and
456 disease management⁷³. Berkman and colleagues argue that individualised patient engagement strategies are essential to the success of
457 interventions for this group, and they describe strategies to optimise the relationship between patients and healthcare providers, including
458 emotional support, self-management skills building and acknowledge of patient disorders⁷⁴. It is essential to understand the nature and extent
459 of mental disorders among this population to plan effective interventions.

460 In terms of future research, the heterogeneity of our findings demonstrates a need for a standardised approach to defining and
461 understanding high and costly healthcare users. An agreed definition of high and/or costly healthcare use in different contexts would be helpful
462 to integrate the estimates of socio-economic and clinical characteristics of this high-need group, and to enable the conduct of cost-
463 effectiveness studies in this area. The Royal College of Emergency Medicine defines frequent use of emergency departments as five
464 attendances or more per year⁷⁵, and a similar, universal definition is indicated for the primary care and secondary care outpatient settings.

465

466 **CONCLUSIONS**

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

475

476 **DECLARATIONS**

477 **Ethics approval and consent to participate**

478 This study is a systematic review of previously published literature and did not involve the collection of primary data or direct interaction with
479 human participants. As all data analysed were already in the public domain, formal ethical approval was not required in accordance with
480 institutional and standard research guidelines. Consequently, no institutional review board or ethics committee approval was sought for this
481 study.

482 **Patient consent for publication**

483 Not applicable.

484 **Availability of data and materials**

485 All data generated or analysed during this study are included in this published article and its supplementary information files.

486 **Competing interests**

487 None declared.

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490 **Contributors**

491 All authors contributed to the focus of this systematic review topic and approved the final version for publication. FJ, OL, AB and EG designed
492 the review and wrote the protocol. FJ and OL completed the initial searches, which were updated by FJ. DR, FJ, AKT, AB and EG contributed
493 to data screening and extraction and quality assessment. DR drafted the manuscript with guidance and feedback from all other authors at all
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496 None

497

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