

1 **Title:** The Prevalence of Depression in General Hospital Inpatients: A Systematic Review and  
2 Meta-Analysis of Interview Based Studies

3

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26

27 **ABSTRACT**

28 **Background**

29 Comorbid depression in the medically ill is clinically important. Admission to a general  
30 hospital offers an opportunity to identify and initiate treatment for depression. However we  
31 first need to know how common depression is in general hospital inpatients. We aimed to  
32 address this question by systematically reviewing the relevant literature.

33

34 **Methods**

35 We reviewed published prevalence studies in any language which had used diagnostic  
36 interviews of general hospital inpatients and met basic methodological quality criteria. We  
37 focussed on interview-based studies in order to estimate the proportion of patients with a  
38 diagnosis of depressive illness.

39

40 **Results**

41 Of 158 relevant articles, 65 (41%) describing 60 separate studies met our inclusion criteria.  
42 The 31 studies that focussed on general medical and surgical inpatients reported prevalence  
43 estimates ranging from 5% to 34%. There was substantial, highly statistically significant,  
44 heterogeneity between studies which was not materially explained by the covariates we  
45 were able to consider. The average of the reported prevalences was 12% (95% C.I. 10% to  
46 15%), with a 95% prediction interval of 4% to 32%. The remaining 29 studies, of a variety of  
47 specific clinical populations, are described.

48

49 **Conclusions**

50 The available evidence suggests a likely prevalence high enough to make it worthwhile  
51 screening hospital inpatients for depression and initiating treatment where appropriate.  
52 Further, higher quality, research is needed to clarify the prevalence of depression in specific  
53 settings and to further explore the reasons for the observed heterogeneity in estimates.

54 **INTRODUCTION**

55 Depression frequently accompanies physical illness (Vos *et al.*, 2012). It is clinically  
56 important because it is associated with worse physical symptoms, poorer quality of life and  
57 greater functional disability (Egede, 2007, Katon, 1996). Patients with depression also spend  
58 more time in hospital, are less likely to adhere to medical treatments, and consequently  
59 incur higher healthcare costs (DiMatteo *et al.*, 2000). Despite its importance the  
60 management of depression comorbid with physical illness is often suboptimal with low rates  
61 of detection and treatment (Balestrieri *et al.*, 2002, Cepoiu *et al.*, 2008, Hirschfeld *et al.*,  
62 1997, Katon and Sullivan, 1990, Kessler *et al.*, 1999, Walker *et al.*, 2014).

63

64 Admission to a general hospital therefore provides an important opportunity to improve the  
65 management of comorbid depression. Detection can be improved by incorporating  
66 systematic screening into hospital admission procedures and treatment can be initiated  
67 where appropriate (Beach *et al.*, 2015). However, in order to plan such a management  
68 strategy we need to know how common depression is in general hospital inpatients.

69 Surprisingly, we currently lack a clear answer to this basic question. This is largely because  
70 previous systematic reviews of the prevalence of depression have focussed on study  
71 populations with specific physical diseases such as cancer, rather than on specific clinical  
72 settings such as general hospital wards (Castro-de-Araujo *et al.*, 2013, Craig *et al.*, 2009,  
73 Davydow *et al.*, 2009, Delville and McDougall, 2008, Kouwenhoven *et al.*, 2011, Mitchell *et*  
74 *al.*, 2011, Poynter *et al.*, 2009, Shanmugasegaram *et al.*, 2012, Singer *et al.*, 2013, Thombs *et*  
75 *al.*, 2006a, Thombs *et al.*, 2006b, Walker *et al.*, 2013, Wilder Schaaf *et al.*, 2013, Wiseman *et*  
76 *al.*, 2013).

77

78 We therefore aimed to conduct a systematic review of studies of the prevalence of  
79 depression in general hospital inpatients. We focussed on interview-based studies in order  
80 to estimate the proportion of patients with a definite diagnosis of depressive illness.

81

## 82 **METHODS**

83

### 84 **Search strategy and selection criteria**

85 We performed a systematic review of studies of the prevalence of depression in general  
86 hospital inpatients, using procedures that accorded with the PRISMA (Preferred Reporting  
87 Items for Systematic Reviews and Meta-Analyses) guidelines (Moher *et al.*, 2009). We  
88 identified studies by searching EMBASE, Medline and PsycINFO (from 1974, 1946 and 1967  
89 respectively) to December 2015. Searches were run for the combination of 'prevalence',  
90 'general hospital inpatient' and 'depression' using both standardised subject terms and free  
91 text terms, including synonyms and alternative spellings. We provide full details of the  
92 searches used in the online appendix. We also manually searched the reference lists of  
93 review articles obtained through the electronic searches.

94

95 We judged studies to be relevant to the review if they met all the following criteria: (1) the  
96 study clearly aimed to estimate the prevalence of depression (i.e. studies that were  
97 designed to address a different research question but happened to include a prevalence  
98 estimate, such as clinical trials or questionnaire validation studies, were not included); (2) all  
99 study participants were adults (aged 16 or older); (3) all study participants (or a clearly  
100 defined subgroup for which there was an estimate of depression prevalence) were general  
101 hospital inpatients at the time of depression assessment; (4) the presence of depressive  
102 illness was determined using a diagnostic interview. We only included primary studies (i.e.

103 not reviews) for which we could obtain the full paper to allow data extraction. No language  
104 restrictions were applied.

105

106 When selecting publications to include in the review, we also applied quality criteria to the  
107 reported study methods. In order to ensure a consistent and transparent approach to this  
108 quality assessment we used a checklist based on the work of Loney et al (Loney *et al.*, 1998,  
109 Walker *et al.*, 2013). We used a checklist rather than a continuous scale to ensure that all  
110 the key aspects of the study methods met basic quality criteria (Juni *et al.*, 1999). The basic  
111 methodological standards required for inclusion were: (1) the study sample was obtained  
112 using a random or consecutive sampling method; (2) data were available for analysis on at  
113 least 70% of the eligible patients (either as reported by the authors or derived from  
114 presented data); (3) depressive illness was defined using standard diagnostic criteria: major  
115 depression from the Diagnostic and Statistical Manual of Mental Disorders (DSM),  
116 depressive episode from the International Classification of Diseases (ICD) or similar  
117 (American Psychiatric Association, 1994, 2013, World Health Organization, 1992). The first  
118 two of these criteria aimed to minimise selection bias, and the third aimed to ensure that  
119 estimates could be compared across studies.

120

## 121 **Data collection**

122 We screened the titles and abstracts of all articles identified by the searches to determine  
123 whether each might meet the selection criteria. We then reviewed the full text of the  
124 article, with the help of a translator where necessary, if there was any possibility that it  
125 might be relevant and would meet our quality criteria. This process (including screening of

126 titles and abstracts) was conducted independently by two researchers with reference to a  
127 third researcher to resolve disagreements.

128

129 Two researchers independently extracted the following data from all the articles included in  
130 the review, using a specially designed, standardised data extraction form: country in which  
131 the study took place; age, sex and clinical characteristics of participants; sample size; type of  
132 depression interview used and profession of interviewer; diagnostic criteria used to  
133 determine the presence of depressive illness; prevalence of depression in the sample (for  
134 cohort studies, we extracted the prevalence of depression at the first time point only).

135

### 136 **Clinical analysis**

137 Two researchers reviewed the data extracted on participants' clinical characteristics in order  
138 to assess their similarity across studies. We found that there was high clinical heterogeneity,  
139 indicating that a meta-analysis of all the studies would not yield meaningful results. Whilst  
140 some studies had recruited general medical and surgical inpatients, others had recruited  
141 inpatients with very specific clinical characteristics, and therefore were of samples  
142 unrepresentative of the general hospital inpatient population. In order to deal with this  
143 clinical heterogeneity, we restricted our statistical analysis to studies of general medical and  
144 surgical inpatients. The studies of more specific patient groups are described in our results  
145 and online appendix in order to provide the reader with a comprehensive overview of the  
146 relevant literature.

147

### 148 **Statistical analysis**



149 We used forest plots to display the proportion (with exact binomial 95% confidence  
150 intervals) of participants diagnosed with depression in each study (Newcombe, 1998).

151

152 We used random-effects models to describe the prevalence of depression in general  
153 medical and surgical inpatients. This is because it is implausible that the underlying study-  
154 specific prevalence of depression (i.e. the prevalence that would be observed were a study  
155 of infinite size) is exactly the same for each study. Prevalence is likely to vary from study to  
156 study according to factors, both measured and unmeasured, that differ between them  
157 (Stroup *et al.*, 2000). Random effects models assume that the populations investigated in  
158 each study are themselves drawn from a wider population of populations and that the  
159 underlying study-specific prevalences in these populations therefore follow a statistical  
160 distribution, rather than taking a single value.

161

162 As is common for proportions, we used the logit transformation expressing each of the  
163 prevalences as a log-odds. Accordingly our random-effects models assume that the logit  
164 transformed prevalences follow a normal distribution with a mean and standard deviation.

165 This mean can be thought of as a “typical” prevalence, while the standard deviation  
166 quantifies the underlying between-study variability in prevalences. This variability is  
167 summarised by a 95% prediction interval, which is the interval within which 95% of  
168 underlying study-specific prevalences are predicted to lie (for a thorough discussion of this  
169 topic see Guddat *et al.*) (Guddat *et al.*, 2012). As such it differs from a 95% confidence  
170 interval which quantifies the precision of the mean of the study-specific prevalences (with  
171 the mean defined after logit transformation).

172

173 We used the inverse variance method of DerSimonian and Laird to estimate between-study  
174 heterogeneity in underlying depression prevalence and the I-squared measure which  
175 represents the proportion of total variance attributable to this heterogeneity (Higgins *et al.*,  
176 2003). The assumption that underlying prevalences are normally distributed after logit  
177 transformation was not contradicted by our data.

178

179 We investigated potential sources of the heterogeneity that we observed between the  
180 studies' prevalence estimates (that is, the large amount of between-study variability  
181 compared with the total variability) by considering some of the known differences between  
182 the studies. To this end, we inspected scatter plots of depression prevalence against year of  
183 study publication, sample size, average (or other available measure for central tendency)  
184 participant age, and percentage of female participants. We used forest plots to compare  
185 depression prevalence in studies grouped by use of DSM major depression versus other  
186 diagnostic criteria for depression, and national income of the country where the study took  
187 place (we used income groupings because the studies had been done in too many different  
188 countries to group by country) (The World Bank, 2015). Where evidence of an association  
189 with depression prevalence was apparent, we performed a mixed-effects meta-regression  
190 and present its I-squared statistic, odds ratio and p-value for the association (Thompson and  
191 Higgins, 2002). We did not present funnel plots for bias assessment because in the presence  
192 of heterogeneity, there is no reason to expect a funnel shape (Terrin *et al.*, 2005). Statistical  
193 analysis was performed in R v3.2.2 using the "meta" package v3.8-0 (R Core Team, 2015,  
194 Schwarzer *et al.*, 2014). Graphs were produced in R and Stata v14 (StataCorp, College  
195 Station, TX, USA).

196

197

198 **RESULTS**

199 Our initial screening of 23,775 titles and abstracts yielded 4,161 articles for full paper  
200 review. We considered 158 of these to be relevant to the review. Of these 158 articles, 65  
201 (41%), describing 60 separate studies, met our quality criteria and were included (see Figure  
202 1, Figure 2 and appendix) (Abiodun and Ogunremi, 1990, Aghanwa and Ndububa, 2002,  
203 Alexander *et al.*, 1993, Annagür *et al.*, 2013, Arnold and Privitera, 1996, Arolt and Driessen,  
204 1996, Arolt *et al.*, 1997, Atesci *et al.*, 2004, Baubet *et al.*, 2011, Blomstedt *et al.*, 1996,  
205 Blumel *et al.*, 2005, Dogar *et al.*, 2008, Dyster-Aas *et al.*, 2008, Feldman *et al.*, 1987, Fenton  
206 *et al.*, 1994, Fritzsche *et al.*, 2003, Hardman *et al.*, 1989, Heeren and Rooymans, 1985,  
207 Hosaka *et al.*, 1999, Jenkins *et al.*, 1994, Kathol and Wenzel, 1992, Kayhan *et al.*, 2013,  
208 Kigamwa, 1991, Kishi *et al.*, 1994, Koenig *et al.*, 1997, Koenig *et al.*, 1991, Koenig *et al.*, 1993,  
209 Kok *et al.*, 1992, Kok *et al.*, 1995, Koroglu and Tural, 2010, Kugaya *et al.*, 2000, Kumar *et al.*,  
210 2011, Lazaro *et al.*, 1991, Lazaro *et al.*, 1995, Linka *et al.*, 1999, Linka *et al.*, 2000, Lykouras  
211 *et al.*, 1996, Madianos *et al.*, 2001, Marchesi *et al.*, 2004, Moayedoddin *et al.*, 2013, Nair  
212 and Pillay, 1997, Ng *et al.*, 1995, O'Riordan *et al.*, 1989, Pakriev *et al.*, 2009, Palmu *et al.*,  
213 2010, 2011, Petrak *et al.*, 2003, Prieto *et al.*, 2002, Regvat *et al.*, 2011, Seltzer, 1989, Sharma  
214 *et al.*, 2002, Silverstone, 1996, Singer *et al.*, 2013, Snyder *et al.*, 1992, Soeiro *et al.*, 2008,  
215 Starkstein *et al.*, 1988, Thalassinou *et al.*, 1992, Topitz *et al.*, 2015, Turner *et al.*, 2011,  
216 Uwakwe, 2000, Wancata *et al.*, 2000, Yan *et al.*, 2013, Yellowlees *et al.*, 1987, Zhao *et al.*,  
217 2014, Zhong *et al.*, 2010).

218

219 These studies had been conducted in 29 countries (see appendix for map) and had included  
220 a total of 12,540 participants (median sample size 109, range 27 to 993).

221

222 A variety of interviews and associated diagnostic criteria were used. The most commonly  
223 used interview (16 studies) was the Structured Clinical Interview for DSM-IV (SCID) and the  
224 most commonly used diagnostic criteria (used in 47 studies) were those for DSM major  
225 depression (American Psychiatric Association, 1994, First *et al.*, 1996). The majority of  
226 studies (40) had employed a psychiatrist or clinical psychologist to conduct the diagnostic  
227 interviews.

228

229 [Figures 1 and 2 about here]

230

231 The study sample was of general medical or surgical inpatients (or both) in 31 of the studies  
232 (median sample size 215, range 65 to 993, with a total of 9,305 participants; see Table 1)  
233 (Abiodun and Ogunremi, 1990, Arolt and Driessen, 1996, Arolt *et al.*, 1997, Feldman *et al.*,  
234 1987, Fenton *et al.*, 1994, Hosaka *et al.*, 1999, Jenkins *et al.*, 1994, Kathol and Wenzel, 1992,  
235 Kayhan *et al.*, 2013, Kigamwa, 1991, Koenig *et al.*, 1997, Koenig *et al.*, 1991, Koenig *et al.*,  
236 1993, Kok *et al.*, 1992, Kok *et al.*, 1995, Koroglu and Tural, 2010, Kumar *et al.*, 2011, Lazaro  
237 *et al.*, 1991, Lazaro *et al.*, 1995, Linka *et al.*, 1999, Linka *et al.*, 2000, Marchesi *et al.*, 2004,  
238 Moayedoddin *et al.*, 2013, Nair and Pillay, 1997, Pakriev *et al.*, 2009, Seltzer, 1989, Sharma  
239 *et al.*, 2002, Silverstone, 1996, Soeiro *et al.*, 2008, Thalassinios *et al.*, 1992, Topitz *et al.*,  
240 2015, Uwakwe, 2000, Wancata *et al.*, 2000, Yan *et al.*, 2013, Zhong *et al.*, 2010). These  
241 studies reported prevalence estimates for depression that ranged from 5% to 34% (see  
242 Figure 3). The high heterogeneity observed between study findings (I-squared 90%)  
243 indicated that no single estimate was sufficient to describe the prevalence of depression in  
244 general medical and/or surgical inpatients. Our random-effects model assumed that the  
245 underlying study-specific prevalences followed a normal distribution (on the log-odds scale).

246 The mean of this distribution corresponded to a prevalence of 12% (95% C.I. 10% to 15%)  
247 with 95% of all populations predicted to have an underlying depression prevalence between  
248 4% and 32% (the prediction interval).

249

250 [Table 1 and Figure 3 about here]

251

252 In our investigations of potential sources of this observed heterogeneity visual inspection of  
253 the scatter and forest plots suggested that percentage of female participants, study sample  
254 size, the income band of the country in which the study was done, and the diagnostic  
255 criteria used (but not year of study publication or average participant age), may all be  
256 associated with the observed prevalence of depression. We therefore tested the association  
257 of these variables with depression prevalence. We found that when expressed as an odds,  
258 studies with a higher percentage of female participants reported a lower prevalence of  
259 depression (OR 0.82 per 10 percentage points increase in female participants, 95% C.I. 0.71  
260 to 0.95,  $p=0.007$ ). Studies with larger sample sizes reported lower prevalences (OR 0.82 per  
261 doubling in size, 95% C.I. 0.68 to 0.99,  $p=0.043$ ). There were also non-significant associations  
262 with national income in the country in which the study was done ( $p=0.292$ ), and the  
263 diagnostic criteria used for depression ( $p=0.154$ ). Notably, in all our investigations the  
264 residual heterogeneity remained high (all I-squared  $>88\%$ , see appendix for scatter plots and  
265 forest plots) meaning that a very high proportion of the heterogeneity remained  
266 unaccounted for by the variables we considered.

267

268 In addition to the 31 studies of general medical and/or surgical patients, we identified 29  
269 studies (median sample size 72, range 27 to 502, with a total of 3,235 participants) of

270 inpatients who were in a variety of specialist units (such as endocrinology or haematology)  
271 or had very specific clinical characteristics (such as a diagnosis of systemic sclerosis)  
272 (Aghanwa and Ndububa, 2002, Alexander *et al.*, 1993, Annagür *et al.*, 2013, Arnold and  
273 Privitera, 1996, Atesci *et al.*, 2004, Baubet *et al.*, 2011, Blomstedt *et al.*, 1996, Blumel *et al.*,  
274 2005, Dogar *et al.*, 2008, Dyster-Aas *et al.*, 2008, Fritzsche *et al.*, 2003, Hardman *et al.*, 1989,  
275 Heeren and Rooymans, 1985, Kishi *et al.*, 1994, Kugaya *et al.*, 2000, Lykouras *et al.*, 1996,  
276 Madianos *et al.*, 2001, Ng *et al.*, 1995, O'Riordan *et al.*, 1989, Palmu *et al.*, 2010, 2011,  
277 Petrak *et al.*, 2003, Prieto *et al.*, 2002, Regvat *et al.*, 2011, Singer *et al.*, 2013, Snyder *et al.*,  
278 1992, Starkstein *et al.*, 1988, Turner *et al.*, 2011, Yellowlees *et al.*, 1987, Zhao *et al.*, 2014).  
279 These studies reported prevalence estimates ranging from 2% to 56%. They are described in  
280 detail in the online appendix.  
281

282 **DISCUSSION**

283

284 This is the first systematic review of studies of the prevalence of depression in general  
285 hospital inpatients. The 60 studies that we found had been conducted in 29 countries and  
286 included a total of 12,540 participants. They reported a wide range of prevalence estimates.  
287 We reduced the clinical heterogeneity by focussing on the 31 studies of general medical  
288 and/or surgical inpatients. However even in these studies the estimated prevalence ranged  
289 from 3% to 34%. There was also a high degree of heterogeneity, indicating that even  
290 'general medical and/or surgical inpatients' cannot be considered as a single population, but  
291 rather as a number of different populations, each with a different prevalence of depression.  
292 These populations had a median prevalence of depression of 12% and we can predict that  
293 95% of them have a prevalence between 4% and 32%. This median prevalence of 12% is  
294 more than twice that in the general population, for which international studies suggest an  
295 average 12-month prevalence of approximately 5% (Kessler and Bromet, 2013).

296

297 Our analyses were unable to adequately explain the observed heterogeneity in prevalence  
298 estimates. The only variables that we found to be significantly associated with prevalence of  
299 depression were sample size and the proportion of female patients in the study samples. As  
300 these explained only a trivial amount of the heterogeneity and the latter association was  
301 not in the expected direction (a higher proportion of female patients was associated with a  
302 lower prevalence of depression), we judge this finding to be of questionable importance.  
303 Our inability to explain the observed heterogeneity indicates that it resulted from variables  
304 we were unable to investigate as they had not been consistently reported in the  
305 publications we reviewed. These unreported variables might be at the population,  
306 healthcare system, patient or methodological level. At the population level, it is likely that

307 national and local prevalence of depression in the general population varies. At the  
308 healthcare system level, hospital type (e.g. university, community), funding systems,  
309 admission pathways and medical staffing vary substantially. At the patient level, it is likely  
310 that the characteristics of patients admitted to general hospitals, and specifically to general  
311 medical and surgical (as opposed to sub-speciality) wards varies. Methodologically, there  
312 are likely to be unreported variations in how the studies were done. These include how the  
313 patients were sampled (e.g. who was excluded), how the diagnosis of depression was made  
314 (e.g. the details of how the diagnostic interviews were conducted, whether physical  
315 symptoms were counted toward the diagnosis of depression or not and exactly how the  
316 diagnostic criteria were applied) and when the assessment was done during the period of  
317 hospitalisation (e.g. soon after admission or later in the stay).

318

319 This review has strengths which include: (a) The use of clearly defined inclusion criteria for  
320 papers to minimise selection bias; (b) the focus on studies where the diagnosis of  
321 depression was made by interview; (c) the exclusion of studies with major design flaws  
322 (Moher *et al.*, 2009, Stroup *et al.*, 2000). It also has limitations which include: (a) a reliance  
323 on the published reports to assess studies' relevance and quality, which may potentially  
324 have led to us excluding studies that were in fact well conducted, but poorly reported; (b)  
325 our inability to investigate all potential sources of heterogeneity because of the limited  
326 potentially relevant data reported in the publications we reviewed.

327

328 Given the importance of the question we addressed in this review, we found a remarkably  
329 small literature, much of which was published some time ago. Furthermore, our quality  
330 assessments indicated that much of that literature was of poor quality. Common



331 shortcomings were poor sampling strategies and the use of unclear case definitions for  
332 depressive disorder. Even the methodologically better studies selected for inclusion in this  
333 review were mostly small in size (median sample size 109) by epidemiological standards.  
334 There is consequently a clear and pressing need for better quality studies of the prevalence  
335 of depression in medical inpatients. If these are to inform service planning these should aim  
336 both to determine the prevalence of depression in specific settings (such as National Health  
337 Service hospitals in the UK) and to clarify the determinants of the substantial apparent  
338 variations in prevalence noted in this review. Suggestions for the design of future studies  
339 are given in Table 2.

340

341 [Table 2 about here]

342

343 Despite the limitations of the available evidence we can reasonably conclude that  
344 depression is sufficiently common in medical inpatients to make planning for its systematic  
345 management worthwhile. This management should include systematic identification of  
346 depression during hospital admissions, monitoring of depression once identified (during the  
347 hospital admission and thereafter, to determine whether it resolves post-discharge) and the  
348 initiation of treatment when it is persistent (Kathol and Wenzel, 1992, Mayou *et al.*, 1988).  
349 Few hospitals currently have such systems. The approach we have tested for depression  
350 management in cancer patients provides a potential model for how we might improve  
351 depression care in all medical settings (Walker and Sharpe, 2014).

352

353

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360

361 **CONFLICTS OF INTEREST**

362 None.

363

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