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Depression prevalence using the HADS-D compared to SCID major depression classification

Citation for published version:

Brehaut, E, Neupane, D, Levis, B, Wu, Y, Sun, Y, Krishnan, A, He, C, Bhandari, PM, Negeri, Z, Riehm, KE, Rice, DB, Azar, M, Yan, XW, Imran, M, Chiovitti, MJ, Saadat, N, Cuijpers, P, Ioannidis, JPA, Markham, S, Patten, SB, Ziegelstein, RC, Henry, M, Ismail, Z, Loiselle, CG, Mitchell, ND, Tonelli, M, Boruff, JT, Kloda, LA, Beraldi, A, Braeken, APBM, Carter, G, Clover, K, Conroy, RM, Cukor, D, da Rocha e Silva, CE, De Souza, J, Downing, MG, Feinstein, A, Ferentinos, PP, Fischer, FH, Flint, AJ, Fujimori, M, Gallagher, P, Goebel, S, Jetté, N, Julião, M, Keller, M, Kjærgaard, M, Love, AW, Löwe, B, Martin-Santos, R, Michopoulos, I, Navines, R, O'Rourke, SJ, Öztürk, A, Pintor, L, Ponsford, JL, Rooney, AG, Sánchez-González, R, Schwarzbald, ML, Sharpe, M, Simard, S, Singer, S, Stone, J, Tung, K-Y, Turner, A, Walker, J, Walterfang, M, White, J, Benedetti, A & Thombs, BD 2020, 'Depression prevalence using the HADS-D compared to SCID major depression classification: An individual participant data meta-analysis', *Journal of Psychosomatic Research*, vol. 139. <https://doi.org/10.1016/j.jpsychores.2020.110256>

Digital Object Identifier (DOI):

[10.1016/j.jpsychores.2020.110256](https://doi.org/10.1016/j.jpsychores.2020.110256)

Link:

[Link to publication record in Edinburgh Research Explorer](#)

Document Version:

Peer reviewed version

Published In:

Journal of Psychosomatic Research

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1 **Depression Prevalence using the HADS-D Compared to SCID Major Depression**

2 **Classification: an Individual Participant Data Meta-Analysis**

3

4 **Running head:** Estimating Depression Prevalence using the HADS-D and SCID

5

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152 **Word Count:** 3, 649

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161 **ABSTRACT**

162 **Objectives:** Validated diagnostic interviews are required to classify depression status and
163 estimate prevalence of disorder, but screening tools are often used instead. We used individual
164 participant data meta-analysis to compare prevalence based on standard Hospital Anxiety and
165 Depression Scale – depression subscale (HADS-D) cutoffs of ≥ 8 and ≥ 11 versus Structured
166 Clinical Interview for DSM (SCID) major depression and determined if an alternative HADS-D
167 cutoff could more accurately estimate prevalence.

168 **Methods:** We searched Medline, Medline In-Process & Other Non-Indexed Citations via Ovid,
169 PsycINFO, and Web of Science (inception-July 11, 2016) for studies comparing HADS-D scores
170 to SCID major depression status. Pooled prevalence and pooled differences in prevalence for
171 HADS-D cutoffs versus SCID major depression were estimated.

172 **Results:** 6,005 participants (689 SCID major depression cases) from 41 primary studies were
173 included. Pooled prevalence was 24.5% (95% Confidence Interval (CI): 20.5%, 29.0%) for
174 HADS-D ≥ 8 , 10.7% (95% CI: 8.3%, 13.8%) for HADS-D ≥ 11 , and 11.6% (95% CI: 9.2%,
175 14.6%) for SCID major depression. HADS-D ≥ 11 was closest to SCID major depression
176 prevalence, but the 95% prediction interval for the difference that could be expected for HADS-
177 D ≥ 11 versus SCID in a new study was -21.1% to 19.5%.

178 **Conclusions:** HADS-D ≥ 8 substantially overestimates depression prevalence. Of all possible
179 cutoff thresholds, HADS-D ≥ 11 was closest to the SCID, but there was substantial heterogeneity
180 in the difference between HADS-D ≥ 11 and SCID-based estimates. HADS-D should not be
181 used as a substitute for a validated diagnostic interview.

182 **Key Words:** depression, Hospital Anxiety and Depression Scale, individual participant data,
183 meta-analysis, screening tools

184 **INTRODUCTION**

185 Accurately measuring depression prevalence in different populations is important to
186 understand disease burden, interpret research on etiology, and utilize healthcare resources as
187 efficiently as possible (Rogan & Gladen, 1978). In mental health research, diagnostic interviews
188 are required for diagnosis of major depression (First, Spitzer, Gibbon, & Williams, 1995;
189 Wittchen, 1994). These interviews, however, are costly to administer, especially in large groups,
190 due to the time and trained personnel required to conduct them properly. Therefore, self-report
191 screening questionnaires are sometimes used as an inexpensive alternative to evaluate depression
192 prevalence, with the percentage of patients scoring above a cutoff threshold being described as
193 the prevalence of depression (Levis et al., 2019; Thombs, Kwakkenbos, Levis, & Benedetti,
194 2018). Screening tool cutoffs, however, are typically set to cast a wide net and identify many
195 more individuals for further assessment than will meet diagnostic criteria. Thus, commonly used
196 screening tools tend to overestimate depression prevalence, sometimes substantially (Thombs et
197 al., 2018).

198 A previous study used an individual participant data meta-analysis (IPDMA) approach to
199 compare prevalence based on a depression screening tool with prevalence based on a validated
200 diagnostic interview. That meta-analysis examined prevalence based on the Patient Health
201 Questionnaire-9 (PHQ-9) using the standard cutoff of ≥ 10 compared to prevalence based on the
202 Structured Clinical Interview for the DSM (SCID) among 9,242 participants from 44 primary
203 studies (Levis et al., 2020). Compared to the SCID, PHQ-9 ≥ 10 overestimated prevalence by
204 11.9%; across included studies, the mean and median ratio of PHQ-9 prevalence to SCID-based
205 prevalence were 2.5 and 1.9. In that study, the authors attempted to identify a PHQ-9 cutoff that

206 would match SCID-based prevalence, but heterogeneity was too high to generate consistently
207 accurate estimates in individual studies for any PHQ-9 cutoff.

208 The Hospital Anxiety and Depression Scale (HADS) is a self-report screening
209 questionnaire designed to be administered to non-psychiatric medical patients. It includes 14
210 items, with 7 assessing symptoms of depression (HADS-D) and 7 assessing symptoms of anxiety
211 (HADS-A) over the past week. To avoid overlap with physical illness, the HADS-D does not
212 include symptoms common to both physical and mental disorders, such as insomnia, loss of
213 appetite, or fatigue. Cutoff thresholds of ≥ 8 and ≥ 11 on the HADS-D are traditionally used as
214 standard cutoffs for identifying people who may have depression (Zigmond & Snaith, 1983).
215 Although not designed for this purpose, the HADS-D is also frequently used to report depression
216 prevalence in primary research studies. A review of recent studies listed in PubMed (2018-2019)
217 identified 32 studies that reported “prevalence” of depression based on a HADS-D cutoff, with \geq
218 8 and ≥ 11 used in 66% and 16% of the studies, respectively (see supplementary material
219 eMethods 1 and eTable 1).

220 Although other screening tools and commonly used cutoffs have been shown to
221 overestimate depression prevalence, it is not clear whether this would be the case with the
222 HADS-D. A previous study that investigated prevalence of major depression among survivors of
223 acute myocardial infarction found a prevalence of 20% (10,785 participants, 8 studies) using
224 structured interviews, compared to 16% using a HADS-D cutoff of ≥ 8 (863 participants, 4
225 studies), and 7% using ≥ 11 (830 participants, 4 studies) (Thombs et al., 2006). This was a
226 between-study comparison, however, and no included studies administered both the HADS-D
227 and a validated diagnostic interview.

228 The objectives of the present study were to use an IPDMA approach to (1) compare
229 pooled prevalence based on HADS-D cutoffs of ≥ 8 and ≥ 11 with major depression prevalence
230 based on the SCID; and (2) use a prevalence-matching approach to determine if any cutoff
231 threshold on the HADS-D matches prevalence based on the SCID with sufficiently low
232 heterogeneity that it could be used to accurately measure depression prevalence in future studies.

233 **METHODS**

234 This study used a subset of data collected for an IPDMA of the diagnostic accuracy of the
235 HADS-D for screening to detect major depression. Detailed methods of the IPDMA were
236 registered in PROSPERO (CRD42015016761), and a protocol was published (Thombs et al.,
237 2016). The present analysis was not included in the original IPDMA protocol, which focused
238 only on diagnostic accuracy. A protocol for the present study was published on the Open Science
239 Framework prior to initiating the study (<https://osf.io/n5a3e/>).

240 **Study Selection**

241 In the main IPDMA, datasets from studies in any language were eligible for inclusion if
242 (1) they included HADS-D scores; (2) they included diagnostic classifications for current Major
243 Depressive Episode (MDE) or Major Depressive Disorder (MDD) based on the Diagnostic and
244 Statistical Manual (DSM) or International Classification of Diseases criteria, using a validated
245 semi-structured or fully structured interview; (3) the HADS-D and diagnostic interview were
246 administered within two weeks of each other, since diagnostic criteria for major depression are
247 for symptoms experienced in the last two weeks; (4) participants were ≥ 18 years and not
248 recruited from youth or school-based settings, since the main IPDMA was designed for adult
249 screening, and although there are some adults in schools, the pathways for identification and
250 management are likely very different from other adult settings; and (5) participants were not

251 recruited from psychiatric settings or because they were identified as having symptoms of
252 depression, since screening is done to identify unrecognized cases. Datasets where not all
253 participants were eligible were included if primary data allowed selection of eligible participants.

254 For the present study, we included only primary studies that based diagnoses on the SCID
255 (First et al., 1995). The SCID is a semi-structured diagnostic interview designed to be conducted
256 by an experienced clinician; it requires professional judgment and allows rephrasing questions
257 and probes to follow up responses. The reason for including only studies that used the SCID is
258 that in recent analyses using three large IPDMA databases (Levis et al., 2018, Levis et al., 2019,
259 Wu et al., 2020) we found that, compared to semi-structured interviews, fully structured
260 interviews, which are designed for administration by lay interviewers, may identify more patients
261 with low-level symptoms as depressed but fewer patients with high-level symptoms. These
262 results are consistent with the idea that semi-structured interviews most closely replicate clinical
263 interviews done by trained professionals, whereas fully structured interviews are less rigorous
264 reference standards; they are less resource-intensive options that can be administered by research
265 staff without diagnostic skills but may misclassify major depression in substantial numbers of
266 patients. An important feature of the SCID is that it allows the interviewer to probe to determine
267 whether a symptom is merely a manifestation of a physical illness. In the HADS IPDMA
268 database, the SCID was the most commonly used semi-structured interview; out of 83 studies, 45
269 used semi-structured interviews, and 41 of the 45 used the SCID. In sensitivity analyses, we also
270 included the 4 studies from the IPDMA database that used semi-structured interviews other than
271 the SCID.

272 **Data Sources and Searches**

273 A medical librarian searched Medline, Medline In-Process & Other Non-Indexed
274 Citations via Ovid, PsycINFO, and Web of Science from inception to July 11, 2016, using a
275 peer-reviewed search strategy (McGowan et al., 2016) (see supplementary material eMethods 2).
276 We also reviewed reference lists of relevant reviews and queried contributing authors about non-
277 published studies. Search results were uploaded into RefWorks (RefWorks-COS, Bethesda, MD,
278 USA). After de-duplication, unique citations were uploaded into DistillerSR (Evidence Partners,
279 Ottawa, Canada) for tracking search results.

280 Two investigators independently reviewed studies by title and abstract for eligibility. If
281 either deemed a study potentially eligible, a full-text review was done by both investigators
282 independently. Any disagreements were resolved by consensus and consulting a third
283 investigator when necessary. For languages other than those in which team members were fluent,
284 translators were consulted.

285 **Data Contribution and Synthesis**

286 Authors of eligible datasets were invited to contribute de-identified primary data,
287 including HADS-D scores and major depression classification status. We emailed corresponding
288 authors of eligible primary studies at least three times, as necessary, with at least two weeks
289 between each email. If we did not receive a response, we emailed co-authors and attempted to
290 contact corresponding authors by phone.

291 Before integrating individual datasets into our synthesized dataset, we compared
292 published participant characteristics and diagnostic accuracy results with results from raw
293 datasets and resolved any discrepancies in consultation with the original investigators.

294 **Data Analysis**

295 *Comparison of HADS-D ≥ 8 and ≥ 11 Prevalence with SCID Major Depression Prevalence*

296 For each primary study, we estimated 7 values: (1) the percentage of participants who
297 scored ≥ 8 on the HADS-D, (2) the percentage of participants who scored ≥ 11 on the HADS-D,
298 (3) the percentage of participants classified as having major depression based on the SCID, (4)
299 the difference between HADS-D ≥ 8 percentage and SCID percentage, (5) the ratio for HADS-D
300 ≥ 8 percentage versus SCID percentage, and the corresponding (6) difference and (7) ratio for
301 HADS-D ≥ 11 versus the SCID. Then, across all studies, we pooled prevalence for HADS-D ≥ 8 ,
302 HADS-D ≥ 11 , and SCID, and we pooled the HADS-D versus SCID differences in prevalence
303 from each study.

304 *Prevalence Matching*

305 To identify which HADS-D cutoff best matches SCID-based prevalence, we estimated
306 the pooled difference in prevalence for each possible HADS-D cutoff compared to the SCID.
307 The HADS-D cutoff with the smallest pooled difference was chosen to be the “prevalence-
308 matched cutoff.” Then, for each included study, we estimated the difference and ratio in
309 prevalence based on the prevalence-matched cutoff versus SCID major depression. We
310 determined the mean and median absolute difference and the range of differences across all
311 studies. To illustrate the range of difference values that would be expected if a new study were to
312 compare prevalence based on the prevalence-matched cutoff to prevalence based on the SCID,
313 we estimated a 95% prediction interval for the difference.

314 All meta-analyses were conducted in R (R version R 3.4.1 and R Studio version 1.0.143)
315 using the lme4 package. To estimate pooled prevalence values, generalized linear mixed-effects
316 models with a logit link function were fit using the glmer function. To estimate pooled difference
317 values, linear mixed-effects models were fit using the lmer function. To account for correlation
318 between subjects within the same primary study, random intercepts were fit for each primary

319 study. To quantify heterogeneity, for each analysis, we calculated τ^2 , which is the estimate of
320 between-study variance, and I^2 , which quantifies the proportion of total variability due to the
321 between-study heterogeneity.

322 We conducted two sets of post hoc analyses. First, some studies had high depression
323 prevalence. Thus, to test whether differences in prevalence between the HADS-D and SCID
324 might be influenced by heterogeneity in depression levels, we repeated the main analysis of
325 prevalence excluding studies with SCID-based prevalence $\geq 20.0\%$. Second, we assessed
326 whether differences in prevalence for the prevalence-matched cutoff and SCID were associated
327 with study or patient characteristics. To do this, we fit an additional linear mixed-effects model
328 for pooled prevalence difference, including age, sex, country human development index category
329 (“very high” [reference group] or “high”, based on the United Nation’s Human Development
330 Index for the year of publication), recruitment setting category (nonmedical care, inpatient care
331 [reference group], outpatient care, or mixed inpatient and outpatient care), and sample size as
332 fixed-effect covariates. For this analysis, we excluded 520 participants (8.7%) who were missing
333 age or sex data. We repeated all analyses including 4 studies that used semi-structured interviews
334 other than the SCID.

335 **RESULTS**

336 The initial search for the main IPDMA found 10,015 unique titles and abstracts for
337 potential eligibility. Of these, we excluded 9,584 studies after reviewing titles and abstracts and
338 238 studies after full-text review. There were 193 eligible studies using data from 133 unique
339 samples from which 75 (56.4%) contributed individual participant data. Authors also contributed
340 data from 8 unpublished studies, resulting in a total of 83 datasets. For our main analyses, we
341 excluded 42 studies that used diagnostic interviews other than the SCID. In total, the main

342 analyses included 41 primary studies involving 6,005 participants (689 SCID major depression
343 cases; 11.5%; Figure 1). Of 58 eligible primary studies with unique samples that did not
344 contribute individual participant data, 26 used the SCID (3,096 participants). Thus, the main
345 analyses in the present study included 61.2% of eligible studies that used the SCID (41 of 67)
346 and 66.0% of eligible participants (6,005 of 9,101). See Table 1 for characteristics of each
347 included study.

348 There were 4 additional studies that used semi-structured diagnostic interviews other than
349 the SCID (635 participants; 65 major depression cases; 10.2%), which we included in sensitivity
350 analyses. Two of these studies used the Monash Interview for Liaison Psychiatry, one used the
351 Schedule for Affective Disorders and Schizophrenia, and one used the Schedules for Clinical
352 Assessment in Neuropsychiatry. Thus, these analyses included 45 primary studies (6,640
353 participants; 754 major depression cases; 11.4%; Table 1).

354 **Objective 1: Comparison of HADS-D \geq 8, HADS-D \geq 11 and SCID Major Depression**

355 **Prevalence**

356 *Pooled Prevalence*

357 The results for individual studies are presented in Table 1. For the 41 studies included in
358 our main analyses, the percentage of participants who scored \geq 8 on the HADS-D ranged from
359 4.2% to 82.7%, with a pooled prevalence of 24.5% (95% CI: 20.5% to 29.0%, τ^2 :0.49, I^2 :
360 97.2%). The percentage of participants who scored \geq 11 on the HADS-D ranged from 0.3% to
361 74.7%, with a pooled prevalence of 10.7% (95% CI: 8.3% to 13.8%, τ^2 : 0.71, I^2 : 97.1%). The
362 percentage of participants classified as having SCID major depression ranged from 0% to 50.0%,
363 with a pooled prevalence of 11.6% (95% CI: 9.2% to 14.6%, τ^2 : 0.6, I^2 :97.1%).

364 Excluding 8 studies (552 participants; 185 major depression cases; 33.5%) with SCID-
365 based prevalence of 20.0% or over, prevalence based on the HADS-D \geq 8 was 21.8% (95% CI:
366 18.4% to 25.6%, τ^2 : 0.31, I^2 = 96.4). Prevalence based on the HADS-D \geq 11 was 9.2% (95% CI:
367 7.3% to 11.6%, τ^2 : 0.41, I^2 = 96.0). Prevalence based on the SCID was 8.9% (95% CI: 7.6% to
368 10.4%, τ^2 : 0.14, I^2 = 94.7).

369 Results were similar when the 4 studies using interviews other than the SCID were
370 included.

371 *Pooled Difference and Ratio*

372 The difference between HADS-D \geq 8 and SCID-based prevalence in the main analyses
373 ranged from -9.5% to 41.3%, and the pooled difference was 12.4% (95% CI: 8.8% to 16%, τ^2 :
374 0.01, I^2 : 97.2%). The difference between HADS-D \geq 11 and SCID-based prevalence ranged from
375 -31.0% to 33.3%, and the pooled difference was -0.8% (95% CI: -4.1% to 2.5%, τ^2 : 0.01, I^2 :
376 97.2%).

377 Results were similar in the sensitivity analyses. Pooled difference for HADS-D \geq 8 was
378 11.9% (95% CI: 8.6% to 15.2%, τ^2 : 0.01, I^2 : 97.4%), and pooled difference for HADS-D \geq 11
379 was -1.0% (95% CI: -4.0% to 2.0%, τ^2 : 0.01, I^2 : 97.5%). The ratio of HADS-D \geq 8 prevalence
380 to SCID major depression prevalence ranged from 0.4 to 7.7 times (mean: 2.6 times; median: 2
381 times). The ratio of HADS-D \geq 11 prevalence to SCID major depression prevalence ranged from
382 0 to 3.8 times (mean: 1.2 times; median: 0.8 times).

383 *Mean Ratio and Difference in Individual Studies*

384 In the main analyses, the mean ratio of HADS-D to SCID-based prevalence was 0.73
385 times for the 3 studies with HADS-D \geq 8-based prevalence $<$ 10.0% (mean difference: -2.7%),
386 1.8 times for the 7 studies with HADS-D \geq 8-based prevalence between 11.0% and 19.0% (mean

387 difference: 6.1%), and 2.9 times for the 31 studies with HADS-D \geq 8-based prevalence of 20.0%
388 or greater (mean difference: 15.2%). The mean ratio was 0.7 times for the 19 studies with
389 HADS-D \geq 11-based prevalence $<$ 10.0% (mean difference: -4.4%), 1.5 times for the 15 studies
390 with HADS-D \geq 11-based prevalence between 11.0% and 19.0% (mean difference: -1.3), and 2
391 times for the 7 studies with HADS-D \geq 11-based prevalence of 20.0% or greater (mean
392 difference: 9.8%). Results were similar when the 4 additional studies were included.

393 **Objective 2: Prevalence Matching**

394 Of all possible HADS-D cutoffs, \geq 11 produced the pooled prevalence estimate that most
395 closely matched SCID major depression prevalence (HADS-D \geq 11: 10.7%, SCID: 11.6%)
396 (Figure 2). This cutoff underestimated depression prevalence compared to the SCID, but only
397 slightly (pooled difference: -0.8%). HADS-D \geq 10 produced a pooled prevalence of 14.7%
398 (pooled difference: 3.1%), and HADS-D \geq 12 a pooled prevalence of 7.9% (pooled difference: -
399 3.7%). The mean absolute difference between HADS-D \geq 11 and SCID was 8.2%, and the
400 median absolute difference was 6.7%. The 95% prediction interval for the difference between
401 HADS-D \geq 11 and SCID-based prevalence was -21.1% to 19.5%. Results were similar in
402 sensitivity analyses. In the post-hoc analysis, no participant or study characteristics were
403 significantly associated with differences in prevalence for the HADS-D prevalence-match cutoff
404 compared to the SCID.

405 **DISCUSSION**

406 Previous research has demonstrated that there may be substantial differences between
407 screening tools and diagnostic tools in estimating depression prevalence (Levis et al., 2020,
408 Thombs et al., 2018, Levis et al., 2019). In the present study, we found that the most commonly
409 used HADS-D cutoff threshold for reporting depression prevalence of \geq 8 overestimated

410 depression prevalence (24.5%) substantially compared to SCID major depression prevalence
411 (11.6%). A HADS-D cutoff of ≥ 11 underestimated prevalence only slightly in aggregate
412 compared to the SCID (10.7%), but heterogeneity in the difference between HADS-D ≥ 11 and
413 SCID-based estimates in individual studies was high. The 95% prediction interval for difference
414 between HADS-D ≥ 11 and SCID-based prevalence ranged from approximately -20% to 20%,
415 which suggests that any single new study using HADS-D ≥ 11 may over or underestimate
416 depression prevalence by up to 20%.

417 Results from the present study are partially consistent with what might be expected
418 theoretically when comparing screening tools and diagnostic tools (Thombs et al., 2018). Since
419 screening tools are designed to cast a wide net and identify individuals who might be depressed,
420 they generally tend to overestimate depression prevalence when compared to diagnostic
421 interviews, which are designed to determine who meets diagnostic criteria. This was indeed the
422 case in our study for results from the HADS-D ≥ 8 , which were in line with those from a
423 previous study that found that the PHQ-9 similarly overestimated prevalence (Levis et al., 2020).
424 A finding that was unique to the present study was that estimates based on another commonly
425 used cutoff threshold, HADS ≥ 11 , were in aggregate consistent with major depression
426 prevalence based on the SCID. The findings from the present study differed from those in a
427 previous synthesis of evidence from post-acute myocardial infarction patients in which
428 depression prevalence estimates based on HADS-D ≥ 8 and ≥ 11 were both lower than estimates
429 based on structured interviews (Thombs et al., 2006). This discrepancy may be due to the
430 specific clinical population eligible for the review or because none of the studies included in that
431 review administered both the HADS-D and a structured interview to the same group of
432 individuals.

433 Identifying a HADS-D cutoff that consistently matches the SCID would allow
434 researchers to use screening questionnaires rather than diagnostic interviews for prevalence
435 estimation, thus conserving time and resources. However, when we used a prevalence-matching
436 approach and identified the closest HADS-D cutoff (≥ 11) to the SCID, although the aggregate
437 estimates were similar, heterogeneity between studies was too high to suggest that HADS-D ≥ 11
438 would accurately estimate prevalence in any particular future study. In fact, it may substantially
439 under or overestimate prevalence in individual studies.

440 Researchers often describe the proportion of individuals scoring at or above a cutoff
441 threshold as prevalence of “depressive symptoms” or “clinically significant depressive
442 symptoms” rather than prevalence of “depression”. However, this does not resolve the problem.
443 There is no evidence that impairment becomes meaningful at or above these thresholds, which
444 have been set for the purpose of screening, and not for impairment delineation. While individuals
445 scoring above these thresholds have greater impairment on average than those scoring below the
446 threshold, this would be the case for any threshold that is set. Reporting the proportion of
447 individuals scoring above a threshold may be useful for comparisons between samples. However,
448 it should not be characterized as “prevalence” or as the percentage of individuals who have
449 “symptoms of depression” versus no symptoms.

450 Ideally, semi-structured interviews should be used for prevalence estimation, since they
451 provide patient-specific details that help interviewers determine whether the diagnostic criteria
452 for depression are met. They also most closely replicate full assessments done by trained
453 professionals (Wu et al., 2020). However, these interviews are not always feasible as they are
454 time-intensive compared to screening questionnaires. Diagnostic interviews also require trained
455 research staff or mental health professionals to conduct them properly. Hiring clinicians or

456 training research staff to do this can be costly and time-consuming, especially when assessing
457 large numbers of study participants. When determining which diagnostic interview to use,
458 researchers should consider the advantages and disadvantages of each, including performance,
459 cost, and required training (Wu et. al., 2020). When publishing studies, researchers should
460 discuss their reasons for selecting a particular interview, as well as the implications of their
461 selection.

462 To our knowledge, this is the first study to synthesize evidence and directly compare
463 depression prevalence based on HADS-D scores versus the SCID. Strengths of this study are that
464 we examined data from 41 primary research studies including 6,005 participants, and that we
465 directly compared status based on HADS-D scores to status based on a validated diagnostic
466 interview. A limitation is that we did not incorporate data from 39% of eligible studies that used
467 the SCID (26 of 61) and 34% of eligible participants (3,096 of 9,101), since they did not provide
468 individual participant data. Furthermore, since not all studies described the qualifications of the
469 individuals administering the SCID, it is possible that interviewer skill-level contributed to
470 heterogeneity. Since the objective of our study was to determine how accurate the HADS-D is
471 for estimating depression prevalence, we did not evaluate whether the correct individuals were
472 identified; that is beyond the scope of this study. Since diagnostic criteria for major depression
473 are for symptoms experienced in the last two weeks, we ensured that all studies administered the
474 HADS-D and SCID within two-weeks of each other. However, studies may not have
475 administered the HADS-D and SCID on the same day. This may have contributed to variability
476 in responses to the SCID and the HADS-D, but it would not be expected to contribute to bias.
477 We included studies where diagnoses were based on DSM or ICD criteria, but only one study
478 used ICD (De Souza et. al., 2009). This study did not use the SCID and was included only in

479 sensitivity analyses. Finally, this study considered only the HADS-D, which is one screening tool
480 out of many that are commonly used in clinical practice. As shown in this study, the degree to
481 which the use of screening tools may accurately estimate prevalence depends on the specific
482 screening tool and cutoff threshold used.

483 In conclusion, we found that the standard HADS-D cutoff of ≥ 8 , which is most
484 commonly used by researchers to estimate depression prevalence, resulted in overestimation
485 when compared to the SCID. The other standard screening cutoff of ≥ 11 most closely matched
486 SCID prevalence, but heterogeneity in the difference between HADS-D and SCID-based
487 estimates in individual studies was high and not associated with study or participant
488 characteristics. Findings are consistent with evidence demonstrating that depression screening
489 tools should not be used for diagnostic purposes. Studies should only report prevalence of
490 depression if they used a validated diagnostic interview designed for case classification.
491 Clinicians and researchers should be aware that the prevalence of depression reported in studies
492 using depression screening tools may not be accurate.

493 **Contributors:**

494 • BLevis, PC, JPAI, SM, SBP, RCZ (DEPRESSD Steering Committee Members), MH, ZI,
495 CGL, NDM, MT (DEPRESSD Knowledge Users), ABenedetti, and BDT (DEPRESSD
496 Directors) were responsible for the conception, design and oversight of the main IPDMA
497 project of which the present study is a part.

498 • EB, DN, BLevis, JPAI, ABenedetti, and BDT were responsible for the conception and
499 design of the present study

500 • JTB and LAK designed and conducted database searches to identify eligible studies.

501 • ABeraldi, APBMB, GC, KC, RMC, DC, CEdReS, JDS, MGD, AF, PPF, FHF, AJF, MF,
502 PG, SG, NJ, MJ, MKeller, MKjærgaard, AWL, BLöwe, RMS, IM, RN, SJO, AÖ, LP,
503 JLP, AGR, RSG, MLS, MS, SSimard, SSinger, JS, KYT, AT, JWalker, MW, and JWhite
504 contributed primary datasets that were included in this study.

505 • EB, DN, BLevis, YW, YS, AK, CH, PMB, ZN, KER, DBR, MA, XWY, MI, MJC, NS
506 and BDT contributed to data extraction and coding for the meta-analysis.

507 • EB, DN, BLevis, ABenedetti, and BDT contributed to the data analysis and
508 interpretation.

509 • EB, DN, BLevis, YW, and BDT contributed to drafting the manuscript.

510 • All authors provided a critical review and approved the final manuscript. ABenedetti and
511 BDT are the guarantors; they had full access to all the data in the study and take
512 responsibility for the integrity of the data and the accuracy of the data analyses.

513

514 **Declaration of Competing Interest:**

515 All authors have completed the Unified Competing Interest form at
516 http://www.icmje.org/coi_disclosure.pdf and declare that: no support from any organisation for
517 the submitted work; no financial relationships with any organisations that might have an interest
518 in the submitted work in the previous three years with the following exceptions: (1) Dr. Ismail
519 declares that he has received personal fees from Avanir, Janssen, Lundbeck, Otsuka, Sunovion,
520 outside the submitted work. (2) Dr. Tonelli declares that he has received a grant from Merck
521 Canada, outside the submitted work. (3) Dr. Feinstein reports that he received speaker's
522 honorariums from Biogen, Sanofi-Genzyme, Merck-Serono, Novartis, Roche, and is on the
523 advisory board for Akili Interactive, outside the submitted work; He has also received royalties
524 from the Cambridge University Press for the Clinical Neuropsychiatry of Multiple Sclerosis, 2nd
525 Edition. (4) Dr. Löwe declares that the primary study by Löwe et al. was supported by
526 unrestricted educational grants from Pfizer, Germany. (5) Dr. Stone declares that he has received
527 personal fees from UptoDate, outside the submitted work. No other relationships or activities
528 that could appear to have influenced the submitted work.

529 **Roles of the Funding Source:**

530 This study was funded by the Canadian Institutes of Health Research (CIHR, KRS-144045 &
531 PCG 155468). Ms. Neupane was supported by a G.R. Caverhill Fellowship from the Faculty of
532 Medicine, McGill University. Drs. Levis and Wu were supported by Fonds de recherche du
533 Québec - Santé (FRQS) Postdoctoral Training Fellowships. Mr. Bhandari was supported by a
534 studentship from the Research Institute of the McGill University Health Centre. Ms. Rice was
535 supported by a Vanier Canada Graduate Scholarship. Dr. Patten was supported by a Senior
536 Health Scholar award from Alberta Innovates, Health Solutions. The primary study by Scott et
537 al. was supported by the Cumming School of Medicine and Alberta Health Services through the
538 Calgary Health Trust, and funding from the Hotchkiss Brain Institute. The primary study by
539 Amoozegar et al. was supported by the Alberta Health Services, the University of Calgary
540 Faculty of Medicine, and the Hotchkiss Brain Institute. The primary study by Cheung et al. was
541 supported by the Waikato Clinical School, University of Auckland, the Waikato Medical
542 Research Foundation and the Waikato Respiratory Research Fund. The primary study by Cukor
543 et al. was supported in part by a Promoting Psychological Research and Training on Health-
544 Disparities Issues at Ethnic Minority Serving Institutions Grants (ProDIGs) awarded to Dr.
545 Cukor from the American Psychological Association. The primary study by De Souza et al. was
546 supported by Birmingham and Solihull Mental Health Foundation Trust. The primary study by
547 Honarmand et al. was supported by a grant from the Multiple Sclerosis Society of Canada. The
548 primary study by Fischer et al. was supported as part of the RECODEHF study by the German
549 Federal Ministry of Education and Research (01GY1150). The primary study by Gagnon et al.
550 was supported by the Drummond Foundation and the Department of Psychiatry, University
551 Health Network. The primary study by Akechi et al. was supported in part by a Grant-in-Aid for

552 Cancer Research (11-2) from the Japanese Ministry of Health, Labour and Welfare and a Grant-
553 in-Aid for Young Scientists (B) from the Japanese Ministry of Education, Culture, Sports,
554 Science and Technology. The primary study by Kugaya et al. was supported in part by a Grant-
555 in-Aid for Cancer Research (9-31) and the Second-Term Comprehensive 10-year Strategy for
556 Cancer Control from the Japanese Ministry of Health, Labour and Welfare. The primary study
557 Ryan et al. was supported by the Irish Cancer Society (Grant CRP08GAL). The primary study by
558 Keller et al. was supported by the Medical Faculty of the University of Heidelberg (grant no.
559 175/2000). The primary study by Love et al. (2004) was supported by the Kathleen Cuninghams
560 Foundation (National Breast Cancer Foundation), the Cancer Council of Victoria and the
561 National Health and Medical Research Council. The primary study by Love et al. (2002) was
562 supported by a grant from the Bethlehem Griffiths Research Foundation. The primary study by
563 Löwe et al. was supported by the medical faculty of the University of Heidelberg, Germany
564 (Project 121/2000). The primary study by Navines et al. was supported in part by the Spanish
565 grants from the Fondo de Investigación en Salud, Instituto de Salud Carlos III (EO PI08/90869
566 and PSIGEN-VHC Study: FIS-E08/00268) and the support of FEDER (one way to make
567 Europe). The primary study by O'Rourke et al. was supported by the Scottish Home and Health
568 Department, Stroke Association, and Medical Research Council. The primary study by Sanchez-
569 Gistau et al. was supported by a grant from the Ministry of Health of Spain (PI040418) and in
570 part by Catalonia Government, DURSI 2009SGR1119. The primary study by Gould et al. was
571 supported by the Transport Accident Commission Grant. The primary study by Rooney et al. was
572 supported by the NHS Lothian Neuro-Oncology Endowment Fund. The primary study by
573 Schwarzbald et al. was supported by PRONEX Program (NENASC Project) and PPSUS
574 Program of Fundação de Amparo a pesquisa e Inovacao do Estado de Santa Catarina (FAPESC)

575 and the National Science and Technology Institute for Translational Medicine (INCT-TM). The
576 primary study by Simard et al. was supported by IDEA grants from the Canadian Prostate Cancer
577 Research Initiative and the Canadian Breast Cancer Research Alliance, as well as a studentship
578 from the Canadian Institutes of Health Research. The primary study by Singer et al. (2009) was
579 supported by a grant from the German Federal Ministry for Education and Research (no.
580 01ZZ0106). The primary study by Singer et al. (2008) was supported by grants from the German
581 Federal Ministry for Education and Research (# 7DZAIQTX) and of the University of Leipzig (#
582 formel. 1-57). The primary study by Meyer et al. was supported by the Federal Ministry of
583 Education and Research (BMBF). The primary study by Stone et al. was supported by the
584 Medical Research Council, UK and Chest Heart and Stroke, Scotland. The primary study by
585 Turner et al. was supported by a bequest from Jennie Thomas through Hunter Medical Research
586 Institute. The primary study by Walterfang et al. was supported by Melbourne Health. Drs.
587 Benedetti and Thombs were supported by FRQS researcher salary awards. No other authors
588 reported funding for primary studies or for their work on this study. No funder had any role in
589 the design and conduct of the study; collection, management, analysis, and interpretation of the
590 data; preparation, review, or approval of the manuscript; and decision to submit the manuscript
591 for publication.

592

593 **Acknowledgements**

594 We thank Dr. Linda Kwakkenbos for helping with translation and coding throughout the project.

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642 Strategies: 2015 Guideline Statement database. DOI: 10.1016/j.jclinepi.2016.01.021.

Table 1. Characteristics of included studies.

Author, year	Country	Population	N total	N (%) Major Depression	Mean Age	% Female	N (%) HADS-D ≥ 8	% Difference: HADS-D ≥ 8 - Major Depression	Ratio: HADS-D ≥ 8 / Major Depression	N (%) HADS-D ≥ 11	% Difference: HADS-D ≥ 11 - Major Depression	Ratio: HADS-D ≥ 11 / Major Depression
Studies from IPDMA that used the SCID and were included in main analyses												
Akechi, 2006	Japan	Outpatients with cancer in palliative care	223	17 (8.0%)	61.1	65.0%	97 (43.0%)	35.9%	5.7	43 (19.0%)	11.7%	2.5
Amoozegar, 2017	Canada	Patients with migraines	102	51 (50.0%)	42.5	81.4%	53 (52.0%)	2.0%	1.0	32 (31.0%)	-18.6%	0.6
Beraldi, 2014	Germany	Patients of haemato-oncology	120	10 (8.0%)	52.1	32.5%	32 (27.0%)	18.3%	3.2	16 (13.0%)	5.0%	1.6
Braeken, 2010	Netherlands	Dutch cancer patients in radiotherapy	13	1 (8.0%)	69.4	NR	4 (31.0%)	23.1%	4.0	2 (15.0%)	7.7%	2.0
Cukor, 2008	USA	Patients with end-stage renal disease	70	14 (20.0%)	53.3	52.9%	18 (26.0%)	5.7%	1.3	7 (10.0%)	-10.0%	0.5
da Rocha e Silva, 2013	Brazil	Patients with stroke	47	14 (30.0%)	59.8	51.1%	16 (34.0%)	4.3%	1.1	7 (15.0%)	-14.9%	0.5
Ferentinos, 2011	Greece	Patients with amyotrophic	36	8 (22.0%)	62.0	41.7%	11 (31.0%)	8.3%	1.4	6 (17.0%)	-5.6%	0.7

		lateral sclerosis										
Fiest, 2014	Canada	Patients with epilepsy	180	30 (17.0%)	41.1	51.4%	31 (17.0%)	0.6%	1.0	18 (10.0%)	-6.7%	0.6
Fischer, 2014	Germany	Patients with heart failure	194	11 (6.0%)	65.9	20.6%	49 (25.0%)	19.6%	4.5	25 (13.0%)	7.2%	2.3
Gagnon, 2005	Canada	Patients admitted to hospital due to fall	108	14 (13.0%)	78.1	87.0%	22 (20.0%)	7.4%	1.6	7 (6.0%)	-6.5%	0.5
Goebel, 2011	Germany	Patients with brain tumors	26	0 (0.0%)	58.3	50.0%	5 (19.0%)	19.2%	–	1 (4.0%)	3.8%	–
Golden, 2006	Ireland	Outpatients with Hepatitis C	86	7 (8.0%)	37.7	25.6%	24 (28.0%)	19.8%	3.4	11 (13.0%)	4.7%	1.6
Gould, 2011	Australia	Patients with traumatic brain injury	189	15 (8.0%)	35.7	21.7%	35 (19.0%)	10.6%	2.3	12 (6.0%)	-1.6%	0.8
Honarmand, 2009	Canada	Patients with multiple sclerosis	140	9 (6.0%)	43.9	74.3%	26 (19.0%)	12.1%	2.9	10 (7.0%)	0.7%	1.1
Juliao, 2013	Portugal	Patients with advanced disease	75	31 (41.0%)	NR	NR	62 (83.0%)	41.3%	2.0	56 (75.0%)	33.3%	1.8
Keller, 2004	Germany	Inpatients with cancer at the department of surgery	76	4 (5.0%)	56.7	38.2%	22 (29.0%)	23.7%	5.5	15 (20.0%)	14.5%	3.8

Kjaergaard, 2014	Norway	Healthy population	357	20 (6.0%)	52.5	100.0%	15 (4.0%)	-1.4%	0.8	1 (0.3%)	-5.3%	0
Kugaya, 2000	Japan	Inpatients with Cancer	81	3 (4.0%)	61.2	25.9%	23 (28.0%)	24.7%	7.7	9 (11.0%)	7.4%	3.0
Lambert, 2015	Australia	Patients with cancer	164	25 (15.0%)	58.5	65.9%	33 (20.0%)	4.9%	1.3	16 (10.0%)	-5.5%	0.6
Löwe, 2002	Germany	Medical outpatients	497	64 (13.0%)	41.8	66.4%	193 (39.0%)	26.0%	3.0	100 (20.0%)	7.2%	1.6
Meyer, 2008	Germany	Patients undergoing laryngectomy	102	4 (4.0%)	60.4	93.1%	25 (25.0%)	20.6%	6.2	13 (13.0%)	8.8%	3.2
Michopoulos, 2010	Greece	Elderly inpatients	194	27 (14.0%)	74.0	47.9%	83 (43.0%)	28.9%	3.1	47 (24.0%)	10.3%	1.7
Navines, 2012	Spain	Patients with chronic hepatitis C	500	32 (6.0%)	43.4	30.6%	74 (15.0%)	8.4%	2.3	31 (6.0%)	-0.2%	1.0
Öztürk, 2013	Turkey	Patients with acne	45	7 (16.0%)	20.9	80.0%	14 (31.0%)	15.6%	2.0	5 (11.0%)	-4.4%	0.7
Patten, 2015	Canada	Patients with multiple sclerosis	42	20 (48.0%)	NR	28.6%	16 (38.0%)	-9.5%	0.8	7 (17.0%)	-31%	0.4
Pintor, 2006	Spain	Patients on waiting list for heart transplantation	73	13 (18.0%)	55.2	16.4%	15 (21.0%)	2.7%	1.2	8 (11.0%)	-6.8%	0.6
Rooney, 2013	UK	Adults with cerebral glioma	133	15 (11.0%)	53.7	42.9%	20 (15.0%)	3.8%	1.3	9 (7.0%)	-4.5%	0.6

Ryan, 2012	Ireland	Patients with advanced cancer	203	8 (4.0%)	61.6	49.3%	46 (23.0%)	18.7%	5.8	16 (8.0%)	3.9%	2.0
Sanchez-Gistau, 2012	Spain	Patients with epilepsy	296	35 (12.0%)	36.1	55.7%	74 (25.0%)	13.2%	2.1	40 (14.0%)	1.7%	1.1
Sanchez, 2012	Spain	Patients undergoing heart transplantation	22	3 (14.0%)	54.2	9.1%	6 (27.0%)	13.6%	2.0	2 (9.0%)	-4.5%	0.7
Sanchez, 2014	Spain	Candidates for heart transplantation	120	8 (7.0%)	55.6	22.5%	26 (22.0%)	15%	3.2	7 (6.0%)	-0.8%	0.9
Schwarzbold, 2014	Brazil	Patients with severe traumatic brain injury	44	14 (32.0%)	32.8	18.2%	12 (27.0%)	-4.5%	0.9	8 (18.0%)	-13.6%	0.6
Simard 2015	Canada	Survivors of cancer	60	7 (12.0%)	60.3	43.3%	3 (5.0%)	-6.7%	0.4	1 (2.0%)	-10%	0.1
Singer, 2008	Germany	Patients with laryngeal cancer	141	8 (6.0%)	63.7	8.5%	38 (27.0%)	21.3%	4.8	16 (11.0%)	5.7%	2.0
Singer, 2009	UK	Patients with cancer in acute care	580	55 (9.0%)	59.4	38.4%	200 (34.0%)	25%	3.6	101 (17.0%)	7.9%	1.8
Stone, 2004	UK	Outpatients after stroke	35	4 (11.0%)	71.2	31.4%	5 (14.0%)	2.9%	1.2	3 (9.0%)	-2.9%	0.8
Tung, 2015	China	Patients with diabetes	136	33 (24.0%)	39.8	56.6%	32 (24.0%)	-0.7%	1.0	12 (9.0%)	-15.4%	0.4

Turner, 2012	Australia	Patients after stroke	72	13 (18.0%)	66.7	47.2%	18 (25.0%)	6.9%	1.4	5 (7.0%)	-11.1%	0.4
Turner, Unpublished	Australia	Patients undergoing cardiac rehabilitation	52	4 (8.0%)	60.3	86.5%	4 (8.0%)	0%	1.0	3 (6.0%)	-1.9%	0.8
Walker, 2007	UK	Patients with cancer	361	30 (8.0%)	NR	23.5%	45 (12.0%)	4.2%	1.5	14 (4.0%)	-4.4%	0.5
Walterfang, 2007	Australia	Sample of Australian Patients with Adrenomyeloneuropathy	10	1 (10.0%)	43.8	10.0%	3 (30.0%)	20%	3.0	2 (20.0%)	10%	2.0

Studies that used other semi-structured interviews and were included in sensitivity analyses

Love, 2002 ¹	Australia	Outpatients with breast cancer	302	28 (9.0%)	46.3	100.0%	35 (12.0%)	2.3%	1.2	8 (3.0%)	-6.60%	0.3
Love, 2004 ²	Australia	Outpatients with breast cancer	227	16 (7.0%)	51.7	100.0%	43 (19.0%)	11.9%	2.7	16 (7.0%)	0%	1.0
O'Rourke, 1998 ³	UK	Patients with stroke	56	9 (16.0%)	67.1	33.9%	13 (23.0%)	7.1%	1.4	7 (13.0%)	-3.60%	0.8
De Souza, 2009 ⁴	UK	Outpatients with Huntington's disease	50	12 (24.0%)	50.8	48.0%	16 (32.0%)	8.0%	1.3	11 (22.0%)	-2.0%	0.9

Author, year	Country	Population	N total	N (%) Major Depression	Mean Age	Percent Female	N (%) HADS-D ≥ 8	% Difference: HADS-D ≥ 8 - Major Depression	Ratio: HADS-D ≥ 8 / Major Depression	N (%) HADS-D ≥ 11	% Difference: HADS-D ≥ 11 - Major Depression	Ratio: HADS-D ≥ 11 / Major Depression
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Ferentinos, 2011	Greece	Patients with amyotrophic lateral sclerosis	36	8 (22.0%)	62.0	41.7	11 (31.0%)	8.3%	1.4	6 (17.0%)	-5.6%	0.7

Fiest, 2014	Canada	Patients with epilepsy	180	30 (17.0%)	41.1	51.4	31 (17.0%)	0.6%	1.0	18 (10.0%)	-6.7%	0.6
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Turner, 2012	Australia	Patients after stroke	72	13 (18.0%)	66.7	47.2	18 (25.0%)	6.9%	1.4	5 (7.0%)	-11.1%	0.4
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Studies that used other semi-structured interviews and were included in sensitivity analyses
39.8

Love, 2002 ¹	Australia	Outpatients with breast cancer	302	28 (9.0%)	46.3	100.0	35 (12.0%)	2.3%	1.2	8 (3.0%)	-6.60%	0.3
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^{1,2} Diagnostic interview = Monash Interview for Liaison Psychiatry

³ Diagnostic interview = Schedule for Affective Disorders and Schizophrenia

⁴ Diagnostic interview = Schedules for Clinical Assessment in Neuropsychiatry

NR= Not reported

Figure 1. Study selection process.

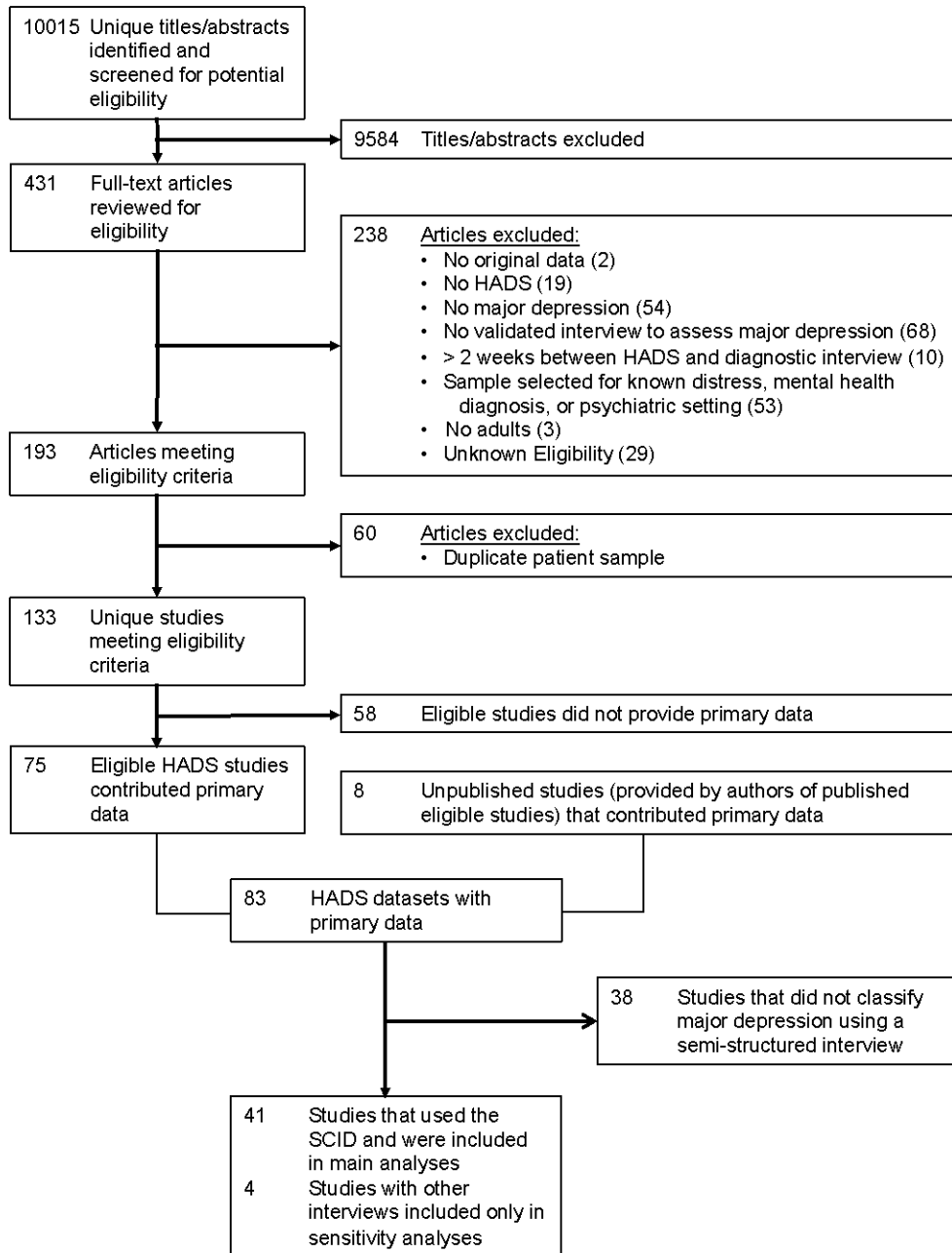


Figure 2. Proportion of participants (%) who scored at or above each possible HADS-D cutoff.

