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Equivalency of the diagnostic accuracy of the PHQ-8 and PHQ-9: A systematic review and individual participant data meta-analysis

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ABSTRACT

Background: Item 9 of the Patient Health Questionnaire-9 (PHQ-9) queries about thoughts of death and self-harm, but not suicidality. Although it is sometimes used to assess suicide risk, most positive responses are not associated with suicidality. The PHQ-8, which omits Item 9, is thus increasingly used in research. We assessed equivalency of total score correlations and the diagnostic accuracy to detect major depression of the PHQ-8 and PHQ-9.

Methods: We conducted an individual patient data meta-analysis. We fit bivariate random-effects models to assess diagnostic accuracy.

Results: 16,742 participants (2,097 major depression cases) from 54 studies were included. The correlation between PHQ-8 and PHQ-9 scores was 0.996 (95% confidence interval 0.996 to 0.996). The standard cutoff score of 10 for the PHQ-9 maximized sensitivity + specificity for the PHQ-8 among studies that used a semi-structured diagnostic interview reference standard (N = 27). At cutoff 10, the PHQ-8 was less sensitive by 0.02 (-0.06 to 0.00) and more specific by 0.01 (0.00 to 0.01) among those studies (N = 27), with similar results for studies that used other types of interviews (N = 27). For all 54 primary studies combined, across all cutoffs, the PHQ-8 was less sensitive than the PHQ-9 by 0.00 to 0.05 (0.03 at cutoff 10), and specificity was within 0.01 for all cutoffs (0.00 to 0.01).

Conclusions: PHQ-8 and PHQ-9 total scores were similar. Sensitivity may be minimally reduced with the PHQ-8, but specificity is similar.

INTRODUCTION

The 9-item Patient Health Questionnaire (PHQ-9) (Kroenke, Spitzer & Williams, 2001) is a self-report questionnaire that is commonly used for identifying people who may have depression based on matching symptoms to diagnostic criteria or, more commonly, on a standard cutoff of a score of 10 or greater (Moriarty et al. 2015; Levis et al. 2019). It is also used as a continuous measure to assess depressive symptom severity in research and clinical care (Kroenke, Spitzer & Williams, 2001). The nine items of the PHQ-9 are designed to capture the nine Diagnostic and Statistical Manual of Mental Disorders (DSM) symptom criteria for a major depressive episode (American Psychiatric Association 2013). Response options on the items range from “not at all” (0 points) to “nearly every day” (3 points). Per the DSM-5, the ninth criterion for major depression requires “Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide” (American Psychiatric Association 2013). Item 9 of the PHQ-9 taps into this criterion but also assesses self-harm, which is not part of the DSM criterion, or passive thoughts of death within the last two weeks: “...how often have you been bothered by...thoughts that you would be better off dead or of hurting yourself in some way?” It does not query specifically about suicidality, and positive responses may be due to thoughts about death or to thoughts about self-harm.

Item 9 is sometimes used as an indicator of suicide risk, and it may be useful as a component of modelling approaches for stratifying suicide risk among participants in psychiatric settings (Simon et al. 2016; Simon et al. 2013). However, responses to the item may not accurately reflect whether or not suicide risk is present, particularly among patients with serious medical conditions for whom thoughts of death may not reflect suicidal ideation, and it appears to perform poorly in identifying individuals at risk in these settings. Four studies in non-

psychiatric settings have compared positive responses on Item 9 to responses to questions that explicitly assess suicidal thoughts or intentionality. In these studies, which included US military veterans in primary care (Corson, Gerrity & Dobscha, 2004), patients with coronary artery disease (Razykov et al. 2012; Suarez et al. 2015), and cancer patients (Walker et al. 2011), 7% to 21% of all study participants had positive responses on Item 9, but of those, only 18% to 35% had thoughts of suicide based on questions designed specifically to address suicide risk, and only 3% to 20% had a plan (Corson, Gerrity & Dobscha, 2004; Razykov et al. 2012; Suarez et al. 2015; Walker et al. 2011). Thus, concerns have been raised that using Item 9 to identify individuals at risk would result in a high rate of false indications, compared to questions designed specifically to assess suicidal thoughts or intentionality (Razykov et al. 2012; Suarez et al. 2015; Walker et al. 2011).

The PHQ-8 omits Item 9 from the PHQ-9. Many research studies use the PHQ-8 as a depression screening tool or to assess depressive symptom severity in order to avoid the high risk of inaccurate indications of suicide risk based on Item 9 (Corson, Gerrity & Dobscha, 2004; Razykov et al. 2012; Kroenke et al. 2009; Wells et al. 2013; Barrera et al. 2017). This is a particularly important consideration in studies that are not focused on depression or psychiatric disorders, but would need to allocate substantial resources to follow-up on responses to Item 9 of the PHQ-9. Similarly, many large epidemiological studies that include assessments of depressive symptoms are not able to provide adequate assessment and intervention with telephone or internet surveys (Kroenke et al. 2009).

Although differences in performance between the PHQ-8 and PHQ-9 might be expected to be minimal, to the best of our knowledge, only one study has attempted to verify this by comparing diagnostic accuracy between the PHQ-8 and PHQ-9 (Razykov et al. 2012). That

study evaluated the diagnostic testing accuracy of the PHQ-8 versus the PHQ-9 and the correlation between PHQ-8 and PHQ-9 scores in a sample of 1,022 coronary artery disease outpatients (233 major depression cases). Differences between sensitivity and specificity for the PHQ-8 (50%, 91%) and PHQ-9 (54%, 90%) based on a cutoff score of 10 or greater were minimal. In addition, PHQ-8 and PHQ-9 scores were highly correlated ($r = 0.997$) (Razykov et al. 2012). One additional study reported correlations between continuous PHQ-8 and PHQ-9 scores (Corson, Gerrity & Dobscha, 2004). That study, which included over 1000 patients from a US Department of Veterans Affairs primary care setting, reported a correlation of $r = 0.998$ (Corson, Gerrity & Dobscha, 2004).

We have synthesized a large database of individual participant data (IPD) from primary studies on the PHQ-9 (Levis et al. 2019; Levis et al. 2018). In the present study we included studies from that database that provided individual item scores (not just total PHQ-9 scores), which allowed for calculation of PHQ-8 scores. The objectives of the present study were (1) to evaluate the equivalency of the correlation between PHQ-8 and PHQ-9 scores for assessing depressive symptom severity; and (2) to assess the equivalency of the diagnostic accuracy of PHQ-8 and PHQ-9 across relevant cutoffs for screening to detect major depression.

METHOD

Data Source

The present study used a subset of participants from an IPD database of PHQ-9 (Levis et al. 2019; Levis et al. 2018). The main PHQ-9 IPD meta-analysis (IPDMA) was registered in PROSPERO (CRD42014010673), and a protocol was published (Thombs et al. 2014). Analyses of the diagnostic accuracy of the PHQ-8 were conducted according to protocol with two exceptions: (1) we stratified results by reference standard categories and (2) we added an

examination of equivalency with the PHQ-9. Results from the main IPDMA of the PHQ-9 are available elsewhere (Levis et al. 2019).

Search Strategy

A medical librarian searched Medline, Medline In-Process & Other Non-Indexed Citations, PsycINFO, and Web of Science from January 1, 2000 through February 7, 2015, using a peer-reviewed search strategy (Canadian Agency for Drugs and Technologies in Health 2016) (SupplementaryMethods1). We limited our search to these databases based on research showing that adding other databases when the Medline search is highly sensitive does not identify additional eligible studies (Rice et al. 2016). The search was limited to the year 2000 forward because the PHQ-9 was originally published in 2001 (Kroenke, Spitzer & Williams, 2001). In addition to the database search, we reviewed reference lists of relevant reviews and queried contributing authors about non-published studies. Search results were uploaded into RefWorks (RefWorks-COS, Bethesda, MD, USA). After de-duplication, unique citations were uploaded into DistillerSR (Evidence Partners, Ottawa, Canada), which was used to store and track search results, conduct screening for eligibility, document correspondence with primary study authors, and extract study characteristics.

Identification of Eligible Studies

Datasets from articles in any language were eligible for inclusion if they included diagnostic classification among participants aged 18 or older for current Major Depressive Disorder (MDD) or Major Depressive Episode (MDE) based on a validated semi-structured or fully structured interview conducted within two weeks of PHQ-9 administration, since diagnostic criteria for major depression are for symptoms in the last two weeks. Datasets where not all participants were at least 18 years of age were included if the primary data allowed us to select

participants who were at least 18 years of age. Datasets where not all participants were administered the PHQ-9 within two weeks of the diagnostic interview were included if the primary data allowed us to select participants who were administered both instruments within two weeks. Data from studies where the PHQ-9 was administered exclusively to individuals with known psychiatric diagnoses or symptoms or who were seeking psychiatric care were excluded, because screening is not indicated for patients already seeking care or managed in psychiatric settings. For defining major depression cases, we considered MDD or MDE based on the DSM or the International Classification of Diseases (ICD). If more than one was reported, we prioritized MDE over MDD and DSM over ICD. Across all studies, there were only 23 discordant diagnoses that depended on classification prioritization (0.1% of participants). For the present study, we only included primary studies that provided individual PHQ-9 item scores and not just PHQ-9 total scores, because only those datasets allowed us to generate PHQ-8 scores and compare the PHQ-8 with the PHQ-9.

Two investigators independently reviewed titles and abstracts for eligibility. If either reviewer deemed a study potentially eligible, full-text article review was done by two investigators, independently. Disagreement between reviewers after full-text review was resolved by consensus, consulting a third investigator when necessary. Translators were consulted to evaluate titles, abstracts and full-text articles for languages other than those for which team members were fluent.

Data Contribution and Synthesis

Authors of eligible datasets were invited to contribute de-identified primary data. Primary study country, clinical setting, language, and diagnostic interview administered were extracted from published reports by two investigators independently, with disagreements resolved by

consensus. Countries were categorized as “very high”, “high”, or “low-medium” development level based on the United Nation’s human development index (Whiting et al. 2011). Recruitment settings were categorized as “non-medical”, “primary care”, “inpatient specialty care”, or “outpatient specialty care.” Participant-level data included age, sex, major depression status, current diagnosis or treatment for a mental health problem, and PHQ-9 item scores. In two primary studies, multiple recruitment settings were included, thus recruitment setting was coded at the participant-level. When primary study datasets included appropriate statistical weighting to reflect sampling procedures, we used the provided weights. For studies where sampling procedures merited weighting, but the original study did not weight, we constructed appropriate weights using inverse selection probabilities. Weighting occurred, for instance, when all participants with positive screens, but only a random subset of participants with negative screens, were administered a diagnostic interview.

Individual participant data were converted to a standard format and entered into a single dataset that also included study-level data. We compared published participant characteristics and diagnostic accuracy results with those obtained using the raw datasets. When primary data and original publications were discrepant, we identified and corrected errors when possible and resolved any outstanding discrepancies in consultation with the original investigators.

Statistical Analyses

To evaluate the equivalence of the PHQ-8 and PHQ-9 scores for assessing depressive symptom severity, a Pearson correlation with a 95% confidence interval (CI) was calculated between the total scores of PHQ-8 (which excluded Item 9) and PHQ-9.

To estimate the diagnostic accuracy of the PHQ-8 and compare with the PHQ-9, we analyzed primary studies separately by the type of diagnostic interview that was used as the

reference standard, as we did in the previously published main PHQ-9 meta-analysis (Levis et al. 2019). This was done because of differences in the performance of the different types of interviews. Semi-structured interviews involve clinical judgement and are designed to be administered by clinically trained professionals; fully structured interviews are completely scripted and designed for lay administration, but the resulting increased standardization and reliability across interviewers may lead to increased misclassification (Brugha, Bebbington & Jenkins, 1999; Nosen & Woody 2008). The Mini International Neuropsychiatric Interview (MINI), which is a fully structured interview, was developed to be administered in a fraction of the time necessary for other fully structured interviews and was described by its developers as designed to be over-inclusive (Robins et al. 1988; Sheehan et al. 1997). In a previous study, we found that semi-structured and fully structured diagnostic interviews are not interchangeable reference standards for major depression and that fully structured interviews may diagnose depression at higher rates than semi-structured interviews at low symptom levels and at lower rates at high symptom levels (Levis et al. 2018). We also found that the MINI classifies approximately twice as many participants as cases compared to the most commonly used fully-structured interview, the Composite International Diagnostic Interview (CIDI) (Levis et al. 2018). In the main PHQ-9 meta-analysis, the diagnostic accuracy of the PHQ-9 differed substantially depending on the reference standard used for the comparison (Levis et al. 2019). Thus, for the present study, we analyzed primary studies separately based on whether they used a semi-structured interview, a fully structured interview (non-MINI), or the MINI.

For each reference standard and for the PHQ-8 and PHQ-9 cutoffs 5-15, separately, bivariate random-effects models were fitted using an adaptive Gauss Hermite quadrature with 1 quadrature point (Riley et al. 2008). This 2-stage meta-analytic approach models sensitivity and

specificity at the same time, taking the inherent correlation between them and the precision of estimates within studies into account. A random-effects model was used as we assumed true values of sensitivity and specificity would likely to vary across primary studies.

In order to examine the equivalence between PHQ-8 and PHQ-9 across reference standards, for each analysis, we used the results of the random-effects meta-analyses at each cutoff to construct separate empirical receiver operating characteristic (ROC) curves based on the pooled estimates. Equivalence tests between PHQ-8 and PHQ-9 sensitivity and specificity were conducted at each cutoff. This allowed us to test whether the sensitivity and specificity of the PHQ-8 was similar to that of the PHQ-9, up to a pre-specified maximum clinically acceptable difference, that is, an equivalence margin (Walker & Nowacki 2011). In the present study, an equivalence margin of $\delta = 0.05$ was used, which is the same margin that was used in a previous study that used the same IPD database (Ishihara et al. 2019). CIs for the differences between PHQ-8 and PHQ-9 sensitivity and specificity at each cutoff were constructed via a cluster bootstrap approach (van der Leeden, Busing & Meijer, 1997; van der Leeden, Meijer & Busing, 2008), with resampling at the study and subject level. For each comparison, we ran 1000 iterations of the bootstrap. For each bootstrap iteration, the bivariate random-effects model was fitted to the PHQ-8 and PHQ-9 data, and the pooled sensitivities and specificities were computed separately, as described above, for each cutoff score. Equivalence tests were done by comparing the CIs around the pooled sensitivity and specificity differences to the equivalence margin of $\delta = 0.05$. If the entire CI was included within the interval of ± 0.05 , then we rejected the hypothesis that there were differences large enough to be important and concluded that equivalence was present. If the entire CI was outside of the interval, then we failed to reject the hypothesis that the

PHQ-8 and PHQ-9 were not equivalent. When the CIs crossed the ± 0.05 threshold, findings were deemed equivocal, and the equivalence was indeterminate.

Although we previously found that sensitivity and specificity of the PHQ-9 differs by type of reference standard, we did not believe that the differences in sensitivity and specificity between the PHQ-8 and PHQ-9 would vary depending on the reference standard. This is because for each included study the PHQ-8 and PHQ-9 were compared to the same reference standard. Thus, we reported pooled sensitivity and specificity only stratified by reference standards, but we investigated equivalence both stratified by reference standards and pooled across all studies. To investigate heterogeneity across studies, by reference standard and overall, we generated forest plots for the differences in sensitivity and specificity estimates between PHQ-8 and PHQ-9 for the standard cutoff 10 for each study. We also quantified heterogeneity at cutoff 10, by reporting the estimated variances of the random effects for the differences in PHQ-8 and PHQ-9 sensitivity and specificity (τ^2) (Fagerland, Lydersen & Laake, 2014; Higgins & Thompson 2002).

All analyses were run in R (R version R 3.5.0 and R Studio version 1.1.423) using the lme4 package.

RESULTS

Search Results and Inclusion of Primary Data

For the main IPDMA, of 5,248 unique titles and abstracts identified from the database search, 5,039 were excluded after title and abstract review and 113 after full-text (SupplementaryList1), leaving 96 eligible articles with data from 69 unique participant samples (SupplementaryFigure1). Of the 69 unique samples, 55 contributed data (80%). In addition, authors of included studies contributed data from three unpublished studies, for a total of 58 PHQ-9 datasets contributed to our IPDMA. Four studies without PHQ-9 individual item scores

were excluded from the present study (see SupplementaryTable1b). Thus, 16,742 participants (2,097 major depression cases) from 54 studies were analyzed (78% of 21,572 participants from the 69 eligible published studies and 3 eligible unpublished studies). Included study characteristics are shown in SupplementaryTable1a. Characteristics of eligible studies that did not provide data, including the 4 studies excluded because they only provided PHQ-9 total scores, are shown in SupplementaryTable1b.

There were 27 included primary studies that used semi-structured interviews to assess major depression (6,362 participants), 13 that used fully structured interviews other than the MINI (7,596 participants), and 14 that used the MINI (2,784 participants). The Structured Clinical Interview for DSM Disorders (SCID) was the most commonly used semi-structured interview (24 studies, 4,378 participants), and the CIDI was the most commonly used fully structured interview (10 studies, 6,291 participants). The average study sample size and number of major depression cases was 236 and 29 for studies that used a semi-structured interview; 584 and 61 for studies that used a fully structured interview; and 199 and 37 for studies that used the MINI.

Participant characteristics are shown in Table 1.

PHQ-8 and PHQ-9 Scores

Among all participants in all studies, the mean (standard deviation [SD]) PHQ-8 score (range = 0–24) was 5·3 (5·2), and the mean (SD) PHQ-9 score (range 0–27) was 5·4 (5·4). Overall, 11·8% of participants had a non-zero score on Item 9 (score of 1-3). As shown in Table 2, this included 1·9% among participants with PHQ-8 scores 0-4 and increased to 64·7% among those with scores 20-24. The correlation (95% CI) between PHQ-8 and PHQ-9 scores was 0·996

(0.996, 0.996). The correlation of the score of Item 9 with PHQ-8 scores was 0.480 (0.469, 0.492).

Diagnostic Accuracy of the PHQ-8 and PHQ-9

ROC curves comparing sensitivity and specificity estimates for cutoffs 5-15 between the PHQ-8 and PHQ-9 for the three reference standard categories, separately, are shown in Figure 1. The curves for the PHQ-8 and PHQ-9 were highly overlapping for each reference standard, and the area under the curve for the PHQ-8 and PHQ-9 were similar for semi-structured interviews (0.930 versus 0.933), fully structured interviews (excluding the MINI; 0.852 versus 0.856), and the MINI (0.894 versus 0.899).

Comparisons of sensitivity and specificity estimates between PHQ-8 and PHQ-9 cutoffs 5-15 across the three reference standard categories are shown in Table 3. Cutoff 10 maximized combined sensitivity and specificity for PHQ-8 (sensitivity [95% CI] = 0.86 [0.80, 0.90], specificity [95% CI] = 0.86 [0.83, 0.89]) and PHQ-9 (sensitivity [95% CI] = 0.88 [0.82, 0.92], specificity [95% CI] = 0.86 [0.82, 0.88]) among studies using a semi-structured interview as the reference standard; cutoff 8 for PHQ-8 (sensitivity [95% CI] = 0.77 [0.66, 0.85], specificity [95% CI] = 0.78 [0.71, 0.84]) and PHQ-9 (sensitivity [95% CI] = 0.79 [0.68, 0.86], specificity [95% CI] = 0.77 [0.70, 0.83]) among studies using a fully structured interview; and cutoff 8 for PHQ-8 (sensitivity [95% CI] = 0.83 [0.75, 0.89], specificity [95% CI] = 0.80 [0.75, 0.84]) and PHQ-9 (sensitivity [95% CI] = 0.86 [0.77, 0.91], specificity [95% CI] = 0.79 [0.74, 0.83]) among studies using the MINI.

In comparisons stratified by reference standard, for sensitivity, results of equivalence tests showed that for semi-structured diagnostic interviews, estimates were equivalent from cutoffs 5 through 9 and indeterminate from cutoffs 10 through 15; for fully structured interviews

(excluding the MINI), they were equivalent on cutoffs 5 and 7 and indeterminate at cutoffs 6 and 8 through 15; and for the MINI, they were equivalent from cutoffs 5 through 7 and indeterminate from cutoffs 8 through 15. Estimates of specificity were equivalent in all analyses, regardless of reference standards and cutoffs. See Table 3.

Overall, including all 54 primary studies, as shown in Table 4, across cutoffs, sensitivity was between 0·00 and 0·05 percentage points lower for the PHQ-8 compared to the PHQ-9. At cutoff 10, the difference (95% CI) was -0·03 (-0·06, -0·02). For specificity, the PHQ-8 and PHQ-9 were within 0·01 for all cutoffs. For sensitivity, estimates were equivalent for cutoffs 5 to 8 and indeterminate for cutoffs 9 to 15. For specificity, estimates were equivalent for all cutoffs.

A forest plot of the difference of sensitivity and specificity estimates for cutoff 10 between PHQ-8 and PHQ-9 for all studies is shown in Figure 2. At the commonly used cutoff of 10 or greater, there was low heterogeneity in the differences across the 54 studies with estimated inter-study heterogeneity (τ^2) <0·01 for sensitivity and <0·01 for specificity. Forest plots of the differences of sensitivity and specificity estimates for cutoff 10 between PHQ-8 and PHQ-9 among studies by reference standard category are shown in SupplementaryFigure2.

DISCUSSION

In the present study, we assessed the correlation of continuous PHQ-8 and PHQ-9 scores for assessing depression severity in research and clinical practice, and we compared the diagnostic accuracy of the PHQ-8 and PHQ-9 across all cutoffs for detecting major depression. There were two main findings. First, the correlation of continuous PHQ-8 and PHQ-9 scores was high (0·996). Second, to screen for major depression, the PHQ-8 at different possible cutoffs including the standard cutoff of 10 or greater, was similarly accurate compared to the PHQ-9 overall and across all three types of reference standards. The cutoffs that maximized combined

sensitivity and specificity were the same for the PHQ-8 and PHQ-9 across reference standard categories.

Overall, for all 54 primary studies combined, across all cutoffs, the PHQ-8 was slightly less sensitive than the PHQ-9 by 0·00 to 0·05 (0·03 at cutoff 10). For specificity, the differences between PHQ-8 and PHQ-9 were within 0·01 for all cutoffs. Although the CIs for the difference in sensitivity for cutoff 10 did not fit the study definition of equivalency, the reduction in sensitivity if the PHQ-8 is used is small, and specificity is equivalent.

Previous studies have shown that Item 9 of the PHQ-9 does not accurately assess suicide risk and identifies far more patients or study participants as at risk than would be identified with items designed to assess suicide risk (Corson, Gerrity & Dobscha, 2004; Razykov et al. 2012; Walker et al. 2011). Thus, unintended consequences of using Item 9 could include substantial additional costs for research, as well as possible harms or inconvenience to patients. Research ethics boards sometimes require follow-up for all patients with positive responses to Item 9. Using the PHQ-8, which is minimally different from PHQ-9 in terms of diagnostic accuracy characteristics, would reduce unintended consequences of false signals of suicide risk without substantive changes to continuous measurement properties or diagnostic accuracy for major depression.

It is possible that use of the PHQ-8 could result in not identifying a small subset of people with suicidal thoughts, although, if the case, based on our findings, this number would be small. Furthermore, there is no evidence that using questionnaires to screen for suicide in general medical settings, above and beyond screening for depression, would reduce risk of suicide (Allaby 2010; Crawford et al. 2011; Siu & the US Preventive Services Task Force 2016). Tools are available to screen patients or stratify by risk for suicidality. However, a review concluded

that they are not accurate enough at this point for use in practice and that alternative methods are more appropriate (Carter & Spittal 2018). Indeed, in mental health settings or when there is reason to suspect possible suicidality, standards of care indicate that engagement with patients is needed to assess suicide risk and determine the best management plan, as appropriate (Carter & Spittal 2018).

To our knowledge, this is the first meta-analysis and also the first study using a large IPD database to compare diagnostic accuracy characteristics of PHQ-8 and PHQ-9. Strengths of this study included the large overall sample size, the ability to compare results for PHQ-8 and PHQ-9 from all cutoffs from all studies (rather than just published cutoff results), and the ability to assess diagnostic accuracy separately in studies that used semi- and fully structured diagnostic interviews as the reference standard. There are also limitations to consider. First, for the full IPDMA data, we were unable to include primary data from 14 of 69 published eligible datasets (20% datasets; 17% of eligible participants), and we restricted our analyses to those with complete data for all individual PHQ-9 item scores (95% of available data). Nonetheless, this sample was much larger than the few previous primary studies that have compared the PHQ-8 and PHQ-9. Second, we categorized studies based on the diagnostic interview that was used, but adaptations to interviews are sometimes made and, thus, all studies may have not used the diagnostic interviews in the way that they were originally designed. However, when we analyzed data from all studies, regardless of reference standard, heterogeneity was minimal, suggesting that findings can be applied across reference standards.

CONCLUSIONS

In summary, although the PHQ-9 was designed to reflect the 9 symptoms included in DSM criteria for major depression, the item assessing suicide risk also assesses self-harm. This study

used a large IPD dataset and found that the PHQ-8 performs similarly to the PHQ-9 in terms of the correlation of continuous scores and the diagnostic accuracy across all cutoffs for detecting major depression. Removing Item 9 and using the PHQ-8 instead of the PHQ-9 has minimal influence on performance of the measure and will likely reduce the number of false positive signals from people who endorse this item but would not be considered to be at risk for suicide based on measures intended to assess suicide risk.

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Conflict of Interest.

Drs. Jetté and Patten declare that they received a grant, outside the submitted work, from the University of Calgary Hotchkiss Brain Institute, which was jointly funded by the Institute and Pfizer. Pfizer was the original sponsor of the development of the PHQ-9, which is now in the public domain. Dr. Chan is a steering committee member or consultant of Astra Zeneca, Bayer, Lilly, MSD and Pfizer. She has received sponsorships and honorarium for giving lectures and providing consultancy and her affiliated institution has received research grants from these companies. Dr. Hegerl declares that within the last three years, he was an advisory board member for Lundbeck and Servier; a consultant for Bayer Pharma; a speaker for Roche Pharma and Servier; and received personal fees from Janssen, all outside the submitted work. Dr. Inagaki declares that he has received a grant from Novartis Pharma, and personal fees from Meiji, Mochida, Takeda, Novartis, Yoshitomi, Pfizer, Eisai, Otsuka, MSD, Technomics, and Sumitomo Dainippon, all outside of the submitted work. All authors declare no other relationships or

activities that could appear to have influenced the submitted work. No funder had any role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Author Contributions.

YW, BLevis, JB, PC, SG, JPAI, LAK, DM, SBP, IS, RCZ, AB, and BDT were responsible for the study conception and design. JB and LAK designed and conducted database searches to identify eligible studies. DHA, BA, LA, HRB, MB, CHB, PB, GC, MHC, JCNC, RC, YC, JMG, JRF, FHF, DF, BG, FGS, CGG, BJH, PAH, MHärter, UH, LH, SEH, MHudson, TH, MI, NJ, MEK, KMK, YK, FL, SL, ML, SRL, BLöwe, AM, SM, TNM, KM, FLO, VP, BWP, PP, AP, KR, AGR, ISS, JS, ASidebottom, ASimming, LS, SS, PLLT, AT, HCvW, JW, MAW, KW, MY, and BDT were responsible for collection of primary data included in this study. BLevis, KER, NS, AWL, MA, DBR, and BDT contributed to data extraction and coding for the meta-analysis. YW, BLevis, AB, and BDT contributed to the data analysis and interpretation. YW, BLevis, AB, and BDT contributed to drafting the manuscript. All authors provided a critical review and approved the final manuscript. AB and BDT are guarantors.

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1008

1009 **Table 1.** Participant characteristics by subgroup

Participant Subgroup	N Participants	N (%) Major Depression
All participants	16,742	2,097 (13)
Type of diagnostic interview		
Semi-structured diagnostic interview	6,362	790 (12)
Fully structured diagnostic interview	7,596	790 (10)
Mini International Neuropsychiatric Interview	2,784	517 (19)
Age^a		
< 60	11,144	1,402 (13)
≥ 60	5,552	692 (12)
Sex^a		
Women	9,552	1,259 (13)
Men	7,180	835 (12)
Care setting		
Non-medical care	1,832	252 (14)
Primary care	7,846	760 (10)
Inpatient specialty care	1,245	136 (11)
Outpatient specialty care	5,819	949 (16)
Country human development index		
Very high	13,297	1,577 (12)
High	1,337	276 (21)
Low-medium	2,108	244 (12)

^a Due to missing participant data, total participant numbers for these variables were <16,742.

1012 **Table 2.** Characteristics of participants who rated Item 9 as present for several days, more than
 1013 half the days, or nearly every day (i.e., scores 1-3) in last two weeks by total PHQ-8 score

Total PHQ-8 Score	N of participants ^a	% with non-zero Item 9	Item 9 Mean (SD)
0-4	11,034	1·9%	0·02 (0·16)
5-9	5,071	13·2%	0·16 (0·45)
10-14	2,231	31·3%	0·44 (0·74)
15-19	1,044	48·3%	0·78 (0·97)
20-24	380	64·7%	1·39 (1·25)

^a Numbers of participants add up to >16,742 as they were weighted by sampling weights.

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 1015

1016 **Table 3a.** Comparison of sensitivity and specificity estimates between PHQ-8 and PHQ-9 among studies that used a semi-structured
1017 reference standard

PHQ-8 ^a					PHQ-9				PHQ-8 – PHQ-9 ^b			
Cutoff	Sensitivity	95% CI	Specificity	95% CI	Sensitivity	95% CI	Specificity	95% CI	Sensitivity	95% CI	Specificity	95% CI
5	0.98	(0.95, 0.99)	0.55	(0.50, 0.60)	0.98	(0.95, 0.99)	0.55	(0.50, 0.60)	0.00	(-0.01, 0.00)	0.00	(0.00, 0.01)
6	0.98	(0.95, 0.99)	0.63	(0.58, 0.68)	0.98	(0.95, 0.99)	0.63	(0.58, 0.67)	0.00	(-0.00, 0.00)	0.00	(0.00, 0.01)
7	0.97	(0.93, 0.99)	0.70	(0.66, 0.74)	0.98	(0.93, 0.99)	0.70	(0.65, 0.74)	-0.01	(-0.02, 0.00)	0.00	(0.00, 0.01)
8	0.94	(0.89, 0.96)	0.76	(0.72, 0.79)	0.95	(0.90, 0.97)	0.75	(0.71, 0.79)	-0.01	(-0.03, 0.00)	0.01	(0.00, 0.01)
9	0.89	(0.84, 0.92)	0.81	(0.78, 0.84)	0.91	(0.87, 0.95)	0.80	(0.77, 0.83)	-0.02	(-0.06, -0.00)	0.01	(0.00, 0.01)
10 ^b	0.86	(0.80, 0.90)	0.86	(0.83, 0.89)	0.88	(0.82, 0.92)	0.86	(0.82, 0.88)	-0.02	(-0.06, -0.00)	0.00	(0.00, 0.02)
11	0.81	(0.75, 0.87)	0.90	(0.87, 0.92)	0.84	(0.84, 0.84)	0.89	(0.89, 0.89)	-0.03	(-0.06, -0.00)	0.01	(0.00, 0.02)
12	0.74	(0.68, 0.79)	0.92	(0.89, 0.93)	0.78	(0.71, 0.83)	0.91	(0.89, 0.93)	-0.04	(-0.09, -0.01)	0.01	(0.00, 0.01)
13	0.67	(0.60, 0.73)	0.94	(0.92, 0.95)	0.69	(0.63, 0.75)	0.93	(0.91, 0.95)	-0.02	(-0.07, -0.00)	0.01	(0.00, 0.01)
14	0.59	(0.53, 0.65)	0.96	(0.94, 0.97)	0.64	(0.57, 0.70)	0.95	(0.93, 0.96)	-0.05	(-0.09, -0.01)	0.01	(0.00, 0.01)
15	0.51	(0.44, 0.57)	0.97	(0.95, 0.98)	0.55	(0.48, 0.62)	0.96	(0.94, 0.97)	-0.04	(-0.09, -0.02)	0.01	(0.00, 0.01)

1018 ^a N Studies = 27; N Participants = 6,362; N major depression = 790

1019 ^b For PHQ-8 cutoff 10, among studies that used semi-structured interviews as the reference standard, the default optimizer in glmer
1020 failed to converge, thus bobyqa was used instead.

1021 CI: confidence interval

1022 **Table 3b.** Comparison of sensitivity and specificity estimates between PHQ-8 and PHQ-9 among studies that used a fully structured
1023 reference standard (MINI excluded)

PHQ-8 ^a					PHQ-9				PHQ-8 – PHQ-9			
Cutoff	Sensitivity	95% CI	Specificity	95% CI	Sensitivity	95% CI	Specificity	95% CI	Sensitivity	95% CI	Specificity	95% CI
5	0.92	(0.85, 0.96)	0.57	(0.49, 0.66)	0.93	(0.85, 0.96)	0.57	(0.48, 0.65)	-0.01	(-0.03, 0.00)	0.00	(0.00, 0.02)
6	0.88	(0.79, 0.93)	0.65	(0.57, 0.73)	0.90	(0.81, 0.95)	0.65	(0.56, 0.72)	-0.02	(-0.07, 0.00)	0.00	(0.00, 0.02)
7	0.83	(0.73, 0.90)	0.72	(0.64, 0.79)	0.84	(0.73, 0.90)	0.71	(0.63, 0.78)	-0.01	(-0.01, 0.00)	0.01	(0.00, 0.02)
8	0.77	(0.66, 0.85)	0.78	(0.71, 0.84)	0.79	(0.68, 0.86)	0.77	(0.70, 0.83)	-0.02	(-0.07, -0.00)	0.01	(0.00, 0.01)
9	0.69	(0.59, 0.77)	0.83	(0.76, 0.87)	0.71	(0.62, 0.80)	0.81	(0.75, 0.86)	-0.02	(-0.07, -0.00)	0.02	(0.01, 0.02)
10	0.63	(0.52, 0.72)	0.86	(0.81, 0.90)	0.67	(0.57, 0.76)	0.85	(0.80, 0.90)	-0.04	(-0.09, -0.01)	0.01	(0.00, 0.02)
11	0.57	(0.45, 0.67)	0.89	(0.85, 0.93)	0.59	(0.49, 0.69)	0.88	(0.84, 0.92)	-0.02	(-0.07, -0.01)	0.01	(0.00, 0.02)
12	0.51	(0.38, 0.64)	0.92	(0.88, 0.94)	0.54	(0.43, 0.65)	0.90	(0.86, 0.93)	-0.03	(-0.16, -0.01)	0.02	(0.01, 0.02)
13	0.43	(0.32, 0.55)	0.94	(0.91, 0.96)	0.47	(0.36, 0.58)	0.93	(0.89, 0.95)	-0.04	(-0.12, -0.01)	0.01	(0.00, 0.01)
14	0.36	(0.26, 0.47)	0.95	(0.93, 0.97)	0.41	(0.31, 0.53)	0.95	(0.92, 0.96)	-0.05	(-0.14, -0.01)	0.00	(0.00, 0.01)
15	0.30	(0.22, 0.39)	0.96	(0.95, 0.98)	0.33	(0.24, 0.42)	0.96	(0.94, 0.97)	-0.03	(-0.07, -0.00)	0.00	(0.00, 0.00)

1024 ^a N Studies = 13; N Participants = 7,596; N major depression = 790

1025 CI: confidence interval

1026

1027 **Table 3c.** Comparison of sensitivity and specificity estimates between PHQ-8 and PHQ-9 among studies that used the MINI reference
1028 standard

PHQ-8 ^a					PHQ-9				PHQ-8 – PHQ-9			
Cutoff	Sensitivity	95% CI	Specificity	95% CI	Sensitivity	95% CI	Specificity	95% CI	Sensitivity	95% CI	Specificity	95% CI
5	0.96	(0.93, 0.98)	0.58	(0.50, 0.65)	0.97	(0.93, 0.98)	0.57	(0.49, 0.65)	-0.01	(-0.01, 0.00)	0.01	(0.00, 0.02)
6	0.92	(0.85, 0.96)	0.67	(0.59, 0.74)	0.93	(0.86, 0.97)	0.66	(0.59, 0.73)	-0.01	(-0.03, 0.00)	0.01	(0.00, 0.02)
7	0.89	(0.81, 0.94)	0.73	(0.67, 0.79)	0.89	(0.81, 0.94)	0.73	(0.66, 0.79)	0.00	(-0.03, 0.00)	0.01	(0.00, 0.01)
8	0.83	(0.75, 0.89)	0.80	(0.75, 0.84)	0.86	(0.77, 0.91)	0.79	(0.74, 0.83)	-0.03	(-0.06, 0.00)	0.01	(0.00, 0.02)
9	0.78	(0.69, 0.85)	0.85	(0.81, 0.89)	0.81	(0.71, 0.88)	0.84	(0.80, 0.88)	-0.03	(-0.07, -0.00)	0.01	(0.00, 0.02)
10	0.72	(0.63, 0.79)	0.88	(0.84, 0.91)	0.75	(0.66, 0.82)	0.88	(0.84, 0.91)	-0.03	(-0.08, -0.01)	0.01	(0.00, 0.02)
11	0.65	(0.57, 0.73)	0.91	(0.88, 0.94)	0.69	(0.61, 0.77)	0.90	(0.87, 0.93)	-0.04	(-0.08, -0.01)	0.01	(0.00, 0.02)
12	0.59	(0.51, 0.66)	0.93	(0.91, 0.95)	0.65	(0.56, 0.73)	0.92	(0.90, 0.94)	-0.06	(-0.11, -0.02)	0.01	(0.00, 0.02)
13	0.53	(0.44, 0.62)	0.95	(0.93, 0.97)	0.57	(0.49, 0.66)	0.94	(0.92, 0.96)	-0.04	(-0.09, -0.01)	0.01	(0.00, 0.02)
14	0.43	(0.35, 0.51)	0.97	(0.95, 0.98)	0.49	(0.49, 0.49)	0.96	(0.96, 0.96)	-0.06	(-0.11, -0.02)	0.01	(0.00, 0.02)
15	0.37	(0.29, 0.45)	0.98	(0.96, 0.99)	0.42	(0.42, 0.42)	0.97	(0.97, 0.97)	-0.05	(-0.10, -0.02)	0.01	(0.00, 0.01)

1029 ^a N Studies = 14; N Participants = 2,784; N major depression = 517

1030 CI: confidence interval; MINI: Mini International Neuropsychiatric Interview

1031 **Table 4.** Comparison of sensitivity and specificity estimates between PHQ-8 and PHQ-9 across
1032 cutoffs 5-15 for all studies

PHQ-8 – PHQ-9				
Cutoff	Sensitivity	95% CI	Specificity	95% CI
5	-0.01	(-0.01, 0.00)	0.00	(0.00, 0.01)
6	0.00	(-0.01, 0.00)	0.01	(0.00, 0.01)
7	-0.01	(-0.02, 0.00)	0.00	(0.00, 0.01)
8	-0.01	(-0.04, -0.01)	0.00	(0.01, 0.01)
9	-0.03	(-0.06, -0.01)	0.01	(0.01, 0.01)
10	-0.03	(-0.06, -0.02)	0.01	(0.00, 0.01)
11	-0.03	(-0.06, -0.01)	0.01	(0.01, 0.01)
12	-0.05	(-0.08, -0.03)	0.01	(0.00, 0.01)
13	-0.04	(-0.06, -0.02)	0.00	(0.00, 0.01)
14	-0.05	(-0.08, -0.03)	0.01	(0.00, 0.01)
15	-0.04	(-0.07, -0.03)	0.01	(0.00, 0.01)

1033 ^a N Studies = 54; N Participants = 16,742; N major depression = 2,097

1034 CI: confidence interval

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1036

Supplementary Material

SupplementaryMethods1. Search strategies

SupplementaryFigure1. Flow diagram of study selection process

SupplementaryFigure2. Forest plots of the difference in sensitivity and specificity estimates at cutoff 10 between PHQ-8 and PHQ-9 for each reference standard category

SupplementaryTable1. Characteristics of included primary studies as well as eligible primary studies not included in the present study

SupplementaryList1. Studies excluded at full-text review level

SupplementaryMethods1. Search strategies

MEDLINE (OvidSP)

1. PHQ*.af.
2. patient health questionnaire*.af.
3. 1 or 2
4. Mass Screening/
5. Psychiatric Status Rating Scales/
6. "Predictive Value of Tests"/
7. "Reproducibility of Results"/
8. exp "Sensitivity and Specificity"/
9. Psychometrics/
10. Prevalence/
11. Reference Values/
- 12.. Reference Standards/
13. exp Diagnostic Errors/
14. Mental Disorders/di, pc [Diagnosis, Prevention & Control]
15. Mood Disorders/di, pc [Diagnosis, Prevention & Control]
16. Depressive Disorder/di, pc [Diagnosis, Prevention & Control]
17. Depressive Disorder, Major/di, pc [Diagnosis, Prevention & Control]
18. Depression, Postpartum/di, pc [Diagnosis, Prevention & Control]
19. Depression/di, pc [Diagnosis, Prevention & Control]
20. validation studies.pt.
21. comparative study.pt.
22. screen*.af.
23. prevalence.af.
24. predictive value*.af.
25. detect*.ti.
26. sensitiv*.ti.
27. valid*.ti.
28. revalid*.ti.
29. predict*.ti.
30. accura*.ti.
31. psychometric*.ti.
32. identif*.ti.
33. specificit*.ab.
34. cut?off*.ab.
35. cut* score*.ab.
36. cut?point*.ab.
37. threshold score*.ab.
38. reference standard*.ab.
39. reference test*.ab.
40. index test*.ab.
41. gold standard.ab.
42. or/4-41
43. 3 and 42

44. limit 43 to yr="2000-Current"

PsycINFO (OvidSP)

1. PHQ*.af.
2. patient health questionnaire*.af.
3. 1 or 2
4. Diagnosis/
5. Medical Diagnosis/
6. Psychodiagnosis/
7. Misdiagnosis/
8. Screening/
9. Health Screening/
10. Screening Tests/
11. Prediction/
12. Cutting Scores/
13. Psychometrics/
14. Test Validity/
15. screen*.af.
16. predictive value*.af.
17. detect*.ti.
18. sensitiv*.ti.
19. valid*.ti.
20. revalid*.ti.
21. accura*.ti.
22. psychometric*.ti.
23. specificit*.ab.
24. cut?off*.ab.
25. cut* score*.ab.
26. cut?point*.ab.
27. threshold score*.ab.
28. reference standard*.ab.
29. reference test*.ab.
30. index test*.ab.
31. gold standard.ab.
32. or/4-31
33. 3 and 32
38. Limit 33 to "2000 to current"

Web of Science (Web of Knowledge)

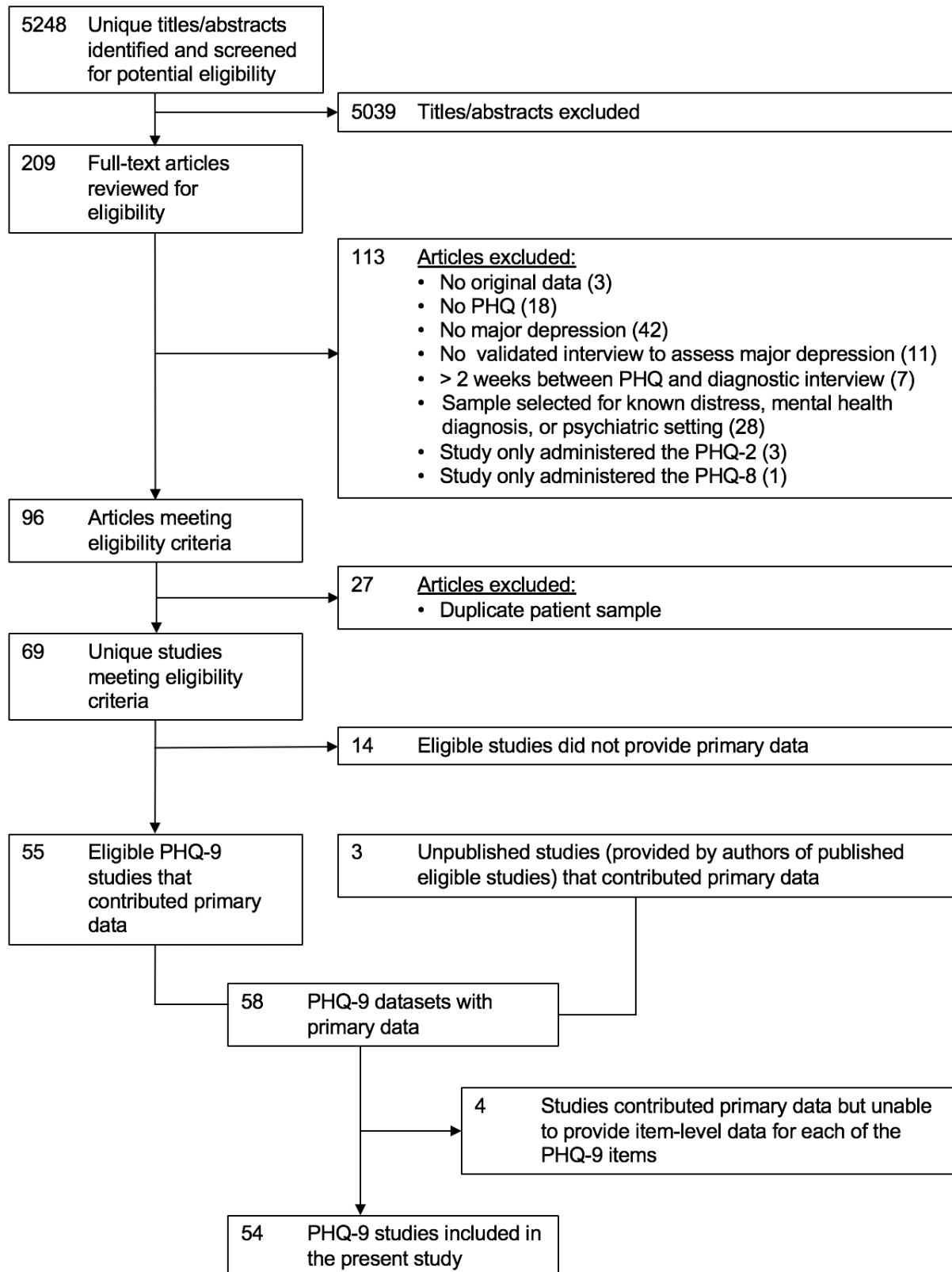
#1: TS=(PHQ* OR "Patient Health Questionnaire*")

#2: TS= (screen* OR prevalence OR "predictive value*" OR detect* OR sensitiv* OR valid* OR revalid* OR predict* OR accura* OR psychometric* OR identif* OR specificit* OR cutoff* OR "cut off*" OR "cut* score*" OR cutpoint* OR "cut point*" OR "threshold score*" OR "reference standard*" OR "reference test*" OR "index test*" OR "gold standard")

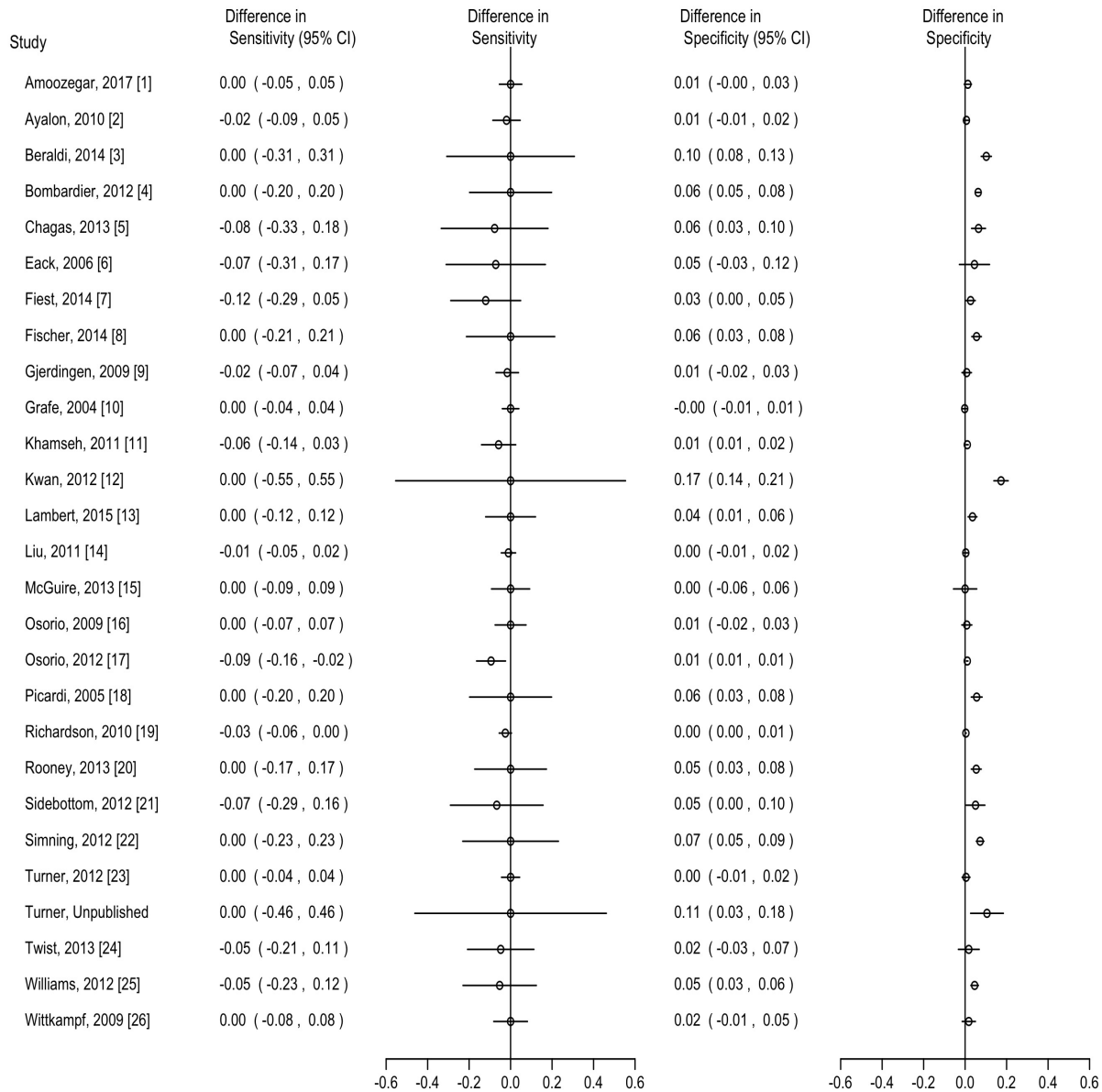
#1 AND #2

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=2000-2015

SupplementaryFigure1. Flow diagram of study selection process

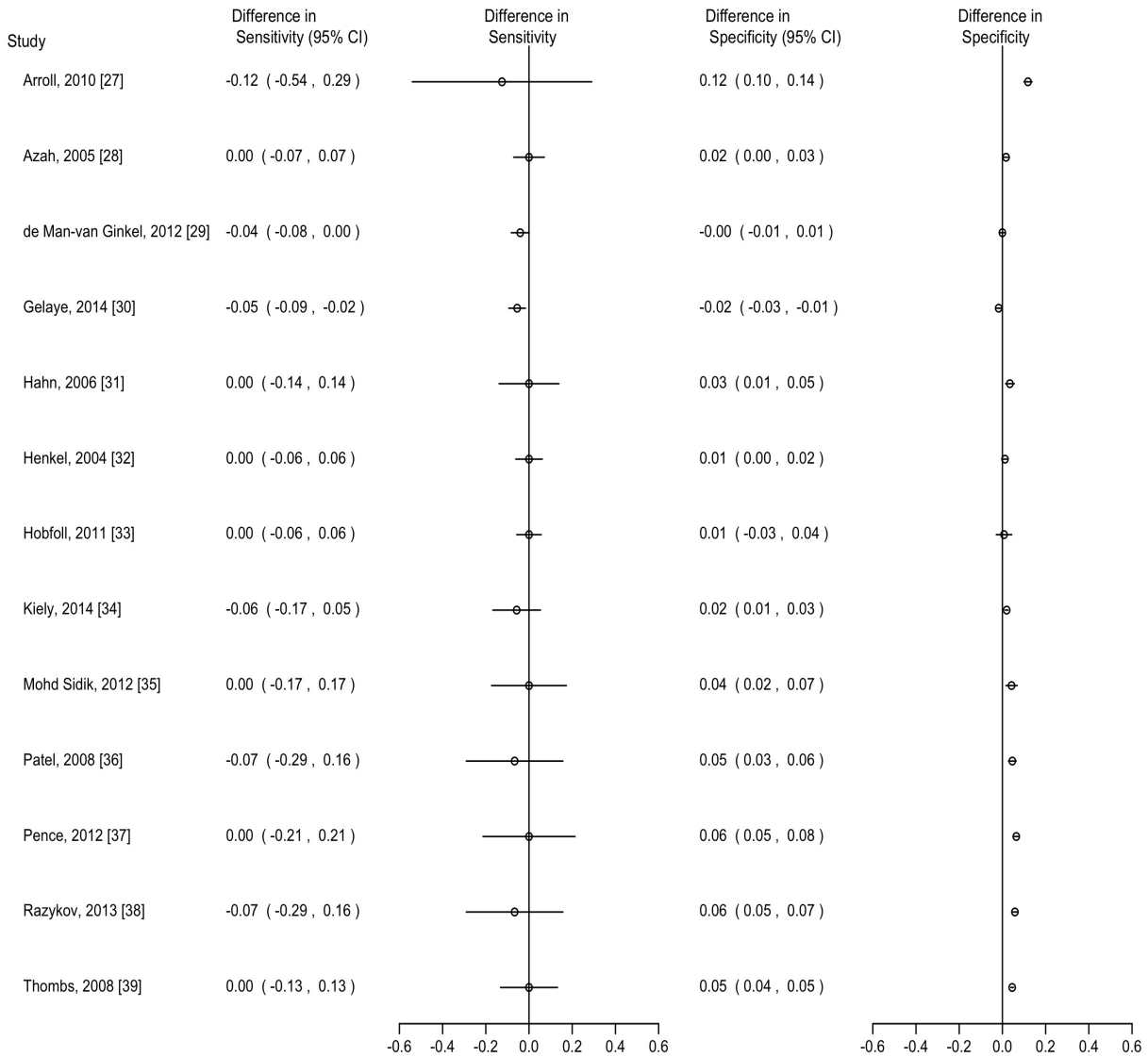


SupplementaryFigure2a. Forest plots of the difference in sensitivity and specificity estimates at cutoff 10 between PHQ-8 and PHQ-9 among studies that used a semi-structured diagnostic interview as the reference standard^a (N Studies = 27; N Participants = 6,362; N major depression = 790)



^a τ^2 for the differences of sensitivity and specificity were both <0.001.

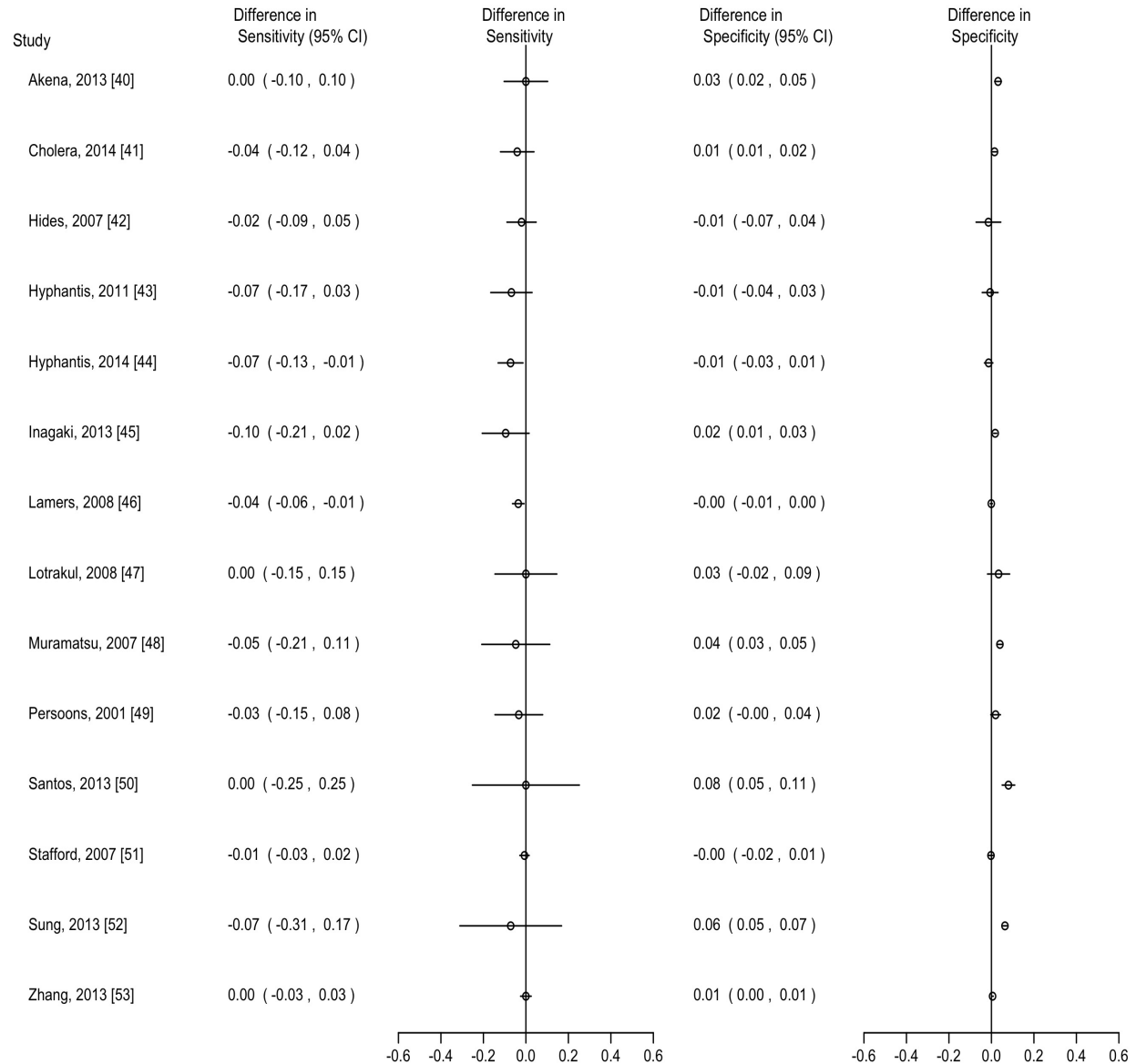
SupplementaryFigure2b. Forest plots of the difference in sensitivity and specificity estimates at cutoff 10 between PHQ-8 and PHQ-9 among studies that used a fully structured diagnostic interview as the reference standard^a (N Studies = 13; N Participants = 7,596; N major depression = 790)



^a τ^2 for the differences of sensitivity and specificity were both <0.001 .

SupplementaryFigure2c. Forest plots of the difference in sensitivity and specificity estimates at cutoff 10 between PHQ-8 and PHQ-9 among studies that used the MINI as the reference

standard^a (N Studies = 14; N Participants = 2,784; N major depression = 517)



^a τ^2 for the differences of sensitivity and specificity were both <0.001.

Supplementary Table 1a. Characteristics of included primary studies

First Author, Year	Country	Recruited Population	Diagnostic Interview	Classification System	Total N	Major Depression N (%)
Semi-structured Interviews						
Amoozegar, 2017^{1a}	Canada	Migraine patients	SCID	DSM-IV	203	49 (24)
Ayalon, 2010²	Israel	Elderly primary care patients	SCID	DSM-IV	151	6 (4)
Beraldi, 2014³	Germany	Cancer inpatients	SCID	DSM-IV	116	7 (6)
Bombardier, 2012⁴	USA	Inpatients with spinal cord injuries	SCID	DSM-IV	160	14 (9)
Chagas, 2013⁵	Brazil	Outpatients with Parkinson's Disease	SCID	DSM-IV	84	19 (23)
Eack, 2006⁶	USA	Women seeking psychiatric services for their children at two mental health centers	SCID	DSM-IV	48	12 (25)
Fiest, 2014⁷	Canada	Epilepsy outpatients	SCID	DSM-IV	169	23 (14)
Fischer, 2014⁸	Germany	Heart failure patients	SCID	DSM-IV	194	11 (5)
Gjerdingen, 2009⁹	USA	Mothers registering their newborns for well-child visits at medical or pediatric clinics	SCID	DSM-IV	419	19 (5)
Gräfe, 2004¹⁰	Germany	Medical and psychosomatic outpatients	SCID	DSM-IV	494	67 (14)
Khamseh, 2011¹¹	Iran	Type 2 diabetes patients	SCID	DSM-IV	122	47 (39)
Kwan, 2012¹²	Singapore	Post-stroke inpatients undergoing rehabilitation	SCID	DSM-IV-TR	113	3 (3)
Lambert, 2015^{13a}	Australia	Cancer patients	SCID	DSM-IV	147	21 (14)
Liu, 2011¹⁴	Taiwan	Primary care patients	SCAN	DSM-IV	1532	50 (3)
McGuire, 2013¹⁵	USA	Acute coronary syndrome inpatients	DISH	DSM-IV	100	9 (9)

Osório, 2009¹⁶	Brazil	Women in primary care	SCID	DSM-IV	177	60 (34)
Osório, 2012¹⁷	Brazil	Inpatients from various clinical wards	SCID	DSM-IV	86	28 (33)
Picardi, 2005¹⁸	Italy	Inpatients with skin diseases	SCID	DSM-IV	138	12 (9)
Richardson, 2010¹⁹	USA	Older adults undergoing in-home aging services care management assessment	SCID	DSM-IV	377	95 (25)
Rooney, 2013²⁰	UK	Adults with cerebral glioma	SCID	DSM-IV	126	14 (11)
Sidebottom, 2012²¹	USA	Pregnant women	SCID	DSM-IV	246	12 (5)
Simning, 2012²²	USA	Older adults living in public housing	SCID	DSM-IV	190	10 (5)
Turner, Unpublished	Australia	Cardiac rehabilitation patients	SCID	DSM-IV	51	4 (8)
Turner, 2012^{23b}	Australia	Stroke patients	SCID	DSM-IV	72	13 (18)
Twist, 2013^{24d}	UK	Type 2 diabetes outpatients	SCAN	DSM-IV	352	79 (22)
Williams, 2012²⁵	USA	Parkinson's Disease patients	SCID	DSM-IV	235	61 (26)
Wittkamp, 2009^{26c}	The Netherlands	Primary care patients at risk for depression	SCID	DSM-IV	260	45 (17)

Fully Structured Interviews						
Arroll, 2010²⁷	New Zealand	Primary care patients	CIDI	DSM-IV	2,528	156 (6)
Azah, 2005^{28c}	Malaysia	Adults attending family medicine clinics	CIDI	ICD-10	180	30 (17)
de Man-van Ginkel, 2012²⁹	The Netherlands	Stroke patients	CIDI	DSM-IV	164	17 (10)
Gelaye, 2014³⁰	Ethiopia	Outpatients at a general hospital	CIDI	DSM-IV	923	162 (18)
Hahn, 2006³¹	Germany	Patients with chronic illnesses from rehabilitation centers	CIDI	DSM-IV	211	18 (9)
Henkel, 2004³²	Germany	Primary care patients	CIDI	ICD-10	430	43 (10)

Hobfoll, 2011³³	Israel	Jewish and Palestinian residents of Jerusalem exposed to war	CIDI	DSM-IV	144	42 (29)
Kiely, 2014³⁴	Australia	Community sample of adults	CIDI	ICD-10	822	33 (4)
Mohd-Sidik, 2012^{35d}	Malaysia	Primary care patients	CIDI	DSM-IV	146	31 (21)
Patel, 2008³⁶	India	Primary care patients	CIS-R	ICD-10	299	13 (4)
Pence, 2012³⁷	Cameroon	HIV-infected patients	CIDI	DSM-IV	398	11 (3)
Razykov, 2013³⁸	Canada	Patients with systemic sclerosis	CIDI	DSM-IV	345	13 (4)
Thombs, 2008³⁹	USA	Outpatients with coronary artery disease	C-DIS	DSM-IV	1,006	221 (22)
Mini International Neuropsychiatric Interviews (MINI)						
Akena, 2013⁴⁰	Uganda	HIV/AIDS patients	MINI	DSM-IV	91	11 (12)
Cholera, 2014⁴¹	South Africa	Patients undergoing routine HIV counseling and testing at a primary health care clinic	MINI	DSM-IV	397	47 (12)
Hides, 2007⁴²	Australia	Injection drug users accessing a needle and syringe program	MINI	DSM-IV	103	47 (46)
Hyphantis, 2011^{43c}	Greece	Patients with various rheumatologic disorders	MINI	DSM-IV	213	69 (32)
Hyphantis, 2014⁴⁴	Greece	Patients with chronic illnesses presenting at the emergency department	MINI	DSM-IV	349	95 (27)
Inagaki, 2013^{45d}	Japan	Internal medicine outpatients	MINI	DSM-III-R	104	21 (20)
Lamers, 2008^{46c}	The Netherlands	Elderly primary care patients with diabetes mellitus or chronic obstructive pulmonary	MINI	DSM-IV	104	59 (57)

		disease				
Lotrakul, 2008⁴⁷	Thailand	Outpatients	MINI	DSM-IV	278	19 (7)
Muramatsu, 2007⁴⁸	Japan	Primary care patients	MINI	DSM-IV	116	32 (28)
Persoons, 2001^{49b}	Belgium	Inpatients and patients at gastroenterological and hepatology wards	MINI	DSM-IV	173	28 (16)
Santos, 2013⁵⁰	Brazil	General population	MINI	DSM-IV	196	25 (13)
Stafford, 2007⁵¹	Australia	Inpatients with coronary artery disease who had undergone surgery	MINI	DSM-IV	193	35 (18)
Sung, 2013⁵²	Singapore	Primary care patients	MINI	DSM-IV	399	12 (3)
Zhang, 2013⁵³	China	Type 2 diabetes patients	MINI	DSM-IV	68	17 (25)

Abbreviations: C-DIS: Computerized Diagnostic Interview Schedule; CIDI: Composite International Diagnostic Interview; CIS-R: Clinical Interview Schedule Revised; DISH: Depression Interview and Structured Hamilton; DSM: Diagnostic and Statistical Manual of Mental Disorders; ICD: International Classification of Diseases; MINI: Mini Neurospsychiatric Diagnostic Interview; PHQ-9: Patient Health Questionnaire-9; SCAN: Schedules for Clinical Assessment in Neuropsychiatry; SCID: Structured Clinical Interview for DSM Disorders; UK: United Kingdom; USA: United States of America.

^aWas unpublished at the time of the electronic database search.

^bMultiple recruitment settings were included, thus recruitment setting was coded at the participant-level.

^cAppropriate statistical weighting to reflect sampling procedures was included in the primary study dataset. The provided weights were used for analysis.

^dSampling procedures merited weighting, but the original dataset did not weight. Appropriate weights were constructed using inverse selection probabilities.

Supplementary Table 1b. Characteristics of eligible primary studies not included in the present study

First Author, Year	Country	Recruited Population	Diagnostic Interview	Classification System	Total N	Major Depression N (%)
Semi-structured Interviews						
Becker, 2002 ⁵⁴	Saudi Arabia	Primary care patients	SCID	DSM-III-R	173	NR
Chen, 2013 ⁵⁵	China	Primary care populations	SCID	DSM-IV	280	NR ^a
Chen, 2012 ⁵⁶	China	Adults over 60 in primary care	SCID	DSM-IV	262	97 (37)
Fann, 2005 ^{57b}	USA	Inpatients with traumatic brain injury	SCID	DSM-IV	134	45 (34)
Lai, 2010 ⁵⁸	Hong Kong	Men with postpartum wives	SCID	DSM-IV	551	8 (1)
Navinés, 2012 ⁵⁹	Spain	Chronic hepatitis C patients	SCID	DSM-IV	104	21 (20)
Phelan, 2010 ⁶⁰	USA	Elderly primary care patients	SCID	DSM-IV	69	8 (12)
Thompson, 2011 ⁶¹	USA	Parkinson's patients	SCID	DSM-IV	214	30 (14)
Vöhringer, 2013 ^{62b}	Chile	Primary care patients	SCID	DSM-IV	190	59 (31)
Watnick, 2005 ⁶³	USA	Long term dialysis patients	SCID	DSM-IV	62	12 (19)
Fully Structured Interviews						
Al-Ghafri, 2014 ⁶⁴	Oman	Medical trainees	CIDI	NR	131	NR ^a
Delgadillo, 2011 ^{65b}	UK	Outpatients in drug addiction treatment	CIS-R	ICD-10	103	51 (50)
Haddad, 2013 ⁶⁶	UK	Coronary heart disease patients	CIS-R	ICD-10	730	32 (4)

Mini International Neuropsychiatric Interviews (MINI)						
Persoons, 2003⁶⁷	Belgium	Otorhinolaryngology outpatients	MINI	DSM-IV	97	16 (16)
Rathore, 2014⁶⁸	USA	Adults with epilepsy	MINI	DSM-IV	172	33 (19)
Scott, 2011⁶⁹	USA	Chronic hepatitis C patients	MINI	DSM-IV and ICD-10	30	NR ^a
van Steenbergen-Weijenburg, 2010^{70b}	The Netherlands	Diabetes patients	MINI	DSM-IV	172	33 (19)
Wang, 2014⁷¹	China	General population	MINI	DSM-IV	1045	28 (3)

Abbreviations: CIDI: Composite International Diagnostic Interview; CIS-R: Clinical Interview Schedule Revised; DSM: Diagnostic and Statistical Manual of Mental Disorders; ICD: International Classification of Diseases; MINI: Mini International Neuropsychiatric Interview; NR: Not Reported; PHQ-9: Patient Health Questionnaire-9; SCID: Structured Clinical Interview for DSM Disorders; UK: United Kingdom; USA: United States of America.

^aReported numbers implausible.

^bContributed primary data to the main individual participant data meta-analysis of PHQ-9, but were excluded from the present study because PHQ-9 individual item scores were not available.

SupplementaryList1. Studies excluded at full-text review level

Studies excluded because no original data was used:

1. Shoukri MM, Donner A. Bivariate modeling of interobserver agreement coefficients. *Stat Med.* 2009;**28**:430-440.
2. Priyanka P, Boyle LL, Tu XM, Conwel YI. Inter-rater reliability and validity of the PHQ-9 and GAD-7 to identify depression and anxiety in older adults receiving aging services care management. *Am J Geriatr Psychiatry.* 2010;**18**:S113-S114.
3. Lowe B, Grafe K, Quenter A, Buchholz C, Wild B, Zipfel S, Herzog W. The Patient Health Questionnaire D as a self-rating instrument for screening mental disorders in internal medicine and in general medicine - Preliminary validation results with 1000 outpatients. *Psychother Psychosom Med Psychol.* 2001;**51**:109-109.

Studies excluded because there was no administration of the PHQ:

4. Fine TH, Contractor AA, Tamburrino M, Elhai JD, Prescott MR, Cohen GH, Shirley E, Chan PK, Goto T, Slembariski R, Liberzon I, Galea S, Calabrese JR. Validation of the telephone-administered PHQ-9 against the in-person administered SCID-I major depression module. *J Affect Disord.* 2013;**150**:1001-1007.
5. Tilli V, Suominen K, Karlsson H. The Autonomic Nervous System Questionnaire and the Brief Patient Health Questionnaire as screening instruments for panic disorder in Finnish primary care. *Eur Psychiatry.* 2013;**28**:442-447.
6. Ryan DA, Gallagher P, Wright S, Cassidy EM. Sensitivity and specificity of the Distress Thermometer and a two-item depression screen (Patient Health Questionnaire-2) with a 'help' question for psychological distress and psychiatric morbidity in patients with advanced cancer.. *Psychooncology.* 2012;**21**:1275-1284.

7. Saliba D, DiFilippo S, Edelen MO, Kroenke K, Buchanan J, Streim J. Testing the PHQ-9 interview and observational versions (PHQ-9 OV) for MDS 3.0. *J Am Med Dir Assoc*. 2012;**13**:618-625.
8. Salve H, Goswami K, Nongkynrih B, Sagar R, Sreenivas V. Prevalence of psychiatric morbidity at Mobile Health Clinic in an urban community in North India. *Gen Hosp Psychiatry*. 2012;**34**:121-126.
9. Morina N, von Lersner U, Prigerson HG. War and bereavement: consequences for mental and physical distress. *PLoS ONE*. 2011;**6**:e22140.
10. Watson LC, Zimmerman S, Cohen LW, Dominik R. Practical depression screening in residential care/assisted living: five methods compared with gold standard diagnoses. *Am J Geriatr Psychiatry*. 2009;**17**:556-564.
11. Mitchell AJ, McGlinchey JB, Young D, Chelminski I, Zimmerman M. Accuracy of specific symptoms in the diagnosis of major depressive disorder in psychiatric outpatients: data from the MIDAS project. *Psychol Med*. 2009;**39**:1107-1116.
12. Husain N, Waheed W, Tomenson B, Creed F. The validation of personal health questionnaire amongst people of Pakistani family origin living in the United Kingdom. *J Affect Disord*. 2007;**97**:261-264.
13. Husain N, Gater R, Tomenson B, Creed F. Comparison of the Personal Health Questionnaire and the Self Reporting Questionnaire in rural Pakistan. *J PMA J Pak Med Assoc*. 2006;**56**:366-370.
14. Lowe B, Grafe K, Zipfel S, Spitzer RL, Herrmann-Lingen C, Witte S, Herzog W. Detecting panic disorder in medical and psychosomatic outpatients: comparative validation of the Hospital Anxiety and Depression Scale, the Patient Health

Questionnaire, a screening question, and physicians' diagnosis. *J Psychosom Res.* 2003;**55**:515-519.

15. Rizzo R, Piccinelli M, Mazzi MA, Bellantuono C, Tansella M. The Personal Health Questionnaire: a new screening instrument for detection of ICD-10 depressive disorders in primary care. *Psychol Med.* 2000;**30**:831-840.
16. Husain N, Creed F, Tomenson B. Depression and social stress in Pakistan. *Psychol Med.* 2000;**30**:395-402.
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18. Creed F. The relationship between somatic symptoms, health anxiety, and outcome in medical out-patients. *Psychiatr Clin North Am.* 2011;**34**:545-564.
19. Allgaier AK, Pietsch K, Fruhe B, Prast E, Sigl-Glockner, Schulte-Korne G. Depression in pediatric care: Is the WHO-Five Well-Being Index a valid screening instrument for children and adolescents?. *Gen Hosp Psychiatry.* 2012;**34**:234-241.
20. Gellis ZD. Depression screening in medically ill homecare elderly. *Best Pract Ment Health.* 2010;**6**:1-16.
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Studies excluded because there was no clinical interview to diagnose current major depression:

22. Muller KW, Beutel ME, Wolfling K. A contribution to the clinical characterization of Internet addiction in a sample of treatment seekers: validity of assessment, severity of psychopathology and type of co-morbidity. *Compr Psychiatry*. 2014;**55**:770-777.
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26. Tabb KM, Gavin AR, Guo Y, Huang H, Debiec K, Katon W. Views and experiences of suicidal ideation during pregnancy and the postpartum: findings from interviews with maternal care clinic patients. *Women Health*. 2013;**53**:519-535.
27. Gold KJ, Spangenberg K, Wobil P, Schwenk TL. Depression and risk factors for depression among mothers of sick infants in Kumasi, Ghana. *Int J Gynaecol Obstet*. 2013;**120**:228-231.
28. Kamphuis MH, Stegenga BT, Zuithoff NP, King M, Nazareth I, de Wit NJ, Geerlings MI. Does recognition of depression in primary care affect outcome? The PREDICT-NL study. *Fam Pract*. 2012;**29**:16-23.

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36. Hausteiner-Wiehle C, Sokollu F. Magical thinking in somatoform disorders: an exploratory study among patients with suspected allergies. *Psychopathology*. 2011;**44**:283-288.
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