Minimal detectable change of the Patient Health Questionnaire-9, Patient Health Questionnaire-8, and Patient Health Questionnaire-2: individual patient data meta-analysis

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ABSTRACT

OBJECTIVE

To estimate the minimal detectable change (MDC) for the Patient Health Questionnaire-9 (PHQ-9) and its eight item (PHQ-8) and two item (PHQ-2) versions including differences by participant and study characteristics.

DESIGN

Individual participant data meta-analysis.

DATA SOURCES

Medline, Medline In-Process and other non-indexed citations, PsycInfo, and Web of Science, 1 January 2000 to 9 May 2018.

ELIGIBILITY CRITERIA FOR SELECTING STUDIES

Datasets from articles in any language if participants were aged ≥18 years, were recruited from any non-psychiatric setting, and were not recruited because they were seeking mental healthcare. Eligible datasets had a classification for major depressive disorder or major depressive episode based on a validated semi-structured or fully structured interview conducted within two weeks of administering the PHQ-9, PHQ-8, or PHQ-2.

RESULTS

Pooled MDCs across studies were estimated for the PHQ-9, PHQ-8, and PHQ-2 with random effects meta-analysis for 95% (MDC95), 90% (MDC90), and 67% (MDC67) confidence that change beyond measurement error occurred. PHQ-9, PHQ-8, and PHQ-2 analyses included 42 548 participants (94 studies), 42 592 participants (94 studies), and 44 085 participants (98 studies), respectively. Mean participant age was 49 years (standard deviation 17), and 60% of participants were women. Overall, 10% of participants had major depression (range 1-57% across studies). MDC95 was 5.72 points (95% confidence interval (CI) 5.54 to 5.90, 95% prediction interval (PI) 4.00 to 7.44) for the PHQ-9, 5.51 points (95% CI 5.33 to 5.68, 95% PI 3.87 to 7.15) for the PHQ-8, and 2.26 points (95% CI 2.15 to 2.37, 95% PI 1.20 to 3.32) for the PHQ-2. For the PHQ-9, MDC95 was highest in inpatient healthcare settings at 6.48 (95% CI 6.05 to 6.92) points. MDC95 for the PHQ-9 increased by 0.40 (95% CI 0.25 to 0.55) points for each 10% increase in the proportion of participants with major depression. Sex and age had minimal or no association. Subgroup and meta-regression findings were similar for the PHQ-8 and PHQ-2.

CONCLUSIONS

Based on the pooled estimate, a six point difference on the PHQ-9, the PHQ version most used in clinical practice, could be an appropriate MDC threshold in general practice. A higher threshold may be preferred in specialty mental healthcare. MDC67 or MDC90 thresholds would provide less certainty that change has occurred. Alternative strategies, such as using the upper end of a prediction interval, would provide more certainty but a greater likelihood of not recognising change.

STUDY REGISTRATION

PROSPERO CRD42014010673.

WHAT IS ALREADY KNOWN ON THIS TOPIC

The minimal detectable change (MDC) of the Patient Health Questionnaire-9 (PHQ-9) and the shorter PHQ-8, and PHQ-2, has not been assessed in a systematic review

Only one primary study in systemic sclerosis has assessed the MDC for the PHQ-8, and none has evaluated PHQ-9 or PHQ-2 MDCs

The UK NHS's Talking Therapies programme uses a six point PHQ-9 reliable change index (equivalent to MDC with 95% confidence, MDC95) to assess change in individuals in treatment, but no supporting analyses have been published

WHAT THIS STUDY ADDS

This study synthesised evidence from 98 studies (44 085 participants) and estimated MDC95, MDC90, and MDC67 for the PHQ-9, PHQ-8, and PHQ-2

A six point threshold for the PHQ-9 could be considered for evaluating individual changes in depression symptoms and as a threshold for assessing estimates for a minimal important difference

A higher threshold for the PHQ-9 may be more appropriate for people in specialty mental health treatment settings

Introduction

Patient reported outcome measures assess people's health and wellbeing from their perspective. Measurement based care involves administering patient reported outcome measures, with scores to evaluate change, and discussing the results collaboratively with patients to inform treatment decisions. Clinical decision making must consider whether changes in scores are clinically important and represent reliable change beyond random fluctuation.[1]

Minimal important differences, also known as minimal clinically important differences, represent

the smallest change likely perceived as worthwhile by patients.[2 3] Minimal important differences are estimated by comparing changes in scores to an anchor that reflects a patient's perspective of whether or how much change has occurred.[4-6] Sometimes, however, estimated minimal important differences are too small to be reliably detected.

The minimal detectable change (MDC) is the smallest change in score that can be detected beyond measurement error.[7 8] Minimal important differences that are smaller than the MDC cannot distinguish meaningful change from chance fluctuations. Determining that meaningful change has occurred requires that a change in score exceeds the minimal important difference threshold and is detectable beyond error fluctuation based on the MDC.

The Patient Health Questionnaire (PHQ)-9, PHQ-8, and PHQ-2 were originally developed as screening tools and are now the most commonly used mental health outcome measures in clinical practice.[2 9-16] The PHQ-9 has nine questions, with each question scored 0-3. Possible total scores range from 0 (least depressed) to 27 (most depressed). The eight item PHQ-8 and two item PHQ-2 are subsets of the PHQ-9 with score ranges of 0-24 and 0-6, respectively. The PHQ-8 differs from the PHQ-9 by excluding an item on suicidal ideation. The PHQ-2 includes the first two items of the PHQ-9 and is mainly used as a first step in screening for depression.

No systematic review has assessed the minimal important difference or MDC of the PHQ-9, PHQ-8, or PHQ-2. Two primary studies, both from the UK, estimated the minimal important difference for the PHQ-9 with patient reported anchors for improvement. One study assessed 1122 participants from two trials on treatments for depression at three month intervals and reported a minimal important difference of 3.7 points.[10] The other study assessed 400 patients in primary care at two week intervals and reported minimal important difference thresholds of 2.0, 1.7, and 2.4 points among participants with low, medium, and high baseline symptoms.[11] Neither study provided estimates of precision, an important consideration in evaluating the credibility of the minimal important difference estimates.[17]

The PHQ-9 is commonly used in measurement based care. The UK NHS's Talking Therapies programme (formerly known as the Improving Access to Psychological Therapies programme) uses a six point PHQ-9 threshold for reliable change, equivalent to 95% confidence that change beyond measurement error has occurred (MDC95). No analysis of estimation of this threshold, however, has been published.[18-20] This threshold has also been adopted in Canadian mental healthcare.[21-23] In the US, the National Committee for Quality Assurance defines a response to treatment for depression as a reduction in PHQ-9 score of ≥50% and remission as a PHQ-9 score of < 5, but has not identified metrics for assessing meaningful or reliable change.[24 25]

The only study that has evaluated the MDC for the PHQ-9, PHQ-8, or PHQ-2 reported an MDC of 5.2 points (95% confidence interval (CI) 5.1 to 5.3) for the PHQ-8 in 2571 people with the rare autoimmune disease systemic sclerosis.[26] This finding suggests that existing estimates of minimal important difference (range 1.7-3.7 points) may be too small to be distinguished from measurement error. Also, the MDC for people with systemic sclerosis, a specific population with a rare disease, may not be generalisable to other populations. No studies have estimated MDCs for the PHQ-9, PHQ-8, or PHQ-2 in large representative samples or evaluated whether MDCs vary by factors such as age, sex, recruitment setting, and major depression status.

Individual participant data meta-analyses (IPDMAs) can be used to generate estimates from data collected in many primary studies, even when those studies did not publish the outcome of interest. We have assembled a large database to conduct IPDMAs on measurement properties of the PHQ-9, PHQ-8, and PHQ-2.[27-30] The objectives of our study were to evaluate the MDC for the PHQ-9, PHQ-8, and PHQ-2, including MDC95, MDC90 (90% confidence), and MDC67 (67% confidence), and examine whether MDCs differ by age, sex, recruitment setting, or major depression status.

Methods

The MDC can be calculated with test-retest reliability, which requires multiple observations and is often not available, or with a cross sectional reliability estimate. We calculated MDC based on Cronbach's alpha, a cross sectional estimation method.

Our main PHQ-9, PHQ-8, and PHQ-2 screening accuracy IPDMAs were registered in the International Prospective Register of Systematic Reviews (PROSPERO CRD42014010673), and the results have been published.[27-30] The protocol for this study was uploaded to the Open Science Framework before the start of the study (https://osf.io/xsyw8). We have reported our study consistent with relevant Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) items.[31] Because data collection methods were similar to our main PHQ-9, PHQ-8, and PHQ-2 IPDMAs,[27-30] and data analysis methods were similar to our study of Geriatric Depression Scale MDCs,[32] we followed the reporting guidance of the Text Recycling Research Project.[33]

Eligible studies and participants

For our main PHQ-9, PHQ-8, and PHQ-2 screening accuracy IPDMAs,[27-30 34] datasets from articles in any language were eligible if participants were aged ≥18 years, were recruited from any non-psychiatric setting, and were not recruited because they were seeking mental healthcare, because screening is done to identify previously unrecognised cases. Examples of eligible studies included studies of participants from the community, general practice, or non-psychiatric specialty inpatient or outpatient settings (eg, oncology or cardiology). Eligible datasets had to include a classification for major depressive

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disorder or major depressive episode based on a validated semi-structured or fully structured interview conducted within two weeks of administering the PHQ-9, PHQ-8, or PHQ-2 because diagnostic criteria for major depression are for symptoms in the past two weeks. Datasets where not all participants were eligible were included if the primary data allowed us to select eligible participants. In defining major depression, we considered major depressive disorder or major depressive episode based on any version of the Diagnostic and Statistical Manual of Mental Disorders or the International Classification of Diseases. If more than one was reported, we prioritised major depressive episode over major depressive disorder and the Diagnostic and Statistical Manual of Mental Disorders over the International Classification of Diseases. For this study, we included only primary study datasets with PHQ-9, PHQ-8, or PHQ-2 item scores (ie, not if only total scores were reported), because item scores are needed to calculate Cronbach's alpha reliability, which was used to calculate the standard error of measurement and thus MDC.[35]

Identification and selection of eligible studies

We searched Medline, Medline In-Process and other non-indexed citations, PsycInfo, and Web of Science from 1 January 2000 to 9 May 2018 with a peer reviewed[36] search strategy (supplementary methods 1). We did not perform searches before 2000 because the PHQ-9 was originally published in 2001.[37] We also 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, ON, Canada) to store and track search results, conduct eligibility screening, record correspondence with primary study authors, and extract study characteristics.

Two investigators independently reviewed titles and abstracts for eligibility. If either investigator considered a study potentially eligible, a full text review was done by two investigators, independently (supplementary methods 2). Any disagreements after full text review were 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 extraction, contribution, and synthesis

We invited authors of eligible datasets to contribute de-identified primary datasets. We emailed corresponding authors of eligible studies at least three times, as necessary. If no response was received, we emailed co-authors and attempted telephone contact.

We compared published participant characteristics and diagnostic accuracy results with results that we generated from raw datasets. We resolved any discrepancies with the primary study investigators. We then converted individual participant data to a standard format and entered the data, along with study level data, into one harmonised dataset. When datasets included statistical weights 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 weights with inverse selection probabilities. For our screening accuracy IPDMAs, we assessed the risk of bias with the Quality Assessment of Diagnostic Accuracy Studies-2 tool.[38] No risk of bias tool exists for studies assessing MDCs, and risk of bias for screening accuracy would not necessarily reflect risk of bias for MDCs, so we did not incorporate a risk of bias assessment into our study.

Data analysis

We used a two stage IPDMA approach. In the first stage, individual participant data were analysed separately within each study to obtain study level MDC estimates. In the second stage, study level estimates were pooled with restricted maximum likelihood random effects meta-analysis and mixed effects meta-regression models.

We calculated MDC95 as $1.96\times\sqrt{2}\times$SEM, MDC90 as $1.64\times\sqrt{2}\times$SEM, and MDC67 as $\sqrt{2}\times$SEM,[39-41] which reflect CIs for a difference. SEM (standard error of measurement) is the standard deviation of test scores multiplied by the square root of one minus the reliability coefficient.[12 35 41 42] We used Cronbach's alpha as the reliability coefficient.[12 35] Ideally, test-retest reliability would be used to reflect reliability in scores over time. Test-retest reliability estimates, however, must be done over a period that is long enough to avoid memory effects but short enough to ensure that symptom status has not changed; few studies provide such estimates.[43 44] Thus Cronbach's alpha is commonly used in estimating MDC[43 45] (supplementary methods 3 has more details).[43 45-47]

For each study, we estimated MDC and its standard deviation (SD) by a bootstrap approach with resampling at the participant level and 1000 bootstrap iterations. We used restricted maximum likelihood random effects meta-analysis to obtain pooled MDC95, MDC90, and MDC67 estimates with 95% CIs and 95% prediction intervals (PIs). CIs were derived with normal based Wald methods and PIs were calculated as the pooled estimate $\pm 1.96\times\sqrt{(\tau^2+\text{Var(pooled estimate)})}$ under a normal predictive distribution. We examined the distributions of the random effects for each model, which were found to be reasonably normal. Because CIs can be sensitive to distributional assumptions, particularly when between study heterogeneity is substantial, we conducted sensitivity analyses with the Hartung-Knapp approach to derive CIs and PIs, with the corresponding t distribution and degrees of freedom based on the number of studies contributing to each analysis minus one. We excluded participants with missing item scores on the PHQ-9, PHQ-8, or PHQ-2. Given the small proportion of missing data (PHQ-9, n=566 (1%); PHQ-8, n=522 (1%); PHQ-2, n=203 (< 1%); and only one study with >15% of participants with missing items), we used complete case analyses.

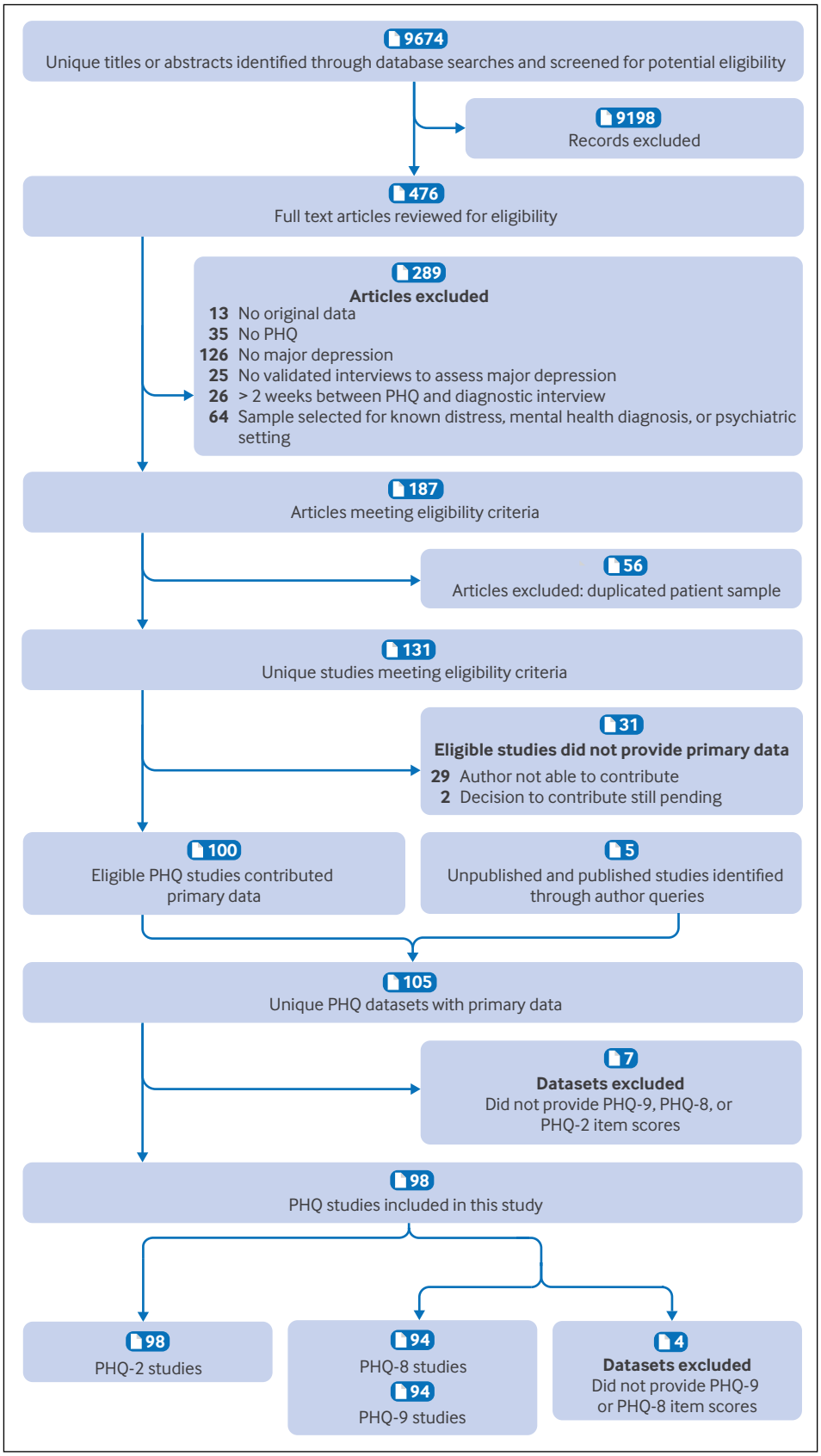


Fig 1 | Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow diagram. PHQ=Patient Health Questionnaire; PHQ-2=Patient Health Questionnaire-2; PHQ-8=Patient Health Questionnaire-8, and PHQ-9=Patient Health Questionnaire-9

Table 1 | Unweighted characteristics of 42 548 participants from 94 studies included in the Patient Health Questionnaire-9 (PHQ-9) analysis

Subgroup	No of participants*	Mean (SD) proportion across studies*	Mean (SD) PHQ-9 score*	No (%) of participants with major depression positive classification status*
Overall sample	42 548	—	4.96 (5.24)	4255 (10)
Age (years)†:				
18-29	6684	16 (18)	5.66 (5.28)	664 (10)
30-44	11 273	25 (17)	5.18 (5.41)	1205 (11)
45-64	16 161	36 (19)	4.82 (5.24)	1616 (10)
≥65	8163	22 (25)	4.35 (4.84)	739 (9)
Missing	267	1 (10)	6.20 (5.78)	31 (12)
Country‡:				
US	4028 (15)	—	5.99 (5.64)	619 (15)
Australia or New Zealand	4299 (9)	—	4.55 (5.08)	315 (7)
UK	613 (3)	—	7.99 (6.88)	108 (18)
Germany	1605 (6)	—	7.13 (5.76)	147 (9)
Canada	5788 (9)	—	4.19 (4.81)	269 (5)
Brazil	543 (4)	—	7.52 (6.61)	132 (24)
Netherlands	7049 (7)	—	3.62 (4.37)	494 (7)
Other European countries§	3817 (7)	—	6.18 (5.37)	532 (14)
Middle Eastern or African countries¶	4817 (14)	—	6.21 (5.67)	833 (17)
Asian countries or regions**	9452 (18)	—	4.24 (4.75)	708 (7)
Central or South American countries††	537 (2)	—	7.05 (5.71)	98 (18)
Sex‡‡:				
Women	25 013	60 (23)	5.38 (5.34)	2797 (11)
Men	17 512	40 (22)	4.37 (5.03)	1455 (8)
Missing	23	0 (1)	7.30 (6.24)	3 (13)
Setting§§:				
Non-medical	15 552	—	3.48 (4.32)	944 (6)
Primary care	13 983	—	5.46 (5.35)	1580 (11)
Outpatient specialty	9822	—	5.99 (5.58)	1369 (14)
Inpatient	3061	—	7.03 (5.94)	357 (12)
Mixed outpatient specialty and inpatient	130	—	3.80 (3.78)	5 (4)

SD=standard deviation.
*Characteristics are based on observed participants and calculated without participant level sampling weights.
†267 participants missing for age across 23 studies.
‡Number of participants with number of studies in parentheses.
§Includes Spain (n=1), Italy (n=1), Greece (n=3), Belgium (n=1), and Latvia (n=1).
¶Includes South Africa (n=4), Israel (n=2), Iran (n=2), Ethiopia (n=1), Kenya (n=1), Zimbabwe (n=1), Cameroon (n=1), and Uganda (n=2).
**Includes China (n=2), Japan (n=4), Hong Kong (n=1), Malaysia (N=3), Singapore (n=2), South Korea (n=1), Taiwan (n=1), India (n=1), Thailand (n=1), Nepal (n=1), and Myanmar (n=1).
††Includes Mexico (n=1) and Argentina (n=1).
‡‡23 participants missing for sex across eight studies.
§§130 participants from one study with mixed outpatient specialty and inpatient settings, without individual classification.

We estimated MDCs for subgroups based on age (18-29, 30-44, 45-64, and ≥65 years),[26] sex (women and men), and recruitment setting (non-medical, primary care, outpatient specialty, and inpatient) with the same analysis method as the main MDC analyses. To estimate MDC differences between age and sex subgroups, we estimated the difference in each study and its SD followed by restricted maximum likelihood random effects meta-analysis. In each subgroup analysis, the subgroup with the largest number of included studies was used as the reference group to maximise study coverage and sample size (age reference subgroup was 45-64 years and sex reference subgroup was women). To compare the age groups 18-29 years and 45-64 years, for example, we performed bootstrap resampling within each study that included participants from both age groups to estimate separate MDCs for each age group. We then calculated within study subgroup differences by subtracting the MDC of the reference age group (45-64 years) from that of the comparison age group. Within study differences were then pooled with restricted maximum likelihood random effects meta-analysis. Participants with missing data on a subgroup defining variable were excluded from that subgroup analysis.

We used meta-regression, rather than meta-analysis of differences within studies, to estimate MDC differences between recruitment sites because all participants in each study were recruited from the same site. We also used meta-regression, rather than a subgroup analysis, for major depression classification status. We used this approach because of the indirect range restriction of PHQ-9, PHQ-8, and PHQ-2 scores, which would have occurred if we had grouped participants based on depression classification status. This grouping would have altered variance within classification groups, thus making the estimation of reliability untenable.[48] We did not conduct a subgroup analysis on symptom severity scores for the same reason. We fitted two stage linear mixed effects meta-regression models in which the MDC95 of each study was used as the outcome. Study recruitment setting

Table 2 | Synthesised estimates of minimal detectable change with 95% (MDC95), 90% (MDC90) and 67% (MDC67) confidence for Patient Health Questionnaire-9 (PHQ-9), Patient Health Questionnaire-8 (PHQ-8), and Patient Health Questionnaire-2 (PHQ-2)

Scale	No of participants (studies)	Mean (SD) score*	MDC95, MDC90, or MDC67	MDC estimate (95% CI)	95% PI	τ^2†
PHQ-9	42 548 (94)	6.14 (5.29)	MDC95	5.72 (5.54 to 5.90)	4.00 to 7.44	0.76
			MDC90	4.79 (4.64 to 4.94)	3.35 to 6.23	0.54
			MDC67	2.92 (2.83 to 3.01)	2.04 to 3.80	0.20
PHQ-8	42 592 (94)	5.95 (5.02)	MDC95	5.51 (5.33 to 5.68)	3.87 to 7.15	0.69
			MDC90	4.61 (4.47 to 4.76)	3.24 to 5.99	0.49
			MDC67	2.81 (2.72 to 2.90)	1.97 to 3.65	0.18
PHQ-2	44 085 (98)	1.45 (1.59)	MDC95	2.26 (2.15 to 2.37)	1.20 to 3.32	0.29
			MDC90	1.89 (1.80 to 1.99)	1.01 to 2.78	0.20
			MDC67	1.15 (1.10 to 1.21)	0.61 to 1.69	0.08

CI=confidence interval; PI= prediction interval; SD=standard deviation.
*Pooled estimates with restricted maximum likelihood random effects meta-analysis. The correlation between study sample size and mean score was -0.38. Although study weights were relatively similar because of high between study variability, this negative correlation may have influenced the results or interpretation of the weighted means.
†Estimated variance of between study heterogeneity.

(reference category was non-medical) and study level proportion of participants with major depression were included as predictors in separate models.

To assess the heterogeneity of MDC across studies, we generated forest plots for the MDC95 estimate for each study and the random effects summary MDC95 estimate. We also reported the estimated between study variance (τ^2), percentage of variability caused by between study heterogeneity (I^2), and PIs.[48 49] All analyses were done in R (R version R 4.4.1[50] and R Studio version 2024.04.2+764[51]) with the lme4 and meta packages.[52 53]

Patient and public involvement

Sarah Markham, an experienced patient advisor and member of the BMJ's international Patient Advisory Panel, was a research team member from project inception. Sarah provided comments on the study protocol and content of this article and is a coauthor.

Results

Search results and selection of eligible studies

Database searches identified 9674 unique titles and abstracts, of which 9198 were excluded at the title and abstract stage and 289 at the full text stage. After removing 56 articles that used the same dataset as another included article, 131 unique primary studies remained, of which 100 (76%) contributed datasets. Five additional unpublished studies were contributed by authors. Seven datasets provided only total PHQ-9, PHQ-8, or PHQ-2 scores, without individual item scores, and were therefore excluded, and four datasets had individual item scores for the PHQ-2 but not the PHQ-9 or PHQ-8. Thus our analyses included 94 studies for the PHQ-9 and PHQ-8, and 98 studies for the PHQ-2 (fig 1).

Included studies and sample characteristics

Mean PHQ-9 (n=42 548 participants), PHQ-8 (n=42 592), and PHQ-2 (n=44 085) scores were 4.96 (SD 5.24), 4.82 (4.99), and 1.18 (1.56), respectively. Table 1 shows unweighted characteristics of participants included in the PHQ-9 analyses (PHQ-8 and PHQ-2 analyses are in supplementary tables 1 and 2, respectively). Across PHQ-9, PHQ-8, and PHQ-2 samples, mean age was 49 years (SD 17) and 60% of participants were women. Overall, 10% of participants had a positive major depression classification status (range 1-57% across studies). Participants were recruited from non-medical (n=14), primary care (n=28), outpatient specialty (n=38), inpatient (n=13), and mixed (n=5) settings. Supplementary Table 3a shows participant characteristics for the primary studies included in our study, and supplementary table 3b shows the characteristics of the eligible studies that did not provide data or provided total scores but not item level data.

Estimated overall and subgroup MDC

Pooled Cronbach's alpha was 0.84 for the PHQ-9 and PHQ-8, and 0.74 for the PHQ-2. Supplementary table 3a shows study specific Cronbach's alpha values. Table 2 shows the pooled estimates of MDC95, MDC90, and MDC67 for the PHQ-9, PHQ-8, and PHQ-2. Overall MDC95 estimates were 5.72 points (95% CI 5.54 to 5.90, 95% PI 4.00 to 7.44, I^2=98%, τ^2=0.76) for the PHQ-9, 5.51 points (95% CI 5.33 to 5.68, 95% PI 3.87 to 7.15, I^2=98%, τ^2=0.69) for the PHQ-8, and 2.26 points (95% CI 2.15 to 2.37, 95% PI 1.20 to 3.32, I^2=96%, τ^2=0.29) for the PHQ-2. Figure 2 shows MDC95 estimates for the PHQ-9 for each study, and pooled MDC95 values. Supplementary figures 1 and 2 show corresponding forest plots for the PHQ-8 and PHQ-2, respectively.

Table 3 shows subgroup estimates for MDCs for the PHQ-9, PHQ-8, and PHQ-2 by participant age, sex, and recruitment setting. Supplementary figures 3a-j, figures 4a-j, and figures 5a-j show forest plots of subgroup estimates for the PHQ-9, PHQ-8, and PHQ-2, respectively. MDC95 estimates for the PHQ-9 were similar across age groups. Table 4 shows a slightly higher MDC95 value for women (5.82 points, 95% CI 5.62 to 6.03, 95% PI 4.02 to 7.64) than men (5.53 points, 95% CI 5.33 to 5.73, 95% PI 3.84 to 7.22; difference 0.29 points, 95% CI 0.21 to 0.38). Subgroup results were similar for the PHQ-8 and PHQ-2.

Table 5 shows meta-regression analyses, based on recruitment setting and proportion of participants

Table 3 | Estimates of minimal detectable change with 95% (MDC95), 90% (MDC90), and 67% (MDC67) confidence for Patient Health Questionnaire-9 (PHQ-9), Patient Health Questionnaire-8 (PHQ-8), and Patient Health Questionnaire-2 (PHQ-2) by age, sex, and recruitment setting subgroups

Scale and subgroup	No of participants (studies)*	Mean (SD) score †	MDC95		MDC90		MDC67	
			Estimate (95% CI)	95% PI	Estimate (95% CI)	95% PI	Estimate (95% CI)	95% PI
PHQ-9								
Age (years):								
18-29	6672 (67)	6.45 (4.83)	5.59 (5.34 to 5.84)	3.72 to 7.46	4.68 (4.47 to 4.89)	3.11 to 6.25	2.85 (2.73 to 2.98)	1.90 to 3.81
30-44	11 268 (85)	6.54 (5.26)	5.60 (5.40 to 5.80)	3.92 to 7.28	4.69 (4.52 to 4.86)	3.28 to 6.10	2.86 (2.76 to 2.96)	2.00 to 3.72
45-64	16 157 (87)	6.15 (5.22)	5.67 (5.47 to 5.88)	3.88 to 7.46	4.75 (4.58 to 4.92)	3.25 to 6.25	2.90 (2.79 to 3.00)	1.98 to 3.81
≥65	8155 (72)	5.12 (4.61)	5.63 (5.37 to 5.88)	3.66 to 7.59	4.71 (4.50 to 4.93)	3.06 to 6.36	2.87 (2.74 to 3.00)	1.87 to 3.88
Sex:								
Women	25 013 (94)	6.54 (5.28)	5.83 (5.64 to 6.03)	4.02 to 7.64	4.89 (4.72 to 5.05)	3.37 to 6.40	2.98 (2.88 to 3.08)	2.05 to 3.90
Men	17 512 (83)	5.48 (5.05)	5.53 (5.33 to 5.73)	3.84 to 7.22	4.63 (4.47 to 4.80)	3.22 to 6.05	2.82 (2.72 to 2.92)	1.96 to 3.69
Setting:								
Non-medical	15 552 (14)	5.64 (5.07)	5.39 (4.82 to 5.96)	3.22 to 7.56	4.51 (4.04 to 4.99)	2.70 to 6.33	2.75 (2.46 to 3.04)	1.64 to 3.86
Primary care	13 983 (28)	6.17 (5.24)	5.58 (5.30 to 5.86)	4.11 to 7.04	4.67 (4.44 to 4.91)	3.45 to 5.90	2.85 (2.70 to 2.99)	2.10 to 3.59
Outpatient specialty	9822 (39)	6.10 (5.31)	5.72 (5.44 to 5.99)	4.05 to 7.39	4.79 (4.56 to 5.02)	3.39 to 6.19	2.92 (2.78 to 3.06)	2.07 to 3.77
Inpatient	3061 (15)	7.01 (5.66)	6.48 (6.05 to 6.92)	4.82 to 8.15	5.43 (5.07 to 5.79)	4.04 to 6.82	3.31 (3.09 to 3.53)	2.46 to 4.16
PHQ-8								
Age (years):								
18-29	6676 (67)	6.24 (4.56)	5.37 (5.14 to 5.61)	3.60 to 7.15	4.50 (4.30 to 4.70)	3.02 to 5.99	2.74 (2.62 to 2.87)	1.84 to 3.65
30-44	11 280 (85)	6.35 (5.00)	5.36 (5.16 to 5.55)	3.75 to 6.97	4.49 (4.33 to 4.65)	3.14 to 5.83	2.74 (2.64 to 2.83)	1.91 to 3.56
45-64	16 181 (87)	5.99 (4.98)	5.46 (5.27 to 5.66)	3.74 to 7.19	4.58 (4.41 to 4.74)	3.13 to 6.02	2.79 (2.69 to 2.89)	1.91 to 3.67
≥65	8158 (72)	4.97 (4.38)	5.45 (5.20 to 5.69)	3.54 to 7.35	4.56 (4.36 to 4.77)	2.97 to 6.16	2.78 (2.65 to 2.91)	1.81 to 3.75
Sex:								
Women	25 039 (94)	6.34 (5.02)	5.61 (5.42 to 5.79)	3.90 to 7.32	4.70 (4.54 to 4.85)	3.26 to 6.13	2.86 (2.77 to 2.96)	1.99 to 3.74
Men	17 530 (83)	5.32 (4.79)	5.33 (5.14 to 5.52)	3.70 to 6.96	4.47 (4.31 to 4.63)	3.10 to 5.83	2.72 (2.63 to 2.82)	1.89 to 3.55
Setting:								
Non-medical	15 568 (14)	5.46 (4.83)	5.17 (4.63 to 5.71)	3.11 to 7.23	4.33 (3.88 to 4.78)	2.60 to 6.06	2.64 (2.36 to 2.91)	1.59 to 3.69
Primary care	13 998 (28)	5.96 (4.97)	5.36 (5.10 to 5.62)	4.00 to 6.72	4.49 (4.27 to 4.71)	3.35 to 5.63	2.74 (2.60 to 2.87)	2.04 to 3.43
Outpatient specialty	9831 (39)	5.92 (5.04)	5.51 (5.25 to 5.77)	3.92 to 7.10	4.62 (4.40 to 4.83)	3.28 to 5.95	2.81 (2.68 to 2.95)	2.00 to 3.63
Inpatient	3065 (15)	6.82 (5.39)	6.25 (5.85 to 6.65)	4.71 to 7.79	5.23 (4.90 to 5.57)	3.94 to 6.52	3.19 (2.99 to 3.40)	2.40 to 3.98
PHQ-2								
Age (years):								
18-29	6765 (68)	1.50 (1.47)	2.24 (2.09 to 2.39)	1.19 to 3.28	1.87 (1.75 to 2.00)	1.00 to 2.75	1.14 (1.06 to 1.22)	0.61 to 1.68
30-44	11 688 (89)	1.52 (1.58)	2.11 (1.98 to 2.23)	1.10 to 3.12	1.76 (1.66 to 1.87)	0.92 to 2.61	1.08 (1.01 to 1.14)	0.56 to 1.59
45-64	16 919 (91)	1.47 (1.58)	2.21 (2.08 to 2.34)	1.10 to 3.32	1.85 (1.74 to 1.96)	0.92 to 2.78	1.13 (1.06 to 1.19)	0.56 to 1.70
≥65	8396 (73)	1.20 (1.51)	2.18 (2.01 to 2.35)	0.95 to 3.42	1.83 (1.69 to 1.97)	0.79 to 2.86	1.11 (1.03 to 1.20)	0.48 to 1.74
Sex:								
Women	25 914 (98)	1.55 (1.60)	2.24 (2.12 to 2.35)	1.18 to 3.29	1.87 (1.78 to 1.97)	0.99 to 2.75	1.14 (1.08 to 1.20)	0.60 to 1.68
Men	18 147 (87)	1.29 (1.52)	2.21 (2.08 to 2.33)	1.16 to 3.25	1.85 (1.74 to 1.95)	0.97 to 2.72	1.13 (1.06 to 1.19)	0.59 to 1.66
Setting:								
Non-medical	15 675 (14)	1.33 (1.50)	2.05 (1.74 to 2.35)	0.90 to 3.19	1.71 (1.46 to 1.97)	0.76 to 2.67	1.04 (0.89 to 1.20)	0.46 to 1.63
Primary care	14 126 (29)	1.59 (1.60)	2.31 (2.11 to 2.52)	1.22 to 3.40	1.94 (1.76 to 2.11)	1.03 to 2.85	1.18 (1.07 to 1.29)	0.63 to 1.74
Outpatient specialty	10 923 (42)	1.37 (1.59)	2.19 (2.02 to 2.35)	1.18 to 3.20	1.83 (1.70 to 1.97)	0.99 to 2.68	1.12 (1.03 to 1.20)	0.60 to 1.63
Inpatient	3231 (16)	1.61 (1.74)	2.52 (2.24 to 2.81)	1.45 to 3.59	2.11 (1.87 to 2.35)	1.21 to 3.01	1.29 (1.14 to 1.43)	0.74 to 1.83

CI=confidence interval; PI= prediction interval; SD=standard deviation.
*Subgroups with only one or two participants or zero variance were excluded to ensure valid estimation of pooled effects (PHQ-8 and PHQ-9: age 18-29 years, n=1 (6 studies), n=2 (3 studies); age 30-44 years, n=1 (1 study), n=2 (2 studies); age 45-64 years, n=2 (2 studies); age ≥65 years, n=1 (3 studies), n=2 (1 study), n=3 (1 study, var=0); PHQ-2: age 18-29 years, n=1 (7 studies), n=2 (3 studies), n=3 (1 study, var=0), n=4 (1 study, var=0); age 30-44 years, n=1 (1 study), n=2 (2 studies); age 45-64 years, n=2 (2 studies); age ≥65 years, n=1 (3 studies), n=2 (1 study), n=3 (2 studies, var=0), n=6 (1 study, var=0)).
†Pooled estimates with restricted maximum likelihood random effects meta-analysis.

with major depression. Compared with participants from non-medical settings (5.39 points, 95% CI 4.82 to 5.96, 95% PI 3.22 to 7.56), the MDC95 for PHQ-9 was higher among participants from inpatient settings (6.48 points, 95% CI 6.05 to 6.92, 95% PI 4.82 to 8.15; difference 1.10 points, 95% CI 0.47 to 1.74). For every 10% increase in the proportion of participants with major depression, the MDC95 increased on average by 0.40 points for the PHQ-9 (95% CI 0.25 to 0.55), 0.35 points for the PHQ-8 (0.20 to 0.49), and 0.17 points for the PHQ-2 (0.07 to 0.27). Sensitivity analyses based on the Hartung-Knapp approach for estimating CIs and PIs were consistent with the main analyses (supplementary tables 4 and 5).

Discussion

Principal findings

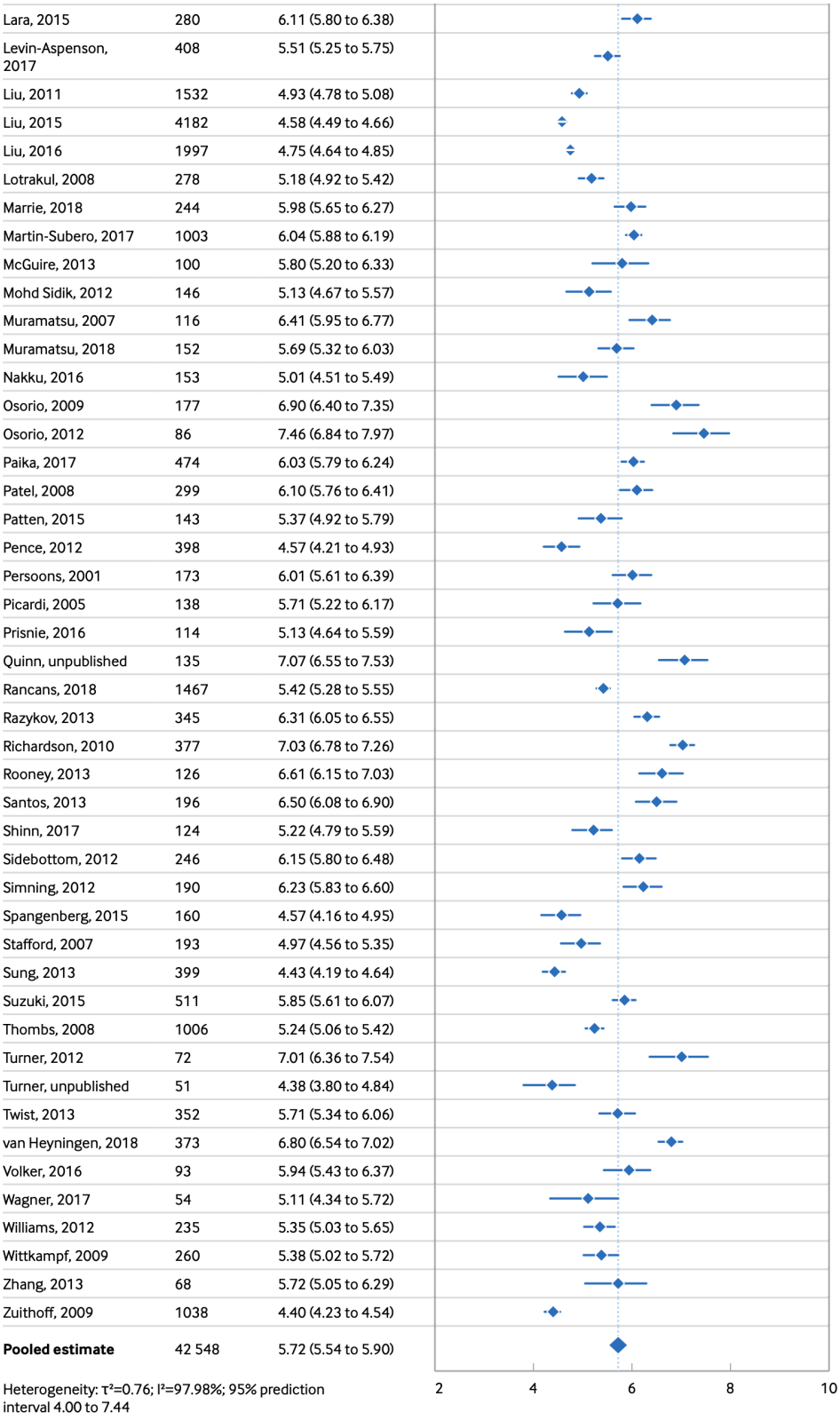
We estimated the MDC95, MDC90, and MDC67 values for the PHQ-9, PHQ-8, and PHQ-2. MDC95 estimates were 5.7 points for the PHQ-9, 5.5 points for the PHQ-8, and 2.3 points for the PHQ-2. Findings for subgroup analyses were consistent across PHQ-9, PHQ-8, and PHQ-2 analyses. MDCs were slightly lower for men than women, and about one point higher for medical inpatients compared with non-medical study participants for the PHQ-9 and PHQ-8 (and about 0.5 points for the PHQ-2). In our meta-regression analysis, the estimated MDC95 for the PHQ-9 was 0.40 points higher for each 10% increase in the proportion of study

Meta-analysis results for MDC95 of Patient Health Questionnaire-9 (PHQ-9)

Pooled MDC95 for PHQ-9 scores based on individual participant data meta-analysis

MDC95 = 1.96 × √2 × SEM, where SEM (standard error of measurement) was calculated as SD (standard deviation) × √(1 − reliability)

Study	No of participants	MDC95 (95% CI)
Akena, 2013	91	7.09 (6.60 to 7.50)
Amoozegar, 2017	203	5.77 (5.45 to 6.05)
Amtmann, 2015	164	5.67 (5.23 to 6.07)
Arroll, 2010	2528	4.80 (4.69 to 4.91)
Ayalon, 2010	151	5.40 (4.81 to 5.97)
Azah, 2005	180	5.74 (5.33 to 6.11)
Baron, 2017	851	5.67 (5.49 to 5.85)
Beraldi, 2014	116	5.42 (5.02 to 5.76)
Bernstein, 2018	240	5.33 (5.02 to 5.62)
Bhana, 2015	679	5.37 (5.13 to 5.60)
Bombardier, 2012	160	6.62 (6.19 to 7.02)
Buji, 2018	130	5.36 (4.84 to 5.83)
Chagas, 2013	84	6.90 (6.30 to 7.37)
Chibanda, 2016	264	7.15 (6.88 to 7.38)
Cholera, 2014	397	7.00 (6.73 to 7.26)
Conway, 2016	26	5.17 (4.08 to 6.01)
de la Torre, 2016	257	6.76 (6.39 to 7.08)
de Man-van Ginkel, 2012	382	7.35 (7.05 to 7.60)
Eack, 2006	48	5.97 (5.36 to 6.44)
Fiest, 2014	169	5.27 (4.88 to 5.61)
Fischer, 2014	194	4.82 (4.47 to 5.15)
Fisher, 2016	357	4.45 (4.16 to 4.71)
Garabiles, unpublished	99	5.71 (5.05 to 6.25)
Gelaye, 2014	923	6.72 (6.54 to 6.91)
Gholizadeh, 2019	79	6.97 (6.17 to 7.68)
Gjerdingen, 2009	419	4.90 (4.63 to 5.15)
Grafe, 2004	494	5.80 (5.60 to 5.99)
Green, 2017	176	5.38 (5.07 to 5.64)
Green, 2018	192	7.72 (7.36 to 8.05)
Grool, 2011	477	4.02 (3.75 to 4.27)
Hahn, 2006	211	6.03 (5.74 to 6.31)
Hantsoo, 2017	321	4.64 (4.33 to 4.92)
Haroz, 2017	132	6.28 (5.78 to 6.73)
Henkel, 2004	430	5.18 (4.97 to 5.38)
Hides, 2007	103	6.76 (6.28 to 7.17)
Hitchon, 2019	148	5.41 (5.03 to 5.76)
Hobfoll, 2011	144	5.16 (4.69 to 5.58)
Hyphantis, 2011	213	6.03 (5.70 to 6.33)
Hyphantis, 2014	349	6.79 (6.51 to 7.05)
Inagaki, 2013	104	4.84 (4.27 to 5.39)
Janssen, 2016	4695	3.83 (3.76 to 3.90)
Khamseh, 2011	122	7.37 (6.95 to 7.70)
Kiely, 2014	822	4.55 (4.37 to 4.72)
Kim, 2017	3071	3.51 (3.41 to 3.62)
Kohrt, 2016	125	6.06 (5.66 to 6.41)
Kwan, 2012	113	6.66 (6.01 to 7.26)
Lambert, 2015	147	5.58 (5.21 to 5.91)
Lamers, 2008	104	5.76 (4.57 to 6.95)



Article DOI: 10.1136/bmj-2026-100119 • Download data
CI=confidence interval; MDC95=minimal detectable change based on 95% confidence of change beyond measurement error

Fig 2 | Meta-analysis results for MDC95 of Patient Health Questionnaire-9 (PHQ-9). An interactive version of this graphic and downloadable data are available at https://public.flourish.studio/visualisation/29605896/

Table 4 | Age and sex subgroup differences in estimates of minimal detectable change with 95% confidence (MDC95) for Patient Health Questionnaire-9 (PHQ-9), Patient Health Questionnaire-8 (PHQ-8), and Patient Health Questionnaire-2 (PHQ-2)

Subgroup*	PHQ-9		PHQ-8		PHQ-2	
	No of studies (participants)	MDC95 (95% CI)	No of studies (participants)	MDC95 (95% CI)	No of studies (participants)	MDC95 (95% CI)
Age (years)						
45-64 (reference)	61 (11 140)	5.72 (5.50 to 5.94)	61 (11 161)	5.50 (5.29 to 5.71)	62 (11 692)	2.27 (2.12 to 2.42)
18-29	61 (5604)	5.54 (5.28 to 5.79)	61 (5608)	5.31 (5.07 to 5.56)	62 (5692)	2.20 (2.04 to 2.35)
Difference†	—	-0.12 (-0.34 to 0.10)	—	-0.13 (-0.35 to 0.09)	—	-0.06 (-0.19 to 0.08)
45-64 (reference)	79 (15 904)	5.65 (5.45 to 5.86)	79 (15 927)	5.44 (5.24 to 5.63)	83 (16 658)	2.19 (2.06 to 2.32)
30-44	79 (10 481)	5.56 (5.36 to 5.77)	79 (10 492)	5.32 (5.12 to 5.52)	83 (10 894)	2.10 (1.97 to 2.23)
Difference†	—	-0.07 (-0.18 to 0.04)	—	-0.09 (-0.21 to 0.02)	—	-0.09 (-0.17 to -0.02)
45-64 (reference)	72 (14 626)	5.69 (5.47 to 5.90)	72 (14 649)	5.48 (5.27 to 5.69)	73 (15 208)	2.22 (2.07 to 2.36)
≥65	72 (8155)	5.63 (5.37 to 5.88)	72 (8158)	5.45 (5.20 to 5.69)	73 (8396)	2.18 (2.01 to 2.35)
Difference†	—	-0.06 (-0.21 to 0.09)	—	-0.03 (-0.17 to 0.11)	—	-0.04 (-0.16 to 0.07)
Sex						
Women (reference)	83 (22 552)	5.82 (5.62 to 6.03)	83 (22 575)	5.60 (5.40 to 5.80)	87 (23 433)	2.21 (2.09 to 2.33)
Men	83 (17 512)	5.53 (5.33 to 5.73)	83 (17 530)	5.33 (5.14 to 5.52)	87 (18 147)	2.21 (2.08 to 2.33)
Difference†	—	-0.29 (-0.38 to -0.21)	—	-0.27 (-0.35 to -0.18)	—	-0.06 (-0.11 to -0.02)

CI=confidence interval.
*Subgroup comparisons and differences were calculated based on data from studies that included participants in both comparison groups.
†Estimated differences diverge somewhat in some cases from what is obtained by subtracting the estimate for each subgroup from the reference group. This result is because of different relative weighting of some studies in models that pooled MDC estimates across studies versus models that pooled the difference between subgroups from each study.

participants with major depression (0.35 points for the PHQ-8 and 0.17 points for the PHQ-2), starting at the overall mean of 10%. Thus in a setting where 50% of patients meet the criteria for major depression, for example, an MDC for the PHQ-9 of seven points might be used (5.7 points + 4 × 0.4 = 7.3 points). We found substantial heterogeneity across all main analyses and most subgroup analyses.

Comparison with other studies

To the best of our knowledge, our study is the first to publish analyses of the MDC for the PHQ-9 and PHQ-2. Our estimated MDC for the PHQ-8 (5.5 points) was similar to the only other study that has evaluated the MDC for the PHQ-8 (5.2 points, 95% CI 5.1 to 5.3; 2571 individuals with systemic sclerosis).[26] Only two primary studies have used anchor based approaches to estimate minimal important differences for the PHQ. Bauer-Staeb et al[10] reported an average minimal important difference of 3.7 points, with the minimal important difference defined as the threshold for a 50% probability of reporting "feeling better". Credible minimal important differences should be based on change ratings with correlations of 0.50 or higher

Table 5 | Simple meta-regressions of minimal detectable change with 95% confidence (MDC95) on study level variables for Patient Health Questionnaire-9 (PHQ-9), Patient Health Questionnaire-8 (PHQ-8), and Patient Health Questionnaire-2 (PHQ-2)

Scale and variable	Raw regression coefficient (95% CI)	τ^2*	I^2 (%)†
PHQ-9			
10% increase in proportion of participants with major depression	0.40 (0.25 to 0.55)	0.58	97.3
Setting‡:			
Non-medical	—	—	—
Primary care	0.20 (-0.36 to 0.75)	0.72	97.7
Outpatient specialty	0.33 (-0.19 to 0.86)	—	—
Inpatient	1.10 (0.47 to 1.74)	—	—
PHQ-8			
10% increase in proportion of participants with major depression	0.35 (0.20 to 0.49)	0.55	97.3
Setting‡:			
Non-medical	—	—	—
Primary care	0.20 (-0.33 to 0.72)	0.64	97.5
Outpatient specialty	0.35 (-0.15 to 0.85)	—	—
Inpatient	1.09 (0.49 to 1.69)	—	—
PHQ-2			
10% increase in proportion of participants with major depression	0.17 (0.07 to 0.27)	0.26	95.6
Setting‡:			
Non-medical	—	—	—
Primary care	0.27 (-0.08 to 0.62)	0.28	95.6
Outpatient specialty	0.15 (-0.19 to 0.48)	—	—
Inpatient	0.48 (0.07 to 0.89)	—	—

CI=confidence interval.
*Estimated amount of (residual) heterogeneity.
†Total variability in the effect size estimates that can be attributed to heterogeneity among the true effects.
‡Estimate represents the increase in MDC95 compared with the non-medical setting.

Table 6 | Thresholds for minimal detectable change with 95% (MDC95), 90% (MDC90), and 67% (MDC67) confidence for Patient Health Questionnaire-9 (PHQ-9), Patient Health Questionnaire-8 (PHQ-8), and Patient Health Questionnaire-2 (PHQ-2) based on standard and alternative approaches

Estimated MDC thresholds	PHQ-9	PHQ-8	PHQ-2
Standard			
Pooled MDC95	6	6	2 to 3
Alternatives			
Pooled MDC90	5	5	2
Pooled MDC67	3	3	1 to 2
MDC95 prediction interval upper limit	7 to 8	7 to 8	3 to 4

The pooled MDC95 is typically used in practice. Alternatively, other methods for setting thresholds could be selected and would increase the likelihood of identifying change but reduce certainty (MDC67 and MDC90) or increase certainty but decrease the likelihood of classifying change when it has occurred (upper limit of prediction interval). Thresholds can be adjusted for different settings; a higher threshold may be more appropriate among people in specialty mental health treatment settings.

with the measure being assessed,[17 54] however, and this value was somewhat lower in this study. Also, the reported minimal important difference range across PHQ-9 scores was wide (0-14 points) and no estimates of precision were provided. Kounali et al[11] reported that the minimal important difference for PHQ-9 ranged from 1.7 to 2.4 points, a score change threshold that best distinguished participants who reported "feeling better" from those who reported "feeling the same". No correlation coefficients, however, were reported to show that changes in PHQ-9 scores were meaningfully correlated with the anchor. Also, the precision of the minimal important difference estimate was not reported, but each analysis included only 83-149 participants. Estimates of minimal important difference from both studies were substantially below our estimated MDC values, which suggests that the values may be too small to be reliably distinguished from measurement error.

Clinical and research implications

The minimal important difference, which represents the smallest change that a patient would likely perceive as important, is used along with patient perception of change to guide treatment decisions. As highlighted in guidelines for measurement based care,[1] however, when the MDC is greater than the minimal important difference, change that exceeds the minimal important difference might be because of measurement error rather than real change. In this case, the MDC should be used as the change threshold. In contrast, if the MDC is smaller than the minimal important difference, then the minimal important difference value can guide interpretation.[55]

Jacobson and Truax introduced the reliable change index,[47] equivalent to MDC95, over 30 years ago. Since then, MDC95 has been the standard for evaluating reliable change. Less stringent thresholds (eg, MDC90 and MDC67) could also be used to inform the likelihood that change has occurred. Historically, the pooled MDC has been used to guide decisions. Alternatively, when MDC is calculated in primary studies, the upper end of a confidence interval around the mean would provide greater certainty that change has occurred. Given the heterogeneity across studies that we identified in our IPDMA, using the upper end of a PI, rather than the mean, would provide greater certainty of change. The PI provides the range of estimates that might be generated in one future study.[56]

Table 6 shows possible MDC thresholds that could be used in practice. Among the three questionnaires, the PHQ-9 is the most used in clinical settings. The UK NHS's Talking Therapies programme[18] and other programmes[21-23] define reliable change, equivalent to MDC95, for the PHQ-9 as a change in score of ≥6 points. We found a pooled MDC95 of 5.72 points on the PHQ-9, which is consistent. The mean baseline PHQ-9 score of patients in the UK NHS's Talking Therapies programme was 14-15,[19 57] however, suggesting that about 50% of participants may have major depression.[58] Considering the possible influence of baseline severity, our analysis suggests that an MDC95 of seven points could be used. Our finding that MDC estimates were similar in primary care and outpatient specialty medical settings suggests that these estimates apply to people with and without co-existing medical conditions, although a higher threshold might be considered in inpatient medical settings.

The PHQ-2 is typically used as a screening tool but can sometimes be used as a brief tool to monitor symptom changes in clinical settings.[14-16] The PHQ-8 is often used in research because item 9 of the PHQ-9 generates high numbers of false positive signals about the risk of suicide. Evaluations of status change in research could incorporate the minimal important difference and MDC to classify participants as changed if both thresholds were exceeded, not changed if neither was exceeded, or uncertain if the minimal important difference was exceeded but not the MDC. Recommended values for PHQ-8 and PHQ-2 MDCs have not been established, and our findings can inform recommendations.

When research studies assess whether group differences or changes, rather than individual differences, are clinically meaningful, the minimal important difference is used. The precision of these magnitudes for groups is assessed with 95% CIs or PIs, which depend chiefly on the adequacy of the sample size,[7 59 60] rather than MDCs.

Strengths and limitations of this study

In this meta-analysis, we estimated MDCs for the PHQ-9, PHQ-8, and PHQ-2. We used a large and diverse individual participant data sample, many times larger than previous studies. Furthermore, the use of individual level data allowed us to conduct subgroup analyses that are not typically possible in individual primary studies or when using study level data in aggregate data meta-analysis.

Our study had some limitations. Primary data from 31 of 131 published eligible datasets (24%) were not obtained. Of the studies that contributed datasets, seven did not provide item level scores for the PHQ-2 and 11 did not provide item level scores for the PHQ-8 and PHQ-9 and therefore could not be included. In our previous IPDMAs on depression screening tool accuracy, however, we found that published sensitivity

and specificity from studies that did not contribute data were similar to the results from those that provided data.[30 61 62]

Standard error of measurement was estimated with Cronbach's alpha, a measure of internal consistency, rather than by test-retest reliability.[63] A meta-analysis on PHQ-9 reliability reported a pooled Cronbach's alpha of 0.86 from 60 studies, similar to our estimate of 0.84, and a pooled test-retest reliability of 0.82 from eight studies.[44] Our estimates for PHQ-8 (0.84) and PHQ-2 (0.74) Cronbach's alpha were also similar to estimates of Cronbach's alpha and test-retest reliability reported in previous studies for the PHQ-8 (Cronbach's alpha 0.85; test-retest over a mean of 11 days, 0.83) and PHQ-2 (Cronbach's alpha 0.76; test-retest over two weeks, 0.70).[64 65] Thus, although possible, it seems unlikely that using Cronbach's alpha for PHQ-9 and PHQ-8 resulted in MDC estimates that were substantively different than if we had obtained test-retest reliability estimates. It is more likely that using Cronbach's alpha could have influenced MDC estimates for the two item PHQ-2 because Cronbach's alpha depends on the number of items in a scale and could have been lower than test-retest estimates.[66]

We found substantial heterogeneity. Heterogeneity is almost always present in the evaluations of tests, but the test results reflect real differences that affect scale properties across studies.[67] Also, because we did not have data on score changes, we could not compare our estimated MDCs with minimal important differences from the same dataset. We also did not incorporate a risk of bias assessment, given the absence of a validated tool for MDC studies. The COSMIN (Consensus Based Standards for the Selection of Health Measurement Instruments) Risk of Bias Checklist,[8] for example, only determines whether internal consistency reliability of a measure was evaluated with Cronbach's alpha but does not establish factors associated with the risk of bias for Cronbach's alpha.

Our study was a secondary analysis of an existing dataset and only included studies published up to May 2018. MDC is considered a stable metric, however, and therefore its estimated value would not likely change meaningfully with the inclusion of data from more recent studies. The main change in assessment methods in recent years has been the increased use of remote assessments; we previously analysed >50 000 participants with scores on three depression screening tools and found no differences in scores by administration modality.[68] Also, we conducted subgroup analyses by age, sex, and setting, but we could not analyse additional factors, such as race or ethnic group or socioeconomic status, because these data were not included in our dataset.

Because our meta-regression analysis was based on study level data, observed associations may be influenced by ecological confounding from other study level characteristics. Also, although many participants in the UK NHS's Talking Therapies programme are referred by general practitioners, others are self-referred and may differ somewhat from our sample, which could limit generalisability. Finally, we used a classical test theory approach because the results of a simulation study that compared classical test with item response theory approaches found that classical test theory more accurately identified change for measures with <20 items.[69] This approach, however, may have limitations because of assumptions such as unidimensionality and approximate tau equivalence.

Conclusions

MDC thresholds can be used in conjunction with patient perspectives to evaluate treatment progress. We found that the pooled MDC95 was 5.7 points for the PHQ-9, 5.5 points for the PHQ-8, and 2.3 points for the PHQ-2. Across the three scales, the effects of individual level and study level factors were similar. MDC was higher in inpatient medical settings than in other healthcare settings. Sex and age had minimal or no association with MDC. About 10% of participants across the included studies were classified as having major depression, and we estimated that MDC increased by about 0.4 points for every 10% increase in the proportion of participants with major depression. Our pooled estimate of MDC95 is consistent with the six point change in PHQ-9 scores that is used in the UK to evaluate improvement in symptoms, although using seven points might be considered, given the likely proportion of patients with major depression in clinical settings. Other methods for setting thresholds could be selected and would increase the likelihood of identifying change but reduce certainty (MDC67, MDC90) or increase certainty but increase the likelihood of not recognising change (upper end of 95% PI).

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