Is the US Gender Gap in Depression Changing Over Time? A Meta-Regression

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Abstract

The depression gap refers to higher rates of depression among women than men. Change in the depression gap over time may elucidate social causes of this disparity—such as unequal college attendance or employment status. We conducted a meta-regression analysis to estimate variation in the depression gap over time by age, accounting for potential sources of variation between studies. Electronic databases and bibliographies were searched for English language studies from January 1980–October 2019. 144 independent estimates from United States-representative samples met selection criteria (n=813,189). The depression gap was summarized as prevalence ratios (PR) among studies using diagnostic instruments, and standardized mean differences among symptom-based studies. Primary study measures were baseline study year (range: 1982-2017), and age (range: 10-60+). Compared with respondents ages 60+, depression prevalence was greater among respondents aged 10-19 (PR=1.26; 95% CI=1.02, 1.56). Over time, the depression gap did not change among adults, but increased among adolescents (age by time interaction PR=1.05; 95% CI=1.01, 1.08). Results were similar for symptom-based studies. The present study finds no evidence of a change in the depression gender gap for US adults, however, the gap increased among adolescents. Greater attention to factors driving this widening disparity in adolescent depression is needed.

Keywords: Depression, depressive symptoms, gender, time trends, United States, health disparities

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INTRODUCTION

Major depressive disorder is the leading cause of disability among Americans ages 15-44 (1), and is more likely to affect women than men (2). This pattern, hereafter referred to as the depression gap, reflects meaningful differences in depression and is not solely an artifact of gender differences in reporting mental health symptoms or seeking treatment (3,4). Also, even though the quantitative surveys providing evidence regarding the depression gap typically rely on binary categories that do not differentiate between sex assigned at birth and gender expression, the gap is typically described using the term gender. Given that caveat, we use gender throughout the present study.

The depression gap emerges in early adolescence, remains relatively stable throughout adulthood, then decreases at later ages (5). Biological (6) and social stress (7) mechanisms have been explored to explain the gap, with the most robust evidence to date supporting social stress. As applied to gender, social stress theory suggests that gender may influence stress exposure and responses (8). In particular, women traditionally have had fewer opportunities in attaining higher education and full-time employment, which may act as social stressors (9). From an early age, women are typically socialized, through gender norms, to respond to stressors in depressogenic ways (10,11). These factors may increase women's depression risk, and explain gender differences in depression (9). If so, changes in women's social positions, and therefore changes in these factors, should change the depression gap in turn.

Since the mid-20th century, education (12) and employment (13,14) opportunities have become increasingly available to women. These changes in gendered social positions likely reflect broader changes in norms and the process of gender socialization, which may influence both exposure and response to stressors, and may decrease the depression gap in adults in turn.

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Among adolescents, depressive symptoms have been increasing since 2012, to a greater extent among girls compared with boys (15). While the underlying factors contributing to the increase remain only speculative, the increase among young women may, unlike adults, suggest an increasing gender gap.

Available evidence suggests that the depression gap may be changing (16,17), but is inconclusive, in part due to three limitations. First, follow-up periods in single longitudinal studies are often too short to identify temporal trends in depression. Second, while existing studies suggest that the depression gap may vary over time, there may also be variation by age across time. Examining variation by both age and time is necessary to identify any temporal variation due to social change. Among reviews that have directly accounted for age in assessing temporal variation in the depression gap, most have focused on a single age group or developmental period (18,19). A wide time span with age groups across the lifecourse is necessary in order to fully characterize variation in the depression gap by both age and time. Third, less attention has been paid to gender differences in levels of depressive symptoms, which may be distinct from diagnostic depression categories (20).

We conducted a systematic review, meta-analysis, and meta-regression to characterize changes in the depression gap over time and across the lifecourse. First, studies of gender differences in depression in recent decades were identified and summarized. Second, data from the systematic review were extracted to form the analytic sample of the meta-regression, which estimated the variation in the gap over time by age and accounted for other potential sources of variation between studies. Trends in the depression gap were considered separately based on diagnostic vs. symptom-based depression tools, to explore whether variation has been different at a diagnostic threshold vs. total depression symptoms.

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METHODS

Identification of studies

The literature search focused on peer-reviewed research published in English language journals between January 1980 and October 2019. The year 1980 was chosen as the lower limit because it coincided with changes to women's social positions in the United States (US) that had been ongoing since the mid 20th Century. The year 1980 also represented the introduction of the Diagnostic and Statistical Manual (DSM) version III that was used to estimate the US population prevalence of psychiatric disorders in community-based psychiatric epidemiological surveys (21,22). Only studies of the US population were included, given the background of changing gendered social positions in the US. Finally, the search focused on studies based on nationally-representative sampling frames to avoid bias from gender-specific selection factors (e.g., clinical samples(23)). Also, US-population-level samples typically have large sample sizes that maximize statistical precision of depression gap estimates.

The literature search and study selection flow chart is detailed in Figure 1. The initial search included five electronic databases: PubMed, JSTOR, Embase, PsychInfo, and Scopus. The initial search yielded 1007 potential abstracts. Bibliographies of related reviews and meta-analyses were also searched, which yielded 20 additional estimates.

After removing 218 duplicate studies, 809 abstracts were screened in more detail and additional studies were excluded based on the following criteria: no quantitative data were presented (e.g., qualitative study, narrative review); the sample included non-human subjects;

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gender-specific estimates were not presented; depression measures were not based on a symptom-level interview (e.g., self-reported doctor diagnosed depression).

A second reviewer independently screened the 809 abstracts. Agreement between the two reviewers was very good (kappa= 0.827, 95% CI=0.788, 0.867) (24), and the reviewers further discussed any conflicting judgments to reach consensus. A resulting 452 studies met exclusion criteria and were removed.

The full text of the 357 remaining studies was reviewed in more detail. In the instance that the same dataset was used for multiple studies, only the study with the most complete sample was included (i.e., the fewest stated restrictions to derive the analytic sample from the full study sample), to ensure the independence between depression gap estimates. The reasons for exclusion of the full-text reviewed studies were: study design (e.g., case control, sampling based on depression status) (n = 158), a non-nationally representative sampling strategy (n = 123), and duplicate data source (n = 35) (see Figure 1).

In total, 41 studies were included. Several of these studies included multiple estimates for different age groups, and each group was considered as an independent estimate (range: 1-17 estimates per study). Among longitudinal studies, only baseline data were included to avoid issues of within-study correlation of depression gap estimates and potential selection bias from attrition. Several studies did not measure depression at baseline but included it in later interviews. Estimates from the first follow-up interview where depression was measured were included, and the proportion lost-to-follow-up was extracted to consider the potential for selection bias. The full meta-analytic dataset contained 144 independent estimates from nationally representative samples. The total sample size was 813,189 (52% women).

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Data Abstraction

For each estimate, the following information was collected: full citation, study name, baseline study year, sample size by gender, age range, depression effect measure, effect estimate and variance, depression instrument, and the period of symptom recall.

Effect measures

The depression gap was summarized as a prevalence ratio (PR) among studies that reported depression based on a diagnostic threshold (i.e., diagnostic studies). Among symptom-based studies, the depression gap was estimated as a standardized mean difference ((SMD), calculated as the mean depression score among women minus the mean score among men, divided by the pooled standard deviation). Null, small, medium, and large effect sizes corresponded with SMD=0<0.2, 0.2<0.5, 0.5<0.8, and 0.8<1.0 respectively (25). Studies were weighted by the inverse of the standard error of the log PR and SMD respectively (26).

Independent variables

Continuous study year at baseline was the main independent variable (range 1982-2017), to estimate temporal variation in the depression gap.

Age was considered as an effect modifier of time, categorized as: ages 10-19 (i.e., childhood/adolescence); 20-39 (i.e., early adulthood); 40-59 (i.e., middle adulthood); 60 or older (i.e., older adults). Groupings were chosen in order to capture meaningful life periods, while also ensuring large enough samples within each group. Studies with wider age ranges (e.g., ages 18-65) were included in the descriptive analysis but not the meta-regression models (3 diagnostic

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studies (3.9%) and 6 symptom studies (8.8%)). Note that age across time also indexes birth cohort, thus age in the present review is a proxy for both age and birth cohort.

The depression instrument was considered as a confounding variable. Symptom-scale instruments included Children's Depression Inventory (CDI), Patient Health Questionnaire 9-item (PHQ-9), other vs. the Center for Epidemiologic Studies Depression scale (CESD). Diagnostic instruments included: DSM version III/version III revised, and Other diagnostic vs. DSM-version IV/version IV-revised. Only one study utilized DSM-version 5 instruments, so it was grouped with DSM-version IV instruments.

Publication bias

We considered the potential for publication bias (27). However, given that the depression gap was often not the main focus of these articles, the magnitude of the depression gap would likely have little influence over whether a study was published. Nonetheless, to explore potential bias, a funnel plot was estimated for each set of studies. The degree of bias was tested using Egger's test (28). Additionally, the trim-and-fill procedure was used to estimate what the actual effect size would have been in the absence of any publication bias (29).

Analysis

In order to characterize variation in the depression gap, the review was structured to estimate cross-study variation over time with meta-regression models. For each depression gap estimate, the baseline study year formed the main independent variable in the meta-regression model, representing change in the depression gap over time, accounting for differences in age and other potential sources of variation.

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First, a descriptive analysis summarized the data sources, study designs, and analytic variables of all included studies. Additionally, a pooled depression gap was estimated to summarize the depression gap across all studies in the analytic sample, with random effects confidence intervals and prediction intervals (30). Second, meta-regression models estimated the average effects of time, age, the interaction between time and age, and instrument in depression gap estimates, using maximum likelihood estimation with robust standard errors. Analyses were implemented with 'meta' (31) and 'metafor' (32) packages in R, version 3.5.1 (Vienna, Austria) (33).

Multiple Imputation

For 27 diagnostic study estimates (40%), data needed to compute the standard error of the effect estimate were not reported (i.e., only an unadjusted PR was reported). To minimize the amount of information lost due to missing data, models were estimated with imputed variance parameters from 100 imputed datasets using chained equations, combined with corrected standard errors, averaging coefficient vectors, variance-covariance matrices, and adding a non-negative correction to variance-covariance matrices inversely proportional to the predictive ability of the imputation models, effectively widening confidence intervals where missing data values are poorly predicted by observed data (34). The large number of imputation models was chosen to achieve stability of imputed estimates and all abstracted study variables were used to imputed missing data. Recent simulations have reported that multiple imputation in meta-regression models are unbiased when missing values are weighting variables (i.e., within-study standard errors), rather than predictor variables (35). Imputed model estimates were compared to complete case models to examine the degree of their robustness to missing data.

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RESULTS

Descriptive summary

Tables 1 and 2 (and Web Tables 1 and 2) provide the descriptive details of the diagnostic and symptom-based studies that comprised the analytic sample. A descriptive summary of the study designs and sampling procedures can be found in Web Appendix 1.

Table 3 summarizes the distributions of all analytic variables. Of the 144 total estimates, 76 measured the depression gap with a diagnostic instrument and 68 measured the gap with symptom scores. Overall, the study year at baseline ranged from 1982 to 2017. The respondent ages ranged from 10 to 99 years old. Estimates from samples of ages 10-19 represented 35.5% of diagnostic and 48.6% of symptom-based estimates. Depression was assessed using DSM-version IV/version IV-revised criteria in 71 diagnostic studies (93.4%), and the CESD scale was used to measure depression in 42 symptom-based studies (61.7%). Among diagnostic studies, 97.4% of studies assessed past-year depression (two studies assessed lifetime depression (36,37)), so symptom period was not included as an independent variable; a sensitivity analysis included only studies of past-year depression to determine whether the meta-regression estimates were biased by the few studies with a longer recall period.

The effect sizes of all diagnostic and symptom-based depression gap estimates and a pooled summary depression gap are presented in Web Figures 1 (diagnostic studies) and 2 (symptom-based studies) and described in Web Appendix 1. Among diagnostic studies, prevalence ratios ranged from 1.26 (95% CI= 0.99, 1.59) to 4.23 (95% CI=3.37, 5.31), and the pooled summary PR was 2.01 (95% CI=1.88, 2.14). Among symptom-based depression gap

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studies, SMDs ranged from -0.12 (95% CI= -0.4, 0.16) to 0.59 (95% CI=0.51, 0.67), the pooled summary SMD was 0.22 (95% CI= 0.19, 0.25), indicating a small effect size.

Meta-regression

Meta-regression results are presented in Table 4. Main effects among diagnostic studies were estimated in Model 1a. The depression gap with all model variables at their reference levels was 2.27 (95% CI=1.48, 3.05). Overall, there was no evidence of change in the depression gap over time. The age effect was most pronounced among ages 10-19 (PR=1.26; 95% CI= 1.02, 1.56), compared with the referent (i.e., respondents ages 60+). Based on the exponentiated combined intercept and age coefficients, the depression gap was 2.86 among ages 10-19. The depression gap did not differ for any other age groups vs. the referent.

Model 2a tested interaction between age group and study year. The interaction term for youngest age group was elevated (PR=1.05; 95% CI=1.01, 1.08), suggesting that, compared with ages 60+, the depression gap had increased among the youngest ages over the study period. There was no evidence of time changes among any other age groups.

Main effects among symptom-based studies were estimated in Model 1b (Table 4). In these studies, the depression gap with all variables at their reference levels was 0.3 (0.09, 0.51). There was no evidence of change over time overall. Compared to age 60+ samples, the depression gap was greater only among the youngest ages (age 10-19) (SMD=0.40, based on combined intercept and age 10-19 model coefficients). In Model 2b, the interaction term for youngest age group was elevated (SMD=0.03; 95% CI=0.01, 0.05), suggesting that, compared to the oldest ages, the symptom-based depression gap increased over the study periods among the youngest ages. Compared to studies that measured depression with the CESD, the depression gap

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was higher in the 7 studies that used the PHQ (SMD=0.14; 95% CI=0, 0.28) and other instruments (SMD=0.13; 95% CI=0.04, 0.22).

Multiple imputation

In a sensitivity analysis, missing variance information was multiply imputed for 27 diagnostic studies. The depression gap with all variables at the reference level was slightly larger than in the unimputed model (PR=2.49; 95% CI=1.28, 4.88), and the age by time interaction tests were similar to the unimputed estimates (ages 10-19 PR=1.20; 95%=1.01, 1.39, no other age differences vs. the referent). The imputed random effects model pooled PR was not appreciably different from the complete case analysis (PR=1.97; 95% CI=1.82, 2.14). Overall, results suggested that the complete case analysis was not appreciably biased by missing data.

Publication bias

Funnel plots are shown in Web Figures 3 (diagnostic studies) and 4 (symptom-based studies). In the symptom-based model, Egger's test indicated no evidence of publication bias (intercept=-1.19 (95% CI=-3.5, 1.1), though the trim-and-fill procedure imputed 23 additional studies to achieve funnel plot symmetry. Imputing these studies increased the pooled effect size from 0.22 to SMD=0.27 (prediction interval=-0.026, 0.57). In the diagnostic-based model, Egger's test indicated no evidence of publication bias (intercept=-0.266 (95% CI=-1.78, 1.24). The trim-and-fill procedure imputed no additional studies.

DISCUSSION

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The purpose of this systematic review and meta-regression was to review studies of the depression gap and characterize changes in the gap over time. To our knowledge, this is the largest study to examine changes in the depression gap over time by age in the U.S. There were four central findings. First, women's depression risk was twice that of men overall, and the effect size was moderate among symptom-based studies. Second, there was no variation over time among adults ages 20 and older, which does not support the hypothesis that changing gendered social positions are narrowing the depression gap. Third, the depression gap increased over time among respondents ages 10-19. Fourth, variation in the magnitude of the symptom-based depression gap was related to differences in depression instrument.

Concordant with nearly all of the depression gap literature, the present meta-analysis identified an appreciable depression gap between men and women. Findings were generally consistent between diagnostic depression and symptom-based depression measures, though more variation in the depression gap was found in studies of depression symptom scales. This variation was likely due in part to differences in the depression instrument across these studies. Symptom scales like the CESD, the most commonly used instrument in these studies, correlate with diagnostic depression, but likely measure more general psychological distress and demoralization constructs (38). This variation should be considered when measuring and interpreting the depression gap using symptom scales in future individual studies.

While the meta-regression results suggested no change in the depression gap over time on average, there was heterogeneity in the time effects by age group, which is potentially indicative of cohort effects. Among adults ages 20 and older, there was no variation over time in the depression gap. Evidence of changes in the adult depression gap to date has been mixed. Some have reported a narrowing gender depression gap among younger adults over time, among

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individuals born from 1905-1965 (21,39), and young adults ages 18-25 from 2005-2014 (16). In contrast, other studies have reported no effects or an increasing depression gap over time, among individuals born from 1936-1975 (40), and individuals born from 1915 to 1955 (41). To some extent, these differences reflected the period of recall, the age and birth year of respondents, and the depression instrument. The present meta-regression sought to account for these sources of heterogeneity across studies and estimate a summary of overall variation in a wider age range to the present day.

The time period covered by the present study coincides with broad changes to women's social positions in the US. It was hypothesized that these changes would narrow the depression gap, but the results do not support a clear effect on the depression gap among adults. While it could be that the depression gap is not influenced by social position, the lack of an effect could also reflect both positive and negative consequences of changing position on the depression gap. On one hand, changing social position is indicated by greater opportunities in the workplace and access to personal socioeconomic (13,42) and psychosocial resources among women (43,44). Greater resources may reduce exposure to stress (45) and mitigate the effects of stressors (46,47) in ways that influence the risk of depression (9,48,49). On the other hand, these changes may increase exposure to role conflict- and overload- related stressors that could increase women's depression risk (50,51). Alternately, regardless of the impact of changing social positions on women's exposure to stress, stress responses may still remain gendered (52,53) in ways that are deleterious to women, thus sustaining the depression gap magnitude. Future research to elucidate these complex and potentially countervailing effects of gendered social and economic changes would add to the current understanding of depression gap trends.

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Among the youngest respondents, however, the depression gap was appreciably larger than among respondents age 60+. This pattern has been reported by individual (54) and meta-analytic (55) studies of age effects in the depression gap, which suggest that the depression gap peaks around age 13-15. This peaking corresponds with the onset of puberty, which marks significant neurobiological changes (56), but also substantial changes in adolescents' social context, marked by increases in psychosocial stressors and interpersonal conflict among peers (57). The development of secondary sex characteristics and other physical changes, such as acne or increased adipose tissue, serve as additional sources of potential negative social interactions (58). These changes have been shown to increase the risk of depression and anxiety, especially in adolescent girls (59), whose experiences may be exacerbated by depressogenic coping strategies such as rumination (10).

In addition to identifying age effects overall, the interaction between age and study year indicated that the depression gap has increased among adolescents since 1982. These results align with previous studies showing that the adolescent depression gap has been increasing and emerging at earlier ages for several generations (16,40). Causes of these trends are not clear, though again, changes in the adolescent social environment have been hypothesized. The prevalence of online harassment and bullying has increased over the past 20 years, and is more frequently experienced by girls (60). While social media use entails a diverse set of exposures with potentially positive effects on adolescent self-esteem (61), problematic use is more common among girls (62). To date, social media use is inconsistently linked to depressed mood (63,64), and more detailed research is needed before any particular mechanism is implicated. Fortunately, recent cohort studies have included more detailed measures of social media use (65). These studies can address the role social media use plays in depression across cohorts (66). Regardless

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of the causes of these emergent trends, clinicians should pay particular attention to adolescent girls as a high-risk group for depression. Additionally, it is unknown if these trends will be limited to adolescence or if the gap will continue to widen through adulthood. To date, there is little evidence of gender differences in depression recurrence (67,68), however, future studies that follow adolescent cohorts longitudinally into adulthood are necessary to fully answer this important question.

The findings of this meta-regression should be interpreted in light of several limitations. First, the majority of national samples were cross-sectional in design, and were only able to assess prevalent depression status. Second, there was significant heterogeneity in age ranges across studies. A consequence of making the age group categories comparable across studies (i.e., observed ages) involved truncating the age ranges within each sample (i.e., true ages), potentially introducing measurement error because observed age range was sometimes different from the true age range. This measurement error was likely non-differential as it was not related to the depression gap outcome, so any bias would attenuate age and age by time interaction estimates. In this study, the reported age effects were robust to an alternative set of age groupings (i.e., 10-17, 18-25, 26-35, 36-45, 46-55, 56+), suggesting that the age trends were not artifactual. Finally, among included studies of diagnostic depression, there were missing data and evidence of potential publication bias, which may have distorted the summary estimates of the depression gap. However, evidence from multiple imputation models, and trim-and-fill sensitivity analyses suggested that this bias was minimal. Finally, this study compliments recent international research showing associations between country-level gender equality and the depression gap (55,69), however, it was not structured to directly test the putative social mechanisms that might explain the depression gap itself. While mental health is the result of multiple interacting

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exposures, identifying changes over time highlights the important role of the social environment, which is more dependent on historical and social context than relatively immutable biological determinants. Future research to directly test the role of changing gender social positions over time in mediating any changes in the depression gap would be an important contribution to understanding determinants of the gender depression gap.

In conclusion, with a sample of 813,189 respondents spanning eight decades of age and a time period of 35 years, the present study finds evidence of a persistent gender gap in depression that appears to be increasing in adolescents over time. Future research is needed to understand the causes of these changes in the gender gap in adolescents, in order to inform depression prevention and treatment efforts, and reverse potentially growing depression disparities among young people.

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Table 1. Studies of gender differences in diagnostic depression, measured as prevalence ratios

Author, Year (Reference No.)	BL Year	PR	SE	Age Min	Age Max[a]	N Men	N Women	Interview & instrument	Study design	Data source	Recall period
Kessler et al, 1993 (70)	1990	3.15	1.455	15	24	1010	990	CIDI DSM-III-R	C	NCS	2
	1990	1.50	0.249	25	34	1231	1207	CIDI DSM-III-R	C	NCS	2
	1990	1.89	0.284	35	44	1108	1086	CIDI DSM-III-R	C	NCS	2
	1990	1.52	0.299	45	54	740	726	CIDI DSM-III-R	C	NCS	2
Alaimo et al, 2002 (36)	1991	2.28	0.968	15	16	365	389	DIS	C	NHANES III	3
Dawson & Grant, 1997 (71)	1992	1.60	0.065	18	99	17819	25043	AUDADIS DSM-IV	C	NLAES	2
Kessler et al, 2010 (72)	2001	1.58	0.196	18	34	1375	1658	CIDI DSM-IV	C	NCS-R	2
	2001	2.73	0.483	35	49	1342	1522	CIDI DSM-IV	C	NCS-R	2
	2001	1.48	0.247	50	64	854	1068	CIDI DSM-IV	C	NCS-R	2
	2001	1.71	0.297	65	99	564	894	CIDI DSM-IV	C	NCS-R	2
CBHSQ, 2004 (73)	2004	2.62	0.131	12	17	11363	10938	CIDI DSM-IV	C	NSDUH	2
CBHSQ, 2005 (74)	2005	2.96	0.154	12	17	11378	11156	CIDI DSM-IV	C	NSDUH	2
	2005	2.09	0.104	18	25	10697	10444	CIDI DSM-IV	C	NSDUH	2
	2005	1.69	0.096	26	49	7823	9132	CIDI DSM-IV	C	NSDUH	2

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	2005	2.00	0.260	50	99	3142	3420	CIDI DSM-IV	C	NSDUH	2
CBHSQ, 2006 (75)	2006	2.81	0.151	12	17	11718	11153	CIDI DSM-IV	C	NSDUH	2
	2006	1.81	0.096	18	25	9158	11526	CIDI DSM-IV	C	NSDUH	2
	2006	1.73	0.100	26	49	7431	8606	CIDI DSM-IV	C	NSDUH	2
	2006	1.67	0.217	50	99	2888	3804	CIDI DSM-IV	C	NSDUH	2
CBHSQ, 2007 (76)	2007	2.59	0.135	12	17	11524	10909	CIDI DSM-IV	C	NSDUH	2
	2007	1.97	0.100	18	25	10645	11542	CIDI DSM-IV	C	NSDUH	2
	2007	1.72	0.097	26	49	7770	9114	CIDI DSM-IV	C	NSDUH	2
	2007	1.67	0.214	50	99	2857	3509	CIDI DSM-IV	C	NSDUH	2
CBHSQ, 2008 (77)	2008	2.91	0.155	12	17	11517	11029	CIDI DSM-IV	C	NSDUH	2
	2008	2.11	0.103	18	25	11166	12039	CIDI DSM-IV	C	NSDUH	2
	2008	1.49	0.091	26	49	7440	8936	CIDI DSM-IV	C	NSDUH	2
	2008	2.14	0.306	50	99	2996	3613	CIDI DSM-IV	C	NSDUH	2
CBHSQ, 2009 (78)	2009	2.49	0.129	12	17	11520	11106	CIDI DSM-IV	C	NSDUH	2
	2009	1.93	0.096	18	25	11104	11900	CIDI DSM-IV	C	NSDUH	2
	2009	1.71	0.104	26	49	7591	8729	CIDI DSM-IV	C	NSDUH	2
	2009	1.67	0.21	50	99	3060	3690	CIDI DSM-IV	C	NSDUH	2

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			3								
CBHSQ, 2010 (79)	2010	2.71	0.146	12	17	11140	10820	CIDI DSM-IV	C	NSDUH	2
	2010	2.27	0.091	18	25	17283	16788	CIDI DSM-IV	C	NSDUH	2
CBHSQ, 2011 (80)	2011	2.69	0.138	12	17	12028	11482	CIDI DSM-IV	C	NSDUH	2
	2011	1.95	0.077	18	25	17178	17123	CIDI DSM-IV	C	NSDUH	2
Verplaetse et al, 2016 (81)	2012	2.01	0.218	18	99	15715	20,386	DSM-V	C	NESARC 3	2
CBHSQ, 2013 (82)	2013	2.07	0.405	12	12	1824	1713	CIDI DSM-IV	C	NSDUH	2
	2013	3.42	0.523	13	13	1963	1849	CIDI DSM-IV	C	NSDUH	2
	2013	4.23	0.550	14	14	2026	1865	CIDI DSM-IV	C	NSDUH	2
	2013	3.34	0.366	15	15	1882	1868	CIDI DSM-IV	C	NSDUH	2
	2013	2.54	0.260	16	16	1940	1890	CIDI DSM-IV	C	NSDUH	2
	2013	2.70	0.283	17	17	1914	1760	CIDI DSM-IV	C	NSDUH	2
	2013	1.96	0.095	18	25	10671	11543	CIDI DSM-IV	C	NSDUH	2
	2013	1.71	0.251	26	29	1376	1603	CIDI DSM-IV	C	NSDUH	2
	2013	1.26	0.171	30	34	1529	1802	CIDI DSM-IV	C	NSDUH	2
	2013	1.64	0.269	35	39	1317	1562	CIDI DSM-IV	C	NSDUH	2
	2013	1.57	0.237	40	44	1437	1671	CIDI DSM-IV	C	NSDUH	2

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	2013	1.31	0.194	45	49	1440	1613	CIDI DSM-IV	C	NSDUH	2
	2013	1.43	0.282	50	54	837	951	CIDI DSM-IV	C	NSDUH	2
	2013	1.54	0.374	55	59	711	909	CIDI DSM-IV	C	NSDUH	2
	2013	1.41	0.376	60	64	674	719	CIDI DSM-IV	C	NSDUH	2
	2013	3.53	1.399	65	99	1302	1659	CIDI DSM-IV	C	NSDUH	2
CBHSQ, 2017 (83)	2017	2.59	0.610	12	12	1329	1269	CIDI DSM-IV	C	NSDUH	2
	2017	4.04	0.696	13	13	1507	1423	CIDI DSM-IV	C	NSDUH	2
	2017	3.63	0.507	14	14	1492	1385	CIDI DSM-IV	C	NSDUH	2
	2017	3.68	0.416	15	15	1460	1427	CIDI DSM-IV	C	NSDUH	2
	2017	2.46	0.246	16	16	1508	1389	CIDI DSM-IV	C	NSDUH	2
	2017	2.20	0.206	17	17	1419	1418	CIDI DSM-IV	C	NSDUH	2
	2017	2.10	0.296	18	18	1070	1036	CIDI DSM-IV	C	NSDUH	2
	2017	1.90	0.263	19	19	976	1002	CIDI DSM-IV	C	NSDUH	2
	2017	1.51	0.180	20	20	973	954	CIDI DSM-IV	C	NSDUH	2
	2017	1.59	0.208	21	21	922	984	CIDI DSM-IV	C	NSDUH	2
	2017	2.21	0.319	22	22	1000	1033	CIDI DSM-IV	C	NSDUH	2
	2017	1.85	0.25	23	23	1006	1155	CIDI DSM-IV	C	NSDUH	2

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2017	1.55	0.203	24	24	975	1139	CIDI DSM-IV	C	NSDUH	2
2017	1.48	0.205	25	25	1061	1183	CIDI DSM-IV	C	NSDUH	2
2017	1.83	0.196	26	29	2117	2580	CIDI DSM-IV	C	NSDUH	2
2017	1.36	0.139	30	34	2631	3088	CIDI DSM-IV	C	NSDUH	2
2017	2.06	0.267	35	39	2231	2551	CIDI DSM-IV	C	NSDUH	2
2017	1.91	0.249	40	44	1945	2387	CIDI DSM-IV	C	NSDUH	2
2017	1.67	0.214	45	49	2075	2450	CIDI DSM-IV	C	NSDUH	2
2017	1.30	0.274	50	54	901	1093	CIDI DSM-IV	C	NSDUH	2
2017	1.64	0.342	55	59	931	1138	CIDI DSM-IV	C	NSDUH	2
2017	1.87	0.448	60	64	948	1013	CIDI DSM-IV	C	NSDUH	2
2017	1.57	0.343	65	99	2077	2381	CIDI DSM-IV	C	NSDUH	2

CBHSQ=Center for Behavioral Health Statistics and Quality; NESARC=National Epidemiologic Survey of Alcoholism and Related Conditions; NCS=National Comorbidity Survey;
NHANES=National Health & Nutrition Epidemiologic Survey; NLAES=National Longitudinal Alcohol Epidemiologic Survey; NCS-R=National Comorbidity Survey Replication; NSDUH=National Survey of Drug Use and Health; DSM=Diagnostic and Statistical Manual of Mental Disorders; CIDI=Composite International Diagnostic Interview; AUDADIS=Alcohol Use Disorder and Associated Disabilities Interview Schedule. Note: BL=baseline; PR=prevalence ratio; SE=standard error; [a] When the sample age range was described as all ages (e.g., 18 and up). Study design: C=cross-sectional, BL=Baseline interview of a longitudinal study, L=other wave of longitudinal study (BL year); Recall period: 2=PY; 3=Lifetime; Race/ Ethnicity: 1=all; 2=NHW; 3=NHB; 4=Hispanic; 5=other

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Table 2. Studies of gender differences in symptom-based depression, measured as standardized mean differences

Author, Year (Reference No.)	BL Year	SMD	SE	Age Min	Age Max[a]	N Men	N Women	Instrument	Study design	Data source	Retention[b]	Recall period
Ferketich et al, 2000 (84)	1982	0.26	0.02	30	99	2886	5007	CESD	C	NHANES I		1
Everson-Rose et al, 2004 (85)	1986	0.31	0.02	24	34	333	407	CESD	BL	ACLS		1
	1986	0.23	0.05	35	44	228	363	CESD	BL	ACLS		1
	1986	-0.01	0.02	45	54	168	222	CESD	BL	ACLS		1
	1986	0.08	0.05	55	64	251	434	CESD	BL	ACLS		1
	1986	0.12	0.05	65	74	239	526	CESD	BL	ACLS		1
	1986	0.23	0.05	75	99	139	307	CESD	BL	ACLS		1
Inaba et al, 2005 (86)	1994	0.27	0.05	28	39	1372	1413	CESD	BL	NSFH-2		1
	1994	0.22	0.05	40	49	1013	987	CESD	BL	NSFH-2		1
	1994	0.38	0.05	50	59	594	716	CESD	BL	NSFH-2		1
	1994	0.29	0.04	60	78	856	1220	CESD	BL	NSFH-2		1
Marmorstein et al, 2009 (87)	1995	0.12	0.02	12	12	262	329	CESD	BL	Add Health		1
	1995	0.22	0.02	13	13	1039	1218	CESD	BL	Add Health		1
	1995	0.3	0.02	14	14	1319	1472	CESD	BL	Add Health		1
	1995	0.34	0.02	15	15	1778	1883	CESD	BL	Add Health		1
	199	0.31	0.0	16	16	206	1991	CESD	BL	Add Health		1

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	5		2			1						
	1995	0.19	0.02	17	17	1981	1940	CESD	BL	Add Health		1
	1995	0.21	0.05	18	18	1512	1427	CESD	BL	Add Health		1
	1995	0.34	0.05	19	19	237	159	CESD	BL	Add Health		1
Neumark-Sztainer et al, 2000 (88)	1997	0.26	0.04	10	10	239	267	CDI	C	CFS		1
	1997	0.02	0.02	11	11	254	305	CDI	C	CFS		1
	1997	0.04	0.05	12	12	386	461	CDI	C	CFS		1
	1997	0.29	0.05	13	13	420	484	CDI	C	CFS		1
	1997	0.22	0.05	14	14	370	462	CDI	C	CFS		1
	1997	0.31	0.02	15	15	361	503	CDI	C	CFS		1
	1997	0.32	0.04	16	16	399	497	CDI	C	CFS		1
	1997	0.25	0.02	17	17	314	372	CDI	C	CFS		1
Mumford et al, 2013 (89)	2000	0.48	0.02	15	15	815	765	MHI-D	L (BL=1997)	NLSY97	88	1
	2000	0.33	0.02	16	16	819	774	MHI-D	L (BL=1997)	NLSY97	88	1
	2000	0.29	0.05	17	17	811	773	MHI-D	L (BL=1997)	NLSY97	88	1
	2000	0.22	0.02	18	18	766	767	MHI-D	L (BL=1997)	NLSY97	88	1
	200	0.23	0.0	19	19	657	681	MHI-D	L	NLSY97	88	1

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	0		5						(BL=1997)		
Song et al, 2011 (90)	2005	0.3	0.04	21	64	167	188	CESD	C	Study-specific	1
	2005	0.21	0.02	21	64	187	225	CESD	C	Study-specific	1
	2005	0.11	0.04	21	64	939	1124	CESD	C	Study-specific	1
Shiovitz-Ezra et al, 2009 (91)	2005	0.23	0.05	57	64	521	484	CESD	C	NSHAP	1
	2005	0.16	0.04	65	74	543	537	CESD	C	NSHAP	1
	2005	0.09	0.05	75	85	373	499	CESD	C	NSHAP	1
Haroz et al, 2014 (92)	2006	0.16	0.14	11	12	95	99	CESD-10R	C	Growing up with Media	1
	2006	0.49	0.10	13	14	201	191	CESD-10R	C	Growing up with Media	1
	2006	0.11	0.11	15	17	192	172	CESD-10R	C	Growing up with Media	1
	2009	0.47	0.06	13	14	585	785	CESD-10R	C	Growing up with Media	1
	2009	0.27	0.05	15	17	856	1096	CESD-10R	C	Teen Health and Tech	1
	2009	0.22	0.04	18	18	954	1404	CESD-10R	C	Teen Health and Tech	1
	2006	0.25	0.14	18	18	94	106	CESD-10R	C	Teen Health and Tech	1
Wang et al, 2010 (93)	2006	0.29	0.05	11	11	1164	1186	DFB	C	HBSC	1
	2006	0.44	0.02	12	12	892	951	DFB	C	HBSC	1
	2006	0.49	0.02	13	13	789	997	DFB	C	HBSC	1
	2006	0.51	0.02	14	14	721	742	DFB	C	HBSC	1

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	2006	0.59	0.02	15	15	793	804	DFB	C	HBSC		1
Oksuzyan et al, 2010 (94)	2006	0.13	0.02	50	54	640	1013	CESD	L (BL=1992)	HRS	85	1
	2006	0.05	0.05	55	59	1051	1472	CESD	L (BL=1992)	HRS	85	1
	2006	0.1	0.05	60	64	936	1463	CESD	L (BL=1992)	HRS	85	1
	2006	0.11	0.05	65	69	1537	1879	CESD	L (BL=1992)	HRS	85	1
	2006	0.12	0.05	70	74	1267	1560	CESD	L (BL=1992)	HRS	85	1
	2006	0.16	0.02	75	79	906	1128	CESD	L (BL=1992)	HRS	85	1
	2006	0.11	0.02	80	84	647	917	CESD	L (BL=1992)	HRS	85	1
	2006	0.04	0.04	85	89	344	649	CESD	L (BL=1992)	HRS	85	1
	2006	0.04	0.02	90	99	142	379	CESD	L (BL=1992)	HRS	85	1
Thibodeau et al, 2014 (95)	2008	0.29	0.02	18	29	550	500	PHQ-9	C	NHANES 2008		1
	2008	0.34	0.05	30	39	431	447	PHQ-9	C	NHANES 2008		1
	2008	0.3	0.05	40	49	391	452	PHQ-9	C	NHANES 2008		1
	200	0.23	0.0	50	59	418	400	PHQ-9	C	NHANES 2008		1

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	8		2								
	200	0.29	0.0	60	69	434	459	PHQ-9	C	NHANES 2008	1
	8		5								
	200	0.25	0.0	70	99	483	482	PHQ-9	C	NHANES 2008	1
	8		5								
Bushman et al, 2012	201	0.14	0.0	18	90	251	549	CESD	C	Study-specific	1
(96)	1		5								
Gettler et al, 2016 (97)	201	0.14	0.0	20	60	150	933	PHQ-9	C	NHANES 2011-	1
	1		4			5				2012	
Margraf et al, 2016	201	-	0.1	18	99	125	1786	DASS-D	BL	Bochum	1
(98)	3	0.12	4			2				Optimism and	
										Mental Health	

NHANES=National Health & Nutrition Epidemiologic Survey; ACLS=American's Changing Lives Survey; NSFH-2=Natl Survey of Families and Households 2; CFS=Commonwealth Fund Survey of Adolescent Girls & Boys; NLSY97=National Longitudinal Survey of Youth 1997; NSHAP=National Social Life, Health, and Aging Project; HBSC=Health Behavior in school-aged children; HRS=Health and Retirement Study; CESD=Center for Epidemiologic Studies Depression scale; CDI=Children's Depression Inventory; MHI-D=Mental Health Inventory-Depression scale; DFB=Depressive feelings and behaviors; PHQ-9=Patient Health Questionnaire-9 item; DASS-D=Depression Anxiety Stress Scales-Depression subscale.

Note: BL=baseline; SMD=Standardized mean difference; SE=standard error; [a] When the sample age range was described as all ages (e.g., 18 and up), upper bound was coded as 99.

[b] if sample was not cross-sectional or BL longitudinal; Study design: C=cross-sectional, BL=Baseline interview of a longitudinal study, L=other wave of longitudinal study (BL year); Race/ Ethnicity: 1=all; 2=NHW; 3=NHB; 4=Hispanic; 5=other.

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Table 3. Distributions of all variables used in meta-regression models

Variable	Diagnostic studies (n=76)		Symptom studies (n=68)	
	No.	%	No.	%
Year[a, b]	2010(6.9)		2001(7.8)	
Age groups				
All[c]	3	(3.9)	6	(8.8)
10-19	27	(35.5)	33	(48.5)
20-39	24	(31.6)	4	(5.9)
40-59	11	(14.5)	9	(13.2)
60+	11	(14.5)	16	(23.5)
Symptom period				
Prior-year	74	(97.4)		
Lifetime	2	(2.6)		
Instrument				
DSM-III/III-R	4	(5.3)		
DSM-IV/IV-R	71	(93.4)		
DSM-5	1	(1.3)		
CESD			42	(61.7)
CDI			8	(11.8)
PHQ-9			7	(10.3)
Other			11	(16.2)

Note: SD=Standard Deviation; DSM=Diagnostic and Statistical Manual; CESD=Center for Epidemiologic Studies Depression scale; CDI=Children's Depression Inventory; PHQ-9=Patient Health Questionnaire; [a]Values are expressed as mean (standard deviation)
[b]Year range: 1990-2017 (diagnostic studies); 1982-2013 (symptom studies)
[c]studies were not included to estimate age effects

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Table 4. Meta-regression model estimates

	Diagnostic depression gap				Symptom-based depression gap			
Variable	PR	95% CI	PR	95% CI	SMD	95% CI	SMD	95% CI
	Model 1a		Model 2a[a]		Model 1b		Model 2b[a]	
Intercept	2.27	1.48, 3.05	2.30	1.58, 3.36	0.30	0.09, 0.51	0.54	0.34, 0.75
Study Year	1.00	0.99, 1.01	1.00	0.98, 1.01	-0.01	-0.02, 0.01	-0.01	-0.02, 0.00
Age (ref=60+)								
10-19	1.26	1.02, 1.56	0.43	0.21, 0.88	0.10	0.03, 0.16	0.08	-0.13, 0.29
20-39	0.89	0.73, 1.08	0.41	0.06, 0.77	0.03	-0.10, 0.15	-0.02	-0.20, 0.16
40-59	0.94	0.59, 1.50	0.86	0.30, 1.43	-0.02	-0.14, 0.11	-0.03	-0.09, 0.03
Age 10-19 x study year			1.05	1.01, 1.08			0.03	0.01, 0.05
Age 20-39 x study year			1.02	0.99, 1.04			0.00	-0.01, 0.01
Age 40-59 x study year			1.00	0.98, 1.03			0.01	-0.01, 0.02
Diagnostic-depression instrument (ref=DSM-IV)								
DSM-III/IIIR	0.94	0.59, 1.50	0.80	0.49, 1.32				
Other	1.08	0.80, 1.48	1.03	0.74, 1.43				
Symptom-based depression instrument (ref=CESD)								
CDI					-0.06	-0.22, 0.09	-0.05	-0.21, 0.11
PHQ-9					0.13	0.03, 0.23	0.14	0.00, 0.28

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Other	0.16	0.02, 0.30	0.13	0.04, 0.22

Note: [a]adjusted for all model 1 variables; PR=prevalence ratio; SMD=standardized mean difference; CI=confidence interval; DSM=Diagnostic and Statistical Manual; CESD=Center for Epidemiologic Studies Depression scale; CDI=Children's Depression Inventory; PHQ-9=Patient Health Questionnaire

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Figure 1. Literature search and study selection flowchart. Note: The general search strategy included: ('gender' OR 'sex') AND (('male' AND 'female') AND (‘depress*’ OR ‘distress’ OR ‘demoraliz*’ OR ‘internaliz*’). * denotes a stem that may encompass various forms a word, e.g., depress* = depressive, depression, depressed, etc. Search terms were optimized using MeSH terms and adapted for each database (PubMed, JSTOR, Embase, PsychInfo, and Scopus).

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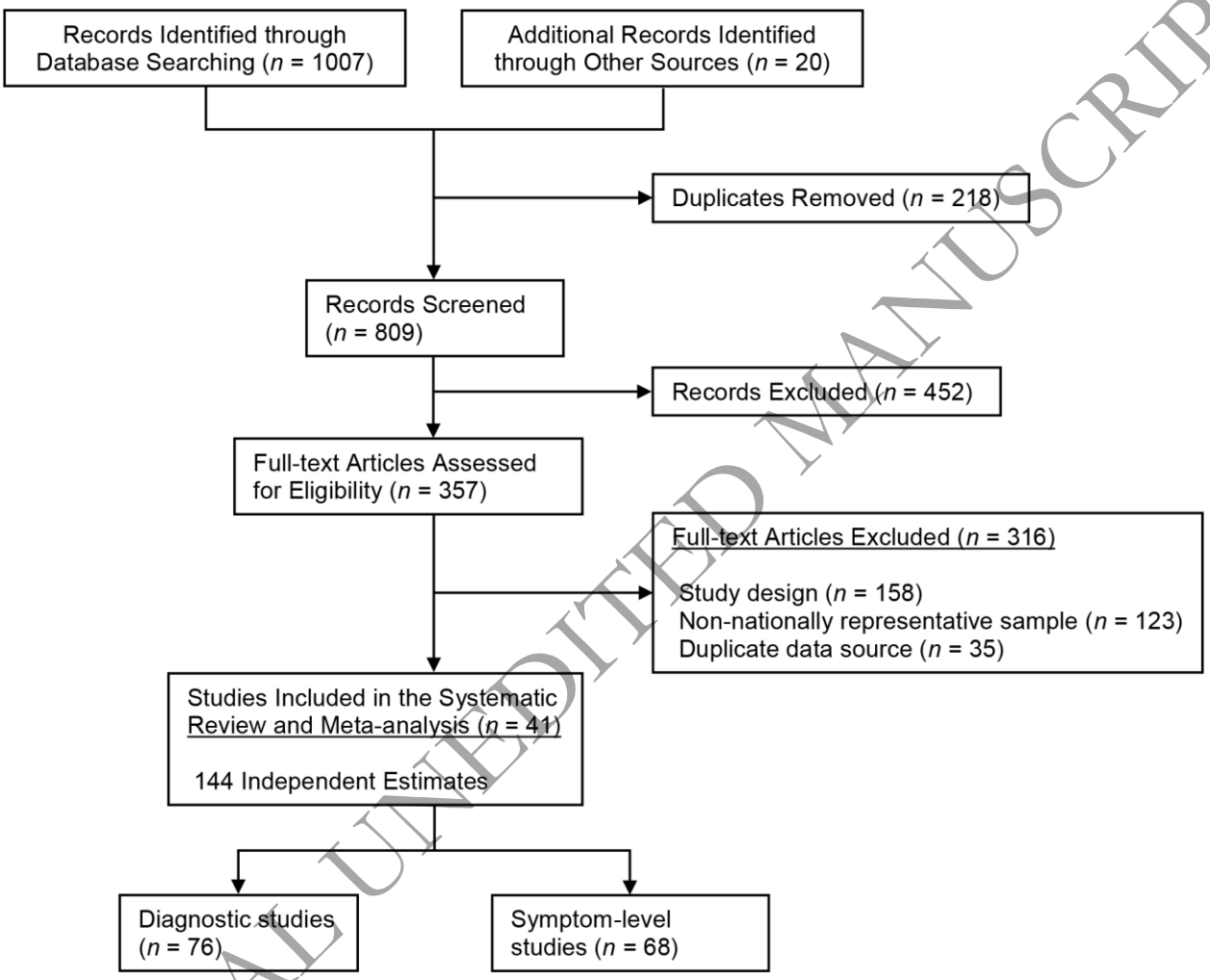

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