Is the global prevalence rate of adult mental illness increasing? Systematic review and meta-analysis

Running title: Is adult mental illness increasing over time?

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Abstract

Objectives: The question whether mental illness prevalence rates are increasing is a controversially debated topic. Epidemiological articles and review publications that look into this research issue are often compromised by methodological problems. The present study aimed at using a meta-analysis technique that is usually applied for the analysis of intervention studies to achieve more transparency and statistical precision.

Methods: We searched Pubmed, PsycInfo, CINAHL, Google Scholar and reference lists for repeated cross-sectional population studies on prevalence rates of adult mental illness based on ICD- or DSM-based diagnoses, symptom scales and distress scales that used the same methodological approach at least twice in the same geographical region. The study is registered with PROSPERO (CRD42018090959).

Results: We included 44 samples from 42 publications, representing 1,035,697 primary observations for the first time point and 783,897 primary observations for the second and last time point. Studies were conducted between 1978 and 2015. Controlling for a hierarchical data structure, we found an overall global prevalence increase odds ratio of 1.179 (95%-CI: 1.065 – 1.305). A multivariate meta-regression suggested relevant associations with methodological characteristics of included studies.

Conclusions: We conclude that the prevalence increase of adult mental illness is small and we assume that this increase is mainly related to demographic changes.

Keywords

Mental illness, prevalence, secular trends, meta-analysis

Summations

- The issue of potentially increasing prevalence rates of mental illness is controversial.
- Using a meta-analysis, we found a small increase of prevalence rates over time.
- The increase may be due to demographic changes in current societies.

Limitations

- There is a scarcity of data from non-western regions.
- The coverage of mental illness is unevenly distributed.
- No data on prevalence changes of psychosis/schizophrenia were available.

Data availability statement

The data will be made available after publication.

Introduction

Currently, numerous media reports and many lay and expert commentators suggest a belief that distress in general and mental illness more specifically are on the rise [1-3]. These claims are usually supported by data on utilization of mental health care and by monitoring of health-related indicators such as suicides. The claim of rising mental illness – if supported by rigorous research – would have important implications not only for public mental health in terms of potential failure of treatment approaches [4] but also for wider society in terms of understanding living conditions that sociologists see to be deteriorating and stress terminologies such as social suffering or social pathology [5].

Empirical research has supported these claims previously by utilizing a variety of study designs and indicators. But those studies and indicators have considerable methodological problems when it comes to generalizing trends of mental illness. Early epidemiological field studies from the 1980s on lifetime prevalence of depression have indicated higher prevalence rates in more recent birth cohorts [6,7]. However, as later re-analyses have shown, the studies were compromised by recall bias [8,9]. Current psychiatric utilization rates are on the rise in many countries. Antidepressant consumption has doubled in OECD-countries between 2000 and 2015 [10] and the rates of disability pensions claimed due to mental illness have increased in recent decades in the UK [11], Australia [12], Switzerland [13] and many other countries. The interpretation of rising utilization rates is, however, not straightforward. Increasing prescription rates may indeed indicate rising prevalence, but they may also indicate an increasing willingness to receive treatment in the population or more overuse and off-label use [14,15]. The rise of disability pensions rates due to mental illness may be a mirror of a changing labour market with less physically damaging workplaces [16]. Next, the WHO Global Burden of Disease-studies have stressed the increasing burden due to depression and other mental disorders [17]. But the increasing burden caused by mental illness is not necessarily caused by an increasing prevalence, but may rather be due to changing demographics [18]. Finally, the United States are currently experiencing a large-scale mental health-related crisis due to prescription and self-administration of opioids [19]. There is, yet, a clear indication that prescription and marketing practices have greatly contributed to this crisis.

Many systematic reviews, utilizing different methodological approaches, have however not supported the assumption of increasing prevalence rates over time. Wittchen et al. reviewed review-papers and re-analysed prevalence data for Europe and identified no relevant changes in recent years [20]. Steel et al. reported a higher prevalence of common mental illness in the 1990s compared to the 2000s when analysing single-point cross-sectional studies [21]. Using the Global Burden of Disease (GBD)-approach that is based on a variety of methodologies, Baxter et al. rejected the claim of a mental illness increase [18].

Repeated cross-sectional studies, utilizing the same instruments and sampling methodologies over at least two timepoints, are currently regarded as the gold-standard for this type of research [22]. Longitudinal cohort studies have the main disadvantage that they cover the ageing process of the sample while repeated cross-sectional samples can only differ in terms of demographics. Richter et al. found no clear trend in terms of prevalence changes when systematically reviewing repeated cross-sectional studies [23,24]. Similarly, Jorm et al. searched for papers on common mental illness that covered more than one time point in Australia, Canada, the UK and the US and found no relevant prevalence changes [25].

The most recent Global Burden of Disease-analysis utilized a different metric when looking into change of mental illness burden. According to this report, the percentage of years lived with disability (YLD) due to mental illness increased globally by 13.5% between 2007 and 2017. However, when age-standardisation was applied to account for demographic changes, the YLD percentage

decreased significantly by 1.1% [26]. YLD percentage changes of substance use disorders were also affected by demographic changes. While the unstandardized percentage increased from 2007 to 2017 by 16.7%, the age-standardized percentage changes were much lower (2.9%). Furthermore, the increase was mainly due to opioid use disorders, whereas alcohol use disorders decreased significantly during this time.

We searched the Global Health Data Exchange database (www.ghdx.healthdata.org) for global prevalence changes over the longer time period between 1990 and 2017. The search yielded the following results. The prevalence of mental disorders, not standardized for age, increased significantly by 2.47% but the age-standardized prevalence decreased significantly by 1.72%. Substance use disorder prevalence, not standardized for age, increased significantly by 5.65%, while the age-standardized prevalence increased non-significantly by 0.05% (see permanent link at the end of the article).

A major methodological weakness of the GBD-approach is the use of meta-regression modelling and estimation processes. For example, the GBD reports provide population-based prevalence data for schizophrenia for every country in the world but only very few studies have actually analysed schizophrenia prevalences in the general population. Most prevalence studies on this disorder are based on hospital and register data. Given the relatively opaque data processing in the GBD study, compared to a black box by some researchers recently [27], there is a need for more precise and transparent estimates in terms of prevalence changes for mental illness using the gold-standard design noted above.

Aims of the study

Our study aims at conducting a systematic review and meta-analysis based on repeated cross-sectional population surveys focusing on any adult mental illness prevalence changes over time. By using the term mental illness, we will refer throughout to mental disorders and distress to encompass the wide range of mental phenomena within the literature. We restricted this study to adults because data gathering procedures in children and adolescent populations (i.e. parent and teacher interviews) differ fundamentally from the procedures in adult populations where respondents report directly about their personal health.

Methods

Search strategy and data extraction

The current study was registered with PROSPERO (registration number CRD42018090959; https://www.crd.york.ac.uk/PROSPERO). We searched the Pubmed, PsycInfo, CINAHL and Google Scholar databases. Reference lists were also searched. Inclusion criteria were publications on repeated cross-sectional studies with at least two time points on any kind of mental illness in adult populations (18 years+). We included a variety of methodological approaches for case definitions that were not restricted to DSM- or ICD-frameworks. This was because both the DSM-/ICD-classifications are increasingly challenged [28] and the use of community survey instruments related to them is not uncontroversial [29,30], especially with regard to case ascertainment [31]. We therefore used clinical diagnostic interviews (for both specific disorders and for all disorders combined), validated self-report symptom scales not used for diagnosis (e.g. Patient Health Questionnaire, PHQ-9), and distress assessment instruments (e.g. General Health Questionnaire, Kessler-6-Scale). Distress assessment instruments were included because they have been shown to be discriminative in terms

of DSM disorder caseness [32]. Included languages were English, French, German, Dutch and Spanish. We did not apply any time restrictions or geographical restrictions.

Exclusion criteria were as follows: longitudinal and cohort studies which assessed the same population at both time points; treatment prevalence studies (incl. consumption of medication or prescriptions) as treatment is not a valid proxy for illness; studies not at the core of the mental illness construct, e.g. substance use/misuse, psychosomatic symptoms or personality traits; studies covering the prevalence of somatic outcomes linked to mental illness (e.g. liver cirrhosis or mortality); studies on suicides, suicidality or self-harm, dementia and related cognitive conditions where specific analyses are already available [33,34].

The initial search process was conducted by DR and was cross-checked by other project members. The study selection process was conducted by AW and AB who independently read abstracts and full texts. Disagreement on inclusion was resolved by consulting the senior project members (DR and RW).

We conducted a quality appraisal of all included studies. As the currently available instruments were not suitable for our purposes of appraising repeated cross-sectional population studies, we adapted an instrument by Munn et al. [35]. Our appraisal tool awarded higher scores for: national representativeness; coverage of ages from 18 to 70 years; census or random sampling; sample size greater than 1,000 per time point; comprehensive data on subjects and settings; response rate of at least 80 percent or more or of at least 50 percent with reasons; utilization of a DSM- or ICD-related tool or any other validated instrument; identical procedure at both timepoints; appropriate statistical analysis. Quality appraisal was conducted by AW and AB; disagreement was again resolved by DR or RW.

Data extraction was conducted by DR and cross-checked by other team members. The following data were entered into a database: authors, publication year, country, world region, first datapoint year, second/last datapoint year, mental health condition (depression, anxiety etc.), type of assessment (clinical diagnosis, symptoms, distress), number of cases per timepoint, sample size per timepoint, number of years between first and last year, and quality appraisal score. In studies where only case percentages were reported with no raw data, we calculated the number by applying the percentage to the total sample size.

Meta-analysis

The meta-analysis was conducted utilizing a methodology usually applied to intervention studies that compare intervention and control conditions with odds ratios and 95%-confidence intervals (CI hereafter) as the effect size metric. Conceptually, therefore, the first time point constituted a baseline or control assessment and the second or last time point was comparable to a post-intervention assessment to find out whether changes have occurred. In other words, we considered ‘time’ as a form of intervention. We used the ‘meta’ (version 4.9-1) and ‘metafor’ (version 2.0-0) packages [36,37], R software (version 3.5.1) for all analyses [38]. A random-effects-model with Paule-Mandel-method for between-study variance estimation was used [39,40]. Heterogeneity was assessed with the Q-Test.

The ‘rma.mv’-function from the ‘metafor’-package was used for multilevel analyses to account for non-independence of some studies (i.e. publications nested within studies or the use of data from one time point for comparisons with several later time points in various publications). For example, we found several publications assessing different mental health conditions using the same data from the US ‘National Epidemiologic Survey on Alcohol and Related Conditions’ or the US ‘National Survey

on Drug Use and Health'. Due to the multilevel data structure of some samples we will indicate whether we report clustered or non-clustered analyses.

Forest plots cannot be provided for the full sample of publications because of the dependent data structure. We will, however, provide a forest plot that – in cases of multiple papers per study – shows either the first publication from the study or the publication with highest sample size when more than one paper in the same year was published.

Finally, we conducted a multivariate meta-regression to analyse the moderators' association with the heterogeneity of the dependent effect size, accounting for the multilevel data structure. For this analysis we used again the rma.mv-function from the R package 'metafor'. This function allows the computing of a multilevel model that adds a random effect for the study from where multiple papers have been published. The R package 'glmulti' in combination with the package 'metafor' with a small-sample corrected Akaike Information Criterion was used for model selection. Publication bias was assessed by a contour-enhanced funnel plot and Egger's Test [41]. There was no funding source for this study.

Results

Our search identified 8545 publications from the databases and further 60 publications from reference lists. We assessed 109 publications in full text and included 44 samples from 42 publications into the meta-analysis (see Table 1 and Figure 1 for PRISMA flowchart). Altogether, 1,035,697 primary observations were included for the first time point and 783,897 primary observations for the second and last time point.

We identified the following study characteristics: 20 samples were from Western Europe, 16 from North America, 3 each from Asia and Oceania and one each from the Middle East and from South America. Four samples used DSM/ICD-related clinical interviews for the entire range of mental disorders (excluding schizophrenia) and 20 samples utilized DSM/ICD-related clinical interviews on single disorders. Seven samples used symptom scales and 13 samples used distress scales. Due to the methodological similarity, we analysed symptom scales and distress scales below as one methodological approach. Prevalence changes of general mental illness were analysed in 4 samples, distress was analysed in 13 samples and 27 samples examined specific symptoms (15 samples looked for depression/depressive symptoms, 5 for drug dependence, 3 for alcohol dependence, and one each for anxiety, bipolar disorder, eating disorders, and medication dependence). The mean time between first and last data collection point was 9.9 years (median 10 years). Our quality appraisal resulted in 3 samples achieving 9 points, 8 samples 8 points, 13 samples 7 points and 20 samples less than 7 points. The visual inspection of the publication bias contour-enhanced funnel plot (Figure 3) revealed an asymmetry that was supported by a significant Egger's test ($p = 0.007$). The funnel plot does not indicate an association between smaller sample size (i.e. higher standard error) and effect size and significant result.

The main result is as follows: For all samples combined and accounting for dependence (i.e. clustered data) we found a univariate pooled odds ratio (OR) of 1.179 (CI 1.065 – 1.305). However, the Q-Test for heterogeneity was highly significant ($Q(df = 43) = 1693.1$, $p < .0001$). A forest plot that contains all single study publications and one publication each from a multiple paper study is provided in Figure 2.

As indicated by the univariate moderator analysis in Table 2, we found the following ORs for the different conditions: general mental illness: 1.046 (CI 0.998 – 1.097), distress: 1.126 (CI 0.946 –

1.340), depression: 1.298 (CI 1.062 – 1.587), alcohol dependence: 1.016 (CI 0.851 – 1.215), drug dependence: 1.999 (CI 1.155 – 3.459), medication dependence: 1.679 (1.187 – 2.374), anxiety: 1.449 (CI 1.055 – 1.989), bipolar disorder: 2.836 (1.599 – 5.029), eating disorders: 0.906 (CI 0.634 – 1.294).

We have conducted a univariate analysis (Table 2) and a multivariate meta-regression (Table 3). In the univariate analysis we found at least one significant odds ratio in every covariate. For example, we found significant ORs indicating increasing prevalence rates for self-report symptoms/distress, several mental illness conditions, world regions Asia, and Middle East, survey start decades 1970s and 1990s, all survey end decades, study periods 6 to 10 years and 16 to 20 years and quality score 8 to 9 points.

According to the model selection procedure we dropped the 'start decade' variable from the final regression model. In the multivariate analysis we found a reduced number of significant moderator variables. Additionally, some variables showed declining Ratio of Odds Ratios (RORs) and estimates when compared to reference categories, while the univariate analyses suggested otherwise. Self-report symptoms/distress ORs indicated a significant increase in the univariate analyses whereas the other methodological approaches did not. In the multivariate analysis, however, we found a significant decreasing ROR and negative estimate for self-report symptoms/distress. Further significant RORs and negative estimates were found for illness conditions alcohol dependence and drug dependence (reference: general mental illness) and the end decade 2000s (reference: 1990s). Increasing significant RORs and positive estimates were found for the Middle East region (reference: Western Europe) and quality score 6 to 7 points (reference: 4 to 5 points). One predictor (mental illness condition 'distress') was dropped from the model by the statistics software due to redundancy. This happens in cases where there is an insufficient number of data points to estimate each coefficient.

Discussion

We have conducted a meta-analysis and a meta-regression on prevalence changes in adult mental illness since the 1970s. Overall, we found evidence of a small but significant increase over time (OR 1.18). This result is based on studies that are very heterogeneous in their characteristics and in their outcomes. While our funnel plot does not suggest that there is a 'small study effect' present as is known from trial meta-analyses, we cannot rule out a publication bias. Although prevalence studies are supposed to be less likely biased than intervention studies, it remains possible that some studies have not been published that, for example, have not found an increase of prevalence rates.

Before discussing our results against the background of previous research, several limitations of our analysis need to be acknowledged. Firstly, as quite often with global epidemiological analyses, the publications used in our data set are based overwhelmingly on samples in Western Europe and North America. Hence, firm conclusions on other world regions cannot be made due to a shortage of studies, sometimes with only one relevant publication that has met our inclusion criteria. Secondly, the coverage of mental illness conditions is unevenly distributed with depression and distress the most commonly surveyed conditions in the original studies. Again, some other conditions were covered by only one study which restricts any conclusions that can be drawn. Thirdly, we did not find any study on psychosis/schizophrenia that has been conducted using a repeated cross-sectional design as required by our inclusion criteria. Thus, there is no information available on this very important diagnostic group. Fourthly, we cannot make any claims on subgroups within each sample, e.g. in terms of gender or age, where different trends may have occurred. Previous reviews have shown that such subgroup variations exist [23,24]. Fifthly, as our analytical approach is focussed on the bigger picture of prevalence change for adult mental illness over time, we cannot rule out that there

are temporal fluctuations in terms of prevalence changes between the two time points that we used in our analysis. Again, previous reviews have shown that this is the case [23,24]. Sixthly, we cannot make any claims about developments in specific countries or regions that lead to contradictory results, e.g. during times of severe economic recession.

Additionally, we have to stress methodological issues inherent to meta-analysis and meta-regression in terms of identifying relevant moderator variables that are associated with the effect size. Meta-analysis and meta-regression have to deal with the same constraints as other statistical procedures, namely the problems of multiple comparisons and statistical power in regression analyses [42,43]. Simulation research has shown that the predictive power of mixed-effects meta-regression models, such as in our case, mainly relies on the number of studies and on the number of participants in the included studies. With more than 40 samples in the regression analysis, and with a comparatively high number of primary observations, we fulfil the basic requirements that are recommended in the methodological literature [44]. However, we have to acknowledge that our data were not sufficient to avoid the deletion of some variables during the regression analysis. Additionally, meta-regression analyses are prone to the risk of spurious and false positive findings [45]. In our meta-regression we found only one world region (Middle East) with a significantly positive estimate compared to the reference region of Western Europe. As this finding is based on only one study, we have to caution against any firm conclusion from this particular result. Finally, the variables in our analyses are heterogeneous in themselves across the included studies and we found some inconsistency when cross-tabulating world regions with mental illness conditions or other variables. However, we decided to keep the global perspective rather than excluding some regions with few available studies.

Keeping these limitations in mind and seen from a broader perspective, our results, using a new methodology, are in line with previous reviews and aggregate analyses. As outlined in the introduction, most such publications have not supported the public impression that mental illness prevalence is on the increase [18,20,23,24,46]. In addition, several meta-analyses on changes in anxiety and depression population mean scores over time have reported mixed results, questioning a clear tendency towards increasing anxiety and depression in western populations [47-49].

Finally, we would like to stress the similarity of our results with the latest GBD-report. As outlined in the introduction of this article, that report [26] and the related prevalence data (www.ghdx.healthdata.org) suggested a small increase in years lived with disability and illness prevalence over time. However, when age-standardization is applied the increase is no longer apparent, and some illnesses are on the decline. Our results also do indicate only a small increase. As our data cannot be standardized or adjusted to age-related demographics, we assume that the small increase in our study may also be related to population ageing or other demographic changes.

Beyond these previous reviews and aggregate analyses, our study is able to provide a more precise estimate of the likelihood of prevalence changes in mental illness for adults as we have only included studies utilizing an identical methodology on at least two time points in combination with a meta-analytical estimation of prevalence changes. In addition, further strengths are that we captured a very high number of primary observations and included a variety of methodological approaches for case ascertainment. We also accounted for the multilevel data structure and conducted a multivariate meta-regression of publication and study characteristics.

Concerning the meta-regression, we found relevant differences between the univariate and the multivariate approaches. Whether these differences are based on 'true' publication characteristics or on methodological artefacts, is difficult to determine. Methodologists caution against firm conclusions from multivariate meta-regressions [42]. We have to deal with a methodological dilemma:

on one hand, a study on specific mental health problems at a specific time in a particular country conducted with a high-quality methodology is not sufficient to generalize its results as they may be limited to this time and place. One the other hand, the multitude of factors that impact mental illness prevalences makes it very difficult to isolate specific characteristics that may be responsible for changing or non-changing prevalence rates.

Looking at concordant estimates, this suggests that prevalence changes in mental illness are only to a minor degree affected by the methodological approach and by the specific mental illness. Concordant estimates between the univariate and multivariate analyses suggest the following: prevalence changes are affected to some extent by the region where the study was conducted. The historical period may be of more importance with earlier decades showing higher prevalence changes although the length of the study period does not seem to be linearly associated to the prevalence changes. However, higher study quality is associated with identifying such changes.

Our main result of a small increase in mental illness prevalence is obviously at odds with the evidence of a tremendous increase in mental health care utilization especially in the developed countries. One reason for the increase in the number of treated persons may be success in closing the treatment gap between those in need and those already in treatment [50]. While this gap clearly exists from the perspective of conventional psychiatry, some experts have assumed that the increase of care provision should have reduced the prevalence of illness [4,25] – and this obviously has not been the case. However, the contrary claim that the increased provision of psychopharmacological treatment has led to an epidemic of mental disability is not supported by our results, either [51].

Given the extension of mental health care provision and the public impression of a mental health epidemic during the same period, further research is needed to analyse the drivers of both developments. Several reasons have been proposed in recent publications, e.g. the de-stigmatization of specific mental disorders or the increasing willingness of primary care professionals to address mental illness in clinical encounters [18,24,46]. In terms of utilization, another major driver might have been a sociocultural change that social scientists have called 'psychologization' [52], which involves the expansion of a "Therapy Culture" [53] into the general population. Alongside the common perception of recent massive social change resulting in an accelerating pace of everyday life, this therapy culture is assumed to be one important factor for a heightened willingness to report distress and to accept psychological and psychiatric treatment. The psychologization of everyday problems such as family conflicts or workplace problems may also have led to a perception of increased distress that for unknown reasons has not resulted in a large-scale increase in mental illness. Which combination of factors eventually leads to an increase of reported utilization rates remains difficult to determine and may be different in different countries.

We conclude from our data that the prevalence of adult mental illness has increased minimally in recent decades and we assume that this increase can be best explained by demographic changes as suggested by the GBD data. From a methodological perspective, we conclude that research on changes in mental illness prevalence is faced with a similar situation to that which is encountered when considering the difference between single trials and meta-analyses. A meta-analysis has the advantages of providing greater statistical precision, dealing with contradictory findings and estimating study heterogeneity. As we have seen in our analysis, it is also necessary to account for the non-independence of several publications that stem from the same data set. Thus, the question of whether mental illness prevalence is generally changing or not cannot reliably be answered by one study or even by a small number of studies. Furthermore, this calls into question any attempt to extrapolate from one disorder (e.g. depression) to mental illness in general. Like in the GBD data, we have seen in our results that different illness conditions may develop in varied ways with the prevalence of one illness condition increasing while others are decreasing.

In addition, the obvious differences between the univariate and the multivariate moderator analysis highlight the methodological issues related to the analysis of prevalence changes over time. The results of single studies may indicate a prevalence change in a specific region. However, the prevalence change may also be related to the choice of methodological approach, the illness condition, the timing of the start and end of the survey, the length of the survey period or the overall study quality and combinations of those study characteristics.

With our results and with the GBD results, we now have two different methodologies based on different data sources that suggest similar conclusions. From a current public health perspective, we can be rather confident that the overall global prevalence of mental illness has not dramatically increased in recent decades if it has at all. However, having found that there was no substantial increase in mental illness prevalence in recent decades, this does not indicate that mental illness should not be taken seriously. Nevertheless, the parallel trends of increasing mental health care utilization and stable prevalence rates suggests that the treatment gap is slowly closing in many countries.

Appendix: Global Burden of Disease prevalence rates – Permanent link

http://ghdx.healthdata.org/gbd-results-tool?params=gbd-api-2017-permalink/0b62acc85fbb00019b66a69face0b39d

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Figure 1: Flow-Chart according to PRISMA

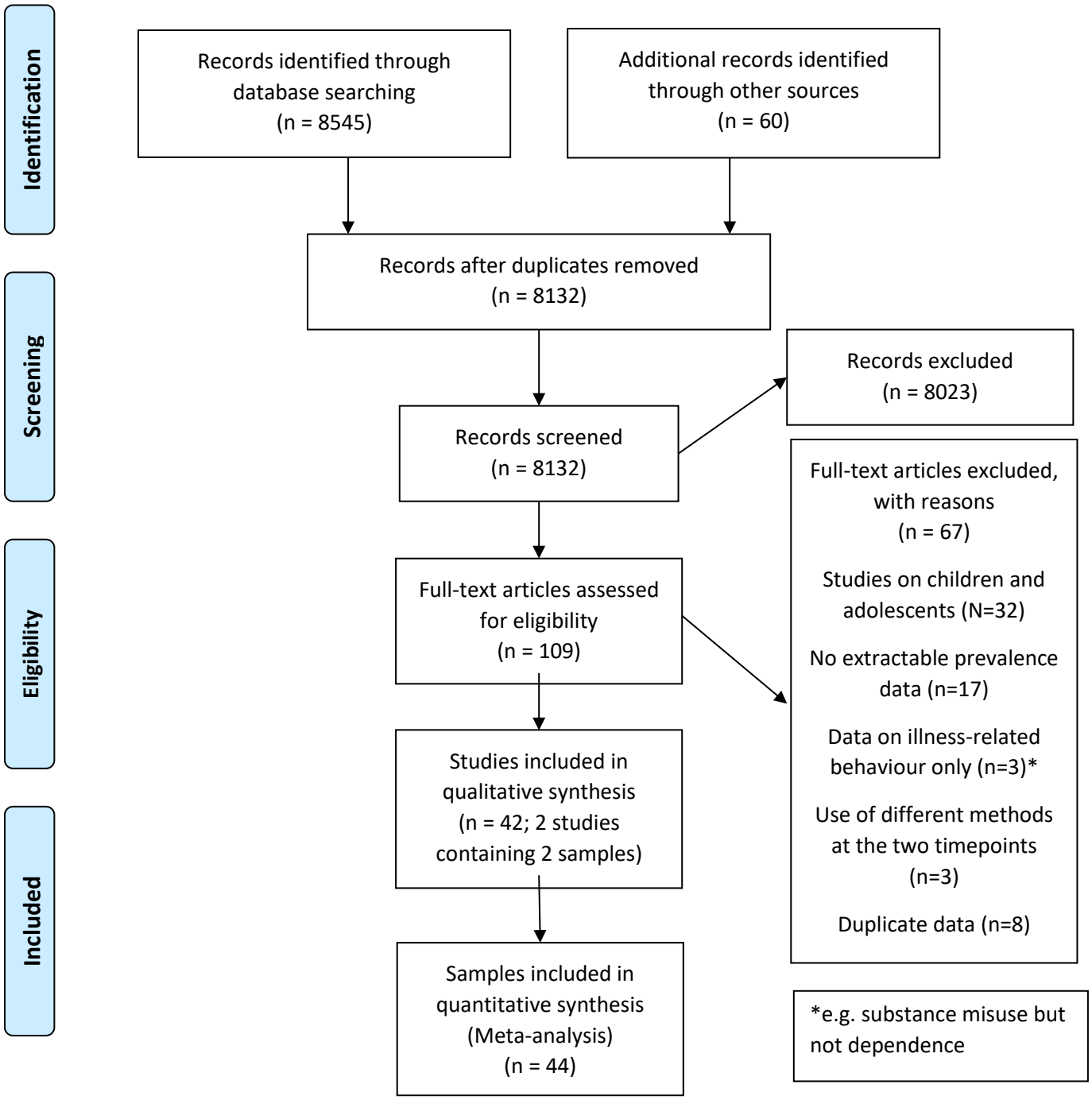
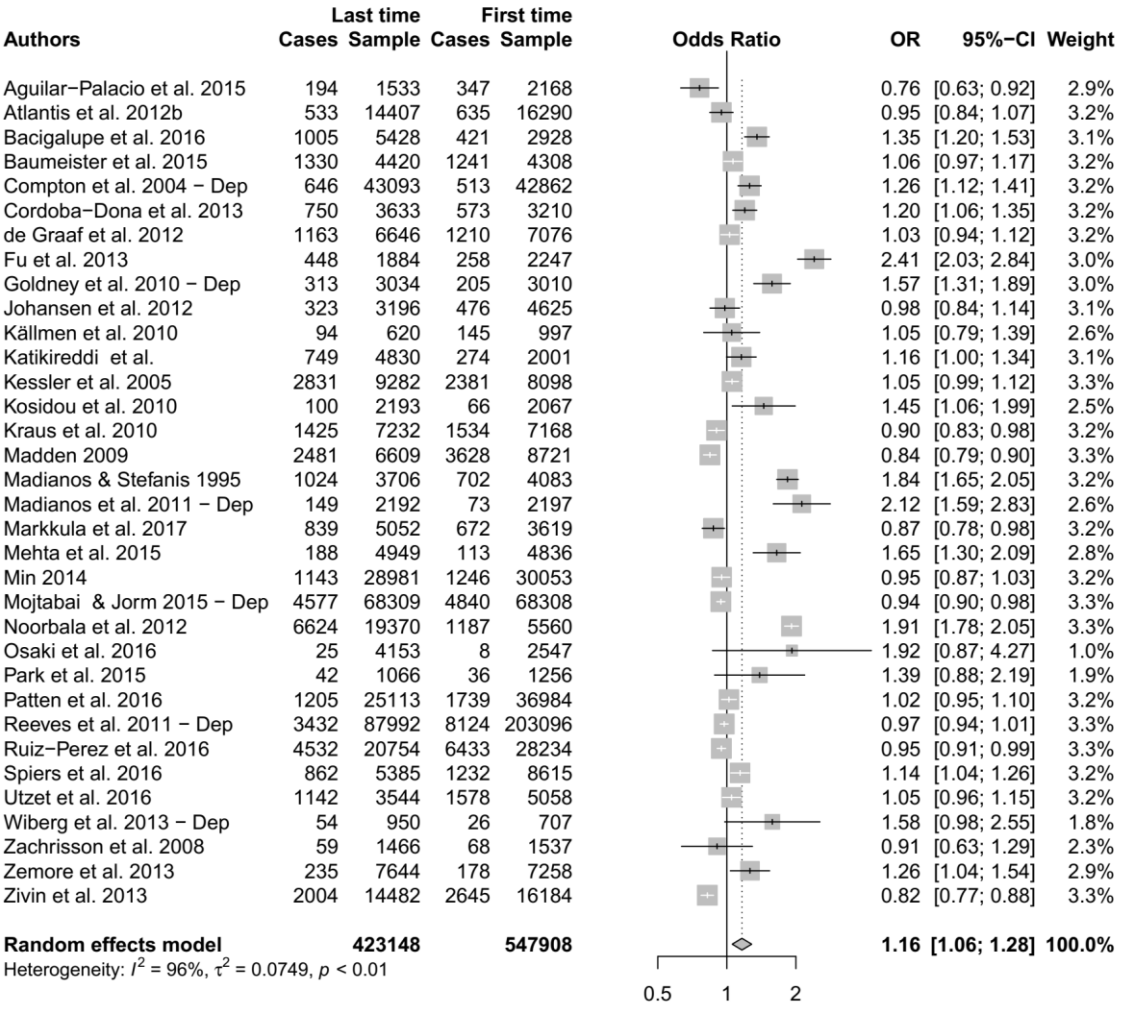


Figure 2: Forest Plot



Dep: Dependent data structure

Figure 3: Contour-enhanced Funnel Plot

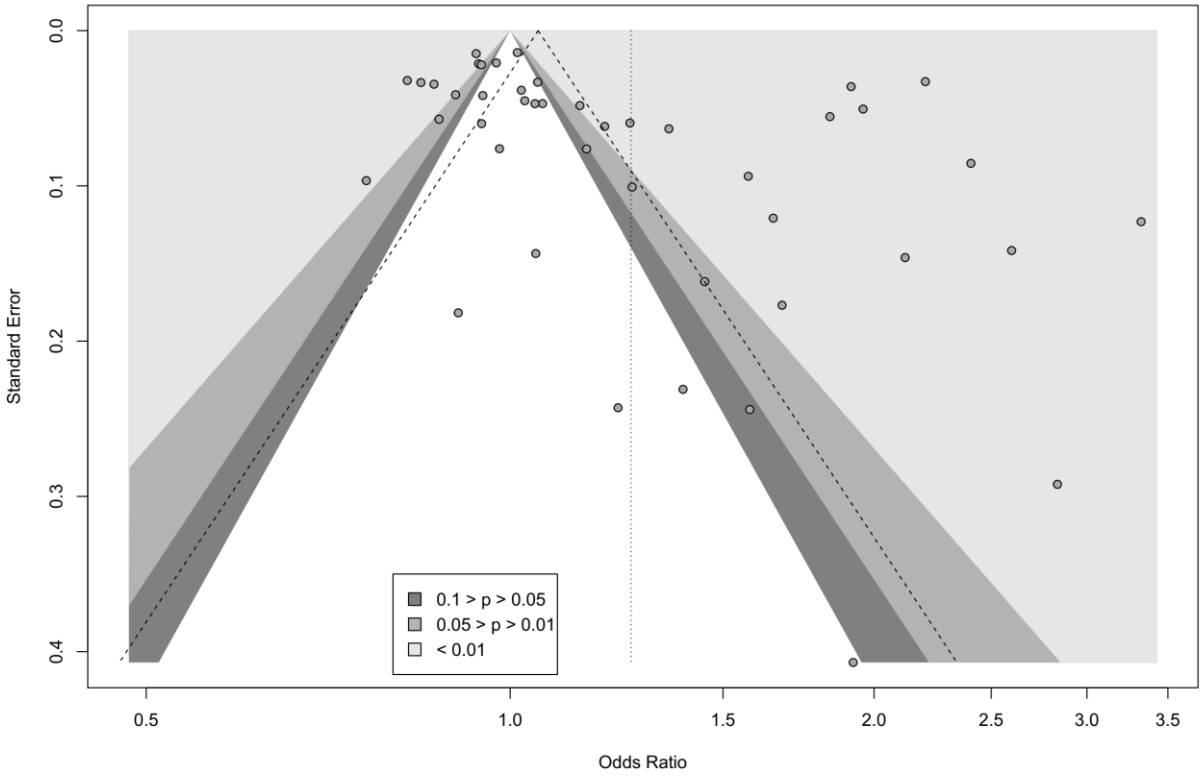


Table 1: Study Characteristics

Authors/ Publication Year	Country	First Time Point	Last Time Point	Dependent Effect Size (Numbers indicate other papers linked to the same study)	Cases First Time Point	Sample Size First Time Point	Cases Last Time Point	Sample Size Last Time Point	Mental Illness Condition	Prevalence First Time Point	Prevalence Last Time Point	Instrument	Methodological Approach	Quality Score
Aguilar-Palacio et al. 2015[54]	Spain	2006	2011	No	347	2168	194	1533	Distress	16.01	12.65	GHQ Cutoff	Distress	7
Atlantis et al. 2012[55]	Australia	1998	2008	No	635	16290	533	14407	Distress	3.90	3.70	Kessler-10	Distress	7
Bacigalupe et al. 2016[56]	Spain	1997	2013	No	421	2928	1005	5428	Distress	14.38	18.52	SF36-MHI	Distress	6
Baumeister et al. 2015[57]	Germany	1997	2008	No	1241	4308	1330	4420	Depression	28.81	30.09	M-CIDI	Clinical Interview	7
Compton et al. 2004[58]	United States of America	1991	2001	Yes 1	513	42862	646	43093	Drug dependence	1.20	1.50	Marihuana abuse/dependence (AUDADIS)	Clinical Interview	7
Compton et al. 2006[59]	United States of America	1991	2001	Yes 1	1427	42862	3042	43093	Depression	3.33	7.06	AUDADIS-IV (DSM-IV)	Clinical Interview	7
Cordoba-Dona et al. 2013[60]	Spain	2007	2011	No	573	3210	750	3633	Distress	17.85	20.64	SF12-MHI	Distress	7
de Graaf et al. 2012[61]	Netherlands	1996	2009	No	1210	7076	1163	6646	General	17.10	17.50	CIDI (DSM-IV)	Clinical Interview	6
Economou et al. 2012[62]	Greece	2008	2011	Yes 2	73	2197	185	2256	Depression	3.32	8.20	SCID, 1-month	Clinical Interview	9
Fu et al. 2013[63]	Taiwan	1990	2010	No	258	2247	448	1884	Distress	11.48	23.78	Chinese Health Questionnaire	Distress	8
Goldney et al. 2010[64]	Australia	1998	2008	Yes 3	205	3010	313	3034	Depression	6.81	10.32	PRIME-MD	Symptoms	9
Grant et al. 2004[65]	United States of America	1991	2001	Yes 1	1877	42862	1642	43093	Alcohol dependence	4.38	3.81	Alcohol dependence	Clinical Interview	6

Authors/ Publication Year	Country	First Time Point	Last Time Point	Dependent Effect Size (Numbers indicate other papers linked to the same study)	Cases First Time Point	Sample Size First Time Point	Cases Last Time Point	Sample Size Last Time Point	Mental Illness Condition	Prevalence First Time Point	Prevalence Last Time Point	Instrument	Methodological Approach	Quality Score
Hasin et al. 2015[66]	United States of America	2001	2012	Yes 1	646	43093	1051	36309	Drugs	1.50	2.89	Marihuana abuse/dependence	Clinical Interview	7
Johansen et al. 2012[67]	Norway	1998	2008	No	476	4625	323	3196	Distress	10.29	10.11	HSCL Cut off	Distress	6
Källmen et al. 2011[68]	Sweden	1997	2009	No	145	997	94	620	Alcohol dependence	14.54	15.16	AUDIT	Clinical Interview	6
Katikireddi et al. 2012[69]	United Kingdom	1991	2010	No	274	2001	749	4830	Distress	13.69	15.51	GHQ-Caseness	Distress	5
Kessler et al. 2005[70]	United States of America	1990	2001	No	2381	8098	2831	9282	General	29.40	30.50	DSM-IIIR/IV based	Clinical Interview	5
Kosidou et al. 2010[71]	Sweden	1997	2005	No	66	2067	100	2193	Anxiety	3.19	4.56	Severe anxiety (one question)	Symptoms	6
Kraus et al. 2010[72]	Germany	1997	2009	No	1534	7168	1425	7232	Alcohol dependence	21.40	19.70	AUDIT, Alcohol misuse	Clinical Interview	7
Madden 2009[73]	Ireland	1994	2000	No	3628	8721	2481	6609	Distress	41.60	37.54	GHQ caseness	Distress	6
Madianos & Stefanis 1992[74]	Greece	1978	1984	No	702	4083	1024	3706	Depression	17.19	27.63	CES-D	Symptoms	9
Madianos et al. 2011[75]	Greece	2008	2009	Yes 2	73	2197	149	2192	Depression	3.32	6.80	DSM-IV/SCID	Clinical Interview	8
Markkula et al. 2017[76]	Chile	2003	2010	No	672	3619	839	5052	Depression	18.57	16.61	CIDI	Clinical Interview	7
Martins et al. 2017[77]	United States of America	2001	2012	Yes 1	90	43093	251	36309	Heroin dependence	0.21	0.69	DSM-IV	Clinical Interview	6
McCabe et al. 2008[78]	United States of America	1991	2001	Yes 1	51	42862	86	43093	Medication	0.12	0.20	Prescription drug dependence/AUDADIS	Clinical Interview	7

Authors/ Publication Year	Country	First Time Point	Last Time Point	Dependent Effect Size (Numbers indicate other papers linked to the same study)	Cases First Time Point	Sample Size First Time Point	Cases Last Time Point	Sample Size Last Time Point	Mental Illness Condition	Prevalence First Time Point	Prevalence Last Time Point	Instrument	Methodological Approach	Quality Score
Mehta et al. 2015[79]	United States of America	2005	2011	No	113	4836	188	4949	Depression	2.34	3.80	PHQ-9	Symptoms	7
Min 2014[80]	United States of America	2005	2011	No	1246	30053	1143	28981	Distress	4.15	3.94	Kessler-6	Distress	4
Mojtabai & Jorm 2015[81]	United States of America	2005	2012	Yes 4	4840	68308	4577	68309	Depression	7.09	6.70	DSM-IV based	Clinical Interview	4
Noorbala et al. 2012[82]	Iran	1998	2007	No	1187	5560	6624	19370	Distress	21.35	34.20	GHQ-28	Distress	8
Center for Behavioral Health Statistics and Quality 2016[83]	United States of America	2008	2015	Yes 4	12166	68736	12185	68073	General	17.70	17.90	Mental Health Survey Study Clinical Interview	Clinical Interview	4
Osaki et al. 2016[84]	Japan	2003	2013	No	8	2547	25	4153	Alcohol dependence	0.31	0.60	ICD-10	Clinical Interview	7
Park et al. 2015[85]	South Korea	2001	2011	No	36	1256	42	1066	Depression	2.87	3.94	CIDI	Clinical Interview	7
Patten et al. 2016[86]	Canada	2002	2012	No	1739	36984	1205	25113	Depression	4.70	4.80	CIDI	Clinical Interview	8
Reeves et al. 2011 - 1[87]	United States of America	2006	2008	Yes 5	17284	198678	6970	85004	Depression	8.70	8.20	PHQ-8	Symptoms	4
Reeves et al. 2011 - 2[87]	United States of America	2007	2009	Yes 5	8124	203096	3432	87992	Distress	4.00	3.90	Kessler-6	Distress	4
Ruiz-Perez et al. 2016[88]	Spain	2006	2012	No	6433	28234	4532	20754	Distress	22.78	21.84	GHQ	Distress	8
Spiers et al. 2016[89]	United Kingdom	1993	2007	No	1232	8615	862	5385	General	14.30	16.01	CIS-R/ICD-10	Clinical Interview	8

Authors/ Publication Year	Country	First Time Point	Last Time Point	Dependent Effect Size (Numbers indicate other papers linked to the same study)	Cases First Time Point	Sample Size First Time Point	Cases Last Time Point	Sample Size Last Time Point	Mental Illness Condition	Prevalence First Time Point	Prevalence Last Time Point	Instrument	Methodological Approach	Quality Score
Utzet et al. 2016[90]	Spain	2005	2010	No	1578	5058	1142	3544	Distress	31.20	32.22	SF36-MHI	Distress	6
Wiberg et al. 2013 - 1[91]	Sweden	1976	2000	Yes 6	31	396	46	487	Depression	7.83	9.45	DSM-IV	Clinical Interview	5
Wiberg et al. 2013 - 2[91]	Sweden	1976	2005	Yes 6	26	707	54	950	Depression	3.68	5.68	Major depression,CPRS	Clinical Interview	5
Zachrisson et al. 2008[92]	Norway	1991	2004	No	68	1537	59	1466	Eating disorder	4.42	4.02	SED; DSM-IIIR/IV based	Clinical Interview	5
Zemore et al. 2013[93]	United States of America	2000	2010	No	178	7258	235	7644	Alcohol dependence	2.45	3.07	DSM-IV	Clinical Interview	6
Zivin et al. 2013[94]	United States of America	1998	2008	No	2645	16184	2004	14482	Depression	16.34	13.84	CESD elevated symptoms	Symptoms	8
Zutshi et al. 2011[95]	Australia	1998	2008	Yes 3	16	3010	45	3014	Bipolar disorder	0.53	1.49	PRIME-MD	Symptoms	8

Table 2: Univariate Meta-Analysis

Methodological approach	**Odds Ratio**	**95% Confidence Interval**
Clinical diagnoses – summarized [2] (k=4)	1.046	0.998 – 1.097
Clinical diagnoses – single [1] (k=20)	1.178	0.999 – 1.389
Self-report symptoms/distress [1] (k=20)	**1.196**	**1.025 – 1.398**
Mental illness condition		
General mental illness [2] (k = 4)	1.046	0.998 – 1.097
Distress [1] (k = 13)	1.126	0.946 – 1.340
Depression [1] (k = 15)	**1.298**	**1.062 – 1.587**
Alcohol dependence [1] (k = 5)	1.016	0.851 – 1.215
Drug dependence [1] (k = 3)	**1.999**	**1.155 – 3.459**
Medication dependence[2] (k = 1)	**1.679**	**1.187 – 2.374**
Anxiety [2] (k = 1)	**1.449**	**1.055 – 1.989**
Bipolar disorder [2] (k = 1)	**2.836**	**1.599 – 5.029**
Eating disorders [2] (k = 1)	0.906	0.634 – 1.294
World region		
Western Europe [1] (k = 20)	1.136	0.997 – 1.292
North America [1] (k = 16)	1.092	0.946 – 1.261
Oceania [1] (k = 3)	1.250	0.720 – 2.170
Asia [1] (k = 3)	**1.945**	**1.322 – 2.861**
Middle East[2] (k = 1)	**1.915**	**1.784 – 2.055**
South America[2] (k = 1)	**0.873**	**0.780 – 0.976**
Start decade		
1970s [1] (k = 3)	**1.678**	**1.298 – 1.343**
1990s [1] (k = 22)	**1.172**	**1.022 – 1.343**
2000s [1] (k = 19)	1.188	0.999 – 1.411
End decade		
1980s [2] (k = 1)	**1.839**	**1.650 – 2.050**
2000s [1] (k = 24)	**1.142**	**1.004 – 1.299**
2010s [1] (k = 19)	**1.272**	**1.070 – 1.514**
Study period		
1 to 5 years [1] (k = 5)	1.379	0.812 – 2.341
6 to 10 years [1] (k = 25)	**1.149**	**1.007 – 1.309**
11 to 15 years [1] (k = 9)	1.125	0.926 – 1.367
16 to 20 years [1] (k = 3)	**1.552**	**1.007 – 2.394**
21 and more years [1] (k = 2)	1.391	0.993 – 1.950
Quality score		
4 to 5 [1] (k = 10)	1.005	0.952 – 1.060
6 to 7 [1] (k = 23)	1.099	0.990 – 1.220
8 to 9 [1] (k = 11)	**1.451**	**1.113 – 1.893**

[1] Clustered analysis

[2] Non-clustered analysis

Bold: Statistically significant

Table 3: Multivariate Meta-Regression

	Ratio of Odds Ratio	95% Confidence Interval	Beta estimate	Standard error	Beta confidence interval	p-value
Methodological approach						
Clinical diagnoses – summarized [2] (k=4)	Reference					
Clinical diagnoses – single [1] (k=20)	0.968	0.902 - 1.039	-0.0325	0.0360	-0.1031 – 0.0381	0.3674
Self-report symptoms/distress [1] (k=20)	**0.664**	**0.466 - 0.946**	**-0.4098**	**0.1810**	**-0.7646 - -0.0550**	**0.0236**
Mental illness condition						
General mental illness [2] (k = 4)	Reference					
Distress [1] (k = 13)	Omitted due to redundancy[3]					
Depression [1] (k = 15)	0.964	0.917 - 1.013	-0.0366	0.0254	-0.0864 - 0.0133	0.1502
Alcohol dependence [1] (k = 5)	**0.390**	**0.351 - 0.433**	**-0.9426**	**0.0533**	**-1.0470 - -0.8381**	**<.0001**
Drug dependence [1] (k = 3)	**0.562**	**0.488 - 0.647**	**-0.5759**	**0.0719**	**-0.7168 - -0.4350**	**<.0001**
Medication dependence[2] (k = 1)	0.745	0.522 - 1.064	-0.2940	0.1816	-0.6500 - 0.0620	0.1053
Anxiety [2] (k = 1)	1.792	0.785 - 4.092	0.5834	0.4212	-0.2422 - 1.4089	0.1661
Bipolar disorder [2] (k = 1)	1.779	0.974 - 3.249	0.5758	0.3075	-0.0269 - 1.1785	0.0611
Eating disorders [2] (k = 1)	1.779	0.974 - 3.249	0.0566	0.4828	-0.8879 - 1.0029	0.9006
World region						
Western Europe [1] (k = 20)	Reference					
North America [1] (k = 16)	1.433	0.964 - 2.132	0.3601	0.2026	-0.0369 - 0.7572	0.0755
Oceania [1] (k = 3)	1.670	0.921 - 3.030	0.5129	0.3039	-0.0828 - 1.086	0.0915
Asia [1] (k = 3)	1.612	0.898 - 2.895	0.4776	0.2987	-0.1077 - 1.0630	0.1098
Middle East[2] (k = 1)	**2.831**	**1.252 - 6.400**	**1.0406**	**0.4126**	**0.2249 - 1.8563**	**0.0124**
South America[2] (k = 1)	0.614	0.273 - 1.382	-0.4872	0.4138	-1.2982 - 0.3238	0.2390
Start decade						
1970s [1] (k = 3)	Not selected due to model fit					

1990s [1] (k = 22)	Not selected due to model fit					
2000s [1] (k = 19)	Not selected due to model fit					
End decade						
1980s [2] (k = 1)	Reference					
2000s [1] (k = 24)	**0.355**	**0.156 - 0.805**	**-0.1036**	**0.4186**	**-1.8574 - -2163**	**0.0133**
2010s [1] (k = 19)	0.444	0.194 - 1.015	-0.8130	0.4222	-1.6406 - -0.0145	0.0542
Study period						
1 to 5 years [1] (k = 5)	Reference					
6 to 10 years [1] (k = 25)	0.633	0.394 - 1.015	-0.4578	0.2412	-0.9306 - 0.0150	0.0577
11 to 15 years [1] (k = 9)	0.633	0.394 - 1.015	-0.1740	0.2523	-0.6685 - 0.3206	0.4905
16 to 20 years [1] (k = 3)	1.076	0.569 - 2.036	0.0733	0.3254	-0.5644 – 0.7110	0.8217
21 and more years [1] (k = 2)	1.417	0.528 - 3.804	0.3845	0.5038	-0.6390 – 1.3360	0.4891
Quality score						
4 to 5 [1] (k = 10)	Reference					
6 to 7 [1] (k = 23)	**1.829**	**1.149 - 2.913**	**0.6038**	**0.2374**	**0.1385 - 1.0692**	**0.0110**
8 to 9 [1] (k = 11)	1.530	0.952 - 2.461	0.4255	0.2423	-0.0494 - 0.9005	0.0804
			Intercept 1.0878	0.5298	0.0494 - 2.1262	0.0400
			Test for Residual Heterogeneity: QE(df = 21) = 479.6122, p-value < .0001 Test of Moderators: QM(df = 22) = 472.8333, p-value < .0001			

[1] Clustered analysis

[2] Non-clustered analysis

[3] Omitted by the statistical software

Bold: Statistically significant