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Metaanalysis of Mood and Substance Use Disorders in Proximal Risk for Suicide Deaths

Kenneth R. Conner, PsyD, MPH, **Jeffrey A. Bridge, PhD**, **Dustin J. Davidson, BA, BS**, **Carly Pilcher, BS**, **David A. Brent, MD**

Kenneth R. Conner, University of Rochester Medical Center, Rochester, NY, USA; Jeffrey A. Bridge, Nationwide Children's Hospital, Columbus, OH and Ohio State University, Columbus, OH, USA; Dustin J. Davidson and Carly Pilcher, Nationwide Children's Hospital, Columbus, OH, USA; David A. Brent, University of Pittsburgh, Pittsburgh, PA, USA.

Abstract

Evidence for proximal risk factors for suicide is based on case–control psychological autopsy studies, with these reports showing that mood and substance use disorders are the most prevalent mental disorders among suicide decedents worldwide and are associated with marked risk. However, moderators of risk and the degree of risk associated with (nonalcohol) drug use disorder are unknown. A comprehensive search was used to identify 35 case–control psychological autopsy studies published worldwide over a 30-year period that were metaanalyzed using random effects models. Major depression, odds ratio (95% confidence interval) = 9.14 (5.53, 15.09), and drug use disorder, OR (95% CI) = 7.18 (3.22, 16.01), had large effect sizes, among other results. Risk estimates associated with major depression were greater in studies with a larger proportion of women and those conducted in Asia compared with other regions. There was no evidence of publication bias or that any one study had a disproportionate impact on findings. Risk for suicide associated with major depression appears to be moderated by sex and/or world region. Drug use disorder is a potent risk factor, illustrating the importance of assessing drug use in clinical risk assessment.

Worldwide, there are more than 800,000 suicide deaths annually, accounting for 50% of all violent deaths in men and 71% in women (World Health Organization, 2014). Although cohort studies have generated much of the evidence for distal risk factors for suicide (Franklin et al., 2017), data on *proximal* risk factors (i.e., present near time of death) is based primarily on case–control psychological autopsy studies. With this design, researchers interview proxy respondents of suicide decedents, most often family members, and gather comparable information on nonsuicide control subjects along with additional information obtained from records when available (e.g., medical records) for the purpose of making systematic comparisons between study groups (Conner et al., 2011, 2012).

Psychological autopsy research shows that mood disorders are the most common category of mental disorders among suicide decedents worldwide (Cavanagh, Carson, Sharpe, & Lawrie,

Address correspondence to Kenneth R. Conner, Department of Emergency Medicine, University of Rochester Medical Center, Box 655C, Rochester, NY 14642; kenneth_conner@urmc.rochester.edu.

2003). Illustrating their central importance in suicide, a metaanalysis concluded that 26.3% of suicides in males and 31.6% in females are “attributable” to a mood disorder, highest among mental disorders, based on a formula that considers both the high prevalence of mood disorders among suicide decedents and the substantially higher likelihood of a mood disorder in suicide cases compared to nonsuicide controls (Li, Page, Martin, & Taylor, 2011). Alcohol or other drug use disorders are the second most common category of mental disorder among suicide decedents (Cavanagh et al., 2003). Prior metaanalyses of case–control psychological autopsy studies have generated pooled estimates of risk for suicide associated with mood disorders and alcohol or drug use disorders (Arsenault-Lapierre, Kim, & Turecki, 2004; Cavanagh et al., 2003; Yoshimasu, Kiyohara, & Miyashita, 2008), but numerous studies with large sample sizes from different regions of the world have been conducted since these reports were published. A more recent metaanalysis by Cho, Na, Cho, Im, and Kang (2016) served to update the literature, but the inclusion criteria required an estimate of risk for any mental disorder, serving to exclude more targeted papers, with implications for results (see Discussion).

As well, prior metaanalyses did not determine whether mood disorders and alcohol or drug use disorders confer differing levels of risk across populations. Along these lines, it is well-established that there are age, sex, and regional differences in the prevalence of mood disorders and alcohol or drug use disorders among suicide decedents, with females generally more likely to have mood disorders compared to males, younger individuals more likely to have alcohol or drug use disorders compared to older individuals (Qin, 2011), and suicide decedents in China showing lower prevalence of depression and alcohol or drug use disorders compared to Western populations (Phillips et al., 2002). Furthermore, the metaanalysis by Cho et al. (2016) examined age, sex, and regional differences in the presence of any mental disorder (but not mood or substance use disorder per se) among suicide cases. Although these reports are useful, they are limited by the examination of suicide cases only, with the potential that results merely reflect underlying population distributions of these disorders as opposed to moderating influences of age and so forth in suicide risk. Addressing this topic will require analysis of case–control data and formal tests of moderating effects, yet, with rare exception (e.g., Conner, Beautrais, & Conwell, 2003), formal tests of moderation that produce statistically significant results in the case–control psychological autopsy research literature are rare, a limitation that can be overcome by combining the results of studies through metaanalysis. A metaanalysis by Li et al. (2011) examined risk for suicide associated with mood disorders and alcohol or drug use disorders using controlled reports that included a focus on moderating effects of sex, age, and region. However, the authors narrowed their search to studies that reported risk estimates for various diagnoses *and* one or more socio-economic variables (e.g., low occupational status), resulting in a restricted number of studies analyzed, with unclear generalizability to the broader case–control psychological autopsy literature.

A recent metaanalysis examined risk for suicide associated with alcohol use disorder, providing a pooled estimate, OR (95% CI) = 2.59 (1.95, 3.23) (Darvishi, Farhadi, Haghtalab, & Poorolajal, 2015). The authors also examined age and sex as moderators of the association between alcohol use disorder and suicide and did not find evidence of moderation. However, the analyses combined the results from studies using different study designs, including

cohort studies that may assess mental disorders years prior to suicide, making the relevance of the findings to proximal risk for suicide unclear. The metaanalysis by Cho et al. (2016) narrowed the focus to psychological autopsy research studies and reported risk estimates for any substance use disorder (i.e., alcohol or drug) and alcohol use disorder broadly defined. However, neither metaanalysis disentangled subcategories of alcohol use disorder, including alcohol abuse and alcohol dependence, or examined nonalcohol drug use disorders. These are critical gaps because case–control psychological autopsy research has been dominated by reports of alcohol use disorder alone or summary substance use disorders variables that combine alcohol and other drug use disorders, making the contribution of (nonalcohol) drug use disorders to risk unclear. Disentangling categories of alcohol use disorder is also needed because some reports suggest that alcohol dependence but not alcohol abuse is greater in suicide decedents compared to nonsuicide controls (Cheng, 1995; Foster, Gillespie, McClelland, & Patterson, 1999; Kolves, Varnik, Tooding, & Wasserman, 2006), which may be attributable to greater alcohol-related severity associated with alcohol dependence.

We conducted a metaanalysis of case–control psychological autopsy studies of suicide to provide updated estimates of risk associated with mood disorders and alcohol or drug use disorders; test the moderating effects of age, sex, and region on these variables; disentangle risk in diagnostic subcategories based on the idea that risk may vary as a function of illness severity; and generate novel proximal risk estimates for nonalcohol drug use disorders.

METHODS

Literature Search

Inclusion criteria were as follows: (1) case–control study design that included a suicide decedent group and a nonsuicide control group, living or dead; (2) descriptive data provided on one or more mood disorder(s) and/or alcohol or drug use disorders in suicide cases and controls and/or the results of adjusted or unadjusted comparisons that were sufficient to calculate an effect size with respect to these disorders; (3) in-person research interviews using a diagnostic instrument with proxy respondents of suicide decedents and with nonsuicide controls and/or proxy respondents of controls; and (4) examinations of all suicides in a given population and/or subgroups defined by age, sex, and/or geographic location but no other criteria (e.g., a study comparing a general population sample of suicides and controls ages 60 and over would be eligible). Exclusion criteria were as follows: (1) non-English reports; (2) nonsuicide studies (e.g., examinations of non-lethal suicide attempt); (3) subpopulations of cases defined other than by age, sex, or geographic location (e.g., hospital patients, prisoners); (4) ineligible study design (e.g., record linkage study); (5) results were unavailable to calculate an effect size for a mood disorder and/or alcohol or drug use disorder and suicide or such results were duplicative of other reports of the same sample; (6) papers published before 1985; and (7) non-peer-reviewed studies (e.g., book chapters).

The identification of reports for the metaanalysis is described in Figure 1. First, electronic searches of PubMed using the terms “case-control” [All Fields] AND “suicide” [All Fields]) OR “psychological autopsy” [All Fields] were used to identify reports between January 1, 1985, and May 9, 2016 (n = 1,559). Second, review of the abstracts and, when necessary, the

full reports of these studies were used to narrow the list to nonduplicative reports that met all eligibility criteria ($n = 32$). Third, the reference lists of the eligible papers, along with the reference sections of prior metaanalyses (Arsenault-Lapierre et al., 2004; Cavanagh et al., 2003; Darvishi et al., 2015; Yoshimasu et al., 2008) and comprehensive reviews (Conner et al., 2011, 2012), were used to identify three additional studies ($N = 35$).

Data Abstraction and Coding

Standardized data collection forms were developed for abstracting data (Lipsey & Wilson, 2001). The studies were coded by one of the authors (DJD) who reviewed the codes regularly with a second author (JAB) and, when there were questions, they consulted with a third author (KRC) to reach a consensus. The codes included: date of publication; region; country; sample size (cases, controls); participation rates (when available); age (mean, range); sex distribution; race/ethnic distribution when available; other demographic characteristics when available (e.g., education); nature of control group (e.g., community sample, injury decedents); instrument used to assess mental disorders; diagnostic system; and relevant results including descriptive, unadjusted, and adjusted findings.

Age, sex, and region were defined by mean age of cases (median age or age range used if mean age not available); proportion of male cases; and region of data collection including Asia, Australia or Oceania, Central America, Europe, and North America. Diagnoses of mood disorders and substance use disorders were used if they were based on one of the versions of the *Diagnostic and Statistical Manual* (e.g., American Psychiatric Association, 1994), *International Classification of Diseases* (e.g., World Health Organization, 1995), or if we determined that they were a reasonable proxy (e.g., substance misuse). Mood disorders included five categories: (1) mood disorder (broadest); (2) minor depression or dysthymic disorder; (3) major depression; (4) depression with psychosis; and (5) bipolar disorder. Alcohol and drug use disorders included five categories: (1) substance misuse or substance use disorder (substance use disorder) (broadest); (2) nonalcohol drug misuse or drug use disorder (drug use disorder); (3) alcohol abuse; (4) alcohol dependence; and (5) alcohol misuse or alcohol use disorder (alcohol use disorder). Data from separate reports of the same data set were included when they provided nonoverlapping results pertinent to the metaanalysis, including estimates for different diagnoses (e.g., Kolves, Sisask, et al., 2006; Kolves, Varnik, et al., 2006) or examinations of different age groups (e.g., Chan et al., 2009; Chiu et al., 2004). Methodological quality ratings were generated by one of the authors (KRC) using a 14-item rating scale (score range 0–18) that included 10 applicable items from a standard measure (Downs & Black, 1998) and four novel items created for the current study; for example, “What was the response rate for cases in the study?” ≥75% (scored 2), 50–74% (scored 1), ≤49% or unreported (scored 0).

Analyses

We obtained pooled estimates of the size of associations between mood disorders and alcohol or drug use disorders with suicide using random effects models (DerSimonian & Laird, 1986). We chose random effects models instead of fixed effects models in anticipation of heterogeneous effect sizes (Cooper, Hedges, & Valentine, 2009). Statistical analyses were performed using Comprehensive Metaanalyses version 2.2 (Biostat, Englewood,

NJ) and SPSS version 24 (SPSS Inc, Chicago, IL). Odds ratios and 95% confidence intervals (OR, 95% CI) generated in these models provided measures of effect size. As data allowed, we examined world region, sex, age, and methodological quality as moderators of risk associated with mood disorders, major depression, minor depression or dysthymia, substance use disorder, and alcohol use disorder; there were too few reports to examine moderating influences on other disorders. World region and age were categorical moderators of outcome. For continuous moderators, mixed effects metaregression was used to explore whether proportion of male cases and methodological quality influenced outcome. Continuous moderators that showed an association with outcome were dichotomized by median split and reexamined as categorical moderators. Heterogeneity of effect sizes was examined using the Cochran Q chi-square statistic ($p \leq .10$) and the I^2 statistic, a transformation of Q that indicates the percentage of variation in the effect size estimate attributable to heterogeneity rather than sampling error (Higgins & Thompson, 2002). Publication bias was assessed visually using funnel plots and quantitatively using an adjusted rank correlation test (Begg & Mazumdar, 1994) and a regression procedure to measure funnel plot asymmetry (Egger, Davey Smith, Schneider, & Minder, 1997). We performed leave-oneout analyses by iteratively deleting each study and calculating the resulting effect to determine whether any study unduly influenced pooled effect size estimates.

RESULTS

Eligible Studies

Characteristics of the 35 studies analyzed are listed in Table 1. Region of studies include Asia (n = 11), Australia or Oceania (n = 5), Central America (n = 1), Europe (n = 12), and North America (6). Age categories include adolescent and/or young adult (n = 10), mixed age (n = 19), and older adult (n = 6). Across all studies, the average proportion of male cases was 0.71 (standard deviation [SD] = 0.14). Quality ratings ranged from 4 to 17, with mean (SD) = 12.7 (3.4). The studies reported the results for the disorders examined in this review.

Main Effects

The primary results of the analyses are shown in Table 2. Mood disorder broadly defined and major depression showed the largest effect sizes in risk for suicide: mood disorder, OR (95% CI) = 14.34 (9.10, 22.57); major depression, OR (95% CI) = 9.14 (5.53, 15.09). The effect sizes for bipolar disorder, depression with psychosis, and minor depression or dysthymic disorder were statistically significant although smaller in magnitude, in the range of three- to fourfold risk. The results of the analyses of the various alcohol and drug use disorders are also shown in Table 2, with each disorder showing statistically significant results in the range of threefold risk for suicide and higher, with the highest risk estimate for drug use disorder, OR (95% CI) = 7.18 (3.22, 16.01). Significant heterogeneity across studies was noted for each disorder (I^2 range, 39%–80%), with the exception of depression with psychosis and bipolar disorder.

Moderator Analyses

There is evidence of a moderating effect of region on risk for suicide associated with mood disorder (Q_3 = 9.60, p = .022) and major depression (Q_2 = 7.63, p = .022), with studies conducted in Asia showing the highest pooled risk estimate for each of these disorders. However, the test for a moderating effect of region on risk for suicide associated with substance use disorder was nonsignificant (Q_3 = 4.98, p = .173). Also, risk for suicide associated with major depression was higher in studies with larger proportions of females (β= 4.48, Q_1 = 6.87, p = .009). Dichotomizing proportion of male cases by median split (≤ 0.70 vs. > .70) revealed significantly larger effect sizes (Q_1 = 3.97, p = .046) in studies where the proportion of male cases was ≤ .70 (OR = 15.34, 95% CI = 7.17–32.83) compared to studies with > .70 proportion of male cases (OR = 5.37, 95% CI = 2.67–10.80). Studies with higher quality ratings generated higher risk estimates associated with alcohol use disorder (p = .003) and drug use disorder (p < .001). There was a lack of evidence of moderating effects of region or gender on risk associated with other disorders, and we found no evidence of moderating effects of age.

Publication Bias and Leave-One-Out Analysis

Separate analyses of publication bias were conducted for each pooled estimate of risk of suicide associated with mood disorders and alcohol or drug use disorders. We did not find evidence of publication bias in any of the models based on visual inspection of the funnel plots, the adjusted rank correlation tests, and the regression intercept approach (data available on request). Sensitivity analyses did not suggest that any individual study unduly influenced the pooled risk estimates reported in Table 2 (data available on request).

DISCUSSION

Mood Disorders

The current metaanalysis of case–control psychological autopsy studies conducted worldwide over a 30-year period provided estimates of proximal risk for suicide associated with various mood and substance use disorders and tested moderators of risk. The risk estimate for major depression was significantly lower than that provided by Cho et al. (2016) which may be presumed to be attributable to the differing search strategies, with the current search uncovering a greater number of relevant reports (n = 19 vs. n = 12). Nonetheless, the risk estimate that we obtained for major depression is on the order of ninefold risk, underscoring that it is a potent risk factor. In contrast, the estimate of proximal risk for suicide associated with minor depression or dysthymia OR (95%) CI = 2.7 (1.5., 4.9) was similar to that provided by Cho et al., with the implication that nonsevere depression confers increased risk for suicide.

Tests of moderation suggest that mood disorder broadly defined and major depression are more potent proximal risk factors in studies conducted in Asia than other world regions. Interestingly, psychological autopsy studies conducted in Asia have generally shown that the percentage of suicide decedents with depressive symptoms or disorders is *lower* compared to Western reports (e.g., Phillips et al., 2002; Vijayakumar et al., 1999). However, it is critical to consider the generally very low prevalence of depressive illness in nonsuicide control

subjects in Asian studies and, as illustrated by the current analysis, when cases and controls from studies conducted in Asia are pooled and compared on major depression, it produces dramatic risk estimates. Tests of moderation also suggest that major depression is associated with greater increased risk for suicide in women than men (Table 3).

Alcohol and Drug Use Disorders

The study provides a novel estimate for proximal risk for suicide associated with nonalcohol drug use disorder, and the high-risk estimate, OR (95% CI) = 7.2 (3.2, 16.0), illustrates the importance of targeting drug abuse in suicide prevention efforts. Drug use disorders are heterogeneous, and prior research suggests that nonmedical use of opiates, cocaine, amphetamine, and other stimulants is associated with suicide (Degenhardt, Roxburgh, & Barker, 2005; Wilcox, Conner, & Caine, 2004). Unfortunately, information on specific drug use disorders is generally lacking in case–control psychological autopsy studies, making it unclear whether similar results would be obtained using this methodology. The risk estimates for alcohol use disorder broadly defined, alcohol abuse, and alcohol dependence are similar to one another, in the area of three- to four-fold risk. These results suggest that it would not represent a significant loss of information to use a unitary measure of alcohol use disorder in case–control psychological autopsy research studies, for example, as defined using current nosology (American Psychiatric Association, 2013). Finally, risk estimates did not differ by region or sex, unlike the results for mood disorder and major depression.

Effect Sizes

The effect sizes in the current study were generally higher than in Franklin et al.'s (2017) landmark metaanalysis of suicidal behavior. However, it is difficult to make head-to-head comparisons of effect sizes of postmortem case–control studies and cohort studies. Cohort studies of suicide deaths have had long lengths of follow-up, with potential that an assessed exposure (e.g., alcohol use disorder) is no longer an active problem at the time of death, among other problems of interpretation. Indeed, the median length to follow-up in Franklin and colleagues' metaanalysis was 6 years, with fewer than 1% of the effect sizes based on reassessments of 1 month or less, and approximately 29% based on follow-ups of 10 years or greater. The study also showed that effect sizes for suicide deaths were modestly reduced with length of follow-up, suggesting longer follow-ups may bias effect sizes downward. Recognizing the limitation of lengthy follow-ups, Franklin and colleagues called for the use of short follow-up periods in cohort studies moving forward. We agree, although the feasibility of such research for studies of suicide deaths is unclear given the low incidence rate. Case–control psychological autopsy studies are focused on the time period prior to death and a comparable exposure period in nonsuicide controls, increasing their capability to estimate risk associated with active symptoms. Accordingly, this study design seems better equipped to estimate proximal risk for suicide deaths associated with mental disorders (and other exposures). Finally, despite generally large effect sizes associated with mood and substance use disorders, suicide is a rare outcome that cannot be predicted with accuracy by clinicians, researchers, or other stakeholders, and the results of the current study do not change this bottom-line conclusion.

Limitations

There were limitations of the meta-analysis. Broad measures were used to create the moderators including age (mean age of study) and sex (proportion male in study). There were no data to allow for examination of several world regions. We examined proximal risk associated with alcohol and drug use disorders, but it was not possible to examine the role of *acute* use of alcohol (e.g., Branas, Richmond, Ten Have, & Wiebe, 2011) or *acute* use of various drugs in risk (e.g., Borges, Bagge, & Orozco, 2016) because such data are rarely available in case–control psychological autopsy studies. Females make up a greater percentage of suicide decedents in Asia, and in China in particular, compared to other regions (World Health Organization, 2014), complicating the interpretation of moderating effects of sex and region on risk for suicide associated with major depression that were identified in the current analyses. More specifically, in our metaanalysis, it was not possible to disentangle main or interactive effects of region and sex in the moderation analysis concerning major depression because all studies in Asia had a low proportion (≤ .70) of male cases. As well, the risk estimate for bipolar disorder, OR (95% CI) = 3.7 (1.6, 8.6), in the current study requires cautious interpretation in light of high risk associated with this disorder that has been reported in studies using prospective designs (Angst, Stassen, Clayton, & Angst, 2002; Chang, Chen, Yen, Chen, & Lee, 2012) and because of the potential for missing the diagnosis using retrospective methodology in individuals who killed themselves during the depressive (rather than manic) phase of the illness (Valtonen et al., 2008). Another limitation is that the available data did not make it feasible to estimate risk associated with mental disorder comorbidity (e.g., mood disorder plus substance use disorder). There are inherent limitations of case–control psychological autopsy research, including retrospective biases, primary reliance on proxy reports, and participation rates that vary widely (Conner et al., 2011, 2012). Future research on suicide, regardless of the methodology used, would be improved by examining acute use of alcohol, investigating social media content (e.g., to identify suicide-related communication before suicide), employing cutting-edge data analytic techniques, and gathering data on other domains of study (e.g., stressful life events, perceived belonging) with widely used and validated measures to allow for pooling such data for metaanalysis (Conner et al., 2011, 2012; Franklin et al., 2017; Luxton, June, & Fairall, 2012).

CONCLUSION

Merits of the current metaanalysis included the focus on a single study design (case–control) and outcome (suicide death) to aid interpretation; examination of the two most prevalent broad categories of mental disorders among suicide decedents worldwide (i.e., mood disorders, substance use disorders); use of several strategies to examine potential biases on results; and a focus on proximal risk for suicide that is uniquely suited for psychological autopsy research designs. In conclusion, the current metaanalysis provides new evidence that major depression and mood disorder may be an especially virulent proximal risk factor for suicide in Asian populations and that major depression may be a more potent risk factor in women. The pooled estimate concerning drug use disorders is novel and underscores the importance of targeting drug abuse in suicide prevention efforts. Results do not suggest differences in suicide risk associated with alcohol abuse and alcohol dependence, suggesting

that the change to simplify substance use disorder nomenclature in DSM-V does not come at a cost to estimations of suicide risk.

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REFERENCES

Almasi K, Belso N, Kapur N, Webb R, Cooper J, Hadley S, et al. (2009). Risk factors for suicide in Hungary: A case-control study. BMC Psychiatry, 9, 45. [PubMed: 19638202]

American Psychiatric Association. (1994). Diagnostic and statistical manual of mental disorders (4th ed.). Washington, DC: Author.

American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). Arlington, VA: Author.

Angst F, Stassen HH, Clayton PJ, & Angst J (2002). Mortality of patients with mood disorders: Follow-up over 34–38 years. Journal of Affective Disorders, 68, 167–181. [PubMed: 12063145]

Appleby L, Cooper J, Amos T, & Faragher B (1999). Psychological autopsy study of suicides by people aged under 35. British Journal of Psychiatry, 175, 168–174.

Arsenault-Lapierre G, Kim C, & Turecki G (2004). Psychiatric diagnoses in 3275 suicides: A meta-analysis. BMC Psychiatry, 4, 1–11. [PubMed: 15018628]

Beautrais AL (2001). Suicides and serious suicide attempts: Two populations or one? Psychological Medicine, 31, 837–845. [PubMed: 11459381]

Begg CB, & Mazumdar M (1994). Operating characteristics of a rank correlation test for publication bias. Biometrics, 50, 1088–1101. [PubMed: 7786990]

Borges G, Bagge CL, & Orozco R (2016). A literature review and meta-analyses of cannabis use and suicidality. Journal of Affective Disorders, 195, 63–74. [PubMed: 26872332]

Branas CC, Richmond TS, Ten Have TR, & Wiebe DJ (2011). Acute alcohol consumption, alcohol outlets, and gun suicide. Substance Use and Misuse, 46, 1592–1603. [PubMed: 21929327]

Brent DA, Baugher M, Bridge J, Chen T, & Chiappetta L (1999). Age- and sex-related risk factors for adolescent suicide. Journal of the American Academy of Child and Adolescent Psychiatry, 38, 1497–1505. [PubMed: 10596249]

Brent DA, Perper JA, Moritz G, Allman C, Friend A, Roth C, et al. (1993). Psychiatric risk factors for adolescent suicide: A case-control study. Journal of the American Academy of Child and Adolescent Psychiatry, 32, 521–529. [PubMed: 8496115]

Cavanagh JTO, Carson AJ, Sharpe M, & Lawrie SM (2003). Psychological autopsy studies of suicide: A systematic review. Psychological Medicine, 33, 395–405. [PubMed: 12701661]

Chan SS, Chiu HF, Chen EY, Chan WS, Wong PW, Chan CL, et al. (2009). Population-attributable risk of suicide conferred by axis I psychiatric diagnoses in a Hong Kong Chinese population. Psychiatric Services, 60, 1135–1138. [PubMed: 19648205]

Chang JC, Chen HH, Yen AM, Chen SL, & Lee CS (2012). Survival of bipolar depression, other type of depression and comorbid ailments: Ten-year longitudinal follow-up of 10,922 Taiwanese patients with depressive disorders. Journal of Psychiatric Research, 46, 1442–1448. [PubMed: 22868046]

Chen EYH, Chan WSC, Wong PWC, Chan SSM, Chan CLW, Law YW, et al. (2006). Suicide in Hong Kong: A case-control psychological autopsy study. Psychological Medicine, 36, 815–825. [PubMed: 16704748]

Cheng AT (1995). Mental illness and suicide: A case-control study in east Taiwan. Archives of General Psychiatry, 52, 594–603. [PubMed: 7598636]

Cheng AT, Chen TH, Chen CC, & Jenkins R (2000). Psychosocial and psychiatric risk factors for suicide: Case-control psychological autopsy study. British Journal of Psychiatry, 177, 360–365.

Chiu HF, Yip PS, Chi I, Chan S, Tsoh J, Kwan CW, et al. (2004). Elderly suicide in Hong Kong: A case-controlled psychological autopsy study. Acta Psychiatrica Scandinavica, 109, 299–305. [PubMed: 15008804]

Cho S-E, Na K-S, Cho S-J, Im J-S, & Kang S-G (2016). Geographical and temporal variations in the prevalence of mental disorders in suicide: Systematic review and meta-analysis. Journal of Affective Disorders, 190, 704–713. [PubMed: 26600412]

Conner KR, Beautrais AL, Brent DA, Conwell Y, Phillips MR, & Schneider B (2011). The next generation of psychological autopsy studies. Part I. Interview content. Suicide and Life-Threatening Behavior, 41, 594–613. [PubMed: 22050639]

Conner KR, Beautrais AL, Brent DA, Conwell Y, Phillips MR, & Schneider B (2012). The next generation of psychological autopsy studies. Part 2. Interview procedures. Suicide and Life-Threatening Behavior, 42, 86–103. [PubMed: 22288728]

Conner KR, Beautrais AL, & Conwell Y (2003). Moderators of the relationship between alcohol dependence and suicide and medically serious suicide attempts: Analyses of Canterbury Suicide Project data. Alcoholism, Clinical and Experimental Research, 27, 1156–1161.

Conwell Y, Duberstein PR, Hirsch JK, Conner KR, Eberly S, & Caine ED (2010). Health status and suicide in the second half of life. International Journal of Geriatric Psychiatry, 25, 371–379. [PubMed: 19582758]

Cooper HM, Hedges LV, & Valentine JC (2009). The handbook of research synthesis and meta-analysis (2nd ed.). New York: Russell Sage Foundation.

Darvishi N, Farhadi M, Haghtalab T, & Poorolajal J (2015). Alcohol-related risk of suicidal ideation, suicide attempt, and completed suicide. PLoS ONE, 10, e0126870. [PubMed: 25993344]

De Leo D, Draper BM, Snowdon J, & Kõlves K (2013a). Contacts with health professionals before suicide: Missed opportunities for prevention? Comprehensive Psychiatry, 54, 1117–1123. [PubMed: 23768696]

De Leo D, Draper BM, Snowdon J, & Kõlves K (2013b). Suicides in older adults: A case-control psychological autopsy study in Australia. Journal of Psychiatric Research, 47, 980–988. [PubMed: 23522934]

Degenhardt L, Roxburgh A, & Barker B (2005). Underlying causes of cocaine, amphetamine and opioid related deaths in Australia. Journal of Clinical Forensic Medicine, 12, 187–195. [PubMed: 16054006]

DerSimonian R, & Laird N (1986). Meta-analysis in clinical trials. Controlled Clinical Trials, 7, 177–188. [PubMed: 3802833]

Downs SH, & Black N (1998). The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. Journal of Epidemiology and Community Health, 52, 377–384. [PubMed: 9764259]

Egger M, Davey Smith G, Schneider M, & Minder C (1997). Bias in meta-analysis detected by a simple, graphical test. BMJ, 315, 629–634. [PubMed: 9310563]

Foster T, Gillespie K, McClelland R, & Patterson R (1999). Risk factors for suicide independent of DSM-III-R Axis I disorder. British Journal of Psychiatry, 175, 175–179.

Franklin JC, Ribeiro JD, Fox KR, Bentley KH, Kleiman EM, Huang X, et al. (2017). Risk factors for suicidal thoughts and behaviors: A meta-analysis of 50 years of research. Psychological Bulletin, 143, 187–232 10.1037/bul0000084 [PubMed: 27841450]

Freuchen A, Kjelsberg E, Lundervold AJ, & Groholt B (2012). Differences between children and adolescents who commit suicide and their peers: A psychological autopsy study of suicide victims compared to accident victims and a community sample. Child and Adolescent Psychiatry and Mental Health, 6, 1. [PubMed: 22216948]

Harwood D, Hawton K, Hope T, & Jacoby R (2001). Psychiatric disorder and personality factors associated with suicide in older people: A descriptive and case-control study. International Journal of Geriatric Psychiatry, 16, 155–165. [PubMed: 11241720]

Higgins JPT, & Thompson SG (2002). Quantifying heterogeneity in a meta-analysis. Statistics in Medicine, 21, 1539–1558. [PubMed: 12111919]

Khan MM, Mahmud S, Karim MS, Zaman M, & Prince M (2008). Case-control study of suicide in Karachi, Pakistan. British Journal of Psychiatry, 193, 402–405.

Kim CD, Lesage A, Seguin M, Chawky N, Vanier C, Lipp O, et al. (2003). Patterns of co-morbidity in male suicide completers. Psychological Medicine, 33, 1299–1309. [PubMed: 14580083]

Kolves K, Sisask M, Anion L, Samm A, & Värnik A (2006). Factors predicting suicide among Russians in Estonia in comparison with Estonians: Case-control study. Croatian Medical Journal, 47, 869–877. [PubMed: 17171808]

Kolves K, Varnik A, Tooding LM, & Wasserman D (2006). The role of alcohol in suicide: A case-control psychological autopsy study. Psychological Medicine, 36, 923–930. [PubMed: 16650347]

Li Z, Page A, Martin G, & Taylor R (2011). Attributable risk of psychiatric and socio-economic factors for suicide from individual-level, population-based studies: A systematic review. Social Science & Medicine, 72, 608–616. [PubMed: 21211874]

Lipsey MW, & Wilson DB (2001). Practical meta-analysis. Thousand Oaks, CA: Sage.

Luxton DD, June JD, & Fairall JM (2012). Social media and suicide: A public health perspective. American Journal of Public Health, 102, S195–S200. [PubMed: 22401525]

Manoranjitham SD, Rajkumar AP, Thangadurai P, Prasad J, Jayakaran R, & Jacob KS (2010). Risk factors for suicide in rural south India. British Journal of Psychiatry, 196, 26–30.

Page A, Morrell S, Hobbs C, Carter G, Dudley M, Duflou J, et al. (2014). Suicide in young adults: Psychiatric and socio-economic factors from a case-control study. BMC Psychiatry, 14, 68. [PubMed: 24597482]

Palacio C, García J, Diago J, Zapata C, Lopez G, Ortiz J, et al. (2007). Identification of suicide risk factors in Medellín, Colombia: A case-control study of psychological autopsy in a developing country. Archives of Suicide Research, 11, 297–308. [PubMed: 17558615]

Phillips MR, Yang G, Zhang Y, Wang L, Ji H, & Zhou M (2002). Risk factors for suicide in China: A national case-control psychological autopsy study. The Lancet, 360, 1728–1736.

Préville M, Hébert R, Boyer R, Bravo G, & Seguin M (2005). Physical health and mental disorder in elderly suicide: A case-control study. Aging and Mental Health, 9, 576–584. [PubMed: 16214706]

Qin P (2011). The impact of psychiatric illness on suicide: Differences by diagnosis of disorders and by sex and age of subjects. Journal of Psychiatric Research, 45, 1445–1452. [PubMed: 21722920]

Renaud J, Berlim MT, McGirr A, Tousignant M, & Turecki G (2008). Current psychiatric morbidity, aggression/impulsivity, and personality dimensions in child and adolescent suicide: A case-control study. Journal of Affective Disorders, 105, 221–228. [PubMed: 17568682]

Schneider B, Wetterling T, Sargk D, Schneider F, Schnabel A, Maurer K, et al. (2006). Axis I disorders and personality disorders as risk factors for suicide. European Archives of Psychiatry and Clinical Neuroscience, 256, 17–27. [PubMed: 16133739]

Shaffer D, Gould MS, Fisher P, Trautman P, Moreau D, Kleinman M, et al. (1996). Psychiatric diagnosis in child and adolescent suicide. Archives of General Psychiatry, 53, 339–348. [PubMed: 8634012]

Shafii M, SteltzLenarsky J, Derrick AM, & Beckner C (1988). Comorbidity of mental disorders in the post-mortem diagnosis of completed suicide in children and adolescents. Journal of Affective Disorders, 15, 227–233. [PubMed: 2975295]

Tong Y, & Phillips MR (2010). Cohort-specific risk of suicide for different mental disorders in China. British Journal of Psychiatry, 196, 467–473.

Valtonen HM, Suominen K, Haukka J, Mantere O, Leppamaki S, Arvilommi P, et al. (2008). Differences in incidence of suicide attempts during phases of bipolar I and bipolar II disorders. Bipolar Disorders, 10, 588–596. [PubMed: 18657243]

Vijayakumar L, & Rajkumar S (1999). Are risk factors for suicide universal? A case-control study in India. Acta Pscyhiatrica Scandinavica, 99, 407–411.

Waern M (2003). Alcohol dependence and misuse in elderly suicides. Alcohol and Alcoholism, 38, 249–254. [PubMed: 12711660]

Waern M, Runeson BS, Allebeck P, Beskow J, Rubenowitz E, Skoog I, et al. (2002). Mental disorder in elderly suicides: A case-control study. American Journal of Psychiatry, 159, 450–455.

Wilcox HC, Conner KR, & Caine ED (2004). Association of alcohol and drug use disorders and completed suicide: An empirical review of cohort studies. Drug and Alcohol Dependence, 76(Suppl), S11–S19. [PubMed: 15555812]

World Health Organization. (1995). International Classification of Diseases, ninth revision, clinical modification (ICD-9-CM). Los Angeles, CA: Practice Management Information Corporation and World Health Organization.

World Health Organization. (2014). Preventing suicide: A global imperative. Geneva: Author. RetrievedOctober 29, 2016, from www.who.int/mental_health/suicide-prevention/exe_summary_english.pdf.

Yoshimasu K, Kiyohara C, Miyashita K, & Stress Research Group of the Japanese Society for Hygiene. (2008). Suicidal risk factors and completed suicide: Meta-analyses based on psychological autopsy studies. Environmental Health and Preventive Medicine, 13, 243–256. [PubMed: 19568911]

Zhang J, Xiao S, & Zhou L (2010). Mental disorders and suicide among young rural Chinese: A case-control psychological autopsy study. American Journal of Psychiatry, 167, 773–781.

Zonda T (2006). One-hundred cases of suicide in Budapest: A case-controlled psychological autopsy study. Crisis, 27, 125–129. [PubMed: 17091822]

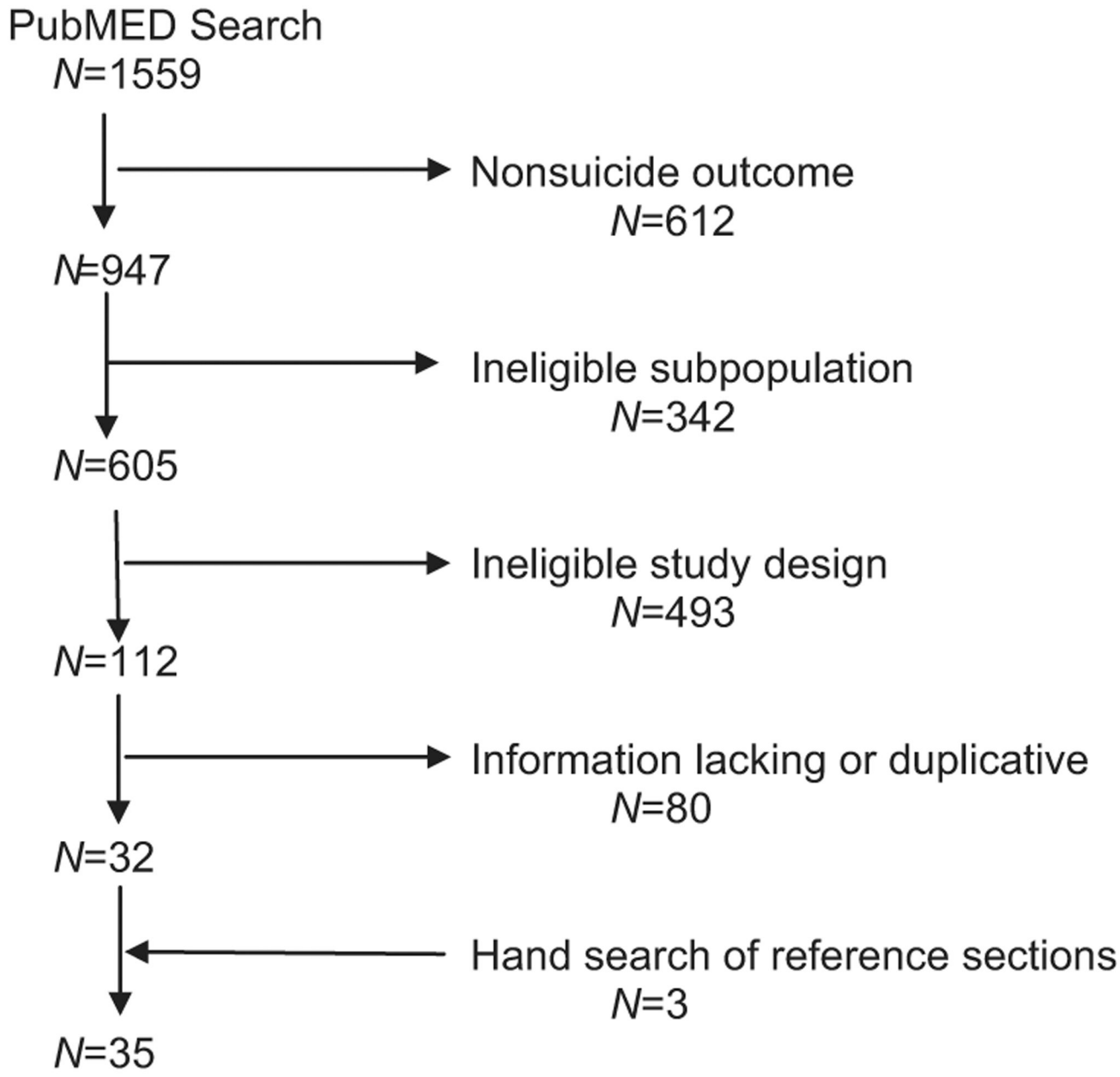

Figure 1.
Selection of studies for metaanalysis.

TABLE 1

Description of Reports Analyzed

Report	*N*	Region	Age category	% Male (cases)	Quality rating	Diagnoses examined
1. Almasi et al. (2009)	194	Europe	Mixed	81	16	Mood disorder, minor depression, SUD
2. Appleby, Cooper, Amos, and Faragher (1999)	84	Europe	Adolescent/young adult	81	8	SUD
3. Beautrais (2001)	202	Australia/Oceania	Mixed	78	16	Mood disorder, SUD
4. Brent, Baugher, Bridge, Chen, and Chiappetta (1999)	140	North America	Adolescent/young adult	85	16	Mood disorder, SUD
5. Brent et al. (1993)	67	North America	Adolescent/young adult	85	13	Major depression, drug use disorder, AUD
6. Chan et al. (2009)	150	Asia	Mixed	64	9	Major depression
7. Chen et al. (2006)	150	Asia	Mixed	64	9	Mood disorder
8. Cheng (1995)	117	Asia	Mixed	62	13	Minor depression, alcohol abuse, alcohol dependence
9. Cheng, Chen, Chen, and Jenkins (2000)	117	Asia	Mixed	62	14	Major depression, SUD
10. Chiu et al. (2004)	70	Asia	Older adult	46	8	Mood disorder, minor depression, major depression, alcohol dependence
11. Conner et al. (2003)	193	Australia/Oceania	Mixed	77	16	Drug use disorder, alcohol dependence
12. Conwell et al. (2010)	86	North America	Older adult	73	15	Mood disorder, major depression, SUD, AUD
13. De Leo, Draper, Snowdon, and Kõlves (2013a)	84	Australia/Oceania	Mixed	85	13	Mood disorder, SUD
14. De Leo, Draper, Snowdon, and Kõlves (2013b)	261	Australia/Oceania	Mixed, Older adult	75	14	Major depression, bipolar disorder, AUD
15. Foster et al. (1999)	117	Europe	Mixed	NR	14	Mood disorder, major depression, SUD, alcohol abuse, alcohol dependence, AUD
16. Freuchen, Kjelsberg, Lundervold, and Groholt (2012)	41	Europe	Adolescent/young adult	71	12	Mood disorder, minor depression
17. Harwood, Hawton, Hope, and Jacoby (2001)	54	Europe	Older adult	41	6	Mood disorder, SUD
18. Khan, Mahmud, Karim, Zaman, and Prince (2008)	100	Asia	Mixed	83	14	SUD
19. Kim et al. (2003)	115	Asia	Mixed	100	11	Major depression, bipolar disorder, drug use disorder, alcohol abuse, alcohol dependence
20. Kolves, Varnik, et al. (2006)	427	Europe	Mixed	80	15	Alcohol abuse, alcohol dependence
21. Kolves, Sisask, et al. (2006)	419	Europe	Mixed	80	15	SUD
22. Manoranjitham et al. (2010)	100	Asia	Mixed	59	14	Minor depression, major depression, alcohol dependence
23. Page et al. (2014)	84	Australia/Oceania	Adolescent/young adult	85	12	Mood disorder, major depression, SUD
24. Palacio et al. (2007)	108	Central America	Mixed	81	12	Minor depression, major depression, SUD

Report	*N*	Region	Age category	% Male (cases)	Quality rating	Diagnoses examined
25. Préville, Hébert, Boyer, Bravo, and Seguin (2005)	95	Europe	Older adult	75	13	Major depression, alcohol abuse, alcohol dependence
26. Renaud, Berlim, McGirr, Tousignant, and Turecki (2008)	55	North America	Adolescent/young adult	78	8	Mood disorder, minor depression, bipolar disorder, SUD, drug use disorder, AUD
27. Schneider et al. (2006)	163	Europe	Mixed	64	13	Mood disorder, minor depression, major depression, bipolar disorder, SUD, AUD
28. Shaffer et al. (1996)	120	North America	Adolescent/young adult	79	16	Mood disorder, major depression, bipolar disorder, SUD, drug use disorder, AUD
29. Shafii, SteltzLenarsky, Derrick, and Beckner (1988)	21	North America	Adolescent/young adult	91	8	Mood disorder, minor depression, major depression, SUD
30. Tong and Phillips (2010)	895	Asia	Mixed	51	17	Mood disorder, SUD
31. Vijayakumar et al. (1999)	100	Asia	Mixed	55	17	Minor depression, major depression, bipolar disorder, drug use disorder, AUD
32. Waern et al. (2002)	85	Europe	Older adult	54	16	Mood disorder, minor depression, major depression, bipolar disorder, SUD
33. Waern (2003)	88	Europe	Adolescent/young adult	56	16	AUD
34. Zhang, Xiao, and Zhou (2010)	392	Asia	Adolescent/young adult	55	11	Mood disorder, minor depression, major depression, bipolar disorder, SUD, drug use disorder, AUD
35. Zonda (2006)	100	Europe	Mixed	67	4	Major depression, drug use disorder, AUD

AUD, alcohol use disorder; SUD, substance use disorder; NR, not reported.

TABLE 2

Risk for Suicide Associated with Mood and Alcohol and Drug Use Disorders

						Heterogeneity		
Disorder	***N* of studies**	**OR**	**95% CI lower**	**95% CI upper**	***p* Value**	**Q_{df} Within**	***p* Value**	**Variance explained, %**
Mood disorder	18	14.34	9.10	22.57	<.001	77.9_{17}	<.001	78
Minor depression	12	2.73	1.53	4.85	.001	18.1_{11}	.08	39
Major depression	19	9.14	5.53	15.09	<.001	72.5_{18}	<.001	75
Depression with psychosis	3	3.37	1.01	11.24	.048	0.6_{2}	.73	0
Bipolar disorder	8	3.70	1.59	8.61	.002	9.6_{7}	.22	27
Substance use disorder	20	4.09	3.10	5.40	<.001	40.7_{19}	.003	53
Drug use disorder	8	7.18	3.22	16.01	<.001	13.6_{7}	.06	49
Alcohol abuse	5	3.90	1.62	9.38	.002	9.1_{4}	.06	56
Alcohol dependence	8	4.40	2.55	7.59	<.001	21.5_{7}	.003	67
Alcohol use disorder	11	3.68	1.99	6.82	<.001	49.4_{10}	<.001	80

Note. All results based on random effects models.

OR, odds ratio; CI, confidence interval; df, degrees of freedom.

TABLE 3

Region-Grouped Risk for Suicide Associated with Mood Disorder, Major Depression, and Substance Use Disorder

							Heterogeneity			Effect of Region	
Disorder	**Region**[a]	***N* of studies**	**OR**	**95% CI lower**	**95% CI upper**	***p* Value**	**Q_{df} Within**	***p* Value**	**Variance explained, %**	**Q_{df} Between**	***p* Value**
Mood disorder	Asia	4	28.61	14.91	54.92	<.001	8.3_3	.04	64	9.60_3	.022[b]
	Australia/Oceania	3	6.90	3.50	13.61	<.001	5.33_2	.07	62		
	Europe	6	10.62	4.50	25.09	<.001	25.13_5	<.001	80		
	North America	5	17.32	9.42	31.85	<.001	3.79_4	.44	0		
Major depression[c]	Asia	6	26.87	15.58	46.36	<.001	2.3_5	.80	0	7.63_2	.022[d]
	Europe	4	7.95	3.30	19.16	<.001	14.5_3	.002	79		
	North America	6	7.68	2.60	22.70	<.001	21.0_5	.001	76		
Substance use disorder	Asia	4	3.35	2.00	5.61	<.001	2.68_2	.26	25	4.98_3	.173
	Australia/Oceania	3	2.64	1.35	5.14	.004	6.76_2	.03	70		
	Europe	7	6.54	3.76	11.39	<.001	16.22_6	.01	63		
	North America	5	3.97	1.99	7.90	<.001	5.48_4	.24	27		

OR, odds ratio; CI, confidence interval; df, degrees of freedom.

[a] Random effects model used to combine studies within each region.

[b] Pairwise comparisons: Asia vs. Australia/Oceania, $Q_1 = 8.77$, $p = .003$; Asia vs. Europe, $Q_1 = 3.24$, $p = .072$; Asia vs. North America, $Q_1 = 1.22$, $p = .270$; Australia/Oceania vs. Europe, $Q_1 = 0.60$, $p = .44$; Australia/Oceania vs. North America, $Q_1 = 3.91$, $p = .048$; Europe vs. North America, $Q_1 = 0.83$, $p = .36$.

[c] Australia/Oceania and Central America were excluded from analyses because there were <3 studies within each region.

[d] Pairwise comparisons: Asia vs. Europe, $Q_1 = 5.32$, $p = .021$; Asia vs. North America, $Q_1 = 4.09$, $p = .043$; Europe vs. North America, $Q_1 = 0.00$, $p = .96$.