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Review article

The association between mental disorders and suicide: A systematic review and meta-analysis of record linkage studies

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ABSTRACT

Background: There has long been debate about the extent to which mental disorders contribute to suicide. We aimed to examine the evidence on the contribution of mental disorders to suicide among record linkage studies.
Methods: We performed a systematic search using eight major health databases for English-language studies published between 1 January 2000 and 11 June 2018 that linked collected data on mental disorders and suicide. We then conducted a meta-analysis to assess risk of suicide conferred by mental disorders.
Results: Our search identified 20 articles representing 13 unique studies. The pooled rate ratio (RR) was 13.2 (95% CI 8.6–20.3) for psychotic disorders, 12.3 (95% CI 8.9–17.1) for mood disorders, 8.1 (95% CI 4.6–14.2) for personality disorders, 4.4 (95% CI 2.9–6.8) for substance use disorders, and 4.1 (95% CI 2.4–6.9) for anxiety disorders in the general population. The overall pooled RR for these mental disorders was 7.5 (95% CI 6.6–8.6). The population attributable risk of mental disorders was up to 21%.
Limitations: The overall heterogeneity between studies was very high.
Conclusions: Our findings underline the important role of mental disorders in suicide. This suggests that ongoing efforts are required to improve access to and quality of mental health care to prevent suicide by people with mental disorders.

1. Introduction

The extent to which mental disorders contribute to suicide has long been debated (Goldney et al., 2008; Goldney, 2015; Haw and Hawton, 2015; Pridmore, 2015; Sara, 2015; Hjelmeland and Knizek, 2017). Those who contend that the risk conferred by mental disorders is overrated tend to argue this is because observed associations often come from psychological autopsy studies (Pridmore, 2015; Hjelmeland and Knizek, 2017). These studies obtain information on those who have died by suicide through interviews with individuals who were close to them, potentially introducing recall biases by priming these informants to think about particular risk factors (e.g., mental disorders) that could explain the suicide (Cavanagh et al., 2003). There are other studies, however, which potentially offer a more objective window into the relationship (Goldney, 2015; Haw and Hawton, 2015). These are studies that used record linkage data (where mental health service use data were linked with suicide data at the individual level). Identifying the presence of mental disorders in this way overcomes the recall bias inherent in psychological autopsy studies; those who have made contact with these services are likely to have been diagnosed with a mental disorder or at least to have presented with mental health concerns.

An increasing number of record linkage studies are being conducted in this area, but no attempt has been made to pool the data from them to more objectively estimate the magnitude of the relationship between mental disorders and suicide. We conducted the current systematic review and meta-analysis of relevant record linkage studies to do just that, arguing that the resultant estimates would be conservative (given the record linkage studies do not identify individuals with mental disorders who do not seek support from mental health services). Our key question was: To what extent are mental disorders associated with suicide, as evidenced by the findings from record linkage studies?

2. Methods

Our systematic review and meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)

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reporting guidelines (Moher et al., 2009).

2.1. Databases and search terms used

We searched eight electronic databases that index literature from the disciplines of medicine, nursing, and health sciences. These databases were: CINAHL, Embase, Medline, ProQuest, PsycINFO, Scopus, The Cochrane Library, and Web of Science. All databases were searched from 1 January 2000 to 11 June 2018. We used a multi-tier search strategy to identify eligible studies. At the first tier, we searched for terms reflecting suicide (suicid* OR "intentional self-harm"). At the second tier, we searched for terms reflecting mental disorders ("psychiat*" OR "mental health service*" OR "community mental health service*" OR "psychiat* hospital*" OR hospitali?at* OR inpatien*). At the third tier, we searched for terms reflecting data linkage ("data collect*" OR registr* OR "vital statistic*" OR "record* link*" OR "data link*" OR "data match*" OR "routine collect*" OR "information system*"). These tiers were guided by our initial database searches. We mapped search terms onto subject headings where applicable and integrated the terms from tiers one, two, and three using "AND" Boolean operator. We also searched the reference lists of key reviews of the subject and eligible studies.

2.2. Inclusion and exclusion criteria

We confined our meta-analysis to studies published as original English-language articles in scientific journals and excluded other publications (e.g., case reports, commentaries, editorials, conference abstracts, dissertations/theses). The criteria for a study to be included were: (i) suicide as the outcome variable; (ii) specific mental disorder or mental health service use for specific mental disorder as the exposure variable; (iii) outcome and exposure data linked at the individual level; (iv) comparisons made between individuals with and without mental disorders; and (v) general population as the study sample. Studies were excluded if: (i) the outcome variable was non-fatal suicide attempts; (ii) the outcome variable was the combination of suicide and non-fatal suicide attempts and these could not be disaggregated; (iii) the exposure variable was reported with only information on undefined mental disorder or mental health service use for undefined mental disorder; and (iv) the study did not include a comparison group. The last criterion meant that only studies using cohort and case-control designs or their variants were included.

2.3. Data collection

Two authors (LB and LST) conducted the initial searches (identification and screening). One author (LST) assessed the full-text articles for eligibility and extracted information from each study. The extracted information was then cross-checked by another author (LR). Inconsistency in extracted information was resolved by LST and LR discussing the discrepancy and reaching consensus. Contact was made with the primary author of one article to obtain relevant study data. The extracted information included: author(s) and date of publication; setting; study design; linked data sources; exposure variable; study sample; comparison group; numbers of suicides in the exposed and unexposed groups; and numbers of non-suicides (i.e., people who remained alive and/or died by causes other than suicide) in the exposed and unexposed groups. Risk ratios (and 95% Confidence Intervals [CIs]) or equivalent ratios (e.g., incidence rate ratios, standardised mortality ratios) were extracted if the numbers of exposed and unexposed suicides and non-suicides were not provided. The information was categorised into disorder subgroups (e.g., mood disorders, psychotic disorders, personality disorders, substance use disorders, anxiety disorders). When data on diagnosis was not available, we included proxy measures as appropriate. For example, hospital admission for mood disorders was classified into 'mood disorders', and substance disorder visit was classified into 'substance use disorders'. Data from disorder subgroups based on fewer than three studies are presented in tables but not included in our meta-analysis.

We classified sets of articles that examined the same exposure across different years using data from the same databases as one study and only included the most recent data. For example, there were five articles that used data on schizophrenia from the same databases that were published in 2000, 2001, 2005, 2006, and 2013 (Mortensen et al., 2000; Hiroeh et al., 2001; Qin and Nordentoft, 2005; Qin et al., 2006; Webb et al., 2013), so we only included data from the 2013 article (Webb et al., 2013) in our meta-analysis. Note that this approach meant that a study may have been represented by one article when a particular disorder was being examined and been represented by another article when a different disorder was being examined.

2.4. Quality assessment

In a review of tools for quality assessment of observation studies, several minimum requirements for a quality assessment tool to be considered 'good' were recommended (Sanderson et al., 2007). We selected checklists for cohort and case-control studies from the Scottish Intercollegiate Guidelines Network (SIGN) for quality assessment of eligible studies (Harbour and Miller, 2001) because they fulfilled most of the minimum requirements for being a 'good' quality assessment tool (e.g., methods for selecting study participants; methods for measuring exposure and outcome variables; design-specific sources of bias; methods to control confounding; statistical methods; relatively specific and simple; and showing evidence of careful development). The quality of eligible studies was assessed by one author (LST) and cross-checked by a second author (LR), with inconsistency in quality outcome resolved by consensus.

2.5. Statistical analysis

Given age and sex are recognised confounders in the association between mental disorders and suicide and are commonly adjusted for in analyses, our minimum requirement for data inclusion in our analysis was therefore data adjusted for these variables. For case-control/case-cohort studies that matched for at least age and sex, we calculated a risk ratio (RR) for each study based on the number of reported suicides and non-suicides associated with the presence and absence of mental disorders. For cohort studies, we included the reported RR or equivalent ratio (e.g., hazard ratio, incidence rate ratio, odds ratio, standardised mortality ratio) adjusted for age and sex. Where such information was not available, we included the RR (or an equivalent ratio) adjusted for age, sex, and other confounders or the age-adjusted RR stratified by sex.

We then estimated a pooled RR using the standard DerSimonian-Laird random-effects estimator. We fitted this for each specific disorder and for all disorders. In this approach, the weights assigned to each study were based on sample size, which means a study with a large sample size was given a greater weight than a study with a small sample size. A sensitivity analysis was performed by excluding any study that focused on particular age cohort.

Heterogeneity between studies was assessed using the I^2 statistic (an estimate of between study variation and expressed as a proportion) and investigated using random-effects meta-regression. Publication bias was assessed using funnel plots and Egger's test.

We also estimated the pooled population attributable risk (PAR) overall and for each mental disorder. To do this, we estimated the proportion of cases exposed to the risk factor in the population by pooling this information from individual studies. We again used random-effect meta-analysis for this calculation. If insufficient information was available from individual studies to make this calculation, we relied on data from those studies where the data were available. The PAR was computed using the following equation:

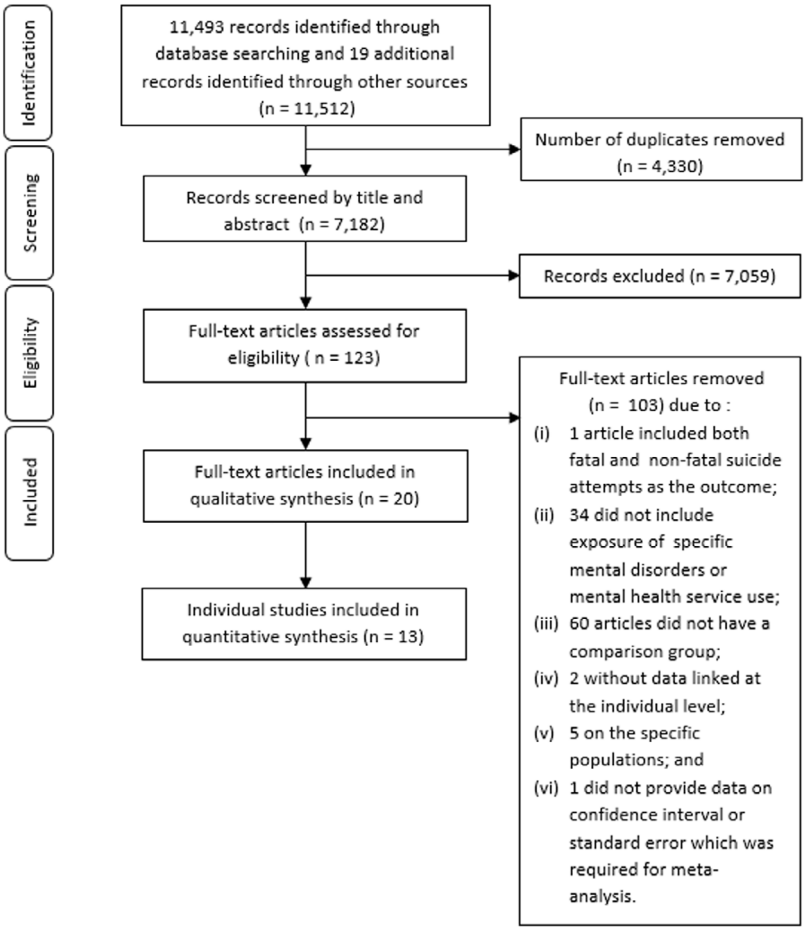

Fig. 1. Flow diagram on study selection.

$$PAR = p(PR - 1)/[1 + p(RR - 1)],$$

where p refers to the prevalence of each mental disorder, and RR refers to the pooled relative risk estimate of suicide for each disorder.

Finally, we estimated the pooled proportion of mental disorders in suicides and non-suicides separately. All meta-analyses were performed using StataSE 14.

3. Results

The search yielded 11,512 articles (Fig. 1). We removed 4330 duplicate records which left us with 7182 unique records. We screened the titles and abstracts of each unique record and identified 123 articles that were potentially eligible for inclusion. We then retrieved the full text of these articles and assessed their eligibility. Finally, we excluded 103 articles and included 20 articles (13 studies) in our review and meta-analysis. Of the 103 articles that were excluded, one used combined fatal and non-fatal suicide attempts as the outcome variable, 34 did not assess an exposure related to specific mental disorders or mental health service use for specific mental disorders, 60 did not have a comparison group, two did not use linked data at the individual level, and five focused on specific populations (e.g., veterans, emergency patients, self-poisoning patients, heroin dependent inpatients) rather than the general population. For example, one study used a sample of heroin dependent inpatients to estimate the risk of suicide for lifetime depressive syndrome by comparing heroin dependent inpatients who were alive with heroin dependent inpatients who died by suicide (Pan et al., 2014). This study therefore did not meet our inclusion criteria iv and v. We also excluded one study that did not report confidence intervals or standard errors which were required for our meta-analysis.

3.1. Overview of studies

Table 1 describes the characteristics of the studies. Of the 13 studies included in the review, five were cohort studies, six were case-control studies (five of which used matched controls and one of which used all available controls), and one was a case-cohort study. One study (study 5 in Table 1) was reported in several articles that used case-control or cohort designs. Four studies were conducted in Denmark, three in Sweden, two in Canada, two in Australia, one in the United Kingdom, and one in Norway. The data coverage ranged between 4 and 45 years. Five studies examined more than one exposure. Seven examined mood disorders, four examined psychotic disorders, three examined personality disorders, six examined substance use disorders, and six examined anxiety disorders.

3.2. Summary of quality assessment

Of the 20 included articles, 17 were judged as being of high quality and three as being of acceptable quality. Studies of high quality met all the requirements for sample selection, measurement methods, controlling for bias and confounders, and statistical methods. Studies of acceptable quality matched cases and controls on specific criteria but did not adjust for potential confounders in the analysis. We retained all acceptable quality studies in our analysis because these studies matched cases and controls at least on age and sex, which met our minimum requirement for data inclusion.

Table 1
Study characteristics.

Study no.	Author(s) and date of publication	Setting and study period	Study design	Linkage data source	Exposure and outcome	Study sample	Comparison group
1	Almeida et al. (2016)	Western Australia (1996–June 2009)	Cohort	Western Australian Data Linkage System (WADLS)	Exposure: - Bipolar disorder Outcome: - Suicide (ICD-8 and ICD-9 codes: E950–E959; ICD-10 codes, X60–X84, Y87.0, and U03)	Men aged 65–85 years without a diagnosis of dementia	Men who did not die by suicide (alive/died by other causes) (37,768 individuals)
2	Doyle et al. (2016)	United Kingdom (2002–2011)	Matched case-control	UK Clinical Practice Research Datalink (CPRD)	Exposure: - Personality disorder - Borderline personality disorder Outcome: - Suicide [ICD-10 codes: X60–84, Y10–Y34 (excluding Y33.9), Y87.0, and Y87.2]	General population registered to primary care practice	Living individuals, matched on gender, age, and registered primary care practice (1 case: 20 matched controls)
3	Fernandez de la Cruz, et al. (2017)	Sweden (1969–2013)	Matched case-control	National Patient Register, Cause of Death Register, Swedish Register of Total Population, Education Register	Exposure: - Obsessive-compulsive disorder (OCD) Outcome: - Suicide (ICD-8 and ICD-9 codes: E950–E959; ICD-10 codes: X60–X84)	General population	Living individuals, matched on sex, birth year, and county of residence at the time of the first OCD diagnosis (1 case: 10 matched controls)
4	Flensborg-Madsen et al. (2009)	Copenhagen, Denmark (1976–1993)	Cohort	Copenhagen City Heart Study, Danish Causes of Death Register, Danish Hospital Discharge Register, Danish Psychiatric Central Register, WINALCO-database	Exposure: - Lifetime alcohol use disorder Outcome: - Suicide (ICD-8 codes: E950–E959; ICD-10 codes: X60–X84)	General populations aged 20–93 years	People aged 20–93 years who did not die by suicide (alive/died by other causes) (23,189 individuals)
5	Gradus et al. (2010a)[21] Gradus et al. (2010b)	Denmark (1994–2006)	Matched case-control	Cause of Death Register, Danish Psychiatric Central Register, National Patients Register, Civil Registration System, Integrated Database for Labour Market Research	Exposure: - Depression - Substance abuse - Anxiety disorder - Post-traumatic stress disorder - Acute stress reaction	General population aged 15–90 years at the time of suicide	Living general population, matched on sex, date of birth, and time of death (1 case: 30 matched controls)
	Hiroeh et al. (2001)	(1973–1993)	Cohort		- Schizophrenia - Affective psychoses - Non-affective psychoses - Neurosis - Personality disorder - Alcoholism - Drug use - Organic psychoses	General population over 21 years	Living general population who died by other causes (72,208 individuals)
	Meier et al. (2016a)	(2002–2011)	Cohort		- Anxiety disorder - Depression - Comorbid anxiety disorder and depression	General population	People who did not die by suicide (alive/died by other causes) (unknown number of individuals)
	Mortensen et al. (2000)	(1982–1994)	Matched case-control		- Schizophrenia - Drug abuse - Alcohol abuse - Manic-depressive psychosis - Reactive psychosis	General population aged 16–78 years	Living people matched on time of suicide (811 cases: 79,871 controls)
	Qin & Nordentoft (2005)	(1981–1997)	Matched case-control		- Schizophrenia spectrum disorders - Affective disorder	General population	Living people matched on age, sex, and time (1 case: 20 matched controls)

(*continued on next page*)

Table 1 (*continued*)

Study no.	Author(s) and date of publication	Setting and study period	Study design	Linkage data source	Exposure and outcome	Study sample	Comparison group
					- Substance abuse disorders		
	Qin et al. (2006)	(1981–1997)	Matched case-control		- Current hospitalization for schizophrenia and schizophrenia-like psychoses - Current hospitalization for affective disorders - Current hospitalization for substance abuse disorders	General population	Living people matched on age, sex, and time (1 case: 20 matched controls)
	Webb et al. (2013)	(1981–2006)	Matched case-control		- Depression - Schizophrenia - Personality disorder - Alcohol/drug disorders (secondary care-treated) Outcome: - Suicide (before 1994, ICD-8 codes: E950–E959; 1994 and after, ICD-10 codes: X60–X84, and/or Y10-Y34)	General population aged 15 years or above	Living people aged 15 or above years matched on age and sex (1 case: up to 25 matched controls)
6	Høye et al. (2016)	Troms and Finnmark, Norway (1980–2012)	Cohort	Hospital case register (The University Hospital of North Norway), Cause of Death Register, Statistics Norway	Exposure: - Affective disorders Outcome: - Suicide (ICD-8 and ICD-9 codes: E950– 959, ICD-10 codes: X60–84)	General population	Living people (unknown number of individuals)
7	Lawrence et al. (2000)	Western Australia (1980–1995)	Cohort	Western Australian Health Services Research Linked Database	Exposure: - Depressive disorder - Schizophrenia - Personality disorder - Alcohol/drug disorders - Neurotic disorder - Affective psychoses Outcome: - Suicide (ICD-9 codes: E950–E959)	Males and females aged 60 and over years, or those whose first contact with mental health services occurred in 1980–1995	People who did not die by suicide (alive/died by other causes) (Unknown number of individuals)
8	Meier et al. (2016b)	Denmark (2002–2011)	Cohort	Danish Psychiatric Central Register, Danish National Patient Register, Danish Register of Causes of Death, and Danish Civil Registration System	Exposure: - Obsessive-compulsive disorder Outcome: - Suicide (ICD-10 codes: X60–X84, and Y87.0)	People born between 1 January 1955 and 31 November 2006	People who did not die by suicide (alive/died by other causes) (3,270,650 individuals)
9	Morrison, & Laing (2011)	Alberta, Canada (2003–2006)	Case-control	Mortality database, Alberta Health and Wellness (AHW) health service registry	Exposure: - Depression diagnosis visit - Substance disorder visit - Anxiety/stress diagnosis visit Outcome: - Suicide (ICD-10 codes X60–X84)	General population aged 25–64 years who were active on the AHW registry during the year of death and one year earlier	Adults who were active on the AHW registry during the year and one year earlier (854 cases: 1,752,323 controls)
10	Nordentoft et al. (2004)	Denmark (1981–1997)	Matched case-control	Danish Civil Registration System, Cause of Death Register, Integrated Database for Longitudinal Labour Market Research, Danish Psychiatric Central Register	Exposure: - Current hospital admission due to schizophrenia - Current hospital admission due to schizophrenia spectrum disorder Outcome:	General population aged less than 76 years	Living people matched on birth year, sex, and calendar time of suicide (1 case: 20 matched controls)

(*continued on next page*)

Table 1 (*continued*)

Study no.	Author(s) and date of publication	Setting and study period	Study design	Linkage data source	Exposure and outcome	Study sample	Comparison group
					- Suicide (before 1994, ICD-8 codes: E950–E959; 1994 and after, ICD-10 codes: X60–X84)		
11	Reutfors et al. (2010)	Sweden (1991–2003)	Matched case-control	Swedish Cause of Death Register, Census register, Swedish Patient Register	Exposure: - Hospital admission for mood disorder in the year before suicide - Hospital admission for schizophrenia spectrum disorder in the year before suicide - Hospital admission for alcohol use disorder in the year before suicide Outcome: - Suicide (ICD-9 codes: E950–E959 and E980–E989; ICD-10 codes: X60–X84 and Y10–Y34)	General adults 18 years and older	Living general adults matched on age, sex, country of residence (1 case: 10 matched controls)
12	Voaklander et al. (2008)	British Columbia, Canada (1993–2002)	Matched case-control	British Columbia (BC) Vital Statistics, BC Health Insurance Registry, PharmaCare database, provincial Physician Claims, Inpatient Hospitalisation database.	Exposure: - Hospital coded alcohol abuse - Hospital coded depression/ psychosis - Hospital coded neurosis Outcome: - Suicide (ICD-9 codes: E950–E959; ICD-10 codes: X60–X84)	General population aged 66 and over years	Living people aged 66 and over years matched on sex and age (1 case: 5 matched controls)
13	Webb et al. (2014)	Sweden (1973–2009)	Matched case-cohort	Patient Register, Cause of Death Register, National Crime Register, Total Population Register, Multi-Generation Register, Migration Register	Exposure: - Two or more outpatient or inpatient episodes with a bipolar disorder diagnosis Outcome: - Suicide (ICD-8 and ICD-9 codes: E950–E959 and E980–E989; ICD-10 codes: X60–X84 and Y10–Y34)	General population	People who did not die by suicide (alive/died by other causes), matched on age and sex (1 case: 20 matched individuals)

Table 2
Risk ratio of mental disorders for individual studies.

Study No.	Author(s) and date of publication	Exposure	Exposed suicide (n)	Unexposed suicide (n)	Exposed non-suicide (n)	Unexposed non-suicide (n)	Adjusted RR (95% CI)	% of exposure in suicide	% of exposure in non-suicide
1	Almeida et al. (2016) (males)	Bipolar disorder	5	53	251	37,459	13.43 (5.35 – 33.73)[c]	8.6	0.7
2	Doyle et al. (2016)	Personality disorder	110	2274	236	46,663	6.84 (5.83 – 8.02)[j]	2.3	0.3
		Borderline personality disorder[b]	16	2368	19	46,880	9.51 (6.61–13.67)[j]	0.7	0.04
3	Fernandez de la Cruz, et al. (2017)	Obsessive-compulsive disorder	545	579	36,243	367,301	9.41 (8.38 – 10.58)[j]	48.5	9.0
4	Flensborg-Madsen et al. (2009)	Alcohol use disorder	57	152	1700	21,280	7.36 (4.82 – 11.23)[d]	27.3	7.4
5	Gradus et al. (2010a)	Depression[a]	1713	7899	2542	196,764	10.43 (10.00 – 10.88)[j]	17.8	1.3
		Substance abuse[a]	1024	8588	2686	196,620	6.60 (6.24 – 6.98)[j]	10.7	1.3
		Anxiety disorder[a]	352	9260	1309	197,997	4.74 (4.31 – 5.22)[j]	3.7	0.7
		Post-traumatic stress disorder[b]	38	9574	95	199,211	6.23 (4.76 – 8.16)[j]	0.4	0
	Gradus et al. (2010b)	Acute stress reaction[b]	95	9517	165	199,141	8.01 (6.82 – 9.41)[j]	1.0	0.1
	Hiroeh et al. (2001) (males)	Schizophrenia[a]	–	–	–	–	10.73 (9.73 – 11.83)[e]	–	–
		Affective psychoses[b]	–	–	–	–	16.44 (15.62 – 17.31)[e]	–	–
		Non-affective psychoses[b]	–	–	–	–	13.81 (12.75 – 14.96)[e]	–	–
		Neurosis[a]	–	–	–	–	8.08 (7.29 – 8.95)[e]	–	–
		Personality disorder[a]	–	–	–	–	11.98 (11.28 – 12.72)[e]	–	–
		Alcoholism[a]	–	–	–	–	10.64 (10.05 – 11.25)[e]	–	–
		Drug use[a]	–	–	–	–	24.60 (22.43 – 26.98)[e]	–	–
		Organic psychoses[b]	–	–	–	–	11.39 (10.28 – 12.63)[e]	–	–
	Hiroeh et al. (2001) (females)	Schizophrenia[a]	–	–	–	–	10.80 (9.36 – 12.46)[e]	–	–
		Affective psychoses[b]	–	–	–	–	16.00 (15.26 – 16.78)[e]	–	–
		Non-affective psychoses[b]	–	–	–	–	11.09 (10.12 – 12.15)[e]	–	–
		Neurosis[a]	–	–	–	–	10.08 (9.42 – 10.78)[e]	–	–
		Personality disorder[a]	–	–	–	–	15.68 (14.71 – 16.72)[e]	–	–
		Alcoholism[a]	–	–	–	–	15.86 (14.25 – 17.64)[e]	–	–
		Drug use[a]	–	–	–	–	23.97 (21.28 – 27.01)[e]	–	–
		Organic psychoses[b]	–	–	–	–	14.61 (13.02 – 16.39)[e]	–	–
	Meier et al. (2016a)	Anxiety disorder	–	–	–	–	5.69 (4.70 – 6.86)[f]	–	–
		Depression	–	–	–	–	13.41 (12.10 – 14.84)[f]	–	–
		Comorbid anxiety disorder and depression[b]	–	–	–	–	18.32 (15.21 – 21.86)[f]	–	–
	Mortensen et al. (2000)	Schizophrenia[a]	40	771	293	79,578	–	4.9	0.4
		Drug abuse[a]	126	685	838	79,033	–	15.5	1.0
		Alcohol abuse[a]	51	760	396	79,475	–	6.3	0.5
		Manic-depressive psychosis[b]	80	731	459	79,412	–	9.9	0.6
		Reactive psychosis[b]	66	745	414	79,457	–	8.1	0.5
	Qin & Nordentoft (2005)	Schizophrenia spectrum disorders[a]	1658	19,511	2942	420,186	8.12 (7.80 – 8.46)[j]	7.8	0.7
		Affective disorders[a]	2736	18,433	4482	418,646	8.99 (8.70 – 9.29)[j]	12.9	1.1
		Substance abuse disorders[a]	1392	19,777	2983	420,145	7.08 (6.76 – 7.41)[j]	6.6	0.7
	Qin et al. (2006)	Current hospitalization for schizophrenia and schizophrenia-like psychoses[a]	436	20,733	406	422,722	11.08 (10.36 – 11.84)[j]	2.1	0.1
		Current hospitalization for affective disorders[a]	630	20,539	139	422,989	17.69 (17.07 – 18.34)[j]	3.0	0
		Current hospitalization for substance abuse disorders[a]	51	21,118	51	423,077	10.52 (8.66 – 12.78)[j]	0.2	0
	Webb et al. (2013)	Depression[a]	252	2132	271	55,745	13.08 (11.86 – 14.43)[j]	10.6	0.5
		Schizophrenia	374	2010	395	55,621	13.94 (12.82 – 15.17)[j]	15.7	0.7
		Personality disorder	299	2085	352	55,664	12.72 (11.59 – 13.97)[j]	12.5	0.6
		Alcohol/drug disorders	286	2098	371	55,645	11.98 (10.88 – 13.20)[j]	12.0	0.7
6	Høye et al. (2016) (males)	Affective disorders	–	–	–	–	21.00 (15.70 – 28.20)[e]	–	–
	Høye et al. (2016) (females)	Affective disorders	–	–	–	–	27.60 (19.80 – 38.70)[e]	–	–

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Table 2 (*continued*)

Study No.	Author(s) and date of publication	Exposure	Exposed suicide (n)	Unexposed suicide (n)	Exposed non-suicide (n)	Unexposed non-suicide (n)	Adjusted RR (95% CI)	% of exposure in suicide	% of exposure in non-suicide
7	Lawrence et al. (2000) (males)	Depressive disorder	–	–	–	–	12.22 (6.88 – 21.70)[e]	–	–
		Schizophrenia	–	–	–	–	3.31 (0.97 – 11.20)[e]	–	–
		Personality disorder	–	–	–	–	2.31 (0.58 – 9.27)[e]	–	–
		Alcohol/drug disorders	–	–	–	–	1.40 (0.71 – 2.73)[e]	–	–
		Neurotic disorder	–	–	–	–	2.67 (1.42 – 5.03)[e]	–	–
		Affective psychoses[b]	–	–	–	–	10.57 (6.68 – 16.70)[e]	–	–
	Lawrence et al. (2000) (females)	Depressive disorder	–	–	–	–	8.35 (3.66 – 19.10)[e]	–	–
		Schizophrenia	–	–	–	–	3.56 (1.13 – 11.20)[e]	–	–
		Personality disorder	–	–	–	–	12.33 (1.72 – 88.30)[e]	–	–
		Alcohol/drug disorders	–	–	–	–	3.56 (1.13 – 11.20)[e]	–	–
		Neurotic disorder	–	–	–	–	4.95 (2.63 – 9.33)[e]	–	–
		Affective psychoses[b]	–	–	–	–	10.83 (6.17 – 19.00)[e]	–	–
8	Meier et al. (2016b)	Obsessive-compulsive disorder	–	–	–	–	3.02 (1.85 – 4.63)[g]	–	–
9	Morrison, & Laing (2011)	Depression diagnosis visit	338	516	140,722	1611,601	3.27 (2.71 – 3.95)[h]	39.6	8.0
		Substance disorder visit	136	718	23,086	1729,237	1.88 (1.50 – 2.35)[h]	15.9	1.3
		Anxiety/stress diagnosis visit	301	553	181,518	1570,805	1.82 (1.52 – 2.17)[h]	35.2	10.4
10	Nordentoft et al. (2004)	Current hospital admission due to schizophrenia	–	–	–	–	18.00 (13.87 – 23.36)[i]	–	–
		Current hospital admission due to schizophrenia spectrum disorder	–	–	–	–	78.26 (39.95 – 153.29)[i]	–	–
11	Reutfors et al. (2010)	Hospital admission for mood disorder	1885	18,790	305	194,017	9.75 (9.54 – 9.96)[j]	9.1	0.2
		Hospital admission for schizophrenia spectrum disorder	1000	19,675	368	193,954	7.94 (7.67 – 8.22)[j]	4.8	0.2
		Hospital admission for alcohol use disorder	1285	19,390	619	193,703	7.42 (7.17 – 7.67)[j]	6.2	0.3
12	Voaklander et al. (2008)	Hospital coded alcohol abuse	18	584	14	2985	3.44 (2.51 – 4.71)[j]	3.0	0.5
		Hospital coded depression/psychosis[b]	74	528	23	2976	5.06 (4.42 – 5.80)[j]	12.3	0.8
		Hospital coded neurosis	56	546	28	2971	4.29 (3.62 – 5.09)[j]	9.3	0.9
13	Webb et al. (2014)	Bipolar disorder	272	289	15,065	306,451	18.82 (15.96 – 22.20)[j]	48.5	4.7

[a] Data was not included in our analyses because same exposure was examined using the same databases across different articles (classified as one study) and only more recent and expansive data was selected.
[b] Data was not included in our analyses because the exposure had data from less than three studies
[c] Hazard ratio (men only), adjusted for age.
[d] Hazard ratio, adjusted for sex (and age was used as the time variable).
[e] Age-standardised mortality ratio.
[f] Rate ratio, adjusted for year, age, sex, maternal and paternal age, place of residence at time of birth, somatic comorbidity and the interaction of age with gender was provided.
[g] Rate ratio, adjusted for calendar year, age, maternal and paternal age, place of residence at time of birth and somatic comorbidity.
[h] Odds ratio, adjusted for age, sex, health region, health care insurance plan premium subsidy category, other health service use.
[i] Incidence rate ratio, adjusted for marital status, being parent of young child, employment status, annual income, place of residence, and absence from work due to sickness, interaction with age by diagnosis.
[j] Case-control/cohort data matched on at least sex and age.

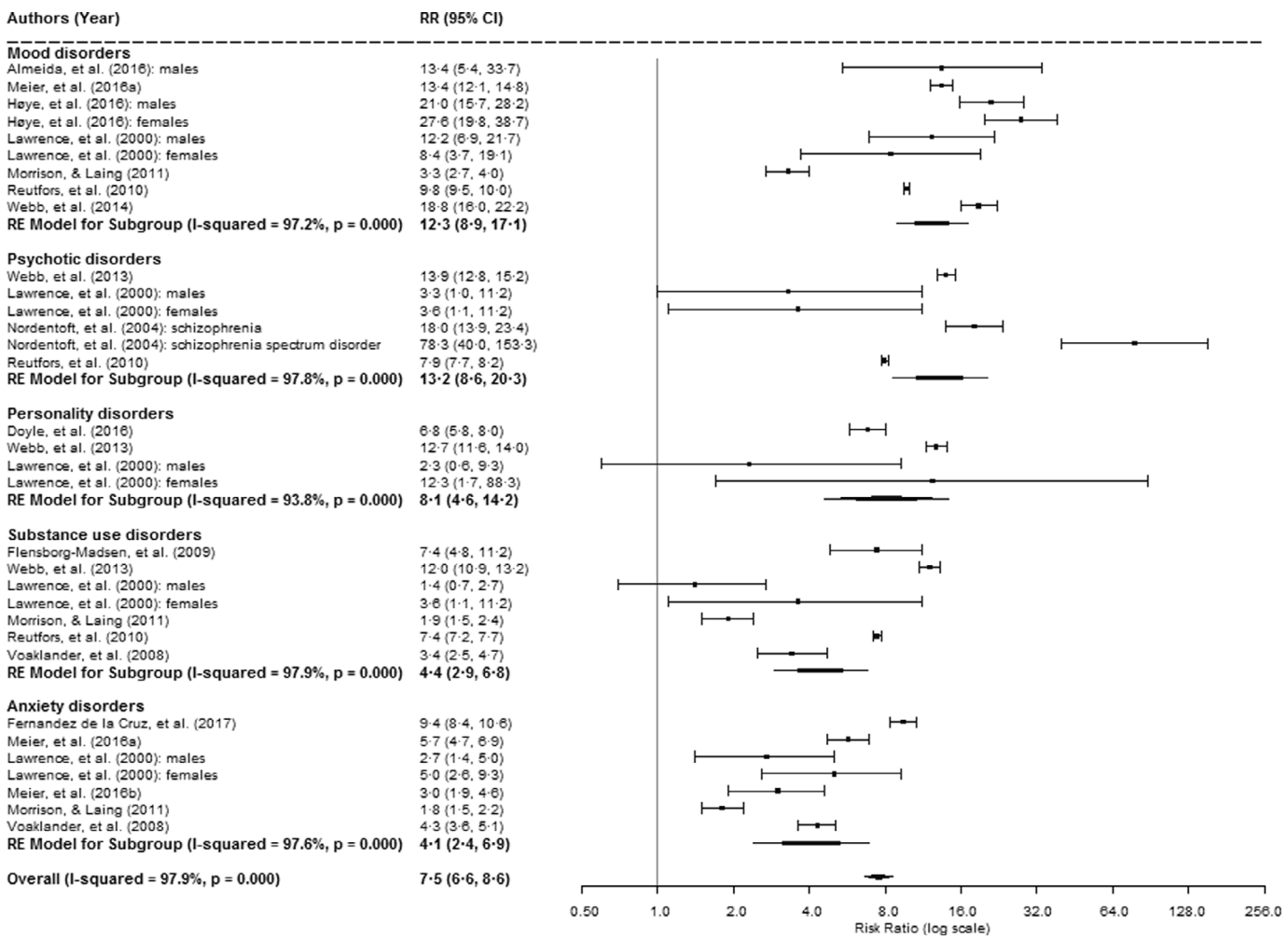

Fig. 2. Risk ratio of suicide associated with mental disorders.

3.3. Pooled estimates of risk ratios

Table 2 shows the unadjusted and adjusted RRs and Fig. 2 shows the pooled estimates of RRs. Psychotic disorders showed a pooled RR of 13.2 (95% CI 8.6–20.3). The pooled RR for mood disorders was 12.3 (95% CI 8.9–17.1) and for personality disorders was 8.1 (95% CI 4.6–14.2). Substance use disorders (RR_{pooled} = 4.4, 95% CI 2.9–6.8) and anxiety disorders (RR_{pooled} = 4.1; 95% CI 2.4–6.9) also showed a high pooled RR. The overall pooled RR for these mental disorders was 7.5 (95% CI 6.6–8.6).

The sensitivity analysis that excluded three studies restricted to older people showed that the pooled RR for psychotic disorders was 17.3 (95% CI 10.8–27.9), for mood disorders was 12.7 (95% CI 8.7–18.6), for personality disorders was 9.4 (95% CI 5.1–17.2), for substance use disorders was 6.0 (95% CI 3.6–9.9), and for anxiety disorders was 4.2 (95% CI 1.8–9.6). The overall pooled RR for these mental disorders was 8.9 (95% CI 7.6–10.4). However, the pooled RR for personality disorders was based on only two studies.

3.4. Pooled population attributable risks

The pooled PAR was 21% for mood disorders, 18% for anxiety disorders, 7% for psychotic disorders, 6% for personality disorders, and 4% for substance use disorders. The overall pooled PAR for these mental disorders was 9%. However, it is worth noting that the pooled PAR for all specific disorders (except substance use disorders) was based on only two studies because the required data were not available for the estimation of PAR in other relevant studies.

3.5. Pooled proportion of mental disorders in suicides and non-suicides

The pooled proportions for mood disorders in suicides and non-suicides were 11.3% and 6.8%; for anxiety disorders were 31.7% and 10.1%; for psychotic disorders were 6.0% and 0.3%; for personality disorders were 8.6% and 0.6%; and for substance use disorders were 7.2% and 1.3%. The pooled proportion for these mental disorders in suicides was 9.1% and in non-suicides was 5.9%. The results on psychotic and personality disorders were based on only two studies.

3.6. Heterogeneity and risk of publication bias

The I^2 statistics indicated a high degree of heterogeneity among the studies included in the meta-analyses, ranging from 93.8% to 97.9%. The results from the meta-regression showed that the I^2 was explained by country of study (50.5%), the type of risk ratio (37.0%), the length of study time frame (34.5%), the type of mental disorder (30.7%), the type of comparison group (23.2%), the type of mental disorder classification (16.6%), and the inclusion of older people (12.3%). Together these factors explained 82.6% of the heterogeneity. Funnel plots for all outcomes also indicate the presence of heterogeneity (Fig. 3). However, Egger's test yielded a non-significant result (p = 0.401), indicating publication bias was unlikely.

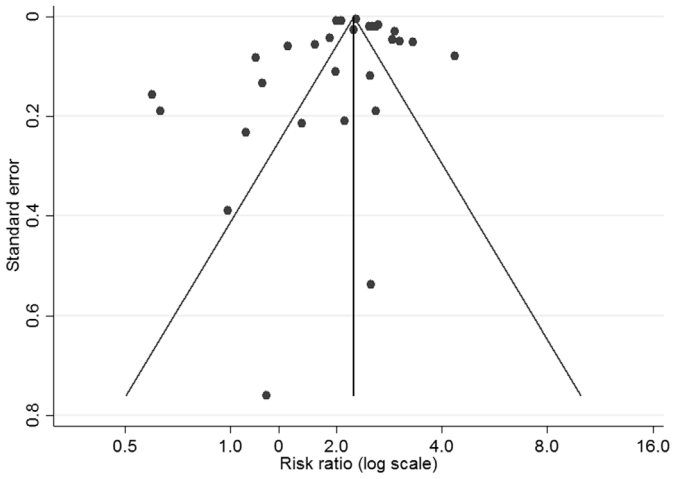

Fig. 3. Funnel plot for pooled mental disorders.

4. Discussion

Our meta-analysis has shown unequivocally that mental disorders are a major risk factor for suicide. Our approach was conservative because we only drew on data from studies that identified the presence or absence of mental disorders in an objective manner via collected data, thereby circumventing the issue of recall bias identified in studies relying on information from informants. Using this conservative approach, we found that people who have been diagnosed with a mental disorder have an eight-fold greater risk for suicide than those who have not. This risk is even greater (nine-fold) after excluding studies focusing exclusively on older people. All measured mental disorders, and particularly psychotic disorders, mood disorders, and personality disorders, confer a strong risk for suicide. We also found that the PAR for mental disorders is up to 21%.

Our findings point in the same direction as those from a recent meta-review by Chesney et al. (2014) that assessed the risks of all-cause and suicide mortality in people with mental disorders. They concluded that the highest suicide risk was associated with borderline personality disorder; people with this disorder had a 45-fold higher risk than that of general population. Suicide risk was also found to be strong in anorexia nervosa in women (31-fold greater risk), depression (20-fold greater risk), bipolar disorder (17-fold greater risk), opioid use (14-fold greater risk), and schizophrenia (13-fold greater risk). Although we were not able to estimate the pooled RR for borderline personality disorder, we identified one study that showed a very strong association for this disorder (OR = 37.3) (Doyle et al., 2016). The meta-review showed stronger risks in depression/bipolar disorder and opioid use than the corresponding pooled risks estimated from our meta-analysis (our pooled RR is 12.3 for mood disorders and 4.4 for substance use disorders). This is mainly because the meta-analyses included in the meta-review used more relaxed inclusion criteria than ours in terms of study design. One exception was that our study showed a similar suicide risk for people diagnosed with psychotic disorders. Our risk estimate for this disorder appears to be increased by the inclusion of the incidence rate ratio for schizophrenia spectrum disorder from one study (Nordentoft et al., 2004).

Our meta-analysis found much lower PARs for mental disorders (up to 21%) compared to those reported in the systematic review by Cavanagh et al. (2003). Cavanagh et al. (2003) reviewed only psychological autopsy studies and estimated that the PAR for mental disorders ranged from 47% to 74%. This estimation was primarily based on PARs for affective disorders (21–57%), but also included PARs for comorbid mental disorders (41–52%) and PARs for comorbidity between mental disorder and substance abuse (23–46%). In addition, their estimation of PARs was based on seven case-control studies that focused on young adults/adolescents and included a study from India (where the PAR for mental disorders was 74%). The inclusion of psychological autopsy studies, younger populations, comorbid mental disorders, and a study from an Asia country with a high suicide rate is likely to contribute to the notable PAR difference between Cavanagh et al. (2003) review and our meta-analysis. Nevertheless, our findings suggest that up to 21% of suicides could be averted if mental disorders could be prevented. Such estimates have significant caveats, such as an assumption of causation and an absence of any residual confounding. However, this PAR suggests that mental disorder is an important modifiable risk factor for suicide.

Of course, our findings do not suggest that all people who die by suicide have or have had mental disorders. Suicide is a complex phenomenon and in most cases is the tragic culmination of a confluence of factors, some of which may be related to underlying mental health issues and some of which may be associated with stressful life events. Many models of suicidal behaviour are underpinned by frameworks that incorporate mental disorders as a distal diathesis, suggesting that more proximal environmental factors or life events may act as triggers in the presence of such background vulnerability. O'Connor et al. (2016)'s Integrated Motivational-Volitional Model of Suicidal Behaviour, for example, suggests that these factors act in a pre-motivational phase, and when these are overlaid by feelings such as defeat/humiliation and then entrapment in a motivational phase, suicidal thoughts and intentions may begin to come to the fore. They further suggest that if these thoughts and intentions are moderated by factors that influence behavioural enactment, like capability or impulsivity, then suicidal behaviour may result.

Mishara and Chagnon (2016) have specifically considered the relationship between mental disorders and suicide and have suggested six models that may explain the mechanisms underpinning the relationship. Model 1 contends that suicide and mental disorders have a common aetiology, such that biogenetic vulnerability and negative life events can lead to both. Model 2 suggests that some mental disorders (e.g., substance use disorders) may develop as an alternative to suicide (e.g., in the context of people trying to avoid suicidal thoughts or impulses). Under Model 3, suicide is viewed as a direct consequence of cognitive distortions that characterise many mental disorders (e.g., command hallucinations in psychotic disorders, feelings of extreme hopelessness in depression). Model 4 argues that suicide occurs as a result of the negative experiences that sometimes accompany mental disorders (e.g., social exclusion, stigma, and discrimination). Model 5 posits that suicide is iatrogenic, resulting from sub-optimal treatment for mental disorders. Model 6 is a combined model which incorporates features of the other five but overlays these with a crisis situation, similar to the diathesis-stress components of O'Connor et al. (2016)'s model and the models posed by others.

It is important to acknowledge the significant role of mental disorders in suicide; underplaying it may result in missed opportunities for suicide prevention. The fact that suicide is complex means that it warrants a multi-faceted response (Hawton and van Heeringen, 2009; Turecki and Brent, 2016; Hawton and Pirkis, 2017), but mental health services and practitioners should be a core part of this response. Our meta-analysis suggests the need for ongoing efforts to maximise the opportunities for mental health services to have a positive impact on suicide risk. Some of these efforts may involve encouraging help-seeking by reducing the stigma attached to mental disorders and improving access for those who do seek help. Others approaches may involve improving the quality of care provided for people with mental disorders in general, ensuring that it is person-centred and promotes recovery. Still others may be more specific to those who present with suicide risk, such as 24-h crisis care or brief intervention and contact after discharge.

4.1. Limitations

Our review and meta-analysis had several limitations which must be acknowledged. First, despite our best efforts, it is possible that we missed some relevant studies. Second, the number of studies available for our meta-analysis was relatively small, particularly for some specific mental disorders. Third, the corpus of studies largely came from Western countries and there are suggestions that the influence of mental disorders on suicide may be less prominent in Asian countries (Vijayakumar, 2005). Fourth, our findings showed high heterogeneity between studies. A large proportion of this heterogeneity was explained by country of study, the type of risk ratio, the length of study time frame, the type of mental disorder, the type of comparison group, the way in which mental disorders were classified, and the inclusion of older people. The remaining heterogeneity may be explained by some unmeasured factors such as phase of mental disorder and time of admission for mental disorder. High heterogeneity may also be explained by the difference in the definition of suicide. While most studies included only certain suicide as the outcome, some other studies included certain suicide, undetermined death, and/or sequelae of intentional self-harm/sequelae of events of undetermined intent. Fifth, we were not able to determine whether those with mental disorders in the various studies had symptoms at the time of their death. Sixth, while we were able to obtain RRs adjusted for only age and/or sex from seven studies, RRs from six studies were adjusted for other confounders in addition to these variables. The inclusion of data adjusted for confounders in addition to age and sex is likely to reduce the size of the effect of mental disorders on suicide. Seventh, some studies did not provide sufficient information to enable calculation of PAR. This meant that the pooled PARs for mental disorders were based on data from fewer studies (two to three studies for each disorder). Finally, we included the subcategories of specific mental disorder when estimating the risk for that disorder (e.g., bipolar disorders, depression, and depression diagnosis visit for mood disorders). This means the estimated risk may be more attributable to particular subcategory or a combination of these subcategories. Relatedly, while two studies had their RR adjusted for somatic comorbidity and twelve studies did not include data on comorbidity with other mental disorders, we acknowledge that individuals with mental disorders may have comorbidity with other risk factors and this is likely to increase their risk for suicide.

5. Conclusions

In conclusion, the present findings, based on pooled data from record linkage studies, offer a conservative estimate for the risk of suicide associated with mental disorders and suggest that the association is strong. The risk of suicide is markedly greater in people with a current or previous diagnosis of mental disorder than those without such a diagnosis. These findings suggest that better mental health care and improved access to this care are essential for people with a mental disorder to reduce their risk of suicide.

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CRediT authorship contribution statement

Lay San Too: Investigation, Formal analysis, Data curation, Writing - review & editing, Writing - original draft. **Matthew J. Spittal:** Formal analysis, Writing - review & editing. **Lyndal Bugeja:** Writing - review & editing. **Lennart Reifels:** Data curation, Writing - review & editing. **Peter Butterworth:** Formal analysis, Writing - review & editing. **Jane Pirkis:** Conceptualization, Writing - review & editing, Formal analysis.

Declaration of Competing Interest

The authors report no conflict in interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2019.08.054.

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