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Review Article

Factors Influencing Risk of Premature Mortality in Community Cases of Depression: A Meta-Analytic Review

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Background. Depressive disorders are associated with substantial risk of premature mortality. A number of factors may contribute to reported risk estimates, making it difficult to determine actual risk of excess mortality in community cases of depression. The aim of this study is to conduct a systematic review and meta-analysis of excess mortality in population-based studies of clinically defined depression. *Methods*. Population-based studies reporting all-cause mortality associated with a clinically defined depressive disorder were included in the systematic review. Estimates of relative risk for excess mortality in population-representative cases of clinical depressive disorders were extracted. A meta-analysis was conducted using Stata to pool estimates of excess mortality and identify sources of heterogeneity within the data. *Results*. Twenty-one studies reporting risk of excess mortality in clinical depression were identified. A significantly higher risk of mortality was found for major depression (RR 1.92 95% CI 1.65–2.23), but no significant difference was found for dysthymia (RR 1.37 95% CI 0.93–2.00). Relative risk of excess mortality was not significantly different following the adjustment of reported risk estimates. *Conclusion*. A mortality gradient was identified with increasing severity of clinical depression. Recognition of depressive symptoms in general practice and appropriate referral for evidence-based treatment may help improve outcomes, particularly in patients with comorbid physical disorders.

1. Introduction

Depressive disorders make a substantial contribution to the global burden of disease [1–3]. Their contribution to disease burden is largely attributed to the high prevalence of, and disability caused by, depression [1]. Contribution to disease burden of premature mortality in individuals with depression is less well studied, with the exception of suicide and more recently coronary heart disease. Depressive disorders are a well-recognized risk factor for suicide [4], and increased treatment of depression has been associated with a decrease in suicide rates [5, 6].

Increased risk of excess all-cause mortality has previously been shown in psychiatric inpatients [7–9]. Excess mortality in psychiatric inpatients has been associated with conditions such as gastrointestinal infection and respiratory disease, and previously attributed to conditions within hospitals or asylums [10], although the introduction of modern psychiatric treatments and shorter duration of stay in hospitals has improved mortality outcomes for individuals hospitalized with depression [11].

Deinstitutionalization of individuals with chronic mental disorders has been continuing over the past 50 years [12], with only a small proportion of those with depression now hospitalized, and then for short periods. Due to both increased reliance on community care [13] and low treatment-seeking rates for depression [14], those hospitalised are more likely to be presenting with severe symptomatology and not representative of depressive disorder in the community. Despite improvements in the treatment of depression, a growing body of literature suggests that persons with depressive disorder in the community still experience excess mortality compared to those without depression.

Two pathways have been proposed leading to increased mortality in depression. The first is increased tendency for adverse health behaviours [15]. Depression has been

associated with greater likelihood of smoking [16, 17], alcohol, and drug abuse [18–20] and more sedentary lifestyles [21]. In those with chronic diseases, depression is associated with noncompliance with medical treatment [22–24] and worse health outcomes including increased deaths [25]. The WHO World Health Survey (WHS) collected data on mental disorders and a range of physical disorders in 60 countries [26]. Respondents with depression and one or more comorbid physical disorders had the worst overall health states of all the disease states, including either combined physical disorders or depression alone.

The second pathway is based on a body of evidence suggesting a biological progression [27], including the dysfunction of inflammatory response [28]. Depression has been described as an independent risk factor for both coronary heart disease [29] and a number of cancers [27]. It has also been independently associated with increased levels of inflammatory markers [30, 31]. While this finding is not always consistent, it may be that methodological differences between studies are having a confounding effect on the relationship. For example, one study where an association was not found reported depression as identified through the General Health Questionnaire (GHQ) [32]. This measure is likely to reflect subthreshold depressive symptomatology, as well as clinical depression. This highlights the importance of a consistent definition of depression when looking at associations with adverse health outcomes. Inflammation has also been implicated in the pathogenesis of a range of chronic diseases including diabetes [33], atherosclerosis, and related high mortality diseases such as coronary artery disease [34]. Thus depression is thought to be a contributing factor to the development of these diseases and also associated with an increased risk of mortality in those with comorbid physical disease.

Previous systematic reviews have shown increased risk of mortality in people suffering from depression [35–40], especially in males and in those with severe depression [35]. However, previous estimates of mortality combined clinical and community samples [35, 37] and nonclinical definitions of depression [36, 38].

Three previous meta-analyses focusing on all-cause mortality in community-based studies of depression [36, 38, 40] found higher mortality in those with depressive disorders compared to those without. Pooled effect sizes ranged from 1.56 to 1.81 [36, 38, 40]. In two of these analyses [36, 38], depression was variably defined, based on both clinically defined depression (i.e., meeting internationally recognized diagnostic criteria such as DSM [41] or ICD [42]) and subclinical depression or depressive symptoms ascertained through symptom scales such as the General Health Survey or CES-D. If severity is a mediating factor, the inclusion of subclinical cases of depression may result in an underestimate of excess mortality for depression.

Synthesis of the current evidence linking clinical depression with premature death, along with the identification of potential modifiers, may be relevant in informing public health policy, and clinical practice aimed at reducing mortality. The aim of this paper and meta-analysis is to examine the risk of premature mortality in clinically defined depression and identify factors which may influence reported mortality estimates.

2. Methods

2.1. Data sources. A systematic search was conducted to identify papers reporting mortality for population-based studies of depressive disorders. The methodology follows the recommendations by the Meta-analysis of Observational Studies in Epidemiology (MOOSE) Group [43]. A broad search string was developed with the assistance of a research librarian to search electronic databases (Medline, Embase, Psychinfo, Scopus and Google Scholar). Broad search terms (mortality* death* fatality*) and (mental* psychiatric*) were employed as well as key words for specific mental disorders, including depression, depending on database requirements. Searches were limited to human participants and individual-level analytic studies (either cohort or case-control studies). No limitations were set on language of publication. Article titles were scanned for relevance, and abstracts of potential papers were read to identify duplicates, further reduced the list according to predetermined criteria.

Prospective cohort or case-control studies were sought reporting excess all-cause mortality. Studies were excluded if they were not observational and analytic (e.g.; case studies or treatment trials), did not report relative associations between exposure and outcome (or provided insufficent data to calculate effect size) or did not contain primary data (such as review articles). If multiple papers were identified from a single study, the most recent or relevant article was included. The full text of all potentially relevant papers was reviewed. Citations from identified primary data papers, reviews, and monographs were examined to locate additional sources of data.

Depressive disorders were defined as those disorders meeting ICD or DSM diagnostic criteria (including where survey tools map to these criteria) for depressive disorders. Only studies based on samples from the general population were included in analyses. Studies based on occupational groups (e.g., veterans) or conducted in clinical settings, or inpatient populations, were excluded to reduce the effects of potential confounders that may be associated with both occurrence of depression and increased risk of mortality, and in the case of inpatient samples, where cases were more likely to be severe [44].

A summary of the studies meeting the review's inclusion criteria is shown in Table 2. Studies meeting inclusion criteria included samples identified with depressive disorders between 1952 and 2001 in Western Europe, North America, Australia, and Africa.

2.2. Data Abstraction. Data extracted from papers included study design, sample ascertainment, diagnostic instrument, geographic location, adjustment for confounding, and loss to followup. Design factors rather than aggregate quality scores are perhaps more important in interpreting heterogeneity across studies [43], hence a range of variables reflecting study methodology and reporting were also abstracted. Other

variables included sample descriptors (e.g., age, gender, characteristics) and measurement parameters (e.g., type of estimate, period of follow-up, error).

Adjusted estimates of relative risk and confidence intervals were extracted where reported. Estimates of relative risk included odds ratios, hazard rate ratios, and standardized mortality ratios. Numbers of exposed (depressed) and nonexposed (controls) were extracted, as well as numbers of deaths in each group. Where an adjusted effect size was not reported, or an adjusted effect size was reported without uncertainty, crude relative risk and confidence intervals were calculated using numbers of exposed and nonexposed and relative numbers of deaths in each group.

2.3. Statistical Methods. Meta-analyses were conducted to estimate pooled relative risk for all-cause mortality. Analyses were carried out on STATA-IC 10 software. Due to the high level of heterogeneity we used the *metan* function which specifies a random-effects model using the DerSimonian and Laird method [45]. I^2 statistics were calculated to determine variation attributable to heterogeneity with a value of 0% indicating no observable heterogeneity between studies and larger values indicating increasing heterogeneity [46, 47]. Egger's regression test for small study effects was conducted using the *metabias* function.

A stepwise metaregression was carried out to explore the degree to which covariates explained the degree of between-study variability [48]. A number of covariates identified through univariate analysis comprised the original regression model. These included follow-up period, gender, age range and definition of depression (major depression, dysthymia or unspecified depression). The meta-regression was carried out in STATA using the *metareg* command which reported an adjusted R^2 statistic. Covariates were then excluded one at a time until the model reflected the greatest between-study variability.

3. Results

Risk statistics for all-cause mortality were identified for twenty studies (see Figure 1). Data were reported for 153,965 participants with 51% from Western Europe, 48% from North America, and <1% each from Australasia and Africa. After reviewing the articles and excluding duplicated samples, twenty studies from twenty-one papers provided an estimate of risk for all-cause mortality in community samples [49–69]. The estimates were based on an estimated total of 13,090 deaths with a median follow-up period of 4.4 years (range 1–17 years).

Excess mortality was significantly higher in those with clinically defined depression compared to those without depression (RR 1.67, 95% CI 1.48–1.90). In addition, a dose-response effect was observed for pooled estimates when depressive disorders were stratified by severity (Figure 2). Relative risk for premature mortality in major depressive disorder was highest with a RR of 1.92 (95% CI 1.65–2.23) compared to studies reporting unspecified depression (RR 1.46 95% CI 1.22–1.76) and dysthymia (RR 1.37 95% CI 0.93–2.00). Heterogeneity between studies was reduced when the definition was narrowed to include only major depressive disorder ($I^2 = 38.2\% P = .066$).

Males with depression had a 78% greater risk of dying prematurely compared to controls and females with depression were at 63% greater risk (see Table 1). *Ad hoc* sensitivity analyses were conducted to explore the relationship between risk of excess mortality and various covariates such as age range, study follow-up period, definition of depression (MDD, unspecified depression, and dysthymia), and type of estimate (RR, OR, SMR, HRR).

Seven studies reported risk of excess mortality for adults in a broad age range [49, 52, 62–65, 68] and thirteen reported on only older adults (60 years and over) [50, 51, 53–61, 66, 67, 69]. No studies were identified that reported risk for children/adolescents or that stratified risk by age. Table 1 shows that risk of excess mortality was slightly higher for samples comprising all adults compared to those only in the older age group (RR 1.85 and 1.59, resp.). A higher risk of excess mortality was also observed in studies that had a follow-up period of less than five years (RR 1.91) compared to those with follow-up periods of five years or greater (RR 1.41).

Approximately one quarter of studies identified reported risk estimates adjusted for age and/or sex and slightly fewer reported estimates adjusted for additional factors such as demographic (marital status, education, or household income), behavioral and health risk factors (smoking, alcohol consumption, or presence of other chronic disease). No substantial differences were found between the pooled effect sizes for studies that adjusted for age and/or sex (RR 1.85), those adjusted for additional risk factors (RR 1.77), and those that reported unadjusted effect size (RR 1.59).

A stepwise metaregression was carried out to identify a model explaining the greatest proportion of between-study variance. The final model, explaining 80.4% of between study variability, included follow-up period, gender, and definition of depression. Residual variation due to heterogeneity (I^2_{res}) was reduced from 69.1% to 17.2%.

A funnel plot was generated with a fitted regression line from the standard regression (Egger) test for presence of asymmetry (Figure 3). The plot of risk for excess mortality is skewed and asymmetric with evidence of smaller studies showing associations that differ systematically from larger studies (Egger's test $P < .02$). It is possible that small studies showing little risk for excess mortality remain unpublished. Alternatively small studies may overestimate risk compared to larger studies.

4. Discussion

The present study found significantly higher risk of excess mortality in community cases of depression compared to those without depression. Previous analyses have reported effect sizes ranging between 1.56 and 1.81 [36, 38, 40]. The present review highlights the increased risk of premature mortality with greater severity of symptoms. While major depression was associated with almost twice the risk of

Table 1: Pooled relative risk of excess all-cause mortality in community cases of depressive disorders.

	Studies[#]	Depressive disorder (deaths/Total)	No depressive disorder (deaths/Total)	RR	95% CI	I^{2*}
Overall	**21**	**1,167/6,687**	**11,650/151,721**	**1.67**	**1.48–1.90**	**69.10%**
Gender[#]						
Males and females	16	982/5,620	9,291/90,765	1.66	1.42–1.94	75.10%
Males	5	82/377	1,263/28,669	1.78	1.27–2.51	61.60%
Females	5	103/690	1,096/32,287	1.63	1.32–2.02	14.10%
Disorder type[#]						
Major depression	12	345/2,284	5,986/79,615	1.92	1.65–2.23	38.20%
Unspecified depressive disorders	8	738/4,183	4,277/67,797	1.46	1.22–1.76	70.00%
Dysthymic disorder	2	84/220	1,387/4,309	1.37	0.93–2.00	76.60%
Age range						
Adults (all ages)	8	479/4,411	6,656/130,033	1.85	1.46–2.35	73.10%
Older adults (60+)	13	688/2,276	4,994/21,688	1.59	1.37–1.83	60.50%
Follow–up period						
Less than 5 years	13	651/5,631	6,651/134,016	1.91	1.70–2.14	15.90%
5 years or more	8	516/1,326	5,089/17,705	1.41	1.23–1.62	55.30%
Adjustment factors						
Unadjusted	10	462/1,151	5,115/17,996	1.59	1.25–2.01	57.50%
Age and/or sex	6	509/3,913	4,768/74,453	1.85	1.60–2.15	28.90%
Age and/or sex and other factors	5	196/1,623	1,767/59,272	1.77	1.32–2.38	61.70%

RR: relative risk; CI: confidence intervals.
*I^2 represents as a percentage of the variation attributable to heterogeneity between studies.
[#]number of studies do not add up to 21 as 5 studies reported estimates for males and females, and 1 study reported estimates for both major depression and dysthymia.

premature mortality, no significant risk was found in association with dysthymia. Inclusion criteria for this meta-analysis were restricted to diagnostic instruments with high specificity for clinically significant depression. Subthreshold disorders are likely to be associated with lower risk of excess mortality. Inclusion of subthreshold depression or depressive symptoms may bias pooled estimates toward the null.

The current review found a pooled estimate for excess mortality higher than that reported by Harris and Barraclough [35] for major depression (SMR = 1.36). However, due to data availability at that time, the earlier review included papers published prior to DSM diagnostic criteria, with diagnoses such as melancholia, unipolar depression, primary depressive illness, and late onset primary clear-cut depression. As this review has demonstrated, definition of risk factor is an important source of variability. Greater consistency of definition for clinical depression provided a more homogenous representation of mortality risk in depressed cases according to modern DSM/ICD diagnostic criteria.

The present study found slightly higher risk in studies of all ages compared to older adult samples, and the study with the youngest age group (15–49 years) reported the highest risk of excess mortality (RR 3.55 95% CI 1.97–6.39). One other review has examined mortality by age group and found increased risk for adult samples over age 40, compared to all adults (adults ≥18 years) or older adults (≥65 years) [36]. The nonlinear trend by age reported in this review may reflect the heterogeneity of age groupings within the data available. One hypothesis for the reduced risk in older age groups is that it reflects survivor bias within depressed samples. It is possible that people with depressive disorders are less likely to survive into older age and hence the risk of excess mortality is reduced in this age group.

Several possible explanations have been advanced for the higher mortality risk associated with depression. First, depression and physical disorders co-occur and frequently complicate each other [39]. Co-occurring disorders may mask the presence of depression, and depression in combination with physical disorders results in poorer health outcomes [26, 39]. Data from the recent World Mental Health Survey show that individuals are more likely to seek treatment for physical disorders than for mental disorders [14]. Other studies have found that even though individuals may not seek treatment specifically for their mental disorders, they often seek treatment for coexisting physical health problems [72]. Although 5.4% of a patient sample attending a General Practice [GP] sought treatment for mental disorders, prevalence of clinical or subclinical criteria for a mental disorder within the GP attending population was over 40% [72]. Individuals may be accessing health care but are not reporting symptoms of mental disorder, or medical professionals are not recognizing symptoms in persons with coexisting physical disorders. It is likely that

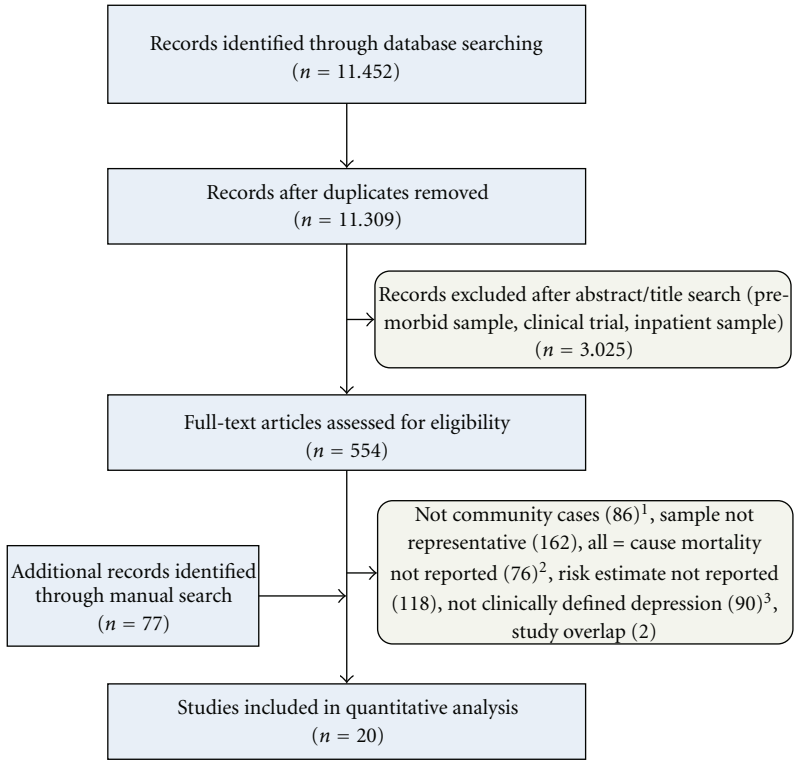
Table 2: Studies reporting risk of all-cause excess mortality in community cases of depressive disorder.

Source	Disorder	Country	Study period	Sample	Survey	Follow-up (years)	Gender	Estimate type	Effect Size	95% CI	Factors adjusted for
Murphy et al. [64]	MDD	USA	1952–1952	Gen pop 18+ yrs	Structured iv	17	M, F	Unadj RR	1.84, 2.13	0.9–3.73, 1.01–4.51	
Davidson et al. [59]	Unspecified depression	UK	1982–1986	Gen pop 65+ yrs	GSM–CATEGO	3	M&F	Unadj RR	1.74	1.03–2.94	
Jorm et al. [54]	MDD	Australia	1982–1983	Gen pop 70+ yrs	GMS + MMSE	5	M&F	Unadj RR	1.5	1.06–2.11	
Aromaa et al. [68]	Unspecified depression	Finland	1978–1981	Gen pop 40–64	PSE–CATEGO	6.6	M&F	Unadj RR	2	1.35–2.96	
Bruce et al. [65]	MDD Dysthymia	USA	1980–1980	Gen pop 40+ yrs	DIS (DSM3)	9	M, F	Unadj RR	1.16, 0.97	0.86–1.57, 0.74–1.29	
Kouzis et al. [62]	MDD	USA	1980–1980	Gen pop 18+ yrs	DIS	1	M&F	OR	2.6	1.1–6.0	Age, sex, marital status, household income
Snowdon and Lane [53]	Unspecified depression	Australia	1985–1987	Gen pop 65+ yrs	Clinical iv (DSM3R)	2	M&F	Unadj RR	2.23	0.8–6.2	
Engedal [60]	Unspecified depression	Norway	1984–1987	Gen pop 75+ yrs	Clinical iv (DSM3R)	3	M&F	OR	1.9	1.0–3.6	Age
Henderson et al. [55]	Unspecified depression	Australia	1990–1994	Gen pop 70+ yrs	CIE	3.6	M&F	Unadj RR	1.26	0.69–2.32	
Pulska et al. [58]	Unspecified depression	Finland	1984–1985	Gen pop 65+ yrs	Clinical iv (DSM3)	5.9	M, F	RR	1.21	0.94–2.06, 0.85–1.69	Age, sex, marital status, low education, smoking
Zheng et al. [63]	MDD	USA	1989–1989	Gen pop (white) 25+	Self-reported (71% males and 79% females report diagnosis by physician)	2.5	M, F	HRR	3.1, 1.7	2.0–4.9, 0.9–3.1	Age, education, marital status & BMI
Pulska et al. [66, 67]	MDD	Finland	1984-1985	Gen pop 65+ yrs	Clinical iv (DSM3)	5.9	M, F	RR	1.88, 2.06	1.11–3.19, 1.25–3.39	Unadj RR

Table 2: Continued.

Source	Disorder	Country	Study period	Sample	Survey	Follow-up (years)	Gender	Estimate type	Effect Size	95% CI	Factors adjusted for
Pulska et al. [66, 67]	Dysthymia	Finland	1989-1990	Gen pop 65+ yrs	Clinical iv (DSM3)	6	M, F	RR	1.52, 1.77	1.04–2.21, 1.30–2.40	Unadj RR
Penninx et al. [61]	MDD	Netherlands	1992–1997	Gen pop 55–85	DIS	4.2	M&F	RR	2.32	1.38–3.89	Age, sex
Vinkers et al. [69]	MDD	Netherlands	1997–1999	Gen pop 85+ yrs	GDS–15 (≥4) MMSE (>18)	3.2	M&F	RR	2.07	1.35–3.17	Sex, smoking, alcohol, and other chronic diseases
Adamson et al. [50]	MDD	England	1996–1998	Gen pop 75+	GDS–15	3	M&F	HR	1.79	1.5–2.13	Age
Bergdahl et al. [56]	MDD	Sweden	2000–2002	Gen pop 85+	Clinical iv (DSM4)	1	M&F	Unadj RR	2.15	1.16–3.97	
Gallo et al. [51]	MDD	USA	2001–2001	Primary Care 60+ yrs	SCAN	2	M&F	OR	1.78	1.06–2.99	Age, sex, marital status, education, and smoking
Mogga et al. [52]	MDD	Ethiopia	1998–2001	Gen pop 15–49	CIDI	3	M&F	SMR	3.55	1.97–6.39	Age, sex
Mykletun et al. [49]	Unspecified depression	Norway	1995–1997	Gen pop 19+ yrs	HADS	4.4	M&F	OR	1.68	1.46–1.92	Age, sex
Schoevers et al. [57]	Unspecified depression	Netherlands	1990–2000	Gen pop 65–84	GMS–AGECAT	10	M&F	Unadj RR	1.18	1.08–1.28	

MDD: major depressive disorder;
RR: Relative risk; Unadj RR: Unadjusted relative risk; OR: Odds ratio; SMR: Standardised mortality ratio; HRR: Hazard Risk Ratio;
M&F: person; M: Males; F: Females.



[1]Not community cases = study featured clinical samples or members of a treatment group only

[2]Risk estimate not reported = reported number of exposed who died but not the denominator therefore not allowing mortality rate to be calculated, or did not report deaths in controls

[1]Not clinically defined depression = study used a scale not validated against dsm or icd criteria therefore reports on depressive symptomatology only

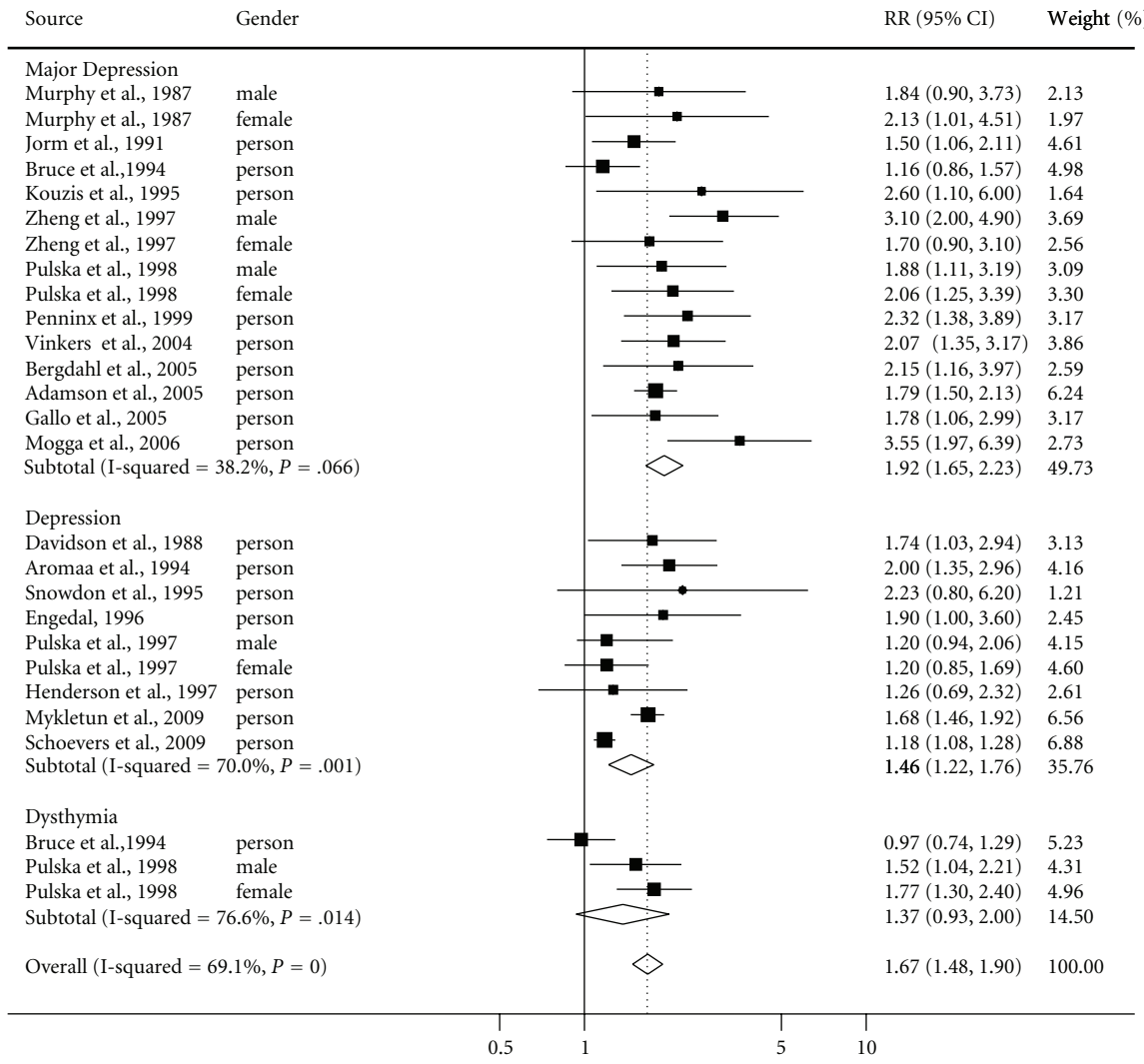
Figure 1: Flowchart showing results of systematic review.

individuals with multiple health problems are not receiving appropriate treatment for a comorbid mental disorder [39]. Underdiagnosis is a concern as depression has been associated with poorer health outcomes including higher fatality rates in those with coronary heart disease [73, 74], cancer [75], and stroke [71].

Persons suffering depression are also more likely to neglect their health and show poor adherence to prescribed medication regimens [15, 22–24]. The causal direction of these relationships is a focus of current research. Possible associations include depression as a result of lifestyle factors, depression leading to lifestyle factors or both depression and lifestyle factors resulting from other independent factors [76]. Improvement of diagnosis and treatment of comorbid physical and mental health problems in primary care may reduce mortality in these groups.

A shorter followup period was associated with increased risk of excess mortality compared to longer follow-up periods. Two of the studies with shorter follow-up period included exposure measures of period prevalence such past-year [52] and lifetime [63] rather than current prevalence. This finding is unexpected as period prevalent cases, which include those without the current disorder, would presumably be less likely to neglect their health and have better adherence to medication at the time of the study baseline [15] which may be expected to show lower relative mortality. Possible recall bias in measures of period and lifetime prevalence may result in misclassification and reduce relative differences in mortality if nondifferential. However, insufficient data were available to look at the association between exposure measure and effect size. The effect of exposure measure deserves further exploration, particularly the possible interaction with follow-up period and age group.

The main strength of this study relates to the inclusion criteria which ensured relatively consistent diagnosis of depressive disorder, limited to population-based studies. Studies were included where estimates for clinically defined depression (depression meeting DSM or ICD diagnostic criteria) were reported while broader mental disorder categories of affective disorders and mood disorder were excluded. Dimensional measures of symptomatology and psychological distress were also excluded. Inclusion of subclinical samples may reduce the risk of excess mortality as severity of depressive symptoms is related to higher rates



RR = relative risk; CI = confidence interval
I-squared represents as a percentage the variation attributable to heterogeneity between studies

Figure 2: Forest plot showing included studies and pooled relative risks of excess all-cause mortality in community cases of depressive disorders, by diagnostic type.

of suicide and self-harm [77]. Whilst acknowledging that mental ill health is a continuum rather than dichotomous (as conceptualized by modern diagnostic standards), it would be inaccurate to compare outcomes for different categories of risk, for example, the inclusion of studies where the "at risk" group comprised major depression, minor depression, and subthreshold depression, compared to studies where the "at risk" group included only major depression [26, 72].

A limitation is the low number of studies focusing on children or adolescents with depression. It may be that the inclusion of studies featuring child and adolescent samples would affect the pooled estimate. More cohort studies involving young people suffering mental disorders are needed to gain a true picture of the long-term outcome of depression across the lifespan.

The only information identified for children and adolescents with depression was on clinical or inpatient samples, or where the focus was on traits and behaviors rather than clinically significant mental disorders [70, 78–84]. The lack of data for long-term followup of community adolescent cases of depression may be due, at least in part, to lack of epidemiological studies which screen for mental disorders in young people. While many countries have carried out regional or national level epidemiologic surveys of mental health in adults, few similar surveys have been conducted for young people. Those studies that have done so have not yet reported long-term outcomes such as mortality [85, 86]. Considering the consistency of the relationship between early mortality and depression, and the link between depression and serious physical disorders, should be given to

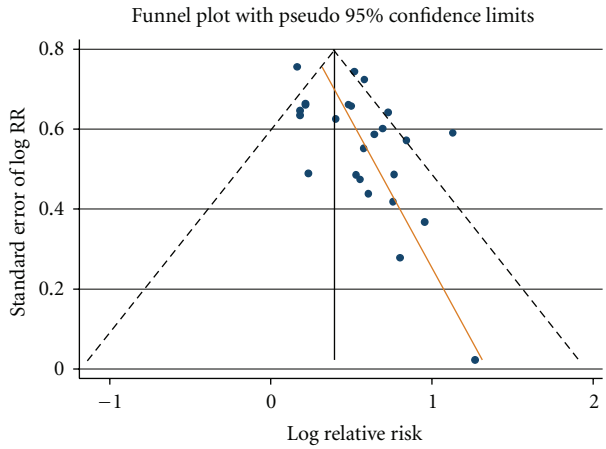


Figure 3: Funnel plot, using data from 21 studies of excess all-cause mortality in cases of clinical depression, with log relative risk displayed on the horizontal axis.

the identification of children and adolescents with depression as early as possible not only to address their mental health but also so that physical health can be monitored.

Analysis of heterogeneity in this review found a high proportion of between-study variance was attributable to follow-up period, gender, and type of depression. Further research is required in order to compare and contrast the risk of premature mortality in mental disorders, other than depression. Similar analyses are needed across the spectrum of mental disorders. If conducted along with similar specifications to this study, the results could be compared to identify those disorders which present the greatest risk of premature death.

Our findings support the importance of identification and treatment of depression in primary care, including where depression is comorbid with physical disorders. Most patients with depression are treated in primary care, and here it should be possible to adequately identify and treat comorbid physical disorders. Where depression is being treated in a mental health service, it is important for clinicians to be vigilant regarding the physical health status of the patient and intervene to minimize lifestyle disease risk factors and have emerging physical disease treated early and effectively.

Appendix

See Table 2.

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