

The Epidemiology of Excess Mortality in People With Mental Illness

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Objective: To investigate the burden of excess mortality among people with mental illness in developed countries, how it is distributed, and whether it has changed over time.

Method: We conducted a systematic search of MEDLINE, restricting our attention to peer-reviewed studies and reviews published in English relating to mortality and mental illness. Because of the large number of studies that have been undertaken during the last 30 years, we have selected a representative cross-section of studies for inclusion in our review.

Results: There is substantial excess mortality in people with mental illness for almost all psychiatric disorders and all main causes of death. Consistently elevated rates have been observed across settings and over time. The highest numbers of excess deaths are due to cardiovascular and respiratory diseases. With life expectancy increasing in the general population, the disparity in mortality outcomes for people with mental illness is increasing.

Conclusions: Without the development of alternative approaches to promoting and treating the physical health of people with mental illness, it is possible that the disparity in mortality outcomes will persist.

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Clinical Implications

- High mortality rates in people with mental illness highlight the importance of treating both physical illness and mental disorder in psychiatric patients, particularly cardiovascular and respiratory diseases.
- People with mental illness have not benefited from improvements in life expectancy seen in the general population, particularly reductions in mortality that are due to cardiovascular disease.

Limitations

- Much of the research on mortality in people with mental illness relies on administrative record linkage. Thus less is known about the psychosocial, demographic, and lifestyle factors that may modify mortality risk.
- Excess mortality from natural causes implies either excess morbidity or worse-case outcome, fatality; however, there has been limited research into the determinants of disease incidence and prognosis, or into their prevention.

Key Words: *mental health, mortality, cause of death, health status*

The excess mortality of people with mental illness has been known for many years. In 1841, William Farr¹ reported to the Royal Statistical Society on mortality within the major asylums and licensed houses of the period in England. He estimated, using life-table methods, the mortality rate in the best facility to be about 3 times that of the general population, and mortality in other facilities to be several times higher again. The report inspired the British parliament to require regular compilation of statistics within all asylums, and established mortality rate as a measure of the quality of care provided. The

high mortality was attributed to infectious diseases and the poor conditions within the asylums, such as lack of exercise and warmth, poor diet, and lack of medical care.

During subsequent years, mortality in people with mental illness has been the subject of hundreds of studies. In the most comprehensive meta-analyses to date, Harris and Barraclough^{2,3} identified 152 reports on all-cause mortality and 249 on suicide. They found that all mental disorders were associated with an increased risk of premature death. Overall

they estimated a mortality risk of more than double for deaths owing to natural causes, and almost 10 times for deaths owing to suicide.

Method and Search Results

We updated Harris and Barraclough's² review of excess mortality through a systematic search of MEDLINE, for peer-reviewed studies and reviews published in English on mortality and mental illness in the 10 years following their review up to January 2010. Because of the large number of studies, we restricted the search to core clinical journals and focused on overall psychiatric morbidity, as well as mood disorders and schizophrenia. We excluded studies restricted to dementia, alcohol or substance use, and anorexia nervosa as increased mortality may be an integral part of the disease process. We used the following search terms: psychiatric disorder; mental disorder; affective disorder; depression; psychosis; schizophrenia; death; and mortality. We did not include studies that collapsed all adverse events, including mortality, into one single measure. We also reviewed the bibliography of retrieved articles.

Our MEDLINE search retrieved 3554 papers, of which we scrutinized 135 abstracts (Figure 1). Among these, we reviewed 104 papers and included 85 in the final review (Figure 1).

Measures of Excess Mortality

The principal measure is the SMR. Synthesizing SMRs reported from multiple studies is complicated by the dependence of SMRs on numerous factors that vary between studies. Relevant factors include follow-up time because the risk of death from unnatural causes is highest in the period after first onset of psychiatric illness and declines over time.⁴⁻⁶ A follow-up cohort of incident cases will return different results than a follow-up cohort of prevalent cases. The age distribution of a cohort is also relevant, as unnatural deaths are highest in younger age groups.⁶

These issues complicate the meta-analyses of mortality studies. No single estimate of risk can accurately reflect the excess risk of mortality with mental illness, as it is clearly dependent on age, diagnosis, and stage of illness. These dependencies are only infrequently described,⁶ and life-table methods are useful in this regard.⁷

Other measures include years or potential life lost, average age at death, and life expectancy.⁸ For instance, years of potential life lost among patients of public mental health services in 8 US states range from 15 to 25 years.⁸ In another

study⁹ comparing sex, estimated mean years of potential life lost were 14 for males and 6 for females.

A further approach is to calculate life expectancy or to estimate life tables. To our knowledge, this has only been done in a Swedish study⁹ where life tables for male and female inpatients were presented by 9 diagnostic categories. Life expectancies were reduced for all diagnostic groups. For example, at age 40 years, conditional life expectancy was 7 years less for patients with schizophrenia or affective psychosis, 13 years less for substance abuse disorders, and 12 years less for personality disorders.

Excess Mortality, by Setting

Most mortality studies have been based on either cohorts or registers of psychiatric patients. In most cases, these are limited to people who have received inpatient treatment for mental illness.¹⁰ For instance, Hiroeh et al¹¹ followed up a population of 4.1 million people of whom 258 000 (6%) had received inpatient treatment for psychiatric illness. Mortality rates were elevated for all psychiatric diagnoses, with highest risks observed for organic psychoses, dementia, and drug and alcohol abuse (SMRs around 3). Mortality rates were also highest for long-stay psychiatric patients.¹¹ Importantly, the elevated risk persists for years after discharge from hospital.

Studies of inpatients have become less relevant as more psychiatric patients are treated in the community. Fortunately, some psychiatric case registers include outpatient and community-based treatment. For example, Amaddeo et al¹² undertook a 10-year follow-up of over 3000 patients, most of whom only received outpatient or community-based care. They estimated an SMR of 2.2 for inpatients and 1.3 for outpatients.¹² A 6-year population follow-up in Nova Scotia using databases covering in- and outpatient psychiatric services and primary care reported SMRs of around 3 for patients of specialist psychiatric services and 1.5 for patients only treated in general practice.¹³

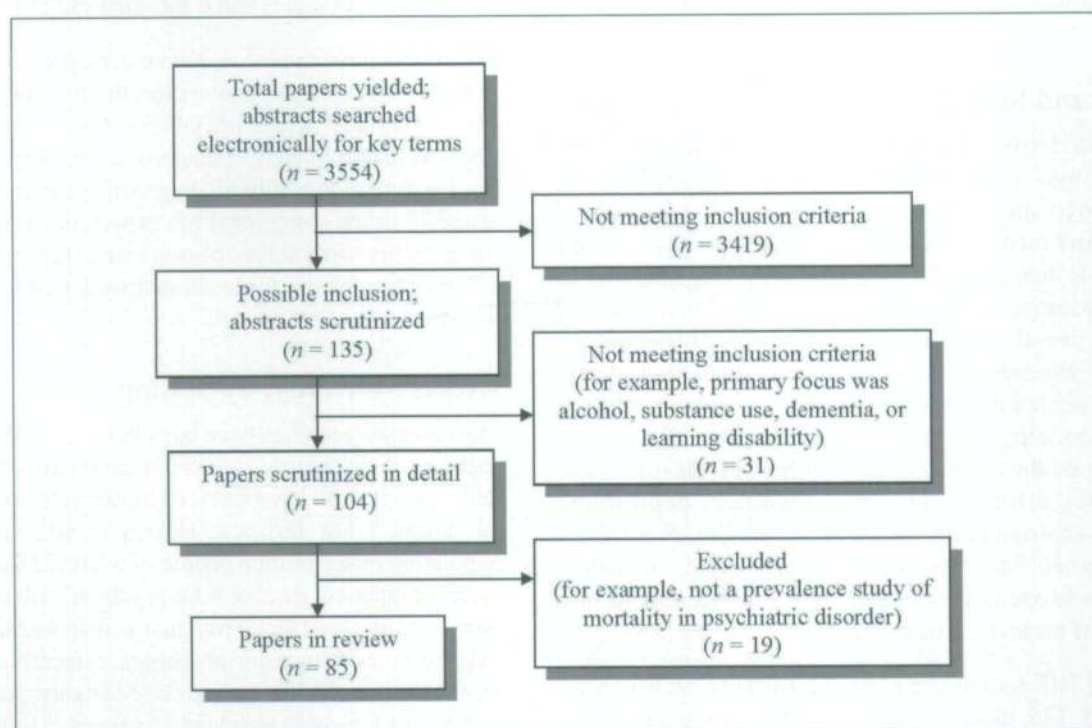
Few studies have examined mortality in population-based cohorts, and these are generally limited by the relatively small number of people who are identified as having psychiatric disorders. Joukamaa et al¹⁴ reported an overall relative risk of mortality of 1.6 in men (95% CI 1.3 to 1.8), and 1.4 in women (95% CI 1.2 to 1.6). Unfortunately, this study did not break down the cohort by those who did or did not receive treatment for their mental illness. Bruce et al¹⁵ reported a mortality ratio of 1.4 from a 9-year follow-up of a population survey including 350 people identified with psychiatric disorders.

While these data are not comprehensive, they suggest a general pattern of elevated mortality rates across all treatment settings, with highest mortality ratios for patients with disorders requiring inpatient specialist treatment, and lower, but still elevated, ratios in community-based and general practice settings. It seems likely that people with untreated mental

Abbreviations used in this article

SMR	standardized mortality ratio
SSRI	selective serotonin reuptake inhibitor

Figure 1 Number of papers yielded by search strategy in systematic review



disorders also have a higher mortality risk, although this remains to be more rigorously tested.

Unnatural Causes of Death

Suicide is the most studied cause of death for people with mental illness, with rates elevated 8 to 14 times among patients with major depression, schizophrenia, or affective psychoses.³ While suicide rates are much higher in people with mental illness than the general community, the absolute number of deaths are small compared with excess deaths owing to natural causes, although these have received considerably less attention in the literature.

There is only a small amount of literature on accidental death and mental illness. In a long-term follow-up of the Danish psychiatric case register, Hiroeh et al¹⁶ found that around 75% of deaths from unnatural causes in psychiatric patients were due to suicide, about 25% were accidental deaths, and 1% were due to homicide. Although the number of deaths are lower, people with mental illness are at higher risk of accidental and violent deaths, particularly where drug and alcohol comorbidities are involved.¹⁷

Natural Causes of Death

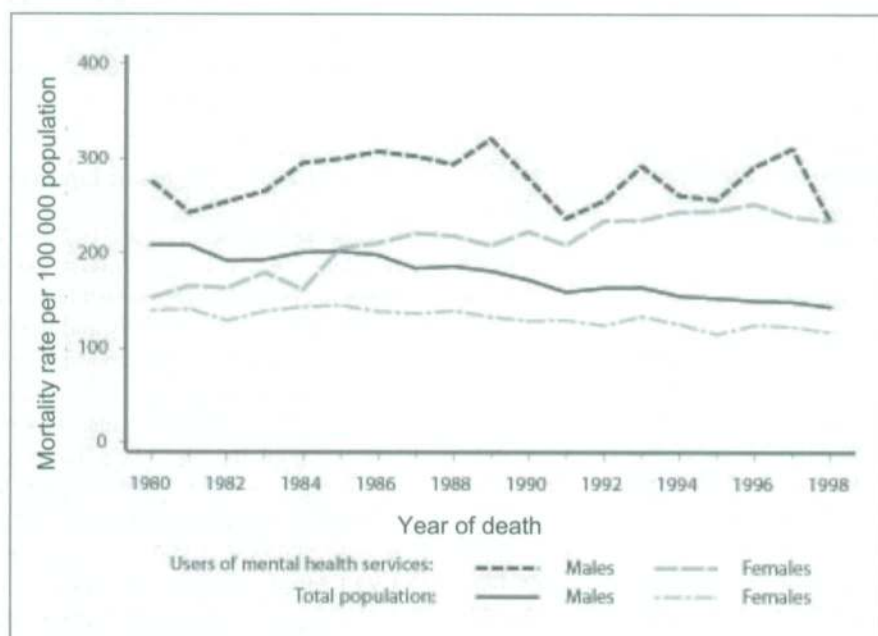
The major causes of death in psychiatric patients are chronic medical diseases not suicide.^{2,5} These include circulatory

disorders such as cardiovascular disease and stroke, chronic lung disease, and infection. Among these, cardiovascular disease is the most common, and, in contrast to the rate in the general population, among people with mental illness, the mortality rate from this cause has not diminished during the last 2 decades (Figure 2).^{14,17,18}

In the case of cancer, the picture is more complicated. Some authors have reported lower than expected cancer incidence or mortality in psychiatric patients, while others have found no association.^{19,20} Still others have found an increased risk of incidence or mortality.²¹⁻²⁵ Schizophrenia has particularly been associated with a reduced incidence of cancer.¹⁹ Explanations have included a tumour suppressor gene, enhanced natural killer cell activity, or the protective effects of some psychotropics.²⁶

Cancer mortality may not always be an ideal marker of the risk of cancer as it is affected both by susceptibility to developing the disorder and by subsequent survival rates. Only 2 population-based studies have evaluated incidence and mortality at the same time and they showed that while people with mental illness did not show an increased incidence rate for many types of cancer, they did have higher cancer mortality, suggesting a higher cancer case fatality.^{21,22}

Figure 2 Ischaemic heart disease mortality rates in Western Australia, 1980–1998^a



^a From Lawrence et al¹⁷; used with permission.

Mortality Risks, by Mental Disorder

Schizophrenia

In 1997, Brown²⁷ published the first meta-analysis of mortality and schizophrenia, based on 18 studies. He estimated an SMR of 1.5, and noted that while the highest SMR was seen for deaths owing to suicide (more than 8), the largest number of deaths were due to cardiovascular disease. A later meta-analysis²⁸ based on 37 papers estimated an SMR of 2.5 (95% CI 2.2 to 2.8) with evidence that the SMR for all-cause mortality has increased in recent decades. The continuing gap in survival between patients with schizophrenia and the general population is confirmed in the latest population-based cohort study.²⁵

About one-third of the excess mortality in schizophrenia is due to unnatural causes, and two-thirds to natural causes.^{29–32} Explanations include direct effects of schizophrenia and its treatment, as well as poor organization of health services, stigma within and outside the health system, and attitudes of medical practitioners.³¹

Mood Disorders

Most studies indicate that major depression is associated with substantial excess mortality.^{33,34} However, results from studies vary.^{34–37} While the 1989 US National Health Interview Study found a mortality risk of 3.1 (95% CI 2.0 to 4.9) for males and 1.7 (95% CI 0.9 to 3.1) for females,³⁵ the Alameda

County study reported no association between depression and mortality after adjusting for physical comorbidity at baseline.³⁶ These differences may be due to differences in case definition or length of follow-up. It had been suggested that mortality risk following depression may wane over several years,³⁸ although this is not a universal finding.³⁹

Increased mortality has also been reported for minor as well as major depression,⁴⁰ and a past history of depression can further increase the risk of inpatient mortality in depressed patients.⁴¹

There is also a large amount of literature on the link between depression and death from myocardial infarction.^{42–47} Severity or persistence of depression following admission for myocardial infarction had been associated with a doubling of mortality during subsequent years.^{42,46,48,49} Timing of depression may also have an influence. Past psychiatric history does not appear to be as important as depression at the time of myocardial infarction.⁴⁷ One study⁵⁰ also reported that it was somatic rather than the cognitive or affective depressive symptoms that were associated with an increased risk of cardiovascular-related mortality and events. The increased mortality risk associated with depression extends to unstable angina,⁵¹ heart failure,^{52–55} and cardiac arrhythmias or arrest.^{56–58} In terms of other disorders, depression has been linked to increased mortality in stroke,⁵⁹ chronic obstructive airways disease,⁶⁰ and HIV infection.^{61,62}

There have been far fewer studies of bipolar affective disorder but they also suggest an increased mortality risk from physical disorder,^{63,64} matching that of schizophrenia.⁶⁴

Depression in the Elderly

For elderly people with psychotic depression, Vythilingam et al⁶⁵ estimated a mortality ratio of 2.3, while Ganguli et al⁶⁶ estimated a mortality hazard rate associated with presence of depressive symptoms of 2.2 after 5 years of follow-up in a general community sample.

Mortality Risks Over Time

Psychiatric care has changed markedly during the last 30 to 40 years, with the availability of new treatments, moves to community-based treatment, and the integration of psychiatric and general medical services. Some of these changes could have been expected to reduce the level of exposure to some mortality risks, such as infectious diseases, and to improve access to physical health care for people with mental illness. At the same time, other risks could have increased with more freedom to make unhealthy lifestyle choices, or experience adverse social circumstances such as homelessness.⁶⁷

As previously noted, the excess mortality of mental illness has not decreased, and may have increased during this period,^{68,69} particularly for cardiovascular and unnatural deaths.⁷⁰ This is at a time when mortality from ischaemic heart disease in the general population has been falling in many developed countries, such as Australia (Figure 2).

Need for Continued Research

With so many studies of mortality and mental illness, the value of performing further studies has been questioned.⁷¹ As the excess mortality observed in people with mental illness has not abated, there is value, at least from a monitoring perspective, in continued measurement. However, there are additional reasons why further research is needed, as much remains unknown about the mechanisms of excess mortality.⁷² Possibilities include the following:

Direct Effects of Mental Illness or Its Treatment

Mental illness may directly affect physical health or the prognosis of a physical illness. For example, chronic organic brain syndromes such as dementia are incurable, progressive, and terminal. Higher mortality could also be associated with the side effects of treatments such as the cardiovascular and metabolic side effects of psychotropic medications, either directly or through weight gain.⁷³⁻⁷⁸ Patients with some diagnoses such as dementia may be particularly susceptible.⁷⁹ Although sudden cardiac death associated with some typical antipsychotic agents generated concern, patients on typical and atypical antipsychotics had similar, dose-related increased risks of sudden cardiac death.⁸⁰ Postmenopausal women taking either tricyclic antidepressants or SSRIs had increased risks of all-cause mortality, and SSRI users seemed

to be at increased risk of hemorrhagic and fatal stroke, although absolute risk were low.⁸¹ However, the relation between such events and psychotropic medications may not always be clear as it is possible that prescription might be a marker of more severe psychiatric symptoms, or other uncontrolled risk factors.^{82,83}

Effect of Mental Illness on Lifestyle and Environment

People with mental illness are more likely to smoke, drink alcohol, and use drugs, to have poorer diets, and are less likely to exercise at recommended levels.⁸⁴⁻⁸⁶ These lifestyle factors are linked to obesity and dyslipidemia, insulin resistance and diabetes, and hypertension, which are major risk factors for cardiovascular disease. Among the total cigarettes consumed in the United States, 44% were smoked by people with a mental disorder.⁸⁷ Similar results have been observed in Australia, with the 20% of adult Australians who had a diagnosable mental disorder in the 12 months before the 2007 National Survey of Mental Health and Wellbeing representing 32.5% of Australian smokers.⁸⁴ Programs can be successful in helping people with mental illness stop smoking, but attitudes of practitioners often undermine these programs.⁸⁸

However, this is unlikely to be the sole explanation in all situations. All-cause mortality remains high, even after adjusting for behavioural risk factors such as smoking, physical activity, and body mass index.⁸⁹ In the case of cancer, the incidence at some sites for psychiatric patients is no higher than that of the general population, although mortality is higher.^{21,22} It is unlikely that lifestyle explains this finding, otherwise incidence should better reflect the increased mortality rate. Although there are less data for other conditions such as cardiovascular disease, these disorders share similar risk factors including tobacco, diet, and alcohol.

Effect of Mental Illness on Physical Health Care

People with mental illness are generally less likely to receive the same level of health care as others in the community with the same level of physical health problems.^{55,90} Despite the higher incidence of cardiovascular disease, rates of procedural interventions are considerably lower in people with mental illness, in Australia, Canada, the United States, and Denmark.^{18,91-93} They are also less likely to receive appropriate medications on discharge such as beta blockers and statins.⁹⁴ The results are consistent with findings from ambulatory and primary care where patients with severe mental illness were less likely to be assessed or treated for hyperlipidaemia.^{95,96} The few exceptions to these findings are in highly specific groups such as patients of Veterans Affairs.⁹⁷ A follow-up of older patients after acute myocardial infarction found that while mental disorders were associated with higher mortality risks, this dependence disappeared once measures of quality of the medical care they received were factored into the model.⁹⁸

It is possible that physicians are reluctant to offer some procedures because of the ensuing psychological stress, concerns about capacity or compliance with postoperative care, or the presence of contraindications such as smoking.⁹⁹ In addition, psychiatric patients may be more at risk of developing complications following medical or surgical interventions,¹⁰⁰ or to have poorer outcomes postoperatively.¹⁰¹ However, contraindications to specialized interventions, such as smoking or problems with informed consent, are less relevant to the prescription of vascular drugs such as angiotensin-converting enzyme inhibitors, beta blockers, or statins known to reduce subsequent morbidity and mortality. It seems that while we are willing to make considerable accommodations to allow people with physical limitations to access health care, there may be a different attitude in terms of accommodating the needs of people with mental illness who may have resulting cognitive impairments that could impair their access to, or compliance with, medical care.

In the case of cancer, a higher mortality in the context of an incidence that is no higher than the general population might be explained by delays in detection or initial presentation, with more advanced staging at presentation.

While it is possible to improve the physical health of people with mental illness, developing programs and models of care that allow for the cognitive, social, and functional impairments associated with mental illness would seem to be an important step forward.¹⁰²

Research Directions

Research in this area has been hampered by the long follow-up times and large cohort sizes required to capture sufficiently large numbers of events for informative analysis. Numerous locations now have long-running population-based registers or administrative data that can be used to track mortality and other outcomes in people with mental illness. However, most are limited in the breadth of the information they collect, with little details available about comorbidities, substance use, diet, exercise, and other lifestyle factors, or social, economic, or demographic factors that would be of interest in exploring the various hypotheses for excess mortality.

Another limitation of administrative data, and register- and hospital-based research is that less than one-half of people with diagnosable psychiatric disorders seek treatment.^{79,99} Little is therefore known about whether there is excess mortality in the community owing to untreated mental illness. This deficiency could be addressed by combining large-scale cross-sectional surveys in the community (and thus including people with treated and untreated psychiatric morbidity), with longitudinal follow-up via linkage to mortality registers.

A final area that is underrepresented in the literature is intervention research. Regarding primary prevention, there have been few attempts to address risk factors for physical illness in people with mental illness. In a trial of physical health checks

and health promotion for patients with severe mental illness, two-thirds of the trial group had not recently undergone any physical health check despite most having at least one modifiable first factor for cardiovascular disease.¹⁰³ Although the program was well received by the participants, its effectiveness was not evaluated. Similarly, interventions for smoking, such as nicotine replacement therapy and bupropion, show promise, but there has been much less research than in the general population.¹⁰⁴ In addition, studies have largely been restricted to psychiatric patients in remission, and data are also lacking for medications such as varenicline in this group.¹⁰⁴ Regarding secondary prevention, results have been disappointing.¹⁰⁵ The Sertraline AntiDepressant Heart Attack Trial investigation demonstrated that sertraline is safe and efficacious in depressed patients with ischemic heart disease but was underpowered to detect a mortality difference between sertraline and placebo.¹⁰⁶ Similarly, in patients with chronic obstructive pulmonary disease and depression, appropriate psychotropic treatment was not significantly associated with decreased mortality during the following 2 years.¹⁰⁷ Larger studies are therefore needed that incorporate both psychological and pharmacological therapy for depression.

Conclusions

Almost all reports of psychiatric and physical comorbidity have found excess mortality associated with mental illness, for all psychiatric diagnoses considered, across all settings, and at all ages. Elevated mortality rates have been reported for all major causes of death, with cardiovascular disease being the most common cause of premature death. Without the development of alternative approaches to promoting and treating the physical health of people with mental illness, it is possible this disparity will persist.

Risk factors for cardiovascular disease (and other major natural causes of death), such as smoking, obesity, and hypertension, are potentially modifiable. There have been extensive efforts to modify risk factors in the general population (such as antismoking campaigns, modification of diets, and increasing promotion of physical activity), and at least some of the decline in cardiovascular mortality observed in the developed world has been attributed to these factors. In contrast, there have been few attempts to address these factors in people with mental illness. Antismoking groups, national heart associations, diabetes associations, and cancer associations should realize that psychiatric patients are a significant proportion of their target audience, and that tailored interventions are required to address their specific needs. Research into ways to improve health care and health promotion in populations with mental illness has the potential to address the excess of mortality associated with mental illness.

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Résumé : L'épidémiologie du taux de mortalité excessif chez les personnes souffrant de maladie mentale

Objectif : Examiner le fardeau du taux de mortalité excessif chez les personnes souffrant de maladie mentale dans les pays développés, la façon dont il est distribué, et s'il a changé avec le temps.

Méthode : Nous avons mené une recherche systématique dans MEDLINE, limitant notre attention aux études révisées par les pairs et aux revues publiées en anglais portant sur la mortalité et la maladie mentale. En raison du grand nombre d'études qui ont été entreprises durant les 30 dernières années, nous avons choisi un échantillon représentatif des études à inclure dans notre revue.

Résultats : Il y a un taux de mortalité excessif substantiel chez les personnes souffrant de maladie mentale pour presque tous les troubles psychiatriques et toutes les principales causes de décès. Des taux constamment élevés ont été observés dans tous les milieux et au fil du temps. Les taux les plus élevés de décès excessifs sont attribuables aux maladies cardiovasculaires et respiratoires. Tandis que l'espérance de vie s'accroît dans la population générale, la disparité des décès pour les personnes souffrant de maladie mentale augmente.

Conclusions : Si l'on n'élabore pas des approches de rechange pour promouvoir et traiter la santé physique des personnes souffrant de maladie mentale, il est possible que la disparité des décès persiste.

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