Mortality of subjects with mood disorders in the Lundby community cohort: A follow-up over 50 years.

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Mortality of subjects with mood disorders in the Lundby Community Cohort: a follow-up over 50 years

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Abstract

Aims: To compare cause of death and mortality among subjects with and without mood disorder in the Lundby Cohort and to analyse other mental disorders as risk factors for mortality in subjects with mood disorders.

Background: The Lundby study is a longitudinal study that investigated mental health in an unselected population. The study commenced in 1947; the population was further investigated in 1957, 1972, and 1997.

Methods: Experienced psychiatrists performed semi-structured diagnostic interviews, and best estimate consensus diagnoses of mental disorders were assessed at each field investigation. Subjects with mood disorder (n= 508, 195 males, 313 females) were identified until 1997. Causes and dates of death between 1947 and 2011 were obtained from the Swedish cause of death register and were compared between subjects diagnosed with mood disorder and other participants.

Mortality was compared between those with mood disorders and the remaining cohort with Cox regression analyses. Other mental disorders were considered as risk factors for death for subjects with mood disorders.

Results: The hazard ratio for mortality in mood disorders was HR=1.18. However, the mortality was elevated only for males, HR=1.5. A total of 6.3% of the participants with mood disorder and 1.2% of the remaining participants committed suicide. Comorbid anxiety disorders, organic disorders, dementia and psychotic disorders were significant risk factors for death.

Conclusions: As expected, the suicide rate was higher among participants with mood disorders. Only males with mood disorders had elevated mortality. The impact on mortality from other mental disorders seems to vary between the genders.

Keywords: Mortality, mood disorder, depression, suicide, causes of death

Introduction

It is a well-established fact that subjects suffering from mental illness die at an earlier age than healthy people. Psychiatric patients have elevated mortality rates, between 36-100% higher than those of the general population (Rorsman, 1974; Murphy et al., 1989). Despite progress in psycho-pharmacologic and psychotherapeutic treatment options, people with psychiatric illness continue to have increased mortality (Hansen et al., 1997). Elevated mortality rates also include subjects with mood disorder (Murphy et al., 1987; Ösby et al., 2001; Angst et al., 2002; Angst et al., 2012); these findings have been demonstrated in both clinical samples of hospitalised subjects and epidemiological studies of general populations (Zheng et al., 1997, Murphy et al., 1987). A review using a systematic method by Wulsin et al. (1999) showed that depression is associated with an increased mortality. Also, cardiovascular mortality and suicide are related to depression according to Wulsin.

In an earlier investigation from the Lundby Study the mortality rate from natural causes of death among subjects with a history of mental disorders was studied. The relative death rate was 1.5 in males and 1.2 in females with histories of mental disorder (Rorsman et al., 1982). For both sexes it was organic brain disorders that accounted wholly for the excess mortality. The mortality rate in the Lundby Study was described also in 1983, when findings of the study showed increased mortality among men with untreated as well as treated mental disorders (Rorsman et al., 1983). It was found that the relative overall death rate for mentally ill subjects compared to the standard population to be 1.8 for males and 1.2 for females. Similarly, a Norwegian study showed minimal improvement in the mortality rate in males

over the previous 50 years in spite of better treatment options (Hansen et al., 1997). The Stirling County Study reported that depressed men had a significant risk of mortality not detected among matched depressed women (Murphy et al., 2010).

Several studies have found increased mortality in patients with major depressive as well as bipolar disorder (Höyer et al., 2001; Ösby et al., 2001; Brådvik et al., 2010; Sharma and Markar, 1994). One exception is the follow-up study of mortality in the Epidemiological Catchment Area Study, which did not confirm higher mortality among subjects with mood disorder (Eaton et al., 2014). The elevated mortality of subjects with mood disorder is mainly due to suicide (Berglund and Nilsson, 1987). In particular, studies of inpatients hospitalised for mood disorder have demonstrated high rates of suicide (Höyer et al., 2001, Angst et al., 2012). It is clear that studies of community and outpatient populations show much lower suicide rates than studies of hospitalised inpatients (Mattisson et al., 2007).

Comorbid non-psychiatric conditions among psychiatric populations have also been suggested as factors that contribute to low life expectancy. It has been suggested that physical disease contributes more to mortality than psychiatric illness (Batty et al., 2012). Cardiovascular and psychiatric conditions often coexist (Huang et al., 2009). It is likely that there are other causes, such as comorbid alcohol and drug use, that contribute to elevated mortality in patients with mood disorders (Yoon et al., 2011).

Earlier, researchers in the Lundby Study have studied in mortality in the Lundby Cohort, which is an unselected population. It was reported within the framework of the Lundby Study that severe depression with psychotic and/ or melancholic features in particular carries a high

risk of accomplished suicidality (Brådvik et al., 2008). Moreover, male gender has been linked to a higher risk of suicide.

In the Lundby Study there is a unique access to information about not only mood disorders but also additional diagnoses. The aim of the present study is to investigate the mortality of subjects with mood disorders in a general population the Lundby Community Cohort. The present study also aimed to assess additional diagnoses in subjects with mood disorder in the Lundby cohort. Finally, another aim is to study whether the presence of an additional mental disorder was associated with an increase in mortality among subjects with mood disorder in the Lundby community cohort.

Background

The present study was performed within the framework of the Lundby Study which is an epidemiological study with a long follow-up period; it commenced in 1947 in a rural area in the south of Sweden. The original population was comprised of 2,550 subjects. In 1957, 10 years after the first survey, follow-up was conducted, and 1,013 subjects who had either moved into the area or had been born were added to the original population. The total cohort thus comprises 3,563 subjects. In 1972, 25 years after the first field investigation, a second follow-up was performed (Hagnell, 1990). In 1997, a 50-year follow-up was performed (Nettelbladt et al., 2005). Survivors of the total cohort, regardless of residence have been followed up in 1972 and in 1997. At the beginning of the study, many of the inhabitants were farmers and farm labourers. In 1997, the Lundby area had changed into a suburban society in which subjects of working age commuted to neighbouring city areas. During the previous decades, migration form the area had been substantial, though limited mostly to nearby municipalities.

Procedure

All individuals in the rural catchment area in the south of Sweden in 1947 (n=2,550) were included and personally examined in the first survey. All persons in 1957 were again examined by a personal interview conducted by psychiatrists. At all investigations, observations of clinical behaviours, the participants subjective report on various personality-related items were scored at the semi structured interviews conducted by psychiatrists. Participants provided written consent. A preliminary diagnosis of an eventual episode of mental disorder was established after the interview. Episodes of mental disorder were assessed at each field investigation, by the fieldworkers (psychiatrists). The participants were also surveyed for mental problems and episodes of mental disorders as well as alcohol abuse during the intervals between follow-up periods. The interview comprised about 150 items that were to be answered and graded. Other sources of information such as medical records, registers, and key-informants were utilised in order to get as much information as possible before the diagnostic evaluation took place within the research team. When a subject had died, nearest next of kin, other persons or key-informants that knew the deceased person well were interviewed. The research team agreed upon the best estimate consensus diagnoses of episodes of mental disorders after gathering all data.

Certified causes of death were obtained from the national cause of death register (Epidemiological Centre, the National Board Health and Welfare). The causes of death were coded according to the ICD-9 (World Health Organization, 1977). On each death certificate in Sweden there is one underlying cause of death and an option to specify contributing causes. For subjects who are hospitalised, the death certificate is made by the consultant in charge,

and for deaths outside the hospital, the physician in charge (mostly a general practitioner) certifies the death as well as the date of death (Statistics, Sweden).

All subjects of working age in the cohort were classified in 1997 according to the principles established in the Swedish socio-economic classification (Swedish Socio-Economic Classification, 1982). Three socioeconomic levels were applied: (1) blue-collar workers, including unskilled, semi-skilled, and skilled workers; (2) white-collar workers, such as assistant non-manual employees, professionals (self-employed or otherwise), higher civil servants, or executives; or (3) self-employed (other than professionals).

Diagnostic criteria

The Lundby Study started before the DSM-system was developed and before structured diagnostic schedules were in use (American Association, 1994). Since 1957, the Lundby Study applied a simple and comprehensive diagnostic system that was adapted to fieldwork and has 11 diagnostic categories. A diagnosis according to the simplified Lundby diagnostic system and a diagnosis according to the ICD-system and the DSM-system were applied. The main groups of the Lundby diagnostic system are: depression, anxiety disorders, mixed neurosis, schizophrenia, other psychoses, organic syndrome, and dementia. After the last field investigation in 1997 it was found that certain diagnostic categories were unevenly distributed before and after 1972 indicating a problem of diagnostic probability over time. The categories concerned were the diagnostic categories: tiredness, mixed neurosis and psychotic disorders. Episodes of mental disorders representing these diagnostic categories were re-evaluated and diagnoses according to the DSM-system were added in retrospect.

The diagnostic criteria for depression used in the Lundby Study have remained the same over the years. Depression includes subjects who mainly have melancholic, endogenous symptoms such as lowered mood, guilty feelings, reduced activity, lack of initiative, are better towards the evening, reduced self-esteem, lowered enjoyment of life, and feelings of low vitality, anxiety, and fear. Sometimes retardation is present. Often the subject has sleep disturbances and wakes up during early morning or suffers from loss of appetite and weight (Hagnell, 1966).

The DSM diagnosis of bipolar disorder is found in the category of other psychosis, but is included in the concept of mood disorders in the present study. Subjects with a mood disorder, depression or bipolar, in the Lundby cohort were thus identified as cases of mood disorders.

An impairment rating according to Leighton (1963) was given for every episode of a mental disorder in a subject during 1947-1997. In reports from the Lundby Study, three degrees of impairment were applied: mild, medium, and severe. Mild impairment means that daily work is usually possible although with a lower achievement. The mental symptoms make a psychiatrist think that something should be done therapeutically. Naturally, there is no sharp limit between severe and medium impairment. Severe impairment involves almost a total inability to work or at least a marked reduction in functional capacity. Individuals in this group either depend on daily help or require complete care. Severe impairment may involve depression with retardation or delusions or schizophrenia (Hagnell, 1990). For caseness an impairment of at least medium degree of impairment was required as well as a diagnosis according to the Lundby diagnostic system and diagnoses of DSM-IV and ICD-10. The Lundby diagnoses of mood disorder and the corresponding DSM-IV diagnoses are presented in Table 3.

Other mental disorders as risk factors for mortality in subjects with mood disorder

Other mental disorders considered in the present study to be risk factors for mortality included anxiety disorders, mixed neurosis, organic syndrome, dementia, psychotic disorders, and alcohol use disorder.

Anxiety disorders in the Lundby Study correspond mainly to panic disorders and generalized anxiety disorder (Gräsbeck et al., 1993). Mixed neurosis comprises neurotic states with symptoms such as fatigue, anxiety, depressiveness, and obsessive-compulsive symptoms, in which no symptom is especially dominant. Organic syndrome comprises subjects with cognitive deficits such as memory difficulties, slow reactions, and concentration difficulties. Dementia in the Lundby Study comprises Alzheimer's disease, multi-infarct dementia, and other varieties of dementia (Hagnell, 1966). Psychotic disorders in the present study include schizophrenia, other psychoses, and substance induced psychotic disorders. Schizophrenia in the Lundby Cohort corresponds to the DSM-IV and ICD-10 diagnoses of schizophrenia. Alcohol abuse disorder comprises alcohol abuse and alcohol dependence. In the latest follow-up period (1972-1997), personality disorders were diagnosed according to DSM-IV criteria, whereas in earlier studies from the Lundby Study, personality disorders referred to a severe deviance of the personality with, for example, psychopathic and aggressive traits. The occurrence of other diagnoses in subjects with and without mood disorder is shown in Table 3.

Sample and correspondence of diagnosis

Sample characteristics are presented in Table 1. In the total cohort, 508 out of 3563 subjects were diagnosed with mood disorder. The observation years for the whole cohort by age-intervals are presented in table 2. The total years of observation were 124, 805. Of those 508

subjects diagnosed with mood disorder, 195 were males (38.4%) and 313 were females (61.6%); 108 subjects (21.3%; 45 males and 63 females) had been admitted to a psychiatric facility. There was information from medical records (both psychiatric and non-psychiatric) for 107/195 (54.9%) males with mood disorder. Further, there were reports from the in-patient register *(*comprising both somatic and psychiatric care*)* for 140/195 (71.8%) males. Outpatient registers provided reports for 90/195 (46.1%) males and key-informants informed the fieldworkers about 76/195 males. For 170/313 (54.3%) females, medical records were provided as well as information from the in-patient register, 258/313 (82.4%) females. Outpatients registers had information about 146/313 (46.6%) females. and key-informants gave information about 120/313 females. In the remaining cohort, there were 3055 participants, 1627 males (53.3%) and 1428 females (46.7%). Among the other subjects (not diagnosed with mood disorder) in the cohort, 6.5% (117 males and 88 females) were admitted for care.

See Table 1 and Table 2

The Lundby diagnoses of mood disorders comprising depressive disorders and psychotic disorders (bipolar disorders) and the corresponding DSM-IV diagnoses are shown in Table 3. The diagnostic categories in DSM corresponding to the Lundby diagnosis of depression and other psychotic disorders (bipolar disorder) include: major depressive disorder (n=249), depressive disorder NOS (n=155), adjustment disorder with depressed mood and dysthymic disorder (n=67), mood disorder due to a medical condition (n=8), substance induced mood disorder (n=3), depressive disorders with psychotic features (n=14), and bipolar disorders (n=12). The most common DSM-IV diagnosis was major depressive disorder; it constituted 51.4% of the diagnoses. There were only 12 subjects (2.4%) diagnosed with bipolar disorder. Few of the subjects (14 subjects, 2.8%) were diagnosed with depressive disorder with

psychotic features. Of 508 participants with a Lundby diagnosis of depression, 354 subjects (134 males and 220 females) were classified with medium degree of impairment. A smaller number of subjects (154, 61 males and 93 females) were categorized with severe degree of impairment.

See Table 3

Statistics

The sample was described with frequencies for discrete data and with medians and quartiles for interval scaled data. The statistical significance of differences in occurrence of other mental disorders between individuals with and without mood disorders was assessed with Fisher's exact test. In order to compare the mortality between participants in the Lundby Cohort who were rated as cases of mood disorder during the study period with those who were not, an analysis using Cox regression was carried out with time from date at entry into the cohort to either death or end of the study as the dependent variable and presence of mood disorder as a time-dependent covariate, controlling for age at entry into the cohort, gender, and marital status; this model was established for the whole cohort as well as separately for each gender. In order to assess the influence of other comorbid mental disorders in individuals with mood disorder, Cox regression models were again considered, with time of diagnosis of the mood disorder until death or end of follow-up as dependent variable. An individual who was diagnosed with another mental episode was assumed to have that disorder from the day the other mental disorder episode was diagnosed until the end of the follow-up period. First, simple models, which included only one of the other mental diagnoses in addition to possible cofounder variables such as age at entry, gender, and marital status, were considered. A model in which all other mental diagnoses were included was then considered, then the non-

significant diagnoses were removed one by one, again controlling for age at entry, gender, and marital status. Such models were made for all participants with mood disorders as well as separately for each gender. Cumulative survival for the main diagnostic categories was illustrated by a Kaplan-Meier curve. The significance level was set at $P<0.05$. The SPSS Statistical Package for Social Sciences version 21.0 was used for statistics and data handling.

Results

Causes of death

Certified causes and dates of death were obtained from the Swedish national cause of death register (Epidemiological Centre, the National Board of Welfare). The causes of death are presented in table 4. Subjects with and without mood disorder had similar causes of death. Causes of death were mostly due to circulatory diseases, neoplasm, and gastrointestinal and endocrine diseases. Among subjects with mood disorder, suicide was a prominent cause of death. In the total cohort 68 subjects committed suicide during follow-up. Thirty-six participants (1.2%; 26 males, 10 females) in the sample without mood disorders committed suicide, whereas 32 (6.3%; 25 males, 7 females) among those diagnosed with mood disorder committed suicide. Of those participants who were diagnosed with mood disorder and committed suicide, 1 participant (aged 44 years) with bipolar disorder committed suicide, 13 subjects had major depressive disorder, 11 subjects had depression NOS, 5 had depressive disorders with psychotic features, 1 person had adjustment disorder with depressed mood, and 1 person had the diagnosis of substance-induced mood disorder. The age at death from suicide was roughly the same for those with and without mood disorder: 59.5 years (range 22-85 years) for those with mood disorder and 59.0 years (range 22-91 years) for those with mood disorder. Twenty participants with mood disorders who committed suicide were assessed as having severe degree of impairment, and 12 had medium degree of impairment. Among the

36 participants in the remaining cohort who had committed suicide, 11 subjects had no diagnosis of mental disorder, whereas 25 had various diagnoses of mental disorder.

See Table 4

Mortality in mood disorder

Of those diagnosed with a mood disorder, 313 (180 males, 133 females) out of 508 died during follow-up (mean age at death 69.0 years for males and 76.3 for females). In the remaining cohort, 1548 (873 males, 675 females) out of 3055 participants died during follow-up; the mean age at death was 73.2 years and 77.2 years for males and females, respectively. The mortality rate among subjects with mood disorder was 18% higher compared to subjects without mood disorder (HR=1.18, P=0.012). The hazard ratio (HR) was 1.5 for males (P< .001) and 1.0 for females 1.0 (P=. 967). It was thus concluded that males with mood disorder had higher rates of mortality than females, and males and females were not affected equally.

In general, females had a statistically significant higher mortality rate if they were married or cohabitating compared to unmarried females, HR=1.45 (P< .001), while married males had a lower mortality rate, HR=0.77 (P< .001).

See Table 5

Comorbidity and other mental disorders as risk factors for mortality

Anxiety and alcohol abuse disorders were found to be the most frequent comorbidities among participants with mood disorders. There was a statistically significant difference between participants with and without mood disorders (P-values below 0.001) for both disorders and

both sexes. Dementia was more common among subjects without mood disorders, but the difference was not statistically significant. For both sexes, personality disorders were more common among participants with mood disorder compared to those without mood disorder to a statistically significant degree.

See table 6

The putative risk factors for mortality was studied in subjects with mood disorder and the results are shown in table 7.

In the simple models, anxiety disorders increased mortality in the entire sample and in females. Organic disorders increased mortality in the entire sample of patients with mood disorders as well as in males. A diagnosis of dementia increased the mortality for the entire sample and for both genders. Personality disorders did not increase mortality. Psychotic disorders increased mortality for the entire sample.

In the multivariate models, anxiety disorders were a risk factor for mortality for the entire sample and for females. Organic disorders were risk factors for the whole sample and for males. Dementia was a risk factor for the whole sample as well as for both genders. Psychotic disorders were risk factors for the whole sample and for females with mood disorders.

See Table 7

Mortality for the main diagnostic groups

Kaplan-Meier survival curves are demonstrated for the three main diagnostic groups: major depressive disorders (n=249), depressive disorder NOS (n=155), and a group comprised of cases of dysthymia and adjustment disorder with depressed mood (n=67). Subjects with a diagnosis of depressive disorder NOS had the lowest rates of survival.

It was found that subjects with major depressive disorder had roughly 40% (HR =1.41) higher mortality than participants with dysthymia and those with adjustment disorder with depressed mood; the difference was not statistically significant, however (P=0.14, CI 0.89-2.23). The category comprising depressive disorder NOS had the highest mortality, 85% (HR=1.85), in comparison with the group with dysthymia and subjects with adjustment disorder with depressed mood (P<0.010, CI 1.16-2.96).

See figure 1

Discussion

The Lundby cohort comprises 3,563 subjects screened for mental disorder over 50 years. The cohort offers an opportunity to study mortality in a general population followed over a long time period. There are few prospective long-term studies of mortality of unselected populations, as most studies evaluate hospital-based samples. The aim of the present study was to investigate whether a diagnosis of mood disorder was related to an elevated mortality and to investigate other mental disorders as putative risk factors. Our results were similar to those of previous studies that showed an elevated mortality rate among subjects with a diagnosis of mood disorder. We also found that depressed men experienced a statistically significant increase in mortality that was not found in depressed women. In fact males had a hazard ratio of 1.5 indicating a high mortality rate. An explanation could be that the increased mortality of cardiovascular and cerebrovascular disease associated with depressive disorder may contribute to the higher mortality in males compared to females (Pan et al., 2011).

The Lundby Study has continued to use its own simple diagnostic system in order to be able to make comparisons over time. The Lundby diagnosis of depression mainly corresponds to

the DSM-IV diagnoses: major depressive disorder, depressive disorder NOS, adjustment disorder with depressed mood, and dysthymia. The Lundby Study is a longitudinal study with a long period of follow-up and with few field-investigations; hence, recall bias could have affected the diagnostic procedures resulting in several unspecific diagnoses. Also, many participants were diagnosed with depressive disorder NOS. Recall bias may explain this, since many diagnoses were assessed in retrospect in the present study, and participants may have forgotten symptoms. However, the use of other sources of information as registers and medical records may have detected forgotten episodes of depression and decreased recall bias. It is a possibility that the use of collateral sources gives a more complete coverage of disease in the population by detecting more cases and maybe this could contribute to the finding of an increased mortality.

There were no differences in the distribution of causes of death between deceased individuals with and without mood disorders other than in the proportion of suicides in the present study. Subjects, especially males, with mood disorders had higher suicide rates. The opposite was found in a study from Denmark that reported higher suicide rates for hospitalised females compared to hospitalised males (Munk-Laursen et al., 2007). The Danish Study compared cause-specific mortality between admitted males and females in subjects with unipolar depressive, disorders, bipolar affective disorder, schizoaffective disorder and schizophrenia. The divergent results are probably due to methodological differences since the Danish Study covered a wider range of diagnostic categories although patients with unipolar depressive disorders, bipolar disorder, and schizoaffective disorder had similar patterns of mortality in the Danish study. Moreover, the different results may be due to different kind of samples, since the Lundby Cohort is a population based and the Danish study was hospital-based.

Elevated mortality in depression has been reported to be unevenly distributed among genders. Time trends in mortality associated with depression were investigated in the well-known Stirling County Study, and the main finding was that depressed males experienced a significant mortality risk that were not matched among females (Murphy et al., 2010). In the present study, depressed males were more likely to die earlier than females, in line with the findings from the Stirling County Study. The hazard ratio for mortality among males with mood disorders was 1.5, which was similar to the Stirling County Study figure of 1.3 from the period 1970-1992. Females with mood disorder did not show an elevated risk for premature death in the present study, a finding that is also similar to the Stirling County Study. Similar results were reported from a study that examined the association between late-life depression and all-cause mortality (Jeong et al., 2012). The authors reported that major depressive disorder seem to directly confer a risk of mortality in elderly men, whereas non-major depression may be an indicator of increased mortality in both genders. On the other hand, in the ECA study, Eaton et al. did not find that there was an increased mortality rate in subjects with mood disorders. Alcohol, drug use, and antisocial personality disorders were associated with increased risk of death, but there was no strong association between risk of death and mood and anxiety disorders (Eaton et al., 2014). One explanation that was offered was that depressive disorder itself was not associated with a high risk of death but rather is concomitant with rapidly declining health and that somatic symptoms of chronic fatal disease overlap with those of depressive disorder. However, severe depression has been linked to a high risk of suicide and hence an increase in mortality (Brådvik et al., 2008).

Another interesting finding was that, whereas marriage and cohabitation were associated with longer survival in males and thus protective, the reverse was found for females. Hence, married females have statistically significant higher rates of mortality than unmarried females in this cohort. This could reflect different expectations and demands correlated to the gender

role. It is possible that even today, females are expected to be more giving and caring than males. However, a protective effect of marriage was found for both genders in the Swiss National Cohort, but the benefit of being married was stronger for men than for women (Staehelin et al., 2012).

During the study period, many participants with mood disorder received additional diagnoses that were used in the regression models. In the simple models, the risk factors that were found to be predictors of mortality in mood disorders were anxiety (though not for males), psychotic disorders for all, and organic syndrome for all and for males in particular. In the multivariate model, additional mental disorders such as anxiety, organic disorders, dementia, and psychotic disorders increased mortality. Some gender differences were detected. Females seem to be more affected by anxiety disorders as a predictor of mortality, whereas males were more vulnerable to organic disorders. The finding of elevated mortality for those with both anxiety disorder and mood disorder could be important, since anxiety disorders also is an independent risk factor for suicide (Schaffer et al., 2000) .In an earlier study of the Lundby Cohort it was found that organic syndrome was found to be the diagnosis group that accounted for excess mortality among persons who had been under psychiatric care (Rorsman et al., 1982). These reports are similar to the finding in the present study showing that the mortality was increased for males with mood disorder and organic disorder. As expected, dementia was a predictor of mortality for all subjects and for both genders. Concurrent alcohol abuse disorder did not, however, turn out to be a risk factor for premature mortality in both the simple and multivariate regression models. Personality disorders also did not affect mortality in the present study.

Comorbidity refers to the presence of two or more distinct co-occurring disorders in the same person. However, the diagnostic system that is applied may affect the rate of comorbidity, and

it has been proposed that comorbidity may be nothing more than an artefact of an imperfect diagnostic system (Cummings et al., 2013). In the Lundby diagnostic system only one diagnosis of mental disorder is allowed at a specific time, except for the diagnoses of alcohol use disorders and personality disorders, consequently it is somewhat difficult to refer to comorbidity in this study.

In the present study during follow-up, the prevalence of other mental disorders as anxiety disorders, personality disorders, and alcohol abuse disorder were markedly higher for subjects diagnosed with a mood disorder compared to subjects without mood disorder. The differences were statistically significant. Anxiety disorder has been reported to be a significant risk factor for major depressive disorder as well as an independent risk factor for suicide (Hettema et al., 2003; Schaffer et al., 2000). Anxiety could also be one of the symptoms in a depressive episode. Further, alcohol abuse disorder has often been reported to be a risk factor for depressive disorder (Swendsen and Merikangas, 2000). Previous studies have reported that alcohol abuse disorder is often present in individuals who suffer from mood disorders; this was (Kessler et al., 2005) also the case in the present study. The relationship between alcohol abuse disorder and depression may be reciprocal. Comorbid personality disorders have been reported to be frequent in subjects with mood disorders and are associated with a range of clinically important indicators such as a higher burden of psychopathology, a longer-lasting reduction in psychosocial and occupational functioning, and a poorer response to treatment (Friborg et al., 2014). According to the same author (Friborg), dysthymia is especially associated with a higher frequency of comorbid personality disorders. There were few subjects with dysthymia in this study. Somewhat surprisingly, dementia was more common among participants who not were affected with mood disorders, but the difference was not statistically significant.

The Kaplan-Meier survival analyses in the present study showed that those participants diagnosed with depressive disorders NOS had the shortest survival, and the diagnostic category composed of subjects with dysthymia and adjustment disorder with depressed mood had the longest survival. Those subjects with major depressive disorder also had higher mortality, but the survival was longer than for subjects with depressive disorder NOS. This finding was somewhat unexpected and may depend on factors in the diagnostic evaluation, as mentioned before.

There is, of course, a difference between a sample of hospitalised inpatients with very severe illness and a community based sample. Previous studies have indicated quite clearly that hospitalised patients with mood disorders may have much higher suicide rates than outpatients or subjects identified with mood disorder in the community (Fredman et al., 1989). Accordingly, a follow-up performed by Angst et al. (2002) found that 10.8% of subjects hospitalised for mood disorder committed suicide. A later follow-up of the same inpatient sample (2012) reported that 15.05% of individuals with major depressive disorders committed suicide. In the present study, 6.3% of the subjects with mood disorder achieved suicide, which probably reflects that the Lundby cohort is a population-based sample. This result is similar to what Inskip reported, namely, a lifetime risk of 6% for affective disorder (Inskip et al., 1998).

Finally, this study showed an increased mortality for males with mood disorder. The presence of other mental disorder for subjects with mood disorder elevated the mortality. For females the increase in mortality seem to be caused by anxiety and by organic disorders for males. Dementia was a significant predictor for both sexes.

Conclusion

Mood disorders are common serious mental disorders in general populations that affect mortality. In the present study that was true only for males. Males with mood disorder should be treated carefully as the risk of suicide is high.

Strengths and limitations

The strength of the present study is that the Lundby Study is a prospective study of a community-based population with a long follow-up period. Another strength is the access to collateral sources of information such as registers, medical records, and key-informants. There are also several important limitations. The Lundby Study was started before structured diagnostic instruments were widely applied. There were somewhat few subjects with bipolar disorders. Causes of death were identified for the time period 1947-2011, whereas diagnoses of mental disorders were identified only until 1997. Thus, new cases of mood disorders and other diagnoses of mental disorders between 1997 and 2011 are not registered. Mortality due to mood disorder and the influence of other mental diagnoses could thus have been somewhat underestimated. On the other hand, as additional mental disorders are assumed to persist throughout the follow-up, there could have been in some cases a slight overestimation of the influence on mortality from these disorders. Also, the recall periods were of considerable length, probably introducing recall bias that resulted in some episodes of mental disorders being forgotten, although this bias could have been mitigated by the use of other sources of information.

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Conflict of interest

None declared.

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Table 1. *Sociodemographic characteristics of subjects with mood disorders at entry into the Lundby Cohort, n=508, and without mood disorder, n=3055. Percentages are given in parentheses (%).*

	N=508, with mood disorders		N=3055, without mood disorders	
	Males	Females	Males	Females
Subjects, n	195	313	1627	1428
Age at entry into the study, median (q1-q3)	27 (10-41)	29 (12-40)	30 (13-48)	32 (11-51)
Age at onset of mood disorder Median (q1-q3)	47.5 (35-61)	48.0 (37-62)	-	-
Marital state (%)				
Unmarried	37 (19.0)	51 (16.3)	248 (15.2)	191 (13.4)
Married, cohabitating	140 (72.0)	199 (64.0)	1119 (68.8)	839 (58.8)
Divorced	14 (7.2)	29 (9.3)	98 (6)	83 (5.8)
Widow/widower	4 (2.1)	34 (10.9)	162 (10)	315 (22.1)
Socio-economic classification (%)				
Blue-collar workers	117 (60)	185 (59.1)	914 (56.2)	802 (56.2)
White-collar workers	47 (24)	80 (25.6)	338 (20.8)	344 (24.1)
Self-employed	29 (14.9)	48 (15.3)	365 (22.4)	279 (19.5)
No information (about disorders)	2 (1.0)	-	10 (0.6)	3 (0.2)

Table 2. *Total observation years n=124 805 in the Lundby Cohort of males and females n= 124805 during the follow-period 1947-1997*

Males	Subjects entering study	Total observation years	Females	Subjects entering study	Total observation years
Age-interval			Age-interval		
0-9	366	1871	0-9	379	1776
10-19	282	5019	10-19	252	5084
20-29	245	7429	20-29	209	7056
30-39	275	9707	30-39	253	9078
40-49	254	11335	40-49	227	10501
50-59	160	10825	50-59	166	10004
60-69	123	8883	60-69	131	8680
70-79	90	5681	70-79	84	6289
80+	28	2339	80+	39	3248
Total	1823	63089		1740	61716

Table 3. *DSM-IV diagnoses for 508 subjects diagnosed with mood disorder, depression, or other psychoses (bipolar disorder)*

Diagnoses	Men	Women	Total
Major depressive disorder 296.22	88	161	249
Depressive disorder NOS 311	64	91	155
Adjustment disorder with depressed mood, Dysthymia 309.0, 300.4	22	45	67
Mood disorder due to a medical condition 293.83	6	2	8
Substance induced mood disorder 292.84, 291.8	2	1	3
Depressive disorder with psychotic features 296.24	7	7	14
Bipolar disorder 296.80, 296.43, 296.04, 296.89	6	6	12
Total	195	313	508

Table 4. *Causes of death for 313 deceased subjects out of 508 with mood disorder in comparison with 1971 subjects out of 3055 without any mood disorder*

	Participants with mood disorder, n=313		Participants without mood disorder, n=1971	
Neoplasm including leukaemia	57	18.2%	406	20.6%
Diseases of the circulatory system	175	55.9%	1157	58.7%
Gastrointestinal and endocrine causes of death	13	5.8%	89	4.5%
Infectious diseases	2	0.6%	25	1.3%
Diseases of the urogenital system	5	1.6%	30	1.5%
Myopathies and diseases of the skeleton	2	0.6%	6	0.3%
Mental disorder and diseases of the central nervous system	9	2.9%	57	2.9%
Congenital malformations	0	-	3	
Dermatological diseases	0	-	2	
Accidents	5	1.6 %	61	3.1%
Suicides	32	10.2%	36	1.8%
Uncertain causes of death	5	1.6%	46	2.3%
Unknown causes of death	8	2.6%	53	2.7%

Table 5. *Survival analysis for 3563 subjects, n=508 with mood disorder and 3055 without mood disorder, in the Lundby Cohort. Males and females are analysed separately.*

	Total N=3563			Males N=1822			Females N=1741		
	HR	CI	P-value	HR	CI	P-value	HR	CI	P-value
Mood disorder	1.18	1.04-1.34	.012*	1.50	1.24-1.81	.000*	1.00	0.84-1.18	.967
Age at entry	1.11	1.10-1.10	< .001*	1.10	1.09-1.10	.000*	1.11	1.10-1.11	< .001*
*Gender**	1.38	1.27-1.51	< .001*	—	—	—	—	—	—
Marital † state	1.0			1.0			1.0		
Married, cohabitating	1.00	0.89-1.13	.933	0.77	0.66-0.89	.001*	1.45	1.21-1.73	.000*
Divorced	1.05	0.84-1.30	.663	0.93	0.70-1.23	.608	1.28	0.81-2.75	1.49
Widow	0.62	0.54-0.71	.000	0.45	0.36-0.56	.000	0.84	0.85-1.46	1.12

Female gender* was regarded as reference category. Unmarried marital state† was regarded as reference category. HR refers to hazard ratio; CI refers to 95 % confidence interval.

Table 6. *Occurrence of other mental disorders considered as risk factors in the Lundby Cohort for those with mood disorder, n=508, and for those without mood disorders n=3055. P-values are given regarding significance of differences in frequencies of occurrence of comorbid disorder. Percentages are given in the parentheses.*

Mental disorders	Males with mood disorder 195	Males without mood disorder 1627	P-values	Females with mood disorder 313	Females without mood disorder 1428	P-values
Anxiety disorders	25 (12.8)	86 (5.3)	.000*	60 (19.2)	129 (9.0)	.000*
Mixed neurosis	4 (2.05)	9 (0.55)	.042	6 (1.9)	23(1.6)	.631
Organic syndrome	5 (2.6)	50 (3.1)	.000*	7 (2.2)	20 (1.4)	.309
Dementia	14 (7.2)	174 (10.7)	.437	27 (8.6)	161 (11.3)	.191
Psychotic disorders	10 (5.1)	63(3.9)	.827	10 (3.2)	49 (3.4)	1.00
Personality disorders	22 (11.2)	61 (3.7)	.000*	33 (10.5)	57 (4.0)	.000*
Alcohol use disorders	68 (34.5%)	322 (19.8)	.000*	17 (5.4)	20 (1.4)	.000*

Table 7. *Cox regression models of risk factors for mortality among individuals with mood disorders in the Lundby Cohort. Males and females are analysed separately.*

	Total N=508			Males N=195			Females N=313		
	HR	CI	P-value	HR	CI	P-value	HR	CI	P-value
Simple models									
Anxiety disorders	1.46	1.09-1.97	.012*	1.19	0.69-2.06	.530	1.62	1.13-2.32	.009*
Mixed neurosis	1.06	0.39-2.86	.905	2.61	0.62-10.98	.189	0.64	0.16-2.58	.529
Organic syndrome	2.51	1.33-4.75	.005*	4.59	1.83-11.53	.001*	1.65	0.67-4.07	.275
Dementia	3.67	2.55-5.29	.000*	5.21	2.72-9.97	.000*	3.06	1.94-4.80	.000*
Psychotic disorder	1.93	1.19-2.86	.007*	1.89	0.87-4.12	.109	1.86	1.00-3.46	.051
Personality disorder	0.99	0.66-1.48	0.96	1.10	0.58-2.08	.770	0.94	0.56-1.58	.800
Alcohol use disorder	1.09	0.78-1.53	.623	1.09	0.75-1.59	.660	1.21	0.54-2.71	.638
Multivariate models									
Anxiety disorders	1.42	1.06-1.92	.021*	_	_	_	1.62	1.13-2.32	.009*
Organic disorders	2.46	1.30-4.67	.006*	3.27	1.25-8.52	.015*	_	_	_
Dementia	3.69	2.56-5.31	.000*	4.58	2.37-8.85	.000*	3.11	1.98-4.90	.000*
Psychotic disorder	2.08	1.28-3.37	.003*	_	_	_	2.24	1.19-4.21	.012*
Gender	2.02	1.59-2.55	.000*						
Age-at-onset	1.06	1.05-1.07	.000*	1.06	1.05-1.07	.000*	1.06	1.05-1.08	.000*
Marital state†									
Married, cohabitate	1.39	0.98-1.95	.063	1.23	0.75-2.03	.403	1.45	0.90-2.34	.127
Divorced	2.47	0.94-2.61	.001*	2.12	0.98-4.61	.058	2.52	1.26-5.02	.009*
Widow	1.56	0.93-2.61	.088	0.90	0.28-2.91	.902	1.74	0.93-3.25	.080

The outcome is time to death. HR refers to hazard rate. CI refers to 95 % confidence interval. Unmarried marital state† was regarded as reference category. All simple models included one of the risk factors as well as the variables of gender, marital state, and age at onset. A divorced marital state was a significant risk factor for females in the simple model. Age at onset was significant in all the simple models (but not shown).

Figure 1. *Kaplan-Meier analysis of the main diagnostic groups according to the Lundby diagnosis of depression corresponding to the DSM-IV diagnoses of major depressive disorder (n=249), depressive disorder NOS (n=155), and adjustment disorder with depressed mood and dysthymia (n=67).*