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Risk factors for suicide in depression in Finland: first-hospitalized patients followed up to 24 years

Running title: "Risk factors for suicide in depression"

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Abstract

Objective: To examine longitudinally risk factors for suicide in depression, and gender differences in risk factors and suicide methods.

Method: We linked data from (a) The Finnish Hospital Discharge Register, (b) the Census Register of Statistics Finland, and (c) Statistics Finland's register on causes of deaths. All 56 826 first-hospitalized patients (25 188 men, 31 638 women) in Finland in 1991-2011 with a principal diagnosis of depressive disorder were followed up until death (2587 suicides) or end of the year 2014 (maximum 24 years).

Results: Clinical characteristics (severe depression adjusted hazard ratio [AHR] 1.19 [95% CI 1.08-1.30]; psychotic depression AHR 1.45 [1.30-1.62]; and co-morbid alcohol dependence AHR 1.26 [1.13-1.41]), male gender (AHR 2.07 [1.91-2.24]), higher socioeconomic status and living alone at first hospitalization were long-term predictors of suicide deaths. Highest risk was associated with previous suicide attempts (cumulative probability 15.4% [13.7-17.3%] in men, 8.5% [7.3-9.7%] in women). Gender differences in risk factors were modest, but in lethal methods prominent.

Conclusion: Sociodemographic and clinical characteristics at first hospitalization predict suicide in the long term. Inpatients with previous suicide attempts constitute a high-risk group. Despite some gender differences in risk factors, those in lethal methods may better explain gender disparity in risk.

Keywords: *Depression, suicide, cohort studies, risk factors, gender differences*

Significant outcomes:

- This national study of risk factors for suicide in depression is the largest cohort study published thus far in terms of sample size and number of suicide deaths. Of 13 risk factors, male sex, previous suicide attempts, severe or psychotic depression, co-morbid alcohol dependence, higher family income, and higher education predicted future suicide.
- During the long-term follow-up, a substantial proportion of patients hospitalized for depression with a history of suicide attempt eventually died by suicide.
- Some gender differences in risk factors for suicide in depression were found to exist. However, there are marked gender differences in lethal methods used, which more likely explain the gender disparity in risk of suicide.

Limitations

- The cohort comprised first-hospitalized psychiatric inpatients. Generalizability of findings pertaining to risk factors among psychiatric outpatients or primary care patients remains to be confirmed.
- Some risk factors remained uninvestigated in the study.

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- The study is based on clinical diagnoses. Diagnostic imprecisions likely exist in assessment of severity of depression, in poor recognition of delusional hopelessness of psychotic depression, and missed diagnoses of co-morbid alcohol dependence.

Introduction

Of all individuals dying by suicide, about one-half have suffered from depressive disorders (1) and nearly one-half have a history of psychiatric hospitalization (2, 3). Hospitalized patients with affective disorders (4, 5) or severe depression (6-8) have high risk of suicide. However, prospective evidence on risk factors for suicide deaths in depression is very limited (9). The same applies to previously hospitalized patients (10). Low incidence of suicides in the short term necessitates very large sample sizes and extended follow-ups to reliably estimate risk factors for suicide in cohort studies. Consequently, most suicide research has focused on proxy outcomes of suicide attempts or ideation, leaving uncertainty in the generalizability of the findings (11).

According to a systematic review of 29 putative risk factors (9) suicide deaths in depression are associated with male gender, family history of psychiatric disorder, previous suicide attempt, depression severity, hopelessness, co-morbid anxiety and personality disorders, and substance use disorders. However, the evidence is mostly based on a limited number of small case-control or cohort studies, and considerable uncertainty persists regarding even clinically relevant risk factors such as psychotic features (9). For several reasons, attempts to identify high-risk groups have thus far been ineffectual (10). Longitudinal large-scale studies on risk factors for suicide in depression are needed to aid clinical evaluations, treatment planning, and preventive efforts (9).

The gender disparity of suicide risk among subjects with depression (9) constitutes a central finding calling for scientific explanation. The excess mortality in men might be explained by gender differences in co-morbid mental disorders (12), suicidal intent (13, 14), impulsive-aggressive traits

(15), or choice of lethal methods (13). Gender differences in risk factors for suicide attempts in depression may exist (16). However, as reliable longitudinal evaluation of gender differences in risk factors necessitates substantially larger cohorts than mere investigation of risk factors overall, gender differences in risk factors for suicide deaths among patients with depression have not been investigated.

The data of the study are based on a Finnish population-based cohort of all first-hospitalized patients (N = 56 826) due to depression in 1991-2011 who were followed up after discharge until the end of the year 2014 (maximum 24 years). In our previous work (8), we have reported the overall cumulative risk of suicide being higher in men than in women and that the risk of suicide declined nationwide to one-half (hazard ratio 0.49) between those hospitalized during years 1991-1995 and those during years 2006-2011.

Aims of the study

In this Finnish national register-based study, we investigate altogether 13 plausible risk factors for suicide after first hospitalization for depression over an extended follow-up period of 24 years at most. We examine gender differences in risk factors and methods for suicide.

Material and methods

Study design, setting, and population

This study stems from the MERTTU research project (17). The database merges data from three national sources: 1) the Finnish Hospital Discharge Register on all inpatient treatments, 2) the census register of Statistics Finland on sociodemographic variables, and 3) the Statistics Finland's

register on causes of death. The Finnish personal identity codes link complete data at the individual level.

We identified all ≥ 18 -year-old patients with first lifetime admission to a psychiatric hospital or a psychiatric ward of a general hospital for depressive disorder (principal diagnosis) in 1991-2011. The overall annual population rate of psychiatric inpatient care in Finland has varied between 5.3 per 1000 inhabitants and 6.3 per 1000 inhabitants in 1994-2011 (18).

A total of 56 826 subjects (25 188 men, 31 638 women) were followed on the registers until death by suicide or other cause or the end of the year 2014 (length of follow-up 628 514 person-years, mean 11.1 years, median 10.7 years, maximum 24 years). The Ethics Committee of the National Institute for Health and Welfare approved the study design.

Finnish Hospital Discharge Register

The Finnish Hospital Discharge Register (FHDR) contains information on all psychiatric and somatic hospitalizations since 1969. In Finland, psychiatric secondary services receive funding through tax revenue, and there are no private psychiatric hospitals. Since 1987, national guidelines have stipulated use of operationalized criteria for clinical psychiatric diagnoses. The Finnish ICD-9 diagnoses (19) used in 1987-1995 were based on the DSM-III-R criteria and the ICD-10 diagnoses since then on the Diagnostic Criteria for Research (DCR). The accuracy of mental health diagnoses in the FHDR is good (20).

We identified from the database a cohort of patients having at least one admission with a psychiatric diagnosis in 1987-2011. Due to the availability of sociodemographic information since 1990, the study period starts in 1991. We identified baseline (first) hospitalizations for depressive disorder as a principal diagnosis in 1991-2011 with the Finnish ICD-9 codes (19) 2961A-G and 2968A and ICD-10 codes F32-33. We obtained for this cohort all hospitalizations with psychiatric diagnoses

in 1980-2011 and excluded patients with any previous psychiatric hospitalizations in 1980-1990 (including hospitalizations before the age of 18 years). Excluded were also patients with baseline co-morbid diagnosis of principal psychotic disorder (ICD-9 codes 2951-2953A-F, 2954A, 2956A-F, 2957A, 2959A-F, 2971A, 2973A, 2988A, 2989X, 3012C; ICD-10 codes F20-29) or bipolar disorder (post-discharge suicide risk in bipolar disorder has been previously reported (21)), or who died by suicide during baseline hospitalization. We extracted data on co-morbid diagnoses of alcohol dependence (ICD-9 code 3039X; ICD-10 code F10.2), date of admission, and discharge. Since 1994, the FHDR provides information on the overall functioning at discharge (Global Assessment Scale [GAS] value recorded by attending doctor) and admission status (voluntary, involuntary). In Finland, a doctor is authorized to refer a person involuntarily for evaluation in a psychiatric hospital when three conditions are met: 1) the patient is mentally ill (i.e. psychotic), 2) he or she needs treatment for a mental illness, which if left untreated would become considerably worse or severely endanger the health or safety of the patient or others, and 3) all other mental health services are considered inapplicable or inadequate.

Suicide deaths and previous attempts

Finland has high medicolegal autopsy rates (about 16-24% of all deaths in 1991-2014) (22, 23). A forensic pathologist performs a medicolegal autopsy in almost every case of unnatural death and determines virtually all suicides (leaving few undetermined deaths in a ratio of less than 1 to 10 relative to suicides) (22). We retrieved information on the dates and causes of death for all cases and then identified suicides (ICD-9 codes E950-E959; ICD-10 codes X60-X84, Y87.0, Z91.5).

We identified previous suicide attempts (codes as above) from somatic and psychiatric records in the FHDR. Previous suicide attempts were classified in one of two non-overlapping categories: 1) a suicide attempt at admission (either somatic hospitalization due to a suicide attempt which

interminably continued thereafter as baseline psychiatric hospitalization or suicide attempts recorded in psychiatric discharge records by attending psychiatrist [latter includes also suicide attempts treated in emergency department and non-medical attention-requiring attempts either preceding admission or attempted during the baseline hospitalization due to identical coding in the register] or 2) suicide attempts during the four years prior to baseline (all had resulted in hospital admission, excludes emergency department visits). The four-year time-frame was determined by establishing equal time-at-risk period for each patient (data available since 1987). Neither data on pre-existing psychiatric diagnoses at the time of the past attempts nor evaluation of suicidal intent (ICD codes include suicide attempts and other intentional self-harm) was available in the registers. However, patients who self-harm without suicidal intent are generally treated in psychiatric outpatient setting. Because suicide attempts in the data have either necessitated somatic inpatient treatment or contributed to baseline psychiatric admissions, we assume that some degree of suicidal intent has been present.

Sociodemographics

The census register of Statistics Finland provided data from the final day of the previous year for baseline hospitalization on the following six variables: 1) Marital status (categorized as single, married, divorced, and widowed; includes same-sex partners since 2002), 2) Habitation (living with family or alone), 3) Having children ≤ 7 years of age (for patients living with the family), 4) Family income (relative within the cohort, divided into thirds), 5) Educational level (basic, upper secondary, and tertiary), and 6) Employment status (at work, unemployed, student, retired, conscript or conscientious objector, unemployment pension, or not in labor force for other reason).

Statistical analyses

The DSM-III-R based diagnoses from the ICD-9 era were converted to corresponding ICD-10-DCR diagnoses. The study diagnoses were then grouped into three mutually exclusive subcategories of severity: 1) reference (henceforth “moderate”) category included mild, moderate, full or partial remissions, other specified, and unspecified types (ICD-9 codes 2961A-C, 2961F-G, 2968A; ICD-10 codes F32.0*, F32.1*, F32.8, F32.9, F33.0*, F33.1*, F33.4, F33.8, F33.9), 2) severe depressive disorder without psychotic features or symptoms (ICD-9 code 2961D; ICD-10 codes F32.2, F33.2), and 3) severe depressive disorder with psychotic features or symptoms (ICD-9 code 2961E; ICD-10 codes F32.3, F33.3).

We followed the patients using register data from the day of discharge to death by suicide or other cause, or 31 December 2014, whichever occurred first. Other causes of death were considered as competing risks for suicides. Observations in which the end of follow-up period was reached were treated as censored. During the naturalistic observation period re-hospitalizations were possible and suicide deaths include all suicides irrespective of the place of death. Because of risk of survival bias, we ignored diagnostic conversions to a principal psychotic disorder or bipolar disorder (only diagnoses of living patients can change).

We used the competing survival analyses to derive the cumulative probability of dying by suicide. Cause-specific Cox proportional hazard regression models were used to provide unadjusted (sex, age, baseline year only) and adjusted hazard ratio (HR) estimates for the association between covariates and risk of suicide. Separate models were estimated for all and for men and women. Statistical significances of gender interactions were estimated by including interaction term for one variable at a time to the model. The selection of variables to the multivariate models was made by a priori hypotheses. Decisions were also based on an aim to limit interdependence of included variables or their susceptibility to changes during the long-term follow-up. We chose variables indicating sociodemographic status being family income, education level, and living alone. Baseline

year was used as a stratification variable in the Cox models. According to observations based on Schoenfeld residuals, the proportional hazards assumption was met. We used the software packages of R (www.r-project-org), and Survo (www.survo.fi).

Results

Patient characteristics at baseline hospitalization are presented in the Supplementary Table 1. The cumulative probability of dying by suicide was 7.7% (95% CI 7.2-8.2%) in men and 3.9% (95% CI 3.6-4.3%) in women (overall 5.6% (95% CI 5.3-5.9%)). The temporal patterns of risk of suicide in men and women are presented in Figure 1. The mean age at the time of suicide was 46.2 (SD 13.9) in men and 48.4 (SD 14.7) in women (overall 47.0; SD 14.3).

Predictors of suicide

The unadjusted (age only) hazard ratios for suicide are provided in the Supplementary Table 2. Suicide deaths were associated with numerous variables including gender, severity of depression, alcohol dependence, previous suicide attempts, education level, family income, living alone, marital status, having small children in the family, employment status, and GAS score.

The multivariable-adjusted models for proportional hazards of suicide (contribution of each variable adjusted for the confounding effects of other variables) are presented for all patients and for men and women separately in adjacent columns of Table 1. Men showed an adjusted hazard ratio (AHR) of 2.07 (95% CI 1.91-2.24; $p < 0.0001$) for suicide. Severity of depression showed an exposure-response gradient (severe depression without psychotic symptoms AHR 1.19; 95% CI 1.08-1.30; $p = 0.0003$; psychotic depression AHR 1.45; 95% CI 1.30-1.62; $p < 0.0001$) and co-morbid alcohol dependence an AHR of 1.26 (95% CI 1.13-1.41; $p < 0.0001$) for risk of suicide. A previous suicide

attempt, either at baseline or during the previous four years, elevated the risk for suicide most by over twofold. Of the sociodemographic factors at baseline, the risk of suicide was increased by living alone, higher level of education, and high family income.

Of those with previous suicide attempts, the overall cumulative probability of suicide was 15.4% (95% CI 13.7-17.3%) in men (suicide attempts at admission 15.5%; 95% CI 13.2-17.9%; and during the previous four years 16.0%; 95% CI 13.5-18.6%), and 8.5% (95% CI 7.3-9.7%) in women (suicide attempts at admission 8.4%; 95% CI 6.9-10.0%; and during the previous four years 8.8%; 95% CI 7.1-10.7%). Of patients with a previous suicide attempt, 9.7% of men and 5.0% of women died by suicide within five years of discharge. The temporal patterns of cumulative probability of suicide in men and women with previous suicide attempts are presented in Figure 2. At baseline, the patients who had a history of a previous suicide attempt within past four years were about five years younger (mean age 39.5 years [SD ± 13.3] in men and 39.5 years [SD ± 15.1] in women) compared to the total cohort. Among these patients, the most common methods for the first attempted suicide were intoxication (90.7%) and cutting (3.5%).

Differences in predictors and methods of suicide in men and women

Some risk factors for suicide were stronger in one gender. First, a diagnosis of co-morbid alcohol dependence increased the risk of suicide proportionally more in women than in men (statistically strongest gender interaction term, $p = 0.002$). Second, tertiary level education specifically increased significantly the risk of suicide in women but not in men (interaction $p = 0.01$). Third, having young children in the family increased the risk of suicide in men but not in women (interaction $p = 0.03$). No other statistically significant gender differences were detected as a whole, except for admission type (interaction $p = 0.11$), involuntary admission seemed to increase the risk for suicide more in

women than men (pairwise interaction $p = 0.046$). Previous suicide attempts and family income showed least evidence for gender differences.

The methods of suicide deaths in men and women are presented in Table 2. Relative to women, men died more often by self-poisoning with gases; hanging, strangulation or suffocation; and use of firearms. Women died more often than men by drowning or self-poisoning.

Discussion

This national study of risk factors for suicide in depression among 56 826 first-time hospitalized patients, followed up to 24 years, is the largest of its kind to date. Unlike in any previous study, the data enabled investigation of gender differences in altogether 13 risk factors. Overall, baseline predictors of suicide were male gender, previous suicide attempts, severe or psychotic depression, co-morbid alcohol dependence, higher socioeconomic status and living alone. Men with previous suicide attempts had very high risk of suicide death. Gender differences in risk factors were found in co-morbid alcohol dependence, tertiary level education and having young children in the family. The order of magnitude of these differences was, however, limited compared with the large gender difference in risk. We found marked gender differences in lethal methods of suicide.

Predictors of suicide

We investigated 13 putative risk factors for suicide in depression, including 11 of the 29 examined in the recent meta-analysis (9), plus income and education level. To our knowledge, this is a wider range than in any previous longitudinal study and enables also examination of adjusted effects. The Hawton et al. meta-analysis (9) included three larger cohorts, of which one was a national sample (24) with an investigation period in 1973-1993 mostly preceding ours and none of these examined

more than five risk factors. In our data, predictors were examined in a national sample with 2587 suicides. By comparison, the pooled meta-analytic data (9) on depression severity or alcohol misuse derived from a limited number of small samples, including less than 300 suicides. The other limitations of previous studies include samples of advanced age, only men, or retrospective study designs. The systematic review (10) of risk factors for suicide of discharged general psychiatric inpatients was based on 1544 suicides.

Diagnosed severity of baseline depressive episode in our data shows a dose-response effect on long-term risk of suicide, thereby confirming the previous tentative findings of a smaller, likely under-powered study (25). Severity of depression, when measured more accurately with the Patient Health Questionnaire (PHQ-9) in a large community sample, has been found to predict suicide death over the next month (26). Those results enable generalizability to less severely depressed outpatient populations, whereas our long-term findings are based on a high number of suicide deaths and involve additionally psychotic depression. Severity of depression has been found to correlate significantly with severity of suicidal ideation, although even among severely depressed patients some have had no suicidal thoughts (27). The role of psychotic symptoms in risk of suicide in depression has been long debated. Our finding of an added influence of diagnosed psychotic depression on risk of suicide substantiates the so far limited evidence base (9), but is contrary to the findings of a recent study (28) applying different study methodologies. According to other studies, baseline severity of depression (25, 29) and psychotic features (30) predict future recurrence and persistence of depressive morbidity. Time spent at risk in gradually more severe depressive episodes likely forms a major determinant of suicide risk and provides a meaningful target for prevention (11).

We found alcohol dependence to elevate risk for suicide by 26% in the adjusted models. This finding is in accordance with the Danish national study (7) and the Hawton et al. meta-analysis (9) but in contrast to the findings of some major studies (10, 24). Given that alcohol use disorders rank as the second most common mental disorder among suicide decedents (1), we believe that depressed inpatients with alcohol use disorders represent a high-risk group needing preventive attention.

Of first-hospitalized patients with depression and previous suicide attempts more than one in seven (15%) men and more than one in twelve (8.5%) women eventually died by suicide. The risk was highest in the early years but persisted over nearly two decades. The twofold adjusted risk is slightly higher, but comparable with the estimations of a Danish national study (7). The gender difference in risk reflected the higher overall risk among men and we found no gender-modifying effects pertaining to previous suicide attempts among inpatients. Overall, our estimations of suicide risk markedly exceed those of a previous meta-analysis of self-harm patients (31), which pooled data mostly on self-poisonings in primary and secondary care settings. In contrast, our data derive from suicide attempts that had mostly necessitated somatic admission among patients later hospitalized for depression with extended follow-up, which may explain the differences. Individuals who use violent methods have high risk of repetition with fatal outcome particularly in the short term (32). However, the methods, medical severity or intent of previous suicide attempts were unmodeled in our study. The high suicide risk of first-hospitalized patients with preceding suicide attempts, highlighted particularly in men, is understandable as a proxy for several important risk indicators for suicide, i.e. preceding suicide attempts (9), psychiatric hospitalizations (2), high-risk post-discharge periods (33), and early illness course (7). The high proportion (56-59%) of suicide attempters dying by their first attempt (34, 35) limits, however, the sensitivity as a risk indicator. Nevertheless, psychiatric evaluation should be provided to all who have attempted suicide. Depressive inpatients who have previously attempted suicide form a particular high-risk group warranting intensive attention in psychiatric care.

Accepted Article

Of sociodemographic factors, living alone, high relative family income, and higher educational level predicted suicide deaths. Our finding that living alone increases the risk of suicide in depression adds to the previously insufficient evidence base (9). The finding of baseline higher socioeconomic status predicting higher risk of suicide among inpatients is counterintuitive, but not without support (36). Contrasting results are found in community-based case-control studies (2, 36, 37), in which suicide deaths have been associated with single marital status, unemployment, sickness-related absence, and low income. However, when in these general population studies the effect of a history of psychiatric hospitalization was controlled for, the associations between socioeconomic status and suicide were often disappeared indicating major role for mental illness. A cohort study as here provides better control for confounding and our finding persisted when controlling for baseline diagnosed severity of depression. However, some residual confounding by illness severity may remain due to complex bidirectional relations between sociodemographic factors and depression (discussed in more detail elsewhere (36, 38)). Moreover, we modelled baseline information on socioeconomic status prior to hospitalization and the socioeconomic status may have changed considerably at the time of death. Accordingly, another longitudinal study of general psychiatric inpatients (39) showed not only that higher socioeconomic status was associated with higher risk of suicide but also that this higher risk was associated with later loss of income or employment status and ending of an intimate relationship. In summary, our findings of higher education and income at first hospitalization for depression to predict higher future suicide risk are consistent, but the causal pathways remain unclear and require further studies. Possible explanations include that higher socioeconomic status could mark some unmeasured baseline vulnerability, or that depressive inpatients with a higher socioeconomic status might have been at greater suicide risk if they later experienced major hardships in living circumstances.

Differences in predictors and methods of suicide in men and women

In women, diagnosed co-morbid alcohol dependence elevated the risk of suicide more than in men. Relative risks should not be confused with absolute risks, which among alcohol-dependent women remain lower than the risk among non-alcohol-dependent men. In the Finnish psychological autopsy study in 1987-1988, male decedents with major depression had more often co-morbid alcohol disorder and less often a history of psychiatric hospitalization (40). We found that high education level increased the risk for suicide more in women than men, whereas another study (41) found an interaction with male gender and medium-level education. In contrast to previous studies (2, 37, 41), we found no evidence on protective effects of having young children in the family. Conversely, in men this was statistically a significant risk factor, although marginal in magnitude of effect.

Gender differences in quality, distribution or potency of underlying risk and protective factors for suicide could partly explain the twofold higher risk among men. In the adjusted analyses, however, the risk associated with male gender remained unaltered. This suggests a role of other factors in explaining the gender disparity in risk. According to the Finnish psychological autopsy studies (34, 42), we found that men died more often than women by potentially more lethal suicide methods.

Gender differences in methods of suicide are marked, whereas variations in prevalence or potency of risk factors are modest. We cannot exclude the possibility of gender differences in some unmeasured risk factors, but our findings are more consistent with differences in lethality of the suicide methods chosen contributing to this disparity.

Strengths and limitations of the study

Strengths of the study design include a population-based cohort of first hospitalized patients (N=56 826) with depression in 1991-2011 followed for a maximum of 24 years (including 2587 suicides). The large data enable in a single study design longitudinal examination of adjusted effects of numerous risk factors overall, and a comparison between men and women. The study strengths include high-quality national-level register data and complete information on post-discharge suicide mortality based on reliable death investigation procedures (22). The data on methods of suicide and on risk factors demonstrates the magnitude of gender differences in both.

Among the limitations are that structural interview-based diagnostics remain unavailable for large-scale studies. The clinical diagnoses, assigned by routine clinical evaluation at various treatment settings, are based on nationally applied operationalized diagnostic criteria and unbiased by hindsight at outcome. Diagnostic imprecisions likely exist in assessment of severity of depression, in poor recognition of delusional hopelessness of psychotic depression, and missed diagnoses of co-morbid alcohol dependence. The previous and subsequent course of depression and clinical status at the time of death remain unknown. Therefore, our results presumably underestimate the actual effects. Bipolar disorder was probably underdiagnosed, and suicide attempts not requiring somatic hospitalization or occurring more than four years earlier remained unexamined. Un-investigated risk factors include hopelessness, impulsive-aggressive tendencies or cluster B traits, and family history of suicide (9, 11). The socioeconomic status was susceptible to change after baseline, except for the highest level of education if attained. Despite the clearance period of 11-31 years some patients could have had previous hospitalizations longer time ago. However, based on the FHDR data the number is likely to be very low because only 3% of consecutive admissions have an interval longer than 11 years and 0.5% longer than 21 years (median length of our clearance period). Psychiatric care represents treatment as usual with known regional differences (17). Possible effects

of treatment and whether gender differences exist in provision of health care services or in treatment practices for depression remains unknown.

The long-term cumulative probability of suicide in men (7.7%) and women (3.9%) of this first-hospitalized cohort (8) is comparable to the findings of a similar Danish long-term study of first-treated depressive patients (7). The results on probability of suicide and age at time of suicide represent lower-boundary estimations because the cohort is not yet followed up throughout the lifetime. The national-level findings enable generalizability, whereas the cohort likely represents the most severe patients with depression. It remains unknown, to what extent risk factors for suicide between outpatient and inpatient populations diverge, or in this study varied over time along with the substantially declining risk for suicide (8). While prediction of suicide at individual level remains a difficult task, the findings may inform clinical practice and preventive efforts.

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Declaration of Interests

The authors declare no competing interests.

Table 1 Adjusted hazard ratios for suicide after first lifetime psychiatric hospitalization for depression followed for 628 514 person-years^a

	All (N = 56 826)			Men (n = 25 188)			Women (n = 31 638)		
	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p
Men	2.069	1.908 - 2.243	<0.0001	-			-		
Depression severity									
Moderate ^b	1.0			1.0			1.0		
Severe without psychotic symptoms	1.188	1.083 - 1.303	0.0003	1.230	1.095 - 1.382	0.0005	1.115	0.956 - 1.299	n.s.
Psychotic depression	1.451	1.301 - 1.619	<0.0001	1.470	1.276 - 1.694	<0.0001	1.423	1.198 - 1.692	<0.0001
Alcohol dependence ^{**}	1.261	1.129 - 1.409	<0.0001	1.147	1.008 - 1.306	0.038	1.647	1.338 - 2.026	<0.0001
Suicide attempt ^c									
At admission	2.110	1.862 - 2.391	<0.0001	2.000	1.700 - 2.355	<0.0001	2.248	1.849 - 2.733	<0.0001
During previous 4 years	2.111	1.845 - 2.415	<0.0001	2.116	1.783 - 2.510	<0.0001	2.083	1.673 - 2.592	<0.0001
Education [*]									
Basic	1.0			1.0			1.0		
Upper secondary	1.147	1.049 - 1.253	0.003	1.128	1.010 - 1.260	0.032	1.177	1.013 - 1.369	0.034
Tertiary ^{d**}	1.295	1.160 - 1.445	<0.0001	1.137	0.984 - 1.315	n.s.	1.536	1.295 - 1.823	<0.0001
Income									
Lowest third	1.0			1.0			1.0		
Middle third	1.065	0.961 - 1.180	n.s.	1.060	0.929 - 1.210	n.s.	1.059	0.899 - 1.248	n.s.
Highest third	1.191	1.068 - 1.329	0.002	1.169	1.018 - 1.343	0.027	1.207	1.011 - 1.442	0.038

Living alone	1.124	1.029 - 1.227	0.009	1.165	1.044 - 1.301	0.007	1.069	0.923 - 1.238	n.s.
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HR - hazard ratio, CI - confidence interval, p – p-value, n.s. – not significant

Statistically significant p-values ($p < 0.05$) are bolded.

* Statistically significant interaction between sex, $p < 0.05$

** Statistically significant interaction between sex, $p < 0.01$

^a adjusted for each other and age, baseline admission year was used as a stratification variable

^b includes mild to moderate, full and partial remissions, other specified and unspecified types of depression

^c non-overlapping categories, an individual may have both

^d lowest level tertiary education or higher

Table 2 Methods of suicide in men and women (n = 2587) dying by suicide after first lifetime psychiatric hospitalization for depression followed for a maximum of 24 years.

Method of suicide	Men (n = 1609)		Women (n = 978)	
	n	%	n	%
Gassing*	74	4.6	8	0.8
Hanging, strangulation, or suffocation*	540	33.6	192	19.6
Drowning*	77	4.8	115	11.8
Firearms and explosives*	193	12.0	19	1.9
Jumping from a height	73	4.5	54	5.5
Cutting and piercing	42	2.6	15	1.5
Self-poisoning*	475	29.5	495	50.6
Traffic	105	6.5	72	7.4
Sequelae of intentional self-harm and other methods	30	1.9	8	0.8

Chi-square 265.7; df 8; p = <0.0001

* relative frequency significantly different between men and women at the 0.0001 level (z-test)

Gassing includes ICD-9 codes E951* and E952* and ICD-10 code X67

Hanging, strangulation, or suffocation includes ICD-9 code E953* and ICD-10 code X70

Drowning includes ICD-9 code E954* and ICD-10 code X71

Firearms and explosives include ICD-9 code E955* and ICD-10 codes X72-X75

Jumping from a height includes ICD-9 code E957* and ICD-10 code X80

Cutting and piercing include ICD-9 code E956* and ICD-10 code X78

Self-poisoning includes ICD-9 code E950* and ICD-10 codes X60-X66, X68-X69

Traffic includes ICD-9 codes E959A, E959B, and E959C and ICD-10 codes X81-X82

Sequelae of intentional self-harm and other methods include ICD-9 code E959X and ICD-10 codes X76, X77, X79, X83-X84, Y870, and Z915

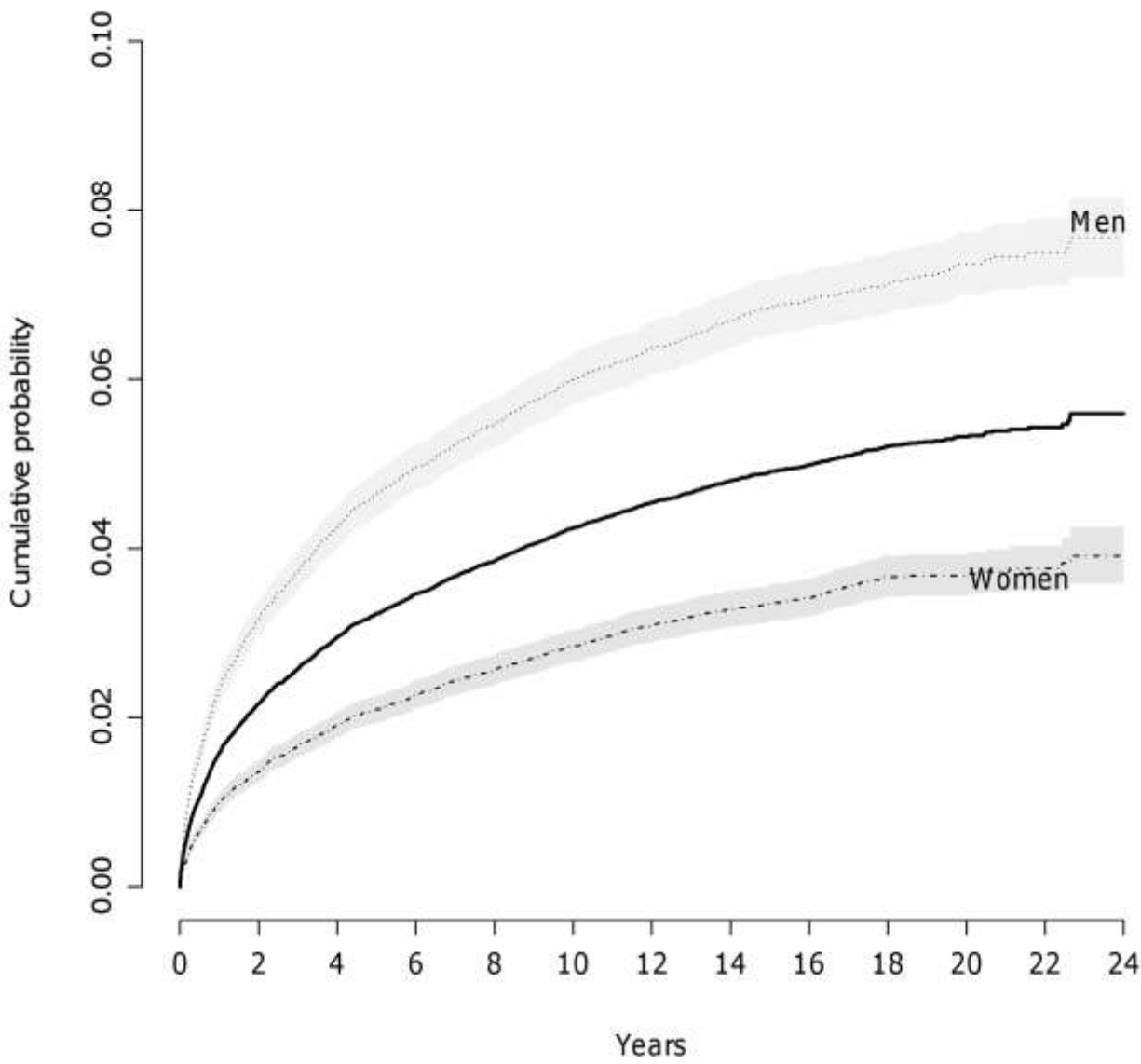


Figure 1. Cumulative probability of dying by suicide in men and women after first lifetime psychiatric hospitalization for depression followed up to a maximum of 24 years.

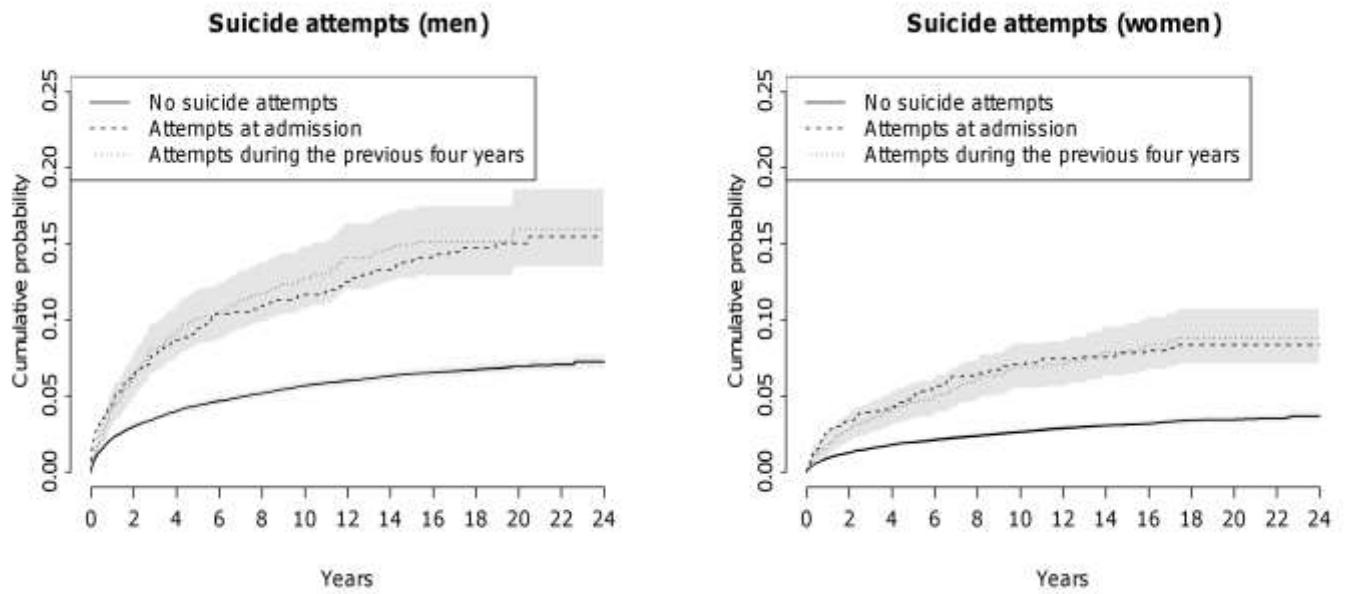


Figure 2. Cumulative probability of dying by suicide after a suicide attempt, either during the previous four years or at the baseline admission, in men and women after first lifetime psychiatric hospitalization for depression.

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