

ORIGINAL ARTICLE

Healthcare resource utilization prior to suicide death or suicide attempt in patients with major depressive disorder—A Danish registry-based cohort study

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Abstract

Introduction: Major depressive disorder (MDD) is associated with suicide events and with increased healthcare resource utilization (HRU). The aim was to analyze the pattern of HRU prior to death by suicide or suicide attempt in patients with MDD using national registries.

Methods: Danish adults with MDD, who died by suicide or had a first-time suicide attempt, were matched with MDD controls on age, sex, and MDD severity and analyzed for psychiatric and non-psychiatric hospital and private practitioner contacts, and prescriptions 1 year prior to the event. For individuals having a second suicide attempt, HRU prior to first and second suicide attempt was analyzed.

Results: Among 1061 individuals dying by suicide and 3759 individuals with suicide attempt, compared with their controls, the proportion with psychiatric hospitalization was more than 50% increased, mainly accounted for by acute contacts. The difference to the matched controls decreased with increasing MDD severity. Non-psychiatric HRU was increased as well. The proportion with psychiatric hospitalizations or ED visits was reduced prior to the second attempt compared with first attempt.

Conclusion: Among individuals with MDD, psychiatric and non-psychiatric HRU was increased 1 year prior to suicide event. The proportion of individuals who had psychiatric HRU decreased from first to second suicide attempt.

KEYWORDS

cohort study, healthcare resource utilization, major depressive disorder, suicide, suicide attempt

INTRODUCTION

Death by suicide and suicide attempt are major public health problems, with suicide ranking the fourth most

common cause of death globally among people aged 15–29 years in both men and women, despite a general declining trend on all continents but the Americas (World Health Organization, 2021). Suicide attempt has an

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estimated lifetime prevalence of 2.7% and a peak during young adulthood (Nock et al., 2008). In a US-based survey the 12-month prevalence of suicide attempt in young adults increased from 1.1% to 1.6% during 2009 to 2015 (Han et al., 2018). Also Danish regional data indicate that suicide attempt rates have been increasing in young adults (Centre for Suicide Research).

Most suicide deaths are related to psychiatric disorders among which major depressive disorder (MDD) is a large risk factor (Moitra et al., 2021). A Swedish study found that men and women suffering from depression have 20.9 and 27 times higher risk, respectively, of dying by suicide compared to the general population (Ösby et al., 2001). The association also applies to suicide attempts. Of Danish individuals with a suicide attempt incurring healthcare costs, 69.5% had a psychiatric diagnosis, of which depression was the most frequent (28.1%; Dyvesether et al., 2021). In addition, the risk of suicide ideation or suicide attempt increases with severity of depression (Eikelenboom et al., 2012).

Suicide death and suicide attempts are associated with increased healthcare resource utilization (HRU; Dyvesether et al., 2021; Strøbæk et al., 2016). A Danish registry-based study of general practitioner (GP) utilization found a larger probability of attending GP among subsequent suicide cases compared to the general population in the year leading up to suicide, and the difference increased particularly in the last month prior to suicide (Schou Pedersen et al., 2019). Also MDD as such is associated with increased HRU documented in several studies, for example, in Sweden (Lundberg et al., 2022), the US (Greenberg et al., 2021), and Finland (Tusa et al., 2019). Furthermore, this may be modified by depression severity; a US healthcare database study found that the risk of 1-month hospital contact increased with increasing depression severity (Voelker et al., 2021). Hence, MDD patients are characterized by both high HRU and high risk of suicidality.

Despite that risk factors are well known, suicidal behavior is often unforeseeable on individual level, and therefore preventive measures are challenging to exercise in a targeted manner. While patients with MDD in general have increased HRU and an increased risk of suicide death, it is not known if healthcare utilization increases in the time before suicide death or attempt. Moreover, it is important to know to what extent patients at risk of suicidal behavior are followed by health professionals or drop out of care, in particular whether patients receive psychiatric healthcare.

The aim of the present study was therefore to investigate if patients with MDD have different healthcare utilization in the year leading up to suicide death or suicide attempt, overall and by different types of HRU, including primary as well as tertiary healthcare, acute versus planned, somatic versus psychiatric, and in-patient versus

out-patient healthcare services. Moreover, for individuals with recurrent suicide attempt, we asked if there were differences in HRU prior to the second attempt compared to the first attempt. The identified patterns of HRU may be investigated in further studies targeting more detailed clinical descriptors than is offered by the national registries.

METHODS

Population

Base population

This register-based cohort study included Danish residents having an in- or out-patient contact with a psychiatric department for MDD as main diagnosis (ICD-10: F32.x-33.x) from 1997 to 2018. In case of several contacts on the same day with different grades of depression, in-patient contacts were given priority over out-patient contacts, and secondly the most severe grade was prioritized.

Suicide death cohort and suicide attempt cohort

From this population, we identified two different cohorts, one cohort consisting of all, who died by suicide (index date) between January 1, 1998, and December 31, 2018 (identified in the Registry of Causes of Death (Helweg-Larsen, 2011) by the value 48 in list 49). The other cohort consisted of all, who had a first-time suicide attempt (index date) between January 1, 1998, and December 31, 2018 (identified in the Danish National Patient Registry; Schmidt et al., 2015) and the Danish Psychiatric Central Research Registry (Mors et al., 2011) using the diagnosis code at discharge: ICD-10 T39, T42, T43, X60-X84 (excluding X65, suicide attempt or self-harm using alcohol, in order to avoid including cases of excess consumption resulting in unintended life danger).

Inclusion criteria were age 18 years or above on the index date, having had at least one qualifying psychiatric hospital contact with MDD as in- or out-patient within 12 months prior to index date. The diagnosis assigned at the last contact prior to index date defined depression severity (mild [ICD-10: F32.0, F32.8, F32.9, F33.0, F33.4, F33.8, F33.9], moderate [ICD-10: F32.1, F33.1], severe [ICD-10: F32.2, F32.3, F33.2, F33.3]). If depression severity was unspecified [ICD-10: F32, F33]), the individual was excluded. Further exclusion criteria were having a migration event within 1 year of index date, or having a diagnosis of comorbid bipolar affective disorder (ICD-10: F30.x, F31.x; ICD-8: 296.19, 296.39, 296.89, 296.99, 298.19), other affective mood disorders (ICD-10: F38.x, F39.x), persistent

mood disorder (ICD-10: F34.x), schizophrenia (ICD-10: F20.x, -F29.x; ICD-8: 295.x9, 297.x9, 298.29–298.99, 299.04, 299.05, 299.09), or dementia (ICD-10: DF00.x–F03.x, DG30.x, DR54.9; ICD-8: 290.x) within 10 years prior to index date. These co-morbidities, on which matching to controls would most likely be imperfect, are known to incur a large HRU and would therefore confound the analyses.

A suicide death was not considered a suicide attempt. A previous suicide attempt did not disqualify a suicide death from being included as a suicide death.

Matching

The two cohorts of suicide death and suicide attempt were both matched 1:2 on sex, birth year (± 2 years), and depression severity (mild, moderate, severe) with Danish residents alive and 18 years or older at the index date. The index date of the person who died by suicide or had a suicide attempt was also assigned to the matched controls. Similar to the suicide death and suicide attempt cohorts, for the matched controls, the last hospital contact with MDD as main diagnoses prior to the index date defined the severity grade. Besides, the same inclusion and exclusion criteria applied to the matched controls. Matching was performed with replacement. Hence, a person included as a control could later die by suicide or have a suicide attempt, thus entering in the analysis in the suicide death cohort or suicide attempt cohort.

Second suicide attempt

We also analyzed the HRU of persons with a first-time suicide attempt followed by a subsequent secondary suicide attempt (before January 1, 2019), where second attempt took place no earlier than 4 months after the first attempt. In the identification of secondary suicide attempts, records in the first month after the first suicide attempt was disregarded, due to the inherent difficulty in discriminating whether early hospital contacts registered with a suicide attempt diagnosis in fact being related to the first attempt and not constitute a new attempt. The minimum time span of 4 months before first and second suicide attempt was required in order to minimize the risk of having spill-over of HRU ensuing from psychiatric and somatic damages caused by the first attempt into the HRU associated with the second attempt.

Healthcare resource utilization

HRU in the given time period prior to the index date was the outcome of interest. Three main categories of HRU

were included, and these were analyzed and reported according to the following specific subcategories. (1) Psychiatric HRU included: hospitalization in a psychiatric hospital department (overall and elective or acute contacts); hospital bed days (overall and elective or acute contacts); emergency department (ED) visits; outpatient hospital contact courses; home visits (visits by psychiatric health personnel in the private home of the patient, SKS code AAF6x, only available from 2006); private psychiatrist visits ('speciale': 24); and private psychologist visits ('speciale': 63). (2) Somatic HRU included hospitalization in a somatic hospital department (overall and elective or acute contacts); hospital bed days (overall and elective or acute contacts); ED visits; outpatient hospital contact courses; general practitioner (GP) visits ('speciale': 80) and other healthcare specialist visits ('speciale': any but 24, 63, 80). Data on diagnoses, hospital contacts and services, including ED visits and electroconvulsive therapy (ECT), were retrieved from the Danish National Patient Registry (Schmidt et al., 2015) and the Danish Psychiatric Central Research Registry (Mors et al., 2011). The data on GP visits and other private healthcare specialist visits including psychologists and psychiatrists were retrieved from the National Health Service Register (Sahl Andersen et al., 2011). (3) Medicine expenses (total transaction price from redemption of prescriptions at community pharmacies, comprising of both the part covered by public subsidies and the part paid by the patient) were retrieved from the Danish National Prescription Registry (Pottegård et al., 2017), presented as total and by the following mutually exclusive subcategories: antidepressant medicine (ATC code N06A), other psychotropic (non-antidepressant) medicine (ATC codes N05A and N05B), other non-psychiatric-related medicine.

For the analysis of death by suicide and first-time (single) suicide attempt, the analyzed HRU period was 1 year prior to index date. For the analysis of first versus second suicide attempt, the analyzed HRU period was the 3 months prior to the first and second attempt, respectively. HRU in the first month after the first attempt was not included in the analysis of HRU prior to the secondary event due to the large risk of spillover HRU ensuing from psychiatric and somatic damages caused by the first attempt.

Descriptive variables

Sex, day of birth, and cohabitation (living with partner or alone) were retrieved from the Danish Civil Registration System (Schmidt et al., 2014). The highest level of education was retrieved from the Danish Education Registers (Jensen & Rasmussen, 2011) and categorized into Primary school or Lower secondary; Upper secondary or Short cycle education; Bachelor, Master, or Doctoral education; Missing or not

classified. Income in the year prior to the event was retrieved from the Registry of Income (Baadsgaard & Quitzau, 2011), and presented as quartiles stratified by age group and 3-year calendar intervals to account for age-dependency in income and changing expected income through life and inflation. For missing observations, the last observation looking further 2 years back was carried forward.

Statistical analysis

Due to the bimodal distribution of the utilization data with a fraction of zero-values (representing non-users), the data were analyzed using a two-step model with suicide death/suicide attempt versus control as independent variable. First, the difference in probability of any use of the health-care resource in question was tested using a Poisson regression. Results from this model are presented as a proportion ratio (PR), meaning the proportion of individuals that have at least one instance of HRU among individuals with a suicide death/suicide attempt divided by the similar proportion among individuals in the control group. Second, the difference in average utilization was tested restricted to individuals having at least one utilization for the specific HRU type using an ANOVA model. Utilization data were non-normally distributed and right-skewed, due to few individuals having a relatively high degree of utilization; hence the utilization data are log-transformed prior to analysis. After back-transforming from the log scale, results are given as percentage increase in utilization in the suicide death/suicide attempt cohort versus controls. In both models, matched pairs were included as clusters. The analysis of HRU before first time attempt comparing

individuals with two attempts versus one attempt was adjusted for sex, depression severity, and age, as these were the matching parameters in the main analyses.

To graphically present the HRU over time, stacked cumulative frequency plots of the daily HRU were generated. Herein, the types of outcomes were ordered according to the following hierarchy: (1) Death; (2) Emigration; (3) Psychiatric acute hospitalization or ED visit; (4) Psychiatric elective hospitalization, outpatient visits, and home visits, and private psychiatrist and psychologist visits; (5) Acute somatic hospitalization or ED visit; (6) Elective somatic hospitalization, somatic outpatient visits, GP visits; (7) No contact. Note that the category 'psychiatric outpatient visits' for the cumulative frequency plots was identified as outpatient contact dates from table SKSUBE in the Danish National Patient Registry.

All analyses were performed in SAS Enterprise Guide, except the sunburst plots made in R. Data are in the domain of Statistics Denmark (www.dst.dk) and cannot be transferred to third party. Access to data can be applied for through Statistics Denmark and the Danish Health Data Authority, respectively. The study was approved by the Danish Data Protection Agency, the Scientific Board of Statistics Denmark (ref. P-2020-88). Ethical permission is not required for anonymized register studies.

RESULTS

In total, 3759 individuals with a first-time suicide attempt and 1061 individuals who died by suicide during 1998–2018 had a hospital contact with MDD within 1 year prior to the event (index date) (Figure 1). After matching successfully

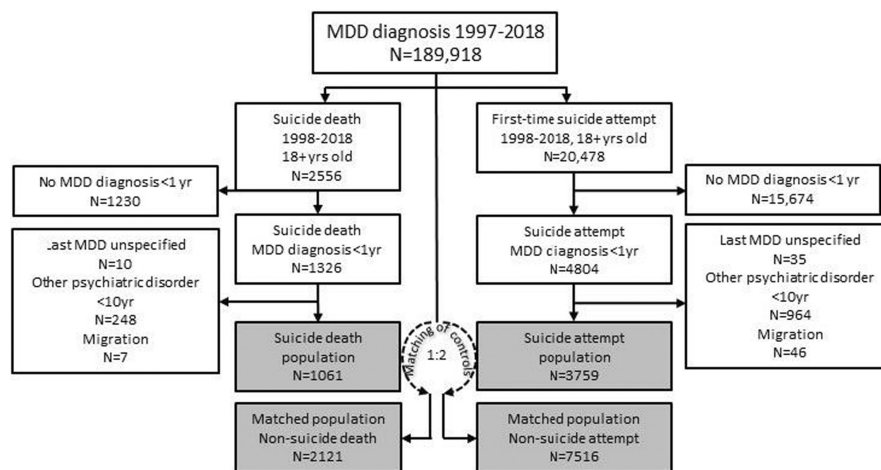


FIGURE 1 Flow chart. Matching 1:2 on sex, birth year (± 2 years) and MDD severity of latest diagnosis before index date (date of suicide death or suicide attempt). Non-suicide death and non-suicide attempt controls had to be alive on the index date, and otherwise fulfilling the same criteria as the population with event, that is, 18 years or above on the index date, Danish residence with no migration event within 1 year prior to index date, at least one hospital contact with the MDD diagnosis within 1 year prior to the index date, no other psychiatric disorder diagnosis within 10 years prior to the index date.

balancing age, sex, and depression severity, individuals with suicide death or suicide attempt had slightly higher educational levels, more persons living alone, and a shorter median time since last hospital contact with MDD compared with their respective controls (Table 1). For the suicide death

and suicide attempt cohorts, one and two individuals could only be matched to a single control, respectively. Of controls to the suicide death cohort, 32 individuals later entered the analysis as suicide decedents; for the suicide attempt cohort, 286 controls later entered as suicide attempters.

TABLE 1 Background characteristics after matching.

Parameter	Suicide death	Suicide control	Suicide attempt	Suicide attempt control
Total	1061	2121	3759	7516
Age at index (years)	56 (46–67)	56 (45–67)	39 (27–53)	39 (27–54)
Age group at index				
18–44	253 (24%)	515 (24%)	2291 (61%)	4590 (61%)
45–64	506 (48%)	995 (47%)	993 (26%)	1970 (26%)
>64	302 (28%)	611 (29%)	475 (13%)	956 (13%)
Sex				
Female	413 (39%)	826 (39%)	2558 (68%)	5116 (68%)
Age group by sex				
Male <65 years	482 (45%)	959 (45%)	1069 (28%)	2138 (28%)
Female <65 years	277 (26%)	551 (26%)	2215 (59%)	4422 (59%)
Male ≥65 years	166 (16%)	336 (16%)	132 (4%)	262 (3%)
Female ≥65 years	136 (13%)	275 (13%)	343 (9%)	694 (9%)
Year of index				
1998–2004	359 (34%)	717 (34%)	1205 (32%)	2410 (32%)
2005–2011	392 (37%)	784 (37%)	1525 (41%)	3050 (41%)
2012–2018	310 (29%)	620 (29%)	1029 (27%)	2056 (27%)
Highest education				
Primary, Lower secondary	337 (32%)	764 (36%)	1738 (46%)	3050 (41%)
Upper secondary, Short cycle	417 (39%)	870 (41%)	1453 (39%)	3097 (41%)
Bachelor, Master, Doctoral	245 (23%)	366 (17%)	459 (12%)	1131 (15%)
Missing or not classified	62 (6%)	121 (6%)	109 (3%)	238 (3%)
Income quartile ^a				
First	228 (21%)	554 (26%)	931 (25%)	1878 (25%)
Second	249 (23%)	551 (26%)	950 (25%)	1870 (25%)
Third	275 (26%)	537 (25%)	988 (26%)	1846 (25%)
Fourth	309 (29%)	479 (23%)	890 (24%)	1922 (26%)
Cohabitation ^a				
No cohabitant	487 (46%)	902 (43%)	1840 (49%)	3412 (45%)
Cohabitant	574 (54%)	1219 (57%)	1918 (51%)	4102 (55%)
Days since last MDD ^b	47 (15–134)	153 (65–250)	75 (26–178)	160 (70–260)
Depression grade ^c				
Mild	308 (29%)	616 (29%)	1243 (33%)	2484 (33%)
Moderate	376 (35%)	752 (35%)	1658 (44%)	3316 (44%)
Severe	377 (36%)	753 (36%)	858 (23%)	1716 (23%)

Note: Continuous variables presented as median (and interquartile range), and categorical variables presented as frequency (and % of total). Income quartile is stratified on age group and calendar year.

^aFor income quartile and partnership status, a few individuals have missing information, and therefore numbers do not sum up to the total.

^bDays since last MDD is the time between date of the last hospital contact with MDD as the primary diagnosis from a psychiatric hospital department and the index date.

^cThe depression degree was defined by the primary diagnosis assigned to the last hospital contact with depression prior to the index date.

Suicide death

The daily HRU for the death by suicide group and the control group is graphically presented in [Figure S1](#), showing elevated total HRU throughout the entire year prior to the index date. Aggregated over the year prior to the index date, 80% of individuals dying by suicide had a psychiatric hospitalization, contrasting 51% of the matched controls, resulting in a proportion ratio (PR) of 1.57 (95% confidence interval: (1.49–1.65)). Similarly, 58% of the suicide death cohort and 40% of the matched controls had at least one psychiatric ED visit (PR: 1.44 (1.34–1.54)) ([Figure 2](#)). Among individuals having at least one utilization of the health service in question, the mean number of psychiatric hospitalizations was 1.5 (1.5–1.6), 11.5% (6.3%–17.0%) larger than among controls. The mean number of psychiatric ED visits was 1.6 (1.6–1.7), 10.8% (4.3%–17.6%) larger than among controls, whereas psychiatric bed days (mean of 17.9 (16.3–19.7) for the suicide death cohort) were 11.1% (0.0%–20.9%) fewer than among controls ([Table 2](#)).

An increased PR of utilization comparing death by suicide to matched controls was also seen for somatic hospital contacts, although the estimates were generally smaller than those for the psychiatric hospital-related HRU, except for somatic ED visits ([Figure S2](#)). Among individuals having at least one utilization of the HRU type in question, compared with controls the average number of somatic hospitalizations was 14.9% (6.4%–24.1%) larger, whereas the average numbers of somatic bed days or somatic ED visits were not different ([Table S1](#)). For both somatic and psychiatric HRU, acute hospital contacts accounted for most of the observed difference.

Of prescription medicine, the PR of individuals incurring costs was 1.18 (1.00–1.39) for antiepileptics, 1.31 (1.22–1.40) for anxiolytics, 1.33 (1.24–1.42) for hypnotics and sedatives and 1.55 (1.27–1.90) for drugs against addictive disorders comparing those who died by suicide with controls. Among users of the drugs, however, the average cost was not significantly different, except for lower average costs for antidepressants and non-psychiatric drugs in the suicide death cohort ([Table S2](#)).

Suicide attempt

For individuals with a first-time suicide attempt, 67% had a psychiatric hospitalization and 58% had a psychiatric

ED visit within 1 year prior to the attempt. Compared with matched controls, the PR estimates of psychiatric HRU ([Figure 2](#)), somatic HRU ([Figure S2](#)), and medicine expenses ([Table S3](#)) resembled the ones for individuals dying by suicide, with the addition that the estimates tended to be slightly larger when studying suicide attempts compared to when studying death by suicide. Among users of the HRU type in question comparing suicide attempt with controls, the mean number of psychiatric hospitalizations was 1.6 (1.5–1.6) in the suicide attempt cohort, 19.5% (16.3%–22.7%) larger than among controls, and the mean number of psychiatric ED visits was 1.7 (1.6–1.7) in the suicide attempt cohort, 23.1% (19.3%–27.0%) larger than among controls, where the numbers of psychiatric bed days was not significantly different ([Table 2](#)).

By depression severity

The proportion of individuals with psychiatric hospital contacts increased with increasing depression severity in both the suicide death and suicide attempt cohorts (except for ED visits), as well as their respective matched controls. However, comparing suicide death with control, and suicide attempt with control, the PR decreased with increasing severity of depression ([Figures 3 and 4](#)). For the PR of somatic HRU, there was no evident dependence on depression severity ([Figures S3 and S4](#)).

Sequences of HRU prior to suicide death or suicide attempt

For the suicide death cohort, 98% had a healthcare contact in the last 3 months before suicide, and more than three quarters had at least one psychiatric healthcare contact, with 31% having an acute psychiatric healthcare contact as the last contact ([Figure S5](#)). For the suicide attempt cohort, the figures were similar, although the fraction with an acute psychiatric healthcare contact as the last contact was smaller (20%).

First and second suicide attempt

Of the 3759 individuals with a first-time attempt, 859 had a second suicide attempt separated by at least 4 months

FIGURE 2 Risk of psychiatric healthcare resource utilization 1 year prior to suicide death or suicide attempt, compared with controls. Proportion (in %) of individuals with the specified type of psychiatric healthcare resource utilization 1 year prior to suicide death or suicide attempt and their respective controls. Proportion ratios (PR) comparing individuals with suicide death or suicide attempt with respective controls, presented with 95% confidence intervals (CIs).

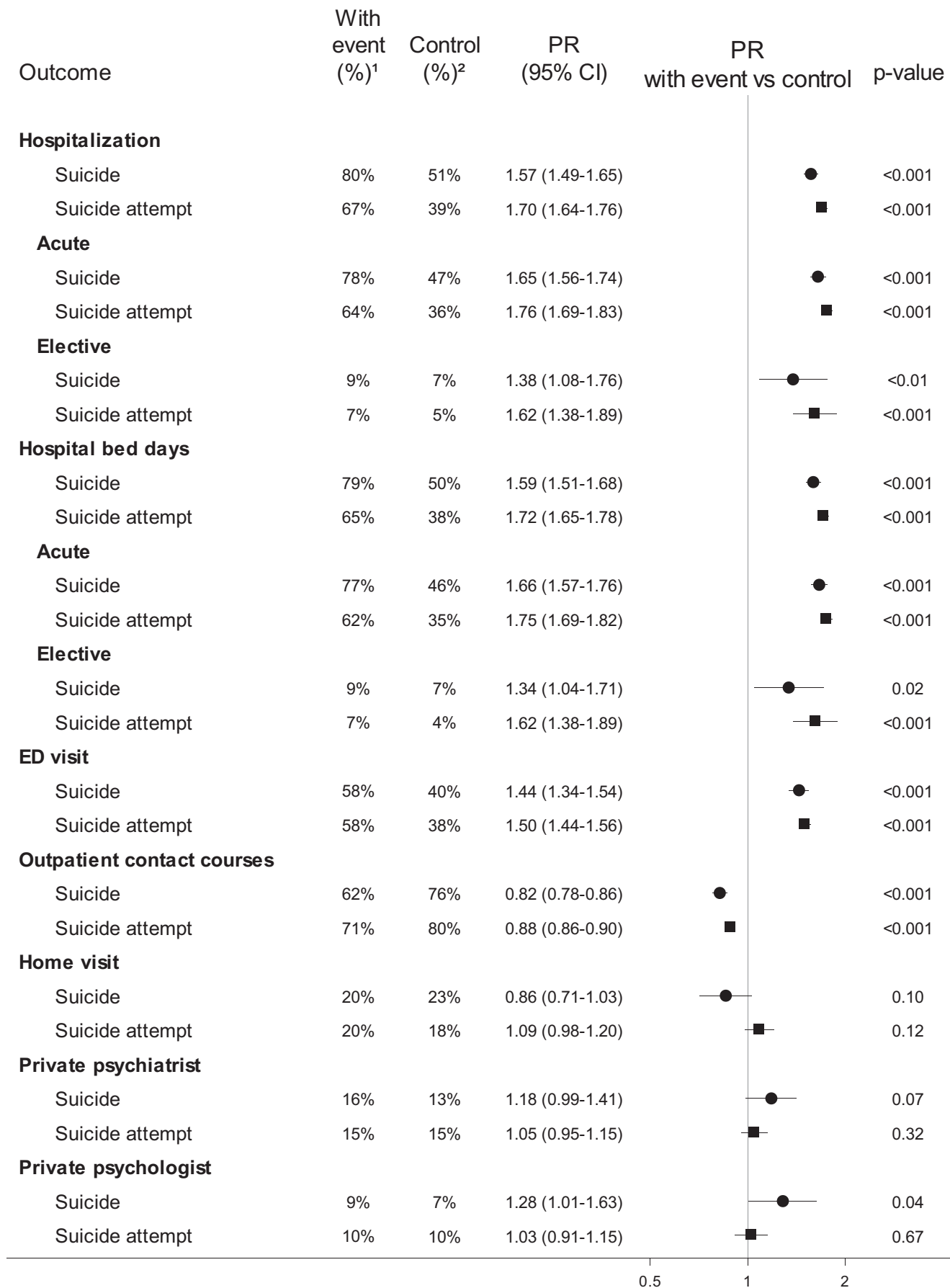


TABLE 2 Difference in psychiatric healthcare resource utilization 1 year prior to suicide death or suicide attempt, compared with controls.

Healthcare resource	Suicide death		Control (no suicide)		Suicide death vs. control		Suicide attempt		Control (no attempt)		Suicide attempt vs. control	
	GM (95% CI)		GM (95% CI)		Difference in utilization (95% CI)	p-Value	GM (95% CI)		GM (95% CI)		Difference in utilization (95% CI)	p-Value
Hospitalization												
Overall	1.5 (1.5–1.6)		1.4 (1.3–1.4)		11.5% (6.3; 17.0)	<0.01	1.6 (1.5–1.6)		1.3 (1.3–1.3)		19.5% (16.3; 22.7)	<0.01
Acute	1.5 (1.4–1.5)		1.3 (1.3–1.4)		11.7% (6.7; 17.0)	<0.01	1.5 (1.5–1.5)		1.3 (1.2–1.3)		18.8% (15.7; 22.0)	<0.01
Elective	1.2 (1.1–1.3)		1.3 (1.1–1.4)		–7.4% (–17.9; 4.6)	0.22	1.2 (1.2–1.3)		1.1 (1.1–1.2)		6.5% (–0.2; 13.8)	0.06
Bed days												
Overall	17.9 (16.3–19.7)		20.3 (18.8–22.0)		–11.1% (–20.9; –0.0)	0.05	16.6 (15.6–17.6)		16.7 (15.8–17.6)		0.4% (–6.9; 8.2)	0.92
Acute	16.3 (14.8–17.9)		18.7 (17.2–20.3)		–11.9% (–22.0; –0.4)	0.04	15.2 (14.3–16.1)		15.2 (14.4–16.0)		0.6% (–6.9; 8.7)	0.88
Elective	18.0 (14.2–22.8)		23.0 (19.2–27.6)		–21.6% (–41.4; 5.0)	0.10	22.1 (18.7–26.1)		22.4 (19.5–25.6)		–0.1% (–19.1; 23.4)	0.99
ED visits	1.6 (1.6–1.7)		1.5 (1.4–1.5)		10.8% (4.3; 17.6)	<0.01	1.7 (1.6–1.7)		1.4 (1.3–1.4)		23.1% (19.3; 27.0)	<0.01
Out-patient contact courses	1.4 (1.4–1.5)		1.4 (1.3–1.4)		5.1% (1.1; 9.3)	0.01	1.5 (1.5–1.5)		1.3 (1.3–1.4)		10.8% (8.6; 13.0)	<0.01
Home visits	2.9 (2.4–3.4)		3.3 (3.0–3.7)		–13.6% (–28.9; 4.9)	0.14	3.1 (2.8–3.4)		3.4 (3.1–3.6)		–7.3% (–17.7; 4.4)	0.21
Priv psychologist visits	6.0 (5.2–7.0)		5.2 (4.7–5.8)		15.3% (–3.5; 37.9)	0.12	5.6 (5.2–6.1)		5.3 (5.1–5.6)		4.7% (–4.6; 14.8)	0.33
Priv psychiatrist visits	3.1 (2.6–3.6)		3.5 (3.0–4.0)		–10.8% (–28.3; 10.8)	0.30	3.0 (2.8–3.3)		4.0 (3.8–4.3)		–24.2% (–31.6; –15.9)	<0.01

Note: Among individuals with any utilization, the difference in frequency or amount of utilization comparing individuals with suicide death or suicide attempt with their respective controls. Estimates are presented with 95% confidence intervals (CI). Home visits only available from 2006; the denominator of the fraction only includes individuals with full observation period from 2006 and onwards.

Abbreviation: GM, geometric mean.

(Table S4). Among these individuals there was a larger fraction of individuals with both psychiatric and somatic acute HRU and a prescription for antiepileptics, anxiolytics, addictive disorders, and hypnotics and sedatives, but a smaller fraction with prescriptions for psychostimulants for ADHD and nootropics in the year leading up to their first attempt compared with the individuals, who had no recurrent suicide attempt during the observation period of the study (Table S5–S7).

In the 3-month period prior to the second attempt, the proportion with a healthcare contacts remained lower compared with the period before the first attempt (Figure S6). For psychiatric hospitalization the PR was 0.63 (0.56–0.71). The proportion of individuals having at least one psychiatric ED visit prior to the second attempt was 23% versus 35% prior to the first attempt, resulting in a PR of 0.65 (0.57–0.74). Among users of HRU, the difference in utilization was for most psychiatric outcomes not significantly different before the second attempt compared with the first attempt with a median of one psychiatric hospitalization and one psychiatric ED visit in both periods, and a median of 18 and 14 bed days, respectively, prior to the first and second attempt.

The proportion of individuals with psychiatric outpatient visits (PR: 0.65 (0.57–0.74)) was lower leading up to the second attempt, but among the fraction of users (27% prior to the second attempt), the average number of psychiatric out-patient contacts was 7.9% (1.5%–14.7%) higher. For private psychologist visits the proportion of users was also reduced prior to the second attempt (PR: 0.41 (0.24–0.69)), whereas among the relatively few users, the number of visits was 73.2% (27.6%–135.0%) higher prior to the second attempt compared with the first attempt (Table 3).

The proportion of individuals with somatic HRU were not significantly different before the first and the second attempts. Among frequenters of GP, the average number of GP visits was 11.4% (4.5%–17.8%) lower prior to the second attempt compared with the first attempt (Table S8). The proportions of individuals having medicine costs prior to the second attempt was lower for antidepressive medicine (PR: 0.92 (0.89–0.96)) and lower for hypnotics and sedatives (PR: 0.87 (0.79–0.96)) compared with the first attempt, whereas the proportion of individuals having costs for psychostimulants for ADHD and nootropics was increased (PR: 3.00 (1.55–5.82)) (Table S9). Among individuals with medicine costs, the amount incurred was increased prior to the second attempt for antidepressants, antiepileptics, anxiolytics, medicine for addictive disorders and non-psychiatric medicine (Table S9).

DISCUSSION

Among individuals with MDD, we analyzed the proportion of specific types of HRU prior to suicide death or suicide attempt. One year prior to death by suicide, 8 out of 10 had a psychiatric hospitalization and almost 6 in every 10 had a psychiatric ED visit; similarly, 1 year prior to suicide attempt, two thirds had a psychiatric hospitalization and almost 6 out of 10 had a psychiatric ED visit.

The comparison with MDD controls matched on age, sex and depression severity yielded a number of differences which we in brief highlight here: (1) In the year prior to suicide death or suicide attempt, the proportion of individuals with psychiatric and somatic hospital-based HRU was 40–70% increased. (2) The psychiatric HRU was generally more increased than the somatic HRU, and more so for acute versus elective contacts. (3) The differences were generally somewhat larger for the suicide attempt cohort than for the suicide death cohort. (4) Among individuals with a hospitalization, the numbers of psychiatric or somatic hospitalizations were also increased in the suicide death and suicide attempt cohorts compared with controls. (5) Despite increased probability of having a bed day, the number of bed days was slightly less in the suicide death cohort compared with controls, when restricting to those with at least one psychiatric bed day. (6) The proportion of individuals with psychiatric hospitalization increased with increasing depression severity, but more so in controls than in individuals with suicide death or suicide attempt, and therefore the proportion ratio (PR) decreased with increasing depression severity; hence the largest PR was seen for the mild depression stratum, despite a lower absolute fraction. (7) For individuals with recurrent suicide attempts, the HRU prior to the second attempt was lower compared to the period leading up to their first suicide attempt. (8) More than 98% of the individuals had a healthcare contact within the last 3 months leading up to their suicide death or suicide attempt, with three quarters having a psychiatric healthcare contact.

Comparison with other studies

Aligning our findings with studies from other settings is challenged by the potential underlying differences in the surveillance and focused resources allocated to individuals of high suicidal risk. Moreover, few studies have restricted the analysis to MDD. Several studies using unmatched control design (Ahmedani et al., 2019; Liu et al., 2012) or matching on sex and age

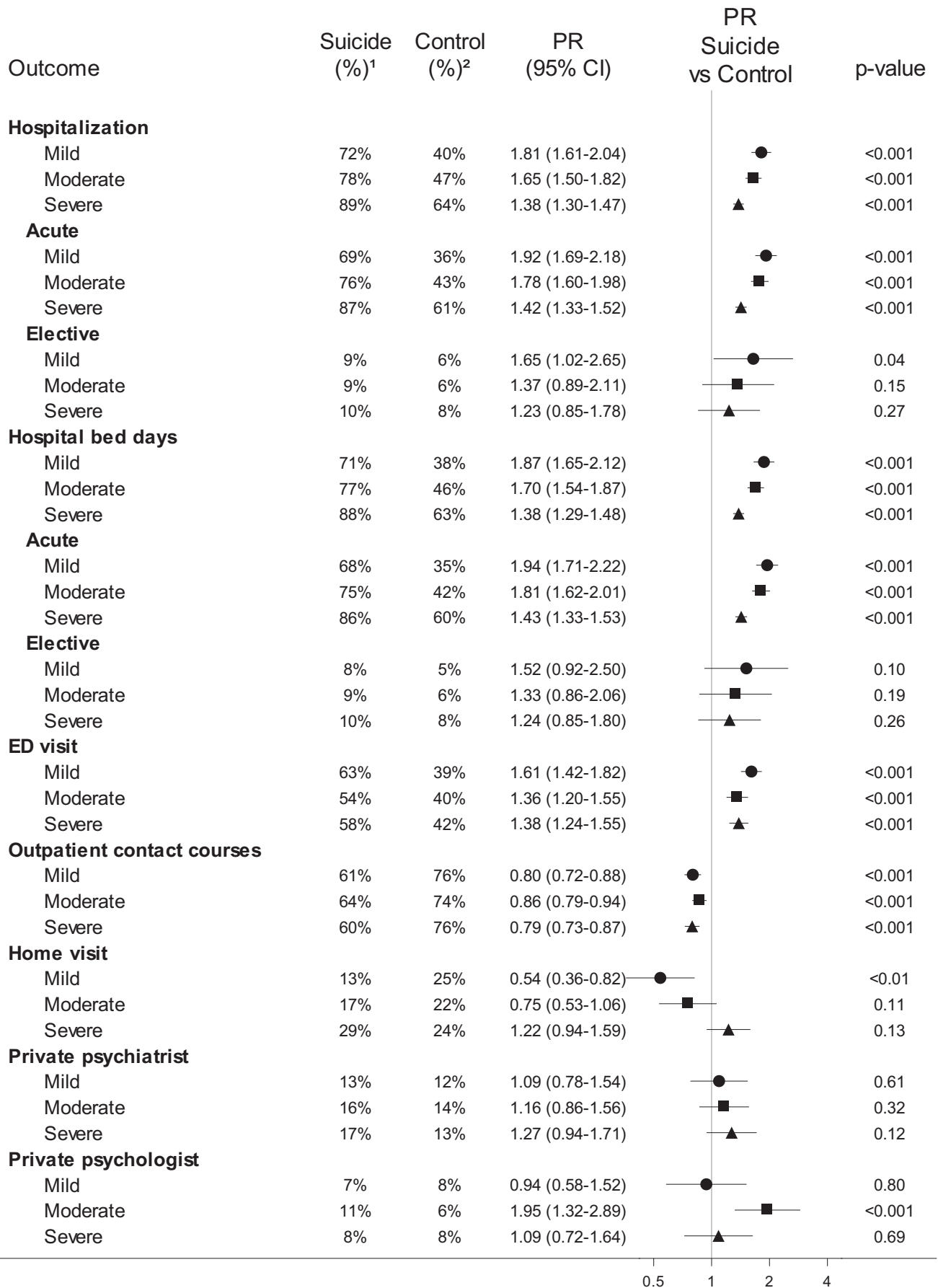


FIGURE 3 Risk of psychiatric healthcare resource utilization 1 year prior to suicide death compared with controls, stratified by MDD severity. Proportion (in %) of individuals with the specified type of psychiatric healthcare resource utilization 1 year prior to date of suicide death, and their respective controls. Proportion ratios (PR) comparing individuals with suicide death with controls, presented with 95% confidence intervals (CI). Estimates are stratified by depression severity.

(Chock et al., 2015; Ribeiro et al., 2017; Schou Pedersen et al., 2019) find increased HRU prior to death by suicide, with differences incrementing towards the suicide date (Ahmedani et al., 2019; Liu et al., 2012; Schou Pedersen et al., 2019).

Considering all suicide cases in Denmark in the period 1997–2013, compared with an age- and sex-matched reference group, Schou Pedersen et al. found an increased proportion attending GP in the year before suicide date (83% vs. 76%; Schou Pedersen et al., 2019). In the present study conditioning on MDD within 1 year prior to the event, 99% of suicide decedents and their matched controls had a GP visit, resulting in no difference in GP utilization. We found that the largest difference was seen for acute psychiatric hospital contacts, which also accounted for most of the HRU. Intriguingly, individuals dying by suicide had a large probability of and more frequent psychiatric hospital contacts, but with shorter average in-hospital stays. The large acute psychiatric HRU is putatively a consequence of inadequately treated mental conditions with overt symptomatic manifestations, which ultimately leads to suicide death or suicide attempt; in addition, it may also reflect a lower threshold for admission to hospital based on clinical assessment of the individuals. Further studies accessing more detailed patient data including medical records may explore the reason for these shorter and more frequent acute contacts, which entails discharge of patients in high risk of suicide.

Additionally, the results indicate that the present registry data on healthcare contacts may be a data source with potential for prediction of suicidal behavior. Prediction, however, was not within the scope of the present study.

MDD severity

The risk of suicide ideation or suicide attempt increases with depression severity (Eikelenboom et al., 2012) and depression symptom severity is a key driver of short-term risk of hospital encounters (Voelker et al., 2021). Moreover, a previous study suggested that anti-depressive therapy reduced suicidal behavior via a modification of the depression severity (Weitz et al., 2014). Corroborating these observations, we found that the risk of HRU increased with increasing depression severity, emphasizing the need to allocate resources to particularly MDD

patients with severe depression, whereas the relative difference between the cohorts with suicide death or suicide attempts and their matched controls decreased with increasing depression severity.

Recurrent suicide attempt

Precedent suicide attempt is a major risk factor for death by suicide and a large proportion have recurrent attempts (Christiansen & Frank Jensen, 2007; Gradus et al., 2020). Almost one in four of the present suicide attempt cohort had a second attempt occurring at least 4 months after the first attempt, and already prior to their first attempt these were characterized by a larger proportion having acute hospitalization compared with individuals attempting suicide only once. It is therefore interesting that the proportion of HRU users was lower before the second attempt compared with the first attempt, particularly for psychiatric healthcare contacts, but not somatic services. The reduction in frequenters was for acute hospital contacts as well as for contacts in the primary sector. The results may indicate that a fraction of individuals with a previous suicide attempt do not subsequently receive adequate psychiatric healthcare, although the reason cannot be elucidated from the present study. From the registries we cannot identify whether the changes in HRU from first to second attempt reflect altered barriers in admission to the healthcare system or refractory healthcare seeking of the individual. The reduction or unaltered utilization of also primary healthcare, which generally has a high accessibility, may indicate that the latter explanation is at least a contributing factor.

Corroborating this speculation, a Danish registry study of all cases of self-harm in Denmark in 2012–2016 presented at hospitals found that more than half of individuals presenting with self-harm received no subsequent specialized psychiatric hospital treatment apart from a psychosocial assessment in the ED. The majority of self-harm presentations had no subsequent psychiatric hospital care within 3 weeks of hospital discharge (Dyvesether et al., 2021). And yet, despite psychiatric in-hospital care, suicide frequently occur as shown in a Danish registry-study of psychiatric patients. The incidence of suicide during the first week of psychiatric admission was 237 (95% CI: 205–274) times higher in men and 322 (256–404) times higher in women than the risk of the background

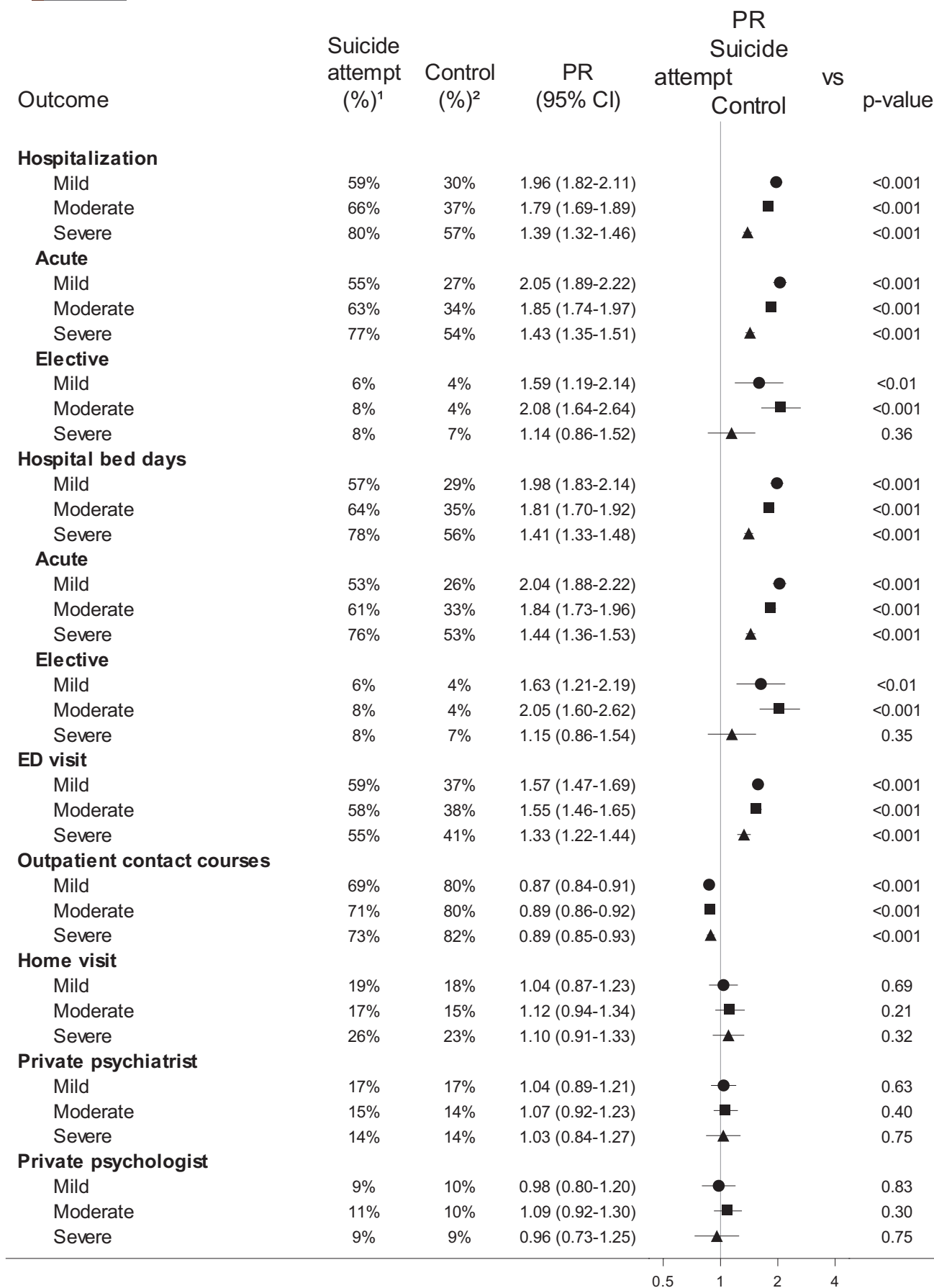


FIGURE 4 Risk of psychiatric healthcare resource utilization 1 year prior to suicide attempt compared with controls, stratified by MDD severity. Proportion (in %) of individuals with the specified type of psychiatric healthcare resource utilization 1 year prior to date of suicide attempt, and their respective controls. Proportion ratios (PR) comparing individuals with suicide attempt with controls, presented with 95% confidence intervals (CI). Estimates are stratified by depression severity.

TABLE 3 Psychiatric HRU for second attempt versus first attempt.

Healthcare resource	First attempt	Second attempt	Second attempt vs. first attempt			
	Proportion ^a (Median [IQR]) ^b	Proportion ^a (Median [IQR]) ^b	PR (95% CI) ^c	<i>p</i> -Value	Difference in utilization (95% CI) ^d	<i>p</i> -Value
Hospitalization						
Overall	45% (1 [1–2])	29% (1 [1–2])	0.63 (0.56–0.71)	<0.001	6.3% (–0.9; 13.9)	0.09
Acute	43% (1 [1–2])	27% (1 [1–2])	0.63 (0.56–0.71)	<0.001	5.8% (–1.3; 13.4)	0.11
Elective	3% (1 [1–1])	3% (1 [1–1])	0.93 (0.57–1.52)	0.77	10.5% (–1.1; 23.5)	0.08
Bed days						
Overall	43% (18 [6–41])	28% (14 [5–34])	0.64 (0.57–0.72)	<0.001	–12.0% (–28.6; 8.5)	0.23
Acute	41% (16 [4–38])	26% (13 [5–32])	0.63 (0.55–0.71)	<0.001	–14.4% (–30.8; 5.7)	0.15
Elective	3% (36 [15–51])	3% (23 [8–50])	0.96 (0.59–1.58)	0.88	–23.7% (–62.6; 56.1)	0.45
ED visits	35% (1 [1–2])	23% (1 [1–2])	0.65 (0.57–0.74)	<0.001	–3.1% (–11.6; 6.1)	0.49
Out-patient contact courses	42% (1 [1–2])	27% (1 [1–2])	0.65 (0.57–0.74)	<0.001	7.9% (1.5; 14.7)	0.01
Home visits	12% (2 [1–4])	12% (3 [1–6])	0.97 (0.72–1.32)	0.87	11.9% (–17.1; 51.2)	0.46
Priv psychiatrist visits	10% (3 [2–4])	9% (3 [2–5])	0.87 (0.67–1.13)	0.30	17.1% (–7.1; 47.7)	0.18
Priv psychologist visits	5% (2 [1–3])	2% (3 [2–5])	0.41 (0.24–0.69)	<0.001	73.2% (27.6; 135.0)	<0.01

Note: Healthcare resource utilization during 3 months prior to the index date in individuals with a first-time attempt followed by a second suicide attempt separated by a minimum span of 4 months.

^aProportion of individuals with the outcome in % of the population.

^bMedian (interquartile range (IQR)) among individuals with any utilization.

^cProportion ratio (PR) of the outcome between the time prior to the second suicide attempt versus the first attempt, presented with 95% confidence interval (CI).

^dAmong individuals with any utilization, the difference in amount of utilization is presented with 95% CI. Home visits only available from 2006; the denominator of the fraction only includes individuals with full observation period from 2006 and onwards.

population never admitted; this increased risk remained alarmingly high during the first week after discharge from the psychiatric hospitalization, with suicide incidences 225 (197–257) and 425 (354–510) times higher than the background population in men and women, respectively (Madsen et al., 2020).

Strengths and limitation

The present study was based on the nationwide Danish health registries which have a very high degree of completeness, capturing the entire population with regard to any type of public and most private healthcare utilization, allowing a detailed analysis of the HRU by type of health care service. As healthcare is tax-financed in Denmark, there is negligible economic or social selection bias in the registers, rendering our study highly generalizable.

Only depression assigned as the primary diagnosis from psychiatric hospital departments were considered,

ensuring a high degree of clinical validity. However, individuals with milder depression symptoms and less complicated disease courses may have been underrepresented, as patients treated solely in the primary health care by private general practitioners or private psychiatrists were not included in the MDD cohort.

As diagnoses or other detailed indicative data on the reason for consultations in the primary healthcare sector are not available in the Danish registries, GP visits could not be differentiated by somatic versus psychiatric type of healthcare utilization.

Due to the progressive subsidy of medicine expenses by the public healthcare, virtually all prescription medicine outside the hospital setting is dispensed from community pharmacies (Medstat.dk, Danish National Health Data Authority) and therefore captured in the Danish National Prescription Registry. The fact that only prescriptions of medicine redeemed at community pharmacies were included, whereas medicine administered at the hospital was not available from the registers would, therefore, have

a negligible influence on the results. However, there may have been a slight underestimation of medicine costs for all patients, particularly patients with very frequent hospital contacts, that is, leading to a slight underestimation of the excess use among the suicide death and suicide attempt cohorts compared with their controls.

Patients with a history of other psychiatric disorders than depression were excluded from the study, as other psychiatric disorders also incur increased HRU, and, as a known risk factor of suicidal behavior, the prevalence of other psychiatric disorders would most likely be higher among persons dying by suicide or attempting suicide, hence confounding the analysis. Similar results may have been obtained if restricting the analysis to, for example, schizophrenia, bipolar disorders, or anxiety disorders.

Despite excluding on other psychiatric disorders, there was yet a high proportion of users of medicine with psychiatric indications other than depression in both the suicide death and the suicide attempt cohorts, with up to half the cohorts redeeming prescriptions for antiepileptics and anxiolytics; compared with controls, the proportion of users was higher in the suicide death and suicide attempt cohorts for antiepileptics, anxiolytics, hypnotics, and sedatives, and drugs for addictive disorders. Almost all also redeemed prescriptions for non-psychiatric medicine. The drug utilization pattern indicating polypharmacy may reflect several concurring or sequential treatment strategies, and the diagnosed and un-diagnosed co-morbidities may have contributed to the complex treatment trajectory. The increased proportion of users of psychiatric medicine other than anti-depressants in the suicide death and suicide attempt cohorts, may reflect an accordingly larger proportion of other psychiatric conditions that have not been diagnosed in the hospital setting, and therefore not eliminated through the applied exclusion criteria. If so, this may have somewhat contributed to an inflation of the observed difference, as other psychiatric conditions most likely would also be associated with increased HRU.

Suicide attempt by excessive alcohol consumption was not included in the study, as the intended lethal intake may not be consistently discernible from the unintended life danger in the available registry-data (Nordentoft & Søgaard, 2005; Reuter Morthorst et al., 2016). However, only approximately 0.2% of the unrestricted MDD population with suicide attempt had alcohol-related suicide attempt as their first attempt. Nonetheless, these caveats may also to some extent apply to other types of suicidal behavior including poisoning. Thus, by including the ICD-10 codes T39, T42, and T43 as part of the definition for deliberate self-harm, we may have overestimated the number of patients with deliberate self-harm, since up to 30% of cases with these specific codes might not be intentional self-harm but accidental.

For the analysis of recurrent suicide attempts, we restricted the analysis to include only recurrent suicide attempts separated by at least 4 months, in order to avoid potential spill-over of HRU arising directly from the first suicide attempt. This criterion may have inferred a selection excluding patients with the most acute mental challenges. A minimum of 1-month gap between the first suicide attempt and the beginning of the HRU observation period associated with the second suicide attempt was granted. However, some healthcare contacts inflicted by the first suicide attempt, for example, treatment of injuries, may have occurred beyond the 1-month grace period. The consequence would be inflation of the HRU prior to the second attempt. The criterion of a psychiatric hospital contact with MDD 1 year prior to the first suicide attempt was not applied to the second attempt. This inherently caused a larger chance of a psychiatric hospital healthcare utilization and of the individual experiencing an ongoing MDD episode during the 3 months prior to the first suicide attempt compared with the second suicide attempt.

CONCLUSION

Among Danish patients with MDD who already have a high healthcare attendance, the present study finds increased utilization of primarily psychiatric hospital-based services, and secondly somatic hospital-based services 1 year prior to suicide or attempted suicide. The contacts become more frequent toward the event. Among individuals with recurrent attempt, fewer had a psychiatric hospital contact prior to the second attempt compared to their first suicide attempt.

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CONFLICT OF INTEREST STATEMENT

The study was performed by the Copenhagen Phase IV Unit (Phase4CPH) and was financed by Janssen Cilag A/S, which holds the license to antidepressant medicine. JP has performed other studies regarding antidepressants involving funding from Janssen Cilag and Eli Lilly, while KJJ and MO have performed other studies regarding antidepressants involving funding from Janssen Cilag. All funds were given to their institution. JR and NB are employees of Janssen Cilag. Janssen Cilag A/S and its employees did not have access to the registry data located on the servers of Statistics Denmark and had therefore no influence on the data management and data analysis of the present work. The authors at Copenhagen Phase IV Unit retained editorial control of the manuscript.

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The study was sponsored by Janssen Cilag A/S. The funder was not involved in data management or data analysis of the present work, nor did the funder have access to the data or the data analysis platform located on the research engines of Statistics Denmark used for the present study.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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