

## Research Article

# High Quality of Early Ischemic Stroke Care but Poorer Clinical Outcomes among Patients with a History of Mental Illness

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Objectives. The aim of this study was to compare early stroke care and clinical outcomes among patients with and without a history of mental illness. Materials/Methods. A nationwide registry-based cohort study of patients with acute ischemic stroke treated in a tax-financed healthcare system. We used process and outcome measures from the Danish Stroke Registry 2007-2018 combined with the data from multiple Danish registries. We combined the process measures in two composite measures: an opportunity-based score (the proportion of all relevant process measures fulfilled for each patient) and an all-or-none score (the proportion of patients fulfilling all relevant process measures). Patients were categorized according to severity of mental health history. Results. We included 117 548 admissions with acute ischemic stroke: 20.8%, 3.5%, and 3.4% of admissions concerned patients with a history of minor, moderate, or major mental illness, respectively. Patients received a median of 85.7% (IQR, 66.7; 100.0) of the relevant processes (opportunity-based score). Patients with a history of mental illness were less likely to receive guideline-recommended acute stroke care within the defined time frames; however, differences were not clinically relevant. Patients with a history of mental illness were significantly more likely to die within 30 days, compared to patients with no history of mental illness: Risk ratios (RR) for 30-day mortality adjusted for age, sex, and country of origin were 1.31 (CI, 1.25; 1.37) for minor, 1.18 (CI, 1.05; 1.33) for moderate, and 1.44 (CI, 1.30; 1.60) for major mental illness. The corresponding adjusted RRs for recurrent stroke/TIA were 1.69 (CI, 1.58; 1.80) for minor, 1.39 (CI, 1.19; 1.61) for moderate, and 1.36 (CI, 1.17; 1.59) for major mental illness. The associations were weakened for 30-day mortality but not recurrent stroke/TIA after additional adjustment for potential mediating factors (comorbidity and stroke severity). Conclusion. More than one-quarter of patients with ischemic stroke had a history of mental illness. The overall performance of acute stroke care was high in all groups. Mental illness was associated with a higher risk of death and recurrent stroke compared to patients without a history of mental illness which may at least partly be due to a more adverse prognostic profile at the time of admission, including a higher stroke severity.

### 1. Introduction

People with severe mental illness have an increased risk of stroke and a higher risk of adverse poststroke outcomes, compared to the general population [1–5].

People with mental illness may experience a systematic failure of the healthcare system to prevent, identify, and treat physical diseases in general [6–8]. Also, patients with mental illness have a higher risk of having a low socioeconomic status, poor social network, impaired bodily sensation, disturbed perception of reality, adverse lifestyle factors, drug abuse, and physical comorbidities all acting as mediating factors contributing to the higher stroke rates, more severe strokes, and poorer poststroke outcomes [9–14].

Some studies have focused on the prognosis for patients with stroke and comorbid mental illness [3–5, 15, 16]. Few studies have investigated disparities in the use of reperfusion therapy [17, 18] and carotid endarterectomy/artery stenting [19]. The evidence of the impact of early stroke care (including organization of care and nonpharmacological care) on clinical outcomes is well known [20–23]. Investigating disparities in guideline-adherence and differences in the delivered quality of acute stroke care may strengthen our possibilities to improve both quality of acute stroke care and patient outcomes.

The aim of this study was to compare quality of acute stroke care and clinical outcomes among ischemic stroke patients with and without a history of mental illness in Denmark.

#### 2. Methods

2.1. Data Availability Statement. Data cannot be shared publicly because of Danish legislation. Data can be accessed through the Danish Health Data Authority and Statistics Denmark for researchers at authorized institutions. Information on data access is available online (http://sundhedsdatastyrelsen.dk/da/ forskerservice). Access to data requires approval from the Danish Data Protection Agency (https://www.datatilsynet.dk/ english/legislation). The authors did not have special access privileges to this data.

2.2. Study Design and Setting. This was a nationwide cohort study combing patient-level data from the Danish Stroke Register (DSR) [24] with other nationwide Danish health registries. The authors of this paper have previously published a paper investigating disparities in reperfusion therapy based on this cohort [17]. Please find detailed description of study setting and the data sources in this paper [17] as well as other sources (the Danish CPR-number [25], the Danish Stroke Registry, and the Danish Clinical Registries [26]). Methods and results from this paper were included in the PhD thesis defended by the corresponding author at Aalborg University, Denmark, in 2022 [25].

The study was reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for observational studies.

Acute stroke care is provided only at public hospitals in Denmark. The organization of acute stroke care in Denmark

is based on the current knowledge about the association between higher patient volumes and higher reperfusion rates [26]. Patients with suspected acute stroke, who are eligible for reperfusion therapy, are received at one of the eight hospitals providing reperfusion therapy. In Denmark, performance of prehospital stroke identification is high [27] Regardless of receiving reperfusion therapy, patients with acute stroke were transferred to one of the twenty-five multidisciplinary stroke units for further treatment and care. In the study period, more than 90% of all acute stroke patients were transferred to a multidisciplinary stroke unit within 48 hours from hospital arrival. The reperfusion rate for patients admitted with ischemic stroke has increased since 2010, where the Danish Health Authority updated their recommendation, making thrombolysis available for all age groups receiving treatment within 4.5 hours. In 2016-2017, the reperfusion rate was 17% [17].

2.3. Identification of Study Population. The study population consisted of consecutive stroke patients admitted from January 1, 2007, to December 31, 2018, identified in the DSR. Since the authors of this paper have previously published another paper using data from this source [17], description of the study population can be found in this paper [17]. Please find a flow-chart regarding this study population in Figure 1.

2.4. Ethics. The study was approved by the local institutional review board. According to Danish law, approval from a national ethical committee is not required for register-based studies.

#### 2.5. Variables

2.5.1. Definition of Exposure: Mental Health History. Patients were categorized according to the severity of their mental health history: major, moderate, minor, or none based on the information from the Danish National Patient Registry, the Danish National Patient Registry-Psychiatry, the Danish Psychiatric Central Research Register, the National Register of Medicinal Product Statistics, and the Danish National Health Service Register. The same definition of exposure has been used previously by the authors of this paper [17]. Please find detailed description of the exposure in the previous papers [17].

- Major mental illness: an inpatient or outpatient contact with schizophrenia or bipolar disorder (ever), or inpatient contacts with severe depression or emotionally unstable personality disorder (within the last 10 years)
- (2) Moderate mental illness: other inpatient or outpatient psychiatric contacts with diagnoses of mental illness (other than "major") or consultations at a private practicing psychiatrist (within the last 5 years)
- (3) Minor mental illness or vulnerability: none of the above. Reimbursement of at least one prescription of selected drugs (antidepressants or benzodiazepines) or two or more sessions of talk therapy or

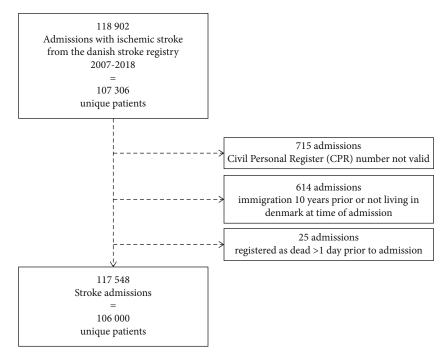


FIGURE 1: Flowchart of the included patients.

psychometric testing in a primary care setting or referral to a private psychologist (within the past 12 months)

(4) No mental illness: none of the above

If the patient fulfilled criteria in several categories, the most severe category defined the patient's exposure. Please see Supplementary Table 1, for details on included ICD-10 diagnoses and codes. Please see Supplementary table 2 for information about timing of most recent mental health disease-related activity.

2.5.2. Definition of Outcomes: Quality of Acute Stroke Care, Mortality, and Recurrent Stroke. We defined guidelinerecommended care using performance measures obtained from the DSR [24] (see Table 1 for details on each measure).

The Danish stroke guidelines including stroke diagnose are in accordance with the guidelines stated by the European Stroke Organization [22]. The measures reflect the provision of the core processes of early stroke care including nine measures regarding diagnostics, treatment, and early rehabilitation.

Based on detailed written instructions, the hospital staff classify every patient as eligible or not for each measure, according to the presence of contraindications. For example, severe dementia in a patient with ischemic stroke and atrial fibrillation can preclude oral anticoagulant therapy; mobilization is not relevant; if the patient was immobilized prior to admission, anticoagulation is not indicated for a patient with recent intracerebral haemorrhage; and rapid spontaneous recovery of motor symptoms makes early assessment by physiotherapist and occupational therapist irrelevant. The medical relevance of each measure is therefore incorporated into the registration and consequently included in this study; i.e., patients with contraindications for a specific clinical intervention were not considered eligible for the corresponding performance measure.

During the study period, the definition of some measures changed, and some measures were added. Also, some measures were redefined in year 2016 (e.g., "CT/MR within with six hours..." rather than the original "...on the day of admission"). In these cases, the original definition of the measures was applied. For an overview of the included measures and the periods in which they were available, see Table 1.

(1) Composite Measures. We combined all process measures and calculated two composite measures: an opportunitybased score, which was defined as the proportion of all relevant process measures which was fulfilled (0-100%) for each patient, and an *all-or-none score*, which is the proportion of patients fulfilling all relevant measures. Due to the availability of measures in different time periods, we calculated the composite scores based on seven measures for the years 2007-2010: same-day CT/MRI, admission to stroke unit, physiotherapy, occupational therapy, mobilization, nutritional screening, and platelet inhibitor/oral anticoagulation-depending on the presence of atrial fibrillation. For the years 2011-2018, we added the following two measures to the score: direct and indirect swallowing tests. A maximum score was calculated for each individual based on the relevance of each measure, as some processes were contraindicated (e.g., mobilization of a patient who was immobilized prior to admission, as described in the methods section).

2.5.3. Covariates. Covariates available for all patients included age, sex, comorbidity, smoking status, socioeco-nomic position, country of origin, cohabitation status, drug

No.	Performance measures	Period available	
Process measures			
(1) CT/MR	Patient is examined with a CT/MRI scan on the day of admission	2007-2018	
(2) Mobilization	Patient is mobilized on the day of admission	2007-2018	
(3) Indirect swallowing test	Patient receives indirect swallowing test on the day of admission before receiving food or fluids to assess swallowing function and risk of aspiration direct swallowing test	2011-2018	
(4) Direct swallowing test	Patient receives direct swallowing test on the day of admission before receiving food or fluids to assess swallowing function and risk of aspiration	2011-2018	
(5) Physiotherapist	Patient is assessed by a physiotherapist about the need for rehabilitation (including type and extent) within the second day of admission	2007-2018	
(6) Occupational therapist	Patient is assessed by an occupational therapist about the need for rehabilitation (including type and extent) within the second day of admission	2007-2018	
(7) Nutrition screening	Patient receives a nutritional risk assessment within the second day of admission	2007-2018	
(8) Stroke unit	Patient is admitted to a stroke unit within the second day of admission	2007-2018	
(9a) Platelet inhibitor	Patient with ischemic stroke without atrial fibrillation receives platelet-inhibitor therapy within the second day of admission	2007-2018	
(9b) Oral anticoagulation	Patient with ischemic stroke with atrial fibrillation receives oral anticoagulation therapy within 14 days after admission	2007-2018	
Outcome measures			
(10) 30-day mortality	30-day mortality	2007-2018	
(11) Recurrent stroke	Admission with new event of stroke or TIA within 1 year	2007-2018	

TABLE 1: Process and outcome performance measures of acute stroke care.

abuse, and stroke severity (Scandinavian Stroke Scale, SSS). The Scandinavian Stroke Scale and the NIH Stroke Score (NIHSS) correlates well [28] and may be converted by the equation NIHSS =  $25.68 - 0.43^*$  SSS [29] or SSS =  $50 - 2 \times$  NIHSS [30]. Detailed definitions of covariates are presented in Supplementary Table 3. Supplementary Figure 1 provides a directed acyclic graph (DAG) presenting covariates as confounders or mediators [14].

2.6. Statistical Methods. We compared all measures according to the severity of mental illness using the group with no history of mental illness as a reference.

For each measure, we calculated risk ratios (RR) as unadjusted and adjusted for potential confounding factors including age, sex, and country of origin (model 1) and additionally adjusted for potential mediating factors including stroke severity, Charlson's comorbidity index (including previous stroke), and atrial fibrillation (model 2). Please see Supplementary Figure 1 "directed acyclic graph (DAG)" for information about the potential confounding and mediating factors.

All estimates included 95% confidence intervals (CI). For all adjusted analyses, we implemented restricted cubic splines for age with three knots at quantiles 0.1, 0.5, and 0.9.

30-day mortality was calculated for each exposure group and stratified according to fulfilment of the all-or-none measure, and according to an opportunity-based score above or below 70% [31]. Doing this, the impact of high quality of acute stroke care on 30-day mortality could be assessed in each exposure group. Statistical analyses were performed using Stata 17 (Stata Corporation, College Station, Texas, USA).

#### 3. Results

We included 117 548 admissions with stroke (Figure 1) of which there was a history of mental illness of minor (20.8%), moderate (3.5%), or major (3.4%) severity, respectively. Characteristics of the population are shown in Table 2.

The 117 548 admissions were registered for 106 000 unique individuals. The median number of admissions per individual was one interquartile range (IQR) [1, 1] (range 1–16) in the period 2007-2018. Supplementary table 2 provides information on available measures of recent mental health disease-related activity.

Patients with a history of mental illness were less likely to receive guideline-recommended acute stroke care within the defined time frames (Figure 2 and Supplementary Table 4). Both for unadjusted and adjusted estimates, patients with any history of mental illness were less likely to receive a CT/MR, be mobilized, and receive a swallowing test on the day of admission and less likely to receive nutritional risk assessment and to be assessed by an occupational and a physiotherapist on the 2<sup>nd</sup> day of admission. Further, patients with a history of minor mental illness were less likely to receive oral anticoagulation within 14 days, if diagnosed with atrial fibrillation. While differences were small, this finding was consistent across all groups.

Combining the individual measures of guidelinerecommended care into composite measures, we found that

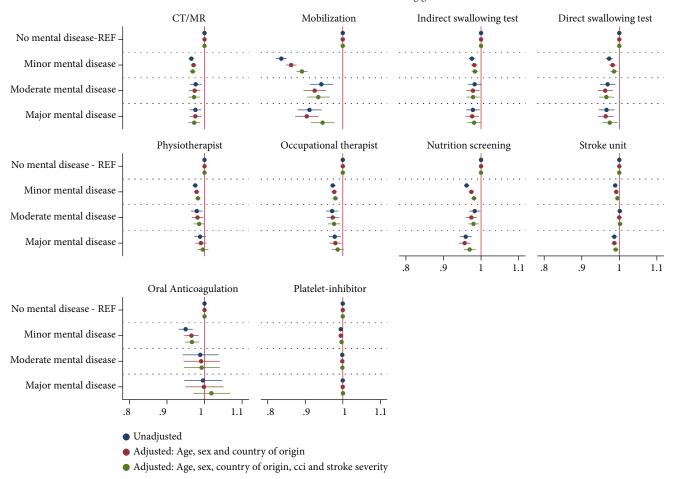
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		No history of mental illness N = 85,056	Minor history of mental illness N = 24,433	Moderate history of mental illness $N = 4,076$	Major history of mental illness N = 3,983	Missing
Sex	Male	50,168 (59%)	9,842 (40%)	1,939 (48%)	1,805 (45%)	0
Age	Years	73 (64-82)	78 (69-86)	65 (54-77)	70 (60-80)	0
Country of origin	Denmark	81,162 (96%)	23,587 (97%)	3,788 (93%)	3,781 (95%)	95
	Western countries	1,966 (2%)	564 (2%)	118 (3%)	103 (3%)	
	Non-Western	1,838 (2%)	279 (1%)	169 (4%)	98 (2%)	
	0	2,675 (3%)	492 (2%)	111 (3%)	142 (3%)	0
Charlson's comorbidity index (CCI)	1-2	59,125 (70%)	14,140 (58%)	2,619 (64%)	2,492 (63%)	
	3-4	16,375 (19%)	6,162 (25%)	888 (22%)	880 (22%)	
	5+	6,881 (8%)	3,639 (15%)	458 (11%)	469 (12%)	
Diabetes		12,588 (15%)	4,142 (17%)	630 (16%)	708 (18%)	1,621
Atrial fibrillation		15,153 (18%)	5,548 (23%)	524 (13%)	536 (14%)	1,964
Hypertension		46,771 (56%)	14,607 (62%)	1,971 (50%)	1,989 (51%)	2,733
Previous stroke		18,552 (22%)	8,484 (36%)	1,210 (30%)	1,129 (29%)	2,267
Smoking	Never smoker	27,246 (37%)	7,016 (35%)	1,013 (29%)	890 (27%)	15,453
	Previous smoker	22,584 (30%)	6,372 (32%)	792 (23%)	780 (23%)	
	Current smoker	24,445 (33%)	6,838 (34%)	1,682 (48%)	1,671 (50%)	
Substance use		2 850 (3%)	1 533 (6%)	842 (21%)	883 (22%)	
Cohabitation	Living alone	37,639 (44%)	14,001 (57%)	2,423 (60%)	2,807 (71%)	345
Income, individual level	Above country average	39,264 (46%)	10,427 (43%)	1,569 (39%)	1,482 (37%)	37
	Below country average	43,957 (52%)	13,660 (56%)	2,323 (57%)	2,431 (61%)	
	Relative poverty	1,802 (2%)	346 (1%)	180 (4%)	70 (2%)	
Adherence to workforce, individual level	Working	16,662 (21%)	1,814 (8%)	593 (16%)	264 (7%)	12,331
	Retirement excl. early retirement	53,601 (69%)	17,428 (81%)	1,832 (49%)	2,232 (62%),	
	Public benefits incl. early retirement	7,759 (10%)	2,439 (11%)	1,298 (35%)	1,098 (31%)	
Level of education	High	13,150 (17%)	3,057 (14%)	701 (18%)	592 (16%)	8,005
	Medium	31,213 (39%)	7,545 (35%)	1,477 (39%)	1,213 (34%)	
	Low	34,545 (44%)	11,924 (51%)	1,644 (43%)	1,866 (50%)	
Scandinavian stroke scale	Mild (45-58)	54,438 (68%)	12,146 (56%)	2,516 (67%)	2,132 (57%)	5,025
	Moderate (30-44)	13,914 (17%)	5,249 (23%)	651 (20%)	860 (23%)	
	Severe (15-29)	6,351 (8%)	2,531 (11%)	312 (8%)	405 (11%)	
	Very severe (0-14)	5,690 (6%)	2,124 (10%)	215 (6%)	308 (8%)	

TABLE 2: Characteristics of patients admitted with ischemic stroke 2007-2018 in Denmark according to mental health history.

patients with a history of mental illness received a total fewer number relevant processes within the defined time frames (opportunity-based score) and they were less likely to receive all relevant measures (all-or-none score) compared to patients with no history of mental illness (Figure 3(a) and Supplementary table 4). The absolute differences were again small, i.e., median opportunity-based score of 87.5% (IQR, 71.4; 100.0) for patients with no history of mental illness compared to a median of 85.7% (IQR, 66.7; 100.0) for each of the groups with a history of minor, moderate, or major mental illness (Supplementary Table 4).

Among patients with no history of mental illness, 3.8% (CI, 3.6; 3.9) had a recurrent stroke within 1 year, compared to 6.2% (CI, 5.9; 6.5) of minor, 5.0% (CI, 4.3; 5.6) of moderate, and 4.9% (CI, 4.2; 5.5) of patients with a history of major mental illness. Considering the estimates adjusted for age, sex, and country of origin (model 1) and further stroke severity, atrial fibrillation, and Charlson's comorbidity



Risk ratio and 95% confidence intervals for recieving guideline-recommended acute stroke care

FIGURE 2: Risk ratio for receiving guideline-recommended care according to the Danish Stroke Registry using patients with no history of mental illness as reference. CCI: Charlson's comorbidity index.

(model 2), patients with a history of mental illness were significantly more likely to have a recurrent stroke within 1 year (Figure 3(b) and Supplementary table 4).

Patients with no history of mental illness has a 30-day mortality of 6.5% (CI, 6.3; 6.7), while 10.8% (CI, 10.4; 11.2) of minor, 5.9% (CI, 5.2; 6.7) of moderate, and 8.4% (CI, 7.5; 9.2) of patients with a history of major mental illness died within 30 days. Considering age- and sex-adjusted estimates, patients with a history of mental illness had a higher risk of death at day 30 (Figure 3(b) and Supplementary Table 4). If also adjusting for stroke severity and comorbidity—both potential mediators rather than confounding factors—differences in 30-day mortality were less pronounced (Figure 3(b)).

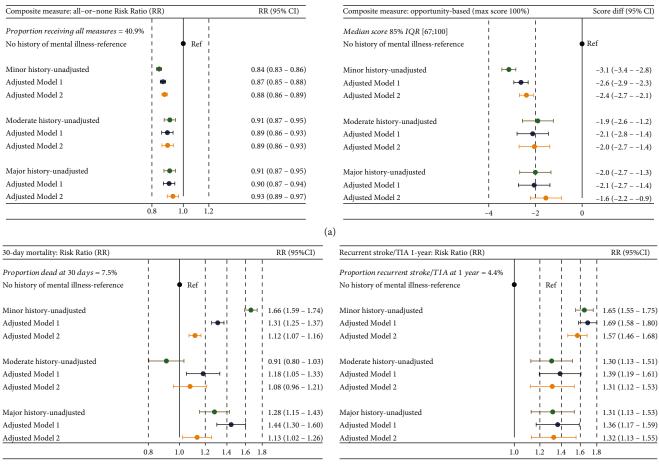
#### 4. Discussion

In this nationwide study comparing the quality of acute stroke care between patients with and without a history of mental illness, we found an overall high performance regarding quality of acute stroke care. Patients with a history of mental illness showed a consistent tendency to be less likely to receive guideline-recommended acute stroke care. However, with the expectation of mobilization, new event of stoke, and mortality, differences were small and most likely not clinically relevant.

4.1. Proportion of Patients with Mental Illness. We found that one in three patients had a history of mental illness; however, one in twelve patients had history of moderate or major mental illness [25]. The proportion of patients with a history of mental illness is comparable to other studies [4, 18] but may depend on the definition of mental illness [5]. Most likely, the proportion of patients with a history of major mental illness should be greater in the stroke population compared to the general population due to the higher prevalence of risk factors in this groups. However, system- and patient-related factors may complicate or obstruct hospital admission with time-critical diseases like ischemic stroke [6–14, 25].

4.2. In-Hospital Measures of Stroke Care. Other studies investigating disparities in acute stroke care have found patients with comorbid mental illness to be less likely to receive cerebrovascular arteriography, carotid endarterectomy, and thrombolysis [17–19, 25]. The overall high

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(b)

FIGURE 3: (a) Forest plots for the composite scores "all-or-none" and "opportunity-based measures" according to mental health history. (b) Forest plots for 30-day mortality and recurrent stroke within 1 year according the mental health history. Model 1: sex, age, and country of origin. Model 2: sex, age, country of origin, comorbidity, stroke severity, and atrial fibrillation.

performance across measures of in-hospital stroke care in the Danish setting is comparable to other European settings [32, 33]. However, the reperfusion rate is higher in Denmark [17] compared to the US [18].

Disparities in stroke care in patients with comorbid mental illness has been investigated in terms of reperfusion therapy [17, 18, 25] and hospital length of stay [15]. However, to our knowledge, disparities in timing of imaging, mobilization, therapy, etc., were not described in subgroups of patients with comorbid mental illness. This fact was also discussed in the thesis defended by the corresponding author of the paper in 2022, including the finding from this paper [25]. While Denmark—like the other Nordic countries—is a welfare state providing equal access to healthcare to all citizens, equal care nor equal outcomes are provided [11, 25, 34].

Reperfusion therapy is a time-critical treatment, and any delay—patient-related or system-related—makes the patient less likely to be eligible for treatment. While the measures in our study are also time-dependent, fulfilment of these measures is not a question of minutes to hours, but rather hours to days. Finding no clinically relevant differences across a large number of process measures is a positive finding suggesting that the clinical staff does not discriminate based on individual factors. Differences regarding mobilization on the day of admission may be due to more severe strokes in patients with a history of mental illness. Delayed mobilization may be caused by being more time-consuming, i.e., prescribing a drug (e.g., platelet inhibitor), and may require stronger interpersonal skills and stronger collaboration between the patient and staff.

4.3. Mortality and Recurrent Stroke. We found patients with a history of mental illness to have a higher risk of 30-day mortality and a higher risk of new event of stroke within 1 year [25]. Especially among patients with a history of minor mental illness, describing causality can be challenging. These patients had the highest proportion of very severe stroke, highest age, highest proportion of previous stroke, and largest burden of comorbidities. Hence, the association between the mental illness itself; the factors defining the mental illness, e.g., being on an antidepressant; and the risk of vascular dementia and clinical outcome after ischemic stroke is complex [35, 36].

Our results regarding higher mortality and higher risk of recurrent stroke are in accordance with other studies finding stroke patients with comorbid mental illness to have longer hospital stays, higher risk of death, and higher risk of readmission compared with people without mental illness [3-5, 15, 16]. However, the patients' prognosis on admission is dependent on several factors, including-especially-stroke severity. Patients with a history of mental illness express patient characteristics associated with higher mortality and more severe strokes (e.g., higher prevalence of atrial fibrillation among patients with a history of minor mental illness, patients with any severity of mental illness living alone, higher prevalence of low socioeconomic position, current smoking, and substance abuse among patients with moderate or major mental illness) [9-14, 37]. In the Swedish Riksstroke registry, including patients admitted with ischemic or haemorrhagic stroke in Sweden, a mediation analysis investigating the association between low income and survival after stroke showed that approximately half of the income-related disparities in stroke outcome were mediated through stroke severity [14]. This is likely to be true for patients with a history of mental illness. Hence, differences in comorbidity and stroke severity between patients with and without mental illness appeared to explain a large part of the mortality disparities.

#### 5. Strengths and Limitations

The data applied in this study represent a key strength. The data had been validated, and the DSR has been found to have a high sensitivity. In addition, the registers have national coverage, and the data were collected prospectively and on an individual level.

The definition of guideline-recommended care was based on up to 9 performance measures of process quality, which is adopted by clinicians in general and is in accordance with international standards. A particular strength is that each measure comes with a registration of medical relevance for the individual patient rather than a yes/no response. It assists in removing potential heterogeneity in individual patient needs from the analysis. However, we cannot entirely exclude that nonrandom misclassification may have occurred in the registration of medical relevance.

However, several limitations should be considered. Firstly, selection bias may have been introduced, since patients with mental illness may be more likely to have undetected (i.e., without hospital admission) or silent events of stroke [38]. We expect this to contribute to more conservative estimates.

Secondly, our estimates may also be skewed due to confounding. While we did adjust for age, sex, comorbidity, and stroke severity, residual confounding may persist, for example, health literacy, prehospital dispositions, and delays and presenting symptoms. Also, considering the differences in baseline characteristics (e.g., patients with a history of minor mental illness being older and more comorbid with more severe strokes), there may be an inherent frailty in exposed groups that we were not able to adjust for using the available measures.

Third, the definition of mental illness is a proxy based on consensus between local experts since there is no gold standard for these definitions. Especially, the definition of minor group may be prone to misclassification, since these measures may express a state of mental vulnerability rather than mental illness.

#### 6. Conclusion

More than one-quarter of patients with ischemic stroke had a history of mental illness, with a majority of patients with a history of minor mental illness and two smaller groups of patients with a history of moderate and major mental illness, respectively. The overall performance of acute stroke care was high in all groups. Mental illness was associated with a higher risk of death and recurrent stroke compared to patients without a history of mental illness, which may at least partly be due to a more adverse prognostic profile at the time of admission, including a higher stroke severity.

#### Abbreviations

- CCI: Charlson's comorbidity index
- DSR: Danish Stroke Registry
- GP: General practitioner
- TIA: Transient ischemic attack.

#### **Data Availability**

Data cannot be shared publicly because of Danish legislation. Data can be accessed through the Danish Health Data Authority and Statistics Denmark for researchers at authorized institutions. Information on data access is available online (http:// sundhedsdatastyrelsen.dk/da/forskerservice). Access to data requires approval from the Danish Data Protection Agency (https://www.datatilsynet.dk/english/legislation). The authors did not have special access privileges to this data.

#### **Conflicts of Interest**

The authors declare that they have no conflicts of interest.

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#### **Supplementary Materials**

Supplementary Table 1: details on included ICD-10 diagnoses and codes for each exposure group. Supplementary table 2: information recent mental health disease-related activity for each exposure group. Supplementary Table 3: definitions of covariates. Supplementary Table 4: proportion of patients receiving guideline-recommended care (process measure 1-9), composite measures, and outcome measures according to history of mental illness. Supplementary Figure 1: directed acyclic graph (DAG) presenting covariates as confounders or mediators. (*Supplementary Materials*)

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