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# Increased risk of depression after Guillain-Barré syndrome

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## Abstract

**Introduction/Aims:** Guillain-Barré syndrome (GBS) is a potentially life-threatening disorder, and some patients may develop subsequent depression related to traumatic stress or permanent loss of motor function. We determined the short-term (0 to 2 years) and long-term (>2 years) risk of depression after GBS.

**Methods:** Individual-level data from nationwide registries were linked in this population-based cohort study of all first-time hospital-diagnosed GBS patients in Denmark between 2005 and 2016 and individuals from the general population. After exclusion of individuals with previous depression, we computed cumulative rates of depression, defined as either antidepressant drug prescription or depression hospital diagnosis. We used Cox regression analyses to calculate adjusted depression hazard ratios (HRs) after GBS.

**Results:** We identified 853 incident GBS patients and recruited 8639 individuals from the general population. Depression within 2 years was observed in 21.3% (95% confidence interval [CI], 18.2% to 25.0%) of GBS patients and in 3.3% (95% CI, 2.9% to 3.7%) of those in the general population, resulting in a HR of 7.6 (95% CI, 6.2 to 9.3). The highest depression HR was observed within the first 3 months after GBS (HR, 20.5; 95% CI, 13.6 to 30.9). After the first 2 years, GBS patients and the general population members had similar long-term depression risks with an HR of 0.8 (95% CI, 0.6 to 1.2).

**Discussion:** During the first 2 years after GBS hospital admission, patients with GBS had a 7.6-fold increased hazard of depression compared with individuals in the general population. Two years after GBS, the risk of depression was similar to that of the background population.

KEYWORDS
AIDP, depression, epidemiology, Guillain-Barré syndrome, prognosis

## 1 | INTRODUCTION

The acute phase of Guillain-Barré syndrome (GBS) is potentially life-threatening and may be associated with considerable morbidity.[1] After a plateau phase, spontaneous recovery usually starts, which in some cases is incomplete. Neuropsychological/neuropsychiatric

**Abbreviations:** aHR, age-, sex-, index date–, and comorbidity-adjusted hazard ratio of depression; ATC, Anatomical Therapeutic Chemical Classification System; CCI, Charlson Comorbidity Index; CRS, Civil Registration System; DNPR, Danish National Patient Registry; GBS, Guillain-Barré syndrome; HR, age-, sex-, and index date–adjusted hazard ratio of depression; NaSSA, specific serotonergic antidepressant; SSRI, serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

disturbances after GBS often are unnoticed. Specifically, GBS patients may develop depression related to traumatic stress and anxiety caused by having a life-threatening illness or due to loss of motor function and residual disability, rendering some GBS patients completely dependent on others.[2–4] Although several studies have addressed residual physical signs after GBS, little is known about the risk of depression. In a recent systematic review of neuropsychiatric comorbidities in patients with inflammatory neuropathies, the main finding was the paucity of publications precluding secondary data analysis.[5] The available studies were characterized by wide variability in depression assessment methods, including psychometric scales, absence of normative values, heterogeneity of study focus, variable timing between the acute GBS manifestation and psychometric assessment, and lack of longitudinal data, all representing major limitations to drawing any clear conclusions about the risk of depression in GBS.[5]

The aim of this study was to determine the excess short- and long-term risk of depression after GBS compared with the general population.

## 2 | METHODS

### 2.1 | Data sources

Since 1968, all Danish citizens have been registered with a 10-digit CPR number in the Civil Registration System (CRS),[6] which is updated daily. The CRS holds information on exact dates of births, deaths, address changes, immigration, and emigration for the entire Danish population.[6] Since 1977, information on all inpatient hospitalizations in Denmark has been recorded in the Danish National Patient Registry (DNPR), with outpatient contacts available since 1995.[7] For each inpatient or outpatient hospital contact, the discharging physician assigns one primary discharge code and an unlimited number of secondary diagnoses.[7] Codes include all types of diagnoses in the *International Classification of Diseases*–10th revision (ICD-10), including psychiatric disorders. Only hospital contacts with nonpsychiatric (somatic) hospitals were available for this study. Since 2004, the Danish National Health Service Prescription Database[8] has provided individual-level information on reimbursable drugs dispensed at all community pharmacies in Denmark. This database records the date on which the drug was dispensed and the type and quantity of drug prescribed according to the Anatomical Therapeutic Chemical (ATC) classification system each time a prescription is redeemed.[8]

### 2.2 | Study design and participants

We applied a population-based cohort study design. The DNPR was used to identify all individuals in Denmark with an incident hospital inpatient GBS diagnosis between January 1, 2005 and December 31, 2016, based on the ICD-10 code (DG61.0). We previously validated medical records of hospital inpatients with a GBS diagnosis in the DNPR and verified a high accuracy (positive predictive value of 84% to 86%).[9,10] In cases of multiple admissions with GBS between 2005 and 2016, we only included the first GBS inpatient admission date. Next, we sampled general population members from the background population for a comparison cohort. On the date of GBS diagnosis, for each GBS patient, up to 10 general population members were randomly selected through the CRS by computer among eligible population members who had no previous record of GBS and who had the same year of birth and sex as the corresponding GBS patient, using risk-set sampling. Participants with previous hospital-diagnosed depression and antidepressant use 1 year before the index date were excluded. Study participants were then followed from the index date until the date of first redemption of an antidepressant drug, a first depression discharge diagnosis, death, emigration, or the end of 2016.

### 2.3 | Covariates

We obtained data for *a priori*–selected confounding factors potentially associated with both GBS and depression. Any differences between GBS patients and general population members in age, sex, and calendar date of GBS diagnosis (index date) were controlled for by the matched cohort study design as well as adjustment. In addition, we retrieved individual-level data for each GBS patient and population member for preceding overall level of pre-existing comorbidity. Comorbidities were assessed based on a complete hospital discharge history for each individual within 10 years before the index date, using the Charlson Comorbidity Index (CCI) score. The CCI categorizes comorbidities using ICD-10 codes, scores each comorbidity category, and then combines all scores to calculate a single comorbidity score.[11] A score of zero indicates that no comorbidities were found, and higher scores indicate higher comorbidity burdens.[11]

### 2.4 | Depression outcome

Our primary study outcome was incident depression, defined as first occurrence of either a first primary or secondary hospital diagnosis of depression (ICD-10 codes DF32 and DF33) and/or a new prescription for any antidepressant drug (ATC code N06A) among GBS patients and general population members after the index date.

### 2.5 | Statistical analyses

All analyses were performed using STATA version 16 (StataCorp, College Station, Texas, USA). The baseline characteristics of GBS patients and the general population members were described in contingency tables. Availability of drug prescription data since 2004 and in- and outpatient hospital contact data since 1995 ensured at least a 1-year lookback for no prevalent antidepressant treatment, and at least 10 years for no recent depression diagnosis, among study participants from 2005 to 2016. We used the Nelson-Aalen method (1 − the

**TABLE 1** Characteristics of GBS patients and matched general population members

| | GBS cohort (N = 853), n (%) | Comparison cohort (N = 8639), n (%) |
|---|---|---|
| Sex | | |
| Female | 319 (37.4%) | 3352 (38.8%) |
| Male | 534 (62.6%) | 5287 (61.2%) |
| Index year | | |
| 2005-2008 | 269 (31.5%) | 2642 (30.6%) |
| 2009-2012 | 331 (38.8%) | 3359 (38.9%) |
| 2013-2016 | 253 (29.7%) | 2638 (30.5%) |
| Age groups (years) | | |
| 0-9 | 50 (5.9%) | 494 (5.7%) |
| 10-19 | 57 (6.7%) | 553 (6.4%) |
| 20-29 | 55 (6.4%) | 548 (6.3%) |
| 30-39 | 111 (13.0%) | 1183 (13.7%) |
| 40-49 | 90 (10.6%) | 942 (10.9%) |
| 50-59 | 140 (16.4%) | 1400 (16.2%) |
| 60-69 | 180 (21.1%) | 1878 (21.7%) |
| 70-79 | 117 (13.7%) | 1191 (13.8%) |
| 80-100 | 53 (6.2%) | 450 (5.2%) |
| CCI score accumulated 10 years before index date | | |
| 0 | 1087 (74.8%) | 7122 (82.4%) |
| 1 | 180 (12.4%) | 791 (9.2%) |
| 2 | 115 (7.9%) | 457 (5.3%) |
| ≥3 | 71 (4.9%) | 269 (3.1%) |
| Individual disease in CCI | | |
| Myocardial infarction | 25 (2.9%) | 148 (1.7%) |
| Congestive heart failure | 17 (2.0%) | 133 (1.5%) |
| Peripheral vascular disease | 17 (2.0%) | 139 (1.6%) |
| Cerebrovascular disease | 36 (4.2%) | 241 (2.8%) |
| Dementia | 0 (0.0%) | 17 (0.2%) |
| Chronic pulmonary disease | 43 (5.0%) | 340 (3.9%) |
| Connective tissue disease | 18 (2.1%) | 126 (1.5%) |
| Ulcer disease | 15 (1.8%) | 88 (1.0%) |
| Mild liver disease | 9 (1.1%) | 43 (0.5%) |
| Diabetes type 1 and 2 | 37 (4.3%) | 247 (2.9%) |
| Hemiplegia | 7 (0.8%) | 11 (0.1%) |
| Moderate to severe renal disease | 8 (0.9%) | 69 (0.8%) |
| Diabetes with end organ | 20 (2.3%) | 104 (1.2%) |
| Any tumor | 32 (3.8%) | 351 (4.1%) |
| Leukemia | ≤5 (0.6%) | 12 (0.1%) |
| Lymphoma | 6 (0.7%) | 29 (0.3%) |
| Moderate to severe liver disease | ≤5 (0.6%) | 12 (0.1%) |
| Metastatic solid tumor | ≤5 (0.6%) | 34 (0.4%) |
| AIDS | ≤5 (0.6%) | ≤5 (<1%) |

Abbreviations: CCI, Charlson Comorbidity Index; GBS, Guillain-Barré syndrome.

survival function) to compute cumulative incidence of depression with corresponding 95% confidence intervals (CIs). We then used Cox regression to compute age-, sex-, and index date–adjusted hazard ratios (HRs) of depression with corresponding 95% CIs, comparing depression risks between GBS patients and the general population in two periods: 0 to 2 years (short-term follow-up) and after 2 years

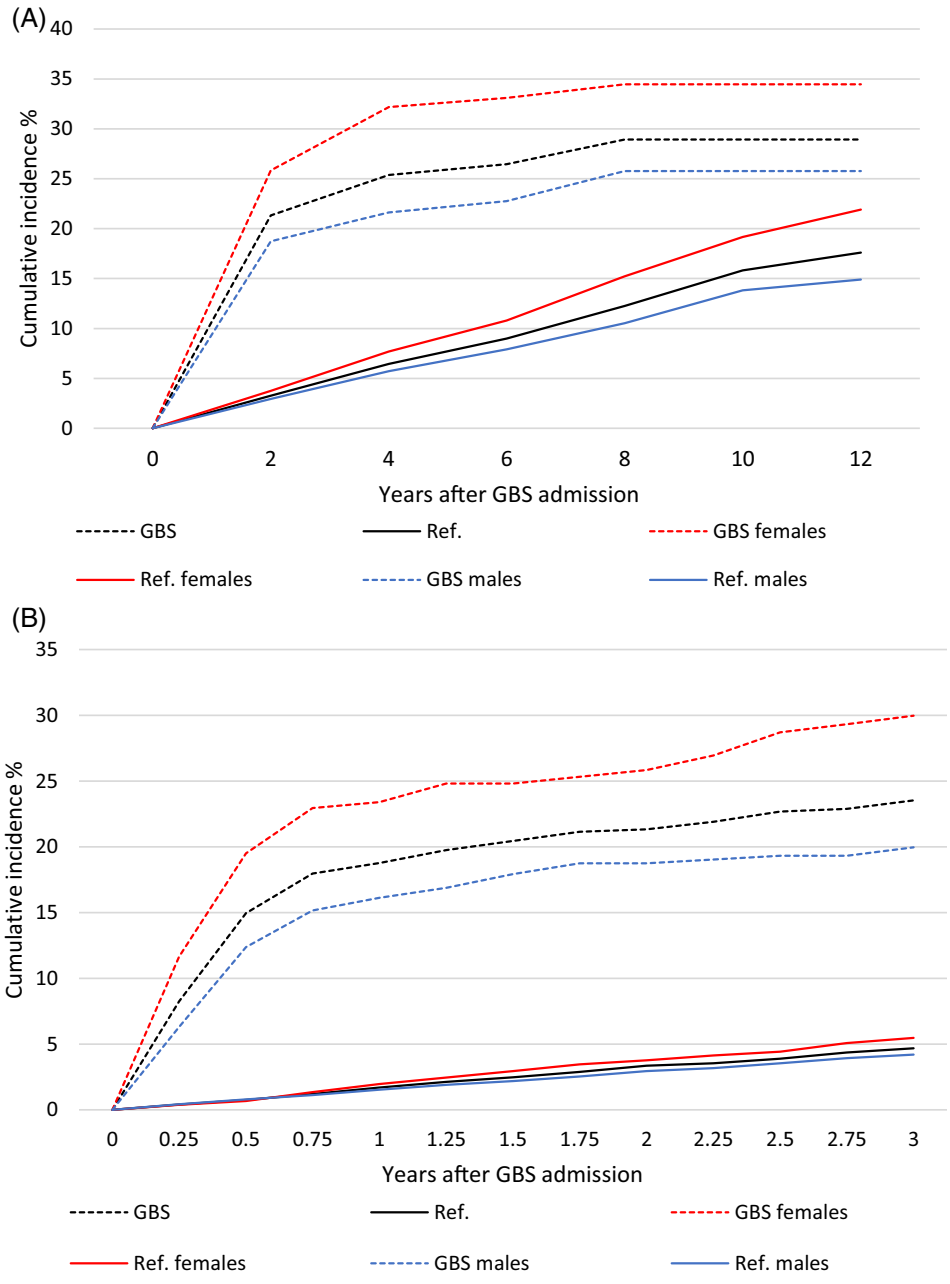


**FIGURE 1** Cumulative incidence of depression within 12 years (A) and 3 years (B) of follow-up.

(long-term follow-up). Furthermore, we computed depression HRs additionally adjusted for comorbidity (adjusted HR [aHR]). In addition, we calculated depression HRs within several shorter consecutive periods during the follow-up period. We performed stratified analyses to assess the impact of GBS on depression risk in different strata of sex, age, level of pre-existing comorbidity, and calendar periods of the index date.

Because GBS patients may be more closely followed for depression than the general population as it relates to admission and ambulant follow-up, we performed a sensitivity analysis of depression outcomes including only GBS patients and those in the general population who had at least one hospital contact during follow-up, adjusted for age, sex, index date, and comorbidity. Because GBS patients may be more prone to have antidepressants prescribed for pain compared with the general population, we performed a sensitivity analysis including hospital-diagnosed depression and only prescriptions for serotonin reuptake inhibitors (SSRIs) in the depression outcome.

## 3 | RESULTS

### 3.1 | Descriptive data

We identified 853 incident GBS patients and recruited 8639 individuals from the general population (Table 1).

In both populations, about 60% were male and median age was 54 (interquartile range [IQR], 34 to 67) years. During the full study period, GBS patients and the general population members were

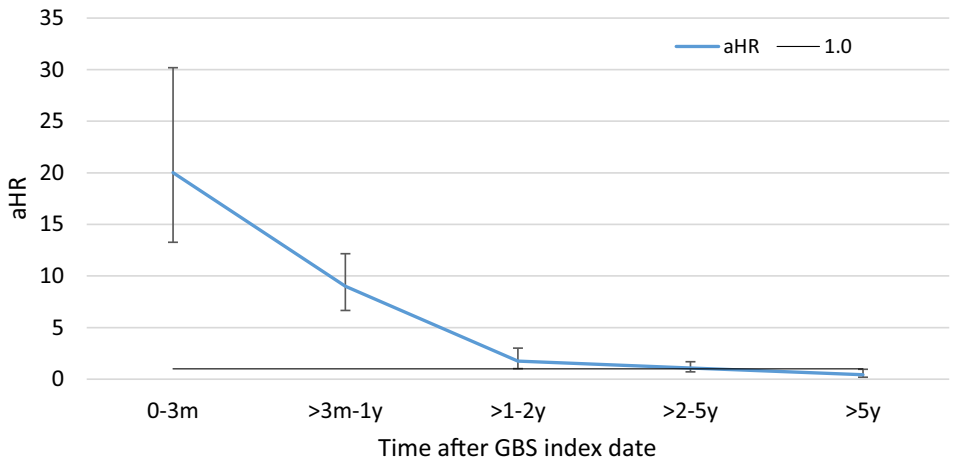


**FIGURE 2** Adjusted hazard ratios for depression after Guillain-Barré syndrome.

followed for a median of 3.4 (IQR, 0.8 to 7.1) years and 5.1 (IQR, 2.4 to 7.8) years, respectively. GBS patients had slightly more somatic comorbidities (23.2% with CCI score >0) than the general population (17.6% had CCI score >0). Similar proportions of GBS patients were diagnosed within the three calendar periods of the study period (Table 1).

During the full study period (maximum, 12 years), cumulative depression risk among GBS patients increased most steeply within the first 3 months (Figure 1A, B). Crude cumulative risk of depression after 3 months of follow-up was 8.3% (95% CI, 6.5% to 10.5%) in GBS patients and 0.4% (95% CI, 0.3% to 0.6%) in the general population members. Yet, the HRs of depression were increased for up to 2 years after GBS (Figure 2). Short-term depression, diagnosed within 2 years after GBS was 21.3% (95% CI, 18.2% to 25.0%) in GBS patients compared with 3.3% (95% CI, 2.9% to 3.7%) for the general population members, corresponding to a highly increased 2-year HR of 7.6 (95% CI, 6.2 to 9.3). Long-term depression, diagnosed more than 2 years after GBS diagnosis (maximum follow-up: 12 years) showed similar rates for GBS patients and the general population members (Figure 1), with an HR close to 1, that is, 0.8 (95% CI, 0.6 to 1.2). Short- and long-term depression HRs were largely unchanged (aHR, 7.5; 95% CI, 6.1 to 9.2; and aHR, 0.8; 95% CI, 0.6 to 1.2, respectively) after adjustment for comorbidities.

Stratified results of short- and long-term depression HR analyses showed similar relative depression risks among sex, age, comorbidity, and calendar time strata (Table 2), but the data were subjected to limited statistical precision (wide 95% CI). The strongest associations of GBS with relative risk of depression was observed in female GBS patients, GBS patients aged 60 years and over, and in the most recent calendar periods within 2 years of follow-up after GBS. However, due to short follow-up time (<2 years) for individuals with an index date in 2015 and 2016, fewer GBS patients and general population members were registered with depression in the most recent calendar period compared with the previous calendar periods.

SSRIs and tricyclic antidepressants (TCAs) were used more frequently by GBS patients (Table 3). Use of other types of prescribed antidepressants was similar for GBS patients and the general population (Table 3). Most GBS patients diagnosed with depression continued to receive antidepressant therapy until the end of 2016 (n = 85 of 182) or death (n = 38 of 182). For the 59 GBS patients who stopped pharmacological treatment before the end of follow-up, 31 redeemed only one antidepressant prescription and the median duration of antidepressant therapy for the remaining 28 GBS patients was 169 days (range, 27.3 days to 3.1 years).

### 3.2 | Sensitivity analyses

After including only general population members with a minimum of one hospital admission after the index date, the comparison cohort was reduced to 7079 individuals. This restriction resulted in similar aHRs compared with the primary analyses, with a depression aHR of 7.9 (95% CI, 3.3 to 18.9) and a long-term aHR of 0.3 (95% CI, 0.4 to 2.1). Upon assessing hospital-diagnosed depression and only prescriptions for SSRI as depression outcome, the short-term depression aHR was 3.7 (95% CI, 2.7 to 5.0) and long-term depression aHR was 0.7 (95% CI, 0.4 to 1.1).

## 4 | DISCUSSION

Compared with the general population, GBS patients had a 7.6-fold increased hazard of depression within the 2 years after GBS. The risk of depression was highest within the first 3 months after GBS hospital admission. After 2 years, the risk of depression after GBS was similar to that seen in members of the general population.

Although GBS has a favorable outcome in most patients, at nadir more than one third of GBS patients are chair-bound or bedridden, and at discharge this applies to one fourth of patients.[12] The primary recovery of function occurred during the first 6 months after GBS symptom onset, according to prospective studies of Swedish patients (n = 42).[13,14] Yet, residual moderate to severe disability and lower frequency of social and lifestyle activities were observed in about 25% of patients at 2 years after onset as compared with levels before

**TABLE 2** Adjusted hazard ratios of depression in incident GBS patients compared with individuals from the general population

| 2005-2016 GBS patients (N = 853) and general population members (N = 8639) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 0-2 years | | | | >2 years | | | |
| | GBS, n with depression | General population, n with depression | HR[a] (95% CI) | CCI-adjusted HR (95% CI) | GBS, n with depression | General population, n with depression | HR[a] (95% CI) | CCI-adjusted HR (95% CI) |
| Total | 154 | 253 | 7,64 (6.25-9.34) | 7.52 (6.14-9.19) | 28 | 466 | 0.84 (0.57-1.23) | 0.82 (0.56-1.20) |
| Females | 68 | 112 | 8.35 (6.17-11.30) | 8.36 (6.17-11.31) | 12 | 214 | 0.82 (0.46-1.47) | 0.80 (0.45-1.43) |
| Males | 86 | 141 | 7.12 (5.45-9.32) | 6.90 (5.27-9.03) | 16 | 252 | 0.85 (0.51-1.41) | 0.83 (0.50-1.38) |
| Age groups | | | | | | | | |
| <60 years | 71 | 124 | 6.57 (4.90-8.79) | 6.40 (4.77-8.59) | 17 | 138 | 0.88 (0.54-1.45) | 0.87 (0.53-1.42) |
| ≥60 years | 83 | 129 | 8.85 (6.71-11.67) | 8.73 (6.61-11.52) | 11 | 228 | 0.80 (0.44-1.46) | 0.79 (0.43-1.44) |
| Comorbidity | | | | | | | | |
| CCI = 0 | 112 | 175 | 8.51 (6.71-10.80) | – | 17 | 348 | 0.69 (0.42-1.12) | – |
| CCI > 0 | 42 | 78 | 5.38 (3.69-7.86) | – | 11 | 118 | 1.15 (0.62-2.14) | – |
| Index year | | | | | | | | |
| 2005-2008 | 72 | 136 | 6.84 (5.13-9.11) | 6.67 (5.00-8.90) | 18 | 369 | 0.68 (0.43-1.10) | 0.67 (0.42-1.08) |
| 2009-2012 | 60 | 93 | 7.97 (5.76-11.04) | 7.88 (5.69-10.93)) | 10 | 97 | 1.41 (0.73-2.70) | 1.35 (0.71-2.60) 19-1.45) |
| 2013-2016 | 22 | 24 | 10.67 (5.98-19.04) | 10.65 (5.97-19.01) | ≤5 | ≤5 | – | – |

Abbreviations: CCI, Charlson Comorbidity Index; CI, confidence interval; GBS, Guillain-Barré syndrome; HR, hazard ratio.
[a]Age-, sex-, and index-adjusted.

**TABLE 3** Antidepressants prescribed to GBS patients and the general population with depression from 2005 to 2016

| Type of antidepressants | GBS patients | General population | *P* value |
|---|---|---|---|
| Total population from 2005 to 2016, N | 853 | 8639 | – |
| Follow-up time, years (IQR) | 3.4 years (0.8-7.1) | 5.1 years (2.4-7.8) | – |
| Antidepressant-treated depression, n | 182 | 715 | – |
| SSRI (citalopram, escitalopram, fluoxetine, paroxetine, sertraline) | 72 (8.4%) | 457 (5.3%) | <.05 |
| SNRI (duloxetine, venlafaxine) | 13 (1.5%) | 89 (1.0%) | .182 |
| NaSSA (mianserine, mirtazapine) | 32 (3.8%) | 249 (2.9%) | .153 |
| TCA (amitriptyline, clomipramine, doxepin, imipramine, nortriptyline, trimipramine) | 113 (13.2%) | 157 (1.8%) | <.05 |
| Other antidepressive (agomelatine, reboxetine) | 0 (0.0%) | ≤10 (<0.1%) | .086 |

*Note*: Number of GBS patients and general population members treated with individual antidepressants does not add up to the total number of individuals with depression because some were treated with more than one type of antidepressant.
Abbreviations: GBS, Guillain-Barré syndrome; IQR, interquartile range; NaSSA, noradrenergic and specific serotonergic antidepressant; SNRI, selective serotonin norepinephrine reuptake inhibitor; SSRI, serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

GBS.[13,14] Psychological distress and depression were not examined in those analyses.[14] Another prospective Swedish follow-up study covering 10 years after GBS onset confirmed that the residual disability still observed at 1 to 2 years after onset may be lifelong.[15] Another study reported that, although 90% of GBS survivors had complete functional recovery, 5 years later 27% had to make substantial changes in their job, hobbies, or social activities.[16] Further, a reduction in leisure and social activities was observed in 44% of GBS survivors (n = 116).[16] Sixty-two percent reported an ongoing detrimental impact upon their life and career 3 to 6 years later.[17]

We believe that, during postacute stages of GBS, depressive disorders may contribute considerably to reduced quality of life. Despite limitations in the existing literature regarding duration of psychological distress after GBS,[5] depression has been described more frequently in patients with preceding GBS, even years after the acute episode, compared with general population members.[3,5,18,19] In a prospective study of 49 GBS patients admitted to the intensive care unit, the proportions with in-hospital anxiety and depression were 82% and 67%, respectively.[4] These are the highest reported risks of depression after GBS in the existing literature,[5,19] but inherently included the most severely affected patients. In interviews after their hospital stay, patients defined loss of communication as the most stressful problem. Ninety percent reported regular visits from relatives as very helpful for coping with the psychological distress induced by their disease.[4] Subacute depression risk was assessed in a prospective study of 20 GBS patients and a matched (age, sex, body mass index) control group.[20] One month after GBS, higher depression scores were found in GBS patients compared with controls (2.6-fold increase).

The long-term risk of depression in GBS survivors has been sparsely studied.[3] In a prospective Australian study including 76 GBS patients, more GBS participants reported moderate to severe levels of depression (18%) after a median of 6 (IQR, 2.9 to 10.0) years, compared with the normative Australian population (13%).[3] These findings are comparable with our results for incident depression as assessed by new antidepressant use among GBS patients (21%), yet were lower for our comparisons (8%). In a recent population-based nationwide study of 4548 GBS patients from 2000 to 2013 in Taiwan, the risk of depressive disorders was also increased after GBS, with an HR of 4.84 (95% CI, 3.81 to 6.16) when compared with a sex- and age-matched control group.[21] Absolute depression risks were 2.6% among the GBS patients and 1.4% in the control group. Analyses within different follow-up periods were not presented, but these results are similar to and consistent with findings from our short-term depression analyses.

The exact mechanisms of the increased risk of depression in patients with GBS remain unclear. Traumatic stress from a life-threatening illness may contribute to the increased short-term depression risk.[2–4] In addition, in some patients, depressive symptoms may develop due to loss of vital functions, such as the ability to move, eat, drink, and communicate. Yet, depression also may occur during the recovery phase, often in combination with pain, anxiety, and fatigue,[22,23] resulting in continued lowered quality of life after the acute phase of GBS.[22] This has major clinical implications for long-term rehabilitation, monitoring, education, support, and counseling of GBS patients and their families.

### 4.1 | Limitations

Our study could not clarify whether the strong association between GBS and subsequent depression is mainly related to the experience of a recent life-threatening illness or whether it is related to the combination of a recent life-threatening illness and GBS-specific neuropsychological/neuropsychiatric effects. Our study has several other limitations that warrant consideration. First, similar to previous studies of GBS using the DNPR,[7,9,24] some clinical detailed data were not recorded. Thus, we were unable to evaluate the neurological severity, weakness severity, availability of rehabilitation, and additional examination findings (e.g., electrophysiological testing). Second, hospital discharge diagnoses for comorbidities may vary in quality; however, the overall positive predictive value for the 19 CCI conditions is 98.0%

(95% CI, 96.9 to 98.8).[25] Third, we assessed depression discharge diagnoses recorded at somatic admissions only, and not those from psychiatric departments. However, depression diagnosed at psychiatric departments would usually be accompanied by previous or subsequent antidepressant prescription as well, which we captured. Fourth, the exact indication for antidepressant use may be unclear (e.g., neuropathic pain vs. depression and insomnia).[26,27] TCAs and selective serotonin norepinephrine reuptake inhibitors are frequently used for treating neuropathic pain, and noradrenergic and specific serotonergic antidepressants (NaSSAs) are prescribed for insomnia, which are frequent comorbidities seen in GBS patients.[26,28] Consequently, our additional analyses of depression evaluated through either diagnoses or prescriptions may be biased toward a falsely strong association of GBS with depression. On the other hand, even when only hospital-diagnosed depression and SSRI were included in the depression outcome, a fourfold increased hazard of depression within 2 years after GBS was found. In addition, sensitivity analyses of only hospital-diagnosed depression supported the primary results. Finally, surveillance bias may have affected our results, as patients with GBS were usually followed in outpatient clinics after the initial admission. This may lead to more referrals and diagnoses compared with the general population. However, our sensitivity analysis, excluding population controls without any hospital admission after the index date, identified similar HRs when compared with the primary analyses.

Overall, we adjusted for possible confounding factors, but we cannot rule out any residual confounding from unmeasured factors, such as baseline genetic, psychosocial, and environmental factors associated with both GBS and depression. Moreover, the homogeneity of the Danish population, with more than 90% being Caucasian, the high life expectancy and socioeconomic status, and the Danish universal tax-financed health-care system, may limit the external validity of our findings in other populations.

In conclusion, during the first 2 years after GBS hospital admission, patients with GBS had a 7.6-fold increased hazard of depression compared with individuals in the general population, with the highest increase observed during the first 3 months after GBS. Two years after GBS, the risk of depression was similar to that of the background population. These findings have major clinical implications for GBS patients and their families. Detection and management of depressive symptoms during the acute phase of GBS may help to mitigate the contribution of this factor during long-term follow-up. Further research is required to understand the relationship between physical and depressive symptoms in GBS as well as the prognostic value and treatment of depression after GBS.

## AUTHOR CONTRIBUTIONS

**Lotte Levison:** Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; resources; software; validation; visualization; writing – original draft. **Reimar Wernich Thomsen:** Conceptualization; data curation; methodology; supervision; writing – review and editing. **Henning Andersen:** Conceptualization; funding acquisition; methodology; resources; supervision; writing – review and editing.

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## CONFLICT OF INTEREST STATEMENT

None of the authors has any conflict of interest to disclose.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the Danish Health Data Authority.[29] Restrictions apply to the availability of these data, which were used under license for this study. Data are available only with the permission of the Danish Health Data Authority.

## ETHICAL PUBLICATION STATEMENT

The study received approval from the Danish Data Protection Agency (File No. 1-16-02-817-17). Further approval from an ethical committee is not required to conduct purely registry-based studies in Denmark.[30]

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