

Validating ICD-10 Diagnosis Codes for Guillain-Barré Syndrome in Taiwan's National Health Insurance Claims Database

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Purpose: To validate the International Classification of Diseases, 10th Revision (ICD-10) codes for Guillain-Barré syndrome (GBS) in Taiwan's insurance claims database.

Methods: We identified adult patients hospitalized at any Chang Gung Memorial Foundation branch hospital between January 1st, 2017, and December 31st, 2022, with ICD-10 code G61.0 in any of the five discharge diagnosis positions, indicating possible Guillain-Barré syndrome. We then validated the possible GBS diagnosis using data from electronic medical records of the identified patients, based on the diagnostic criteria established by the National Institute of Neurological Disorders and Stroke. We determined the positive predictive values (PPV) of various operational definitions, including the position (primary or other) where the code was recorded in the discharge diagnosis, nerve conduction study (NCS) claims, and / or specific GBS treatments.

Results: The final validation cohort of 484 patients with ICD-10 code for GBS in the discharge diagnosis was found to include 368 true GBS patients. Identifying inpatients using only the ICD-10 code for GBS in any of the five positions for discharge diagnosis yielded a PPV of 76.0%. With more restrictive definitions (primary diagnosis only, or requiring additional claims for NCS and/or treatments), the PPV tended to increase, but with fewer true GBS patients identified. Using ICD-10 GBS code in the primary diagnosis plus NCS and treatment claims yielded the highest PPV (98.3%); however, 140 (38.0%) of the true GBS patients were missed using this definition. In contrast, using the ICD-10 GBS code in any position, plus claims for NCS, achieved a relatively good PPV (85.8%) with minimal loss of true GBS patients (13, ie, 3.5%).

Conclusion: In Taiwan's NHI claims data, identifying true GBS patients using only the ICD-10 code yielded a PPV of 76.0%; however, adding claims for diagnostic procedure and GBS treatment increased the PPV to 98.3%.

Keywords: validation, positive predictive value, diagnostic codes, ICD-10, Guillain-Barré syndrome

Introduction

Guillain-Barré syndrome (GBS) is a rare, immune-mediated illness causing inflammation of peripheral nerves and nerve roots with a diverse range of clinical manifestations.¹ Its classical clinical presentations include acute progressive muscle weakness starting from the bilateral lower limbs and spreading upwards, as well as absent deep tendon reflexes, cranial nerve palsies, or even respiratory failure leading to death.¹⁻³ Miller Fisher syndrome (MFS) is a well-known variant syndrome of GBS that typically presents as ophthalmoplegia, ataxia and areflexia.^{1,4} Overall, GBS is the leading cause of acute flaccid paralysis worldwide, with an estimated global incidence of 1 to 2 per 100,000 person-years.^{1,5-7} Though the

specific cause of GBS is still uncertain, evidence suggests that a process potentially triggered by molecular mimicry of an antecedent infection or vaccine exposure is responsible for the development of autoimmune antibodies and the activation of inflammatory cells targeting peripheral nerves and nerve roots.^{1,2}

Given the rare but potentially fatal nature of GBS, and its potential association with vaccination, active nationwide surveillance programs for vaccine safety usually need to include GBS when monitoring the incidence rates of severe adverse events as compared to the background rate.^{8–13} Administrative claims databases, such as Taiwan's National Health Insurance Research Database (NHIRD), contain comprehensive population-level health outcomes^{14,15} and are therefore suitable as resources for both timely disease surveillance⁶ and outcome studies of GBS.^{16,17} In a claims database, GBS is usually identified with diagnosis codes; however, because these diagnosis codes are primarily used by healthcare providers for insurance reimbursement, their validity and hence suitability for research purposes are not guaranteed. In prior validation studies focusing on nationwide claims databases, the positive predictive value (PPV) of diagnosis codes for GBS ranged from 45.3% in the United States,¹⁸ 75.0% in Korea,⁵ and 83.8% in Denmark,⁷ to 92.5% in Canada,¹⁹ while the PPV for Taiwan's NHIRD has not yet been determined.

We therefore conducted the present study to validate the International Classification of Diseases, 10th Revision (ICD-10) codes for GBS in Taiwan's National Health Insurance (NHI) claims database, by using electronic medical records to verify the diagnoses.

Materials and Methods

Study Setting and Ethics

The Chang Gung Medical Foundation (CGMF), founded in 1976, is the largest healthcare group in Taiwan. Our study setting encompassed all eight CGMF branch hospitals (Keelung, Linkou, Taipei, Taoyuan, Kaohsiung, Chiayi, Yunlin and Fengshan), located across the northeastern, northwestern, central, and southern regions of Taiwan. All CGMF branch hospitals have contracted with Taiwan's NHI, and their accreditation levels include academic medical centers, regional teaching hospitals, and district community hospitals. The CGMF branch hospitals have a total of more than 10,000 beds and serve 280,000 hospitalized patients annually, covering around 12% of the entire Taiwanese population.^{20–22} Therefore, our study setting may be considered sufficiently representative of all hospitals in Taiwan's NHIRD. The same setting has previously been used to validate ICD-10 codes for several other critical conditions or diseases.^{23–27}

The protocol used in the current study adhered to the principles outlined in the Declaration of Helsinki and has been approved by the Institutional Review Board of the CGMF (IRB NO: 202200229B0). Because of its retrospective design, informed consent was not required.

Data Sources

Both the NHI claims data and electronic medical records data from the CGMF hospitals were utilized in this study. To protect patient confidentiality, the study data were stored in a secure system with restricted access granted only to authorized personnel. The hospitalization claims data reported to Taiwan's NHI Administration was extracted from the hospital information system. Consistent with the inpatient dataset of the NHIRD, a patient can have up to five discharge diagnoses documented for each hospitalization episode.¹⁴ We identified adult patients who were hospitalized at any of the CGMF branch hospitals between January 1st, 2017, and December 31st, 2022, and who were subsequently discharged with an ICD-10 code of G61.0 in any of the five positions for recording discharge diagnosis, indicating possible Guillain-Barré syndrome. The hospital admission date was defined as the index date. We excluded patients whose medical records were unavailable or whose diagnostic work-up was incomplete due to premature discharge. For patients with multiple hospitalization records including a GBS discharge diagnosis during the study period, only the initial hospital stay was included in the analysis.

Ascertainment of Guillain-Barré Syndrome

Information from the electronic medical records was utilized to validate the identified patients' suspected GBS. In the first step, a manual review of all medical records was conducted by one specialist physician (SCL) to determine whether the patients

could be confirmed as true GBS patients. After the initial review, inconclusive cases were reviewed again in conjunction with a senior neurologist (CYH) for final case ascertainment. Patients were classified as either GBS or non-GBS based on the diagnostic criteria established by the NINDS (National Institute of Neurological Disorders and Stroke), using a combination of clinical features, cerebrospinal fluid (CSF) findings, and nerve conduction studies (NCS) to make the judgment²⁸ ([Supplementary Table 1](#)). The MFS was also included. Subsequently, we classified all GBS patients based on the Brighton criteria.²⁹ We applied the Brighton criteria (www.brightoncollaboration.org) in order to increase the level of diagnostic certainty (graded 1–4) ([Supplementary Table 1](#)) and to ensure comparability with prior GBS studies.^{3,4,7,13,30,31}

Variables

We collected demographic and general clinical variables from the medical records. Seasonality was defined by the month of hospitalization as spring (March, April, May), summer (June, July, August), fall (September, October, November), and winter (December, January, February). We used the GBS disability score to assess the level of disability at admission from 0 (normal), 1 (minor symptoms and capable of running), 2 (able to walk 10 m or more without assistance but unable to run), 3 (able to walk 10 m across an open space with help), 4 (bedridden or chair bound), 5 (requiring assisted ventilation for at least part of the day), to 6 (death),³² and manually reviewed the results of NCS to group the patients into subtypes as per the criteria defined by Hadden et al.³³ We also extracted data on CSF cell count and protein concentration, whereby we considered CSF protein concentration >45 mg/dL as elevated. We documented the specific treatment for GBS, such as plasma exchange, intravenous immunoglobulin, or intravenous immunoglobulin plus methylprednisolone. We also used the medical records to assess outcomes including ability to walk independently and all-cause death at 6 months from the index date. Patients were considered non-GBS if they were diagnosed with acute-onset chronic inflammatory demyelinating polyneuropathy or other diseases during this 6-month follow-up period.

Statistical Analyses

We presented descriptive statistics using either mean with standard deviation (SD) or number (N) with percentage (%), as appropriate. The PPV was calculated as the number of true GBS patients divided by the total number of patients suspected to have GBS based on the ICD-10 code, and the 95% confidence interval (CI) for the PPV was estimated using the Clopper-Pearson exact method.³⁴ We determined the PPV of various operational definitions, including whether the diagnosis was recorded in the primary or other position of the discharge diagnosis, as well as claims for NCS and / or specific treatments for GBS. We further compared the position of the ICD-10 GBS code in the discharge diagnoses and the Brighton levels of diagnostic certainty. The data was analyzed using SAS 9.4 for Windows (SAS Institute, Inc., Cary, NC, USA).

Results

From the electronic claims data, we identified 491 inpatients in CGMF hospitals who were discharged with ICD-10 code of G61.0 for GBS in their discharge diagnoses between January 1st, 2017, and December 31st, 2022. Of these, we excluded three patients whose medical records were not readily available, two patients with duplicate records from different CGMF branch hospitals, and two patients prematurely discharged against medical advice ([Figure 1](#)). In the final validation cohort of 484 patients, a total of 368 patients were confirmed as true GBS patients. Of these true GBS patients, 43.8% met the Brighton criteria level 1, while 27.7%, 15.2% and 13.3% were classified as levels 2, 3 and 4, respectively. MFS accounted for 53 (14.4%) of the true GBS patients. Of the 116 non-GBS patients, the top four diagnoses [N (%)] were “polyneuropathy, other causes” [35 (30.2)], “autoimmune neurological disorders, other causes” [15 (12.9)], “radiculopathy, other causes” [12 (10.3)], and “psychiatric disorders” [10 (8.6)]. For further details, please see [Supplementary Table 2](#).

The demographics and general clinical characteristics of the 368 true GBS patients are presented in [Table 1](#). The mean (SD) age was 47.1 (19.4) years old, and 162 (44.0%) of the true GBS patients were female. Their disease onset appeared to show seasonality and was most common in spring (29.3%), followed by winter (27.4%). At entry, 40.5% were unable to walk independently (ie, a Guillain-Barré syndrome disability score ≥ 3), and 41.8% had cranial nerve involvement. At disease nadir, 14.9% used a ventilator. Of these true GBS patients, 51.3% had an NCS finding classified as demyelinating, while 19.8% exhibited an abnormal NCS finding consistent with peripheral nerve (root) involvement, but did not meet the criteria for any of the defined subtypes (demyelinating, axonal, or unexcitable). The CSF cell count

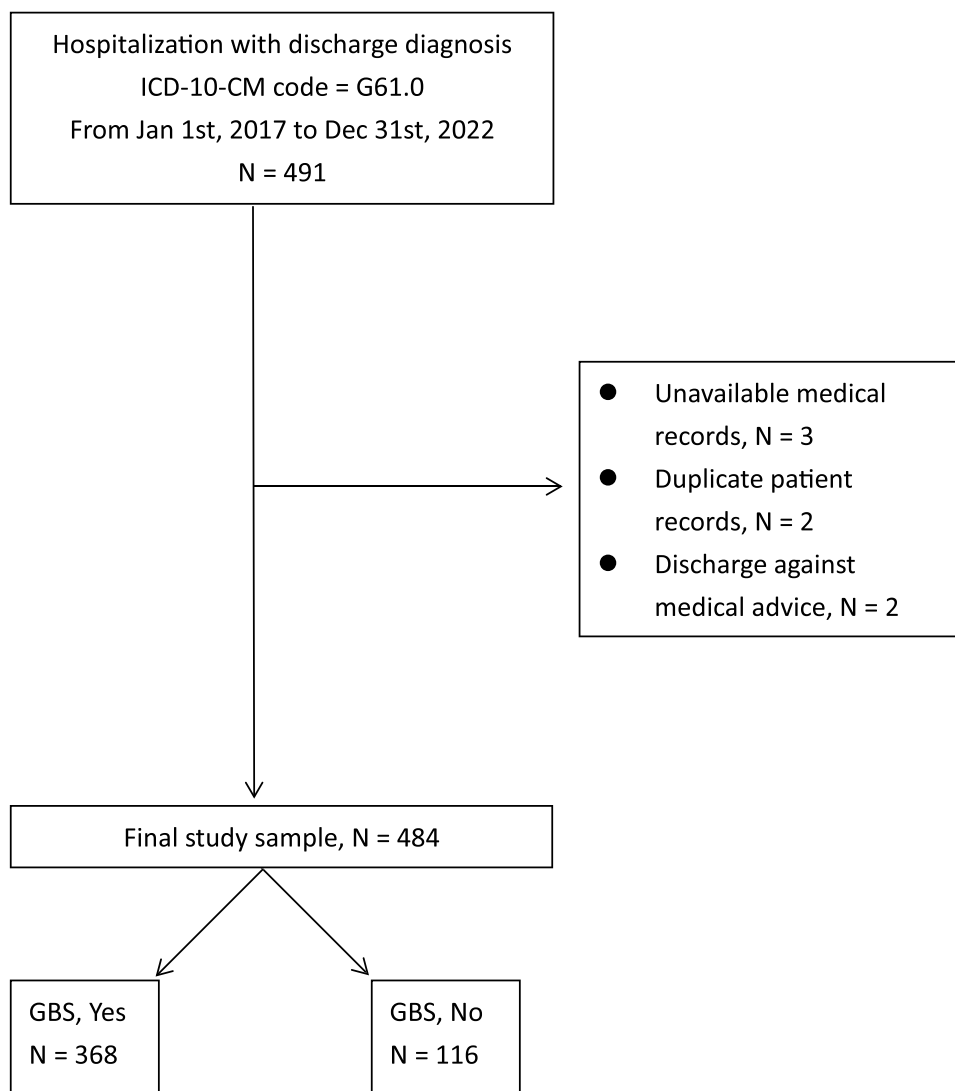


Figure 1 Study flowchart to identify true Guillain-Barré syndrome (GBS) patients from the claims database validated with electronic medical records.

was $<5/\mu\text{L}$ and CSF protein concentration was higher than 45 mg/dL in 248 (67.4%) and 229 (62.2%) of these patients, respectively. More than half (53.8%) of them received plasma exchange, while about a quarter (25.3%) received intravenous immunoglobulin during hospitalization. At the 6-month follow-up, about two-thirds of the patients could walk without assistance, but 2.2% died.

Table 2 shows the PPV of various operational definitions for GBS, based on the data in the claims database. Using only an inpatient claim with the ICD-10 code for GBS in any of the five positions of the discharge diagnosis produced a PPV of 76.0% (definition #1). As the definitions became more restrictive (primary position diagnosis only, or adding claims for NCS and/or treatments), the PPV tended to improve, but at the expense of a lower number of the true GBS patients identified. For example, the definition using the ICD-10 code for GBS in the primary position plus claims for NCS and treatment (definition #16) resulted in the highest PPV (98.3%). However, under such a restrictive definition, 140 (38.0%) of the true GBS patients were not identified. By contrast, a definition using the ICD-10 code for GBS in any position of the discharge diagnosis plus claims for NCS (definition #5) achieved a relatively high PPV (85.8%) with a minimal loss of true GBS patients (3.5%).

As shown in Table 3, among the true GBS patients, more than 90% of the Brighton level 1 GBS patients (highest level of certainty) were discharged with the ICD-10 GBS code in the primary position. As the level of diagnostic

Table 1 Baseline Characteristics, Treatments, and Outcomes of Patients with Confirmed Guillain-Barré Syndrome (N = 368)

Age, years, mean (SD)	47.1 (19.4)
Sex, female, N (%)	162 (44.0)
Miller Fisher variant syndrome, N (%)	53 (14.4)
Seasonality	
Spring, N (%)	108 (29.3)
Summer, N (%)	76 (20.7)
Fall, N (%)	83 (22.6)
Winter, N (%)	101 (27.4)
Neurological symptoms at admission	
GBS disability score (0–6)	
0, N (%)	0 (0.0)
1, N (%)	129 (35.1)
2, N (%)	90 (24.5)
3, N (%)	61 (16.6)
4, N (%)	79 (21.5)
5, N (%)	9 (2.4)
6, N (%)	0 (0.0)
Cranial nerve involvement, N (%)	154 (41.8)
Sensory deficits, N (%)	297 (80.7)
Pain, N (%)	42 (11.4)
Neurological symptoms at nadir	
Cranial nerve involvement, N (%)	171 (46.5)
Ventilator dependent, N (%)	55 (14.9)
Nerve conduction study	
Normal, N (%)	51 (13.9)
Demyelinating, N (%)	189 (51.3)
Axonal, N (%)	41 (11.1)
Unexcitable, N (%)	1 (0.3)
Equivocal, N (%)	73 (19.8)
Not available, N (%)	13 (3.6)
CSF cell count	
< 5/ μ L, N (%)	248 (67.4)
5–10/ μ L, N (%)	6 (1.6)
10–30/ μ L, N (%)	9 (2.5)

(Continued)

Table 1 (Continued).

30–50/ μ L, N (%)	13 (3.5)
>50/ μ L, N (%)	38 (10.3)
Not available, N (%)	54 (14.7)
CSF protein concentration > 45 mg/dL, N (%)	229 (62.2)
Specific treatment for GBS*	
Plasma exchange, N (%)	198 (53.8)
IVIG, N (%)	93 (25.3)
IVIG and Methylprednisolone, N (%)	22 (6.0)
None	76 (20.6)
Outcomes at 6 months	
Walking without assistance, N (%)	249 (67.7)
Death, N (%)	8 (2.2)

Note: *A patient may receive > 1 specific treatment for GBS.

Abbreviations: SD, standard deviation; N, number; %, percentage; GBS, Guillain-Barré syndrome; spring, March, April, May; summer, June, July, August; fall, September, October, November; winter, December, January, February; CSF, cerebrospinal fluid; IVIG, intravenous immunoglobulin.

Table 2 Positive Predictive Value of Various Operational Definitions of Guillain-Barré Syndrome in the Claims Database (N = 484)

Operational Definition	PPV, %	95% CI,	% (N) of true GBS patients not identified
#1. Any of the five positions of the discharge diagnosis	76.0% (368/484)	76.3–83.6	0.0% (0)
#2. Primary, secondary, or tertiary diagnosis	79.2% (354/447)	75.1–82.9	3.8% (14)
#3. Primary or secondary diagnosis	81.2% (341/420)	77.1–84.8	7.3% (27)
#4. Primary diagnosis	85.8% (307/358)	81.7–89.2	16.6% (61)
#5. Any of the five positions of the diagnosis + NCS	85.7% (355/414)	82.0–89.0	3.5% (13)
#6. Primary, secondary, or tertiary diagnosis + NCS	88.1% (341/387)	84.5–91.2	7.3% (27)
#7. Primary or secondary diagnosis + NCS	89.2% (329/369)	85.5–92.1	10.6% (39)
#8. Primary diagnosis + NCS	91.2% (302/331)	87.7–94.1	17.9% (66)
#9. Any of the five positions of the diagnosis + Tx	96.8% (269/278)	93.9–98.5	26.9% (99)
#10. Primary or secondary or tertiary diagnosis + Tx	97.0% (261/269)	94.2–98.7	29.1% (107)
#11. Primary or secondary diagnosis + Tx	96.9% (253/261)	94.1–98.7	31.3% (115)
#12. Primary diagnosis + Tx	97.9% (230/235)	95.1–99.3	37.5% (138)
#13. Any of the five positions of the diagnosis + NCS + Tx	97.8% (263/269)	95.2–99.2	28.5% (105)
#14. Primary, secondary or tertiary diagnosis + NCS + Tx	98.1% (255/260)	95.6–99.4	30.7% (113)

(Continued)

Table 2 (Continued).

Operational Definition	PPV, %	95% CI,	% (N) of true GBS patients not identified
#15. Primary or secondary diagnosis+ NCS + Tx	98.0% (247/252)	95.4–99.4	32.9% (121)
#16. Primary diagnosis + NCS + Tx	98.3% (228/232)	95.6–99.5	38.0% (140)

Note: Tx, claims for treatment of plasma exchange, intravenous immunoglobulin, or methylprednisolone.

Abbreviations: N, number; PPV, positive predictive value; %, percentage; CI, confidence interval; GBS, Guillain-Barré syndrome; NCS, claims for nerve conduction study.

Table 3 Distributions of Guillain-Barré Syndrome Diagnosis Code Position and Brighton Levels of Diagnostic Certainty

GBS Diagnosis Code Position	Brighton Levels Of Diagnostic Certainty				
	Level 1 (n=161)	Level 2 (n=102)	Level 3 (n=56)	Level 4 (n=49)	Level 5 (n=116)
1 (n=307)	146 (90.7)	84 (82.4)	44 (78.6)	33 (67.3)	51 (44.0)
2 (n=34)	8 (5.0)	9 (8.8)	7 (12.5)	10 (20.4)	28 (24.1)
3 (n=13)	1 (0.6)	5 (4.9)	4 (7.1)	3 (6.1)	14 (12.1)
4 (n=10)	5 (3.1)	3 (2.9)	0 (0.0)	2 (4.1)	16 (13.8)
5 (n=4)	1 (0.6)	1 (1.0)	1 (1.8)	1 (2.0)	7 (6.0)

Abbreviations: GBS, Guillain-Barré syndrome; n, number; Brighton level 5, non-GBS cases.

certainty decreased (Brighton levels 2–4), the ICD-10 code was more likely to be found in the secondary, tertiary, or other positions of the discharge diagnosis.

Discussion

In this validation study using medical records from the largest healthcare group in Taiwan, we found that the presence of the ICD-10 code for GBS at any position of the discharge diagnosis carried a PPV of 76.0% (95% CI: 76.3–83.6%). The PPV increased by about 10–20% when the code position was restricted to the primary diagnosis column, or if a combination with diagnostic procedure and / or treatment specific to GBS was required. Requiring a combination of primary diagnosis position with NCS and treatment for GBS achieved a nearly perfect PPV, but at the expense of missing about two fifths of the true GBS patients.

Comparison with the Literature

In the current study, our PPV results from various permutations of the GBS definition (76.0% to 98.3%) are comparable to those found in other claims databases of different countries; as such, it is likely that the PPV in those databases also increases when additional definitions and restrictions are applied. For example, in a Korean study,⁵ the PPV was only 35% when combining outpatient and inpatient claims, but increased to 75% when restricted to inpatient claims only, and even to 85% when restricted to inpatient claims plus specific department data (eg, neurology). When such a definition (inpatient claims plus specific departments) was applied to the national claims database of Denmark, the PPV was 83.8%.⁷ In a recent validation study of the US Medicare database,¹⁸ the presence of the ICD-10 GBS code in any position and in the primary position of the discharge diagnosis yielded a PPV of 45.3% (95% CI: 34.8–55.9%) and 79.5% (95% CI: 67.6–91.5%), respectively. The PPV increased to 81.6% (95% CI: 69.3–93.9%) when claims for a diagnostic procedure within 45 days of admission were added though the 95% confidence interval was wide and overlapping because of the smaller sample size (40 true GBS patients). In a Canadian study,¹⁹ the ICD-10 code for GBS had a PPV of

92.5% when the reference standard was physician diagnosis. However, it deteriorated to 68.0% when the reference standard was changed to clinical criteria.

Notably, the mortality rate at 6 months was 2.2%, which might be lower than the 3% to 10% range found in the literature.^{1,2} However, the proportion of being able to walk independently was 67.7%, which was lower than the range of 77% to 82% reported.^{1,3} The exact cause of such a lower mortality rate, but poorer recovery of walking ability in our GBS patients is unclear. It may warrant further research.

Strengths

One of the strengths of our present study was that it used a validation sample (N = 484) from the largest and most representative healthcare group in Taiwan. The true GBS patients (368 of the 484) mostly underwent complete diagnostic studies, (NCS and lumbar puncture), and had a wide range of clinical severities, treatments, and clinical outcomes. Notably, GBS is a heterogeneous disorder, and no accurate biomarkers have been identified yet. The Brighton criteria were proposed to help establish consistent and high-quality case definitions for assessing vaccine safety internationally. The criteria define GBS certainty from level 1 (highest level of diagnostic certainty) to level 4 (reported as GBS, possibly due to insufficient data for further classification, or “physician diagnosis of GBS”). A novel finding of our study was that as the diagnostic certainty decreased, the entry position of the diagnosis code for GBS in the discharge diagnosis tended to move to lower-ranking position after the primary position (Table 3). It appears that our hospital coders, to some extent, follow the diagnostic confidence of the attending physicians, when manually coding the discharge diagnosis claims. While 49 (13.3%) of the patients in the current study were classified as Brighton level 4 due to incompleteness of required diagnostic work-ups, this number is comparable to the 6% to 22% found for level 4 GBS patients who participated in randomized clinical trials or therapeutic pilot studies involving the Brighton criteria.³ To improve the sensitivity when the goal is to identify as many true positive GBS patients as possible in a real-world setting with limited resources, it may be desirable to include the Brighton level 4 patients, as seen in prior vaccine safety outcome studies.^{13,30,31}

Implications for Future Researchers

For future researchers using Taiwan’s NHIRD or another claims database to study GBS, our study results may have the following implications. Based on the PPVs and the numbers of GBS patients identified through the 16 operational definitions, researchers can select the most appropriate one for their study purposes. For example, if the occurrence of GBS is the outcome, they may choose definition #5 (any of the five discharge diagnosis positions plus NCS), given its relatively high PPV (85.7%), as well as the high number of true GBS patients identified (355 out of 368 true GBS patients). By contrast, if the researchers intend to conduct a cohort study and GBS patients are the study subject, they may choose the stricter definitions (definitions #9 to #16) given that they yield the highest PPVs (all >95%). Finally, for studies comparing observed incidence versus background incidence (ie, vaccine safety studies), researchers may choose the strictest definition (#16) for the main analysis and the other 15 definitions for sensitivity analyses to test the robustness of their findings.

Limitations

Our study has some limitations. First, because the target population was those identified from the claims database in the first step, we could not determine the sensitivity, specificity and negative predictive value of the ICD-10 diagnosis code for GBS in our claims database. This is only achievable if the starting point of a study is to identify patients from the medical records. However, given the rarity of GBS, it would not be pragmatic to review all the medical records during the study period to identify the GBS patients without using the ICD-10 diagnosis code. Second, we did not determine the PPV resulting from a combination of diagnosis code and admission to a specific department (eg, neurology department), as was done in the prior studies.^{5,7}

Conclusion

The PPV of the ICD-10 code for GBS in Taiwan’s NHI claims data was high and comparable to that in other similar national claims databases worldwide. Our validation results based on a range of different operational definitions for GBS

in the claims data may be useful for researchers to conduct future GBS research using Taiwan's NHIRD, or other claims databases.

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Disclosure

The authors report no conflicts of interest.

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