

Risk-Factor-Stratified Positive Predictive Values of an Algorithm for Guillain-Barré Syndrome

Candace C. Fuller, PhD, MPH^{1,2}; Jenny W. Sun, PhD³; Stanley Xu, PhD, MS⁴; Abel Wu, MD⁵; Jianing Liu, MD⁵; Chunyi Hsu, MPH⁴; Jose Pio, MD, MPH⁴; Nancy M. Canul⁴; Candelaria Garcia, MPH⁴; Rossy Perez, BA⁴; Margaret B. Nolan, MD, MS⁶; Terese A. DeFor, MS⁶; Casie Horgan, MPH¹; Soowoo Back, MPH¹; Diane Emerton, MS¹; Elizabeth J. Bell, PhD, MPH¹; Katherine E. Round, MPH¹; Shannon T. Walsh, MPH, MBA¹; David V. Cole¹; Rajani Rajbhandari, MS¹; Anne Vasquez, MPH¹; Fang Zhang, PhD ^{1,2}; Jia Weng, PhD¹; Judith C. Maro, PhD^{1,2}; Richard Platt, MD, MSc ^{1,2}; Noelle M. Cocoros, DSc, MPH^{1,2}

¹Harvard Pilgrim Health Care Institute; ²Harvard Medical School; ³Pfizer, Inc.; ⁴Research and Evaluation, Kaiser Permanente Southern California; ⁵Department of Neurology, Los Angeles Medical Center, Kaiser Permanente Southern California; ⁶HealthPartners

Background

- Guillain-Barré Syndrome (GBS) is an outcome of interest in numerous vaccine safety studies, including the vaccines for Respiratory Syncytial Virus (RSV).
- The positive predictive value (PPV) of a claims-based GBS algorithm commonly used in the United States (US) has been reported as ~75% but may vary by key patient characteristics such as age and underlying conditions.
- As a part of a post-authorization safety study to monitor the incidence of GBS in ABRYSVO-vaccinated adults 18-59 years of age at increased risk of RSV-associated Lower Respiratory Tract Disease (LRTD), we validated an ICD-10-CM code-based algorithm for GBS.

Objective

- To estimate the PPV of an ICD-10-CM code-based GBS algorithm in subgroups relevant to vaccine safety studies.

Methods

Population

- Potential GBS was identified among patients aged ≥18 years in 2017 through 2024 using electronic health record and claims data from two US integrated delivery systems.
- Patients were required to have ≥365 days of medical and pharmacy coverage prior to GBS diagnosis.

Claims-based algorithm

- Potential GBS** was defined with an ICD-10-CM code-based algorithm, comprising of an inpatient ICD-10-CM code G61.0 in the principal position.
- Index date** was the hospital admission date, unless an outpatient visit with G61.0 occurred in the preceding 7 days, in which case the earlier date was used.
- Incidence** was defined as no GBS diagnosis code (G61.0; G65.0; GBS sequelae) in the 365 days prior to index (any position, any setting).

Medical Record Review

- The study aimed to review approximately 300 cases. One site reviewed all identified cases, whereas the other reviewed a random sample of identified cases.
- Cases were adjudicated at each site based on Brighton Collaboration criteria:
 - Confirmed cases:** Cases classified as Brighton Levels 1-3.
 - Insufficient evidence:** Cases classified as Brighton Level 4.
 - Not a case:** Cases classified as Brighton Level 5; this category also included cases without mention of Miller-Fisher Syndrome or GBS noted in the medical record, and cases with an alternative diagnosis for weakness identified in the medical record.
- Based on information in the medical records, clinicians identified potential causes of GBS (e.g., infection, vaccination, surgery, medication) among confirmed cases (Brighton Levels 1-3).

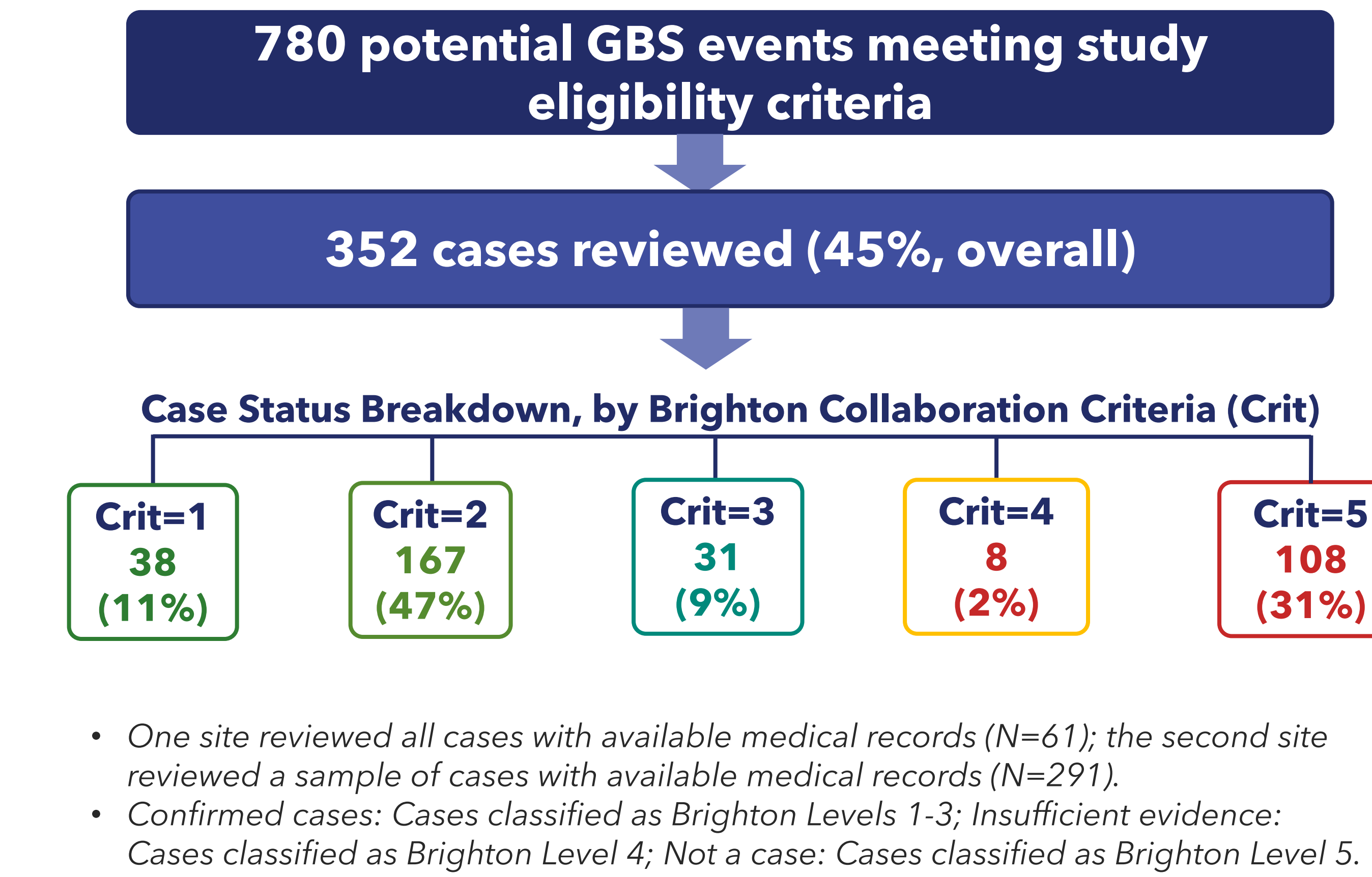
Statistical Analyses

- PPV:** Calculated as follows:

PPV = $\frac{\text{Confirmed cases (Levels 1-3)}}{\text{Algorithm-defined GBS cases with available, abstracted charts (Levels 1-5 + N/A)}}$
- Subgroups:** PPVs were calculated overall and by age, sex, year, comorbidity score, risk of severe RSV-LRTD, any vaccination in the previous 42 days, and infection in the previous 60 days.

Results

Figure 1. Disposition of Potential GBS Cases



- Among 352 cases included in medical record review, 67.0% were confirmed GBS (Brighton Levels 1-3).

Disclosure Statement: This project was funded by Pfizer; some co-authors are employees and stockholders of Pfizer. Some co-authors are or were employed at nonprofit organizations (Harvard Pilgrim Health Care Institute, Kaiser Permanente Southern California, HealthPartners) that conduct work for government and private organizations, including pharmaceutical companies.

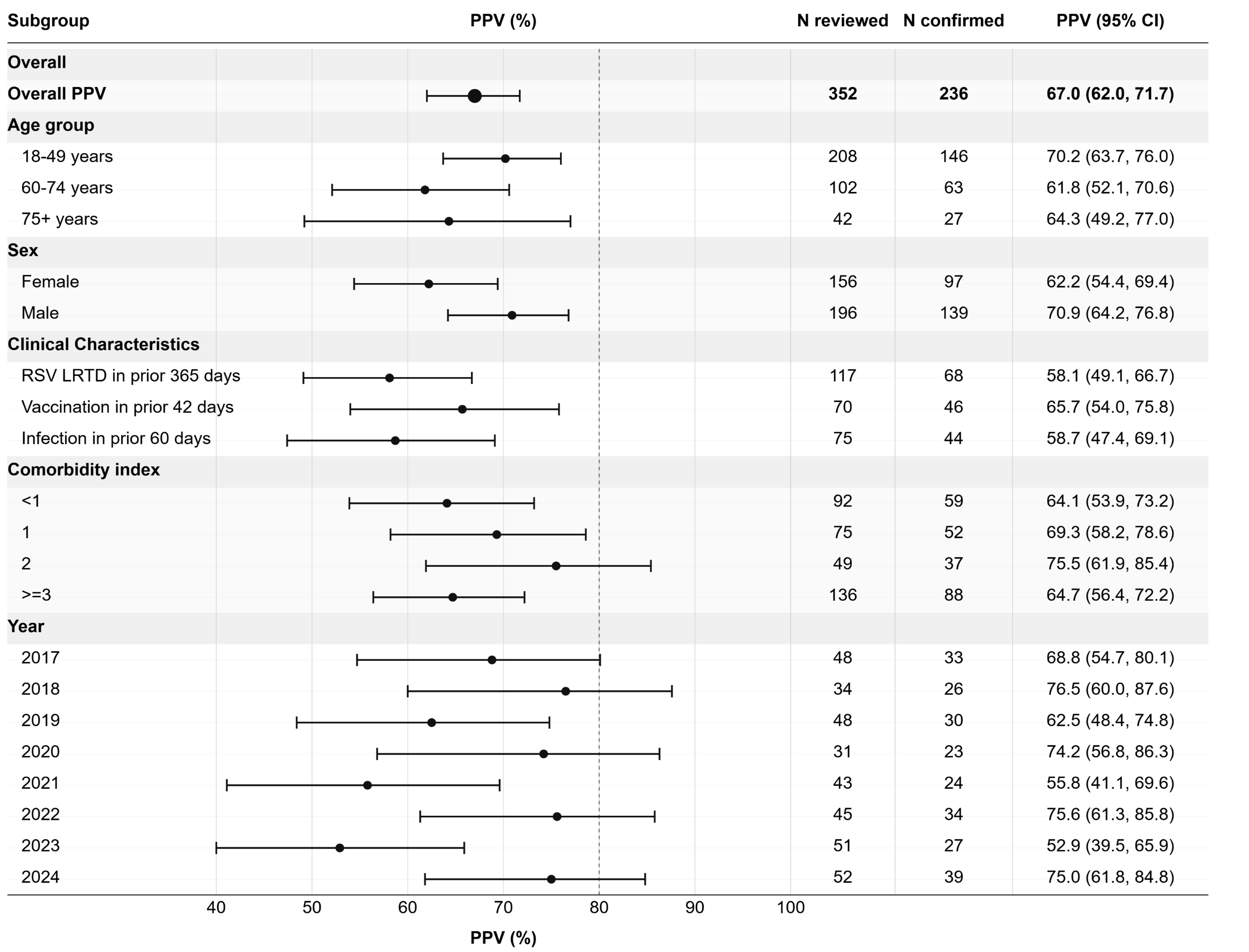
Acknowledgements: HealthPartners: Dianne Eggen, Laurie Van Arman

Contact: Candace_Fuller@hphci.harvard.edu
rwe@hphci.harvard.edu
Harvard Pilgrim Health Care Institute

Table 1. Characteristics of Potential GBS Cases Included in Medical Record Review (N=352)

Characteristic	N	Percent	%
Overall	352		100%
Age			
18-59 years	208		59%
60-74 years	102		29%
>=75 years	42		12%
Sex			
Female	156		44%
Male	196		56%
Combined Comorbidity Index (CCI)			
<1	92		26%
1	75		21%
2	49		14%
>=3	136		39%
Clinical Conditions			
Had a condition associated with RSV-LRTD in the prior 365 days	117		33%
Had an infection in the prior 60 days	75		21%
Had a vaccination in the prior 42 days	70		20%
Potential etiology among cases confirmed as Brighton Level 1-3			
Infection	116		49%
Not available or unable to determine	111		47%
Other(e.g. surgery/medication)	6		3%
Vaccine	3		1%

Figure 2. PPVs of the GBS ICD-10-CM Based Algorithm



Footnotes, Table 1 and Figure 2

- CCI: Combined Comorbidity Score, reference: Sun JW, et al. Med Care. 2017;55(12):1046-1051
- Demographic characteristics, vaccination in the prior 42 days, CCI, and RSV-LRTD was from claims/billing data.
- Potential etiology and infection in the prior 60 days was attained from medical records review; patients could have >1.
- The vertical dotted line at PPV=80% is provided as a visual reference for interpreting subgroup estimates.

Conclusions

- The GBS algorithm demonstrated a moderate PPV, with estimates generally ranging from 55% to 75% across subgroups.
- Variation in PPVs across demographic and clinical characteristics was modest, with overlapping confidence intervals.
- Adjudicators noted that 49% of confirmed GBS cases had infection and 1% had vaccination as potential etiologies.
- Findings are consistent with prior validation studies* and provide information on algorithm performance across clinically relevant subgroups.
- These results inform the design and interpretation of epidemiologic and vaccine safety studies of GBS and support the use of medical record review to improve outcome ascertainment.

*References:

- Goud R, Lufkin B, Duffy J, et al. Risk of Guillain-Barré Syndrome Following Recombinant Zoster Vaccine in Medicare Beneficiaries. JAMA Intern Med. 2021;181(12):1623-1630. doi:10.1001/jamainternmed.2021.
- Eiffert SR, Wright B, Nardin J, Howard JF, Traub R. Evaluating algorithms for identifying incident Guillain-Barré Syndrome in Medicare fee-for-service claims. Glob Epidemiol. 2024;7:100145. doi:10.1016/j.gloepi.2024.
- Funch D, Holick C, Velentgas P, et al. Algorithms for identification of Guillain-Barré Syndrome among adolescents in claims databases. Vaccine. 2013;31(16):2075-2079. doi:10.1016/j.vaccine.2013.
- Bogliun G, Beghi E, Guillain-Barré Syndrome Registry Study Group. Validity of hospital discharge diagnoses for public health surveillance of the Guillain-Barré syndrome. Neurol Sci. 2002;23(3):113-117.

