HHS Public Access

Author manuscript

Epidemiol Infect. Author manuscript; available in PMC 2019 April 01.

Published in final edited form as:

Epidemiol Infect. 2018 October ; 146(13): 1740–1745. doi:10.1017/S0950268818001802.

Post-*Campylobacter* Guillain Barré Syndrome in the United States: Secondary Analysis of Surveillance Data Collected during the 2009–2010 Novel Influenza A (H1N1) Vaccination Campaign

A. Laufer Halpin[1,2], **W. Gu**[1], **M. Wise**[3], **J.J. Sejvar**[4], **R.M. Hoekstra**[1], and **B.E. Mahon**[1]

[1]Division of Foodborne, Waterborne and Environmental Diseases, CDC, Atlanta, GA

[2]Epidemic Intelligence Service, Scientific Education and Professional Development Program, CDC, Atlanta, GA

[3]Division of Healthcare Quality Promotion, CDC, Atlanta, GA

[4]Division of High-Consequence Pathogens and Pathology, CDC, Atlanta, GA

Summary

Guillain Barré syndrome (GBS), which is triggered by autoantibodies produced in response to antigenic stimuli such as certain infections and vaccinations, is the most common cause of acute flaccid paralysis worldwide. *Campylobacter*, the most common bacterial enteric infection in the United States, is reported to be the most commonly diagnosed antecedent of GBS, yet little information is available about the risk of post-*Campylobacter* GBS. Data collected through active, population-based surveillance in the Emerging Infections Program during the 2009–2010 novel Influenza A (H1N1) vaccination campaign allowed us to compare confirmed and probable GBS cases to non-cases to determine whether antecedent *Campylobacter* infection (or a diarrheal illness consistent with campylobacteriosis) was more common among cases and to assess the risk of GBS following *Campylobacter* infection. We estimate that 8-12% of GBS cases in the United States are attributable to *Campylobacter* infection (or a diarrheal illness consistent with campylobacteriosis), with 434 to 650 cases of post-diarrheal GBS annually and about 49 cases of GBS per 100000 *Campylobacter* infections. These results provide updated estimates for post-*Campylobacter* GBS incidence in the United States and highlight an important benefit of effective measures to prevent *Campylobacter* infections.

Corresponding author for both manuscript and reprints Alison Laufer Halpin, 1600 Clifton Rd NE, Mail Stop C-16, Atlanta, GA 30329, ALaufer@cdc.gov.

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

Potential conflicts of interest

A.L.H – None
W.G. – None
M.W. – None
J.J.S. – None
R.M.H. – None
B.E.M. – None

Introduction

Guillain Barré syndrome (GBS) is an autoimmune disorder of the peripheral nervous system triggered by autoantibodies formed in response to antigenic stimuli [1]. Antecedent exposures can include certain vaccinations (e.g., influenza) and viral or bacterial (especially *Campylobacter*) infections [2–6]. GBS is the most common cause of acute flaccid paralysis worldwide [1]; studies in Europe and North America report estimates of GBS incidence of 0.6 to 3.0 cases per 100000 person-years [1, 7]. GBS is associated with severe morbidity, with patients frequently requiring extended ICU stays and up to 67% experiencing at least one major complication [8, 9]. The economic cost is estimated to be $1.7 billion annually in the United States [10].

Campylobacter causes an estimated 1.3 million enteric illnesses annually in the United States, making it the most common bacterial cause of gastroenteritis [11]. *C. jejuni* accounts for most *Campylobacter* infections and has been estimated in various settings and countries to precede 20%– 31% of GBS cases with incidence estimated at 20-65 GBS cases per 100000 *Campylobacter* infections [2, 12–20]. However, recent estimates for US populations are not available [7, 20].

Determining the risk of post-*Campylobacter* GBS is challenging for several reasons. *Campylobacter* infection is often undetectable by the time GBS symptoms begin, because *Campylobacter* is typically shed for less than 2 weeks after onset of diarrhoea, whereas GBS symptoms typically present between 1 and 3 weeks after diarrhoea onset [2, 16, 20, 21]. In addition, due to mild symptoms or asymptomatic infection, many *Campylobacter* infections go undiagnosed, with an estimated 30 undiagnosed infections occurring for each laboratory-confirmed infection [11]. Diarrhoea can be mild [22], so infected persons may not seek care. Even if a stool sample is submitted, *Campylobacter* can be difficult to detect [23]. In the United States, surveillance for *Campylobacter* infection is conducted by the Centers for Disease Control and Prevention's (CDC) Foodborne Diseases Active Surveillance Network (FoodNet), the foodborne disease component of the Emerging Infections Program (EIP) [24]; however, no routine surveillance for GBS exists [7].

An increased risk of GBS following vaccination with a specific formulation of the vaccine targeted at an H1N1 influenza virus was identified in 1976 [25, 26], though no significant increased risk was observed with subsequent seasonal influenza vaccines formulations [27–29]. However, when a novel influenza A (H1N1) virus similar to the type identified in 1976 emerged in 2009 [30–32], concerns about post-vaccination GBS arose, and CDC initiated a special EIP surveillance activity. This surveillance activity, conducted during the 2009–2010 novel influenza A vaccination campaign to assess the risk of post-vaccination GBS found no additional excess risk beyond typical that of seasonal influenza vaccines [33], and offered the opportunity for secondary analysis focused on post-*Campylobacter* GBS. This included extensive data collection on persons who were determined to not have GBS, providing a unique, well-characterized comparison group. Here, we report analysis of the association of GBS with laboratory-confirmed *Campylobacter* infection (the most specific measure for campylobacteriosis) and with diarrheal illness (the most sensitive, available measure) to

estimate the fraction of GBS attributable to laboratory-confirmed *Campylobacter* infection or diarrheal illness. We also present estimated rates of post-*Campylobacter* GBS.

METHODS

EIP GBS Surveillance Activity

We used data from the EIP GBS surveillance activity conducted during the 2009-2010 novel influenza A vaccination campaign to analyse the association of GBS with diarrheal illness or laboratory-confirmed *Campylobacter* infection and to calculate the fraction of GBS attributable to diarrheal illness or laboratory-confirmed *Campylobacter* infection.

EIP GBS surveillance activity population—The EIP includes ten sites and a population that is approximately representative of the U.S. population with respect to demographic and other health indicators, such as poverty (www.cdc.gov/ncezid/dpei/eip/). The catchment area for the GBS surveillance activity included 44.9 million persons. Data were collected between 1 October 2009 and 31 May 2010, yielding 22.9 million person-years under surveillance [33]. Possible GBS cases were identified by exhaustive, active, population-based case-finding to identify every resident of the catchment area presenting with symptoms possibly consistent with GBS. This case-finding was conducted through several avenues, including a network of clinicians (e.g., neurologists, clinical pharmacists, other providers), review of hospital admission and discharge data for the International Classification of Diseases-9-Clinical Modification code for GBS (357.0; acute infective polyneuritis), and monitoring of the Vaccine Adverse Events Reporting System (VAERS). For additional details, see Wise et al. [33].

GBS and non-GBS diagnoses—Data were collected by review of inpatient and outpatient medical records for all possible GBS cases identified with onset of symptoms during the surveillance period [33]. After data collection and review, all possible GBS cases were classified using the Brighton Collaboration criteria for GBS, a classification of diagnostic certainty [34]. Cases were classified as confirmed (meeting Brighton level 1 or 2 criteria) or probable (Brighton level 3 criteria) based on clinical, cerebrospinal fluid, and electrophysiologic criteria. We considered cases that did not meet the Brighton criteria for levels 1, 2, or 3 or cases in which an alternative diagnosis was reported as non-GBS controls.

Antecedent illness—Information about signs, symptoms, and infections experienced in the 42 days before presentation, including diarrhea, influenza-like illness (ILI), upper respiratory tract infection (URI), and laboratory-confirmed *Campylobacter* infection, was collected for all of the reported possible GBS cases, including persons ultimately determined to not have GBS. GBS is known to be strongly associated with *Campylobacter* infection but less with other common causes of diarrheal illness, so we examined the association of antecedent illness with GBS diagnosis using five definitions that ranged from highly specific and less sensitive to highly sensitive and less specific for *Campylobacter* infection. The most specific, least sensitive definition was laboratory-confirmed *Campylobacter* infection. The most sensitive, least specific was any diarrheal illness, which, as described above, was used because *Campylobacter* infection is usually not laboratory-confirmed. Three additional

definitions of intermediate specificity and sensitivity included diarrhoea without ILI, diarrhoea without URI, and diarrhoea without either ILI or URI. These were used because ILI and URI can also precede GBS and can sometimes include diarrhoea [12].

FoodNet

FoodNet, the foodborne diseases component of the EIP, is a collaboration among CDC, ten state health departments, the U.S. Department of Agriculture's Food Safety and Inspection Service (USDA-FSIS), and the Food and Drug Administration (FDA). It conducts active, laboratory-based surveillance for selected pathogens transmitted commonly by food, including *Campylobacter*, and publishes annual estimates of incidence. The FoodNet population is similar though not completely identical to the 2009-2010 GBS surveillance population. Based on 2010 U.S. Census data, about 18% of the FoodNet surveillance population resided in areas not included in the EIP catchment and about 15% of the EIP GBS surveillance population was not included in the FoodNet catchment. We used FoodNet data on laboratory-confirmed *Campylobacter* infections reported from 15 September 2009 to 14 September 2010. Since the EIP GBS surveillance activity did not cover a full year, we used FoodNet data from 2009-2010 on the timing of laboratory-confirmed *Campylobacter* infection in our extrapolation from 8-month to 12-month estimates. Thus, we calculated the proportion of laboratory-confirmed *Campylobacter* infections reported to FoodNet that occurred during 15 September 2009 – 15 May 2010, a period shifted 2 weeks earlier than the GBS surveillance activity, to account for an average 2-week lag between onset of *Campylobacter*-related diarrhoea and onset of GBS.

Statistical analyses

Confirmed and probable GBS cases (Brighton 1–3) were compared to non-cases to determine whether antecedent illness, as determined using the five definitions detailed above, was more common in cases. We calculated odds ratios (OR) to evaluate the association between each definition of antecedent illness and GBS, and we used these OR to estimate the attributable risk (AR) [35].

The AR estimates in turn were used to estimate the number of post-*Campylobacter* and post-diarrheal GBS cases that occurred in the EIP GBS surveillance activity population during the surveillance period. Next, incorporating the national estimate of *Campylobacter* incidence data, we estimated national rates of post-*Campylobacter* (post-diarrheal) GBS in the United States using each of the five definitions of antecedent illness. All analyses were performed in SAS 9.3 (Cary, NC), Microsoft Excel, or the R Package, epiR.

For sensitivity analysis, we also used a more specific definition of GBS limited to confirmed GBS (Brighton levels 1 and 2). We also repeated analyses excluding the 11% of patients referred for possible GBS who had a previous history of GBS.

RESULTS

EIP GBS Surveillance Activity

GBS and non-GBS diagnoses—The GBS surveillance activity identified 638 persons with possible GBS, of whom 398 were determined to have confirmed (Brighton levels 1 or 2, n=349) or probable (Brighton level 3, n=62) GBS. The other 227 patients were classified as not cases of GBS and served as controls. These included persons whose illness did not meet the criteria for Brighton levels 1-3 and persons who received another diagnosis. These other diagnoses were not collected systematically but included cancer or cancer-related treatment (N=8), cardiac-related conditions (7), conversion disorder/seizures (6), radiculopathy (6), drug or alcohol abuse (4), chronic obstructive pulmonary disease (3), diabetes-related conditions (3), stroke (3), multiple sclerosis (2), renal failure (2), and other conditions.

Antecedent illness—Complete antecedent illness reports were available for all 638 patients (Figure 1, Table 1). From most sensitive to most specific for *Campylobacter* infection, antecedent illnesses in the 42 days before onset of symptoms of possible GBS included, 79 (12%) with diarrhea, 68 (11%) with diarrhoea without ILI, 63 (10%) with diarrhoea without URI, 55 (9%) with diarrhoea without ILI or URI, and 6 (1%) with laboratory-confirmed *Campylobacter* infection. The number of laboratory-confirmed *Campylobacter* infections was, as expected, substantially smaller than for the other antecedent illness definitions, though generally consistent with the other definitions (Table 1). Therefore, we focus on the other, more sensitive, antecedent illness definitions. Estimates of association with GBS ranged from OR = 3.2 to 4.2. Attributable risk percent ranged from 8.2% to 12.3%, indicating that 33.7 to 50.5 of the 411 GBS cases diagnosed in the EIP GBS surveillance were attributable to *Campylobacter* infection, as measured by the various antecedent illness definitions (Table 1).

FoodNet

From 15 September 2009 through 15 May 2010, 3,394 cases of *Campylobacter* infection were reported in FoodNet, representing 53% of all *Campylobacter* cases reported to FoodNet during the 1-year period from 15 September 2009 to 14 September 2010 (N=6353). Applying this proportion to the estimate for each antecedent illness definition shows that, for the more sensitive case definitions (i.e., definitions based on symptomatology rather than laboratory-confirmation) an estimated 63.1 to 94.6 attributable GBS cases occurred in the EIP catchment population during the 1-year period from 1 October 2009 to 30 September 2010 (Table 1). Extrapolating from the EIP population, an estimated 433.8 to 650.4 post-*Campylobacter* GBS cases occurred in the United States during this 1-year period, yielding a rate of 0.1 to 0.2 cases per 100000 person-years. Using our 1-year estimates of post-antecedent illness GBS and the 1-year estimate of *Campylobacter* infections (1322137 infections) [11], approximately 32.8 to 49.2 cases of GBS occurred for every 100000 *Campylobacter* infections in the United States. Table 1 also shows the lower estimates obtained using the highly specific definition of laboratory-confirmed *Campylobacter* infection; they are in the expected range, given the known underreporting of *Campylobacter* infection.

Assessment of more or less specific definitions—Analyses repeated using the more specific GBS case definition (confirmed cases only) and excluding persons with a previous history of GBS yielded similar results (data not shown).

DISCUSSION

High quality, comprehensive, population-based, active surveillance data are rarely available for GBS, which, though uncommon, is responsible for high morbidity and economic burden [8–10]. We conducted a secondary analysis of GBS surveillance data collected during the 2009-2010 novel influenza A vaccination campaign to generate contemporaneous estimates of the burden of GBS attributable to *Campylobacter* infection in the United States; the primary analysis demonstrated that the risk of GBS following novel H1N1 vaccination was extremely low, and not greater than what is typically observed for seasonal influenza vaccines. We estimate that 8.2-12.3% of GBS is attributable to antecedent *Campylobacter* infection, with 433 to 650 cases of GBS occurring annually in the United States (32.8-49.2 per 100000 *Campylobacter* infections) that are attributable to antecedent *Campylobacter* infection. Although attributable risk estimates are at the lower end of the range of previous estimates for the US and other developed countries, the incidence estimates are in the mid- to upper- range [17–20].

The EIP GBS surveillance activity provided a unique opportunity to investigate the association between *Campylobacter* and GBS. Strengths of the project include detailed health history collected through intensive, active, population-based surveillance not only from individuals who met the GBS case definitions but also from a comparison group. Given that *Campylobacter* infection is usually not laboratory-confirmed (only six laboratory-confirmed cases were reported in the project), and diarrhoea often resolves before GBS symptom onset [2, 16, 20, 21], the collection of signs and symptoms in the 42 days prior allowed exploration of multiple definitions of varying sensitivity and specificity to represent antecedent *Campylobacter* illness. Of note, although the catchment areas of the EIP GBS surveillance activity and FoodNet did not perfectly overlap and *Campylobacter* incidence estimates were geographically contingent, the low proportion of mismatch in the catchment areas would not be expected to lead to a large difference in our results.

Campylobacter is the most common bacterial cause of domestically-acquired acute gastroenteritis in the US [11, 36]. With rare exceptions [3, 37], the other top three acute gastroenteritis pathogens (norovirus, *Salmonella*, and *Clostridium perfringens*) have not been consistently associated with GBS. However, the less specific but more sensitive definitions of antecedent *Campylobacter* illness based on diarrheal symptoms may have misclassified other diarrheal infections that are rare antecedents of GBS. The impact of these biases is hard to predict. On one hand, using diarrhoea as a proxy for campylobacteriosis should overestimate antecedent illness in both cases and controls, leading to underestimation of the association between *Campylobacter* infection and GBS. On the other hand, to the extent that other diarrheal syndromes are truly associated with GBS, attributing them to *Campylobacter* would lead to an overestimate of the post-*Campylobacter* association.

A limitation of this project is that some patients with *Campylobacter* infection may not have reported diarrhea. For example, one patient with culture-confirmed *Campylobacter* infection did not report diarrhoea and therefore was not captured by the definition of antecedent diarrheal illness. However, GBS diagnosis (case versus non-case) would not have influenced testing for *Campylobacter* or report of diarrhoea in the previous 42 days because these occurred before the onset of the symptoms that led to reporting of possible GBS. In addition, identification of *Campylobacter* infection was limited to reported symptoms and clinical culture; serological testing was not performed. This may have led to underreporting of *Campylobacter* infection, thus underestimating the reported association.

Campylobacteriosis was not nationally notifiable at the time of the EIP GBS surveillance project. Therefore, a major strength of using FoodNet surveillance data for the annual incidence of *Campylobacter* infection in the United States is that the data were collected through active laboratory-based surveillance, which estimates infections and incidence rates more accurately than passive surveillance. The estimated annual incidence of campylobacteriosis was generated using 2006 data, while the EIP GBS surveillance project covered an 8-month period during 2009 to 2010. This is unlikely to have substantially affected our results, as the incidence of *Campylobacter* infection remained relatively stable between 2006 and 2010 [38].

This analysis provides updated estimates related to GBS cases following *Campylobacter* infection in the United States. Post-*Campylobacter* GBS tends to be more severe than GBS following other antecedent events, with worse outcomes and slower recovery [14]. *Campylobacter* infections in the US have an estimated economic burden of ($1.9 billion), over half which is attributed to GBS-related morbidity and mortality [39]. Efforts to decrease *Campylobacter* infections, a priority of the Food Safety Modernization Act, would likely contribute to a decrease in GBS, specifically the most severe GBS cases, thereby substantially mitigating morbidity and mortality associated with *Campylobacter* infection.

Acknowledgments

We gratefully acknowledge Patricia M. Griffin for the initial idea for the analysis and for helpful suggestions on the manuscript. We also thank the many Emerging Infections Program staff for their contributions to the active, population-based surveillance during the 2009–2010 novel Influenza A (H1N1) vaccination campaign.

Funding: This work was not supported by grant funding from any agency, commercial or non-for-profit organization.

References

1. Sejvar JJ, et al. Population incidence of Guillain-Barré syndrome: A systematic review and meta-analysis. Neuroepidemiology. 2011; 36:123–133. [PubMed: 21422765]
2. Hadden RD, et al. Preceding infections, immune factors, and outcome in Guillain-Barré syndrome. Neurology. 2001; 56:758–765. [PubMed: 11274311]
3. Rhodes KM, Tattersfield AE. Guillain-Barre syndrome associated with Campylobacter infection. British Medical Journal (Clin Res Ed). 1982; 285:173–174.
4. Dowling PC, Cook SD. Role of infection in Guillain-Barré syndrome: Laboratory confirmation of herpesviruses in 41 cases. Annals of Neurology. 1981; 9(Suppl):44–55. [PubMed: 6261680]
5. Ju YY, et al. *Haemophilus influenzae* as a possible cause of guillain-barre syndrome. Journal of Neuroimmunology. 2004; 149:160–166. [PubMed: 15020076]

6. Sencer DJ, Millar JD. Reflections on the 1976 swine flu vaccination program. Emerging Infectious Diseases. 2006; 12:29–33. [PubMed: 16494713]
7. McGrogan A, et al. The epidemiology of Guillain-Barré syndrome worldwide. A systematic literature review. Neuroepidemiology. 2009; 32:150–163. [PubMed: 19088488]
8. Henderson RD, et al. The morbidity of Guillain-Barré syndrome admitted to the intensive care unit. Neurology. 2003; 60:17–21. [PubMed: 12530364]
9. Dhar R, Stitt L, Hahn AF. The morbidity and outcome of patients with Guillain–Barré syndrome admitted to the intensive care unit. Journal of the Neurological Sciences. 2008; 264:121–128. [PubMed: 17881005]
10. Frenzen PD. Economic cost of Guillain-Barré syndrome in the United States. Neurology. 2008; 71:21–27. [PubMed: 18591502]
11. Scallan E, et al. Foodborne illness acquired in the United States–major pathogens. Emerging Infectous Diseases. 2011; 17:7–15.
12. Tam CC, et al. Guillain-Barré syndrome and preceding infection with campylobacter, influenza and Epstein-Barr virus in the general practice research database. PLoS One. 2007; 2:e344. [PubMed: 17406668]
13. Poropatich KO, Walker CL, Black RE. Quantifying the association between Campylobacter infection and Guillain-Barré syndrome: A systematic review. Journal of Health, Population and Nutrition. 2010; 28:545–552.
14. Rees JH, et al. *Campylobacter jejuni* infection and Guillain-Barré syndrome. New England Journal of Medicine. 1995; 333:1374–1379. [PubMed: 7477117]
15. Hughes RA, Rees JH. Clinical and epidemiologic features of Guillain-Barré syndrome. Journal of Infectious Diseases. 1997; 176(Suppl 2):S92–98. [PubMed: 9396689]
16. Nachamkin I, Blaser MJ. Campylobacter. 2nd. Washington, D.C.: ASM Press; 2000. xxiii, 545
17. McCarthy N, Giesecke J. Incidence of Guillain-Barré syndrome following infection with *Campylobacter jejuni*. American Journal of Epidemiology. 2001; 153:610–614. [PubMed: 11257070]
18. Tam CC, et al. Incidence of Guillain-Barré syndrome among patients with Campylobacter infection: A general practice research database study. Journal of Infectious Diseases. 2006; 194:95–97. [PubMed: 16741887]
19. Orlikowski D, et al. Guillain-Barré syndrome following primary cytomegalovirus infection: A prospective cohort study. Clinical Infectious Diseases. 2011; 52:837–844. [PubMed: 21427390]
20. Mishu B, Blaser MJ. Role of infection due to *Campylobacter jejuni* in the initiation of Guillain-Barré syndrome. Clinical Infectious Diseases. 1993; 17:104–108. [PubMed: 8353228]
21. Svedhem A, Kaijser B. *Campylobacter fetus* subspecies *jejuni*: A common cause of diarrhea in Sweden. Journal of Infectious Diseases. 1980; 142:353–359. [PubMed: 7441005]
22. Blaser MJ. Epidemiologic and clinical features of *Campylobacter jejuni* infections. Journal of Infectious Diseases. 1997; 176(Suppl 2):S103–105. [PubMed: 9396691]
23. Voetsch AC, et al. Laboratory practices for stool-specimen culture for bacterial pathogens, including *Escherichia coli* O157:H7, in the FoodNet sites, 1995-2000. Clinical Infectious Diseases. 2004; 38(Suppl 3):S190–197. [PubMed: 15095189]
24. Henao OL, et al. Foodborne diseases active surveillance network—2 decades of achievements, 1996–2015. Emerging Infectious Diseases. 2015; 21:1529–1536. [PubMed: 26292181]
25. Schonberger LB, et al. Guillain-Barré syndrome following vaccination in the national influenza immunization program, United States, 1976–1977. American Journal of Epidemiology. 1979; 110:105–123. [PubMed: 463869]
26. Langmuir AD, et al. An epidemiologic and clinical evaluation of Guillain-Barré syndrome reported in association with the administration of swine influenza vaccines. American Journal of Epidemiology. 1984; 119:841–879. [PubMed: 6328974]
27. Lasky T, et al. The Guillain–Barré syndrome and the 1992–1993 and 1993–1994 influenza vaccines. New England Journal of Medicine. 1998; 339:1797–1802. [PubMed: 9854114]
28. Roscelli JD, Bass JW, Pang L. Guillain-Barré syndrome and influenza vaccination in the US Army, 1980–1988. American Journal of Epidemiology. 1991; 133:952–955. [PubMed: 2028981]

29. Haber P, et al. Vaccines and Guillain-Barré syndrome. Drug Safety. 2009; 32:309–323. [PubMed: 19388722]
30. Louie JK, et al. Factors associated with death or hospitalization due to pandemic 2009 influenza A (H1N1) infection in California. JAMA: The Journal of the American Medical Association. 2009; 302:1896–1902. [PubMed: 19887665]
31. Perez-Padilla R, et al. Pneumonia and respiratory failure from swine-origin influenza A (H1N1) in Mexico. New England Journal of Medicine. 2009; 361:680–689. [PubMed: 19564631]
32. Novel Swine-OriginInfluenza A. (H1N1) Virus Investigation Team. Emergence of a novel swine-origin influenza A (H1N1) virus in humans. New England Journal of Medicine. 2009; 360:2605–2615. [PubMed: 19423869]
33. Wise ME, et al. Guillain-Barré syndrome during the 2009-2010 H1N1 influenza vaccination campaign: Population-based surveillance among 45 million Americans. American Journal of Epidemiology. 2012; 175:1110–1119. [PubMed: 22582209]
34. Sejvar JJ, et al. Guillain-Barré syndrome and Fisher syndrome: Case definitions and guidelines for collection, analysis, and presentation of immunization safety data. Vaccine. 2011; 29:599–612. [PubMed: 20600491]
35. Jewell NP. Statistics for epidemiology. Boca Raton: Chapman & Hall/CRC; 2004. xiv, 333
36. Centers for Disease Control and Prevention. Surveillance for foodborne disease outbreaks–United States, 2009-2010. MMWR Morbidity and Mortality Weekly Report. 2013; 62:41–47. [PubMed: 23344696]
37. Eltayeb KG, Crowley P. Guillain–Barré syndrome associated with norovirus infection. BMJ Case Reports. 2012; 2012
38. Crim SM, et al. Incidence and trends of infection with pathogens transmitted commonly through food—foodborne diseases active surveillance network, 10 US sites, 2006–2013. MMWR Morbidity and Mortality Weekly Report. 2014; 63:328–332. [PubMed: 24739341]
39. Hoffmann S, Maculloch B, Batz M. Economic burden of major foodborne illnesses acquired in the United States EIB-140. US Department of Agriculture, Economic Research Service; 2015.

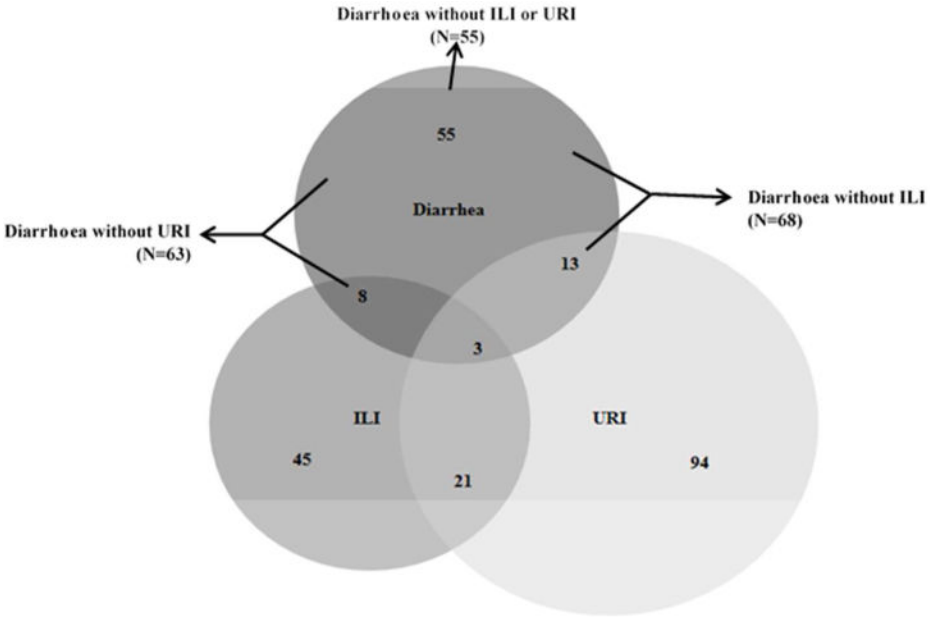

Figure 1.

Diarrhoea, influenza-like illness (ILI), and upper respiratory illness (URI) during the 42 days before onset of symptoms of possible Guillain Barré syndrome (GBS), Emerging Infections Program GBS surveillance, October 2009 – May 2010

Table 1

Association of antecedent illness, based on definitions ranging from highly sensitive to highly specific for *Campylobacter* infection, and association with Guillain Barré Syndrome (GBS) (Brighton Criteria 1-3).

		EIP GBS Surveillance Catchment							US Population		
Antecedent Illness definition (within 42 days before GBS onset)	**Expected sensitivity/ specificity of antecedent illness definition**	**Patients with antecedent illness (N)**	**GBS cases with antecedent illness n (%)**	**Non-cases with antecedent illness n (%)**	**Odds ratio [95% CI]**	**Fraction of GBS attributable to antecedent illness (AR%)**	**Post-antecedent illness-GBS cases n [95% CI]**	**Annual post-antecedent illness-GBS cases n [95% CI][1]**	**Annual post-antecedent illness-GBS cases n [95% CI][1]**	**Post-antecedent illness-GBS Cases, per 100000 person-years [95% CI][1]**	**Rate GBS, per 100000 *Campylobacter* infections [95% CI][3]**
Diarrhoea reported[3]	Most sensitive Least specific	79	68 (86)	11 (14)	3.9 [2.0, 7.5]	12.3%	50.5 [31.3, 68.8]	94.6 [58.5, 128.8]	650.4 [402.3, 886.0]	0.2 [0.1, 0.3]	49.2 [30.4, 67.0]
Diarrhea, without ILI reported	Intermediate	68	57 (84)	11 (16)	3.2 [1.6, 6.2]	9.5%	39.0 [20.4, 56.6]	73.0 [38.2, 106.0]	501.6 [262.9, 729.0]	0.2 [0.1, 0.2]	37.9 [19.9, 55.1]
Diarrhea, without URI reported	Intermediate	63	55 (87)	8 (13)	4.2 [2.0, 9.0]	10.2%	42.0 [24.9, 58.4]	78.6 [46.5, 109.3]	540.5 [319.9, 751.4]	0.2 [0.1, 0.2]	40.9 [24.2, 56.8]
Diarrhoea without ILI or URI reported	Intermediate	55	47 (85)	8 (15)	3.5 [1.6, 7.6]	8.2%	33.7 [17.2, 49.5]	63.1 [32.3, 92.6]	433.8 [221.8, 636.9]	0.1 [0.1, 0.2]	32.8 [16.8, 48.2]
Laboratory-confirmed *Campylobacter* infection[3]	Most specific Least sensitive	6	5 (83)	1 (17)	2.8 [0, 2.1]	0.8%	3.2 [0, 8.8]	6.0 [4.6, 16.5]	41.2 [0, 113.1]	0.01 [0, 0.04]	3.1 [0, 8.6]

[1]Results of main analyses extrapolated using 2009-2010 FoodNet data

[2]Results of main analyses extrapolated using annual estimates for *Campylobacter* infections [11]

[3]Estimated 1 in 30 *Campylobacter* infections are laboratory confirmed [11]