

Declining Guillain-Barré Syndrome after Campylobacteriosis Control, New Zealand, 1988–2010

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Learning Objectives

Upon completion of this activity, participants will be able to:

- Distinguish the infection most closely associated with GBS
- Analyze the temporal relationship between campylobacteriosis and GBS
- Assess differences in the association between campylobacteriosis and GBS based on age
- Evaluate the effect of infection-control measures on rates of campylobacteriosis and GBS

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Infection with *Campylobacter* spp. commonly precedes Guillain-Barré syndrome (GBS). We therefore hypothesized that GBS incidence may have followed a marked rise and then decline in campylobacteriosis rates in New Zealand. We reviewed records for 1988–2010: hospitalization records for GBS case-patients and campylobacteriosis case-patients plus notifications of campylobacteriosis. We identified 2,056 first hospitalizations for GBS, an average rate of 2.32 hospitalizations/100,000 population/year. Annual rates of hospitalization for GBS were significantly correlated with rates of notifications of campylobacteriosis. For patients hospitalized for campylobacteriosis, risk of being hospitalized for GBS during the next month was greatly increased. Three years after successful interventions to lower *Campylobacter* spp. contamination of fresh poultry meat, notifications of campylobacteriosis had declined by 52% and hospitalizations for GBS by 13%. Therefore, regulatory measures to prevent foodborne campylobacteriosis probably have an additional health and economic benefit of preventing GBS.

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Guillain-Barré syndrome (GBS) is an autoimmune condition that affects the peripheral nervous system. Patients typically describe ascending weakness and sensory disturbance that evolve over several days; during this acute phase, approximately one third of patients require ventilatory support. The condition is generally self-limiting, but for 3%–10% of patients, it is fatal (1).

An estimated 40%–70% of patients with GBS had an infection before GBS onset; for 6%–39% of these patients, the infection affected the gastrointestinal system (2). Campylobacteriosis is the most commonly identified antecedent infection; several studies have shown that in industrialized countries (Europe, North and South America, Japan, and Australia), *Campylobacter* spp. infection preceded GBS for 20%–50% of patients (3,4).

During 1980–2006 in New Zealand, incidence of campylobacteriosis steadily increased. The notification rate in 2006 (379 cases/100,000 population) remains the highest national rate reported in the literature (5,6). In 2006, in response to this high incidence, New Zealand introduced an array of voluntary and regulatory interventions to reduce contamination of poultry with *Campylobacter* spp. (7). By 2008, the rate of campylobacteriosis notifications had dropped to 157 cases/100,000 population, a decrease of 59% over 2 years (7); this decline has persisted (8). Given the known association between *Campylobacter* spp. infection and GBS and the marked recent changes in reported rates of campylobacteriosis in New Zealand, we examined GBS hospitalization data for evidence of responsiveness to trends in campylobacteriosis incidence.

Methods

Identification of GBS Incidence

Because GBS is a serious illness that nearly always results in hospitalization, hospitalization data provided the most accurate available measure of GBS incidence. We obtained national hospital discharge data for the 23-year period 1988–2010 in New Zealand. To estimate the case-fatality proportion, we also obtained data on deaths from GBS for 1988–2008 (the most recent year available). Both datasets are collated and maintained by the New Zealand Ministry of Health.

Although hospitalization data are available for earlier years, we used 1988 as the starting point because that is when use of unique patient identifiers, the National Health Index (NHI), became universal in New Zealand. Use of the NHI enables identification and removal of repeat GBS hospitalizations for the same patient, thereby identifying the first GBS hospitalization for each case (hereafter called GBS hospitalization), which provides an estimate of the number of incident cases of GBS.

We selected all cases from 1988 on that had International Classification of Diseases, 9th and 10th Revisions, Clinical Modification and Australian Modification, codes for GBS (ICD-9 CM 357.0 and ICD-10 AM G61.0) recorded as the principal or additional diagnosis. Records of patients who had been transferred between hospitals were merged to create 1 hospitalization event. We identified repeat hospitalizations for the current year and for previous years, i.e., case-patients with the same NHI number previously admitted in the same or a previous year. Some patients were readmitted before universal use of the NHI in 1988, so the calculation needed to take these estimated repeat hospitalizations into account. (See online Technical Appendix Tables 1, 2, wwwnc.cdc.gov/EID/pdfs/11-1126-Techapp.pdf, for a description of how estimated repeat hospitalizations and incident cases were calculated.)

Identification of Campylobacteriosis Incidence

Since 1980, campylobacteriosis has been a notifiable disease in New Zealand. Medical practitioners are required to report all identified and suspected cases to the local medical officer of health. These data are in turn collated nationally by the Institute of Environmental Science and Research for the New Zealand Ministry of Health. We used published annual totals of notifications (9) as well as anonymized datasets of notified cases. Most cases were culture confirmed (>96% during 1997–2008 [7]), although the case definition also allows for cases epidemiologically linked to a confirmed case.

Hospitalizations for campylobacteriosis are recorded in hospital discharge data, which are electronically available for a similar period. However, a specific diagnostic code for *Campylobacter* spp. infection was not introduced until July 1995. Hospitalizations for campylobacteriosis were defined as those with ICD-9 CM code 008.43 from July 1995 on and ICD-10 AM code A04.5 from July 1999 on. To create a dataset of incident cases, we included principal or additional diagnoses, merged records for those transferred with records from preceding hospitalizations, and removed repeat hospitalizations in the current and previous years.

Analysis of Hospitalizations for GBS after Campylobacteriosis

To assess the association between the 2 conditions, we investigated the incidence of GBS among patients hospitalized for campylobacteriosis. Because campylobacteriosis was only specifically identified in hospitalization data from July 1995, this analysis focused on the period starting in July 1995. To allow a follow-up period for GBS cases to emerge, we continued the inclusion period through December 2008.

For those cases identified, we first analyzed the time from hospital admission for campylobacteriosis to

admission for GBS. For epidemiologic purposes, the risk period for GBS after *Campylobacter* spp. infection is ≈ 2 months (10); neurologic signs of GBS usually develop 1–3 weeks after a preceding infection (3). In our dataset, a clear trend was seen toward a close temporal association between hospitalization dates: for most (34/35, 97.1%) patients, hospitalizations for GBS and campylobacteriosis were concurrent (patients were discharged with a diagnosis of both), or hospitalization for GBS occurred within 1 month of hospitalization for campylobacteriosis.

To assess the risk for GBS associated with campylobacteriosis, we calculated GBS hospitalization rates for comparison conditions, notably other infections that might be associated with an elevated risk for GBS. We used the GBS rate in the total New Zealand population as our reference rate for calculating age-standardized rate ratios for GBS after campylobacteriosis and other conditions of interest.

We also evaluated which age groups might be more vulnerable to development of GBS. To do so, we compared the age distributions of all patients hospitalized for GBS and those associated with campylobacteriosis with the age distributions for those with campylobacteriosis alone (hospitalized or with notified case).

Statistical Analyses

Because of marked changes in campylobacteriosis disease incidence and some changes in case identification during the 23-year study period, some outcomes were measured over a shorter time. The periods associated with implementation of the *Campylobacter* spp. control interventions used a baseline period similar to that used in a previous study (7).

Data were analyzed by using Stata version 11.0 (StataCorp LP, College Station, TX, USA) and SAS version 9.1 (SAS Institute, Cary, NC, USA). CIs are given at the 95% level throughout. We used well-documented methods for calculating adjusted rates, rate ratios (RRs),

and 95% CIs (11). Rates were calculated by using mean population estimates published by Statistics New Zealand (www.stats.govt.nz/browse_for_stats/population/estimates_and_projections/national-pop-estimates.aspx) as denominators. To calculate age-standardized rates, we used the population age structure determined by the New Zealand 2006 Census of Population and Dwellings (www.stats.govt.nz/Census/2006CensusHomePage/classification-counts-tables/about-people/age.aspx).

Results

GBS Incidence

This study identified 2,056 first hospitalizations for GBS that occurred during 1988–2010, resulting in an average rate of 2.32 hospitalizations/100,000 population/year (online Technical Appendix Table 1). Incidence was not stable over the period of the study (Figure). The minimum recorded rate was 1.53 hospitalizations/100,000 population/year in 1989; the maximum was 2.93 in 2005. During 1989–2008, a total of 56 deaths from GBS were recorded; case-fatality proportion (56 deaths/1,873 cases) was 3.0%.

Changes in GBS and Campylobacteriosis Incidence

For 1988–2010, there was a significant direct correlation between annual rates of hospitalization for GBS and annual rates of notification of campylobacteriosis cases (Spearman $\rho = 0.52$, $p = 0.012$). During 1988–2006, incidence of campylobacteriosis notifications and of GBS hospitalizations increased (Figure; online Technical Appendix Table 3). Subsequently, campylobacteriosis notifications then decreased markedly, and GBS hospitalizations decreased, although less dramatically. The fall in campylobacteriosis notifications followed the introduction of countrywide campylobacteriosis control measures focused on reducing contamination levels in fresh poultry meat (7).

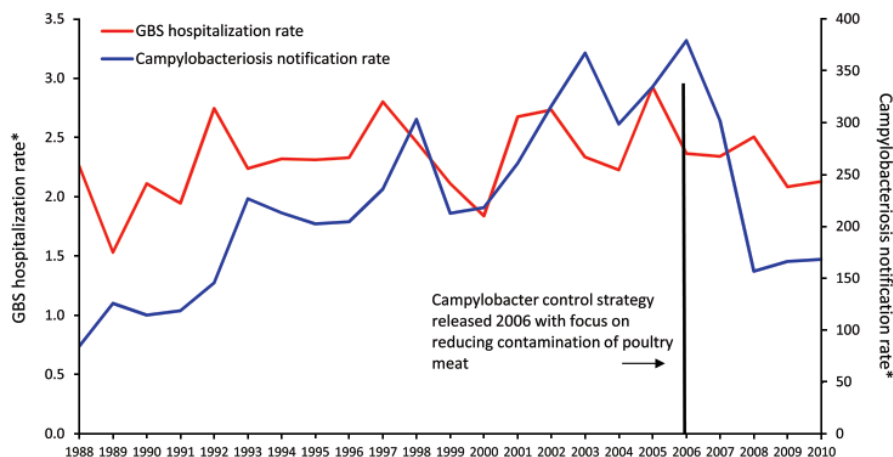


Figure. Guillain-Barré syndrome (GBS) hospitalization rates and campylobacteriosis notification rates, by year, New Zealand, 1988–2010. *Per 100,000 population.

Table 1 summarizes the changes between the 2 periods: 1) 2002–2006, the baseline period, when rising campylobacteriosis rates became an urgent public health concern, and 2) 2008–2010, the postintervention period, after implementation of wide-ranging control measures. The transition year, 2007, was excluded.

During the postintervention period, notifications and hospitalizations decreased by $\approx 50\%$ (online Technical Appendix Tables 3, 4). Incidence of GBS declined by 13%, which was statistically significant (RR 0.87, 95% CI 0.81–0.93), suggesting that $\approx 25\%$ of GBS was caused by preceding campylobacteriosis.

GBS among Patients Hospitalized for Campylobacteriosis or Other Conditions

During 1995–2008, among the 8,448 patients hospitalized for campylobacteriosis, 35 were also hospitalized for GBS. The frequency distribution of time delays is shown in Table 2. These data show that most (29) of these 35 patients had diagnoses of GBS and campylobacteriosis at time of hospital discharge. Another 5 patients were hospitalized for GBS within 4 weeks of being hospitalized for campylobacteriosis. The time difference for the remaining patient was $>1,500$ days (this patient was excluded from subsequent analyses). This striking distribution further supports a causative association between campylobacteriosis and GBS in New Zealand.

We calculated the rate of GBS hospitalizations among the cohort of patients hospitalized for campylobacteriosis and compared this with rates of GBS hospitalization among other patient cohorts hospitalized for infectious diseases (Table 3). This analysis used the overall rate of GBS hospitalizations among the New Zealand population as a reference for calculating age-standardized RRs.

The age-standardized rate of GBS was 810.0 hospitalizations/100,000 person-years (95% CI 41.4–1,578.7) in the month after hospitalization for campylobacteriosis. The RR, compared with the rate of GBS hospitalizations among the New Zealand population,

was 319.4 (95% CI 201.5–506.4). This rate was markedly higher than rates for the other patient cohorts examined (Table 3).

Patients with GBS (median age 52.5 years) were significantly older than those hospitalized for campylobacteriosis (median 41 years), who in turn were significantly older than those with campylobacteriosis notifications (median 31 years) (Tables 4, 5). The age of the subpopulation of patients with GBS associated with campylobacteriosis was similar (median 54 years) to that of the total population with GBS.

Discussion

This study shows how the incidence of an acute infectious disease, campylobacteriosis, can influence incidence of a serious neurologic condition, GBS. At the population level, hospitalizations for GBS were significantly correlated with notifications of campylobacteriosis for the same year. At the individual level, compared with rates for the New Zealand population as a whole, hospitalizations for campylobacteriosis were associated with an almost 320-fold increased risk for subsequent hospital admission for GBS in the next month.

Results also show that food safety measures to reduce contamination of fresh poultry meat with *Campylobacter* spp. not only reduced incidence of campylobacteriosis but also were associated with reduced incidence of GBS. In the 3 years after introduction of these control measures, campylobacteriosis notifications and hospitalizations decreased by $\approx 50\%$, and GBS hospitalizations dropped by 13%. These findings suggest that in New Zealand, *Campylobacter* spp. infection may be responsible for $\approx 25\%$ of GBS cases, which is consistent with data from other industrialized countries (3).

A recent systematic review (12) summarized attempts to quantify the association between campylobacteriosis and GBS incidence. There is general agreement that measuring GBS population rates is useful, for example, for monitoring vaccine adverse effects (13,14). However,

Table 1. Incidence of campylobacteriosis and GBS before and after intervention to reduce *Campylobacter* spp. in poultry, New Zealand 2002–2010*

| Incident condition | Before intervention, 2002–2006 | | | After intervention, 2008–2010† | | | Change | |
|--------------------------------------|--------------------------------|--------------|-------|--------------------------------|--------------|-------|---------------------|---------|
| | Total no. | Average/year | Rate‡ | Total no. | Average/year | Rate‡ | Rate ratio (95% CI) | p value |
| Campylobacteriosis notifications§ | 69,207 | 13,841 | 339.4 | 21,217 | 7,072 | 163.8 | 0.48 (0.48–0.49) | <0.0001 |
| Campylobacteriosis hospitalizations¶ | 4,669 | 934 | 23.2 | 1,603 | 534 | 12.2 | 0.53 (0.51–0.54) | <0.0001 |
| GBS hospitalizations¶ | 513 | 103 | 2.6 | 290 | 97 | 2.2 | 0.87 (0.81–0.93) | 0.0496 |

*GBS, Guillain-Barré syndrome.

†Excludes 2007, which was a transitional year.

‡Annual no. cases/100,000 person-years at risk. Denominator populations based on mean population estimates published by Statistics New Zealand (www.stats.govt.nz/browse_for_stats/population/estimates_and_projections/national-pop-estimates.aspx). Campylobacteriosis and Guillain-Barré syndrome hospitalizations used age-standardized rates based on the age structure of the New Zealand 2006 Census of Population and Dwellings (www.stats.govt.nz/Census/2006CensusHomePage/classification-counts-tables/about-people/age.aspx).

§Published campylobacteriosis notification data (9).

¶Hospitalization data from New Zealand Ministry of Health.

Table 2. Hospitalization for Guillain-Barré syndrome during or after hospitalization for campylobacteriosis, New Zealand, July 1995–December 2008

| Interval, d | No. (%) persons hospitalized | Cumulative % |
|---------------|------------------------------|----------------|
| Concurrent | 29 (82.9) | 82.9 |
| 1–7 | 2 (5.7) | 88.6 |
| 8–28 | 3 (8.6) | 97.1 |
| 1,524 (4.2 y) | 1 (2.9) | 100 |
| Total | 35 (100) | Not applicable |

to our knowledge, no similar population-based analysis of the relationship between GBS and campylobacteriosis has been conducted for other countries, probably because few countries collect similarly detailed national-level hospitalization data. An earlier population-based study in New Zealand did not show an association between notifications for campylobacteriosis and GBS incidence (15). However, that study was over a shorter period and did not use a correction factor to account for undetected repeat hospitalizations in the early years of the observation period, which would have made it harder to detect an association between incidence rates for the 2 conditions.

Compared with global estimates, rates of GBS in New Zealand are high. In a review of reported GBS rates during 1980–2000, worldwide incidence varied between 1.0 and 1.8 cases/100,000 population/year (2). The average reported rate for New Zealand during this period was at the upper end of this range (1.8/100,000). A more recent study from the United States estimated that annual hospitalization rates for GBS varied between 1.65 and 1.79/100,000 during

2000–2004 (16). In New Zealand during the same period, the annual hospitalization rates varied between 1.8 and 2.7/100,000.

The 320-fold increased risk for GBS in the month after hospitalization for campylobacteriosis found in this study is higher than that previously reported. In a case-control study of GBS and potential antecedent infections in the United Kingdom, Tam et al. reported that persons with *Campylobacter* enteritis had a 38-fold increased risk that GBS would develop in the next 2 months (17). However, when they added a correction factor to account for under-ascertainment of campylobacteriosis, the risk increased to 60-fold. Similarly, a population-based study in Sweden estimated that patients with laboratory-confirmed *C. jejuni* infection had a 100-fold increased risk that GBS would develop in the next 2 months (10). We used a 1-month risk period because the GBS cases we identified subsequent to hospitalizations for campylobacteriosis were confined to this period. Using a 2-month risk period would have halved our estimated age-standardized RR, but the elevated risk would still be higher than that reported elsewhere.

The proportion of GBS cases attributable to preceding *Campylobacter* spp. infection estimated for New Zealand ($\approx 25\%$) is within the range described elsewhere. Studies from other countries and regions have reported serologic evidence of previous *C. jejuni* infection in 13%–72% of GBS case-patients (18). A systematic review, based on 32 eligible studies, estimated that 31% of GBS cases were attributable to *Campylobacter* spp. infection (12).

Table 3. Incidence of GBS after hospitalization for campylobacteriosis and other infectious diseases compared with total population incidence rate for GBS, New Zealand, July 1995–December 2008*

| Initial hospitalization condition | ICD-9 codes | ICD-10 codes | Denominator population† | Subsequent GBS hospitalizations (concurrent hospitalizations)‡ | Crude rate§ | Age-standardized rate¶ (95% CI) | Age-standardized rate ratio (95% CI) |
|-------------------------------------|---------------------------------------|-----------------------------------|-------------------------|----------------------------------------------------------------|-------------|---------------------------------|--------------------------------------|
| Infectious diseases (ICD chapter 1) | 001–139 | A00–B99 | 732,254 | 56 (273) | 90.7 | 87.0 (56.9–116.4) | 34.3 (29.2–40.3) |
| Pneumonia and influenza | 480–488 | J09–J18 | 250,399 | 19 (82) | 91.1 | 96.2 (25.1–167.3) | 37.9 (26.5–54.3) |
| Enteric diseases# | 001–002 004–008.42 008.44–009.3 | A00–A01 A03–A04.4 A04.6–A09 | 77,793 | 6 (21) | 93.3 | 132.0 (1.2–262.7) | 52.0 (32.2–84.2) |
| Campylobacteriosis | 008.43 | A04.5 | 8,448 | 5 (29) | 710.2 | 810.0 (41.4–1,578.7) | 319.4 (201.5–506.4) |
| Salmonellosis | 003 | A02 | 2,148 | 0 (0) | 0 | 0 | 0 |
| New Zealand population GBS rate | NA | NA | 53,617,400 | 1,320 | 2.5 | 2.5 (2.4–2.7) | Referent |

*GBS, Guillain-Barré syndrome; ICD, International Classification of Diseases; ICD-9, ICD 9th Revision; ICD-10, ICD 10th Revision; NA, not applicable.
†Denominator population based on either 1) incident hospitalizations for specific condition (number of acute and arranged first overnight hospitalizations as principal or additional diagnosis); or 2) total New Zealand population person-years for July 1995–December 2008 for calculating the New Zealand population GBS rate.

‡First hospitalization of GBS either 1) among those with a previous hospitalization in the preceding 30 d and excluding those with concurrent diagnoses (numbers in parentheses); or 2) in the total New Zealand population for July 1995–December 2008.

§Rate per 100,000 person-years at risk. For GBS hospitalizations after specific conditions, monthly rate has been multiplied by 12 to convert to annual rate.

¶Standard population is population of New Zealand according to the New Zealand 2006 Census of Population and Dwellings (www.stats.govt.nz/Census/2006CensusHomePage/classification-counts-tables/about-people/age.aspx).

#Excluding campylobacteriosis and salmonellosis.

Table 4. Distribution of campylobacteriosis and GBS cases, by age, New Zealand, July 1995–December 2008*

| Age group, y | Campylobacteriosis notifications | | Campylobacteriosis hospitalizations | | GBS hospitalizations | | GBS hospitalizations associated with campylobacteriosis | |
|--------------|----------------------------------|-------|-------------------------------------|-------|----------------------|-------|---------------------------------------------------------|-------|
| | No. (%) | Rate‡ | No. (%) | Rate‡ | No. (%) | Rate‡ | No. (%) | Rate‡ |
| <5 | 15,232 (11.7) | 442.5 | 538 (6.4) | 13.9 | 45 (3.4) | 1.2 | 0 | 0 |
| 5–9 | 6,295 (4.9) | 176.9 | 200 (2.4) | 5.0 | 33 (2.5) | 0.8 | 2 (5.9) | 0.1 |
| 10–19 | 14,481 (11.2) | 203.7 | 965 (11.4) | 12.2 | 113 (8.6) | 1.4 | 3 (8.8) | 0 |
| 20–29 | 25,063 (19.3) | 385.9 | 1,509 (17.9) | 20.6 | 115 (8.7) | 1.6 | 1 (2.9) | 0 |
| 30–39 | 19,511 (15.0) | 270.7 | 935 (11.1) | 11.5 | 146 (11.1) | 1.8 | 3 (8.8) | 0 |
| 40–49 | 16,572 (12.8) | 237.0 | 747 (8.8) | 9.6 | 149 (11.3) | 1.9 | 5 (14.7) | 0.1 |
| 50–59 | 14,311 (11.0) | 261.9 | 778 (9.2) | 13.0 | 226 (17.1) | 3.8 | 6 (17.7) | 0.1 |
| 60–69 | 9,559 (7.4) | 255.7 | 824 (9.8) | 19.9 | 209 (15.8) | 5.0 | 7 (20.6) | 0.2 |
| 70–79 | 6,174 (4.8) | 235.9 | 1,046 (12.4) | 35.9 | 200 (15.2) | 6.9 | 5 (14.7) | 0.2 |
| ≥80 | 2,712 (2.1) | 190.8 | 906 (10.7) | 57.9 | 84 (6.4) | 5.4 | 2 (5.9) | 0.1 |
| Total | 129,910 (100.0) | 270.4 | 8,448 (100.0) | 15.8 | 1,320 (100.0) | 2.5 | 34 (100.0) | 0.1 |

*GBS, Guillain-Barré syndrome.

†Association with hospitalization for campylobacteriosis. Includes subsequent and concurrent hospitalizations (campylobacteriosis and GBS diagnoses at time of hospital discharge).

‡Average annual no./100,000 population.

The strength of the association with GBS may vary geographically, according to the neuropathic propensity of local *Campylobacter* strains. We would also expect the percentage contribution of preceding *Campylobacter* spp. infection to vary according to the incidence of this infection in the population and the incidence of other causal infections and exposures.

The results of our study suggest that risk for GBS may not be uniform for different degrees of campylobacteriosis severity. Our study found that risk for GBS was ≈1 in 1,690 (5 in 8,448) among patients hospitalized for campylobacteriosis and that ≈25% of GBS cases were caused by campylobacteriosis. On the basis of an annual incidence of ≈100 GBS cases, these data suggest that ≈42,000 cases of campylobacteriosis occur each year in New Zealand. Current estimates of total campylobacteriosis incidence are higher. Annual notifications remain at ≈7,000 cases. A study from the United Kingdom estimated that 9.3 cases of campylobacteriosis occurred in the community for every notified case (19); a study from Australia estimated this number to be 10 (20). Applied to New Zealand, these multipliers suggest an incidence among the population of 65,000 to 70,000 cases per year. These findings suggest that the causal association between campylobacteriosis and GBS is probably weaker for patients with less severe infections, who do not require hospitalization.

Analysis of the age distribution of patients with campylobacteriosis and GBS suggests that older age is a major risk factor for more severe outcomes (hospitalization and GBS) from this enteric infection. The rising incidence of GBS with increasing age in New Zealand is consistent with incidence observed in other countries (21).

One strength of this study is that it has been able to monitor a natural experiment in which campylobacteriosis incidence decreased by 50% within a few months, providing an unusual opportunity to assess the effect of this change on incidence of GBS. New Zealand's comprehensive recording of national hospitalization data and use of a unique patient number also provided us with a consistent base for estimating population rates of GBS over a prolonged period. Although the spectrum of GBS includes extremely mild cases, studies elsewhere indicate that only ≈3.0%–5.8% of patients with GBS are not hospitalized (22,23). In addition, patients with *Campylobacter*-associated GBS are believed to experience more severe disease (24,25), which would minimize the number of *Campylobacter*-associated GBS cases missed by this investigation.

One limitation of this study is the group used to compare risk for GBS: the total New Zealand population. A variety of conditions and events have been identified as possible GBS triggers (1,24,26–29). Consequently, because it is not possible with current knowledge to identify a

Table 5. Comparison of ages of patients with campylobacteriosis and GBS, New Zealand, July 1995–December 2008*

| Calculation | A. Patients with campylobacteriosis | B. Patients hospitalized for campylobacteriosis | p value for age compared with A§ | C. Patients hospitalized for GBS | p value for age compared with B§ | D. Patients hospitalized for GBS and campylobacteriosis† | p value for age compared with C‡ |
|-------------|-------------------------------------|-------------------------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------------------------------|----------------------------------|
| | Age, y | Age, y | | Age, y | | Age, y | |
| Mean | 33.7 | 43.7 | <0.0001 | 48.8 | <0.0001 | 50.3 | 0.7063 |
| Median | 31 | 41 | <0.0001 | 52.5 | <0.0001 | 54 | 0.7280 |

*GBS, Guillain-Barré syndrome.

†Includes subsequent and concurrent hospitalizations (campylobacteriosis and GBS diagnoses at time of hospital discharge).

‡Means compared with Student t-test medians compared with median 2-sample test.

reference patient population with no additional GBS risk factors, we considered that the total population provided the most appropriate reference rate.

The association between campylobacteriosis and GBS in New Zealand needs further investigation. It will be useful to continue to follow the trends identified here to assess the stability of the decrease in GBS, which will eventually give greater precision to the estimated contribution of campylobacteriosis. Ongoing monitoring of GBS should be included in the comprehensive surveillance of infectious diseases (30). The hypothesis that patients not hospitalized for campylobacteriosis have a lower risk for GBS should be tested by investigation of incidence of GBS among these patients.

Our findings suggest the value of further research to identify other potentially preventable infectious causes of GBS. Table 3 shows a markedly elevated risk for GBS after hospitalization for infectious diseases in general. Investigating these associations in detail may identify other potentially preventable causes of GBS.

Findings of this study have relevant implications for food safety programs. Although GBS is rare, the toll it takes on the individual patient is often high (1). Even with treatment, 9%–17% of patients die or remain disabled (31), and repeat hospitalizations are common, representing ≈60% of total hospitalizations (online Technical Appendix Table 1). Almost half of all patients report ongoing difficulties 3–6 years after GBS onset (32). Consequently, ongoing health care costs for each GBS patient are considerable. In New Zealand during 1988–2008, the GBS case-fatality proportion was 3.0%, and a recent article (33) estimated that 204 (13%) of 1,568 disability-adjusted life years for campylobacteriosis in New Zealand were caused by GBS.

This study shows that food safety programs that successfully lower rates of campylobacteriosis might have the additional benefit of preventing GBS. This finding adds to the health and economic arguments for such control measures. The justification for such interventions is particularly strong where a substantial proportion of human disease can be linked to a widely consumed food source, such as contaminated poultry products, as it is in New Zealand (7).

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Dr Baker is an associate professor at the University of Otago, Wellington. He is actively investigating the potential for public health surveillance to guide more effective interventions

in a range of settings. His research includes a strong focus on infectious diseases and their determinants, particularly the effects of housing conditions and social and ethnic inequalities.

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Declining Guillain-Barré Syndrome after Campylobacteriosis Control, New Zealand, 1988–2010

Technical Appendix

Technical Appendix Table 1. Incidence of GBS hospitalizations and adjusted estimates of hospitalization rates for incident cases by year, New Zealand, 1988–2010*

| Year | Total New Zealand population | GBS total hospitalizations (principal and additional), T | GBS repeat hospitalizations in current year, Rc | GBS repeat hospitalizations from previous years, Rp | GBS repeat hospitalizations estimated from before 1988, Re (Re = C × [T - Rc]) | GBS incident hospitalizations, I (I = T - Rc - Rp - Re) | GBS rate/100,000 (based on incident cases I) |
|-------|------------------------------|----------------------------------------------------------|-------------------------------------------------|-----------------------------------------------------|--------------------------------------------------------------------------------|---------------------------------------------------------|----------------------------------------------|
| 1988 | 3,317,000 | 140 | 41 | 13 | 11 | 75 | 2.26 |
| 1989 | 3,330,200 | 97 | 29 | 11 | 6 | 51 | 1.53 |
| 1990 | 3,362,500 | 147 | 56 | 12 | 8 | 71 | 2.11 |
| 1991 | 3,495,800 | 147 | 57 | 16 | 6 | 68 | 1.95 |
| 1992 | 3,533,000 | 205 | 87 | 15 | 6 | 97 | 2.75 |
| 1993 | 3,573,600 | 181 | 84 | 14 | 3 | 80 | 2.24 |
| 1994 | 3,621,600 | 261 | 150 | 24 | 3 | 84 | 2.32 |
| 1995 | 3,675,800 | 194 | 86 | 21 | 2 | 85 | 2.31 |
| 1996 | 3,733,900 | 214 | 102 | 23 | 2 | 87 | 2.33 |
| 1997 | 3,782,600 | 244 | 110 | 28 | – | 106 | 2.80 |
| 1998 | 3,815,800 | 215 | 100 | 21 | – | 94 | 2.46 |
| 1999 | 3,837,300 | 210 | 101 | 28 | – | 81 | 2.11 |
| 2000 | 3,860,100 | 211 | 111 | 29 | – | 71 | 1.84 |
| 2001 | 3,887,000 | 282 | 148 | 30 | – | 104 | 2.68 |
| 2002 | 3,951,200 | 300 | 163 | 29 | – | 108 | 2.73 |
| 2003 | 4,027,700 | 295 | 175 | 26 | – | 94 | 2.33 |
| 2004 | 4,088,700 | 262 | 143 | 28 | – | 91 | 2.23 |
| 2005 | 4,136,000 | 302 | 149 | 32 | – | 121 | 2.93 |
| 2006 | 4,186,900 | 212 | 90 | 23 | – | 99 | 2.36 |
| 2007 | 4,230,700 | 223 | 97 | 27 | – | 99 | 2.34 |
| 2008 | 4,271,100 | 276 | 141 | 28 | – | 107 | 2.51 |
| 2009 | 4,318,100 | 203 | 96 | 17 | – | 90 | 2.08 |
| 2010 | 4,367,800 | 207 | 84 | 20 | – | 93 | 2.13 |
| Total | | 5,028 | 2,400 | 515 | 47 | 2,056 | 2.32 |

*GBS, Guillain-Barré syndrome

Notes:

1. The populations used in this paper are from Statistics New Zealand: 1991-2010: "National population estimates, mean year ended 31 December 1991–2010 – tables", (http://www.stats.govt.nz/browse_for_stats/population/estimates_and_projections/national-pop-estimates.aspx) 1988-1990: "Estimated total population by sex, year ended 30 December (1926–2010) and 30 June (1937–2011) – tables", (http://www.stats.govt.nz/browse_for_stats/population/estimates_and_projections/historical-population-tables.aspx)
2. T = total hospitalizations with a GBS diagnostic code as the principal or additional diagnosis. These hospitalization data were provided by the New Zealand Ministry of Health.
3. Rc = repeat GBS hospitalizations during that year (i.e., same NHI number with GBS diagnostic code as the principal or additional diagnosis).
4. Rp = GBS cases with hospitalization in a previous year.
5. Re = estimated GBS repeat hospitalizations of cases first admitted before 1988, based on applying a correction factor C to cases seen in that year (T-Rc) where Re = C*(T-Rc). See the notes to Technical Appendix Table 2 for a description of how C was calculated.
6. GBS incident hospitalizations (I) where I = T-Rc-Rp-Re.

Technical Appendix Table 2. Estimating a correction factor (C) for the early years of the study by using empirical data from more recent years

| Year | 2000 | | 1999 | | 1998 | | 1997 | | 1996 | | Average C |
|------|------|-------|------|-------|------|-------|------|-------|------|-------|-----------|
| | Rb | C | Rb | C | Rb | C | Rb | C | Rb | C | |
| S | 29 | 0.290 | 28 | 0.257 | 21 | 0.183 | 28 | 0.209 | 23 | 0.205 | 0.229 |
| S+1 | 16 | 0.133 | 15 | 0.174 | 14 | 0.147 | 5 | 0.051 | 16 | 0.131 | 0.127 |
| S+2 | 12 | 0.100 | 15 | 0.126 | 14 | 0.165 | 12 | 0.129 | 2 | 0.021 | 0.108 |
| S+3 | 5 | 0.051 | 10 | 0.085 | 12 | 0.103 | 11 | 0.134 | 9 | 0.100 | 0.095 |
| S+4 | 5 | 0.052 | 4 | 0.041 | 7 | 0.061 | 11 | 0.096 | 11 | 0.134 | 0.077 |
| S+5 | 10 | 0.076 | 5 | 0.052 | 3 | 0.031 | 5 | 0.044 | 9 | 0.080 | 0.057 |
| S+6 | 0 | 0.000 | 9 | 0.069 | 5 | 0.052 | 2 | 0.021 | 5 | 0.044 | 0.037 |
| S+7 | 3 | 0.029 | 0 | 0.000 | 9 | 0.069 | 5 | 0.052 | 2 | 0.021 | 0.034 |
| S+8 | 1 | 0.009 | 3 | 0.029 | 0 | 0.000 | 8 | 0.062 | 3 | 0.032 | 0.027 |
| S+9 | 1 | 0.011 | 1 | 0.009 | 1 | 0.010 | 0 | 0.000 | 8 | 0.062 | 0.018 |

Notes:

1. S = the start year for each series, e.g., 2000, for the first series; 1999 for the second series, 1998 for the third series.
2. Rb = the number of repeat hospitalizations in that year of GBS cases first admitted before the specified start year S, but with no repeat hospitalizations between year S and the current year.
3. C = the correction factor, i.e., the proportion of cases in each year with a previous hospitalization before the start year S. It is calculated using the formula $C = Rb / (T - Rb)$. See Appendix Table 1 for values for T and Rb.
4. Averaging C over the 5 series produced a set of C values for years 0–9, which were then applied to the first 10 years of the study period (1988 to 2007).

Technical Appendix Table 3. Incidence of campylobacteriosis notifications by year, New Zealand 1988–2010

| Year | Total New Zealand population | Campylobacteriosis notifications | Campylobacteriosis notification rate/100,000 population |
|------|------------------------------|----------------------------------|---------------------------------------------------------|
| 1988 | 3,317,000 | 2,796 | 84.29 |
| 1989 | 3,330,200 | 4,187 | 125.73 |
| 1990 | 3,362,500 | 3,850 | 114.50 |
| 1991 | 3,495,800 | 4,148 | 118.66 |
| 1992 | 3,533,000 | 5,144 | 145.60 |
| 1993 | 3,573,600 | 8,101 | 226.69 |
| 1994 | 3,621,600 | 7,714 | 213.00 |
| 1995 | 3,675,800 | 7,442 | 202.46 |
| 1996 | 3,733,900 | 7,635 | 204.48 |
| 1997 | 3,782,600 | 8,924 | 235.92 |
| 1998 | 3,815,800 | 11,572 | 303.27 |
| 1999 | 3,837,300 | 8,161 | 212.68 |
| 2000 | 3,860,100 | 8,418 | 218.08 |
| 2001 | 3,887,000 | 10,146 | 261.02 |
| 2002 | 3,951,200 | 12,494 | 316.21 |
| 2003 | 4,027,700 | 14,788 | 367.16 |
| 2004 | 4,088,700 | 12,215 | 298.75 |
| 2005 | 4,136,000 | 13,836 | 334.53 |
| 2006 | 4,186,900 | 15,874 | 379.13 |
| 2007 | 4,230,700 | 12,778 | 302.03 |
| 2008 | 4,271,100 | 6,694 | 156.73 |
| 2009 | 4,318,100 | 7,177 | 166.21 |
| 2010 | 4,367,800 | 7,346 | 168.19 |

Notes:

1. Population data are estimates from Statistics New Zealand (see Table 1 footnote for details).
2. Campylobacteriosis notification data are from the Institute of Environmental Science and Research (ESR). See reference 9 in main paper.

Technical Appendix Table 4. Campylobacteriosis hospitalizations by year, New Zealand 1995–2010

| Year | Total New Zealand population | Principal diagnosis | Additional diagnosis | Total, T | Repeat hospitalizations in current year, Rc | Repeat hospitalizations from previous years, Rp | Incident hospitalizations, I | Hospitalization rate per 100,000 population (based on incident cases (I)) |
|------|------------------------------|---------------------|----------------------|----------|---------------------------------------------|-------------------------------------------------|------------------------------|---------------------------------------------------------------------------|
| | | | | | | | $I = T - Rc - Rp$ | |
| 1995 | 3,675,800 | 127 | 61 | 188 | 4 | 0 | 184 | 5.01 |
| 1996 | 3,733,900 | 225 | 150 | 375 | 7 | 1 | 367 | 9.83 |
| 1997 | 3,782,600 | 306 | 155 | 461 | 13 | 6 | 442 | 11.69 |
| 1998 | 3,815,800 | 363 | 161 | 524 | 18 | 4 | 502 | 13.16 |
| 1999 | 3,837,300 | 278 | 119 | 397 | 14 | 2 | 381 | 9.93 |
| 2000 | 3,860,100 | 410 | 101 | 511 | 16 | 8 | 487 | 12.62 |
| 2001 | 3,887,000 | 520 | 120 | 640 | 15 | 4 | 621 | 15.98 |
| 2002 | 3,951,200 | 586 | 147 | 733 | 21 | 5 | 707 | 17.89 |
| 2003 | 4,027,700 | 770 | 197 | 967 | 28 | 8 | 931 | 23.11 |
| 2004 | 4,088,700 | 749 | 174 | 923 | 35 | 10 | 878 | 21.47 |
| 2005 | 4,136,000 | 885 | 212 | 1,097 | 52 | 19 | 1026 | 24.81 |
| 2006 | 4,186,900 | 990 | 213 | 1,203 | 62 | 14 | 1127 | 26.92 |
| 2007 | 4,230,700 | 750 | 183 | 933 | 45 | 17 | 871 | 20.59 |
| 2008 | 4,271,100 | 395 | 101 | 496 | 24 | 10 | 462 | 10.82 |
| 2009 | 4,318,100 | 480 | 104 | 584 | 23 | 10 | 551 | 12.76 |
| 2010 | 4,367,800 | 516 | 101 | 617 | 19 | 8 | 590 | 13.51 |

Notes:

1. Because campylobacteriosis was recorded as a separate diagnosis from July 1995, figures for that year are incomplete.
2. Data from 2010 are provisional and may undercount hospitalizations.