Correspondence

Indirect Protection and Indirect Measures of Protection From Rotavirus in Adults

To the Editor—We read with interest the recent article by Lopman et al [1], who used *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9CM*) data from the Nationwide Inpatient Sample (NIS) to document a decline in rotavirus and cause-unspecified gastroenteritis in 2008 in patients <24 years of age following widespread implementation of pediatric rotavirus vaccination. Despite the fact that administrative coding (*ICD-9CM*) data have been widely used [1–6], we are unaware of data regarding how well these codes identify hospitalized adults with all-cause gastroenteritis. In addition, important differences exist in the *ICD-9CM* codes used in studies, depending on whether the focus was on foodborne illness or all-cause gastroenteritis. Analysis of administrative data that was performed for rotavirus in children showed an underestimation of rotavirus in that population [7]. As part of an institutional review board–approved study of the prevalence of rotavirus among adults hospitalized at Northwestern Memorial Hospital (Chicago, Illinois) from 1 December 2005 through 30 November 2006, who had a stool specimen submitted for bacterial stool culture (BSC) [8], we compared how well *ICD-9CM* codes were able to identify patients with gastroenteritis when compared with having a BSC obtained, a surrogate for a clinical diagnosis of gastroenteritis.

We used the criteria from the sentinel study of Mounts et al [3]. Any patient with an *ICD-9CM* code of 008.45 (*Clostridium difficile*) was reviewed and

Table 1. Comparison Between Patients With an *ICD-9CM* Code Consistent With Gastroenteritis and Those Who Have a Bacterial Stool Culture Saved

Characteristic	Coded With *ICD-9CM*, BSC Not Sent (n = 109)	Not Coded With *ICD-9CM*, BSC Saved (n = 109)	*P* Value
Age			
Mean (SD)	54.2 (19.48)	54.0 (17.47)	NS[a]
Min, max	18, 100	22, 92	
Sex			
Male	44 (40.4%)	47 (43.1%)	NS[b]
Female	65 (59.6%)	62 (56.9%)	
Ethnicity			
White	63 (57.8%)	74 (67.9%)	NS[c]
Black	25 (22.9%)	23 (21.1%)	
Hispanic	13 (11.9%)	7 (6.4%)	
Asian	2 (1.8%)	2 (1.8%)	
Other	2 (1.8%)	1 (0.9%)	
Missing	4 (3.7%)	2 (1.8%)	
Preceding hospitalizations			
Yes	65 (59.6%)	61 (56.0%)	NS[b]
No	44 (40.4%)	48 (44.0%)	
Pregnancy[d]			
Yes	8 (12.3%)	1 (1.6%)	.03[c]
No	57 (87.7%)	61 (98.4%)	
Cancer			
Yes	28 (25.7%)	28 (25.7%)	NS[b]
No	81 (74.3%)	81 (74.3%)	
Diabetes			
Yes	24 (22.0%)	23 (21.1%)	NS[b]
No	85 (78.0%)	86 (78.9%)	
SCT or SOT			
Yes	17 (15.6%)	13 (11.9%)	NS[b]
No	92 (84.4%)	96 (88.1%)	
HIV/AIDS			
Yes	3 (2.7%)	11 (10.1%)	<.03[b]
No	106 (97.3%)	98 (89.9%)	
Inflammatory bowel disease			
Yes	7 (6.4%)	6 (5.5%)	NS[b]
No	102 (93.6%)	102 (93.6%)	
Missing	0 (0%)	1 (0.9%)	
Liver disease			
Yes	9 (8.3%)	17 (15.6%)	.095[b]
No	100 (91.7%)	92 (84.4%)	
Renal disease			
Yes	17 (15.6%)	8 (7.3%)	.056[b]
No	92 (84.4%)	101 (92.7%)	

Table 1 continued.

Characteristic	Coded With *ICD-9CM*, BSC Not Sent (n = 109)	Not Coded With *ICD-9CM*, BSC Saved (n = 109)	*P* Value
Prolonged steroid administration (>14 days)			
Yes	9 (8.3%)	2 (1.8%)	.03[b]
No	100 (91.7%)	107 (98.2%)	
Clostridium difficile			
Yes	35 (32.1%)	20 (18.4%)	<.0001[b]
No	16 (14.7%)	62 (56.9%)	
Missing	58 (53.2%)	27 (24.8%)	
Preceding antibiotic administration			
Yes	45 (41.3%)	49 (45.0%)	NS[b]
No	64 (58.7%)	60 (55.0%)	
Admission source			
Home	93 (85.3%)	102 (93.6%)	.006[c]
Nursing home	5 (4.6%)	3 (2.8%)	
Rehabilitation Hospital	9 (8.3%)	0 (0%)	
Other	2 (1.8%)	4 (3.7%)	
Duration of admission, days			
Mean (SD)	5.67 (5.877)	6.53 (8.344)	NS[a]
Min, max	0.6, 34.8	0.8, 66.9	
Rehospitalization (yes/no)			
Yes	53 (48.6%)	56 (51.4%)	NS[b]
No	56 (51.4%)	53 (48.6%)	
Rehospitalization (weeks after initial admission)			
Mean (SD)	4.20 (7.683)	5.17 (8.874)	NS[e]
Median	0	0.29	
Min, max	0, 39	0, 37	
Survival			
Yes	98 (89.9%)	97 (89.0%)	NS[b]
No	11 (10.1%)	11 (10.1%)	
Missing[f]	0 (0%)	1 (0.9%)	

Abbreviations: BSC, bacterial stool culture; HIV, human immunodeficiency virus; *ICD-9CM*, *International Classification of Diseases, Ninth Revision*; NS, not significant; SCT, stem cell transplant; SOT, solid organ transplant.

[a] *P* values obtained using a 2-sample *t* test assuming unequal variances with Satterthwaite degrees of freedom.

[b] *P* values obtained using χ^2 test.

[c] *P* values obtained using Fisher exact test.

[d] Analysis only includes women from both groups.

[e] *P* values obtained using nonparametric methods (Wilcoxon rank sum test).

[f] Records reference hospice care but the current vital status of patient is unknown.

included only if diarrhea was present on admission or occurred within 72 hours of hospitalization. A random sample of 200 adult subjects coded with gastroenteritis was then compared to 200 randomly selected subjects from whom BSCs were submitted and saved. Subjects who had a stool submitted for BSC were eligible if they were >18 years, had unformed stool, and the BSC was not a duplicate [8]. Because overlap of 91 subjects existed between these groups, the remaining 109 subjects in each group were compared with one another. We have previously reported that no difference existed between those who had a BSC saved for additional testing and a randomly selected group of those who did not have a BSC saved [8]. Data were collected and compared, including demographic information, risk factors for diarrhea, underlying medical comorbidities, symptoms, laboratory findings, and outcomes (see Table 1).

BSC better identified patients who were positive for human immunodeficiency virus with gastroenteritis than did administrative criteria. In contrast, administrative coding identified additional patients with pregnancy or who were on steroids. Additional differences in *C. difficile* testing and the source of the admission existed between the groups. It has been shown from prior FoodNet data that BSCs tend to be sent in patients with bloody diarrhea and in those with diarrhea lasting for ≥3 days [9]. Thus, neither administrative coding nor the sending of a BSC identifies all patients with gastroenteritis. Variability in the *ICD-9CM* coding between different institutions and variability in the *ICD-9CM* codes used in different studies undoubtedly further compound such differences.

Despite the limitations of administrative data, the data from Lopman et al [1] are important and consistent with previous literature. Rotavirus is known to be a significant pathogen during the winter–spring months in adults [8, 10]. The prior *ICD-9CM*–based study of Lopman et al [1] estimated rotavirus at 3%–5% of hospitalizations for gastroenteritis in patients ≥18 years before implementation of pediatric vaccination; our results from direct antigen testing of adult BSCs (5% in February–May) correlate well with this estimate [2, 8]. Interestingly, in our study among the 896 adult inpatients who had an administrative code assigned that was consistent with gastroenteritis, the rotavirus-specific code 008.61 was never used. Additionally, rotavirus testing was not sent as a standard of care test by the treating physician of any patient in whom we identified rotavirus [8]. Thus, the failure to identify a decline in rotavirus-specific coding in adults ≥25 years of age is not surprising.

Administrative coding was developed for billing purposes; therefore, it is not surprising that limitations exist in the extent to which it can be relied on for

epidemiological purposes. Direct patient-related data are necessary to validate the important conclusions of Lopman et al [1] about the indirect impact of pediatric rotavirus vaccination on the prevalence of adult rotavirus gastroenteritis.

Notes

Disclaimer. The opinions expressed in this paper are those of the authors and do not necessarily represent those of Merck Sharp & Dohme Corp, a subsidiary of Merck & Co, Inc.

Financial support. This work was supported in part by a research grant from the Investigator-Initiated Studies Program of Merck Sharp & Dohme Corp, a subsidiary of Merck & Co, Inc. We also thank Meridian Biosciences, Inc, for partial funding.

Potential conflicts of interest. E. J. A. has served as a consultant for Merck and GlaxoSmithKline and has received honoraria from Medscape. E. J. A. and B. Z. K. have served on the speakers' bureau for Merck. All other authors report no potential conflicts.

The authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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Received 20 October 2011; accepted 15 December 2011; electronically published 28 March 2012.

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The Journal of Infectious Diseases 2012;205:1762–4

DOI: 10.1093/infdis/jis262

Reply to Anderson et al

To the Editor—Anderson and colleagues [1] highlight some important limitations of using administrative data to assess burden of gastroenteritis hospitalizations and the impact of interventions such as rotavirus vaccination.

Validation studies have shown that in children <5 years of age, the rotavirus-specific *International Classification of Diseases* (*ICD*) code (*Ninth Revision*, 008.61; *Tenth Revision*, A08.0) is reasonably specific (ie, the vast majority of *ICD*-coded rotavirus hospitalizations are laboratory confirmed) but insensitive in that it may be assigned to only about half of all laboratory-confirmed rotavirus hospitalizations identified through active surveillance [2, 3]. In adults, validity of this code has not been assessed but is likely to be substantially poorer than it is for children because diagnostic testing for rotavirus is less likely to be performed in adults. In addition, pathogens such as *Clostridium difficile* [4] and noninfectious pathologies are much more common among adults, especially among the elderly, and thus general gastroenteritis codes are likely to be less specific to detect rotavirus events. These shortcomings of administrative data reduce our ability to detect effects that may be attributable to rotavirus vaccination, particularly among adults.

Despite these substantial limitations, we were able to detect indirect impacts of the rotavirus vaccination program across several age groups [5]. We detected reductions in both rotavirus-coded and cause-unspecified gastroenteritis discharges in all age groups up to 24 years. Even in adults and the elderly, for whom rotavirus coding is exceedingly rare, we detected fewer cause-unspecified gastroenteritis discharges. The fact that these declines were only seen during the month(s) of the year in which rotavirus was known to circulate in prevaccine years increases our confidence that they represent true declines in rotavirus hospitalizations in these age groups.

We agree wholeheartedly that direct diagnostic data are needed to confirm the etiological importance of rotavirus outside of pediatric age groups. However, as Anderson and colleagues [1] note, using stool specimens taken for bacterial culture also has important limitations [6]. For example, when a patient's symptoms are consistent with viral gastroenteritis, physicians are probably less likely to order a stool culture, resulting in underestimation of the role of rotavirus. Active collection of stool for patients admitted for gastroenteritis may provide the most robust estimates of prevalence. Indeed, a recently published article in the *Journal of Infectious Diseases* demonstrated 18% rotavirus prevalence, mainly in adults of child-rearing age admitted with gastroenteritis, using such an approach [7].

Even well-conducted active surveillance studies, however, have limitations in terms of generalizability. Administrative