

## The rate of acute gastrointestinal illness in developed countries

Sharon L. Roy, Elaine Scallan and Michael J. Beach

### ABSTRACT

This paper reviews estimates of the incidence and prevalence of acute gastrointestinal illness (AGI) from 33 studies. These studies include prospective cohort studies, retrospective cross-sectional population-based surveys, and intervention trials from the United States and six other developed countries published since 1953. The incidence and prevalence estimates for AGI reported in these studies range from 0.1 to 3.5 episodes per person-year. However, comparisons of these rates are problematic owing to significant variation in study design, sampling methodology, and case definitions and should be made with caution. In the United States, the Centers for Disease Control and Prevention's (CDC) Foodborne Diseases Active Surveillance Network (FoodNet) estimates a rate of 0.65 episodes of AGI per person-year. This estimate includes diarrhea and/or vomiting of infectious or non-infectious origin, with a measure of severity (impairment of daily activities or diarrhea duration greater than 1 day), and has been adjusted for combined respiratory–gastrointestinal illnesses. However, it excludes episodes of diarrhea or vomiting due to any long-lasting or chronic illness or condition. Limitations in study design result in an unknown degree of uncertainty around this point estimate.

**Key words** | diarrhea, gastroenteritis, incidence, prevalence, review, vomiting

**Sharon L. Roy** (corresponding author)

**Michael J. Beach**

Water and Environment Activity, Division of  
Parasitic Diseases,  
Centers for Disease Control and Prevention,  
4770 Buford Highway, N.E., Mailstop F22,  
Atlanta, GA 30341-3724,  
USA  
E-mail: [str2@cdc.gov](mailto:str2@cdc.gov)

**Elaine Scallan**

Foodborne Diseases Active Surveillance Network  
(FoodNet),  
Foodborne and Diarrheal Diseases Branch,  
Centers for Disease Control and Prevention,  
1600 Clifton Road, Mailstop D63,  
Atlanta, GA 30333,  
USA

### INTRODUCTION

Acute gastrointestinal illness (AGI) is caused by a variety of different agents and conditions and comprises a constellation of symptoms that may include diarrhea, nausea, vomiting, abdominal pain, abdominal cramps, fever, and other systemic symptoms. Because of its various causes and variable symptomatology, no standard definition of AGI has been presented in the medical literature, making comparisons of studies difficult. Furthermore, investigators use different terms to describe AGI, such as intestinal infectious disease (IID) (Garthright *et al.* 1988; Roderick *et al.* 1995) and highly credible gastrointestinal symptoms (HCGI) (Payment *et al.* 1991). For the purposes of this review, the

generic term “AGI” will be used to refer to gastrointestinal illness involving diarrhea, nausea, or vomiting, which may or may not also be combined with abdominal pain, abdominal cramps, or systemic symptoms, such as fever. Diarrhea and diarrheal illness, which considers the degree of severity of diarrhea, are the most frequently studied components of AGI. Currently, studies focusing on diarrhea provide the majority of the information available on the rate of AGI.

Diarrheal illness is a common problem worldwide but is well recognized as a significant cause of morbidity and mortality in developing countries. Recent estimates suggest that children younger than 5 years of age in developing countries experience a median of two to three diarrhea episodes per person-year. Moreover, children six to eleven

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months of age experience the highest median rate of diarrhea at five episodes per person-year (Snyder & Merson 1982; Kosek *et al.* 2003). According to 2002–2003 World Health Organization statistics, diarrheal diseases accounted for 17% of all deaths worldwide in children younger than 5 years of age, resulting in approximately 1.8 million deaths annually (WHO 2005). When all ages were considered, diarrheal diseases accounted for 3.2% of all deaths worldwide each year. Diarrheal diseases have the 5th highest burden of disease, expressed in DALYs, surpassed only by perinatal conditions, respiratory infections, HIV/AIDS, and depression (WHO 2004).

While AGI mortality is low in developed countries, AGI morbidity remains important. In the United States, children younger than 5 years of age are estimated to experience one to two episodes of diarrhea annually, with 300–400 deaths attributed to AGI each year (Glass *et al.* 1991). A study of approximately 300,000 American children younger than 5 years of age estimated that diarrhea accounted for 4% of all hospitalizations and 2% of all outpatient visits in this population. Based on the total outpatient and inpatient payments in this group, researchers estimated that the total national payment for diarrhea-associated disease in this age group was \$411 million per year (in 1998 US dollars) (Zimmerman *et al.* 2001). This estimate would have been greater if the costs associated with morbidity and mortality in older children and adults were included.

Accurate estimates of AGI incidence and prevalence are essential for the development of sound public health policy. An overall estimate of the prevalence of AGI due to all etiologies is the necessary first step in developing an estimate of the prevalence of gastrointestinal illness due to specific exposures or etiologies, such as drinking water consumption. Disease surveillance plays an important role in developing these estimates. However, the data available from outbreak surveillance, laboratory-based communicable disease reporting, and other public health surveillance systems underestimate the rate of disease because they usually only capture case-patients in contact with the healthcare system. Not all persons infected by enteric pathogens develop gastrointestinal symptoms (Figuroa *et al.* 1983; Ish-Horowicz *et al.* 1989; Pettoello-Mantovani *et al.* 1995). Furthermore, less than a third of persons with

an AGI seek medical care and stool samples for laboratory diagnoses are only obtained in a minority of these patients (Hawkins *et al.* 2002; Herikstad *et al.* 2002; Imhoff *et al.* 2004; Jones *et al.* in press). Most persons consulting a healthcare provider for a gastrointestinal illness are either treated with supportive care, regardless of the cause, or are treated presumptively without confirming the etiology through laboratory testing. Even if laboratory testing is ordered, different disease agents require different testing methodologies and laboratories may not perform the necessary diagnostic tests in every case (Jones *et al.* 2004; Voetsch *et al.* 2004). Furthermore, most stool tests fail to identify a pathogen (Magliani *et al.* 1985; Essers *et al.* 2000; Denno *et al.* 2005). While some cases of gastrointestinal illness due to laboratory-confirmed pathogens are required to be reported to public health agencies, most are not (CDC 2005a). Even when reporting is required, a large proportion of laboratory-confirmed notifiable diseases go unreported (Standaert *et al.* 1995). This phenomenon results in underreporting of AGI, particularly of mild cases. Therefore, passive surveillance captures only a small fraction of the true rate of disease.

Because so many episodes of AGI are treated at home without contact with the healthcare system, special studies within communities are required to estimate the incidence and prevalence of gastrointestinal illness in the general population. In the United States, information on AGI incidence and prevalence has come from prospective community-based cohort studies, intervention trials, and retrospective population-based cross-sectional surveys. Similar studies have been conducted in other developed countries. However, using the data from these studies to derive an estimate of AGI prevalence is still problematic. The definition of what constitutes AGI is inconsistent between studies. Some studies only measure a single symptom – diarrhea – but even the definition of diarrhea varies. This paper reviews studies estimating the AGI incidence and prevalence in developed countries, examines the strengths and weaknesses of these studies, compares the estimated rates, discusses the limitations associated with such a comparison, and proposes an estimate of AGI prevalence in the United States based on available information.

## METHODS

To identify the information available on the rate of AGI in developed countries, we conducted a literature review of peer-reviewed journal articles, scientific conference abstracts, and public health and environmental health agency documents available on the Internet. To identify the journal articles, we performed a PubMed search through the US National Library of Medicine using various combinations of the following key words: diarrhea, vomiting, gastroenteritis, gastrointestinal, prevalence, incidence, and human. Reference lists from relevant articles identified in the PubMed search were reviewed to find other relevant journal articles, abstracts, and agency reports. Using this approach, we identified 33 studies published since 1953 that provide estimates of AGI incidence and prevalence in the United States and in other developed countries.

## RESULTS

### Estimates from prospective community-based cohort studies and intervention trials in the United States

Since the mid-1900s, there have been several large-scale prospective community-based cohort studies and intervention trials to determine the rate of AGI in the United States. The first of these studies was conducted by [Dingle \*et al.\* \(1953, 1964\)](#) from January 1 1948 to May 31 1957. Investigators observed the occurrence of respiratory illness and unexplained gastrointestinal illness among families in Cleveland, Ohio over a 10-year study period. Families were selected in a non-random fashion through referral by family physicians or pediatricians. All had young children, belonged to the middle or upper socioeconomic classes, and were located within a specified residential area. Data was collected on the occurrence of diarrhea, vomiting, abdominal pain, and respiratory symptoms. One adult per family, usually the mother, kept a daily record of symptoms present in each family member. Field workers visited the homes weekly to check the records. During the early years of the study, staff physicians visited most of the ill study participants. During the later years of the study, persons with mild afebrile illnesses were not routinely examined.

In this study, illness was defined as the presence of one or more symptoms abnormal for that individual. Only gastrointestinal symptoms judged to be the result of primary gastrointestinal disease were considered in this 10-year study. Gastrointestinal symptoms thought to be secondary to another non-gastrointestinal illness or to some cause other than illness, and those thought to be too minor to warrant consideration as true symptoms were excluded. Those illnesses determined to be primary gastroenteritis were further categorized as infectious or noninfectious. Noninfectious gastroenteritis cases due to dietary causes (120 cases), infant diarrhea (8 cases), functional symptoms (e.g. constipation, globus hystericus – 192 cases), and miscellaneous disorders (e.g. peptic ulcer, diverticulitis, ulcerative colitis – 22 cases) were excluded from analysis. The remaining gastrointestinal illnesses were assumed to be infectious in nature. An infectious gastroenteritis case was defined as two or more of the following symptoms: vomiting, abdominal pain, diarrhea, and fever (2139 cases). An infectious gastroenteritis-epidemiological case was defined as one of the above major symptoms (vomiting, abdominal pain, diarrhea, or fever) or minor symptoms (nausea, anorexia, etc.) occurring within 10 days of another infectious gastroenteritis case or infectious gastroenteritis-epidemiological case in the same family (1169 cases). A probable infectious gastroenteritis case was defined as the same symptoms as an infectious gastroenteritis-epidemiological case but was not associated, within 10 days, with the onset of another case of infectious gastroenteritis (749 cases). In total, 439 members from 85 different families participated in the study and contributed 2692 person-years of follow-up. The median enrollment time per person was 2100 days (range 35–3439 days). There were a total of 4057 reported episodes of infectious gastroenteritis for an incidence of 1.52 episodes per person-year.

A second study to examine gastroenteritis of unknown etiology was performed by the same investigators using the 1948–1950 subset of the data from the above study ([Dingle \*et al.\* 1953, 1964](#); [Hodges \*et al.\* 1956](#)). In this subset study, gastroenteritis was defined as any one or more of the following three conditions preceded by at least 5 symptom-free days: (1) diarrhea, (2) vomiting, or (3) abdominal pain. Participants reported 1466 episodes of gastroenteritis defined using these criteria. However, 362

episodes were considered to be secondary to other causes as explained by descriptions found in the records – these cases were not included in the analysis. Among these excluded cases were 116 episodes of gastrointestinal symptoms attributed to acute infectious diseases, such as streptococcal infections, measles, chickenpox, and bacterial gastroenteritis. Therefore, only 1104 episodes of infectious gastroenteritis of unknown etiology were analyzed for an overall incidence of 1.6 episodes per person-year (Hodges *et al.* 1956; Dingle *et al.* 1964). A large number of these unexplained episodes were hypothesized to represent acute, infectious, nonbacterial gastroenteritis. Among the children in this cohort, infants younger than 1 year of age had the lowest incidence of infectious gastroenteritis of unknown etiology (1.2 episodes per person-year) and children 4 years of age had the highest incidence (2.6 episodes per person-year). Adults had an incidence of 1.2 episodes per person-year. The incidence of infectious gastroenteritis of unknown etiology was lowest in the summer from May to August and highest in the late autumn and early winter, peaking in October and November (Hodges *et al.* 1956). The proportion of the 1104 episodes associated with either diarrhea or vomiting cannot be determined from the information provided, but diarrhea occurred in 56% and vomiting in 53% of a subset of 683 cases of gastroenteritis that occurred at least 6 days after the onset of respiratory symptoms (Dingle *et al.* 1956, 1964). Investigators observed that when gastrointestinal and respiratory symptoms in the same case-patient were temporally related, the onset of gastrointestinal symptoms was concurrent with or followed the onset of respiratory symptoms; gastrointestinal symptoms did not precede respiratory symptoms. Of the 1104 unexplained gastrointestinal illness cases analyzed, approximately 20% comprised what investigators termed respiratory–gastrointestinal syndrome. This syndrome consisted of cases in which the gastrointestinal and respiratory symptoms presumably had a common etiology and in which gastrointestinal symptoms began the same day as or within a few days after respiratory symptoms. Similarly, this syndrome accounted for an estimated 5% of common respiratory disease in this population (McCorkle *et al.* 1956). When persons with respiratory–gastrointestinal syndrome were excluded, the incidence of infectious

gastroenteritis of unknown etiology was 1.3 episodes per person-year. This figure would likely have been slightly higher if some of the cases of known bacterial gastroenteritis had been included in the analysis.

From August 1 1961 to March 31 1965, the New York Virus Watch Program followed a highly select population in the metropolitan New York area to gain information concerning viral agents detectable by *in vitro* culture methods available at that time (Fox *et al.* 1966). Two contrasting communities were selected for the study: a large urban housing project and a relatively isolated rural island community. Both were middle-income, predominantly white communities. Investigators used non-random selection techniques to enroll families with children 1–10 years of age. Families with newborns were recruited partway through the study. In each family, a parent recorded any illness in the family on a form that a nurse would pick up and review on a bi-weekly basis. At this time, routine fecal and respiratory samples were collected. Specimens were also collected upon report of illness. Signs and symptoms were coded by the field nurse and later reviewed by a pediatrician or a supervising nurse. Illnesses were then classified into categories based on the predominant symptoms. In total, 178 families with 791 persons were enrolled and contributed 882 person-years of observation. The investigators analyzed the occurrence of enteric and respiratory illness, though they did not provide a definition for enteric illness in their paper. There were approximately 844 episodes of enteric illness for a rate of 1.0 episode per person-year. When cases with combined respiratory and gastrointestinal symptoms were excluded, there remained approximately 630 cases of enteric illness alone for a rate of 0.7 episodes per person year.

From November 1965 to August 1969, the Seattle Virus Watch Program followed a cohort of families to assess infections with respiratory or enteric viruses recoverable in cell cultures (Fox *et al.* 1972). Two groups of families were non-randomly recruited throughout the study period from a large comprehensive prepaid medical care plan. This plan covered approximately 10% of the population of the Seattle, WA metropolitan area. For logistical reasons, participants came from the northern two-thirds of metropolitan Seattle. In total, 215 predominantly white middle-income families with newborn infants were enrolled for 2-year periods of

observation. A nurse visited the first group of 149 families on a bi-weekly basis to collect and review illness records kept by the mother for the entire family. During these visits, routine fecal and respiratory specimens were collected. Supplemental specimens were collected upon report of illness. Mothers were requested to notify investigators when illness occurred between visits. The 149 Group 1 families contributed 965 person-years of observation and approximately 85% of these families stayed in the study until their 2-year observation periods were completed or the study terminated. The 66 Group 2 families were either recruited after the monthly quota for Group 1 families was filled or preferred the less intense form of observation provided for Group 2. In Group 2, the mother was contacted weekly by telephone for information about illnesses in the family. Fecal and respiratory specimens were collected only upon report of illness and no more than twice a year. The 66 Group 2 families contributed 431 person-years of observation but 51% of these families withdrew from the study before their 2-year observation periods were completed or the study terminated. This study used the same classification of enteric and respiratory illnesses as the New York Virus Watch study, although, again, the symptomatology of enteric illness was not defined. When the cases with enteric symptoms alone, without respiratory symptoms, were analyzed, the Group 2 families reported fewer enteric illness episodes than the Group 1 families (0.2 vs. 0.3 episodes per person-year), although both groups had similar age distributions. Overall, participants reported 0.3 enteric illness episodes per person-year. Children 2–9 years of age had the highest age-specific rate of 0.5 episodes per person-year.

From November 1965 to December of 1971, the incidence of acute enteric illness was assessed in Tecumseh, MI (Monto *et al.* 1970, 1971; Monto & Koopman 1980), a city of approximately 10,000 persons. Following a census of the entire community, households were randomly sampled and recruited for a 1-year observation period, after which time they were replaced by other households. Recruitment continued throughout the 6-year study period. From November 1965 to May 1969, investigators only enrolled households with at least one child of school age or younger and with all adults younger than 45 years of age. These eligibility criteria changed in May 1967 to also include families with older adult members (Monto *et al.* 1971) and by

1968 these older families constituted approximately half of the participating households (Monto *et al.* 1970). One adult member of each household was contacted weekly, usually by telephone, and asked about the onset of acute illnesses among family members; illnesses were followed to their conclusion date during subsequent weekly telephone calls. If at least 2 symptom-free days had passed between periods of reported illness, the latter illness was recorded as a new event (Monto *et al.* 1971). Families were questioned about general symptoms and about specific respiratory and gastrointestinal symptoms. Enteric symptoms were divided into four syndromes: (1) diarrhea without vomiting; (2) vomiting without diarrhea; (3) diarrhea and vomiting combined; and (4) upset stomach and/or nausea without the other symptoms. Respiratory specimens were collected from persons reporting respiratory symptoms. In total, 4905 participants who remained for a full year of surveillance were included in the analyses (Monto & Koopman 1980). The overall incidence of self-reported enteric illness (which included all four syndromes) was 1.20 episodes per person-year. The incidence of enteric illness was highest in children younger than 5 years of age (1.95 episodes per person-year) and declined in older children. Adults 20 years of age and older experienced the lowest rate of enteric illness at 1.00 episode per person-year (Monto & Koopman 1980). Enteric illness frequency was highest in the winter from December to February and lowest in the summer from June to August. The incidence rates for diarrhea with or without vomiting, diarrhea alone, and vomiting without diarrhea were 0.63, 0.40, and 0.35 episodes per person-year, respectively. These incidence estimates included persons with concurrent respiratory symptoms, defined by five syndromes including lower respiratory symptoms, upper respiratory symptoms, laryngotracheal symptoms, nonproductive cough, and earache (Monto & Koopman 1980). Respiratory symptoms were reported in 27% of cases of enteric illness and enteric symptoms were reported in 11% of cases of respiratory illness. Investigators found that, in general, concurrent respiratory and enteric symptoms appeared to be the result of a single illness and not due to overlapping simultaneous infections with different pathogens. When persons with combined enteric and respiratory symptoms were excluded, the overall incidence of enteric illness (including all 4 enteric illness syndromes) was 0.88 episodes per person-year.

Insufficient data were provided by the authors to determine the separate incidence rates of each of the four enteric illness syndromes in the absence of respiratory symptoms. Overall, 52% of enteric illness cases were accompanied by restriction of ordinary daily activity for an incidence of 0.63 activity-restricting enteric illness episodes per person-year. The types of restriction of daily activity were not further defined.

From August 1975 to July 1977 investigators conducted a prospective community-based study of suburban families with one to four children in Charlottesville, VA (Hughes *et al.* 1978; Guerrant *et al.* 1990). Participants kept daily records of AGI symptoms, defined as (1) vomiting, (2) diarrhea, or (3) a combination of two or more gastrointestinal and systemic symptoms, including nausea, abdominal cramps, malaise, fever, chills, headaches, myalgia, and anorexia. Families were visited at least once every 2 weeks. Fecal swabs were taken when symptoms were reported. Forty-five families (169 individuals) were observed for a total of 173.6 person-years. Investigators found 334 cases of AGI for an incidence of 1.9 cases per person-year. This estimate included cases of vomiting alone and cases consisting only of milder non-diarrheal symptoms. The highest attack rate for AGI was in children younger than 3 years of age (2.46 episodes per person-year) and the rate decreased with increasing age. A seasonal peak was noticed in the winter months, with 38% of all cases occurring in November to January.

In 1988, Garthright *et al.* (1988) recalculated the rates of intestinal infectious disease (IID) for both the Cleveland (Dingle *et al.* 1964) and Tecumseh (Monto & Koopman 1980) studies, adjusting to the 1980 US Census age distribution and population estimates. They defined IID as an acute episode of vomiting or diarrhea without a plausible noninfectious origin (such as chemical poisoning or an adverse reaction to medication) and without respiratory symptoms. Therefore, this definition excluded some cases of enteric illness that occurred at the same time as an unrelated respiratory illness, as well as mild enteric illnesses that may have included other gastrointestinal symptoms (such as nausea or abdominal pain) but that lacked vomiting or diarrhea. For the Cleveland study, researchers estimated that the 1980 US incidence of IID would have been 0.71 cases per person-year (compared to the

1948–1950 rate of 1.3 cases of infectious gastroenteritis of unknown etiology per person-year excluding respiratory symptoms). For the Tecumseh study, researchers estimated that the 1980 US incidence of IID would have been 0.62 cases per person-year (compared to the 1965–1971 rate of 0.88 cases of enteric illness per person-year excluding respiratory symptoms). From the Tecumseh study, the researchers were also able to estimate rates of activity restriction associated with IID. They calculated that the 1980 US incidence for IID with at least 1 full day of restricted activity was 0.32 cases per person-year.

In 1999, Colford *et al.* (2002) conducted the Pilot Water Evaluation Trial (Pilot WET), a randomized, controlled, triple-blinded intervention trial of water treatment devices in private residences. The primary purpose of the study was to determine if participants could be successfully blinded to the type of treatment device, in preparation for a larger study at a later date. A secondary purpose of the study was to estimate the annualized incidence of highly credible gastrointestinal illness (HCGI). The study area included single-family dwellings served by the Contra Costa Water District in northern California. All households in this water district were contacted by flyers, followed by mailings, and asked to participate. Households were eligible if the families owned the home, used municipal tap water as their primary drinking water source, and had no household members with serious immunosuppression. Eligible households willing to participate were randomized to the different treatment groups. Each family was asked to participate for 16 weeks. Individual household members were each asked to complete a health diary. An adult completed the diary for children younger than 12 years of age and for persons unable to do so. The health diaries were to be mailed to the investigators every 2 weeks. HCGI was defined as any of the following four conditions preceded by at least 6 symptom-free days: (1) vomiting; (2) watery diarrhea; (3) soft diarrhea and abdominal cramps occurring together on any day; or (4) nausea and abdominal cramps occurring together on any day. Participants with diarrhea were asked to indicate the days on which they had two or more loose stools. HCGI episodes due to other plausible etiologies (e.g. pregnancy) were *not* excluded, unlike in other studies. Of the 29 415 homes that received flyers, 573 households contacted the investigators but only 77 households with 236 persons were

eligible to participate. Ninety-six percent of these households completed all 16 weeks of the trial. There were 103 episodes of HCGI during 29.6 person-years at risk in the sham treatment group (3.48 episodes per person-year). This rate is much higher than those reported in other studies. Investigators hypothesized that, because this trial was fairly short, participants may have been more likely to report, or even over-report, illness symptoms when enrollment and participation instructions had been recently emphasized. Furthermore, study participants had a visible treatment device installed in their homes and were paid for the return of health diaries throughout the study which may have further encouraged symptom reporting. Also, the case definition used was not as strict as in other studies and may have captured more instances of mild illness.

From October 2000 to May 2002, Colford *et al.* (2005) conducted the larger companion trial to the Pilot WET study just described. This was a randomized, controlled, triple-blinded, crossover intervention study performed in the Davenport/Bettendorf area of Scott County, Iowa. The principle objective was to measure the change in incidence of HCGI from the use of a supplemental in-home drinking water treatment device. This community was served by a single drinking water treatment facility, taking its water from a microbiologically-challenged surface water source. The water utility supplied investigators with a list of all 40,403 residential addresses it served. Apartments, post office boxes, out-of-service addresses, and addresses outside the service area were excluded. The remaining households were contacted and asked to participate. A total of 1421 households responded and were assessed for eligibility. Households were excluded if they contained an employee of the water utility, consumed less than 75% of their in-home drinking water from the tap, or contained an immunocompromised member or one who had been advised to drink only specially treated water. Households were randomly assigned to 26 weeks of either an active or a sham treatment device (Cycle A), a 2-week washout period, then a crossover period of 26 weeks using the alternate device (Cycle B). Participants recorded daily occurrences of illness in health records. Adults recorded illnesses for children younger than 12 years of age. The health records were to be mailed back to investigators every week (personal communication with investigators). HCGI was defined as any of the following four conditions preceded by at

least 6 symptom-free days: (1) vomiting; (2) watery diarrhea; (3) soft diarrhea and abdominal cramps; or (4) nausea and abdominal cramps. Final enrollment included 456 households and 1296 individuals for 1123 person-years of observation. Overall, 84% of the participants completed the full 1-year study period. In the sham treatment group, there were 672 reported episodes of HCGI in Cycle A and 476 reported episodes of HCGI in Cycle B for rates of 2.40 and 1.82 episodes per person-year, respectively (average 2.11). As with the Pilot WET study, these rates are much higher than the rates reported in other studies. Again, the case definition used was not as strict as in other studies and may have captured more instances of mild illness. Furthermore, the presence of a visible device may have altered participant behavior or illness reporting in unknown ways to change the estimated incidence of HCGI. When only diarrhea was considered (that is, three or more instances of diarrhea during the day), 208 episodes were reported in Cycle A for an incidence of 0.74 episodes per person-year and 142 episodes were reported in Cycle B for an incidence of 0.54 episodes per person-year (average 0.64). These rates of diarrhea are more in keeping with estimates from other studies. Investigators noticed a decline in the frequency of reported gastrointestinal illness episodes over time, similar to that observed in other intervention trials in Canada (Payment *et al.* 1991, 1997) and Australia (Hellard *et al.* 2001). They hypothesized that this was likely due to a loss of enthusiasm for the study.

### Estimates from retrospective cross-sectional studies in the United States

In addition to the prospective cohort studies and intervention trials, there have been several recent retrospective population-based cross-sectional surveys conducted in different populations across the United States to estimate the rate of AGI. In 1993, investigators performed a random-digit dialed telephone survey of 1197 household members from 462 households in all 22 Washington, DC residential zipcode areas (representing approximately 0.2% of residents) (Akhter *et al.* 1994). Participants were asked about the occurrence of diarrhea, defined as three or more loose or watery stools in a 24-hour period, from November 22 to December 5 1993. This was the 2-week period prior to the failure of a filtration device in a local drinking water-treatment facility. During this

period, 2.8% of respondents reported diarrhea, for an annualized incidence of 0.7 episodes per person-year.

Between August 11 and October 6 1997, investigators conducted a national, retrospective, cross-sectional, household, telephone survey to estimate the prevalence of abdominal pain, bloating, and diarrhea in the US adult population (Sandler *et al.* 2000). They used the Genesys Sampling System to first identify and remove business and nonworking telephone numbers from directory listings (Abt Associates Inc. 2002) and then generate a random sample of telephone numbers from the 48 contiguous states and Washington, DC. The telephone numbers were called in order until a household was reached. At that time, the first eligible permanent resident was interviewed. Persons were eligible to participate if they were 18–75 years of age, a permanent resident of the household, able to converse in English, and mentally competent to be interviewed. Following the interview, a household census was conducted and one person was then selected at random. If this person was the one already interviewed, the household was considered complete. If another person was randomly chosen, arrangements were made to interview that person but only in a sample of the households. Only the interviews from the randomly selected household members were retained for analysis if more than one interview was conducted per household. Persons were asked if they had experienced (1) lower abdominal pain or discomfort; (2) bloating or distension; and (3) loose stools or diarrhea during the month prior to interview. These symptoms were not otherwise explained or defined. In total, 4908 households were contacted but 788 (16%) were ineligible, primarily due to age and language barrier. From the eligible households, 2684 adults agreed to participate and 2510 (94%) completed the interview and were included in the analyses. Only 17% of these participants were selected completely at random. Nearly 80% of the 2510 participants were white, 62% were women, 56% were married, and the majority had a high school education. Of the demographics collected, only the reported household income was similar to that of the United States population. Overall, 674 participants (26.9%) reported loose stools or diarrhea in the previous month, for an annualized prevalence of 3.2 episodes per person-year.

From 1996 to 2003, the Foodborne Diseases Active Surveillance Network (FoodNet) conducted four 12-month

cycles of a population-based telephone survey to determine the prevalence of self-reported diarrheal illness. Approximately 150 persons were interviewed per month in each FoodNet site and the number of FoodNet sites increased over the four survey cycles (Jones *et al.* in press). During the first 12-month cycle, conducted from July 1996 to June 1997, 9003 completed interviews were obtained from persons residing in five FoodNet sites with a population of 14.3 million people, representing approximately 5% of the US population (Herikstad *et al.* 2002). During the second cycle, conducted from July 1998 to June 1999, 12,755 completed interviews were obtained from persons residing in seven FoodNet sites with a population of 29 million, representing approximately 11% of the US population (Imhoff *et al.* 2004). During the third cycle, conducted from February 2000 to January 2001, 14,647 completed interviews were obtained from eight FoodNet sites with a population of 33 million, representing approximately 12% of the US population (CDC 2005b). During the fourth cycle, conducted from March 2002 (CDC 2005b) to February 2003 (Jones *et al.* in press), 16,435 completed interviews were obtained from nine FoodNet sites with a population of 37.6 million, representing 14% of the US population (Jones *et al.* in press).

FoodNet investigators employed the same survey methodology developed by CDC's Behavioral Risk Factor Surveillance System (BRFSS) (Gentry *et al.* 1985; Remington *et al.* 1988; Tourangeau 2004; Jones *et al.* in press). Telephone numbers in the FoodNet catchment area were screened using Genesys-ID software (Abt Associates Inc. 2002) to remove business and non-working numbers before contacting households using a single-stage random digit dialing sampling method (Jones *et al.* in press). One person per household was randomly selected to participate in the survey from a roster of household members of all ages. Parents or guardians responded for children younger than 12 years of age (Imhoff *et al.* 2004). Only English-speaking persons were interviewed until the fourth survey when the survey was also administered in Spanish (Jones *et al.* in press).

Respondents were asked about episodes of diarrhea in the four weeks (1996–1997 and 1998–1999 survey cycles) or month (2000–2001 and 2002–2003 survey cycles) prior to the interview (Jones *et al.* in press). Diarrhea was defined



as three or more loose stools in a 24-hour period. Diarrheal illness was defined as diarrhea resulting in an impairment of daily activities (e.g. missing time from work, school, recreation or vacation activities, or work in the home) or diarrhea with a duration greater than 1 day. In the first and second cycles, respondents reporting diarrhea were asked about other symptoms experienced during their illness, including vomiting, fever, and abdominal pain. In the third and fourth cycles, all respondents, including those without diarrhea, were asked about vomiting; those respondents reporting any diarrhea or vomiting were also asked about concurrent respiratory symptoms.

A comparison of the prevalence of diarrheal illness from all four cycles of the FoodNet survey (1996–1997, 1998–1999, 2000–2001, and 2002–2003) is awaiting publication (Jones *et al.* in press). For this comparison, investigators equated the 28-day period used in the first two cycles with the 1-month period used in the last two cycles. If more than one diarrheal episode occurred during the period of interest, only the most recent episode was considered. Respondents who indicated they had any long-lasting or chronic illness or condition in which diarrhea or vomiting was a major symptom (such as irritable bowel syndrome, ulcerative colitis, partial removal of stomach or intestines, stomach or esophagus problems, or Crohn's disease) were excluded from the analysis. Persons reporting concurrent diarrhea and respiratory symptoms were not excluded.

Data from each cycle were weighted by age, sex, and location, using the projected census numbers from the corresponding years, to ensure that the survey populations were demographically representative of the FoodNet catchment areas. Data were also weighted using the number of eligible respondents per household and the number of telephone lines per household to compensate for the unequal probabilities of selection between and within households. Cooperation rates were calculated using the upper bound response rate formula provided by the Council of American Survey Research Organizations (CASRO) (White 1983; Remington *et al.* 1988). These rates include survey refusals, terminations, and completed interviews. The upper bound CASRO response rate declined over time from 71% in the 1996–1997 survey cycle to 33% in the 2002–2003 survey cycle (Jones *et al.* in press).

For the purposes of this paper, we used the FoodNet population survey data to estimate the prevalence of AGI in the United States for the period 2000–2003. As discussed, the first and second survey cycles did not record information on respiratory symptoms or vomiting without diarrhea. Therefore, only data from the third and fourth cycles were used for this estimate. We defined AGI as diarrheal illness and/or vomiting of infectious or non-infectious origin, excluding cases with concurrent respiratory symptoms (defined as cough and/or sore throat). Overall, 8.8% of respondents reported diarrheal illness and/or vomiting in the month prior to interview; of these, 39% reported having respiratory symptoms. Therefore, the overall prevalence of self-reported AGI in the month prior to interview was 5.4%, a rate of 0.65 episodes per person-year. The prevalence of AGI did not differ significantly between the third and fourth cycles (Table 1). The prevalence of AGI was higher in females than males. Children younger than 5 years of age reported the highest prevalence while persons 65 years of age and older reported the lowest prevalence. White respondents reported a higher prevalence than African Americans or Hispanics. The prevalence reported by adults with less than a high school education was lower than that of high school graduates. The prevalence of AGI was higher in the winter months compared to the summer months.

## Studies from other developed countries

### Australia

During the late 1990s, Hellard *et al.* (2001) conducted a drinking water intervention study in Australia. In this randomized, double-blinded controlled trial, households in Melbourne that (1) received their water from a defined catchment area; (2) had at least four eligible family members, including at least two children aged 1–15 years; and (3) owned or would be purchasing their homes were eligible for the study. In addition to the household eligibility criteria, each participant had to consume at least one glass of tap water per day. Individuals who had immunosuppression, had a chronic diarrheal illness, or were on long-term antibiotic therapy were excluded. Invitations to participate were distributed by mail, through advertisements in local

**Table 1** | Prevalence and factors associated with reporting AGI in the month before interview, FoodNet Population Survey 2000–2003

	AGI	Bivariate	Multivariate	
	%	OR	OR	95%CI
<b>Cycle</b>				
3 <sup>rd</sup> (2000–2001)	5.1	0.93	0.89	0.75–1.05
4 <sup>th</sup> (2002–2003)	5.6	1.00	1.00	–
<b>Sex</b>				
Male	4.7	0.74	0.71	0.61–0.83
Female	6.1	1.00	1.00	–
<b>Age (years)</b>				
< 5	8.3	1.94	2.18	1.60–2.95
5–17	5.9	1.29	1.52	1.14–2.05
18–35	7.0	1.51	1.56	1.30–1.86
36–54	4.6	1.00	1.00	–
55–64	3.8	0.79	0.79	0.61–1.01
≥ 65	2.6	0.54	0.53	0.40–0.71
<b>Race</b>				
White	5.7	1.00	1.00	–
African American	4.2	0.72	0.68	0.49–0.94
Hispanic	4.1	0.73	0.64	0.47–0.87
<b>Education</b>				
Less than high school	5.3	0.92	0.79	0.60–1.04
High School graduate	5.7	1.00	1.00	–
College graduate	5.2	0.93	0.90	0.77–1.06
<b>Residence</b>				
Urban	4.9	0.81	0.96	0.76–1.22
Suburban/town	5.8	1.06	1.07	0.85–1.35
Rural	5.4	1.00	1.00	–
<b>Medically insured</b>				
Yes	5.3	1.00	1.00	–
No	6.4	1.15	1.18	0.90–1.53
<b>Season</b>				
Spring	5.6	1.13	1.17	0.94–1.45
Summer	5.2	1.00	1.00	–
Autumn	4.4	0.82	0.83	0.66–1.05
Winter	5.8	1.22	1.29	1.04–1.60

newspapers, and through primary schools, child-care centers, maternal health centers, and shopping malls. Interested families were asked to phone the study center if they met the inclusion criteria. Eligible families who called the study center were then mailed an information booklet about the study, visited at home, and enrolled. In total, 600 families (2811 individuals) were recruited and were randomly assigned to receive real or sham water treatment units installed in their kitchens. Families were blinded as to the type of unit they received. Highly credible gastroenteritis (HCG) was defined as any of the following symptoms in a 24-hour period: (1) two or more loose stools; (2) two or more episodes of vomiting; (3) one loose stool with abdominal pain or nausea or vomiting; or (4) one episode of vomiting with abdominal pain or nausea. Cases were considered distinct if the participant experienced at least 6 symptom-free days in between episodes. Families completed and returned health diaries by mail every 4 weeks. Participants were asked to collect fecal specimens during any episodes of HCG. A total of 600 families (2811 persons) were enrolled in the study and contributed 3333 person-years of health diary data during a 68-week period between September 1997 and February 1999 (excluding two 4-week periods over each Christmas season). There were 1352 cases of HCG reported during this period among persons with the sham units, for an incidence of 0.82 cases per person-year. Investigators noticed a decline in the reported incidence of HCG from the first 13 weeks of the study compared to the last 13 weeks. They believed this reflected an underreporting of symptoms due to declining motivation over time. Investigators found no significant difference in the incidence of HCG between the different treatment groups.

During a 12-month period from September 2001 to August 2002, the National Centre for Epidemiology and Population Health, on behalf of OzFoodNet, conducted a national cross-sectional computer-assisted telephone interview (CATI) survey to estimate the incidence of infectious gastroenteritis (Ashbolt *et al.* 2002; Hall *et al.* 2002, 2005; Scallan *et al.* 2005). In this national gastroenteritis survey, private households across Australia with fixed telephone lines were sampled using random-digit dialing. The household member with the last birthday was selected to be interviewed. Interviews were conducted in seven languages.

Participants were asked about symptoms in the 4 weeks preceding the interview. Infectious gastroenteritis was defined as: (1) three or more loose stools; or (2) two or more episodes of vomiting; or, if respiratory symptoms were present, (3) four or more loose stools; or (4) three or more episodes of vomiting in a 24-hour period in the previous 4 weeks. Persons were excluded if they identified a noninfectious cause for their symptoms, and an adjustment made for persons with gastrointestinal symptoms secondary to a respiratory infection. The study interviewed 6087 participants over the 12-month period. The cooperation rate was 68.2%, defined as the number of completed interviews divided by the number of completed interviews plus the number of non-interviews that involved the identification of, and contact with, an eligible respondent (Scallan *et al.* 2005). Data were weighted to the Australian population by age and sex and the estimated incidence of infectious gastroenteritis was 0.92 cases per person-year (Hall *et al.* 2005). Analysis suggested that the incidence of gastroenteritis varied by region, age, and medical history of chronic illness (Ashbolt *et al.* 2002). To make the results nationally representative, data were weighted by age, sex, geographic location, household size, and the number of residential telephone lines. Using diarrhea as the outcome, defined as three or more loose stools or bowel movements in any 24-hour period, the weighted rate of diarrhea was 0.83 episodes per person-year. The incidence of diarrhea was highest among children younger than 5 years of age (8.2%) and adults 25–44 years of age (7.8%) and lowest among adults 65 years of age and older (3.6%) (Scallan *et al.* 2005).

The Victoria Department of Human Services estimated the annualized incidence of gastroenteritis in persons 18 years of age or older using questions included in the Victorian Population Health Survey conducted between August and November 2001 (Ashbolt *et al.* 2002). This was a computer-assisted telephone interview (CATI) survey. Participants aged 18 years or older were randomly selected and asked if they had experienced gastroenteritis in the 4 weeks preceding the interview. An episode of gastroenteritis was defined as (1) three or more loose stools or (2) two or more episodes of vomiting in a 24-hour period. Participants who reported a chronic condition in which diarrhea or vomiting was a predominant symptom were excluded from analysis. Of the 7494 adults interviewed, 760 reported having

gastroenteritis in the previous 4 weeks, for an unweighted annualized incidence of 1.3 episodes per person-year.

Similarly, the Queensland Department of Health estimated the statewide incidence of diarrhea using relevant questions included in the Queensland Health 2001 Omnibus Survey (Ashbolt *et al.* 2002; Queensland OzFoodNet 2002). This survey was conducted between March 12 and May 3 2001. A random sample of private households with fixed telephone lines was selected from numbers listed in at least one of the telephone directories for Queensland published over the previous 5 years. Eligible households had at least one person 18 years of age or older. Persons unable to speak English, having a mental or physical disability preventing the interview, absent from the household, or visiting the household were excluded. Data was collected on two age groups: adults 18 years of age or older, and children 7 months to 4 years of age (through a nested survey of parents or caregivers). Within the household, the person in the age group of interest who had the most recent birthday was asked to participate. Participants were asked about the occurrence of diarrhea in the 1 month preceding the interview. Diarrhea was defined as three or more loose stools in a 24-hour period. A person with a known chronic condition in which diarrhea was a predominant symptom was excluded unless the respondent believed that the diarrhea was unrelated to the chronic condition. Estimates of the incidence of diarrhea assumed each case-patient had only one episode during the previous month. Of the 3081 adults interviewed, 418 were identified as having had acute diarrhea in the preceding month. Of the 386 children aged 7 months through 4 years enrolled in the study, 73 were identified as having had acute diarrhea in the preceding month. When adjusted for seasonality and the age distribution of persons in Queensland, the estimated annualized incidence of diarrhea for adults was 1.46 episodes per person-year and for children was 1.89 episodes per person-year. Assuming the incidence of acute diarrheal illness among children 5 through 17 years of age was between that of adults and young children, investigators estimated the annual incidence of diarrhea in Queensland for this age group was 1.49 episodes per person year, adjusted for seasonality. Since this study was conducted over a 2-month period, investigators adjusted the incidence rates for seasonality by reducing the total monthly episodes of

diarrhea to 83% of their original values. This factor was chosen because Queensland surveillance data of *Salmonella* and *Campylobacter* cases over a 3-year period revealed that, on average, the monthly reported case totals in May to January were 83% of those in February to April.

## Canada

In 1988–1989, [Payment \*et al.\* \(1991\)](#) conducted a randomized intervention study in a relatively homogeneous middle-class suburban area of Montreal to estimate the level of gastrointestinal illness attributable to tap water consumption. Households were randomly contacted using a directory of inhabited addresses for the study area. Households were eligible if they (1) were owner-occupied; (2) had French-speaking occupants; (3) had occupants who regularly consumed tap water; (4) had at least one child between the ages of 2–18 years living in the household; and (5) were willing to participate. Eligible households were then randomized to a regular tap water group and a filtered water group. Households in the latter group were supplied with under-the-sink filtration units. No attempt was made to blind participants as to which treatment group they were in. The health of household participants was monitored from March 1988 to June 1989, with a 2-month gap in surveillance in July and August 1988 due to summer vacation. Family health diaries were maintained and one family member completed and returned a self-administered questionnaire for all family members every 2 weeks. Follow-up with a staff nurse occurred by telephone every 2 weeks. Highly credible gastrointestinal (HCGI) symptoms were defined as (1) at least 1 symptomatic day of vomiting or liquid diarrhea with or without confinement to bed, medical consultation, or hospitalization; or (2) at least 1 symptomatic day of nausea or soft diarrhea combined with abdominal cramps with or without absence from school/work, confinement to bed, medical consultation, or hospitalization. Episodes with plausible etiologies other than waterborne disease (e.g. pregnancy) were excluded. New cases could occur in the same person only after 6 consecutive symptom-free days. A total of 3741 households were contacted and 606 (with 2408 individuals) were enrolled. Over the entire study period, household participation rates were 86% in the group consuming regular tap

water and 93% in the group consuming filtered water. The incidence for HCGI symptoms in the regular tap water group was 0.76 episodes per person-year. This rate was adjusted using Poisson regression methods to account for the correlation between repeated episodes in the same person. The incidence of HCGI symptoms was highest among children younger than 6 years of age and lowest among adults 50 years of age or older. As in the Davenport intervention trial ([Colford \*et al.\* 2005](#)), reports of HCGI symptoms declined across the study period, which could have resulted in an underestimate of the incidence.

Four years later, [Payment \*et al.\* \(1997\)](#) conducted another intervention trial in the same suburban Montreal community. This time households were randomly chosen from a list of families in the study area who were enrolled in a government income supplement program for families with children younger than 18 years of age (this program was independent of income level). Households were eligible if they (1) were located within the distribution system of the water filtration plant; (2) had French-speaking occupants; (3) had occupants who regularly consumed tap water; (4) had at least one child between the ages of 2–12 years living in the household; and (5) were willing to participate. For 16 months (September 1993 to December 1994), families with young children were randomly assigned to one of four groups: (1) regular tap water; (2) tap water from a continuously purged tap valve; (3) bottled plant water; and (4) purified bottled water. Participants were not blinded to their treatment status. A family diary of gastrointestinal and respiratory symptoms was kept and families were contacted by telephone every 2 weeks to obtain the information. The definition for an episode of highly credible gastrointestinal (HCGI) illness was the same as that used in the previous study. In total, 1062 families (5253 individuals) participated in the trial. The incidence of HCGI illness among the regular tap water group was 0.66 episodes per person-year. As with the previous study, this rate was adjusted using Poisson regression methods to account for the correlation between repeated episodes in the same person. The incidence of HCGI illness was highest among children younger than 6 years of age and lowest among adults 50 years of age or older. The highest incidence of HCGI illness was observed during autumn and winter and the lowest during the summer. The incidence was highest at the beginning of the trial in September 1993 and dropped steadily

as the trial progressed. A similar trend was seen in the Davenport (Colford *et al.* 2005) and earlier Montreal (Payment *et al.* 1991) trials, as well as in an Australian study (Hellard *et al.* 2001). However, owing to a 16-month study period, a rising trend beginning in September 1994 was observed, suggesting that the seasonal increase in the winter months may have been present in spite of what appeared to be reporting fatigue.

From February 1994 to February 1995, Raina *et al.* (1999) conducted a prospective cohort study of rural families drinking untreated well water to determine the relationship between consumption of *E. coli*-contaminated well water and gastrointestinal illness. Families from southern Ontario were recruited from participants in the Ontario Farm Groundwater Quality Survey (1991–1992) (Goss *et al.* 1998). This earlier study sampled water from 1292 of the estimated 500 000 water wells in Ontario, and the study conformed to a stratified random survey. It is unclear how the families participating in the Raina study were selected from this earlier study. Families in the Raina study were excluded if (1) they no longer used the same well as in the 1991–1992 study; (2) the household would contain fewer than two full-time residents during the study period; (3) the family did not drink well water; or (4) the family routinely treated the water. Children younger than 1 year of age at the start of the study and any persons absent from the household for more than 2 months during the study period were excluded from analysis. One contact person in each household completed a health diary for each family member. Interviewers telephoned the contact persons approximately once per month to collect the diary information. Gastrointestinal illness episodes were defined as diarrhea, with or without vomiting, occurring for 1 or more days with at least 5 symptom-free days separating episodes. The definition of diarrhea used in this study was not provided. Of the 442 families identified for potential inclusion in the study, 156 (35%) were enrolled and included in the final analysis. These 156 families included 531 individuals. Of these, 414 persons were considered to have non-contaminated water supplies during the study period because their wells tested negative for *E. coli* in all of five separate water quality tests staggered throughout the year. Among these 414 persons with non-contaminated well water, 25.8% reported at least one episode of gastrointestinal illness during the year, for an incidence of at least

0.26 episodes per person-year (counting only one episode per person per year). Gastrointestinal illness episodes were most frequent in February and March and fluctuated throughout the study period.

For the 3-month period from April 3 1995 to July 22 1995, Strauss *et al.* (2001) conducted a study to examine the relationship between microbiologic contamination of drinking water from private wells in rural communities in eastern Ontario and the incidence of AGI. Four rural communities were selected, representing a cross section of rural population in the area. The selection criteria for the communities were not described. Households within these communities were randomly selected using a phone book database. All households within each community were eligible for participation except those not consuming drinking water from a private well, and residents of retirement or nursing homes. Health information was collected on each household member using self-reported health diaries for a 28-day period. AGI episodes were defined as either (1) vomiting or liquid diarrhea, or (2) nausea or soft, loose diarrhea with abdominal cramps. Episodes included 1 or more symptomatic days, with at least 6 consecutive symptom-free days between episodes. For analytic purposes, only the first episode was considered. Of the 327 households initially contacted, 235 (72%) representing 647 persons agreed to participate. Of these persons, 619 (96%) completed the diaries for the full 28 days and were included in the analysis. One or more AGI episodes were identified in 51 (8.2%) participants for an annualized incidence of 1.1 episodes per person-year. Seasonality was not accounted for in this 3-month study period. Children 10 years of age or younger were found to be more likely to have AGI symptoms.

From February 2001 to February 2002, Majowicz *et al.* (2004) conducted a retrospective cross-sectional telephone survey in the city of Hamilton to assess the magnitude and distribution of self-reported AGI. Participants were randomly selected from a list of Hamilton residential telephone numbers in an electronic directory. One individual per household was randomly selected to participate by identifying the person with the next birthday. Interviews were conducted over 12 months, with approximately the same number of interviews completed each month. AGI was defined as any vomiting or diarrhea (loose stool or stool

with abnormal liquidity) in the 28 days prior to the interview. Episodes due to other plausible etiologies (e.g. excess alcohol intake) were not excluded. Episodes due to pre-existing conditions (e.g. Crohn's disease, irritable bowel syndrome, lactose intolerance, and pregnancy) were excluded from the numerator but not the denominator. Incidence rates were adjusted to account for the likely proportion of pre-existing cases that actually began before the 28-day period. Of the 9543 persons contacted to participate in the study, 3496 (37%) agreed to participate. Of these, 351 reported an episode of AGI in the preceding 28 days; 138 reported more than one episode; however only the last episode was counted to minimize the potential for recall bias. The adjusted incidence was 1.3 episodes per person-year. The incidence of AGI was highest among children 0–9 years of age (16%) and adults 20–24 years of age (18%) and lowest among adults 70–74 years of age (4%). The incidence peaked in April, with another smaller peak in October.

### France

Between October 1998 and June 1999, *Gofti-Laroche et al. (2003)* conducted a prospective cohort study in the French Alps as part of a larger study to assess the risks of acute digestive conditions (ADC) in relation to protozoal contamination of drinking water. Volunteer families in communities in the Isère and Savoie departments of southeast France that were supplied by four public drinking water systems were recruited through notices distributed through the media, schools, and town councils, and from drinking water utility files. All four water systems were considered vulnerable to microbial contamination. Each family completed self-administered daily questionnaires concerning the health problems of each family member. Each weekday, 20% of the families were telephoned by an interviewer who recorded all incident cases of ADC occurring since the previous call. An ADC was defined as an episode of abdominal pain, nausea, vomiting, and/or diarrhea. The definition of diarrhea used in this study was not provided. A diarrheic episode (DE) was defined as diarrhea with at least one other digestive condition (unspecified) or fever. A case of gastroenteritis (GE) was defined as an episode of diarrhea with fever or

vomiting. A total of 176 households, representing 544 persons, were enrolled in the study providing 252.6 person-years of observation. These persons were not representative of the local population with respect to socioeconomic status (white-collar workers and employees were over-represented; blue-collar workers and farmers were under-represented) and age (children were over-represented). There were 712 reported cases of ADC, 105 cases of DE, and 46 cases of GE among all 4 drinking water systems combined. The overall annualized incidence rates per person-year were 2.8 for ADC, 0.4 for DE, and 0.2 for GE.

### The Netherlands

Between March and July 1991, a population-based prospective cohort study was conducted in four regions of the Netherlands (*Hoogenboom-Verdegaal et al. 1994; de Wit et al. 2000*). Ten municipalities were chosen to represent the different geographical regions across the country: three rural, two urban, and five mixed rural/urban. Participants were randomly selected from the population registers of each municipality; only one person per household was eligible for the study. Participants were asked to return weekly questionnaires about the presence and duration of gastroenteritis. Two grades of gastroenteritis were defined. Grade 1 constituted diarrhea (two or more stools a day) or vomiting with two or more additional symptoms occurring within the 1-week period. Grade 2 constituted diarrhea or vomiting with two or more additional symptoms occurring on the same day and lasting at least 2 days within the 1-week period. The additional symptoms included nausea, abdominal pain, cramps, and blood or mucus in the stool. Grade 2 gastroenteritis was more severe and defined a subset of Grade 1 gastroenteritis. An episode of gastroenteritis was considered to be over if 2 weeks had passed without further symptoms. Participants were also asked to submit a stool sample if symptoms developed. Of the 6243 persons invited, 2257 (36%) agreed to participate. Over the 17-week study period, there were 425 Grade 1 cases (0.57 cases per person-year), of which 115 (0.15 cases per person-year) could also be classified as Grade 2. The annualized incidence of acute gastroenteritis was highest among children younger than 10 years of age (0.98 cases per

person-year) and lowest among persons 60 years of age or older (0.30 cases per person-year) (de Wit *et al.* 2000). Several years later, de Wit *et al.* (2000) recalculated the annualized incidence of Grade 1 gastroenteritis standardizing for age and sex using the 1991 Dutch mid-year population and estimated it at 0.45 cases per person-year. Investigators stated that the standardized incidence was lower because of an over-representation of children under 10 years of age.

In the late 1990s, de Wit *et al.* (2001) conducted a prospective medical practice-based cohort study (called Sensor) to assess the incidence of gastroenteritis in the Netherlands. To include an entire year of data in the study, the investigators used two consecutive 6-month cohorts from December 14 1998 to June 13 1999 and from June 14 1999 to December 13 1999. Participants were recruited by age-stratified random sampling of all persons registered at 44 general practices within a sentinel network. Participants were asked to return a history card every week reporting the presence or absence of gastrointestinal symptoms in the previous 7 days. Those who developed diarrhea or vomiting were also asked to telephone the study coordinator and submit a stool specimen. Gastroenteritis was defined as (1) diarrhea (three or more loose stools in 24 hours); or (2) vomiting (three or more times in 24 hours); or (3) diarrhea with two or more additional symptoms; or (4) vomiting with two or more additional symptoms in 24 hours. The additional symptoms were diarrhea, vomiting, abdominal pain, cramps, fever, nausea, and blood or mucus in the stool. Cases with an obvious noninfectious cause were excluded. New cases could occur in the same person only after a 2-week symptom-free period. In total, 11,569 persons were invited and 4860 (42%) participated. The total follow-up time was 2229 person-years with 76% of participants completing the full 26 weeks of observation. During the follow-up period, 1050 case episodes occurred. This figure included multiple cases in the same persons. The overall incidence, standardized by cohort, age, and sex (according to the distribution in the Dutch population in 1999), was 0.28 episodes per person-year. The incidence of gastroenteritis was highest among children 1–4 years of age (0.90 episodes per person-year) and lowest among children 12–17 years of age (0.16 episodes per person-year). Adults 65 years of age or older also had a low incidence (0.19 cases

per person-year). A seasonal variation in incidence was observed, with the highest rates during the winter months. The incidence reported in this study was lower than that reported in the previous Dutch study. The investigators speculated that this decrease may have been due to an actual decrease over the decade but stated that it was more likely that the incidence in 1991 was overestimated because the response seemed to be strongly influenced by gastrointestinal symptoms. Other explanations could be that slightly different case definitions were used between the studies and that the earlier study period only covered part of a year and did not account for seasonality.

### Norway

From June 15 1999 to June 14 2000, Kuusi *et al.* (2003) conducted a cross-sectional survey to determine the incidence of gastroenteritis in Norway. A self-administered questionnaire was mailed to 3000 persons randomly selected from a governmental registry of all Norwegian residents. Equal proportions of participants were mailed surveys in each month of the 12-month study period to account for seasonal variation in the incidence of gastroenteritis. Participants were asked about the occurrence of gastroenteritis in the 4 weeks before the questionnaire was completed. Gastroenteritis was defined as (1) diarrhea (three or more loose stools in 24 hours), or (2) at least three of the following symptoms: vomiting, nausea, abdominal cramps, or fever  $\geq 38^{\circ}\text{C}$ . Persons with chronic diarrheal illnesses were excluded. A total of 1843 persons completed the questionnaire for a 61% response rate. Gastrointestinal symptoms meeting the case definition were reported by 171 persons for an incidence of 1.2 cases per person-year. The incidence of gastroenteritis was highest among children younger than 5 years of age (12.9%) and lowest among adults 65 years of age or older (3.1%). The incidence peaked in September to October and again in December to March, with the lowest rates observed in late spring and early summer.

### United Kingdom and Ireland

Since the early 1990s, four studies in Great Britain and one in Ireland have estimated the incidence of AGI. The first

study was conducted by Roderick *et al.* (1995) between October 1991 and May 1992. This was a pilot study of infectious intestinal disease (IID) among persons registered at select general practices belonging to the Medical Research Council's General Practice Research Framework in England. The purpose of the study was to assess the feasibility of a larger study, subsequently conducted by Wheeler *et al.* (1999) and Sethi *et al.* (1999). Four general practices in the same area of England in both rural and urban settings were selected for a population-based cohort study. Practice registries were used to sample study participants. Random samples of individuals (in two practices) and households (in the other two practices) were drawn from the age–sex patient registers. Subjects and households were initially contacted by mail but a low response rate (31%) prompted a second round of contact during this pilot study using both mail and a follow-up telephone call, where possible. The response rate in the second round was 49% and was similar for individuals and households. A total of 192 persons were recruited for this study. Individuals and households were randomly allocated to either a 3- or 6-month follow-up group. The 6-month follow-up did not reduce compliance. Participants were asked to mail a postcard to the practice each week stating whether the individual in question or a household member had developed IID, defined as any of the following symptoms preceded by a symptom-free period of at least 3 weeks in the absence of a known noninfectious cause: (1) loose stools present for fewer than 14 days, or (2) significant vomiting for less than 48 hours that either incapacitated the patient or was forceful and accompanied by systemic symptoms. The number of loose stools required to meet the definition of IID was not specified. Similarly, significant vomiting was also not defined. If a participant experienced symptoms, the nurse was to be contacted and a stool sample was to be submitted. The incidence among individuals was higher than that among households (0.14 vs. 0.03 episodes per person-year). The overall annualized incidence of IID was 0.10 episodes per person-year.

From August 1993 to January 1996, Wheeler *et al.* (1999) and Sethi *et al.* (1999) conducted a prospective medical practice-based cohort study in England to estimate the incidence infectious intestinal disease (IID) in the community. This was the follow-up study to the pilot study

conducted by Roderick *et al.* (1995) just described. Seventy general practices were chosen from across the country to participate in the study. They were representative of general practices in England by geographical area and rural/urban location, but with fewer small and affluent practices. Practice registries were used to sample study participants and enrollment was staggered over the 18 months of the study. Within each practice, persons were selected to be contacted using stratified random sampling by age and sex from the patient register. Two consecutive cohorts of patients were each followed for 6 months, rather than one cohort of 12 months, in order to increase the level of participation (Sethi *et al.* 1999). Participants returned weekly postcards for 6 months declaring the absence of intestinal illness. IID was defined as loose stools or significant vomiting (more than once in 24 hours, incapacitating, or accompanied by cramps or fever) lasting less than 2 weeks, in the absence of a known noninfectious cause and preceded by a 3-week symptom-free period (Sethi *et al.* 1999). Those who developed symptoms were asked to contact the study nurse, complete a risk factor questionnaire, and submit a stool sample. When recruited, each person was also asked to recall episodes of diarrhea in the month preceding recruitment to provide a retrospective estimate of the incidence of diarrhea. A total of 9776 patients (40% of invited patients [9776/24,399]) were recruited into the study and provided 4026 person-years of observation. Sixty-one percent of participants completed the full 26 weeks. Participants reported 781 cases of IID for a prospective incidence of 0.19 episodes per person-year. While this incidence is comparable to that reported in the pilot study by Roderick *et al.* (1995) (0.10 episodes per person-year), it is much lower than the incidence reported in other international studies. The reason for the low incidence in these two studies is unclear. Perhaps the request for a stool sample if IID occurred negatively impacted reporting. However, other prospective cohort studies requesting stool specimens, some still to be discussed, reported higher incidence rates (Fox *et al.* 1966, 1972; Hughes *et al.* 1978; Hoogenboom-Verdegaal *et al.* 1994; de Wit *et al.* 2000, 2001). The retrospective estimate of diarrhea incidence from this study was 0.55 episodes per person-year, which was nearly three times the prospective estimate. This finding has significant implications for



comparisons made between retrospective and prospective studies of AGI, which will be discussed in greater detail in a subsequent section.

In 1992, Palmer *et al.* (1996) conducted a postal survey of patients in a convenience sample of four large urban general practices in Wales. Investigators asked about self-reported acute infective gastroenteritis (worded in the questionnaires as a “tummy upset”, vomiting, or diarrhea). For analysis, diarrhea was defined as three or more loose or watery stools in a 24-hour period. Two study periods were chosen to cover known seasonal peaks in viral and bacterial infection: the 90-day period from January 1 to March 31 1992 (winter) and the 49-day period from August 31 (a Bank Holiday) through October 18 1992 (autumn). At the end of March and at the end of October, questionnaires were mailed to random samples of 250 patients in each of the four practices. During these two study periods, a total of 1977 randomly selected patients were asked about the occurrence of gastroenteritis. The overall response rate was 79% (1557/1977), with a 76% (757/1001) response rate in the winter months and an 82% (800/976) response rate in the autumn months. In total, 286 patients reported a gastrointestinal illness during the periods in question (144 during the winter months and 142 during the autumn months) for an annualized incidence of 1.0 episode per person-year. The rate of diarrhea alone was 0.5 episodes per person-year.

From October 1992 to January 1993, Feldman & Banatvala (1994) used the Office of Population Censuses and Surveys Omnibus Survey to measure the annualized rate of diarrhea in adult respondents aged 16 years and older in Great Britain. Approximately 2000 adults were interviewed each month from private households randomly selected using postcode addresses. Postal sectors were stratified by region, proportion of home ownership, and socio-economic group. One adult per household was randomly selected for a face-to-face interview. Participants were asked about the occurrence of diarrhea (three or more loose bowel movements in a 24-hour period) in the previous month. Over the 4-month study period, 8143 adults were interviewed with a 77% response rate (8143/10,535). A total of 633 adults (7.9%) reported one or more episodes of diarrhea in the preceding month, equating to an annualized rate of 0.95 episodes per person per year. Persons 65–74

years of age had the lowest incidence. Since this study was conducted among adults only, the results are not generalizable to children, who have been shown to have a higher incidence of diarrhea, particularly children younger than 5 years of age (Hodges *et al.* 1956; Monto & Koopman 1980; Jones *et al.* in press).

Scallan *et al.* (2004) conducted a random-digit dialing telephone survey of acute gastroenteritis over a 12-month period from December 2000 to November 2001 in Northern Ireland and the Republic of Ireland. All private households with fixed-line telephones were included in the sampling frame. One person per household was chosen based on the next closest birthday to the day of the interview. Approximately 800 surveys were conducted each month (half in Northern Ireland and half in the Republic of Ireland). Participants were asked about the presence of acute gastroenteritis in the 4 weeks before the interview. Acute gastroenteritis was defined as diarrhea with three or more loose stools in a 24-hour period or bloody diarrhea or vomiting together with at least one other symptom (diarrhea, abdominal pain/cramps, or fever), in the absence of a known noninfectious cause. Participants who believed their acute gastroenteritis was due to a noninfectious cause were excluded. A total of 9903 interviews were conducted (Scallan *et al.* 2005). At least one episode of acute gastroenteritis was reported by 4.5% of participants in the 4 weeks prior to the interview for a rate of 0.60 episodes per person-year (Scallan *et al.* 2004). This rate was weighted to adjust for the age and sex distributions based on recent census estimates and to adjust for the sampling fractions in Northern Ireland and the Republic of Ireland. The rate of acute gastroenteritis was highest among children younger than 5 years of age (10.5%) and lowest among persons 65 years of age or older (2.0%). The rate of acute gastroenteritis was higher during the winter months (December to April) and lower during the remainder of the year.

### Multinational

While numerous studies have been conducted in developed countries to estimate the national prevalence of AGI, comparisons of these studies have been hindered by different study designs and different case definitions. Using a uniform

case definition for comparative analysis, Scallan *et al.* (2005) reviewed data from four retrospective cross-sectional population-based telephone surveys using similar methodologies that were conducted in Australia (Ashbolt *et al.* 2002; Hall *et al.* 2002), Canada (Majowicz *et al.* 2004), Republic of Ireland and Northern Ireland (Scallan *et al.* 2004), and the United States (Hawkins *et al.* 2002; Jones *et al.* in press) over 12-month periods between 2000 and 2002. All four surveys have been previously described. For each survey, a sample of telephone numbers was generated either by using random-digit dialing or by randomly selecting from a list of residential telephone numbers. One person per household was randomly selected to be interviewed. Investigators in Australia and Ireland conducted nation-wide surveys. Investigators in Canada surveyed one municipality. Investigators in the United States conducted their survey in eight FoodNet sites across the country. The American, Canadian, and Irish surveys were all conducted in English. The Australian survey was conducted in seven languages, including English. For comparative analysis, a uniform case definition of diarrhea was employed: three or more loose stools or bowel movements in any 24-hour period. Participants who reported a chronic diarrheal illness were excluded. Participants were asked about the occurrence of diarrhea in the 4 weeks prior to the interview. To be nationally representative in America, Australia, and Ireland, the data were weighted by age, sex, and geographic location. The Canadian data were weighted by age and sex to the population in the municipality under study. The American and Australian data were also weighted by the number of residential telephone lines. Finally, the Australian data were also weighted by household size. Cooperation rates were calculated and used to compare participation in each survey. The cooperation rate was defined as the number of completed interviews divided by the number of completed interviews plus the number of non-interviews that involved the identification of, and contact with, an eligible respondent. The number of participants varied by country: 6087 in Australia, 3496 in Canada, 9903 in Ireland, and 14,647 in the United States (Jones *et al.* in press). The cooperation rate was highest in Ireland (84.1%), then Australia (67.5%), the United States (36.4%), and Canada (34.7%). Canada and the United States had the highest prevalence of diarrhea at 0.99 episodes per person-year, followed by Australia (0.83) and Ireland (0.44). These rates

were slightly different than those previously described in the individual studies because of the different case definition and different weightings used for this comparison. In this comparative analysis, the prevalence of diarrhea in Ireland was approximately half of that reported in the other countries. When investigators modified the case definition to consider diarrhea and vomiting together, the prevalence was almost identical in all four countries; a rate of 0.26 episodes per person-year in Australia, Canada and Ireland and a rate of 0.34 episodes per person-year in the United States. The investigators speculated that cultural differences in Ireland might have resulted in reduced reporting of mild episodes of diarrhea.

## DISCUSSION

In this chapter we have reviewed 14 American and 19 international studies estimating the rate of AGI. The range of estimates provided varies both among and within countries. Some of this variation is due to differences in study methodology and design; this makes comparisons between studies problematic.

Of the 33 studies reviewed, 16 were retrospective studies and 18 were prospective studies (of which five were intervention trials with a prospective component and one was a recalculation of existing data). One study from England had both a retrospective and prospective component (Table 2). Both retrospective and prospective studies have some limitations. Retrospective studies suffer from a number of recall errors. One such error is telescoping. This phenomenon involves compression of time whereby an event is remembered as having occurred more recently than it actually did (Sudman & Bradburn 1973; Wheeler *et al.* 1999). The result is that events, such as the occurrence of AGI, may be over-reported, particularly if the event is severe, and thus, more memorable. This problem is more pronounced with proxy interviews for children (Bruijnzeels *et al.* 1998). At the same time, milder, less memorable symptoms may be underrepresented or even forgotten, particularly if the recall period is long. In the retrospective studies reviewed, the recall periods for AGI symptoms ranged from 2 weeks (Akhter *et al.* 1994) to 3 months (Palmer *et al.* 1996) but most were 1 month. Therefore, because of recall

errors, retrospective studies may result in higher estimates of morbidity. Consequently, prospective studies are sometimes considered more reliable than retrospective studies because they reduce or eliminate recall errors. Wheeler *et al.* (1999) found that, within the same study, the retrospective estimate of infectious intestinal disease was almost three times higher than the prospective estimate. However, prospective studies also have difficulties. Four of the five intervention trials reviewed (Payment *et al.* 1991, 1997; Hellard *et al.* 2001; Colford *et al.* 2005) showed signs of reporting fatigue. Each of these trials required individual participation for over 1 year. Over time, the rate of reported symptoms declined. Investigators hypothesized that participants lost interest in prospectively reporting their symptoms, which may have resulted in an underestimation of the disease rate. Furthermore, some prospective studies collected stool samples when symptoms were reported. Participants in these studies may have been unwilling to report symptoms because of the follow-up such a report triggered, once again leading to underreporting. Given the types of errors associated with retrospective and prospective studies, one would anticipate that retrospective studies would, in general, provide higher estimates of AGI rates than prospective studies. This is true in a comparison of Australia, British, and Canadian studies in which all estimates from retrospective studies were higher than those provided by the prospective studies in the same country. However, this trend does not appear to be true in the American studies. In the United States, the range of estimated AGI rates from retrospective and prospective studies overlapped: 0.6 episodes per person-year (Hawkins *et al.* 2002; Jones *et al.* in press) to 3.2 (Sandler *et al.* 2000) in the retrospective studies, and 0.3 (Fox *et al.* 1972) to 3.48 (Colford *et al.* 2002) in the prospective studies. The cause of this discrepancy is unclear but may be related to the use of different case definitions in the different countries. These case definitions used in the retrospective Australian, Canadian, and British studies tended to be similar to those used in the prospective studies from the same countries. These case definitions often referred to both diarrhea and vomiting. In contrast, all of the retrospective American studies used a restrictive definition of AGI that included diarrhea only, whereas the prospective American studies used broader definitions of AGI that included diarrhea and vomiting, with many also including a combination of other

symptoms. The two prospective studies by Fox *et al.* (1966, 1972) did not provide detailed case definitions so comparisons using these studies are not possible. The use of restrictive case definitions in the retrospective American studies may have reduced the estimates of the rate of AGI, thereby creating the overlap with the range of estimates provided by the prospective American studies. One anomaly should be noted in the range of estimates provided by the retrospective American studies. Sandler *et al.* (2000) estimated a prevalence of 3.2 episodes of loose stools or diarrhea per person-year. This estimate was more than twice as high as any other retrospective study reviewed from any country. The reasons for this outlying estimate are unknown but may reflect bias due to nonrandom participant selection resulting in a sample population not demographically representative of the US population. Furthermore, this was the only retrospective study to use the term “diarrhea” without further definition. Therefore, the case definition used in this study may have been interpreted much more liberally than those used in the other retrospective studies and may have resulted in a higher estimate.

The varying definitions of AGI used in the studies we have reviewed significantly reduce their comparability. Not only are different symptoms considered in the definitions (Table 2), even the definitions of the symptoms themselves vary. For example, diarrhea was defined as loose stools or stools with abnormal liquidity (Majowicz *et al.* 2004), loose stools present for fewer than 14 days (Roderick *et al.* 1995), two or more loose stools a day (Hoogenboom-Verdegaal *et al.* 1994; de Wit *et al.* 2000; Hellard *et al.* 2001), or liquid versus soft stools (Payment *et al.* 1991, 1997). However, diarrhea was most commonly defined as three or more loose or watery stools in a 24-hour period. The use of this last definition is supported by data in the scientific literature. Denno *et al.* (2005) showed a statistically significant trend exists between the number of stools in a 24-hour period and the presence of detectable bacterial and viral enteric pathogens. Denno *et al.* suggested that an incidence of fewer than three loose stools in the previous 24 hours should be used as an exclusion criterion for stool cultures. Connell *et al.* (1965) studied persons from industrial communities around London who were not seeking healthcare and patients attending a general medical practitioner’s surgery who did not have known gastrointes-

**Table 2** | Studies providing estimates of the rate of gastrointestinal disease in developed countries<sup>a</sup>

Country	Author	Study period	Study design <sup>b</sup>	Sampling method <sup>c</sup>	Sample size <sup>c</sup>	Participant contact <sup>d</sup>	Main components of case definition <sup>e</sup>	Case definition	Incidence (per person-year)
<b>Retrospective Data Collection</b>									
United States	Akhter <i>et al.</i> (1994)	Nov. 22 – Dec. 5 1993	CC	Random sampling of HH in Washington, DC	1197 persons (all ages)	T	D	≥ 3 loose or watery stools in 24 hours	0.7
United States	Sandler <i>et al.</i> (2000)	Aug. 11 – Oct. 6 1997	CP	Random sampling of HH in 48 states and Washington, DC; only 17% of individuals from HH randomly sampled	2510 adults (18–75 years)	T	D	Loose stools or diarrhea in the month prior to the interview	3.2
United States	Herikstad <i>et al.</i> (2002)	1996 – 1997	CP	Random sampling of HH within FoodNet catchment area then random selection of 1 person per HH	8624 persons (all ages)	T	D	≥ 3 loose stools or bowel movements in 24 hours that either lasted > 1 day or resulted in impairment of daily activities	0.7 (1.4 – D regardless of duration or impairment)
United States	Imhoff <i>et al.</i> (2004)	1998 – 1999	CP	Random sampling of HH within FoodNet catchment area then random selection of 1 person per HH	12,075 persons (all ages)	T	D	≥ 3 loose stools in 24 hours that either lasted > 1 day or resulted in impairment of daily activities	0.7 (1.3 – D regardless of duration or impairment)

Table 2 | (continued)

Country	Author	Study period	Study design <sup>b</sup>	Sampling method <sup>c</sup>	Sample size <sup>c</sup>	Participant contact <sup>d</sup>	Main components of case definition <sup>e</sup>	Case definition	Incidence (per person-year)
United States	Hawkins <i>et al.</i> (2002)	2000–2001	CP	Random sampling of HH within FoodNet catchment area then random selection of 1 person per HH	14,046 persons (all ages)	T	D	≥ 3 loose stools or bowel movements in 24 hours that either lasted > 1 day or resulted in impairment of daily activities	0.6
United States	Jones <i>et al.</i> (in press)	1996–2003	CP	Random sample of HH within FoodNet area then random sample of 1 person per HH	50,323 persons (all ages)	T	D	≥ 3 loose stools or bowel movements in 24 hours that either lasted > 1 day or resulted in impairment of daily activities	0.6
Australia	Hall <i>et al.</i> (2002); Ashbolt <i>et al.</i> (2002)	September 2001 – August 2002	CP	Random sampling of HH then random selection of 1 person per HH	6087 persons (all ages)	T	D	≥ 3 loose stools or bowel movements in any 24 hour period	0.92
Australia	Ashbolt <i>et al.</i> (2002)	August – November 2001	CP	Randomly selected persons across Victoria	7494 adults	T	D or V	≥ 3 loose stools or two or more episodes of vomiting in 24 hours	1.3
Australia	Ashbolt <i>et al.</i> (2002); Queensland OzFoodNet (2002)	March 12 – May 3 2001	CP	Random sampling of HH across Queensland then random selection of 1 person per age group per HH	3081 adults, 386 children aged 7 months through 4 years	T	D	≥ 3 loose stools in 24 hours	1.46 for adults; 1.89 for children 7 months to 4 yrs

Table 2 | (continued)

Country	Author	Study period	Study design <sup>b</sup>	Sampling method <sup>c</sup>	Sample size <sup>c</sup>	Participant contact <sup>d</sup>	Main components of case definition <sup>e</sup>	Case definition	Incidence (per person-year)
Canada	Majowicz <i>et al.</i> (2004)	February 2001 – February 2002	CC	Random sampling of HH then random selection of 1 person per HH	3496 persons (all ages)	T	V or D	Any vomiting or diarrhea (loose stool or stool with abnormal liquidity) in the 28 days prior to the interview	1.3
England	Wheeler <i>et al.</i> (1999); Sethi <i>et al.</i> (1999)	August 1993 – January 1996	CM <sup>1</sup>	Age and sex-stratified random samples from 70 GP registers across England	9776 persons (all ages)	M	D or V	Loose stools or significant vomiting (> 1 in 24 hours, incapacitating, or with cramps or fever) lasting < 2 weeks, without a noninfectious cause, preceded by a 3-week symptom-free period	0.55 <sup>1</sup>
Great Britain	Feldman & Banatvala (1994)	October 1992 – January 1993	CP	Random sampling of 1 adult per HH within postcode sectors stratified by region, home ownership, and socio-economic group	8143 adults (aged ≥ 16 years)	I	D	≥ 3 loose bowel movements in 24 hours	0.95

Table 2 | (continued)

Country	Author	Study period	Study design <sup>b</sup>	Sampling method <sup>c</sup>	Sample size <sup>c</sup>	Participant contact <sup>d</sup>	Main components of case definition <sup>e</sup>	Case definition	Incidence (per person-year)
Northern Ireland and the Republic of Ireland	Scallan <i>et al.</i> (2004)	December 2000 – November 2001	CP	Random-digit dialing of all private HH across Northern Ireland and the Republic of Ireland with telephones sampling 1 person per HH	9903 persons (all ages)	T	D or V	Diarrhea with $\geq 3$ loose stools in 24 hours, or bloody diarrhea, or vomiting with $\geq 1$ other symptom (diarrhea, abdominal pain/cramps, or fever), in the absence of a known non-infectious cause	0.60
Multinational (Australia, Canada, Ireland, United States)	Scallan <i>et al.</i> (2005)	12-month periods from 2000 – 2002	CP	Random sampling of HH then random selection of 1 person per HH	Varied by survey: 3496 to 14 647 persons (all ages)	T	D	$\geq 3$ loose stools or bowel movements in 24 hours	Canada: 0.99 USA: 0.99 Australia: 0.83 Ireland: 0.44
Norway	Kuusi <i>et al.</i> (2003)	June 15 1999 – June 14 2000	CP	Random sampling from a governmental registry of all Norwegian residents	1843 persons (all ages)	M	(1) D, or (2) V, or (3) 3 of V, N, cramps, or fever	(1) Diarrhea ( $\geq 3$ loose stools in 24 hours), or (2) at least 3 of: vomiting, nausea, abdominal cramps, or fever $\geq 38^\circ\text{C}$	1.2
Wales	Palmer <i>et al.</i> 1996	January 1 to March 31 1992 and August 31 to October 18 1992	CM	Random sampling from convenience sample of 4 urban general practice registers	1557 persons (all ages)	M	D or V	“Tummy upset”, vomiting, or diarrhea ( $\geq 3$ loose or watery stools in 24 hours)	1.0 (0.5 for diarrhea alone)

Table 2 | (continued)

Country	Author	Study period	Study design <sup>b</sup>	Sampling method <sup>c</sup>	Sample size <sup>c</sup>	Participant contact <sup>d</sup>	Main components of case definition <sup>e</sup>	Case definition	Incidence (per person-year)
<b>Prospective Data Collection</b>									
United States	Dingle <i>et al.</i> (1953, 1956, 1964); Hodges <i>et al.</i> (1956)	January 1 1948 – May 31 1957	CBC	Non-random selection of HH from a suburban area of Cleveland	85 different HH with 439 persons – HH with young children	I	(1) D, or (2) V, or (3) abdominal pain, or (4) F, or (5) minor symptoms within 10 days of another family case	Any one of vomiting, abdominal pain, diarrhea, or fever; or a minor symptom (e.g. nausea, anorexia) within 10 days of another case in the same family	1.5–1.6 (1.3 without respiratory symptoms)
United States	Fox <i>et al.</i> (1966)	August 1 1961 – March 31 1965	CBC	Non-random selection of HH from 2 contrasting communities in metropolitan New York area	178 HH with 791 persons (HH with children < 11 years of age)	I	Enteric illness (undefined)	Enteric illness (undefined)	1.0 (includes respiratory symptoms), 0.7 (excludes respiratory symptoms)
United States	Fox <i>et al.</i> (1972)	November 1965 – August 1969	HBC	Non-random selection of HH from the metropolitan Seattle area	215 HH with newborn infants (1397 person-years)	I and T	Enteric illness (undefined)	Enteric illness (undefined)	0.3
United States	Monto & Koopman (1980); Monto <i>et al.</i> (1970, 1971)	November 1965 to end of 1971	CBC	Random sampling of HH in Tecumseh, Michigan	4905 persons from HH with school-age children	T	(1) D, or (2) V, or (3) D and V, or (4) N	Any of (1) diarrhea without vomiting; (2) vomiting without diarrhea; (3) diarrhea and vomiting combined; or (4) upset stomach and/or nausea without the other symptoms	1.20 (0.63 D ± V; 0.40 D alone; 0.88 D ± V without concomitant respiratory symptoms)



Table 2 | (continued)

Country	Author	Study period	Study design <sup>b</sup>	Sampling method <sup>c</sup>	Sample size <sup>c</sup>	Participant contact <sup>d</sup>	Main components of case definition <sup>e</sup>	Case definition	Incidence (per person-year)
United States	Hughes <i>et al.</i> (1978); Guerrant <i>et al.</i> (1990)	August 1975 – July 1977	CBC	Unknown sampling method in Charlottesville	45 young families with 169 persons (all ages)	I	V or D or 2 or more milder intestinal and systemic symptoms	(1) Vomiting, (2) diarrhea or (3) $\geq 2$ of nausea, cramps, malaise, fever, chills, headaches, myalgia, anorexia	1.9
United States	Garthright <i>et al.</i> (1988)	See Cleveland and Tecumseh studies above	R	See Cleveland and Tecumseh studies above	See Cleveland and Tecumseh studies above	Not applicable	V or D without respiratory symptoms	Vomiting or diarrhea without (1) noninfectious origin and (2) respiratory symptoms	Cleveland: 0.71; Tecumseh: 0.62
United States	Colford <i>et al.</i> (2002)	16 weeks in 1999	CBI	Willing families among eligible HH in Contra Costa County study area – participating HH randomized to different study groups	77 HH with 236 persons (all ages)	M	(1) V, or (2) watery D, or (3) soft D & cramps together on any day, or (4) N & cramps together on any day	Any one of four conditions below preceded by $\geq 6$ symptom-free days: (1) vomiting; (2) watery diarrhea; (3) soft diarrhea and abdominal cramps together on any day; or (4) nausea and abdominal cramps together on any day	Sham treatment group 3.48

Table 2 | (continued)

Country	Author	Study period	Study design <sup>b</sup>	Sampling method <sup>c</sup>	Sample size <sup>c</sup>	Participant contact <sup>d</sup>	Main components of case definition <sup>e</sup>	Case definition	Incidence (per person-year)
United States	Colford <i>et al.</i> (2005)	54 weeks from October 2000 to May 2002	CBI	Willing families among all eligible HH in Davenport study area – participating HH randomized to different study groups	456 HH with 1296 persons (all ages)	M	(1) V, or (2) watery D, or (3) soft D & cramps, or (4) N & cramps	Any of the following 4 conditions preceded by $\geq 6$ symptom-free days: (1) vomiting; (2) watery diarrhea; (3) soft diarrhea and abdominal cramps; or (4) nausea and abdominal cramps	Sham treatment group: 2.40 Cycle A, 1.82 Cycle B (average 2.11); diarrhea alone ( $\geq 3$ diarrheal stools in 24 hours): 0.74 Cycle A, 0.54 Cycle B (average 0.64)
Australia	Hellard <i>et al.</i> (2001)	September 1997 – February 1999 (not including two 4-week periods over Christmas)	CBI	Willing families among eligible HH in Melbourne study area	600 HH with 2811 persons (all ages)	M	(1) D, or (2) V, or (3) D not meeting case definition but with abdominal pain or nausea, or (4) V not meeting case definition but with abdominal pain or nausea	Any of the following in 24 hours: (1) $\geq 2$ loose stools; (2) $\geq 2$ episodes of vomiting; (3) 1 loose stool with abdominal pain or nausea or vomiting; or (4) one episode of vomiting with abdominal pain or nausea	0.82 for persons with sham units

Table 2 | (continued)

Country	Author	Study period	Study design <sup>b</sup>	Sampling method <sup>c</sup>	Sample size <sup>c</sup>	Participant contact <sup>d</sup>	Main components of case definition <sup>e</sup>	Case definition	Incidence (per person-year)
Canada	Payment <i>et al.</i> (1991)	March to June 1988 and September 1988 to June 1989	CBI	Random sampling of HH from a directory of inhabited addresses for a suburban Montreal study area	606 HH with 2408 persons (all ages)	M and T	(1) V or D, or (2) N or D with cramps	(1) $\geq 1$ symptomatic day of vomiting or liquid diarrhea; or (2) $\geq 1$ symptomatic day of nausea or soft diarrhea combined with abdominal cramps	0.76 for regular tap water group
Canada	Payment <i>et al.</i> (1997)	September 1993 – December 1994	CBI	Random sampling of HH from a list of families enrolled in a government income supplement program in a suburban Montreal study area	1062 HH with 5253 persons (all ages)	T	(1) V or D, or (2) N or D with cramps	(1) $\geq 1$ symptomatic day of vomiting or liquid diarrhea; or (2) $\geq 1$ symptomatic day of nausea or soft diarrhea combined with abdominal cramps	0.66 for regular tap water group
Canada	Raina <i>et al.</i> (1999)	February 1994 – February 1995	PBC	Unknown selection process for rural HH using well water in southern Ontario – these HH had participated in an earlier study	156 HH with 531 persons (all ages) – 414 persons drinking non- <i>E.coli</i> well water; 117 drinking <i>E.coli</i> well water	T	D $\pm$ V	Diarrhea, with or without vomiting, occurring for $\geq 1$ days with $\geq 5$ symptom-free days separating episodes	At least 0.26 (counting only one episode) in non-contaminated wells

Table 2 | (continued)

Country	Author	Study period	Study design <sup>b</sup>	Sampling method <sup>c</sup>	Sample size <sup>c</sup>	Participant contact <sup>d</sup>	Main components of case definition <sup>e</sup>	Case definition	Incidence (per person-year)
Canada	Strauss <i>et al.</i> (2001)	April 3 – July 22 1995	CBC	Random selection of HH from among 4 rural communities	235 HH with 619 persons completing study (all ages)	Unknown	(1) V or D, or (2) N or D with cramps	(1) Vomiting or liquid diarrhea, or (2) nausea or soft, loose diarrhea with abdominal cramps – episodes included $\geq 1$ symptomatic days with $\geq 6$ consecutive symptom-free days between episodes	1.1
England	Roderick <i>et al.</i> (1995)	October 1991 – May 1992	MBC	Age and sex-stratified random sampling from convenience sample 4 general practice registers in England	192 + persons (all ages) – sample size only provided for second round of recruiting	M	D or V	Any of the following symptoms preceded by a symptom-free period of $\geq 3$ weeks in the absence of a known non-infectious cause: (1) loose stools present for < 14 days, or (2) significant vomiting for < 48 hours that either incapacitated the patient or was forceful and accompanied by systemic symptoms	0.10

Table 2 | (continued)

Country	Author	Study period	Study design <sup>b</sup>	Sampling method <sup>c</sup>	Sample size <sup>c</sup>	Participant contact <sup>d</sup>	Main components of case definition <sup>e</sup>	Case definition	Incidence (per person-year)
England	Wheeler <i>et al.</i> (1999); Sethi <i>et al.</i> (1999)	August 1993 – January 1996	MBC <sup>2</sup>	Age and sex-stratified random sampling from 70 general practice registers across England	9776 persons	M	D or V	Loose stools or significant vomiting (> once in 24 hours, incapacitating, or accompanied by cramps or fever) lasting <2 weeks in absence of non-infectious cause and preceded by a 3-week symptom-free period	0.19 <sup>2</sup>
France	Gofti-Laroche <i>et al.</i> (2003)	October 1998 – June 1999	CBC	Willing families among eligible HH in southeast France supplied by 4 vulnerable public drinking water systems	176 HH with 544 persons (all ages)	T	(1) Cramps, N, V, and/or D, (2) D + 1 digestive condition or fever, (3) D + F or V	<ul style="list-style-type: none"> <li>• Acute digestive conditions: abdominal pain, nausea, vomiting, and/or diarrhea</li> <li>• Diarrheal episode: diarrhea with 1 other digestive condition (unspecified) or fever</li> <li>• Gastroenteritis: diarrhea + (fever or vomiting)</li> </ul>	(1) ADC 2.8 (2) DE 0.4 (3) GE 0.2

Table 2 | (continued)

Country	Author	Study period	Study design <sup>b</sup>	Sampling method <sup>c</sup>	Sample size <sup>c</sup>	Participant contact <sup>d</sup>	Main components of case definition <sup>e</sup>	Case definition	Incidence (per person-year)
Netherlands	Hoogenboom-Verdegaal <i>et al.</i> (1994); de Wit <i>et al.</i> (2000)	March 1991 – July 1991	PBC	Random sampling of 1 person per HH from the population registers of 10 municipalities from rural, urban, and mixed rural/urban settings across the country	2257 persons (all ages)	M	D or V with at least 2 additional symptoms	<ul style="list-style-type: none"> <li>Grade 1: diarrhea (<math>\geq 2</math> stools a day) or vomiting with <math>\geq 2</math> additional symptoms occurring within preceding 7 days</li> <li>Grade 2: above + symptoms occurred on same day and lasted <math>\geq 2</math> days</li> </ul>	Grade 1: 0.57 (Hoogenboom-Verdegaal <i>et al.</i> 1994); 0.45 (de Wit <i>et al.</i> 2000) Grade 2: 0.15 (Hoogenboom-Verdegaal <i>et al.</i> 1994)
Netherlands	de Wit <i>et al.</i> (2001)	December 14 1998 to December 13 1999	MBC	Age-stratified random sampling of all persons registered at 44 participating sentinel general practices	4860 persons (all ages)	M	(1) D, or (2) V, or (3) D or V not meeting case definition but with at least 2 additional symptoms	(1) Diarrhea ( $\geq 3$ loose stools in 24 hours); or (2) vomiting ( $\geq 3$ times in 24 hours); or (3) diarrhea or vomiting not meeting the case definition with $\geq 2$ additional symptoms	0.28

<sup>a</sup>Adapted from Table 3 in Majowicz *et al.* (2004).

<sup>b</sup>CC, cross-sectional community-based survey; CP, cross-sectional population-based survey; CM, cross-sectional medical practice-based survey; CBC, community-based cohort; HBC, health insurance plan-based cohort; R, recalculation of incidence rates for 1980 population; CBI, community-based intervention trial; PBC, population-based cohort; MBC, medical practice-based cohort.

<sup>c</sup>HH, household(s).

<sup>d</sup>I, in-person; M, mail; T, telephone.

<sup>e</sup>D, diarrhea; V, vomiting; N, nausea; F, fever.

<sup>1</sup>Same study contained a prospective component.

<sup>2</sup>Same study contained a retrospective component.

tinal illness and found that 99% of the combined study population had bowel movements ranging from three per week to three per day. More recent studies have also found similar rates in adults (Drossman *et al.* 1982; Bassotti *et al.* 2004) and children 1–4 years of age (Weaver & Steiner 1984). Connell *et al.* (1965) concluded that more than three bowel movements per day might be considered unusual. They also observed a correlation between increasing stool frequency and the person's opinion of the stool as loose. However, limited information is available about the validity of self-reported diarrhea where specific symptoms are not defined. Baqui *et al.* (1991) tested various definitions of diarrhea in Bangladeshi children younger than 5 years of age using prospective community-based surveillance data and found that reports of either (1) three or more loose stools in a 24-hour period or (2) any number of loose stools containing blood in a 24-hour period seemed to be the most sensitive (78%) and specific (96%) definition compared to the mothers' perceptions of diarrhea. Sandler & Drossman (1987) studied young adult university students and new hospital employees and asked them to define diarrhea. Most (84%) included loose or watery stools in their definitions while only about a quarter of participants included urgency (27%), frequent stools (26%), and abdominal discomfort (24%). These definitions were not mutually exclusive. Talley *et al.* (1994) studied an age- and gender-stratified random sample of residents 20–64 years of age in Olmsted County, Minnesota and found that self-reported diarrhea identified only 39% of the participants who reported one or more of four major diarrheal symptoms: (1) loose or watery stools more than 25% of the time; (2) a stool frequency often of more than three per day; (3) a stool frequency usually of more than 21 per week; and (4) urgency. Investigators found that the overlap between self-reported diarrhea and the presence of individual symptoms was greatest for loose or watery stools and urgency, with estimates of stool frequency of lesser importance. They also found that diarrheal symptoms inadequately discriminated between self-reported diarrhea and self-reported normal bowel habit, thereby raising the philosophical question about what constitutes diarrhea and whether the definition of diarrhea should encompass some measure of a change from normal bowel habit or, as a surrogate, a measure of severity (such as the duration of diarrhea or the effect of diarrhea on

behavior). These studies indicate that self-reported diarrhea alone, without clarification of the symptoms, is not an adequate measure of diarrheal illness and should be used with caution in clinical trials and epidemiological studies. The study by Sandler *et al.* (2000), previously discussed, that provided the outlying estimate of AGI prevalence might be an example of this phenomenon. Alternatively, specification of loose or watery stools and the frequency of stools (i.e. three or more in a 24-hour period) in the definition of diarrhea may improve the clinical and epidemiologic validity of the response. Some studies have attempted to address these issues by defining diarrhea and incorporating a measure of severity into their definitions of AGI. For example, the four FoodNet survey cycles (Herikstad *et al.* 2002; Hawkins *et al.* 2002; Imhoff *et al.* 2004; Jones *et al.* in press) define diarrheal illness as diarrhea (three or more loose stools in a 24-hour period) resulting in an impairment of daily activities (e.g. missing time from work, school, recreation or vacation activities, or work in the home) or diarrhea duration greater than 1 day. Such a definition addresses the departure from normal bowel habits (of which there is a range) and identifies more severe cases that have a personal impact. However, by using a more specific definition of AGI, the sensitivity for mild cases is reduced. Therefore, the balance between sensitivity and specificity of the definition of AGI needs to be determined by the purpose of the investigation in which the definition is being used.

The definition of an episode of AGI not only requires specification of the symptoms involved, it also requires identification of the end of an illness episode. One study has found that 3 intervening diarrhea-free days seemed to be the optimal interval to define new episodes of diarrheal illness (Baqui *et al.* 1991). This finding is supported by Morris *et al.* (1994), who modeled the distribution of illness episodes and found that an interval of 2 or 3 days without symptoms generally marked a new episode of diarrhea. However, the intervals used in the studies reviewed in this paper ranged from 2 days (Monto & Koopman 1980) to 3 weeks (Roderick *et al.* 1995; Wheeler *et al.* 1999), with a median of 6 days. Therefore, some of these studies may have misclassified two or more distinct AGI episodes as a continuation of a single episode. Misclassification was not the only mechanism by which underreporting of AGI may have occurred. All the retrospective studies counted only

one episode of AGI during the period of interest, even if more than one episode was experienced. Regardless of the definition used, those persons with mild symptoms that did not meet the case definitions were not counted. Therefore, all but the very broadest case definitions may have underestimated the rate of mild cases.

Another way in which the 33 studies reviewed varied was in the method of contact with study participants. Four studies (Hodges *et al.* 1956; Fox *et al.* 1966; Hughes *et al.* 1978; Feldman & Banatvala 1994) conducted in-person interviews to gather information on symptoms and illness. Nine studies (Hoogenboom-Verdegaal *et al.* 1994; Roderick *et al.* 1995; Palmer *et al.* 1996; Wheeler *et al.* 1999; de Wit *et al.* 2001; Hellard *et al.* 2001; Colford *et al.* 2002, 2005; Kuusi *et al.* 2003) relied on the mail to collect this information from respondents. Sixteen studies (Monto & Koopman 1980; Akhter *et al.* 1994; Payment *et al.* 1997; Raina *et al.* 1999; Sandler *et al.* 2000; Ashbolt *et al.* 2002; Hall *et al.* 2002; Hawkins *et al.* 2002; Herikstad *et al.* 2002; Queensland OzFoodNet 2002; Gofiti-Laroche *et al.* 2003; Imhoff *et al.* 2004; Majowicz *et al.* 2004; Scallan *et al.* 2004, 2005; Jones *et al.* in press) conducted telephone interviews. Two studies (Fox *et al.* 1972; Payment *et al.* 1991) used a combination of methods, and the authors of one study (Strauss *et al.* 2001) did not specify the method of participant contact. These differing methodologies are subject to different response rates and nonresponse biases. Studies have found that in-person interviews tend to have the highest response rates, followed by mail surveys, then telephone surveys (Marcus & Crane 1986; Picavet 2001). Only one of the in-person studies reviewed supplied a response rate (77%) (Feldman & Banatvala 1994). The response rates for nine of the mail studies ranged from 31% (Roderick *et al.* 1995) to 96% (Colford *et al.* 2002). The response rates for eight of the telephone studies were comparable to those by mail. Of note, the FoodNet population telephone survey response rate declined over the four survey cycles, from 71% in the first cycle (Herikstad *et al.* 2002) to 33% in the fourth cycle (Jones *et al.* in press). This is representative of an overall decline in survey response rates (Atrostic *et al.* 2001; Tourangeau 2004). In particular, telephone surveys in the United States have been affected by the increase in private telemarketing, and the introduction of “do-not-call” lists and caller screening

devices (Tourangeau 2004). The growth in households using only cellular telephones (without a land line) may also be of concern. During the first half of 2005, CDC’s National Health Interview Survey found that 6.7% of adults had access only to cellular telephones. Cellular-only usage was more common among certain groups, such as young adults and persons renting their homes. However, investigators concluded that, while the percent of adults without land line telephones has increased, it is still low, which minimizes the bias resulting from their exclusion from telephone surveys (Blumberg *et al.*, 2006). While several recent studies have demonstrated little relationship between nonresponse rates and nonresponse bias (Curtin *et al.* 2000; Keeter *et al.* 2000; Tourangeau 2004), low response rates are still problematic when trying to generalize results to both the population under study and to a wider population. In-person interviews, mail surveys, and telephone surveys are also each subject to different nonresponse biases, whereby the group of people not interviewed may be systematically different from those that are interviewed. Compared to in-person interviews, mail surveys are less likely to be completed by persons with lower levels of education and literacy (Picavet 2001). Telephone surveys are also less likely to reach low-income minorities and persons with lower educational levels (Marcus & Crane 1986; Imhoff *et al.* 2004). All three methods exclude institutionalized persons (e.g. persons in long-term healthcare facilities, mental institutions, and jail), persons who could not respond because of physical or mental impairment, and persons speaking languages that are different than the language(s) of the interview or survey. If these excluded persons are different from the larger population concerning the event of interest (i.e. AGI), then bias may be introduced and estimates of AGI extrapolated to the US population may be inaccurate (Imhoff *et al.* 2004).

Selection bias is another means by which persons under study differ from the rest of the population, thereby limiting the generalizability of the results. This bias may be present at the level of the respondent. Persons with AGI may be more likely to complete a survey or interview, thereby creating a selection bias. Selection bias may also be present within the sampling frame. Most of the studies reviewed in this chapter evaluated relatively small specific groups of people. Eight studies (Hodges *et al.* 1956; Fox *et al.* 1966,



1972; Monto & Koopman 1980; Guerrant *et al.* 1990; Payment *et al.* 1991, 1997; Hellard *et al.* 2001) were limited to families with young children. Therefore, children were overrepresented in these studies, which could have inflated the estimated AGI rate because children are known to experience higher rates of AGI than adults (Hodges *et al.* 1956; Monto & Koopman 1980; Hawkins *et al.* 2002; Herikstad *et al.* 2002; Imhoff *et al.* 2004; Jones *et al.* in press). Five studies were conducted in populations served by specific medical practices or health insurance organizations (Fox *et al.* 1972; Roderick *et al.* 1995; Palmer *et al.* 1996; Wheeler *et al.* 1999; de Wit *et al.* 2001), eliminating the medically indigent and those outside the service areas. Fourteen studies (Hodges *et al.* 1956; Fox *et al.* 1966; Monto & Koopman 1980; Guerrant *et al.* 1990; Payment *et al.* 1991, 1997; Akhter *et al.* 1994; Feldman & Banatvala 1994; Raina *et al.* 1999; Hellard *et al.* 2001; Strauss *et al.* 2001; Colford *et al.* 2002, 2005; Majowicz *et al.* 2004) were conducted in specific communities, some with very homogeneous demographic characteristics that were not generalizable to larger populations. Finally, five intervention trials (Payment *et al.* 1991, 1997; Hellard *et al.* 2001; Colford *et al.* 2002, 2005), one retrospective survey (Akhter *et al.* 1994), and three prospective studies (Raina *et al.* 1999; Strauss *et al.* 2001; Gofti-Laroche *et al.* 2003) limited their study populations to those served by specific water systems. These different sampling frames were not mutually exclusive. Random selection of study participants is one method used to reduce selection bias. However, one study (Sandler *et al.* 2000) had only 17% of its participants selected completely at random, at least four studies (Hodges *et al.* 1956; Fox *et al.* 1966, 1972; Hellard *et al.* 2001) recruited participants through nonrandom selection techniques, and five studies (Roderick *et al.* 1995; Palmer *et al.* 1996; Wheeler *et al.* 1999; de Wit *et al.* 2001; Gofti-Laroche *et al.* 2003) randomly chose participants only after medical practices or communities were selected using nonrandom sampling schemes.

Only four international studies (Hoogenboom-Verdegaal *et al.* 1994; Hall *et al.* 2002; Kuusi *et al.* 2003; Scallan *et al.* 2004) assessed the national rate of AGI using a representative sample of the nationwide population. In the United States, Sandler *et al.* (2000) conducted a nationwide survey but, as just mentioned, only a small proportion of participants were randomly selected. The four cycles of

the US FoodNet population survey (Hawkins *et al.* 2002; Herikstad *et al.* 2002; Imhoff *et al.* 2004; Jones *et al.* in press) were population-based but the FoodNet sites were not chosen to be representative of the US general population. Rather, these sites were chosen based on their ability to conduct population-based surveillance and to achieve geographic diversity within their areas (Hardnett *et al.* 2004). However, this geographic diversity presents a problem. Studies of different enteric pathogens have demonstrated regional differences in the incidence of specific laboratory-confirmed infections (Hedberg *et al.* 1997; Bender *et al.* 2004; Ray *et al.* 2004) and have suggested that these variations in incidence reflect regional differences in physician and laboratory practices and perhaps regional differences in the risk of exposure (Hedberg *et al.* 1997; Hardnett *et al.* 2004). FoodNet has conducted surveys of physician and laboratory practices in FoodNet catchment areas and no differences were observed between FoodNet sites. However, because true regional differences in infection rates appear to exist based on other studies, these regional differences may have impacted the crude rate of AGI as estimated by the FoodNet population surveys as new sites were included in subsequent survey cycles (Hardnett *et al.* 2004). Demographic differences between the FoodNet and US populations must also be considered if generalizations using these data are to be made. In 1996, investigators compared the FoodNet and US populations and found that the age and sex distributions were similar but that the FoodNet population overrepresented Asians, underrepresented Hispanics, had a lower population density in FoodNet counties, and had a smaller percentage of persons living at or below the poverty level (Hardnett *et al.* 2002, 2004). A similar comparison of the FoodNet and US populations in 2000 again found similar age and sex distributions but, this time, a similar proportion of Asians in both populations, although Hispanics were still underrepresented in the FoodNet population (6% in FoodNet areas in 2000 compared to 12% nationally) (Hardnett *et al.* 2004). Overall, FoodNet researchers believe that the demographic differences appear to be limited. Furthermore, after accounting for the changing composition of the FoodNet sites between cycles by weighting for age, sex, location, and number of residential telephone lines, the estimates of diarrheal illness are comparable across the four

survey cycles. Therefore, the FoodNet population survey data have been generalized to the US population. However, whenever this is done, it is important that the limitations of the data be well understood.

Seasonality of AGI is yet another issue to consider when comparing these studies or generalizing their findings. Studies conducted over periods of less than one year (Akhter *et al.* 1994; Feldman & Banatvala 1994; Hoogenboom-Verdegaal *et al.* 1994; Roderick *et al.* 1995; Palmer *et al.* 1996; Sandler *et al.* 2000; Strauss *et al.* 2001; Ashbolt *et al.* 2002; Colford *et al.* 2002; Queensland OzFoodNet 2002; Gofti-Laroche *et al.* 2003) fail to capture the seasonal variation of AGI and, therefore, may overestimate or underestimate the annual rate of disease, depending on what time of year the study was conducted. In temperate climates, gastrointestinal illness is reported to have a bimodal distribution. Bacterial gastroenteritis tends to peak in the summer months (Gurwith & Williams 1977; Michel *et al.* 1999; Denno *et al.* 2005) while viral gastroenteritis, which may be more common (Gurwith & Williams 1977), tends to peak during the winter months (Gurwith & Williams 1977; Cook *et al.* 1990; Mounts *et al.* 2000; Denno *et al.* 2005) with lower rates in the summer (Hodges *et al.* 1956; Monto & Koopman 1980; Payment *et al.* 1997; Kuusi *et al.* 2003; Jones *et al.* in press).

Another barrier to comparability is that different studies used different exclusion criteria for individual participants or cases. Therefore, the estimated AGI rates were calculated from different groups of people, making comparisons problematic. Eight studies (Hughes *et al.* 1978; Akhter *et al.* 1994; Feldman & Banatvala 1994; Palmer *et al.* 1996; Hoogenboom-Verdegaal *et al.* 1994; Colford *et al.* 2002, 2005; Gofti-Laroche *et al.* 2003) did not report any exclusion criteria for individual participants or cases. Eleven studies (Hellard *et al.* 2001; Ashbolt *et al.* 2002; Hall *et al.* 2002; Herikstad *et al.* 2002; Kuusi *et al.* 2003; Imhoff *et al.* 2004; Hawkins *et al.* 2002; Queensland OzFoodNet 2002; Majowicz *et al.* 2004; Scallan *et al.* 2005; Jones *et al.* in press) excluded persons reporting a chronic illness in which diarrhea was a major symptom. Therefore, their estimated rates failed to account for AGI episodes in chronically ill persons that were unrelated to their chronic illnesses or conditions. The first two FoodNet surveys (Herikstad *et al.* 2002; Imhoff *et al.* 2004) also excluded persons who had

surgery to remove parts of their stomachs or intestines because these surgeries predisposed them to recurrent noninfectious diarrhea. However, this meant that AGI episodes unrelated to surgery were not counted. The Cleveland study (Dingle *et al.* 1953, 1964; Hodges *et al.* 1956) excluded cases of AGI with known etiologies, some of which were bacterial gastroenteritis. Therefore, this study underestimated the rate of infectious gastroenteritis. Six studies (Payment *et al.* 1991, 1997; Roderick *et al.* 1995; Wheeler *et al.* 1999; de Wit *et al.* 2001; Scallan *et al.* 2004) excluded noninfectious causes. Therefore, their estimated rates of AGI were limited to infectious etiologies and may have excluded environmental causes, such as chemical exposure.

Five studies (Hodges *et al.* 1956; Fox *et al.* 1966, 1972; Monto & Koopman 1980; Garthright *et al.* 1988) provided estimates of AGI rates in the absence of respiratory symptoms. The Cleveland study found that gastrointestinal illness was associated with respiratory symptoms in 20% of cases (Hodges *et al.* 1956; McCorkle *et al.* 1956), often with gastrointestinal symptoms beginning at the same time as respiratory symptoms or shortly thereafter (McCorkle *et al.* 1956). In contrast, respiratory illness was associated with gastrointestinal symptoms in 5% (McCorkle *et al.* 1956) of cases. In the Cleveland study, respiratory illness included common respiratory diseases (e.g. common cold, rhinitis, laryngitis, bronchitis, and other acute respiratory illnesses of undifferentiated type) and specific respiratory diseases (e.g. streptococcal tonsillitis and pharyngitis, nonstreptococcal exudative tonsillitis and pharyngitis, primary atypical pneumonia, pneumococcal pneumonia, and influenza) (Dingle *et al.* 1953). In the Tecumseh study (Monto & Koopman 1980), gastrointestinal illness was associated with respiratory symptoms in 27% of cases and respiratory illness was associated with gastrointestinal symptoms in 11% of cases. In this study, respiratory illness was divided into five syndromes: (1) lower respiratory illness with a productive cough, wheezing, or pain on respiration, (2) upper respiratory illness with coryza, without lower respiratory symptoms, (3) laryngotracheal illness with sore throat or hoarseness, without lower or upper respiratory symptoms, (4) nonproductive cough, and (5) earache alone (Monto & Koopman 1980). In the Cleveland and Tecumseh studies, many cases with combined gastrointestinal and respiratory symptoms appeared to have a common etiology. However,

because it was unclear as to whether these were primarily gastrointestinal or respiratory illnesses, cases with combined symptoms were excluded from these analyses.

Recent studies have attempted to exclude persons with gastrointestinal symptoms secondary to respiratory infections to more accurately reflect the true rate of AGI (Mead *et al.* 1999; Hall *et al.* 2005). Hall *et al.* (2005) used the results from the Australian national gastroenteritis survey previously described (Ashbolt *et al.* 2002) and excluded cases with concurrent sore throat, runny nose, sneezing, and/or cough. Using this revised case definition and weighting the results to the Australian population by age and sex, Hall estimated a national incidence of 0.92 AGI episodes per person-year. Mead *et al.* (1999) estimated the rate of AGI in the US population using the AGI rate calculated in the first cycle of the FoodNet population survey. Since this cycle did not collect data on the frequency of concurrent respiratory symptoms, Mead adjusted for combined gastrointestinal-respiratory illness using a value based on the Cleveland and Tecumseh studies. Mead's final estimate for the rate of AGI was 0.79 cases per person-year. As discussed, the third and fourth cycles of the FoodNet population survey collected information on respiratory symptoms among those persons with AGI. Therefore, the FoodNet estimate of AGI presented in this paper did not have to rely on the Cleveland and Tecumseh studies to adjust for concurrent respiratory illness. Data from the third and fourth FoodNet cycles indicated that 39% of those with AGI had concurrent respiratory symptoms. When these cases were excluded, the rate of AGI was estimated at 0.65 episodes per person-year.

All of these methodological variations make comparisons between the studies difficult and interpretations of the estimated AGI rates should be made with caution. Rates of AGI differ within and between study types, and within and among countries. Taken as a whole, these 33 studies suggest that the rate of AGI (including diarrhea) in developed countries is somewhere in the range of 0.1 (Roderick *et al.* 1995) to 3.5 (Colford *et al.* 2002) episodes per person-year, depending on location and type of study. Among the international studies, the range is 0.1 (Roderick *et al.* 1995) to 2.8 (Gofti-Laroche *et al.* 2003). In the United States, the same range is 0.3 (Fox *et al.* 1972) to 3.5 (Colford *et al.* 2002). These estimates come from a variety of different study types, including retrospective cross-sectional

population-based surveys, prospective cohort studies, and intervention trials designed to assess the rate of diarrhea and AGI. Other study types peripherally capturing information on AGI can also inform estimates of the rate of AGI. For example, a convenience sample of three randomized, double-blind, placebo-controlled drug trials in the US (Tilley *et al.* 1995; Black *et al.* 1997; Szapary *et al.* 2003) reported a range in the rates of diarrhea among their placebo groups (adults with active rheumatoid arthritis, essential hypertension, and primary hypercholesterolemia, respectively) of 0.05 (hypertensive placebo group) to 0.87 episodes per person-year (hypercholesterolemic placebo group). This range overlaps with the ranges presented in the studies specifically assessing AGI.

## CONCLUSIONS

Within the limitations described previously, the FoodNet studies are the most generalizable to the US population given their study design. They likely provide the best data currently available for an estimate of the rate of AGI in the United States. Their retrospective study designs could have resulted in over-reporting and may have led to an overestimate of the rate of AGI. Using the data from the third and fourth FoodNet survey cycles, the estimated rate of AGI in the U.S. is 0.65 episodes per person-year, with an unknown degree of uncertainty around this point estimate. However, this estimate does fall within the range of estimates presented by other national and international studies of varying designs. For this FoodNet estimate, AGI was defined as diarrheal illness (three or more loose stools in a 24-hour period resulting in an impairment of daily activities or diarrhea duration greater than 1 day) and/or vomiting, excluding those with respiratory symptoms (cough and/or sore throat). The diarrhea and/or vomiting could have been of either infectious or non-infectious origin. However, this definition excluded episodes of diarrhea or vomiting due to any long-lasting or chronic illness or condition. This case-definition of AGI is supported by studies in the literature that indicate that the validity of self-reported diarrhea is improved by including "three or more stools in 24 hours" and "loose stools" in the case definition. A measure of severity was added to ensure mild, noninfectious causes of AGI were excluded. Vomiting

was included in the case definition to estimate the rate of AGI rather than just the rate of diarrheal illness. Other AGI symptoms (e.g. nausea, abdominal pain) were not considered sufficient to meet the case definition in the absence of diarrhea or vomiting. Finally, cases with gastrointestinal symptoms secondary to respiratory illnesses were excluded to improve the specificity of AGI rate estimates. We believe that this case definition and the estimate of 0.65 AGI episodes per person-year can serve as a basis for the calculation of the rate of endemic gastrointestinal illness due to public drinking water systems in the United States.

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## DISCLAIMER

The findings and conclusions in this report are those of the author(s) and do not necessarily represent the views of the Centers for Disease Control and Prevention.

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- World Health Organization 2004 World Health Report 2004 – Annex Table 3 Burden of disease in DALYs by cause, sex and mortality stratum in WHO regions, estimates for 2002, Available at: [http://www.who.int/whr/2004/annex/topic/en/annex\\_3\\_en.pdf](http://www.who.int/whr/2004/annex/topic/en/annex_3_en.pdf).
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