Severity and Economic Burden of Recreational Waterborne Illness in the United States

BY

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DISSERTATION

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This thesis is dedicated to my husband, Mike Barker, without whom it would have never been accomplished.

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LIST OF ABBREVIATIONS

ACS	American Community Survey
AF	Attributable Fraction
AHRQ	Agency For Healthcare Research and Quality
AOE	Acute Otitis Externa
AOR	Adjusted Odds Ratio
AR	Attributable Risk
AF	Attributable Fraction
CAWS	Chicago Area Waterways
CBC	Complete Blood Count
CCR	Cost-To-Charge Ratio
CHEERS	Chicago Health Environmental Exposure and Recreation Study
CI	Confidence Interval
COI	Cost Of Illness
COVIS	Cholera and Other Vibrio Illness Surveillance
CPI	Consumer Price Index
CPT	Current Procedural Terminology
DALY	Disability Adjusted Life Years
E/M	Evaluation And Management
ED	Emergency Department
EPA	Environmental Protection Agency
ESRD	End Stage Renal Disease
FIB	Fecal Indicator Bacteria
FoodNet	Foodborne Diseases Active Surveillance Network
GBS	Guillain-Barré Syndrome
GI	Gastrointestinal
GUW	General Use Water
HAB	Harmful Algal Blooms
HCP	Healthcare Provider
HCUP	Healthcare Cost And Utilization Project
HUS	Hemolytic-Uremic Syndrome
ICC	Interclass Correlation
ICD-9-CM	*International Classification Of Diseases* Version 9
IHDD	Illinois Hospital Discharge Database
IV	Intravenous
LOS	Length of Stay
NEDS	Nationwide Emergency Department Sample
NEEAR	National Epidemiological and Environmental Assessment of Recreational Water
NIS	Nationwide Inpatient Sample
NSRE	National Survey on Recreation and the Environment

LIST OF ABBREVIATIONS (continued)

OR	Odds Ratio
OTC	Over-the-Counter
PAM	Primary Amoebic Meningoencephalitis
POA	Proportional Odds Assumption
QALY	Quality Adjusted Life Years
qPCR	Quantitative Polymerase Chain Reaction
RD	Risk Difference
ReA	Reactive Arthritis
RR	Relative Risk
SES	Socioeconomic Status
UCR	Usual, Customary, and Reasonable
VSL	Value Of A Statistical Life
WBDO	Waterborne Disease Outbreak
WBDOSS	Waterborne Disease Outbreak Surveillance System
WHO	World Health Organization
WTP	Willingness To Pay
WWTP	Wastewater Treatment Plant

SUMMARY

An analysis of the severity of illness and the cost of gastrointestinal illness among water recreators on untreated surface water, such as lakes, oceans, and rivers, and a national estimate of the overall economic burden due to recreational waterborne illness on untreated surface water was calculated. All analyses used two large comprehensive prospective cohort studies consisting of persons exposed to recreational water and other outdoor recreators or beachgoers. The Chicago Health Environmental Exposure and Recreation Study (CHEERS) focused its investigation on those participating in incidental-contact water recreation, which includes kayaking, rowing, canoeing, boating, and fishing. Some locations in the CHEERS study were directly impacted by non-disinfected wastewater effluent. The National Epidemiological and Environmental Assessment of Recreational Water (NEEAR) study examined those engaged in full-contact water recreation, such as swimming and wading at beaches impacted by human fecal pollution in six different states.

Overall, assessing only the occurrence of illness, defined according to a predetermined case definition, may not adequately describe the impact of water recreation on human health. This study observed a spectrum of illness severity among all those who water recreate. In general, most individuals who develop symptoms have mild and self-limiting illness; however, some individuals develop more severe symptoms that require use of the healthcare system and loss in productivity. Specifically, measures of water quality and the degree of water contact were observed to be associated with increased severity of symptoms among all water recreators.

The per case cost of gastrointestinal illness within NEEAR and CHEERS was assessed according to costs associated with medications, visits with a healthcare provider (HCP), visits to an emergency department (ED), hospitalizations, and costs associated with lost productivity. In general, the costs of gastrointestinal illness attributable to water recreation were found to range between approximately $500 to $2,000, per 1,000 individuals engaged in any type of water recreation including swimming, wading, kayaking, rowing, canoeing, boating, and fishing. The variation in costs attributable to water recreation depended primarily on assumptions concerning the monetization of lost productivity. In general, costs of gastrointestinal (GI) illness among all water recreators were observed to be larger among those with greater exposure to recreational water, after controlling for potential confounding variables.

Data from recreational waterborne disease outbreaks, in addition to data from the CHEERS and NEEAR studies, were used to calculate an estimate of the total economic burden due to recreational waterborne illness on untreated surface water impacted by fecal contamination in the United States. The total economic burden due to recreational waterborne illness, including sporadic GI, respiratory, eye, ear, and skin illnesses, as well as illnesses associated with outbreaks, was estimated to range between $3.1 and $4.7 billion annually. This estimate included costs associated with medications, visits with an HCP, visits to an ED, hospitalizations, as well as costs related to time missed from work, mortality, and sequelae. In general, costs associated with GI illness were estimated to account for more than 50% of the total economic burden due to recreational waterborne illness on untreated surface water. Additionally, it was found that almost 40% of the total economic burden was estimated to be associated with time missed from work and mortality due to recreational waterborne illness.

1. INTRODUCTION

1.1 <u>Overview of Epidemiologic Basis for Recreational Water Quality Criteria</u>

Historically, epidemiologic studies have been the primary basis for the development of recommendations to protect human health at untreated recreational waters. Untreated recreational water includes lakes, streams, rivers, oceans, and other naturally occurring bodies of water, while treated recreational water includes spas and swimming pools. A study published in 1953 reported a markedly higher incidence of ear, eye, nose, and throat symptoms, as well as GI and skin symptoms among swimmers versus nonswimmers at recreational beaches (Stevenson, 1953). This epidemiologic study was used as part of the basis for the microbiological guidelines for contact with untreated recreational waters set in 1968 by the National Technical Advisory Committee to the Federal Water Pollution Control Administration (US NTAC, 1968).

Fecal indicator bacteria (FIB), such as enterococci and *Escherichia coli* (*E. coli*), are measured as a surrogate for fecal contamination as well as several disease-causing pathogenic microbes present in recreational water. Potential sources of fecal indicator organisms include human sewage, nonpoint sources such as urban runoff, or animals shedding fecal indicator organisms (Colford et al., 2007). Several known disease-causing pathogens may be present in recreational water due the presence of human fecal pollution, including organisms such as *Cryptosporidium* and *Giardia*, among others (Pond, 2005).

Numerous epidemiological studies have been conducted to characterize the relationship between FIB concentrations in surface waters and the risk of GI illness (Cabelli, 1983; Dorevitch et al., 2012a; Dufour, 1984; Wade et al., 2008). Recent epidemiologic studies, examining the relationship between FIB and GI illness have primarily focused on novel indicators of fecal contamination (Colford et al., 2007) and have included the use of rapid molecular methods for quantifying indicator bacteria (Wade et al., 2006). Other studies have evaluated different types of source water, such as inland lakes (Marion et al., 2010), or have focused on the potential use of different guide values for indicators in setting recreational water quality standards (Wiedenmann et al., 2006). All of these studies evaluated GI illness, respiratory illness, as well as ear, eye, and skin symptoms as a binary variable: illness was present or absent. Very few recent studies have addressed the range of severity of illness observed among study participants.

1.2 Severity of Illness

In contrast to studies of health effects of exposure to contaminated recreational water, the severity of illness has been used extensively to evaluate the relationship between air pollution and health. Previous studies have evaluated relationships between air pollutants and a spectrum of asthma severity, including medication use (Slaughter et al., 2003; Schildcrout et al., 2006), missed school, emergency department (ED) visits (Gilliland et al., 2011), hospitalizations, and death. Additionally, research done to examine the relationship between cardiovascular disease and exposure to air pollutants has also gone beyond only measuring the occurrence of disease, but also in assessing a range of outcomes that could lead to more serious cardiovascular consequences (Brook et al., 2004).

Few epidemiology studies have directly assessed the severity of illness attributed to water recreation. In the 1990s a randomized intervention trial conducted at four separate swimming locations in the United Kingdom was the first epidemiologic study to evaluate and assess the severity of illness due to water recreation. Healthy volunteers were recruited and randomly assigned to bather or non-bather groups. Participants assigned to the bather group were asked to spend a minimum of ten minutes in the water and perform head immersion a total of three times. Information was collected from bathers and non-bathers who developed illness, specifically about the duration of symptoms, whether medical attention was sought, and if any time was lost from regular activities due to illness. Severity was assessed among those who developed gastroenteritis, acute febrile respiratory illness, as well as ear or eye ailments. However, no significant difference was observed between the duration of symptoms, the proportion that seek medical attention, and the proportion that report missing time from normal daily activities for bathers compared non-bathers for any of the outcomes (Fleisher et al., 1998).

Waterborne disease outbreaks (WBDOs) occur in both treated (swimming pools) and untreated (lakes, oceans) surface water. In the United States, from 2009 to 2010, 29% of WBDOs occurring in untreated recreational water have resulted in at least one hospital admission (Hlavsa et al., 2014). However, only a small percentage of the more severe outbreaks are investigated and not all outbreak investigations report information regarding the severity of illness (Yoder et al., 2008). These investigations only consider hospital admissions and the number of deaths, rather than lesser, but significant, degrees of illness severity that resulted in physician office or ED visits that did not lead to hospital admission.

In 2005, a World Health Organization (WHO) report highlighted the development of a Severity Index (Pond, 2005) designed to aid public health professionals in setting priorities for recreational water management, with a goal of decreasing the chance of severe illness among recreational surface water users. The Severity Index is based on several factors such as the case fatality rate, duration of illness, hospital admissions, and the frequency and the severity of sequelae (Pond, 2005). The report suggests that the pathogen concentration, the degree of water exposure, and the immune status of the individual play critical roles in determining the severity of illness. The Index is pathogen-specific and has not been able to inform monitoring at beaches since pathogens responsible for illness are rarely identified for surface water recreators (Dorevitch et al., 2012b; Jones et al., 1991) except in the context of recognized outbreaks (Dziuban et al., 2006; Yoder et al., 2004; Yoder et al., 2008). Furthermore, FIB rather than a broad constellation of pathogens are analyzed and reported in beach water monitoring efforts (US EPA, 2012).

It is not well understood which particular infectious agents are directly responsible for excess cases of GI illness among water recreators in epidemiology studies. In previous analyses, specific pathogens responsible for waterborne illnesses have not been able to be identified in stool samples of symptomatic study participants (Dorevitch et al., 2012b; Jones et al., 1991). Additionally, on an individual level it is difficult to ascertain which water recreators have GI symptoms due to water recreation versus a GI infection due to another cause versus symptoms that are due to a noninfectious cause. Some agents, including *Cryptosporidium* and *Giardia*, may be present in recreational water, which can cause illness among water recreators (Pond, 2005). These pathogens are known to be often associated with recreational waterborne disease outbreaks (Dziuban et al., 2006; Yoder et al., 2004; Yoder et al., 2008).

The severity of illness can be assessed among water recreators. Currently, in epidemiologic studies, illness is described using a predefined case definition. Individuals in these epidemiology studies are either ill or not ill based on the conditions outlined in the case definition. It is unclear how sensitive or specific the current illness criteria are for assessing illness, since there is no “gold standard” for describing recreational waterborne illness. It is anticipated that exposure to recreational water contaminated with fecal pollution may result in a range of symptom severity. However, only a portion of those with symptoms will be considered ill based on the case definition. Evaluating measures of symptom severity in addition to the occurrence of illness, can allow for an understanding of where current presence/absence illness definitions fall on the spectrum of severity.

The severity of symptoms may be useful in the future for identifying new thresholds for illness outcomes among water recreators. The use of severity to define waterborne illness can either create an extremely sensitive definition of illness, or create a very specific definition of illness. However, by examining the relationship between severity and water exposures, one can determine where the difference in severity is maximized, and where the potential new illness threshold should be placed. Thus, the use of severity to describe health outcomes may therefore improve the sensitivity and specificity of the current definition of illness.

The relationship between exposure and severity of GI illness is demonstrated in Figure 1. Several factors may be related to the relationship between exposure and the subsequent manifestation and the severity of symptoms. Dose itself has been demonstrated to be related to the occurrence of illness (Keene et al., 1994) and has been suggested to be directly related to the severity of symptoms. Previous outbreaks of salmonella (Glynn and Bradley, 1992; Mertens et al., 2013; Taylor et al., 1984) and studies related to hepatitis E (Purcell and Emerson, 2008) have indicated that increased dose is related to more severe outcomes, but often depends on the strain and virulence of the organism. It is expected that age and certain comorbid conditions may modify the association between exposure and increased severity. Previous studies have suggested that children and the elderly may be more likely to have more severe symptoms relative to healthy adults (Glynn and Bradley, 1992; Fisker et al., 2003; Rocourt and Motarjemi, 2014). Evidence from studies of foodborne illness have suggested that those with decreased immune function often develop more severe illness outcomes (Lund and O'Brien, 2011; Rocourt and Motarjemi, 2014). Additionally, further evidence from the literature indicates that exposure to enteric microorganisms can exacerbate symptoms among those with preexisting GI conditions (Karaoglu et al., 2004; Szilagyi et al., 1985).

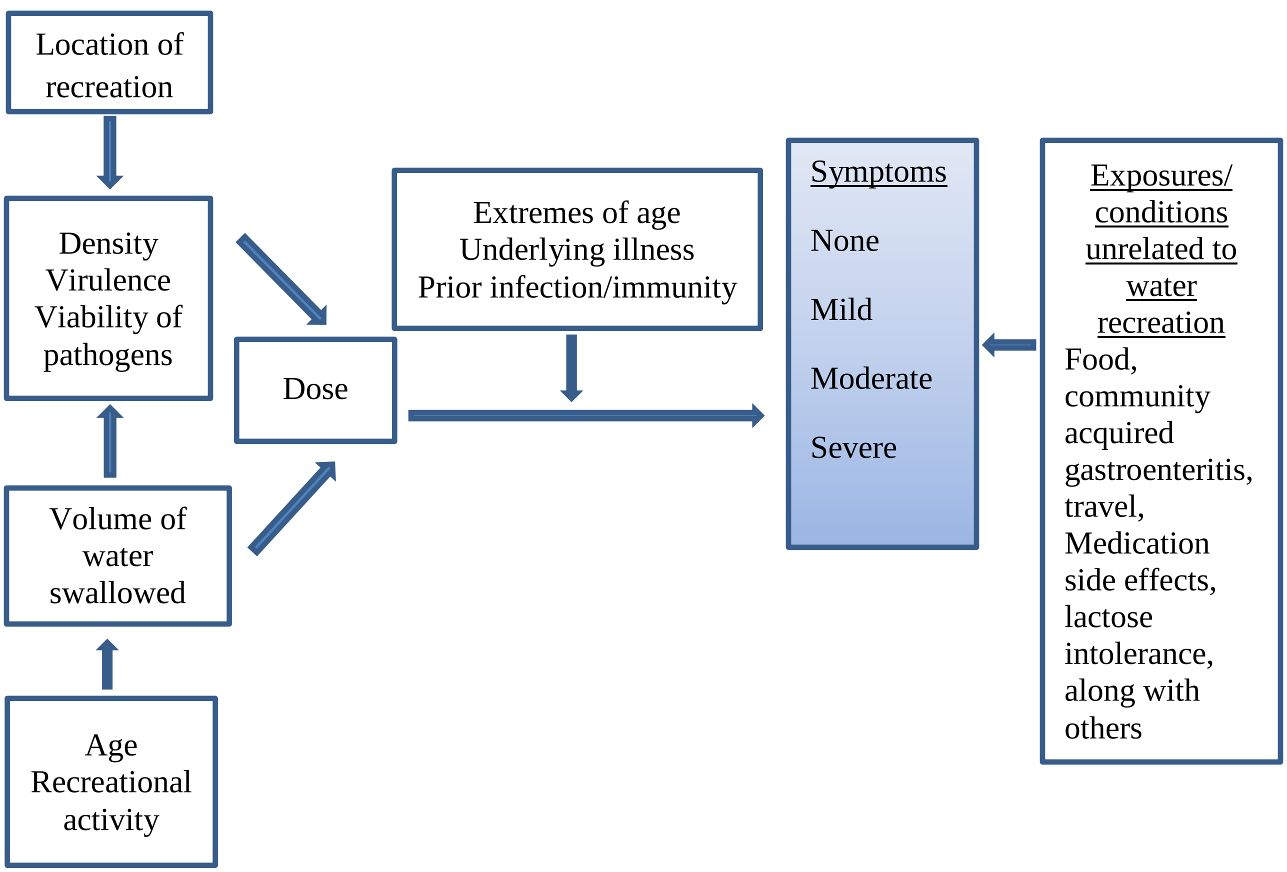

Figure 1. Causal diagram for the relationship between severity and exposure.

1.3 Burden of Disease

The frequency and the severity of illness are elements of the burden of disease. More specifically, burden of disease encompasses the total number of cases of illness, the severity of those cases, and can include the economic impacts associated with those illnesses (Rice et al., 2006). Burden analysis typically utilizes data from epidemiologic studies in order to determine the number of cases of illness, the typical symptoms experienced by each case, as well as the duration and frequency of the symptoms (Murray et al., 1996). There is no universally accepted method of measurement for disease burden. However, disease burden metrics should be useful in helping to set health service priorities, set research goals, identify sensitive subgroups, as well as for evaluation and planning (Murray, 1994).

A common measure of disease burden is the disability adjusted life year (DALY), which is used extensively in the health economics literature (Rice et al., 2006). The WHO defines DALYs as the sum of the years of life lost due to disease and the amount of time spent living with a disability (Mathers et al., 2008; Murray et al., 1996). The DALYs are good for describing and comparing the burden of disease across large communities with diverse health experiences. For example, the burden of a disease that causes premature death with little to no disability, such as drowning, can directly be compared to other diseases that cause chronic disability without death, such as blindness (Mathers et al., 2008). Previously, DALYs have been used to compare the global impact of bathing and consuming raw or undercooked shellfish in coastal waters polluted by wastewater to other global diseases (Shuval, 2003).

Another common burden of disease metric, the quality adjusted life year (QALY), incorporates measures of quality of life (Philips, 2009; Rice et al., 2006). Quality of life is described by health utilities, which can be calculated using several different mechanisms. Health utilities can range between 0, a state equivalent to death, to 1, a state equivalent to perfect health, and are multiplied by the number of years in that particular health state (Philips, 2009). The QALYs are typically used to assess interventions (Philips, 2009; Sassi, 2006). Other studies have measured burden of foodborne illness in the United States using QALY losses (Hoffmann et al., 2012).

Other burden of disease measures are monetary measures such as willingness to pay (WTP) and cost of illness (COI). The WTP approach involves establishing the amount an individual is willing to pay in order to avoid illness, and has been used extensively in the field of health economics. The COI approach is more direct and incorporates the costs of lost productivity and medical expenses (Rice et al., 2006). Following the *Cryptosporidium* drinking water outbreak in Milwaukee, Wisconsin in 1993, a COI approach was used in order to quantify the economic impact due to the contaminated water source. It was determined that approximately 1% of the 403,000 who experienced symptoms were hospitalized and 11% sought medical care, for a total cost of $96.2 million, in 1993 dollars (Corso et al., 2003). Another COI analysis was used to assess the economic burden due to a *Salmonella* drinking water outbreak in Alamosa, Colorado. This outbreak was estimated to cost approximately $1.5 million to the residents and businesses within the outbreak area (Ailes et al., 2013).

The COI has also been evaluated for illnesses associated with water recreation in Orange County, California (Dwight et al., 2005). The authors sought to characterize the cost of medical visits and costs associated with missed daily activities for waterborne illness among users of two California beaches, using the distribution of illness severity described by Fleisher et al. (1998). Dwight and colleagues then utilized an estimate of the number of cases of illness at the beaches derived from a modeling study (Turbow et al., 2003) and applied cost data specific from Southern California. Costs of GI, respiratory, ear, and eye illness were estimated. Due to lack of data, costs associated with hospital admission, ED visits, and medication use were not included in the estimates for this study. The authors concluded that the estimated annual COI at the two beaches studied was approximately $3.3 million in 2001 dollars, or $36.58, $76.76, $37.86, and $27.31 per case of GI, respiratory, ear, and eye illness, respectively (Dwight et al., 2005). This estimate would be much greater if cost data for hospitalizations, ED visits, and medications were included in the calculation.

A limitation of the COI approach is that it does not incorporate information regarding a person's preference for avoiding illness and suffering, which would be captured in a WTP approach. However, the COI approach is favored by many regulatory agencies, such as the Environmental Protection Agency (EPA), because it can be easily interpreted. The EPA utilizes the COI to evaluate severe illnesses due to environmental exposures because it can be useful for policy evaluation or development, economic analysis, and for environmental decision making (US EPA, 2007). The use of the COI to evaluate the burden of disease may be the best choice for assessing costs associated with recreational waterborne illness, since other burden of disease metrics may lack sensitivity when evaluating less severe health outcomes (Phillips, 2009). Evaluating illness among water recreators in terms of dollars may serve as a novel method by which to evaluate potential adverse effects due to water recreation in future studies.

1.4 National Estimate of Burden of Waterborne Disease

A recent study (Collier et al., 2012) estimated the total economic burden due to hospitalizations from drinking and recreational water using medical and pharmaceutical claims data from Medicare and commercial insurance carriers. Illnesses thought to be primarily transmitted by water, including giardiasis, cryptosporidiosis, Legionnaires' disease, otitis externa, and non-tuberculosis mycobacterium infections were estimated to cost more than $970 million (in 2007 dollars) annually. Illnesses considered partially transmitted by water, including campylobacteriosis, salmonellosis, shigellosis, hemolytic uremic syndrome, and toxoplasmosis were estimated to cost $860 million annually. The authors estimated the number of cases that may have been waterborne based on the pathogens found to be primarily responsible for their illness, since no data were available regarding potential water exposures for those who were ill. In addition, the study only was able to characterize the most severe cases that resulted in a hospital admission. No data were available for any other medical costs, or an estimate of the number of days of work or school that were missed due to illness.

Estimates of the costs associated with waterborne disease would be useful for determining resource allocation and helping to prioritize waterborne disease prevention initiatives (Collier et al., 2012). Using illness information from epidemiology datasets along with the costs associated with illness will aid in determining an approximate national estimate of the burden of disease due to water recreation. This information may be useful to public health researchers in comparing the economic burden of recreational waterborne illness to the costs of beach monitoring programs or to the costs associated with illness acquired through drinking water or food.

1.5 Objectives

The current literature is quite limited regarding the severity of illness and economic burden of disease attributable to water recreation in light of the ubiquity of water recreation in the United States. Two similar epidemiologic studies of water recreation and health risk have been conducted in the past decade, one of full-contact recreators (swimmers) (NEEAR) and one of people who engage in incidental-contact water recreation, such as boating, fishing, and paddling (CHEERS). The primary objectives of the current study are to use the available epidemiologic data to (1) characterize the severity of illness among water recreators and describe predictors of illness severity, such as demographics, water exposure and water quality; (2) characterize the economic burden of GI illness attributable to water recreation and compare burden estimates among water recreation subgroups; and (3) estimate the burden of recreational waterborne illness on untreated surface water at a national level.

2. WATER RECREATION AND ILLNESS SEVERITY

Historically, epidemiologic studies have evaluated risk due to water recreation on US surface waters by assessing the occurrence of cases of GI illness, or non-enteric illnesses such as respiratory, eye, ear, and skin symptoms among water recreators compared to non-water recreators (Cabelli, 1983; Dorevitch et al., 2012a; Dufour, 1984; Wade et al., 2008). Many of these epidemiologic studies assessing exposure to recreational surface waters in the United States (Cabelli, 1983; Dufour, 1984; Stevenson, 1953; Wade et al., 2008) have been used to inform policy for setting water quality criteria recommendations (US EPA, 1986; US EPA, 2012; US NTAC, 1968), because FIB, primarily *E. coli* and enterococci, indicators of the presence of fecal pollution, have been identified as predictors of the occurrence of GI illness among water recreators (Cabelli, 1983; Dufour, 1984).

Waterborne disease outbreaks (Dziuban et al., 2006; Yoder et al., 2004; Yoder et al., 2008) and a handful of epidemiologic studies (Dorevitch et al., 2012a; Fleisher et al., 1998; Wade et al., 2013) demonstrate that illness severity varies among water recreators who develop disease following water recreation. However, current epidemiologic studies on water recreation and health do not differentiate between the risk of developing mild symptoms versus life-threatening disease. Certain factors, including comorbidities and age, have been known to influence severity (Fisker et al., 2003; Glynn and Bradley, 1992; Karaoglu et al., 2004; Lund and O'Brien, 2011; Pond, 2005; Rocourt and Motarjemi, 2014; Szilagyi et al., 1985). Additionally, the presence of other comorbid conditions, such as diabetes, has been known to influence whether or not an individual will develop a serious infection (Joshi et al. 1999).

The severity of illness has been a common outcome measure in previous studies on air pollution and health. These studies have assessed outcomes due to exposure to air pollution such as the number of school days missed (Gilliland et al., 2001), and the frequency of medication use (Schildcrout et al., 2006; Slaughter et al., 2003), among others (Brook et al., 2004). However, there is a lack of knowledge regarding the severity of illnesses attributed to water recreation (Fleisher et al., 1998). Assessing only the occurrence of recreational waterborne illness may fail to characterize the burden of disease, which takes into account both the occurrence and severity of illness that can be related to water exposure (Pond, 2005). By evaluating severity, the relationship between water exposure and illness can be further explored.

The severity of illness among water recreators was originally assumed to be relatively mild and thus not of large public health significance (Fleisher et al., 1998; US EPA, 1986). However, the findings of the study conducted by Fleisher et al. (1998) and evidence from outbreaks (Yoder et al., 2008) indicate that illness associated with recreational waterborne illness result in losses in daily activities and use of the healthcare system, thus implying that recreational waterborne illness is relatively significant and warrants further investigation. In the study by Fleisher et al. (1998), the proportion or fraction of illnesses attributable to water recreation varied from 35% for GI illness to 66% for ear illnesses, implying that water contaminated by domestic sewage is responsible for a large proportion of illnesses among water recreators. Additionally, foodborne outbreaks (Glynn and Bradley, 1992; Mertens et al., 2013; Taylor et al., 1984) and other studies (Purcell and Emerson, 2008) have indicated that increased dose of exposure is associated with more severe outcomes. Therefore, it is hypothesized that exposure to contaminated surface water may be related to increased severity observed among those who are exposed to recreational surface water (Figure 1).

To more fully explore the severity of symptoms associated with recreational water exposure, I utilized data from two epidemiologic studies of water recreation to characterize the severity of illness among water recreators. The studies were also used to describe predictors of illness severity including demographics and certain water exposures, as well as water quality. Severity among full-contact water recreators engaged in swimming was evaluated among participants in the NEEAR study from 2003–2007 (Wade et al., 2008; Wade et al., 2006; Wade et al., 2010a), while severity among incidental-contact water recreators, engaged in fishing, boating, rowing, kayaking, and canoeing, was evaluated among participants in the CHEERS from 2007–2009 (Dorevitch et al., 2012a).

2.1 Methods

2.1.1 Study Population

Participants for the NEEAR study were recruited at seven different marine and freshwater beaches impacted by human fecal pollution, located in Alabama, Indiana, Michigan, Mississippi, Ohio, and Rhode Island. Recruited beachgoers included those with and without beach water contact. Recruiting, survey administration, and corresponding water sampling methods have been described previously (Wade et al., 2008; Wade et al., 2006; Wade et al., 2010a). The CHEERS participants were recruited from 39 locations in Chicago along the Chicago Area Waterway System (CAWS), which includes the Chicago River; the General Use Waterways (GUW), which includes Lake Michigan and other inland lakes; and an unexposed group composed of outdoor recreators not engaged in water recreation. On the CAWS, over 90% of the flow during dry weather is non-disinfected wastewater. The GUW waters are significantly less polluted by wastewater. Methods regarding survey administration and water quality sampling methodology have been described previously (Dorevitch et al., 2012a) (Appendix A: Section A).

Both NEEAR and CHEERS followed similar methodological approaches for evaluation of the development of illness and illness severity. In general, participants were interviewed directly before and after recreation and participated in telephone follow-up. In the NEEAR study, n=27,276 participants were engaged by telephone follow-up 10–12 days following recreation (Wade et al., 2008; Wade et al., 2006; Wade et al., 2010a); while CHEERS participants (n=11,297) were contacted approximately 2, 5, and 21 days following recreation (Dorevitch et al., 2012a).

2.1.2 Case Definitions and Exclusion Criteria

Both studies had similar case definitions for GI, respiratory, ear, eye, and skin symptoms (TABLE I), which were used in previous analyses (Dorevitch et al., 2012a; Wade et al., 2008; Wade et al., 2006) to define the occurrence of illness. Since CHEERS had a longer follow-up period, symptoms that developed among CHEERS participants 12 or more days following recreation were excluded to match the NEEAR study definition of illness. In CHEERS, a greater odds of the occurrence of GI illness was observed among water recreators compared to non-water recreators for those meeting the case definition within 0–3 days following recreation. The GI illness that developed outside of this time window appeared to be less related to water exposure (Dorevitch et al., 2012a). Therefore, GI illness severity was also assessed among those with GI illness developing within 0–12 days and within 0–3 days of recreation in both studies. Any study participants experiencing baseline symptoms at the time of enrollment and women who were pregnant or experiencing stomach cramps due to menstruation were excluded from the analysis (Appendix A: Section B).

TABLE I
CASE DEFINITIONS USED TO DEFINE ILLNESS IN CHEERS AND NEEAR

	CHEERS	NEEAR
GI illness	(1) three episodes of diarrhea in 24 hours, or (2) vomiting, or (3) nausea with stomachache, or (4) nausea that interferes with daily activities, or (5) stomachache that interferes with daily activities.	(1) three episodes of diarrhea in 24 hours, or (2) vomiting, or (3) nausea with stomachache, or (4) nausea that interferes with daily activities, or (5) stomachache that interferes with daily activities.
Respiratory illness	Fever and nasal congestion, or fever and sore throat, or cough with phlegm	Two of the following: sore throat, cough, runny nose, cold, or fever
Eye illness	Eye redness, crusting, itching, or draining of the eyes	Eye infection or watery eyes
Ear illness	Ear pain or ear infection	Earache, ear infection, or runny ears
Skin illness	Symptoms related to skin rash	Rash or itchy skin

2.1.3 Severity Metrics

There is no consensus on the best measures for evaluating the severity of illness due to illness. Prior studies of recreational waterborne illness have assessed severity according to the duration of symptoms (Fleisher et al., 1998), or the frequency of hospitalization (Dziuban et al., 2006; Pond, 2005; Yoder et al., 2004; Yoder et al., 2008). In the current analysis, severity of GI symptoms and the severity of a combination of all symptoms (either GI, respiratory, ear, eye, or skin) were evaluated. The majority of waterborne pathogens are transmitted via the fecal-oral route and therefore most commonly result in the development of symptoms of GI illness (Pruss, 1998). However, illness severity would be potentially greater among persons experiencing multiple symptoms associated with multiple organ systems compared to those who have symptoms only associated with GI. Several metrics were used (Figure 2) to evaluate illness severity and are described individually below.

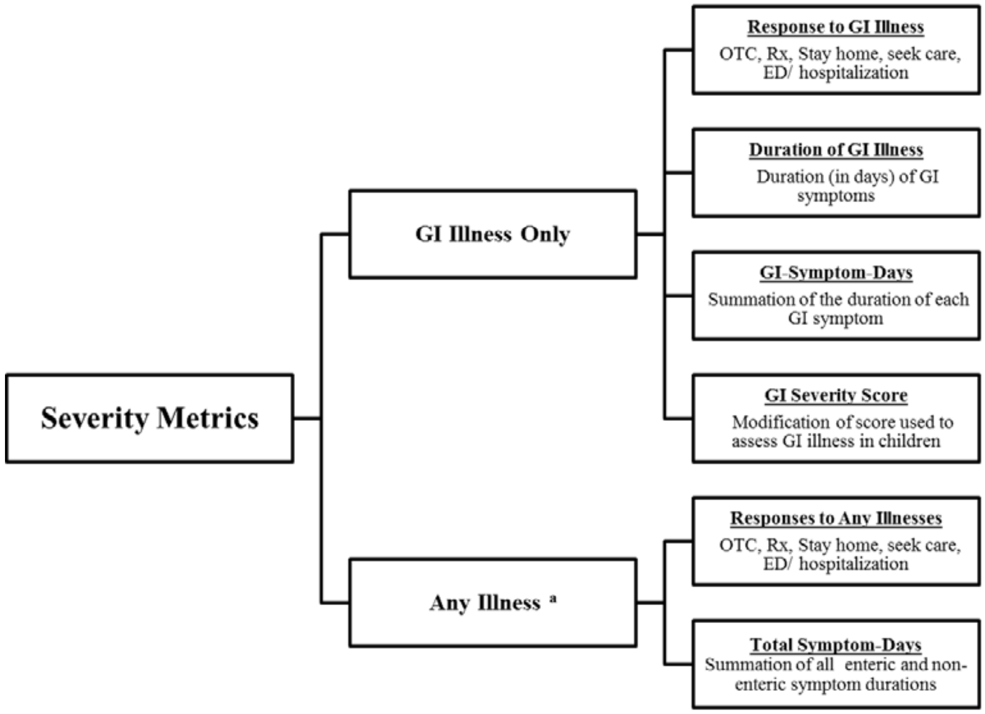

Figure 2. Description and definition of severity metrics.
[a] Either GI, respiratory, ear, eye, or skin

2.1.3.1 Responses to Illness

Illness severity directly influences the decision to visit an HCP (Scallan et al., 2006; Stratmann, 1999) or to stay home from work (Stratmann, 1999). In telephone follow-up for both NEEAR and CHEERS, participants were asked if they stayed home from work or school, took over-the-counter (OTC) medication, took prescription medication, contacted an HCP, or were admitted to an ED or hospital. These are referred to as "responses to illness." Responses to illness could be related to socioeconomic status (SES) and issues concerning access to healthcare (Adler et al., 1993; Anderson et al., 1997; Blackwell et al., 2009; Stratmann, 1999). Thus, SES could influence whether or not a person responds to their symptoms. To evaluate whether responses to illness were independent, median household income was obtained from the US Census and matched to NEEAR and CHEERS participants using zip code of residence. Further analyses of income and other SES characteristics among water recreators and non-water recreators are described in Appendix B.

In the current analyses, responses to illness were evaluated for all participants from both studies for GI symptoms alone (diarrhea, vomiting, nausea, and stomachache) and for any symptoms (either GI, respiratory, ear, eye, or skin symptoms). In the NEEAR study, telephone follow-up responses to illness were evaluated individually for each type of symptom (GI, respiratory, ear, eye, and skin). In contrast, during each round of telephone follow-up in CHEERS, participants were asked about responses to illness without differentiating, among those with more than one type of symptom, which symptom(s) prompted each response. Therefore, separate analyses of data from CHEERS, were conducted to evaluate the severity of illness for those only with GI symptoms, and for those with GI and other symptoms (Appendix A: Section B).

Certain responses to illness were considered to be more severe than other responses. Previous analyses of foodborne illness have considered illnesses that result in contact with an HCP to be more severe than illnesses that require no contact with an HCP (Hoffman et al., 2012). Additionally, the severity of illness has been demonstrated to be directly related to one's decision to miss work (Scallan et al., 2006; Stratmann, 1999). Therefore, it was assumed that those only taking OTCs had less severe illness and those that indicated lost time from daily activities or work, taking prescription medication, contacting an HCP, or going to an ED or hospital, had more severe symptoms.

Responses to illness were dichotomized in two different ways: (1) those with any response to illness (stayed home from work or school, took OTC or prescription medications, contacted an HCP, visited an ED, or hospitalized) were compared to those who did not indicate a response to their illness; and (2) those who had more severe responses to illness (stayed home from work or school, took prescription medications, contacted an HCP, visited an ED, or hospitalized) were compared to those who either had less severe responses to illness (took OTC medications) or denied any response to their illness. Therefore, these two dichotomizations differed by either including those who take OTC medications in the high severity group or the reference group. Taking only OTC medications may not be associated with severe illness outcomes. Responses to illness were also evaluated as a multilevel outcome and were categorized according to severe response to illness (stayed home from work or school, took prescription medications, contacted an HCP, visited an ED, or were hospitalized), those who responded in a less severe manner (took OTC medication), with those with no response to their symptoms as the reference group.

2.1.3.2 Gastrointestinal Severity Score

For enteric illnesses, scoring systems have been developed to assess GI severity using information such as the duration of diarrhea, maximum number of diarrheal stools in 24 hours, body temperature, the duration of vomiting (Hjelt et al., 1987), dehydration, type of treatment (Flores et al., 1987), the maximum episodes of vomiting in 24 hours (Ruuska and Vesikari, 1990), and changes in behavior (Clark et al., 2004; Clark et al., 1988). Different versions of the GI severity score have been utilized in randomized control trials to test the efficacy of rotavirus vaccinations in children (Clark et al., 2004; Clark et al., 1988; Flores et al., 1987). These scoring systems were modified to accommodate the data available from the two epidemiological studies and included six different scoring criteria with a maximum GI severity score of 18 points (TABLE II). The GI severity score was dichotomized at a score of six, which corresponded to a definition of moderate GI illness in a study of rotavirus infection in children (Freedman et al., 2010). Additionally, tertiles of GI severity score were created with the lowest tertile of GI severity score as the reference group.

TABLE II

MODIFIED GASTROINTESTINAL SEVERITY SCORE

Component of score	**0 Points**	**1 Point**	**2 Points**	**3 Points**
Duration of diarrhea (days)	0	1–4	5	≥6
Maximum number of loose stools in 24 hours	0	1–3	4–5	≥6
Duration of vomiting (days)	0	1	2	≥3
Body Temperature (°F)	≤98.6	98.7–101.1	101.2–102.0	≥102.1
Healthcare Provider	None		Contact with HCP	ED
Treatment	None	OTC Medication	Prescription medication	Hospitalization

2.1.3.3 Duration of Gastrointestinal Illness

The duration of GI illness is a common metric for describing the severity of illness in WBDOs (MacKenzie et al., 1995) and has been used in one previous randomized control study of beach water exposure (Fleisher et al., 1998). In the current study, GI illness duration was calculated based on the self-reported start and end dates of stomachache or stomach cramps, diarrhea, nausea, and vomiting reported during telephone follow-up (Appendix A: Section B). It was expected that duration may vary according to age (Van Den Brandhof et al., 2004) and other comorbidities. It has been recommended by the National Digestive Diseases

Information Clearinghouse, that individuals with GI symptoms lasting for two or more days should contact an HCP (NDDIC, 2013). Previous analyses have indicated that contact with an HCP is indicative of more severe illness (Hoffman et al. 2012). For this reason I dichotomized duration of GI illness at two days, which also corresponded to the median duration of GI illness in both studies.

2.1.3.4 Symptom-Days

Illness could be considered more severe if an individual had numerous symptoms for a given number of days compared to having a single symptom. In the current study, to define severity as it relates to symptom duration, I applied a symptom-days metric (*Equation I*), which sums the number of symptoms and the duration of each symptom during illness. Symptom-day measures were developed for participants from both studies with respect to GI symptoms alone (diarrhea, vomiting, nausea, and stomachache), and for total symptoms (either GI, respiratory, ear, eye, or skin symptoms). Others have suggested that greater weight should be placed on symptoms considered more severe (Freedman et al., 2010). Therefore, I multiplied the duration of vomiting and diarrhea by a factor of two (while other symptoms were not weighted). Other weighting approaches, such as using a factor of five or ten, were considered. However, it was thought that a factor of two would be reasonable, as to not overstate the occurrence of vomiting or diarrhea among those who develop symptoms. Unlike duration of GI illness, symptom-days measure severity as a function of duration, type, and number of symptoms. As with duration of illness, it was expected that symptom-days would be influenced by age (Van Den Brandhof et al., 2004) and preexisting illnesses. Symptom-days, for only GI symptoms and total symptoms (either GI, respiratory, ear, eye, or skin), were dichotomized at four symptom-days, which corresponded to the median value in either study. Additionally, tertiles of GI and total symptom-days were created using the lowest tertile of symptom-days as the reference group.

Equation I:

$$symptom\text{-}days = \sum_{i=0}^{n} duration\ of\ symptom\ (i)\ \times f_i$$

where f_i=2 for diarrhea or vomiting and f_i=1 otherwise

All severity metrics occur on a continuum, but in the current analysis were evaluated as binary or ordinal outcomes since they were highly skewed. The different severity categories were created using clinically relevant cut points. Specifically, previous studies have indicated contact with an HCP (Hoffmann et al., 2012) and missing work or daily activities (Scallan et al., 2006; Stratmann, 1999) is indicative of more severe illness. Additionally, GI symptoms lasting for two or more days have been suggested as a threshold for when one should seek care from a medical professional (NDDIC, 2013). The creation of these categories can allow for a further understanding of the distribution of severity for those with certain types of water exposure compared to those who do not have the exposure.

2.1.4 Defining Exposures

I assessed different types of recreational water exposures in the current analysis. First, the distribution of severity metrics were assessed among water recreators was compared to non-water recreators. Water recreators in CHEERS were defined as participants engaged in limited contact water recreation, while non-water recreators were defined as those participating in other outdoor recreation activities. In the NEEAR study, water recreators were defined as those who had any contact with beach water, whether they only waded (wet below their waist only) or swam (wet above the waist), while non-water recreators were those who were at the beach, but did not have any beach water contact.

It was hypothesized that the degree of contact with recreational water would be related to severity (Figure 1). Illness severity was assessed among water recreators who swallowed water compared to water recreators that did not swallow water. Additionally, severity was assessed by comparing those exposed to high levels of fecal indicators to those exposed to lower levels of fecal indicators. In CHEERS, severity was also assessed among water recreators getting their face wet compared to water recreators not getting their face wet and among CAWS compared to GUW recreators, due to the differences in fecal indicator organism concentrations at these two locations. In the NEEAR study, the relationship between severity and digging in beach sand compared to not digging in beach sand was also evaluated, while controlling for beach water exposure. Past studies have observed an elevated risk of GI illness among beach goers with direct contact (digging or being buried in) with beach sand (Heaney et al., 2012).

The degree of water exposure among water recreators was also assessed as an ordinal variable. For CHEERS water recreators, three exposure groups were defined: (1) those that swallowed water; (2) those who did not swallow water but who got their face, torso, or hands wet; and (3) those that were water recreators but did not report any water exposure (reference group). Since the NEEAR study evaluated risk among swimmers, all of those considered water recreators had direct contact with water. Those NEEAR participants who only were wet below their waist were considered waders, while those who got wet above the waist, whether or not they had head submersion or swallowed water were considered swimmers (Wade et al., 2008). To evaluate the degree of water exposure among water recreators as an ordinal variable in

NEEAR, three categories were created: swimmers who swallowed water, swimmers that did not swallow water, and waders (reference group).

Water quality was hypothesized to be related to the severity of illness (Figure 1). Surface water was sampled during water recreation in both epidemiologic studies (Appendix A: Section A). In CHEERS, six different water quality measurements were available for analysis: enterococci by US EPA Method 1600, *E. coli* by US EPA Method 1603, Coliphages (F+ and somatic) by US EPA Method 1602, and *Giardia* and *Cryptosporidium* by US EPA Method 1623. In the NEEAR study, two water quality measurements were available for analysis: enterococci by US EPA Method 1600 and enterococci by quantitative polymerase chain reaction (qPCR). The US EPA Method 1600 is a culture-based method that requires viable enterococci organisms for proper quantification, whereas qPCR measures enterococci DNA, regardless of whether bacteria are viable (Wade et al., 2006). At some locations in CHEERS, on certain days, some measures of water quality, especially F+ Coliphage, *Giardia*, and *Cryptosporidium*, were below the limit of detection (Nieh et al., 2014). Furthermore, measures of these microbes were neither normally nor lognormally distributed. Water quality measurements in both studies were dichotomized at the 75th percentile.

Past tracer studies have found that incidental-contact water recreators who swallowed a mouthful, teaspoon, a drop, or no recreational water, swallowed on average 20.3 mL, 10.8 mL, 10.8 mL, and 3.5 mL, respectively every 60 minutes (Dorevitch et al., 2011). It has also been estimated using similar methods that on average every 45 minutes swimmers under the age of 18 ingest 37 mL and those over 18 ingest 16 mL (Dufour et al., 2006). No other information was available to determine if younger children ingest a greater volume of water compared to older children during water recreation. This information, combined with the concentration (organisms/mL) of F+ and somatic coliphages in CHEERS, and enterococci by Method 1600 and by qPCR in NEEAR, was used to calculate the dose of organisms ingested ((organisms/mL) × (mL of ingested recreational water)). Dose was analyzed as a three-level exposure variable among water recreators in each of the studies, with the lowest tertile as the reference group. Among CHEERS water recreators, tertiles of dose were calculated for CAWS and GUW recreators separately, since CAWS water quality was significantly poorer than GUW water quality (Appendix A: Table LXI).

2.1.5 Statistical Analysis

Severity metrics were analyzed for normality, and bivariate analyses were conducted to evaluate the relationships within the severity metrics. Bivariate analyses were also used to explore the associations between the severity metrics and recreational water exposure or water quality. Initial bivariate analyses evaluated the relative risk (RR) between certain water exposures and severity. In both studies, crude RRs showed a similar relationship between water exposure and severity among those with illness developing within 0–12 days and within 0–3 days following recreation (Appendix A: Table XLI). Since no differences in severity were observed, subsequent analyses focus on those who developed symptoms within 0–12 days of recreation.

The current analysis assessed severity in two different ways. First, severity was assessed among study participants meeting the case definition for illness (TABLE I) (GI for analyses assessing GI illness, or any case definition for analyses assessing any illness). Therefore, among all individuals with illness, those with more severe illness were compared to those with less severe illness, to determine if increased exposure to recreational water was related to more severe symptoms. Previous studies have suggested that increased dose of pathogenic microorganisms may be related to increased severity of symptoms (Glynn and Bradley, 1992; Mertens et al., 2013; Purcell and Emerson, 2008; Taylor et al., 1984). Second, severity was also assessed among all participants, regardless of whether they met the conditions to be considered a case of illness. In these analyses, severity metrics, and not the presence or absence of illness (TABLE I) was used to assess the potential consequences of exposure to recreational water. Therefore, those with symptoms of higher severity were compared to study participants with less severe symptoms, or no symptoms at all. It was expected that a spectrum of severity exists that includes symptoms and responses to illness even among those who do not meet any of the formal case definitions.

2.1.5.1 Separate Analyses of the National Epidemiological and Environmental Assessment of Recreational Water Study and the Chicago Health Environmental Exposure and Recreation Study

Logistic regression was used to evaluate the relationship between exposure and severity in the two epidemiologic studies. Several models assessing different severity outcomes and exposures were examined. Logistic regression was chosen in order to obtain a consistent measure of association (an odds ratio [OR]) for the relationship between each of the severity metrics and the chosen exposure. Adjusted odds ratios (aORs) were calculated using logistic regression analysis in SAS (version 9.3; SAS Institute Inc., Cary, North Carolina). Potential confounders of the association between illness severity and exposure were identified based on the suspected relationship between severity and exposure (Figure 1). All logistic models controlled for age as a dummy variable. Participants 18 years of age or younger and those over

65 were compared to the reference group of adults aged 19 to 65. These groupings were based on the bivariate distribution between age and swallowing water. Those under 18 were more likely to swallow water, followed by those over 65, with those 19 to 65 reporting the least amount of swallowing water. Previous studies have indicated that for every 45 minutes of swimming, those under 18 swallow approximately 37 mL, while those over 18 swallow 16 mL (Dufour et al., 2006). No data were available to determine if younger children ingest a greater volume of water compared to older children. Other confounders (Figure 1), chosen from the list of potential confounders, were included based on a change-in-estimate approach. Covariates were retained if they contributed to at least a 5% change in the crude OR of the association between severity and the primary exposure variable of interest.

Dichotomous measures of severity were evaluated as a function of water exposure in each study. Exposure variables were either assessed as dichotomous (exposure versus no exposure) variables, or as ordinal variables, which assessed the degree of water exposure among water recreators as it relates to severity. When assessing the relationship between severity, measured as responses to illness (OTC use, visits to the ED), and exposure, separate analyses among CHEERS participants with GI illness were conducted for those with only GI illness and those with GI illness in addition to one or more other illnesses, since it was not clear which responses to illness were specifically due to GI symptoms.

Each study (NEEAR and CHEERS) was conducted at multiple locations. Therefore, the effect of potential clustering based on recruitment location within these locations was addressed. Additional analyses included the use of random effect multivariable logit model to determine if there was any effect of location of recruitment on the relationship between severity and exposure. Random effect models were assessed using xtlogit in Stata 11 (StataCorp LP, College

Station, Texas) using the default of 12 quadrature points. The potential effect due to clustering was evaluated by examining the interclass correlation coefficient (ICC) (Appendix A: Section E). The ICCs calculated from random intercept models were extremely small in models of illness among incidental-contact (CHEERS) water recreators (ICC range 10^{-14}-10^{-3}), indicating a lack of clustering due to location in CHEERS (Appendix A: Section E). Therefore, all CHEERS analyses do not control for recruitment location. However, slightly greater ICCs were observed among full-contact water recreators (ICC range 10^{-3}-10^{-1}), with some suggestion that there may be some effect due to recruitment location when evaluating exposure and illness severity in NEEAR. In the NEEAR study, participants could be recruited within households and one person from the household answered follow-up questions as a proxy for the rest of the household members. Therefore, further analyses of NEEAR data control for beach as a fixed effect, and utilize robust estimates of variance to account for household cluster, since severity may be correlated within clusters.

2.1.5.1.1 Effect Modification

It was postulated that the relationship between severity and water exposure could be modified by age and the presence of comorbid conditions (Figure 1). Previous studies have indicated that age can impact illness severity, with children and adults over the age of 65 being prone to more severe illness outcomes (Glynn and Bradley, 1992; Rocourt and Motarjemi, 2014), even without the presence of other comorbid conditions (Fisker et al., 2003). Comorbidities, such as having decreased immune function, may modify the relationship between severity and exposure similarly to what has been observed in studies of foodborne illness (Lund and O'Brien, 2011; Rocourt and Motarjemi, 2014) and what was observed during the 1993 *Cryptosporidium* outbreak (MacKenzie et al., 1994). Those with diabetes have also been found to be at increased risk for a serious infection (Joshi et al., 1999). Additionally, having a preexisting GI condition, such as Crohn's disease or an increased number of daily bowel movements at baseline, which was collected in CHEERS, was also thought to modify the relationship between exposure and severity. Previous analyses have indicated that exposure to enteric microorganisms can exacerbate GI symptoms among those with a preexisting GI condition (Karaoglu et al., 2004; Szilagyi et al., 1985). Effect modification was analyzed using logistic models that contained the two main effects (exposure and effect modifier) and the interaction between the two. Covariates were considered effect modifiers if the interaction between the exposure and the potential effect modifier had p-value<.20 in the fully adjusted model. A high interaction p-value was chosen to increase the power of the analyses (Rothman et al., 2008) and thus identify potentially important interactions that may exist between severity and exposure.

2.1.5.1.2 Ordinal and Multinomial Regression

Logistic models were also assessed using a multilevel severity outcome, among those who met the case definition(s) for illness. Ordinal or cumulative logit assumes the multilevel outcome variable is ordinal and thus the proportional odds assumption (POA) holds. The POA states that the odds of being in one category, compared to the rest of the categories, is proportional to the odds of being in the first two categories, compared to the rest of the categories, and is tested according to a χ^2 test (Ananth and Kleinbaum, 1997; Rothman et al., 2008). When the POA is violated (χ^2<.05), generalized or multinomial logit is preferred, which treats the outcome as a nominal, rather than an ordinal variable (Derr, 2013). In the current analysis, both the single summary OR from ordinal logistic regression, and the multiple ORs, calculated from multinomial logistic regression, comparing each category of severity to the reference group, were calculated when the POA was violated (χ^2<.05).

2.1.5.1.3 Model-Based Standardization

Logistic regression is commonly used in epidemiology since it can adequately and efficiently predict the probability of illness (Rothman et al., 2008). The main measure of association, the OR, produced by logistic regression, is sometimes inadequate for assessing risk, especially when the outcome is common (Greenland, 2004; McNutt et al., 2003). In this analysis, increased severity was relatively common among those meeting a case definition for illness. Other regression models such as the linear risk and log-linear risk, which produce measures of association such as the RR and the attributable risk (AR) or risk difference (RD) respectively, are not as stable and often fail to converge, especially when there are several parameters in the model (Rothman et al., 2008). Model-based standardization, a method that can rely on the robust nature of the logistic model, can produce parameters other than an OR. This was accomplished by calculating a predicted probability of increased severity for each level of the exposure (Greenland, 2004). Model-based standardization was used to assess exposure as an ordinal variable and predicted probabilities of increased severity were calculated for each level of exposure, while controlling for covariates using the change-in-estimate approach. In the case of swallowing water, a predicted probability of increased severity assuming all water recreators swallow water (p_1), and the predicted probability of increased severity assuming no water recreators swallow water (p_0) were calculated to produce the RD (p_1-p_0) and the RR (p_1/p_0). Bias-corrected bootstrapping was performed (1,000 iterations) to obtain confidence intervals for these standardized measures of association, using Stata version 11 (StataCorp LP, College Station, Texas).

To evaluate any potential dose-response relationships between exposure and severity, predicted probabilities of severe illness (stayed home from work or school, took prescription medication, contacted an HCP, visited an ED, or admitted to a hospital) among incidental-contact (CHEERS) water recreators with GI illness were calculated for the four levels of swallowing water (none, a drop, teaspoon, and a mouthful) indicated during follow-up. Plots of the probability of severe illness were created for water recreators with GI illness and differentiated between those with only GI illness and those with GI illness in addition to one or more other illnesses.

2.1.5.1.4 Water Quality and Severity

Exposure was also evaluated as a dichotomous water quality variable and multilevel dose variable. Binary logistic models were used to assess severity and dichotomized water quality, while ordinal and multinomial models were used to assess the relationship between illness severity and tertiles of dose of indicator microbes among NEEAR and CHEERS water recreators. Rather than dichotomizing dose or choosing to leave it continuous, dose was chosen to be measured in tertiles based on the distribution of the data, which indicated three distinct categories of microbe dose.

2.1.5.2 Combined Analyses of the National Epidemiological and Environmental Assessment of Recreational Water Study and the Chicago Health Environmental Exposure and Recreation Study

To further assess severity among all water recreators, regardless of the type of water recreation, the NEEAR and CHEERS datasets were merged and binary severity was predicted, using water ingestion as a main predictor of interest, compared to those not reporting swallowing or ingesting any water. The interaction between exposure (water ingestion) and study

(CHEERS or NEEAR) was evaluated to determine differences in the effect of exposure among the two studies. Using the CONTRAST statement in SAS, study-specific estimates (full (NEEAR) or incidental-contact (CHEERS) water exposure) were calculated for specific severity metrics. All severity metrics were assessed, except for the responses to GI illness. Responses to GI illness specifically among CHEERS participants are indistinguishable from responses to non-enteric illness, since telephone follow-up did not distinguish between responses to illness for each symptom reported, as was done in the NEEAR. All logistic models controlled for age, race, gender, study group, and enterococci density measured by culture.

2.2 <u>**Results**</u>

The CHEERS had 11,297 participants and the NEEAR study had 27,276 participants engage in telephone follow-up. Basic demographics and the proportion of water recreators and non-water recreators with illness were compared within the two studies. In general, water recreators were younger than non-water recreators. In CHEERS, a greater fraction of water recreators developed GI illness within 0–3 days of recreation compared to non-water recreators. However, in the 0–12 day window, a greater fraction of non-water recreators developed GI illness than did water recreators. In the NEEAR study, a greater proportion of water recreators developed GI illness, regardless of the time to illness (0–3 versus 0–12 days) compared to non-water recreators. In CHEERS, water recreators had a greater median household income, according to zip code of residence compared to non-water recreators, which was not observed in the NEEAR study (TABLE III). Differences in estimated income based on zip code of residence are described in Appendix B.

TABLE III

CHARACTERISTICS OF CHEERS AND NEEAR PARTICIPANTS

	CHEERS			NEEAR		
	Water Recreators [a]	Non-Water Recreators	χ^2 p-value	Water Recreators [b]	Non-Water Recreators	χ^2 p-value
No.	7,710	3,587		17,571	9,705	
Race/ethnicity (%)			<.01			<.01
White	79.5	63.5		79.2	79.3	
Black	5.4	16.0		5.6	7.1	
Hispanic	5.9	9.5		10.9	9.8	
Other/mixed	9.3	11.0		4.3	3.8	
Age (mean years) [c]	35.4	38.5	<.01	25.1	35.3	<.01
Age (%)						
<18	16.9	11.4	<.01	42.3	17.3	<.01
18–64	79.5	82.3		56.6	77.4	
≥65	3.6	6.1		1.3	5.3	
Males (%)	49.0	54.7	<.01	45.5	41.3	<.01
Illness after recreation (%) [d]						<.01
GI (0–12 days)	8.7	10.0	0.03	8.0	6.0	<.01
GI (0–3 days)	4.2	3.3	0.04	3.9	2.4	<.01
Respiratory	22.6	25.5	<.01	5.9	4.7	<.01
Ear	1.6	1.3	0.30	1.6	1.2	<.01
Eye	8.1	7.5	0.25	2.8	3.2	0.06
Skin	8.7	8.7	0.94	3.1	2.2	<.01
Response to Illness (%) [e]						
Missed days of school or work	23.4	27.4	<.01	17.6	17.1	0.54
Contact with healthcare provider	11.2	15.4	<.01	10.0	9.9	0.85
OTC Medication	53.6	52.7	0.60	47.4	45.7	0.13
Prescription	5.7	7.7	0.02	7.5	8.0	0.44
Hospitalized/ED	0.7	2.4	<.01	0.9	0.8	0.63
Median Household income [a f] *($52,762)*	71,427	63,655	<.01	56,540	56,540	0.49

[a] Individuals participating in incidental-contact water recreation (kayaking, canoeing, rowing, boating, fishing)
[b] Individuals with any contact with recreational water (swimming, wading)
[c] T-test
[d] Cases that met formal case definition for each study, excluding those with baseline symptoms (TABLE I)
[e] For all symptoms, for those who met any case definition
[f] Obtained from US Census according to zip code of residence

2.2.1 Severity Metrics

In CHEERS, a modest increase in the proportion of non-water recreators with any illness responded to their illness, compared to water recreators (TABLE III). However, in NEEAR, no statistically significant differences in responses to illness between water recreators and non-water recreators were observed. When evaluating CHEERS participants with GI illness, those with GI and other symptoms were more likely to respond to their illness than those with only GI illness (Appendix A: Section B).

The distributions and characteristics of the other severity metrics were similar in the two studies (TABLE IV). The duration of GI illness, GI symptom-days, and the GI severity score were metrics to describe the severity of GI outcomes, while total symptom-days evaluated severity in terms of all potential organ-system outcomes. However, compared to the GI severity score, fewer participants had complete information, including start and end dates for their symptoms, to calculate the duration of GI illness and GI symptom-days (TABLE IV, TABLE V).

In general, symptom duration and responses to illness were associated with one another. Duration of illness (Appendix A:Table XXXIX) and number of symptom-days (Appendix A: Table XL) were larger among those indicating a response to their illness (use of healthcare, taking medication). However, duration of GI illness, symptom-days, and the GI severity score were skewered, with few individuals having values above the mean. Additionally, there was some degree of correlation among the different metrics in both studies (r=.35 to .83) with lowest correlation noted between the GI severity score and duration of GI illness, and the highest correlation noted between GI symptom-days and the duration of GI illness. Participants with symptoms not meeting the case definitions also demonstrated a range of severity (TABLE V), which was generally less severe than those meeting the case definition.

TABLE IV

SEVERITY METRICS FOR PARTICIPANTS MEETING THE CASE DEFINTIONS, BY STUDY AND WATER RECREATION STATUS [a]

		Water Recreators [b]				Non-Water Recreators			
		N	Range	Mean	Median	N	Range	Mean	Median
CHEERS	Duration of GI illness (days)	526	1–26	3.5	2.0	263	1–20	3.6	2.0
	GI symptom-days	526	1–70	7.5	4.0	263	1–70	7.5	4.0
	GI severity score	636	1–11	2.9	3.0	334	1–13	3.2	3.0
	Total symptom-days [c]	1,217	1–70	6.9	4.0	542	1–89	7.4	4.0
NEEAR	Duration of GI illness (days)	1,365	1–13	2.5	2.0	557	1–13	2.8	2.0
	GI symptom-days	1,365	1–55	5.8	4.0	557	1–64	6.0	4.0
	GI severity score	1,377	1–12	2.7	2.0	562	1–15	3.0	2.0
	Total symptom-days [c]	2,606	1–105	7.2	4.0	1,068	1–141	7.2	4.0

[a] All meet the case definition for either GI illness or any illness (either GI, respiratory, eye, ear, or skin) See TABLE I

[b] CHEERS water recreators participated in incidental-contact water recreation (kayaking, canoeing, rowing, boating, fishing), NEEAR water recreators participated in full-contact water recreation (swimming, wading)

[c] Any illness: including GI, respiratory, ear, eye, or skin

TABLE V

SEVERITY METRICS AMONG PARTICIPANTS WITH SYMPTOMS NOT MEETING THE CASE DEFINITION, BY STUDY AND WATER RECREATION STATUS

		Water Recreators [a]				Non-Water Recreators			
		N	Range	Mean	Median	N	Range	Mean	Median
CHEERS	Duration of GI symptoms (days)	515	1–22	1.8	1.0	216	1–22	2.1	1.0
	GI symptom-days	515	1–27	3.1	2.0	216	1–22	3.3	2.0
	GI severity score	652	1–6	1.4	1.0	300	1–7	1.5	1.0
	Total symptom-days [b]	448	1–44	3.3	2.0	171	1–34	3.3	2.0
NEEAR	Duration of GI symptoms (days)	430	1–11	1.9	1.0	229	1–11	1.9	1.0
	GI symptom-days	430	1–11	2.0	1.0	229	1–11	2.0	1.0
	GI severity score	443	1–7	1.6	1.0	240	1–6	1.5	1.0
	Total symptom-days [b]	760	1–13	2.7	2.0	400	1–20	2.8	2.0

[a] CHEERS water recreators participated in incidental-contact water recreation (kayaking, canoeing, rowing, boating, fishing), NEEAR water recreators participated in full-contact water recreation (swimming, wading)

[b] Any illness: including GI, respiratory, ear, eye, or skin

2.2.2 Relationship between Severity and Exposure

2.2.2.1 Separate Analyses of the National Epidemiological and Environmental Assessment of Recreational Water Study and the Chicago Health Environmental Exposure and Recreation Study

The relationship between water exposure and severity was confounded by several different covariates, depending on the outcome and the exposure. All models controlled for age, since it consistently confounded the association between severity and exposure. Based on the change-in-estimate selection process, models for specific severity metrics included one or more of the following: race, gender, frequency of water use, contact with animals, ingestion of either raw meat, hamburger, or fish, contact with someone with GI symptoms, washing hands prior to eating or drinking, and digging in sand (NEEAR participants only) (Appendix A: Table XLII). Additionally, models assessing NEEAR data also controlled for beach as a fixed effect and robust estimates of variance were used to account for household cluster.

In both studies, at least one severity metric was significantly associated with swallowing water among water recreators (Figure 3). In CHEERS, the subset of water recreators with illness meeting the case definition (TABLE I) who swallowed water were more likely to have a severe response to their GI illness (either staying home from work or school, taking prescription medication, contacting an HCP, visiting an ED, or being admitted to the hospital versus to those only taking OTCs or having no response to their symptoms) compared to water recreators that did not swallow water. Among CHEERS water recreators with GI illness, it could not be determined which symptom(s) prompted each of the responses to illness, therefore separate analyses were conducted among all of those with GI illness (with or without other symptoms), those with GI symptoms only, and for those with GI and other symptoms (respiratory, ear, eye, or skin) for the relationship between severity and swallowing water (Appendix A: Table XLVI). The observed aOR for the relationship between severe responses to GI illness and swallowing water compared to not swallowing water among those with GI illness with or without other symptoms was 2.19 (95% CI: 1.08, 4.40), while for those with GI illness only it was 1.19 (95% CI: 0.40, 3.56), and those with GI illness combined with another illness it was 3.21 (95% CI: 1.14, 9.05). Based on these results a stronger relationship is observed for CHEERS water recreators who have GI illness in addition to other symptoms, compared to those who only have GI illness. No significant associations were observed among the subset of NEEAR water recreators with illness among those who swallowed water compared to those who did not swallow water.

Additionally, among all CHEERS water recreators, those who swallowed water were more likely to have four or more GI symptom-days, and four or more total symptom-days compared to water recreators that did not swallow water (Figure 3). In NEEAR, among all water recreators, those who swallowed water were more likely to have four or more GI symptom-days, a GI severity score greater than six, and four or more total symptom-days, compared to water recreators that did not swallow water. The aORs for the relationship between CAWS versus GUW water recreators (not shown), face wetness among CHEERS participants (Appendix A:Table XLVIII), and any contact with the water (Appendix A:Table XLIX) or digging in sand (Appendix A: Table L) among NEEAR participants were generally insignificant regardless of the subset of participants of interest.

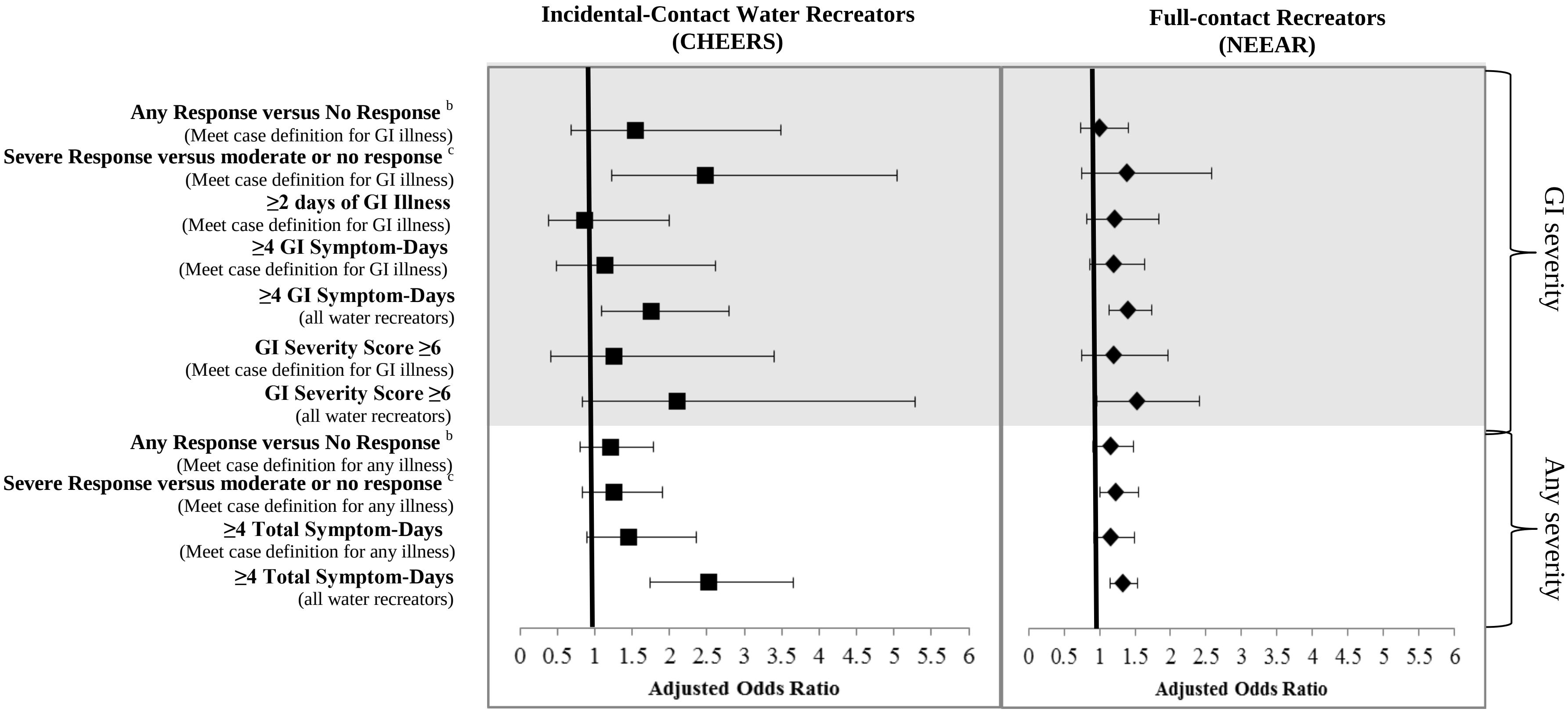

Figure 3. Adjusted OR (95% CI) of the association between severity and swallowing water among incidental-contact (CHEERS) and full-contact water recreators (NEEAR). [a]

Shaded area represents severity due to GI symptoms; white area represents severity of any symptoms (GI, respiratory, eye, or ear)

[a] All models controlled for age and other confounders (Appendix A:TABLE XLVI–TABLE XLVII), NEEAR models additionally control for beach as a fixed effect and account for household cluster

[b] Responded to illness by either staying home from work or school, taking OTC or prescription medication, contacting an HCP, or visiting an ED or being admitted to the hospital versus those who did none of these

[c] Responded to illness by either staying home from work or school, taking prescription medication, contact with an HCP, or visiting an ED/being admitted to the hospital versus those only taking OTCs or who did none of these

Water exposure was also assessed as an ordinal variable among those meeting the case definition (TABLE VI) and among all water recreators (TABLE VII). In CHEERS, water recreators swallowing water and water recreators with body wetness were compared to water recreators without direct water contact. In CHEERS, among the subset of ill water recreators, there were no statistically significant associations observed between water exposure and severity (TABLE VI). In NEEAR, swimmers (getting wet above the waist) who swallowed water, and swimmers not swallowing water were both compared to waders (only wet below the waist). Among the subset of NEEAR water recreators with illness, there were also no statistically significant associations observed between increased water exposure and severity (TABLE IV).

When assessing severity and the ordinal exposure variable among all water recreators, a dose-response relationship was observed, with increasing odds of severity associated with greater water exposure separately noted in both the NEEAR and CHEERS (TABLE VII). Particularly, CHEERS water recreators who swallowed water were more likely to have four or more GI symptom-days and four or more total symptom-days compared to the reference group of water recreators with no water contact. The full model for assessing the relationship between ordinal water exposure and the presence of four or more symptom-days among CHEERS water recreators can be found in Appendix A: Table LIV. When assessing severity among all water recreators in NEEAR, swimmers who swallowed water were more likely to have four or more GI symptom-days, or have four or more total symptom-days compared to waders. The full model for assessing the relationship between ordinal water exposure and the presence of four or more symptom-days among NEEAR water recreators can be found in Appendix A:Table LIII.

TABLE VI

AORS (95% CI) FOR SEVERITY AND ORDINAL EXPOSURE AMONG WATER RECREATORS MEETING A CASE DEFINITION [a]

	Incidental-contact recreators (CHEERS)		Full-contact recreators (NEEAR)	
	Swallow water Body Wetness only No-contact water recreators (reference)		Swallow water Swimmers not swallowing water Waders (reference)	
	N [b]	**(95% CI)**	**N [b]**	**(95% CI)**
Severity of GI Symptoms				
Responses to Illness				
Any response versus none [c]	28/36 281/406 146/194	1.11 (0.47,2.67) 0.71 (0.47,1.06) 1.00	145/228 538/852 178/300	1.13 (0.75,1.71) 1.17 (0.87,1.55) 1.00
Severe response versus moderate or no response [d]	23/36 186/406 100/194	1.94 (0.92, 4.13) 0.85 (0.60, 1.21) 1.00	109/228 381/852 131/300	1.14 (0.75,1.70) 1.05 (0.79,1.39) 1.00
Duration of GI Illness				
≥2 days	20/29 237/337 103/160	1.05 (0.44,2.53) 1.29 (0.84,1.97) 1.00	125/221 467/848 172/296	0.99 (0.66,1.49) 0.89 (0.67,1.18) 1.00
GI Symptom-Days				
≥4 symptom-days	20/29 214/337 96/160	1.17 (0.49,2.81) 1.02 (0.67,1.54) 1.00	127/221 460/848 156/296	1.18 (0.79,1.76) 1.04 (0.78,1.37) 1.00
GI Severity Score				
Score of ≥6	6/36 43/406 24/2,043	1.27 (0.43,3.73) 1.01 (0.56,1.84) 1.00	28/228 74/850 24/299	1.15 (0.54,2.43) 1.04 (0.60,1.78) 1.00
Severity of Any Symptoms				
Responses to Illness				
Any response versus none [c]	76/118 869/1,433 395/638	1.13 (0.75,1.71) 0.97 (0.80,1.16) 1.00	357/469 1,247/1,757 486/675	1.01 (0.74,1.37) 0.90 (0.72,1.11) 1.00
Severe response versus moderate or no response [d]	37/118 405/1,433 177/638	1.45 (0.91, 2.26) 1.16 (0.94, 1.44) 1.00	222/469 710/1,757 264/675	1.24 (0.94,1.63) 1.01 (0.83,1.24) 1.00
Total Symptom-Days				
≥4 symptom-days	39/72 346/786 153/356	1.60 (0.95,2.67) 1.06 (0.82,1.38) 1.00	303/433 1,036/1,581 396/591	1.07 (0.79,1.45) 0.93 (0.74,1.15) 1.00

[a] All models controlled for age and other confounders (Appendix A:Table LI–Table LII), NEEAR models additionally control for beach as a fixed effect and account for household cluster

[b] Proportion in the "higher risk" category, out of total n

[c] Responded to illness by either staying home from work or school, taking OTC or prescription medication, contacting an HCP, or visiting an ED or being admitted to the hospital versus those who did none of these

[d] Responded to illness by either staying home from work or school, taking prescription medication, contact with an HCP, or visiting an ED/being admitted to the hospital versus those only taking OTCs or who did none of these

TABLE VII
AORS (95% CI) FOR SEVERITY AND ORDINAL EXPOSURE AMONG ALL WATER RECREATORS [a]

	Incidental-contact recreators (CHEERS)		Full-contact recreators (NEEAR)	
	Swallow water Body Wetness only No-contact water recreators (reference)		Swallow water Swimmers not swallowing water Waders (reference)	
	N [b]	(95% CI)	N [b]	(95% CI)
Severity of GI Symptoms				
GI Symptom-Days				
≥4 symptom-days	29/270 292/4,556 124/2,369	2.32 (1.51,3.56) 1.32 (1.06,1.65) 1.00	127/2,315 460/10,552 156/4,303	1.72 (1.29, 2.30) 1.30 (1.06,1.59) 1.00
GI Severity Score				
Score of ≥6	6/277 43/4,624 24/194	1.57 (0.35,7.14) 1.02 (0.49,2.10) 1.00	30/2,332 75/10,554 25/4,306	1.75 (0.88,3.49) 1.18 (0.70,1.99) 1.00
Severity of Any Symptoms				
Total Symptom-Days				
≥4 symptom-days	53/257 523/4,184 208/2,184	2.61 (1.86,3.66) 1.42 (1.20,1.70) 1.00	337/2,323 1,184/10,472 456/4,293	1.45 (1.20,1. 72) 1.08 (0.96,1.24) 1.00

[a] All models controlled for age and other confounders (Appendix A:Table LI–Table LII), NEEAR models additionally control for beach as a fixed effect and account for household cluster
[b] Proportion in the "higher risk" category, out of total n

2.2.2.1.1 Effect Modification

The average number of daily bowel movements at baseline consistently modified the association between water ingestion and severity among CHEERS participants both among all water recreators and the subset of water recreators with illness. Overall, those with two or more bowel movements per day at baseline had greater odds of severe illness associated with swallowing recreational water compared to those with only one bowel movement per day at baseline (Appendix A: Table LV). Age was not found to be an important effect modifier, with no interaction p-values <.20) (not shown). Additionally, other comorbid conditions like diabetes, being prone to infection, having a preexisting GI condition, and asthma also modified the relationship between swallowing water and severe illness among participants in either study. Among all water recreators, those with any comorbid condition were consistently more likely to have a greater aOR for the associations between water ingestion and severity compared to participants without any condition (TABLE VIII). However, cell sizes for the relationship between ingestion and severity were small among water recreators with comorbidities, implying that estimates should be viewed with caution. Comorbidities also modified some of the associations between severity and any contact with the water (Appendix A: TABLE LVI) or digging in sand (Appendix A:Table LVII) among NEEAR participants. Similar interaction effects were observed when assessing ordinal exposures in either study (Appendix A:Table LVIII–Table LX).

TABLE VIII
MODIFICATION OF THE ASSOCIATIONS BETWEEN SEVERITY AND SWALLOWING WATER (95% CI) BY PRESENCE OF A COMORBID CONDITION, ALL WATER RECREATORS [a]

	Severity metric	**Comorbid condition**	**Interaction p-value**	**Ingest Water**	**Absence of condition**			**Presence of condition**		
					N with outcome	N without outcome	AOR	N with outcome	N without outcome	AOR
CHEERS	**≥4 Total symptom-days** (all water recreators)	Preexisting GI condition	0.13	Yes	48	197	**1.96 (1.41,2.73)**	5	7	**5.18 (1.49, 17.97)**
				No	696	5,448		36	229	
NEEAR	**GI Severity Score of ≥6** (all water recreators)	Preexisting GI condition	0.17	Yes	25	2,270	1.38 (0.81,2.33)	3	24	3.99 (0.95,16,74)
				No	87	13,673		6	315	
	≥4 GI symptom-days (all water recreators)	Preexisting GI condition	0.15	Yes	123	2,167	**1.30 (1.03,1.65)**	4	21	3.16 (0.96,10.47)
				No	576	13,180		17	303	

[a] Controlling for confounders (Appendix A:Table XLVI–Table XLVII), NEEAR models additionally control for beach as a fixed effect and account for household cluster

2.2.2.1.2 **Ordinal Outcome**

Severity metrics were also evaluated as tertiles and assessed among the subset of water recreators with illness using ordinal and multinomial logistic regression methods. Controlling for covariates resulted in violations of the POA, therefore generalized logit, or multinomial regression was utilized rather than ordinal or cumulative logit. Cumulative logit assumes the multilevel outcome variable is ordinal, while generalized logit assumes the outcome is nominal, and thus treats it similarly to a dummy variable (Derr, 2013). In general, greater aORs were observed for the highest levels of the severity categories, compared to the reference group (least severe category), yet no associations were statistically significant with $p < .05$, except for the relationship between the ordinal response to all illnesses and swallowing water among water recreators in the NEEAR study (TABLE IX).

TABLE IX

MULTINOMIAL SEVERITY OUTCOMES AND SWALLOWING WATER (95% CI) AMONG WATER RECREATORS MEETING THE CASE DEFINITION FOR ILLNESS

	Severity Outcome [a] Severe Moderate Not severe (reference)	**Ordinal Logit**		**Multinomial Logit**	**Additional Confounders** [c]
		Crude	Adjusted [b]	Adjusted	
Incidental-Contact (CHEERS)	Response to GI Illness [d]	1.79 (0.96,3.52)	2.01 (1.01,3.97)	2.00 (0.87,4.62) 0.81 (0.26,2.53)	Gender, recent antacid use, wash hands before eating/drinking
	Response to all Illness [d]	1.17 (0.83,1.64)	1.23 (0.87,1.75)	1.34 (0.84,2.13) 1.09 (0.70,1.73)	Gender, same water use
	GI Symptom-Days	1.37 (0.69,2.73)	1.11 (0.53,2.25)	1.15 (0.43,3.04) 1.13 (0.44,2.90)	Gender, same water use, recent contact with animals
	GI Severity Score	1.30 (0.70,2.43)	1.16 (0.61,2.19)	1.17 (0.54,2.57) 0.81 (0.31,2.12)	Same water use, recently ate hamburger
	Total Symptom-Days	1.37 (0.88,2.13)	1.28 (0.82,2.00)	1.36 (0.78,2.38) 1.29 (0.69,2.43)	Gender, recent contact with animals, average daily bowels at baseline
Full-Contact (NEEAR)	Response to GI Illness [d]	1.13 (0.86,1.48)	1.05 (0.79,1.40)	1.06 (0.76,1.36) 0.86 (0.55,1.37)	Gender, race, digging in sand
	Response to all Illness [d]	1.32 (1.09,1.59)	1.28 (1.05,1.55)	**1.37 (1.05,1.78)** **1.07 (0.81,1.42)**	Gender, digging in sand, comorbid condition, same water use
	GI Symptom-Days	1.18 (0.90,1.55)	1.19 (0.88,1.58)	1.32 (0.89,1.95) 0.97 (0.67,1.42)	Gender, digging in sand
	GI Severity Score	1.36 (1.04,1.78)	1.08 (0.80,1.45)	1.06 (0.73,1.55) 1.12 (0.75,1.66)	Race, digging in sand
	Total Symptom-Days	1.20 (0.98,1.47)	1.13 (0.91,1.39)	1.15 (0.89,1.49) 1.05 (0.75,1.47)	Gender, digging in sand

[a] Lowest tertile (least severe) is the reference group
[b] Ordinal logit models violated the POA
[c] All models controlled for age, NEEAR models also control for beach location as a fixed effect
[d] Staying home from work or school, prescription medication use, contacting an HCP, or admission to ED or hospital, compared to those who only took OTC medication compared to those that did not indicate any response to their illness (reference group)

2.2.2.1.3 Model-Based Standardization

Model-based standardization was applied to models assessing the degree of water exposure and severity for both incidental- and full-contact water recreators for those meeting any case definition (TABLE X), and among all water recreators (TABLE XI). No statistically significant associations were noted when assessing exposure among the subset of water recreators with illness (TABLE X). In general, water exposure was associated with an increased probability of severe illness when assessing all water recreators (TABLE XI). An RD of 0.14 corresponded to a 14% increase in the probability of four or more total symptom-days among all incidental-contact water recreators in CHEERS compared to water recreators without any direct water contact. In NEEAR, a 3% increase in the probability of four or more total symptom-days was observed among swimmers swallowing water compared to waders. Relative risks approximated the ORs when all water recreators were included in the model, when controlling for the appropriate covariates, since the outcome of interest was rare (Rothman et al., 2008).

TABLE X

PREDICTED PROBABILITIES, RRS, AND RDS (95% CI) OF THE RELATIONSHIP BETWEEN SEVERE ILLNESS AND DEGREE OF WATER EXPOSURE AMONG INCIDENTAL- (CHEERS) AND FULL-CONTACT (NEEAR) WATER USERS MEETING A CASE DEFINITION [a]

			Severity of GI Illness	Severity of Any Illnesses
			Responses to Illness Severe response [c]	**Responses to Illness** Severe response [c]
Incidental-Contact (CHEERS)	Predicted Probability [b]	Ingested Water	0.65 (0.50, 0.81)	0.35 (0.26, 0.44)
		Body Contact	0.43 (0.39, 0.48)	0.29 (0.26, 0.31)
		No Contact	0.49 (0.41, 0.56)	0.27 (0.24, 0.31)
	Ingesting water versus no contact	RD (95% CI)	0.13 (-0.06,0.32)	0.08 (-0.01,0.17)
		RR (95% CI)	1.27 (0.90,1.66)	1.28 (0.93,1.67)
	Body contact versus no body contact	RD (95% CI)	-0.04 (-0.13,0.04)	0.03 (-0.01,0.07)
		RR (95% CI)	0.93 (0.77,1.10)	1.15 (0.95,1.45)
Full-contact (NEEAR)	Predicted Probability [b]	Swim: Ingestion of water	0.45 (0.38, 0.52)	0.44 (0.40, 0.50)
		Swim: No ingestion of water	0.45 (0.42,0.48)	0.45 (0.39, 0.51)
		Wading	0.44 (0.40, 0.52)	0.42 (0.38, 0.46)
	Swim (ingesting water) versus wading	RD (95% CI)	-0.001 (-0.10,0.08)	0.02 (-0.04,0.10)
		RR (95% CI)	0.99 (0.79,1.20)	1.06 (0.91,1.25)
	Swim (no ingestion of water) versus wading	RD (95% CI)	0.02 (-0.05,0.09)	0.05 (-0.01,0.11)
		RR (95% CI)	1.04 (0.90,1.23)	1.13 (0.98,1.27)

[a] Controlling for confounders (Appendix A:TABLE LI–TABLE LII), NEEAR models additionally control for beach as a fixed effect and account for household cluster
[b] Predicted probability of severe illness among water recreators with GI illness
[c] Responded to illness by either staying home from work or school, taking OTC or prescription medications, contacting an HCP, or went to an ED or hospital

TABLE XI

PREDICTED PROBABILITIES, RRS, AND RDS (95% CI) OF THE RELATIONSHIP BETWEEN SEVERE ILLNESS AND DEGREE OF WATER EXPOSURE AMONG ALL INCIDENTAL (CHEERS) AND FULL-CONTACT (NEEAR) WATER USERS[a]

			Severity of GI Illness		Severity of Any Illnesses
			GI Symptom-Days ≥4 symptom-days	**GI Severity Score** Score of ≥6	**Total Symptom-Days** ≥4 symptom-days
Incidental-Contact (CHEERS)	Predicted Probability[b]	Ingested Water	0.08 (0.05, 0.11)	0.03 (0.01, 0.05)	0.23 (0.16, 0.29)
		Body Contact	0.05 (0.04, 0.05)	0.01 (0.01, 0.01)	0.11 (0.10, 0.12)
		No Contact	0.04 (0.03, 0.05)	0.01 (0.01, 0.01)	0.09 (0.07, 0.10)
	Ingesting water versus no contact	RD (95% CI)	**0.04 (0.01,0.08)**	0.02 (-0.001,0.04)	**0.14 (0.08,0.21)**
		RR (95% CI)	**2.00 (1.04,2.96)**	2.71 (0.87,6.06)	**2.56 (1.89,3.57)**
	Body contact versus no body contact	RD (95% CI)	0.01 (-0.00,0.02)	0.00 (-0.01,0.01)	**0.03 (0.01,0.04)**
		RR (95% CI)	1.23 (0.95,1.52)	1.07 (0.65,1.82)	**1.32 (1.08,1.57)**
Full-contact (NEEAR)	Predicted Probability[b]	Swim: Ingestion of water	0.05 (0.04, 0.07)	0.01 (0.01, 0.01)	0.13 (0.11, 0.14)
		Swim: No ingestion of water	0.05 (0.04, 0.05)	0.01 (0.00,0.02)	0.10 (0.09, 0.11)
		Wading	0.04 (0.03, 0.04)	0.01 (0.01, 0.01)	0.10 (0.09, 0.11)
	Swim (ingesting water) versus wading	RD (95% CI)	0.02 (0.00,0.4)	0.00 (-0.00,0.01)	**0.03 (0.01,0.05)**
		RR (95% CI)	**1.48 (1.07,2.01)**	1.65 (0.78,3.09)	**1.31 (1.11,1.55)**
	Swim (no ingestion of water) versus wading	RD (95% CI)	**0.01 (0.00, 0.02)**	0.00 (-0.00,0.01)	0.01 (-0.00,0.02)
		RR (95% CI)	**1.29 (1.07,1.56)**	1.30 (0.57,2.44)	1.07 (0.96,1.21)

[a] Controlling for confounders (Appendix A:Table LI–Table LII), NEEAR models additionally control for beach as a fixed effect and account for household cluster
[b] Predicted probability of severe illness among water recreators with GI illness
[c] Responded to illness by either staying home from work or school, taking OTC or prescription medications, contacting an HCP, or went to an ED or hospital

A relationship between swallowing of recreational water and probability of severe illness (stayed home from work or school, took prescription medication, visited an ED, or admitted to a hospital) was observed among incidental-contact water recreators with GI illness in CHEERS who engaged in water recreation activities such as kayaking, canoeing, rowing, boating, and fishing. The lowest predicted probability for severe responses to illness was noted among water recreators who did not swallow water or who only swallowed drops, and the highest was observed among water recreators who ingested a teaspoon or a mouthful of water (Figure 4). Higher predicted probabilities for severe illness were observed among water recreators with GI illness with other non-enteric illnesses (respiratory, ear, eye, or skin).

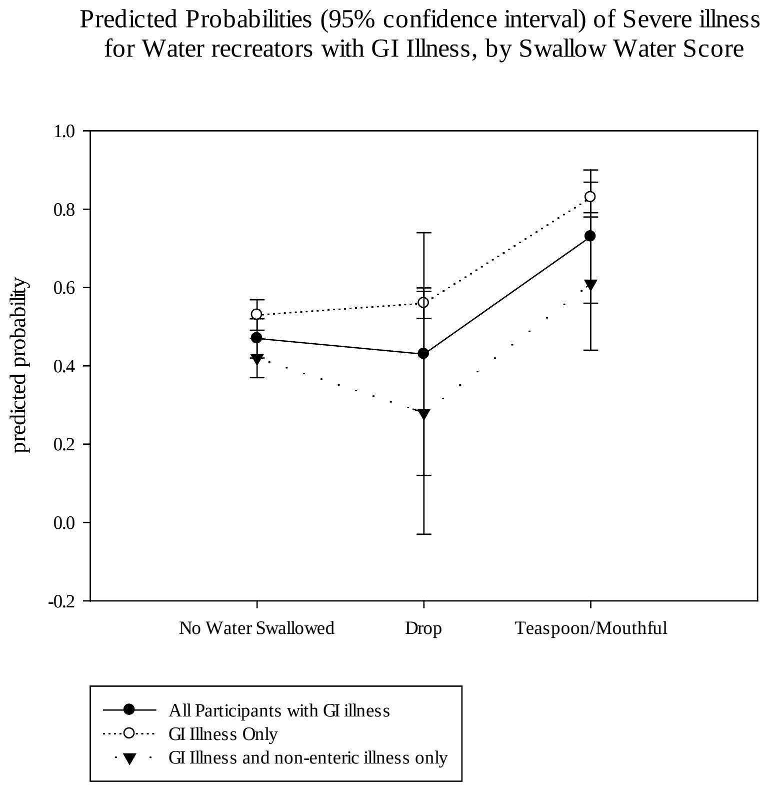

Figure 4. Predicted probability (95% CI) of four or more total symptom-days according to swallow water score.

2.2.2.1.4 <u>Water Quality and Severity</u>

An association was observed between water quality and severity among incidental-contact water recreators (CHEERS), when evaluating water quality measurements above and below the 75th percentile, after controlling for potential confounders (Appendix A: Table LXII). The large, yet not statistically significant association (aOR: 1.52 (95% CI: 0.91–2.53)) was observed between four or more total symptom-days (either GI, respiratory, ear, eye, or skin) among participants with any illness, and exposure to concentrations F+ coliphage above the 75th percentile. Additionally, a relationship was observed between severity and dose of microbes among CHEERS water recreators (Appendix A: Table LXIII). When examining only those with illness, there was an association between tertiles of the GI severity score and tertiles of the dose F+ coliphage measured in GUW water. Among water recreators in the highest tertile of the GI severity score exposed to the highest tertile of dose of F+ coliphage, the aOR was 2.01 (95% CI: 1.00–4.05) compared to water recreators within the lowest tertile of GI severity score and exposed to the lowest tertile of dose. Additionally, water recreators in the middle tertile of the GI severity score exposed to the highest tertile of dose of F+ coliphage, the aOR was 2.35 (95% CI: 1.02–5.48) compared to those lowest tertile of GI severity score and exposed to the lowest tertile of dose. However, the relationship observed between the highest and the middle tertiles of the GI severity score and the middle tertile of F+ coliphage were not statistically significant at 0.82 (95% CI: 0.25–2.66) and 2.49 (95% CI: 0.77–8.14) respectively.

An association was observed between water quality dichotomized at the 75th percentile and severity among full-contact water recreators participating in swimming and wading in the NEEAR study. Age, race, were controlled for in these models since they were the only covariates that contributed to at least a 5% change in the crude OR. Additionally, beach was controlled for as a fixed effect, while clustering within households was also taken into account. In general, dichotomous enterococci measurements by qPCR were not associated with severity, while enterococci measurements using EPA method 1600, a culture-based method, were negatively associated with the presence of four or more total symptom-days among water recreators with illness (TABLE XII). Enterococci by culture and by qPCR were moderately correlated (r=.56) within the NEEAR study. Furthermore, when $\log_{10}$ transformed, the relationship between enterococci by qPCR was similar to what was observed when assessing enterococci concentration dichotomized at the 75th percentile, yet when enterococci by culture was $\log_{10}$

transformed, the relationship was insignificant. However, among all water recreators enterococcus by qPCR was positively associated with four or more total symptom-days (TABLE XIII). No association was noted between culture and severity among all water recreators.

TABLE XII

AORS (95% CI) BETWEEN SEVERITY AND ENTEROCOCCI BY QPCR AND EPA METHOD 1600, DICHOTOMIZED AT THE 75TH PERCENTILE AMONG FULL-CONTACT RECREATORS MEETING A CASE DEFINITION (NEEAR) [a]

	qPCR aOR (95% CI)	EPA Method 1600 aOR (95% CI)
≥4 GI Symptom-Days	1.09 (0.76,1.56)	0.76 (0.57,1.02)
GI Severity Score ≥6	0.72 (0.34,1.55)	0.83 (0.51,1.37)
≥4 Total Symptom-Days	1.17 (0.90,1.53)	**0.79 (0.63,0.99)**

[a] Controlling for age, race, beach, and household cluster

TABLE XIII

AORS (95% CI) BETWEEN SEVERITY AND ENTEROCOCCI BY QPCR AND EPA METHOD 1600, DICHOTOMIZED AT THE 75TH PERCENTILE AMONG ALL FULL-CONTACT RECREATORS (NEEAR) [a]

	qPCR aOR (95% CI)	EPA Method 1600 aOR (95% CI)
≥4 GI Symptom-Days	1.19 (0.93,1.52)	0.91 (0.72,1.13)
GI Severity Score ≥6	0.99 (0.53,1.82)	0.90 (0.56,1.44)
≥4 Total Symptom-Days	**1.24 (1.05,1.46)**	1.00 (0.86,1.15)

[a] Controlling for age, race, beach, and household cluster

In general, among full-contact water recreators in the NEEAR study with illness, the tertiles of dose of enterococci were not generally associated with of severity (Appendix A: Table LXIII). The strongest associations were observed for tertiles of enterococci by qPCR and of responses to GI illness defined as either staying home from work or school, taking prescription medications, contacting an HCP, visiting an ED, or hospital, compared those who only took OTC medication, compared to those with no response to their symptoms as the reference group. The highest tertiles of responses to GI illness and the highest tertile of dose of enterococci by qPCR were not statistically significant compared to the lowest tertiles, with aORs of 1.86 (95% CI: 0.83, 4.20). However, a statistically significant association was observed among those only taking OTCs for their GI illness (the middle tertile) and the highest tertile of dose of enterococci by qPCR. Lastly, the middle tertile of enterococci dose was not associated with either tertile of responses to GI illness aOR 2.40 (95% CI: 0.70, 8.27) and 2.76 (95% CI: 0.67, 11.38) for the third and second tertiles of response to GI illness, respectively.

2.2.2.2 Combined Analyses of the National Epidemiological and Environmental Assessment of Recreational Water Study and the Chicago Health Environmental Exposure and Recreation Study

Combining the CHEERS and NEEAR datasets indicated an association between severe illness and swallowing recreational water among all water recreators and among the subset of water recreators with illness (Figure 5). All models in the combined analysis controlled for age, race, gender, and mean daily enterococci by culture, since they were consistent across the studies, and considered to be confounders of the relationships between severity and exposure when examined in each study separately. Other covariates were not considered since they were only present in one of the datasets. Daily mean enterococci by culture was controlled for to account for the difference in water quality observed in the studies. Interaction terms between swallowing water and study group (CHEERS versus NEEAR) were generally not significant, implying that in most cases, associations between illness severity and water exposure were not modified by study. However when evaluating those with a GI severity score greater than six and presence of four or more total symptom-days (either GI, respiratory, ear, eye, or skin symptoms), significant interaction terms were observed between study group and water ingestion during recreation.

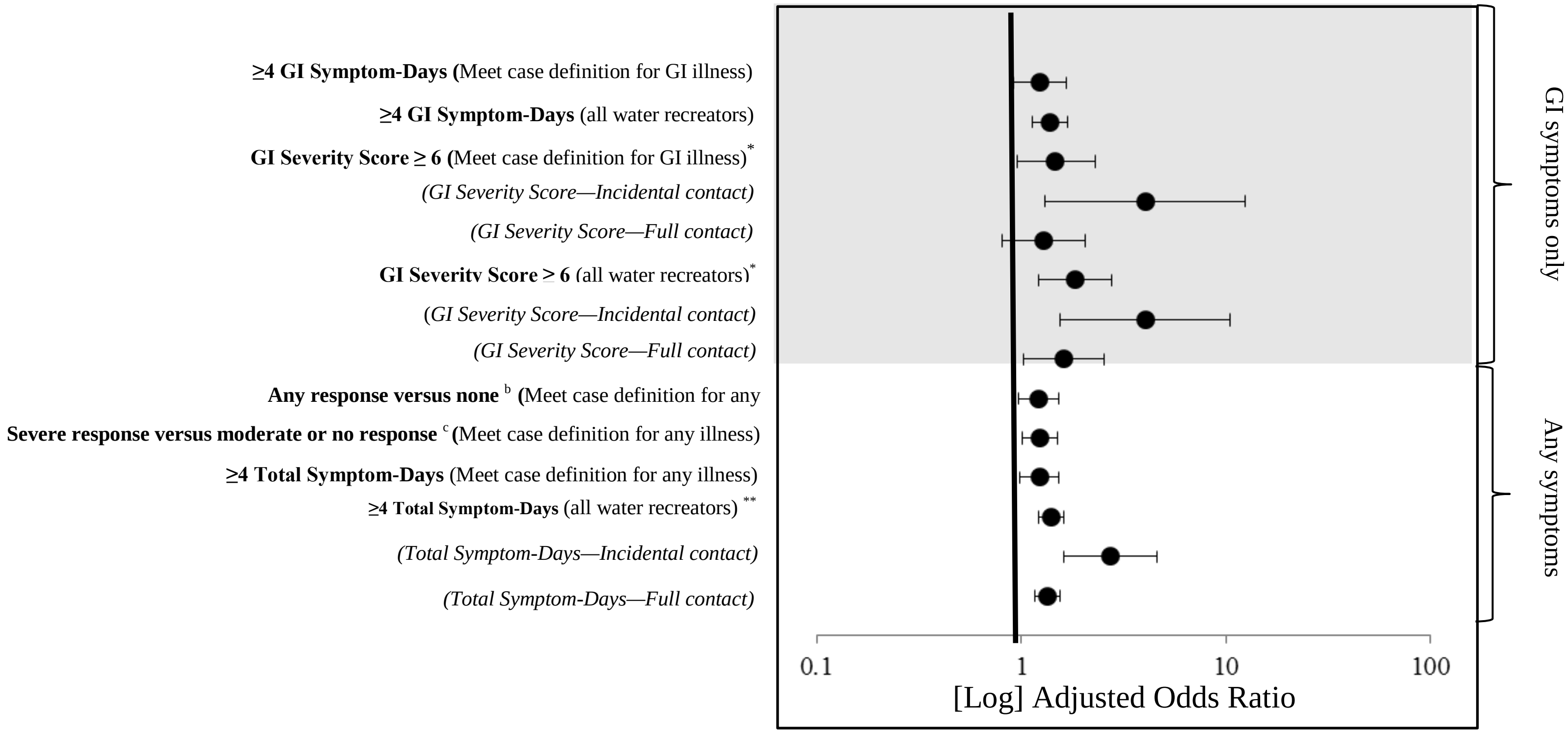

Figure 5. AOR (95% CI) of the association between severity and swallowing water among all water recreators (combined incidental-contact (CHEERS) water recreators and full-contact (NEEAR) water recreators). [a]

[a] All models controlled for age, race, gender, and mean daily enterococci by culture

[b] Responding to illness by either staying home from work or school, taking OTC or prescription medication, contacting an HCP, or visiting an ED or being admitted to the hospital versus those who did none of these

[c] Responding to illness by either staying home from work or school, taking prescription medication, contacting an HCP, or visiting an ED/being admitted to the hospital versus those with only took OTC medication or who did none of these

* Interaction between study and swallowing water p <.1

** Interaction between study and swallowing water p<.05

Shaded area represents severity of illness due to GI illness; white area represents severity of illness due to all illnesses (GI, respiratory, eye , ear, and skin)

2.3 Discussion

The severity of illness varied among participants in epidemiologic studies of short-term health risks of water recreation. No differences in severity were noted for water recreators developing illness within 0–3 days compared to water recreators developing illness within 0–12 days. Severity, regardless of the metrics used to define it, can be predicted according to certain types of water exposures, mainly water ingestion (Figure 3, TABLE VII, TABLE XI). The relationship between some definitions of severity and swallowing water was modified by comorbidities, with those with comorbid conditions having a greater odds of severe illness (TABLE VIII). However, associations observed between severity and water ingestion were generally not modified by study (NEEAR versus CHEERS) (Figure 5).

2.3.1 Severity Metrics

The severity of illness metrics have a broad range of variability (TABLE IV and TABLE V) among participants in the CHEERS and NEEAR studies. A majority of participants who become ill have mild to moderate illnesses, while a smaller, yet substantial, proportion develop more severe illness. However, the proportion of severe cases varies by the choice of severity metric (TABLE IV and TABLE V). In studies of water recreation, severity has previously been assessed according to the number of deaths and hospitalizations (Dziuban et al., 2006; Yoder et al., 2004; Yoder et al., 2008), or according to the duration of illness (Fleisher et al., 1998). This study indicates that healthcare utilization and duration of GI symptoms were not associated with water exposure among water recreators with illness.

However, symptoms related to GI or other organ systems were reported by participants who did not meet the case definitions for illness (TABLE V), thus, indicating a range of severity among those with and without illness. Symptom-days, which combine severity as a function of duration, type, and number of symptoms, when examined among all water recreators, may be informative for understanding severity among water recreators in future studies, and may be a useful metric for describing illness outcomes, opposed to relying on the presence or absence of illness. The examination of GI symptom-days and total symptom-days (either GI, respiratory, ear, eye, or skin symptoms) were consistently related to different types of water exposure in both studies (Figure 3, TABLE VII, TABLE XI, TABLE XIII) among all water recreators (Appendix A: Section F).

It is important to note, that a greater number of CHEERS water recreators were observed to have symptoms not meeting the case definition for GI or any other illness, compared to NEEAR participants, despite the vast difference in sample size. In CHEERS, each individual answered their own follow-up questions, whereas in NEEAR, one person was chosen to answer all symptom-related questions for each person in their household. It is possible that in the NEEAR study the individual responding for the entire household may not have been fully aware of all minor symptoms (one instance of diarrhea, a half a day of nausea) experienced by the entire household. This slight difference in the methods may explain the differences in the number of those in either study who have symptoms and measureable severity yet do not meet any case definitions. However, it is unclear if proxy report would over- or underestimate these measures.

Severity of illness has been assessed, to a limited degree, in some studies of water recreators with sporadic illness. A randomized controlled exposure study was conducted to evaluate illness among participants who were randomized to immerse their head three times in marine recreational water, compared to those who did not have water contact (Fleisher et al., 1998). That particular study evaluated the duration of GI, respiratory, ear, and eye illnesses and assessed the proportion of those who sought medical treatment or lost at least one day of normal activity. Participants in that study who developed GI illness had a mean and median duration of GI illness of 4 and 2 days, respectively (Fleisher et al., 1998). These results are comparable to the current study, which had observed a mean and median duration of GI illness of 3.5 and 2 days, respectively, among CHEERS water recreators, and 2.5 and 2 days, respectively, among NEEAR water recreators. The Fleisher et al. (1998) study also observed that 12% of bathers with GI illness contacted an HCP, and 15% missed at least one day of normal activity. In CHEERS, approximately 17% of water recreators with GI illness contacted an HCP (in person or by phone), while close to 45% stayed home from work or school. In NEEAR, approximately 10% of water recreators contacted an HCP (in person or by phone), while almost 43% missed work or daily activities due to GI illness. While the proportion who contacted an HCP in NEEAR and CHEERS is similar to the findings in the Fleisher (1998) study, the NEEAR and CHEERS found a greater proportion of participants with GI illness who reported missing daily activities or staying home from work or school. These differences may be due to differences in the way missed activities were measured according to Fleisher et al. (1998) compared to the current epidemiologic studies, or due to differences in exposure. The Fleisher study assessed exposure differently (immersing the head), which may not be similar to exposures due to swimming or incidental-contact recreation.

2.3.2 <u>Relationship between Severity and Exposure</u>

Severe illness, among all water recreators, was most consistently predicted by the degree of water exposure, particularly water ingestion (Figure 3, TABLE VII, TABLE XI), especially among incidental-contact (CHEERS) water recreators. Other exposures were examined, but did not suggest a strong relationship with severity. Of particular interest was the lack of relationship between severity and CAWS versus GUW recreators (Appendix A: Table XLI). On the CAWS, approximately 90% of the flow during dry weather is non-disinfected wastewater while GUW waters are less impacted by human fecal pollution. Therefore, microbe densities at CAWS locations were significantly higher than those at GUW locations (Appendix A: Table LXI). However, there was no difference in the odds in the occurrence of illness on the CAWS compared to the GUW (Dorevitch et al., 2012a), and in the current analysis increased severity was not observed among recreators in the CAWS compared to GUW. This observation may in part be due to differences of perceived risk, or in water ingestion while recreating in polluted waters such as the CAWS. It was identified that CAWS and GUW recreators were equally likely to swallow water, but GUW water recreators were more likely to submerge their head or face in water (2.9% versus 0.4%; p-value<.001) (Dorevitch et al., 2012a). However, perceived risk regarding exposure to CAWS water may result in increased reporting of severity, due to preconceived ideas regarding the quality of the water.

When evaluating water quality and severity in CHEERS, a moderate relationship between those exposed to the upper 25th percentile F+ coliphage and increased severity compared to those exposed to the lower 75th percentile. The literature suggests that coliphages, viruses that infect *E. coli*, may be better at predicting pathogenic viruses in recreational water, due to similar fate and transport properties, compared to bacterial indicators of water quality (Bosch, 2010; Colford et al., 2007). Viruses are identified as the main etiologic agent in about 10% of recreational water outbreaks; in approximately 16% of outbreaks, the agent is unknown (Yoder et al., 2004) and thus could be due to viruses. Current technology can accurately identify waterborne viruses, but is not widely used (Bosch, 2010). This suggests that coliphages may merit further investigation in predicting severe illness.

The relationship between water quality and severity was also assessed among full-contact water recreators. Greater illness severity was noted among all NEEAR water recreators exposed to higher concentrations of enterococci measured by qPCR in the NEEAR study (TABLE XII and TABLE XIII). However, the associations between enterococci measured by culture (US EPA Method 1600) among only ill water recreators were inversely associated with severity. The literature suggests that enterococci measured by qPCR is a better predictor of the occurrence of illness compared to using culture (Wade et al., 2008), and the current analyses suggests that enterococci measured by qPCR may be an important predictor of illness severity. It is unclear why severity differs when enterococci is measured using two different methods, but could be consistent with the fact that there was only a moderate correlation (r=.56) between qPCR and culture. Previous studies have found similar correlations between qPCR and culture (Noble et al., 2010), and that the persistence of the microbial DNA often results in higher quantities of organisms detected using molecular methods (Walters et al., 2009).

The dose of indicator organisms takes into account microbe density and volume of water ingested. The use of dose was relatively inconsistent for predicting increased severity (Appendix A: Table LXIII and Table LXIV). However, dose still has the potential of being an important exposure metric. The calculation of dose should continue to be explored in future studies, especially where water quality is expected to predict illness occurrence.

Severity was also assessed by combining the CHEERS and NEEAR datasets, which further indicated increased odds of developing severe illness from swallowing recreational water

(Figure 5), even after controlling for important covariates such as age, race, gender, and water quality measured by culture. Interaction terms between swallowing water and study group (CHEERS versus NEEAR) were included, but were generally not statistically significant. Given that the two studies used very similar methods, the associations between illness severity and water exposure appear to be similar in both types of water recreation (full- versus incidental-contact) in the specific settings studied in NEEAR and CHEERS.

Additionally, the results suggest that certain comorbid conditions may modify the association between severity and exposure, particularly swallowing water (TABLE VIII). Elevated aORs were observed for the association between severity and water ingestion, among those with any comorbid condition compared to those without a comorbid condition. However, since cell sizes were relatively small, results should be viewed with caution. Previous studies have indicated that exposure to enteric microorganisms has been known to exacerbate GI symptoms that develop among those with a preexisting GI condition (Karaoglu et al., 2004; Szilagyi et al., 1985). Additionally, evaluations of people with diabetes have found that they are generally more likely to develop serious infections, regardless of the exposure medium (Joshi et al., 1999), which may support their likelihood of severe illness associated with swallowing recreational water. Vulnerable groups, including those with comorbid or preexisting conditions, were also more likely to develop severe symptoms, which corresponds with findings related to illness severity and foodborne illness (Lund and O'Brien, 2011; Rocourt and Motarjemi, 2014), as well as drinking-water-associated *Cryptosporidium* (MacKenzie et al., 1994).

Analysis of all water recreators, as opposed to only water recreators meeting the case definitions, resulted in measures of association that were more likely to reach statistical significance. Severity was independently assessed among water recreators with illness and among all water recreators to answer a very important question. It was hypothesized that increased exposure to recreational water would be associated with increased severity, based on previous studies that have indicated an increased dose of microorganisms is suggested to be associated with increased illness severity (Glynn and Bradley, 1992; Mertens et al., 2013; Purcell and Emerson, 2008; Taylor et al., 1984). The current analysis did not indicate a significant relationship between severity and water exposure among those with illness. However, using severity metrics among all water recreators to assess health effects due to exposure may be useful for understanding health outcomes related to water recreation in future studies. The stronger association between exposure and severity among all participants (compared to the subset only with illness) indicates a spectrum of severity that includes symptoms and responses to illness even among those who do not meet any of the case definitions. Additionally, some recreators who would have been considered a case of illness had less severe outcomes.

The severity of symptoms may be useful in the future for identifying new thresholds for illness outcomes among water recreators. Evidence from this analysis indicates that the current definition of illness includes some individuals with low severity and excludes some individuals with high severity. By examining the relationship between severity and water exposures, one can determine where the difference in severity can be maximized, and where the potential new illness threshold should be placed. Thus, the use of severity to describe health outcomes may improve the sensitivity and specificity of the current definition of illness.

2.3.3 Strengths and Limitations

The current study had several strengths. First, the severity of illness was evaluated among two large cohort studies containing either incidental-contact or full-contact water recreators having similar protocols. The studies were set in several US locations impacted by human fecal pollution and evaluated exposures in urban (Dorevitch et al., 2012a) and less-urban environments (Wade et al., 2008; Wade et al., 2010a). This study also evaluated severity using several metrics relating to different types of water exposures. Additionally, the results between the two studies were relatively consistent, which can help support the validity of the findings.

The current study also had several limitations. First, the ascertainment of severity relied on self-reported information. Several metrics, including the duration of illness, symptom-days metrics, and the GI severity score, relied on self-reported start and end dates of symptoms. The ability for participants to recall specific information regarding the date their individual symptoms began may be problematic, and could bias the results. Additionally, in CHEERS, participants were asked about responses to illness without differentiating, among those with more than one type of symptom, which symptom(s) prompted each response. Therefore, estimated responses to GI illness may be overestimated, since it was unclear which response corresponded to GI illness.

Additionally, these two epidemiology studies took place on waters impacted by fecal pollution. Therefore, the results of this analysis concerning severity may not be generalizable to the general population of water recreators. The distribution of severity may differ on cleaner waters, not impacted by human sewage.

A major difference between the two cohort studies was related to follow-up. While both studies engaged participants in telephone follow-up, time to follow-up differed substantially, with NEEAR follow-up being at 10–12 days and CHEERS being at approximately 2, 5, and 21 days. However, about 9% of NEEAR recreators were still experiencing symptoms at the time of the follow-up interview, regardless of examining the 0–12 or 0–3 day time frame to the development of symptoms. Therefore, the length of symptoms reported by these individuals would be underestimated, and thus could have impacted the duration of GI illness and the symptom-days calculations. However, approximately 95% of those with diarrhea who still had symptoms of diarrhea at the time of the interview had a duration of diarrhea that was greater than two days. In this analysis, the duration of illness was dichotomized at two days. A similar observation was noted for other symptoms as well. Therefore, based on the dichotomization of the severity metrics, it would be expected that a majority of participants in NEEAR would have been correctly classified into the high or low severity groups, even with a truncated symptom duration. However, a more precise approach in future analyses is necessary, but is not anticipated to have a significant impact on the overall conclusions.

In further analysis of this data, a Kaplan-Meier modeling approach may be appropriate, as these participants who were still experiencing symptoms at the time of the follow-up phone call, follow a right-censored distribution. This approach would help to maximize those data available in both epidemiology studies. An alternative approach would be to potentially impute an individual symptom duration for those still experiencing symptoms at the time of follow up either using complete NEEAR data, or using data from CHEERS. In CHEERS it was not common for participants to still be experiencing symptoms at the time of the last interview date.

Additionally, SES could have also been an important factor regarding responses to illness (Adler et al., 1993; Anderson et al., 1997; Blackwell et al., 2009; Stratmann, 1999). Among CHEERS participants, median household income in the zip code of the mailing address was significantly higher ($p<.01$) among water recreators compared to non-water recreators and those with higher income were more likely to report indicators of severity in either study (Appendix B). However, income alone may not be perfectly correlated with one’s insurance status, use of the healthcare system, or ability to miss work, and the use of an ecologic measure of income may introduce bias. In addition to severity of illness, other SES factors, such as education, which were unmeasured in either of the cohort studies, may also influence responses to illness (Blackwell et al., 2009).

2.4 Conclusions

Increased exposure to recreational water either through incidental or full contact is associated with increased illness severity within these two studies. This is especially apparent among water recreators who swallow water. In both NEEAR and CHEERS, there were several recreators not considered cases of illness that had increased severity metrics, while there were also several recreators who were considered cases of illness, who had low severity metrics. Thus, the use of severity to describe negative health outcomes may improve the sensitivity and specificity of the current definition of illness in future studies.

The occurrence of illness may not adequately describe the impact of water recreation on human health. Among those who recreate and develop illness, a range of illness severity was observed among participants meeting the case definition(s) and among those with symptoms not meeting the case definition(s). The majority of those who become ill have mild and self-limiting illness; however some individuals develop more severe symptoms, requiring use of the healthcare system and loss in productivity. Use of the healthcare system and lost productivity have been associated with substantial costs to society when evaluating the impact of recreational water exposure (Dwight et al., 2005) or drinking-water contamination (Corso et al., 2003) in communities. In a study with lower rates of missed daily activities (lost productivity) than the current analysis, it has been estimated that the annual COI due to water recreation can be almost

$3.3 million at two beaches in Orange County, California (Dwight et al., 2005). Additionally, the 1993 drinking-water outbreak of *Cryptosporidium* in Milwaukee was estimated to cost close to $96 million in healthcare and lost productivity costs, with almost two-thirds being related to lost productivity ($64.6 million) (Corso et al., 2003).

Fecal indicator organisms appear to only moderately be able to predict severity, especially when evaluating F+ coliphages and enterococci by qPCR. Water quality has been known to influence the occurrence of illness (Pruss, 1998; Wade et al., 2003); however, weak-to-moderate associations between increased severity and microbe density were observed in the current study. Alternative fecal indicators may be more predictive of severity, and further research is necessary.

The use of enterococci measured by qPCR and F+ coliphages may show value in predicting severe illness. However, stronger associations were observed regarding actual water exposure, suggesting that water ingestion and head immersion puts people at greater risk for more severe outcomes. Additionally, increased severity was suggested among those with comorbid conditions. These findings suggest that severity, rather than occurrence, may be a useful metric to help protect vulnerable subgroups, and further research is warranted. In the future, targeted education may be necessary to help reduce water exposure and to aid in lowering the risk of developing severe illness. Therefore, knowledge regarding the severity of symptoms, not necessarily just the occurrence of illness, may be important for identifying cases with negative health effects due to water recreation. Overall, severity of illness has potential significant public health importance, and may be useful for future epidemiology studies and for prioritizing locations for mitigation in the future.

3. COSTS OF SPORADIC GASTROINTESTINAL ILLNESS ASSOCIATED WITH SURFACE WATER RECREATION

Epidemiological studies indicate a relationship between recreational water exposure and the sporadic occurrence of several health outcomes, including GI illness, and non-enteric illnesses including respiratory, ear, eye, and skin symptoms (Cabelli, 1983; Dorevitch et al., 2012a; Dufour, 1984; Stevenson, 1953; Wade et al., 2008). Cases of sporadic GI illness that develop following surface water recreation are generally mild and self-limited, but in rare cases can lead to ED visits or hospitalization (Dorevitch et al., 2012a; Fleisher et al., 1998; Wade et al., 2013). Similarly, some cases that develop during WBDOs can be debilitating and place demand on the healthcare system (Dziuban et al., 2006; Hlavsa et al., 2011; Hlavsa et al., 2014; Yoder et al., 2004; Yoder et al., 2008).

The burden of disease incorporates both the occurrence and the severity of illness, and can be useful for comparing the impact of diseases across locations, exposures, and sensitive subgroups (Murray et al., 1996; Rice et al., 2006). Monetary disease-burden metrics include WTP and COI. The WTP approach involves establishing the amount an individual is willing to pay in order to avoid illness, and has not been applied to water-borne diseases to date. The COI approach tabulates direct and indirect costs associated with illness. Direct costs include costs associated with medications, visits with an HCP, ED visits, and hospitalizations; while indirect costs are associated with lost productivity due to illness (Corso et al., 2003; Dwight et al., 2005; Hoffmann et al., 2012; Majowicz et al., 2006; Tariq et al., 2011). Following the waterborne outbreak of cryptosporidiosis in Milwaukee, Wisconsin in 1993, a COI approach was used in order to quantify the economic impact of illness due to the contaminated drinking-water source

(Corso et al., 2003). More recently, the COI approach was also used to assess the burden of a drinking water outbreak due to *Salmonella* in Alamosa, Colorado (Ailes et al 2013). The COI has also been applied to illnesses associated with surface-water recreation at two beaches in Orange County, California (Dwight et al., 2005).

A limitation of the COI approach is that it does not reflect an individual's preference for avoiding illness and suffering and does not consider the benefits of reduced pain or illness, which would be captured in a WTP approach (Kenkel, 1994). These preferences, however, do not necessarily result in economic burdens that are substantially different than the COI (Alberini and Krupnick, 2000; Chestnut et al., 1996; Guh et al., 2008). The COI approach is favored by many regulatory agencies for its ease of interpretation and comparability. The EPA currently uses COI to evaluate illnesses due to environmental exposures since it can be used directly for policy evaluation or development, economic analysis, and for environmental decision making (US EPA, 2007).

The DALY, a burden metric commonly used in the health economics literature, has been used to compare disease burden and life expectancy, across several populations (Rice et al., 2006). The WHO describes DALYs as the sum of the years of life lost due to disease as well as the amount of time spent living with a disability. Time spent living with a disability is a function of both the duration of illness and an illness-specific disability weight. Disability weights are calculated based on global surveys and may vary according to age (Salomon et al., 2013) and can range between a value of zero representing perfect health and one representing a health state equivalent to death (Murray et al., 1996; WHO, 2013). Previously, DALYs have been used to estimate the global burden of bathing and consuming raw or undercooked shellfish in coastal waters polluted by wastewater (Shuval, 2003); to estimate the global burden of disease due to water, sanitation, and hygiene (Pruss et al., 2002); and to characterize disease burden due to *E. coli* O157 in the Netherlands (Havelaar et al., 2004; Tariq et al., 2011).

Quality Adjusted Life Years, another burden metric, take into account life expectancy and the quality of life in the remaining years. The QALYs are calculated based on health utilities, which represent a person's preference for different health outcomes, with a value of zero representing a health state equivalent with death and a value of one representing perfect health. Each health utility is multiplied by the number of years in that particular health state to yield QALYs (Philips, 2009). The QALY losses have been used to characterize the burden of foodborne illness in the United States (Hoffmann et al., 2012). Indirect costs, or costs associated with lost productivity, have been calculated in previous studies by monetizing QALYs. Monetized QALYs incorporate costs associated with pain and suffering into the COI estimate (Scharff, 2011; Scharff et al., 2009). In these burden estimates, one QALY has been estimated to be equivalent to between $100,000 and $357,000 (Luce et al., 2006; Scharff, 2011; Scharff et al., 2009).

In the current study, burden of GI illness was evaluated using the COI approach. This approach was selected because sporadic recreational waterborne illnesses observed in epidemiologic studies have low morbidity and no long-term disability (Fleisher et al., 1998; Dorevitch et al., 2012; Wade et al., 2013), a context best suited for the COI approach. Healthcare utilization data were available from two cohort studies of water recreation in the United States: the NEEAR from 2003–2007 and the CHEERS from 2007–2009. The NEEAR study evaluated health risks of full-contact water recreation (swimming and wading) at marine and freshwater beaches impacted directly by human fecal pollution, while CHEERS evaluated incidental-contact water recreation such as kayaking, canoeing, rowing, motor boating, and fishing in rivers heavily dominated by non-disinfected wastewater effluent and freshwater lakes.

The overall aim of this study was to characterize the economic burden of GI illness attributable to water recreation in epidemiological studies of full-contact (NEEAR) and incidental-contact (CHEERS) water recreation, impacted by fecal pollution. Secondary goals of this study were to compare burden estimates among water recreation subgroups and to evaluate the individual monetary components that contribute to the total costs within NEEAR and CHEERS.

3.1 Methods

3.1.1 Epidemiologic Studies

The CHEERS and NEEAR studies were prospective cohorts of water recreation that included field recruitment of water recreators and non-water recreators. Participants in CHEERS were recruited from 39 locations in the Chicago area. Recruitment sites included the CAWS, which includes the Chicago River and is mainly composed of non-disinfected secondary wastewater effluent; and Lake Michigan, rivers, and inland lakes, referred to as GUW. Additionally, a group of outdoor recreators, not exposed to recreational surface water were recruited (Dorevitch et al., 2012a). Beachgoers with and without beach-water contact from the NEEAR study were recruited from seven different marine and freshwater beaches impacted by fecal pollution, across six states (Wade et al., 2008; Wade et al., 2006; Wade et al., 2010a). Both studies included measurements of fecal indicator microbes.

The CHEERS study was designed using the NEEAR protocol as a template. Recreators from both studies were contacted by telephone following recreation to identify the development of symptoms. The symptoms that defined of the occurrence of GI illness were identical in both studies. The case definition for the occurrence of GI illness was defined as either (1) three episodes of diarrhea in 24 hours, (2) vomiting, (3) nausea with stomachache, (4) nausea that interferes with daily activities, or (5) stomachache that interferes with daily activities. The NEEAR participants were evaluated in a single telephone follow-up interview 10 to 12 days following their initial interview and recreational event (Wade et al., 2008; Wade et al., 2006; Wade et al., 2010a), while CHEERS participants were contacted via telephone follow-up approximately 2, 5, and 21 days after recreation (Dorevitch et al., 2012a). Questionnaire design and water sampling methodology for NEEAR (Wade et al., 2008; Wade et al., 2006; Wade et al., 2010a) and CHEERS (Dorevitch et al., 2012a) have been described previously (Appendix A: Section A).

Since CHEERS used a longer follow-up, illnesses that developed among CHEERS participants 12 or more days following recreation were excluded to match the NEEAR study follow-up period. In CHEERS, the odds of GI illness among those developing illness within 0–3 days were greater comparing water recreators to non-water recreators. A GI illness that developed outside of this time window was considered less likely to be related to water exposure (Dorevitch et al., 2012a). Likewise a recent study of swimming at a marine beach found that the 0–3 day time frame for illness development was the preferred interval for identifying GI illness associations with water recreation (Arnold et al., 2013). Therefore, economic burden of GI illness was assessed separately among participants who met the case definition for GI illness within 0–3 days and 0–12 days of recreation in both studies. Any study participants experiencing baseline symptoms at the time of enrollment, and women who were pregnant or experiencing stomach cramps due to menstruation, were excluded from the analysis.

3.1.2 Cost of Illness

Methods widely used in other health economic studies to estimate COI (Corso et al., 2003; Dwight et al., 2005; Hoffmann et al., 2012; Majowicz et al., 2006) were utilized to calculate costs per case of GI illness in each study. The total COI for GI illness *(*subscript *GI)* ($Cost_{GI}$) was the sum of direct and indirect medical costs. Direct medical costs included OTC (OTC_{GI}) and prescription (Rx_{GI}) medications, evaluation by an HCP (HCP_{GI}), ED (ED_{GI}), and hospitalizations ($Hospital_{GI}$). Indirect costs included the costs associated with missed daily activities or missing a day of work ($Productivity_{GI}$), and the costs of others missing work, due to another person's illness ($ProductivityOthers_{GI}$). The tabulation is shown in *Equation II.*

*Equation II***:**

$$Cost_{GI} = OTC_{GI} + Rx_{GI} + HCP_{GI} + ED_{GI} + Hospital_{GI} + Productivity_{GI} + ProductivityOthers_{GI}$$

The data sources used to define each component of *Equation II* are described in the following sections. Information regarding others missing work were only available in the NEEAR dataset, so $ProductivityOthers_{GI}$ was set to zero for CHEERS participants. $Cost_{GI}$ was calculated for all participants who met the case definition for GI illness within 0–3 days or within 0–12 days following recreation, and were adjusted for inflation to 2007 dollars, since both studies collected data in 2007. The use of specific consumer price indices (CPI) for medical care commodities and services were utilized to transform costs into 2007 dollars. A medical care commodity includes prescription and OTC medications, while medical care services include physician office visits, ED visits, and hospitalizations (BLS, 2010). These medical-specific CPIs were utilized since there were expected to most accurately describe inflation for each of these health components. All COI analyses were performed using SAS version 9.3 (SAS Institute Inc., Cary, North Carolina) and Stata version 11 (StataCorp LP., College Station, Texas).

3.1.3 Calculation of Components to the Total Cost of Illness

Participants in NEEAR were asked about their response to each symptom category (GI, respiratory, skin, eye, and ear) separately; only response to GI illness was considered in this analysis. Response included OTC medication use, prescription medication use, visits or phone calls with an HCP, visits to an ED or hospital, and missing work or daily activities according to each symptom. In CHEERS, participants were asked about these responses to illness, but for participants with more than one type of symptom, which symptom(s) prompted each response (for example, use of OTC medication) were not specified (Appendix C: Table LXVII). To increase the likelihood that responses are specific to GI illness, only responses that occurred within the self-reported dates of GI illness (Appendix A: Section B) were utilized. It was assumed that reported responses to illness occurring outside the specified dates of GI symptoms were likely not due to GI symptoms if other illnesses (ear, respiratory, eye, and/or skin) were also reported. However, approximately 15% of cases of GI illness indicated symptoms other than GI during the GI illness time frame.

3.1.3.1 Medications

Participants in the NEEAR study were asked about the total amount of money personally spent on either OTC or prescription medications per symptom. From 2003 to 2004, participants responded categorically (TABLE XIV) while from 2005 to 2007 participants responded to the nearest whole dollar. The CPI for medical care commodities, including prescription and OTC medications (BLS, 2010), was used to adjust the self-reported medication costs for inflation into 2007 dollars.

The CHEERS participants were not asked about costs for their medications and their medication costs were estimated using NEEAR data. Since more than one illness could be reported during the period of GI illness, symptom-complexes were defined (for example, GI illness with eye illness, GI illness with skin illness). Prescription and OTC medication costs were defined for each symptom-complex using NEEAR self-reported medication expenditures from 2005 to 2007. Thus, the same medication cost for each symptom-complex was applied to CHEERS and NEEAR participants who had the same set of symptoms (Appendix C:Table LXVIII). In so doing, medication costs were aggregated for all symptoms reported within the time interval of GI illness for both studies, and the same resolution of medication use and cost information was applied to NEEAR and CHEERS participants.

TABLE XIV

CATEGORICAL RESPONSES TO THE AMOUNT OF MONEY SPENT ON OTC OR PRESCRIPTION MEDICATIONS FOR NEEAR PARTICIPANTS FROM 2003 TO 2004

Categories of OTC Costs ($)	Median OTC cost ($) (imputed value)	Categories of Prescription Costs ($)	Median prescription cost ($) (imputed value)
0–10.00	5.00	0–25.00	12.5
11.00–25.00	18.00	26.00–50.00	38.00
26.00–50.00	38.00	51.00–75.00	63.00
51.00–75.00	63.00	76.00–100.00	88.00
76.00–100.00	88.00	101.00–150.00	125.50
101.00–150.00	125.50	151.00–200.00	175.50
151.00–200.00	175.50	>200.00	250.00
>200.00	250.00	--	--

Directly measured self-reported medication expenditures were also utilized in calculations of COI for GI illness among NEEAR participants. To make use of NEEAR data from 2003 to 2004, when categories rather than dollar amounts were recorded, the median value of the range of each category was imputed for OTC and prescription medication costs (TABLE XIV). These self-reported costs were used in alternative versions of the total COI for NEEAR participants and were directly compared to the medication estimates calculated according to symptom-complex.

3.1.3.2 Contact with Healthcare Provider

Cost data for doctor office visits were obtained from FairHealth using Current Procedural Terminology (CPT) code and geozip code of the participant's residence (the first three digits zip code). FairHealth is an organization established in 2009 in order to standardize cost data from multiple private insurance databases (FairHealth, 2014), and aggregates cost details according to geozip code. The Evaluation and Management (E/M) CPT codes were utilized to assess the costs associated with visiting an HCP. The E/M codes represent nontechnical services provided by physicians or HCPs with the purpose of diagnosis, treatment, and evaluation of diseases (PMIC, 2007). The CPI for medical care services, which includes professional medical and hospital services (BLS, 2010), was used to translate HCP costs from 2014 to 2007 dollars.

The level of E/M services can range from level one to level five, and are based on the elements of the medical history taken at the time of visit, the type of examination, and the amount of medical decision making necessary. The more complex the E/M service, the higher the level of coding and the higher the cost for the service (CMS, 2014). It was assumed that the E/M service for a person presenting with GI symptoms would be equivalent to level three, based on the amount of information necessary from a history and physical exam, as well as the complexity of decision-making and management.

Within each level of E/M services, costs are almost twice as high (PMIC, 2007) for new patients (individuals who seek medical care from an HCP group or practice for the first time, or there has been more than three years since the previous visit) (CMS, 2014) compared to established patients. Approximately 17% of people in the United States visit an HCP as a new patient (Hing et al., 2010). Insurance status also greatly influences the cost of illness. According to the FairHealth data, insured individuals pay almost 70% less than uninsured individuals on average. In 2005, approximately 16% of the US population was uninsured, and the proportion varied by race/ethnicity, and more drastically, by age (TABLE XV) (DeNavas-Walt et al., 2006). Information regarding insurance status (insured versus uninsured) and patient type (new versus established) was not obtained from participants in NEEAR or CHEERS.

To estimate the costs of contacting an HCP, insurance status (insured versus uninsured) and patient type (new versus established) of the CHEERS and NEEAR participants with GI illness who contacted an HCP was equated with the US population. A weighted average was calculated for each participant who indicated contact with an HCP in each study by multiplying the geozip-specific costs for new insured patients ($cost_{n,i}$), established insured patients ($cost_{e,i}$), new uninsured patients ($cost_{n,u}$) or ($cost_{e,u}$) by the probability of patients be of each type *(Equation III*). The probability of being insured or uninsured was age dependent (TABLE XV) (DeNavas-Walt et al., 2006).

Equation III:

$$HCP_{GI} = (cost_{n,i} \times p_{n,i}) + (cost_{n,u} \times p_{n,u}) + (cost_{e,i} \times p_{e,i}) + (cost_{e,u} \times p_{e,u})$$

In the NEEAR study, visits and phone calls to an HCP were differentiated from one another (Appendix C: Table LXVII). Out of 220 NEEAR participants with GI illness who sought medical care due to GI symptoms, approximately 84 (38%) only spoke to their HCP over the phone. Phone or email consultations are not reimbursed by insurance, and therefore not assumed to be associated with costs (West, 2012). The distinction between visits and phone calls was not made in CHEERS. Therefore, costs of contacting an HCP may be overestimated in CHEERS, since at the level of individual participants there was no way to distinguish between visits and phone calls.

3.1.3.3 Emergency Department Visits

Data for ED visits were also collected from FairHealth according to CPT code and geozip code. Level-three E/M CPT codes and other procedural codes for insured and uninsured individuals were utilized to assess the costs associated with visiting an ED. For ED visits, no distinction is made between new or established patients. In addition to E/M services, I assumed that procedures and tests were utilized for participants with GI illness who visit an ED. Common tests to assess GI illness include an electrolyte panel (CPT 80051), blood glucose (CPT 82947), renal function panel (CPT 80069), complete blood count (CBC) (CPT 85025), urinalysis (CPT 81000), stool culture (CPT 87046), and for females aged 13–55 only, a urine pregnancy test (CPT 81025) (TABLE XV). Common ED procedures for GI illness are intravenous (IV) hydration infusion initial set up and secondary service (CPT 96360 and 96361). The ED costs were collected in 2014, and were adjusted for inflation to 2007 dollars, using the CPI for medical care services (BLS, 2010).

Information regarding the frequency with which tests or procedures were performed in the ED for those with GI illness was estimated using the 2010 Illinois Hospital Discharge Database (IHDD). This database contains approximately 97% of all ED and hospitalizations in

Illinois. Patients diagnosed with *International Classification of Diseases* 9th Revision, *Clinical Modification* (ICD-9-CM) codes 009.0–009.3 (Infectious colitis, enteritis, and gastroenteritis) and 008.8 (Viral gastroenteritis) were selected for further analysis. The rates of tests and procedures among patients being seen in the ED (outpatients) are summarized in TABLE XV**.**

Similar to calculating costs for those who visited an HCP, a weighted average was calculated for those visiting an ED. Insurance status and the probability of certain tests or procedures (TABLE XV) being conducted were taken into consideration for the calculation of total ED costs. A weighted average was calculated according to *Equation IV*, by multiplying the geo-specific costs (*cost*) associated with being a level-three ED patient who is insured (*i*) or uninsured (*u*) multiplied by the corresponding probabilities (*p*); and adding the costs of t = {1, 2,…,8} tests or procedures that were considered possible in the ED, weighted by the probability of the patient receiving the test (TABLE XV). This cost was added to the sum of the costs of the eight different tests or procedures potentially encountered in the ED according to insurance status multiplied by the probability of the test (*t*).

Equation IV:

$$\boldsymbol{ED_{GI}} = cost_i \times p_i + cost_u \times p_u + \sum_{t=1}^{8} \left[\left(cost_{t,i} \times p_t \right) + \left(cost_{t,u} \times p_t \right) \right]$$

TABLE XV
ESTIMATED PATIENT INFORMATION TO BE USED TO ESTIMATE COI

Parameter	Probability (CI) [a]	Source
Uninsured status (Probability being uninsured (90% CI))		(DeNavas-Walt et al., 2006)
Total	0.159 (0.157, 0.161)	
By age category		
under 18	0.112 (0.109, 0.115)	
18–24	0.306 (0.299, 0.313)	
25–34	0.264 (0.258, 0.300)	
35–44	0.188 (0.183, 0.193)	
45–64	0.145 (0.142, 0.148)	
≥65	0.130 (0.110, 0.150)	
Patient Type		(Hing et al., 2010)
New	0.171 (0.168, 0.173)	
Established	0.829 (0.827, 0.832)	
Type of Contact with HCP		NEEAR
Visit (with or without phone contact)	0.618 (0.553, 0.682)	
Phone contact only	0.382 (0.317, 0.447)	
ED Test and Procedures		2010 Illinois Hospital Discharge Database
Electrolyte panel	0.189 (0.113, 0.264)	
Blood Glucose	0.189 (0.113, 0.264)	
Renal Function	0.189 (0.113, 0.264)	
CBC	0.189 (0.113, 0.264)	
Urinalysis	0.132 (0.070, 0.200)	
Urine Pregnancy Test [b]	0.650 (0.001, 0.127)	
Stool Culture	0.280 (0.000, 0.600)	
IV Hydration Infusion	0.104 (0.004, 0.163)	
Rate of Uninsured Status in IHDD		2010 Illinois Hospital Discharge Database
Uninsured [c]	0.250 (0.110, 0.390)	

[a] 95% CIs are provided, unless otherwise specified
[b] Assessed among females 13–55
[c] Rate among those hospitalized in Illinois with GI symptoms (ICD-9-CM: 009, 008.8)

3.1.3.4 **Hospitalizations**

Data for hospitalization costs were collected from the 2010 IHDD. Data were only obtained for Illinois, since only participants in CHEERS indicated hospitalization. Median hospital charges for patients with ICD-9-CM codes 009.0–009.3 and 008.8 were estimated for CHEERS participants who were hospitalized according to age category and sex. The IHDD contains detailed charge information for each patient, including charges for pharmaceuticals, radiology, diagnostic and therapeutic services, laboratory, and room charges. Charges refer to the amount billed, not necessarily the amount actually paid (Shwartz et al., 1995). Costs were calculated by multiplying total charges by the cost-to-charge ratio (CCR). The CCR is specific to each hospital and based on total expenses, excluding debt, gross patient revenue, and other operating revenue (AHA, 2010). The CCRs have been shown to adequately predict the actual costs for hospital admission (Shwartz et al., 1995). The CCR for each hospital in Illinois was not available for the IHDD, but the average CCR in the state of Illinois in 2010 was 0.33 (HCUP Cost-to-Charge Ratio Files [CCR], 2010) and was applied to all hospital charges. Hospitalization charges were adjusted to 2007 dollars using the CPI for medical care services (BLS, 2010).

Similar to the calculations used to determine costs of visits with an HCP or to an ED, a weighted average was created to calculate total hospital costs according to *Equation V* by multiplying the costs (*cost*) associated with hospitalization for insured (subscript *i*) or uninsured (subscript *u*) patients multiplied by the corresponding probabilities (*p*). In general uninsured or "self-pay" patients pay approximately 2.5 times what health insurers actually pay for hospital services (Anderson, 2007). It was assumed in the current analysis, that those with health insurance would pay the amount adjusted for the CCR, while those without health insurance would be responsible for the total charged amount (not adjusted for CCR). The rate of uninsured status in the IHDD among patients with ICD-9-CM 009.0–009.3 and 008.8 was considerably lower (2.5%), than the uninsured rate (16%) for all individuals in the United States (TABLE XV). This different insurance rate was applied to some versions of the COI estimate.

Equation V:

$$Hospital_{GI} = (cost_i \times p_i) + (cost_u \times p_u)$$

3.1.3.5 <u>Indirect Costs</u>

Costs associated with individuals who missed work or daily activities were calculated using estimates of the approximate daily wage, multiplied by the number of days lost reported during telephone follow-up. Different versions of the COI assumed that only missed days of work should be monetized, while other versions assumed monetization for missed work and missed daily activities. Per capita earnings for males and females, according to each participant's zip code of residence, were obtained from the 2011 US Census Bureau's American Community Survey (ACS), which includes five-year estimates from the years 2006–2010 (US Census, 2011a). The ACS is an annual continuous nationwide survey, which gathers more detailed economic, demographic and housing data, than the decennial census questionnaire (US Census, 2008). Per capita income by males and females is the average income received in the past 12 months for every individual over the age of 15 in a specified geographic area and divided by the total population of males or females in that area, respectively (US Census, 2011b). To adjust for inflation, income estimates from the ACS were converted from 2010 to 2007 dollars using the CPI-U-RS (CPI research series). The CPI-U-RS is used by the ACS to adjust for inflation of income during the time period evaluated (US Census, 2008).

Per capita income was estimated for all participants in either data set according to zip code, regardless of age. The cost of lost productivity ($Productivity_{GI}$) was equated with each participant's estimated daily income, where daily income equaled annual income divided by 365 days per year. Since days that participants missed from normal activities may not have been workdays, the daily income rather than workday income was judged most appropriate (Dwight et al., 2005).

An ongoing debate among economists is whether the cost of missing out on leisure time or daily activities is equivalent to the costs of missing work. One approach is to assume that lost daily activities or leisure time is equivalent to the daily wage (Drummond et al., 1997; Dwight et al., 2005). However, Drummond et al. (1997) also has argued that lost leisure time can range from zero to an average overtime wage (1.5–2 times the daily wage). Of the 820 NEEAR participants who missed work or daily activities, only 159 (19.4%) specifically missed work, while the rest missed daily activities/leisure time. Since people may value their vacation or leisure time equal to their work time (Drummond et al., 1997; Dwight et al., 2005), an assumption can be made that the cost of missing daily activities is either equivalent to the individual's daily wage or that it is worth 1.5 times the daily wage (Drummond et al., 1997). However, since it is unclear how to value lost leisure time (Drummond et al., 1997), a conservative assumption can be that lost daily activities is worth zero times the daily wage and thus assume only actual time away from work contributes to lost productivity (Hoffmann et al., 2012; Majowicz et al., 2006; Scharff, 2011; Scharff et al., 2009). These different assumptions regarding lost productivity were assessed in different versions of the COI.

In the NEEAR study, participants were asked three separate survey questions about the number of days of work missed, the number of days in which illness prevented normal activities, and the number of days someone else missed work due to the participant's illness. In CHEERS, participants were asked one question regarding the number of days of work, school, or daily activities missed due to any GI, eye, ear or respiratory illness (Appendix C: Table LXVII). Therefore, to make the NEEAR results more comparable to CHEERS when including daily activities in the calculation of lost productivity, the larger of the two responses (number of days of work missed or days in which illness prevented normal activities) was used to estimate lost productivity. The larger of the two was chosen since there may be potential overlap in reporting of these two outcomes. It was assumed that the larger value reported would be more equivalent to what was reported in CHEERS. However, the reported number of work days missed specified among NEEAR participants was utilized in estimations that assumed lost productivity was only associated with missed time away from work. In CHEERS, the number of days of missed activities due to GI illness was not directly reported and needed to be estimated. Days of missed activity that were reported to occur within the specified duration of GI symptoms was used to estimate the number of days of activity missed due to GI illness. Alternative versions of the total cost estimate, also included costs incurred among NEEAR participants due to others missing work for another individuals' GI illness ($ProductivityOthers_{GI}$), which was calculated the same as $Productivity_{GI}$, using the daily waged multiplied by the number of days missed due to another's illness.

3.1.4 Calculation of the Total Cost of Illness

Total COI was calculated using *Equation II,* for each individual in CHEERS or NEEAR who reported any response to their GI illness that developed either within 0–3 days or 0–12 days of recreation. Some data were not available in either of the studies. In some instances measures from the NEEAR study were used to estimate costs in CHEERS, or outside data sources were utilized in order to adequately determine total costs. Overall total costs of illness were calculated based on several different data sources and relied on many different assumptions (TABLE XVI).

TABLE XVI

DATA SOURCES AND ASSUMPTIONS UTILIZED IN CALCULATING THE COST OF GI ILLNESS

Cost Component		**Source of Data**	**Assumptions**
Medications	Price	NEEAR	Cost of OTC and prescription medications self-reported in NEEAR, were assumed to be equivalent to medication costs in CHEERS.
	Quantity	NEEAR and CHEERS	Medications taken during the interval of GI illness among CHEERS participants were taken for GI symptoms.
HCP	Price	FairHealth; ; DeNavas-Walt et al., 2006; Hing et al., 2010	Those visiting the doctor would be coded as E/M level 3
	Quantity	NEEAR and CHEERS	Proportion that indicated visiting an HCP in the NEEAR study was assumed to the same as the proportion visiting an HCP in CHEERS. Contact with an HCP during the interval of GI illness among CHEERS participants was due to GI symptoms.
ED	Price	FairHealth; DeNavas-Walt et al., 2006; IHDD	Those visiting an ED would be coded as E/M level 3, and would be likely to undergo a variety of tests and procedures
	Quantity	NEEAR and CHEERS	Visits to the ED during the interval of GI illness among CHEERS participants was due to GI symptoms
Hospital Admission	Price	IHDD	Insurance rate observed in IHDD was most appropriate to apply to CHEERS participants who indicated hospitalization.
	Quantity	NEEAR and CHEERS	Hospitalizations during the interval of GI illness among CHEERS participants was due to GI symptoms
Missed days of work or daily activity	Price	US Census	Daily wage calculated from Per capita income for males and females by zip code of residence would be representative of daily wage for those who water recreate within NEEAR and CHEERS.
	Quantity	NEEAR and CHEERS; Drummond et al., 1997	The proportion of those who indicate specifically missing work in NEEAR, can be applied to CHEERS. That missed daily activities can be monetized as 0, 1, or 1.5 times the daily wage. Missed daily activities during the interval of GI illness among CHEERS participants was due to GI symptoms

Several critical components to calculating the COI were known, unknown, or could potentially vary based on different assumptions (TABLE XVII). Therefore, 20 different versions of total cost were calculated to determine a range of potential costs associated with GI illness. These COI variations incorporated different assumptions regarding insurance status, patient type, and the frequency of tests in the ED (TABLE XV). The mean, upper confidence limit, or lower confidence limit of these estimates (such as insurance status) was utilized in several different versions to help define variability and uncertainty in the COI.

TABLE XVII

ASSUMPTIONS AND UNKNOWNS IN CHEERS AND NEEAR

Component	Known	Unknown	Assumptions
Meds.	• Cost of medications for NEEAR 2005–2007 participants • Which NEEAR participants took medications for GI illness	• Costs of medications for NEEAR 2003–2004 participants (• TABLE XIV) • Cost of medications for CHEERS participants • If medications taken by CHEERS participants were taken specifically to treat GI symptoms	• The distribution of medications (according to symptom-complex) taken by NEEAR participants from 2005 to 2007 can be applied to all NEEAR and CHEERS participants
Contact with HCP	• Which NEEAR participants visited an HCP for GI illness • Costs for visits to an HCP by geozip, insurance status, and patient type	• Insurance status and patient type for participants • Which CHEERS participants only spoke to an HCP by phone • If contact with HCP by CHEERS participants was in response to GI illness • Costs associated with talking to an HCP over the phone	• Combine insurance status and patient type into a weighted average for costs of contacting an HCP (TABLE XV) • Approximately 60% of those contacting HCP visit in person, while 40% speak only by phone. • Phone calls to HCP cost $0
Visit to an ED	• Which NEEAR participants visited an ED for GI illness • Costs for visits to an ED visit and procedures by CPT code by geozip and insurance status	• Insurance status for participants • Which tests and procedures were performed in the ED • If visits to the ED by CHEERS participants was in response to GI symptoms	• Combine insurance status and the probability of certain tests and procedures into a weighted average for costs of visiting an ED (TABLE XV) • The proportion of tests/procedures according to IHDD can be applied to ED visits for both study areas • Only females aged 13–55 have pregnancy tests in the ED
Hospital Admission	• Hospital charges for patients in Illinois in 2010 with ICD-9-CM codes 009.0–009.3 and 008.8	• Insurance status for participants • If hospitalizations of CHEERS participants was in response to GI symptoms	• Combine insurance status into a weighted average for costs of visiting an hospital (TABLE XV)
Lost productivity	• Gender-specific daily wage by zipcode • Which NEEAR participants missed work or daily activities due to of GI symptoms	• If the cost of missing daily activities is equivalent, greater, or less than the cost of missing work • If missed daily activities reported by CHEERS participants were in response to GI symptoms	• Per capita income by zipcode is adequate for calculating daily wage • Cost of missed daily activities is either equal to, 1.5× or 0×, the cost of missing a day of work

3.1.5 Total Cost of Illness by Group

Different versions of the cost of illness were compared among different water recreation groups. In both studies the COI for individual participants was compared between water recreators and non-water recreators. Additionally, the COI among water recreators who reported swallowing water was compared to those who did not. Among CHEERS water recreators, the COI for CAWS recreators was compared to GUW recreators, and among NEEAR water recreators, the COI of those swimming in freshwater was compared to those swimming in marine water.

To facilitate these statistical comparisons, the normality of COI was assessed. The distributions of cost were skewed, but were close to normal when natural log-transformed. However, some individual costs approached $0 and other costs were identical for multiple individuals. Therefore, rather than evaluate cost as a continuous variable, untransformed cost was assessed as categorical variable, by classifying COI <$10, COI $10–$50, COI $50–$200, and COI >$200. These categories were based on the distribution of COI. Ordinal and multinomial logistic regression models were constructed using SAS (Derr, 2013). The ordinal cumulative logit model produced a single summary OR for the entire model and assumed the POA was not violated. The POA states that the odds of being in the first category versus all other categories is proportional to the odds of being in the first two categories versus all other categories and so on (Ananth and Kleinbaum, 1997; Rothman et al., 2008). When the POA did not hold (according to the χ^2 test), generalized logit was used, treating the outcome as a dummy variable, using the lowest category (<$10) as the reference group (Derr, 2013). First, unadjusted models, only containing the exposure group of interest (water contact versus no water contact, swallowing water versus not swallowing water, CAWS versus GUW among CHEERS recreators, and marine versus fresh among NEEAR recreators) were evaluated. Next, all potential confounders for the relationship between exposure and COI, determined a priori, were included in the logistic models to determine if costs differed based on type of exposure. These covariates included demographics such as gender, race, and age, as well as other potential confounders including frequency of water use, contact with animals, ingestion of either raw meat, hamburger, or fish, contact with someone with GI symptoms, washing hands prior to eating or drinking, and digging in sand, for NEEAR participants only. These covariates were thought to affect the relationship between increased exposure to recreational water and the burden of GI illness (Figure 1). In the NEEAR study beach location was controlled for as a fixed effect to control for any differences between beaches. Linear regression models were also fitted, to predict the natural log-transformed continuous cost variable and were compared to the results of the ordinal and multinomial regression.

Multicollinearity was assessed using PROC CORR to determine if any variables in the models were highly correlated with one another. Additionally, using PROC REG, the variance inflation factor (VIF) was examined to quantify multicollinearity. The model's adjusted R^2 was also examined to estimate the fraction of the total cost explained by the independent variables.

Additionally, total costs of GI illness within 0–3 and 0–12 days of water recreation was determined and presented as the total costs per 1,000 water recreators. To determine the contribution of direct and indirect costs to total costs, each component of the COI was summed and divided by the total number of water recreators in each study (7,710 in CHEERS and 17,571 in NEEAR) and multiplied by 1,000.

3.1.6 Total Costs Attributable to Water Recreation

In these epidemiology studies, it is not possible to determine which illnesses were attributable to water recreation on an individual level. However, calculation of the attributable fraction (AF), which is the fraction of disease incidence in the exposed group due to exposure (Rothman et al., 2008), was used to determine the overall costs attributable to water recreation in each study. The AF can be estimated using the RR according to *Equation VI.* Model-based standardization, which can use logistic regression to produce parameters other than the OR (Greenland, 2004), was used to calculate both the RR and the AF.

Logistic regression was used to identify the association between the development of GI illness and any exposure to recreational water. For CHEERS this included any individuals participating in incidental-contact water recreation, compared to the unexposed group who had no water contact. Similarly in NEEAR, the water-exposed group included all those with any water contact, compared to beachgoers with no water contact. Models assessing the occurrence of GI illness included all potential covariates, determined a priori (Appendix A: Table XLII), based on prior studies that have analyzed the association between water exposure and the occurrence of illness (Dorevitch et al., 2012a; Wade et al., 2010a). Covariates that had the potential to affect the relationship between water recreation and the occurrence of GI illness included gender, race, and age, frequency of water use, contact with animals, ingestion of either raw meat, hamburger, or fish, contact with someone with GI symptoms, washing hands prior to eating or drinking, and digging in sand, for NEEAR participants only. In the NEEAR study, household was an important clustering variable that impacted the association between exposure and the occurrence of illness. Therefore, robust estimates of variance were utilized to account for household cluster, while beach location was controlled for as a fixed effect to control for any differences between beaches. The AF calculated based on this model represented the fraction of water recreators in the epidemiologic studies with GI illness specifically due to any recreational water exposure. Bias-corrected bootstrapping (1,000 iterations) was utilized to estimate CIs for the AF. Subsequently, the AF was multiplied by the estimated total costs among water recreators, to thus determine the total costs attributable to water recreation in each study and the total costs attributable to water recreation per 1,000 water recreators.

Equation VI:

$$AF = \left(\frac{RR - 1}{RR}\right) \times 100$$

3.2 Results

3.2.1 Responses to Illness

The CHEERS had 11,297 participants who participated in telephone follow-up, of which 970 (8.6%) developed GI illness within 0–12 days and 431 (3.8%) developed illness within 0–3 days following recreation. The NEEAR study had 27,276 participants who participated in telephone follow-up, of which 1,944 (7.1%) developed GI illness within 0–12 days and 917 (3.4%) developed GI illness within 0–3 days following recreation. Demographics (TABLE XVIII), the different proportions of those with GI illness who responded to their symptoms, and the corresponding mean costs for those who develop symptoms (TABLE XIX) are described for both studies. In general, the proportion of those who responded to their GI symptoms was slightly greater among those who developed illness within 0–3 days compared to 0–12 days after recreation. Additionally, the cost of medications tabulated using the symptom-complex method was relatively similar to, but larger than individual self-reported costs of medications.

TABLE XVIII
CHARACTERISTICS OF CHEERS AND NEEAR PARTICIPANTS

	CHEERS Participants	NEEAR Participants
Total No. Participants	11,297	27,276
Total No. Water Recreators [a] (%)	7,710 (68.2%)	17,571 (64.4%)
CAWS Water Recreators [a], No. (%)	3,744 (48.6%)	--
Marine Water Recreators [a], No. (%)	--	6,350 (23.2%)
Black Race, No. (%)	1,043 (9.2%)	1,877 (7.0%)
Age, mean years	36.4	28.8
Males, No (%)	5,972 (52.9%)	12,019 (44.0%)

[a] CHEERS water recreators participated in incidental-contact water recreation (kayaking, canoeing, rowing, boating, fishing), NEEAR water recreators participated in full-contact water recreation (swimming, wading)

TABLE XIX
CHARACTERISTICS OF CHEERS AND NEEAR RESPONSE TO GI ILLNESS AND MEAN COSTS

	CHEERS		NEEAR	
	0–12 days	0–3 days	0–12 days	0–3 days
Develop GI Symptoms, No. (%)	970 (8.6%)	431 (3.8%)	1,944 (7.1%)	917 (3.4%)
Proportion of those with GI illness responding to their symptoms				
Any response to GI Symptoms No. (%)	610 (62.9%)	291 (67.5%)	1,191 (61.3%)	568 (61.9%)
OTC medication, (%)	439 (45.3%)	218 (51.8%)	797 (41.0%)	407 (44.8%)
Prescription Medication, No. (%)	52 (5.4%)	24 (5.6%)	110 (5.7%)	61 (6.6%)
Contact with HCP, No. (%) [a]	120 (12.4%)	50 (11.6%)	136 (7.0%)	74 (8.1%)
Visit ED, No. (%)	10 (1.0%)	3 (0.7%) [b]	37 (1.9%)	18 (2.0%)
Admitted to hospital, No. (%)	9 (0.9%)	3 (0.7%) [b]	0 (0.0%)	0 (0.0%)
Lost work or daily activities No. (%)	388 (40.0%)	189 (43.8%)	808 (41.6%)	382 (41.6%)
Mean days lost of work or daily activities (median)	1.6 (1.0)	1.4 (1.0)	1.7 (1.0)	1.9 (1.0)
Missed work, No. (%)	--	--	159 (8.2%)	83 (9.1%)
Lost daily activities, No. (%)	--	--	797 (41.0%)	377 (41.1%)
Others missed work, No. (%)	--	--	69 (3.5%)	45 (4.9%)
Mean costs for responses to illness for those with GI illness (2007 dollars)				
OTC medications, symptom-complex [b]	$11.18	$11.67	$9.27	$9.33
OTC medications, self-reported [c]	--	--	$7.97	$8.52
Prescription medications, symptom-complex [b]	$27.23	$30.06	$35.08	$35.93
Prescription medications, self-reported [c]	--	--	$26.08	$26.74
Contact with HCP; Insured, Established	$36.45	$35.81	$27.79	$27.97
Contact with HCP; Insured, New	$58.82	$59.61	$45.44	$45.43
Contact with HCP; Uninsured, Established	$126.52	$136.13	$92.64	$92.24
Contact with HCP; Uninsured, New	$196.09	$198.70	$151.48	$151.44
ED Visit; Insured [E]	$265.29	$244.84 [d]	$201.38	$200.33
ED Visit; Uninsured [E]	$884.42	$816.14 [d]	$671.26	$667.76
Hospitalization, Insured	$11,346.89	$7,281.28 [d]	--	--
Hospitalization, Uninsured	$34,378.66	$9,621.64 [d]	--	--
Lost productivity	$210.41	$188.97	$186.82	$207.24

[a] Contact with HCP measured as phone calls or visits for CHEERS participants, and measured actual visits (not phone calls) for NEEAR participants
[b] Estimated based on all symptoms reported (See Methods: Section 3.2.3.1)
[c] Self-reported medication costs for GI illness, NEEAR only (See Methods: Section 3.2.3.1)
[d] ED visits and hospitalizations occurring only among non-water recreators who develop illness within 0–3 days
[e] Estimated total ED cost; individual costs for tests/procedures by insurance status (insured versus uninsured) are in Appendix C: Table LXIX

3.2.2 Total Costs of Illness Estimates

Several different versions of the COI were created (TABLE XX) based on various assumptions, described in TABLE XVI and TABLE XVII. The proportion that each component contributed to the total cost varied according to each version of the COI (Appendix C: Table LXX–Table LXXIII). Variations of the COI (in bold) (TABLE XX) were used consistently throughout the analyses, since they were most representative of low, moderate, and high estimates of the total COI. In general, different assumptions, based on the US population, regarding insurance status (insured versus not insured) for doctor and ED visits, and patient type (new versus established), did not greatly impact any of the versions of the overall total costs. However, changes in the assumptions regarding insurance status among those hospitalized and different assumptions related to lost productivity had a significant impact on highest and lowest estimates of the total costs (TABLE XXI and TABLE XXII).

Total costs of GI illness among all participants with illness in CHEERS and NEEAR were summarized. The total costs for all CHEERS participants with GI illness ranged from $159,699.19 to $259,642.28 for participants developing illness 0–12 days after recreation and $42,403.25 to $85,514.81 for participants developing illness 0–3 days after recreation. In the NEEAR study, the total costs ranged from $52,668.09 to $256,563.41 for participants developing symptoms 0–12 days after recreation, and $29,424.47 to $141,350.88, for participants developing symptoms within 0–3 days of recreation. In general, regardless of the time frame, the mean COI for individual CHEERS participants was higher than for individual NEEAR participants, though the reverse was true for the median COI. This indicates that CHEERS had a higher proportion of individuals with very high COI. Slightly lower mean and median COIs were noted among CHEERS participants who developed GI illness within 0–3 days, compared to those who developed GI illness within 0–12 days. However, the mean and median COIs were larger or unchanged among NEEAR participants who developed GI illness within 0–3 days compared to 0–12 days (TABLE XXI and TABLE XXII).

Among participants in CHEERS with GI illness developing within 0–3 days of recreation, the costs per individual in the study ranged between $6.00 and $16,203.91, while the cost of GI illness among those exposed to recreational water in CHEERS ranged from $6.00 and $805.80. Participants in the NEEAR study developing GI illness within 0–3 days, the costs per individual ranged between $0.00 and $1,151 for all participants and for those exposed to recreational beach water.

TABLE XX

ASSUMPTIONS CONSIDERED IN EACH VERSION OF THE COI [a b c]

COI Version	Medication	Contact with HCP	Visit to ED	Hospitalization (CHEERS only)	Lost Productivity
1 (original)	**NEEAR symptom-complex**	**Average uninsured rate by age**	**Average insurance rate by age, average rate of tests**	**Average insurance rate by age**	**All days lost, equivalent to daily wage**
1a	**N:NEEAR Self-report [d]**				
1b		C: Assume 38% contact HCP by phone only			
2		Lowest uninsured	Lowest uninsured	C: Lowest uninsured [e]	
2a		Lowest uninsured	Lowest uninsured	C: Insured rate from IHDD	
3			Lowest rate of tests		
4		**Lowest uninsured**	**Lowest uninsured Lowest rate of tests**	**C: Lowest uninsured [e]**	
4a		**Lowest uninsured**	**Lowest uninsured Lowest rate of tests**	**C: Insured rate from IHDD**	
4b		**Lowest uninsured C: Assume 38% contact HCP by phone only**	**Lowest uninsured Lowest rate of tests**	**C: Lowest uninsured [e]**	
4c		Lowest uninsured C: Assume 38% contact HCP by phone only	Lowest uninsured Lowest rate of tests	C: Insured rate from IHDD	
5			Highest rate of tests		
6		Lowest uninsured	Lowest uninsured Highest rate of tests	C: Lowest uninsured [e]	
7		Highest uninsured	Highest uninsured	C: Highest uninsured [e]	
8		Highest uninsured	Highest uninsured Lowest rate of tests	C: Highest uninsured [e]	
9		Highest uninsured	Highest uninsured Highest rate of tests	C: Highest uninsured [e]	
10					**C: 80% of days lost are missed daily activities (DA) DA equivalent to 1.5× daily wage**
10a					DA equivalent to 1.5× daily wage N: Others miss work
11		**Highest uninsured**	**Highest uninsured Highest rate of tests**	**C: Highest uninsured [e]**	**C: 80% of days lost are missed DA DA equivalent to 1.5× daily wage**
11a		**Highest uninsured**	**Highest uninsured Highest rate of tests**	**C: Highest uninsured [e]**	**DA equivalent to 1.5× daily wage N: Others miss work**
12					**C: 80% of days lost are missed DA DA equivalent to 0× daily wage**

Bolded versions refer to estimates representing high, medium, and low assumptions

[a] Assume original Assumption, unless otherwise specified

[b] N=assumption applied to NEEAR only, C=assumption applied to CHEERS only

[c] "Highest" and "Lowest" refer to the upper and lower bound of the age specific insurance rates or rates of tests/procedures in the ED where appropriate (TABLE XV)

[d] Assume all NEEAR estimates (except version 1) use NEEAR Self-reported estimates for medication costs

[e] Lowest uninsured/highest uninsured refer to the age specific insurance rates for the whole US population (not hospital specific insurance rate) (TABLE XV)

TABLE XXI
ESTIMATES OF EACH VERSION OF THE TOTAL COST OF GI ILLNESS, ALL CHEERS PARTICIPANTS (2007 DOLLARS)

COI Version [a]	**GI, 0–12 days**				**GI, 0–3 days**			
	N	Total Cost ($)	Cost ($) per Individual		N	Total Cost ($)	Cost ($) per Individual	
			Median	Mean			Median	Mean
1	**610**	**225,009.99**	**97.99**	**368.87**	**291**	**70,975.49**	**92.49**	**243.90**
1a	-	-	-	-	-	-	-	-
1b	610	222,413.45	97.45	364.61	291	69,923.12	92.49	240.29
2	610	224,165.12	97.99	367.48	291	70,787.38	92.49	243.26
2a.	610	191,818.70	97.99	314.46	291	63,937.73	92.49	219.72
3	610	224,844.61	97.99	368.60	291	70,930.61	92.49	243.75
4	610	224,000.93	97.99	367.21	291	70,742.83	92.49	243.11
4a	**610**	**191,654.51**	**97.99**	**314.19**	**291**	**63,893.18**	**92.49**	**219.56**
4b	**610**	**221,422.76**	**97.45**	**362.99**	**291**	**69,697.57**	**92.49**	**239.51**
4c	610	189,076.34	97.45	309.96	291	62,847.92	92.49	215.97
5	610	225,167.25	97.99	369.13	291	71,018.13	92.49	244.05
6	610	224,321.24	97.99	367.74	291	70,829.70	92.49	243.40
7	610	226,826.24	98.39	371.85	291	71,184.94	92.49	244.62
8	610	226,657.31	98.39	371.57	291	71,138.88	92.49	244.63
9	610	226,986.87	98.39	372.11	291	71,228.69	92.49	244.77
10	**610**	**257,665.40**	**132.09**	**422.40**	**291**	**85,261.61**	**129.24**	**293.00**
10a	-	-	-	-	-	-	-	-
11	**610**	**259,642.28**	**132.09**	**425.64**	**291**	**85,514.81**	**129.24**	**293.87**
11a	-	-	-	-	-	-	-	-
12	**610**	**159,699.19**	**27.40**	**261.80**	**291**	**42,403.25**	**25.90**	**145.72**

Bolded figures represent low, moderate, and high end estimates for total costs, and were analyzed further
[a] Assumptions for each version described in TABLE XX

TABLE XXII
ESTIMATES OF EACH VERSION OF THE TOTAL COST OF GI ILLNESS, ALL NEEAR PARTICIPANTS (2007 DOLLARS)

COI Version [a]	GI, 0-12 days				GI, 0-3 days			
	N	Total Cost ($)	Cost ($) per Individual		N	Total Cost ($)	Cost ($) per Individual	
			Median	Mean			Median	Mean
1	**1,175**	**173,397.39**	**107.52**	**147.57**	**568**	**93,993.48**	**115.48**	**165.48**
1a	**1,175**	**171,397.13**	**105.78**	**145.87**	**568**	**92,882.80**	**113.49**	**163.53**
1b	-	-	-	-	-	-	-	-
2	1,175	171,311.72	105.78	145.80	568	92,835.47	113.49	163.44
2a.	-	-	-	-	-	-	-	-
3	1,175	171,020.46	105.78	145.55	568	92,699.62	113.49	163.20
4	**1,175**	**170,938.00**	**105.78**	**145.48**	**568**	**92,653.78**	**113.49**	**163.12**
4a	-	-	-	-	-	-	-	-
4b	-	-	-	-	-	-	-	-
4c	-	-	-	-	-	-	-	-
5	1,175	171,758.06	105.78	146.18	568	93,058.04	113.49	163.83
6	1,175	171,669.84	105.78	146.10	568	93,009.28	113.49	163.75
7	1,175	171,577.52	105.78	146.02	568	92,982.76	113.49	163.70
8	1,175	171,193.95	105.78	145.70	568	92,796.20	113.49	163.37
9	1,175	171,945.08	105.78	146.34	568	93,161.24	113.49	164.02
10	1,175	245,067.88	154.51	208.57	568	132,872.17	164.28	233.93
10a	1,179	182,754.41	108.70	155.01	568	101,083.07	116.91	177.34
11	**1,175**	**245,615.83**	**154.51**	**209.03**	**568**	**133,150.61**	**164.28**	**234.42**
11a	**1,179**	**256,563.41**	**155.67**	**217.61**	**570**	**141,350.88**	**168.55**	**247.98**
12	**909**	**52,668.09**	**5.49**	**57.94**	**467**	**29,424.47**	**5.49**	**63.01**

Bolded figures represent low, moderate, and high-end estimates for total costs, and were analyzed further
[a] Assumptions for each version described in TABLE XX

3.2.3 Total Cost of Illness by Group

Costs were evaluated according to exposure group to determine if certain exposures, such as any water exposure compared to the unexposed group, water recreators swallowing water compared to water recreators not swallowing water, CHEERS participants being in CAWS versus GUW waters, and NEEAR participants being in marine versus freshwater, were associated with COI. Similar associations with exposure were noted regardless of the version of COI used in the analysis (Appendix C: Table LXXIV–Table LXXV). Therefore, analyses of the relationship between COI and exposure, rely on the COI with moderate assumptions (Version 1 for CHEERS, Version 1a for NEEAR) (TABLE XX). Crude non-parametric tests (Wilcoxon) did not indicate any statistically different costs for any of the groups assessed (not shown). Among CHEERS participants with GI illness developing within 0–12 days, the COI among non-water recreators was greater than the COI among non-water recreators, and approached statistical significance at the $p<.05$ (Appendix C: Table LXXVI). However, no statistically significant differences in COI were observed among CHEERS exposure groups among those who developed GI illness within 0–3 days of recreation (TABLE XXIII). Among NEEAR participants, regardless of the time window (Appendix C: Table LXXVI), there was no significant difference in the COI comparing water recreators to non-water recreators. The unadjusted relationship between marine water recreators indicated a potential difference in COI from fresh water recreators, but the difference was not statistically significant when other covariates were included.

TABLE XXIII

COSTS OF GI ILLNESS DEVELOPING WITHIN 0–3 DAYS AND MULTINOMIAL LOGISTIC REGRESSION BY EXPOSURE AMONG CHEERS AND NEEAR PARTICIPANTS WITH GI ILLNESS (0–3 DAYS)

	Category	Costs			Ordinal Logit		Multinomial Logit
		Total ($)	Costs ($) per Individual with GI: Mean	Costs ($) per Individual with GI: Median	Crude OR	Adjusted OR [c]	Adjusted OR $200 and over $50–$200 $10–$50 Under $10 (reference)
Incidental-Contact (CHEERS(V1)[a])	Water Rec [b]	29,882.31	145.77	87.17	1.07 (0.67, 1.70)	0.97 (0.58, 1.62)	1.08 (0.45, 2.64) 1.06 (0.48, 2.33) 1.44 (0.50, 4.17) 1.00
	Ref: Non-Water Rec	41,093.17	470.45	98.88			
	CAWS	15,243.38	145.18	81.31	0.89 (0.54, 1.47)	0.92 (0.53, 1.59)	1.38 (0.49, 3.92) 1.50 (0.58, 3.89) 3.26 (0.98, 10.78) 1.00
	Ref: GUW	14,638.94	146.39	95.42			
	Swallow	2,450.64	188.51	141.48	1.84 (0.65, 5.23)	1.63 (0.54, 5.00)	2.83(0.26, 30.63) 2.06 (0.19, 21.90) 3.56 (0.24, 53.52) 1.00
	Ref: Don't Swallow	27,431.68	142.87	79.14			
Full-Contact (NEEAR(V1a)[a])	Water Rec [b]	68,997.74	163.50	113.49	0.93 (0.70, 1.24)	0.97 (0.79, 1.20)	1.03 (0.74, 1.43) 0.91 (0.71, 1.17) 1.35 (0.69, 2.65) 1.00
	Ref: Non-Water Rec	23,377.45	163.48	109.64			
	Marine	17,147.77	194.86	123.65	1.67 (1.17, 2.38)	0.61 (0.36, 1.03)	0.61 (0.29, 1.31) 0.54 (0.27, 1.06) 1.53 (0.41, 5.74) 1.00
	Ref: Fresh	51,849.96	155.24	109.00			
	Swallow	14,729.22	206.65	121.93	1.14 (0.78, 1.66)	0.99 (0.65, 1.51)	1.02 (0.61, 1.97) 0.71 (0.40, 1.25) 1.96 (0.52, 7.40) 1.00
	Ref: Don't Swallow	51,851.71	155.71	112.14			

[a] Assumes all moderate assumptions (TABLE XX)
[b] CHEERS water recreators participated in incidental-contact water recreation (kayaking, canoeing, rowing, boating, fishing), NEEAR water recreators participated in full-contact water recreation (swimming, wading)
[c] POA was violated (χ^2<.05)

Differences in COI between exposure groups were also assessed among all participants, not only among those with illness with assigned costs (TABLE XXIV), since the impact of COI may also be related to the frequency of illness as well as the severity. Overall, among CHEERS participants, the COI per non-water recreator was greater than the COI for water recreators, but did not approach statistical significance. Additionally, there also was no observed differences in the COI among all CAWS recreators compared to GUW recreators. However, a statistically significant difference in COI was observed among CHEERS water recreators that swallowed water compared to water recreators that did not swallow water. Among NEEAR participants, there was a significant difference in COI per person comparing water recreators to non-water recreators. Additionally, adjusting for covariates found marine recreators had significantly lower COI compared to freshwater recreators. Lastly, NEEAR water recreators who swallowed water had greater COI compared to water recreators who did not swallow water, but was not statistically significant at $p<.05$.

TABLE XXIV
COSTS OF GI ILLNESS DEVELOPING WITHIN 0–3 DAYS AND MULTINOMIAL LOGISTIC REGRESSION BY EXPOSURE AMONG ALL CHEERS AND NEEAR PARTICIPANTS

	Category	**Costs**			**Ordinal Logit**		**Multinomial Logit**
		Total ($)	Costs ($) per Individual		Crude OR	Adjusted OR [c]	Adjusted OR $200 and over $50–$200 $10–$50 Under $10 (reference)
			Mean	Median			
Incidental-Contact (CHEERS(V1)[a])	Water Rec [b]	29,882.31	3.93	0.00	1.18 (0.89, 1.58)	1.33 (0.99, 1.79)	1.15 (0.69, 1.93) 1.36 (0.91, 2.05) 1.68 (0.77, 3.63) 1.00
	Ref: Non-Water Rec	41,093.17	11.55	0.00			
	CAWS	15,243.38	3.90	0.00	1.05 (0.77, 1.42)	0.94 (0.69, 1.29)	0.79 (0.45, 1.38) 0.86 (0.56, 1.33) 1.81 (0.82, 4.00) 1.00
	Ref: GUW	14,638.94	3.97	0.00			
	Swallow	2,450.64	8.25	0.00	**1.94** **(1.06, 3.50)**	**1.97** **(1.08, 3.60)**	**2.76 (1.09, 7.04)** **1.47 (0.56, 3.69)** **2.13 (0.49, 9.07)** **1.00**
	Ref: Don't Swallow	27,431.68	3.75	0.00			
Full-Contact (NEEAR(V1a)[a])	Water Rec [b]	68,997.74	3.98	0.00	**1.51** **(1.21, 1.88)**	**1.53** **(1.21, 1.95)**	**1.67 (1.12, 2.51)** **1.46 (1.07, 2.02)** **1.43 (0.62, 3.32)** **1.00**
	Ref: Non-Water Rec	23,377.45	2.43	0.00			
	Marine	17,147.77	4.93	0.00	1.25 (0.96, 1.63)	**0.43** **(0.24, 0.75)**	**0.43 (0.18, 0.98)** **0.35 (0.15, 0.85)** **1.04 (0.18, 5.85)** **1.00**
	Ref: Fresh	51,849.96	3.74	0.00			
	Swallow	14,729.22	6.32	0.00	**1.46** **(1.09, 1.95)**	1.31 (0.96, 1.81)	1.58 (0.99, 2.53) 1.04 (0.64, 1.61) 2.64 (0.79, 8.85) 1.00
	Ref: Don't Swallow	51,851.71	3.65	0.00			

[a] Assumes all moderate assumptions (TABLE XX)
[b] CHEERS water recreators participated in incidental-contact water recreation (kayaking, canoeing, rowing, boating, fishing), NEEAR water recreators participated in full-contact water recreation (swimming, wading)
[c] POA was violated (χ^2<.05)

Similar conclusions regarding the relationship between water exposure and COI were also observed using linear regression (Appendix C:Table LXXVII–Table LXXVIII). In both studies, COI was natural-log transformed. The adjusted R^2 was examined to determine the fraction of cost that can be explained by the set of independent variables in each model. The exposure variables and covariates only explained approximately 1% of the variability in the COI, regardless of the time to illness (0–3 days versus 0–12 days) among those with illness.

Costs per 1,000 water recreators were calculated by dividing the total costs by the number of water recreators in each study and multiplying that figure by 1,000. The contribution of each cost component per 1,000 water recreators for CHEERS (Figure 6 and Figure 7) differed depending on the time window for the development of illness. No CHEERS water recreators developing GI illness within 0–3 days of recreation reported any ED visits or hospitalizations, which had a large impact on total costs, since hospitalization and ED visits were reported among water recreators developing GI illness within 0–12 days. The NEEAR costs per 1,000 water recreators (Figure 8 and Figure 9) indicated similar patterns regardless of the time window of the development of illness. Approximately half of the participants were included when GI illness was defined as symptoms erupting within 0–3 days, compared to 0–12 days, resulting in lower costs per 1,000 recreators. Additionally, lost productivity contributed significantly to the total costs for both studies, and varied greatly when different assumptions were considered (TABLE XX).

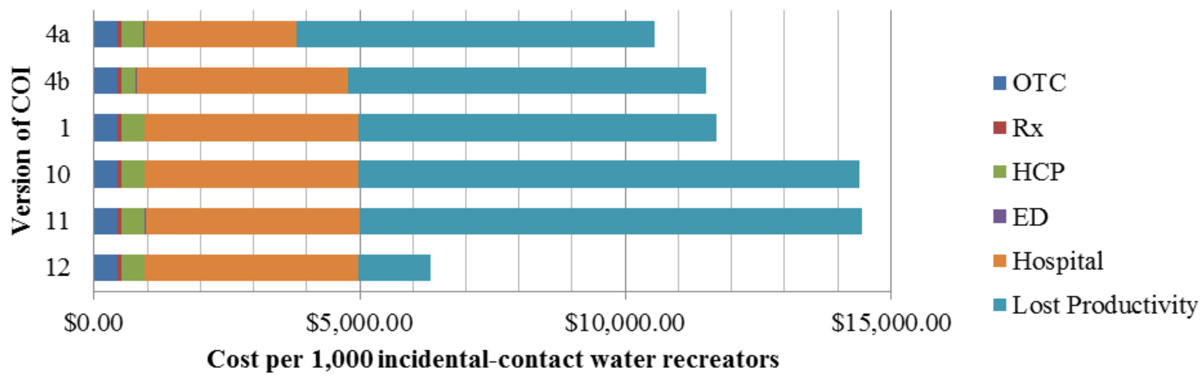

Figure 6: Total cost breakdown, per 1,000 water recreators, CHEERS, GI 0–12 days (2007 dollars).

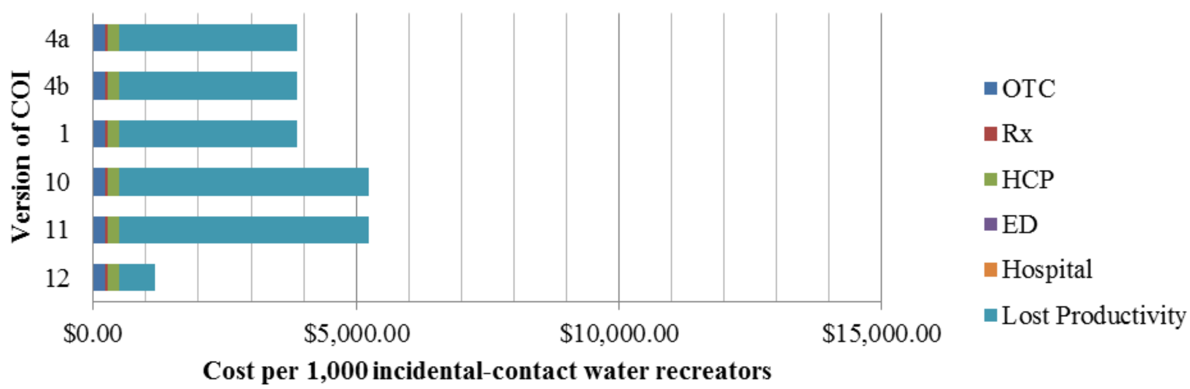

Figure 7. Total cost breakdown, per 1,000 water recreators, CHEERS, GI 0–3 days (2007 dollars).

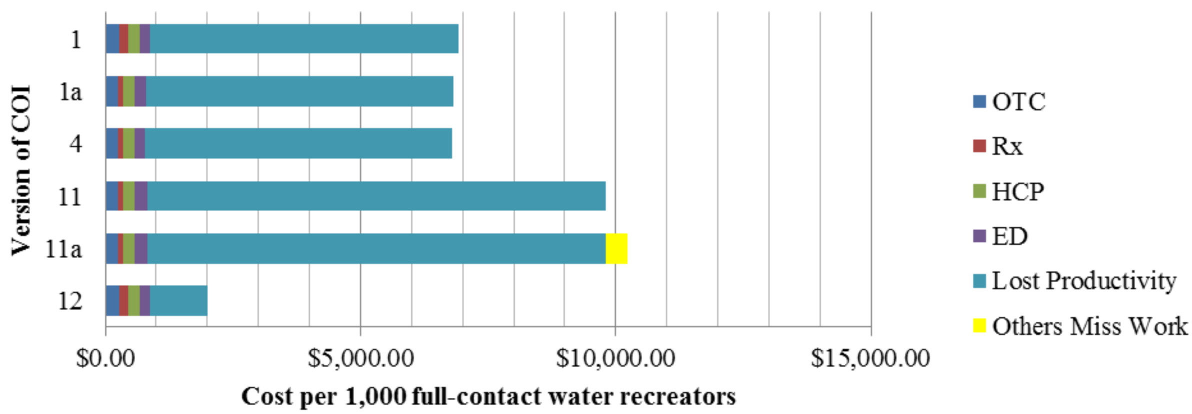

Figure 8. Total cost breakdown, per 1,000 water recreators, NEEAR, GI 0–12 days (2007 dollars).

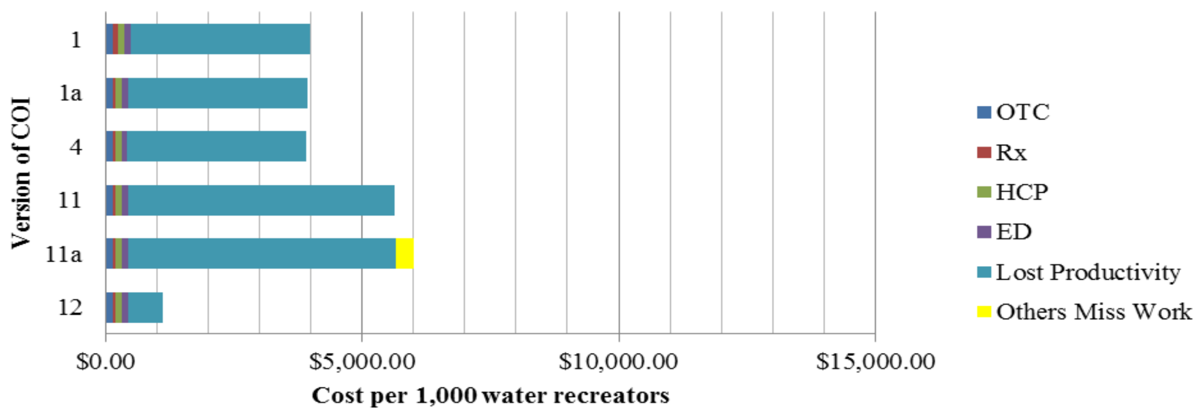

Figure 9. Total cost breakdown, per 1,000 water recreators, NEEAR, GI 0–3 days (2007 dollars).

3.2.4 Costs Attributable to Water Recreation

The AF represents the percentage of GI illness acquired by water recreators that is attributable to water recreation. The AF's for CHEERS and NEEAR were 22.4% and 37.3% respectively, which is similar to another study that observed an AF of 34.5% among bathers exposed to recreational water contaminated with human sewage (Fleisher et al., 1998). Costs attributable to water recreation were calculated by multiplying AF, derived from a logistic model of the association between water recreators compared to non-water recreators and the occurrence of GI illness, by the total costs among water recreators.

The average total costs attributable to water recreation were estimated to be between $2,010.55 and $9,039.95 or between $260.77 and $1,172.50 per 1,000 water recreators for CHEERS participants developing illness within 0–3 days of recreation, assuming an AF of 22.4% (TABLE XXV). The RR for GI illnesses among CHEERS participants that developed within 0–12 days after recreation was 0.92 (95% CI: 0.86, 1.12). This corresponds to an AF of

-0.03%, or approximately $0 attributable to water recreation (Appendix C: Table LXXIX). Among NEEAR water recreators, the average costs attributable to water recreation were between $7,386.20 and $39,414.75 or between $420.36 and $2,243.17 per 1,000 water recreators for those developing illness within 0–3 days of recreation, assuming an AF of 37.3% (TABLE XXV). These estimates are similar to those for the 0–12 day definition ($458.69 to $2,474.30) per 1,000 water recreators (Appendix C: Table LXXIX).

TABLE XXV

COSTS ATTRIBUTABLE TO WATER RECREATION, GI 0–3 DAYS (2007 DOLLARS)

	Probability of GI illness if exposed to water (95% CI)	Probability of GI illness if not exposed to water (95% CI)	Relative Risk (95% CI)	Attributable Fraction (95% CI)	Version	Total Costs Among Water Recreators ($)	Costs per 1,000 water recreators [a]($)	Total Costs Attributable to Water Recreation ($) (95% CI)	Costs per 1,000 water recreators attributable to water recreation [a]($) (95% CI)
CHEERS	0.042 (0.038, 0.048)	0.033 (0.026, 0.039)	1.29 (1.09, 1.64)	28.9% (11.4, 43.1)	12	8,975.67	1,164.16	2,010.55 (215–3.509)	260.77 (28–455)
					4	29,882.31	3,875.79	6,693.64 (717–11,684)	868.18 (93–1,515)
					4a	29,871.29	3,874.36	6,691.17 (717–11,680)	867.86 (93–1,515)
					1	29,239.22	3,792.38	6,549.59 (701–11,432)	849.49 (701–1,482)
					10	40,335.64	5,231.60	9,035.18 (968–15,771)	1,171.88 (126–2,046)
					11	40,356.92	5,234.36	9,039.95 (969–15,779)	1,172.50 (126–2,047)
NEEAR	0.039 (0.035, 0.042)	0.024 (0.022, 0.028)	1.60 (1.34, 1.85)	37.3% (25.7, 46.1)	12	19,802.15	1,126.98	7,386.20 (5,089–9,129)	420.36 (290–520)
					4	68,814.41	3,916.36	25,667.77 (17,685–31,723)	1,460.80 (1,007–1,805)
					1	70,052.07	3,986.80	26,129.42 (18,003–32,294)	1,487.08 (1,025–1,838)
					1a	68,997.74	3,926.80	25,736.16 (17,732–31,808)	1,464.70 (1,009–1,810)
					11	99,328.26	5,652.97	37,049.44 (25,527–45,790)	2,108.56 (1,453–2,606)
					11a	105,669.64	6,013.87	39,414.78 (27,157–48,714)	2,243.17 (1,546–2,772)

[a] 7,710 water recreators in CHEERS, and 17,571 water recreators in the NEEAR study

3.3 Discussion

Based on the analyses of cohort studies containing more than 35,000 participants, the estimated costs of sporadic GI illness attributable with water recreation (as opposed to the total costs of illness) within the two studies were estimated to be between $2,010.55 and $9,039.95 in CHEERS and between $7,386.20 and $39,414.75 in the NEEAR study. Data from both studies indicate that for 1,000 water recreators, the costs attributable to water recreation ranged from $260.77 to $2,243.17 depending on assumptions about insurance status and lost productivity (TABLE XXV). Costs were elevated among water recreators in CHEERS who swallowed water compared to water recreators that did not swallow water. Additionally, in the NEEAR study, differences between costs of marine water recreators were noted compared to freshwater recreators, and in general, the costs of those with any contact with recreational water were higher compared to non-water recreators (TABLE XXIV). Qualitatively, indirect costs associated with illness accounted for the largest proportion of cost under most sets of assumptions, and was a major source of variability in the total cost estimate (Figure 6–Figure 9). In general, depending on the assumptions considered, the total costs of GI illness attributable to water recreation were similar for full-contact (NEEAR) recreation at inland and coastal beaches and incidental-contact (CHEERS) recreation at surface waters that included locations with high concentrations of fecal indicators (TABLE XXV).

3.3.1 Utility and Assumptions in the Cost of Illness Approach

The COI approach is one of many for evaluating disease burden and provides a cost estimate that is representative of the real societal costs of illness (Buzby and Roberts, 2009). However, the COI is influenced by an individual’s SES and the cost associated with lost productivity is often difficult to estimate (Drummond et al., 1997). Evaluating one's WTP to avoid illness due to water recreation would have been informative, but data were not collected in the NEEAR and CHEERS that would support this type of analysis. The DALYs are useful for characterizing more severe outcomes, or illnesses that have long-term complications, but are very small for illnesses that are mild and self-limiting (Havelaar et al., 2004), which makes comparisons difficult. In 2000, a WBDO in Walkerton, Ontario, Canada occurred in an agricultural area after drinking-water wells were contaminated with livestock waste containing *E. coli* O157:H7 and *Campylobacter* spp. This outbreak resulted in more than 2,300 cases of GI illness, including more than 750 ED visits and 65 hospital admissions, as well as long-term health effects such as hypertension, renal impairment, and cardiovascular disease (Clark et al., 2010). The use of DALYs or QALYs would be appropriate in this context owing to the severity of disease. I am not aware of the occurrence of sequelae of acute illness in NEEAR and CHEERS; though long-term follow-up was not conducted as cases of severe illness were not anticipated (and did not occur).

The costs calculated in this study varied according to different assumptions (TABLE XX). First, insurance status in the United States varies according to race/ethnicity and age (DeNavas-Walt et al., 2006). Insurance status for the US population was considered to vary by age groups (TABLE XV), but had little effect on the cost of HCP and ED visits; however, it greatly impacted hospitalization costs (TABLE XXI and TABLE XXII). Hospitalization is costly and the costs of hospitalization were assumed to be equivalent to hospital charges among the uninsured, without the CCR adjustment (Shwartz et al., 1995). Based on the IHDD, mean hospitalization costs for GI illness for insured and uninsured Illinois residents was $11,346.89 and $34,378.66 respectively. However, hospitalizations were only reported among CHEERS water recreators developing illness within 0–12 days, and not among NEEAR water recreators or CHEERS water recreators whose GI illness developed within 0–3 days. In this study, based on the 2010 IHDD approximately 3% of those who were hospitalized with GI illness were considered “self-pay,” which is substantially smaller than the rate of 16% approximated for the US population in 2005 (DeNavas-Walt et al., 2006) and more consistent with the 2007 Nationwide Inpatient Sample (NIS), Healthcare Cost and Utilization Project (H-CUP), Agency for Healthcare Research and Quality (AHRQ) (HCUP Nationwide Inpatient Sample, 2007), finding that approximately 5% of those hospitalized in the United States are uninsured, or considered “self-pay.” It appears that the general rate of insurance status in the United States is not the same as the rate among those who are hospitalized.

In both studies, a significant portion of the total costs, regardless of the time to the development of symptoms, was due to lost productivity. In either study, lost productivity was responsible for anywhere between 21% and 92% of the total cost of illness (Figure 6–Figure 9), depending on certain assumptions considered regarding the monetization of missed daily activities (TABLE XX). The high end of that range is consistent with findings from other studies on gastroenteritis that estimate that lost productivity contributes 73%–80% to the total COI (Hellard et al., 2003; Majowicz et al., 2006). In the current analysis, the proportion of the total costs due to lost productivity varied based on how lost productivity was calculated. The first assumption, which was applied to most scenarios in this analysis, was that every day missed was associated with costs, regardless of the age or working status of the individual. Several studies using a daily wage to estimate lost productivity either assume a specific rate of employment among the population (Hoffmann et al., 2012; Scharff, 2011), apply the daily wage to only members of the population between certain ages (Majowicz et al., 2006; Tariq et al., 2011), or assume a daily wage applies to all members in the study population regardless of workforce status (Corso et al., 2003; Dwight et al., 2005). Children 15 years and under make up approximately 12% of incidental-contact water recreators (CHEERS) and 37% of full-contact water recreators (NEEAR) and are typically not employed. However, several studies have indicated that sick children often require a caregiver to remain home from work, which results in lost productivity (Carabin et al., 1999; Hardy et al., 1994). In NEEAR, approximately 15% of children who developed GI illness within 0–3 days caused another person in the household to miss work due to their illness. However, no lost productivity would be expected for stay-at-home caregivers.

By assuming all days of missed activities are equivalent to the daily wage, both potential costs of missed work by caregivers and the monetary value that individuals may assign to their lost vacation or leisure time can be included. Another variation of lost productivity is to assume that costs of missed leisure time are valued as greater (1.5×) than the cost of a missed work day (Drummond et al., 1997). This assumption resulted in a large increase in the total costs for lost productivity and subsequently the total COI (Figure 6–Figure 9). Other studies of COI (Scharff, 2011; Scharff et al., 2009) have used an enhanced COI model that incorporated the costs of "pain and suffering" using the monetized QALY, which yielded much higher cost estimates than obtained from using the daily wage and the proportion of the population that works. However, placing greater emphasis on the costs of missed leisure time is not the same as using the monetized QALY approach. Furthermore, if people value their lost leisure time more than lost work time, this could be incorporating "pain and suffering" (using lost leisure time as a proxy) into the total cost estimate. Therefore, more time away from leisure could imply a greater amount of "pain and suffering," and using a 1.5× daily wage could be a reasonable assumption.

Another variation in lost productivity assumed that no costs were associated with missed leisure time and only missed work days contributed to lost productivity (Drummond et al., 1997). This assumption resulted in a large decrease in the total costs for lost productivity and thus the total cost of illness (Figure 6–Figure 9). The assumption that only time missed from work contributes to lost productivity is similar to assumptions used in several other COI studies (Hoffmann et al., 2012; Majowicz et al., 2006; Scharff, 2011; Scharff et al., 2009).

Lost productivity is an important component of the COI. However, more accurate information is needed on how individuals value their leisure time to properly assign monetary values to lost productivity (Dwight et al., 2005; Garthright et al., 1988). Additionally, estimates regarding the costs associated with missed vacation time would also provide a more complete picture of the COI. Since people tend to spend a lot of money on vacation, any vacation days missed due to illness, could greatly impact the COI (Dwight et al., 2005).

3.3.2 Cost of Illness Estimates

The mean and median COI for all participants in both studies was relatively similar when examining illnesses that developed within 0–12 days compared to those that developed within 0–3 days of recreation (TABLE XXI and TABLE XXII). However, the total cost for those developing illness within 0–12 days was larger than those developing illness within 0–3 days, due to more people meeting the case definition. Overall, time to illness (0–3 versus 0–12 days) influenced the estimates in CHEERS, but had very little effect on estimates in the NEEAR study.

Among CHEERS water recreators, there were no statistically significant differences observed between CAWS and GUW recreators regardless of the time to illness (0–3 versus 0–12 days). The CAWS was greatly impacted by non-disinfected secondary effluent, while GUW waters were significantly less impacted by fecal pollution. Despite the lack of a statistical difference in cost of illness among these two groups, there also was no observable increase in the odds of the occurrence of GI illness among CAWS recreators compared to GUW (Dorevitch et al., 2012a). However, it was observed that more GUW water recreators were more likely to report face or head immersion, compared to CAWS recreators (2.9% versus 0.4%, $p<.001$) (Dorevitch et al., 2012a). Thus, it is possible that the average dose of microbes (concentration of microbes × volume of recreational water swallowed) CAWS and GUW recreators were exposed to may be similar for the two groups, and why no differences in COI were observed.

The costs attributable to water recreation were similar for incidental-contact recreators at locations with relatively high-indicator bacteria concentrations and full-contact water recreators at inland and coastal beaches. The cost estimates ranged between $260.77 and $1,172.50 per 1,000 incidental-contact water recreators (CHEERS) and between $420.36 and $2,243.17 per 1,000 full-contact water recreators (NEEAR) developing symptoms within 0–3 days. However, in CHEERS, the time to illness had a considerable impact on the estimation of the costs attributable to water recreation. The observed RR for illness developing within 0–12 days was 0.92 (95% CI: 0.86, 1.12), but for illness that developed within 0–3 days was 1.29 (95% CI: 1.02, 1.64), implying that illness that developed 0–12 days following recreation was not attributable to water recreation, but illness that developed within the shorter time frame (0–3 days) may be more closely related to water recreation. Therefore, the costs attributable to water recreation using the 0–12 day time frame would be roughly equivalent to $0 but, when using the 0–3 day time frame, costs attributable to water recreation were similar to NEEAR estimates (TABLE XXV). Conversely, time to illness had very little impact on the costs attributable to water recreation in the NEEAR study. The observed RR for the relationship between water exposure and the development of GI symptoms for the 0–12 day time frame was 1.31 (95% CI: 1.18, 1.46), and for the 0–3 day time frame was 1.60 (95% CI: 1.35, 1.85). Studies have suggested that illnesses that develop within 0–3 days of water recreation are likely the most relevant to water exposure (Arnold et al., 2013; Dorevitch et al., 2012a).

The average COIs among water recreators reported in the current study are within the range of costs reported in other studies of GI illness (TABLE XXVI). Several COI studies have focused on foodborne illness, while others have estimated community or endemic gastroenteritis. A study of the COI among water recreators conducted by Dwight et al. (2005), based on epidemiologic data on sporadic recreational waterborne illness (Fleisher et al., 1998) assumed all missed activities, including lost leisure time, were equivalent to the daily wage. However, Dwight et al. (2005) reported a much lower proportion of water recreators with GI illness who miss work or daily activities (14.7%) compared to CHEERS (43.0%) and NEEAR (42.7%). When using the same assumptions as Dwight et al. (2005) (all missed daily activities are associated with cost equivalent to the daily wage), the mean COI in the current analysis was much higher ($145 to $229) than what was observed by Dwight et al. (2005) ($43). However, when assuming only missed days of work contributed to lost productivity, the mean estimate in the current analysis is closer to what was observed by Dwight et al. (2005) ($43 to $124).

TABLE XXVI
REPORTED COSTS PER CASE OF GI AND OTHER RELATED ILLNESS (2007 DOLLARS)

Type of Case	Cost details	Cost in original report	Cost in 2007 US Dollars [a]	Reference
GI, swimming	current study, 0–12 day		$145.87 [b]	--
GI, swimming	current study, 0–3 day		$163.50 [b]	--
GI, incidental contact	current study, 0–12 day		$229.22 [b]	--
GI, incidental contact	current study, 0–3 day		$145.76 [b]	--
GI, recreational water exposure		$36.58	$42.83	(Dwight et al., 2005) (2001 dollars)
GI, *Cryptosporidium* drinking water exposure	Mild illness	$116.00	$166.45	(Corso et al., 2003) (1993 dollars)
	Moderate illness	$475.00	$681.57	
	Severe Illness	$7,808.00	$11,203.64	
Community GI		A$18.08	$17.73	(Hellard et al., 2003)
Intestinal Infectious Disease	No physician consult	$215.00	$414.30	(Garthright et al., 1988) (1985 dollars)
	Physician consult	$348.00	$670.59	
	Hospitalization	$3,038.00	$5,854.14	
Community GI		Can$1,089.00	$1,057.77	(Majowicz et al., 2006)
GI, foodborne		NZ$462.00	$317.85	(Scott et al., 2000)
GI, foodborne	Basic model assumptions [c]	$1,068.00	$1,032.18	(Scharff, 2011) (2009 dollars)
	Enhanced model [d]	$1,626.00	$1,571.47	
GI, STEC [e]	GI only	€126.00	$179.08	(Tariq et al., 2011)
	HUS [f]	€25,713.00	$36,545.08	
	ESRD [g] (discounted)	€1,223,998.00	$1,739,629.95	

[a] Published costs per case in foreign currency were converted to US dollars. All studies were adjusted to 2007 dollar values
[b] Among water recreators, assuming moderate assumptions (Version 1 (CHEERS) or Version 1a (NEEAR)) see TABLE XX
[c] Assume lost productivity calculated using the daily wage among the proportion that work
[d] Monetized QALY, instead of daily wage
[e] STEC: Shiga toxin-producing *E. coli*
[f] HUS: Hemolytic uremic syndrome
[g] ESRD: End-stage renal disease

3.3.3 Study Strengths and Limitations

This study had several strengths. Both CHEERS and the NEEAR study were prospective epidemiological studies that evaluated the development of illness following water recreation, thus supporting the requirement for temporality of the relationship between GI illness and water exposure. Additionally, both studies collected data regarding the utilization of healthcare services and lost productivity, all of which were incorporated into the estimated total COI of GI illness. Other studies that have evaluated the total COI excluded certain cost estimates that were not available at the time of the analysis, such as costs associated with medications (Dwight et al., 2005; Garthright et al., 1988; Hoffmann et al., 2012), and ED visits or hospitalizations (Dwight et al., 2005). The current analysis used as much individual-level data as possible. Medication costs were self-reported in the NEEAR study and were applied to both epidemiological studies. For the costs of medications, other studies have used estimates from either drug indices (Majowicz et al., 2006) or from national surveys (Frenzen et al., 2005). Application of these indices or surveys to COI estimates requires knowledge about specific medications taken, the amount of medicine taken, and other factors such as insurance status (Majowicz et al., 2006), that may greatly impact the costs. The use of self-reported medication costs required no assumptions regarding frequency or type of medication. Geo-specific cost estimates for contact with an HCP and ED visits were obtained based on estimates from the US population for insurance status and patient type. Additionally, geo-specific costs from a wide range of tests and procedures likely to occur in the ED for patients with GI illness were factored in to the total COI. Lastly, the level of detail available for each cost estimate allowed for a several versions of the COI to be calculated, resulting in a range of potential COI, rather than a single point estimate.

The current study also had several limitations. First, these two large cohort studies were not designed for the purpose of evaluating the economic burden. While severity information was collected from study participants, crucial cost-related information, such as insurance status, patient type, or actual costs spent on illness (other than medications) were not collected in either study. Therefore, several different assumptions regarding costs needed to be estimated. Additionally, the burden within these two cohorts was assessed side-by-side, and often required further incorporation of additional assumptions to thus make the COI estimates comparable between the two studies. The addition of these assumptions could have subsequently either under or overestimated costs of illness.

It was assumed that for purposes of estimating HCP costs, the distribution of participant insurance status (insured versus uninsured) and patient type (new versus established) were the same as those in national datasets, since information regarding insurance status and patient type were unknown in either study. Insurance rates were estimated based on age. However, age is not the only contributor to whether or not an individual is insured or not. Other factors, such as location of residence, income, and race may also influence whether or not a person is insured (DeNavas et al., 2006). Only factoring age into insurance status may have inaccurately described insurance status among NEEAR and CHEERS participants. Additionally, it can be inferred that those with insurance may pay considerably less than what is estimated throughout this analysis. Many people with insurance coverage often pay a copay for medical services or prescription medication. Since insurance status was not available, the costs incurred by the individual due to illness may be overestimated for those with insurance.

Additionally, in CHEERS, among participants with symptoms referable to multiple organ systems during the same period, it was unclear which responses to illness were specifically due to GI illness. It was also unclear which CHEERS participants visited or only spoke to an HCP over the phone, while in the NEEAR study these were noted separately by participants. In some versions of the COI I applied the distribution of office visits versus phone calls observed in the NEEAR study to CHEERS, making the assumption that the ratio of those visiting versus calling an HCP is consistent across studies. It is unclear if it was suitable to assume a similar proportion of participants visiting versus calling an HCP in CHEERS compared to NEEAR. It is possible that CHEERS costs associated with an HCP are either over- or underestimated when applying information collected from NEEAR. Additionally, all CHEERS COI models that do not differentiate callers from visits, may overestimate costs associated with contact with an HCP. In addition, the use of symptom-complex aggregated using NEEAR data may have overestimated medication costs, since costs calculated according to symptom-complex were generally greater than what was strictly self-reported in the NEEAR study. I also assumed that the proportion of those that miss work compared to daily activities was equivalent in both studies.

To calculate costs associated with lost productivity the per capita income rate for males and females was utilized. Per capita income is the average income by males and females in the past 12 months, divided by the total population of males and females over the age of 15 respectively in that geographic area (US Census, 2011b). The use of per capita income may have potentially underestimated costs, since it can be postulated that outdoor water recreators may have more money to spend on leisure, and thus their daily wage or income may not be adequately reflected using per capita income.

In the current analysis, ED costs were estimated based on geo-zip and included professional fees for ED visits and costs for specific tests and procedures thought to be administered in the ED. The average cost of an insured and uninsured ED visit was $227.96 and $759.90 respectively. However, the estimated cost of an ED visit for ICD-9-CM 009-009.3 and 008.8 in 2007 according to the Nationwide Emergency Department Sample (NEDS), H-CUP, AHRQ (HCUP Nationwide Emergency Department Sample, 2007), was $791.41. The cost estimate calculated using the NEDS was adjusted for the CCR (Freidman and Owens, 2007) and accounted for physician fees (PMIC, 2007). This ED cost estimate represents an average cost from all payers (insured, uninsured, Medicare) and is nationally representative. The costs in the current analysis for ED visits are generally lower than those obtained from the NEDS, since only physician fees and procedure costs were considered. Therefore, it is possible that ED costs are underestimated in the current analysis. However, there were only a combined 27 or 15 ED visits among all NEEAR and CHEERS water recreators with illness within 0–12 days and 0–3 days respectively. Therefore, the potential impact of ED visits on total costs among water recreators may be negligible.

The calculated costs in this analysis were expected to reflect the costs to the individual. However, a more complete cost analysis could have incorporated costs related to insurance claims processing, among others. The current analysis generally utilized the human capital method of valuing individual costs, which counts costs incurred to the sick individual, thus counting days not worked as days lost. Alternatively, the friction cost method could have been applied, which takes the “employer’s perspective” and considers costs of missed work until another employee takes over the work of the ill individual (Van den Hout, 2010). Additionally, a more complete estimate of costs would have also incorporated costs estimated to be associated with unpaid work, including household work, caregiving, or volunteering. Valuing unpaid work is becoming more prominent in several economic analyses (Krol et al., 2013).

It is also important to consider that the CHEERS and NEEAR cohort studies explored recreational water heavily impacted by wastewater effluent. Certain sites within CHEERS were known to contain high levels of fecal indicator organisms. The current analysis assesses costs within the context of these two studies, or the costs associated with water recreation in effluent-dominated inland and coastal waters. Therefore, these cost estimates may not be generalizable to all types of water recreation, especially recreation in pristine waters not impacted by effluent.

Lastly, a weighted average was used to estimate costs of visiting an HCP, visits to an ED, and hospitalizations, which introduced no variability in a single estimate of total COI for a set of assumptions. This lack of variability in a single estimate was to some degree mitigated by incorporating several different sets of assumptions with to create a range of total costs of GI illness within the two studies.

3.4 Conclusions

It was estimated that the costs of sporadic GI illness attributable to water recreation within the context of these two cohort studies to be in the range of $500 to $2,000 per 1,000 people who engage in swimming, fishing, boating, kayaking, canoeing, and rowing in water impacted by fecal pollution. The economic burden attributable to water recreation is similar among incidental- and full-contact water recreators in the settings evaluated in two studies that used very similar methods. This study adds to the literature of costs attributable to water recreation and the cost per case of GI illness among water recreators. The prior estimate for cost per case of GI illness among water recreators was based on a much smaller dataset (Dwight et al., 2005) and was lower than the estimates that were obtained from larger and more comprehensive datasets.

An assessment of the COI per 1,000 water recreators provides relevant information concerning the burden of recreational waterborne illness at certain water recreation locations. The costs per 1,000 water recreators could be reduced if illness becomes less frequent or is less severe and thus requires less use of the healthcare system. This burden estimate can potentially be used to prioritize beach cleanup efforts, since the COI per 1,000 recreators incorporates both the frequency and severity of illness. Therefore, the reduction in the overall burden of recreational waterborne illness can be maximized by prioritizing beaches with high burden, which are heavily used, where illness is either common and/or frequently severe. Given the hundreds of millions of water recreation events that take place per year in the United States

(Cordell, 2012), and the costs of sporadic illness that exceed $500 per 1,000 recreators, the COIs attributable to water recreation in waters with high levels of fecal contamination, are likely run in the hundreds of millions to billions of dollars each year.

4. ECONOMIC BURDEN OF SURFACE WATER RECREATIONAL WATERBORNE ILLNESS IN THE UNITED STATES

Surface water recreation waterbodies such as lakes, ponds, and the ocean is popular in the United States. According to the National Survey on Recreation and Environment (NSRE), it is estimated that more than 61% of the US population over the age of 16, equivalent to approximately 143 million people in 2008, engage in certain recreational surface water activities such as swimming in lakes, streams, or the ocean, kayaking, canoeing, and other nonmotorized water sports (Cordell, 2012).

Several health risks are associated with surface water recreation. Numerous epidemiologic studies have found an increased incidence fraction of GI illness, as well as non-enteric illnesses, including respiratory, ear, eye, and skin symptoms among water recreators (Colford et al., 2007; Dorevitch et al., 2012a; Wade et al., 2008; Wade et al., 2006). In addition to sporadic illness, outbreaks among surface-water recreators are documented each year. According to the waterborne disease and outbreak surveillance system (WBDOSS), from 2000 to 2010 there have been 102 outbreaks associated with untreated recreational water, including lakes and oceans, corresponding to more than 1,559 cases of illness. However, the outbreak cases described in WBDOSS are thought to represent only a fraction of the illnesses that are associated with recreational water exposure. Estimates of the number of WBDOs not detected by surveillance are unknown because WBDOSS is a passive surveillance system that relies upon state and local health departments to submit information about any WBDOs that they may have become aware of and investigated (Dziuban et al., 2006; Hlavsa et al., 2011; Hlavsa et al., 2014; Yoder et al., 2004; Yoder et al., 2008).

Limited assessments of the economic burden due to illnesses resulting from water recreation have been published in recent years. The local economic burden of sporadic recreational waterborne illness at two beaches in California was estimated to be $3.3 million in 2001 dollars (Dwight et al., 2005). However, the authors did not include several important components of the economic burden, including costs associated with hospital admission, ED visits, and medication use. The US national economic burden of hospitalization for diseases that are transmitted primarily by water (giardiasis, cryptosporidiosis, Legionnaires' disease, otitis externa, and non-tuberculosis mycobacterium) has been estimated at $970 million, while the burden of diseases only considered to be partially transmitted by water (campylobacteriosis, salmonellosis, shigellosis, hemolytic uremic syndrome, and toxoplasmosis) has been estimated at $860 million in 2007 dollars (Collier et al., 2012). These hospitalizations were thought to include all types of water exposures, including drinking water, treated recreational water (swimming pools, spas), as well as untreated recreational surface water. Collier and colleagues did not include other components of cost, such as lost productivity, in their estimate. Information was not available about any potential water exposures of individuals who were ill. Instead, the authors tried to estimate the percent of cases that may have been waterborne based on pathogens found to be responsible for illness.

A more precise estimate of the national economic burden due to surface-water recreation may help make waterborne disease prevention a priority (Collier et al., 2012). The primary objective of this work was to estimate the economic cost of surface-water recreation at a national level. To accomplish this, data from two epidemiological studies of water recreation, combined with outbreak and surveillance data, and nationally representative data on direct (medical) and indirect (lost productivity) costs of illness were utilized to determine an estimate the total costs associated with recreational waterborne illness due to surface-water exposure in the United States.

4.1 Methods

Previous estimates of the economic burden of foodborne illness (Hoffmann et al., 2012; Scharff, 2011; Scharff et al., 2009) and community gastroenteritis (Majowicz et al., 2006) were used as a template for estimating the economic burden of recreational waterborne illness. These previous burden estimates were able to utilize available data either through surveillance (Hoffmann et al., 2012; Scharff, 2011; Scharff et al., 2009) or surveys (Majowicz et al., 2006). For example, the Foodborne Diseases Active Surveillance Network (FoodNet), along with other surveillance systems, has been used to identify the number of cases of foodborne illness due to known and unknown pathogens (Scallan et al., 2011b; Scallan et al., 2011a). These surveillance systems have been utilized in calculating the total economic burden due to foodborne illness in the United States (Scharff, 2011).

Currently, no active surveillance systems identify cases of waterborne illness. Therefore, several data sources were used to estimate the number of cases of recreational waterborne illness. Data from two prospective cohort studies on water recreation were utilized. The NEEAR study evaluated the occurrence of illness among swimmers at several sites in the United States impacted by fecal pollution (Wade et al., 2008; Wade et al., 2006; Wade et al., 2010a). The CHEERS measured the occurrence of illness among water recreators participating in incidental-contact recreation (kayaking, canoeing, rowing, motor boating, and fishing) in an urban setting in the Chicago, Illinois area. Some sites in CHEERS were significantly impacted by wastewater (Dorevitch et al., 2012a). In addition, the estimated total number of water recreators in the

United States was obtained from the NSRE (Cordell, 2012) and outbreak data were obtained from WBDOSS.

Sporadic cases of illness that develop among water recreators in epidemiologic studies are generally mild to moderate in severity (Dorevitch et al., 2012a; Fleisher et al., 1998; Wade et al., 2013), and specific pathogens responsible for waterborne illnesses have not been identified in stool samples of symptomatic study participants (Dorevitch et al., 2012b; Jones et al., 1991). However, over the past thirty years, WBDOSS has consistently identified pathogen-specific and nonpathogen-specific hospitalizations in US outbreaks due to untreated surface-water recreation.

To be defined as a WBDO in WBDOSS, two or more people must have had exposure to the same recreational water, and there must be sufficient epidemiological evidence to suggest recreational-water exposure is the probable cause of the illness (Dziuban et al., 2006; Hlavsa et al., 2011; Hlavsa et al., 2014; Yoder et al., 2004; Yoder et al., 2008). Prior to 2007, single cases of primary amoebic meningoencephalitis (PAM) caused by *Naegleria fowleri*, thermophilic free-living amoeba found in freshwater (Yoder et al., 2010; Yoder et al., 2008) or *Vibrio* spp. were considered "outbreaks" in WBDOSS. Symptoms of PAM are similar to bacterial or viral meningitis, with death occurring approximately 3–7 days following the start of symptoms in more than 99% of those infected (Yoder et al., 2010). *Vibrio* spp. are responsible for vibriosis, which is caused by pathogenic species of the family *Vibrionacaea*, particularly *Vibrio alginolyticus, Vibrio parahaemolyticus,* and *Vibrio vulnificus* (Dziuban et al., 2006; Hlavsa et al., 2011; Yoder et al., 2008). The majority of recreational waterborne illnesses caused by *Vibrio* spp. occur through preexisting wounds exposed to contaminated marine water (Dechet et al., 2008; Morris and Acheson, 2003). Infections can lead to septicemia, which may lead to amputation or death (Dziuban et al., 2006; Hlavsa et al., 2011; Yoder et al., 2008). The Cholera and Other *Vibrio* Illness Surveillance (COVIS) system uses passive surveillance to identify cases of vibriosis in the United States (CDC, 2012). Cases of vibriosis suspected to be due to recreational-water exposure identified in COVIS, are reported in WBDOSS. From 2003 to 2008, approximately 565 cases of vibriosis due to exposure to marine recreational water were identified, resulting in 232 hospitalizations and 36 deaths (Dziuban et al., 2006; Hlavsa et al., 2011; Yoder et al., 2008).

Previous estimates of the burden of foodborne illness have created three mutually exclusive ordinal categories of symptom severity: mild (does not seek care from an HCP), moderate (seeking care from an HCP), and severe (requiring hospitalization), since economic burden varies according to severity (Hoffmann et al., 2012). The logic used to determine the number of mild, moderate, and severe illnesses due to water recreation and their associated costs is shown in Figure 10. This national estimate is for 2007, a year in which both epidemiologic studies occurred. An estimate of the number of individuals in the United States who water recreate was determined based on the US population in 2007 (US Census, 2009) and the reported proportion of the US population that participates in water recreation each year (Cordell, 2012). The mean frequency in which each individual in the United States engages in certain water-recreation activities (Cordell, 2012) was obtained to estimate the total number of water-recreation events that occur annually. Next, data from two prospective cohorts on water recreation were used to estimate the total projected number of mild and moderate recreational waterborne illnesses. Data from WBDOSS (Dziuban et al., 2006; Hlavsa et al., 2011; Hlavsa et al., 2014; Yoder et al., 2004; Yoder et al., 2008) and other sources (Dechet et al., 2008; Goarant et al., 2009; Mead et al., 1999; Pond, 2005; Scallan et al., 2011a; Yoder et al., 2010) were used to estimate the annual number of severe illnesses (hospitalizations) due to recreational waterborne illness. Nonhospitalized cases of illness from WBDOSS were not included in the current analysis, so as to not over-count the number of mild and moderate cases of recreational waterborne illness. Nationally, representative costs associated with mild, moderate, and severe illnesses were applied to determine a national estimate of economic burden. All methods to calculate and evaluate the national estimate of recreational waterborne illness were performed using SAS version 9.3 (SAS Institute Inc., Cary, North Carolina), Stata 11 (StataCorp LP., College Station, Texas), and Crystal Ball ® version 11.1.

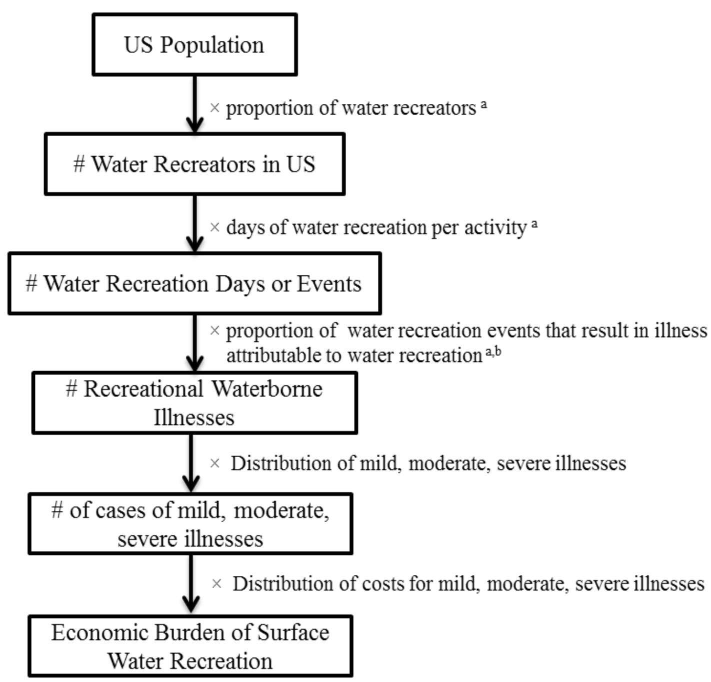

Figure 10. Determination of the number of mild and moderate cases and total economic burden due to recreational waterborne illness.
[a] Varies according of water recreation activity (swimming, kayaking, canoeing, rowing, motor boating, fishing)
[b] Illness specific (GI, respiratory, ear, eye, skin)

4.1.1 Estimated Number of Mild and Moderate Illnesses

The number of people who water recreate in the United States was estimated the NSRE, an ongoing random-digit dialed household survey that has been used to estimate more than 80 different outdoor recreation activities in the US noninstitutionalized population aged 16 and over. The NSRE data are weighted to represent the US population and evaluate several surface-water activities, including swimming, kayaking canoeing, rowing, motor boating, and fishing (Cordell, 2012). The average annual percentage of the US population from 2005 to 2008 engaged in these activities reported by NSRE was applied to the noninstitutionalized US population 16 and over in 2007 equal to 233.5 million persons (US Census, 2009) to determine the total number of people, aged 16 and over who participate annually in each activity in the United States. The NSRE does not capture the number of children aged 15 and under participating in each activity. Instead, the proportion of participants in the NEEAR and CHEERS studies aged 15 and under participating in each activity was identified, and multiplied by the NSRE-based number of adults 16 and older who participate in each activity in the United States to determine the total number of children 15 and under in the United States who participate in each activity. Subsequently, the percentage of children in the US population who engage in each water recreation activity, was also estimated based on this calculation and the total number of children 15 and under in the United States (63.3 million) (US Census, 2009).

The average number of days in which a person engages in a particular water activity reported in NSRE (Cordell, 2012) was applied to the estimated number of water recreators engaged in that activity to determine the total number of person-days per activity. Other information, such as the median number of days, was not available for the activities of interest. The NSRE did not contain a direct measurement of the mean number of days each angler spends fishing. Therefore, the mean number of days of general fishing was calculated from four different types of fishing (saltwater, warm-water, cold-water, and anadromous fishing) reported in NSRE (Cordell, 2012). A combination of the estimated total number of water recreators (composed of children and adults in the United States), multiplied by the mean number of days a person engages in each type of water-recreation activity yielded the estimated total number of water-recreation events occurring on untreated surface water that occurred in the United States in 2007.

Epidemiological data from CHEERS and NEEAR were applied to the total number of untreated surface-water recreation events to approximate the number of sporadic illnesses attributable to water recreation. The CHEERS study design used the NEEAR protocol as a template. Recreators from both studies were contacted by telephone to identify symptoms that developed since the time of recreation. Symptom-based case definitions for illness (GI, respiratory, eye, ear, skin) were similar in both studies (TABLE I). Recreators in the NEEAR study participated in a single telephone follow-up interview 10–12 days following their initial water-recreational event (Wade et al., 2008; Wade et al., 2010a), while CHEERS participants were contacted via telephone 2, 5, and 21 days following recreation (Dorevitch et al., 2012a). Questionnaire design and water sampling methodology for NEEAR (Wade et al., 2008; Wade et al., 2010a) and CHEERS (Dorevitch et al., 2012a) have been described previously (Appendix A: Section A). Since CHEERS had a longer follow-up, symptoms that developed among CHEERS participants 12 or more days following recreation were excluded to match the NEEAR study definition of illness. Previous analyses have found that GI illness that develops within 0–3 days of recreation is likely to be more closely related to water recreation (Arnold et al., 2013; Dorevitch et al., 2012a). Therefore, subsequent analyses assess GI illness developing within 0–3 days, and all other illnesses (respiratory, eye, ear, and skin symptoms) developing within 0–12 days.

The AR, also known as the RD, is the probability of illness in the exposed minus the probability of illness in a group of people who are demographically comparable but unexposed (Rothman et al., 2008). The AR for the relationship between water exposure and the subsequent development of illness was calculated using logistic regression. The margins command in Stata was used to create ARs from the logistic model and relied on 1,000 iterations of the bootstrap to determine CIs. The ARs were estimated for each health endpoint (GI, respiratory, eye, ear, and skin) and each type of water-recreation activity (swimming, kayaking, canoeing, rowing, motor boating, and fishing). The ARs were each applied to the total number of estimated water-recreation events by activity to determine the total number of individual sporadic illnesses attributable to each type of water-recreation activity.

The NEEAR study was used to assess the relationship between swimming (any beach-water contact) and the development of illness compared to the unexposed group of beachgoers with no water contact. Logistic models included all identified potential covariates that were assumed to be relevant to the relationship between water exposure and the occurrence of illness. All logistic models using the NEEAR data controlled for age, gender, any contact with animals, frequency of water use, digging in sand, and eating eggs, fish, or raw meat. Additionally, logistic models for the occurrence of GI illness also controlled for a chronic GI condition and previous contact with someone with GI illness; models assessing the occurrence of ear symptoms also controlled for the wearing of ear plugs; models of respiratory symptoms also controlled for asthma; and models assessing the occurrence of skin symptoms additionally controlled for sunburn and the presence of any chronic skin condition. In the NEEAR study, household was an important clustering variable that impacted the association between exposure and the occurrence of illness. Therefore, robust estimates of variance were utilized to account for household cluster, while beach location was controlled for as a fixed effect to control for any differences between beaches. The ARs for swimming were calculated based on the logistic models for all water types and the interaction between water exposure and water type (marine versus fresh) was examined to determine if there are differences in risk based on the type of water exposure.

Similarly, CHEERS was used to assess the relationship between incidental-contact recreation and the development of illness compared to an unexposed group of outdoor recreators. The CHEERS data were used to estimate the individual associations between kayaking, canoeing, rowing, motor boating, and fishing compared to the unexposed group for each health end point. All logistic models using CHEERS data controlled for age; gender; any contact with animals; frequency of water use; having diabetes; being prone to infection; washing hands prior to eating or drinking; and eating eggs, fish, raw meat, hamburger, prepackaged sandwiches, or fresh produce. The models assessing the occurrence of GI illness also included covariates such as the average number of daily bowel movements at baseline, presence of a preexisting GI condition and previous contact with someone with GI symptoms. Additionally, models assessing respiratory illness also controlled for the presence of a preexisting respiratory condition and recent contact with someone with a respiratory condition, while models assessing occurrence of eye illness controlled for previous contact with someone who has eye symptoms, and models assessing the occurrence of skin illness controlled for the presence of bug bites or sunburn. Similar ARs were observed for all incidental-contact activities in CHEERS, except the observed AR for GI illness was higher among those who fish compared to people who engaged in other incidental-contact activities. This may be due to the fact that anglers are exposed to microbes from multiple sources, including bait and fish they handle, which may result in an increased risk of developing GI illness (Roberts et al., 2007). Excess respiratory, ear, and eye illnesses were not expected among anglers, since their head or face has no contact with the water. The ARs were subsequently estimated for the incidental-contact group that excluded people who fish, compared to the unexposed group, and separate ARs were calculated for people who fish, also compared to the unexposed group.

Evidence from the literature suggests that individuals who recreate frequently (>7 times per year) have a reduced rate of illness due to exposure to recreational surface water, compared to those who recreate less frequently (Lee et al., 1997). This could be due to possible increased immunity due to multiple exposures to recreational water, or that those with recurrent exposures are in general "healthier" compared to those with less-frequent exposure to recreational water. In CHEERS, approximately 15% of water recreators recreated ten or more times each year, which is similar to estimates from NSRE, which indicates that 12%–17% engage in fishing, kayaking, rowing, and canoeing ten or more times per year (Cordell, 2004). In NEEAR, approximately 15% of swimmers indicated participation in swimming ten or more times per year, while according to NSRE, close to 30% of swimmers indicate swimming more than ten times per year (Cordell, 2004). Therefore, the interaction between those recreating either ten or more times per year or less than ten times per year and water exposure was examined, to determine if any differences in risk were present due to the frequency of water recreation among those in the NEEAR study.

The epidemiologic studies included measures of severity: OTC medication use, prescription medication use, contact with an HCP, visits to an ED, hospitalizations, and missed days of work or activities. In the NEEAR study, measures of severity, or responses to illness, were evaluated individually for each type of symptom (GI, respiratory, ear, eye, and skin). In contrast, participants in CHEERS were asked about responses to illness without differentiating which symptom prompted each response among those with more than one type of symptom (Appendix C: Table LXVII). As a result, the proportions of ill water recreators who respond to their individual symptoms may be overestimated since the response cannot be related to a specific symptom when a recreator had more than one category of symptoms. The participants in the CHEERS and NEEAR study were assumed to be samples from a single distribution of illness severity, which is consistent with the similar rates of responses in both studies (TABLE III; TABLE XIX). This assumption allows the proportion of mild and moderate sporadic illnesses identified for each water recreation activity to be estimated using NEEAR data, for which participants responses to specific illness symptoms are known. To determine the number of moderate cases of illness, the symptom-specific proportions of those that contacted an HCP or went to an ED observed in NEEAR were applied to the estimated number of cases of illness (GI, respiratory, ear, eye, and skin). This approach was also used to estimate the number of mild cases of recreational waterborne illness in the United States.

4.1.2 Estimated Number of Severe Illness Cases

To estimate the number of severe illnesses due to water recreation, outbreak cases of illness, and other non-outbreak illnesses (PAM and *Vibrio* spp. illnesses) reported in WBDOSS were used. Outbreak data summaries have been released by WBDOSS for two-year periods since 1978 (Hlavsa et al., 2011). Outbreak data from 2001 to 2010 were used to estimate the average annual number of recreational waterborne outbreaks that occur in untreated waters (lakes, ponds, ocean). This ten-year time period was chosen since it overlapped with the study periods of CHEERS and NEEAR. Recognized WBDOs in untreated recreational water are relatively uncommon. On average, only a few dozen outbreaks involving a few hundred cases are identified each year. Outbreaks are typically pathogen-specific, and certain pathogens may be responsible for several outbreaks in one year, but none in another year (Dziuban et al., 2006; Hlavsa et al., 2011; Hlavsa et al., 2014; Yoder et al., 2004; Yoder et al., 2008). A ten-year average of outbreak associated cases was calculated for each pathogen, and for severe GI illness not found to be associated with a pathogen. Illnesses due to *Vibrio* spp. became nationally notifiable in 2011, but almost 100% of states have been voluntarily reporting *Vibrio* spp. illnesses since the early 2000s (CDC, 2012). Complete data for *Vibrio* illnesses related to recreational-water exposure were available through WBDOSS from 2003 to 2008 (Dziuban et al., 2006; Hlavsa et al., 2011; Yoder et al., 2008). Cases of PAM are rare and it has been estimated that on average there are 0–8 cases diagnosed each year (Yoder et al., 2010).

The number of cases identified in reported outbreaks represent an unknown fraction of total number of cases of illness that occur as a result of water recreation and it is unclear how many WBDOs occur that are not captured by WBDOSS (Dziuban et al., 2006; Hlavsa et al., 2011; Hlavsa et al., 2014; Yoder et al., 2004; Yoder et al., 2008). Previous analyses by Scallan et al (2011) have estimated the projected number of laboratory-confirmed foodborne illnesses from food-related outbreak data by applying an underreporting multiplier. These underreporting multipliers were derived by calculating several pathogen-specific ratios of the number of laboratory-confirmed cases identified through active surveillance to cases identified through outbreak surveillance (Scallan et al., 2011a). Based on this approach, Scallan et al (2011) used 25.5 as a multiplier to account for underreporting in outbreaks. For every case of illness identified during an outbreak, 25.5 other cases were estimated not reported or captured by the outbreak surveillance system. This multiplier of 25.5 was applied to the annual number of outbreak cases in the current analysis of recreational waterborne illness. The surveillance system for identifying single cases of vibriosis, COVIS, relies on passive surveillance. An underreporting multiplier of 1.1, also derived by Scallan et al. (2011) using pathogen-specific ratios of the number of laboratory-confirmed cases to the number of cases identified via passive surveillance, was applied to estimate the projected number of cases of vibriosis that are estimated from passive surveillance. Currently, there are no active surveillance systems in place to identify cases of recreational waterborne illnesses. Therefore, it is not possible to create underreporting multipliers similar to the methods presented by Scallan et al. (2011). The use of these foodborne pathogen-specific multipliers was utilized to help estimate the potential number of cases of severe illness due to exposure to recreational water, since it has been suggested that the current outbreak surveillance may not be capturing all potential cases (Yoder et al., 2008). It was assumed that all cases of PAM due to *N. fowleri* would be identified since the illness is rare and associated with high case-fatality rate, especially among children (Yoder et al., 2010).

Hospitalization defined severe illness in the current analysis. However, specific hospital and mortality information are often not available in WBDOSS summaries. The WBDOSS reports the total number of hospitalizations and deaths in some years, but until recently did not differentiate the number of hospitalizations or deaths among recreators at untreated versus treated recreational water (Dziuban et al., 2006; Hlavsa et al., 2011; Yoder et al., 2004; Yoder et al., 2008). Additionally, WBDOSS has not always specified the number hospitalized due infections caused by specific pathogens (Hlavsa et al., 2014). Therefore, in order to estimate the number of hospitalizations and deaths due to each pathogen; pathogen-specific hospitalization and death rates among laboratory-confirmed illnesses were applied (Dechet et al., 2008; Dziuban et al., 2006; Goarant et al., 2009; Hlavsa et al., 2011; Hlavsa et al., 2014; Mead et al., 1999;

Pond, 2005; Scallan et al., 2011a; Yoder et al., 2010; Yoder et al., 2008). Based on assumptions from FoodNet researchers, it is expected that not all illnesses resulting in hospitalization are necessarily reported or diagnosed (Mead et al., 1999; Scallan et al., 2011a). The doubling of hospitalizations and deaths is common practice in determining the number of illnesses due to foodborne exposures (Mead et al., 1999; Scallan et al., 2011a). Therefore, the number of hospitalizations and deaths due to illness were doubled in the current analysis to attempt to account for underdiagnosis and underreporting (Mead et al., 1999; Scallan et al., 2011a). Hospitalizations and deaths due to infections caused by *N. fowleri* were not doubled, since it was expected that all cases are identified each year due to the high morbidity and mortality of the condition.

4.1.3 Costs of Illness

Health-related costs among the projected number of ill water recreators were summarized for mild, moderate, and severe waterborne illnesses using methods common in studies estimating total economic burden of ill health (Hoffmann et al., 2012; Majowicz et al., 2006; Scharff, 2011). The total costs associated with each outcome (i={mild, moderate, severe}) were estimated according to *Equation VII*, using the total cost of OTC medications (OTC_i), prescription medications (Rx_i), visits to an HCP (HCP_i), ED visits (ED_i), hospitalizations ($Hospital_i$), and sequelae ($Sequelae_i$) that develop as a result of illness. Additionally, total costs included indirect costs resulting from missing time from work ($Productivity_i$), as well as costs associated with mortality (VSL_i) due to illness. All costs were adjusted for inflation to 2007 dollars, using the appropriate consumer price index for medical care commodities (medications) and medical care services (medical and hospital services) (BLS, 2010).

Equation VII:

$$Cost_i = OTC_I + Rx_i + HCP_i + ED_i + Hospital_i + Sequelae_i + Productivity_i + VSL_i$$

4.1.3.1 Assumptions and Inputs for Calculating Total Costs of Mild Illness

The total cost of mild illness arose from medication use (OTC and prescriptions) and lost time away from work. (Appendix D: Table LXXXVI). In NEEAR, participants were asked about the amount of money they spent on OTC and prescription medications, for each individual illness (GI, respiratory, ear, eye, and skin). The cost of OTC or prescription medication use was estimated using the number of mild cases of illness multiplied by the proportion of mild cases in the NEEAR that took OTC or prescription medication multiplied by the self-reported medication costs. Lost productivity due to time missed from work for each illness (GI, respiratory, eye, ear, and skin) was calculated by multiplying the number of mild cases of illness by the proportion of mild cases that stayed home from work, the self-reported number of work days missed, and the daily wage. Daily wage ($119.33) was calculated by dividing the median earnings of the US part-time and full-time population in 2007 ($28,640) (US Census, 2007) by the estimated number of annual workdays (240) (Dwight et al., 2005).

4.1.3.2 Assumptions and Inputs for Calculating Total Costs of Moderate Illness

The cost of moderate illness arose from medication use (OTC and prescription), visits with a physician or HCP, ED visits, and time missed from work. Similar to mild illness, the number of moderate cases of illness was multiplied by the proportion of moderate cases that take medications in NEEAR, multiplied by the self-reported medication costs (Appendix D: TABLE LXXXVI). Lost productivity due to time missed from work, for all moderate illnesses was also estimated similarly to mild illness, by taking the product of the number of moderate cases of illness, the proportion of those with moderate illness that stay home from work in NEEAR, the number of work days missed, and the daily wage ($119.33).

The cost of visiting an HCP was determined by multiplying the number of moderate cases by the proportion of water recreators with moderate illness who visit an HCP by the costs of such a visit. Costs associated with these visits were estimated using the “Usual, Customary and Reasonable” (UCR) rates for specific CPT codes to estimate physicians fees associated with office visits (PMIC, 2007). Physician fees are based on the elements of the medical history taken at the time of visit, the type of examination, and the amount of medical decision-making necessary. The more complex the E/M service, the higher the level of coding and thus the higher the cost for the service (CMS, 2014). Fees for visits to an HCP were assumed to vary depending on the type of illness. Respiratory or GI illnesses were assumed to require level-three care, and eye, ear, or skin symptoms were assumed to only require level-two care (Appendix D: Table LXXX). Established patients, who regularly see their physician, are charged approximately half of what new patients are charged (PMIC, 2007). Approximately 17% of patients are considered new (Hing et al., 2010), which was taken into account when calculating total costs for physician office visits.

The cost of visiting an ED was determined by multiplying the number of moderate cases by the proportion of water recreators with moderate illness who visit an ED by the costs of such a visit. The ED charges were estimated using discharge data from the 2007 NEDS, H-CUP, AHRQ (HCUP Nationwide Emergency Department Sample, 2007). Charges for ED visits were estimated according to ICD-9-CM codes listed as the primary diagnosis (TABLE XXVII). Charges in the NEDS refer to the amount billed by the hospital, not the amount actually paid by the patient (Shwartz et al., 1995). Costs can be calculated by multiplying total charges by the

CCR. There were no CCRs available to convert charges in the NEDS into costs, however preliminary findings from the US AHRQ, have determined that a CCR of 0.46 may be a suitable multiplier to estimate ED costs (Freidman and Owens, 2007), which was applied in the current analysis. Costs of ED visits were calculated using appropriate weights to account for the sampling design (Houchens and Elixhauser, 2014) and included all payers (insured, uninsured). Physician fees were not included in the charges listed in the NEDS. Therefore, the UCR rates for ED specific E/M CPTs (Appendix D: Table LXXX) were applied, assuming that those that go to an ED with GI or respiratory illness would be charged for level-three care, while those with either eye, ear, or skin symptoms would be charged for level-two care.

TABLE XXVII

ICD-9-CM CODES TO DETERMINE ED AND HOSPITAL COSTS [a]

Symptom	ICD-9-CM	ICD-9-CM Description
GI	009	Infectious colitis, enteritis, and gastroenteritis
	008.8	Viral gastroenteritis
Ear	380.1	Acute otitis externa
	380.12	Acute swimmers' ear
	380.14	Malignant otitis externa
Eye	379.93	Redness or discharge of eye
	V74.4	Bacterial conjunctivitis
	372.0	Acute conjunctivitis
	372.00	Acute conjunctivitis, unspecified
Respiratory	465	Acute upper respiratory infections of multiple or unspecified sites
	465.8	Acute upper respiratory infections of other multiple sites
	465.9	Acute upper respiratory infections of unspecified site
	786.2	Cough
	460	Acute nasopharyngitis (common cold)
	462	Acute pharyngitis
Skin	782.1	Rash and other nonspecific skin eruption
	692.9	Dermatitis
Pathogens	004	Shigellosis
	007.1	Giardiasis
	007.4	Cryptosporidiosis
	008	Intestinal infection due to *E. coli*
	008.43	Campylobacter
	008.63	Norwalk virus
	100	Leptospirosis
	136.2 [b]	Specific infections by free-living amebae; Meningoencephalitis due to *Naegleria*

[a] *Vibrio* spp. cell sizes were too small (<10) to estimate costs from NEDS and NIS, used costs reported by EDS for *Vibrio*

[b] Not included in 2007 NEDS or NIS, Bacterial Meningitis (ICD-9-CM 320.0) used as a surrogate

4.1.3.3 Assumptions and Inputs for Calculating Total Costs of Severe Illness

The cost of severe illness arose from medication use (OTC and prescription), visits with an HCP, ED visits, hospitalizations, sequelae, lost productivity due to time missed from work, and mortality. The number of severe cases who take OTC medication was estimated based on the product of the number of severe illnesses, the proportion of moderate cases with GI illness in the NEEAR study who take OTC medication, and the corresponding self-reported cost of OTC medication (Appendix D: Table LXXXVI). No other information was available regarding OTC medication use and costs for those with severe illness. It was assumed that all cases of severe illness take prescription medication at an estimated cost of $44.67 in 2007 dollars (Frenzen, 2007; Scharff, 2011) for all outcomes.

It was estimated that for every case of severe illness there are 0.7 doctor visits prior to hospitalization, and 1 doctor visit following hospitalization (ERS, 2014). The CPTs for a level-four office visit (Appendix D: Table LXXX) were used to estimate costs of office visits for severe illnesses, taking into account the cost differences observed between new and established patients (PMIC, 2007). It was also assumed that there were 0.3 ED visits per severe case (ERS, 2014). The ED costs were estimated using the NEDS according to the primary diagnosis ICD-9-CM code (TABLE XXVII), the estimated CCR to convert charges into costs (Freidman and Owens, 2007), and the appropriate ED physician fees for E/M level-four care (Appendix D: Table LXXX). Costs for outbreak cases of GI illness of unknown etiology, were estimated using the nonspecific GI ICD-9-CM codes (009-008.8). Hospital charges were estimated using discharge data from the 2007 NIS, H-CUP, AHRQ (HCUP Nationwide Inpatient Sample, 2007). Hospital-specific CCRs (HCUP Cost-to-Charge Ratio Files, 2007) were applied to total hospital charges to estimate hospital costs according to ICD-9-CM code (TABLE XXVII). Costs from

NEDS and NIS were calculated using appropriate weights to account for the sampling design in both databases. Physician fees were not included in the NIS. Hospitalization E/M CPTs are broken down into initial care visits, subsequent care visits, and discharge visits (Appendix D: Table LXXX). Subsequent care visits were multiplied by the length of stay (LOS) listed in the NIS for each pathogen (Appendix D: Table LXXXVII). All hospital physician fees were added to the estimated costs of hospitalization from the NIS. Costs for ED and hospitalization for PAM and *Vibrio* spp. illnesses were not calculated in the NEDS or NIS, due to insufficient sample size (n<10). Instead, costs for PAM were estimated using bacterial meningitis (ICD-9-CM: 320.0) as a surrogate in NEDS and NIS, while *Vibrio* spp. illnesses were estimated from foodborne illness studies (ERS, 2014).

Lost productivity due to time missed from work for severe illnesses was estimated by multiplying the number of severe illnesses by the number of work days missed (Appendix D: Table LXXXVII), estimated based on data used to calculate the economic burden of foodborne illness (ERS, 2014), the proportion of the population that works (55%) (US Census, 2007; US Census, 2009), and the daily wage ($119.33). Incorporating the proportion of the US population that works into the estimate of lost productivity ensures that only missed days of work are included in the estimate (Hoffmann et al., 2012; Majowicz et al., 2006; Scharff, 2011; Scharff et al., 2009).

The economic value of deaths due to recreational waterborne illness was calculated by taking the product of the value of a statistical life (VSL) and the number of deaths expected. The VSL can be described as the amount each person is willing to pay to avoid 1/100,000 decrease in the risk of death in the next year. For example, if each person is willing to pay on average $50 then the VSL would be equivalent to $50 x 100,000 or $5 million (Robinson, 2007). The value of the VSL chosen in the current analysis is based on the age-invariant estimate (Hoffmann et al., 2012) recommended by the US EPA, which in 2007 dollars is equivalent to $7.6 million (SD: $4.8 million) (BLS, 2010; US EPA, 2010).

Many potentially waterborne infections can manifest into chronic or acute sequelae distinct from the original infection. Costs of sequelae were estimated for Guillain-Barré syndrome (GBS) (*Campylobacter*), hemolytic-uremic syndrome (HUS) with or without end stage renal disease (ESRD) (*E. coli*), and reactive arthritis (ReA) (*Campylobacter*, *Shigella*). Total excess costs per case due to the development of sequelae were obtained from studies of foodborne illness (Scharff, 2011; Scharff et al., 2009) and adjusted for inflation to 2007 dollars (BLS, 2010). Costs of HUS/ESRD was estimated to be an extra $2,359.90 per case of *E. coli* (Frenzen et al., 2005; Scharff, 2011) adjusting for the use of the US EPA recommended VSL of $7.6 million (Robinson, 2007; US EPA, 2010). Costs for GBS were estimated to be an extra $344.39 per case of *Campylobacter* (Frenzen, 2008; Scharff, 2011), while costs for ReA were estimated to be $52.94 per case of *Campylobacter* or *Shigella* (Glennås et al., 1994; Scharff, 2011; Townes et al., 2008).

Overall, to calculate total costs for mild, moderate, and severe illnesses, several assumptions regarding costs were applied to the final burden estimates. In general, the sources of cost and their general assumptions are summarized in TABLE XXVIII. In order to estimate economic burden for recreational waterborne illness in the United States, several assumptions regarding costs and the number of those affected came from several different data sources.

TABLE XXVIII

DATA SOURCES AND ASSUMPTIONS UTILIZED IN CALCULATING THE ECONOMIC BURDEN OF RECREATIONAL WATERBORNE ILLNESS

Cost Component		**Source of Data**	**Assumptions**
Medications	Price	NEEAR; Frenzen, 2007; Scharff, 2011	Costs of medications for mild and moderate illnesses reported in NEEAR representative of US population. Cost of OTC medications among those with moderate GI illness was the same as the cost of OTC medications for those with severe illness. Assumed cost of $44.67 for prescription medications for all cases of severe illness.
	Quantity	NEEAR	Proportion of NEEAR water recreators taking medications for illness is representative of the US population.
HCP	Price	PMIC, 2007	Moderate ear, eye, and skin illness equivalent to E/M level-2, GI and respiratory illnesses equivalent to E/M level-3. Severe illnesses equivalent to E/M level-4
	Quantity	NEEAR; ERS, 2014	Proportion of cases with moderate illness that visit an HCP due to illness reported in NEEAR is representative of the US population. Cases with severe illnesses due to foodborne illness are similar to cases with severe illness due to recreational waterborne illness.
ED	Price	NEDS; ERS, 2014	Moderate ear, eye, and skin illness equivalent to E/M level-2, GI and respiratory illnesses equivalent to E/M level-3. ED cost of Bacterial Meningitis (ICD-9-CM: 320.0) reflective of ED costs related to PAM. ED costs aggregated for foodborne *Vibrio* infections (ERS, 2014) are reflective of ED costs for waterborne *Vibrio* infections.
	Quantity	NEEAR; ERS, 2014	Proportion of cases with moderate illness that visit an ED due to illness reported in NEEAR is representative of the US population. Cases with severe illnesses due to foodborne illness are similar to cases with severe illness due to recreational waterborne illness.
Hospital Admission	Price	NIS	Hospitalization cost of Bacterial Meningitis (ICD-9-CM: 320.0) reflective of hospitalization costs related to PAM. Hospitalization costs aggregated for foodborne *Vibrio* infections (ERS, 2014) are reflective of hospitalization costs for waterborne *Vibrio* infections.
	Quantity	Dechet et al., 2008; Dziuban et al., 2006; Goarant et al., 2009; Hlavsa et al., 2011; Hlavsa et al., 2014; Mead et al., 1999; Pond, 2005; Scallan et al., 2011a; Yoder et al., 2010; Yoder et al., 2008	Wide range of estimated proportion of pathogen-specific illnesses that result in hospitalization.
Missed days of work or daily activity	Price	US Census	Daily wage calculated from median income for the US population would be representative of daily wage for those who water recreate.
	Quantity	NEEAR; ERS, 2014	Proportion of those who specifically miss work out of those who miss work or daily activities in NEEAR is representative of the US population.

4.1.4 Uncertainty and Variability

Measures of uncertainty were incorporated to account for measurement error (Scharff et al., 2009). Several data sources were integrated in order to calculate the economic burden.

Uncertainty for each proportion or percent used in the analysis was estimated using the Beta-Pert distribution, which has parameters minimum, maximum, and "most likely" value (Scallan et al., 2011a). Several sources of data were used to estimate the proportion of outbreak cases that were hospitalized or who died due to illness. The Beta-Pert distribution has been used frequently in other analyses for determining the total number of foodborne illnesses because it is especially good for incorporating estimates from several sources into a single distribution (Scallan et al., 2011a).

Individual mean costs associated with visits with an HCP, ED visits, hospital visits, and the VSL, were assumed to approach a normal distribution and were truncated at 0 to ensure estimates would not incorrectly be calculated from negative values. Estimates of the number of work days missed, for mild and moderate illnesses, and length of hospital stay, for those with severe illness were fit to a triangular distribution, with parameters minimum, maximum, and mode. As a normal distribution, a large portion of the values were negative, so the range of the triangular distributions were equated with the 5th and 95th percentiles of the normal distribution, and the mode with the mean.

Costs for medications were skewed in the NEEAR dataset and were assumed to have a lognormal distribution, based on the distribution of the costs within the study. I also chose to represent outbreak case counts as lognormal distributions to approximate the variability of the assumption. Point estimates were used when no distribution information was available for the specific parameter (ERS, 2014). The model input parameters are described in detail in Appendix D (Table LXXXI–Table LXXXV). Uncertainty and variability associated with the number of illnesses and the individual economic components were characterized using a Monte Carlo simulation (Scharff, 2011) using Crystal Ball version 11.1. The Monte Carlo simulation used

1,000 iterations to calculate 95% CIs around the mean national estimate of economic burden due to surface water recreation.

4.2 Results

4.2.1 Determination of the Number of Water Recreators Who Develop Mild and Moderate Illness

Water recreation in the United States is very popular, with an approximated 4.4 billion water recreation events per year occurring among the entire noninstitutionalized US population in 2007 (296.8 million) (US Census, 2009) (TABLE XXIX). This estimate is based on data regarding the proportion of the US population that recreates, the number of people in the US population in 2007, and the mean number of days people engage in water recreation. Swimming was estimated to be the most common activity, with an estimated 41.5% of the US population 16 and over participating annually (Cordell, 2012). Based on data from NSRE, combined with data from NEEAR and CHEERS, the estimated proportion of children in the US population who water recreate varied according to activity; with close to 1% of children rowing or kayaking and more than 88% swimming each year in untreated recreational water. Approximately 44% of the water-recreation events were associated with swimming, while fishing was the most common incidental-contact activity, contributing to a total of 59% of all incidental-contact recreation events each year.

TABLE XXIX

ESTIMATED NUMBER OF WATER RECREATORS AND PERSON-DAYS OF WATER ACTIVITY (95% CI)

Activity	% of Population 16 and over	Millions of Recreators 16 and over [a] (95% CI)	% of population under 16 [b]	Millions of Recreators Under 16 [c] (95% CI)	Mean days per recreator	Millions of Person Days (95% CI)
Swimming	41.5 (40.9–42.0)	96. 9 (96.1–97.7)	88.4 (88.0–89.5)	56.3 (55.8–56.7)	12.6	1,928.9 (1,913.4–1,944.8)
Kayaking	6.0 (5.8–6.3)	14.1 (13.7–14.4)	1.7 (1.6–1.7)	1.1 (1.0–1.1)	5.6	84.7 (82.6–86.8)
Rowing	4.0 (3.8–4.2)	9.3 (9.4–9.3)	1.3 (1.2–1.3)	0.8 (0.8–0.8)	5.5	55.8 (54.1–57.6)
Canoeing	9.7 (9.4–10.0)	22.7 (22.2–23.1)	4.9 (4.8–5.0)	3.1 (3.1–3.2)	4.7	121.1 (118.7–123.3)
Motor boating	23.4 (22.9–23.9)	54.7 (53.9–55.4)	12.7 (12.5–12.8)	8.0 (7.9–8.1)	11.9	745.8 (735.8–755.8)
Fishing	34.2 (33.5–35.0)	79.9 (78.8–81.0)	46.4 (45.8–47.0)	29.4 (29.0–29.8)	13.1	1,432.2 (1,412.6–1,451.1)

[a] Estimated based of US noninstitutionalized population 16 and over (233.5 million) in 2007 (US Census, 2009)
[b] Estimated number of recreators under 16/Estimated US population under 16 (63.3 million in 2007) (US Census, 2009)
[c] Estimated based on the proportion of children under 16 in NEEAR and CHEERS and the number of adult recreators in the US population

The risk of illness attributable to water recreation varied according to the type of water-recreation activity (incidental-contact fishing, incidental-contact activities besides fishing, and swimming) (TABLE XXX). For swimmers (any contact with beach water), interaction between frequency and water exposure was not statistically significant at $p<.05$ in the logistic model for the relationship between any exposure to recreational water and the occurrence of GI illness in the NEEAR study. Therefore, the frequency of use did not have a strong impact on the risk for GI illness, unlike what was observed in other studies (Lee et al., 1997) and no further adjustment was made to account for frequent users. Similarly, the interaction between water type (marine versus freshwater) was not significant at $p<.05$, implying that there is no difference in the risk of developing GI illness observed for marine compared to freshwater recreators in the NEEAR study, In general no respiratory or skin symptoms were attributable to any type of incidental-contact water recreation, while no eye symptoms were found to be attributable to swimming. Fishing (from a boat, shore, or pier) resulted in a higher attributable risk of the development of GI symptoms compared to other incidental-contact water recreation or swimming. The AR for eye symptoms was highest among those participating in incidental-contact water-recreation activities other than fishing.

TABLE XXX

ATTRIBUTABLE RISKS (95% CI) FOR THE DEVELOPMENT OF SYMPTOMS AMONG WATER RECREATORS, BY ACTIVITY, FOR ALL WATER TYPES

	Incidental-Contact Fishing [a]			Incidental-Contact No Fishing [b]			Swimming [c]		
	Probability of illness if exposed water and fish/bait (95% CI)	Probability of illness if unexposed (non-water recreator) (95% CI)	**Attributable Risk (95% CI)**	Probability of illness if exposed to water (95% CI)	Probability of illness if unexposed (non-water recreator) (95% CI)	**Attributable Risk (95% CI)**	Probability of illness if exposed to water (95% CI)	Probability of illness if unexposed (non-water recreator) (95% CI)	**Attributable Risk (95% CI)**
GI	0.053 (0.041, 0.067)	0.036 (0.030, 0.043)	**0.017 (0.001, 0.031)**	0.039 (0.035, 0	0.033 (0.025, 0.037)	**0.007 (-0.002, 0.015)**	0.039 (0.036, 0.042)	0.024 (0.022, 0.028)	**0.015 (0.009, 0.019)**
Respiratory	--[d]	--[d]	--	0.079 (0.55, 0.104)	0.082 (0.050, 0.115)	--[e]	0.054 (0.050-0.058)	0.048 (0.043, 0.053)	**0.006 (-0.001, 0.012)**
Eye	--[d]	--[d]	--	0.080 (0.074, 0.087)	0.068 (0.060, 0.078)	**0.012 (0.004, 0.023)**	0.029 (0.027, 0.032)	0.029 (0.026, 0.032)	--[e]
Ear	--[d]	--[d]	--	0.015 (0.012, 0.018)	0.013 (0.010, 0.018)	**0.001 (-0.001, 0.007)**	0.016 (0.014, 0.018)	0.012 (0.010, 0.015)	**0.004 (0.000, 0.007)**
Skin	0.090 (0.081, 0.101)	0.091 (0.073, 0.107)	--[e]	0.083 (0.076, 0.090)	0.088 (0.077, 0.098)	--[e]	0.029 (0.027, 0.032)	0.023 (0.020, 0.027)	**0.006 (0.002, 0.010)**

[a] Comparing those who fish to the unexposed group (non-water recreators) in CHEERS
[b] Comparing those who engage in incidental-contact water recreation (kayaking, canoeing, boating, rowing) compared to unexposed group (non-water recreators) in CHEERS
[c] Comparing those who have any contact with beach water to the unexposed group (non-water recreators) in the NEEAR study
[d] Anglers not expected to have excess risk of respiratory, eye, ear, or skin illness due to nature of fishing exposure
[e] No AR calculated, since no excess of illness among the exposed compared to unexposed

Water recreation was estimated to be responsible for approximately 107 million cases of sporadic illnesses in the United States (TABLE XXXI). The most common outcome was GI illness, with 62.85 million illnesses (59% of total), which is consistent with the epidemiologic literature (Pruss, 1998; Wade et al., 2003), followed by eye and skin symptoms. A majority of GI illnesses predicted were among swimmers (47%) and those who fish (42%). Additionally, the majority (75%) of ear illnesses were estimated to occur among swimmers, with a small number of cases occurring among incidental-contact water recreators. The proportion of illnesses that can be considered moderate (contact with an HCP or visit to an ED) varied according to each symptom. For example, based on NEEAR data, approximately 36% of all cases of eye symptoms were estimated to be moderate, while only 7% of those with GI symptoms were moderate, requiring a physician office visit or an ED visit.

TABLE XXXI
ESTIMATED ANNUAL NUMBER OF CASES OF SPORADIC ILLNESS (95% CONFIDENCE INTERVAL) DUE TO WATER RECREATION, BY ACTIVITY, IN MILLIONS [a]

Activity	GI	Respiratory	Eye	Ear	Skin
Swimming	29.80 (23.80–34.82)	6.15 (2.09–9.24)	--[b]	7.36 (3.17–11.50)	13.62 (8.65, 17.74)
Kayaking	0.68 (0.24–1.09)	--[b]	1.21 (0.70–1.47)	0.21 (0.0.02–0.43)	--[b]
Rowing	0.45 (0.16–0.72)	--[b]	0.80 (0.46–1.13)	0.14 (0.02–0.28)	--[b]
Canoeing	0.99 (0.33–1.57)	--[b]	1.73 (0.1.0–2.43)	0.30 (0.03–0.62)	--[b]
Motor boating	6.01 (2.17–9.62)	--[b]	10.67 (6.17-14.92)	1.85 (0.21–3.79)	--[b]
Fishing	26.16 (12.77–39.05)	--[b]	--[b]	--[b]	--[b]
Total	**62.85 (46.88–77.36)**	**6.15 (2.09–9.24)**	**14.42 (8.34–20.11)**	**9.86 (5.10–14.63)**	**13.62 (8.65, 17.74)**
Moderate Severity [c]	**7%**	**13%**	**36%**	**24%**	**8%**

[a] Calculated based on estimated number of water recreation events (TABLE XXIX) and the attributable risk of illness (TABLE XXX), based off of NEEAR and CHEERS
[b] No excess illnesses expected, based on the attributable risks presented in (TABLE XXX)
[c] Percent that contact their HCP or go to an ED

4.2.2 Determination of the Number of Water Recreators Who Develop Severe Illness

The estimated total number of severe cases of illness due to water recreation was substantially smaller than the number of mild and moderate illnesses (TABLE XXXII). The number of outbreak cases varied from year to year. For example, outbreaks due to *E. coli* O157:H7 ranged from zero cases in some years, to as many as 69 reported cases (1,760 cases with outbreak underreporting multiplier) in other years (Dziuban et al., 2006). Therefore, there is a substantial amount of variability around the number of outbreak cases for each pathogen each year, which was incorporated into the Monte Carlo analysis to estimate the number of severe (hospitalized) cases. Additionally, a great deal of uncertainty was observed in the literature regarding the percent of hospitalizations and deaths due to each pathogen (Dechet et al., 2008;

Dziuban et al., 2006; Goarant et al., 2009; Hlavsa et al., 2011; Hlavsa et al., 2014; Mead et al., 1999; Pond, 2005; Scallan et al., 2011a; Yoder et al., 2010; Yoder et al., 2008).

TABLE XXXII indicates that hospitalizations due to waterborne illnesses are rare, with only approximately 778 (95% CI: 333–1,696) cases hospitalized for specific waterborne pathogens each year. Most hospitalizations were determined to be due to *Shigella* spp. (32%), followed by *E. coli* O157:H7 (22%); infection with *Leptospira* was responsible for 15% of all hospitalizations. Additionally, leptospirosis due to infection with *Leptospira* contributes the most (33%) to the estimated total number of deaths due to recreational waterborne pathogens, followed by deaths due to *V. vulnificus* (26%), most likely due to sepsis, with PAM due to *N. fowleri* contributing to approximately 11% of deaths each year.

TABLE XXXII

ESTIMATED NUMBER OF SEVERE CASES AND DEATHS DUE TO WATER RECREATION (95% CI)

Pathogen	Number of Outbreak Cases Mean (95% CI)	Percent Hospitalized [ab]	Number hospitalized Mean (95% CI)	Percent died [ab]	Number of deaths Mean (95% CI)
Campylobacter spp.	130 (4–495)	13.0–25.0	31.6 (1.1–123.5)	0–0.4	0.4 (0.0–1.4)
Cryptosporidium parvum	191 (27–570)	13.0–25.0	61.7 (9.5–179.2)	0–0.3	0.3 (0.0–0.7)
Escherichia coli O157:H7	252 (12–922)	29.5–46.0	167.5 (7.8–647.2)	0.5–0.8	2.7 (0.1–10.1)
Giardia lamblia	28 (1–106)	0–13.0	5.0 (0.1–18.2)	0–0.1	0.1 (0.0–0.2)
Leptospira	125 (3–479)	30.0–65.2	113.7 (2.9–484.8)	1.0–14.0	11.6 (0.3–45.2)
Naegleria fowleri	4 (1–7)	100.0 [c]	4.0 (4.0–4.0)	99.9–100	4.0 (4.0–4.0)
Norovirus [d]	880 (200–2,250)	0.03	51.5 (12.9–123.6)	0.01	0.2 (0.0–0.4)
Shigella spp.	627 (76–1,952)	13.9–22.0	246.1 (26.5–821.5)	0.1–0.2	2.0 (0.2–6.5)
Vibrio parahaemolyticus [e]	22 (12–31)	33.3–50.0	17.3 (9.9–24.9)	0–4.8	0.6 (0.1–1.3)
Vibrio ahaemolyticus [e]	38 (11–65)	13.9–21.1	10.4 (4.3–23.8)	0–4.2	1.2 (0.2–2.7)
Vibrio spp., other [e]	8 (4–11)	11.1–55.6	5.1 (2.2–8.8)	5.2–20.0	1.0 (0.2–2.3)
Vibrio vulnificus [e]	30 (8–51)	62.5–79.0	47.8 (14.2–83.0)	5.0–23.5	9.1 (2.7–16.5)
Vibrio cholera [e]	4 (1–7)	0–80.0	2.9 (0.6–6.1)	0–10.0	0.5 (0.1–1.0)
Unknown GI illness	87 (7–296)	0.06–0.17	0.93 (0.24–1.85)	0.001–0.002 [f]	0.03 (0.0–0.01)
Total	**2,417 (1,097–4,624)**	--	**778 (333–1,696)**	--	**32 (16–67)**

[a] Doubled to account for underdiagnoses (Mead et al., 1999; Scallan et al., 2011a)
[b] According to: Dechet et al., 2008; Dziuban et al., 2006; Goarant et al., 2009; Hlavsa et al., 2011; Hlavsa et al., 2014; Mead et al., 1999; Pond, 2005; Scallan et al., 2011a; Yoder et al., 2008; Yoder et al., 2010;
[c] Assumed to be 100% based on the severity of the illness
[d] No variation in hospitalization or death rates
[e] Proportion hospitalized and died based on COVIS data presented in WBDOSS (Dziuban et al., 2006; Hlavsa et al., 2011; Yoder et al., 2008)
[f] Estimated from 2007 NIS

4.2.3 Economic Burden of Recreational Waterborne Illness

Individual costs used to calculate the economic burden varied according to severity (Appendix D: Table LXXXVI–Table LXXXVII). For example, in the NEEAR study the cost of prescription medication for those with mild GI symptoms was reported as $19.98 (14.24–25.71), whereas prescription medication for moderate illness was slightly higher at $27.31 (14.04–40.57) (Appendix D: Table LXXXVI–Table LXXXVII). Additionally, the proportion of cases having specific responses to their illness (TABLE XXXIII) varied according to symptom and severity (mild, moderate, severe).

TABLE XXXIII
PROPORTION OF WATER RECREATORS WHO RESPOND TO ILLNESS (95% CI), BY SYMPTOM

		Healthcare Provider	OTC	Prescription	ED	Miss Work	Days of work missed
GI [a]	**Mild**	-	0.39 (0.36–0.41)	0.01 (0.01–0.02)	-	0.06 (0.05–0.08)	1.05 (1.01–1.08)
	Moderate	0.93 (0.88–0.98)	0.62 (0.52–0.72)	0.58 (0.48–0.68)	0.26 (0.17–0.35)	0.23 (0.14–0.31)	1.28 (0.97–1.59)
Respiratory [a]	**Mild**	-	0.65 (0.61–0.68)	0.04 (0.02–0.05)	-	0.04 (0.03–0.06)	1.32 (1.00–1.63)
	Moderate	0.97 (0.95–1.00)	0.63 (0.55–0.72)	0.67 (0.59–0.75)	0.11 (0.06–0.16)	0.16 (0.10–0.22)	1.48 (1.02–1.93)
Eye [a]	**Mild**	-	0.47 (0.39–0.48)	0.17 (0.07–0.28)	-	-	--
	Moderate	1.00	0.28 (0.24–0.51)	0.81 (0.69–0.91)	0.06 (0.01–0.13)	0.06 (0.01–0.16)	2.33 (1.00–7.00)
Ear [a]	**Mild**	-	0.36 (0.30–0.43)	0.05 (0.02–0.09)	-	0.03 (0.01–0.06)	1.08 (0.71–1.44)
	Moderate	0.97 (0.93–1.00)	0.33 (0.22–0.45)	0.88 (0.80–0.96)	0.12 (0.04–0.19)	0.10 (0.03–0.18)	1.14 (0.56–1.72)
Skin [a]	**Mild**	-	0.52 (0.47–0.56)	0.03 (0.02–0.05)	-	0.01 (0.00–0.02)	1.50 (0.58–2.42)
	Moderate	1.00	0.38 (0.22–0.53)	0.73 (0.58–0.87)	0.05 (0.02–0.12)	0.05 (0.02–0.12)	1.50 (0.00–7.85)
Severe Illnesses		1.7 visits per case [b]	0.62 [c] (0.52–0.72)	1.00 [d]	0.3 visits per case	1.00 [d]	Varied based on pathogen [e]

[a] Estimated proportion of water recreators with mild or moderate illness responding to their symptoms.
[b] 0.7 visits/ case prior to hospitalization; 1 visit/case following hospitalization (ERS, 2014)
[c] Estimated using NEEAR data for moderate illness (ERS, 2014)
[d] Assumed all hospitalized cases take prescription medication and miss work (ERS, 2014)
[e] See Appendix D: Table LXXXVII for individual number of days missed by pathogen (ERS, 2014)

Overall, mild illnesses due to water recreation were estimated to cost $916.2 million (95% CI: $730.3 million to $1,091.6 million) annually (TABLE XXXIV). Approximately 39% of the total cost ($355.5 million) was from OTC and prescription medication, while the rest of the total cost was due to lost productivity. A small portion, 1.5% (95% CI: 0.8%–2.2%) of those with mild symptoms reported taking prescription medication, even though they did not report seeing a physician or going to an ED, which is consistent with previous studies (Sargeant et al., 2008). Therefore, the majority (>80%) of total medication costs was due to OTC medications. Overall, a large fraction of costs due to mild illness were due to mild GI illness (71%). The other four illnesses contributed less than 10% each to the total cost of mild illness.

TABLE XXXIV

TOTAL COST OF MILD WATERBORNE ILLNESS; MEAN (95% CI)

Outcome	**Total cost in Millions of US dollars [a]**			**US dollars**
	Meds [b]	Lost Productivity	Total Cost	**Cost per case**
GI	187.5 (138.7–233.4)	467.5 (339.9–603.0)	655.0 (482.7–826.9)	**10.89 (9.74–12.04)**
Respiratory	32.1 (11.9–50.0)	39.4 (14.5–63.1)	71.5 (26.5–111.4)	**12.81 (11. 26–14.53)**
Eye	60.2 (35.3–104.9)	--	66.2 (35.3–104.9)	**7.05 (5.24–9.45)**
Ear	25.1 (11.7–39.7)	37.1 (15.4–64.0)	62.1 (29.4–97.5)	**8.34 (5.93–10.79)**
Skin	46.5 (28.6–62.4)	18.2 (6.1–32.1)	64.6 (39.3–90.8)	**5.12 (4.10–6.15)**
Total Cost of Mild Illness	355.5 (288.3–419.9)	560.7 (423.4–695.3)	916.2 (730.3–1,091.6)	**9.66 (8.81–10.54)**

[a] Estimated costs (in millions of 2007 dollars) may not sum to estimated totals due to rounding
[b] Combined OTC and prescription medication costs

Moderate illnesses due to water recreation were estimated to cost $2.67 billion annually (95% CI: $2.08 billion to $3.30 billion) (TABLE XXXV). Approximately 38% of the total cost ($1.02 billion) was due to physician office visits, while another 37% of the total cost ($0.99 billion) was due to ED visits. The cost of moderate GI illness contributed substantially (52%) to the total cost of moderate illnesses. Moderate eye illnesses accounted for the second largest contributor (27%) to total costs of moderate illness.

TABLE XXXV

TOTAL COST OF MODERATE WATERBORNE ILLNESS; MEAN (95% CI)

Outcome	**Total cost in Millions of US dollars [a]**					**US dollars**
	Meds [b]	Doctor visit	ED visit	Lost Productivity	Total Cost	**Cost per case**
GI	85.9 (56.6–122.7)	390.7 (243.6–551.1)	764.7 (515.3–1,087.1)	149.3 (96.1–214.7)	1,390.6 (978.3–1,868.6)	**321.35 (271.67–379.59)**
Respiratory	16.7 (5.8–27.7)	77.7 (26.9–132.1)	39.3 (13.8–70.9)	24.2 (8.6–41.3)	157.9 (57.8–256.0)	**183.1 (148.50–215.56)**
Eye	117.4 (62.3–184.9)	343.1 (171.1–551.7)	97.9 (29.7–189.9)	174.2 (40.8–398.6)	732.6 (384.8–1,168.2)	**137.94 (102.84–181.54)**
Ear	36.3 (16.8–59.4)	147.3 (61.6–245.0)	73.7 (29.0–133.7)	32.3 (11.7–60.0)	289.5 (136.1–454.8)	**126.03 (97.60–153.50)**
Skin	16.8 (9.4–25.7)	65.8 (34.8–101.1)	17.2 (5.1–32.2)	20.8 (3.1–54.9)	120.5 (67.2–185.2)	**117.00 (85.83–154.75)**
Total Cost of Moderate Illness	268.5 (200.0–347.3)	1,018.2 (760.4–1,298.0)	986.7 (714.5–1,318.7)	394.1 (245.5–613.1)	2,667.5 (2,079.4–3,299.8)	**196.03 (168.83–226.77)**

[z] Estimated costs (in millions of 2007 dollars) may not sum to estimated totals due to rounding

[b] Combined OTC and prescription medication costs

Severe illnesses due to water recreation were estimated to be $287 million (TABLE XXXVI). The majority of the costs (94%) were due to deaths, based on the VSL (Robinson, 2007; US EPA, 2010). Hospitalizations contributed approximately 2.4% ($6.9 million) to the total costs of severe illness. Leptospirosis was responsible for approximately 35% ($100.7 million), followed illness due to *V. vulnificus* contributing 26% ($74.2 million), with PAM due to *N. fowleri* contributing 11% ($32.8 million) to the total cost of severe illness. Illnesses due to *N. fowleri* had the highest per case cost of illness ($8.2 million), due to the high (>99.9%) mortality rate (Yoder et al., 2010).

TABLE XXXVI
TOTAL COST OF SEVERE WATERBORNE ILLNESS; MEAN (95% CI)

	Total cost in Millions of US dollars [a]							
	Meds	Doctor/ED visit	Hospital visit	Lost Productivity [b]	Death	Sequelae	Total Cost	**Cost per case**
Campylobacter spp.	0.00 [c] (0.00–0.00)	0.02 (0.00 [c] –0.06)	0.19 (0.00 [c] –0.68)	0.01 (0.00 [c] –0.05)	3.45 (0.50–13.22)	0.01 (0.00 [c] –0.05)	3.71 (0.07–13.65)	**0.09 (0.00 [c] –0.21)**
C. parvum	0.00 [c] (0.00–0.00)	0.03 (0.00 [c] –0.09)	0.42 (0.06–1.19)	0.03 (0.00 [c] –0.09)	1.66 (0.03–5.95)	--	2.14 (0.15–6.91)	**0.03 (0.00 [c] –0.08)**
E. coli O157:H7	0.00 [c] (0.00–0.03)	0.08 (0.00 [c] –0.28)	1.13 (0.58–4.47)	0.07 (0.00 [c] –0.27)	19.01 (0.52–70.06)	0.37 (0.02–1.49)	20.72 (0.68–78.33)	**0.14 (0.03–0.26)**
Giardia lamblia	0.00 [c] (0.00–0.00)	0.00 [c] (0.00–0.00)	0.03 (0.00 [c] –0.10)	0.00 [c] (0.00–0.00)	0.48 (0.00 [c] –1.67)	--	0.52 (0.01–1.76)	**0.12 (0.03–0.28)**
Leptospira	0.00 [c] (0.00–0.02)	0.06 (0.00 [c] –0.29)	1.49 (0.03–5.37)	0.07 (0.00 [c] –0.26)	103.07 (1.09–361.27)	--	100.70 (1.17–363.4)	**0.86 (0.12–2.03)**
N. fowleri	0.00 [c] (0.00–0.00)	0.00 [c] (0.00–0.00)	0.08 (0.08–0.09)	-- [d]	32.73 (6.72–66.27)	--	32.82 (6.81–66.36)	**8.2 (1.7–16.6)**
Norovirus	0.00 [c] (0.00–0.00)	0.02 (0.00 [c] –0.06)	0.36 (0.08–0.96)	0.00 [c] (0.00–0.03)	1.45 (0.13–4.13)	--	1.74 (0.30–5.05)	**0.03 (0.01–0.06)**
Shigella spp.	0.01 [c] (0.00–0.04)	0.13 (0.01–0.39)	1.30 (0.15–3.76)	0.06 (0.00 [c] –0.18)	16.06 (0.85–52.85)	0.01 (0.00 [c] –0.04)	17.46 (1.24–58.20)	**0.08 (0.02–0.15)**
V. parahaemolyticus	0.00 [c] (0.00–0.00)	0.00 [c] (0.00–0.00)	0.16 (0.10–0.23)	0.01 (0.00 [c] –0.02)	4.73 (0.32–14.4)	--	4.91 (0.47–14.58)	**0.29 (0.03–0.82)**
V. ahaemolyticus	0.00 [c] (0.00–0.00)	0.00 [c] (0.00–0.00)	0.10 (0.03–0.22)	0.00 [c] (0.00–0.01)	9.59 (0.71–26.3)	--	9.73 (0.85–26.47)	**0.76 (0.08–1.94)**
Vibrio spp., other	0.00 [c] (0.00–0.00)	0.00 [c] (0.00–0.00)	0.05 (0.02–0.09)	0.00 [c] (0.00–0.00)	8.08 (0.72–21.9)	--	8.13 (0.76–21.94)	**1.18 (0.18–4.36)**
V. vulnificus	0.00 [c] (0.00–0.00)	0.03 (0.00 [c] –0.05)	1.52 (0.51–2.57)	0.03 (0.00–0.05)	74.39 (8.33–179.46)	--	74.24 (9.15–181.84)	**1.58 (0.29–3.21)**
V. cholera	0.00 [c] (0.00–0.00)	0.00 [c] (0.00–0.00)	0.03 (0.00 [c] –0.06)	0.00 [c] (0.00–0.00)	3.81 (0.37–10.14)	--	3.92 (0.37–10.17)	**1.82 (0.22–5.02)**
Unknown GI	0.00 [c] (0.00–0.00)	0.00 [c] (0.00–0.00)	0.09 (0.00 [c] –0.28)	0.0 [c] (0.00–0.01)	0.51 (0.01–1.80)	--	0.61 (0.03–2.13)	**0.03 (0.01–0.06)**
Total Cost of Severe Symptoms	0.04 (0.01–0.08)	0.37 (0.15–0.84)	6.92 (3.11–13.96)	0.31 (0.13–0.67)	270.79 (106.89–523.18)	0.40 (0.03–1.52)	287.19 (103.02–609.86)	**0.49 (0.18–1.07)**

[a] Estimated costs (in millions of 2007 dollars) may not sum to estimated totals due to rounding
[b] Estimated only for nonfatal cases
[c] Estimated cost <.01 million
[d] No lost productivity estimated, >99.9% cases are fatal

The national total annual estimate of surface-water recreational waterborne illness was $3.9 billion (95% CI: $3.1 billion to $4.7 billion) in the United States (Figure 11). The majority of the national estimate (70%) was due to moderate illnesses. Combined mild and moderate sporadic GI illness was approximately 51% ($2.0 billion) of the total cost. Indirect costs contributed substantially to the total costs with lost productivity due to missed time away from work, equivalent to 33% and mortality responsible for almost 7% of the total economic burden. The average cost per case of severe illness was substantially higher ($0.49 million) than the costs for moderate ($196.03) and mild ($9.66) illnesses. Overall, the average cost for any illness (mild, moderate, or severe) among water recreators was $35.82, while the average cost per water recreator was $0.87.

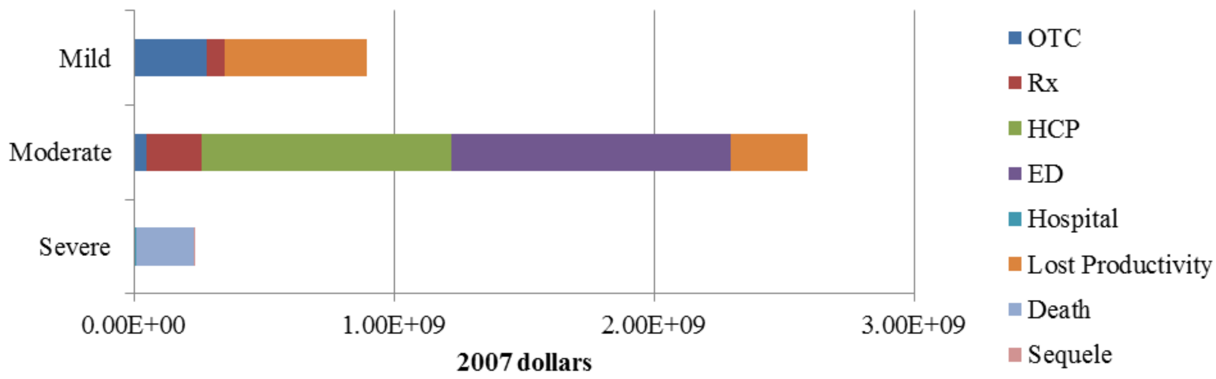

Figure 11. Total cost breakdown by mild, moderate, and severe illnesses.

4.3 Discussion

The estimated total number of annual surface-water recreation events (4.4 billion) was estimated to result in approximately $3.9 billion (95% CI: $3.1 billion to $4.7 billion) in medical costs and lost productivity due to missed time from work each year. Moderate illness, defined as seeking care from a doctor at a physician's office or an ED, but not being hospitalized, accounted for the majority (70%) of the costs associated with surface-water recreation in the United States. Approximately 38% of the total estimated economic burden is due to lost productivity, measured as economic losses directly associated with missing work due to illness, and mortality.

4.3.1 Costs in Context to Other National and Regional Studies of Economic Burden

4.3.1.1 Waterborne Disease Estimates

A recent study by Collier et al. (2012) found that hospitalization costs for illnesses that were primarily transmitted by water (giardiasis, cryptosporidiosis, Legionnaires' disease, otitis externa, and non-tuberculosis mycobacterial infection) were $970 million annually in the United States. The same study also estimated that illnesses only partially transmitted by water (campylobacteriosis, salmonellosis, shigellosis, HUS, and toxoplasmosis) accounted for $860 million in hospitalizations annually, but it was not possible to estimate the proportion that were due to water (Collier et al., 2012). In the current study, it was estimated that costs due to hospitalizations from recreational exposure to untreated surface water was $6.9 million (95% CI: $3.1 million to $14.0 million), or approximately 4% of the estimate from Collier et al. (2012). The costs reported by Collier and colleagues included illnesses that can result from all types of water exposures, including drinking water, treated recreational water (swimming pools, spas) as well as untreated recreational surface water. From 2007 to 2008, approximately 90% of all outbreaks and 95% of all outbreak cases were associated with treated recreational water (Hlavsa et al., 2011). Therefore, it was to be expected that only a small fraction of hospitalization costs found by Collier et al. (2012) would be associated with recreation on untreated US surface water.

A recreational surface-water study by Dwight et al. (2005) estimated the annual economic burden (direct and indirect costs) due to water recreation at two beaches in Orange County California to be $3.3 million in 2001 dollars ($3.9 million in 2007 dollars). In the current analysis, it was estimated that 1.9 billion swimming events occur annually in the United States (TABLE XXIX). At the two beaches in Orange County, California it was estimated that swimming occurred more than 5.5 million times annually (Turbow et al., 2003), which is equivalent to approximately 0.3% of the estimated number of swimming events in the United States. If the costs estimated by Dwight and colleagues were scaled up, the national estimate of the annual economic burden due to swimming in polluted untreated surface water would be more than $1 billion.

An examination of the total economic burden of acute otitis externa (AOE), or swimmers ear, in the United States was estimated to be $489 million in ambulatory-care (office visits) and ED visits in 2007 (CDC, 2011). Cases of AOE are characterized by inflammation and pain of the external ear canal associated with water exposures, including recreational water exposure (Agius et al., 1992), or a humid environment (CDC, 2011). The total cost of ear symptoms (not necessarily due to AOE) in the current analysis was estimated to be $352 million, with $221 million being directly due to outpatient visits (office visits and ED visits). Another study suggested that earache (not necessarily due to AOE) is responsible for approximately $4 million in medication costs alone, but was expected to be an underestimate, since only the number of swimmers, not the frequency of swimming was included in the calculation (Wade et al., 2013).

4.3.1.2 The Burden of Waterborne Illness Compared to Foodborne Illness

Foodborne illness of known and unknown etiologies has been estimated to cost between $51 and $77 billion each year, depending on certain assumptions regarding lost productivity and pain and suffering (Scharff, 2011). It was expected that illnesses due to surface-water recreation would be a fraction of the costs of foodborne illnesses. It is expected that the concentration of microbes in surface water may be much lower than what is found in food. Additionally, water recreators, including those engaged in incidental-contact or swimming, have been found to only ingest milliliters of surface water (Dorevitch et al., 2011; Dufour et al., 2006) during their water-recreation event, with those engaged in swimming activities swallowing more water compared to incidental-contact water recreators. Therefore, it is anticipated that the dose of pathogenic organisms water recreators are exposed to is much less, and would cause fewer illnesses, compared to individuals who eat contaminated food. Evidence from the literature suggests that the dose of pathogenic organisms in water is typically lower than what it is in food (Glynn and Bradley, 1992). Additionally, evidence from previous analyses has also observed a smaller fraction of cases of illness due to outdoor water recreation compared to foodborne illness. An examination of *E. coli* O157 outbreaks found that out of 350 total outbreaks, 183 (52%) were foodborne, while 14 (4%) were associated with recreational water exposure in lakes or ponds (Rangel et al., 2005). Similarly, a case control study found that approximately 55% of *Campylobacter* infections were foodborne, while only 3% were associated with water from lakes, rivers, or streams (Friedman et al., 2004).

Based on the current study, it is suspected that the severity of waterborne GI illness is milder than illnesses associated with food exposure. In the current analysis, 7% of those with GI symptoms sought medical care (office visits or ED visits). However, the estimated rate of those with foodborne GI illness who seek medical care ranges from 13% to 23% (Scallan et al., 2011a; Scharff, 2011; Scharff et al., 2009).

The methods used in the current analysis to calculate lost productivity for mild and moderate illnesses differed from methods used to estimate the lost productivity due to foodborne illness. The current study estimated lost productivity of mild and moderate illness by taking the product of the self-reported proportion that miss work, the number of work days missed from the NEEAR study, and multiplied it by the estimated daily wage according to the US Census (US Census, 2007). In studies that estimate the economic burden of foodborne illness, it is assumed that workdays lost are a direct function of the duration of illness (Hoffmann et al., 2012). To estimate lost productivity for mild and moderate foodborne illness Hoffman et al. (2012) assumed that 0.25 or 0.33 workdays for mild and moderate illnesses, respectively, are missed for each day of illness. This estimated number of workdays missed per person, was then multiplied by the proportion of part-time and full-time workers in the US population (55%) (US Census, 2007; US Census, 2009) and then by the daily wage (US Census, 2007). The estimate for lost productivity for mild GI illness using the Hoffman et al. (2012) methodology was more than ten times the estimate for lost productivity using the estimates derived from the epidemiology studies ($4.56 billion versus $467 million). The estimate for lost productivity for all moderate cases of GI illness using the Hoffman et al. (2012) method was only about four times greater compared to the lost productivity estimate using epidemiological data ($483 million versus $149 million). This difference suggests that mild GI illness among water recreators may be less severe than mild foodborne illness caused by a pathogen or that lost productivity of mild illness may possibly be overestimated for foodborne illness.

Some studies on the economic burden of foodborne illness (Scharff, 2011; Scharff et al., 2009) use an alternative approach for calculating lost productivity. A QALY takes into account life expectancy and quality of life. Economic burden estimates that incorporate QALYs value them as one QALY being equivalent to $100,000 to $357,000 (Luce et al., 2006; Scharff, 2011; Scharff et al., 2009). While some researchers believe lost productivity measured only as time missed from work is a significant underestimate of costs (Scharff, 2011; Scharff et al., 2009), others believe that monetization of QALYs is controversial, and not supported by empirical evidence (Hoffmann et al., 2012). The current analysis estimated lost productivity by approximating costs associated with loss of work only. Incorporating aspects regarding pain and suffering into the calculation, such as through the use of monetized QALYs, would have significantly increased the total lost productivity estimates and ultimately the total cost of recreational waterborne illness. Additionally, monetization of missed days of daily activity or leisure time would have also significantly increased costs as well, since approximately 20% of those with GI illness in NEEAR who missed either work or daily activities specifically missed work due to illness. Further research into the most appropriate way to characterize lost productivity among water recreators with illness is necessary.

4.3.2 Assumptions Used to Estimate National Economic Burden Due to Surface Water Recreation

The assumptions made in the current analysis were chosen in order to arrive at a reasonable estimate of the total economic burden of surface-water recreation. The number of annual water recreators was determined based off of recreational surveys for those 16 and over (Cordell, 2012), and the ratio of adult to child recreators was assumed to be similar to what was observed in the epidemiology studies. However, it is unclear whether the ratio of adults to children participating in incidental-contact water recreation (kayaking, canoeing, rowing, motor boating, and fishing) in an urban setting is the same as the adult to child ratio in nonurban settings. If more or less children engage in water sports in rural areas compared to urban areas, than the estimates of the total number of water recreation events would be underestimated or overestimated.

Additionally, it was assumed that the ARs calculated for all illnesses in NEEAR and CHEERS would be nationally representative. The NEEAR and CHEERS sites were significantly impacted by pollution; therefore, the risk of illness among water recreators calculated within these contexts may not be generalizable to all instances of water recreation. This assumption may have significant impact on the results and may overestimate the total economic burden attributable to water recreation.

Severe cases were estimated based on outbreak and non-outbreak illnesses reported in WBDOSS. The fraction of illnesses due to water recreation that are captured in outbreaks is unknown (Dziuban et al., 2006; Hlavsa et al., 2011; Hlavsa et al., 2014; Yoder et al., 2004; Yoder et al., 2008). An estimated 1.4 million cases of foodborne *Salmonella* infections occur each year in the United States, yet only an average of 30,000 are identified through outbreaks (Olsen et al., 2000), thus indicating that only 2% of cases of *Salmonella* infections are captured by outbreak surveillance systems. In the current analysis, I used FoodNet assumptions that assumed that for every reported outbreak case, 25.5 others occur but are not reported (Scallan et al., 2011a), therefore assuming that approximately 4% of cases of illness are captured by outbreaks.

The use of outbreak and passive surveillance multipliers based off of data related to foodborne illness may not necessarily be appropriate for determining the number of recreational waterborne illnesses not captured by outbreak surveillance. Currently, there is extensive surveillance data for foodborne illnesses, which were used in the construction of the multipliers (Scallan et al., 2011a). Unfortunately, no surveillance systems are in place for recreational waterborne illnesses. Therefore, there is no way to confirm whether or not the outbreak multiplier of 25.5 or the passive surveillance multiplier of 1.1 are appropriate for estimating the projected number of illnesses not captured in WBDOSS. It is unclear if the outbreak and passive surveillance multipliers are over- or underestimating the number of waterborne outbreak-related illnesses. However, the use of no multipliers would underestimate the number of cases, since it is expected that outbreaks are only capturing a fraction of the total number of cases that occur as a result of water recreation (Dziuban et al., 2006; Hlavsa et al., 2011; Hlavsa et al., 2014; Yoder et al., 2004; Yoder et al., 2008). The use of these multipliers, based on several ratios of laboratory-confirmed cases of foodborne illness to cases identified through foodborne outbreak surveillance, are the best estimate to date, for attempting to estimate the number of cases of illness not identified from outbreak reporting systems.

Additionally, it was assumed that outbreak cases of waterborne illness had the same or similar pattern of hospitalizations and deaths as laboratory-confirmed cases of foodborne illness (Mead et al., 1999; Scallan et al., 2011a). The WBDOSS did not typically provide data concerning the number of hospitalizations among outbreak cases associated with untreated recreational water. Evidence from this study suggests the potential for waterborne illnesses to be generally less severe than foodborne illness, based on the proportion that seek care (7% among those with sporadic GI illness compared to 13%–23% with foodborne illness (Scallan et al., 2011a; Scharff, 2011; Scharff et al., 2009)). Therefore, it is possible that the projected number of hospitalizations associated with untreated surface water may be overestimated. However, cases of severe illness accounted for a very small proportion of the estimated waterborne disease costs, and if hospitalization costs were overestimated, the impact on total costs would have little impact on the overall disease burden estimate.

Year-to-year there was a great deal of variability in the number of reported outbreak cases per pathogen. This variability was chosen to be represented as a lognormal distribution based on calculations of the mean and standard deviation of the annual number of outbreak cases. However, a different probability distribution may have been more appropriate for describing the outbreak data. During the analysis, several alternative distributions were applied, all of which had a very minor effect on the total economic burden estimate. However, a more appropriate method for characterizing outbreak cases of illness over a ten-year period may be necessary.

Outbreaks of cercarial dermatitis, or swimmer's itch, potentially caused by avian schistosomes, occur relatively frequently. From 2007 to 2008 there were four outbreaks involving 300 cases of swimmer's itch (Hlavsa et al., 2011). While outbreaks of illness due to avian schistosomes are captured by outbreak surveillance, the illness is relatively mild and self-limiting and does not typically result in hospitalization (Chamot et al., 1998). Therefore, cases of swimmer's itch were not included in the estimates for severe illness, even though they were identified in WBDOSS. However, those with swimmer's itch often take OTC medications and approximately 4% of those infected will seek care from a physician (Chamot et al., 1998). Thus, cases of cercarial dermatitis would be considered mild or moderate, and would have been captured by the review of CHEERS and NEEAR data. Thus, I avoided double-counting the cases by not including data from outbreaks of cercarial dermatitis. However, this may have resulted in an underestimation of the total economic burden of skin symptoms.

Harmful algal blooms (HABs) are accumulations of phytoplankton that produce toxins that can result in several adverse effects. The symptoms associated with HABs are typically nonspecific and can include GI, respiratory, skin, eye, ear, and neurological outcomes (Hilborn et al., 2014). From 2009 to 2010 there were four outbreaks due to cyanobacterial toxins (due to HABs) corresponding to 38 cases. Seven additional outbreaks, involving 23 cases, were suspected to be due to cyanobacterial toxins but were not able to be confirmed because algal toxins were not detected in sufficient quantities to be identified as the etiologic agent (Hlavsa et al., 2014). Despite the nonspecific nature of the symptoms, outbreak illnesses due to HABs resulted in two hospitalizations (among identified and suspected outbreak cases) from 2009 to 2010 (Hlavsa et al., 2014). Algal blooms caused by *Karenia brevis* have been shown to be specifically associated with respiratory symptoms (Hlavsa et al., 2011; Hoagland et al., 2009) and have been estimated to be responsible for $0.5–$4 million in respiratory ED visits in Sarasota Country, Florida annually (Hoagland et al., 2009). Exposures to HABs may have a significant economic impact, yet the HAB outbreak data were not included in the current analysis. Rather I assumed that the economic burden due to HABs was captured in the burden estimates for mild and moderate illness. Specific economic burden analyses for illnesses due to HABs may be more transparent in the future. Newer versions of the ICD-9-CM diagnosis codes includes an E code (E928.6) that can allow an HCP to indicate that a specific illness is suspected to be due to environmental exposures to harmful algae or toxins (Buck, 2014). The use of this E code could be beneficial for beginning to understand the economic impact of algal blooms.

Several common sequelae may develop after infections by certain waterborne pathogens, including GBS (*Campylobacter*), HUS/ESRD (*E. coli*) and ReA (*Campylobacter*, *Shigella*). Evidence suggests that shiga toxins, produced by *E. coli* O157:H7, can have physiological impacts that can also lead to hypertension and systemic endothelial dysfunction, (which can lead to cardiovascular disease), along with renal impairment (Brenner et al., 1996; Clark et al., 2010; Ohmi et al., 1998). Epidemiologic studies on the long-term effects from exposure to drinking water contaminated with *E. coli* O157:H7 and *Campylobacter* have found an association with increased risk of cardiovascular disease, hypertension, as well as renal impairment (Clark et al., 2010). In the United States, the combined economic burden due to all cardiovascular outcomes was approximately $273 billion in 2010 and is expected to rise to close to $800 billion by 2030 due to anticipated increases in cardiovascular disease in the United States (Heidenreich et al., 2011). While I did include cost estimates of sequelae such as HUS and ESRD, I did not include estimates of the burden of hypertension or other cardiovascular outcomes that may result from these infections.

4.3.3 **Strengths and Limitations**

The current analysis had several strengths. First, large prospective cohort studies containing a combination of more than 35,000 participants were used to estimate excess risks, by symptom, due to water recreation. These epidemiology studies prospectively obtained data directly from those engaged in water recreation regarding illness, healthcare utilization, and lost productivity. The observed attributable risks were used to inform the estimate of the total number of water recreators that develop illness in the United States. Second, data from the NEEAR study were used to help estimate responses to mild and moderate illness (OTC and prescription medication use, visits with an HCP, ED visits, hospitalizations, and lost productivity). The information available to help estimate lost productivity, including the proportion of mild and moderate cases that miss work combined with the self-reported number of workdays missed contributed to a suspected more accurate estimation of productivity losses due to sporadic illness associated with untreated surface-water exposure.

Additionally, several data sources were used to estimate the cost of illness. Self-reported medication expenditures from the NEEAR study were used to estimate OTC and prescription costs. Furthermore, both the NEDS and the NIS were utilized in calculating costs associated with ED visits and hospitalizations, respectively (HCUP Nationwide Emergency Department Sample (NEDS), 2007; HCUP Nationwide Inpatient Sample (NIS), 2007), while hospital- and ED-specific professional fees were estimated using the UCR for each E/M CPT (PMIC, 2007). The variability and uncertainty of costs and the number of mild, moderate, and severe illnesses were taken into account in the Monte Carlo simulation, which led to the calculation of 95% CIs around the estimate.

The estimate of the total economic burden due to surface-water recreation should be considered in light of several important limitations. The economic burden estimate is based in part on an accurate estimation of the total number of people in the United States who engage in water recreation and an estimate of the total number of person-days associated with a particular water activity. Fishing, for example, is a popular water activity, and an estimated 34% of the US population over 16 years fishes each year. The mean number of days a person in the United States fished was estimated to be 13.4 days/year, based on a weighted average of four different fishing activities (saltwater, warm-water, cold-water, and anadromous fishing), since a combined average for all fishing activities was not reported (Cordell, 2012). It is possible that fishing person-days was over- or underestimated based on this assumption, which could have a substantial impact on the total economic burden estimate. Additionally, only the mean number of days a person engages in water recreation was available for these analyses. Therefore, these values needed to be incorporated into the Monte Carlo simulation as a point estimate. Use of the mean number of days could have subsequently overestimated the number of water-recreation events that occur annually.

A major limitation of this work is related to the use of the AR to estimate the number of mild and moderate recreational waterborne illnesses in the United States. These ARs were calculated based on the relationship between the occurrence of illness among water recreators compared to the unexposed group of non-water recreators, in two very specific studies of water recreation. The CHEERS and NEEAR were conducted at certain study locations that were heavily impacted by human fecal pollution. Specifically, CAWS locations in CHEERS were composed of approximately 75% of non-disinfected wastewater effluent (Rijal et al., 2011). Therefore, it is anticipated that the ARs calculated within the context of these two epidemiology studies may potentially be overestimating the risk of recreational waterborne illnesses in all contexts and thus the total number of illnesses attributable to water recreation. It is expected that recreation occurring in pristine surface waters, unlike the study locations utilized in this analysis, would result in significantly less risk of illness. In fact, illness rates at Boqueròn beach in Puerto Rico, another site included in the NEEAR study, but not included in the current analysis, saw GI illness rates (4%) much lower than what was reported in the current analysis (Wade et al., 2010b). This beach had lower geometric means of fecal indicators compared to the other

NEEAR sites used in this analysis as well (Wade et al., 2010b), suggesting that cleaner beaches would result in lower rates of illness. Ultimately, an overestimation of the number of recreational waterborne illnesses would lead to an overestimation of the total economic burden due to illness attributed to surface-water recreation.

Additionally, the current analysis needed to rely on several assumptions and uncertainties to construct an estimate of the economic burden due to recreational waterborne illness. These various assumptions were necessary because no active surveillance systems are in place for recreational waterborne illness. Also, it is unclear which methodology best describes lost productivity. In the current analysis, I estimated costs according to days of work missed, using an estimation of the national daily wage. This daily wage estimate may not be reflective of individuals who participate in water recreation. It can be postulated that those who engage in any type of water recreation may have more money to spend on leisure, and thus their daily wage or income may not be adequately reflected using the national average income. Additionally, alternative analyses could have also incorporated lost days of activity, which are not specific to work days. It has been suggested that individuals may value their leisure or vacation time equal to or greater than their missed work time (Drummond et al., 1997). If missed leisure time were to be considered, costs would have been substantially greater. These uncertainties and assumptions may significantly influence the accuracy of the total estimate.

The uncertainty surrounding these estimates of the number of illnesses due to water recreation suggests that better surveillance systems may be necessary. The economic burden estimate may be inaccurate based on the assumptions needed to determine the number of recreational waterborne illnesses that occur annually. FoodNet, an active surveillance system set in place to identify cases of foodborne illness in the United States, has been used in several analyses to determine the economic burden due to foodborne illness (Hoffman et al., 2012; Scharff et al., 2011). If similar surveillance systems were in place to identify cases of recreational waterborne illness, fewer assumptions would need to be incorporated into the estimate of economic burden due to untreated surface-water recreation. Moreover, active surveillance systems can be costly and the benefits of a surveillance system for waterborne illnesses may not outweigh the costs for implementing such a system. However, FoodNet currently consists of surveys disseminated to laboratories, physicians, and the general population within the surveillance areas, as well as regularly conducted case-control, cohort, and other epidemiology studies (CDC, 2014). Perhaps restructuring of the survey questionnaire to include specific questions related to recreational-water exposures could enhance the current FoodNet system—to not only inquire about exposures to specific foods, but also regarding waterborne exposures as well. This could potentially increase our knowledge regarding waterborne illnesses while building off of an existing and successful surveillance system.

4.4 Conclusions

It is estimated that the economic burden of surface-water recreation ranges between $3.1 and $4.7 billion each year. Estimates of the cost of prevention activities, such as beach monitoring and notification programs, should be viewed in context of this burden estimate. To date, approximately $130 million has been allocated toward beach-water protection programs since 2001 (US EPA, 2014), which is only a small fraction of the estimated burden. Almost 70% of this burden estimate is due to moderate sporadic illnesses, which has great public health impact. Moderate illnesses, requiring care from an HCP or ED, contribute more to the total economic burden than severe cases of illness that could result in death.

While the costs associated with recreational water exposure are substantial, there are also several health benefits associated with outdoor water recreation. Water recreation, and specifically, aquatic exercise, has been demonstrated to be associated with reducing blood pressure in post-menopausal women (Arca et al., 2013) and for reducing pain and increasing the quality of life among those with musculoskeletal disorders (Barker et al., 2014). People who swim have also been shown to have a decrease in all-cause mortality compared to those who are sedentary or engaged in other physical activities such as running (Chase et al., 2008). Additionally, the physical demands of kayaking have been shown to have extensive health benefits (Michael et al., 2008), while rowing has been associated with decreased risk of type 2 diabetes (Olsen et al., 2011). Efforts to reduce the severity of illness among water recreators should be explored to reduce the total economic burden and encourage more individuals to enjoy the several health benefits associated with outdoor water recreation.

5. CONCLUSIONS

These studies assessing severity and the economic burden of recreational waterborne illness will add to the current literature on water recreation and health. This work advances our thinking about illness attributed to water recreation as a spectrum of severity rather than an "either/or" event. The current analyses explored novel ways in which to describe illness severity among water recreators and used several assumptions and variations to calculate the total cost of illness per water recreator. This work also identified relationships between recreational water exposures and COI. Additionally, the estimate of the economic burden due to recreational waterborne illness in untreated surface water was the first attempt in determining cost at a national level and will have a significant impact on future public health studies on water recreation and health.

A range of illness severity exists among water recreators who develop symptoms. Most symptoms are mild and self-limiting, but some water recreators develop illnesses severe enough to require use of the healthcare system or time away from regular daily activities or work. The severity of symptoms may be useful in the future for identifying new thresholds for illness outcomes among water recreators. Evidence from this analysis indicates that the current definition of illness includes some individuals with low severity and excludes some individuals with high severity. By examining the relationship between severity and water exposures, one can determine where the difference in severity can maximized, and where the potential new illness threshold should be placed. Water quality was associated with increased severity of illnesses, yet exposures such as swallowing water were more strongly associated with severity. In the future, targeted education may be necessary to help reduce risky behaviors (swallowing water, head immersion) in order to avoid more severe illnesses among water recreators. Severity, not just the occurrence of illness, potentially has public health importance and may be useful for guiding future epidemiology studies of water recreation and health.

Sporadic illnesses attributable to water recreation are expected to cost between $500 and $2,000 per 1,000 water recreators within the context of the NEEAR and CHEERS studies. These cost estimates are sensitive to ways of valuing lost productivity, which has the most significant impact on the total cost of illness. Future studies are necessary to determine the most suitable assumptions for determining the valuation of lost productivity due to illness as a result of environmental exposures. Increased costs were noted among all water recreators with greater water contact, implying that increased water exposure is associated with a higher COI. Assessing costs per 1,000 water recreators, rather than costs per individual with symptoms, provides relevant information for adequately assessing burden. Beach cleanup efforts can be time-consuming and costly. However, a metric such as the cost of illness per 1,000 water recreators can help prioritize locations with a higher burden, where illness is either common or frequently severe. By prioritizing such locations for cleanup, the overall burden due to recreational waterborne illness can be expected to decrease.

The total economic burden due to recreational waterborne illness was estimated to cost between $3.1 billion and $4.7 billion annually. These costs are only a fraction of the costs of foodborne illness, estimated to be between $51 billion and $77 billion each year (Scharff, 2011). These findings can have a significant impact on the cost-benefit analyses for prevention or mitigation strategies in the future. Since 2001 approximately $130 million has been allocated towards beach-water protection programs (US EPA, 2014), only a fraction of the estimated economic burden due to recreational waterborne illness. Approximately 70% of the total economic burden was among the subset who sought medical care either at a physician office or ED. These moderate illnesses are associated with a much larger burden than illnesses that are more severe and life-threatening that result in hospitalization. While the per-case cost of hospitalizations was much higher than the per-case cost of doctor or ED visits, illnesses that result in hospitalization are very rare and only contribute to approximately 6% of the total economic burden.

This overall estimate of the national burden due to recreational waterborne illness was primarily based off of epidemiology studies that were conducted in waters impacted by fecal pollution. Therefore, the estimates of the risks attributable to water recreation may not be generalizable for all surface water in the United States. It is expected that the incidence of illness would be close to zero in pristine waters, not impacted by human sewage. Therefore, the projected total number of recreational waterborne illnesses that occur annually in the United States may be overstated, and thus the estimated economic burden due to recreational waterborne illness could also be overestimated as well. Nevertheless, this economic burden assessment provides some important groundwork in which we can continue to build a more appropriate estimate of the economic burden associated with recreational waterborne illness in the future.

In light of these analyses, several data gaps have been highlighted. Illness severity may be a promising metric (opposed to the occurrence of illness) for guiding future epidemiology and risk assessment studies. Also, adequate active surveillance systems are not in place for assessing illnesses among water recreators and may be necessary to get a more accurate representation of the total number of recreational waterborne illnesses in the United States. Currently, I can only at best, come up with an estimate of the total number of recreational waterborne illnesses using several distinct data sources. These sources include epidemiology studies, estimates of the proportion of the United States participating in water recreation annually (Cordell, 2012) and limited outbreak data collected via passive surveillance (Dziuban et al., 2006; Hlavsa et al., 2011; Hlavsa et al., 2014; Yoder et al., 2004; Yoder et al., 2008). Better surveillance tools targeted at identifying illnesses due to water recreation are needed to obtain a better estimate of the overall burden due to recreational waterborne illness. While surveillance would provide a more accurate estimate of the number of recreational waterborne illnesses, these types of systems are costly. The benefit of an active surveillance system may not outweigh the potential costs. In order to reduce the costs of implementing such a system, incorporating waterborne illness surveillance into preexisting surveillance systems, such as FoodNet, may be beneficial. However, further research into the practicality and plausibility of this is necessary.

These analyses were not only the first to estimate economic burden due to surface-water recreation, but also the first to estimate an approximation of the total number of annual water recreators, the number of water recreation events, as well as the total number of recreational waterborne illnesses on a national scale. The findings from these analyses are expected to help advance to field of environmental epidemiology as it pertains to water recreation and health.

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APPENDICES

APPENDIX A

Severity of illness

A. **Epidemiology Studies**

1. **National Epidemiologic and Environmental Assessment of Recreational Water (NEEAR)**

The NEEAR study was a prospective cohort conducted by the EPA to help develop new or revised recreational water criteria. Since the recreational water criteria set by EPA are for exposures related to swimming, the NEEAR study enrolled swimmers in order to determine a relationship between FIB and illness. The study was conducted on weekends and holidays during the summer at seven marine and freshwater US beaches in six different states impacted by wastewater treatment plants (WWTP) in 2003, 2004, 2005, and 2007(Wade et al., 2008; Wade et al., 2010a).

Individuals directly exposed to beach water by swimming as well as those who had no contact with water were recruited to partake in the study. Recruited participants first completed an enrollment interview, followed by an exit interview, which occurred after recreation. Study participants were asked about water exposure at the beach, demographics, GI risk factors such as eating undercooked meat, as well as information regarding underlying medical conditions. A follow-up phone interview was conducted 10–12 days after water recreation and inquired about health symptoms since the beach visit. An adult over the age of 18 was responsible for responding to questions pertaining to themselves and other members of their household who were enrolled in the study. Approximately 27,373 participants were enrolled in the NEEAR study (Wade et al., 2008; Wade et al., 2010a).

Since the goal of the NEEAR study was to establish the exposures experienced by swimmers, it was important to utilize a rigorous water sampling approach. At each beach, samples were taken at three separate transects at 8:00 a.m., 11:00 a.m., and 3:00 p.m. Samples were taken at two different depths along the transects; shin depth (0.3 meters) and waist depth (1 meter). Overall, there were 18 total samples taken per day at each of the beaches studied. All samples were analyzed for indicators of fecal contamination, specifically for enterococcus, by culture (by EPA Method 1600) and by qPCR (Wade et al., 2008; Wade et al., 2010a).

2. **Chicago Health Environmental Exposure and Recreation Study (CHEERS)**

CHEERS was also a prospective cohort, and the study methods, including the survey instruments, were developed using NEEAR study documents as a template (provided by

T. Wade, PI of the NEEAR study). However, CHEERS was conducted during the summer from 2007 to 2009 at 39 distinct different locations in and around Chicago and focused entirely on limited-contact recreation that includes fishing, motor boating, canoeing, rowing, and kayaking (Dorevitch et al., 2012a).

The CHEERS had three target study populations from which to recruit. Groups of participants were recruited to be part of either the GUW exposure group, indicating contact with Lake Michigan, inland lakes, or rivers the CAWS group, indicating contact with the Chicago River, which is directly impacted by two WWTPs; and the unexposed (UNX) group that consisted of participants who did not engage in any water activity. Similar to the NEEAR study, participants completed a series of interviews both in the field and over the phone. The field interviews collected data pertaining to water exposure, as well as information regarding comorbidities and other high-risk exposures. The CHEERS had three follow-up telephone interviews at days 2, 5, and 21, which collected data on the development of symptoms as well as symptom severity. However, unlike the NEEAR study, each individual recruited was responsible for responding to their own set of surveys, as opposed to having one member of the household being responsible for answering for all of the household members. A total of 11,297 participants were enrolled in CHEERS, for whom telephone follow-up was available (Dorevitch et al., 2012a).

Water samples for CHEERS were collected for fecal indicators every 2 hours and every 6 hours for pathogens during participant recruitment at designated access points. Similar to the NEEAR study, ancillary information about the sampling site was also collected, including information about the weather conditions and the presence of boats in the water. Samples collected for fecal indicators were analyzed for enterococci and *E. coli* using culture methods (EPA Method 1600 and EPA Method 1603 respectively), for all three sampling years, and for enterococci by qPCR in 2009. Additionally, samples were also analyzed for male-specific and somatic coliphages, which are viral indicators of fecal pollution, by EPA Method 1602 for all three sampling years. In addition to fecal indicators, pathogens such as *Giardia* and *Cryptosporidium* were analyzed according to EPA Method 1623, among several others throughout the study period (Dorevitch et al., 2012a).

B. <u>Severity Metrics</u>

A total of 511 CHEERS participants only had GI symptoms, while the other 459 participants had GI as well as other non-enteric symptoms. Those with GI and other symptoms were statistically significantly more likely to respond to their illness, compared to those only with GI illness (TABLE XXXVII).

TABLE XXXVII

FREQUENCY OF INDIVIDUAL RESPONSE TO ILLNESS AMONG CHEERS PARTITIONS ONLY WITH GI ILLNESS COMPARED TO THOSE WITH GI ILLNESS AND OTHER NON-ENTERIC SYMPTOMS

	Only GI (n=511)		GI and Other Symptoms (n=459)			
	%	N	%	N	χ^2(df=1)	p-value [a]
Stay home from work/school	42.3	216	52.7	242	10.6	<.01
Seek Medical Care	12.3	63	22.2	102	16.7	<.01
OTC medication use	47.4	242	64.9	298	30.2	<.01
Prescription medication use	5.7	29	10.9	50	8.8	<.01
ED/hospitalization	1.0	5	3.1	14	5.4	0.02

[a] Comparisons evaluated using Chi-square test

The duration of GI illness was determined using the start and end dates indicated during telephone follow-up for CHEERS participants. Participants in NEEAR provided the start date of their symptoms and the length of their illness. With this information, a symptom end date was calculated. It was assumed the durations of the four symptoms could overlap or be several days after the end of another symptom. Using two arrays, first the symptom with the earliest start date was identified, then the next symptom with the second earliest start date was identified. This second symptom only contributed to the duration of GI illness if its start date was no more than two days following the first symptom's end date (Cheng, 2006). This process was repeated until all potential symptoms were considered, and ensured no large gaps between symptoms existed, which would ultimately cause an overestimation of the duration of illness. Using this methodology, CHEERS participants with less than 24 hours of illness, were recorded as a duration of 0 days. The NEEAR participants could have interpreted less than 24 hours of illness as either 0 or 1 day of illness, based on how the question was worded. Therefore, all those reporting an illness duration of 0, were increased by 1, in order to aid in the comparability of the two studies. Figure 12 describes an example of a participant with all four GI symptoms. This participant's duration of GI illness would be three days, and the duration of diarrhea symptoms would not be included in their duration of GI illness due to recreation, since it is two or more days past the end date of the other symptoms.

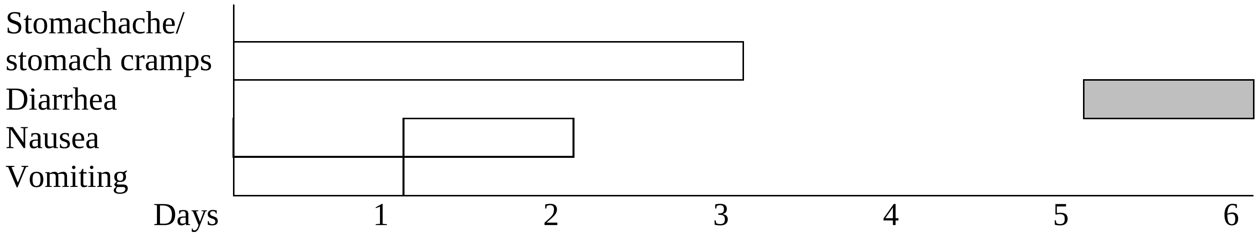

Figure 12. Example duration of GI illness for a study participant. [a]

[a] White boxes contribute to the duration of GI illness, while grey boxes, which correspond to symptoms occurring ≥2 days after the end date of another symptom, would not be included in the duration of GI illness

In several cases, CHEERS participants were still experiencing symptoms on the day of the follow-up interview, and therefore were unable to indicate an end date for their symptoms at that time. In some cases, an end date could be established by information obtained in a following phone call. However, there were several cases in which there is no reported symptom end date. The duration of GI illness was not calculated for participants without end dates. Using an imputed end date, such as the date of the appropriate telephone follow-up interview, could potentially have overestimated the duration of GI illness.

In CHEERS, 181 individuals were missing key information to calculate the duration of GI illness. Participants in CHEERS with GI illness and an incomplete duration of GI illness either did not know the start date of the illness, provided a start date that occurred prior to their date of recreation, or never indicated an end date for their symptoms. Missing end dates can either be due to incomplete telephone follow-up, or having symptoms resolved between phone calls. Each phone call only captured symptoms that began since the previous phone call. A few demographic and severity variables were used to compare CHEERS participants with incomplete duration information to those with complete duration information (TABLE XXVIII). Demographic variables were similar between the two groups; however individual responses to illness were more commonly reported among the group with complete information for calculating the duration of illness compared to those with incomplete information for the calculation of the duration of GI Illness.

In the NEEAR study, participants directly indicated the length of the duration of each reported symptom. Only 22 participants were missing the duration of GI illness. These participants either reported symptoms, but no length of duration, or they did not know the start date of their illness. The start date was a key variable in determining the total duration of illness.

TABLE XXXVIII

COMPARISON OF THOSE WITH COMPLETE DURATION INFORMATION AND THOSE WHO ONLY INDICATE A START DATE USING THE χ^2 TEST, T-TEST, OR FISHER'S EXACT TEST WHERE SPECIFIED

	Proportion with Complete Duration Information **(n=789)**	Proportion with Incomplete Duration Information **(n=181)**	p-value
Male (%)	47.5	42.8	0.25
Age (%)			0.42
0–10	5.7	4.4	
11–-64	91.9	94.5	
≥65	2.4	1.1	
% Black	14.2	18.1	0.18
% Water Recreators	66.7	61.0	0.15
% in CAWS	51.9	47.8	0.42
Responses to Illness (%)			
Missed work/school	32.4	19.9	0.001
Seek Care	10.3	3.3	0.003
OTC Medication	38.6	25.4	0.001
Prescription	4.8	0.5	0.008 [a]
Hospitalized/ED	1.6	0	0.23 [a]

[a] Fisher's Exact Test

1. **<u>Comparison between severity metrics</u>**

The duration of illness is greater among participants who responded to their illness by either staying home from work or school or utilizing the healthcare system, for both CHEERS and NEEAR participants. In general the duration of GI illness is statistically significantly greater among participants reporting more severe outcomes (TABLE XXIX). Similar to the duration of GI illness, the average number of GI symptom-days is larger among participants responding to their illness including staying home from work or school or utilizing the healthcare system (TABLE XL).

TABLE XXXIX
MEAN DURATION OF GI ILLNESS AND RESPONSES TO ILLNESS AMONG CHEERS AND NEEAR PARTICIPANTS

	CHEERS Participants			NEEAR Participants			
	Yes	**No**	**p-value** [a]		**Yes**	**No**	**p-value** [a]
Stay home from work or school	3.0	1.9	<.01	Stay home	3.6	2.7	<.01
				Stop daily activities	2.8	<.01	<.01
				Cause others to miss work	4.0	<.01	<.01
Seek Medical Care	4.4	2.0	<.01	Call	4.2	2.5	<.01
				Visit	4.5	2.4	<.01
OTC medication use	3.1	1.7	<.01		2.9	2.4	<.01
Prescription medication	4.1	2.2	0.03		4.8	2.5	<.01
ED/ Hospitalization	4.7	2.3	0.04		4.4	2.5	<.01

[a] Non-parametric, Wilcoxon-Mann-Whitney test

TABLE XL
GI SYMPTOM-DAYS AND SEVERITY INDICATORS AMONG CHEERS AND NEEAR PARTICIPANTS

	CHEERS Participants					NEEAR Participants					
	Yes		**No**		**p-value** [a]		**Yes**		**No**		**p-value** [a]
	Mean	Mean Score	Mean	Mean			Mean	Mean Score	Mean	Mean Score	
Stay home from work or school	5.7	360.5	4.0	318.4	<.01	Stay home	8.4	489.9	5.8	360.4	<.01
						Stop daily activities	6.4	1,015.5	5.3	929.2	<.01
						Cause others to miss work	10.5	1,319.4	5.6	952.1	<.01
Seek Medical Care	8.3	425.4	4.1	322.5	<.01	Call	10.0	1,312.5	5.5	938.3	<.01
						Visit	10.0	1,332.1	5.6	936.3	<.01
OTC medication use	6.2	367.0	3.3	308.2	<.01		6.5	1,068.4	5.2	888.0	<.01
Prescription medication	8.8	394.3	4.4	331.4	0.05		10.9	1,372.7	5.5	938.6	<.01
ED/ Hospitalization	9.4	464.9	4.5	332.8	0.02		10.7	1,318.9	5.7	957.6	<.01

[a] Non-parametric, Wilcoxon-Mann-Whitney test

APPENDIX A (continued)

C. Time to Illness Comparison

TABLE XLI
COMPARISON OF CRUDE RRS FOR CHEERS AND NEEAR PARTICIPANTS DEVELOPING ILLNESS WITHIN 0–12 DAYS AND 0–3 DAYS POST-RECREATION

		GI 0-12 days post recreation				GI 0-3 days post recreation			
		Severity Indicators		Duration of GI illness	GI Symptom-Days	Severity Indicators		Duration of GI illness	GI Symptom-Days
		Any versus none	Severe versus Mild or Moderate	≥2 days	≥4 symptom-days	Any versus none	Severe versus Mild or Moderate	≥2 days	≥4 symptom-days
Incidental-Contact (CHEERS)	Water recreators versus Non Water recreators	1.07 (0.94,1.15)	0.81 (0.71,0.92)	1.03 (0.92,1.14)	0.93 (0.77,1.12)	0.92 (0.81,1.02)	0.95 (0.8,1.2)	1.18 (0.81,1.7)	1.09 (0.74,1.6)
	CAWS versus GUW	0.94 (0.86,1.04)	0.90 (0.76,1.07)	0.93 (0.83,1.05)	0.95 (0.77,1.18)	0.97 (0.85,1.12)	0.86 (0.7,1.1)	0.94 (0.7,1.3)	0.85 (0.57,1.25)
	Swallow water versus Non Swallow water	1.09 (0.91,1.31)	1.42 (1.10,1.85)	1.01 (0.78,1.29)	1.66 (1.08,2.57)	1.14 (0.92,1.42)	1.35 (0.97,1.91)	1.04 (0.79,1.43)	2.0 (1.21,3.31)
Full-Contact (NEEAR)	Water recreators versus Non Water recreators	1.02 (0.94,1.10)	0.91 (0.65,1.32)	0.88 (0.73,1.08)	1.28 (1.13,1.46)	1.02 (0.91,1.14)	0.88 (0.52,1.48)	0.77 (0.61,0.97)	0.91 (0.81,1.01)
	Swallow water versus Non Swallow water	1.03 (0.92,1.14)	1.25 (0.74,2.12)	1.01 (0.75,1.36)	1.30 (1.08,1.57)	0.97 (0.84,1.13)	1.15 (0.57,2.34)	1.04 (0.74,1.48)	1.12 (0.97,1.29)

D. Confounders and Effect Modifiers

TABLE XLII
POTENTIAL CONFOUNDERS AND EFFECT MODIFIERS

CHEERS	**NEEAR**
Age **(C, EM)** <18 18–64 (referent group) ≥65	Age **(C, EM)** <18 18–64 (referent group) ≥65
Gender **(C)**	Gender **(C)**
Race (black versus not black) **(C)**	Race (black versus not black) **(C)**
Recent contact with dog or cat **(C)**	Recent contact with any animal **(C)**
Recent contact with other animal **(C)**	
Recently ate raw fish or shell fish **(C)**	Recently ate raw fish **(C)**
Recently ate raw meat **(C)**	Recently ate raw meat **(C)**
Recently ate hamburger **(C)**	--
Recently ate raw/runny eggs **(C)**	Recently ate runny eggs **(C)**
Recently ate packaged sandwich **(C)**	--
Chronic GI Condition **(C, EM)**	Chronic GI Condition **(C, EM)**
Preexisting respiratory condition **(C, EM)**	Chronic asthma **(C, EM)**
Preexisting diabetes **(C, EM)**	--
Prone to infection **(C, EM)**	--
--	Chronic skin condition **(C, EM)**
Comorbid (combination of prone to infection, preexisting GI condition, and preexisting diabetes) **(C, EM)**	Any chronic illness (GI, Skin, Respiratory) **(C, EM)**
Previous contact to someone with respiratory symptoms **(C)**	--
Recent contact to someone with GI symptoms **(C)**	Contact with persons with GI symptoms **(C)**
Recent contact to someone with eye symptoms **(C)**	--
Antibiotic use in past 7 days **(C)**	--
Recent antacid use **(C)**	--
Average daily bowel movements **(C, EM)**	--
Washing hands before eating/drinking after water recreation**(C)**	Washing hands before eating after playing in sand or with algae **(C)**
Frequency of recreation at location of enrollment (0-365) **(C)** 0 (referent group) 1-4 times 5-19 times ≥20 times	How many times did you visit this beach over the summer? **(C)** 0-1 times 2-5 times ≥5 times
--	Dug into the sand **(C)**

E. <u>Hierarchical Modeling</u>

Recall that CHEERS recruited participants from 39 different Chicago area locations. These locations can be grouped into seven different categories, based on geographic location, and include CAWS-North, CAWS-South, CAWS-central, Inland Lake, Lake Michigan, Non-CAWS River, and other. In general, participants recreating in CAWS waters potentially were exposed to a greater amount of FIB because more than 90% of the flow during dry weather on the CAWS is non-disinfected wastewater. The NEEAR study recruited from seven different beaches. The four freshwater beaches were along Lake Michigan and Lake Erie, and the three marine beaches were from locations in Rhode Island and Alabama (Wade et al., 2010a).

In both studies, there were participants who were part of the same family or household. In CHEERS, less than 5% of participants enrolled from the same family, but there were 4.6% of participants who participated in the study twice, while 1.1% participated in the study more than twice. In the NEEAR study, approximately 48% of all households only contained 1 participant, while 44% of households contained 2–4 participants. There was one household that contained 11 participants.

In general, individuals from the same neighborhood are more similar to one another than people from other neighborhoods. People from the same neighborhood often share similar cultural, economic, or political similarities (Merlo et al., 2005). Additionally, participants who are part of the same family or household also share the same SES characteristics. In the case of participants from the CHEERS and NEEAR studies, it was hypothesized that people recruited at the same location would share characteristics similar to those living within the same neighborhood, which may affect the reporting of the severity of illness.

A hierarchical modeling approach was applied to this analysis since there may be unmeasured factors present among participants at each recruitment location or household that may not be accounted for using traditional logistic regression. Correlation within clusters violates the independence assumptions made by traditional regression approaches, such as logistic regression (Hubbard et al., 2010). Cluster analysis may also provide an unbiased estimate of the standard errors for regression parameters (Merlo et al., 2005). Several hierarchical modeling approaches are available for analyzing the data. For this analysis, a random intercept model was chosen to evaluate clusters. Random intercept models estimate the between-cluster variation, yet assume that the errors are normally distributed.

TABLE XLIII

RANDOM INTERCEPT MODEL FOR THE EFFECT OF LOCATION GROUP (CLUSTERS=7) ON CHEERS PARTICIPANTS [a]

		Intercept Only		Swallow Water		Face Wet		Multi-Level	
		ICC [d]	SE (95%)	ICC [d]	SE (95%)	ICC [d]	SE (95%)	ICC [d]	SE (95%)
Severity of GI Illness	**Severity Indicators**								
	Any response versus none [b]	0.006	0.008 (3.4x10^{-4}, 0.089)	6.9x10^{-7}	4.8x10^{-5} (2.36x10^{-66}, 1.0)	8.2x10^{-7}	5.9x10^{-5} (2.3x10^{-68}, 1.0)	3.2x10^{-7}	2.1x10^{-5} (1.0x10^{-64}, 1.0)
	Severe response versus moderate or no response [c]	0.008	0.009 (8.7x10^{-4}, 0.069)	4.8x10^{-7}	3.2x10^{-5} (1.61x10^{-64}, 1.0)	5.9x10^{-7}	3.8x10^{-4} (1.5x10^{-61}, 1.0)	2.5x10^{-7}	1.7x10^{-5} (2.0x10^{-64}, 1.0)
	Duration of GI Illness								
	≥2 days	1.4x10^{-7}	4.2x10^{-6} (3.9x10^{-33}, 1.0)	7.0x10^{-8}	4.8x10^{-6} (7.4x10^{-67}, 1.0)	1.4x10^{-7}	7.4x10^{-6} (1.6x10^{-51}, 1.0)	4.6x10^{-8}	3.2x10^{-6} (2.3x10^{-67}, 1.0)
	GI Symptom-Days								
	≥4 symptom-days (participants meeting case definition)	5.3x10^{-8}	3.6x10^{-06} (3.5x10^{-66}, 1.0)	1.6x10^{-7}	1.1x10^{-5} (8.3x10^{-65}, 1.0)	2.1x10^{-7}	1.4x10^{-5} (1.5x10^{-63}, 1.0)	1.5x10^{-7}	7.4x10^{-6} (1.5x10^{-49}, 1.0)
	≥4 symptom-days (all participants)	6.1x10^{-14}	1.31x10^{-8} (0, 1.0)	3.3x10^{-7}	6.1x10^{-6} (4.3x10^{-23}, 1.0)	1.1x10^{-7}	7.6x10^{-6} (1.5x10^{-65}, 1.0)	3.0x10^{-7}	8.1x10^{-6} (2.2x10^{-30}, 1.0)
	GI Severity Score								
	Score of ≥6 (participants meeting case definition)	0.015	0.016 (0.002, 0.12)	2.2x10^{-7}	1.5x10^{-5} (4.0x10^{-66}, 1.0)	2.7x10^{-7}	1.2x10^{-5} (2.5x10^{-44}, 1.0)	5.1x10^{-8}	3.6x10^{-6} (1.3x10^{-67}, 1.0)
	Score of ≥6 (all participants)	0.024	0.021 (0.004, 0.13)	2.8x10^{-7}	1.9x10^{-5} (6.04x10^{-65}, 1.0)	9.3x10^{-7}	3.0x10^{-5} (7.9x10^{34}, 1.0)	2.5x10^{-7}	1.7x10^{-5} (5.2x10^{-65}, 1.0)
Severity of Any Illness	**Severity Indicators**								
	Any response versus none [b]	0.002	0.002 (1.8x10^{-4}, 0.021)	1.7x10^{-4}	0.002 (1.2x10^{-14}, 1.0)	0.002	0.003 (8.9x10^{-5}, 0.038)	0.002	0.003 (7.7x10^{-5}, 0.038)
	Severe response versus moderate or no response [c]	0.008	0.007 (0.002, 0.043)	0.002	0.0026 (6.9x10^{-5}, 0.037)	1.1x10^{-4}	0.002 (2.5x10^{-21}, 1.0)	0.001	0.003 (4.0x10^{-5}, 0.048)
	Total Symptom-Days								
	≥4 symptom-days (participants meeting case definition)	5.0x10^{-14}	1.0x10^{-8} (0, 0)	1.2x10^{-6}	2.5x10^{-5} (6.6x10^{-24}, 1.0)	1.4x10^{-6}	2.2x10^{-5} (1.4x10^{-20}, 1.0)	5.6x10^{-7}	1.4x10^{-4} (1.2x10^{-28}, 1.0)
	≥4 symptom-days (all participants)	2.5x10^{-7}	4.2x10^{-7} (8.2x10^{-22}, 1.0)	8.4x10^{-8}	2.8x10^{-6} (2.6x10^{-36}, 1.0)	2.2x10^{-12}	8.4x10^{-8} (0, 1.0)	3.5x10^{-7}	6.2x10^{6} (4.3x10^{-22}, 1.0)

[a] Controlling for confounders (See Section Fa)
[b] Responded to illness by either staying home from work or school, taking OTC or prescription medication, contacting an HCP or visiting an ED or being admitted to the hospital versus those who did none of these
[c] Responded to illness by either staying home from work or school, taking prescription medication, contact with an HCP or visiting an ED/being admitted to the hospital versus those only taking OTCs or who did none of these
[d] Interclass Correlation

APPENDIX A (continued)

TABLE XLIV

RANDOM INTERCEPT MODEL FOR THE EFFECT OF START LOCATION (CLUSTERS=37) ON CHEERS PARTICIPANTS [a b]

		Intercept Only		Swallow Water		Face Wet		Multi-Level	
		ICC [e]	SE (95%)	ICC [e]	SE (95%)	ICC [e]	SE (95%)	ICC [e]	SE (95%)
Severity of GI Illness	**Severity Indicators**								
	Any response versus none [c]	1.8x10^{-6}	5.7x10^{-5} (1.4 x10^{-33}, 1.0)	3.3x10^{-7}	1.1x10^{-5} (1.2x10^{-34}, 1.0)	1.8x10^{-7}	5.8x10^{-6} (5.8x10^{-35}, 1.0)	1.7x10^{-7}	5.8x10^{-6} (1.3x10^{-36}, 1.0)
	Severe response versus moderate or no response [d]	0.005	0.011 (4.5x10^{-5}, 0.34)	1.5x10^{-7}	4.8x10^{-6} (1.5x10^{-35}, 1.0)	1.1x10^{-7}	3.7x10^{-6} (4.5x10^{-37}, 1.0)	1.1x10^{-7}	3.7x10^{-6} (1.0x10^{-35}, 1.0)
	Duration of GI Illness								
	≥2 days	1.2x10^{-6}	3.9x10^{-5} (2.9x10^{-34}, 1.0)	4.4x10^{-7}	1.4x10^{-5} (1.0x10^{-36}, 1.0)	5.7x10^{-7}	2.0x10^{-5} (3.0x10^{-36}, 1.0)	1.5x10^{-6}	5.2x10^{-5} (1.9x10^{-35}, 1.0)
	GI Symptom-Days								
	≥4 symptom-days (participants meeting case definition)	3.7x10^{-7}	1.2x10^{-5} (2.0x10^{-34}, 1.0)	5.5x10^{-7}	1.9x10^{-5} (6.0x10^{-36}, 1.0)	5.6x10^{-7}	1.8x10^{-5} (7.1x10^{-35}, 1.0)	5.5x10^{-7}	1.9x10^{-5} (3.7x10^{-36}, 1.0)
	≥4 symptom-days (all participants)	3.7x10^{-3}	5.77x10^{-3} (1.7x10^{-4}, 0.075)	5.1x10^{-7}	1.1x10^{-5} (8.1x10^{-25}, 1.0)	8.3x10^{-7}	1.2x10^{-5} (5.5x10^{-19}, 1.0)	8.6x10^{-7}	1.3x10^{-5} (8.8x10^{-20}, 1.0)
	GI Severity Score								
	Score of ≥6 (participants meeting case definition)	0.009	0.018 (1.7x10^{-4}, 0.32)	3.6x10^{-7}	1.4x10^{-5} (1.0x10^{-36}, 1.0)	2.3x10^{-7}	7.6x10^{-6} (2.2x10^{-35}, 1.0)	2.6x10^{-7}	9.1x10^{-6} (7.3x10^{-37}, 1.0)
	Score of ≥6 (all participants)	**0.05**	0.03 (0.017, 0.15)	1.4x10^{-6}	4.8x10^{-5} (1.6x10^{-36}, 1.0)	8.5x10^{-7}	3.3x10^{-5} (5.9x10^{-40}, 1.0)	4.1x10-7	1.4x10^{-5} (1.4x10^{-35}, 1.0)
Severity of Any Illness	**Severity Indicators**								
	Any response versus none [c]	**0.005**	0.004 (9.1x10^{-5}, 0.026)	0.006	0.006 (1.1x10^{-3}, 3.9x10^{-2})	0.007	0.006 (0.001, 0.036)	0.007	0.006 (0.001, 0.036)
	Severe response versus moderate or no response [d]	**0.011**	0.007 (0.003, 0.039)	0.006	0.006 (0.001, 0.035)	0.007	0.006 (1.1x10^{-3}, 0.038)	0.007	0.006 (0.001, 0.036)
	Total Symptom-Days								
	≥4 symptom-days (participants meeting case definition)	2.2x10^{-6}	3.1x10^{-5} (1.3x10^{-18}, 1.0)	3.0x10^{-3}	0.008 (2.1x10^{-5}, 0.3)	2.8x10^{-3}	0.002 (1.9x10^{-5}, 0.3)	2.1x10^{-3}	0.007 (3.2x10^{-6}, 0.57)
	≥4 symptom-days (all participants)	**4.5x10^{-3}**	3.7x10^{-3} (9.1x10^{-4}, 0.022)	3.1x10^{-3}	4.9x10^{-3} (1.3x10^{-4}, 0.068)	5.2x10^{-3}	5.8x10^{-3} (5.7x10^{-4}, 0.045)	0.005	6.0x10^{-3} (6.0x10^{-4}, 0.046)

[a] Controlling for confounders (See Section Fa)
[b] Bold and underlined are significant at p<.05
[c] Responded to illness by either staying home from work or school, taking OTC or prescription medication, contacting an HCP or visiting an ED or being admitted to the hospital versus those who did none of these
[d] Responded to illness by either staying home from work or school, taking prescription medication, contact with an HCP or visiting an ED/being admitted to the hospital versus those only taking OTCs or who did none of these
[e] Interclass Correlation

APPENDIX A (continued)

TABLE XLV
RANDOM INTERCEPT MODEL FOR THE EFFECT OF BEACH LOCATION (CLUSTERS=7) ON NEEAR PARTICIPANTS [a b]

		Intercept Only		Any Contact		Swallow Water		Digging in Sand		Multi-Level	
		ICC [e]	SE (95%)	ICC [e]	SE (95%)	ICC [e]	SE (95%)	ICC [e]	SE (95%)	ICC [e]	SE (95%)
Severity of GI Illness	**Severity Indicators**										
	Any response versus none [c]	**0.012**	0.01 (0.003, 0.055)	**0.011**	0.009 (0.002, 0.053)	0.001	0.005 (1.6x10^{-6}, 0.52)	0.012	0.009 (0.003, 0.055)	**0.019**	0.018 (0.005, 0.088)
	Severe response versus moderate or no response [d]	**0.039**	0.032 (7.4x10^{-4}, 0.18)	**0.037**	0.032 (0.007, 0.18)	0.025	0.031 (0.002, 0.23)	**0.039**	0.032 (0.007, 0.18)	**0.041**	0.042 (0.005, 0.26)
	Duration of GI Illness										
	≥2 days	0.015	0.014 (0.002, 0.087)	0.011	0.012 (0.001, 0.092)	0.012	0.014 (0.001, 0.12)	0.013	0.013 (0.002, 0.088)	0.014	0.015 (0.002, 0.11)
	GI Symptom-Days										
	≥4 symptom-days (participants meeting case definition)	**0.022**	0.015 (0.006, 0.08)	**0.021**	0.014 (0.006, 0.075)	**0.025**	0.018 (0.006, 0.099)	**0.023**	0.015 (0.006, 0.081)	0.022	0.016 (0.005, 0.09)
	≥4 symptom-days (all participants)	0.016	0.01 (0.005, 0.053)	0.013	0.008 (0.004, 0.045)	0.007	0.005 (0.001, 0.032)	0.008	0.006 (0.002, 0.034)	0.009	0.007 (0.002, 0.037)
	GI Severity Score										
	Score of ≥6 (participants meeting case definition)	0.087	0.057 (0.023, 0.28)	0.022	0.021 (0.003, 0.13)	**0.021**	0.021 (0.003, 0.14)	0.087	0.057 (0.023, 0.28)	**0.021**	0.021 (0.003, 0.14)
	Score of ≥6 (all participants)	0.081	0.052 (0.022, 0.26)	0.081	0.052 (0.022, 0.23)	**0.035**	0.029 (0.007, 0.16)	0.053	0.053 (0.023, 0.26)	**0.037**	0.03 (0.007, 0.17)
Severity of Any Illness	**Severity Indicators**										
	Any response versus none [c]	0.0084	0.007 (0.002, 0.039)	0.009	0.007 (0.002, 0.041)	**0.015**	0.012 (0.003, 0.069)	0.009	0.007 (0.002, 0.041)	**0.013**	0.011 (0.003, 0.065)
	Severe response versus moderate or no response [d]	0.009	0.007 (0.002, 0.038)	0.009	0.007 (0.002, 0.038)	0.003	0.004 (2.1x10^{-4}, 0.033)	0.009	0.007 (0.002, 0.038)	**0.008**	0.007 (0.001, 0.044)
	Total Symptom-Days										
	≥4 symptom-days (participants meeting case definition)	0.0095	0.002 (2.0x10^{-5}, 0.044)	9.3x10^{-4}	0.002 (1.8x10^{-5}, 0.046)	6.1x10^{-4}	0.002 (2.4x10^{-7}, 0.6)	0.001	0.002 (2.7x10^{-5}, 0.041)	5.8x10^{-4}	0.002 (2.3x10^{-7}, 0.59)
	≥4 symptom-days (all participants)	**0.0057**	0.004 (0.002, 0.021)	**0.005**	0.003 (0.001, 0.018)	**0.0025**	0.003 (3.4x10^{-4}, 0.018)	**0.005**	0.003 (0.001, 0.019)	**0.003**	0.003 (4.2x10^{-4}, 0.018)

[a] Controlling for confounders (See Section Fa)
[b] Bold and underlined are significant at p<.05
[c] Responded to illness by either staying home from work or school, taking OTC or prescription medication, contacting an HCP or visiting an ED or being admitted to the hospital versus those who did none of these
[d] Responded to illness by either staying home from work or school, taking prescription medication, contact with an HCP or visiting an ED/being admitted to the hospital versus those only taking OTCs or who did none of these
[e] Interclass Correlation

F. Adjusted Odds Ratio Tables

1. Binary severity outcome, binary exposure

TABLE XLVI

AOR FOR THE RELATIONSHIP BETWEEN SEVERITY AND SWALLOWING WATER AMONG CHEERS WATER RECREATORS

	Severity Category	**N** [a]	**Unadjusted OR** (95% CI)	**Adjusted OR** (95% CI)	**Adjusted OR** p-value	**Wald χ^2** p-value	**HL GOF $\chi 2$** [b] (p-value)	**Additional Confounders** [c]
Severity of GI Illness	**Responses to Illness**							
	Any response versus none [d]	455/637 (71.5%)	1.41 (0.63, 3.17)	1.55 (0.69, 3.49)	0.29	0.07	2.98 (0.56)	
	Only those with GI	210/329	0.75 (0.25, 2.22)	0.80 (0.27, 2.42)	0.70	0.12	0.39 (0.94)	gender, recent antacid use
	Only those with GI and other conditions	245/307	2.67 (0.61, 11.72)	2.89 (0.65, 12.76)	0.16	0.13	0.03 (0.98)	
	Severe response versus moderate or no response [e]	309/637 (48.5%)	2.19 (1.08, 4.40)	2.19 (1.08, 4.40)	0.03	<.01	0.81 (0.94)	
	Only those with GI	137/329	1.19 (0.40, 3.56)	1.19 (0.40, 3.56)	0.75	0.31	0.53 (0.77)	gender, recent contact with someone with GI symptoms, wash hands before eating/drinking
	Only those with GI and other conditions	172/308	3.21 (1.14, 9.05)	3.21 (1.14, 9.05)	0.03	0.02	0.69 (0.71)	
	Duration of GI Illness							
	≥2 days	360/526 (68.4%)	1.03 (0.46, 2.30)	0.87 (0.38, 2.00)	0.75	0.12	5.32 (0.50)	gender, same water use, recent contact with animals
	GI Symptom-Days							
	≥4 symptom-days (participants meeting case definition)	330/526 (62.7%)	1.34 (0.60, 3.00)	1.14 (0.49, 2.61	0.77	0.04	6.06 (0.30)	gender, same water use, recent contact with animals
	≥4 symptom-days (all participants)	330/7,232 (4.56%)	1.72 (1.07, 2.75)	1.75 (1.09, 2.79)	0.02	<.01	2.22 (0.70)	race, average daily bowel movements
	GI Severity Score							
	Score of ≥6 (participants meeting case definition)	73/637 (11.5%)	1.59 (0.64, 3.96)	1.26 (0.41, 3.40)	0.65	0.14	8.12 (0.15)	Same water use, recently ate hamburger
	Score of ≥6 (all participants)	73/7,473 (1.00%)	2.31 (1.00, 5.38)	2.10 (0.83, 5.29)	0.12	<.01	3.60 (0.61)	race, same water use

APPENDIX A (continued)

AOR FOR THE RELATIONSHIP BETWEEN SEVERITY AND SWALLOWING WATER AMONG CHEERS WATER RECREATORS

Severity of Any Illness	**Severity Indicators**							
	Any response versus none [d]	1,343/2,195 (61.8%)	1.16 (0.79, 1.70)	1.21 (0.81, 1.79)	0.36	<.01	3.24 (0.86)	race, gender, same water use
	Severe response versus moderate or no response [e]	619/2,195 (25.5%)	1.29 (0.86, 1.94)	1.26 (0.83, 1.91)	0.28	<.01	1.26 (0.87)	gender, recently ate raw fish or shellfish
	Total Symptom-Days							
	≥4 symptom-days (participants meeting case definition)	539/1,217 (44.3%)	1.53 (0.95, 2.46)	1.46 (0.90, 2.36)	0.12	0.08	2.91 (0.57)	gender, recent contact with animals
	≥4 symptom-days (all participants)	785/5,884 (10.6%)	2.41 (1.67, 3.48)	2.52 (1.74, 3.66)	<.01	<.01	4.10 (0.39)	same water use

[a] Proportion in the "higher risk" category, out of total n
[b] Failure to reject the null (p>0.05) indicates good model fit
[c] All models controlled for age
[d] Responded to illness by either staying home from work or school, taking OTC or prescription medication, contacting an HCP or visiting an ED or being admitted to the hospital versus those who did none of these
[e] Responded to illness by either staying home from work or school, taking prescription medication, contact with an HCP or visiting an ED/being admitted to the hospital versus those only taking OTCs or who did none of these

APPENDIX A (continued)

TABLE XLVII
AORS FOR THE RELATIONSHIP BETWEEN SEVERITY AND SWALLOWING WATER AMONG NEEAR WATER RECREATORS

	Severity Category	N [a]	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted OR p-value	Wald χ^2 p-value	HL GOF $\chi2$ [b] (p-value)	Additional Confounders [c]
Severity of GI Illness	**Severity Indicators**							
	Any response versus none [d]	861/1,380 (62.4%)	1.07 (0.80, 1.44)	1.01 (0.74, 1.40)	0.93	<.01	5.31 (0.62)	gender, race, recent contact with someone with GI symptoms
	Severe response versus moderate or no response [e]	570/1,380 (41.3%)	1.27 (0.72, 2.24)	1.39 (0.75,2.58)	0.30	0.40	7.6 (0.47)	digging in sand, gender
	Duration of GI Illness							
	≥2 days	764/1,365 (55.9%)	1.01 (0.70, 1.46)	1.22 (0.82, 1.83)	0.34	0.14	5.1 (0.53)	digging in sand, gender
	GI Symptom-Days							
	≥4 symptom-days (participants meeting case definition)	705/1,365 (70.0%)	1.15 (0.86, 1.54)	1.20 (0.87, 1.64)	0.26	0.33	3.78 (0.80)	digging in sand, gender
	≥4 symptom-days (all participants)	708/16,035 (4.32%)	1.32 (1.09, 1.61)	1.40 (1.13, 1.73)	<.01	<.01	5.1 (0.64)	digging in sand, gender, race
	GI Severity Score							
	Score of ≥6 (participants meeting case definition)	119/1,373 (9.15%)	1.52 (0.97, 2.38)	1.21 (0.75, 1.96)	0.44	<.01	6.57 (0.36)	race, digging in sand
	Score of ≥6 (all participants)	126/17,204 (0.73%)	1.84 (1.20, 2.81)	1.53 (0.97, 2.41)	0.06	0.002	4.95 (0.55)	Race, digging in sand
Severity of Any Illness	**Severity Indicators**							
	Any response versus none [d]	2,091/2,902 (72.0%)	1.29 (1.02, 1.62)	1.16 (0.90, 1.48)	0.25	<.01	2.1 (0.95)	digging in sand, gender, comorbid condition
	Severe response versus moderate or no response [e]	1,104/2,902 (38.0%)	1.29 (1.06, 1.58)	1.24 (1.00, 1.55)	0.05	<.01	2.3 (0.94)	gender, race, same water use
	Total Symptom-Days							
	≥4 symptom-days (participants meeting case definition)	1,450/2,714 (71.5%)	1.21 (0.96, 1.51)	1.17 (0.92, 1.49)	0.20	0.03	7.80 (0.25)	gender, digging in sand
	≥4 symptom-days (all participants)	1,693/15,914 (10.2%)	1.39 (1.21, 1.59)	1.33 (1.15, 1.53)	<.01	<.01	0.37 (0.95)	digging in sand

[a] Proportion in the "higher risk" category, out of total n
[b] Failure to reject the null (p>0.05) indicates good model fit
[c] All models controlled for age
[d] Responded to illness by either staying home from work or school, taking OTC or prescription medication, contacting an HCP or visiting an ED or being admitted to the hospital versus those who did none of these
[e] Responded to illness by either staying home from work or school, taking prescription medication, contact with an HCP or visiting an ED/being admitted to the hospital versus those only taking OTCs or who did none of these

TABLE XLVIII

AORS FOR THE RELATIONSHIP BETWEEN SEVERITY AND GETTING THE FACE WET AMONG CHEERS WATER RECREATOR

	Severity Category	N [a]	Unadjusted OR (95% CI)	Adjusted OR		Wald χ^2 p-value	HL GOF $\chi2$ [b] (p-value)	Additional Confounders [c]
				(95% CI)	p-value			
Severity of GI Illness	**Responses to Illness**							
	Any response versus none [d]	455/637 (71.5%)	1.09 (0.70, 1.68)	1.03 (0.67, 1.60)	0.89	0.11	8.8 (0.26)	gender, antacid use, recently ate hamburger
	Severe response versus other response [e]	292/637 (45.9%)	1.21 (0.82, 1.77)	1.32 (0.88, 1.98)	0.81	0.12	1.77 (0.88)	same water use
	Duration of GI Illness							
	≥2 days	360/526 (68.4%)	1.36 (0.85, 2.20)	1.46 (0.88, 2.43)	0.15	0.10	4.86 (0.56)	gender, same water use, recent contact with animals
	GI Symptom-Days							
	≥4 symptom-days (Meet case definition for GI illness)	330/526 (62.7%)	1.33 (0.85, 2.09)	1.20 (0.76, 1.90)	0.44	0.03	3.00 (0.39)	recent contact with animals
	≥4 symptom-days (all participants)	330/7,232 (4.56%)	1.77 (1.36, 2.33)	1.87 1.42, 2.47	<.01	<.01	2.18 (0.83)	race, same water use,
	GI Severity Score							
	Score of ≥6 (Meet case definition for GI illness)	73/637 (11.5%)	1.22 (0.68, 2.19)	1.35 (0.75, 2.43)	0.33	0.18	0.40 (0.98)	race
	Score of ≥6 (all participants)	73/7,473 (1.00%)	1.87 (1.08, 3.23)	1.99 (1.15, 3.46)	0.01	<.01	0.80 (0.85)	race
Severity of Any Illness	**Responses to Illness**							
	Any response versus none [d]	1,343/2,195 (61.8%)	1.21 (0.96, 1.52)	1.15 (0.91, 1.46)	0.23	<.01	1.26 (0.74)	preexisting respiratory condition
	Severe response versus moderate or no response [e]	552/2,195 (25.5%)	1.16 (0.90, 1.49)	1.23 (0.95, 1.59)	0.12	0.04	2.24 (0.81)	Same water use
	Total Symptom-Days							
	≥4 symptom-days (Meet case definition for any illness)	539/1,217 (44.3%)	1.47 (1.10, 1.98)	1.51 (1.13, 2.02)	<.01	0.02	1.00 (0.91)	race, gender
	≥4 symptom-days (all water recreators)	539/5,068 (10.6%)	1.90 (1.52, 2.37)	1.95 (1.56, 2.43)	<.01	<.01	3.91 (0.56)	race

[a] Proportion in the "higher risk" category, out of total n

[b] Failure to reject the null (p>0.05) indicates good model fit

[c] All models controlled for age

[d] Responded to illness by either staying home from work or school, taking OTC or prescription medication, contacting an HCP or visiting an ED or being admitted to the hospital versus those who did none of these

[e] Responded to illness by either staying home from work or school, taking prescription medication, contact with an HCP or visiting an ED/being admitted to the hospital versus those only taking OTCs or who did none of these

TABLE XLIX

AORS FOR THE RELATIONSHIP BETWEEN SEVERITY AND WATER CONTACT AMONG NEEAR PARTICIPANTS

	Severity Category	N [a]	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted OR p-value	Wald χ^2 p-value	HL GOF $\chi 2$ [b] (p-value)	Additional Confounders [c]
Severity of GI Illness	**Severity Indicators**							
	Any response versus none [d]	1,207/1,944 (62.1%)	1.05 (0.86, 1.28)	1.11 (0.89, 1.38)	0.35	0.05	5.70 (0.77)	same water use, digging in sand
	Severe response versus moderate or no response [e]	119/1,944 (6.12%)	0.90 (0.60, 1.34)	0.95 (0.63, 1.44)	0.81	0.45	0.30 (0.96)	preexisting GI condition
	Duration of GI Illness							
	≥2 days	1,099/1,922 (57.8%)	0.86 (0.67, 1.10)	0.98 (0.76, 1.27)	0.89	<.01	7.23 (0.41)	preexisting GI condition, same water use
	GI Symptom-Days							
	≥4 symptom-days (participants meeting case definition)	1,061/1,922 (55.2%)	0.90 (0.74, 1.10)	0.86 (0.70, 1.07)	0.19	0.09	3.18 (0.87)	digging in sand, recent contact with animals
	≥4 symptom-days (all participants)	1,061/26,614 (4.00%)	1.29 (1.13, 1.48)	1.23 (1.06, 1.42)	<.01	<.01	3.53 (0.83)	digging in sand, race
	GI Severity Score							
	Score of ≥6 (participants meeting case definition)	173/1,946 (8.92%)	1.10 (0.78, 1.57)	0.97 (0.67, 1.42)	0.88	<.01	5.14 (0.53)	race, digging in sand, preexisting GI condition
	Score of ≥6 (all participants)	173/26,631 (0.65%)	1.47 (1.05, 2.06)	1.23 (0.86, 1.75)	0.26	0.01	1.86 (0.87)	digging in sand
Severity of Any Illness	**Severity Indicators**							
	Any response versus none [d]	2,972/4,201 (71.0%)	1.19 (1.03, 1.37)	1.13 (0.97, 1.32)	0.11	<.01	2.90 (0.82)	digging in sand
	Severe response versus moderate or no response [e]	1,556/4,201 (37.1%)	1.13 (0.99, 1.30)	1.09 (0.95, 1.26)	0.23	0.05	0.23 (0.97)	--
	Total Symptom-Days							
	≥4 symptom-days (participants meeting case definition)	2,440/3,674 (66.4%)	1.03 (0.89, 1.20)	0.97 (0.83, 1.14)	0.75	0.03	2.73 (0.60)	digging in sand
	≥4 symptom-days (all participants)	2,440/26,411 (9.24%)	1.39 (1.27, 1.53)	1.25 (1.13, 1.38)	<.01	<.01	6.18 (0.52)	digging in sand, any contact with animals

[a] Proportion in the "higher risk" category, out of total n
[b] Failure to reject the null (p>.05) indicates good model fit
[c] All models controlled for age
[d] Responded to illness by either staying home from work or school, taking OTC or prescription medication, contacting an HCP or visiting an ED or being admitted to the hospital versus those who did none of these
[e] Responded to illness by either staying home from work or school, taking prescription medication, contact with an HCP or visiting an ED/being admitted to the hospital versus those only taking OTCs or who did none of these

APPENDIX A (continued)

TABLE L

AOR FOR THE RELATIONSHIP BETWEEN SEVERITY AND DIGGING IN SAND AMONG NEEAR PARTICIPANTS

	Severity Category	N [a]	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted OR p-value	Wald χ^2 p-value	HL GOF $\chi2$ [b] (p-value)	Additional Confounders [c]
Severity of GI Illness	**Severity Indicators**							
	Any response versus none [d]	1,207/1,944 (62.1%)	0.93 (0.77, 1.12)	0.86 (0.72, 1.09)	0.25	0.41	2.15 (0.83)	any contact with water
	Severe response versus moderate or no response [e]	119/1,944 (6.12%)	0.95 (0.65, 1.38)	1.01 (0.67, 1.53)	0.97	0.08	3.44 (0.63)	submerging head under water
	Duration of GI Illness							
	≥2 days	1,099/1,922 (57.8%)	0.95 (0.76, 1.20)	1.14 (0.88, 1.47)	0.31	0.01	3.75 (0.59)	submerging head under water
	GI Symptom-Days							
	≥4 symptom-days (participants meeting case definition)	1,061/1,922 (55.2%)	1.21 (1.05, 1.39)	1.16 (1.00, 1.36)	0.05	0.08	1.07 (0.90)	swallow water
	≥4 symptom-days (all participants)	1,061/26,614 (4.00%)	1.38 (1.27, 1.50)	1.24 (1.13, 1.36)	<.01	<.01	0.32 (0.99)	any contact with water
	GI Severity Score							
	Score of ≥6 (participants meeting case definition)	173/1,946 (8.92%)	1.33 (0.97, 1.82)	1.18 (0.83, 1.67)	0.36	0.21	1.03 (0.91)	submerging head under water
	Score of ≥6 (all participants)	173/26,631 (0.65%)	1.67 (1.23, 2.24)	1.46 (1.04, 2.04)	0.03	<.01	1.54 (0.96)	any contact with water, chronic GI condition
Severity of Any Illness	**Severity Indicators**							
	Any response versus none [d]	2,972/4,201 (71.0%)	1.14 (0.99, 1.30)	0.99 (0.85, 1.15)	0.92	<.01	2.60 (0.76)	any contact with water
	Severe response versus moderate or no response [e]	1,556/4,201 (37.1%)	1.13 (1.00, 1.28)	1.07 (0.91, 1.21)	0.47	0.07	3.65 (0.72)	any contact with water
	Total Symptom-Days							
	≥4 symptom-days (participants meeting case definition)	2,440/3,674 (66.4%)	1.18 (1.03, 1.34)	1.13 (0.98, 1.31)	0.10	0.07	0.18 (0.99)	swallow water
	≥4 symptom-days (all participants)	2,440/26,411 (9.24%)	1.38 (1.26, 1.51)	1.24 (1.12, 1.37)	<.01	<.01	0.40 (0.99)	any contact with water

[a] Proportion in the "higher risk" category, out of total n
[b] Failure to reject the null (p>.05) indicates good model fit
[c] All models controlled for age
[d] Responded to illness by either staying home from work or school, taking OTC or prescription medication, contacting an HCP or visiting an ED or being admitted to the hospital versus those who did none of these
[e] Responded to illness by either staying home from work or school, taking prescription medication, contact with an HCP or visiting an ED/being admitted to the hospital versus those only taking OTCs or who did none of these

APPENDIX A (continued)

2. Binary severity outcome, ordinal exposure

TABLE LI

AORS FOR SEVERITY AND ORDINAL EXPOSURE AMONG CHEERS PARTICIPANTS

Section		N [a]	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted OR p-value	Additional Confounders [b]
		Swallow water Body Wetness only No-contact water recreators (reference)				
Severity of GI Illness	**Responses to Illness**					
	Any response versus none [c]	28/36 281/406 146/194	1.15 (0.49, 2.69) 0.74 (0.50, 1.09) 1.00	1.11 (0.47, 2.67) 0.71 (0.47, 1.06) 1.00	0.80 0.09	gender, same water use, recently ate hamburger
	Severe response versus moderate or no response [d]	23/36 186/406 100/194	1.66 (0.80, 3.47) 0.80 (0.56, 1.12) 1.00	1.94 (0.92, 4.13) 0.85 (0.60, 1.21) 1.00	0.08 0.37	gender, recent contact with someone with GI illness, recently ate raw meat
	Duration of GI Illness					
	≥2 days	20/29 237/337 103/160	1.23 (0.53, 2.89) 1.31 (0.88, 1.96) 1.00	1.05 (0.44, 2.53) 1.29 (0.84, 1.97) 1.00	0.91 0.24	gender, same water use, recent contact with animals
	GI Symptom-Days					
	≥4 symptom-days (participants meeting case definition)	20/29 214/337 96/160	1.48 (0.64, 3.46) 1.16 (0.79, 1.71) 1.00	1.17 (0.49, 2.81) 1.02 (0.67, 1.54) 1.00	0.73 0.94	gender, same water use, recent contact with animals
	≥4 symptom-days (all participants)	29/270 292/4,556 124/2,369	1.89 (1.15, 3.12) 1.17 (0.91, 1.49) 1.00	**2.32 (1.51,3.56)** **1.32 (1.06,1.65)** 1.00	<.01 0.08	race
	GI Severity Score					
	Score of ≥6 (participants meeting case definition)	6/36 43/406 24/2,043	1.42 (0.53, 3.76) 0.84 (0.49, 1.43) 1.00	1.27 (0.43, 3.73) 1.01 (0.56, 1.84) 1.00	0.67 0.97	same water use, recently ate hamburger
	Score of ≥6 (all participants)	6/277 43/4,624 24/194	2.20 (0.89, 5.42) 0.93 (0.56, 1.54) 1.00	**1.57 (0.35,7.14)** 1.02 (0.49,2.10) 1.00	0.56 0.96	race, recently ate hamburger
Severity of Any Illness	**Responses to Illness**					
	Any response versus none [c]	76/118 869/1,433 395/638	1.11 (0.74, 1.68) 0.95 (0.78, 1.15) 1.00	1.13 (0.75, 1.71) 0.97 (0.80, 1.16) 1.00	0.57 0.59	gender
	Severe response versus moderate or no response [d]	37/118 405/1,433 177/638	1.19 (0.78, 1.82) 1.03 (0.83, 1.26) 1.00	1.45 (0.91, 2.26) 1.16 (0.94, 1.44) 1.00	0.09 0.17	gender, race, recently ate raw fish or shell fish
	Total Symptom-Days					
	≥4 symptom-days (participants meeting case definition)	39/72 346/786 153/356	1.57 (0.94, 2.61) 1.04 (0.81, 1.34) 1.00	1.60 (0.95, 2.67) 1.06 (0.82, 1.38) 1.00	0.08 0.65	race
	≥4 symptom-days (all participants)	53/257 523/4,184 208/2,184	2.82 (1.91, 4.17) 1.27 (1.04, 1.55) 1.00	**2.61 (1.86,3.66)** **1.42 (1.20,1.70)** 1.00	<.01 <.01	race

[a] Proportion in the "higher risk" category, out of total n
[b] All models controlled for age
[c] Responded to illness by either staying home from work or school, taking OTC or prescription medication, contacting an HCP or visiting an ED or being admitted to the hospital versus those who did none of these
[d] Responded to illness by either staying home from work or school, taking prescription medication, contact with an HCP or visiting an ED/being admitted to the hospital versus those only taking OTCs or who did none of these

APPENDIX A (continued)

TABLE LII
AORS FOR SEVERITY AND ORDINAL EXPOSURE AMONG NEEAR PARTICIPANTS

		N [a]	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	p-value	Additional Confounders [b]
			Swallow water Swimmers not swallowing water Waders (reference)			
Severity of GI Illness	**Responses to Illness**					
	Any response versus none [c]	145/228 538/852 178/300	1.20 (0.84,1.71) 1.17 (0.90,1.54) 1.00	1.13 (0.75,1.71) 1.17 (0.87,1.55) 1.00	0.25 0.21	gender, digging in sand
	Severe response versus moderate or no response [d]	109/228 381/852 131/300	1.18 (0.84,1.67) 1.04 (0.80,1.36) 1.00	1.14 (0.75,1.70) 1.05 (0.79,1.39) 1.00	0.32 0.43	gender, digging in sand
	Duration of GI Illness					
	≥2 days	125/221 467/848 172/296	0.98 (0.62,1.53) 0.94 (0.67,1.32) 1.00	0.99 (0.66,1.49) 0.89 (0.67,1.18) 1.00	0.67 0.62	digging in sand
	GI Symptom-Days					
	≥4 symptom-days (participants meeting case definition)	127/221 460/848 156/296	1.21 (0.85,1.72) 1.06 (0.82,1.39) 1.00	1.18 (0.79,1.76) 1.04 (0.78,1.37) 1.00	0.41 0.81	gender
	≥4 symptom-days (all participants)	127/2,315 460/10,552 156/4,303	1.54 (1.21,1.96) 1.21 (1.00,1.49) 1.00	**1.72 (1.29, 2.30)** **1.30 (1.06,1.59)** **1.00**	<.01 <.01	gender, race,
	GI Severity Score					
	Score of ≥6 (participants meeting case definition)	28/228 74/850 24/299	1.60 (0.90,2.85) 1.09 (0.68,1.77) 1.00	1.15 (0.54,2.43) 1.04 (0.60,1.78) 1.00	0.47 0.95	race, digging in sand
	Score of ≥6 (all participants)	30/2,332 75/10,554 25/4,306	2.18 (1.26,3.77) 1.26 (0.79,2.00) 1.00	1.75 (0.88,3.49) 1.18 (0.70,1.99) 1.00	0.04 0.60	race, digging in sand
Severity of Any Illness	**Responses to Illness**					
	Any response versus none [c]	357/469 1,247/1,757 486/675	1.24 (0.95,1.63) 0.95 (0.78,1.16) 1.00	1.01 (0.74,1.37) 0.90 (0.72,1.11) 1.00	0.56 0.47	gender, digging in sand
	Severe response versus moderate or no response [d]	222/469 710/1,757 264/675	1.40 (1.10,1.77) 1.06 (0.88,1.27) 1.00	1.24 (0.94,1.63) 1.01 (0.83,1.24) 1.00	0.03 0.58	gender, digging in sand
	Total Symptom-Days					
	≥4 symptom-days (participants meeting case definition)	303/433 1,036/1,581 396/591	1.15 (0.88,1.50) 0.94 (0.77,1.14) 1.00	1.07 (0.79,1.45) 0.93 (0.74,1.15) 1.00	0.50 0.49	gender, digging in sand
	≥4 symptom-days (all participants)	337/2,323 1,184/10,472 456/4,293	1.48 (1.26,1.73) 1.08 (0.96,1.22) 1.00	1.45 (1.20,1. 72) 1.08 (0.96,1.24)	<.01 0.38	gender, digging in sand

[a] Proportion in the "higher risk" category, out of total n
[b] All models controlled for age and beach location
[c] Responded to illness by either staying home from work or school, taking OTC or prescription medication, contacting an HCP or visiting an ED or being admitted to the hospital versus those who did none of these
[d] Responded to illness by either staying home from work or school, taking prescription medication, contact with an HCP or visiting an ED/being admitted to the hospital versus those only taking OTCs or who did none of these

TABLE LIII

FULL MODEL FOR THE RELATIONSHIP BETWEEN DEGREE OF WATER EXPOSURE AND FOUR OR MORE TOTAL SYMPTOM-DAYS, NEEAR WATER RECREATORS

Covariate	**Level**	**OR (95% CI)**
Water Exposure (ref=waders)	Swimmers, swallow water	1.45 [a] (1.20, 1.72)
	Swimmers, no swallow water	1.08 (0.96, 1.24)
Age category (ref=19–65)	18 and under	0.96 (0.86, 1.07)
	65 and over	0.48 [b] (0.26, 0.87)
Gender (ref=female)	Male	1.28 [a] (1.16, 1.41)
Digging in sand (ref=no)	Yes	1.23 [a] (1.10, 1.37)
Beach (ref=WP)	EB	1.11 (0.86, 1.44)
	FB	0.89 (0.69, 1.16)
	GB	0.93 (0.74, 1.18)
	HB	1.27 [b] (1.02, 1.60)
	SP	0.91 (0.77, 1.06)
	WB	1.06 (0.86, 1.30)

[a] $p<.01$
[b] $p<.05$

TABLE LIV

FULL MODEL FOR THE RELATIONSHIP BETWEEN DEGREE OF WATER EXPOSURE AND FOUR OR MORE TOTAL SYMPTOM-DAYS, CHEERS WATER RECREATORS

Covariate	**Level**	**OR (95% CI)**
Water Exposure (ref=no contact water recreators)	Swallow water	2.61 [a] (1.86, 3.66)
	Body wetness only	1.42 [a] (1.20, 1.70)
Age category (ref=19–65)	18 and under	1.21 (1.00, 1.47)
	65 and over	0.65 (0.41, 1.03)
Black Race (ref=not black)	Black	1.66 [a] (1.23, 2.24)

[a] $p<.01$

APPENDIX A (continued)

G. Effect Modification

1. Binary severity outcome, binary exposure

TABLE LV

MODIFICATION OF THE ASSOCIATIONS BETWEEN SEVERITY AND SWALLOWING WATER BY AVERAGE DAILY BOWEL MOVEMENTS [a]

Severity Metric	**Interaction p-value**	**Average daily bowel movements (Incidental-contact recreators only)**		
		Less than 2	Exactly 2	2 or more
GI Severity Score of ≥6 (participants meeting case definition)	0.07	0.30 (0.04, 2.50)	1.29 (0.40, 4.18)	5.64 (0.96, 33.33)
GI Severity Score of ≥6 (all participants)	0.01	0.42 (0.05, 3.25)	2.36 (0.81, 6.93)	13.22 (3.28, 53.21)
Severe response versus moderate or no response (Enteric and Non-Enteric Symptoms) [b]	0.02	0.85 (0.49, 1.49)	1.79 (1.08, 2.97)	3.79 (1.44, 9.99)

[a] Controlling for confounders

[b] Responded to illness by either staying home from work or school, taking prescription medication, contact with an HCP or visiting an ED/being admitted to the hospital versus those only taking OTCs or who did none of these

TABLE LVI

STRATUM SPECIFIC AORS FOR THE SEVERITY OF ILLNESS AND ANY WATER CONTACT AMONG NEEAR PARTICIPANTS, MODIFIED BY A COMORBID CONDITION [a]

Severity Category	**Modifying factor**	**Interaction p-value**	**Stratum Specific Adjusted OR for the presence of a comorbid condition (Confidence Interval)**	
			Presence of condition	No presence of condition
Any response versus none (GI Symptoms only) [b]	Preexisting GI condition	0.12	2.29 (0.90, 5.84)	1.08 (0.86, 1.35)
≥4 Total symptom-days (all participants)	Preexisting GI condition	0.02	0.68 (0.37, 1.22)	1.36 (1.18, 1.57)
Any response versus none (Enteric and Non-Enteric Symptoms) [b]	Asthma	0.04	1.82 (1.13, 2.92)	1.07 (0.92, 1.26)
Any response versus none (Enteric and Non-Enteric Symptoms) [b]	Chronic Illness	0.09	1.35 (1.05, 1.73)	1.04 (0.86, 1.25)
Severe response versus moderate or no response (Enteric and Non-Enteric Symptoms) [c]	Asthma	0.12	1.52 (0.99, 2.35)	1.06 (0.91, 1.23)
≥4 Total symptom-days (participants meeting case definition)	Chronic Illness	0.10	1.15 (0.89, 1.50)	0.89 (0.73, 1.08)

[a] Controlling for confounders

[b] Responded to illness by either staying home from work or school, taking OTC or prescription medication, contacting an HCP or visiting an ED or being admitted to the hospital versus those who did none of these

[c] Responded to illness by either staying home from work or school, taking prescription medication, contact with an HCP or visiting an ED/being admitted to the hospital versus those only taking OTCs or who did none of these

APPENDIX A (continued)

TABLE LVII

STRATUM SPECIFIC AORS FOR THE SEVERITY OF ILLNESS AND DIGGING IN SAND AMONG NEEAR PARTICIPANTS, MODIFIED BY A COMORBID CONDITION [a]

Severity Category	**Modifying factor**	**Interaction p-value**	**Stratum Specific Adjusted OR for the presence of a comorbid condition (Confidence Interval)**	
			Presence of condition	No presence of condition
Any response versus none (GI Symptoms only) [b]	Preexisting GI condition	0.17	1.50 (0.68, 3.27)	0.86 (0.70, 1.06)
Duration of GI Illness ≥2 days	Preexisting GI condition	0.03	2.55 (1.19, 5.45)	1.09 (0.84, 1.40)
≥4 GI symptom-days (participants meeting case definition)	Preexisting GI condition	0.01	2.35 (1.59, 3.47)	1.22 (1.11, 1.34)
Any response versus none (Enteric and Non-Enteric Symptoms) [b]	Asthma	0.03	1.46 (1.00, 2.14)	0.96 (0.82, 1.12)
Any response versus none (Enteric and Non-Enteric Symptoms) [b]	Preexisting GI condition	0.09	1.80 (0.90, 3.61)	0.97 (0.83, 1.13)
Any response versus none (Enteric and Non-Enteric Symptoms) [b]	Chronic Illness	<.01	1.41 (1.13, 1.76)	0.83 (0.70, 0.99)
Severe response versus moderate or no response (Enteric and Non-Enteric Symptoms) [c]	Asthma	0.01	1.54 (1.12, 2.11)	1.01 (0.87, 1.17)
Severe response versus moderate or no response (Enteric and Non-Enteric Symptoms) [c]	Preexisting GI condition	0.01	1.50 (0.84, 2.69)	1.40 (1.18, 1.68)
Severe response versus moderate or no response (Enteric and Non-Enteric Symptoms) [c]	Chronic Illness	<.01	1.32 (1.09, 1.59)	0.93 (0.79, 1.09)
≥4 Total symptom-days (all participants)	Asthma	<.01	1.68 (1.34, 2.11)	1.21 (1.10, 1.33)
≥4 Total symptom-days (all participants)	Preexisting GI condition	<.01	2.60 (1.75, 3.86)	1.22 (1.10, 1.34)
≥4 Total symptom-days (all participants)	Chronic Illness	<.01	1.61 (1.40, 1.85)	1.11 (1.00, 1.24)

[a] Controlling for confounders
[b] Responded to illness by either staying home from work or school, taking OTC or prescription medication, contacting an HCP or visiting an ED or being admitted to the hospital versus those who did none of these
[c] Responded to illness by either staying home from work or school, taking prescription medication, contact with an HCP or visiting an ED/being admitted to the hospital versus those only taking OTCs or who did none of these

APPENDIX A (continued)

2. <u>Binary severity outcome, ordinal exposure</u>

TABLE LVIII

STRATUM SPECIFIC AORS FOR THE SEVERITY OF ILLNESS AND MULTILEVEL WATER EXPOSURE MODIFIED BY THE NUMBER OF BOWEL MOVEMENTS AT BASELINE AMONG CHEERS PARTICIPANTS [a]

Severity Outcome	Interaction p-value [b]	Stratum Specific Adjusted OR for the number of bowel movements at baseline (Confidence Interval) [b]		
		2 or more	Exactly 2	Less than 2
≥4 GI symptom-days	0.38	0.59 (0.09, 3.88)	1.0 (0.37, 2.70)	1.69 (0.49, 5.86)
(participants meeting case definition)	0.11	1.89 (0.68,5.25)	1.26 (0.75, 2.10)	0.84 (0.49, 1.42)
GI Severity Score of ≥6	0.12	4.65 (0.66, 33.00)	1.26 (0.36, 4.45)	0.34 (0.04, 3.10)
(participants meeting case definition)	0.37	0.61 (0.17, 2.20)	0.89 (0.45, 1.76)	1.30 (0.59, 2.87)
GI Severity Score of ≥6	0.06	10.84 (2.24, 52.39)	3.24 (1.22, 8.56)	0.97 (0.19, 4.83)
(all participants)	0.56	0.79 (0.25, 2.54)	0.99 (0.54, 1.81)	1.23 (0.63, 2.40)
Severe response versus moderate or no response	0.02	4.63 (1.62, 13.26)	2.11 (1.22, 3.64)	0.96 (0.54, 1.72)
(Enteric and Non-Enteric Symptoms) [c]	0.90	1.22 (0.67, 2.20)	1.20 (0.89, 1.61)	1.18 (0.89, 1.54)

[a] Controlling for confounders
[b] p-values and AORs in calculated relative to the reference group (water recreators that did not get wet)
[c] Responded to illness by either staying home from work or school, taking prescription medication, contact with an HCP or visiting an ED/being admitted to the hospital versus those only taking OTCs or who did none of these

TABLE LIX

STRATUM SPECIFIC AORS FOR THE SEVERITY OF ILLNESS AND MULTILEVEL WATER EXPOSURE MODIFIED BY THE NUMBER OF BOWEL MOVEMENTS AT BASELINE AMONG CHEERS PARTICIPANTS [a]

Severity Outcome	Modifying factor	Interaction p-value [b]	Stratum Specific Adjusted OR for the presence of a comorbid condition (Confidence Interval) [b]	
			Presence of condition	No presence of condition
≥4 Total symptom-days	Diabetes	0.64	5.54 (0.43, 71.00)	3.01 (2.02, 4.50)
(all participants)		0.18	2.53 (0.19, 33.31)	1.37 (1.12, 1.69)
≥4 Total symptom-days	Preexisting GI	0.08	15.71 (2.41, 102.30)	2.82 (1.87, 4.25)
(all participants)	condition	0.67	7.48 (1.10, 50.64)	1.34 (1.09, 1.66)

[a] Controlling for confounders
[b] p-values and AORs in calculated relative to the reference group (water recreators that did not get wet)

APPENDIX A (continued)

TABLE LX

STRATUM SPECIFIC AORS FOR THE SEVERITY OF ILLNESS AND MULTILEVEL WATER EXPOSURE AMONG NEEAR PARTICIPANTS [a]

Severity Outcome	**Modifying factor**	**Interaction p-value** [b]	**Stratum Specific Adjusted OR for the presence of a comorbid condition (Confidence Interval)** [b]	
			Presence of condition	No presence of condition
Duration of GI Illness ≥2 days	Preexisting GI condition	0.10 0.43	8.51 (0.79, 91.50) 7.19 (0.65, 79.43)	1.14 (0.70, 1.86) 0.96 (0.68, 1.37)
GI Severity Score of ≥6 (all participants)	Preexisting GI condition	0.09 0.42	12.75 (1.26, 129.40) 8.77 (0.83, 92.52)	1.60 (0.87, 2.92) 1.10 (0.68, 1.78)
≥4 Total symptom-days (all participants)	Asthma	0.83 0.09	1.50 (0.84, 2.69) 1.51 (0.98, 2.33)	1.40 (1.18, 1.68) 1.03 (0.90, 1.17)

[a] Controlling for confounders

[b] p-values and AORs in calculated relative to the reference group (waders [only got wet below the waist])

H. Fecal Indicator Bacteria and Severity

1. Fecal indicator concentrations

TABLE LXI

DISTRIBUTIONS OF FECAL INDICATORS IN CHEERS AND NEEAR

	CHEERS						**NEEAR**	
	All Locations		**CAWS**		**GUW**		**All Locations**	
	Mean	Median	Mean	Median	Mean	Median	Mean	Median
Enterococci / 100 mL (Method 1600)	8,997.6	181.5	18,798.7	385.8	526.6	92.2	41.8	20.7
Enterococci / 100 mL (qPCR)	-	-	-	-	-	-	158.5	77.7
E. coli/ 100 mL	7,752.6	204.9	16,089.3	2,033.3	106.5	290.9	-	-
Somatic coliphage / 100 mL	702.5	63.3	1,383.1	494.2	96.2	11.3	-	-
F+ coliphage / 100 mL	32.3	2	61.3	18.0	6.2	1	-	-
Cryptosporidium oocysts / 10L	1.9	0	3.7	0.5	0.4	0	-	-
Giardia cysts / 10L	20.9	1.5	41.9	12.0	2.1	0.1	-	-
Turbidity NTU	18.6	17.1	17.5	16.2	19.6	20.9	-	-

2. Dichotomous water quality measures

TABLE LXII
AORS FOR THE RELATIONSHIP BETWEEN SEVERITY AND FIB AMONG INCIDENTAL-CONTACT WATER RECREATORS (CHEERS)

	Water Quality Measurement	N	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted OR p-value	Additional Confounders [a]
Severity of GI Illness: GI Symptom-Days						
≥4 symptom-days (participants meeting case definition)	Enterococci	287	1.04 (0.62, 1.73)	1.18 (0.68, 2.03)	0.56	Race, gender
	E. coli	308	1.02 (0.61, 1.68)	1.18 (0.70, 2.15)	0.55	Race, gender
	Somatic coliphage	351	1.02 (0.62, 1.66)	1.20 (0.72, 2.00)	0.49	Gender
	F+ coliphage	351	1.33 (0.82, 2.17)	1.52 (0.91, 2.53)	0.11	Recently ate packaged sandwich, gender
	Cryptosporidium spp.	351	1.04 (0.65, 1.66)	1.16 (0.65, 1.65)	0.55	--
	Giardia	351	1.19 (0.74, 1.91)	1.28 (0.78, 2.08)	0.33	Prone to infection
	Turbidity	351	1.15 (0.71, 1.87)	1.30 (0.79, 2.15)	0.31	Recently ate raw fish or shellfish
≥4 symptom-days (all participants)	Enterococci	3,955	1.11 (0.76, 1.63)	1.15 (0.77, 1.72)	0.48	Race
	E. coli	4,106	1.17 (0.80, 1.70)	1.24 (0.84, 1.82)	0.28	--
	Somatic coliphage	4,731	1.15 (0.80, 1.64)	1.21 (0.84, 1.75)	0.31	Gender
	F+ coliphage	4,731	1.10 (0.77, 1.57)	1.14 (0.79, 1.66)	0.47	Gender
	Cryptosporidium spp.	4,731	1.13 (0.80, 1.59)	1.19 (0.83, 1.70)	0.34	--
	Giardia	4,731	1.08 (0.66, 1.53)	1.14 (0.79, 1.63)	0.49	--
	Turbidity	4,731	0.94 (0.76, 1.36)	0.99 (0.67, 1.37)	0.96	--
Severity of Any Illness: Total Symptom-Days						
≥4 symptom-days (all participants)	Enterococci	3,027	0.88 (0.66, 1.17)	0.93 (0.70, 1.24)		Age, race
	E. coli	3,201	0.82 (0.62, 1.08)	0.93 (0.70, 1.24)	0.63	Age, race, preexisting respiratory condition
	Somatic coliphage	3,635	0.90 (0.70, 1.18)	1.00 (0.76, 1.32)	0.35	Age, race
	F+ coliphage	3,635	0.91 (0.70, 1.19)	0.99 (0.71, 1.21)	0.93	Age, race
	Cryptosporidium spp.	3,635	1.02 (0.80, 1.31)	1.15 (0.89, 1.49)	0.29	Age, race
	Giardia	3,635	0.98 (0.76, 1.26)	1.06 (0.82, 1.38)	0.66	Race
	Turbidity	3,635	0.92 (0.71, 1.18)	0.89 (0.71, 1.18	0.39	--

[a] All models adjusted for same water use

APPENDIX A (continued)

3. Dose of microbes

TABLE LXIII

MULTINOMIAL SEVERITY OUTCOME BY DOSE OF SOMATIC AND F+ COLIPHAGES IN CAWS AND GUW WATERS AMONG INCIDENTAL-CONTACT WATER RECREATORS (CHEERS)

	Response to GI Illness		**GI Symptom-Days**		**GI Severity Score**		**Total Symptom-Days**	
	Tertile 3 versus 1	Tertile 2 versus 1	Tertile 3 versus 1	Tertile 2 versus 1	Tertile 3 versus 1	Tertile 2 versus 1	Tertile 3 versus 1	Tertile 2 versus 1
CAWS-Somatic Coliphage								
Tertile 3 versus 1	QCS	QCS	2.13 (0.82, 5.52)	1.07 (0.45, 2.55)	QCS	QCS	1.15 (0.67, 1.99)	1.17 (0.64, 2.14)
Tertile 2 versus1	QCS	QCS	1.49 (0.50, 4.45)	1.00 (0.37, 2.66)	QCS	QCS	1.31 (0.73, 2.35)	0.93 (0.47, 1.86)
GUW- Somatic Coliphage								
Tertile 3 versus 1	QCS	QCS	QCS	QCS	1.23 (0.60, 2.54)	1.77 (0.76, 4.12)	1.12 (0.67, 1.89)	1.29 (0.72, 2.31)
Tertile 2 versus1	QCS	QCS	QCS	QCS	0.71 (0.76, 4.12)	1.03 (0.35, 3.18)	1.79 (0.87, 3.72)	1.75 (0.77, 3.97)
CAWS-F+ Coliphage								
Tertile 3 versus 1	QCS	QCS	1.91 (0.70, 5.2)	1.29 (0.50, 3.36)	QCS	QCS	1.00 (0.57, 1.78)	1.10 (0.58, 2.08)
Tertile 2 versus1	QCS	QCS	1.09 (0.41, 2.85)	0.82 (0.34, 1.97)	QCS	QCS	1.02 (0.58, 1.78)	0.93 (0.49, 1.77)
GUW-F+ Coliphage								
Tertile 3 versus 1	QCS	QCS	QCS	QCS	**2.01 (1.00, 4.05)**	**2.35 (1.02, 5.48)**	1.37 (0.82, 2.28)	1.22 (0.69, 2.16)
Tertile 2 versus1	QCS	QCS	QCS	QCS	0.82 (0.25, 2.66)	2.49 (0.77, 8.14)	1.52 (0.66, 3.48)	1.34 (0.53, 3.40)

QCS: "quasi-complete separation of data points"

TABLE LXIV
MULTINOMIAL SEVERITY OUTCOME BY DOSE OF ENTEROCOCCI BY METHOD 1600 AND QPCR AMONG SWIMMERS AND WADERS IN THE NEEAR STUDY

	Response to GI Illness		**GI Symptom-Days**		**GI Severity Score**		**Total Symptom-Days**	
	Tertile 3 versus 1	Tertile 2 versus 1	Tertile 3 versus 1	Tertile 2 versus 1	Tertile 3 versus 1	Tertile 2 versus 1	Tertile 3 versus 1	Tertile 2 versus 1
Enterococci by Method 1600								
Tertile 3 versus 1	1.70 (0.71, 4.10)	1.52 (0.60, 3.85)	0.76 (0.28, 2.04	1.20 (0.41, 3.46)	0.77 (0.29, 2.04)	0.81 (0.28, 2.91)	0.70 (0.37, 1.34)	1.57 (0.77, 3.22)
Tertile 2 versus1	1.16 (0.35, 3.79)	0.80 (0.22, 2.94)	1.02 (0.38, 2.71)	1.34 (0.41, 3.46)	1.02 (0.36,2.91)	0.93 (0.31,2.79)	0.90 (0.39, 2.04)	1.14 (0.45, 2.90)
Enterococci qPCR								
Tertile 3 versus 1	1.62 (0.63, 4.20)	**3.43 (1.30, 9.05)**	0.96 (0.34, 3.74)	0.73 (0.26, 2.04)	1.07 (0.38, 3.03)	1.36 (0.48,3.83)	1.19 (0.62, 2.32)	1.41 (0.72, 2.73)
Tertile 2 versus1	1.78 (0.54, 7.01)	2.46 (0.60, 10.17)	0.69 (0.25, 1.91)	0.58 (0.22, 1.56)	1.08 (0.37, 3.21)	1.70 (0.62, 4.72)	1.11 (0.47, 2.60)	1.22 (0.52, 2.84)

APPENDIX B

Socioeconomic Status and Healthcare Utilization

Responses to illness, such as staying home from work or school, taking over-the-counter (OTC) medication, taking prescription medication, seeing a doctor, or being admitted to an emergency department (ED) or hospital can be dependent on socioeconomic status (SES). The indicators are measures of an individual's utilization of healthcare, and may rely on insurance status, employment status, or whether an adult cares for others, making it difficult for an individual to find time to seek medical care for themselves (Adler et al., 1993; Anderson et al., 1997). It has also been suggested that SES factors such as income and education level can also be associated with a person's use of healthcare services (Adler et al., 1993). The use of responses to illness may only be reliable when the SES of the exposed and unexposed groups is similar.

Approaches to Evaluating Comparability of Water Recreators and Non-Water Recreators in the NEEAR And CHEERS

1. Published sources

A literature review was conducted in order to determine if there are any known SES differences among those who participate in non-water-related outdoor recreation and water-related outdoor recreation. The literature search was conducted using several computerized databases: MEDLINE (http://www.ncbi.nlm.nih.gov/pubmed), GOOGLE SCHOLAR (http://scholar.google.com/) and SUMMON (http://uichicago.summon.serialssolutions.com/). The search terms included "income water recreation," "SES water recreation," "income outdoor recreation," and "swimmers income."

Databases such as the National Survey on Recreation and the Environment (NSRE) and the Behavioral Risk Factor Surveillance System (BRFSS) were examined for the presence of economic data, such as income, along with data specific to outdoor recreational activities. Data related to outdoor activities (including water-recreation activities) and income are present in both of these databases. The variables in these databases could be examined in future studies to examine SES and water versus non-water recreation activities.

A study conducted in 1977 by the Heritage and Conservation Service (Heritage and Conservation Service, 1979) determined the distribution of water recreation activities by income categories. The study size included 3,310 participants who were grouped into four different categories of family income ranging between less than $10,000 to greater than $25,100 (Rorholm, 1983). Rorholm et al. (1983), indicates the distribution of income across each of the water activities is similar to the distribution of income for the US population, except for those who participate in sailing. Those that sail have statistically significant differences in income compared to the US population in 1977. Overall it was clear that one income group did not dominate a specific water recreational category.

2. **Analysis of SES in the two epidemiologic studies**

The CHEERS and the NEEAR study datasets were explored for any trends in SES among the study participants. Zip codes provided in the CHEERS and NEEAR studies were matched to SES data obtained by the US Census. In CHEERS, participants were asked to provide a zip code during each of the three follow-up phone interviews. Most individuals resided in the state of Illinois and provided complete and identical zip codes across the three phone interviews. There were some participants who changed zip codes during the course of the study, or provided incomplete zip codes to the interviewer. These incomplete zip codes could be due to data entry error or may be an error on part of the participant. In cases where more than one zip code was provided, the zip code listed the most frequently was used in the analysis.

Median household income, per capita income, and median income for full-time male and female workers were obtained from the 2011 US Census Bureau's American Community Survey (ACS). The ACS is an annual continuous nationwide survey that gathers more detailed economic, demographic and housing data than the decennial census questionnaire (US Census, 2008). Median household income data was of particular interest since it characterizes the combined income of all individuals over the age of 15 living in a household, whether they are related or not. Median household income is commonly used to assess SES within communities, when individual-level SES information is unavailable (Anderson et al., 1997). Additionally, per-capita income was also collected from the ACS, which is the average income received in the past 12 months for every individual over the age of 15 in a specified geographic area and divided by the total population in that area (US Census, 2011b). Other SES measures such as median income for full-time male and females were also obtained from the ACS. These measures separate median incomes in a geographic area by gender.

Preliminary analyses were conducted to determine the comparability of SES across water recreators and non-water recreators. All of the data obtained from the census were tested for normality using the Kolmogorov-Smirnov test. A t-test was conducted in order to compare median household income, per-capita income, and male and female specific earnings water recreators and non-water recreators. A χ^2 test was conducted to compare race/ethnicity of CHEERS and NEEAR participants across the water and non-water recreator groups.

The results indicate that there is a significant difference in median household income between water recreators and non-water recreators for CHEERS participants, yet there appeared to not be a significant difference among NEEAR participants. Tests comparing per-capita income showed no significant differences among CHEERS participants, but significant differences among NEEAR participants. Additionally, test of zip code earnings stratified by sex differed significantly between the two recreation groups. The US figures were included in order to compare the national averages to the figures determined for the CHEERS and NEEAR study participants. It is clear that the CHEERS participants tend to live in zip codes that are wealthier compared to NEEAR participants and the United States as a whole.

The overall χ^2 test for race/ethnicity is highly significant, and examining the percentages in each group it is clear that there are a greater number of whites and a fewer number of blacks in the water-exposed group compared to the unexposed group. Additionally, there also appears to be fewer Hispanics in the exposed group. These initial results in TABLE LXV indicate that the water-exposed and unexposed groups may not be similar in SES.

TABLE LXV

COMPARISON OF SES FACTORS BY EXPOSURE GROUP, OBTAINED FROM THE US CENSUS

	CHEERS PARTICIPANTS			**NEEAR PARTICIPANTS**			
	Water Recreators	**Non- Water Recreators**	**p-value**	**Water Recreators**	**Non- Water Recreators**	**p-value**	**US QuickFacts**
N	7,656	3,566		17,279	9,535		
Per-capita Income	38,794	38,868	.84	28,091	28,932	<.01	$27,915
Median Household income	71,427	63,655	<.01	56,540	56,540	0.49	$52,762
Median Earnings for males	64,412	59,320	<.01	52,396	52,877	0.01	$47,549
Median Earnings for females	47,440	46,693	.01	37,918	38,503	<.01	$37,160
Race (%)							
White	79.5	63.5		79.5	79.4		
Black	5.4	16.0		5.6	7.1		
Hispanic	5.9	9.5		11.0	9.8		
Asian	5.6	5.0		1.3	1.8		
Other	3.7	6.0		2.6	1.9		
	χ^2=479.4 (df=4) p-value <.0001			χ^2=479.4 (df=4) p-value <.0001			

Next, median household income was used to evaluate those who responded to the severity indicator questions posed during CHEERS and NEEAR telephone follow-up. Severity indicators for NEEAR were condensed to reflect the questions posed during CHEERS. The student t-tests indicate that there may be a difference in median household income between those who answered yes or no to the severity indicator questions at p<.05 (TABLE LXVI). The general trend suggests that those not responding to severity indicators have significantly larger median household incomes compared to participants who responded to severity indicators in both studies.

TABLE LXVI

MEDIAN HOUSEHOLD INCOME BY SEVERITY INDICATORS FOR CHEERS AND NEEAR PARTICIPANTS

	CHEERS					NEEAR				
	Response to Illness					Response to Illness				
	Yes		No		P-value	Yes		No		P-value
	Mean ($)	N	Mean ($)	N		Mean ($)		Mean ($)	N	
Stay home from work/school	66,500	1,159	68,843	5,113	<.01	54,729	N	56,632	7,541	<.01
Seek Medical Care	66,671	661	68,615	5,611	0.078	54,770	905	56,475	8,882	0.011
OTC medication use	67,597	3,250	69,284	3,022	0.013	56,117	4,279	56,478	4,846	0.368
Prescription medication use	68,210	338	68,421	5,934	0.888	55,482	689	56,381	8,440	0.236
Hospitalization/ ED visit	57,961	59	68,509	1,236	<.01	54,426	81	56,355	9,052	0.006

Overall, median household income was found to differ between water recreators and non-water recreations, with water recreators living in zip codes with a higher median household income. However, while they were statistically significant from one another, the absolute difference in income did not differ appreciably between the two groups. It is unclear if a difference of $2,000 (when average income is more than $50,000 per household) would be the difference between an individual who seeks care due to illness versus someone who does not. All of those in the epidemiology studies had higher incomes than the average for the United States. Therefore, it is unclear if the observed differences in income would mean that water recreators are more likely to report different rates of healthcare utilization due to illness compared to non-water recreators.

APPENDIX C
Cost of Illness Associated with Water Recreation

TABLE LXVII
COMPARISON BETWEEN NEEAR AND CHEERS RESPONSE TO ILLNESS VARIABLES

Component of Severity	NEEAR definition	CHEERS definition
	Asked for each symptom, one person answered for entire household	Each participant over the age of 7 answered for themselves; parents answered for children under that age
Medications		
OTC medication	Did you use any OTC medications, including things like special drinks, only because of this illness?	Did you use any OTC medications, including things like special drinks, for symptoms?
	About how much of your own household's money was spent altogether for OTC medicines?	
Prescription medication	Did you receive a prescription for an antibiotic or other drug for illness?	Did you receive a prescription for an antibiotic or other drug for illness?
	About how much of your own household's money was spent altogether for these prescription medicines?	
HCP		
Consult	Consult an HCP over the phone?	Consult healthcare provider on phone or in person about any symptoms
	Visit an HCP in person? Number of times?	
Diagnoses	Illness healthcare provider said you had	Illness healthcare provider said you had
Visit to ED		
ED visit	Did you visit an ED? Number of times?	Did you visit an ED?
Hospitalization		
Admitted to hospital	Were you admitted to the hospital? How many days?	Were you admitted to the hospital?
	Given IV fluids?	
Lost Productivity		
Miss work or school	During illness did you miss time from work?	Did symptoms prevent you from performing daily activities such as school, work, or recreation?
	Did illness prevent you from performing daily activities such as school, recreation, vacation activities, or work around the home?	
	Did your illness cause other household members to lose time at work?	
Number of days missed	(If yes to each of the above) How many days? Recorded only if 1 entire day or more were missed	How long were you prevented from daily activities? Recorded only if 1 entire day or more were missed

APPENDIX C (continued)

TABLE LXVIII
OTC AND PRESCRIPTION MEDICATION COSTS ACCORDING TO SYMPTOM-COMPLEX

	Prescription Medication						OTC Medication					
	Percentiles			Mean	Min	Max	Percentiles			Mean	Min	Max
Symptom	**25th**	**50th**	**75th**				**25th**	**50th**	**75th**			
Ear	5.00	16.00	27.50	18.38	0.00	50.00	5.00	8.00	10.00	8.93	1.00	30.00
Ear and Respiratory	0.00	0.00	4.00	1.33	0.00	4.00	7.00	10.00	10.00	10.90	5.00	30.00
Ear and Skin	10.00	10.00	10.00	10.00	10.00	10.00	5.00	11.00	14.50	9.75	0.00	17.00
Eye	9.00	20.00	40.00	36.38	0.00	200.00	3.00	6.00	10.00	6.65	0.00	25.00
Eye and Ear	10.00	10.00	10.00	10.00	10.00	10.00	6.00	10.00	130.00	48.67	6.00	130.00
Eye and Respiratory	20.00	57.00	100.00	71.83	17.00	180.00	8.50	15.50	29.00	23.13	3.00	100.00
Eye and Skin	10.00	10.00	10.00	10.00	10.00	10.00	15.00	20.00	30.00	21.67	15.00	30.00
Eye, Ear, and Respiratory	20.00	40.00	60.00	40.00	20.00	60.00	13.00	20.00	27.50	20.25	11.00	30.00
Eye, Skin, and Respiratory	0.00	0.00	52.00	17.33	0.00	52.00	10.00	12.00	15.00	12.33	10.00	15.00
Eye, Ear, Skin, and Respiratory	0.00	25.50	51.00	25.50	0.00	51.00	55.00	102.50	150.00	102.50	55.00	150.00
GI	13.00	27.00	39.00	26.35	0.00	60.00	5.00	7.00	11.00	9.66	0.00	65.00
GI and Ear	0.00	0.00	0.00	0.00	0.00	0.00	6.00	6.00	9.00	8.00	4.00	15.00
GI and Eye	0.00	25.50	51.00	25.50	0.00	51.00	7.00	9.00	17.00	11.89	0.00	30.00
GI and Respiratory	0.00	3.00	30.00	30.54	0.00	150.00	7.00	12.50	20.00	14.74	0.00	40.00
GI and Skin	0.00	20.00	40.00	20.00	0.00	40.00	6.00	8.00	17.00	11.00	5.00	25.00
GI, Ear, and Respiratory	30.00	165.00	300.00	165.00	30.00	300.00	6.50	7.50	24.00	15.25	6.00	40.00
GI, Ear, and Skin	13.00	27.00	39.00	26.35	0.00	60.00	18.00	18.00	18.00	18.00	18.00	18.00
GI, Eye, and Respiratory	9.00	39.50	70.00	39.00	9.00	70.00	11.00	23.00	70.00	36.38	0.00	83.00
GI, Eye, and Skin	50.00	50.00	50.00	50.00	50.00	50.00	15.00	24.00	26.00	20.60	5.00	33.00
GI, Skin, and Respiratory	25.00	90.00	150.00	88.33	25.00	150.00	19.00	20.00	22.00	20.17	0.00	40.00
GI, Eye, Ear, and Respiratory	3.00	3.00	3.00	3.00	3.00	3.00	15.00	25.00	113.00	51.00	15.00	113.00
GI, Eye, Skin, and Respiratory	0.00	10.00	0.00	0.00	0.00	0.00	6.50	16.50	35.00	20.75	5.00	45.00
Respiratory	0.00	8.00	23.00	21.22	0.00	120.00	5.00	8.00	14.00	9.55	0.00	30.00
Skin	12.00	30.00	50.00	34.41	0.00	100.00	4.00	5.00	10.00	6.94	0.00	30.00
Skin and Respiratory	10.00	10.00	10.00	10.00	10.00	10.00	10.50	14.00	20.50	14.13	1.00	22.00

APPENDIX C (continued)

TABLE LXIX
MEAN COSTS OF TESTS AND PROCEDURES PERFORMED IN ED FOR INSURED AND UNINSURED PATIENTS

	CHEERS		**NEEAR**	
	GI 0–12 days	**GI 0–3 days**	**GI 0–12 days**	**GI 0–3 days**
ED Test and Procedures				
Insured				
Electrolyte panel	$7.44	$9.08	$11.46	$10.10
Blood Glucose	$6.78	$6.79	$6.03	$5.89
Renal Function	$20.43	$13.11	$13.11	$12.59
CBC	$12.66	$12.39	$10.00	$9.75
Urinalysis	$5.83	$5.51	$4.56	$4.51
Urine Pregnancy Test [a]	$10.47	$9.99	$7.08	$7.01
IV Hydration Infusion, Initial	$70.27	$64.73	$40.89	$40.61
IV Hydration Infusion, Secondary	$42.65	$40.76	$14.77	$13.94
Stool Culture	$13.83	$13.43	$8.25	$7.75
Uninsured				
Electrolyte panel	$24.80	$30.26	$38.20	$33.68
Blood Glucose	$22.62	$22.64	$20.10	$19.63
Renal Function	$68.11	$43.69	$43.70	$41.95
CBC	$42.20	$41.30	$33.35	$32.49
Urinalysis	$19.41	$18.38	$15.18	$15.03
Urine Pregnancy Test [a]	$34.93	$33.30	$23.59	$23.37
IV Hydration Infusion, Initial	$234.23	$215.77	$136.31	$135.36
IV Hydration Infusion, Secondary	$142.25	$135.86	$49.22	$46.47
Stool Culture	$46.11	$44.75	$27.51	$23.84

[a] Assessed among females 13–55

APPENDIX C (continued)

TABLE LXX

INDIVIDUAL COMPONENTS OF COI IN 2007 DOLLARS, CHEERS, GI 0–12 DAYS

Component	N	CHEERS Version Estimates				
		Low		Medium	High	
		4a	4b	1	10	11
OTC	440					
Mean		11.39	11.39	11.39	11.39	11.39
Median		8.19	8.19	8.19	8.19	8.19
Sum		5,009.75	5,009.75	5,009.75	5,009.75	5,009.75
Prescription	52					
Mean		27.38	27.38	27.38	27.38	27.38
Median		27.00	27.00	27.00	27.00	27.00
Sum		1,423.76	1,423.76	1,423.76	1,423.76	1,423.76
HCP	120					
Mean		56.53	35.03	56.95	56.94	57.89
Median		55.99	34.72	56.28	56.29	56.58
Sum		6,784.66	4,206.49	6,833.00	6,833.00	6,946.40
ED	10					
Mean		120.33	120.33	137.74	137.74	156.72
Median		113.90	113.90	130.60	130.60	146.61
Sum		1,203.29	1,203.29	1,377.39	1,377.39	1,567.16
Hospitalization	9					
Mean		10,621.62	14,215.66	14,303.07	14,303.07	14,489.03
Median		10,195.27	14,354.66	14,426.17	14,426.17	14,497.68
Sum		95,594.55	127,940.97	128,727.59	128,727.59	130,401.30
Lost Productivity	388					
Mean		210.41	210.41	210.41	294.57	294.57
Median		137.14	137.14	137.14	192.00	192.00
Sum		81,638.51	81,638.51	81,638.51	114,293.91	114,293.91
TOTAL COI		**191,654.50**	**221,422.80**	**225,010.00**	**257,665.40**	**259,642.30**

APPENDIX C (continued)

TABLE LXXI
INDIVIDUAL COMPONENTS OF COI IN 2007 DOLLARS, CHEERS, GI 0–3 DAYS

Component	N	CHEERS Version Estimates				
		Low		Medium	High	
		4a	4b	1	10	11
OTC	218					
Mean		11.67	11.67	11.67	11.67	11.67
Median		8.19	8.19	8.19	8.19	8.19
Sum		2,542.97	2,542.97	2,542.97	2,542.97	2,542.97
Prescription	24					
Mean		30.06	30.06	30.06	30.06	30.06
Median		27.00	27.00	27.00	27.00	27.00
Sum		721.41	721.41	721.41	721.41	721.41
HCP	50					
Mean		55.01	34.11	56.08	55.39	56.08
Median		53.89	33.41	55.81	54.26	55.81
Sum		2,750.68	1,705.42	2,804.21	2,769.38	2,804.21
ED	3					
Mean		111.31	111.31	144.98	127.11	144.98
Median		110.51	110.51	141.36	126.26	141.36
Sum		333.92	333.92	434.95	381.33	434.95
Hospitalization	3					
Mean		7,276.30	9,559.52	9,615.03	9,615.03	9,669.95
Median		7,948.56	10,901.32	10,982.79	10,982.79	11,063.35
Sum		21,828.90	28,678.55	28,845.10	28,845.10	29,009.85
Lost Productivity	189					
Mean		188.97	188.97	188.97	264.56	264.56
Median		127.42	127.42	127.42	178.38	178.38
Sum		35,715.30	35,715.30	35,715.30	50,001.42	50,001.42
TOTAL COI		**63,893.18**	**69,697.57**	**70,975.49**	**85,261.61**	**85,514.81**

APPENDIX C (continued)

TABLE LXXII
INDIVIDUAL COMPONENTS OF COI IN DOLLARS, NEEAR, GI 0–12 DAYS

Component	N	NEEAR Version Estimates				
		Low	Medium		High	
		4	1	1a	11	11a
OTC	787					
Mean		7.97	9.27	7.97	7.97	7.97
Median		5.37	7.17	5.37	5.37	5.37
Sum		6,274.87	7,294.45	6,274.87	6,274.87	6,274.87
Prescription	109					
Mean		26.08	35.08	26.08	26.08	26.08
Median		13.71	27.00	13.71	13.71	13.71
Sum		2,843.13	3,823.82	2,843.13	2,843.13	2,843.13
HCP	134					
Mean		135.58	146.83	146.83	159.42	159.42
Median		134.33	146.37	146.37	154.69	154.69
Sum		5,016.59	5,432.84	5,432.84	5,898.57	5,898.57
ED	37					
Mean		43.69	44.01	44.01	44.62	44.62
Median		42.30	42.52	42.52	42.94	42.94
Sum		5,854.20	5,897.07	5,897.07	5,979.30	5,979.30
Lost Productivity	808					
Mean		186.82	186.82	186.82	277.99	277.99
Median		133.27	133.27	133.27	199.70	199.70
Sum		150,949.21	150,949.21	150,949.21	224,619.96	224,619.96
Others miss work	66					
Mean		--	--	--	--	165.87
Median		--	--	--	--	113.94
Sum		--	--	--	--	10,947.58
TOTAL COI		**170,938.00**	**173,397.39**	**171,397.13**	**245,615.83**	**256,563.41**

APPENDIX C (continued)

TABLE LXXIII
INDIVIDUAL COMPONENTS OF COI IN DOLLARS, NEEAR, GI 0–3 DAYS

Component	N	NEEAR Version Estimates				
		Low	Medium		High	
		4	1	1a	11	11a
OTC	478					
Mean		9.35	8.57	8.57	8.57	8.57
Median		7.17	5.37	5.37	5.37	5.37
Sum		4,467.58	4,096.17	4,096.17	4,096.17	4,096.17
Prescription	70					
Mean		35.93	26.74	26.74	26.74	26.74
Median		27.00	13.71	13.71	13.71	13.71
Sum		2,514.79	1,871.47	1,871.47	1,871.47	1,871.47
HCP	86					
Mean		45.06	45.06	45.06	45.06	45.06
Median		43.89	43.89	43.89	43.89	43.89
Sum		3,875.06	3,875.06	3,875.06	3,875.06	3,875.06
ED	21					
Mean		165.48	165.48	165.48	165.48	165.48
Median		154.69	154.69	154.69	154.69	154.69
Sum		3,475.03	3,475.03	3,475.03	3,475.03	3,475.03
Lost Productivity	462					
Mean		207.24	207.24	207.24	308.70	308.70
Median		152.22	152.22	152.22	226.78	226.78
Sum		95,745.95	95,745.95	95,745.95	142,619.33	142,619.33
Others miss work	52					
Mean		--	--	--	--	180.73
Median		--	--	--	--	120.38
Sum		--	--	--	--	9,397.87
TOTAL COI		**109,756.66**	**108,741.91**	**108,741.91**	**155,937.04**	**165,334.92**

TABLE LXXIV
CRUDE ASSOCIATION BETWEEN EXPOSURE AND COST (ORDINAL LOGIT), CHEERS

	Version	Water Rec Ref: Non-Water Rec	CAWS Ref: GUW	Swallow Ref: Don't Swallow
GI 0–12	4a	0.75 (0.55, 1.02)	1.10 (0.77, 1.57)	1.72 (0.83, 3.58)
	4b	0.75 (0.56, 1.02)	1.06 (0.75, 1.52)	1.84 (0.89, 3.50)
	1	0.75 (0.55, 1.02)	1.10 (0.77, 1.57)	1.72 (0.83, 3.58)
	10	0.77 (0.57, 1.04)	1.08 (0.76, 1.54)	2.04 (0.97, 4.29)
	11	0.76 (0.57, 1.04)	1.08 (0.76, 1.54)	2.04 (0.97, 4.93)
	12	0.72 (0.53, 0.99)	1.13 (0.78, 1.64)	1.72 (0.81, 3.63)
GI 0–3	4a	1.07 (0.68, 1.70)	0.89 (0.54, 1.47)	1.84 (0.65, 5.23)
	4b	1.09 (0.69, 1.72)	0.87 (0.53, 1.43)	1.92 (0.69, 5.51)
	1	1.07 (0.68, 1.70)	0.89 (0.54, 1.47)	1.84 (0.65, 5.23)
	10	1.06 (0.67, 1.68)	0.92 (0.56, 1.52)	1.72 (0.60, 4.88)
	11	1.06 (0.67, 1.68)	0.92 (0.56, 1.52)	1.73 (0.60, 4.88)
	12	1.10 (0.69, 1.78)	1.06 (0.63, 1.77)	1.58 (0.55, 4.60)

APPENDIX C (continued)

TABLE LXXV
CRUDE ASSOCIATION BETWEEN EXPOSURE AND COST (ORDINAL LOGIT), NEEAR

	Version	Water Rec Ref: Non-Water Rec	Marine Ref: Freshwater	Swallow Ref: Don't Swallow
GI 0–12	4	0.95 (0.79, 1.15)	1.48 (1.15, 1.91)	1.25 (0.95, 1.64)
	1	0.96 (0.79, 1.16)	1.45 (1.13, 1.88)	1.12 (0.85, 1.47)
	1a	0.95 (0.79, 1.15)	1.48 (1.15, 1.91)	1.25 (0.95, 1.64)
	11	0.95 (0.79, 1.15)	1.46 (1.13, 1.88)	1.14 (0.87, 1.50)
	11a	0.97 (0.80, 1.17)	1.49 (1.16, 1.92)	1.14 (0.86, 1.49)
	12	0.83 (0.65, 1.05)	2.59 (1.91, 3.50)	1.18 (0.83, 1.68)
GI 0–3	4	0.98 (0.75, 1.27)	1.51 (1.08, 2.10)	1.20 (0.86, 1.70)
	1	0.96 (0.74, 1.25)	1.55 (1.12, 2.15)	1.20 (0.86, 1.70)
	1a	0.97 (0.75, 1.26)	1.53 (1.12, 2.15)	1.14 (0.81, 1.62)
	11	0.95 (0.73, 1.23)	1.45 (1.05, 2.01)	1.12 (0.79,1.58)
	11a	0.96 (0.74, 1.25)	1.49 (1.07, 2.07)	1.09 (0.77, 1.54)
	12	0.77 (0.57, 1.06)	2.64 (1.81, 3.85)	1.14 (0.74, 1.76)

TABLE LXXVI
COSTS OF GI ILLNESS DEVELOPING WITHIN 0–12 DAYS AND MULTINOMIAL LOGISTIC REGRESSION BY EXPOSURE AMONG CHEERS AND NEEAR PARTICIPANTS WITH GI ILLNESS

	Category	Costs			Ordinal Logit		Multinomial Logit
		Total ($)	Costs ($) per Individual Mean	Costs ($) per Individual Median	Crude OR	Adjusted OR [b]	Adjusted OR $200 and over $50–$200 $10–$50 Under $10 (reference)
Incidental-Contact (CHEERS (V1)[a])	Water Rec	90,312.40	80.73	229.22	0.75 (0.55, 1.02)	0.73 (0.53, 1.01)	0.74 (0.42, 1.30) 0.66 (0.39, 1.10) 1.46 (0.72, 3.00)
	Ref: Non-Water Rec	134,697.59	111.67	623.60			
	CAWS	47,826.89	97.54	245.27	1.10 (0.77, 1.57)	1.16 (0.79, 1.69)	1.32 (0.69, 2.54) 1.04 (0.57, 1.88) 1.00 (0.46, 2.04)
	Ref: GUW	42,485.51	76.72	213.50			
	Swallow	21,817.29	143.31	839.13	1.72 (0.83, 3.58)	1.51 (0.71, 3.22)	1.73 (0.41, 7.22) 1.73 (0.43, 6.87) 1.00 (0.17, 5.43)
	Ref: Don't Swallow	68,495.11	78.29	186.13			
Full-Contact (NEEAR (V1a)[a])	Water Rec	121,137.62	105.40	145.77	0.95 (0.79, 1.15)	0.97 (0.79, 1.20)	1.03 (0.74, 1.43) 0.91 (0.71, 1.17) 1.35 (0.69, 2.65)
	Ref: Non-Water Rec	49,105.70	108.15	145.71			
	Marine	28,328.14	117.76	165.66	1.48 (1.15, 1.91)	0.61 (0.36, 1.03)	0.62 (1.29, 2.31) 0.53 (0.27, 1.06) 1.53 (0.41, 5.73)
	Ref: Fresh	92,809.48	102.96	140.62			
	Swallow	24,229.12	109.35	174.31	1.25 (0.95, 1.64)	1.08 (0.79, 1.45)	1.18 (0.77, 1.84) 0.95 (0.64, 1.39) 1.16 (0.43, 3.15)
	Ref: Don't Swallow	93,544.15	104.64	141.09			

[a] Assumes all moderate assumptions (Chapter 3: TABLE XX)
[b] Proportional odds assumption was violated (χ^2<.05)

TABLE LXXVII

COSTS AND MULTIPLE LINEAR REGRESSION BY EXPOSURE AMONG CHEERS AND NEEAR PARTICIPANTS, GI 0–3 DAYS

	Category	Costs			Unadjusted		Multiple Linear Regression			
							Adjusted			
		Total ($)	Costs($) per Individual				Adjusted for Demographics		Adjusted for Covariates	
			Mean	Median	β, p-value	Adj. R^2	β, p-value	Adj. R^2	β, p-value	Adj. R^2
CHEERS (V1)[a]	Water Rec	29,882.31	145.77	87.17	-0.046, 0.81	0.00	-0.152, 0.44	0.023	-0.120, 0.56	0.044
	Ref: Non-Water Rec	41,093.17	470.45	98.88						
	CAWS	15,243.38	145.18	81.31	-0.028, 0.89	0.00	-0.042, 0.84	0.017	-0.028, 0.89	0.060
	Ref: GUW	14,638.94	146.39	95.42						
	Swallow	2,450.64	188.51	141.48	0.455, 0.26	0.001	0.458, 0.25	0.023	0.265, 0.52	0.062
	Ref: Don't Swallow	27,431.68	142.87	79.14						
NEEAR (V1a)[a]	Water Rec	80,101.51	159.25	111.46	-0.051, 0.72	0.00	-0.100, 0.51	0.005	-0.093, 0.55	0.014
	Ref: Non-Water Rec	28,025.83	160.15	111.54						
	Marine	18,908.19	181.81	121.70	0.329, 0.07	0.005	0.217, 0.24	0.007	0.129, 0.50	0.013
	Ref: Fresh	61,193.32	153.37	104.59						
	Swallow	17,306.43	196.66	120.47	0.386, 0.05	0.006	0.370, 0.08	0.011	0.363, 0.09	0.018
	Ref: Don't Swallow	60,174.43	152.34	104.70						

[a] Assumes all moderate assumptions (Chapter 3: TABLE XX)

APPENDIX C (continued)

TABLE LXXVIII
COSTS AND MULTIPLE LINEAR REGRESSION BY EXPOSURE AMONG CHEERS AND NEEAR PARTICIPANTS, GI 0–12 DAYS

	Category	Costs			Unadjusted		Multiple Linear Regression			
							Adjusted			
		Total ($)	Costs ($) per Individual				Adjusted for Demographics		Adjusted for Covariates	
			Mean	Median	β, p-value	Adj. R^2	β, p-value	Adj. R^2	β, p-value	Adj. R^2
CHEERS (V1) [a]	Water Rec	90,312.40	80.73	229.22	-0.39, 0.004	0.012	-0.44, 0.003	0.023	-0.42, 0.003	0.068
	Ref: Non-Water Rec	134,697.59	111.67	623.60						
	CAWS	47,826.89	97.54	245.27	0.13, 0.44	-0.001	0.09, 0.55	0.008	0.14, 0.38	0.065
	Ref: GUW	42,485.51	76.72	213.50						
	Swallow	21,817.29	143.31	839.13	0.74, 0.02	0.012	0.72, 0.02	0.021	0.60, 0.05	0.072
	Ref: Don't Swallow	68,495.11	78.29	186.13						
NEEAR (V1a) [a]	Water Rec	121,137.62	105.40	145.77	-0.08, 0.47	-0.0004	-0.11, 0.13	0.023	-0.15, 0.20	0.018
	Ref: Non-Water Rec	49,105.70	108.15	145.71						
	Marine	28,328.14	117.76	165.66	0.32, 0.03	0.005	0.05, 0.57	0.020	0.15, 0.34	0.024
	Ref: Fresh	92,809.48	102.96	140.62						
	Swallow	24,229.12	109.35	174.31	0.29, 0.06	0.003	0.08, 0.46	0.020	0.24, 0.15	0.025
	Ref: Don't Swallow	93,544.15	104.64	141.09						

[a] Assumes all moderate assumptions (Chapter 3: TABLE XX)

TABLE LXXIX

COSTS ATTRIBUTABLE TO WATER RECREATION, GI 0–12 DAYS (2007 DOLLARS)

	Probability of GI illness if exposed to water (95% CI)	Probability of GI illness if not exposed to water (95% CI)	Relative Risk (95% CI)	Attributable Fraction (95% CI)	Version	Total Costs Among Water Recreators ($)	Costs per 1,000 water recreators [a] ($)	Total Costs Attributable to Water Recreation ($) (95% CI)	Costs per 1,000 water recreators attributable to water recreation [a] ($) (95% CI)
CHEERS	0.09 (0.08, 0.09)	0.09 (0.08, 0.10)	0.92 (0.86, 1.12)	-0.03% (-18.5, 11.2)	12	48,750.39	6,323.01	--	--
					4	81,266.95	11,518.98	--	--
					4a	90,312.40	11,713.67	--	--
					1	88,811.30	10,540.46	--	--
					10	111,093.41	14,409.00	--	--
					11	111,373.33	14,445.31	--	--
NEEAR	0.08 (0.07, 0.08)	0.06 (0.05, 0.07)	1.31 (1.18, 1.46)	24.0 (15.3, 31.5)	12	33,925.84	1,930.79	8,142.20 (5,190.65–10,686.64)	458.69 (292.41–602.03)
					4	120,805.54	6,805.56	28,993.33 (18,483.25–38,053.75)	1,633.34 (1,041.25–2,143.75)
					1	122,726.41	6,913.77	29,454.34 (18,777.14–38,658.82)	1,659.31 (1,057.81–2,177.84)
					1a	121,137.62	6,824.27	29,073.03 (18,534.06–38,158.35)	1,637.83 (1,044.11–2,149.65)
					11	174,255.12	9,816.64	41,821.23 (26,661.03–54,890.36)	2,355.99 (1,501.95–3,092.24)
					11a	183,005.09	10,309.57	43,921.22 (26,661.03–54,890.36)	2,474.30 (1,577.36–3,247.51)

[a] 7,710 water recreators in CHEERS, and 17,571 water recreators in the NEEAR study

APPENDIX D

National Estimate of the Total Economic Burden of Recreational Waterborne Illness in the United States

TABLE LXXX
PHYSICIAN FEES FOR OFFICE VISITS, ED VISITS, AND HOSPITALIZATIONS

Cost Type	Description	Symptom/Pathogen [a]	CPT	UCR 50 [b]	UCR 75 [b]	UCR 90 [b]
Office Visit	New, Level 2	Ear, Eye, Skin	99202	96.00	110.00	131.00
	Existing, Level 2	Ear, Eye, Skin	99212	58.00	66.00	77.00
	New, Level 3	Respiratory, GI	99303	137.00	158.00	187.00
	Existing, Level 3	Respiratory, GI	99213	78.00	89.00	103.00
	New, Level 4	All Pathogens	99204	192.00	221.00	262.00
	Existing, Level 4	All Pathogens	99214	118.00	135.00	158.00
ED Visit	Level 2	Ear, Eye, Skin	99282	107.00	126.00	144.00
	Level 3	Respiratory, GI	99283	180.00	211.00	241.00
	Level 4	All Pathogens	99284	269.00	316.00	360.00
Hospital	Initial Care, Level 2	All Pathogens except NF and Vibrio	99222	198.00	233.00	272.00
	Initial Care, Level 3	NF, Vibrio	99223	260.00	306.00	357.00
	Subsequent Care, Level 2	All Pathogens except NF and Vibrio	99232	101.00	119.00	139.00
	Subsequent Care, Level 3	NF, Vibrio	99233	148.00	174.00	203.00
	Discharge Visit, Level 1	All Pathogens except NF and Vibrio	99238	116.00	136.00	159.00
	Discharge Visit, Level 2	Vibrio	99329	158.00	185.00	216.00

[a] NF: *N.fowleri*, Vibrio: All *Vibrio* spp
[b] UCR:"Usual, Customary and Reasonable" rates, 2007 dollars

TABLE LXXXI
PARAMETERS USED TO ESTIMATE THE NUMBER OF MILD AND MODERATE ILLNESSES

Pathogen and Model Input	Distribution	Parameters
Proportion of US population 16 and over participating		
Motor boat	Beta-Pert (min, modal, max)	0.23, 0.23, 0.24
Kayak	Beta-Pert (min, modal, max)	0.06, 0.06, 0.06
Canoe	Beta-Pert (min, modal, max)	0.09, 0.1, 0.1
Row	Beta-Pert (min, modal, max)	0.04, 0.04, 0.04
Fish	Beta-Pert (min, modal, max)	0.34, 0.34, 0.35
Swim	Beta-Pert (min, modal, max)	0.41, 0.42, 0.42
Moderate illness assumptions		
GI illnesses that are moderate	Beta-Pert (min, modal, max)	0.05, 0.07, 0.08
Respiratory illnesses that are moderate	Beta-Pert (min, modal, max)	0.11, 0.13, 0.16
Eye illnesses that are moderate	Beta-Pert (min, modal, max)	0.26, 0.36, 0.46
Ear illnesses that are moderate	Beta-Pert (min, modal, max)	0.19, 0.24, 0.29
Skin illnesses that are moderate	Beta-Pert (min, modal, max)	0.53, 0.08, 0.1
Attributable Fractions, by illness		
GI		
swimming	Beta-Pert (min, modal, max)	0.011, 0.016, 0.021
Incidental contact, no fishing	Beta-Pert (min, modal, max)	-0.002, 0.007, 0.015
Incidental contact, fishing	Beta-Pert (min, modal, max)	0.001, 0.017, 0.031
Respiratory		
swimming	Beta-Pert (min, modal, max)	-0.001, 0.006, 0.012
Eye		
Incidental contact, no fishing	Beta-Pert (min, modal, max)	0.004, 0.012, 0.023
Ear		
swimming	Beta-Pert (min, modal, max)	0.000, 0.004, 0.007
Incidental contact, no fishing	Beta-Pert (min, modal, max)	-0.001, 0.001, 0.007
Skin		
swimming	Beta-Pert (min, modal, max)	0.002, 0.006, 0.010

APPENDIX D (continued)

TABLE LXXXII
PARAMETERS USED TO ESTIMATE THE NUMBER OF SEVERE ILLNESSES

Pathogen and Model Input	Distribution	Parameters
Campylobacter		
Number in outbreaks	Lognormal, mean (sd)	130.05 (360.7)
Proportion hospitalized	Beta-Pert (min, modal, max)	0.17, 0.13, 0.25
Proportion dead	Beta-Pert (min, modal, max)	0, 0.001, 0.004
Cryptosporidium		
Number in outbreaks	Lognormal, mean (sd)	191.25 (221.65)
Proportion hospitalized	Beta-Pert (min, modal, max)	0.13, 0.15, 0.25
Proportion dead	Beta-Pert (min, modal, max)	0, 0.0001, 0.003
E. coli 0157H7		
Number in outbreaks	Lognormal, mean (sd)	252.45 (536.97)
Proportion hospitalized	Beta-Pert (min, modal, max)	0.29, 0.3,0.46
Proportion dead	Uniform (min, max)	0.005, 0.008
Giardia		
Number in outbreaks	Lognormal, mean (sd)	28.05 (72.57)
Proportion hospitalized	Beta-Pert (min, modal, max)	0, 0.09, 0.13
Proportion dead	Uniform (min, max)	0, 0.001
Leptospira		
Number in outbreaks	Lognormal, mean (sd)	124.95 (369.03)
Proportion hospitalized	Beta-Pert (min, modal, max)	0.3, 0.5, 0.652
Proportion dead	Beta-Pert (min, modal, max)	0.01, 0.035, 0.14
Naegleria fowleri		
Number in outbreaks	Triangular (min, modal, max)	0, 4, 8
Proportion hospitalized	Point Estimate	1.0
Proportion dead	Uniform (min, max)	0.99, 1.0
Norovirus		
Number in outbreaks	Lognormal, mean (sd)	879.75 (744.73)
Proportion hospitalized	Point Estimate	0.03
Proportion dead	Point Estimate	0.001
Shigella		
Number in outbreaks	Lognormal, mean (sd)	627.3 (802.81)
Proportion hospitalized	Beta-Pert (min, modal, max)	0.139, 0.2, 0.22
Proportion dead	Beta-Pert (min, modal, max)	0.001, 0.002, 0.002
Vibrio parahaemolyticus		
Number in outbreaks	Lognormal, mean (sd)	21.63 (5.63)
Proportion hospitalized	Beta-Pert (min, modal, max)	0.33, 0.39, 0.5
Proportion dead	Beta-Pert (min, modal, max)	0, 0.008, 0.048
Vibrio ahaemolyticus		
Number in outbreaks	Lognormal, mean (sd)	38.32 (16.38)
Proportion hospitalized	Beta-Pert (min, modal, max)	0.034, 0.14, 0.21
Proportion dead	Beta-Pert (min, modal, max)	0, 0.013, 0.042
***Vibrio* spp., other**		
Number in outbreaks	Lognormal, mean (sd)	7.52 (2.25)
Proportion hospitalized	Beta-Pert (min, modal, max)	0.11, 0.34, 0.56
Proportion dead	Beta-Pert (min, modal, max)	0, 0.052, 0.2
Vibrio vulnificus		
Number in outbreaks	Lognormal, mean (sd)	29.7 (12.98)
Proportion hospitalized	Beta-Pert (min, modal, max)	0.63, 0.79, 1.0
Proportion dead	Beta-Pert (min, modal, max)	0.05, 0.16, 0.24
Vibrio cholera		
Number in outbreaks	Lognormal, mean (sd)	4.24 (1.73)
Proportion hospitalized	Beta-Pert (min, modal, max)	0, 0.32, 0.8
Proportion dead	Beta-Pert (min, modal, max)	0, 0.06, 0.1

APPENDIX D (continued)

TABLE LXXXIII
PARAMETERS USED TO ESTIMATE THE COST OF MILD ILLNESS

Pathogen and Model Input for Mild Illness	**Distribution**	**Parameters**
GI illness		
Proportion that take OTC	Beta-Pert (min, modal, max)	0.36, 0.39, 0.41
OTC medication cost	Lognormal, mean (sd)	7.20 (0.34)
Proportion that take prescription	Beta-Pert (min, modal, max)	0.01, 0.02, 0.02
Prescription medication cost	Lognormal, mean (sd)	19.98 (3.52)
Proportion that miss work	Beta-Pert (min, modal, max)	0.05, 0.06, 0.08
Days of work missed	Triangular (min, modal, max)	1.02, 1.05, 1.08
Respiratory illness		
Proportion that take OTC	Beta-Pert (min, modal, max)	0.62, 0.65, 0.68
OTC medication cost	Lognormal, mean (sd)	7.42 (0.35)
Proportion that take prescription	Beta-Pert (min, modal, max)	0.02, 0.04, 0.05
Prescription medication cost	Lognormal, mean (sd)	27.31 (8.31)
Proportion that miss work	Beta-Pert (min, modal, max)	0.03, 0.04, 0.06
Days of work missed	Triangular (min, modal, max)	1.00, 1.32, 1.63
Eye illness		
Proportion that take OTC	Beta-Pert (min, modal, max)	0.39, 0.47, 0.48
OTC medication cost	Lognormal, mean (sd)	7.39 (0.56)
Proportion that take prescription	Beta-Pert (min, modal, max)	0.07, 0.17, 0.28
Prescription medication cost	Lognormal, mean (sd)	23.45 (5.37)
Ear illness		
Proportion that take OTC	Beta-Pert (min, modal, max)	0.30, 0.36, 0.43
OTC medication cost	Lognormal, mean (sd)	6.79 (0.88)
Proportion that take prescription	Beta-Pert (min, modal, max)	0.03, 0.05, 0.09
Prescription medication cost	Lognormal, mean (sd)	17.79 (3.96)
Proportion that miss work	Beta-Pert (min, modal, max)	0.01, 0.03, 0.06
Days of work missed	Triangular (min, modal, max)	0.45, 1.29, 2.12
Skin illness		
Proportion that take OTC	Beta-Pert (min, modal, max)	0.47, 0.52, 0.56
OTC medication cost	Lognormal, mean (sd)	5.80 (0.27)
Proportion that take prescription	Beta-Pert (min, modal, max)	0.02, 0.03, 0.05
Prescription medication cost	Lognormal, mean (sd)	24.90 (8.85)
Proportion that miss work	Beta-Pert (min, modal, max)	0.0002, 0.01, 0.02
Days of work missed	Triangular (min, modal, max)	0.58, 1.50, 2.42

TABLE LXXXIV
PARAMETERS USED TO ESTIMATE THE COST OF MODERATE ILLNESS

Pathogen and Model Input for Moderate Illness	Distribution	Parameters
GI illness		
Proportion that take OTC	Beta-Pert (min, modal, max)	0.52, 0.62, 0.72
OTC medication cost	Lognormal, mean (sd)	8.32 (1.14)
Proportion that take prescription	Beta-Pert (min, modal, max)	0.48, 0.58, 0.68
Prescription medication cost	Lognormal, mean (sd)	27.54 (5.97)
Proportion that go to the ED	Beta-Pert (min, modal, max)	0.17, 0.26, 0.35
ED visit charge [a]	Normal, mean (sd) [b]	1,328.61 (46.52)
Proportion that miss work	Beta-Pert (min, modal, max)	0.14, 0.23, 0.31
Days of work missed	Triangular (min, modal, max)	0.98, 1.28, 1.60
Respiratory illness		
Proportion that take OTC	Beta-Pert (min, modal, max)	0.55, 0.63, 0.72
OTC medication cost	Lognormal, mean (sd)	7.70 (0.81)
Proportion that take prescription	Beta-Pert (min, modal, max)	0.59, 0.67, 0.75
Prescription medication cost	Lognormal, mean (sd)	22.22 (3.57)
Proportion that go to the ED	Beta-Pert (min, modal, max)	0.06, 0.11, 0.16
ED visit charge [a]	Normal, mean (sd) [b]	617.00 (14.62)
Proportion that miss work	Beta-Pert (min, modal, max)	0.097, 0.16, 0.22
Days of work missed	Triangular (min, modal, max)	1.02, 1.48, 1.93
Eye illness		
Proportion that take OTC	Beta-Pert (min, modal, max)	0.24, 0.28, 0.51
OTC medication cost	Lognormal, mean (sd)	9.67 (1.91)
Proportion that take prescription	Beta-Pert (min, modal, max)	0.69, 0.81, 0.92
Prescription medication cost	Lognormal, mean (sd)	23.09 (4.30)
Proportion that go to the ED	Beta-Pert (min, modal, max)	0, 0.063, 0.13
ED visit charge [a]	Normal, mean (sd) [b]	426.06 (19.10)
Proportion that miss work	Beta-Pert (min, modal, max)	0, 0.063, 0.17
Days of work missed	Triangular (min, modal, max)	1.00, 2.33, 7.00
Ear illness		
Proportion that take OTC	Beta-Pert (min, modal, max)	0.22, 0.33, 0.45
OTC medication cost	Lognormal, mean (sd)	6.23 (1.26)
Proportion that take prescription	Beta-Pert (min, modal, max)	0.80, 0.88, 0.96
Prescription medication cost	Lognormal, mean (sd)	16.02 (3.30)
Proportion that go to the ED	Beta-Pert (min, modal, max)	0.038, 0.12, 0.19
ED visit charge [a]	Normal, mean (sd) [b]	467.30 (10.40)
Proportion that miss work	Beta-Pert (min, modal, max)	0.03, 0.10, 0.18
Days of work missed	Triangular (min, modal, max)	0.56, 1.14, 1.72
Skin illness		
Proportion that take OTC	Beta-Pert (min, modal, max)	0.22, 0.38, 0.53
OTC medication cost	Lognormal, mean (sd)	7.86 (2.10)
Proportion that take prescription	Beta-Pert (min, modal, max)	0.58, 0.73, 0.87
Prescription medication cost	Lognormal, mean (sd)	19.22 (3.77)
Proportion that go to the ED	Beta-Pert (min, modal, max)	0.00, 0.05, 0.12
ED visit charge [a]	Normal, mean (sd) [b]	459.38 (10.90)
Proportion that miss work	Beta-Pert (min, modal, max)	0.00, 0.05, 0.12
Days of work missed	Triangular (min, modal, max)	0.00, 1.50, 7.85
Doctor Visit (Level 3) GI/Respiratory illness		
Cost for new patients	Normal, mean (sd) [b]	114.47 (187.00)
Cost for existing patients	Normal, mean (sd) [b]	78.00 (19.51)
Doctor Visit (Level 2) Eye/Ear/Skin illness		
Cost for new patients	Normal, mean (sd) [b]	96.00 (27.31)
Cost for existing patients	Normal, mean (sd) [b]	58.00 (14.83)
ED professional fee (Level 3) GI/Respiratory illness	Normal, mean (sd) [b]	180.00 (47.60)
ED professional fee (Level 2) Eye/Ear/Skin illness	Normal, mean (sd) [b]	107.00 (28.87)

[a] Charge for ED visit, not adjusted for CCR
[b] Normal distributions were bound at 0

APPENDIX D (continued)

TABLE LXXXV
PARAMETERS USED TO ESTIMATE THE COST OF SEVERE ILLNESS

Campylobacter	**Distribution**	**Parameters**
ED Charge [a]	Normal, mean (sd) [c]	1,334.29 (92.88)
Hospital Cost [b]	Normal, mean (sd) [c]	5,547.03 (322.20)
Length of Stay	Triangular (min, modal, max)	3.39, 3.59, 3.81
Cryptosporidium		
ED Charge [a]	Normal, mean (sd) [c]	1,513.90 (236.42)
Hospital Cost [b]	Normal, mean (sd) [c]	6,699.30 (1,044.86)
Length of Stay	Triangular (min, modal, max)	3.97, 4.93, 5.89
E. coli 0157H7		
ED Charge [a]	Normal, mean (sd) [c]	1,085.07 (75.31)
Hospital Cost [b]	Normal, mean (sd) [c]	7,244.61 (946.87)
Length of Stay	Triangular (min, modal, max)	3.92, 4.46, 5.00
Giardia		
ED Charge [a]	Normal, mean (sd) [c]	1,331.32 (149.77)
Hospital Cost [b]	Normal, mean (sd) [c]	6,205.95 (644.23)
Length of Stay	Triangular (min, modal, max)	3.28, 3.93, 4.60
Leptospira		
ED Charge [a]	Normal, mean (sd) [c]	1,797.20 (372.44)
Hospital Cost [b]	Normal, mean (sd) [c]	12,064.55 (3,319.52)
Length of Stay	Triangular (min, modal, max)	4.02, 5.95, 7.88
Naegleria fowleri		
ED Charge [a]	Normal, mean (sd) [c]	1,967.20 (146.32)
Hospital Cost [b]	Normal, mean (sd) [c]	20,456.73 (963.72)
Length of Stay	Triangular (min, modal, max)	10.00, 10.65, 11.30
Norovirus		
ED Charge [a]	Normal, mean (sd) [c]	1,174.24 (193.43)
Hospital Cost [b]	Normal, mean (sd) [c]	6,758.24 (1,737.04)
Length of Stay	Triangular (min, modal, max)	3.17, 4.24, 5.31
Shigella		
ED Charge [a]	Normal, mean (sd) [c]	1,560.63 (193.53)
Hospital Cost [b]	Normal, mean (sd) [c]	5,159.32 (431.68)
Length of Stay	Triangular (min, modal, max)	3.32, 3.73, 4.15
Unknown GI		
ED Charge [a]	Normal, mean (sd) [c]	1,328.61 (46.52)
Hospital Cost [b]	Normal, mean (sd) [c]	4,421.99 (96.24)
Length of Stay	Triangular (min, modal, max)	2.72, 2.77, 2.83
Doctor visit Level 4 (new)	Normal, mean (sd) [c]	118.00 (31.21)
Doctor visit Level 4 (established)	Normal, mean (sd) [c]	192.00 (54.62)
ED professional fee	Normal, mean (sd) [c]	297.26 (48.95)
Hospital initial fee (all pathogen, except NF and Vibrio)	Normal, mean (sd) [c]	218.39 (32.39)
Hospital initial fee (NF and Vibrio)	Normal, mean (sd) [c]	261.22 (58.23)
Subsequent care (hospitalization)	Normal, mean (sd) [c]	113.53 (19.88)
Discharge (Hospital) (all pathogens except NF and Vibrio)	Normal, mean (sd) [c]	127.96 (18.87)
Discharge (Hospital) (NF and Vibrio)	Normal, mean (sd) [c]	156.46 (36.20)
VSL (Millions of $)	Normal, mean (sd) [c]	7.6 (4.8)

[a] Charge for ED visit, not adjusted for CCR
[b] Cost for Hospital, adjusted for CCR, not including professional fees
[c] Normal distributions were bound at 0
Vibrio spp. estimated from (ERS, 2014), no variability

APPENDIX D (continued)

TABLE LXXXVI

INDIVIDUAL COSTS USED TO ESTIMATE MILD AND MODERATE ILLNESS (2007 DOLLARS)

		OTC	RX	Doctor Visit	ED Visit	Lost Productivity
GI	Mild	7.20 (6.64–7.76)	19.98 (14.24–25.71)	-	-	124.75 (121.15–128.46)
	Moderate [a]	8.32 [b] (6.46–10.17)	27.54 (17.87–37.21)	90.96 (64.17–117.14)	792.71 (708.69–875.63)	152.29 (114.02–189.07)
Respiratory	Mild	7.42 (6.85–7.99)	27.31 (14.04–40.57)	-	-	157.25 (117.93–196.73)
	Moderate [a]	7.70 (6.37–9.02)	22.22 (16.39–28.05)	90.96 (64.17–117.14)	463.78 (391.67–546.67)	175.99 (122.11–228.18)
Eye	Mild	7.39 (6.47–8.32)	23.45 (14.77–32.14)	-	-	-
	Moderate [a]	9.67 (6.57–12.77)	23.09 (16.09–30.08)	64.50 (43.44–85.05)	301.53 (252.60–350.39)	478.39 (117.90–828.75)
Ear	Mild	6.79 (5.35–8.23)	17.79 (11.38–24.40)	-	-	155.21 (46.60–260.89)
	Moderate [a]	6.23 (4.18–8.27)	16.02 (10.67–21.37)	64.50 (43.44–85.05)	322.11 (274.68–370.64)	136.38 (63.61–207.54)
Skin	Mild	5.80 (5.36–6.23)	24.90 (10.98–38.82)	-	-	179.07 (70.34–283.82)
	Moderate [a]	7.86 (4.48–11.23)	19.22 (13.09–25.35)	64.50 (43.44–85.05)	318.95 (271.65–364.42)	487.92 (37.81–950.46)

[a] Cost per person that uses medications, goes to the doctor, or goes to an Emergency Department
[b] Moderate OTC costs were used to estimate severe OTC costs

APPENDIX D (continued)

TABLE LXXXVII
INDIVIDUAL COSTS USED TO ESTIMATE SEVERE ILLNESS

	Costs for Severe, Mean (95% CI)								
	OTC	**RX**	**Doc**	**ED**	**Hospitalization**	**Length of Stay**	**Sequelae**	**Lost productivity**	**Estimated Number of Workdays missed [a]**
Campylobacter	8.32 (6.46–10.17)	44.67	249.91 (154.83–345.03)	912.51 (804.77–1,187.93)	5,574.06 (5,017.06–6,077.00)	3.59 (3.39–3.81)	397.33	439.15	6.75
Cryptosporidium	8.32 (6.46–10.17)	44.67	249.91 (154.83–345.03)	997.88 (793.95–1,187.93)	6,699.30 (4,980.66–8,417.94)	4.93 (3.97–5.89)	-	494.45	7.60
E. coli 0157H7	8.32 (6.46–10.17)	44.67	249.91 (154.83–345.03)	794.81 (697.45–893.42)	7,244.61 (5,687.15–8,802.08)	4.46 (3.92–5.00)	2,359.91	439.15	6.75
Giardia	8.32 (6.46–10.17)	44.67	249.91 (154.83–345.03)	915.51 (773.17–1,049.14)	6,205.95 (5,146.28–7,265.62)	3.93 (3.28–4.60)	-	494.45	7.60
Leptospira	8.32 (6.46–10.17)	44.67	249.91 (154.83–345.03)	1,126.79 (850.09–1,410.90)	12,065.00 (6,604.42–17,524.68)	5.95 (4.02–7.88)	-	650.59	10.00
Naegleria fowleri [a]	8.32 (6.46–10.17)	44.67	130.72 (87.43–173.88)	1,202.76 (1,067.59–1,340.53)	20,457.00 (18,871.55–22,041.91)	10.65 (10.00–11.30)	-	-	0.00 [c]
Norovirus	8.32 (6.46–10.17)	44.67	249.91 (154.83–345.03)	836.37 (663.99–1,005.65)	6,758.24 (3,901.06–9,615.43)	4.24 (3.17–5.31)	-	232.26	3.57
Shigella	8.32 (6.46–10.17)	44.67	249.91 (154.83–345.03)	1,016.76 (853.33–1,177.47)	5,159.32 (4,449.27–5,869.38)	3.73 (3.32–4.15)	52.94	240.72	3.70
Vibrio parahaemolyticus	8.32 (6.46–10.17)	44.67	249.91 (154.83–345.03)	392.79	9,555.69	[d]	-	650.59	10.00
Vibrio ahaemolyticus	8.32 (6.46–10.17)	44.67	249.91 (154.83–345.03)	392.79	9,555.69	[d]	-	697.43	10.72
***Vibrio* spp., other**	8.32 (6.46–10.17)	44.67	249.91 (154.83–345.03)	392.79	9,555.69	[d]	-	697.43	10.72
Vibrio vulnificus (sepsis)	8.32 (6.46–10.17)	44.67	249.91 (154.83–345.03)	392.79 (342.105)	22,459.75 (67,377.38)	[d]	-	1,063.17	10.72
Vibrio cholera	8.32 (6.46–10.17)	44.67	249.91 (154.83–345.03)	392.79	9,555.69	[d]	-	697.43	10.72
Unknown GI	8.32 (6.46–10.17)	44.67	249.91 (154.83–345.03)	792.71 (708.69–875.63)	4,421.99 (4,263.69–4,580.29)	2.77 (2.72–2.83)		232.26†	3.57 [e]

[a] Estimated from ERS 2014
[b] Bacterial Meningitis used as a surrogate
[c] Due to 100% mortality rate, 0 works days missed
[d] *Vibrio* spp. not estimated using NIS
[e] Estimated based on Norovirus

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DeFlorio, S. and S. Dorevitch. “Evaluation of Quantitative Microbial Risk Assessment (QMRA) Assumptions Using Observational Data.”

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