DRINKING WATER RISKS TO HEALTH 40 YEARS AFTER PASSAGE OF THE SAFE DINKING WATER ACT: A COUNTY-BY-COUNTY ANALYSIS IN NORTH CAROLINA

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ABSTRACT

Nicholas B. DeFelice: Drinking Water Risks to Health 40 Years After Passage of the Safe Drinking Water Act: A County-by-County Analysis in North Carolina
(Under the direction of Jacqueline MacDonald Gibson)

The advent of community water services was one of the greatest public health advances of the twentieth century, yet disparities in the quality of water may persist and may reflect similar disparities in health outcomes. These disparities have not yet been investigated in North Carolina, home to 2120 community water systems (CWSs) and tens of thousands of domestic water systems (DWSs). This study used novel quantitative methods to compare North Carolina's statewide health outcomes associated with drinking water quality at a county level to estimate the magnitude and spatial variability of cancer attributable to chemicals in CWSs along with acute gastrointestinal illness (AGI) attributable to microbial contamination of drinking water.

Using a stochastic risk model we examined the cancer risks attributable to chemical exposure though drinking water for all chemicals covered under the Safe Drinking Water Act (SDWA) in North Carolina. Of the 67 contaminants, three (total trihalomethanes, arsenic and alpha radiation) dominated the cancer risk, suggesting opportunities may exist to streamline SDWA enforcement by reducing the monitoring requirements for low-risk chemicals and focusing on high-risk chemicals. We also characterized the magnitude and spatial variability of AGI cases attributable to microbial contamination of CWSs. We compared three approaches (population intervention model, drinking water attributable risk, and quantitative microbial risk assessment) to estimate the percentage of emergency department visits for AGI

attributable to microorganisms in North Carolina CWSs. Of the three models, the population intervention model had the highest internal validity and is therefore the most informative for decision making, since risks associated with exposure are specific to the local population.

Finally, using the population intervention model we compared the burden of AGI attributable to CWSs with that attributable to DWSs. In total, an estimated 47,250 (95% CI 32,000 – 62,400) annual cases of AGI were attributable to microbial contamination in drinking water, constituting approximately 11.7% (95% CI 8.0-15.4) of all ED visits for AGI. We determined that each 10% shift in the percentage of the county population from DWSs to CWSs could reduce emergency department visits for AGI by 1.6%. Providing regulated water to current DWS users may provide substantial health benefits.

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PREFACE

This dissertation is organized in a nontraditional format, which includes three manuscripts. Chapter 1 provides and introduction and description of the overall significance of the research. Chapters 2-4 can stand-alone as manuscripts submitted for publication and thus may have some redundancies with the earlier chapters. Chapter 5 presents a summary of the findings, research implications, and directions for future research.

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LIST OF ABBREVIATIONS

AF	Attributable Fraction
CWS	Community Water System
DBP	Disinfection Byporduct
DWAR	Drinking Water Attributable Risk
DWS	Domestic Water System
ECR	Excess Cancer Risk
ED	Emergency Department
EPA	Environmental Protection Agency
IOC	Inorganic Compounds
MCL	Maximum Contmaninat Level
NAS	National Acadamy of Science
NPDWR	National Public Drinking Water Regulation
PIM	Population Intervention Model
PW	Private Well
QMRA	Quantitive Microbaial Risk Assessment
RMCL	Recommended Maximum Contmaninat Level
RN	Radionuclide
RR	Relative Risk
SDWA	Safe Drinking Water Act
SOC	synthetic organic compounds
VOC	volatile organic compounds

Chapter 1:
Introduction

Environmental pollutants are an important contributor to the total US disease burden.[1] One of the most influential public health advances leading to the reduction of the environmental burden of disease in the twentieth century was the introduction of improved municipal water and sewer services. This intervention is credited with a 50% reduction in total mortality, 75% reduction in infant mortality, and 67% decrease in child mortality between 1900 and 1936.[2] A major portion of these mortality reductions was due to the introduction of filtration and chlorination systems, which were highly effective in preventing common causes of waterborne enteric disease. However, not all pathogens are vulnerable to chlorine (e.g. *Giardia*, *Cryptosporidium,* and enteric viruses), and the resistant ones have been recognized as important causes of waterborne disease outbreaks. Furthermore, the publication of *Silent Spring* in the early 1960s brought society's attention to the possibility that long-term ingestion of trace chemicals may be carcinogenic.[3] Unfortunately, little is known about the magnitude or spatial variability of exposure to chemicals and microbial contaminants in drinking water and the resulting health impacts.[4]

U.S. environmental policy analysts have called for comprehensive assessments of the US environmental disease burden to identify and target risk factors with the greatest potential to improve population health.[5] However, previous studies have been limited as information sources for decisions because the studies either relied on expert opinion instead of scientific data or the studies were done at such a large spatial scale that they overlooked potential impacts at a more focused level and did not identify areas that will benefit from the intervention.[1,6] To avoid the cognitive biases in risk perception from expert opinion (a tendency to overestimate high risks and underestimate low risks

and for experts to be over-confident in their risk judgments) we employed formal principles of risk assessment to quantitatively estimate the fraction of observed health outcomes attributable to a variety of water pollutants in North Carolina.[7] The analysis was carried out at the county level to identify which populations or regions were most susceptible to contaminated water, provide information useful in estimating benefits of improving water service, and help inform prevention planning efforts. The remainder of this section gives a brief overview of drinking water service in NC, public health threats associated with drinking water contamination, and the need for a quantitative assessment of the burden of disease attributable to drinking water.

1.1 Water Service and Public Health

Despite decades of federal, state, and local governments implementing policies to improve drinking water quality and increasing the number of people who have access to regulated tap water in North Carolina, the effectiveness of these policies is unknown. North Carolina has over 2,000 CWSs along with tens of thousands of private wells, which together serve the state population of over 9.7 million (Table 1.1). Nearly 90% of the CWSs in North Carolina serve less than 3,300 people each--small-scale decentralized rural systems historically have been more susceptible to water quality problems and have been linked to a disproportionate number of disease outbreaks.[8] Nationally, CWSs serving fewer than 3,300 people have been shown to be 1.5 times more likely to have a violation than systems serving over 10,000 people.[9]

One quarter of North Carolina's population is served by DWSs (private wells)—the fifth largest state population relying on DWSs in the United States.[10] Previous studies have estimated that DWSs across the US carry a five times higher lifetime risk than CWSs of bladder and lung cancer due to arsenic.[11] Another study concluded that DWSs posed five times greater risk of AGI than regulated water systems.[12]

Previous studies have sought to quantify the risks associated with contaminated drinking water but have focused on national, regional or system-level populations. No known studies have

provided county-level estimates for an entire state of the burden of cancer attributable to all carcinogenic chemicals regulated under the SDWA or the burden of AGI attributable to microbially contaminated drinking water. Further, the previous studies have not examined differences in quantified health risks in CWSs by size, and few studies have compared CWSs to DWSs. Limited knowledge of health implications of CWSs and the differences between small and large CWSs and/or CWSs and DWSs suggests that a comprehensive burden of disease assessment could inform future steps to reduce health risks due to drinking water contamination.

1.2 State of Current Knowledge

1.2.1 Chemical Contaminants in CWSs

The majority of existing literature has sought to quantify cancer risk from chemical contaminants in CWSs. The text below identifies chemicals that have previously been studied and describes the existing evidence regarding cancer risk attributable to drinking water.

- **Trihalomethanes** – In 1995, Morris[13] estimated 5,000 (95% CI: 2,000 – 7,000) annual cases of bladder cancer and 8,000 (95% CI: 200 – 14,000) annual cases of rectal cancer in the U.S. attributable to exposure to trihalomethanes in CWSs.
- **Arsenic** – In 1995, Morris[13] estimated 3,000 annual cases of liver, lung, bladder, or kidney cancer attributable to exposure to arsenic in community water systems. Additionally, in 2010 Kumar et al.[11] estimated a national lifetime risk for lung and bladder cancer of 0.2 cases per million annually. Kumar presented results by seven geographic regions. Within the Mid-Atlantic Region, in which North Carolina was grouped, Kumar and colleagues estimated that arsenic contributes to 0.4 and 0.2 annual cases of lung and bladder cancer per million people served by public groundwater and surface water systems, respectively. [11]
- **Radon** – In 1987, Crawford-Brown and Cothern[14] estimated 6,000 (95% CI: 1,000-30,000) excess lifetime lung cancer cases occur in the U.S. population as a result of radon emanation from public water supplies into indoor air. Crawford-Brown[15] updated this estimate in 1991 to include ingestion risks as well as inhalation risks; the resulting estimate was 25,000 (95% CI: 5,000-125,000) premature deaths due to stomach, colon, liver, and lung cancer. Based on the risk estimates from the 1987 Crawford-Brown and Cothern study, Morris estimated that fewer than 100 cases of stomach, colon, liver, or lung cancer occur from radon exposure via drinking water annually.[13]
- **Volatile Organic Compounds (VOCs)** – Studies have compared the cancer risks of different VOCs but have not predicted the number of cases attributable to each chemical. In 2002, Williams and colleagues[16] examined six different VOCs throughout California to determine which posed the greatest cancer risk and concluded that the risk from these six compounds "is not necessarily significant" without further information regarding exposure from specific

drinking water sources. Williams et al. found that chloroform (a disinfection byproduct), followed by tetrachloroethylene (PCE) and 1,1-dicloroethylene (1,1-DCE), posed higher risks than either trichloroethylene (TCE), benzene or methyl tertiary butyl ether (MTBE). The risk of cancer from chloroform were twice as high as those from PCE and more than 2.5 times as high as those from 1,1-DCE. In 2004, Williams and colleagues[17] expanded their analysis to include 12 VOCs and a longer historic data record (1985-2002 instead of 1995-2001, as in the 2002 study). In this expanded analysis, they found that risks from PCE and chloroform were about equal and posed the highest risks among the 12 VOCs. In Taiwan, Fan et al. 2009 evaluated 6 VOCs for cancer risk in ground water sites and found 1,1-DCE, vinyl chloride and benzene were the only contaminants to result in a greater than 10^{-6} cancer risk, while PCE, TCE and 1,1-DCEA did not exceed the 10^{-6} cancer risk.[18]

1.2.2 Microbial Contaminants in CWSs

AGI is the most common infectious disease class attributed to contaminated drinking water.[19] Three research groups have developed national estimates of the number of cases of AGI associated with CWSs across the US. Their estimates ranged from 4 million to 32 million cases (2-18% of all cases) of AGI attributable to CWSs per year.[6,20,21] None of the groups evaluated AGI risk at a scale smaller than the national level. These studies point out that the burden of AGI attributable to drinking water is substantial but do not provide information on the spatial variability in these risks—an important consideration in making decisions about steps to improve drinking water quality.

Others have evaluated a specific type of CWS--non-disinfected groundwater. Macler and Merkle[22] estimated that microbial contamination of non-disinfected community ground water systems contributed between 750,000 and 5.0 million AGI cases annually in the US. Borchardt et al.[23] examined non-disinfected municipal wells in Wisconsin and found that between 6% and 22% of AGI cases were attributable to tap-water-borne viruses.

Other developed countries have conducted studies to determine the role of microbially contaminated water in the burden of AGI. Richardson and colleagues[24] found that in England small private water systems (serving less than 5,000 people) that did not have effective treatment were 1.8 times (95% CI 1.5 -2.3) more likely to be contaminated than water systems with treatment (principal treatments used: chlorination, UCV irradiation and filtration). Hunter et al.[25] estimated the median

annual risk of infection associated with being connected to a small private water systems to be 25-28% for *Cryptosporidium* and 0.4% to 0.7% for *Giardia*. A recent study conducted in British Columbia, Canada, concluded that people connected to mixed systems of municipal surface and groundwater were 2.3 times more likely to suffer from AGI than those who used only a municipal groundwater system.[12]

Source water contamination and deficiencies in treatment (e.g., lack of disinfection) are not the only causes of exposure to microbial contaminants in drinking water. Distribution systems also can be sources of contamination. Lambertini and colleagues[26] estimated that 0.1-4.9% of all cases of AGI were attributable to a lack of residual disinfectant in the distribution system. Hunter et al.[27] concluded that distribution systems were associated with a high proportion of all cases of AGI in the United Kingdom. He found that burst water mains or other factors that caused a loss of pressure in the distribution system might contribute to 15% of AGI in the United Kingdom.

Many studies have developed estimates of the number of AGI cases attributable to poor drinking water quality. These studies have either produced estimates for a single system type or at a national level. A limitation of some of the previous studies is that they considered only a single pathogen and hence accounted for only a small portion of the potential risk. Others have tried to evaluate the problem using previous epidemiological studies, but these efforts are limited by the high variability in the results of previous studies (e.g., attributable risks ranging from below the limits of detection to 0.26 cases per person-year) and by the fact that these studies fail to account for potentially unobserved differences between the study population and the population evaluated in previous epidemiologic investigations. In our study we estimated the risk associated with the exposure to microbial contaminants in North Carolina drinking water from data on occurrence of organisms that indicate the potential presence of microbial pathogens and health outcomes specific to North Carolina. The approach overcomes the deficiencies of previous efforts by considering multiple possible pathogens (the potential exposure to which is represented by indicator organisms) and by

using local health outcome data rather than the results of previous epidemiologic studies of other populations, hence providing higher internal validity than previous estimates. This study was the first to apply a population intervention model to U.S. drinking water quality and health data at a state level. These results will provide insights into the degree to which microbiological quality of drinking water affects health in North Carolina and also will identify counties that may benefit from improved drinking water systems.

1.2.3 Microbial Contaminants in DWSs

Drinking water from DWSs is not regulated at the federal level and typically does not receive the same level of treatment or monitoring as that from CWSs.[28] In an attempt to reduce the risk from DWSs, the North Carolina legislature passed a law requiring all counties to institute a private drinking water well permit program by July 1, 2008. Under this program, all new DWSs must obtain a license and, in order to do so, must undergo water quality testing. However, this program may not be as effective as desired, because routine monitoring is not required after the permit is granted and because wells constructed before 2008 are grandfathered from the permitting requirement.

Few studies have compared the risk of exposure to microbial contamination in DWSs to that in CWSs. A recent study conducted in British Columbia, Canada, estimated that individuals receiving drinking water from private wells had a fivefold increase in AGI risk over those benefiting from centralized public systems.[12] Wedgworth and Brown[29] conducted a cross-sectional case study in Alabama and found that individuals who drank water that sampled positive for fecal coliforms were 4.0 (95% CI 1.3 -14) times more likely to be sick with AGI than those who drank water with no fecal coliforms. They also found that 20% of samples from private wells were positive for fecal coliforms ($\geq$ 1 cuf/100 ml) and were 2.5 times more likely to test positive for fecal coliforms than samples from households connected to a community water system. Heaney et al.[30] tested 12 private wells and 8 households connected to CWSs in a neighborhood in Chapel Hill, North Carolina, and found that 5 of the 12 private wells tested positive for fecal indicator bacteria while none of the

houses connected to CWSs tested positive. Allevi et al.[31] published a study on private wells in Virginia and found that of 538 samples, 41% tested positive for total coliforms and 10% tested positive for *E. coli*. These previous studies suggest that households relying on DWSs might be exposed to more waterborne pathogens than those served by CWSs.

1.3 Objectives

In pursuing this dissertation, I aimed to contribute to the scientific understanding of and practical methods for assessing risks of exposure to contaminants in drinking water. Specifically, I used stochastic models to examine the effects of drinking water contamination (chemical and microbial) on public health in the counties of North Carolina. In conducting this study, I had the following goals: 1) to quantify the number of cancer cases attributable to chemically contaminated drinking water in CWSs; 2) to estimate the number of cases of AGI attributable to microbiologically contaminated drinking water; 3) to compare the risks between counties; 4) to evaluate the role of CWS size and water source on risk levels; and 5) to compare differences in risks among those relying on DWSs and those served by CWSs. This was the first study to evaluate all carcinogenic chemicals regulated under the SDWA for an entire state at the county level, and it was also the first to apply the PIM approach to determine the burden of AGI attributable to microbial contaminants in drinking water. The results of this study will help policymakers understand which counties are in greatest need of resources, help to inform prevention planning efforts and provide information useful in estimating benefits of improving water service.

The remainder of this dissertation is organized into four chapters. Chapter 2 is a quantitative county-level cancer risk assessment for the entire state for all potentially carcinogenic chemicals regulated under the SDWA. Chapter 3 compares three approaches (population intervention model, drinking water attributable risk, and quantitative microbial risk assessment) to determine the most appropriate model to estimate the percentage of emergency department visits for AGI attributable to microorganisms in North Carolina CWSs. Chapter 4 uses the most appropriate method to compares

the burden of AGI attributable to microbial contamination in CWSs to that in DWSs. Finally, Chapter 5 discusses key findings and implications from these analyses as well as future research needs.

Table 1.1 Water systems and population served in North Carolina

Community water system size and source water type		Description	Number of systems	Served population	Percent ground water systems	Percent surface water systems	Percent of state population
Community Water Systems Size	Very Small	Service 25 to 500 people	1,510	227,000	91%	9%	3%
	Small	501 to 3,300	345	487,000	64%	36%	5%
	Medium	3,301 to 10,000	136	798,000	39%	61%	8%
	Large	10,001 to 100,000	117	3,061,000	28%	72%	31%
	Very Large	Greater than 100,000	12	2,941,000	8%	92%	30%
Private Wells		Individual Household	-	2,238,000	100%	0%	23%

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Chapter 2:
Burden of Cancer from Chemicals In North Carolina Drinking Water

2.1 Introduction

The Safe Drinking Water Act (SDWA), first enacted by the U.S. Congress in 1974, provides a comprehensive framework for local, state, and federal agencies to regulate drinking water quality.[1] One essential component of the SDWA is monitoring the quality of water delivered to consumers, in order to protect consumers from adverse health effects resulting from acute and chronic exposure to contaminants. However, several previous analyses have suggested that current SDWA monitoring requirements are inefficient, in part because they fail to consider the relative public health risks of the contaminants.[2-7] These previous analyses have suggested that drinking water monitoring programs—and, indeed, the SDWA in general—could be improved by considering differential contaminant exposures by geographic region and the relative health risks of regionally varying exposures.

In order to support future analyses of the potential risks and benefits of a revised drinking water monitoring protocol that emphasizes regional variation and potential health risk, this study uses a mathematical model to estimate the annual number of cancer cases potentially attributable to chemical contaminants regulated by the SDWA in North Carolina (NC) and compares the relative cancer risks of the regulated contaminants. For each regulated contaminant, we estimate the number of cancer cases in 2010 that were potentially attributable to contamination in community water supply systems (those serving at least 15 connections or 25 people, denoted as CWSs) based on conservatively derived slope factors. We provide separate estimates for each North Carolina county in order to illustrate geographic variation across the state. The goal is to identify the contaminants or contaminant groups that pose the greatest health risk—and hence could be considered highest priority

for monitoring—by county. To our knowledge, this study is the first to quantify cancer risks by county for an entire state for all carcinogenic chemicals regulated under the SDWA.

The remainder of this section describes the origins of current monitoring requirements under the SDWA and summarizes some of the previous critiques of those requirements. It also summarizes previous estimates of cancer risks attributable to drinking water. Section 2 describes the methods and data sources employed in this analysis. The remaining sections present the results and limitations of this analysis and implications for future monitoring under the SDWA.

2.1.1 Origins of Chemical Monitoring Requirements Under the SDWA

Although President Ford signed the SDWA into law in 1974, Congress added the majority of contaminants to the SDWA under amendments enacted in 1986 in response to the Environmental Protection Agency's (EPA) perceived lack of regulatory progress in addressing emerging chemicals of concern, including many cancer-causing chemicals.[8]

The 1986 amendments required that EPA establish National Primary Drinking Water Regulations (NPDWRs) for 83 specific contaminants (listed by Congress in the amendments) within five years and add 25 new contaminants every three years thereafter. The EPA then developed Recommended Maximum Contaminant Levels (RMCLs) for each chemical. The RMCL is a non-enforceable goal set to the exposure level at which no known health effects occur, while the Maximum Contaminant Level (MCL) is an enforceable standard set as close to the RMCL as is possible.[9] In 1996 Congress passed another set of SDWA amendments, which eliminated the requirement to add 25 new contaminants every 3 years and instead established a scientific risk-based framework used to periodically determine whether to add new contaminants. However, the existing list of NPDWRs from the 1986 amendments was unchanged.[8,10]

The original 83 contaminants added under the 1986 amendments were selected primarily based on a National Academy of Sciences (NAS) report titled *Drinking Water and Health*. This report provided a detailed toxicological assessment of contaminants that *might* be found in drinking water.

However, the report did not consider occurrence and concentration of chemicals in community water systems.[9] The three main criteria for selection of NPDWRs were "(1) The analytical ability to detect a contaminant in drinking water, (2) the potential health risk, and (3) the occurrence or potential occurrence in drinking water".[9] Because the NAS study did not address contaminant occurrence, the EPA performed sampling to evaluate occurrence. In press releases describing the results of EPA's sampling, the USEPA Administrator stated, "for most of the [83] contaminants, the common factor was that they rarely occurred in drinking water and seldom at levels of public health concern."[6] Nonetheless, the original 83 contaminants remain the basis for SDWA regulations today.

The SDWA requires six-year reviews to determine which existing NPDWRs remain appropriate and which are candidates for regulatory revision. To date, the EPA has conducted two six-year reviews, completed in 2003 and 2010. Table 2.1 lists all contaminants ever regulated under the SDWA, including those that have been removed and revised as well as the 91 currently monitored contaminants. As the table shows, the majority of the original NPDWRs remain unchanged.[11,12]

2.1.2 Monitoring Under the SDWA

As previously noted, prior research suggests that the current protocol for monitoring community drinking water systems for chemical contaminants is inefficient, because it does not consider adequately the frequency of or regional variations in contaminant occurrence.[2-7] Additionally, monitoring and reporting (M/R) violations are by far the most frequent SDWA violations. A 2004 study performed by Dziegielewski and Bik[5] classified violations in four categories: MCL, TT (treatment technique), M/R (monitoring and reporting), and "other" violations. M/R violations accounted for 80,635 out of 99,495 total violations (81%) in all system sizes, with the most violations in small and very small water systems, which tend to have higher costs of compliance on a per-unit basis.[5,6] Regional variability, rigid enforcement of national standards, and the high number of M/R violations suggest that current-monitoring practices may be financially inefficient. The financial burden of water monitoring can be high, especially in small water systems, further

highlighting the potential benefits of a streamlined monitoring approach.[7] Streamlined monitoring also could help ease the workload of state personnel charged with SDWA enforcement.[13]

As a solution to current problems in SDWA monitoring, Brands and Rajagopal[2,3,7] have proposed a new approach called "place-based" monitoring, which allows for flexible monitoring based on contaminant occurrence data specific to each water system. Under the place-based strategy "contaminants [are] selected [for monitoring] based on their historical occurrence, rather than their appearance on the SDWA contaminant list." Brands and Rajagopal estimated that if the place-based strategy were implemented in 19 Iowa surface water systems, monitoring costs would decrease to about 12% of current costs, and the probability of detecting MCL violations would increase.[2,3,7] These results suggest that place-based monitoring could be effectively applied elsewhere in the United States. It follows that further research regarding which water contaminants pose risks in different regions should be performed to see if a more efficient and cost-effective mode of monitoring can be developed. Toward that end, this research evaluates the occurrence and cancer risks at the county scale of all chemical contaminants regulated under the SDWA in North Carolina.

2.1.3 Previous Estimates of Cancer Risks Attributable to Drinking Water

Previous studies have sought to quantify cancer risk from contaminants in community drinking water systems, but none has provided the spatial (county-level) resolution of our analysis for all carcinogenic chemicals regulated under the SDWA:

- **Trihalomethanes** - In 1995, Morris[14] estimated that 5,000 (95% CI: 2,000 – 7,000) annual cases of bladder cancer and 8,000 (95% CI: 200 – 14,000) annual cases of rectal cancer in the United States are attributable to exposure to trihalomethanes.
- **Arsenic** – In 1995, Morris[14] estimated that 3,000 annual cases of liver, lung, bladder, or kidney cancer are attributable to exposure to arsenic in drinking water. Additionally, in 2010 Kumar[15] estimated a national lifetime risk for lung and bladder cancer of 0.2 cases per million annually. Kumar presented results by geographic region. Within the Mid-Atlantic Region, in which North Carolina was grouped, Kumar estimated that arsenic contributes to 0.4 and 0.2 annual cases of lung and bladder cancer per million people served by public groundwater and surface water systems, respectively.[15]
- **Radon** – In 1987, Crawford-Brown and Cothern[16] estimated that 6,000 (95% CI: 1,000-30,000) excess lifetime lung cancer cases occur in the U.S. population among the 216 million persons served by public water supplies as a result of radon emanation from public water

supplies into indoor air. Crawford-Brown[17] updated this estimate in 1991 to include ingestion risks as well as inhalation risks; the resulting estimate was 25,000 (95% CI: 5,000-125,000) premature deaths in a U.S. population of approximately 250 million due to stomach, colon, liver, and lung cancer. Based on the risk estimates from the 1987 Crawford-Brown and Cothern study, Morris estimated that fewer than 100 cases of stomach, colon, liver, or lung cancer occur from radon exposure via drinking water annually.[14]

- **Volatile Organic Compounds (VOCs)** – Studies have compared the cancer risks of different VOCs but have not predicted the number of cases attributable to each chemical. In 2002, Williams and colleagues[18] investigated six different VOCs throughout California to determine which posed the greatest cancer risk and concluded that the risk from the six compounds "is not necessarily significant" without further information regarding exposure from specific drinking water sources. Williams et al. found that chloroform, followed by tetrachloroethylene (PCE) and 1,1-dicloroethylene (1,1-DCE), posed higher risks than trichloroethylene (TCE), benzene, or methyl tertiary butyl ether (MTBE); risks of chloroform (a disinfection byproduct) were twice as high as those from PCE and more than 2.5 times as high as those from 1,1-DCE. In 2004, Williams and colleagues [19] expanded their analysis to include 12 VOCs and a longer historic data record (1985-2002 instead of 1995-2001, as in the 2002 study). In this expanded analysis, they found that risks from PCE and chloroform were about equal and posed the highest risks among the 12 VOCs.

The objective of the present study is to estimate the number of annual cancer cases potentially attributable to regulated chemical contaminants in North Carolina community drinking water systems. We develop separate risk estimates for each of North Carolina's 100 counties. The results provide insight into the relative importance of currently monitored chemicals, from a public health perspective. The information gained can inform future debates about place-based or other alternative drinking water monitoring schemes to promote efficiency and cost-effectiveness. Decreased monitoring requirements for low-risk contaminants could theoretically increase attention paid to high-risk contaminants by both water utilities and regulators and hence also could improve public health protection.

2.2 Methods

We developed stochastic models based on North Carolina drinking water monitoring data, public health records, and previous epidemiological and toxicological studies to estimate the cancer burden potentially attributable to drinking water contaminants across the North Carolina population in the year 2010. We first identified regulated contaminants that potentially pose cancer risk through drinking water exposure in North Carolina. For those contaminants identified, we estimated the

number of people exposed and the probability distribution of the exposure concentration in each water system. Using a linear, no-threshold dose-response function for carcinogenicity (based on EPA-derived slope factors or relative risk functions from epidemiological meta-analyses), we quantified the probability of developing cancer based on the estimated exposure distribution of each contaminant. The probability of developing cancer was then extrapolated to the population level to quantify the number of cancer cases potentially attributable to drinking water. Simulations were performed in Analytica 4.3 (Lumina Decision Systems, Los Gatos, CA, USA), and each CWS was simulated 1,000 times for each contaminant. The remainder of this section explains the data sources, choice of contaminants for evaluation, and risk estimation methods.

2.2.1 Data Collection

We obtained monitoring data for North Carolina's 2,120 CWSs (Table 2.2) from the North Carolina Department of Environment and Natural Resources Public Water Supply Section and the EPA.[20,21] Data checking was performed using information from the Safe Drinking Water Information System (SDWIS).[22] Monitoring data from 1998-2011were collected for 67 regulated chemical contaminants (the remaining SDWA contaminants were excluded because they are microbial, are regulated by treatment technique rather than concentration, or are waived for regulation in North Carolina). The chemicals included were

- 26 synthetic organic contaminants (SOCs),
- 21 volatile organic contaminants (VOCs),
- 14 inorganic contaminants (IOCs),
- four radionuclides (RNs), and
- two disinfection byproducts (DBPs).

DBP data were available only for 2006-2011. The frequency of the reported data varied by chemical group, source water, population served, and history of violation. Among CWSs, 98% reported on

SOCs, VOCs, and IOCs (covering 99% of the population served by CWSs), 81% reported data on RNs (96% of the population served), and 95% reported on DBPs (99% of the population served).

2.2.2 Hazard Identification

The reported CWS chemical concentrations were compared against EPA's current MCL. If at least one CWS in the state reported at least one sample with a concentration exceeding the MCL for a given contaminant, we reviewed the EPA cancer guidelines to determine if the chemical may be carcinogenic.[23,24] The EPA has employed different sets of cancer classifications; we used those from both the 1986 and 2005 *Guidelines for Carcinogen Risk Assessment*. The cancer classifications of a chemical are based on a descriptive weight-of-evidence judgment regarding the likelihood that an agent is a human carcinogen as well as the conditions under which the carcinogenic effects may be expressed. For each contaminant, we obtained cancer classifications from the EPA drinking water standards and health advisories.[25] All chemicals with minimum cancer classifications of "possible human carcinogen" as defined in the 1986 guidelines, "suggestive evidence of carcinogenic potential" as defined in the 2005 guidelines, or higher cancer risk classifications were included in the analysis. Of the 67 contaminants evaluated, at least one CWS reported at least one MCL violation for 37; of these, 25 are potentially carcinogenic. Table 2.3 shows the resulting list of 25 contaminants along with information about their carcinogenic potential, number of North Carolina CWSs in which the contaminant was detected during the time period of the data set, and number of systems reporting MCL violations at any time during the period covered by the data set.

Risks of five of the 25 contaminants in Table 2.3 could not be evaluated due to insufficient exposure or dose-response information. We were unable to evaluate gross beta particle and photon radioactivity because concentrations (in total pCi/L) were reported as a chemical group rather than for the individual components that contribute to the gross beta activity measure, so it was not possible to assign a dose-response function. Uranium, para-dichlorobenzene, radium 226 and 228, and haloacetic acids (HAA5) were not evaluated due to limited information on their dose-response

functions; slope factors for these contaminants were not available from data sources used in this study (see "Dose Response Assessment" below).

Figure 2.1 summarizes the steps for identifying the 20 chemicals included in this analysis.

2.2.3 Exposure Assessment

For each of the 20 chemicals included in the risk assessment (Figure 2.1), we developed an exposure distribution specific to each community water system. Based on the collected monitoring data, we first estimated the probability of detection of each contaminant in each CWS. Then, we estimated probability distributions for chemical concentrations for samples testing positive. Due to the small sample sizes in some CWSs, we employed a Bayesian approach to develop lognormal distribution parameters for each CWS and chemical, following the method in Price et al. (1996).[26] We log-transformed the data and then calculated the statewide geometric mean of all reported concentrations above the detection limit and the corresponding statewide geometric variance. These values are defined as the "grand mean" (μ) and the "grand variance" (σ^2). Additionally, for each CWS, the prior geometric mean (μ_i) and geometric variance (k_i^2) were calculated (where i is an index representing a particular CWS). The statewide grand mean and variance as well as the CWS-specific geometric mean and variance were used to calculate an updated (posterior) estimate for the mean (μ_{i_est}) and standard deviation (σ_{i_est}) at each CWS, using the following equations (where n_i is the number of observations at the i^{th} CWS):

$$\mu_{i\_est} = \frac{\frac{1}{\sigma^2}\mu + \frac{n_i}{k_i^2}\mu_i}{\frac{1}{\sigma^2} + \frac{n_i}{k_i^2}} \quad (1)$$

$$\mu_{i\_est} = \frac{\frac{1}{\sigma^2}\mu + \frac{n_i}{k_i^2}\mu_i}{\frac{1}{\sigma^2} + \frac{n_i}{k_i^2}} \quad (2)$$

The posterior estimates account for the lower reliability of reported values from CWSs where few samples were taken. If the system did not report at all we used state-wide detection probabilities and the concentration distributions.

2.2.4 Dose-Response Assessment

The lifetime average daily dose (*LADD*, mg/kg-day) for an individual was estimated by aggregating the doses from three exposure pathways (ingestion of contaminated water, inhalation of volatilized vapors in the home, and dermal contact during household activities, such as showering). These calculations were based on standard risk assessment formulas for evaluating multiple sources of exposure and were calculated using the following equations:

Ingestion of drinking water

$$LADD_{ingest} = \frac{C \times IR}{BW} \quad (3)$$

Inhalation of volatilized contaminants

$$LADD_{inhale} = \frac{(C_s \times ET_s + C_b \times ET_b + C_h \times ET_h) \times BR \times A_{inhale}}{BW} \quad (4)$$

Dermal contact during showering

$$LADD_{dermal} = \frac{C \times SA \times PC \times F \times ET_s \times CF}{BW} \quad (5)$$

where C is the contaminant concentration (mg/L) in tap water; I is the daily volume of tap water ingested (L/day); BW is body weight (kg); C_s, C_b, and C_h are the contaminant concentration in shower air, bathroom air and household air, respectively (mg/L); ET_s, ET_b, and ET_h are exposure times in the shower, bathroom and household, respectively (h/day); BR is breathing rate (L/min); A_{inhale} is the lung absorption of each chemical (unitless); SA is the surface area of skin (cm^2); PC is the permeability coefficient between the contaminant and skin (cm/h); and F is the fraction of skin exposed (unitless). In each simulation run, chemical concentrations in water were estimated as pX, where p represents a

Bernoulli random variable with parameter equal to the contaminant detection frequency in a given water system and *X* represents a lognormal variable of the contaminant concentration in water samples with positive detections (see "Exposure Assessment" section). Table 2.4 summarizes values of all other variables in equation 5, which were derived from the EPA *Exposure Factors Handbook* and other literature sources. [27-29]

For all contaminants except TTHMs, the excess cancer risk (*ECR*) was calculated by multiplying the *LADD* for the exposure pathway by the appropriate slope factor (*SF* (mg/kg-day)$^{-1}$) for the chemical exposure pathway:

$$ECR = SF_{oral} \times LADD_{ingest} + (SF_{oral}/Abs) \times LADD_{dermal)} + SF_{inhale} \times LADD_{inhale} \quad (6)$$

where *Abs* represents the fraction of contaminant absorbed during ingestion. According to the Department of Energy Risk Assessment Information System (RAIS) and EPA guidance documents, slope factors for dermal absorption are estimated by dividing the oral ingestion slope factor by a fraction (*Abs*) representing the portion of an ingested chemical absorbed into the gastrointestinal system.[30,31] For all chemicals in this analysis, *Abs* is assumed to equal 1 based on a review of chemical-specific data in RAIS and the Integrated Risk Information System.[32]

The ECR from exposure to a chemical is defined as the probability of developing cancer by age 70 due to a lifetime of exposure. For all chemicals except arsenic, the oral and inhalation cancer *SF* values were obtained from the Integrated Risk Information Systems (IRIS)[32] database, California Environmental Protection Agency (CALEPA),[33] Office of Pesticide Program's Registration Eligibility Decision (OPP RED),[34] or Drinking Water Standards and Health Advisories (DWSHA).[25] The arsenic slope factor was obtained from a 2001 National Research Council comprehensive review of arsenic dose-response studies.[35] Slope factors for the chemicals evaluated using a slope factor are shown in supporting information A, Table 1.A1.

Risks of TTHM exposure were estimated using dose-response information from meta-analyses of epidemiologic studies.[36] Rather than providing slope factors, these studies provide estimates of relative risk (*RR*), which is the probability of contracting cancer if exposed to TTHMs divided by the probability of cancer if unexposed. Using epidemiologic meta-analyses is preferable to using slope factors from toxicologic studies, since the estimates are based on human exposures rather than on extrapolation from animal studies. Furthermore, the *RR* estimates from epidemiologic studies account for all three exposure routes (ingestion, inhalation, and absorption), so there is no need for separate risk calculations for each route. Table 1.A2 contains the *RR* estimate used in this assessment.[36]

2.2.5 Risk Characterization

We characterized the cancer risk for each CWS-chemical pair by using the *ECR* or relative risk function to calculate an attributable fraction (*AF*), defined as the proportion of cancer cases observed in the exposed population that can be attributed to the chemical exposure.[37-39]

For the chemicals for which we computed *ECR*s, we employed the following equation to convert the *ECR* to an *AF*:

$$AF = \frac{ECR}{ECR+1} \qquad (7)$$

In equation 7, the calculated *ECR* is added to the background probability of cancer for the unexposed population (I_u) in order to determine the total probability of cancer for the exposed group in the denominator. The background cancer probabilities (I_u) for each chemical-cancer pair were determined from the national average cancer rate in the U.S. from 2005 to 2008 for all cancer types evaluated.[40] Table 2.3 shows the cancer type evaluated for each contaminant. Supporting ininformation B provides background rates for each cancer type considered.

From the epidemiologic studies of total trihalomethanes, we derived the attributable fraction based on equation 8:[37]

$$AF = \frac{\sum RR(c)P(c) - 1}{\sum RR(c)P(c)} \quad (8)$$

where *RR(c)* is the relative risk associated with exposure concentration *c* and *P(c)* is the proportion of the population exposed at concentration *c*. Exposure concentrations and the population fractions exposed to these concentrations were obtained by discretizing the probability distributions for each CWS and chemical.

Using the estimated *AF*s plus observed cancer case counts in each county, we estimated the number of cancer cases potentially attributable to each chemical (*AC*) in each CWS:

$$AC = AF \times I \quad (9)$$

The observed incidence rate for each county (I_o) was provided by the North Carolina State Center for Health Statistics.[41,42]

Annual estimated attributable cancer rates were aggregated to the county level using a weighted average based on the population served by each water system in the county.

2.3. Results

In total, an estimated 295 (95% CI 163-427) cancer cases in 2010 were potentially attributable to the 20 regulated chemicals in drinking water that are carcinogenic, occur in North Carolina community water supplies, and have sufficient dose-response data available to support a risk assessment (Table 2.5). Across the state, about 48,000 new cancer cases are diagnosed annually.[42] Hence, about 0.6% of the 48,000 observed annual cases are potentially attributable to chemicals in community drinking water systems. On a per-person basis, cancer risks attributable to chemicals in community drinking water systems vary little by county (Figure 2). The mean per-person annual risk across all counties is about 4×10^{-5}; the highest risk occurs in Clay County, with a per-person annual risk estimated to be 5×10^{-4}. Annual per-person risks in all other counties are less than 10^{-4}.

Exposure to TTHMs accounted for approximately 90% of cancer cases potentially attributable to chemicals in community drinking water systems. We estimated that around 267 (95%

CI 132 – 396) cases of male bladder cancer were potentially attributable to TTHM exposure in 2010. The risk was lower among CWSs obtaining their water from groundwater sources, with a mean estimated rate of 2.7 (95% CI 1.5 – 4.0) annual cases per 100,000 served, compared to surface water systems, with a mean estimated rate of 3.8 (95% CI 1.9 – 5.6) annual cases per 100,000 served.

Approximately 15 (95% CI 3.9-65) cancer cases in 2010 were attributed to arsenic exposure in CWSs. Of these 15 cases, 5.2 (95% CI 1.4-23) were bladder and 9.8 (95% CI 2.5-42) were lung cancers. Only 1 (95% CI 0.1-3.4) of the 15 cases was attributed to exposure in a CWS with reported arsenic concentrations above the MCL. The remaining 14 cases were attributed to very low arsenic concentrations in systems that complied with the MCL. Clay County had the arsenic-associated cancer risk among CWS users, with an estimated rate of 16 (95% CI 0.7 – 66) cases per 100,000 served. The attributable cancer risk associated with arsenic in CWSs in all other counties was less than 3.2 per 100,000 (i.e., less than 3.2×10^{-5}) On average across the state, water from CWSs using groundwater as a source posed a slightly higher arsenic-associated cancer risk (0.22 cases per 100,000 served, 95% CI 0.03-0.68) than that from surface water systems (0.20 cases per 100,000 served, 95% CI 0.04-1.0).

Approximately 12 (95% CI 2-45) cancer cases in 2010 were attributed to gross alpha particle activity in CWSs. As was the case for arsenic, risks in groundwater systems were slightly higher than in surface water systems, at 0.4 (95% CI 0.09-1.3) and 0.1 (95% CI 0.01-0.5) annual cancer cases per 100,000 served, respectively. The majority of estimated cases from surface water were in Mecklenburg and Nash counties, even though neither county reported gross alpha particle activity above the MCL, 15 pCi/L. The majority of cases from Mecklenburg County were associated with the Charlotte CWS, which reported a maximum concentration of 5 pCi/L (one-third of the MCL). In total, approximately 50% of cases attributed to alpha particle activity arose from exposure concentrations below 5 pCi/L. The majority of groundwater cases were estimated to occur in Wake, Scotland and Cumberland counties.

Fewer than two potential statistical cases of cancer per year across the entire state were attributed to all 17 other chemicals combined (Table 2.5). The risks from the remaining 17 contaminants were one to five orders of magnitude less than those from TTHMs (Table 2.5, column 3).

2.4 Discussion

2.4.1 Comparison with Previous Risk Estimates

Our results are consistent with previous reviews of cancer risks associated with U.S. drinking water, which also concluded that TTHMs, radionuclides, and arsenic tend to dominate cancer risks associated with CWSs.[14,43-48] Like the previous study by Morris (1995), we conclude that cancer risks potentially associated with exposure to chemicals in CWSs arise mostly from TTHMs.[14] The Morris study concluded that approximately "5,000 (95% CI 2,000-7,000) cases of bladder cancer per year may be associated with consumption of chlorinated drinking water." At the time of the Morris study, approximately 250 million U.S. residents were served by community water supplies[1]; thus, Morris's estimate is equivalent to about 2.0 (95% CI 0.8 – 2.8) bladder cancer cases per 100,000 people per year. Similarly, the estimated 132-396 cases attributed to TTHMs from North Carolina systems serving a total of 7.5 million water system customers is equivalent to 1.8-3.9 cases per 100,000 people. On the other hand, our estimate of the arsenic cancer risk in North Carolina drinking water is about one-sixth of that estimated by Morris (1995) for the United States as a whole but about 10 times that estimated by Kumar (2010) for the Mid-Atlantic region; we estimated a risk of approximately 0.2 (95% CI 0.05 -0.9) cases per 100,000 people per year, whereas Morris's estimate was about 1.2 annual cases per 100,000 people and Kumar's was 0.022 cases per 100,000.[14,15] These differences most likely result from the large local variation in arsenic concentrations and the finer scale of analysis used in our study, as compared to the Morris and Kumar studies.

Alpha radiation, consisting of total alpha radiation minus uranium and radium-226 and -228, was the third highest contributor to cancer risk from drinking water in our study. To our knowledge,

the burden of cancer attributable to alpha radiation has not been previously estimated. The World Health Organization and the U.S. National Research Council have concluded that radionuclides follow a linear no-threshold model of carcinogenicity, meaning that ionizing radiation can increase the risk of cancer even at the lowest doses.[47] In our study we found that approximately 50% of cases came from exposure below 5 pCi/L, which is one-third of the MCL.

2.4.2 Sensitivity Analysis

As might be expected, the risk estimates are most sensitive to the uncertainty in the estimates of the relative risk of male bladder cancer associated with TTHM exposure (Figure 2.3). If male bladder relative risk is fixed at the lower end of its 95% confidence interval for each exposure concentration range (see Table 2.A2), then the total estimated cancer risk attributed to chemicals in CWSs decreases from 295 to about 180 cases in 2010, whereas fixing this parameter at its upper 95% confidence interval increases the estimated cases to more than 400. (. Variability in the frequency of detection of the evaluated chemicals in each water system and in chemical concentrations in systems in which contaminants are detected are the next most influential variables in the analysis. Uncertainty and variability in other random variables in the risk model, including the daily water intake rate, have a relatively small influence on the overall risk estimates. Notably, even when the TTHM bladder cancer relative risk estimates are set at very low values, risks attributed to TTHM exposure still dominate those attributed to other chemical contaminants.

2.4.3 Limitations

A principal limitation of this analysis is uncertainty regarding the relationships between TTHM exposures and cancer risks. The pooled analysis of six case-control studies of bladder cancer risks upon which our estimates rely found a positive association between TTHM exposure and male but not female bladder cancer risk.[36] Thus we only evaluated male bladder cancer associated with TTHMs. Nonetheless, recent research has identified a possible biological mechanism linking TTHM exposure to bladder cancer risk in both genders, strengthening confidence in the significance of

associations observed in previous epidemiologic studies.[48] Colon and rectal cancers have also been studied, and a pooled analysis of three cohort and ten case-control studies also provides evidence of a positive association between colon and rectal cancer and exposures to high concentrations of TTHMs in both genders.[49] However, a recent report from the International Agency for Research on Cancer noted that the meta-analysis included studies with poor exposure assessment.[50] In addition, the meta-analysis did not provide sufficient information to estimate a dose-response function. Therefore, our analysis excludes female bladder cancer and colorectal cancer risks potentially associated with TTHM exposure. If TTHM is a risk factor for these cancer end points, then we may have under-estimated the total cancer risk.

A second limitation is that the dose-response function used to estimate cancer risks potentially attributable to arsenic exposure relies on extrapolations from higher exposure doses observed in a Taiwanese population to lower doses typical of the U.S. population. This dose-response function was developed by the National Research Council (NRC) Committee on Toxicology, Subcommittee to Update the 1999 Arsenic in Drinking Water Report, based on a comprehensive review of available arsenic dose-response information.[35] The NRC tested the predictions of the dose-response model to alternative assumptions and found that other plausible alternatives yielded similar risks results. Nonetheless, the uncertainties in this extrapolation should be recognized.

Another limitation is that alpha radiation represents a group of contaminants, and the individual components that make up the group have different toxicities.[45,47] We evaluated alpha radiation based on information from the NRC and the EPA Drinking Water Standards and Health Advisories.[25,47] However, we do not know the individual components of alpha radiation found in the drinking water systems studied. Thus, we may have over- or under-estimated the potential impacts of this exposure, depending on the particular mixtures in North Carolina CWSs.

We excluded dermal and inhalation routes for radionuclide exposure based on recent studies indicating that inhalation from water contributes less than 2% of total household radiation exposure, since in most U.S. households the soil underlying and adjacent to the foundation contributes the

majority of indoor airborne radiation.[51,52] By excluding inhalation exposure from alpha radiation in drinking water, we may have underestimated the potential risk associated with this class of contaminants.

Lack of information on uncertainties in the EPA slope factors that we employed for all chemicals except TTHMs and arsenic is another limitation. These slope factors assume a linear no-threshold model of carcinogenicity for all contaminants. Further, they typically represent the upper 95th percentile of the estimated probability distribution of risk. In addition, most of these slope factors are extrapolated from studies in rodents, adding another potential source of error.[53] However, it is likely that these uncertainties have little to no impact on the overall results we present, because the contaminants causing most of the risk all were evaluated on the basis of human studies.

An additional limitation is that the risk estimates assume that CWS customers use the same drinking water source for a lifetime. Hence, the analysis fails to consider the effects of changes in exposure due to, for example, population in-migration or out-migration. Furthermore, the estimated number of cases reflects those attributable only to the North Carolina population as of 2010 and therefore does not reflect potential changes in risks as the population continues to grow.

A final limitation is that available public health data were insufficiently refined at the spatial scale to assign a cancer rate separately for each CWS. Therefore, we assumed a homogenous distribution of cancers across each county. As a result, we may under- or over-estimate rates in certain counties.

Due to the large uncertainties in the strength of association between contaminant exposures and cancer risks and to the limitations of available exposure and health outcome data, the results of this analysis are best viewed as providing relative rather than absolute estimates of cancer risks potentially attributable to chemicals in drinking water. The third column of Table 2.5 shows the number of cases potentially attributable to each chemical relative to the number of cases attributable to the lowest-risk chemical, lindane. As shown, the risk estimate for TTHMs is nearly 30,000 times the lindane risk estimate, and the estimates for arsenic and gross alpha radiation are approximately

8,000 and 5,000 times higher than the estimate for lindane, respectively. Similarly, these three chemicals dominate risks from all other chemicals included in the analysis. The major conclusion of this analysis is therefore that nearly 100% of any cancer risk attributable to chemicals in North Carolina community water supply systems appears to arise from just three of the dozens of regulated chemicals.

2.5 Conclusions

This paper attributed 295 (0.6%) of the 48,000 cancer cases in North Carolina in 2010 to regulated chemicals in community drinking water systems. Even though the Safe Drinking Water Act requires regulation and monitoring of 34 chemicals thought to be carcinogens, in North Carolina nearly all of the cancer risk potentially associated with drinking water arises from just three contaminants. Disinfection byproducts are estimated to be responsible for 90% of the risk (267 of 295 attributable cancers in 2010) and arsenic and alpha radiation for the remaining 10%. Thus, not only do the vast majority of regulated chemicals pose negligible to zero cancer risk, but the overall cancer risk attributable to drinking water is extremely low, representing a very small fraction of all North Carolina cancer cases.

The results of this research underscore the potential benefits of reconsidering the contaminant-by-contaminant monitoring approach currently mandated by the SDWA. A place-based regulatory strategy emphasizing the contaminants posing the most risk and considering the regional variation in exposures could reduce the overall costs to water utilities and state regulators of implementing the SDWA while increasing protection of public health. Indeed, the EPA has recognized the need for an approach that moves beyond contaminant-by-contaminant regulation and is gathering information on potential alternative approaches under a drinking water strategy (*A New Approach to Protecting Drinking Water and Public Health*). This research can inform the ongoing debates over strategies for ensuring the public is protected from risks posed by drinking water contamination

Table 2.1: Contaminants Regulated by the SDWA [53-56]

	Contaminant	Type	Added	Revised	Removed
1	Acrylamide *	OC	1991		
2	Alachlor *,#	OC	1991		
3	Aldicarb *	OC	1991		
4	Aldicarb sulfone *,+	OC	1991		
5	Aldicarb sulfoxide *,+	OC	1991		
6	Alpha/photon emitters *,#	R	1976		
7	Aluminum *,X	IOC	--		X
8	Antimony *,#	IOC	1992		
9	Arsenic *,#	IOC	1976		
10	Asbestos *,#	IOC	1991		
11	Atrazine *,#	OC	1991		
12	Barium *,#	IOC	1976	1991	
13	Benzene *,#	OC	1987		
14	Benzo(a)pyrene (PAHs) *,#	OC	1992		
15	Beryllium *,#	IOC	1992		
16	Beta photon emitters *,#	R	1976		
17	Bromate	DBP	1998		
18	Cadmium *,#	IOC	1976	1991	
19	Carbofuran *,#	OC	1991		
20	Carbon tetrachloride *,#	OC	1987		
21	Chloramines (as Cl_2)	D	1998		
22	Chlordane *,#	OC	1991		
23	Chlorine (as Cl_2)	D	1998		
24	Chlorine dioxide (as ClO_2)	D	1998		
25	Chlorite	DBP	1998		
26	(mono) Chlorobenzene *,#	OC	1991		
27	Chromium (total) *,#	IOC	1976	1991	
28	Copper *	IOC	1991		
29	*Cryptosporidium*	M	1998		
30	Cyanide (as free cyanide) *,#	IOC	1992		
31	2,4-D *,#	OC	1976	1991	
32	Dalapon *,#	OC	1992		
33	1,2-Dibromo-3-chloropropane (DBCP) *,#	OC	1991		
34	Dibromomethane *, X	OC	--		X
35	o-Dichlorobenzene *,#	OC	1991		
36	p-Dichlorobenzene *,#	OC	1987		

	Contaminant	Type	Added	Revised	Removed
37	1,2-Dichloroethane *,#	OC	1987		
38	1,1-Dichloroethylene *,#	OC	1987		
39	cis-1,2-Dichloroethylene *,#	OC	1991		
40	trans-1,2-Dichloroethylene *,#	OC	1991		
41	Dichloromethane *,#	OC	1992		
42	1,2-Dichloropropane *,#	OC	1991		
43	Di(2-ethylhexyl) adipate *,#	OC	1992		
44	Di(2-ethylhexyl)phthalate *,#	OC	1992		
45	Dinoseb *,#	OC	1992		
46	Dioxin (2,3,7,8-TCDD) *, ~	OC	1992		
47	Diquat *, ~	OC	1992		
48	Endothall *, ~	OC	1992		
49	Endrin *,#	OC	1976	1992	
50	Epichlorohydrin *	OC	1991		
51	Ethylbenzene *,+,#	OC	1991		
52	Ethylene dibromide (EDB) *,#	OC	1991		
53	Fluoride *,#	IOC	1976	1986	
54	Giardia lamblia *	M	1989		
55	Glyphosate *, ~	OC	1992		
56	Haloacetic acids (HAA5)	DBP	1998		
57	Heptachlor *,+,#	OC	1991		
58	Heptachlor epoxide *,+,#	OC	1991		
59	Hexachlorobenzene #	OC	1992		
60	Hexachlorocyclopentadiene *,#	OC	1992		
61	Lead *	IOC	1976	1991	
62	*Legionella* *	M	1989		
63	Lindane *,#	OC	1976	1991	
64	Mercury (inorganic) *,#	IOC	1976	1991	
65	Methoxychlor *,#	OC	1976	1991	
66	Molybdenum *,X	IOC	--		X
67	Nickel *,#	IOC	1992		1995 remand
68	Nitrate (measured as Nitrogen) *,#	IOC	1976	1991	
69	Nitrite (measured as Nitrogen) *,+,#	IOC	1991		
70	Oxamyl (Vydate) *,#	OC	1992		
71	Pentachlorophenol *,#	OC	1991		

	Contaminant	Type	Added	Revised	Removed
72	Picloram *,#	OC	1992		
73	Polychlorinated biphenyls (PCBs) *,#	OC	1991		
74	Radium 226 *,#	R	1976		
75	Radium 228 *,#	R	1976		
76	Radon *	R	--		X
77	Selenium *,#	IOC	1976	1991	
78	Silver *, X	IOC	1976		X (1991)
70	Simazine *,#	OC	1992		
80	Sodium *, X	IOC	--		X
81	Styrene *,+,#	OC	1991		
82	Sulfate *	IOC	--		
83	Tetrachloroethylene *,#	OC	1991		
84	Thallium *,#	IOC	1992		
85	Toluene *,#	OC	1991		
86	Total Coliforms –(including Fecal coliform and *E. coli)* *,#	M	1976	1989	
87	Total Trihalomethanes (TTHMs)	DBP	1979		
88	Toxaphene *,#	OC	1976	1991	
89	2,4,5-TP (Silvex) *,#	OC	1976	1991	
90	1,2,4-Trichlorobenzene *,#	OC	1992		
91	1,1,1-Trichloroethane *,#	OC	1987		
92	1,1,2-Trichloroethane *,#	OC	1992		
93	Trichloroethylene *,#	OC	1987		
94	Turbidity *	M	1976	1989	
95	Uranium *,#	R	2000		
96	Vanadium *, X	IOC	--		X
97	Vinyl chloride *,#	OC	1987		
98	Viruses (enteric) *	M	1989		
99	Xylenes (total) *,#	OC	1991		
100	Zinc *, X	IOC	--		X

Types of Contaminants: D – Disinfectant; DBP – Disinfection Byproduct; IOC – Inorganic Chemical; M – Microorganism; OC – Organic Chemical; R – Radionuclides

*- Denotes the 83 contaminants required to be regulated under SDWA Amendments of 1986

X - Denotes the 7 contaminants added to then removed from the SDWA list of 83 contaminants

+ - Denotes the 7 contaminants substituted for the above removed contaminants

- Monitored in NC (according to the 2010 Public Water Systems Compliance Report)

~ – NC State-wide waiver (according to the 2010 Public Water Systems Compliance Report)

^ – Perchlorate is not yet regulated but in 2011 the process to develop a NPDWR was initiated [58]

Table 2.2: Size Distribution, Source Water Type, and Population Served by Community Water Systems in North Carolina

Size Category	Description	Number of Systems	Population Served	Percent Ground Water Systems	Percent Surface Water Systems
Very Small	Serve 25-500 people	1,510	227,341	91%	9%
Small	Serve 501-3,300	345	487,176	64%	36%
Medium	Serve 3,301-10,000	136	798,471	39%	61%
Large	Serve 10,001-100,000	117	3,061,791	28%	72%
Very Large	Serve more than 100,000	12	2,941,601	8%	92%

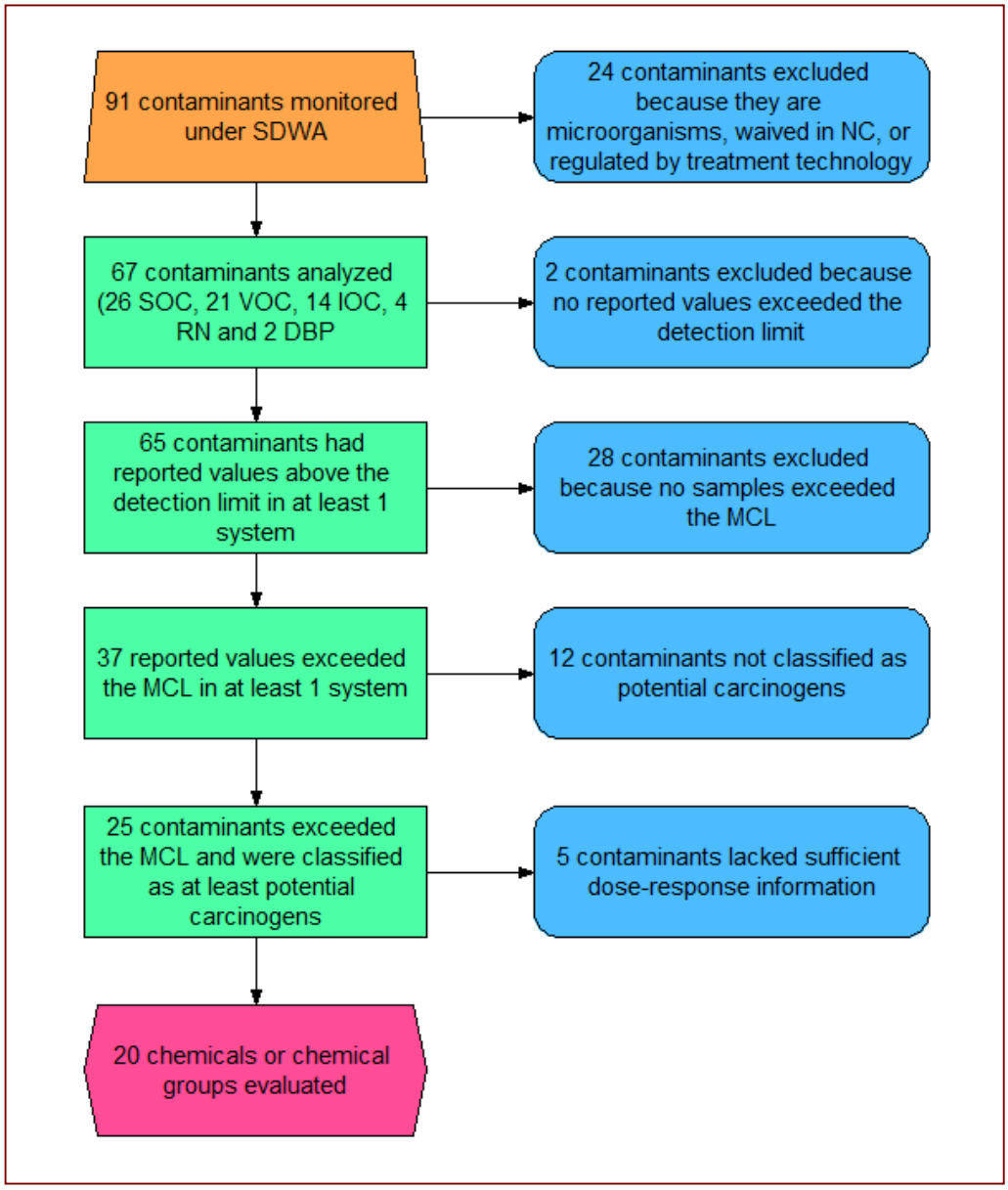

Figure 2.1 Schematic of the process used to determine which contaminants to include in assessing cancer risks attributable to NC community water supplies.

*SDWA (Safe Drinking Water Act), SOC (Synthetic Organic Compound), VOC (Volatile Organic Compound), IOC (Inorganic Compound), RN (Radionuclide), DBP (Disinfection Byproduct), MCL (Maximum Contaminant Level)

Table 2.3: Prevalence of 25 Carcinogenic Contaminants in NC Community Water Supply Systems, 1998-2011[a]

Chemical	Sources	MCL (mg/L)	Cancer Class[b]	Cancer Type(s)	Systems Detecting Contaminant	Systems Reporting Above MCL	Population Exposed	Population Exposed Above MCL
1,1-Dichloroethylene[30,32,34]	Discharge from industrial chemical factories	0.007	S	Liver	68	3	148,427	3,810
1,2-Dibromo-3-chloropropane (DBCP) [30,32]	Runoff/leaching from soil fumigant used on soybeans, cotton, pineapples, and orchards	0.0002	B2	Kidney	45	2	47,174	17,074
1,2-Dichloroethane[30,32]	Discharge from drug and chemical factories	0.005	B2	Lung/ bronchus, stomach, liver, leukemia	67	3	42,379	3,399
1,2-Dichloropropane[30-32]	Discharge from industrial chemical factories	0.005	B2	All cancer	92	5	51,224	1,026
Arsenic[35,56,57]	Erosion of natural deposits; runoff from orchards, runoff from glass & electronics production wastes	0.01	A	Lung/ bronchus, bladder	168	12	1,579,520	22,750
Asbestos@ [25,30,32]	Decay of asbestos cement in water mains	7-MFL	A	Lung/bronchus	878	2	2,587,951	27,577
Benzo(a)pyrene[30,32]	Leaching water storage tanks and distribution lines	0.0002	B2	Lung/bronchus, stomach	55	1	1,044,873	950
Carbon tetrachloride[30,32]	Discharge from chemical plants and other industrial activities	0.005	B2	Liver	124	1	647,051	85
Chlordane[30,32]	Residue of banned termiticide	0.002	B2	Liver	62	4	38,331	561
Di(2-ethylhexyl)phthalate (DEHP) [30,32]	Discharge from rubber and chemical factories	0.006	B2	All cancer	411	26	2,847,784	63,441
Dichloromethane[30,32]	Discharge from drug and chemical factories	0.005	L	Lung/bronchus, liver	129	5	944,969	850
Ethylene dibromide (EDB) [30,32]	Discharge from petroleum refineries	0.00005	L	Stomach	78	13	162,516	65,959
Gross alpha particle activity@[25,47]	Natural deposits of certain minerals that are radioactive	15 pCi/L	A	All cancer	1,514	96	5,026,307	94,069

Chemical	Sources	MCL (mg/L)	Cancer Class[b]	Cancer Type(s)	Systems Detecting Contaminant	Systems Reporting Above MCL	Population Exposed	Population Exposed Above MCL
Gross beta particle activity[25]	Decay of natural and man-made deposits of certain minerals that are radioactive	4 mrem/yr	A		1,498	20	6,918,252	461,337
Haloacetic acids (HAA5) [25]	Byproduct of drinking water disinfection	0.06	B2		1,136	288	7,231,074	3,782,238
Heptachlor epoxide[30,32]	Breakdown of heptachlor	0.0002	B2	Liver, bladder	77	5	65,099	1,032
Lindane[30,32,33]	Runoff/leaching from insecticide used on cattle, lumber, gardens	0.0002	S	All cancer	77	2	132,191	5,592
para-Dichlorobenzene[32]	Discharge from industrial chemical factories	0.075	C		29	1	148,044	229
Radium 226 & 228[25]	Erosion of natural deposits	5 pCi/L	A		773	104	3,920,522	207,064
Tetrachloroethylene (PCE) [30,32]	Discharge from factories and dry cleaners	0.005	L	Liver, kidney	112	4	236,526	9,147
Toxaphene[30,32]	Runoff/leaching from insecticide used on cotton and cattle	0.003	B2	Liver	43	1	29,914	305
Trichloroethylene (TCE) [30,32]	Discharge from metal degreasing sites and other factories	0.005	H	Liver, kidney, non-Hodgkin lymphoma	83	5	124,560	12,644
Total trihalomethanes (TTHM) [30,32,33,36]	Byproduct of drinking water disinfection	0.08	B2	Male Bladder	1,464	419	7,414,271	5,950,785
Uranium[25]	Erosion of natural deposits	0.03	A		374	62	2,706,568	32,441
Vinyl Chloride[30,32]	Leaching from PVC pipes; discharge from plastic factories	0.002	H	Liver	52	2	44,572	14,801

[a]Data represent occurrence during 1998-2011 for all contaminants except TTHMs. TTHM data cover the years 2006-2011.
[b]H–carcinogenic to humans (EPA 2005); L–likely to be carcinogenic to humans (EPA 2005); S-suggestive evidence of carcinogenic potential (EPA 2005); A–human carcinogen (EPA 1986); B2–sufficient evidence in animals and inadequate or no evidence in humans (EPA 1986); C–possible human carcinogen (EPA 1986)

Table 2.4: Parameters Used to Estimate Potential Household Exposures to Chemicals in Drinking Water

Exposure Parameters	Distribution	Mean (SD)	Data Source
General Parameters			
Water concentration (mg/L)	Lognormal	CWS specific	NCDENR or EPA[20-22]
Body weight (kg)	Normal	65 (24.5)[B] 59(18.3)[F] 69(17.8)[M]	EPA exposures factors handbook[29]
Ingestion			
Intake (L/day)	Lognormal	1.129 (0.67)	Study on water intake [28]
Inhalation			
Water use rate, shower (L/day)	Normal	386 (76.5)	EPA exposures factors handbook[29]
Water use rate, bathroom (L/day)	Normal	300 (66.3)	EPA exposures factors handbook[29]
Water use rate, house (L/day)	Normal	400 (84.2)	EPA exposures factors handbook[29]
Transfer efficiency from shower/bath water to air (unitless)	Deterministic	0.37[a], 0.016[b], 0.15[c], 0.0013[d], 0.50[e], 0.051[f], 0.078[g], 0.032[h], 0.53[i], 0.51[j], 0.47[k], 0.48[l], 0.57[m], 0.45[n], 0.49[o], 0.13[p], 0[q], 0[r], 0[s], 0[t], 0.52[u], 0.46[v], 0.52[w], 0.50[x]	McKone (1987) and EPA 2012 [27,59]
Transfer efficiency from toilet water to air (unitless)	Deterministic	0.17[a], 0.0072[b], 0.068[c], 0.00058[d], 0.23[e], 0.024[f], 0.036[g], 0.015[h], 0.25[i], 0.23[j], 0.22[k], 0.22[l], 0.26[m], 0.21[n], 0.22[o], 0.059[p], 0[q], 0[r], 0[s], 0[t], 0.24[u], 0.21[v], 0.24[w], 0.23[x]	McKone (1987) and EPA 2012 [27,59]
Transfer efficiency from other household water use to air (unitless)	Deterministic	0.45[a], 0.019[b], 0.18[c], 0.0016[d], 0.61[e], 0.063[f], 0.096[g], 0.039[h], 0.66[i], 0.62[j], 0.58[k], 0.59[l], 0.70[m], 0.56[n], 0.60[o], 0.16[p], 0[q], 0[r], 0[s], 0[t], 0.64[u], 0.57[v], 0.65[w], 0.61[x]	McKone (1987) and EPA 2012 [27,59]

Exposure Parameters	Distribution	Mean (SD)	Data Source
Air exchange rate, bathroom (L/min)	Normal	34 (19.5)	McKone (1987) [27]
Air exchange rate, house (L/min)	Normal	100 (34.5)	McKone (1987) [27]
Breathing rate, awake (L/min)	Uniform	(16,23)	EPA exposures factors handbook[29]
Breathing rate, sleep (L/min)	Uniform	(6.6,10)	EPA exposures factors handbook[29]
Absorption fraction (unitless)	Deterministic	1	
Exposure time, shower (hours)	Deterministic	1/6 hour between 7 and 7:40 am	McKone (1987) and EPA exposures factors handbook [27,29]
Exposure time, bathroom (hours)	Deterministic	1/3 hour between 7 and 9 and 1/3 hour rest of the day	McKone (1987) and EPA exposures factors handbook [27,29]
Exposure time, house (hours)	Deterministic	8 hours sleeping 4 hours awake	McKone (1987) and EPA exposures factors handbook [27,29]
Dermal			
Skin surface area (m^3)	Lognormal	1.92 (0.23)	EPA exposures factors handbook[29]
Fraction of skin contacting water (unitless)	Deterministic	0.9	EPA exposures factors handbook[29]
Exposure time (hours)	Deterministic	1/6	McKone (1987) and EPA exposures factors handbook [27,29]
Permeability coefficient (cm/hour)	Deterministic	0.033[a], 1.2[b], 0.052[c], 0.033[d], 0.0033[e], 0.01[f], 0.014[g], 0.015[h], 0.016[i], 0.0053[j], 0.01[k], 0.022[l], 0.0045[m], 0.37[n], 0.23[o], 0.0073[p], 0.001[q], 0[r], 0[s], 0[t], 0.089[u], 0.026[v], 0.058[w], 0.039[x]	EPA [60]

[a]1,2-Dibromo-3-chloropropane (DBCP). [b]Benzo(a)pyrene. [c]Chlordane. [d]Di(2-ethylhexyl)phthalate (DEHP). [e]Ethylene dibromide (EDB). [f]Heptachlor Epoxide. [g]Lindane. [h]Toxaphene. [i]1,1-Dichloroethylene. [j]1,2-Dichloroethane. [k]1,2-Dichloropropane. [l]Carbon tetrachloride. [m]Dichloromethane. [n]Tetrachloroethylene (PCE). [o]Trichloroethylene (TCE). [p]Vinyl Chloride. [q]Arsenic. [r]Asbestos. [s]Gross Alpha. [t]TTHMs. [u]Chloroform. [v]Bromoform. [w]Bromodichloromethane. [x]Dibromochloromethane. [B]Both male and female body weight. [F]Female body weight. [M]Male body weight.

Table 2.5. Annual Cancer Cases Potentially Attributable to Contaminants in North Carolina Community Water Systems

Chemical	Attributable Cancer Cases (95% CI)	Risk Relative to Lowest-Risk Contaminant (Lindane)
TTHM	267 (132-396)	29,700 (4,300-1,000,000)
Arsenic	15 (3.9-65)	8,200 (210-35,000)
Gross alpha activity	12 (2-45)	5,200 (290-22,000)
1,1-Dichloroethylene	0.7 (0.06-4)	369 (6-1,900)
Carbon tetrachloride	0.2 (0.002-1)	79 (0.1-650)
1,2-Dibromo-3-chloropropane (DBCP)	0.1 (0.003-0.5)	72 (0.4-397)
Benzo(a)pyrene	0.1 (0-1.3)	67 (0-495)
Tetrachloroethylene (PCE)	0.1 (0.009-0.3)	54 (0.9-290)
1,2-Dichloropropane	0.1 (0.03-0.3)	51 (1.8-217)
Heptachlor epoxide	0.1 (0.02-0.4)	50 (1.7-273)
Toxaphene	0.09 (0.02-0.3)	41 (1.5-186)
Di(2-ethylhexyl)phthalate (DEHP)	0.08 (0.005-0.4)	34 (0.7-235)
Trichloroethylene (TCE)	0.06 (0.006-0.3)	29 (0.5-165)
Chlordane	0.05 (0.01-0.2)	26 (0.8-130)
Ethylene dibromide (EDB)	0.04 (0.001-0.2)	15 (0.2-79)
Asbestos	0.04 (0.008-0.1)	15 (0.8-61)
Dichloromethane	0.03 (0.0004 -0.3)	12 (0.03-87)
Vinyl chloride	0.02 (0.0002-0.1)	10 (0.02-64)
1,2-Dichloroethane	0.02 (0.001 -0.05)	6 (0.1-32)
Lindane	0.009 (0.0003-0.05)	1

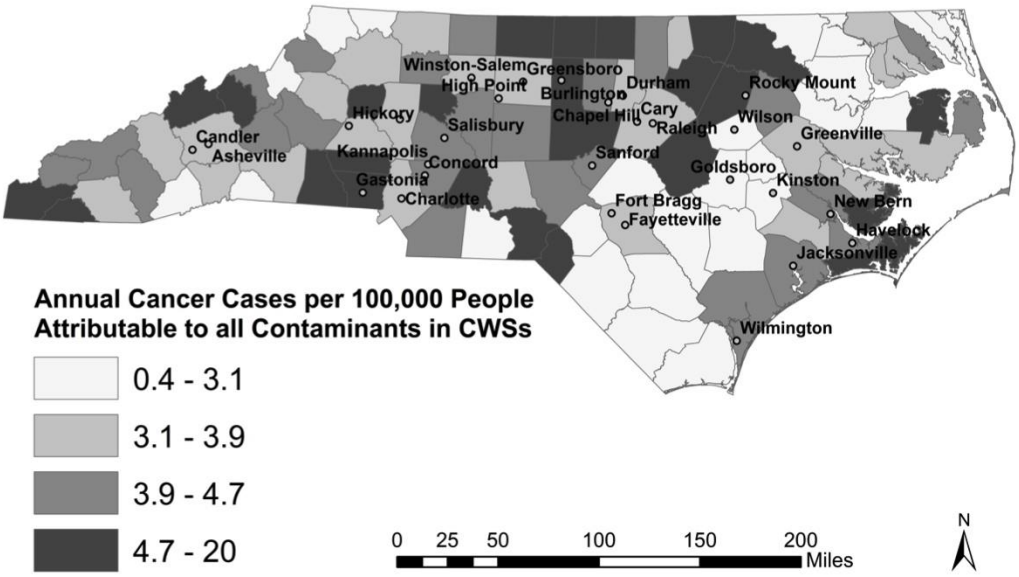

Figure 2.2: Spatial distribution of cancer risks potentially attributable to all chemical contaminants in NC community drinking water systems. Shading denotes risk quartiles among NC's 100 counties (i.e., 25 counties in which attributable risk is lowest among NC counties, etc.). Overall, the risks are low (less than 10^{-4} in all but one county), and the variance in risk by county also is relatively small (coefficient of variation = 0.55).

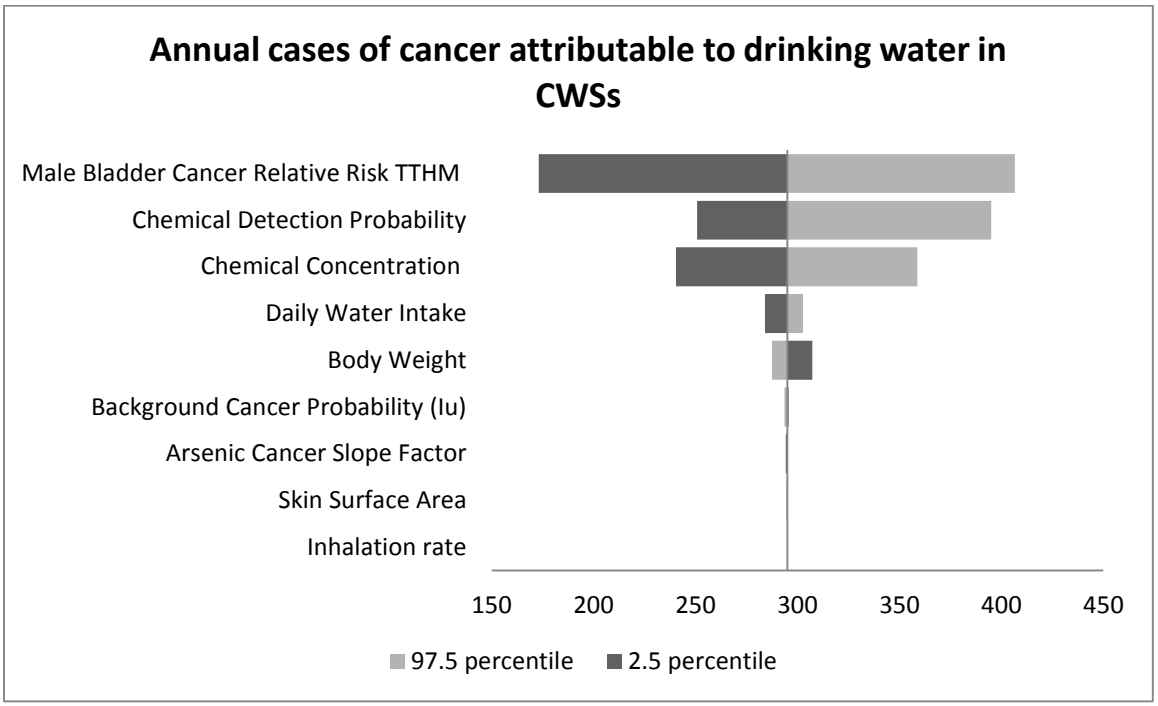

Figure 2.3: Sensitivity of the risk estimates presented here to changes in risk model input variables. The bars show the number of cancer cases that would be estimated if each variable noted on the left side of the chart were fixed at its 2.5 percentile or 97.5 percentile value while holding all other values as in the main analysis. Hence, the wider the bar, the more sensitive is the result to the indicated variable. The "chemical detection probability" and "chemical concentration" variables represent the aggregate effects of changing these variables for each water system and chemical from low to high values.

2.6 Supporting Information

Supporting information A

This contains model input values associated with the slope factors and relative risks used to calculate the excess cancer rate associated with contaminant exposure via drinking water.

Table 2.A1. Oral and Inhalation Slope Factors

Chemical	Oral Slope Factor (per mg/kg-day)	Inhalation Slope Factor (per mg/kg-day)
1,1-Dichloroethylene[30,32,34]	0.581	0.18
1,2-Dibromo-3-Chloropropane (DBCP) [30,32]	0.82	7
1,2-Dichloroethane[30,32]	0.0912	0.072
1,2-Dichloropropane[30,32,33]	0.0363	0.036
Alpha Radiation@[25,47]	15 pCi/L	-
Arsenic[35]	13.6^{MB}, 8.4^{FB}, 9.5^{ML}, 10.8^{FL}	-
Asbestos@ [25]	700-MFL*,[2]	-
Benzo(a)pyrene[30,32]	7.32	0.137
Carbon tetrachloride[30,32]	0.072	0.15
Chlordane[30,31]	0.352	0.35
Di(2-ethylhexyl)phthalate (DEHP) [30,32]	0.0142	7
Dichloromethane[30,32]	0.0022	0.0035
Ethylene dibromide (EDB) [30,32]	1.752	-
Heptachlor Epoxide[30,32]	9.12	
Lindane[33]	1.13	-
Tetrachloroethylene (PCE) [30,32]	0.00212	0.021
Toxaphene[30,32]	1.12	-
Trichloroethylene (TCE) [30,32]	0.0462	0.007
Vinyl Chloride[30,32]	1.52	0.027

*MFL-million fibers per liter; @slope factor was derived from the 10^{-4} cancer rate; MB-male bladder cancer; FB-female bladder cancer; ML- male lung cancer; FL-female lung cancer

Table 2.A2. Relative Risk of Male Bladder Cancer Associated with Exposure to TTHMs[36]

TTHM Concentration	RR (95% CI)
<5 ug/L	1
5-25 ug/L	1.26 (1.05-1.51)
25-50 ug/L	1.25 (1.04-1.50)
> 50 ug/L	1.44 (1.20-1.73)

Supporting information B

This section contains the background cancer rate associated with each chemical and the associated cancer type evaluated.

Table 2.B1. National Cancer Rates Per 100,000 People[39]

Chemical	Cancer Type Evaluated	National Cancer Rate per 100,000 People (95% CI)
1,1-Dichloroethylene	Liver	23.7
1,2-Dibromo-3-Chloropropane (DBCP)	Kidney	15.8
1,2-Dichloroethane	Lung/ Bronchus, Stomach, Liver, Leukemia	96.9 (87.3-102.4)
1,2-Dichloropropane	All cancer	473 (452-497)
Alpha Radiation	All cancer	473 (452-497)
Arsenic	Male Bladder	35(33-36)
	Female Bladder	10.1 (9.8-10.5)
	Male Lung	75(66-84)
	Female Lung	54(47-59)
Asbestos	Lung/Bronchus	65(57-72
Benzo(a)pyrene	Lung/Bronchus, Stomach	74(66-82)
Carbon tetrachloride	Liver	7.95
Chlordane	Liver	7.95
Di(2-ethylhexyl)phthalate (DEHP)	All cancer	473 (452-497)
Dichloromethane	Lung/Bronchus, Liver	73(65-80)
Ethylene dibromide (EDB)	Stomach	9.5(8.1-10.8)
Heptachlor Epoxide	Liver, Bladder	30.6(29.7-31.3)
Lindane	All cancer	473 (452-497)
Tetrachloroethylene (PCE)	Liver, Kidney	23.75
Toxaphene	Liver	7.95
Trichloroethylene (TCE)	Liver, Kidney, Non-Hodgkin Lymphoma	43.45
Total Trihalomethanes (TTHM)	Male Bladder	76(68-83)
Vinyl Chloride	Liver	7.95

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Chapter 3:
Burden of Acute Gastrointestinal Illness from Microbial Contaminants in North Carolina Community Water Systems

3.1 Introduction

The introduction of improved municipal water and sewer services in the United States (US) was one of the most influential public health advances during the twentieth century, leading to a major reduction in the environmental burden of disease. These interventions are credited with a 75% reduction in infant mortality, a 67% decrease in child mortality, and a 50% reduction in total mortality between 1900 and 1936.[1] Filtration and chlorination of drinking water contributed to the majority of observed mortality reductions; these methods are highly effective at preventing common causes of waterborne enteric disease. Nonetheless, pathogens can still enter the drinking water stream due to pathogen resistance to disinfection (e.g. *Giardia*, *Cryptosporidium*, and enteric viruses), periodic water treatment failures, or contamination in the distribution system. As a result, disease risk from drinking water persists even in areas with community water systems (CWSs, defined as drinking water systems serving at least 25 residents or at least 15 residential connections year-round). The magnitude of waterborne disease risk in US communities with CWSs is thought to be substantial but is not well quantified.

Improved methods for estimating the disease burden attributable to microbial contamination of CWSs could identify CWSs and geographic regions most in need of assistance and inform future drinking water policy decisions.[2-4] Toward this end, this paper uses three different approaches to quantify the annual acute gastrointestinal illness (AGI) rate attributable to microbial contamination of CWSs in North Carolina (NC) by combining public health and drinking water quality data. We

compare the results of the three approaches, two of which were used in previous studies (though not in NC) and one not previously employed for assessing waterborne disease risks from US CWSs. Questions have been raised concerning how well US waterborne disease risks can be quantified; thus, using all three models with the same raw data will help identify the shortfalls within each model. [5-7] We also conduct the first county-level statistical analyses of associations between NC emergency department (ED) visits for AGI and CWS violations of Safe Drinking Water Act (SDWA) microbiological standards. Because 26% of the NC population lacks access to a CWS and therefore relies on private well water, [8] this latter analysis controls for the effects of exposure to microbial contamination in private wells, which are not subject to SDWA requirements.

The two previously used risk assessment approaches compared in this study are quantitative microbial risk assessment (QMRA) and drinking water attributable risk (DWAR) analyses. The third approach, the population intervention model (PIM), has been used to evaluate health benefits of water and sanitation interventions in developing countries and interventions targeted at risk factors such as smoking, HIV, social disparities, and depression. [9-12] The PIM estimates risk based exclusively on data specific to the at-risk population, whereas the QMRA and DWAR methods rely partially on dose-response estimates from previous epidemiologic studies of other populations. [6,13] This article compares the three approaches and identifies the strengths and limitations of each. In so doing, it also provides estimates of the geographic distribution and magnitude of waterborne disease risks in NC.

3.1.1 Previous risk estimates in developed nations

Three research groups have developed national estimates of the number of AGI cases attributable to US CWSs. Their results ranged from 4–32 million annual cases (2–18% of all cases). [3,6,14] None of the studies provides information about the spatial variability in risks—an important consideration in decision-making to improve water quality.

Others studies have estimated AGI risks among populations served by CWSs using non-disinfected groundwater. Macler and Merkle[15] estimated that microbial contamination of non-

disinfected groundwater CWSs contributed 0.75–5.0 million US AGI cases annually (5%-32% of all cases among the population served by these CWSs). Borchardt et al. [16] found that 6%–22% of AGI cases were attributable to tap-waterborne viruses in 13 Wisconsin communities with undisinfected groundwater supplies.

Similar research in England found that water systems serving fewer than 5,000 people and lacking treatment were more likely (OR 1.8, 95% CI 1.5 -2.3) to be contaminated than water systems with treatment (chlorination, UV radiation, and/or filtration) and that, as a result, the mean annual risk of infection was 57% for *Cryptosporidium* and 9.1% for *Giardia*. [17,18] A recent Canadian study concluded that residents of communities with mixed surface and groundwater systems were 2.3 times more likely to suffer from AGI than those in communities relying on groundwater. [19]

Source water contamination and deficiencies in treatment are not the only causes of exposure to microbial contaminants in drinking water. A Wisconsin community study estimated that 0.1–4.9% of all AGI cases were attributable to a lack of residual disinfectant in the distribution system. [20] A U.K. study concluded that distribution systems might contribute to 15% of AGI cases. [21]

These previous studies have important limitations, which we seek to overcome in this paper. First, some of the studies considered only a single pathogen or pathogen group and hence may account for only a small portion of the potential risk. Second, the previous US national risk estimates relied on previous epidemiologic studies of targeted populations (for example, residents of a single city), the findings of which may not generalize to other populations with different demographic and water supply characteristics (e.g., access to a public water system). As evidence of such differences, in a review of previous US epidemiologic studies Colford et al. found that AGI risks varied from one population to the next by a factor of 42—from 0.02 to 0.85 cases per person-year. [14]

This study estimates the AGI risk associated with exposure to microbial contaminants in NC CWSs using data on occurrence of indicator organisms (microbes that indicate the potential presence

of fecal pathogens) and health outcomes specific to NC. The approach overcomes some of the deficiencies of previous efforts by considering multiple pathogens and by using local health outcome data to produce context- and population-specific estimates.

3.2 Methods

3.2.1 Data

3.2.1.1 Water Quality Data

The Safe Drinking Water Act (SDWA) requires all CWSs to monitor total coliform bacteria as indicators of potential fecal contamination. If more than 5% of samples over a 30-day period test positive for total coliform bacteria, then the system is in violation of the monthly maximum contamination level (MCL). [22] Follow-up analysis for *E. coli* or fecal coliforms is required for any sample testing positive for total coliforms; a positive result indicates the system had violated the acute MCL. The NC Department of Environment and Natural Resources (NCDENR) provided microbial water quality violation data for all 2,120 active NC CWSs for 2006–2013 (Table 3.S1). [23]

3.2.1.2 AGI Reported Cases

We used ED visits for AGI as a proxy for AGI incidence, while recognizing that only a fraction of those with AGI will seek treatment in an ED. ED visit data for 2007– 2013 were extracted from the NC Disease Event Tracking and Epidemiologic Collection Tool (NCDETECT), which contains near real-time electronic data from all 122 NC EDs, as mandated by state law 130A-480. [24] In keeping with prior research, AGI visits were defined using the following diagnostic codes: infectious GI illness (001 to 009), non-infectious GI illness (558.9), and nausea and vomiting (787.01–787.03, 787.91). [2, 6, 14, 25, 26,27]

To compare NC with national rates, we estimated the mean national AGI ED visit rate from data in Jones et al., who estimated the mean total US AGI rate=0.62 (95% CI: 0.57-0.65) cases per person-year and the mean ED visit rate per AGI case=0.064 (95% CI: 0.05-0.078). [27] Representing both rates as normally distributed and multiplying them yields a mean national AGI visit rate=0.040

(95% CI: 0.031-0.049) per person-year. From the inverse of this rate, every AGI ED visit represents approximately 16 (95% CI: 13-20) AGI cases.

3.2.2 Models

3.2.2.1 Population Intervention Model (PIM)

To implement the PIM, a longitudinal multivariate linear feasible generalized least squares regression model with ar1 autocorrelation was fitted to monthly county-level health outcome and water quality data. The model form is

$$Y_{i,j} = \alpha + \beta_1 C_{cws,i,j} + \beta_2 E_{cws,i,j} + \beta_3 C_{Dws,i,j} + \beta_4 N_i + \beta_5 Pov_i + \left(\sum_{m=6}^{17} \beta_m I_{j,m}\right) + \varepsilon_{i,j} \quad (1)$$

where $Y_{i,j}$ is the number of observed AGI ED visits in county i during month j, $C_{CWS,i,j}$ is the number of CWS customers in county i exposed to a monthly MCL violation during month j (determined by assuming all customers of systems with monthly MCL violations were exposed), $E_{CWS,i,j}$ is the number of CWS customers exposed to an acute MCL violation, $C_{DWS,i,j}$ is the number of private well users exposed to total coliform bacteria in county i during month j (determined by multiplying the fraction of private wells testing positive by the population served by private wells), $I_{j,m}$ is an indicator variable equal to 1 if $m = j$ and zero otherwise, N_i is the county population, and Pov_i is the population in poverty. Population and poverty data were obtained from the 2010 US Census.[28] Private well sampling data were provided by the NC Department of Health and Human Services. The latter data set included total coliform (presence-absence) test results for all newly constructed wells during 2009–2013 (n=16,138) by county. Data on the size of the population relying on private wells (and hence without CWS access) in each county were obtained from the U.S. Geological Survey.[8] Regression models were fit using STATA IC 12 (College Station, TX).

Using the fitted regression model (equation 1), AGI cases in each county were estimated under two scenarios: current conditions and a counterfactual scenario wherein no SDWA violations occur ($C_{CWS,i,j} = E_{CWS,i,j} = 0$). Cases under current conditions were computed by using all parameters

in the regression model to estimate $Y_{i,j}$. Cases under the counterfactual scenario ($Y_{i,j,counterfactual}$) were estimated as

$$Y_{i,j,counterfactual} = \alpha + \beta_3 C_{Dws,i,j} + \beta_4 N_i + \beta_5 Pov_i + \left(\sum_{m=6}^{17} \beta_m I_{j,m}\right) + \varepsilon_{i,j} \quad (2)$$

Next, the fraction of cases attributable to microbial contamination from CWSs was estimated as

$$AF_{cws,i,j} = 1 - \frac{Y_{i,j,counterfactual}}{Y_{i,j}} \quad (3)$$

where $AF_{CWS,i,j}$ is the fraction of AGI cases attributable to microbial contamination of CWSs in county *i* during month *j*. We then multiplied *AF* by the observed number of ED visits for month *j* and used the monthly estimates to estimate annual attributable ED visits for each county.

3.2.2.2 Drinking Water Attributable Risk (DWAR)

The DWAR approach, proposed by Messner and others in the US Environmental Protection Agency (EPA) Office of Ground Water and Drinking Water, matches the distribution of microbial contamination in CWSs to a probability distribution representing *AF* (defined as in Equation 3).[6] To develop an *AF* probability distribution (which we use in this analysis), Messner and colleagues employed data from a previous randomized control trial in which some homes served by CWSs were equipped with point-of-use water filters that removed all microbes, while others were not (Figure 3.S1).[6]

To compute the fraction of AGI associated with NC CWSs using the DWAR approach, we first fit a lognormal distribution to the monthly MCL violation rates of all 2,120 NC CWSs using the previously described data from NCDENR. Next, we matched the location of each CWS on the cumulative probability distribution function (CDF) of MCL violations to the equivalent location on the *AF* CDF (Figure 3.S1). For each county, we then calculated the population-weighted average of the *AF*s across all CWSs. We multiplied the result by the county-specific yearly AGI ED visit rate to estimate the visits attributable to CWSs.

3.2.2.3 Quantitative Microbial Risk Assessment (QMRA)

The QMRA follows the approach of Haas et al. 1999. [29] Since QMRA is pathogen-specific, we selected pathogens to evaluate based on the etiologic agents identified in waterborne disease outbreak data from the US Centers for Disease Control and Prevention (CDC). The CDC categorizes etiologic agents in three groups: parasites, non-legionella bacteria and viruses. [4] In keeping with prior research, we chose representative organisms within each pathogen group, emphasizing organisms that were documented as major causes of previous outbreaks. [3-5] Parasites were represented by *Giardia* (84.8% of identified parasitic outbreaks), non-legionella bacteria by *Campylobacter* (26.8% of identified outbreaks), and viruses by rotavirus (1.6% of identified viral outbreaks). [4] Dose-response, pathogen concentration, and morbidity information for each pathogen were drawn from previous QMRAs (Table 3.S2). [29-34]

Because the SDWA does not require CWSs to monitor for pathogens, we estimated pathogen exposure from total coliform data by multiplying total coliform concentrations by pathogen to total coliform ratios derived from previous studies: 3.0×10^{-4} (SD=2.2×10^{-4}), 1.9×10^{-2} (SD=1.2×10^{-2}), and 1.2×10^{-2} (SD=5.8×10^{-2}) for *Giardia*, *Campylobacter* and rotavirus, respectively. [5] The mean total coliform concentration was computed from presence-absence data using a maximum likelihood approach:[29]

$$\mu_{i,j} = \frac{-1}{V} ln\left(\frac{n_{i,j} - p_{i,j}}{n_{i,j}}\right) \quad (4)$$

where $\mu_{i,j}$ is the mean concentration of total coliform in CWS *i* during month *j*, *V* is the volume of water sampled, $n_{i,j}$ is the number of samples taken in the distribution system of CWS *i* during month *j* and $p_{i,j}$ is the corresponding number of positive samples.

The number of pathogens ingested by an individual was computed as

$$P_{exposure,d,i,j}=\mu_{i,j}\, R_{pathogen} I \quad (5)$$

where $P_{exposure,d,i,j}$ is the number of pathogens ingested by a random customer of CWS i on day d in month j, $\mu_{i,j}$ is the mean estimated total coliform concentration in CWS i during month j, $R_{pathogen}$ is the lognormally distributed ratio of pathogens to total coliforms, and I is a lognormal distribution representing daily tap water consumption (mean = 1.129 liters; SD =0.674).[35]

Daily infection risk ($P_{inf,d,}$) was simulated using dose-response models from previous studies (Table 3.S2).[5,30,31,34] Daily illness probability ($P_{ill,d}$) was calculated by multiplying daily infection risk ($P_{inf,d}$) by morbidity ratios from previous studies (Table 3.S2).[29-34] The risk of illness per fecal contamination event ($P_{ill,e}$) was then computed as

$$P_{ill,e} = 1 - (1 - P_{ill,d})^t \quad (6)$$

where t is the duration of the contamination event. We assumed that the daily probability of illness does not vary by day, that daily risks are independent, and that each contamination event lasts 30 days (since the total coliform rule requires monthly monitoring).

The number of cases per event was calculated by multiplying the population of the CWS by $P_{ill,e}$ for each monitoring event. The total number of AGI cases attributable to CWSs was aggregated to the county level for each month. Using equation 7, we then computed the county attributable AF to scale the QMRA results to match the reported county AGI ED visits:

$$AF_{ij} = \frac{E_{AGI,i,j}}{E_{AGI,i,j}+AGI_{NR}\times CWS\_population_i} \quad (7)$$

where $E_{AGI,i,j}$ is the estimated number of total AGI cases attributable to CWS in county i for month j, $CWS\_population_i$ is the aggregated population served by CWSs for county i, and AGI_{NR} is a normal distribution representing the previously described national monthly all-cause AGI rate as estimated by

Jones et al.[27] We then multiplied $AF_{i,j}$ by the observed AGI ED visits and summed the monthly results to obtain annual estimates.

Monte Carlo QMRA simulations (1,000 iterations) were carried out using *Analytica* 4.3 (Lumina Decision Systems, Los Gatos, CA).

3.3 Results

3.3.1 Descriptive Results for the Source Data

Statistical analysis of the NCDETECT data, which track causes of illness reported in visit data from all 122 NC EDs, shows that the number of ED visits for AGI in NC during 2007-2013 averaged 405,000 (SD=38,500) per year or approximately 1 visit for every 24 people per year (0.04 visits per person-year), the same as the rate estimated by Jones et al. in 2007 from telephone surveys of 52,840 individuals in nine states.[27] As expected, the distribution of annual AGI visit rates varied considerably by county (Figure 3.S2), from a low of 0.014 to a high of 0.11 visits per person-year. The incidence rate of AGI is seasonal, with the majority of cases occurring during winter months (December–March) (Figure 3.S3).

Statistical analysis of the SDWA microbiological water quality data provided by NCDENR shows that, on average, 0.7% (SD=0.39%) of NC CWSs experienced an MCL violation and approximately 1.3% (SD=1.7%) of the population served by CWSs was exposed to an MCL violation during any given month in the time period 2006-2013. Total coliform MCL violations followed a seasonal pattern, with the majority of violations occurring during summer (Figure 3.S7). MCL violations were more frequent for surface water than groundwater systems, with statewide average monthly MCL violation rates of 0.94% (SD=0.66%) and 0.63% (SD=0.37%) for surface water and groundwater systems, respectively. The probability of individual exposure to an MCL violation varied both by county and by source water type (Figures 3.S4-3.S6). Although served predominantly by groundwater systems, counties located in the east and northeast of the state had, on average,

slightly higher violation rates than most other counties: in 13 out of 24 (54%) counties in this region, the individual risk of exposure to water violating the MCL was 2.5%, nearly double the average for the state as a whole (Figure 3.S4).

3.3.2 Associations Between AGI Rates and Drinking Water Quality

The multivariate linear regression showed significant positive associations between AGI ED visit rates and the microbiological quality of drinking water (Table 3.1). On average, the AGI visit rate in any given month increased when monthly or acute violations were reported in CWSs. For a CWS customer population of 100,000, the occurrence of a monthly CWS violation was associated with an increase in the number of AGI ED visits by 4.9 (95% CI: 1.3-8.5) per month, equivalent to 59 visits per year (assuming a violation occurred every month). The effect was stronger for acute MCL violations: an acute violation was associated with an increase in the number of AGI visits by 14 (95% CI: 5.6-22) per month, equivalent to 164 per year. Private well water quality also showed significant associations with AGI visit rates, with effects stronger than those for CWSs. For a population of 100,000 served by private wells, any detection of total coliform bacteria in all wells was associated with an increase in the number of AGI visits by 452 (95% CI: 298-606) per month, equivalent to 5,424 visits per year. These results suggest that being served by CWSs has a protective benefit against AGI, as compared to being served by private wells, since coliform bacteria detections in CWSs are associated with lower AGI rates than in private wells.

3.3.3 Risk Assessment Results

The three different risk assessment methods yield significantly different estimates of ED AGI visit rates attributable to microbial contamination in CWSs (Table 3.2), although they tended to show similar geospatial distributions when mapped according to within-method risk percentiles. The DWAR method estimated that 32,200 (95% CI: 31,200-33,100) AGI ED visits annually may be attributed to microbial contamination in NC CWSs. This estimate is one order of magnitude higher than the rate estimated with the QMRA method, which attributed 4,000 (95% CI: 2,900-5,400)

annual ED visits to microbial contamination of drinking water. The QMRA method risk estimate is an order of magnitude higher than the estimate from the PIM method, which attributed 380 (95% CI: 150-630) annual ED AGI visits to microbial CWS contamination. Notably, none of the estimated 95% confidence intervals overlapped.

The PIM and QMRA models appeared to capture much more spatial variability than the DWAR method, with the PIM method capturing the most variability. Reflecting this increased capability to reflect variability, the coefficient of variation (standard deviation divided by the mean) of the PIM risk estimates across all the counties was 1.6, in comparison to 1.1 and 0.5 for the QMRA and DWAR methods, respectively (for estimates by county, see Table 3.S3). Using the PIM approach, the mean estimated per-person annual risks ranged across counties from 0 to 0.00018 visits per person-year; the QMRA yielded county-level risks ranging from 0 to 0.0025 visits per person-year; and the DWAR model estimated risks ranging across counties from 0.0011 to 0.013 per person-year. Notably, the DWAR method, unlike the other two methods, suggests that in all counties, the per-person risk exceeds zero.

Despite the differences in the magnitude of the risk estimates among methods, all three showed similar geospatial distributions across the state (Figures 3.1, 3.S8, 3.S9). Specifically, all three methods identified 13 counties in the upper quartile of estimated risks; these counties are Anson, Beaufort, Bertie, Carteret, Chowan, Columbus, Craven, Edgecombe, Onslow, Pamlico, Perquimans, Wake, and Wayne (Table 3.S3). Eight of these 13 counties are located in the eastern-northeastern region of the state.

3.3.4 Sensitivity Analysis

A sensitivity analysis conducted by changing PIM model parameters to their lower and then upper 95% confidence interval (CI) values while leaving other parameters unchanged showed that the PIM estimates are most sensitive to uncertainty in the regression parameter describing the relationship between ED visits for AGI and monthly MCL violations (Figure 3.S10). Changing the parameter to

its lower 95% CI value decreased the estimated ED visits attributable to CWSs from 380 to 150, while increasing the parameter to its upper 95% CI value increased the estimated visits to more than 600. All other variables had a much smaller effect on the estimated risks. This result suggests that credible data on CWS compliance with microbiological standards are key to using the PIM approach to estimate AGI risks attributable to CWSs.

A similar sensitivity analysis indicated that the DWAR model is most sensitive to uncertainty in the function relating MCL violation rates to the fraction of AGI cases attributable to CWSs (Figure 3.S11). As previously discussed, Messner et al. developed this function from previous randomized, controlled trials in which some homes were provided with drinking water treatment systems and others with sham systems. Using the lower or upper 95% CIs of this function changed the estimated number of attributable AGI visits from 32,200 to about 11,000 and 55,000, respectively.

Finally, QMRA risk estimates are most sensitive to the uncertainty in the estimated total coliform concentrations in each CWS in each month, which are used to estimate pathogen concentrations (Figure 3.S12). Changing these parameters for each CWS to their lower or upper 95% CI values changes the attributable AGI visits from 4,000 to 260 and 27,000, respectively. The results are generally insensitive to uncertainty in all other model parameters. Hence, the QMRA estimates could be improved if CWSs reported coliform concentration data, rather than just presence/absence data.

3.4 Discussion

The PIM approach to characterizing AGI risks attributable to drinking water required developing a multivariate linear regression model to predict the number of AGI ED visits in each county each month from demographic variables and data on the microbiological quality of CWSs and private wells. In conducting the regression analysis, we found significant associations between microbiological water quality and rates of ED visits for AGI. Counties with higher risks of exposure

to total coliform bacteria and/or *E. coli* in drinking water showed higher rates of AGI visits than counties with lower exposure risks. These effects were two orders of magnitude stronger for private wells than for CWSs, suggesting that CWSs provide important protective benefits against AGI, in comparison to private wells.

We found that the estimated AGI risk attributable to CWSs varies highly depending on the risk estimation method used. The mean values of estimated annual AGI ED visits were 380, 4,000, and 32,200 for the PIM, QMRA, and DWAR methods, respectively. All methods showed similar spatial patterns of risk, however, with counties in eastern and northeastern NC generally at higher risk than other counties. This spatial variability is mostly likely due to the comparatively high MCL violation rates (Figures 3.S4 and 3.S6) in these counties, in comparison to other parts of the state.

3.4.1 Comparison to Previous Risk Estimates

The DWAR results are consistent with previous national estimates by Messner et al.,[6] who estimated that 8% (95% CI 3-16) of AGI nationally is potentially attributable to CWSs. Likewise, the DWAR method estimated that 8% (95% CI 7.7-8.2) of AGI in NC is attributable to CWSs. Our estimate expanded on the Messner et al. method by incorporating local reported health data instead of using a uniform rate calculated at the national level.

The QMRA estimate (1% [95% CI 0.7-1.3] of AGI attributable to CWSs) was an order of magnitude less than a national point estimate (10%) calculated via QMRA by Reynolds et al.[3] This apparent discrepancy is due to a difference in how exposure was defined. Unlike Reynolds,[3] who assumed a fixed proportion of the population is exposed at all times, we accounted for variability in exposure by month. The desirability of incorporating temporal fluctuations is confirmed by the variability in the rates of violations and the health outcomes shown in Figures 3.S3 and 3.S7. Reynolds et al.[3] also assumed the theoretical case distribution was correct while we take into account the number of reported cases by converting the estimated number of attributable AGI cases to a fraction and then multiplying the fraction by the reported incidence rate in a given month. This

approach controls for the seasonal variability in the number of AGI cases (Figure 3.S3).

Because the PIM and QMRA models both account for temporal variability while the DWAR approach cannot, the QMRA and PIM models predicted orders of magnitude fewer attributable AGI ED visits than the DWAR method. The DWAR model assumes a constant attributable fraction and hence does not account for the seasonal variability in water quality or health outcomes. The DWAR model further assumes exposures are constant and that the magnitude of exposure is based on the probability of a system violating the total coliform rule, while the PIM and QMRA models assume exposure only occurs when a total coliform rule violation is detected. On average, the reported number of AGI cases is higher during the months when MCL total coliform violations are lower (Figures 3.S3 and 3.S7). Therefore, the DWAR model may overestimate exposures and attributable AGI cases. On the other hand, the PIM and QMRA models may underestimate risk since exposures in those models are assumed to occur only when MCL violations occur (PIM model) or when total coliform bacteria are detected (QMRA model), but outbreaks can occur during periods when total coliform bacteria are not detected at frequencies that violate the MCL (e.g., Milwakee).[4, 37]

Defining pathogen exposure in CWSs is challenging, because health risks can occur at very low pathogen concentrations in finished water, and detecting such low concentrations is difficult. As Figure 3.S12 shows, the QMRA model is highly sensitive to exposure characterization. Our QMRA approach, which uses a ratio of pathogens to microbial indicators in the manner specified by van Lieverloo et al.,[5] may be vulnerable to bias since the presence or absence of an indicator organism (total coliform bacteria) does not necessarily correspond to the presence or absence of a pathogen. Exposure calculations also require pathogen concentrations n order to quantify illness probabilities. These pathogen-specific exposures are believed to underestimate the total risk since not all pathogens with the potential to cause AGI from drinking water have dose-response profiles, and pathogen-specific morbidity risks in the QMRA model are also based on studies of infectivity and morbidity

among healthy volunteers and do not account for the immune-compromised or other sensitive subpopulations. [7]

The PIM and DWAR models do not need specific pathogen information to predict health outcomes but rather assume poor health outcomes are caused by an array of pathogens. In our implementation, the PIM model uses a regression approach to identify a longitudinal state-wide relationship between MCL total coliform rule violations and an observed disease rate. The use of this population-specific statistical relationship between exposure and AGI ED visits is a strength of the PIM approach since it enables the specification of the dose-response relationship to the NC population. The DWAR method relies on risk estimates from randomized controlled drinking water trials conducted on other populations, and the populations of control trials do not always resemble the general population or that of a specific location, such as an NC county. These efforts are also limited by the high variability in the source studies' results (e.g., attributable risks ranging from 0.02 to 0.85 cases per person-year). [14]

The PIM model is a time-dependent model that relates exposures to reported health outcomes. Our implementation of the model estimates the increase in observed ED visits for AGI given a violation has occurred in the county while controlling for the population, population in poverty, population relying on private wells and the month that the violation occurred. Controlling for these variables allows us to incorporate the seasonal variability in exposures along with the role the ED plays in providing medical services to different subsets of the population. Representation of seasonal variability is an advantage of the PIM model, but it is possible that the reliance on MCL violations as the exposure indicator may upwardly bias our estimate since an MCL violation does not necessarily signal the presence of harmful pathogens. However, even with the potential additional bias that may occur due to the aggregation of exposure and health outcomes at the county level the model still has a high degree of internal validity compared to the other two models because it does not rely on dose-response estimates from other populations.

3.4.2 Limitations

There are a number of limitations in this study. First, all three methods rely on the presence of total coliform bacteria as the indicator of potential exposure to microbial pathogens, as this is the data routinely collected by US CWSs. The total coliform rule requires CWSs to monitor for and report the presence of microbial indicators but for practical and cost reasons does not require them to monitor for pathogens (e.g. *Giardia* and viruses).[31, 38-40] The presence of a microbial indicator does not necessarily mean that pathogens are present, although it increases the likelihood that they are present; likewise, the absence of indicator organisms does not guarantee the water is pathogen free.[41] Therefore, our understanding of the presence of pathogens is conditional on the indicator organism, so we may have over- or under-estimated exposure.[15, 41-43] This limitation may have a greater impact on the QMRA results than on those from the PIM and DWAR approaches, since the QMRA method estimates exposure concentrations for pathogens based on total coliform detection data, whereas the PIM and DWAR methods use coliform detection data as an indicator of overall CWS performance relative to other CWSs.

A second limitation common to all three models is the assumed uniform exposure across the population served by each system. This assumption could over- or under-estimate the number of people exposed if detected contamination events affect some parts of the distribution system but not others, if events in one part of the system are undetected, or if some members of the population follow boil-water orders or other mitigation measures. A related limitation is that exposure at the county level is based on the population weighting of CWSs within a given county. The aggregation of exposure to the county level thus has the potential to be biased due to the influence of larger systems. These limitations were unavoidable given the nature of reported data on microbial indicator organisms in CWSs and the availability of NCDETECT data on AGI ED visits only at the county level of aggregation.

A third limitation is that the health outcome dataset captures only a fraction of all AGI cases. The Foodborne Diseases Active Surveillance Network (FOODNET) study, which estimated the national AGI rate, showed that 6.4% (95% CI 5.0-7.8%) of persons with AGI visited the ED; thus, every ED visit potentially represents approximately 16 total cases of AGI. [25,27,36,44] A related limitation is that the classification of the resulting ED visits is based on ICD-9 codes and thus may contribute to further under- or over-estimation of the true health risk, because ICD-9 codes are used for billing purposes and do not necessarily represent the main cause of the ED visit.

A final limitation is that available public health data were insufficiently refined at the spatial scale to assign an AGI rate separately for each CWS. The finest resolution available to assign an AGI rate was at the county scale. Therefore, we assumed a homogenous distribution of AGI across each county and, as a result, may have introduced bias in our estimates.

The limitations of this analysis are inherent not only to this study but also to previous estimates of waterborne disease risks over large populations. [3, 5, 6, 14] These kinds of limitations further highlight the importance of comparing estimates across methods.

3.5 Research Implications

The PIM approach better addresses the limitations of available data by developing dose-response models specific to the local population (i.e., the regression model predicting county-level ED visits from county-level monthly and acute MCL violation rates). As such, the PIM approach has higher internal validity, relative to the DWAR and QMRA approaches, and therefore we believe it is the most appropriate for quantifying AGI attributable to CWSs at a county level for an entire state.

According to the PIM approach, 380 (0.09%) of the 405,000 annual ED visits for AGI in NC are potentially attributable to microbial contaminates in CWSs. If one assumes that each ED visit potentially represents about 16 AGI cases (as estimated by Jones et al. [27]), then 6,080 (95% CI: 2,400-10,080) AGI cases may be attributable to microbial contaminants in NC CWSs each year. This

equates to an individual risk of about 6 x 10^{-4} per year (obtained by dividing the total number of cases by the 2010 NC population of 9.5 million). This risk varies considerably by location, with risks levels in some counties approaching 3 x 10^{-3}—more than four orders of magnitude higher than in the lowest-risk counties. Notably, the other methods' results predict much higher per-person risks: 7 x 10^{-3} and 5 x 10^{-2} on average across the state and 4 x 10^{-2} and 0.2 in the highest-risk counties for the QMRA and DWAR methods, respectively.

Overall, waterborne disease risks in NC are extremely low by global standards. For example, according to the World Health Organization, the lowest and highest country rates worldwide of diarrheal diseases attributable to deficiencies in water and sanitation systems are 2 x 10^{-4} and 0.107 disability-adjusted life years per person-year, respectively—equivalent to about 2 x 10^{-3}–1 AGI cases per person-year, respectively.[45] By comparison to this estimated global risk range, estimated waterborne disease risks in NC are low regardless of the risk estimation method used. Nonetheless, EPA policy is that annual infection risks above 1 x 10^{-4} should be targeted for interventions.[30,46] While vast improvements have been made in the provision of safe drinking water and while this research clearly shows that CWSs provide substantial health benefits in comparison to reliance on private well water, efforts are still necessary to reduce the burden of disease to the 10^{-4} risk level recommended by the EPA. Furthermore, efforts are needed to improve the characterization of exposure to pathogens in NC drinking water and to link pathogen exposure data to medical visits for AGI across the state, in order to identify specific communities that could benefit from interventions. Ideally, future data collection could occur at a fine spatial scale, such as in Census blocks, in order to improve linkages between exposure and health outcome estimates.

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Table 3.1. Beta coefficients from a generalized linear model used in the PIM model

Variable	Beta (95% CI)
Population exposed to monthly MCL violation ($C_{CWSi,j}$)	0.000049* (0.000013 - 0.000085)
Population exposed to acute MCL violation ($E_{CWSi,j}$)	0.000137* (0.000056 - 0.00022)
Total county population (N_i)	0.00181** (0.00157 -0.00204)
Population exposed to total coliform bacteria in private wells ($C_{DWSi,j}$)	0.00452** (0.00298 -0.00606)
Population living in poverty (Pov_i)	0.0045** (0.00259 - 0.0064)
Month (m)	
January	50.02** (34.12 -65.91)
February	59.12* (42.28 - 75.95)
March	82.91** (65.37 - 100.4)
April	25.39** (7.350 - 43.43)
May	11.25** (-7.14 - 29.64)
June	-4.45** (-23.06 - 14.15)
July	-2.77** (-21.47 - 15.91)
August	-0.92** (-19.58 - 17.73)
September	-2.90** (-21.40 - 15.59)
October	0.686** (-17.51 - 18.88)
November	1.78** (-15.92 - 19.50)
December	35.49** (18.52 - 52.45)

*p<0.01, **p<0.001

Table 3.2. Annual AGI ED visits potentially attributable to ingestion of water from NC CWSs

Method	**Mean AGI ED visits potentially attributable to CWSs (95% CI)**	**Mean percent of total AGI ED visits potentially attributable to CWSs (95% CI)**
Quantitative Microbial Risk Assessment (QMRA)	4,000 (2,900-5,400)	1.0% (0.7-1.3)
Drinking Water Attributable Risk (DWAR)	32,200 (31,200-33,100)	8.0% (7.7-8.2)
Population Intervention Model (PIM)	380 (150-630)	0.09% (0.04-0.16)

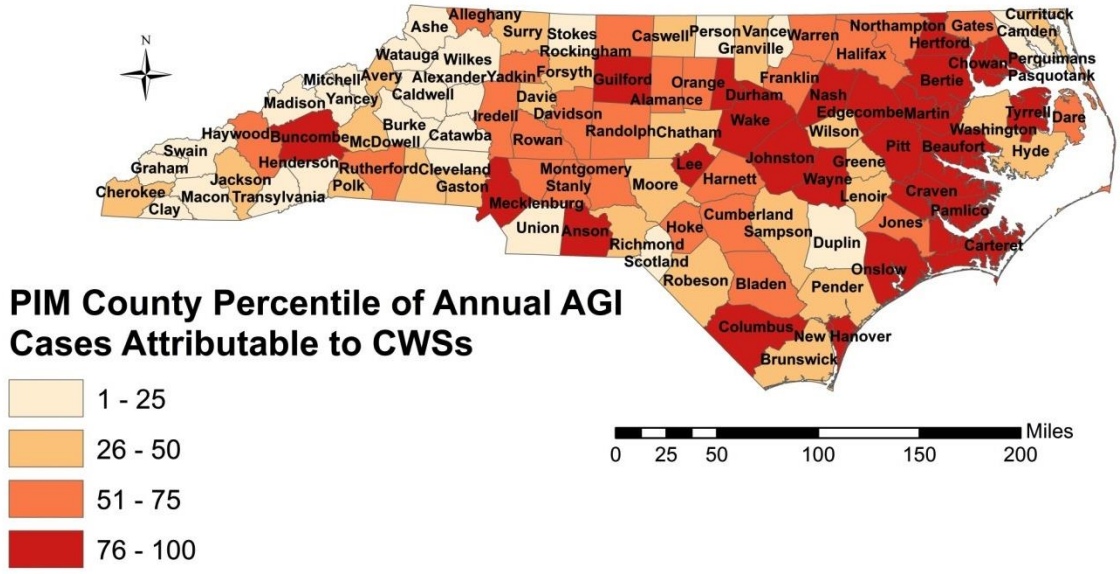

Figure 3.1. Annual county rate of ED visits for AGI attributable to CWSs using the PIM approach. Quartiles correspond to the following risk ranges: first quartile, < 1/1,000,000; second quartile, 1/1,000,000-1/100,000; third quartile, 1/100,000-1/50,000; fourth quartile, 1/50,000-1/5,000.

3.6 Supplementary Information

Table 3.S1. Size distribution, source water type, and population served by community water systems in North Carolina

Size category	Description	Number of systems	Total population served	Percent ground water systems	Percent surface water systems
Very Small	Serve 25-500 people	1,510	227,341	91%	9%
Small	Serve 501-3,300	345	487,176	64%	36%
Medium	Serve 3,301-10,000	136	798,471	39%	61%
Large	Serve 10,001-100,000	117	3,061,791	28%	72%
Very Large	Serve more than 100,000	12	2,941,601	8%	92%

Table 3.S2. Dose-response and morbidity information[5,29-34]

Reference Pathogen	Published Dose-response model	Model parameters	Morbidity Ratio (% of infections resulting in illness)	Reference
Girardia	Exponential	LN(0.0199,0.066)*	Triangular (0.39, 0.58, 0.91)	Rose et al. 1993
Campylobacter	Beta Poisson	BivariateLN (α (0.024,0.03) * β(0.011, 0.04)* Corr(0.82))	α/(α+β)	Teunis et al. 2005; Black et al. 1988; Evans et al. 1996; van den Kerkhof et al. 2003
Rotavirus	Beta Poisson	BivariateLN (α (0.265,0.08) * β(0.442, 1.2)* Corr(0.74))	Triangular (0.01, 0.5, 0.97)	Haas et al. 1993; Ward et al. 1986

* mean and standard deviation of the non-logarithmized sample values.

Table 3.S3. County estimates of ED visits for AGI attributable to CWSs, coefficients of variation and matching ranking from mean estimated rate of ED visits for AGI attributable to CWSs!

	PIM		DWAR		QMRA	
County	Attributable Rate of AGI from CWS	County Ranking	Attributable Rate of AGI from CWS	County Ranking	Attributable Rate of AGI from CWS	County Ranking
ALAMANCE	0.000014 (0.0000038-0.000024)	0.63	0.0032 (0.0028-0.0036)	0.35	0.00023 (0.000026-0.00052)	0.43
ALEXANDER	0 (0-0)	0.12	0.0033 (0.0022-0.0043)	0.39	0 (0-0)	0.11
ALLEGHANY	0.000013 (0.0000049-0.000024)	0.62	0.0064 (0.0058-0.007)	0.84	0.00056 (0.0001-0.00091)	0.64
ANSON	0.000057 (0.000029-0.000087)	0.95	0.012 (0.011-0.013)	0.99	0.0019 (0.0014-0.0021)	0.97
ASHE	0 (0-0)	0.12	0.0032 (0.0024-0.004)	0.36	0 (0-0)	0.11
AVERY	0.0000012 (0.00000032-0.0000024)	0.3	0.0026 (0.0022-0.003)	0.19	0.000044 (0-0.000062)	0.25
BEAUFORT	0.00003 (0.0000082-0.000053)	0.83	0.0091 (0.0082-0.011)	0.94	0.0022 (0.0013-0.0033)	0.99
BERTIE	0.000054 (0.000015-0.000095)	0.94	0.012 (0.01-0.015)	0.98	0.0025 (0.00085-0.0038)	1

	PIM		DWAR		QMRA	
County	Attributable Rate of AGI from CWS	County Ranking	Attributable Rate of AGI from CWS	County Ranking	Attributable Rate of AGI from CWS	County Ranking
BLADEN	0.000012 (0.0000032-0.000021)	0.57	0.005 (0.0046-0.0053)	0.7	0.00053 (0.00025-0.00081)	0.62
BRUNSWICK	0.0000022 (0.0000006-0.0000038)	0.31	0.0032 (0.0024-0.0039)	0.34	0.000073 (0.000033-0.00011)	0.29
BUNCOMBE	0.000025 (0.0000069-0.000044)	0.78	0.0028 (0.0026-0.0031)	0.27	0.00034 (0.000048-0.00079)	0.53
BURKE	0 (0-0)	0.12	0.0048 (0.0036-0.0058)	0.66	0 (0-0)	0.11
CABARRUS	0.0000098 (0.0000028-0.000017)	0.52	0.0028 (0.0019-0.0035)	0.25	0.00022 (0.000024-0.00066)	0.41
CALDWELL	0 (0-0)	0.12	0.0048 (0.0037-0.0059)	0.68	0 (0-0)	0.11
CAMDEN	0 (0-0)	0.12	0.0015 (0.00093-0.002)	0.04	0 (0-0)	0.11
CARTERET	0.000046 (0.000017-0.000078)	0.92	0.011 (0.011-0.012)	0.97	0.0015 (0.001-0.002)	0.94
CASWELL	0.0000029 (0.0000008-0.0000052)	0.36	0.0022 (0.002-0.0025)	0.12	0.00018 (0.0000045-0.00024)	0.4

	PIM		DWAR		QMRA	
County	Attributable Rate of AGI from CWS	County Ranking	Attributable Rate of AGI from CWS	County Ranking	Attributable Rate of AGI from CWS	County Ranking
CATAWBA	0.000000025 (0.0000000068-0.000000045)	0.13	0.0033 (0.0023-0.0041)	0.41	0.0001 (0.00000037-0.00059)	0.31
CHATHAM	0.0000054 (0.0000015-0.0000097)	0.43	0.0021 (0.0018-0.0023)	0.11	0.00017 (0.000059-0.00029)	0.39
CHEROKEE	0.00000084 (0.00000023-0.0000016)	0.26	0.0018 (0.0013-0.0023)	0.07	0.000042 (0-0.000053)	0.24
CHOWAN	0.000072 (0.000031-0.00013)	0.97	0.01 (0.0096-0.011)	0.96	0.0014 (0.00031-0.0025)	0.93
CLAY	0 (0-0)	0.12	0.0011 (0.00067-0.0014)	0.01	0 (0-0)	0.11
CLEVELAND	0.0000035 (0.00000094-0.0000062)	0.38	0.0045 (0.0034-0.0055)	0.63	0.00027 (0.00014-0.00049)	0.45
COLUMBUS	0.000029 (0.000013-0.000044)	0.81	0.0085 (0.0075-0.01)	0.92	0.001 (0.00057-0.0015)	0.86
CRAVEN	0.000028 (0.0000076-0.000049)	0.8	0.0093 (0.0083-0.01)	0.95	0.0011 (0.00067-0.0016)	0.9
CUMBERLAND	0.000018 (0.0000064-0.00003)	0.71	0.0025 (0.0018-0.0031)	0.17	0.00034 (0.000062-0.00089)	0.51

	PIM		DWAR		QMRA	
County	Attributable Rate of AGI from CWS	County Ranking	Attributable Rate of AGI from CWS	County Ranking	Attributable Rate of AGI from CWS	County Ranking
CURRITUCK	0.00000089 (0.00000024-0.0000016)	0.27	0.0013 (0.00099-0.0017)	0.02	0.000038 (0.000015-0.000049)	0.23
DARE	0.00002 (0.0000055-0.000035)	0.74	0.0054 (0.0052-0.0057)	0.74	0.00087 (0.00069-0.0011)	0.82
DAVIDSON	0.000011 (0.0000029-0.000019)	0.53	0.0042 (0.0031-0.0053)	0.61	0.00057 (0.0004-0.00075)	0.66
DAVIE	0.0000035 (0.00000099-0.0000063)	0.39	0.0055 (0.0048-0.0073)	0.76	0.00065 (0.00015-0.0013)	0.72
DUPLIN	0.00000011 (0.000000031-0.0000002)	0.16	0.0028 (0.002-0.0034)	0.24	0.0000068 (0.0000055-0.0000071)	0.16
DURHAM	0.000022 (0.0000094-0.000034)	0.76	0.0047 (0.0042-0.0053)	0.65	0.00039 (0.0000044-0.001)	0.55
EDGECOMBE	0.000039 (0.000011-0.000069)	0.87	0.0061 (0.0055-0.0073)	0.81	0.0021 (0.0016-0.0027)	0.98
FORSYTH	0.0000077 (0.0000022-0.000013)	0.47	0.0026 (0.0013-0.0037)	0.2	0.000032 (0.0000064-0.00037)	0.22
FRANKLIN	0.000013 (0.0000036-0.000023)	0.61	0.0034 (0.0031-0.0036)	0.42	0.00048 (0.00013-0.0008)	0.59

	PIM		DWAR		QMRA	
County	Attributable Rate of AGI from CWS	County Ranking	Attributable Rate of AGI from CWS	County Ranking	Attributable Rate of AGI from CWS	County Ranking
GASTON	0.0000081 (0.0000023-0.000014)	0.5	0.004 (0.0032-0.0048)	0.58	0.00028 (0.00016-0.00042)	0.46
GATES	0.0000093 (0.0000026-0.000017)	0.51	0.002 (0.0019-0.0021)	0.08	0.00033 (0-0.00066)	0.5
GRAHAM	0 (0-0)	0.12	0.002 (0.0013-0.0026)	0.09	0 (0-0)	0.11
GRANVILLE	0.0000038 (0.0000011-0.0000069)	0.4	0.0034 (0.0026-0.0041)	0.43	0.00011 (0.0000036-0.00021)	0.32
GREENE	0.0000076 (0.0000022-0.000013)	0.46	0.0034 (0.0032-0.0036)	0.45	0.00026 (0.00012-0.00039)	0.44
GUILFORD	0.000062 (0.000018-0.00011)	0.96	0.0041 (0.0036-0.0046)	0.59	0.00064 (0.000042-0.0016)	0.71
HALIFAX	0.000022 (0.0000061-0.000038)	0.75	0.013 (0.012-0.014)	1	0.00084 (0.00027-0.0017)	0.78
HARNETT	0.000011 (0.0000031-0.00002)	0.54	0.0036 (0.0034-0.0039)	0.49	0.0012 (0.00031-0.0022)	0.92
HAYWOOD	0.000012 (0.0000066-0.000018)	0.59	0.0034 (0.0031-0.0037)	0.44	0.00036 (0.00011-0.00057)	0.54

	PIM		DWAR		QMRA	
County	Attributable Rate of AGI from CWS	County Ranking	Attributable Rate of AGI from CWS	County Ranking	Attributable Rate of AGI from CWS	County Ranking
HENDERSON	0.00000035 (0.000000098-0.00000062)	0.22	0.0038 (0.0034-0.0042)	0.53	0.0005 (0.0000099-0.0014)	0.61
HERTFORD	0.000022 (0.00001-0.000034)	0.77	0.0038 (0.0035-0.0041)	0.54	0.0006 (0.00022-0.00091)	0.69
HOKE	0.000012 (0.0000035-0.000021)	0.58	0.0061 (0.0054-0.0075)	0.8	0.0009 (0.0004-0.0016)	0.83
HYDE	0.0000064 (0.0000017-0.000012)	0.45	0.0039 (0.0036-0.0042)	0.56	0.00086 (0-0.0014)	0.81
IREDELL	0.000016 (0.0000087-0.000023)	0.68	0.0065 (0.0058-0.0077)	0.86	0.00054 (0.00011-0.0011)	0.63
JACKSON	0.00000099 (0.00000033-0.0000017)	0.28	0.0022 (0.0017-0.0027)	0.14	0.000048 (0.000033-0.000056)	0.26
JOHNSTON	0.000044 (0.00002-0.000067)	0.91	0.0058 (0.0047-0.0067)	0.77	0.00061 (0.00022-0.0011)	0.7
JONES	0.000014 (0.000003-0.000037)	0.65	0.0064 (0.0058-0.0071)	0.83	0.00031 (0-0.00058)	0.48
LEE	0.000029 (0.000008-0.00005)	0.82	0.0023 (0.0014-0.0031)	0.15	0.00073 (0.000082-0.0017)	0.73

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	PIM		DWAR		QMRA	
County	Attributable Rate of AGI from CWS	County Ranking	Attributable Rate of AGI from CWS	County Ranking	Attributable Rate of AGI from CWS	County Ranking
LENOIR	0.0000025 (0.00000071-0.0000044)	0.34	0.0069 (0.0054-0.0083)	0.88	0.00033 (0.000057-0.00067)	0.49
LINCOLN	0 (0-0)	0.12	0.0036 (0.003-0.0041)	0.48	0.000092 (0-0.00039)	0.3
MACON	0.00000011 (0.00000003-0.0000002)	0.17	0.0029 (0.0021-0.0037)	0.29	0.0000029 (0.0000003-0.0000035)	0.14
MADISON	0.0000007 (0.0000002-0.0000013)	0.25	0.0016 (0.0014-0.0019)	0.05	0.00014 (0-0.00021)	0.35
MARTIN	0.000036 (0.00001-0.000065)	0.85	0.0054 (0.005-0.0059)	0.73	0.0018 (0.0011-0.0026)	0.96
MCDOWELL	0.0000049 (0.0000026-0.0000073)	0.42	0.0064 (0.006-0.007)	0.85	0.00016 (0.000068-0.00025)	0.36
MECKLENBURG	0.00018 (0.000076-0.00029)	1	0.004 (0.0037-0.0043)	0.57	0.00056 (0.0000015-0.0015)	0.65
MITCHELL	0 (0-0)	0.12	0.006 (0.0053-0.0067)	0.78	0 (0-0)	0.11
MONTGOMERY	0.000017 (0.0000046-0.000029)	0.69	0.0055 (0.0047-0.0071)	0.75	0.00095 (0.0002-0.0018)	0.85

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	PIM		DWAR		QMRA	
County	Attributable Rate of AGI from CWS	County Ranking	Attributable Rate of AGI from CWS	County Ranking	Attributable Rate of AGI from CWS	County Ranking
MOORE	0.0000078 (0.0000025-0.000014)	0.48	0.0043 (0.004-0.0046)	0.62	0.00034 (0.00015-0.00055)	0.52
NASH	0.000027 (0.0000076-0.000046)	0.79	0.0028 (0.0027-0.003)	0.26	0.00049 (0.00013-0.001)	0.6
NEW HANOVER	0.000041 (0.000013-0.000071)	0.9	0.0037 (0.0027-0.0046)	0.51	0.001 (0.00063-0.0015)	0.87
NORTHAMPTON	0.000012 (0.0000033-0.000021)	0.55	0.0082 (0.0077-0.0087)	0.91	0.00045 (0.00011-0.00078)	0.58
ONSLOW	0.000099 (0.000038-0.00016)	0.98	0.0062 (0.0057-0.0067)	0.82	0.0012 (0.00073-0.0017)	0.91
ORANGE	0.000013 (0.0000047-0.000021)	0.6	0.0016 (0.001-0.0021)	0.06	0.00016 (0.000007-0.0004)	0.37
PAMLICO	0.000048 (0.000013-0.000095)	0.93	0.0074 (0.0064-0.01)	0.9	0.001 (0.00016-0.002)	0.89
PASQUOTANK	0 (0-0)	0.12	0.0026 (0.0016-0.0035)	0.21	0 (0-0)	0.11
PENDER	0.0000044 (0.0000012-0.0000078)	0.41	0.003 (0.0024-0.0036)	0.32	0.00022 (0.000099-0.00028)	0.42

	PIM		DWAR		QMRA	
County	Attributable Rate of AGI from CWS	County Ranking	Attributable Rate of AGI from CWS	County Ranking	Attributable Rate of AGI from CWS	County Ranking
PERQUIMANS	0.000036 (0.000009-0.000075)	0.84	0.0066 (0.0056-0.0089)	0.87	0.00086 (0.000074-0.0016)	0.8
PERSON	0.000000028 (0.0000000079-0.000000051)	0.14	0.0029 (0.0014-0.0041)	0.28	0.0000018 (0.0000017-0.0000019)	0.12
PITT	0.000041 (0.000021-0.000061)	0.89	0.0048 (0.0045-0.0052)	0.67	0.00074 (0.00042-0.0012)	0.74
POLK	0.0000025 (0.00000063-0.0000047)	0.33	0.003 (0.0021-0.0038)	0.31	0.00013 (0-0.00015)	0.34
RANDOLPH	0.000014 (0.000004-0.000025)	0.64	0.0053 (0.0049-0.0059)	0.72	0.00076 (0.00054-0.00094)	0.75
RICHMOND	0.0000026 (0.0000007-0.0000047)	0.35	0.0032 (0.0024-0.0039)	0.37	0.00012 (0-0.00033)	0.33
ROBESON	0.0000022 (0.0000011-0.0000033)	0.32	0.0042 (0.0028-0.0053)	0.6	0.000053 (0.000021-0.000073)	0.27
ROCKINGHAM	0.000017 (0.0000047-0.00003)	0.7	0.0088 (0.0077-0.011)	0.93	0.00091 (0.0003-0.0014)	0.84
ROWAN	0.000015 (0.0000041-0.000026)	0.66	0.0023 (0.0016-0.003)	0.16	0.0004 (0.00006-0.00084)	0.56

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County	PIM		DWAR		QMRA	
	Attributable Rate of AGI from CWS	County Ranking	Attributable Rate of AGI from CWS	County Ranking	Attributable Rate of AGI from CWS	County Ranking
RUTHERFORD	0.000012 (0.0000033-0.000021)	0.56	0.0047 (0.0041-0.0053)	0.64	0.00081 (0.00059-0.00087)	0.76
SAMPSON	0.000001 (0.00000029-0.0000019)	0.29	0.0036 (0.0027-0.0043)	0.47	0.000069 (0.000013-0.000084)	0.28
SCOTLAND	0 (0-0)	0.12	0.0037 (0.0023-0.0049)	0.52	0 (0-0)	0.11
STANLY	0.000015 (0.0000041-0.000027)	0.67	0.0036 (0.0031-0.0041)	0.5	0.0006 (0.00032-0.00082)	0.68
STOKES	0.00000024 (0.000000066-0.00000044)	0.2	0.0029 (0.0016-0.004)	0.3	0.00001 (0.0000012-0.000014)	0.18
SURRY	0.0000063 (0.0000017-0.000011)	0.44	0.0049 (0.0039-0.0058)	0.69	0.00031 (0.000096-0.00041)	0.47
SWAIN	0.00000014 (0.000000033-0.00000028)	0.19	0.0033 (0.0019-0.0044)	0.38	0.0000091 (0.0000075-0.0000097)	0.17
TRANSYLVANIA	0.00000033 (0.000000088-0.00000058)	0.21	0.0026 (0.0018-0.0033)	0.18	0.000014 (0.0000093-0.000017)	0.19
TYRRELL	0.00004 (0.0000036-0.00019)	0.88	0.005 (0.0047-0.0053)	0.71	0.001 (0.00037-0.0014)	0.88

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	PIM		DWAR		QMRA	
County	Attributable Rate of AGI from CWS	County Ranking	Attributable Rate of AGI from CWS	County Ranking	Attributable Rate of AGI from CWS	County Ranking
UNION	0.00000013 (0.000000038-0.00000024)	0.18	0.002 (0.0013-0.0028)	0.1	0.0000038 (0-0.0000067)	0.15
VANCE	0.00000043 (0.00000022-0.00000064)	0.23	0.0027 (0.0015-0.0038)	0.22	0.000015 (0.0000056-0.000019)	0.2
WAKE	0.00013 (0.000052-0.00021)	0.99	0.006 (0.0057-0.0065)	0.79	0.00085 (0.00013-0.002)	0.79
WARREN	0.000019 (0.0000053-0.000033)	0.72	0.0035 (0.0034-0.0037)	0.46	0.00082 (0.000061-0.0014)	0.77
WASHINGTON	0.0000081 (0.0000023-0.000015)	0.49	0.0033 (0.0031-0.0035)	0.4	0.00042 (0.000013-0.0009)	0.57
WATAUGA	0.00000044 (0.00000013-0.00000078)	0.24	0.0014 (0.0011-0.0018)	0.03	0.000026 (0.0000067-0.000032)	0.21
WAYNE	0.000038 (0.000018-0.00006)	0.86	0.0072 (0.0068-0.0077)	0.89	0.0018 (0.00095-0.0025)	0.95
WILKES	0.000000034 (0.0000000095-0.00000006)	0.15	0.0022 (0.0017-0.0027)	0.13	0.0000023 (0-0.0000029)	0.13
WILSON	0.0000033 (0.00000091-0.0000058)	0.37	0.003 (0.002-0.0039)	0.33	0.00017 (0.0001-0.00021)	0.38

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	PIM		DWAR		QMRA	
County	Attributable Rate of AGI from CWS	County Ranking	Attributable Rate of AGI from CWS	County Ranking	Attributable Rate of AGI from CWS	County Ranking
YADKIN	0.000019 (0.0000095-0.000029)	0.73	0.0038 (0.0033-0.0043)	0.55	0.00059 (0.00037-0.0008)	0.67
YANCEY	0 (0-0)	0.12	0.0028 (0.0017-0.0037)	0.2	0 (0-0)	0.11

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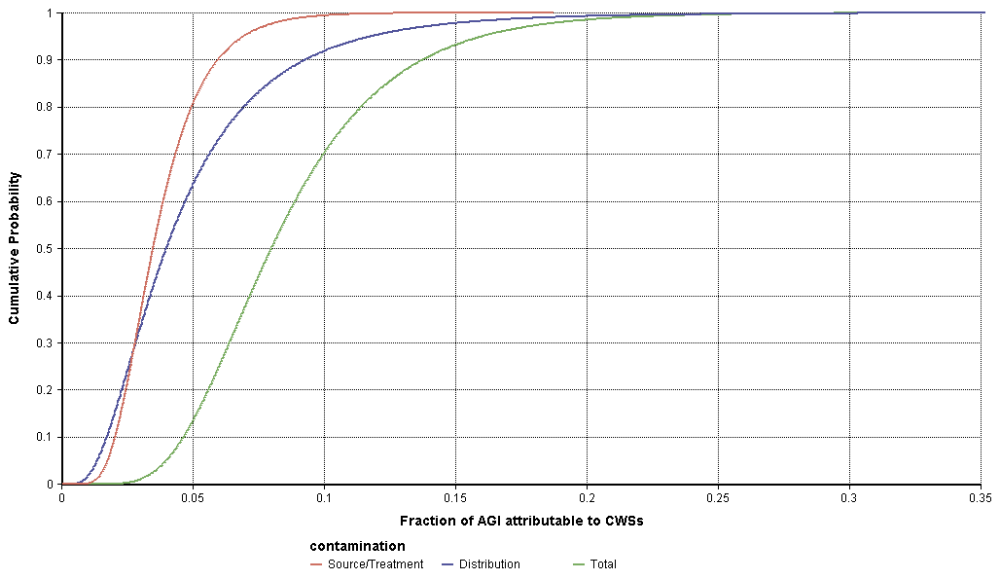

Figure 3.S1. Cumulative probability distribution representing the fraction of AGI attributable to microbial contamination of drinking water in a randomly selected NC community water system.

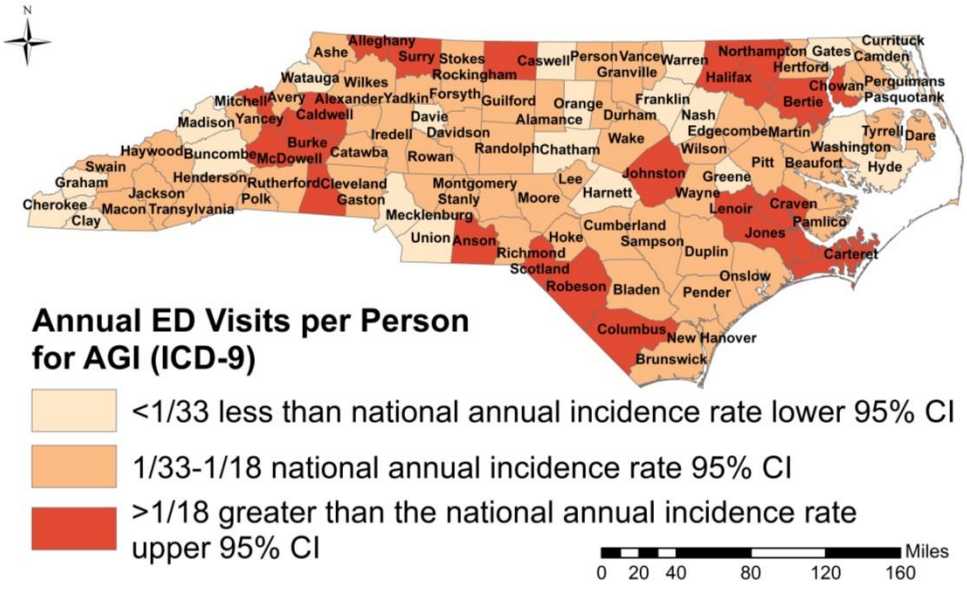

Figure 3.S2. Annual rate of ED visits for AGI by county. In 21 counties, the annual incidence rate exceeds the 97.5th percentile of the national annual incidence rate.

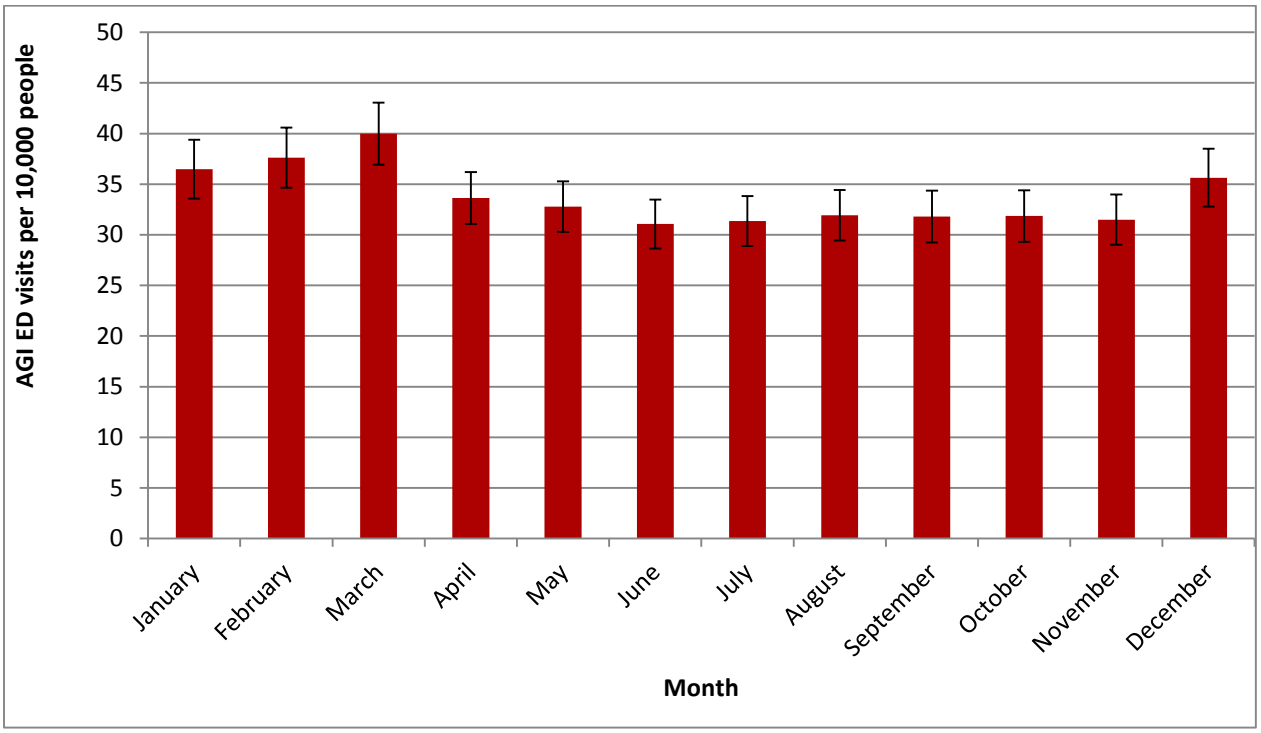

Figure 3.S3. Monthly incidence rate of ED visits for AGI per 10,000 people. The winter months (December to March) have a higher incidence rate of AGI than the summer months (July to September).

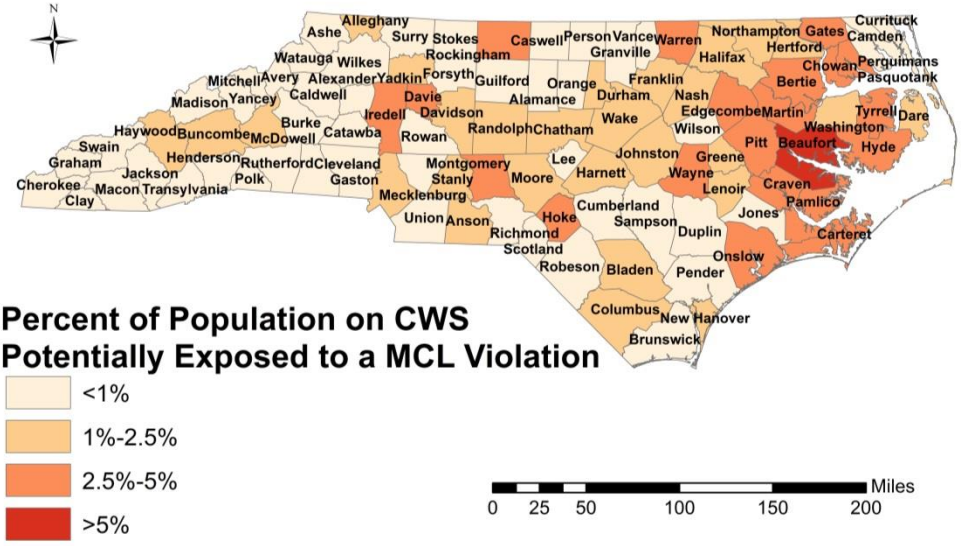

Figure 3.S4. Proportion of the population served by CWSs with detected *E. Coli* or greater than 5% of total coliform samples positive over a month.

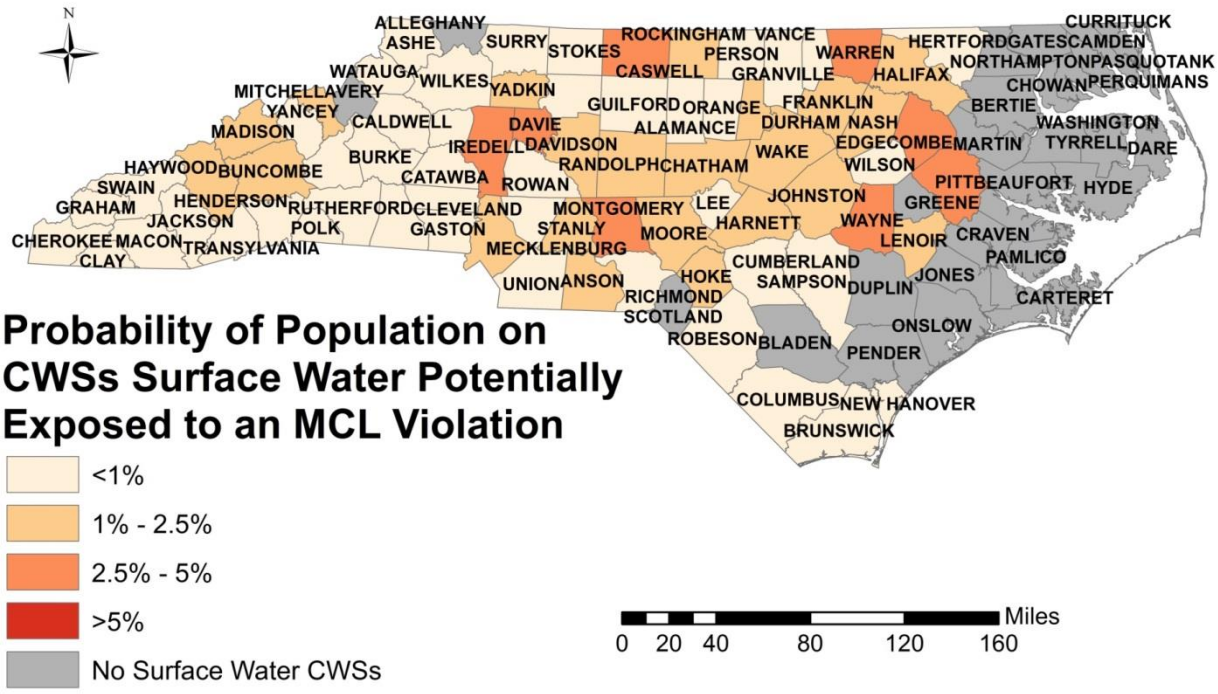

Figure 3.S5. Mean proportion of population potentially exposed to a monthly MCL violation in CWSs using surface water as a source.

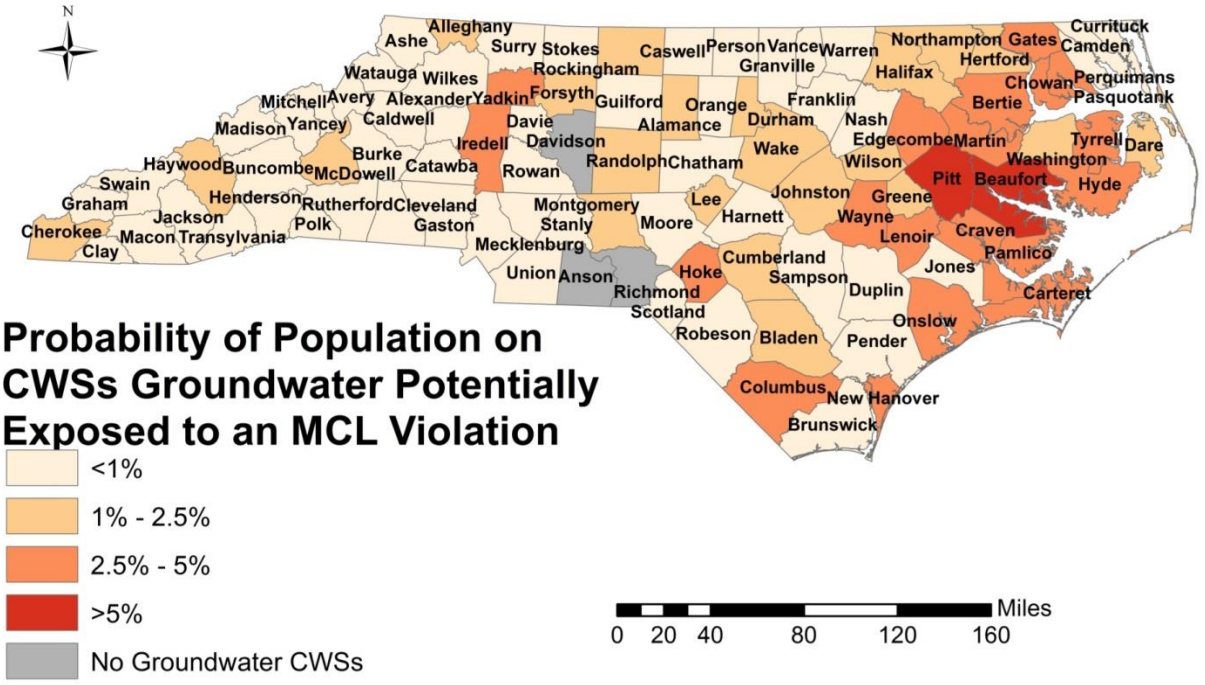

Figure 3.S6. Mean proportion of population potentially exposed to a monthly MCL violation in CWSs using groundwater as a source.

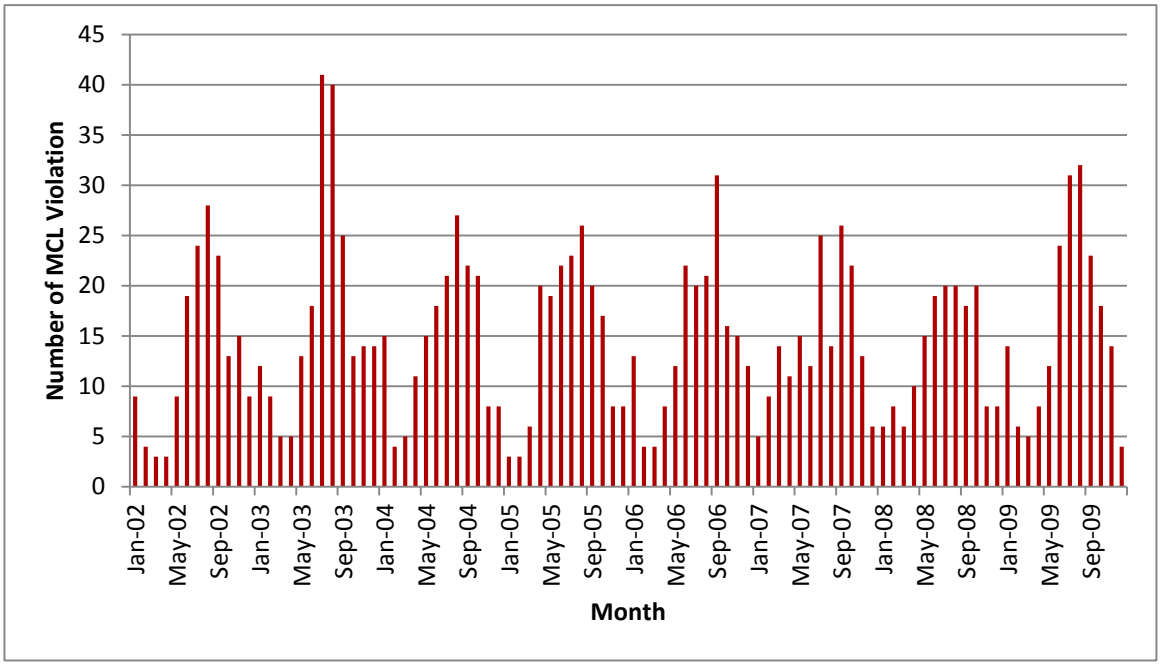

Figure 3.S7. Detection of *E. Coli* or greater than 5% of total coliform samples positive over a month showed a consistent seasonal trend from year to year. The summer months (July to September) have a higher rate of MCL violations than the winter months (December to March).

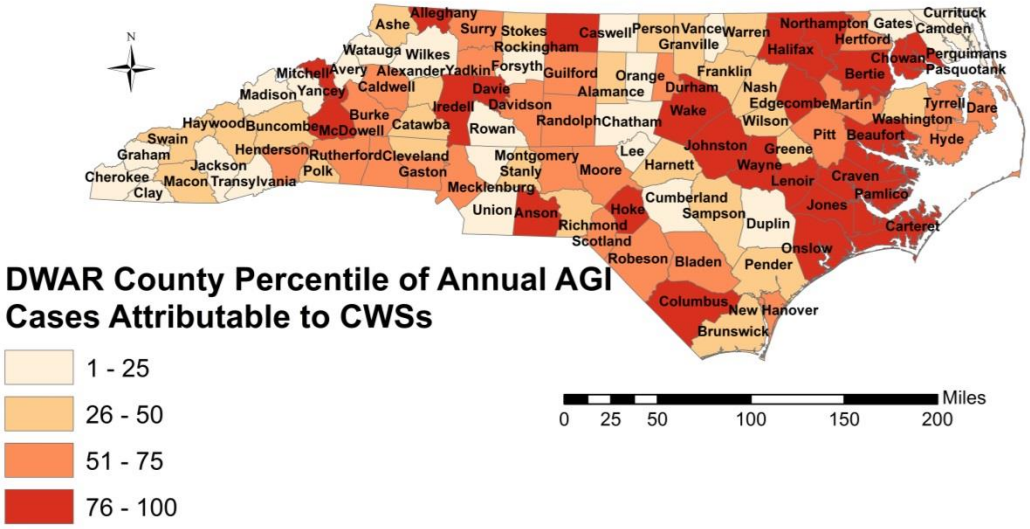

Figure 3.S8. Annual county rate of ED visits for AGI attributable to CWSs using the DWAR approach. Percentiles correspond to the following risk levels: first quartile, 1/900-1/400; second quartile: 1/400-1/300; third quartile, 1/300-1/200; fourth quartile: 1/200-1/75.

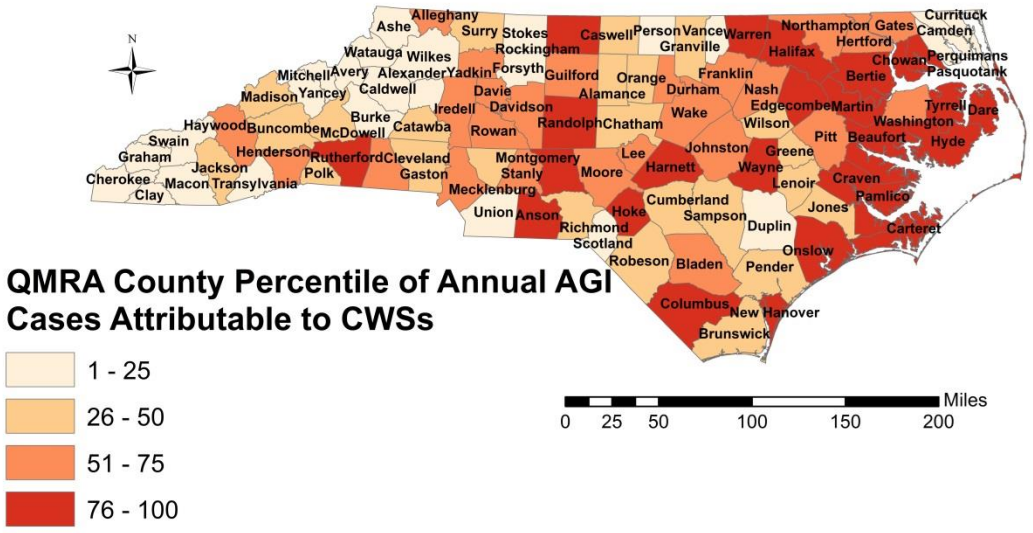

Figure 3.S9. Annual county rate of ED visits for AGI attributable to CWSs using the QMRA approach. Quartiles correspond to the following risk levels: first quartile, 1/1,000,000-1/20,000; second quartile, 1/20,000-1/3,000; third quartile, 1/3,000-1/,1000; fourth quartile, 1/1,000-1/400.

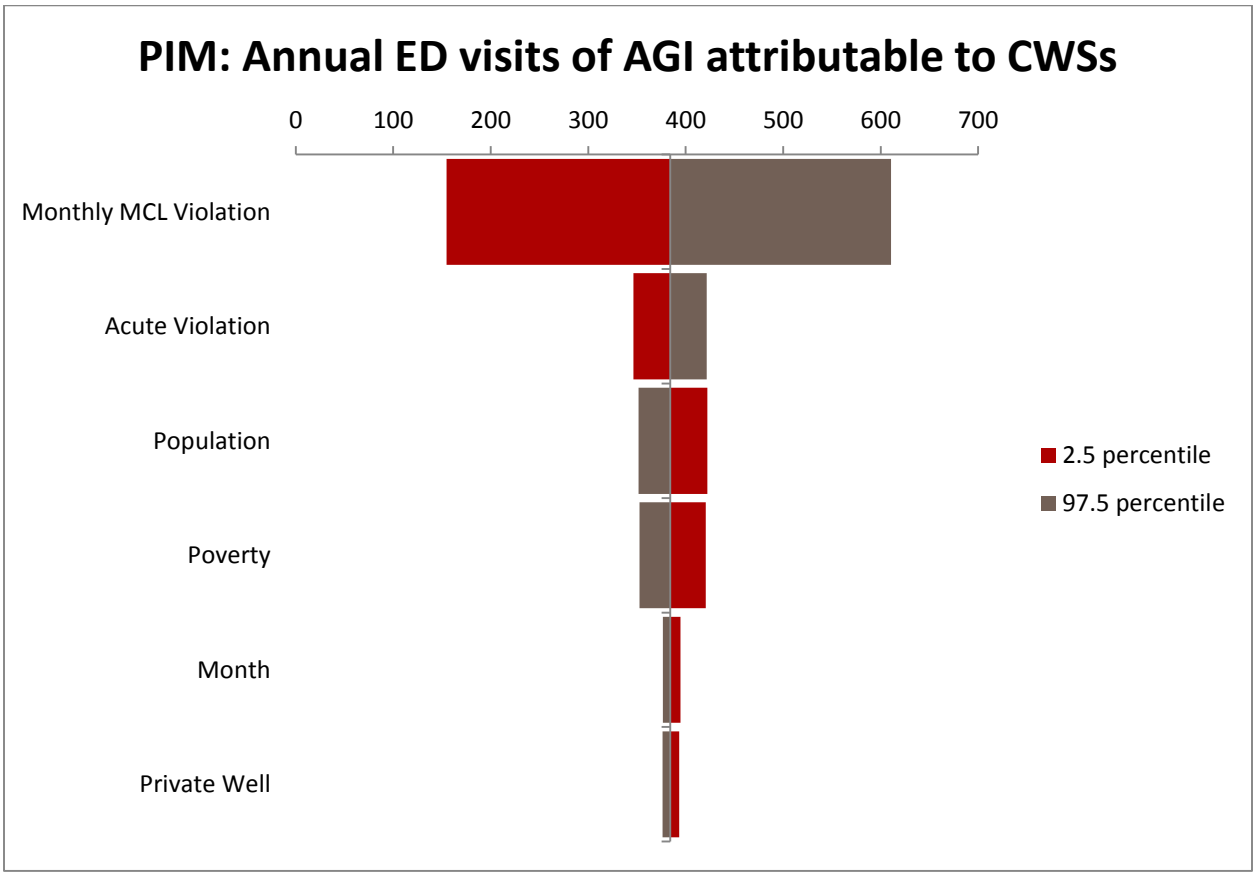

Figure 3.S10. Sensitivity of the risk estimates to changes in input variables of the PIM model.

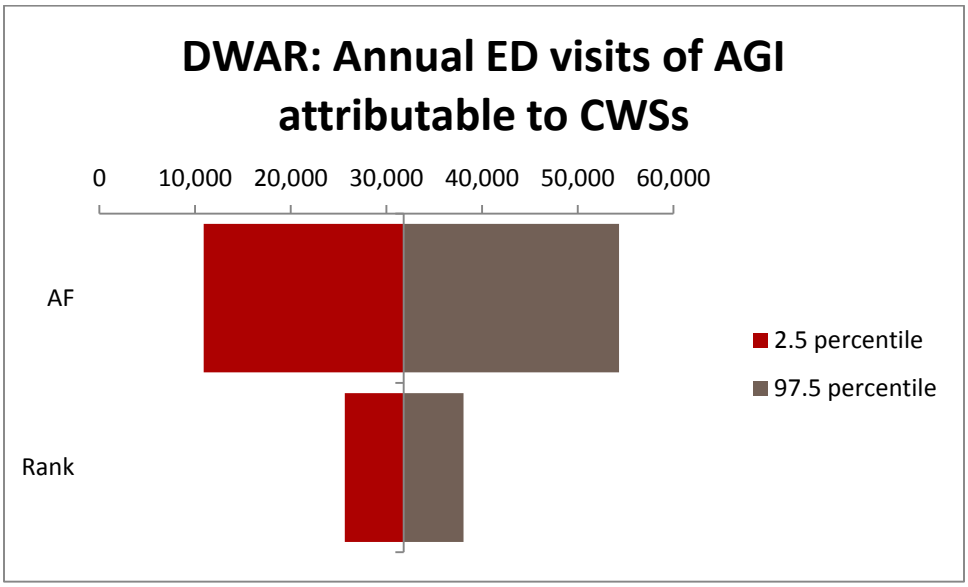

Figure 3.S11. Sensitivity of the risk estimates to changes in input variables of the DWAR model.

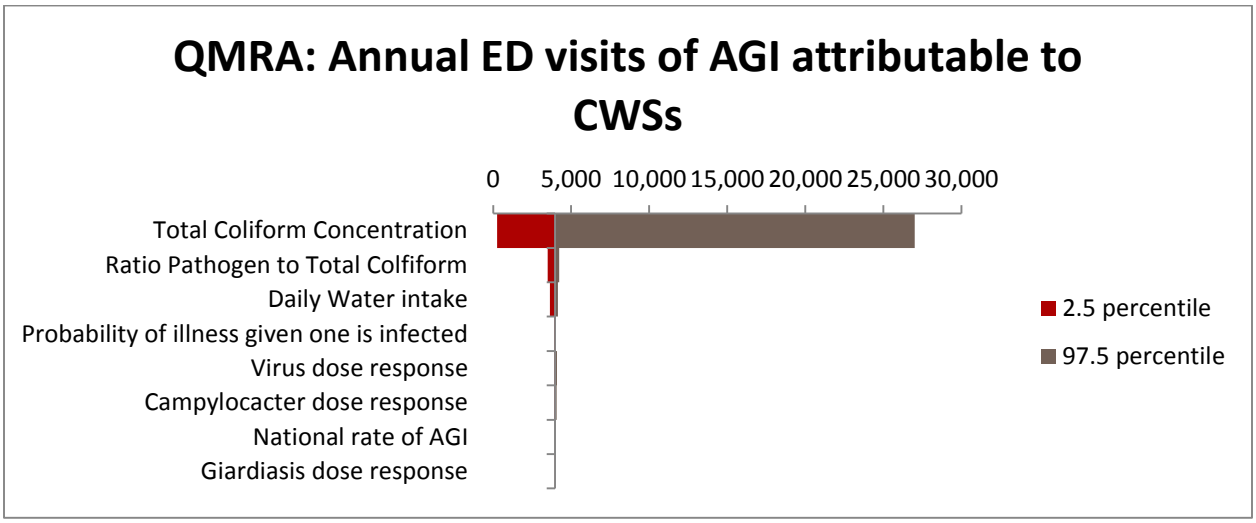

Figure 3.S12. Sensitivity of the risk estimates to changes in input variables of the QMRA model.

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Chapter 4:
Reducing Risks of Acute Gastrointestinal Illnesses due to Microbial Contaminants in North Carolina Drinking Water by Expanding Community Water Systems

4.1 Introduction

The introduction of the community water system (CWS) was one of the twentieth century's most significant public health advances.[1] In the US, this intervention is credited with decreasing infant, child, and total mortality by 75%, 67%, and 50%, respectively, between 1900 and 1936.[1] However, despite the potential benefits of service provided by CWSs and decades of investment in expanding the drinking water infrastructure, 23% of North Carolina's population lacks access to a regulated community water supply and instead obtains drinking water from a domestic water system (DWS), such as a backyard well (Figure 4.SM1, Supporting Material). [2,3] For regulatory purposes, a DWS is defined as an individual household well or other water system with fewer than 15 connections that serves fewer than 25 people year round. As of 2010, approximately 2,232,000 North Carolina (NC) residents relied on DWSs for their water, making NC the fifth-highest ranked state in terms of numbers served by DWSs.[2-4]

Drinking water from DWSs is not regulated at the federal level and therefore does not receive the same level of monitoring as that from a CWS. [5] In an attempt to reduce the risk from DWSs, the NC legislature passed a law requiring all counties to institute a private drinking water well permit program by July 1, 2008. [6] Under this program, all new DWSs must obtain a permit and, in order to do so, must undergo water quality testing. However, this program may not be as effective as desired, because routine monitoring is not required after the permit is granted, and wells constructed before 2008 are exempted from the permitting requirement.

The magnitude of waterborne disease attributable to contaminants in US DWSs is thought to be substantial but is not well quantified. Previous US studies have sought to quantify microbial pathogen concentrations in DWSs and in CWSs using groundwater as a source,[7-11] and a few studies have sought to establish relationships between self-reported health systems and microbial contaminant concentrations in drinking water.[12-16] However, to our knowledge, no known US study has provided county-level estimates for an entire state of the burden of infectious diseases attributable to microbial contaminants in DWSs. The limited knowledge of health risks associated with microbial contamination of DWSs suggests that a comprehensive burden of disease assessment could inform future decisions about whether to extend community water service to unserved/underserved areas or to establish other policies to protect the health of those relying on domestic wells.

To help fill the information gap on waterborne disease risks associated with US DWSs and the potential health benefits of interventions to reduce risks, this paper develops a population intervention model (PIM) to quantify acute gastrointestinal illness (AGI) risks attributable to microbial contaminants in NC DWSs. We focus on AGI, because analyses of US waterborne disease outbreak data over the past four decades indicate that AGI was the health outcome in 87.8% of outbreaks.[17] The PIM model enables not only estimation of current risks but also potential risk reductions achievable if CWSs were extended to portions of the population currently relying on DWSs. While the PIM approach is a well-established method for estimating the effects of public health interventions, it has not previously been used to assess strategies for reducing waterborne disease risks from US DWSs.[18-20] The main advantage of the PIM approach, in comparison to other risk assessment models, is its exclusive reliance on data specific to the at-risk population. In contrast, previously used quantitative microbial risk assessment approaches rely on dose-response estimates from studies of other populations, which may differ in susceptibility from the population on which the risk analysis is focused.[21]

Application of the PIM method to assess NC waterborne disease risks is made possible by the establishment of two relatively new NC databases: one that tracks illnesses reported in every NC emergency department and another that collects all private well water quality sampling data collected through NC's private well permitting program. The integrated analysis of these two databases represents an example of environmental health tracking research, which the US Centers for Disease Control and Prevention and other organizations have promoted to improve understanding of the links between environmental quality and human health.[22] As such, this analysis can serve as an example for future environmental health tracking projects.

4.1.1 Previous Studies of Health Risks Associated with Microbial Contamination in DWSs

The majority of previous studies of US waterborne disease risks from private well groundwater quantified microbial contaminant concentrations but did not extend their analyses to estimate the associated health risks. A recent US Geological Survey study of approximately 400 private wells throughout the US found that 34% were contaminated with total coliform bacteria and 8% were contaminated with *E. coli*.[7] A study of microbial contaminants in DWSs in Virginia found that 41% of 538 samples tested positive for total coliforms and 10% tested positive for *E. coli*.[8] A study in Wisconsin found that 28% of private wells tested positive for total coliforms and 8% for enteric viruses.[9] In Preston County, West Virginia, a study of 155 private wells found that 68% were positive for total coliform bacteria.[10] Finally, a study of three rural South Carolina counties randomly sampled 460 private wells (representing approximately 10% of private well users) and found that 85% of samples were positive for total coliforms.[11] These studies suggest that the detection rate of fecal indicator bacteria in private wells is substantially higher than the current rate (no more than 5% of samples testing positive in any given month) permitted in municipal water systems by US Environmental Protection Agency (US EPA) regulations.

Very few recent US studies have sought to link AGI risks to microbial contamination of private drinking water wells.[12-14] A recent cross-sectional case study in Alabama found that drinking water that tested positive for fecal coliforms increased the odds of contracting AGI by a factor of 4.0 (95% CI 1.3 -14).[15] This study also found that 20% of samples from private wells tested positive for fecal coliforms, a rate that was 2.5 times higher than samples from households connected to a CWS. One prior study in a central NC neighborhood found that 5 of 12 private wells tested positive for fecal indicator bacteria but none of the 8 houses connected to a CWS tested positive.[16] In addition to these two US studies, a recent study in British Columbia, Canada, estimated that individuals drinking water from private wells had a five-fold increase in AGI risk compared to those supplied with water from CWSs.[13] These past findings suggest that households relying on DWSs are exposed to more waterborne pathogens than those served by CWSs and thus may suffer more negative health outcomes compared to municipally supplied households.

This study estimates the risk associated with exposure to microbial contaminants in NC DWSs and CWSs using data from state agencies and then estimates the potential reduction in AGI rates in each county if private well users were connected to nearby CWSs. This is the first study to provide such a quantitative, comparative analysis for an entire state at the county level using local health outcome and water quality data to produce population-specific estimates. The results not only provide insights into modeling the burden of disease attributable to microbially contaminated drinking water but also identify the NC counties that may benefit the most from expanding CWSs.

4.2 Methods

4.2.1 Data

4.2.1.1 Water Quality Data

The NC private drinking water well permit program requires all new DWSs to test for total coliforms and *E. coli*. We received monitoring data for the period January 1, 2009 –December 31,

2013, from the Occupational and Environmental Epidemiology Branch of the NC Department of Health and Human Services.[23] The data set included 16,138 observations with data on test results, the county in which the well was located, and the microbial indicator assessed. Data were received for 91 of the 100 NC counties. For the nine counties that did not report, we assumed exposure for each non-reporting county was equal to the mean of all counties that border the county for which data was missing.

The NC Division of Environment and Natural Resources (NCDENR) provided us with microbial water quality violation data for each of the 2,120 active NC CWSs from January 1, 2007–December 31, 2013.[3] The data set contained information on monthly violations, which were defined as events wherein greater than 5% of samples over a 30-day period tested positive for total coliform bacteria, and acute violations, defined as the presence of *E. coli* in one or more follow-up analyses of samples testing positive for total coliform bacteria.[24]

4.2.1.2 AGI Reported Cases

Since most AGI cases are unreported, we used data on emergency department (ED) visits for AGI as a proxy for total AGI incidence. Data on the total number of reported visits for AGI between January 1, 2007, and October 31, 2013, in EDs across the state were extracted from the NC Disease Event Tracking and Epidemiologic Collection Tool (NCDETECT), a database containing records of all 122 emergency departments throughout the state.[25] In keeping with prior research on AGI, records from NCDETECT containing the following diagnostic codes were retrieved: infectious GI illness (001–009), non-infectious GI illness (558.9), and nausea and vomiting (787.01–787.03, 787.91).[26-30] In total, the database contained 2,769,620 ED visits that matched these criteria.

4.2.1.3 Population Served by Water System Type

The population served by CWSs and by DWSs was determined using the 2010 census data together with CWS data reported by NCDENR.[3-5] We calculated the county-specific population on CWSs by summing all individual CWS populations within a given county. We assumed those not

served by a CWS relied on DWSs. To determine the population on DWSs we therefore subtracted the aggregated population served by CWSs from the total county population.

4.2.2 Population Intervention Model (PIM)

The PIM approach, which is based on modern causal inference theory, was used to estimate AGI cases per county attributable to microbially contaminated CWSs and DWSs under different exposure scenarios.[21] The PIM method was selected partly because our previous experience using it to evaluate AGI risks attributable to microbial contamination in CWSs suggested that the PIM method preformed better than other models and showed the highest internal validity.[31] To implement the PIM, a longitudinal multivariate linear feasible generalized least squares regression model with first-order autoregressive serial correlation was fitted to monthly county-level health outcome and water quality data. The model form is as follows:

$$Y_{i,j} = \alpha + \beta_1 C_{CWS_{i,j}} + \beta_2 E_{CWS_{i,j}} + \beta_3 C_{DWS_i} + \beta_4 N_i + \beta_5 Pov_i + \left(\sum_{m=6}^{17} \beta_m I_{j.m}\right) + \varepsilon_{i,j} \quad (1)$$

where $Y_{i,j}$ is the number of observed AGI ED visits in county i during month j, $C_{CWS,i,j}$ is the potential number of CWS customers in county i exposed to a monthly MCL violation during month j, $E_{CWSi,j}$ is the number of CWS customers exposed to an acute MCL violation in month j, C_{DWSi} is the number of private well (DWS) users exposed to total coliform bacteria in county i, N_i is the total county population, $Pov_{,i}$ is the population in poverty, $I_{j,m}$ is an indicator variable equal to 1 if $m = j$ and zero otherwise, and ε_{ij} is the serially correlated error term. The number of individuals exposed by CWS violations was determined by assuming that all customers of the systems with monthly or acute MCL violations were equally exposed. The number of exposed private well users was determined by multiplying the fraction of private wells testing positive by the total county population served by private wells and was assumed to be constant over time (an assumption necessary because private well sampling data were undated). Population and poverty data for each county were taken from the

2010 US Census.[5] The regression model was fitted for the time period January 1, 2007–October 31, 2013 (the time period for which both AGI ED visit and CWS water quality data were available).

Regression models were fit using STATA IC 12 (College Station, TX). The fully parameterized, fitted regression model (equation 1) was used to estimate the observed AGI cases in each county attributable to microbial contamination of CWSs and DWSs. The expected number of AGI cases for each county was estimated both under current conditions and under multiple counterfactual scenarios in which different proportions of the population relying on DWSs were provided with a connection to the nearest CWS. Risks under actual conditions were computed by using all parameters in the regression model to estimate $Y_{i,j}$ (the mean estimated number of AGI ED visits in county *i* during month *j*) under the current exposure scenario. Risks under counterfactual scenarios were computed in the same manner under multiple different scenarios: (a) zero exposure to contaminants in drinking water (either in CWSs or DWSs); (b) zero exposure to contaminants in CWSs; (c) zero exposure to contaminants in DWSs; (d) connection of portions of the population currently relying on DWSs to the nearest CWS. $Y_{i,j,counterfactual}$ for each county and month was estimated under each counterfactual exposure scenario by changing the relevant independent variables in equation 1 (e.g., for scenario b, $C_{CWS,i,j}$=0) to estimate the number of AGI cases under that scenario for each county and each month. The decrease in cases given the changes in exposure under each counterfactual scenario was then computed by subtracting the estimated counterfactual cases from the mean regression model estimate of current cases:

$$\Delta Y_{i,j} = Y_{i,j} - Y_{i,j-counterfactual} = \beta_1 \left(C_{CWS_{i,j}} - C_{CWS_{i,j-counterfactual}}\right) + \beta_2 \left(E_{CWS_{i,j}} - E_{CWS_{i,j-counterfactual}}\right) \quad (2)$$

where $\Delta Y_{i,j}$ is the decrease in AGI ED visits attributable to microbial contamination of drinking water in county *i* during month *j* under the counterfactual scenario. For each county, we summed the estimates of prevented cases across months for each data year, in order to develop annual estimates of

avoided cases by county. We then averaged these annual estimates across the seven years of data (correcting for the fact that only 10 months of data were available for 2013).

4.3 Results

The longitudinal multivariate regression model showed that emergency department visits for AGI in NC counties are significantly ($p<0.001$) associated with water quality in DWSs (Table 4.1). Employing this regression model in the PIM analysis suggests that an estimated 47,250 (95% CI 32,000 – 62,400) annual AGI ED visits were attributable to microbial contamination in drinking water, constituting approximately 11.7% (95% CI 8.0–15.4) of all ED visits for AGI. Approximately 99% of the attributable cases (46,700; 95% CI 31,700–61,600) were associated with DWS contamination, and the remaining 1% of cases were associated with CWS contamination. The PIM model estimates that every 10% shift in the percentage of the population in each county from DWSs to CWSs is expected to decrease the number of ED visits for AGI statewide by 1.6%. However, the potential benefits of extending CWS services vary by county: the proportion of AGI ED visits attributable to DWSs ranges by county from 0.9%–30% (Figure 4.1 and Supporting Material, Table 4.SM1), and county rates of attributable AGI visits range from 0.4–26 (Figure 4.2).

Considering the high costs of providing medical treatment in EDs, as compared to primary care settings (which may be more appropriate venues for addressing AGI cases), the financial burden of AGI cases attributable to DWS contamination is considerable. McAndrews et al. estimated that ED visits for non-critical conditions cost approximately $1,099 in Mecklenburg County, NC.[32] Applying this cost estimate to the attributable AGI

cases yields a total annual cost burden of $51 million for ED visits associated with microbial contamination of DWSs.

4.3.1 Statewide Variation in ED Visits for AGI

Overall, the rate of AGI ED visits in NC was comparable to that reported in previous national estimates, but visit rates varied considerably by county (Figure 4.SM2, Supporting Material). An average of 405,000 (SD=38,500) AGI ED visits per year were reported in NC between 2007 and 2013, equivalent to a rate of 42 visits per 1,000 people—the same as the national rate previously estimated by the Foodborne Disease Active Surveillance Network (FoodNet). [29,33-35] In 22 counties, the rate was below the national lower 95th percentile of 30 visits per 1,000 people, and in 21 counties the rate exceeded the national upper 95th percentile of 55 visits per 1,000 people reported in the previous FoodNet estimate. [29,33-35]

4.3.2 Statewide Variation in Exposure to Microbial Contaminants in Drinking Water

Detection of total coliforms was much more common in private wells than in CWSs. Among DWSs, 35% of the 16,138 samples collected during 2009-2013 tested positive for total coliforms, and 1.4% tested positive for *E. coli*. In comparison, 0.4% of 539,710 CWS samples collected during 2007-2013 tested positive for total coliforms and 0.1% of 72,899 samples were positive for *E. coli*. Detection probabilities were higher in the eastern part of the state for both DWSs and CWSs (Supporting Material, Figures 4.SM3-4), potentially due to the region's shallow groundwater and high density of industrial animal operations.

4.4 Discussion

We estimated that approximately 11.7% (95% CI 8.0–15.4%) of all ED visits for AGI were attributable to microbial contamination of NC drinking water . About 99% of the attributable cases were associated with contamination in DWSs. On average, these attributable ED visits are estimated to cost a total of $51 million per year. There have not been any previous assessments of AGI risk due to DWSs in the US; the closest equivalent we could find in the literature were two studies of non-

disinfected groundwater. Macler and Merkle [14] estimated that microbial contamination of non-disinfected community groundwater systems contributed 0.75–5.0 million AGI cases annually in the US (5-32% of all cases among the population using non-disinfected community groundwater systems). Borchardt et al. [36] found that 6–22% of AGI cases were attributable to viruses in tap water in 13 Wisconsin communities that did not disinfect their community groundwater supplies. Our results for private wells are comparable to those of the non-disinfected groundwater CWS studies.

While most NC communities lacking water service are located in rural areas, especially in the mountainous western part of the state (Figure 4.SM1), some are located in relatively population-dense neighborhoods on the fringes of, or entirely surrounded by, cities and towns served by CWSs.[37] In the latter case, the NC Center for Civil Rights has documented multiple low-income, minority communities that are excluded from municipal services such as CWSs, thereby denying them the potential health benefits associated with regulated water service. [38] A handful of community-level case studies documenting such disparities exist. The best-known examples are in Mebane, a town of about 8,000 located 50 miles northwest of Raleigh, and Pinehurst, a community of 10,000 that has hosted the US Open Golf Championships. [39,40] Recently, as a result of more than a decade of action by a local community group, Mebane extended services to 90 homes, but more than 400 homes remain without service. [41,42] Such population-dense areas near existing infrastructure may be the most appropriate targets for future CWS expansion due to the likely relatively lower cost (compared to rural areas) of extending existing water distribution networks.

Decisions about water service are traditionally are made by local governments and utility providers and a large portion of these decisions are made on a cost-benefit basis. Constructing water mains is expensive, and it is not feasible to provide regulated water state-wide. However, identifying areas of greater population density that may be in close proximity to existing infrastructure along with

factoring in the potential health benefits may make expansion economically feasible. Future research should identify such eligible communities.

4.4.1 Limitations

A number of limitations are inherent in the data available to support this research. First, due to a lack of pathogen monitoring, we relied on the presence of total coliform bacteria as the indicator of potential exposure to microbial pathogens, because these data are routinely collected by CWSs and when new DWSs are constructed. Such microbial indicators are used for reasons of practicality and cost since large water samples are required to detect pathogens and sampling techniques are costly (e.g. *Giardia* and viruses).[43-45] The presence of a microbial indicator does not confirm but rather increases the probability of pathogen presence; likewise, the absence of indicator organisms does not guarantee the water is pathogen free.[46] Therefore, our understanding of the presence of pathogens is conditional on the indicator organism, so we may have over- or under-estimated exposure.[36,46-48]

A second limitation is the assumed uniform exposure across the population served by each CWS for a given month with a violation and the similar uniform exposure assumed for DWSs within a county within the time period analyzed. These assumptions could result in over-estimates of the number of people exposed if the proportion of DWS users exposed to fecal indicator organisms in a given county was not constant over the course of the analysis time period or if the CWSs population was not uniformly exposed during a given month. On the other hand, underestimates of exposure could have occurred if DWS water quality deteriorated after construction. Our DWS data set included only newly constructed wells, which may not be reprehensive of older DWSs with aging components. Similarly, we could have underestimated exposure to CWS contamination, since exposure for CWSs was defined as an MCL violation (more than 5% of samples tested positive in a given month), while in fact exposure may still occur when fewer than 5% of samples test positive.

A third limitation arises from the geopolitical level of the analysis. The finest resolution of NCDETECT's data on AGI ED visits was at the county level, so exposure estimates needed to be aggregated to the county level, as well. Exposure due to a given water system type (DWS or CWS) at the county level was estimated using a population weighting approach. CWSs thus contributed to the risk estimates proportional to their population size, while DWSs were assumed to have a uniform size across all systems in the county. Further, the aggregation of CWS exposure to the county level has the potential to be biased due to the influence of larger systems. These assumptions were unavoidable given the nature of reported data on microbial indicator organisms.

The health outcome dataset captures only a fraction of all AGI cases. The FoodNet study found that only 6.4% (95% CI 5.0-7.8%) of persons with AGI visited the ED; thus, every ED visit potentially represents approximately 16 AGI cases.[29,33-35] Furthermore, the population using EDs for routine medical care is likely to be of lower socioeconomic status than the general population,[49] possibly biasing our estimates of county-level AGI ED visit rates.

A related limitation is that ED visits are classified based on ICD-9 codes, which are used for billing rather than diagnosis and thus may contribute to further under- or over-estimation of the true health risk. Under estimation may occur when two or more conditions are present during a visit, and medical personnel elect to report the more severe or more important billing code, neglecting to mention the AGI that was in fact present. Over estimation may occur due to general coding protocols of an ED and the assumption of which comorbidities are present for a given condition.

A final limitation is that available public health data were insufficiently refined at the spatial scale to assign an AGI rate separately for CWSs and DWSs. The finest resolution available was at the county scale. Therefore, we assumed a homogeneous distribution of AGI across each county and, as a result, may have introduced bias in our estimates.

4.5 Research Implications

Despite the limitations, this analysis demonstrates a new method for estimating US waterborne disease risks associated with lack of community water service. Concerns about disparities in water service levels have been reported recently in communities ranging from Alaska Native villages to agricultural areas in central California to the southeastern US.[50] The method demonstrated in this paper could be used to quantify the public health implications of these disparities.

Historically, public health practitioners have played a critical role in persuading municipalities to adopt water treatment systems. Our finding that every 10% of the county population shifted from DWSs to CWSs reduces AGI cases by 1.6% demonstrates that expanding regulated water services has the potential for substantial health benefits. Public health practitioners could use this information to encourage a new dialogue with local water utilities and governments about options for extending municipal water service into un-served areas.

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Table 4.1. Beta coefficients from a generalized feasible linear model used in the population intervention method.

Variable	Definition	Beta	(95% CI)
Monthly MCL violation	Population on CWSs exposed to total coliform	0.0000671**	(0.000032 - 0.000103)
Acute MCL violation	Population on CWSs exposed to a E. Coli	0.000163*	(0.000085 - 0.00024)
Private well contamination	Population on DWS exposed to total coliforms	0.0044**	(0.0028 -0.0059)
Population	Total population in county	0.0012**	(0.00098 -0.0016)
Poverty	County population in poverty	0.0077**	(0.0055 - 0.0098)
Month of Assessment			
January		43.79**	(29.65 – 57.95)
February		53.38*	(38.31 – 68.44)
March		75.45**	(59.72 – 91.18)
April		23.59**	(7.38 – 39.81)
May		9.53**	(-7.02 – 26.09)
June		-5.38**	(-22.13 – 11.38)
July		-4.38**	(-21.22 – 12.45)
August		-3.04**	(-19.85 – 13.76)
September		-4.62**	(-21.27 – 12.03)
October		-3.17**	(-19.55 – 13.20)
November		-3.11**	(-19.01 – 12.8)
December		26.85**	(11.66 - 42.04)

*p<0.01, **p<0.0

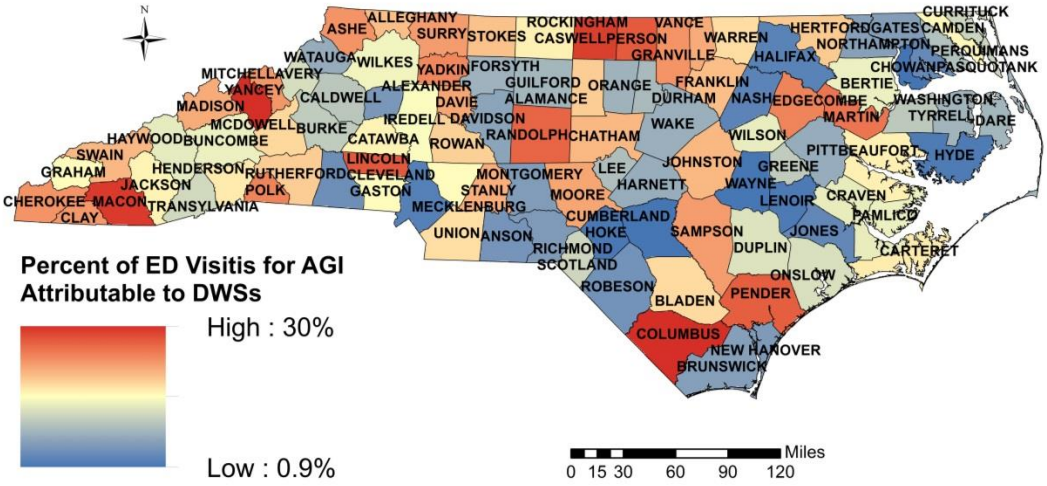

Figure 4.1. Estimated percentage of ED visits for AGI attributable to DWSs.

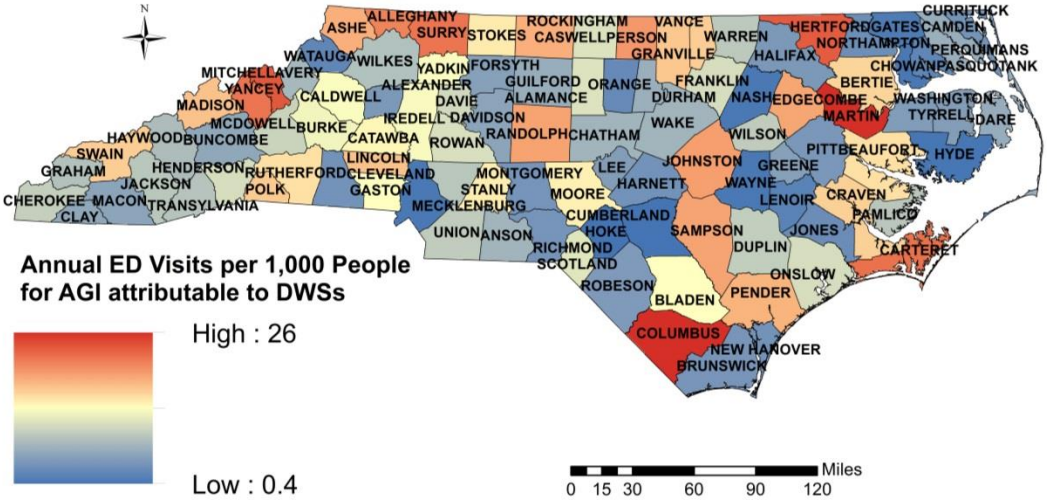

Figure 4.2. Estimated annual rate of ED visits per 1,000 people for AGI attributable to DWS.

4.6 Supporting Information

Table 4.S1: County-by-county assessment of emergency department visits for AGI potentially attributable to domestic water systems (DWSs).

County	County Population	County Population on DWS	Fraction of AGI potentially attributable to DWSs	Number of ED visits for AGI potentially attributable to DWSs
ALAMANCE	151,200	55,700	0.19 (0.13-0.25)	980 (700-1300)
ALEXANDER	37,151	7,751	0.05 (0.033-0.068)	93 (62-130)
ALLEGHANY	11,155	8,113	0.21 (0.15-0.27)	140 (100-180)
ANSON	26,938	2,838	0.048 (0.032-0.066)	110 (75-150)
ASHE	27,240	22,100	0.23 (0.17-0.29)	290 (210-370)
AVERY	17,752	6,952	0.12 (0.083-0.16)	75 (52-99)
BEAUFORT	47,781	8,881	0.17 (0.12-0.22)	430 (300-560)
BERTIE	21,269	4,069	0.15 (0.1-0.19)	210 (140-270)
BLADEN	35,200	13,000	0.19 (0.14-0.25)	290 (210-380)
BRUNSWICK	107,472	7,472	0.059 (0.039-0.08)	260 (170-350)
BUNCOMBE	237,900	63,900	0.14 (0.097-0.18)	820 (570-1100)
BURKE	91,000	30,600	0.11 (0.074-0.14)	680 (470-910)
CABARRUS	178,400	47,400	0.15 (0.1-0.2)	860 (590-1100)
CALDWELL	83,000	23,000	0.1 (0.071-0.14)	640 (440-860)
CAMDEN	9,980	1,744	0.14 (0.096-0.18)	32 (22-42)
CARTERET	66,400	14,400	0.16 (0.11-0.21)	820 (570-1100)
CASWELL	23,746	20,200	0.3 (0.22-0.37)	160 (120-200)
CATAWBA	154,400	56,300	0.16 (0.11-0.21)	1200 (850-1600)
CHATHAM	63,500	31,100	0.2 (0.14-0.25)	250 (180-320)
CHEROKEE	27,500	17,300	0.22 (0.16-0.28)	140 (100-180)
CHOWAN	14,812	312	0.009 (0.0058-0.013)	9.3 (6-13)
CLAY	10,587	8,656	0.23 (0.16-0.29)	37 (26-47)

County	County Population	County Population on DWS	Fraction of AGI potentially attributable to DWSs	Number of ED visits for AGI potentially attributable to DWSs
CLEVELAND	98,090	8,490	0.044 (0.029-0.06)	230 (150-310)
COLUMBUS	58,100	30,600	0.31 (0.23-0.39)	1200 (900-1500)
CRAVEN	103,500	16,400	0.14 (0.096-0.18)	970 (670-1300)
CUMBERLAND	319,602	7,602	0.011 (0.0075-0.016)	120 (78-160)
CURRITUCK	23,561	3,061	0.1 (0.069-0.14)	48 (32-63)
DARE	33,923	5,523	0.078 (0.052-0.1)	110 (75-150)
DAVIDSON	162,600	26,600	0.066 (0.044-0.089)	530 (350-710)
DAVIE	41,200	11,500	0.21 (0.15-0.27)	240 (170-300)
DUPLIN	58,500	17,000	0.14 (0.096-0.18)	340 (240-450)
DURHAM	267,100	47,100	0.088 (0.06-0.12)	1000 (690-1400)
EDGECOMBE	56,600	28,200	0.25 (0.18-0.32)	650 (470-830)
FORSYTH	351,200	60,200	0.08 (0.054-0.11)	1100 (730-1500)
FRANKLIN	60,700	40,000	0.2 (0.14-0.25)	370 (260-480)
GASTON	206,200	56,200	0.16 (0.11-0.21)	1700 (1200-2200)
GATES	12,168	1,468	0.059 (0.039-0.082)	9.7 (6.4-14)
GRAHAM	8,861	4,227	0.15 (0.11-0.2)	42 (29-55)
GRANVILLE	60,000	31,800	0.22 (0.16-0.28)	560 (400-720)
GREENE	21,315	2,515	0.11 (0.072-0.14)	63 (43-84)
GUILFORD	488,200	99,200	0.085 (0.057-0.11)	1800 (1200-2400)
HALIFAX	54,652	2,352	0.027 (0.018-0.037)	150 (100-210)
HARNETT	114,700	22,300	0.074 (0.05-0.1)	250 (170-330)
HAYWOOD	59,000	16,900	0.13 (0.089-0.17)	260 (180-340)
HENDERSON	106,800	41,600	0.16 (0.11-0.22)	640 (440-840)
HERTFORD	24,687	9,387	0.065 (0.044-0.089)	52 (35-71)
HOKE	46,910	1,710	0.013 (0.0087-0.018)	21 (13-28)

County	County Population	County Population on DWS	Fraction of AGI potentially attributable to DWSs	Number of ED visits for AGI potentially attributable to DWSs
HYDE	5,810	99	0.016 (0.0087-0.029)	2.6 (1.4-4.9)
IREDELL	159,900	54,900	0.15 (0.1-0.19)	1200 (800-1500)
JACKSON	40,300	16,600	0.17 (0.12-0.22)	210 (150-270)
JOHNSTON	168,700	61,700	0.2 (0.14-0.26)	1900 (1300-2400)
JONES	10,153	625	0.031 (0.02-0.045)	19 (12-27)
LEE	57,913	8,113	0.092 (0.062-0.12)	170 (110-220)
LENOIR	59,453	1,453	0.018 (0.012-0.026)	74 (49-100)
LINCOLN	78,300	40,800	0.27 (0.19-0.34)	770 (560-970)
MACON	33,910	22,600	0.29 (0.22-0.37)	110 (82-140)
MADISON	20,771	8,471	0.21 (0.15-0.27)	200 (150-260)
MARTIN	24,540	16,800	0.26 (0.19-0.33)	670 (490-850)
MCDOWELL	45,000	22,700	0.19 (0.13-0.24)	260 (190-340)
MECKLENBURG	919,200	24,200	0.021 (0.014-0.029)	560 (370-780)
MITCHELL	15,579	8,965	0.22 (0.16-0.28)	210 (150-270)
MONTGOMERY	27,774	6,674	0.06 (0.04-0.082)	68 (45-92)
MOORE	88,200	31,900	0.21 (0.15-0.27)	720 (510-920)
NASH	95,878	5,778	0.026 (0.017-0.035)	54 (36-74)
NEW HANOVER	203,100	15,100	0.056 (0.037-0.076)	440 (290-590)
NORTHAMPTON	22,115	8,115	0.2 (0.14-0.25)	310 (220-400)
ONSLOW	177,600	23,600	0.12 (0.082-0.16)	1100 (730-1400)
ORANGE	133,600	21,600	0.08 (0.054-0.11)	230 (150-300)
PAMLICO	13,103	1,903	0.12 (0.086-0.16)	59 (40-78)
PASQUOTANK	40,683	5,683	0.097 (0.066-0.13)	150 (110-210)
PENDER	52,200	26,600	0.26 (0.19-0.33)	540 (390-680)
PERQUIMANS	13,436	736	0.036 (0.023-0.05)	19 (12-27)

County	County Population	County Population on DWS	Fraction of AGI potentially attributable to DWSs	Number of ED visits for AGI potentially attributable to DWSs
PERSON	39,500	25,700	0.27 (0.2-0.34)	450 (330-560)
PITT	168,400	16,400	0.078 (0.053-0.11)	460 (310-630)
POLK	20,534	11,800	0.23 (0.16-0.29)	190 (140-240)
RANDOLPH	141,800	76,900	0.27 (0.2-0.34)	1600 (1200-2000)
RICHMOND	46,609	6,309	0.061 (0.04-0.083)	120 (79-160)
ROBESON	133,800	18,800	0.05 (0.033-0.069)	400 (260-550)
ROCKINGHAM	93,700	39,900	0.17 (0.12-0.22)	1000 (710-1300)
ROWAN	138,400	49,100	0.19 (0.13-0.24)	880 (620-1100)
RUTHERFORD	67,800	30,100	0.2 (0.14-0.25)	630 (450-820)
SAMPSON	63,400	36,900	0.23 (0.17-0.3)	730 (530-930)
SCOTLAND	36,100	10,300	0.13 (0.089-0.17)	260 (180-350)
STANLY	60,600	24,500	0.2 (0.14-0.26)	500 (350-640)
STOKES	47,400	24,100	0.19 (0.13-0.24)	390 (280-510)
SURRY	73,600	48,000	0.23 (0.16-0.29)	950 (680-1200)
SWAIN	13,981	9,534	0.21 (0.15-0.27)	140 (97-180)
TRANSYLVANIA	33,100	16,200	0.12 (0.079-0.15)	160 (110-210)
TYRRELL	4,407	557	0.076 (0.049-0.11)	12 (7.5-17)
UNION	201,100	50,100	0.16 (0.11-0.21)	980 (680-1300)
VANCE	45,400	25,900	0.23 (0.16-0.3)	470 (340-610)
WAKE	901,000	115,000	0.07 (0.047-0.095)	3400 (2200-4500)
WARREN	20,994	11,100	0.19 (0.14-0.25)	120 (84-160)
WASHINGTON	13,247	2,047	0.11 (0.075-0.15)	38 (26-52)
WATAUGA	51,100	12,600	0.077 (0.052-0.1)	79 (53-110)
WAYNE	122,605	1,605	0.013 (0.0085-0.018)	78 (52-110)
WILKES	69,400	27,100	0.15 (0.1-0.2)	340 (240-450)

County	County Population	County Population on DWS	Fraction of AGI potentially attributable to DWSs	Number of ED visits for AGI potentially attributable to DWSs
WILSON	81,200	21,900	0.15 (0.1-0.19)	460 (320-600)
YADKIN	38,400	26,300	0.23 (0.17-0.3)	290 (210-370)
YANCEY	17,852	13,400	0.3 (0.22-0.37)	230 (170-280)

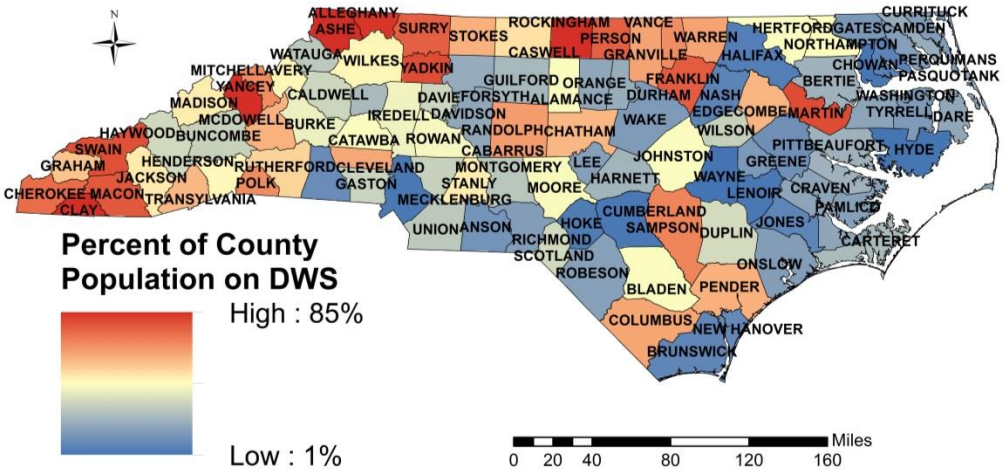

Figure 4.SM1. Percent of the county population served by domestic water systems.

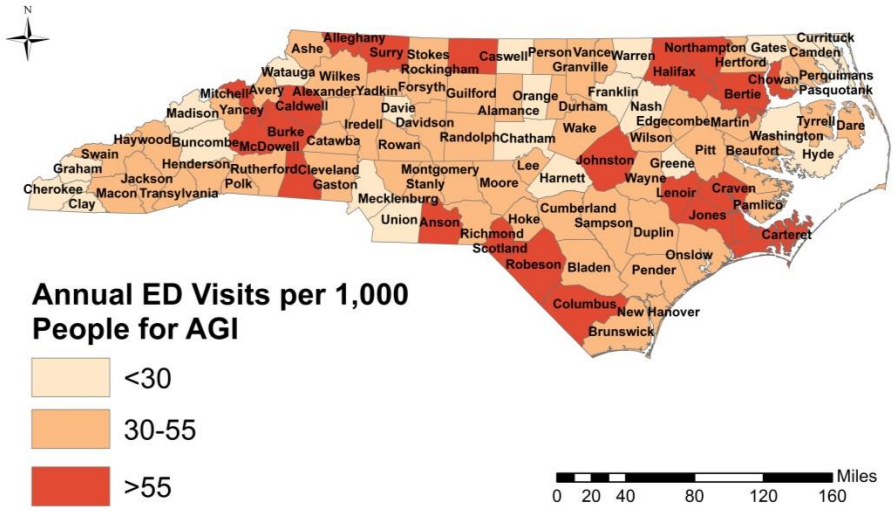

Figure 4.SM2. Annual number of ED visits for AGI (ICD-9) per 1,000 people in each county**.**

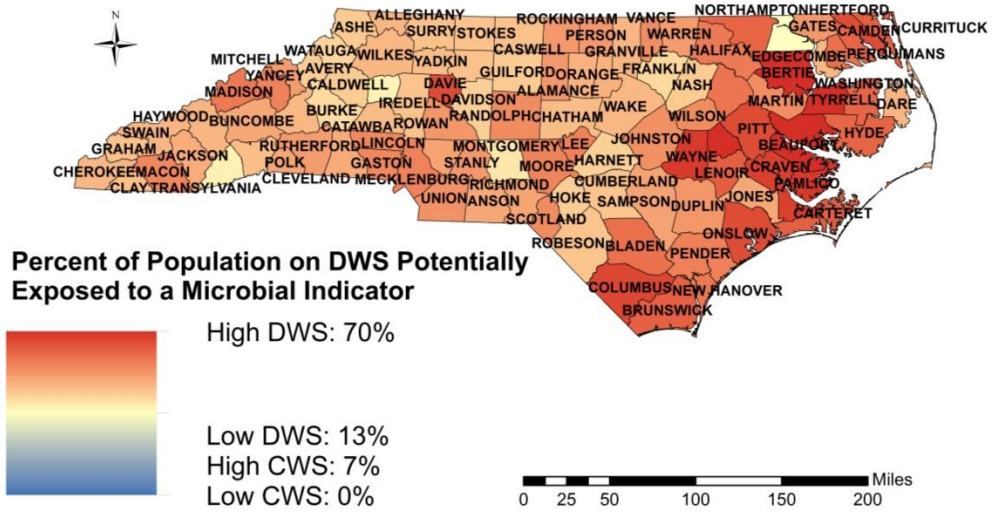

Figure 4.SM3. Percent of the population served by DWSs exposed to total coliform contamination.

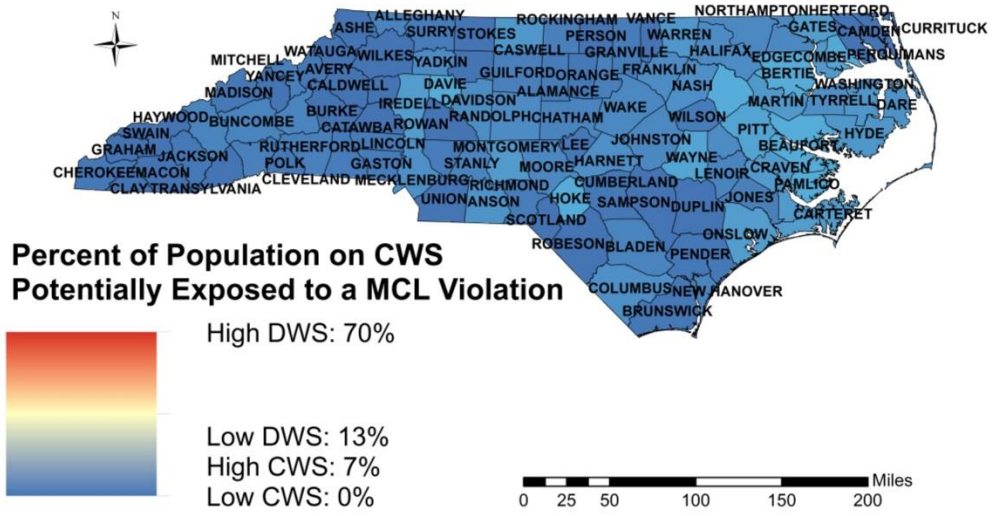

Figure 4.SM4. Percent of the population served by CWSs exposed to *E*. *Coli* or total coliform

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Chapter 5:
Conclusions

5.1 Key Findings and Implications

In this dissertation, I have presented results on the spatial variability of the burden of disease attributable to drinking water. I have demonstrated a method to evaluate the burden of cancer attributable to chemical contaminants in CWSs at the county level (Chapter 2) and to estimate the burden of AGI attributable to microbial contaminants in drinking water at the county level (Chapter 3). I have also identified the potential health benefits from expanding CWSs in each county (Chapter 4). The results presented in the dissertation improve our understanding of how drinking water contributes to the burden of cancer and AGI.

Chapter 2 estimated that 295 (95% CI 163-427) of the 48,000 annual cancer cases in North Carolina are potentially attributable to regulated chemicals in community drinking water systems. Disinfection byproducts are estimated to be responsible for the vast majority (90%) of these cases, with the remaining 10% of cases attributable almost entirely to arsenic and alpha radiation. Around 80% of the population served by CWSs in North Carolina was exposed to water with TTHM concentrations greater than the MCL at least once during the period 2006-2011.

These results underscore the potential benefits of reconsidering the contaminant-by-contaminant monitoring approach currently mandated by the SDWA. The SDWA requires water utilities to monitor their water regularly for 34 carcinogenic chemicals; state regulators then must review these monitoring results and address any violations. However, the results

shown here reveal that health risks appear to be extremely low for most of these chemicals. At the same time, increased attention to TTHMs, arsenic, and alpha radiation in selected regions of the state could yield substantial health dividends. A place-based regulatory strategy emphasizing the three contaminants posing the most risk and considering the regional variation in exposures could reduce the overall costs to water utilities and state regulators of implementing the SDWA while increasing protection of public health. Indeed, the EPA has recognized the need for an approach that moves beyond contaminant-by-contaminant regulation and is gathering information on potential alternative approaches under a drinking water strategy (*A New Approach to Protecting Drinking Water and Public Health*). This research can inform the ongoing debates over strategies for ensuring the public is protected from risks posed by drinking water contamination.

In Chapter 3, I showed that the PIM approach better addresses the limitations of available data by developing dose-response models specific to the local population (i.e., the regression model predicting county-level ED visits from county-level monthly and acute MCL violation rates). As such, the PIM approach has higher internal validity, relative to the DWAR and QMRA approaches, and therefore I believe it is the most appropriate for quantifying AGI attributable to CWSs at a county level for an entire state.

According to the PIM approach, 380 (0.09%) of the 405,000 annual ED visits for AGI in NC are potentially attributable to microbial contaminates in CWSs. If each ED visit potentially represents about 16 AGI cases (as estimated by Jones et al.[1]), then 6,080 (95% CI: 2,400-10,080) AGI cases may be attributable to microbial contaminants in CWSs in NC each year. This equates to an individual risk of about 6×10^{-4} per year. This risk varies considerably by location, with risks levels in some counties approaching 3×10^{-3}—more than

four orders of magnitude higher than in the lowest-risk counties. Notably, the other methods' results predict much higher per-person risks: 7×10^{-3} and 5×10^{-2} on average across the state and 4×10^{-2} and 2×10^{-1} in the highest-risk counties for the QMRA and DWAR methods, respectively.

Overall, waterborne disease risks in NC are extremely low by global standards. For example, according to the World Health Organization, the lowest and highest country rates worldwide of diarrheal diseases attributable to deficiencies in water and sanitation systems are 2×10^{-4} and 1.07×10^{-1} disability-adjusted life years per person-year, respectively—equivalent to between 2×10^{-3} and 1 cases of AGI per person-year, respectively.[2] By comparison to this estimated global risk range, estimated waterborne disease risks in NC are low regardless of the risk estimation method used. Nonetheless, EPA policy is that annual infection risks above 1×10^{-4} should be targeted for interventions.[3,4] While vast improvements have been made in the provision of safe drinking water and while this research clearly shows that CWSs provide substantial health benefits in comparison to reliance on private well water, efforts are still necessary to reduce the burden of disease to the 10^{-4} risk level recommended by the EPA.

Chapter 4 estimated that between 2007 and 2013 there were 47,250 (95% CI 32,000-62,400) annual ED visits for AGI potentially attributable to microbial contamination in drinking water (including water from DWSs and CWSs), constituting approximately 11.7% (95%CI 8.0-15.4) of all ED visits for AGI. The majority of ED visits (46,700 [95% CI 31,700 – 61,600]) arose from contamination in DWSs and only a few (550 [95% CI 300-800]) were attributable to CWSs. The county-level burden of AGI attributable to DWSs was highly variable, ranging from 0.4 to 26 cases per 1,000 people, constituting 0.9% to 30% of

the individual counties' burden of AGI. I showed that each 10% shift in the percentage of the county population from DWSs to CWSs could reduce ED visits for AGI by 1.6%. Although it is impossible to conduct a cost-benefit analysis without knowing the county-specific figures for expansion, providing regulated water to current DWSs users may provide substantial health benefits.

Historically, public health practitioners have played a critical role in persuading municipalities to adopt water treatment systems. The finding that providing county populations on DWSs with access to CWSs may result in a reduction of AGI cases demonstrates that expanding regulated water services has the potential for substantial health benefits. Public health practitioners could use this information to encourage a new dialogue with local water utilities and governments about options for extending municipal water service into un-served areas.

5.2 Future Research Needs

The current study evaluated exposure and health data at the county level, which is an improvement on previous studies, but still leaves room for advancement. One area for improvement is the level of geospatial analysis -- the relationship between drinking water and health outcomes could be evaluated at a finer resolution. This would require a better understanding of the service areas of CWSs and DWSs along with reported health data at a township level. Service area identifcation would also provide valuable information not only on the sources of drinking water but also on potential areas for expansion of CWSs.

Efforts are also needed to improve the characterization of exposure to pathogens in NC drinking water and to link pathogen exposure data to medical visits for AGI across the

state, in order to identify specific communities that could benefit from interventions. Ideally, future data collection could occur at a finer spatial scale, such as at the level of Census blocks, in order to improve linkages between exposure and health outcome estimates.

The current study only compared microbial contaminants in DWSs with CWSs and did not evaluate the differences in risks from chemical contaminants. Potential risk differences due to differential chemical exposures also need to be evaluated to fully understand the benefits of extending CWS service to unserved areas.

Finally, efforts should also try to identify the potential seasonal effect of contaminants in DWSs. The rate of MCL violations occurring in CWSs exhibits a seasonal pattern, but whether DWSs display a similar pattern is unknown. Information on seasonal variability in DWS contamination would potentially help inform private well users when they should test their well or when more treatment may be required.

5.3 Final Thoughts

While the introduction of improved municipal water and sewer services is considered one of the most influential public health advances the twentieth century there are still advancements that can be made in providing safe, clean drinking water. Overall, it appears that regulated drinking water in North Carolina at the county level is of a high quality and provides substantial health benefits compared to private wells. Given the potential health benefits associated with drinking water and the large proportions of the population in North Carolina that is currently relies on private wells, the state may gain substantial benefits from expanding services into those populated regions underserved by public water systems.

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