# A RISK ASSESSMENT OF LIFETIME EXPOSURE TO ARSENIC-CONTAMINATED GROUNDWATER AND COMPARISON WITH URINARY BLADDER CANCER INCIDENCE RATES IN NORTHEASTERN WORCESTER COUNTY AND WESTERN MIDDLESEX COUNTY IN CENTRAL MASSACHUSETTS

A thesis

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## ABSTRACT

Arsenic, a toxic metalloid in Group 15 of the periodic table, is associated with chronic and acute health effects due to its ability to inhibit enzymes associated with adenosine tri-phosphate (ATP) production, resulting in multi-organ damage and carcinogenic effects. The risks from exposure to low concentrations of arsenic in drinking water are not well documented. This thesis investigated the cancer risks to human health associated with lifetime consumption of groundwater contaminated with low concentrations of arsenic. In order to test my hypothesis, I utilized analytical techniques including risk assessment, geographic information system (GIS) software tools that integrate hardware, software, and data for capturing, managing, analyzing, and displaying all forms of geographically referenced information, and Standardized Incidence Ratios (SIRs) for bladder cancer in two counties in north central Massachusetts. I reviewed the results of these assessments through a series of comparisons. My study found that bladder and urinary cancer incidence rates obtained from the Massachusetts Cancer Registry for selected towns where people drink water that is likely to contain more than 10 µg/liter arsenic were not related to arsenic concentration in the bedrock aquifer, but my risk assessment demonstrated that there is possible increased risk. Further research on levels of arsenic in untreated private well drinking water is needed for conclusive results.

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## LIST OF ACRONYMS

| Acronym | Definition of acronym |
|---|---|
| ACGIH | American Conference of Industrial Hygienists |
| $Ag_3AsO_3$ | Silver Arsenite |
| AP-1 | Activating Protein 1 |
| APHO | Association of Public Health Observatories |
| As | Arsenic |
| AS (III) | Trivalent Arsenic / Arsenite |
| As (V) | Pentavalent Arsenic /Arsenate |
| $As_2S_3$ | Orpiment |
| AsS | Realgar |
| ATP | Adenosine Tri-Phosphate |
| ATSDR | Agency for Toxic Substances and Disease Registry |
| BFD | Black Foot Disease |
| BOH | Board of Health |
| Ca | Calcium |
| Ca-Mg ratios | Calcium - Magnesium ratios |
| CF | Conversion Factor |
| CFR | Cancer / Case Fatality Rate |
| CI | Confidence Interval |
| CMRs | Cumulative Mortality Rates |
| CPF / q1 | Carcinogenic Potency Factor |
| CRAVE | Carcinogenic Risk Assessment Verification Endeavor |
| CSF | Cancer / Carcinogenic Slope Factor |
| DMA | Di-methylarsinic acid |
| DMA III | Di-methylarsinous acid |
| DMAV | Di-methylarsinic acid |
| DWR | Drinking Water Regulations |
| ELCR | Excess Lifetime Cancer Risk |
| EOHHS | The Official Website of the Office of Health and Human Services |
| EPA | Environmental Protection Agency |
| EPC | Exposure Point Concentration |
| EPC | Exposure Point Concentration |

| | |
|---|---|
| Fe | Iron |
| FeAsS | Arsenopyrite |
| GIS | Geographic Information Systems |
| GSH | Glutathione |
| GSSG | Glutathione disulfide reductase |
| $H_3AsO_4$ | Arsenic Acid |
| IRIS | Integrated Risk Information System |
| IV | Intravenous |
| LADD | Lifetime Average Daily Dose |
| LMS | Linearized Multistage |
| MassDEP | Massachusetts Department of Environmental Protection |
| MCL | Maximum Contaminant Level |
| MCLG | Maximum Contaminant Level Goal |
| MCR | Massachusetts Cancer Registry |
| Mg | Magnesium |
| mg/kg | miligrams per kilogram |
| MMA III | Mono-methylarsonous acid |
| MMA/ MMA V | Mono-methylarsonic acid |
| NAACR | North American Association of Central Cancer Registries |
| NCI | National Cancer Institute |
| NH - Maine | New Hampshire - Maine sequence |
| NHDH | New Hampshire Department of Health |
| NIPDWR | National Interim Primary Drinking Water Regulations |
| NRC | National Research Council |
| NYDH | New York Department of Health |
| PB-PK | Physiologically-Based Pharmacokinetic Model |
| PDH | Pennsylvania Department of Health |
| PPB | Parts Per Billion |
| RAF | Relative Absorption Factor |
| RBCs | Red Blood Cells |
| RfD | Reference Doses |
| SAMe | S-adenosyl-l-methionine |
| SEER | Surveillance, Epidemiology and End Results |
| SFDPH | San Francisco Department of Public Health |
| SIR | Standardized Incidence Ratio |
| SIR | Standardized Incidence Ratio |
| SMRs | Standard Mortality Rates |

| | |
|---|---|
| TCC | Transitional Cell Carcinoma |
| TMAO | Trimethylarsine oxide |
| Ug / Liter | Micrograms per Liter |
| UROtsa’s | Urothelial cells |
| USCB | United States Census Bureau |
| USEPA | United States Environmental Protection Agency |
| USGS | United States Geological Survey |
| WHO | World Health Organization |
| WOE | Weight of Evidence |
| WSC | Water Supply Certificate |

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## 1.0 INTRODUCTION

Arsenic, a toxic metalloid in Group 15 of the periodic table, is associated with chronic and acute health effects due to its ability to inhibit enzymes associated with adenosine tri-phosphate (ATP) production, resulting in multi-organ damage and carcinogenic effects. There is no method of treatment for cases with chronic/long-term exposure, although antidotes exist for acute poisoning. According to the World Health Organization (WHO) Factsheet on Arsenic in drinking water, depending on the severity and duration of exposure, arsenic can lead to diseases such as cirrhosis, hyperkeratosis, and Blackfoot Disease for chronic exposures whereas acute exposures result in vomiting, esophageal and abdominal pain, and bloody "rice water" diarrhea (WHO, 2001). Inorganic arsenic is a human carcinogen; ingesting arsenic in drinking water increases the risk of developing cancer of the bladder, liver, kidney and skin. As stated in the Toxicological Profile for Arsenic developed by the Agency for Toxic Substances and Disease Registry (ATSDR), inorganic arsenic occurs primarily in two oxidation states, As (V), also called pentavalent arsenic and arsenate, and As (III), referred to as trivalent arsenic and arsenite. As (V) generally dominates in oxidizing environments such as surface water and As (III) dominates under reducing conditions that may occur in groundwater (ATSDR, 2007). Arsenic is readily absorbed by the body after ingestion and undergoes a two-step metabolic pathway of reduction and methylation to produce mono-methylarsonic acid (MMA) and di-methylarsinic acid (DMA). As (V) is reduced to As (III), which then undergoes oxidative methylation to form MMA. This is then further reduced

and methylated to DMA (Hayakawa, Kobayashi, Cui, and Hirano, 2004). Many toxicological and epidemiologic investigations, as presented in reviews by the Agency for Toxic Substances and Disease Registry (ATSDR) and the U. S. Environmental Protection Agency (USEPA), conclude that ingestion of arsenic in high concentrations via drinking water can lead to bladder cancer (ATSDR, 2007: USEPA, 2003). Arsenic-related bladder cancer is a current concern in parts of China, Taiwan, Bangladesh and India as a result of increasing arsenic contamination of groundwater.

Risks from exposure to low concentrations of arsenic are not well documented. According to the 1999 National Research Council Subcommittee on Arsenic in Drinking Water, "Additional epidemiologic evaluations are needed to characterize the dose-response relationship for arsenic-associated cancer and non-cancer endpoints, especially at low doses. Such studies are of critical importance for improving the scientific validity of risk assessment" (Subcommittee on Arsenic in Drinking Water, National Research Council, 1999). In the past, spatial studies have provided the means to map arsenic concentrations (Ayotte et al., 2002; Colt et al., 2002) some of these studies demonstrated epidemiological associations between bladder cancer and consumption of low concentrations of arsenic in drinking water (Bates et al., 1995; Lewis, 1999). Existing studies also address the speciation of arsenic in groundwater and soil chemical effects. (Aurilio et al., 1995; Bednar et al., 2004) However, it is important to note that there is no

quantitative inference of the risk to human health posed by low levels of arsenic exposure as found in some U.S. water supplies, such as those in New England.

The objective of this thesis is to test the hypothesis that lifetime consumption of groundwater contaminated with low concentrations of arsenic can increase risk of cancer. In relation to this a secondary hypothesis will also be tested, that bladder and urinary cancer incidence rates are reflective of arsenic contamination in relation to lifetime exposure to arsenic in drinking water.

## 2.0 BACKGROUND

> *"It is an uncanny thought that this lurking poison (arsenic) is everywhere about us, ready to gain unsuspected entrance to our bodies from the food we eat, the water we drink and the air we breathe"* Karl Vogel, 1928

Arsenic is a naturally occurring and abundant metalloid that is found in trace quantities in rock, soil, water, and air and is widely distributed in the Earth's crust. It is present in over 200 mineral species, the most common of which is arsenopyrite. It is used in manufactures of certain goods and as an agricultural product and is a known human health toxicant.

### 2.1 Health Effects

Use of arsenic can be traced far back into history and was first documented by Albertus Magnus in 1250, although it is reported to have been known and in use since 3000 B.C. (Emsley, 2000). It was known as Zamikh to the Persians, Arsenikos to the Greeks, and in Latin was referred to as Arsenicum (Online Encyclopedia, 2009). It was used in the Bronze Age to form a hardened arsenical bronze alloy (Gale and Stos-Gale, 1982), and has also had medicinal uses such as in treating syphilis and in homeopathic medicine; and has also been considered as a possible treatment for leukemia (Soignet et al., 1998). Due to its toxic nature, one of its primary uses, however, has been as a poison. It is commonly referred to as *Poison of Kings* and the *King of Poisons* (Vahidnia et al., 2007). The first recorded instance of intentional arsenic poisoning was that of Britanicus by Nero in 55 A.D and its notoriety continued through in Louis XIV's court in 1679 where

arsenic was used as a poison by prospective heirs (Bentley and Chasteen, 2002; Vahidnia et al., 2007). Despite its acute and chronic toxic effects, arsenic has many uses in agricultural and industrial applications such as in the manufacture of cosmetics, foods, glass, insecticides, medications, pigments, pyrotechnics, rodenticides, and wood preservatives, as well as in embalming, metallurgy, tanning, and taxidermy (Bentley and Chasteen, 2002). Increasing awareness due to extensive toxicological and epdemiological investigations over the years led to regulatory efforts to control its anthropogenic release into the environment (Thirunavukkarasu et al., 2002).

### 2.1.1. Physical And Chemical Properties of Arsenic

Arsenic is the chemical element that has the symbol As and atomic number 33. Its atomic mass is 74.92. Arsenic is a metalloid with many allotropic forms, including a yellow (molecular non-metallic) and several black and grey forms (metalloids) (ATSDR, 2007; Findlay, 2007; J. R. Meliker and Nriagu, 2008; Rensing and Rosen, 2009). Table 2-1 lists chemical and physical properties of metallic arsenic and Table 2-2 lists properties of inorganic arsenic compounds.

| | |
|---|---|
| Symbol | **As** |
| Number | **33** |
| Group | **15** |
| Period | **4** |
| Block | **P** |
| Standard Atomic Weight | **74.92160 g·mol$^{-1}$** |
| Electronic Configuration | **4s$^2$ 3d$^{10}$ 4p$^3$** |
| Melting Point | **1090 K** |
| Boiling Point | **887 K** |
| Most stable Isotope | **$^{75}$As (naturally abundant)** |
| Density | **5.727 g·cm$^{-3}$** |
| Crystal Structure | **Rhombohedral** |
| Oxidation States | **–3, 0, +3 and +5** |

**Table 2-1: Arsenic Properties** (Emsley, 2000)

| | **$As_2O_3$** | **$As_2O_5$** |
|---|---|---|
| Name | Arsenic Trioxide | Arsenic Pentoxide |
| Valence | +3 | +5 |
| Molecular Weight | 197.8 | 229.8 |
| Boiling Point | 465 | - |
| Melting Point | 312 | 315 |
| Density | 3.738 | 4.32 |
| Water Solubility | 11.5@100ºC<br>$NaAsO_2$ very soluble | 76.7@100ºC<br>$Na_2HAsO_4$ very soluble |

**Table 2-2: Properties of Inorganic Arsenic Compounds** (Findlay, 2007; J. R. Meliker and Nriagu, 2008)

Arsenite and arsenate are the trivalent (AsIII) and pentavalent (AsV) compounds of arsenic, respectively. Arsenite contains an arsenic oxoanion leading to the +3 oxidation state and the arsenate ion is $AsO_4^{3-}$ where arsenic has the +5 oxidation state.

Arsenites include sodium arsenite with the ion $[AsO_2^-]_n$ and silver arsenite, $Ag_3AsO_3$. Arsenites can inhibit the pyruvate dehydrogenase enzyme complex, which affects energy production in the human body. Arsenate can exist in acidic conditions as arsenic acid ($H_3AsO_4$) and in basic conditions as the arsenate ion $AsO_4^{3-}$. Arsenates inhibit glycolysis by replacing inorganic phosphate to produce 1-arseno-3-phosphoglycerate instead of 1,3-bisphosphoglycerate (Findlay, 2007; J. R. Meliker and Nriagu, 2008).

### 2.1.2. Toxicological review

The relationship between systemic exposures to arsenic determined through experimentation in animals to establish its toxicity provides a basis for human health risk inference. Toxicokinetic models examining the absorption, distribution, metabolism and elimination of arsenic assist in human health risk assessment and in pharmaceutical research and development.

#### 2.1.2.1 Absorption

Arsenic can be absorbed into the human body through dermal, inhalation and oral exposures; the oral route is the usual route of exposure to arsenic in drinking water. The rates of retention, metabolism, and elimination depend not only on the route of exposure but also on the oxidation state and organo-metalloid form of arsenic absorbed (Hostynek, 2003). The tissue binding affinities vary, causing differences in toxication and detoxification mechanisms (Thompson, 1993).

Some studies have shown that almost 80-90% of an ingested inorganic water-soluble trivalent and pentavalent arsenic dose is absorbed in humans and animals (Freeman et al., 1995; Pomroy et al., 1980) and 75-85% of the organic arsenic species monomethylarsonic acid (MMA V) and dimethylarsinic acid (DMA V) is absorbed (Stevens et al., 1977; Yamauchi and Yamamura, 1984). Absorption also varies depending on the compound ingested, for example, lead arsenate, arsenic tri-sulfide, and arsenic selenide are low-solubility compounds and have low gastrointestinal rates of absorption (Webb et al., 1984; Webb et al., 1986; Yamauchi et al., 1986).

#### 2.1.2.2 Distribution

Arsenic distribution within the human body is dependent on its chemical properties and on the species present. Properties such as affinity for binding to sulfhydryl groups (Kitchin and Wallace, 2008) is higher for trivalent arsenic, but DMA is more readily excreted than MMA (Hughes et al., 2003; Hughes et al., 2008)., Cellular transport of arsenite (AsIII) is through aquaglycoporins (Tapio and Grosche, 2006) and of arsenate (AsV) via phosphate transporters (Villa-Bellosta and Sorribas, 2008; Wang and Duan, 2009). After absorption, arsenic is transported via the blood to different organs in the human body. It binds to sulfhydryl groups of proteins and other low-molecular weight compounds like glutathione (GSH) and cysteine (Rosen and Liu, 2009).

The tissue distribution also varies with chemical form of arsenic. Repeated daily dosing of small concentrations of radioactive arsenic [73As] arsenate (0.5 mg As/kg) for nine days resulted in the highest accumulation of radioactivity in bladder, kidney, and skin. However MMA(V) was present in all tissues except the bladder, where the concentration of DMA(V) was predominant as shown in Figure 2-1 (Hughes et al., 2003).

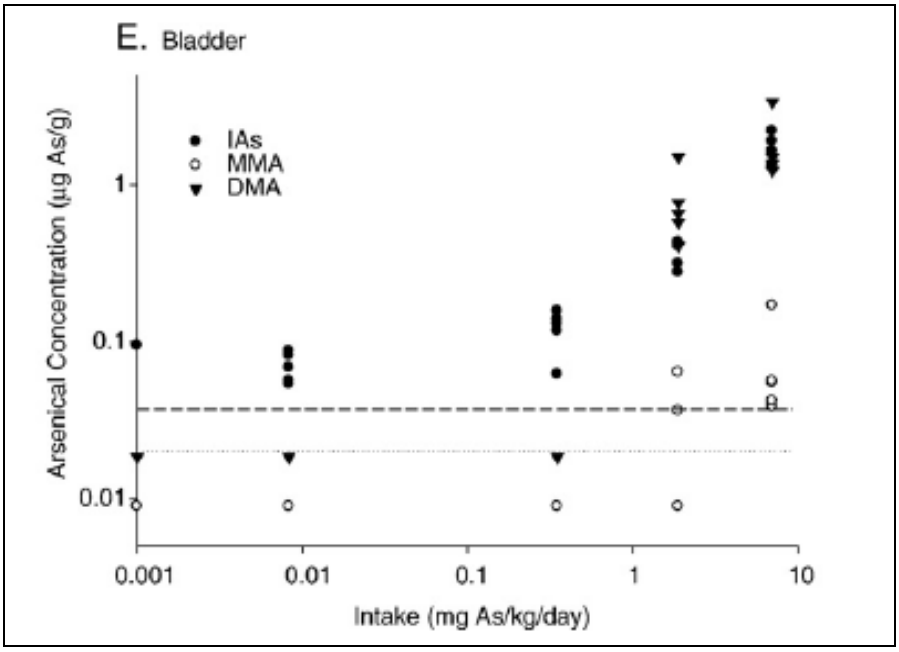


**Figure 2-1 : Concentration of iAs, MMA and DMA in blood bladder (E) after 12 weeks of exposure to 0.5, 2, 10 and 50 ppm AsV in drinking water. Individual data (n=5) are plotted against estimated arsenic intake and non-detects are plotted as 1/2 the LD. The dotted line is the approximate LD for iAs and MMA and the dashed line is the approximate LD for DMA.** (Kenyon et al., 2008)

Factors known to affect the transport and tissue and intracellular distribution of arsenic also include the arsenic species and dietary considerations. Diets low in

methionine, choline and other proteins can lead to a reduction in methylating ability and promote sulfhydryl binding (Mukherjee et al., 2006; Ruan et al., 2000).

### 2.1.2.3 Metabolism

The human body metabolizes arsenic through a process of repetitive reduction and oxidative methylation reactions (Hayakawa et al., 2004; Thomas et al., 2004; Thompson, 1993; Tseng, 2009). Arsenate is methylated to DMA in a sequential pathway through arsenite and methylarsonic acid. Figure 2-2 shows this process.

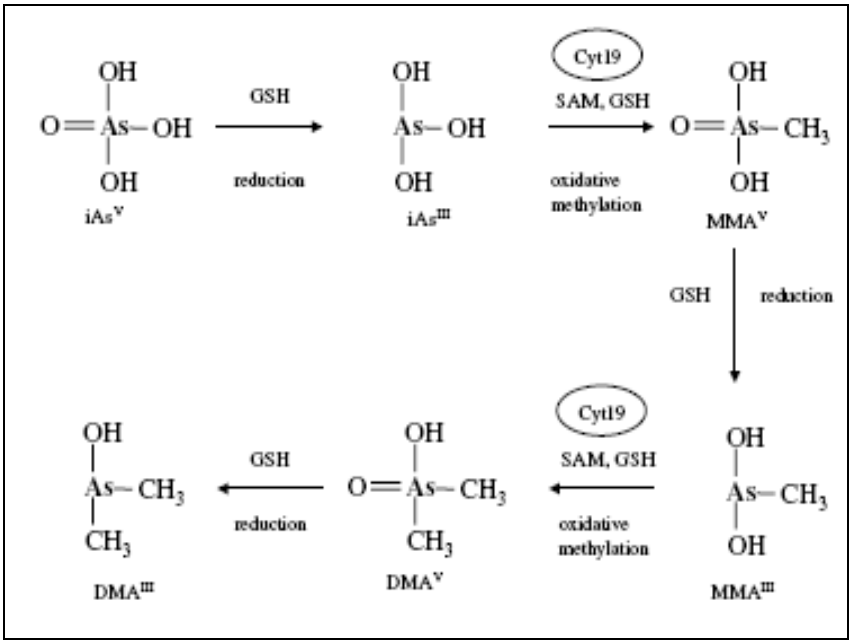


**Figure 2-2: The classical metabolic pathway of inorganic arsenic in mammals (iAsIII arsenite, iAsV arsenate, MMAIII monomethylarsonous acid, MMAV monomethylarsonic acid, DMAIII dimethylarsinous acid, DMAV di-methylarsinic acid, Cyt19 arsenic methyltransferase, GSH reduced glutathione, SAMS-adenosyl-L-methionine)** (Hayakawa et al., 2004)**.**

Glutathione (GSH) acts on pentavalent arsenic species *in vivo* to reduce them to trivalent states by providing two electrons. GSH also reduces methylarsonic acid (MMA V) and Di-methylarsonic acid (DMA V) in aqueous solutions (Sty'blo et al., 2002; Zakharyan et al., 1996).

Monomethylation and dimethylation occur via an enzymatic pathway by oxidative addition of a methyl group from the trialkylsulfonium ion (As III methyltransferases) of S-adenosyl-I-methionine (SAMe) to the lone pair of electrons of arsenite (Thompson, 1993). Methylated arsenicals that are chemically consistent with trivalent methylated metabolites act as potent enzyme inhibitors and cytotoxins: glutathione disulfide reductase (GSSG), pyruvate dehydrogenase and thioredoxin reductase (J. P. Buchet and Lauwerys, 1987; Li et al., 2005; Marafante et al., 1985; Sty'blo et al., 2002). A study examining cytotoxicity of arsenicals found that trivalent arsenicals, particularly MMA III, induce activating protein dependent gene transcription by inducing c-Jun phosphorylation in urothelial cells ( UROtsa's) (Sty'blo et al., 2002).

#### 2.1.2.4 Elimination

The primary excretionary process for arsenic elimination within the human body is through urine in the pentavalent and trivalent forms of DMA and MMA. The biological half-life of ingested inorganic As (III) is approximately four days and this is time is slightly reduced following exposure As (V) (J. P. Buchet et al., 2004). A study conducted by Tam showed that 38% of ingested arsenic was excreted within 48 hours and 58% within 5 days, indicating a tri-compartmental

exponential function with half-life of 2.1 days. In another study, 30% of the ingested As (V) was excreted with a half-life of 9.5 days and 3.7% with a half-life of 38 days (Pomroy et al., 1980).

A study conducted on mice exposed to 0, 0.5, 2, 10 or 50 ppm arsenate in their drinking water for 12 weeks found a linear increase with respect to dose in concentrations of MMAIII, DMAIII, dimethylarsinic acid (DMAV), and trimethylarsine oxide (TMAO) in urinary excretion of AsV; urinary excretion of monomethylarsonic acid (MMAV) was non-linear (Kenyon et al., 2008).

Figure 2-3 shows the graphical representation of these results.

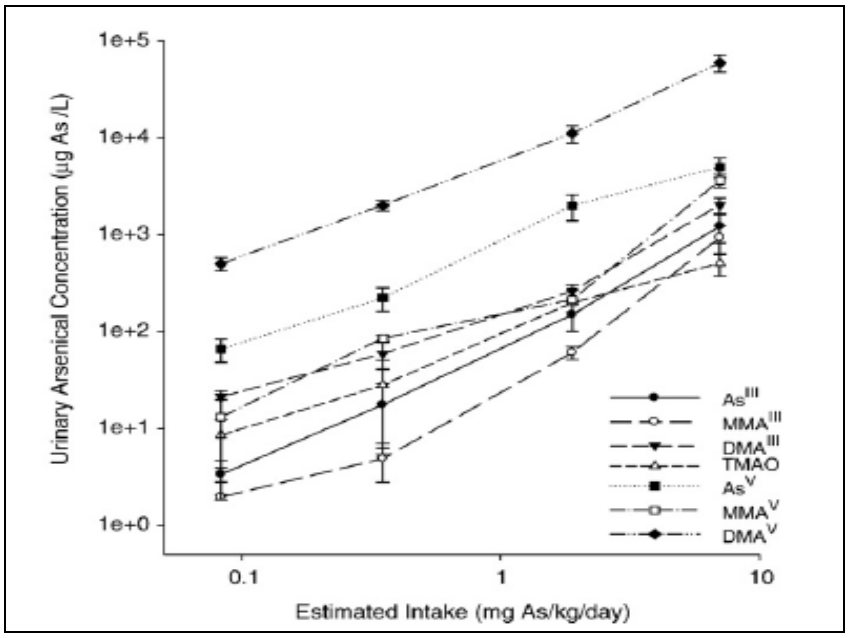


**Figure 2-3: Concentration of arsenical metabolites in urine after 12 weeks of exposure to AsV in drinking water** (Kenyon et al., 2008)

Other routes for elimination of arsenic are via skin, sweat, hair, nails and breast milk (ASTDR 2000; Brown, 1999).

#### 2.1.2.5 Physiologically Based Pharmacokinetic Models

Physiologically Based Pharmacokinetic Models (PB-PK) are mathematically based biological models that are used in chemical risk assessment by predicting the kinetic behaviors of a chemical within the human body. These models are adjusted for variables such as body and organ weights, dosing structures, different exposure scenarios, and therefore go beyond the conventional observations using animal bioassays (D. Yu, 1999a). The following PB–PK models for arsenic exposure are directed towards the study of kinetic behavior of inorganic arsenic and its metabolites using different routes of exposure and tissue parameters in organs.

The first PB-PK model was developed by Mann (S. Mann et al., 1996a) to study exposure to inorganic arsenic in hamsters and rabbits (S. Mann et al., 1996a). It presented three routes of exposure, oral intake, IV injection, and intratracheal instillation, and analyzed tissue compartments based on arsenic affinities, specifically liver, GI tract, kidneys, lungs (naso-pharynx, trachea bronchial and pulmonary), skin, plasma, keratin, red blood cells (RBCs), bone, and other tissues. Figure 2-4 shows the schematic representation of the model Mann constructed in hamsters and rabbits.

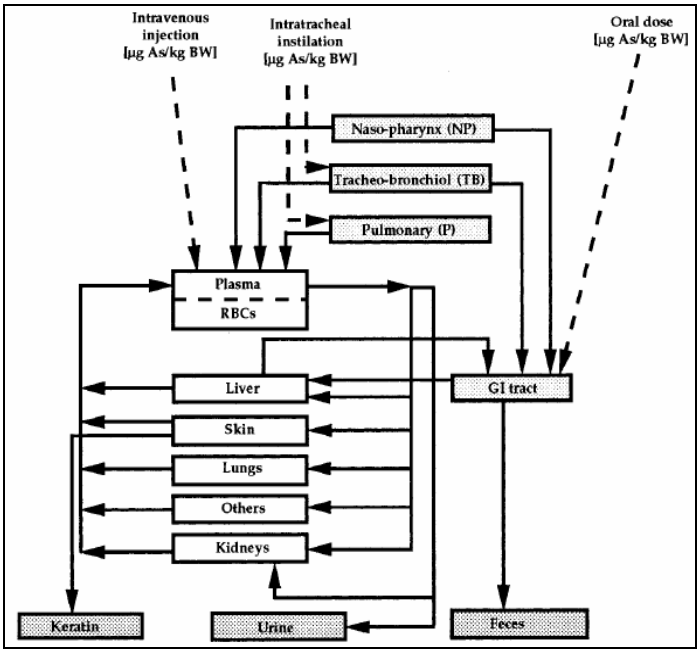


**Figure 2-4**: **Schematic presentation of the PB-PK model showing the exposure routes, the tissues distribution, and the excretion routes for one arsenic metabolite. This diagram is repeated four times, one for each arsenic metabolite** (S. Mann et al., 1996a)

The model estimated tissue concentrations and fecal and urinary excretion of the primary metabolites of arsenic as inorganic As (III) and As (V), methylarsonic acid (MMA) and di-methylarsinic Acid (DMA). The model predicts oral absorption of As (III), As (V) and DMA as a first order transport directly from the GI tract to the liver. Urinary, billiary, and fecal excretion are also depicted as first-order processes. The model found distinct differences in the predicted As metabolite distribution in urine among both animal species used to develop the model. These differences related to methylation rates and highlighted variation in methylation efficiency in species comparison and extrapolation (Marafante and Vahter, 1987).

This model was extrapolated for validation and application in humans by adjusting physiological parameters such as organ weights, blood flows, metabolic rates and absorption rates. It described the absorption, distribution, metabolism and excretion of arsenate, arsenite, methyl arsenate and di-methyl arsenate (S. Mann, Droz, and Vahter, 1996b). This model was fit to literature data on the urinary excretion of total arsenic in prior human studies and was found to have good accuracy for both inhalation and oral exposures. Absorption by inhalation was validated using data on urinary excretion after occupational exposure to arsenic trioxide dust and fumes. Both routes of exposure resulted in urinary excretion of the four As metabolites. Figure 2-5 depicts the kinetic processes of ingested and inhaled arsenic in the human body.

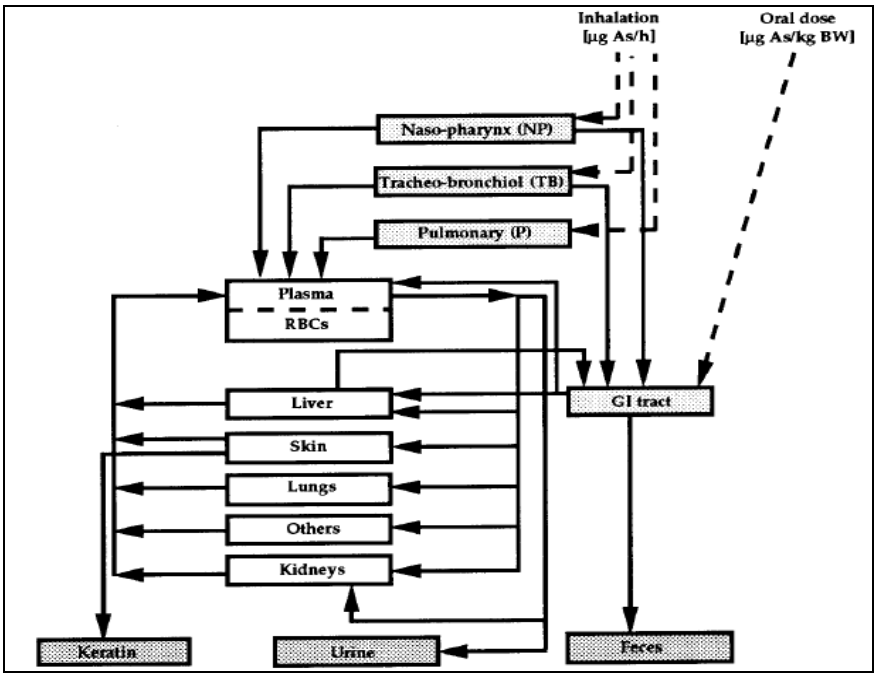


Figure 2-5: **Schematic presentation of the PB-PK model showing the exposure routes, the tissues *i*, and the excretion routes for one arsenic metabolite. This diagram is repeated four times in the model, once for each arsenic metabolite** (S. Mann et al., 1996b)

The model predicted a decrease in the methylation capacity with the decline of DMA proportion in urine and this applied more towards As (III) exposures suggesting that perhaps this was the rate-limiting step in metabolism of arsenic (Marafante et al., 1985). It suggested a saturation of the first methyl step. The results also indicated that consumption of drinking water containing 50 μg As/L led to a higher urinary arsenic excretion than occupational inhalation exposures to 10 $\mu g/m^3$ as per the ACGIH threshold limits, highlighting the susceptibility of a larger population through contaminated drinking water (S. Mann et al., 1996b; Bae et al., 2008).

Yu provided another PB – PK model to include the reduction of As (V) to As (III) via chemical reaction with tissue glutathione and the subsequent transformation of As (III) in two metabolites (MMA and DMA) based on the experimental observations (D. Yu, 1999b). This model was created specifically for extrapolation of the kinetic behavior of inorganic arsenic following exposure to drinking water. The model included five primary parameters, tissue and blood partition coefficients for various tissue groups, physiological constants, and biochemical constants for metabolism, first-order rate constants, and GSH concentrations. Figure 2-6 summarizes this PB – PK model.

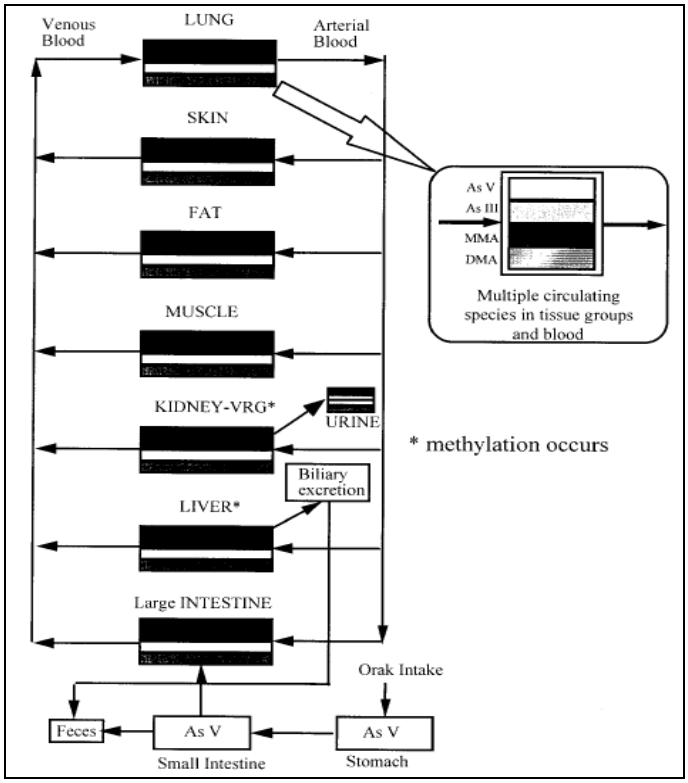


**Figure 2-6: Structure of the PBPK model for inorganic arsenic.** (D. Yu, 1999b)

Oral absorption, reductive metabolism of As (V) to As (III), and urinary, billiary and fecal excretion were modeled as first order processes and glutathione dependency was also studied. The model predicted that at high doses the detoxification process was less effective than at low doses, suggesting that reduction in methylation efficiency increases with dose. This model was not validated against external data (D. Yu, 1999a).

### 2.1.2.6 Systemic Toxicity

Chronic and acute exposures to arsenic vary with route of exposure and

frequency of exposure. Some of the systemic toxic effects of acute poisoning lead to severe nausea, anorexia, vomiting, epigastric and abdominal pain, and diarrhea. (DiNapoli, Hall, Drake, and Rumack, 1989; Fesmire, Schauben, and Roberge, 1988) Severe exposures can result in acute encephalopathy, congestive heart failure, stupor, convulsions, paralysis, coma, and death (Levin-Scherz, Patrick, Weber, and Garabedian, 1987; Luh, Baker, and Henley, 1973). According to the ASTDR the acute lethal dose to humans has been estimated to be about 0.6 mg/kg/day (ATSDR, 2007)

The primary target organs of chronic arsenic exposures are skin, brain and bladder. Hyperpigmentation and hyperkeratosis have been reported in the severely affected areas of Bangladesh, Taiwan parts of India and China (WHO, 2001). This disease is referred to locally as Blackfoot Disease as it leads to a gangrenous appearance in the extremities as a result of arterial occlusion and peripheral vascular damage. (Bae et al., 2008; Sun, 2004; Tseng et al., 1996) Chronic arsenic poisoning can also lead to peripheral neuropathy resulting in sensory nerves being more sensitive than motor nerves to arsenic effects, and neurons with large axons being more affected than neurons with short axons. Clinical symptoms are symmetric sensory effects such as numbness and paresthesiae of the distal extremities with legs being more severely affected than the arms (Rodríguez et al., 2003; Vahidnia et al., 2008). Bladder carcinogenesis is another significant disease caused by chronic As poisoning and is discussed in detail below.

#### 2.1.2.7 Carcinogenicity

Inorganic Arsenic has been classified as a Group A known human carcinogen by the U. S. EPA since almost all intermediate arsenicals have genotoxic traits or may affect the promotion and progression of cancer (Hayakawa et al., 2004; Sty'blo et al., 2002).

The carcinogenic mode of action for inorganic arsenic and its intermediate arsenicals is believed to progress through a few different processes. Data on chromosomal abnormalities observed in human and animal models suggests that arsenic is genotoxic and various researchers classify arsenic as an aneugen at low doses and a clastogen at high doses (Avani and Rao, 2007; Kitchin and Ahmad, 2003; Kligerman and Tennant, 2007; Rossman, 2003). Some studies demonstrate that arsenic can induce aberrant gene or protein expression via DNA hypo- or hypermethylation and gene amplification (Cohen et al., 2007; Drobná et al., 2005; X. Yu et al., 2008). Reactive Oxygen Species (ROS) cause cancer by lipid peroxidation, DNA and protein modification, and sequence amplification and can modulate gene expression. Although neither arsenates nor arsenites are ROS, trivalent, methylated, and relatively less ionizable arsenic metabolites interact with cellular targets such as proteins and even DNA. Oxidative methylation followed by reduction to trivalency serves not as a detoxification pathway but as an activating reaction. Thus arsenite can cause oxidative damage to DNA by the abovementioned processes (Hei and Filipic, 2004; Kim et al., 2005; Kitchin and Ahmad, 2003). Arsenicals can also inhibit DNA repair processes by inhibiting

ligase activity and excision (Andrew et al., 2009). Arsenic can alter gene expression by activating signal transduction pathways that enhance cell proliferation and supersede cell division checks (Chen and Shi, 2002; Luster and Simeonova, 2004; Qian et al., 2003). Figure 2-7 shows an example of signal transduction pathways being affected by metal exposure. Arsenic is known to activate p53 (tumor suppressor) through activation of DNA damaging-dependent protein kinase, arresting the cell cycle at G1 and ultimately leading to inhibition of the cell division cycle.

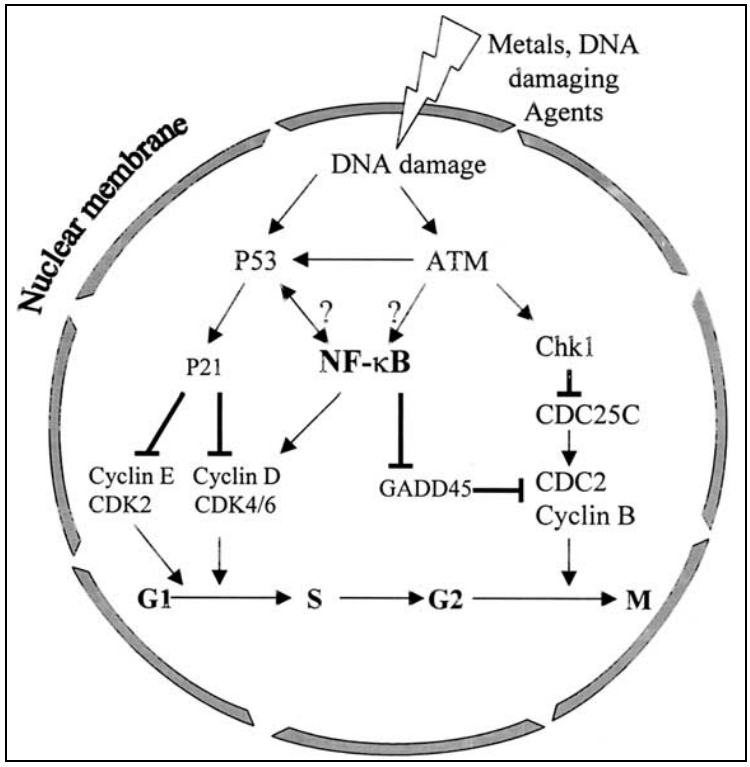


**Figure 2-7: Cell cycle regulation by metals (**Qian et al., 2003)

Studies conducted on the UROtsa (of the urothelium) cells prove them to be malignantly transformed following low-level exposure to both As (III) and MMA

(III). Trivalent arsenicals, particularly MMA, are likely to induce activating protein-1 (AP-1) dependent gene transcription in the human bladder leading to chronic increased cell proliferation (Eblin et al., 2008; Valenzuela et al., 2007; Waalkes et al., 2006).

### 2.1.3 Epidemiological Review

Epidemiological investigations have shed light on the association between bladder cancer and consumption of drinking water contaminated with arsenic. Although the studies have limitation in terms of sample population sizes, examination of confounding variables such as diet, use of alternative sources of water such as bottled water or filtered water, variation in age, duration of exposure, smoking status, and migration, they can provide a basis for the possible links between environmental exposure and bladder cancer.

A cohort study conducted in the Blackfoot Disease (BFD) endemic area of Taiwan examined the relationship between Transitional Cell Carcinoma (TCC) of the bladder and exposure to arsenic in drinking water (Chiou et al., 2001). The study population included 8,102 residents (4,056 male and 4,046 female); their individual exposures were determined based on concentrations of arsenic in private wells. A total of 3,901 households were studied and the exposure point concentration (EPC) range was 0.15 μg/L – 3.59mg/L. The researchers determined cancer incidence through annual personal interviews, hospital records, national death certificates, and cancer registry data. During a follow up period of

six years, 18 new bladder cancer cases were found and upon comparison with overall population increase during the same period the researchers found a significant increase in the BFD Area. The Standardized Incidence Ratio (SIR) was calculated to be 2.05, with a 95% Confidence Interval of 1.22 to 3.24.

Bates et al. conducted a case-control study in Utah in 1995 (Bates et al., 1995). They used 117 bladder cancer cases and 266 population-based controls and tested associations between exposure to low levels of arsenic in drinking water where 92% of the households had concentrations < 10μg/L. The study found no significant correlation between drinking arsenic in drinking water and bladder cancer, by a method of calculating Odds Ratios.

Kurttio et al. evaluated relative risks of 61 bladder cancer cases diagnosed between 1981 and 95 in people who drank water from drilled wells in Finland and compared them to an age and sex balanced cohort of 275 subjects (Kurttio et al., 1999). The study found a strong association for short latency exposures but a weak association for long latency exposures. Short latency was defined by use of well only two years before diagnosis and long latency periods were defined as at least 10 years. Local officials collected the cancer data using questionnaires and the well water was sampled in these households. The questionnaires also sought to clarify if the well water was the primary drinking water source. This study could have possibly been hampered by recall bias and also there is no inclusion of dietary and other lifetime influences.

A case-control study conducted in six counties of Nevada and California focused on populations historically exposed to As concentrations in drinking water sometimes as high as 100 µg/L. The researchers collected individual data on water sources, water consumption patterns, smoking, and other factors were for 181 cases and 328 controls. The 181 cases were in the age group 20-85 years and were matched to 248 people in five-year age groups that were selected through random digit dialing. The study found no significant cancer association for arsenic intakes greater than 80 µg/day (odds ratio = 0.94, 95% confidence interval: 0.56, 1.57; linear trend, $p = 0.48$) but smoking was found to cause a significant increase in bladder cancer incidence and therefore is a confounder (Steinmaus et al., 2003).

### 2.1.4 Susceptible Populations

According to ASTDR children are less efficient at methylation and therefore their tissue distribution and retention times may differ from those of adults and make them more susceptible to the toxic and carcinogenic effects of ingested arsenic (ATSDR, 2007). For chronic exposures, lifetime susceptibility varies although there is not much variation in consumption patterns (amount of water ingested as drinking water per day). Gender differences may play a role in arsenic methylation. A study by Hopenhayn-Rich found higher MMA:DMA ratios in men than in women (Hopenhayn-Rich et al., 1999) and one possible theory for is the protective influence of estrogen receptors -α and –β in women (Shen et al., 2006). Arsenic is also capable of crossing the placental barrier and as such pregnant

women and fetuses are also a susceptible population. Pregnant women have been shown to secrete more than 90% of plasma DMA in their urine, indicating possible hormonal effects on methylation (Concha et al., 1998; Ferrario et al., 2008; Hopenhayn-Rich et al., 1999).

## 2.2 Geologic Review

The bedrock aquifers in New England have high concentrations due to the presence of certain rock types in geologic provinces, i.e. host-rock arsenic concentrations. The concentration of arsenic present in groundwater is influenced by geochemical features of the Pleistocene marine inundations, hydrologic factors, and concentrations of arsenic in stream sediments. It is also dependent on the solubility and mobility of arsenic in groundwater as well as residence time.

Bedrock aquifers store and transmit water through intersecting fractures formed by various processes. The orientation, density and hydraulic properties of fractures vary by rock type and structural setting and affect groundwater chemistry and flow. Bedrock aquifers in New England consist primarily of fractured crystalline rocks; there are studies that show flow and transport of arsenic through the fractures into private well water (Ayotte et al., 2003; Colt et al., 2002). Unconsolidated aquifers are the principal water-yielding aquifers in New England and along with surface water resources satisfy the majority of the drinking water needs of the population. The most commonly found aquifers in New England are sand and gravel unconsolidated aquifers. They are grouped into

four categories: basin-fill aquifers, blanket sand and gravel aquifers; glacial-deposit aquifers; and stream-valley aquifers. All four types have intergranular porosity, and all contain water primarily under unconfined or water-table conditions. The hydraulic conductivity of the aquifers is generally high and they are the preferred aquifers for well drilling as they are not susceptible to the fractures and chemical contamination found in bedrock aquifers (Ayotte et al., 2003; Peters andBlum, 2003; Peters et al., 2006).

### 2.2.1 Sources Of Arsenic

Arsenic is present in over 200 minerals as a primary and major constituent. Some of these minerals include elemental arsenic, arsenides, and arsenates. The principal ores of arsenic are arsenopyrite (FeAsS), which has 46% arsenic content, orpiment ($As_2S_3$), and realgar (AsS) (Smedley and Kinniburgh, 2002; Welch et al., 1999). When deposits of arsenopyrite become exposed to the atmosphere, the mineral undergoes slow oxidization, converting the arsenic into oxides that are more soluble in water than the parent mineral and that may leach into water bodies. Arsenic also occurs as a constituent of rock-forming minerals in varying concentrations. Due to its diagonal placement from sulfur in the periodic table leading to crystalline and structural similarities, its greatest concentrations are found in sulfur-containing minerals such pyrite. It acts as a replacement for sulfur in many sulfide minerals because it has similar chemical properties and valences. Pyrite is formed in low-temperature sedimentary environments under reducing conditions such as those found in the northern

Appalachian Highlands (Peters and Burkert, 2008). This authigenic pyrite is present in the sediments of many lakes, rivers, oceans and aquifers in New England and hence we find higher concentrations of arsenic in bedrock here. High oxide concentrations are also found in many oxide minerals and hydrous metal oxides as sorbed species or in the crystalline structure. Arsenic concentrations in pyrite range from 10 – 77,000 mg/kg (Boyle and Jonasson, 1973), whereas in silicate minerals such as quartz or feldspar the range is much smaller; 0.4-1.3 mg/kg (Smedley and Kinniburgh, 2002). Oxide minerals have concentrations ranging from <1 mg/kg in Illeminite to up to 160 mg/kg in Hematite (Onishi and Sandell, 1955).

Arsenic is also found in rocks, soil, and sediments in varying concentrations. Igneous rocks have relatively low concentrations of arsenic ranging from 1.5 mg/kg in ultrabasic rocks to 5.9 mg/kg in volcanic glasses (Boyle and Jonasson, 1973; Smedley and Kinniburgh, 2002). Concentrations in metamorphic rocks closely resemble the concentrations found in their source igneous or sedimentary rocks, and as a consequence have a larger range. Pelitic rocks, found in some regions of Massachusetts, tend to have the highest concentrations of arsenic with an average of 18 mg/kg and ranging from 0.5 to 143 mg/kg (Smedley and Kinniburgh, 2002), as found in some slates. Quartzite and Feldspar such as those found in the coastal regions of New England display much lower concentrations. Sedimentary rocks display concentrations within the range of 5-10 mg/kg, which is marginally higher than terrestrial abundance. Coal and bituminous deposits have variable arsenic content, but depending on the area and mining use arsenic

concentrations can range from 0.3-35,000 mg/kg and 100-900 mg/kg, respectively (Boyle and Jonasson, 1973; Onishi and Sandell, 1955; Welch et al., 1999). Sandstones and other sands have the lowest arsenic content because they are formed from their dominant minerals quartz and feldspar, which have low arsenic content. Unconsolidated sediments have lower concentrations of arsenic than those reflected in their parent rocks. Samples of muds and clays found in Bangladesh had arsenic concentrations of 1 mg/kg – 14.7 mg/kg (Polizzotto et al., 2006). Higher concentrations are hypothesized to result from pyrites or iron oxides present, therefore altering the texture and mineralogy. Stream sediments in also contain arsenic in minimal concentrations and a study in New England found only 13% of the stream samples collected to have concentrations higher than 10 mg/kg. Although this may be attributed to anthropogenic sources such as rodenticides or pesticides, the concentrations were largely attributed to geologic sources in the study (Robinson and Ayotte, 2006). Natural soils have low arsenic concentrations, usually within the range of 5-10 mg/kg; peats and bog soils have higher concentrations because of elevated levels of sulfide minerals present under reducing conditions (Boyle and Jonasson, 1973).

Anthropogenic sources may also contribute to arsenic concentrations in soil and stream sediments, but the primary sources of arsenic are geological and the concentrations depend on the parent rock. Human activities that may contribute to arsenic concentrations include industrial smelting, refuse combustion, use of agricultural arsenic-containing pesticides, and landfill leachate. Most

anthropogenic arsenic in soil and stream sediments results from deposition from industrial sources such as smelting and from fossil fuel combustion. A study conducted in New England in the Connecticut River Valley, coastal Massachusetts and northern Maine compared pesticide use maps and arsenic concentrations in groundwater along with lead isotope data and found no significant correlation, therefore confirming the geologic nature of arsenic occurrence in groundwater within that particular region (Robinson and Ayuso, 2004).

### 2.2.2 Lithogeochemistry

Groundwater contamination of arsenic runs parallel to the Northern Appalachian Mountain Belt and is located primarily in crystalline bedrock. Aquifers in the fractured rock are particularly inclined towards higher concentrations of arsenic (Peters and Blum, 2003; Peters et al., 2006; Smedley and Kinniburgh, 2002). Figure 2-8 shows the Arsenic Province in the Northern Appalachian Belt and the sources of it in Bedrock Aquifers.

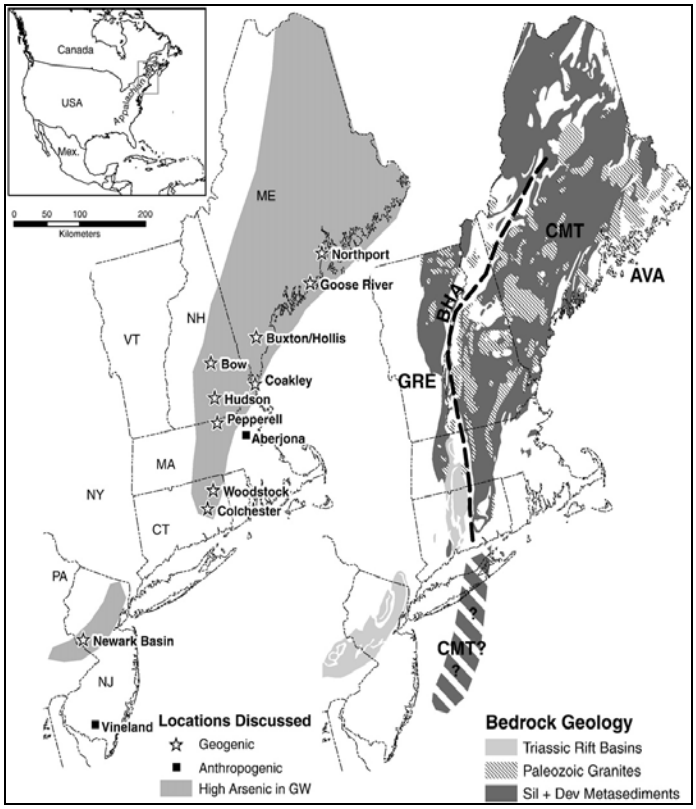


**Figure 2-8: Map of high arsenic belt (left) in the northern Appalachian Mountain belt, USA (inset)** (Peters, 2008)

In New England, the bedrock units are grouped into geologic provinces based upon lithology, age of formation, geologic setting and tectonic history (USGS, 2000). The provinces in the arsenic belt are New Hampshire-Maine sequence, Eugeosynclinal Sequence, Waits River-Gile Mountain Belt, Mesozoic Basin, Bronson Hill Sequence, and the Avalon Province (Robinson and Kapo, 2003; Robinson and Ayotte, 2006). Based upon the Arsenic Belt and the map of the geologic provinces and counties as shown in Figure 2-9, the provinces of interest are NH – Maine sequence and the Avalon Province and the counties of primary interest in Massachusetts are Worcester and Middlesex counties

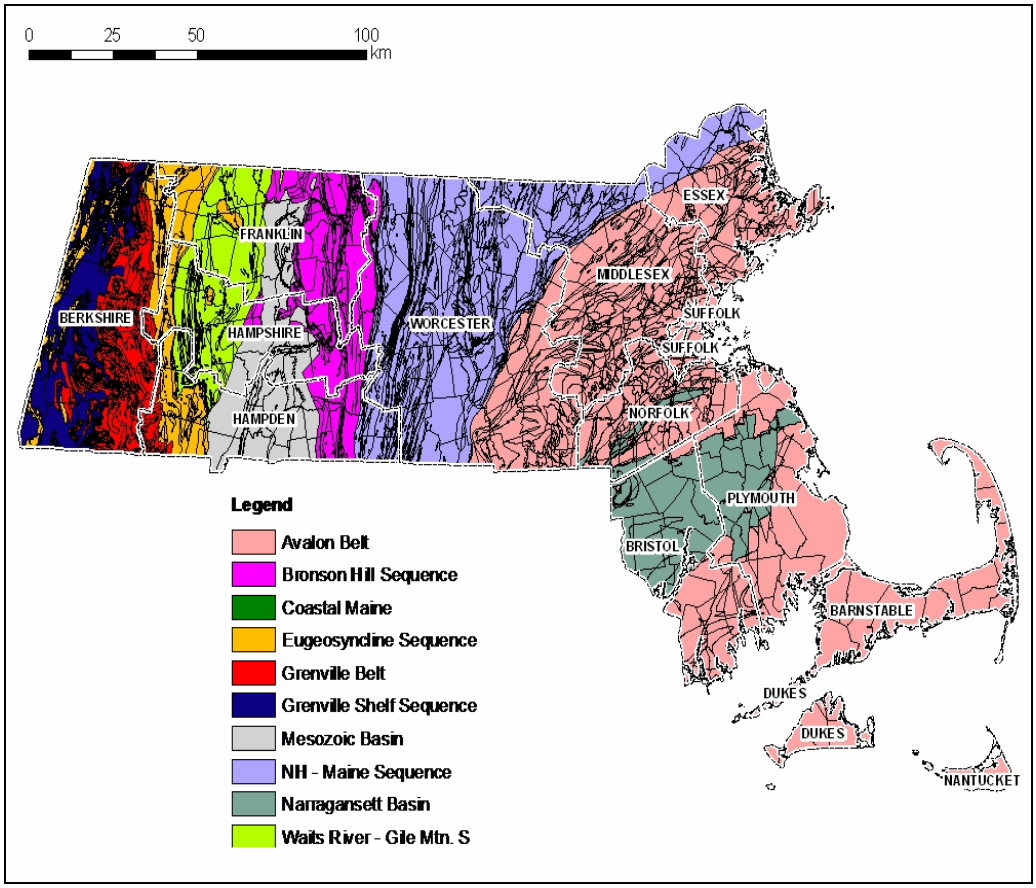


**Figure 2-9: Geologic Provinces of Massachusetts.**
Maps based on GIS data layers provided by Mass GIS

The New Hampshire – Maine sequence trends from south to north across New England covering eastern Connecticut, central Massachusetts, eastern New Hampshire and central Maine. It was formed during the Silurodevonian era and consists of metasedimentary and igneous rocks. It has principally granitic rocks (Robinson and Kapo, 2003).

The Avalon Province lies in eastern Massachusetts, Rhode Island, and coastal Connecticut. It formed during the Precambrian Age and consists of granite and

granitic gneiss and metasedimentary rocks with peraluminous granitic intrusions (Robinson and Kapo, 2003).

Further classification defines 37 lithogeochemical units based on the mineral and textural properties of each bedrock unit's constituent minerals, presence of carbonate and sulfide minerals, depositional setting, and in some granitic units, the magma chemistry. Of these 37 units, the units of relevance with respect to arsenic in groundwater in Massachusetts are Pelitic Rocks, Mafic Rocks and Peraluminous Granites (Ayotte et al., 2003; Robinson and Kapo, 2003; Robinson and Ayotte, 2006). These rocks occur primarily in the NH-Maine sequence and the Avalon province but are also present in smaller quantities in other provinces in Massachusetts. Figure 2-10 shows the different types of rocks found in Massachusetts.

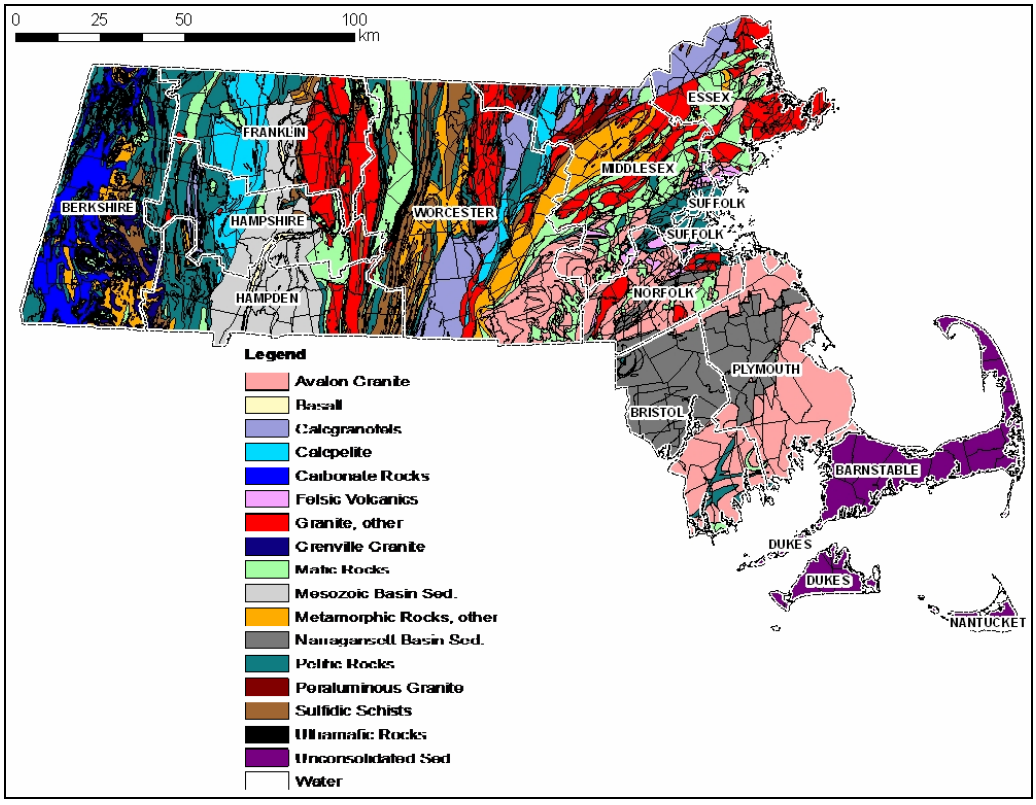


**Figure 2-10: Bedrock Lithology of Massachusettes** (Robinson and Kapo, 2003)
Maps based on GIS data layers provided by Mass GIS

Pelitic rocks **c**onsist of graphitic and sulfidic slate and greywacke and are primarily noncalcareous, clastic sedimentary rocks at or above biotite-grade of regional metamorphism. They may also include some minor amounts of pyrite and (or) pyrhotite and (or) variable amounts of organic materials, sufficient to cause a rusty-weathering characteristic. There may also be traces of politic schist, phyllite, granofels, and gneiss. For sulfidic schists, iron concentrations may be high in groundwater where eH and pH are low and sulfate concentrations may be high. There is also a heightened sensitivity to acid deposition for sulfidic rocks, and endemic flora may occur in acidic metal-rich soils over sulfide-rich horizons (Robinson and Kapo, 2003). The presence of arsenopyrite and sulfidic schists in

this region coupled with low pH are both common is regions with high arsenic concentrations in bedrock.

Peraluminous Granites consist mainly of granitoid plutonic rocks such as granite, quartz monzonite, granodiorite, tonalite, trondhemite, nepheline syenite and equivalent gneiss. The chemical character of natural waters in these rocks is characterized by low solute concentrations, relatively high bicarbonate and silica concentrations, low calcium and magnesium concentrations, relatively low pH, and fluoride, but uranium and radon concentrations may be high. These conditions are conducive to the presence of arsenic in bedrock as the presence of strong reducing conditions in the presence of calcium, iron, and manganese areas is associated with it (Robinson and Kapo, 2003).

Mafic Rocks display characteristics of mafic gneiss and mafic lithologies mixed with felsic volcanoes and metaclastic lithologies and therefore have a large sample of rock types. They consist of mafic plutonic rocks such as gabbro, diorite, monzodiorite, and diabase. They may also consist of amphibolite, greenstone, greenschist facies, and schistose mafic rocks with minor carbonate influences. Natural waters have high Ca-Mg ratios, variable silica concentrations, and, where the pH is low, the concentrations of Fe and Mg are high. High iron and magnesium conditions make it feasible for the redox processes to go forward in strongly reducing conditions. These conditions are associated with the presence of arsenic in groundwater (Robinson and Kapo, 2003; Robinson and Ayotte, 2006).

### 2.2.3 Arsenic Mobilization and Transport

Geochemical controls such as pH, oxides, presence of organic matter, and other factors affecting solid solution interactions control the concentration of arsenic in groundwater in the bedrock aquifers.

pH dependent desorption affects the mobility of arsenic in groundwater as exhibited in the laboratory through sand column and water pumping experiments by Gulens (Gulens et al., 1979). His findings showed that As (III) moved faster than As (V) at pH (5.7) in oxidizing conditions. At neutral pH, As (V) transport rate increased but remained less than that of As (III), and at pH 8.3 at reducing conditions both displayed rapid movement. This experiment was conducted using radioactive $^{74}$ As and $^{76}$ As. The experiment also showed reduction of As concentrations caused a reduction in transport rate. There is a regional association between high arsenic in groundwater and high pH in the New England region (Lipfert et al., 2006) and one of the factors affecting the pH levels can be the characteristics of the adsorbing surface of the mineral surface. As-Fe plots are commonly used to plot the rate of movement since there exists a stoichiometric dissolution of arsenopyrite followed by transport of both Fe and As (Boyle and Jonasson, 1973; Peters and Blum, 2003; Peters and Burkert, 2008; Smedley and Kinniburgh, 2002). In New England the pH of groundwater is usually low or near-neutral but development of strong reducing conditions leads to the desorption of As from mineral oxides.

Sulfide-bearing minerals are common in the Northern Appalachian Mountain Belt and their oxidation is cited as primary source of As in groundwater (Lipfert et al., 2006; Peters and Burkert, 2008; Welch et al., 1999). These minerals are released in to the groundwater through a process of oxidation followed by dissolution. Nano-crystalline phases are also said to impact this process as minerals undergo hydrothermal alteration to convert them into intermediate minerals that can undergo oxidation with greater ease (Deditius et al., 2008).

Reductive dissolution of arsenic bearing oxides results in liberation of arsenic into solution in the groundwater. This occurs under reducing conditions in iron phases and dissolution of these hydrous iron oxides; release of adsorbed combined As will result in Fe concentrations higher than arsenic. This process is also affected by the ratio As:Fe in the mineral (Peters and Burkert, 2008).

Reduction of nitrates causes oxidation of arsenic and higher concentrations of nitrate correspond to higher lower concentrations of arsenic. Nitrate acts as an electron acceptor in surface and groundwater systems and promotes formation of As (V). Nitrates cause the formation of iron oxides and adsorption of arsenic to those arsenic oxides (Durant et al., 2004).

These factors, coupled with flow paths, groundwater contact time and solution maturities, have been suggested as mechanisms for high arsenic concentration in groundwater in aquifers. Well depth and type of aquifer have also been shown to

impact arsenic concentration. Wells constructed in shallow unconsolidated aquifers have reportedly lower concentration of As compared to wells in deeper fractured crystalline aquifers (Peters et al., 2006).

A study by Meliker et al. in 2009 statistically analyzed arsenic concentrations in bedrock and unconsolidated wells through multiple linear regression analyses and found that arsenic contamination is more prevalent in bedrock wells that are cased in proximity to the bedrock-unconsolidated interface than wells found in unconsolidated aquifers. No other factors were associated with arsenic contamination in water drawn from bedrock or unconsolidated aquifers. The researchers concluded that conditions appropriate for arsenic mobilization might be found along the bedrock-unconsolidated interface, including changes in reduction/oxidation potential and enhanced biogeochemical activity because of differences between geologic strata (J. R. Meliker et al., 2009).

## 3.0 METHODS

My thesis was designed to investigate possible human health hazards associated with arsenic contamination in wells drawing from bedrock aquifers in north central Massachusetts. The objective of my thesis was to test the hypothesis that lifetime consumption of groundwater contaminated by low concentrations of arsenic can increase lifetime risk of bladder cancer. A secondary hypothesis was also tested: that bladder and urinary cancer incidence rates are reflective of arsenic contamination in relation to lifetime exposure to arsenic in drinking water. To do this I conducted a literature review to select the study area and then to further evaluate this study area I collected demographic, cancer incidence, and geologic data. In order to test my hypothesis, I utilized analytical techniques including risk assessment, geographic information system (GIS) software tools that integrate hardware, software, and data for capturing, managing, analyzing, and displaying all forms of geographically referenced information, and Standardized Incidence Ratios (SIRs) for bladder cancer. After collecting and assessing the data, I evaluated the results of hypothesis testing through a series of comparisons.

### 3.1 Literature Review

I compartmentalized my literature review into three primary sections: health effects review, geologic review, and municipality profile review. I started by assessing the physical and chemical properties of arsenic and wrote a brief overview of its historical uses. Next, I described and discussed several recent

toxicokinetic and epidemiologic studies. Based upon the findings from these studies, I decided to use bladder and urinary cancer as the health outcome of interest in my study population.

My geologic review focused on north central Massachusetts because the Arsenic Belt in the bedrock is parallel to the Northern Appalachian belt, which is near the region. Several recent studies identified the sources of arsenic in the bedrock aquifer, the lithogeochemistry of Massachusetts, and the mobilization of groundwater. I selected communities where there were private wells drawing from the bedrock aquifer. I determined that the wells were drawing from the bedrock aquifer based on review of information from each community. I did not, however, study any individual wells. I used GIS techniques to overlay the lithological layers (geological provinces and rock types) with county and municipality maps to identify this region.

### 3.2 Selection and Evaluation of Study Area

Based upon the literature review presented in Chapters 1.0 and 2.0, I demonstrated that arsenic was a contaminant of concern in north central Massachusetts. Arsenic is present in rock in a formation that trends parallel to the Northern Appalachian Mountain Belt. I focused on portions of Worcester and Middlesex counties as counties of concern because they are located within the Arsenic Belt. Figure 3-1 shows the location of towns in Worcester and Middlesex Counties.

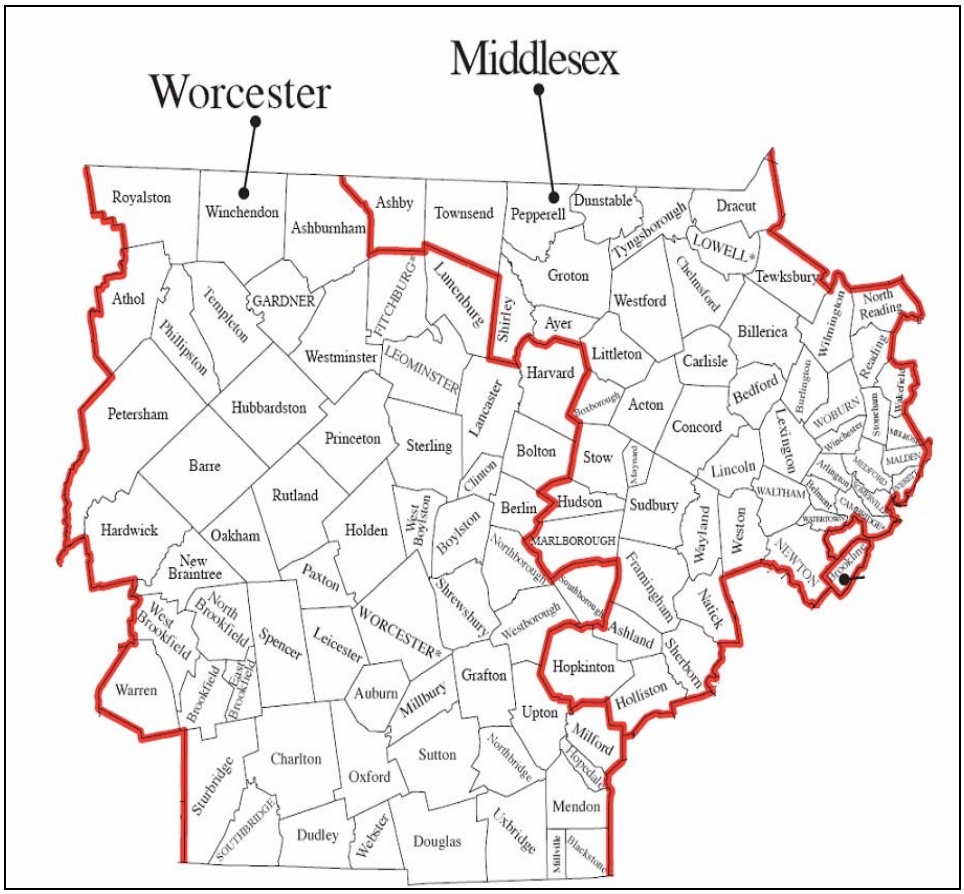


**Figure 3-1. Worcester County and Middlesex County, Massachusetts** (CIS, 2008)

My literature review also included the lithology of Massachusetts, particularly in the two counties. My review evaluated potential for the presence, flow and transport of arsenic-contaminated groundwater in these two counties. Figure 3-2 shows lithology of Worcester and Middlesex Counties.

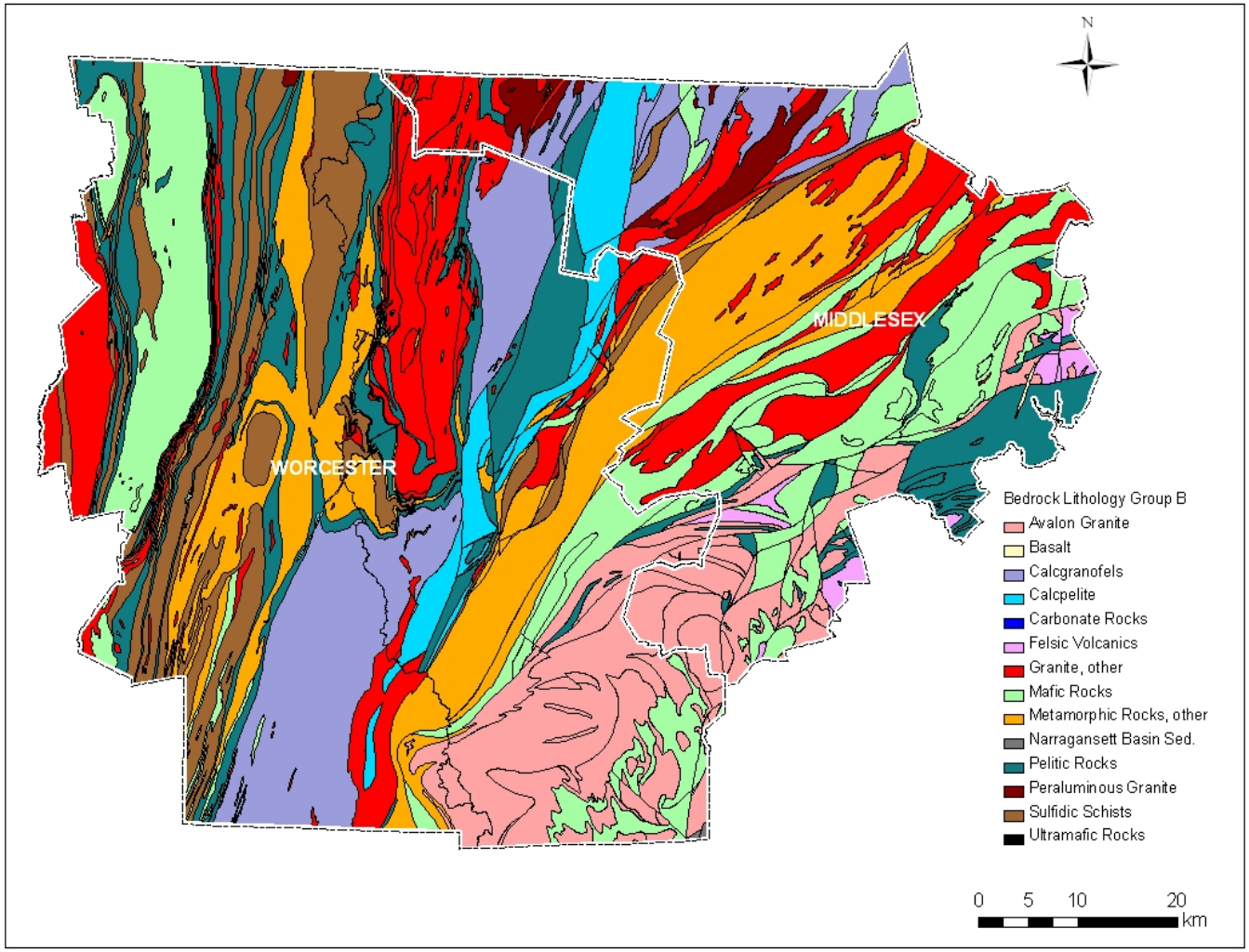


**Figure 3-2. Lithology of Worcester County and Middlesex County, Massachusetts. Obtained from USGS GIS Metadata**

I then further narrowed my scope of research to municipalities where residents would likely be exposed to arsenic in drinking water from private bedrock wells because people who are served by a public water system most likely did not drink water that originated in the bedrock aquifer. Most public water supplies in Massachusetts are from overburden wells or from surface supplies. Therefore, I selected those communities where the public water supply served less than 50 percent of the population and where the private water supplies were primarily from bedrock wells. To do this I conducted telephone interviews with officials from local water departments, public works departments, boards of health and other municipal offices. Figure 3-3 shows the communities that were selected for this study.

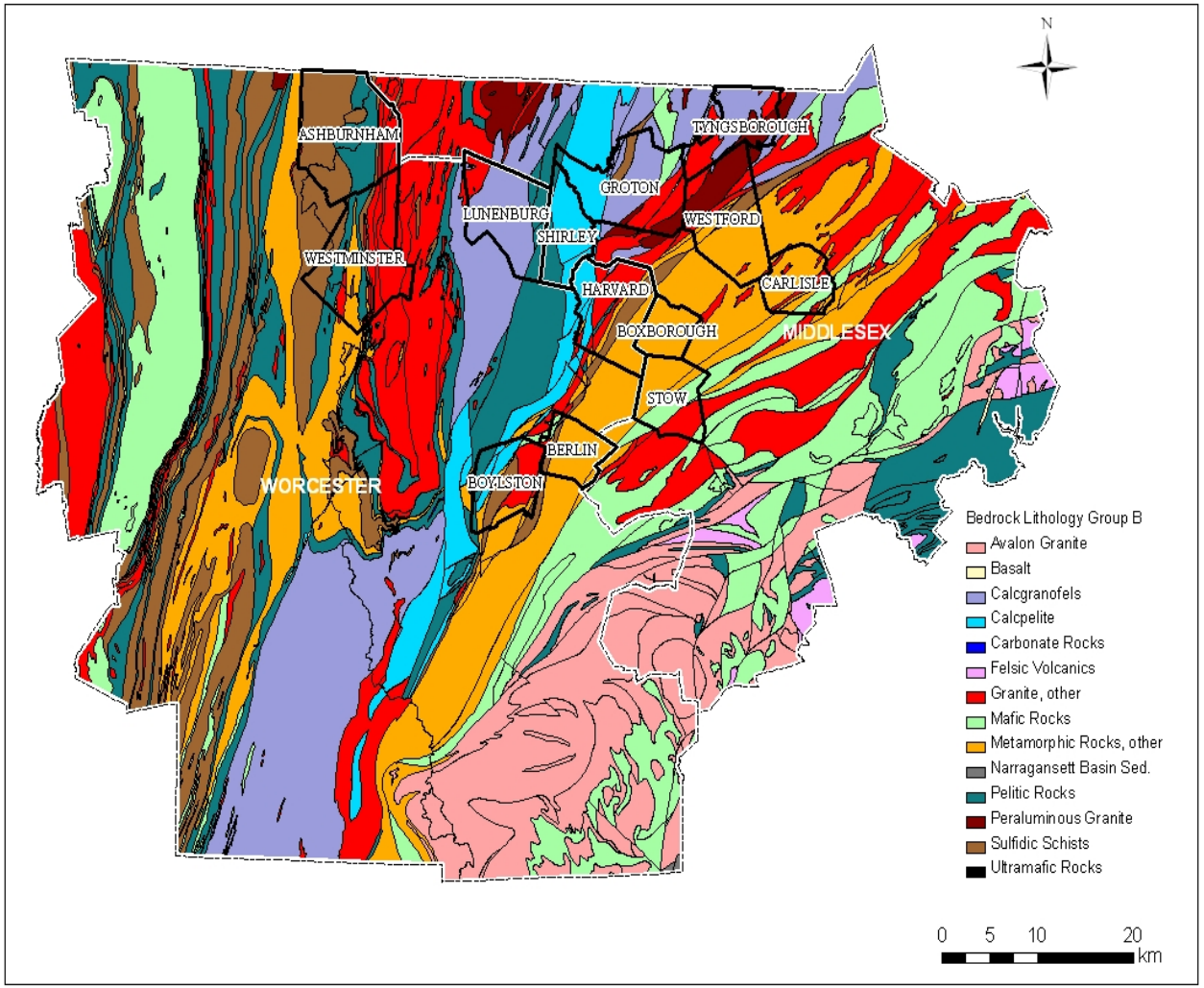


**Figure 3-3. Municipalities of interest in Worcester County and Middlesex County, Massachusetts. Obtained from USGS GIS Metadata**

I further assessed these municipalities by gathering demographic, cancer incidence and geologic data. I gathered data for urban and rural demographics, sex by age, median age by sex, household and populations in households. I also assessed the economic status and healthcare status of the communities to provide a comprehensive picture of the municipalities to be studied. I gathered these data from the United States Census Bureau, Census 2000 report. The data were geographically stratified by municipality and were accessible through the website's American Fact finder feature. I selected the geographic strata as county subdivision and then selected the municipalities I was interested in based on the literature review. I then made selective demographic inquiries and tabulated the desired information. I also accessed the Map feature as available on the Census Bureau website and mapped all towns.

I then collected cancer incidence data from the Massachusetts Cancer Registry (MCR) regarding all newly diagnosed cases of cancer in Massachusetts. This information was available on "The Official Website of the Office of Health and Human Services (EOHHS), Massachusetts" City and Town Series Section. The purpose of these reports was to provide standardized incidence ratios (SIRs) for twenty-three types of cancer in the 351 cities and towns of Massachusetts for a five-year time period. I accessed the City/Town Supplement series with town-specific cancer incidence information on the observed and expected cases in men and women. The SIRs were also part of this information series along with the 95% confidence intervals for SIRs with large numbers. These data were collected

over a five-year period in two different city/town supplements, 2000-2004 and 2001-2005. I collected this information for all cancers and then created tables including only the bladder and urinary cancer cases.

For the geologic data I obtained two data sets; one was the range of concentrations of arsenic found in bedrock aquifer in Worcester and Middlesex towns and the other was a GIS layer giving the probabilities of finding arsenic in excess of 5 µg/L in the bedrock aquifer in each municipality. Both these data sets were United States Geological Survey (USGS) data sets provided to me by Mr. Joseph Ayotte, P.G., of the USGS office in New Hampshire.

### 3.3 Risk Assessment

I next conducted risk assessments using the Massachusetts Department of Environmental Protection (MassDEP) Risk Assessment Guidance. (MassDEP, 2008). I used the guidance to define my exposure parameters based upon the route of exposure, individuals exposed, and the exposure point concentrations found in well water based upon the availability of applicable data.

To assess risks from exposure to arsenic, I collected qualitative and quantitative toxicity information and used dose-response data from the USEPA Integrated Risk Information System (IRIS) database. I did two sets of comparisons; I first grouped the communities in Worcester and Middlesex Counties independently and did the risk assessment based within these ranges in increments of 5 µg/l of

arsenic in drinking water. However, since some towns in each county had higher probabilities of having elevated arsenic in the bedrock aquifer and some had lower; to get a clearer comparison I grouped them together into three levels. The higher probability towns had probabilities greater than 0.2, the medium probability towns from 0.1-0.2, and the lowest probability, less than 0.1. In order to group municipalities under the abovementioned categories I found the minimum and maximum values, the range, and the mean of the probabilities in each town of interest using GIS statistical tools.

Standard toxicological methodologies for assessing the toxicity include dose-response relationships for adverse human health effects associated with exposure to specific chemicals. For carcinogenic effects, Carcinogenic Slope Factors (CSF) are used to estimate the Excess Lifetime Cancer Risk (ELCR) that corresponds to Exposure Point Concentrations (EPCs). CSFs are applied to specific routes of exposure.

The potential for the occurrence of non-carcinogenic adverse health effects from oral exposures typically is evaluated by comparison of estimated daily intakes with Reference Doses (RfD) that represent daily intakes below which no adverse health effects are expected to occur. The reference dose values were based on the toxicological review as found on the EPA's Integrated Risk Information System database (EPA IRIS, 2011). My risk assessment, however, did not calculate the non-cancer end-points because that there is no registry for non-cancer health

effects and my health outcome of interest is bladder cancer. Therefore I used the oral slope factor (also found on IRIS, 2011) to estimate lifetime cancer risk. I included a brief weight-of-evidence characterization for the data collected from IRIS based on a discussion of uncertainty factors used in deriving this.

For characterizing the risks to human health I combined the Lifetime Average Daily Doses of arsenic from drinking contaminated water with the data discussed in this section and applied default drinking water consumption parameters to calculate lifetime exposures.

### 3.4 Aggregating SIRs

To test my secondary hypothesis that bladder and urinary cancer incidence rates are reflective of arsenic contamination in relation to lifetime exposure to arsenic in drinking water I grouped the SIRs in the same way as I did for the risk assessment. In addition to this the grouping the towns together resulted in larger sample sizes with respect to observed and expected cases giving me a more statistically significant SIR. SIRs are calculated as Observed Cases / Expected Cases (calculated as population multiplied with age specific incidence). The data were also differentiated by sex so I could aggregate them to assess for differences among groups.

To aggregate the SIRs I tabulated the total observed cases of bladder cancer in males and females separately along with the total expected cases for males and

females separately. I did this for the selected towns in Worcester County and in Middlesex County, also for the towns with low, medium, and high probabilities of having groundwater containing elevated arsenic in both counties. I then divided the total observed cases by the total expected cases and multiplied that by a hundred and found the Confidence Intervals of these values. In order to calculate the CIs I used the formulae used by the MCR (MCR, 2009 and PDH, 2000).

The 95% Confidence interval shows if the observed number of cases is significantly different from the expected number and is represented by a range of values around a measurement that indicates the precision of the measurement. The equations used to calculate the confidence intervals are:

$95\%\ CI = SIR \pm (1.96 \times SE)$

$SE = SIR/\sqrt{O}$

Where, SIR = Standardized Incidence Ratio

O = Observed number of cases

E = Expected number of cases

### 3.5 Selection of control

I selected Barnstable County as a control based upon the geologic profile of the region. I verified the absence of arsenic in groundwater and no bedrock wells in Barnstable County through literature review. Since all wells in Barnstable County draw from a sand and gravel sole-source aquifer there was no arsenic as a result of bedrock fracturing. Since the SIRs were age adjusted and differentiated by sex I did not compare age distributions or sex ratios to see if the data were comparable on a demographic level.

### 3.6 Comparisons

I analyzed the risk assessment and SIRs independently and made the following sets of comparisons.

- Towns of Worcester County vs. towns of Middlesex County to assess differences in exposed populations.
- Towns of Worcester vs. towns in Barnstable County
- Town in Middlesex vs. towns in Barnstable County
- Towns with high, medium and low probabilities of having elevated arsenic in the bedrock aquifer. I compared the results of my risk assessments and SIRs of each with Barnstable County and to each other.

### 3.7 Discussion and Conclusions

I discussed my findings in the results section, the reasoning behind my selected methodology and the study design. I critiqued the strengths and weaknesses of my evaluation methods and concluded my research with a summary of my findings and made suggestions for further research.

## 4.0 RESULTS

This section provides the results of the GIS data analysis, risk assessment and cancer incidence SIR calculations as discussed in the Methods, Chapter 2.0

### 4.1 GIS Data output

Table 4-1 shows the minimum and maximum probabilities that arsenic will be present in groundwater from bedrock wells at concentrations greater than or equal to 5 micrograms per liter (μg/L) in the selected towns. It also shows the range based on the minimum and maximum values along with the mean and standard deviation (SD). These values are based upon the model provided by Mr. Joseph Ayotte of the New Hampshire USGS office.

This model is a process-based model to predict the probability of arsenic exceeding 5 μg/L in drinking water wells in New England bedrock aquifers. The probability was modeled based on results of a logistic regression where the dependent variable was the concentration of arsenic measured in water samples between 1995 and 2003 from 2,470 bedrock-aquifer wells. The explanatory variables used were geologic and anthropogenic sources of arsenic, geochemical processes, and hydrogeologic and land use factors, mainly related to groundwater flow (Ayotte et al., 2006). Table 4-1 also lists the grouping of towns based on probabilities if finding As in excess of 5 μg/L for selected cities and towns in Middlesex and Worcester County.

| TOWN | MEAN | SD | MIN | MAX |
|---|---|---|---|---|
| Ashburnham | 0.1686 | 0.0439 | 0.0766 | 0.3106 |
| Berlin | 0.0780 | 0.0258 | 0.0299 | 0.3452 |
| Boxborough | 0.1019 | 0.0161 | 0.0509 | 0.1498 |
| Boylston | 0.1059 | 0.0673 | 0.0239 | 0.3299 |
| Carlisle | 0.0885 | 0.0142 | 0.0332 | 0.1180 |
| Groton | 0.3512 | 0.0749 | 0.0866 | 0.5218 |
| Harvard | 0.2667 | 0.1402 | 0.0629 | 0.5773 |
| Lunenburg | 0.3179 | 0.0781 | 0.0443 | 0.5010 |
| Shirley | 0.3100 | 0.0738 | 0.0698 | 0.4778 |
| Stow | 0.0802 | 0.0173 | 0.0112 | 0.1281 |
| Tyngsborough | 0.2936 | 0.0980 | 0.0464 | 0.4397 |
| Westford | 0.1682 | 0.1034 | 0.0196 | 0.4659 |
| Westminster | 0.1846 | 0.0589 | 0.0597 | 0.4018 |

| |
|---|
| low probability |
| medium probability |
| high probability |

**Table 4-1: Range, Mean and Standard Deviation of the probabilities of finding As in excess of 5 µg/L for Selected Cities and Towns in Middlesex and Worcester Counties (Ayotte, 2009)**

Based on these values I grouped the towns into three categories low (probabilities ranging from 0 – 0.1), medium (probabilities ranging from 0.1– 0.2) and high (probabilities ranging from 0.12 and above).

- The concentrations in these groups ranged from <0.2 – 10, 10-22 and 22-26 µg/L respectively.
- The concentrations for all towns of interest in Worcester County ranged from <0.2 – 12 µg/L
- The concentrations for all towns of interest in Middlesex County ranged from <0.2 – 26 µg/L

- The concentrations for all towns in Barnstable county were below <0.2 µg/L

As stated in the Methods section, the source of the data in Table 4-1 is unpublished data obtained from the New Hampshire USGS through Mr. Ayotte.

### 4.2 Risk Assessment

Table 4-2 shows the variables used in the risk assessment and the values I assigned to them based upon the particular exposure scenarios. I evaluated these values based upon lifetime adult residential exposure. I did not calculate non-cancer end-points as the concentrations found in the region are too low to see acute health effects and there is also no database of non-cancer endpoints for comparison like that of the Massachusetts Cancer Registry.

| | | |
|---|---|---|
| **RAF** | unitless | 1 |
| **INTAKE** | L/day | 2 |
| **FREQ** | day/wk | 7 |
| **DURATION** | wk/yr | 50 |
| **EXP. PERIOD** | Yr | 30 |
| **CF** | unitless | 0.001 |
| **BW** | Kg | 65 |
| **AP** | Days | 27375 |
| **SF** | (mg/kg*day)^1 | 1.5E+00 |

**Table 4-2: Risk Assessment variables and values**

Where:
RAF – Relative Absorption Factor, FREQ – Frequency of exposure, EXP. PERIOD – Period of exposure, CF – Conversion Factor (0.001 to convert µg to mg), BW – Body weight, AP – Averaging Period, SF – Slope factor for cancer risk.

I then used these values to calculate the Lifetime Average Daily Dose (LADD) and the Estimated Lifetime Cancer Risk (ELCR). Table 4-3 shows the ELCRs corresponding to the Exposure Point Concentrations (EPC) in towns of Worcester, Middlesex and Barnstable based upon the ranges provided by Mr. Ayotte.

| **County of Concern** | **EPC** µg/L | **ELCR** |
|---|---|---|
| | | |
| Worcester | 0.2 | 3.54E-06 |
| | 1 | 1.77E-05 |
| | 5 | 8.85E-05 |
| | 10 | 1.77E-04 |
| | 12 | 2.12E-04 |
| Middlesex | 0.2 | 3.54E-06 |
| | 1 | 1.77E-05 |
| | 5 | 8.85E-05 |
| | 10 | 1.77E-04 |
| | 15 | 2.66E-04 |
| | 20 | 3.54E-04 |
| | 25 | 4.43E-04 |
| | 26 | 4.60E-04 |
| Barnstable | less than 0.2 | 3.54E-06 |

**Table 4-3: Exposure Point Concentrations and the corresponding ELCRs**

Table 4-4 shows the ELCRs corresponding to the Exposure Point Concentrations in the towns with low, medium and high probabilities of having more than 5 µg/L

arsenic in groundwater based upon the GIS data layer and the ranges provided by Mr. Ayotte.

| **Probabilities of As at > 5 µg/liter** | **EPC** µg/L | **ELCR** |
|---|---|---|
| | | |
| less than 0.2µg/L -10 µg/L | 0.2 | 3.54E-06 |
| | 1 | 1.77E-05 |
| | 5 | 8.85E-05 |
| | 10 | 1.77E-04 |
| less than 0.2µg/L -22 µg/L | 0.2 | 3.54E-06 |
| | 1 | 1.77E-05 |
| | 5 | 8.85E-05 |
| | 10 | 1.77E-04 |
| | 15 | 2.66E-04 |
| | 20 | 3.54E-04 |
| | 22 | 3.89E-04 |
| less than 0.2µg/L -26 µg/L | 0.2 | 3.54E-06 |
| | 1 | 1.77E-05 |
| | 5 | 8.85E-05 |
| | 10 | 1.77E-04 |
| | 15 | 2.66E-04 |
| | 20 | 3.54E-04 |
| | 25 | 4.43E-04 |
| | 26 | 4.60E-04 |
| | | |

**Table 4-4: Exposure Point Concentrations and the corresponding ELCRs**

Figure 4-1 shows the linear dose-response curve drawn from the risks calculated based on the range of arsenic EPCs in drinking water and the Estimated Lifetime Cancer Risk.

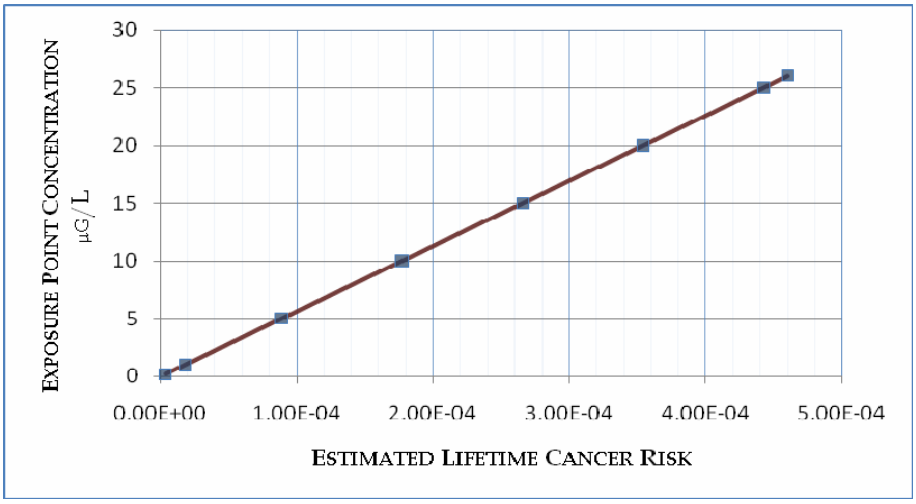


**Figure 4-1: Dose- Response Relationship between estimated Lifetime Cancer Risk and Exposure Point Concentration in Bedrock Wells**

### 4.3 Cancer Incidence

The following tables show the results of aggregating the cancer incidence data. Tables 4-5, 4-6, and 4-7 show the SIRs and confidence intervals of the towns in Worcester, Middlesex, and Barnstable County respectively. Tables 4-8, 4-9, and 4-10 show the SIRs and confidence intervals of the towns used in this study based upon probabilities: low, medium and high. The observed and expected cases were used to calculate the SIR for males and females separately. The cancer incidence data are for Urinary Bladder Cancer International Classification of Diseases (ICD) codes 188.0-188.9. ICD is the International Classification of Disease coding system set by the World Health Organization.

The towns studied in Worcester County are Ashburnham, Berlin, Boylston, Harvard, Lunenberg, and Westminster.

| WORCESTER COUNTY | | |
|---|---|---|
| | **Male** | **Female** |
| Total Observed | 34 | 11 |
| Total expected | 34.80 | 11.20 |
| SIR | 97.70 | 98.21 |
| 95% Confidence Interval | 130.54<br>64.86 | 156.25<br>40.17 |

**Table 4-5: Observed and Expected Cases, SIRs and 95% C.I. in studied towns from Worcester County**

The towns in Middlesex County are Boxborough, Carlisle, Groton, Shirley, Stow, Tyngsborough, and Westford.

| MIDDLESEX COUNTY | | |
|---|---|---|
| | **Male** | **Female** |
| Total Observed | 59.00 | 20.00 |
| Total expected | 49.10 | 16.80 |
| SIR | 120.16 | 119.05 |
| 95% Confidence Interval | 150.82<br>89.50 | 171.23<br>66.87 |

**Table 4-6: Observed and Expected Cases, SIRs and 95% C.I. in studied towns from Middlesex County**

| BARNSTABLE | | |
|---|---|---|
| | Male | Female |
| Total Observed | 465.00 | 163.00 |
| Total expected | 389.60 | 139.00 |
| SIR | 119.35 | 117.27 |
| 95% Confidence Interval | 130.20<br>108.50 | 135.27<br>99.27 |

**Table 4-7: Observed and Expected Cases, SIRs and 95% C.I. in all towns of Barnstable County**

The town with low probabilities of As >5 µg/L in the bedrock aquifer are Berlin, Carlisle, and Stow. Berlin is in Worcester County; Carlisle and Stow are in Middlesex County.

| LOW PROBABILITY | | |
|---|---|---|
| | | |
| | Male | Female |
| Total Observed | 14.00 | 3.00 |
| Total expected | 12.50 | 4.10 |
| SIR | 112.00 | 73.17 |
| 95% Confidence Interval | 170.67<br>53.33 | 155.97<br>-9.63 |

**Table 4-8: Observed and Expected Cases, SIRs and 95% C.I. in towns with low probabilities of As >5 µg/liter in the bedrock aquifer**

The towns with medium probabilities of As >5 µg/liter in the bedrock aquifer are Boxborough and Westford in Middlesex County and Ashburnham, Boylston, and Westminster in Worcester County.

| MEDIUM PROBABILITY | | |
|---|---|---|
| | | |
| | Male | Female |
| Total Observed | 35.00 | 14.00 |
| Total expected | 34.40 | 11.80 |
| SIR | 101.74 | 118.64 |
| 95% Confidence Interval | 135.45<br>68.03 | 180.79<br>56.49 |

**Table 4-9: Observed and Expected Cases, SIRs and 95% C.I. in towns with medium probabilities of As >5 µg/liter in the bedrock aquifer**

The towns with high probabilities of As >5 µg/liter in the bedrock aquifer are Groton and Tyngsborough in Middlezex County and Harvard, Lunenburg, Shirley in Worcester County.

| HIGH PROBABILTY | | |
|---|---|---|
| | | |
| | Male | Female |
| Total Observed | 44.00 | 14.00 |
| Total expected | 37.00 | 12.10 |
| SIR | 118.92 | 115.70 |
| 95% Confidence Interval | 154.06<br>83.78 | 176.31<br>55.09 |

**Table 4-10: Observed and Expected Cases, SIRs and 95% C.I. in towns with high probabilities of As >5 µg/liter in the bedrock aquifer**

These figures are discussed in greater detail in the context of the current scenario and methodology applied in Section 5.0 Discussion and Section 6.0 Conclusions and Recommendations.

## 5.0 DISCUSSION

This section provides the details of selection of study methods, the reasons for their selection and the strengths and weaknesses of my study design and results

### 5.1 Risk Assessment

Risk assessment involves estimating or measuring the magnitude, frequency and duration of exposure to an agent, along with the characteristics of the population exposed. It describes the sources, pathways, routes, and the uncertainties in the assessment. It describes how an individual or population comes in contact with a contaminant, including quantification of the amount of contact across space and time. It is used to measure how much of a contaminant can be absorbed by an exposed target organism, in what form, at what rate and how much of the absorbed amount is actually available to produce a biological effect. Risk assessment also evaluates the magnitude of the hazard along with the intensity of the exposure and estimates the probability that the receptor will develop adverse health effects.

The results of my risk assessment and comparison with the cancer incidence data are further described in this section with a focus on selection parameters and methodology.

The results of the risk assessment based on maximum individual exposure estimates a higher cancer risk than that reflected by the cancer incidence data

from the Massachusetts Cancer Registry. My primary hypothesis that the lifetime consumption of groundwater contaminated by low concentrations of arsenic can increase risk of cancer is supported by the results of the risk assessments and high Excess Lifetime Cancer Risks (ELCRs).

The Human Health Risk Characterization is comprised of four assessments that are taken from the National Research Council (NRC) paradigm, from which both U.S. EPA and MassDEP developed their guidance. These four steps include:

- Hazard identification – The determination of whether a particular chemical is or isn't causally linked to a particular health effect.
- Dose-response assessment – The determination of the relation between the magnitude of exposure and the probability of occurrence of the health effects in question
- Exposure Assessment – The determination of the extent of human exposure before or after application of regulatory controls
- Risk Characterization – The description of the nature and often the magnitude of human risk, including attendant uncertainty (NRC, 1983).

I chose cancer risk as the outcome due to the association between bladder cancer and consumption of arsenic in drinking water (Tseng, 1977 and Tseng, 1968) and also the availability of a cancer database, Massachusetts Cancer Registry (MCR) for comparison with the results (MCR, 2009).

### 5.1.1 Hazard Identification

In Sections 1.0 and 2.0 I described the toxic effects of arsenic, as well as its toxicokinetics, human and animal mechanisms of toxicity, genotoxicity and carcinogenicity. I relied mainly on peer-reviewed studies and included information on epidemiologic investigations, clinical and experimental studies and pharmacokinetic models. My geologic review was also based on peer reviewed journal articles in addition to the USGS geological information on lithogeochemistry. I covered the occurrence, flow and transport so as to create a complete picture of the source of contamination to how it affects human health. Based upon this research I focused on drinking water potentially contaminated with arsenic and its relationship to bladder cancer in certain towns of central Massachusetts.

Arsenic is a known human carcinogen and ingestion of inorganic arsenic is positively associated with increased incidence of bladder, liver, kidney and skin cancers. There is sufficient toxicokinetic and epidemiological evidence to causally link chronic exposure to inorganic arsenic through drinking water and bladder cancer, as highlighted in Chapter 2.

### 5.1.2 Dose-response Assessment

I used the information from the Integrated Risk Information System (IRIS) for my cancer risk dose-response values. IRIS is a USEPA database of information on toxicity and is updated monthly under the guidance of the USEPA Carcinogenic

Risk Assessment Verification Endeavor (CRAVE). The carcinogenic assessment is based on two aspects, weight-of-evidence (WOE) and the quantitative risk estimates from oral and inhalation exposures, most often from animal testing but, in the case of arsenic, from epidemiological studies.

The USEPA uses a cancer weight-of-evidence (WOE) descriptor to describe a substance's potential to cause cancer in humans and the conditions under which the carcinogenic effects may be expressed. This description is independent of the agent's carcinogenic potency. Under EPA's 1986 (U.S. EPA, 1986) guidelines for carcinogen risk assessment, the WOE was described by categories "A through E":

- A (Human carcinogen) based on epidemiological evidence
- B1 (Probable human carcinogen - based on limited evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in animals)
- B2 (Probable human carcinogen - based on sufficient evidence of carcinogenicity in animals) and absent or conflicting evidence in humans
- C (Possible human carcinogen) – based on weak or limited evidence of carcinogenicity in animals
- D (Not classifiable as to human carcinogenicity)
- E (Evidence of non-carcinogenicity for humans)

However under the EPA's 2005 (U.S. EPA, 2005) guidelines for carcinogen risk assessment, a narrative approach, rather than categories, is used to characterize

carcinogenicity. Five standard weight-of-evidence descriptors are used as part of the narrative.

- Carcinogenic to humans
- Likely to be carcinogenic to humans
- Suggestive evidence of carcinogenic potential
- Inadequate information to assess carcinogenic potential
- Not likely to be carcinogenic to humans

The weight-of-evidence classification for arsenic is A: Human carcinogen based upon considerable human evidence along with supporting animal data for carcinogenicity. Increased mortality from multiple internal organ cancers was observed in populations that drink water high in inorganic arsenic.

The USEPA formed this classification based on multiple epidemiologic and toxicological studies. One of the bladder cancer studies was a retrospective case-control study conducted in Taiwan. The cases were cancer deaths in the Blackfoot disease endemic area in between January 1980 and December 1982 and the 400 controls were age and sex matched. The bladder, lung and liver cancer deaths were confirmed through histological, radiological tests and biopsies. The age-sex adjusted odds ratios were increased for all three for people who drank artesian well water for 40 years (Chen et al., 1986), Another study, also conducted in the Blackfoot Disease (BFD) area in Taiwan looked at the Cumulative Mortality Rates (CMRs) and the Standard Mortality Rates (SMRs) for bladder, kidney and skin cancers. The study found that the CMRs and the SMRs were higher in the

BFD areas and within the BFD area were higher in areas with primarily artesian well water consumption (Chen, 1985). A significant dose-response relationship was found among arsenic levels in artesian well water in 42 villages in south-western Taiwan and age-adjusted mortality rates from cancers at all sites, cancers of the bladder, kidney and skin, lung, liver, and prostate (Wu, 1989). An ecologic study of cancer mortality rates and arsenic levels in drinking water in 314 townships also corroborated the association between arsenic levels and mortality from internal cancers (Chen and Wang, 1990).

Toxicology studies have reviewed the mutagenicity of inorganic arsenic, and also its genotoxicity and cytotoxicity. Studies have shown that inorganic arsenic is weak in inducing gene mutations in vitro but its clastogenic with trivalent arsenic being an order of magnitude more potent than pentavalent arsenic (Jacobson-kram, Wan et al 1982). Studies have found that arsenate, arsenite and MMA are clastogenic but the aberration response with DMA is insufficient to consider it a clastogen and arsenic exerts is toxicity by causing chromosomal mutations (Moore L.E. et al., 2002). The cytotoxic effects of sodium arsenite were measured in Chinese hamster ovary cells (CHO) and correlated with the intracellular glutathione levels (Lee et al., 1989). Arsenic has an inhibitory effect on strand breaking and rejoining during DNA repair and influenced by glutathione concentrations is cell cultures (Huang et al., 1993).

Supporting animal studies show that in general the incidence of arsenic-induced cancer is dramatically lower in animals than it is in humans; however, arsenic is

known be a teratogen in several species of animals as well as in humans (Ming H.Y., 2005).

If a contaminant is classified as a carcinogen, USEPA uses mathematical models to estimate an upper bound excess cancer risk associated with lifetime exposure through drinking water. EPA generally uses the linearized multistage (LMS) model, which fits linear dose-response curves to low doses. It is consistent with a no-threshold model of carcinogenesis; i.e., exposure to even a very small amount of the substance theoretically produces a finite increased risk of cancer. The LMS model uses dose response data from an appropriate study to calculate a carcinogenic potency factor (q1*) which is then used to determine concentrations of water that are associated with the theoretical upper bound excess lifetime cancer risk of one in ten thousand (10-4) to one in one million (10-6) (EPA, 2008).

The dose response data used in the classification of arsenic was obtained from studies conducted by Tseng in 1977 and 1968 where data on 40,000 people exposed to arsenic in drinking water were tabulated and compared against 7500 relative unexposed controls (Tseng, 1977 and Tseng, 1968).

The Cancer Slope Factor (CSF) I used in my risk assessment was derived using mathematical extrapolation of time- and dose-related formulation of the multistage model (U.S. EPA, 1988) consistent with the data available. The slope factor is the result of application of a low-dose extrapolation procedure and is

presented as the risk per (mg/kg)/day or risk/(mg/kg/day)$^{-1}$. The unit risk is the quantitative estimate in terms of the risk per μg/L of drinking water. Risk may also be represented as 1 in 10,000 or 100,000 or 1 in 10, 00,000.

The values below are obtained from the U.S. EPA's Integrated Risk Information System (IRIS)

Oral Slope Factor — 1.5E+0 per (mg/kg)/day

Drinking Water Unit Risk — 5E-5 per (μg/L)

Extrapolation Method — Time- and dose-related formulation of the multistage model (U.S. EPA, 1988)

Drinking Water Concentrations at Specified Risk Levels:

| **Risk Level** | **Concentration** |
|---|---|
| E-4 (1 in 10,000) | 2E+0 μg/L |
| E-5 (1 in 100,000) | 2E-1 μg/L |
| E-6 (1 in 1,000,000) | 2E-2 μg/L |

By doing the above I determined that arsenic had the potential to cause cancer and described the need to study this chemical as a contaminant of concern for health

effects. I also described the level (acute, chronic and the varying concentrations) of exposure and the related systemic and genotoxicity of arsenic.

### 5.1.3 Exposure Assessment

This step involves identifying potential routes of exposure, characterizing the population exposed and determining the frequency, extent and duration of exposure. In order to do this I created an exposure profile and used quantitative estimates of exposure. From the given study area I selected towns based on groundwater usage through private wells, which are only partially regulated by state or federal environmental and health agencies and are not required to test for arsenic. I relied on data obtained through telephone conversations with local boards of health public works departments and town hall officials, in the absence of detailed well usage data and demographic data associated with use of such private wells. I then used the data provided by Mr. Joseph Ayotte of the New Hampshire office of the US Geological Survey (USGS) to develop the Exposure Point Concentrations (EPCs). I could not use well-specific EPCs because the data were not available; the data for the wells were scheduled to be released by the USGS in Dec 2009 but were not released at that time. The discrete well data are not available as of the current date, and communications with Mr. Ayotte indicated that there is no updated information on when they will be released (Ayotte). The analysis I performed using the consolidated data provided by Mr. Ayotte in 2009 is still appropriate.

The USGS study was conducted in Essex, Middlesex and Worcester Counties; 1,600 residents received letters and sampling kits to help scientists determine if arsenic or uranium concentrations are elevated in their well water. The study aimed to assess the number of private wells with arsenic or uranium concentrations greater than the current drinking water standards and the degree to which bedrock units correlate with concentrations of uranium and arsenic. Mr. Ayotte provided me with the ranges for arsenic concentrations in both Middlesex and Worcester County wells. He could not release the data from individual wells because the water samples were collected and analyzed after the owners of the wells were ensured the confidentiality of the data. Because I could not get the actual discrete data, I took alternative steps to analyze my hypothesis. In the absence of well-specific data I used the range of concentrations found in the counties of interest. The concentrations were expressed in µg/liter (ppb).

I then used the following values for general exposure factors to estimate the Lifetime Average Daily Dose experienced by a potential adult receptor. I chose to study the adult receptor since bladder and urinary cancers occur primarily in adults and I was studying chronic exposures at low doses.

The usual default value for intake of drinking water is 2 liters per day irrespective of gender for all adults, and I used this value in my risk assessment.

A receptor's body weight is a significant factor since the dose is expressed the mass of contaminant per unit of body weight per day (mg/kg/day As). I chose to study the exposure to an adult resident and used a bodyweight of 65 kg as a more conservative figure to account for more women in the population. The body weight was expressed in kilograms (kg).

The adult resident is exposed to the arsenic through drinking water continuously since people drink water everyday. I used the value of 7 days per week as my frequency of exposure.

The duration of exposure describes the length of time over which the receptor came into contact with a contaminant of concern. I used 50 weeks per year as this value to account for time away from home.

For a residential scenario I used a 30-year exposure period to account for the population living in the same area for a conservative longer duration.

The averaging period is the actual time over which the exposure took place, expressed in days. However for cancer risk the averaging period is 75 years x 365 days/year = 27,375 days/ lifetime. This figure accounts for lifetime incremental risk.

The relative absorption factor (RAF) relates to the exposure and absorption estimated for the exposure pathway and the toxicological information. is dimensionless. For ingestion of arsenic through drinking water the RAF = 1.

The above values were then used to calculate the Lifetime Average Daily Dose (LADD) using the equation:

$$LADD = \frac{EPC \times RAF \times Intake \times Freq \times Duration \times Exp.\ Period \times CF}{BW \times AP}$$

The LADD is expressed in mg/kg/day and is reflective of the lifetime exposure rates experienced by the receptor.

### 5.1.4 Risk Characterization

The risk characterization involves using the information gathered in the above three steps to describe the magnitude of carcinogenic and non-carcinogenic risks to the exposed population. Because the counties of interest are in Massachusetts, I used the MassDEP risk limit of 1.0E-05 as the upper bound of risks that I considered to be unacceptable lifetime risks of cancer.

Carcinogenic risk is calculated as the incremental probability of an individual developing cancer over a lifetime (75 years) due to exposure to a carcinogenic compound. This is also called Excess Lifetime Cancer Risk (ELCR) and represents the increased risk of developing cancer above the background rate.

The dose-response relationship is considered linear under the low dose conditions usually encountered in environmental exposures. In consideration of this assumption, the SF is a constant and risk is directly related to intake. The linear low-dose cancer risk equation is:

ELCR = LADD x SF

where:

ELCR = a unitless excess probability of developing cancer;

LADD = Lifetime Average Daily Dose averaged over 70 years (mg/kg-day);

SF = Slope Factor, expressed in $(mg/kg\text{-}day)^{-1}$.

My results showed that for EPCs of 1 µg/L the ELCR was 1.7 E-05 which is in excess of the 1 E-05 Cancer Risk Limit (CRL) despite the current standard being set at 5µg/L. Sub-section 5.4 explores this in further detail. Due to the linear progression of the data there is a clear linear dose response curve between increase in exposure point concentrations and ELCRs. This curve is linear because I used a linear array of EPCs and illustrates that for an EPC of 2 µg/L, the risk will be double that with an EPC of 1 µg/L . All the ELCRs reported for

EPCs higher than 0 µg/L are beyond the CRL and the highest EPC of 26 µg/Lcorresponds to an ELCR of 4.6 E-04, significantly higher than the Massachusetts CRL. The risks were higher for residents drinking private well water from Middlesex county and highest for those in the high probability areas. An ELCR of 4.6 E-04 indicates a high level for cancer risk for the exposed. My result highlighted the incremental probability of an individual drinking water from wells with increased concentrations of arsenic in drinking water, developing cancer over a lifetime as a result of exposure to the carcinogen. At an EPC of 0.2 µg/L the ELCR was 3.54E-06 and at 1 µg/L it was higher. For EPC's of 10 µg/L or higher the ELCRs were more by an order of magnitude, resulting in a significant increase above the regulatory limit. For human health, the chemical specific risk estimate for arsenic was above a regulatory target of 1E-06 under a hypothetical consumption scenario.

### 5.2 Cancer Incidence

A cancer incidence rate is the number of new cancers of a specific site/type occurring in a specified population during a year. As stated in the Methods section, I collected data on the cancer incidence in the selected towns in Massachusetts from the website of the Massachusetts Cancer Registry (MCR). The following sub-section provides a detailed explanation of the data collection, data processing and statistical techniques employed by the MCR and the applicability in my research.

### 5.2.1 Data collection and SIRs

Facilities reporting to the MCR include acute care hospitals, medical practice associations, laboratories, radiation and oncology facilities, dermatologists and urologists. The MCR also collects information from reporting hospitals on diagnosed cases and the MCR reports include previously unreported cases that were discovered through death certificates. Each year, the North American Association of Central Cancer Registries (NAACCR) reviews cancer registry data for quality, completeness, and timeliness. For diagnosis years 2001-2005, the MCR's annual case count was estimated by NAACCR to be more than 95% complete each year (NAACCR, 2009). Typically, published incidence rates do not combine invasive and in situ cancers due to differences in the biologic significance, survival prognosis and types of treatment of the tumors. However urinary and bladder cancers are the only exception, due to the specific nature of the diagnostic techniques and treatment patterns.

The data I obtained from the MCR website were presented as observed and expected case counts and standardized incidence ratios (SIRs). The observed case count for a particular type of cancer in a city/town is the actual number of newly diagnosed cases among residents of that city/town for a given time period. The expected case count is based on that city/town's population distribution (by sex and among eighteen age groups, in five-year age groups) for the time period 2001-2005, and the corresponding statewide average annual age-specific

incidence rates (MCR, 2009). It is a product of the age-specific incidence rate in each five-year group by the population in that age group.

The SIR is calculated as the observed cases divided by the expected cases multiplied by a hundred. The SIR is adjusted for age and sex differences and describes in numerical form a town's cancer experience in a given time period compared with that of the state as a whole and with other towns. An SIR of 100 denotes that the observed incidence and expected incidence are the same. An SIR more than 100 denotes that the incidence is higher than expected for that cancer based on statewide average annual age-specific incidence rates. An SIR of less than a 100 denotes that the incidence is lower than expected for that cancer based on statewide average annual age-specific incidence rates.

The stability of an SIR is determined by its 95% confidence interval (95% CI). A confidence interval (CI) is a particular kind of interval estimate of a population parameter that instead of estimating the parameter by a single value includes the interval within which the parameter is given. Thus, confidence intervals are used to indicate the reliability of an estimate and are the measures that determine statistical significance and stability. The stability of an SIR depends on how large it is because small increases and decreases will affect larger case numbers less than small numbers. For example, 7 observed cases and 3 expected cases and 700 observed and 300 expected cases will have the same SIRs but the addition of one observed case in each data set will cause a much more drastic change in the

smaller sized SIR. Thus when the observed and expected numbers of cases are relatively large, the value of the SIR is stable. The SIRs of bladder cancer were tabulated as shown in Section 4.0 in Tables 4-5 through 4-10.

Confidence intervals also indicate more than just the possible range around the estimate. They also highlight the stability of the estimate. A stable estimate is one that would be close to the same value if the observation were repeated. An unstable estimate is one that would vary from one observation to another. Wider confidence intervals in relation to the estimate itself indicate instability. Variability can depend on the frequency of the health event, the population size and lack of regularity in the occurrence of the health effects. It is therefore difficult to interpret confidence intervals of calculations based on few observed and expected cases (NMDOH, 2009).

Most epidemiologic and other public health studies use a 95% confidence interval, but it is not uncommon to see alternatives. Within the Association of Public Health Observatories (APHO) community 99.8% confidence intervals are frequently used alongside 95% confidence intervals to reflect the control limits used in Statistical Process Control approaches. Increasing confidence interval levels results in wider limits (APHO, 2008).

The observed and expected case counts for Transitional Cell Carcinoma bladder cancer for the towns of interests were very small and therefore to get a more

stable SIR I aggregated the data as shown in the Results section. Despite this aggregation, however, the resulting SIRs were small and the resulting data were not very stable as illustrated by the wide confidence intervals. If the confidence interval is very wide, the ratio is probably based on a very small number of observed cases and, therefore, any reliable conclusions cannot be made. A “very wide” range can be defined as 50 or more. Because of small sample sizes, the confidence intervals for my SIRs were wide and overlapped each other and therefore no statistically significant relationships could be determined based on the SIRs.

There is also variability on formulae used to calculate CIs for SIRs. Since I was working with data obtained from the MCR I used the formulae prescribed by them. The formula I used was CI = SIR (1.96 x SE) (Knowlton, 2009). This method of calculation is also used by the Pennsylvania Department of Health and the New Hampshire Department of Health. However, the New York Department of Health uses confidence limits that are based on the Byar's approximation of the exact Poisson distribution, which is extremely accurate even with small numbers (Breslow and Day, 1987). The San Francisco Department of Public Health also uses the same. The formula for calculation of $SIR_L$ and $SIR_U$ is

$$SIR_L = SIR\left(1 - \frac{1}{9O} - \frac{Z_{\alpha/2}}{\sqrt{3O}}\right)^3$$

$$SIR_U = SIR\left(\frac{O+1}{O}\right)\left(1 - \frac{1}{9(O+1)} + \frac{Z_{\alpha/2}}{\sqrt{3(O+1)}}\right)^3$$

The National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) Program uses a formula put forth by Sahai and Khurshid to discuss the exact and confidence limit for the true SIR, (Sahai and Khurshid, 1993, 1996).

$$\mathrm{SIR}_L = \frac{\chi^2_{2D,\alpha/2}}{2E^*} \qquad \text{and} \qquad \mathrm{SIR}_U = \frac{\chi^2_{2(D+1),1-\alpha/2}}{2E^*}$$

where $\chi^2_{v,\alpha}$ 100$\alpha$ percentile of the chi-square distribution with *v* degrees of freedom.

My results, using the MCR calculation, were as follows:

- The SIRs for Worcester County were 97.70 and 98.21 for males and females, respectively, indicating that there was a 2.3% and 1.79% reduced incidence in studied towns from Worcester County compared to the statewide average.
- The SIRs for Middlesex County were 120.16 and 119.05 for males and females, respectively, indicating that there was a 20.16% and 19.05% increased incidence in studied towns from Middlesex County compared to the statewide average
- The SIRs for Barnstable County were 119.35 and 117.27 for males and females, respectively, indicating that there was a 19.35% and 17.27% increased incidence in Barnstable County compared to the statewide average

- The SIRs for towns with low probabilities of As >5 µg/liter in the bedrock aquifer were 112.00 and 73.17 for males and females, respectively, indicating a 12% increase in incidence for males and a 26.83% reduced incidence for females compared to the statewide average.
- The SIRs for towns with medium probabilities of As >5 µg/liter in the bedrock aquifer were 101.74 and 118.64 for males and females, respectively, indicating a 1.74% and 18.64 % increased incidence when compared to the statewide average.
- The SIRs for towns with high probabilities of As >5 µg/liter in the bedrock aquifer were 118.92 and 115.70 for males and females, respectively, indicating a 18.92% and 15.7 % increased incidence when compared to the statewide average.

Large differences exist between the SIRs in males and females in towns with low probabilities and medium probabilities. Other than these, the differences between men and women are minimal and there is also very little difference based on towns in Worcester, Middlesex, and Barnstable Counties.

Bladder Cancer is more prevalent in men than in women as stated in research published by NCI's SEER Cancer Statistics Review. On January 1, 2007, in the United States there were approximately 535,236 men and women alive who had a history of cancer of the urinary bladder, 395,480 men and 139,756 women. The SEER Incidence from 2003-2007 was 37.2 per 100,000 men and 9.2 per 100,000

women and the mortality was 7.5 per 100,000 men and 2.2 per 100,000 women. Prior research has pointed towards the role male hormones working in concert with the androgen receptor might play, as well as exposures in the workplace and smoking (Chang et. al, 2007; Sohel, 2009; Smith et. al 1992).

### 5.3 Private Wells

The term "private well" is typically used for a well that provides drinking water for a single-family residence. However as per the MassDEP a private well is defined as a water supply system that provides water for human consumption and consists of a system that has fewer than fifteen service connections and either (1) serves fewer than twenty-five individuals or (2) serves an average of twenty-five or more individuals daily for fewer than sixty days of the year (MassDEP, 2007). Under the Massachusetts General Law, MGL Ch.111 s.122, local Boards of Health (BOHs) have primary jurisdiction over the regulation of private wells. The local BOHs are empowered to adopt a Private Well Regulation that establishes criteria for private well siting, construction, water quality, and quantity. MassDEP recommends the intervals between water quality tests in terms of years if the well is properly constructed and located in a safe area. Under certain condition however they recommend more frequent testing. MassDEP also recommends that residents should test initially for all contaminants of concern, and then at a minimum of once every ten years (except for bacteria and nitrate/nitrite which should be sampled yearly), or as otherwise

required or recommended by the local Board of Health. MassDEP recommends the use of a state-certified analytical laboratory for all water quality testing and the private well owner is responsible for the costs of the water quality analyses. These, however, are recommendations and not requirements.

The "Drinking Water Regulations," 310 CMR 22.00**,** promulgated by the MassDEP, pertain only to public water systems. These regulations include water quality standards that can serve as useful guidelines for interpreting the results of analyses performed on water samples obtained from private water systems. These guidelines, however, do not serve as regulations for private wells and testing is required only for community water systems as per a schedule determined by the local Board of Health (BOH). The testing schedule is determined based on knowledge of naturally occurring contaminants and past and present land uses are of as well as land uses that have the potential to adversely impact water quality (DWP, 2008). A community water system is one that serves more than 25 people or that has more than 15 connections. Examples include restaurants, apartment complexes, and institutions such as schools and daycare centers that are not connected to the public water system.

After a well is drilled in a community, the local BOH issues a Water Supply Certificate (WSC) to verify that the private well may be used as a drinking water supply. This certificate must be issued for a private well before an occupancy permit for an existing structure is issued or before a building permit for new construction to be served by the well is issued. A well completion report and a water quality report must be submitted to the BOH for issuance of the WSC

based upon which the BOH may issue the certificate, place conditions on the certificate, or deny it entirely. Some Boards of Health require testing for arsenic in the initial water quality report but there is no requirement for testing after the WSP has been issued unless so stated in the conditional issuance of a certificate (DWP, 2008).

### 5.4 Current Standard

In regulating a contaminant for public water supplies, EPA first sets a Maximum Contaminant Level Goal (MCLG), which establishes the contaminant level at which no known or anticipated adverse health effects occur. MCLGs are non-enforceable health goals. For this rulemaking, EPA starts by setting an MCLG of zero for carcinogens like arsenic and then sets an enforceable Maximum Contaminant Level (MCL) as close as technologically possible to the MCLG. In addition, EPA uses its discretion in setting the MCL by choosing an MCL that is protective of public health while also assessing the costs-benefit analyses and the economic impact analyses of the rule. Some factors that affect this decision include the analytical capability and laboratory capacity, the likelihood of water systems choosing various compliance technologies for several sizes of systems based on source water properties, the natural occurrence of the contaminant in water supplies, quantified and non-quantified costs associated with control technologies, health risk reduction benefits likely to occur at the MCLs considered, and the effects on sensitive subpopulations (EPA, 2000). Based upon the above, EPA promulgated an enforceable standard of 10 µg/L for arsenic in public water systems under the National Interim Primary Drinking Water

Regulations (40 CFR 59566). In promulgating the standard, which replaced the previous standard of 50 µg/L, EPA stated that the standard for arsenic "is .010 parts per million (10 parts per billion) to protect consumers served by public water systems from the effects of long-term, chronic exposure to arsenic. Public water systems had to comply with this standard by January 23, 2006, providing additional protection to an estimated 13 million Americans" (EPA, 2000).

### 5.5 Uncertainty Analysis

The major weakness in my thesis was the lack of discrete data for arsenic in private wells. Although the USGS has been gathering data on arsenic and uranium concentrations in private well drinking water, these data are not yet available publicly. When they are available, these data will include the concentrations of arsenic found in private well water and the number of people with regular access to this drinking water. Once this information is available, the risk estimate can be determined based on actual data on exposure point concentrations rather than using estimated values based on the range on concentrations founding the study area. This information will help in inferences drawn from results real information on ground reality of exposure data rather than from proxy data.

Due to the small numbers of observed and expected cancer cases in the calculation of SIRs, the 95% CIs were wide indicating unstable SIR estimates. A more detailed cancer data set inclusive of the target population and case-by-case reflection with respect to intake of private well water would provide a more

accurate picture of the magnitude of impact of confounders like smoking, well use duration, location extent of contamination. Within a Confidence Interval the best estimate is always a point estimate and given that most of my point estimates were fairly close to 100 it is unlikely that SIRs such as 300 or 400 occur with a larger data set.

There is also the potential for misclassification error due to the fact that people may not have been exposed to drinking water from that particular well all their lives and might have moved from other regions. Random misclassification is quite likely to be extensive in these data and would drive any SIR towards 100 since random misclassification always results in an underestimate of the true association and pushes the study results away from truth towards the null hypothesis. Barnstable County is known as a preferred region for retirement and people exposed to contaminants during their lifetime in other locations might skew the cancer statistics due to distortion of exposure metrics. Also the study doesn't account for people drinking water from alternative sources of water such as bottled water, or people may also have purifications systems that filter arsenic from drinking water.

Smoking may be a confounder. However, although there is a positive association between smoking and bladder cancer, there is no evidence to suggest that the smoking rates differ among the towns of interest. To establish smoking as a

definitive confounder for my study a detailed report on smokers will be needed to ascertain the differences between communities.

## 6.0 CONCLUSIONS AND RECOMMENDATIONS

There primary source of arsenic in groundwater in regions of north central Massachusetts situated parallel to the Northern Appalachian Mountain Belt is geological. Arsenic from bedrock leaches into groundwater under varying stoichiometric, spatial, and environmental conditions and affects groundwater quality. People in Ashburnham, Berlin, Boxborough, Boylston, Carlisle, Groton, Harvard, Lunenburg, Shirley, Stow, Tyngsborough, Westford and Westminster are particularly susceptible to this as they drink water primarily from bedrock wells and the majority of the town populations use private wells.

### 6.1 Conclusions

Based upon the toxicological review and the geologic review, I found that inorganic arsenic present in drinking water in the study area is causally linked to bladder cancer. I was able to determine that it has toxic effects on the human body through literature review of its toxicokinetics, human and animal mechanisms of toxicity, genotoxicity and carcinogeniety.

I then determined the relation between the magnitude of exposure and the probability of occurrence of bladder cancer through a detailed dose-response assessment as available on IRIS that qualifies Arsenic as a Group A human carcinogen. The results of the risk assessment based on a range of exposures that included the maximum concentrations in each county show a higher cancer

probability risk than that reflected by the cancer incidence data. My primary hypothesis that lifetime consumption of groundwater contaminated with low concentrations of arsenic can increase risk of cancer is satisfied by the results of the risk assessments and high Estimated Lifetime Cancer Risks (ELCRs).

However due to the wide and overlapping confidence intervals I cannot disprove or prove my secondary hypothesis that that bladder and urinary cancer incidence rates are associated with arsenic contamination in relation to lifetime exposure to arsenic in drinking water. The number of observed and expected Urinary Bladder Cancer (ICD: 188.0-188.9) cases in the study areas was fairly small and in order to increase stability SIRs I aggregated the data. However this didn't necessarily affect the stability and the confidence intervals remained extremely wide despite aggregation.

Unlike public water supplies, private wells are not required to meet the new arsenic standard of 10 µg/L (EPA, 2006). The Safe Drinking Water Act is the enabling legislation that ensures safe drinking water for the public. Pursuant to the act, the U. S. Environmental Protection Agency (EPA) is required to set standards for drinking water quality and oversee all states, localities, and public water suppliers who implement these standards. This ensures that no one served by public water supplies will have arsenic concentrations greater than 10 µg/L. Private drinking water sources are not regulated and do not have to meet the Safe Drinking Water Act standards. Since private supplies, however, are not regulated

or mandated to reduce arsenic concentrations people with private wells may continue to consume water containing arsenic greater than the current drinking water standard unless preventive or corrective action is taken by individual well owners.

### 6.2 Recommendations

Due to the large number of people consuming possibly contaminated water in the prescribed study area and given the risks associated with drinking that water, a multi-pronged mitigation and adaptation approach including surveillance, outreach, and education would reduce cancer risk in this population. I recommend a program that includes monitoring of private water supplies, along with public outreach and education, along with treatment where needed to protect public health. I also recommend exploration of sources of funding for this type of program.

I recommend that well owners have their well water tested by certified laboratories prior to use. Private wells in Massachusetts are governed by the local Boards of Health. Testing schedules and range of contaminants to be monitored is based on a existing knowledge of geology, background levels and land use.

I recommend that local Boards of Health in areas where elevated concenterations of arsenic are likely in groundwater make testing for arsenic mandatory in the

initial water quality report prior to issuing a Water Supply Certificate (WSC) to declare that the private well may be used as a drinking water supply. I also recommend that in addition to new wells, all existing private wells in areas where there is likely to be high concentrations of arsenic in groundwater be tested if they were not tested prior to issuance of a certificate. In Massachusetts, there is no requirement for testing after the WSC has been issued unless so stated in the conditional issuance of a certificate, but Boards of Health should educate residents regarding the importance of testing each well for arsenic at least once.

I further recommend that prospective and future home-owners in the study areas with private wells have their well tested for arsenic prior to purchase. Local Boards of Health can promulgate this type of regulation. Commercial laboratory test costs range from about $30 to about $50, and depend upon the number of analyses requested. The USGS also has a program where well owners are encouraged to collect samples by means of a do-it-yourself kit. USGS also uses confidentiality agreements that protect the well owner's interests.

People drinking water from private wells in my study areas need to be made aware about the potential risks of drinking arsenic-contaminated water over a lifetime and also be educated about the alternative resources available.
I also recommend that well owners are adequately educated about the risks associated with drinking arsenic-contaminated water and the need for surveillance and monitoring. This is possible through informational seminars, outreach

program, amendments to school educational series, community discussion forums and town hall meetings. There needs to be coordinated and well planned risk communication so as not to create panic, but to create awareness of the need for monitoring the situation.

Based upon my study I would suggest studying individual exposures to seek possible explanations for the occurrence of bladder cancer. Individual studies of private wells and the number of people experiencing cancer will provide better insight into the need for regulation. Local Boards of Health, in collaboration with physicians and hospitals in the area, can assist with outreach in effectively communicating the risks. I recommend a program to sensitize doctors to the need for creating awareness and encourage testing.

Moreover, given the potential for harm to human health, there needs to be further study on the issue. This needs further geologic and epidemiological study. Massachusetts has some of the highest rates of bladder cancer in the nation (MCR, 2000) and if it reflective of the bladder cancer rates as proved by risk assessment then the private wells need to be assessed so as to minimize the cancer risks. I recommend that further study on the physical basis subsurface water occurrence and flow and its applicability to the range of concentrations found in the wells, the impacts and vulnerability of the affected populations, and possible mitigation activities.

For the private well owner, good quality drinking water depends on a multi-barrier approach to contamination that includes well monitoring and maintenance, locating the well away from points of contamination such as in gravel-packed aquifers and unconsolidated aquifers, typically not associated with arsenic contamination. Given that it is rare for private well owners to be able to find a favorable bedrock location to drill especially in overburden, it may be useful for well owners and drillers to be educated out the location and source of contamination.

In areas where a gravel pack may not be feasible option water treatment options such as home filtration systems may be used. In some cases remediation might be beneficial whereas in some cases filtration or use of bottled water may be the best solution. In some cases where public water systems are not available residents may like to opt for bottled water for drinking and cooking.

In order to find the most effective solution to curtail the negative health effects from contaminated wells, I recommend that that a detailed cost benefit analysis of each solution is conducted. The study should include effectiveness of existing remediation and treatment technologies as well as their capability and success rate.

Because there are no registries for non-cancer effects associated with arsenic, non-cancer effects cannot be tested against mortality data but the vast availability

of toxicology information can be assessed for morbidity data. The concentrations in New England are too low to assess acute health effects and also to study for non-cancer endpoints. Exposure to arsenic should be tested through measuring concentrations in private well water and also through the hair, skin and urine samples of people exposed to contaminated water. More extensive research is needed on biomarkers and personal exposure. I suggest that this research should be conducted in collaboration with spatial studies, as well as risk assessment studies for an accurate picture of the extent of contamination.

It is essential to safeguard the health and general welfare of the general public dependent on private water supply systems so that citizens are assured of consuming potable water. It is thus crucial for regulators, local Boards of Health, researchers and citizens to be aware of the risks and understand the extent of contamination and the risks posed by varied levels of contamination so that the measure adopted to ameliorate negative health effects are adopted. Efficient management of sources and distribution systems can ensure that people are able to maximize upon the quantity and quality of drinking water.

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## APPENDIX A

Demographic Data

Barnstable County

| | Barnstable | Bourne | Brewster | Chatham | Dennis | Eastham | Falmouth |
|---|---|---|---|---|---|---|---|
| Total: | 47,821 | 18,721 | 10,094 | 6,625 | 15,973 | 5,453 | 32,660 |
| Male: | 22,864 | 9,223 | 4,685 | 3,126 | 7,367 | 2,637 | 15,252 |
| Under 5 years | 1,294 | 609 | 166 | 97 | 314 | 109 | 751 |
| 5 to 9 years | 1,509 | 552 | 328 | 117 | 358 | 132 | 959 |
| 10 to 14 years | 1,657 | 585 | 349 | 156 | 431 | 187 | 1,106 |
| 15 to 17 years | 942 | 315 | 239 | 110 | 254 | 95 | 624 |
| 18 and 19 years | 461 | 349 | 79 | 54 | 123 | 50 | 281 |
| 20 years | 215 | 215 | 29 | 18 | 52 | 17 | 91 |
| 21 years | 166 | 184 | 29 | 22 | 46 | 19 | 98 |
| 22 to 24 years | 552 | 372 | 79 | 65 | 137 | 56 | 284 |
| 25 to 29 years | 1,019 | 521 | 141 | 131 | 292 | 106 | 599 |
| 30 to 34 years | 1,395 | 638 | 192 | 127 | 396 | 138 | 814 |
| 35 to 39 years | 1,848 | 669 | 283 | 173 | 481 | 168 | 1,123 |
| 40 to 44 years | 1,925 | 672 | 379 | 211 | 507 | 188 | 1,240 |
| 45 to 49 years | 1,746 | 654 | 401 | 217 | 509 | 194 | 1,159 |
| 50 to 54 years | 1,679 | 615 | 414 | 241 | 524 | 200 | 1,114 |
| 55 to 59 years | 1,253 | 473 | 239 | 213 | 498 | 167 | 981 |
| 60 and 61 years | 414 | 155 | 79 | 77 | 188 | 56 | 331 |
| 62 to 64 years | 657 | 227 | 133 | 125 | 302 | 102 | 555 |
| 65 and 66 years | 461 | 194 | 92 | 94 | 204 | 70 | 399 |
| 67 to 69 years | 721 | 246 | 177 | 145 | 312 | 104 | 546 |
| 70 to 74 years | 1,116 | 398 | 290 | 273 | 577 | 182 | 866 |
| 75 to 79 years | 898 | 289 | 279 | 210 | 432 | 171 | 691 |
| 80 to 84 years | 565 | 188 | 156 | 140 | 268 | 82 | 373 |
| 85 years and over | 371 | 103 | 132 | 110 | 162 | 44 | 267 |
| Female: | 24,957 | 9,498 | 5,409 | 3,499 | 8,606 | 2,816 | 17,408 |
| Under 5 years | 1,215 | 562 | 187 | 96 | 293 | 99 | 715 |
| 5 to 9 years | 1,485 | 584 | 272 | 103 | 360 | 117 | 937 |
| 10 to 14 years | 1,517 | 577 | 368 | 110 | 434 | 147 | 1,082 |
| 15 to 17 years | 879 | 307 | 197 | 90 | 253 | 79 | 590 |
| 18 and 19 years | 408 | 198 | 97 | 30 | 123 | 39 | 272 |
| 20 years | 145 | 93 | 26 | 29 | 59 | 17 | 117 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 21 years | 201 | 90 | 26 | 12 | 35 | 12 | 96 |
| 22 to 24 years | 553 | 255 | 73 | 61 | 163 | 60 | 330 |
| 25 to 29 years | 1,063 | 519 | 134 | 91 | 319 | 119 | 627 |
| 30 to 34 years | 1,485 | 677 | 240 | 142 | 436 | 151 | 966 |
| 35 to 39 years | 1,995 | 704 | 362 | 201 | 523 | 190 | 1,266 |
| 40 to 44 years | 2,079 | 711 | 443 | 235 | 597 | 232 | 1,371 |
| 45 to 49 years | 1,953 | 637 | 472 | 216 | 617 | 196 | 1,294 |
| 50 to 54 years | 1,746 | 692 | 428 | 259 | 650 | 232 | 1,295 |
| 55 to 59 years | 1,483 | 532 | 284 | 246 | 599 | 196 | 1,213 |
| 60 and 61 years | 522 | 197 | 110 | 108 | 197 | 56 | 417 |
| 62 to 64 years | 761 | 282 | 169 | 169 | 361 | 108 | 624 |
| 65 and 66 years | 497 | 198 | 138 | 110 | 250 | 92 | 405 |
| 67 to 69 years | 884 | 279 | 209 | 162 | 431 | 131 | 672 |
| 70 to 74 years | 1,328 | 468 | 354 | 278 | 633 | 211 | 1,038 |
| 75 to 79 years | 1,211 | 379 | 305 | 279 | 553 | 181 | 882 |
| 80 to 84 years | 812 | 282 | 196 | 222 | 436 | 90 | 603 |
| 85 years and over | 735 | 275 | 319 | 250 | 284 | 61 | 596 |

| | **Harwich** | **Mashpee** | **Orleans** | **Province-town** | **Sandwich** | **Truro** | **Wellfleet** | **Yarmouth** |
|---|---|---|---|---|---|---|---|---|
| Total: | 12,386 | 12,946 | 6,341 | 3,431 | 20,136 | 2,087 | 2,749 | 24,807 |
| Male: | 5,672 | 6,091 | 2,958 | 1,839 | 9,783 | 968 | 1,296 | 11,438 |
| Under 5 years | 279 | 393 | 87 | 33 | 689 | 33 | 66 | 551 |
| 5 to 9 years | 331 | 508 | 114 | 31 | 867 | 52 | 51 | 675 |
| 10 to 14 years | 377 | 494 | 160 | 48 | 979 | 67 | 83 | 662 |
| 15 to 17 years | 194 | 213 | 97 | 30 | 449 | 26 | 68 | 372 |
| 18 and 19 years | 107 | 95 | 47 | 33 | 217 | 23 | 25 | 206 |
| 20 years | 43 | 50 | 12 | 11 | 88 | 2 | 7 | 71 |
| 21 years | 27 | 37 | 13 | 9 | 82 | 5 | 7 | 81 |
| 22 to 24 years | 92 | 103 | 42 | 46 | 166 | 16 | 31 | 220 |
| 25 to 29 years | 178 | 245 | 91 | 104 | 305 | 31 | 34 | 540 |
| 30 to 34 years | 295 | 403 | 105 | 165 | 568 | 54 | 58 | 629 |
| 35 to 39 years | 397 | 518 | 137 | 263 | 803 | 88 | 86 | 740 |
| 40 to 44 years | 414 | 535 | 195 | 202 | 949 | 83 | 107 | 811 |
| 45 to 49 years | 400 | 412 | 228 | 184 | 865 | 88 | 116 | 773 |
| 50 to 54 years | 401 | 371 | 232 | 206 | 668 | 109 | 135 | 744 |
| 55 to 59 years | 318 | 344 | 210 | 135 | 533 | 72 | 83 | 663 |
| 60 and 61 years | 128 | 112 | 71 | 35 | 142 | 19 | 25 | 231 |
| 62 to 64 years | 199 | 178 | 143 | 43 | 238 | 37 | 48 | 409 |

| | Harwich | Mashpee | Orleans | Province-town | Sandwich | Truro | Wellfleet | Yarmouth |
|---|---|---|---|---|---|---|---|---|
| 65 and 66 years | 140 | 124 | 87 | 30 | 128 | 14 | 27 | 294 |
| 67 to 69 years | 252 | 231 | 175 | 45 | 219 | 32 | 42 | 455 |
| 70 to 74 years | 413 | 322 | 267 | 73 | 331 | 44 | 78 | 778 |
| 75 to 79 years | 309 | 209 | 240 | 54 | 247 | 37 | 64 | 727 |
| 80 to 84 years | 216 | 124 | 109 | 31 | 167 | 22 | 27 | 448 |
| 85 years and over | 162 | 70 | 96 | 28 | 83 | 14 | 28 | 358 |
| Female: | 6,714 | 6,855 | 3,383 | 1,592 | 10,353 | 1,119 | 1,453 | 13,369 |
| Under 5 years | 225 | 373 | 72 | 27 | 640 | 39 | 52 | 533 |
| 5 to 9 years | 321 | 488 | 113 | 36 | 792 | 47 | 52 | 520 |
| 10 to 14 years | 327 | 491 | 145 | 39 | 866 | 69 | 68 | 627 |
| 15 to 17 years | 209 | 234 | 85 | 29 | 431 | 31 | 50 | 330 |
| 18 and 19 years | 82 | 100 | 31 | 20 | 167 | 11 | 21 | 154 |
| 20 years | 41 | 42 | 17 | 12 | 66 | 6 | 7 | 99 |
| 21 years | 32 | 42 | 21 | 11 | 55 | 6 | 10 | 58 |
| 22 to 24 years | 101 | 125 | 39 | 38 | 153 | 16 | 27 | 251 |
| 25 to 29 years | 219 | 326 | 90 | 78 | 360 | 44 | 57 | 584 |
| 30 to 34 years | 344 | 472 | 104 | 112 | 633 | 69 | 79 | 741 |
| 35 to 39 years | 403 | 583 | 183 | 147 | 909 | 93 | 91 | 855 |
| 40 to 44 years | 491 | 599 | 191 | 168 | 1,042 | 105 | 129 | 889 |
| 45 to 49 years | 464 | 473 | 216 | 174 | 908 | 128 | 142 | 829 |
| 50 to 54 years | 474 | 418 | 254 | 180 | 733 | 102 | 142 | 879 |
| 55 to 59 years | 390 | 406 | 256 | 104 | 619 | 96 | 106 | 812 |
| 60 and 61 years | 168 | 151 | 86 | 26 | 168 | 23 | 32 | 348 |
| 62 to 64 years | 249 | 201 | 170 | 42 | 229 | 43 | 57 | 451 |
| 65 and 66 years | 184 | 157 | 104 | 34 | 150 | 17 | 27 | 356 |
| 67 to 69 years | 278 | 272 | 220 | 50 | 242 | 27 | 55 | 606 |
| 70 to 74 years | 520 | 355 | 291 | 80 | 378 | 56 | 105 | 957 |
| 75 to 79 years | 442 | 258 | 271 | 54 | 347 | 39 | 60 | 957 |
| 80 to 84 years | 352 | 150 | 221 | 56 | 237 | 31 | 44 | 738 |
| 85 years and over | 398 | 139 | 203 | 75 | 228 | 21 | 40 | 795 |

Selected towns in Worcester County

| | Ashburnham | Berlin | Boylston | Harvard | Lunenburg | Westminster |
|---|---|---|---|---|---|---|
| Total: | 5,546 | 2,380 | 4,008 | 5,981 | 9,401 | 6,907 |
| **Male:** | **2,817** | **1,189** | **1,994** | **3,319** | **4,655** | **3,445** |
| Under 5 years | 178 | 93 | 113 | 164 | 275 | 211 |
| 5 to 9 years | 214 | 71 | 151 | 237 | 355 | 280 |
| 10 to 14 years | 304 | 93 | 154 | 277 | 399 | 305 |
| 15 to 17 years | 158 | 52 | 86 | 130 | 223 | 180 |
| 18 and 19 years | 80 | 25 | 27 | 43 | 116 | 88 |
| 20 years | 32 | 12 | 10 | 18 | 36 | 25 |
| 21 years | 26 | 7 | 15 | 14 | 27 | 32 |
| 22 to 24 years | 70 | 31 | 47 | 70 | 107 | 63 |
| 25 to 29 years | 112 | 49 | 106 | 178 | 183 | 129 |
| 30 to 34 years | 172 | 87 | 123 | 222 | 300 | 196 |
| 35 to 39 years | 236 | 105 | 203 | 311 | 424 | 321 |
| 40 to 44 years | 302 | 108 | 187 | 383 | 446 | 318 |
| 45 to 49 years | 268 | 99 | 187 | 359 | 444 | 346 |
| 50 to 54 years | 220 | 98 | 158 | 317 | 379 | 318 |
| 55 to 59 years | 142 | 82 | 118 | 226 | 260 | 199 |
| 60 and 61 years | 36 | 28 | 49 | 65 | 78 | 44 |
| 62 to 64 years | 46 | 27 | 45 | 80 | 105 | 60 |
| 65 and 66 years | 33 | 16 | 23 | 35 | 69 | 39 |
| 67 to 69 years | 44 | 18 | 51 | 39 | 86 | 59 |
| 70 to 74 years | 61 | 47 | 62 | 66 | 138 | 90 |
| 75 to 79 years | 47 | 19 | 42 | 42 | 96 | 65 |
| 80 to 84 years | 24 | 10 | 22 | 23 | 75 | 51 |
| 85 years and over | 12 | 12 | 15 | 20 | 34 | 26 |
| **Female:** | **2,729** | **1,191** | **2,014** | **2,662** | **4,746** | **3,462** |
| Under 5 years | 154 | 79 | 125 | 178 | 279 | 204 |
| 5 to 9 years | 209 | 87 | 148 | 220 | 317 | 234 |
| 10 to 14 years | 245 | 84 | 128 | 260 | 372 | 281 |
| 15 to 17 years | 144 | 37 | 69 | 124 | 207 | 155 |
| 18 and 19 years | 60 | 18 | 24 | 42 | 88 | 78 |
| 20 years | 31 | 6 | 14 | 11 | 32 | 30 |
| 21 years | 22 | 4 | 8 | 9 | 29 | 26 |
| 22 to 24 years | 53 | 22 | 30 | 32 | 89 | 77 |
| 25 to 29 years | 123 | 40 | 106 | 47 | 192 | 157 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 30 to 34 years | 172 | 85 | 141 | 111 | 329 | 223 |
| 35 to 39 years | 269 | 133 | 193 | 212 | 428 | 329 |
| 40 to 44 years | 328 | 112 | 196 | 301 | 495 | 324 |
| 45 to 49 years | 259 | 116 | 194 | 289 | 425 | 346 |
| 50 to 54 years | 180 | 82 | 154 | 281 | 381 | 298 |
| 55 to 59 years | 119 | 70 | 127 | 206 | 259 | 175 |
| 60 and 61 years | 40 | 20 | 34 | 53 | 79 | 44 |
| 62 to 64 years | 50 | 23 | 47 | 54 | 114 | 58 |
| 65 and 66 years | 33 | 23 | 28 | 37 | 71 | 43 |
| 67 to 69 years | 42 | 29 | 56 | 32 | 118 | 60 |
| 70 to 74 years | 68 | 47 | 68 | 55 | 153 | 111 |
| 75 to 79 years | 62 | 33 | 66 | 57 | 126 | 94 |
| 80 to 84 years | 40 | 24 | 34 | 24 | 90 | 69 |
| 85 years and over | 26 | 17 | 24 | 27 | 73 | 46 |

Selected towns in Middlesex County

| | BOXBOROUGH | CARLISLE | GROTON | SHIRLEY | STOW | TYNGSBOROUGH | WESTFORD |
|---|---|---|---|---|---|---|---|
| Total: | 4,868 | 4,717 | 9,547 | 6,373 | 5,902 | 11,081 | 20,754 |
| **Male:** | **2,483** | **2,338** | **4,731** | **3,693** | **2,948** | **5,470** | **10,324** |
| Under 5 years | 173 | 158 | 411 | 183 | 273 | 520 | 921 |
| 5 to 9 years | 259 | 213 | 507 | 198 | 271 | 472 | 1,067 |
| 10 to 14 years | 243 | 242 | 468 | 214 | 245 | 467 | 980 |
| 15 to 17 years | 101 | 119 | 221 | 89 | 128 | 260 | 446 |
| 18 and 19 years | 33 | 50 | 80 | 74 | 44 | 96 | 216 |
| 20 years | 21 | 13 | 31 | 36 | 25 | 47 | 65 |
| 21 years | 12 | 7 | 23 | 60 | 16 | 50 | 57 |
| 22 to 24 years | 56 | 26 | 66 | 171 | 41 | 120 | 155 |
| 25 to 29 years | 121 | 26 | 160 | 376 | 86 | 289 | 299 |
| 30 to 34 years | 149 | 71 | 294 | 370 | 182 | 457 | 634 |
| 35 to 39 years | 264 | 165 | 524 | 444 | 288 | 597 | 1,173 |
| 40 to 44 | 300 | 239 | 526 | 435 | 283 | 578 | 1,179 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| years | | | | | | | |
| 45 to 49 years | 260 | 243 | 427 | 297 | 258 | 483 | 875 |
| 50 to 54 years | 190 | 261 | 332 | 232 | 257 | 367 | 740 |
| 55 to 59 years | 124 | 188 | 237 | 156 | 204 | 195 | 524 |
| 60 and 61 years | 33 | 53 | 58 | 41 | 50 | 70 | 174 |
| 62 to 64 years | 31 | 62 | 71 | 65 | 85 | 93 | 175 |
| 65 and 66 years | 23 | 34 | 41 | 36 | 40 | 49 | 104 |
| 67 to 69 years | 27 | 58 | 50 | 51 | 53 | 62 | 166 |
| 70 to 74 years | 23 | 61 | 81 | 74 | 51 | 78 | 142 |
| 75 to 79 years | 18 | 28 | 61 | 52 | 38 | 59 | 132 |
| 80 to 84 years | 13 | 11 | 42 | 30 | 19 | 40 | 58 |
| 85 years and over | 9 | 10 | 20 | 9 | 11 | 21 | 42 |
| **Female:** | **2,385** | **2,379** | **4,816** | **2,680** | **2,954** | **5,611** | **10,430** |
| Under 5 years | 185 | 182 | 426 | 196 | 237 | 467 | 921 |
| 5 to 9 years | 211 | 226 | 448 | 199 | 199 | 447 | 996 |
| 10 to 14 years | 221 | 219 | 440 | 196 | 197 | 500 | 830 |
| 15 to 17 years | 94 | 86 | 196 | 107 | 117 | 227 | 440 |
| 18 and 19 years | 29 | 25 | 76 | 39 | 46 | 103 | 156 |
| 20 years | 11 | 7 | 22 | 24 | 11 | 48 | 52 |
| 21 years | 15 | 6 | 26 | 12 | 16 | 39 | 45 |
| 22 to 24 years | 69 | 26 | 76 | 70 | 47 | 131 | 129 |
| 25 to 29 years | 95 | 24 | 163 | 141 | 114 | 318 | 348 |
| 30 to 34 years | 163 | 92 | 351 | 210 | 193 | 544 | 806 |
| 35 to 39 years | 286 | 197 | 561 | 262 | 327 | 624 | 1,176 |
| 40 to 44 years | 294 | 283 | 544 | 259 | 332 | 551 | 1,192 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 45 to 49 years | 238 | 284 | 435 | 232 | 276 | 448 | 899 |
| 50 to 54 years | 170 | 245 | 311 | 183 | 248 | 367 | 714 |
| 55 to 59 years | 109 | 151 | 213 | 126 | 189 | 226 | 539 |
| 60 and 61 years | 36 | 65 | 65 | 43 | 66 | 71 | 163 |
| 62 to 64 years | 42 | 68 | 90 | 47 | 66 | 77 | 167 |
| 65 and 66 years | 20 | 31 | 37 | 32 | 42 | 51 | 92 |
| 67 to 69 years | 27 | 50 | 61 | 53 | 53 | 62 | 131 |
| 70 to 74 years | 28 | 43 | 92 | 90 | 48 | 107 | 206 |
| 75 to 79 years | 26 | 25 | 82 | 85 | 50 | 90 | 157 |
| 80 to 84 years | 9 | 17 | 51 | 34 | 43 | 76 | 129 |
| 85 years and over | 7 | 27 | 50 | 40 | 37 | 37 | 142 |

**APPENDIX B**

Cancer Incidence Massachusetts

City/Town Supplement 2001-2005 Summary

| |
|---|
| Obs = observed case count; Exp = expected case count; |
| SIR = standardized incidence ratio ( (Obs / Exp) X 100); |
| 95% CI = 95% confidence intervals, measure of the statistical significance of the SIR; |
| Shading indicates the statistical significance of the SIR at 95% level of probability; |
| nc = The SIR and 95% CI were not calculated when Obs < 5; |

| ASHBURNHAM | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 2 | 4.8 | nc | (nc-nc) |
| Female | 2 | 1.6 | nc | (nc-nc) |

| BERLIN | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 4 | 2.7 | nc | (nc-nc) |
| Female | 0 | 0.9 | nc | (nc-nc) |

| BOXBOROUGH | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 2 | 3 | nc | (nc-nc) |
| Female | 1 | 0.9 | nc | (nc-nc) |

| BOYLSTON | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 5 | 4.4 | 113.8 | (36.7-265.7) |
| Female | 3 | 1.5 | nc | (nc-nc) |

| CARLISLE | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 4 | 4.6 | nc | (nc-nc) |
| Female | 0 | 1.4 | nc | (nc-nc) |

| GROTON | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 13 | 7.4 | 176.3 | (93.8-301.5) |
| Female | 2 | 2.5 | nc | (nc-nc) |

| HARVARD | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 5 | 5.6 | 89.1 | (28.7-207.9) |
| Female | 1 | 1.5 | nc | (nc-nc) |

| LUNENBURG | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 10 | 10.3 | 96.7 | (46.3-177.8) |
| Female | 4 | 3.4 | nc | (nc-nc) |

| SHIRLEY | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 5 | 6.3 | 78.8 | (25.4-184.0) |
| Female | 0 | 2.1 | nc | (nc-nc) |

| STOW | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 6 | 5.2 | 116.5 | (42.5-253.5) |
| Female | 3 | 1.8 | nc | (nc-nc) |

| TYNGSBOROUGH | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 11 | 7.4 | 149 | (74.3-266.6) |
| Female | 7 | 2.6 | 265.6 | (106.4-547.3) |

| WESTFORD | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 18 | 15.2 | 118.7 | (70.3-187.5) |
| Female | 7 | 5.5 | 128.3 | (51.4-264.3) |

| WESTMINSTER | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 8 | 7 | 113.6 | (48.9-223.8) |
| Female | 1 | 2.3 | nc | (nc-nc) |

**Source:-**

Mass.gov. "The Official Website of the Office of Health and Human Services (EOHHS)." *Cancer Incidence in Massachusetts - City/Town Supplement 2000-2004.* 2009. You do not have to show the entire citation here.

City/Town Supplement 2000-2004 Summary

| ASHBURNHAM | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 2 | 4.8 | nc | (nc-nc) |
| Female | 2 | 1.5 | nc | (nc-nc) |

| BERLIN | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 2 | 2.7 | nc | (nc-nc) |
| Female | 0 | 0.9 | nc | (nc-nc) |

| BOXBOROUGH | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 1 | 3 | nc | (nc-nc) |
| Female | 1 | 0.9 | nc | (nc-nc) |

| BOYLSTON | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 5 | 4.4 | 114 | (36.7-265.9) |
| Female | 3 | 1.4 | nc | (nc-nc) |

| CARLISLE | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 3 | 4.6 | nc | (nc-nc) |
| Female | 0 | 1.3 | nc | (nc-nc) |

| GROTON | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 14 | 7.3 | 192.7 | (105.2-323.3) |
| Female | 1 | 2.4 | nc | (nc-nc) |

| HARVARD | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 6 | 5.7 | 105.5 | (38.5-229.6) |
| Female | 1 | 1.5 | nc | (nc-nc) |

| SHIRLEY | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 6 | 6.4 | 94.2 | (34.4-204.9) |
| Female | 0 | 2 | nc | (nc-nc) |

| STOW | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 4 | 5.1 | nc | (nc-nc) |
| Female | 3 | 1.7 | nc | (nc-nc) |

| TYNGSBOROUGH | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 11 | 7.4 | 149.3 | (74.4-267.2) |
| Female | 5 | 2.6 | 195.3 | (62.9-455.8) |

| WESTFORD | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 16 | 15.2 | 105.6 | (60.3-171.4) |
| Female | 6 | 5.3 | 112.8 | (41.2-245.5) |

| WESTMINSTER | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 9 | 7 | 128.1 | (58.4-243.2) |
| Female | 0 | 2.3 | nc | (nc-nc) |

**Source:-**

Mass.gov. "The Official Website of the Office of Health and Human Services (EOHHS)." *Cancer Incidence in Massachusetts - City/Town Supplement 2000-2004.* 2009.

Cancer Incidence for all towns in Barnstable County

| BARNSTABLE | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 83 | 73.9 | 112.4 | (89.5-139.3) |
| Female | 19 | 25.9 | 73.2 | (44.1-114.4) |

| BREWSTER | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 16 | 20.1 | 79.4 | (45.4-129.0) |
| Female | 12 | 7.1 | 169.8 | (87.7-296.7) |

| BOURNE | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 24 | 25.4 | 94.3 | (60.4-140.4) |
| Female | 14 | 9.2 | 152.4 | (83.2-255.7) |

| CHATHAM | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 23 | 16.9 | 135.9 | (86.1-204.0) |
| Female | 11 | 6 | 183.4 | (91.4-328.2) |

| DENNIS | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 39 | 33.6 | 116.2 | (82.6-158.8) |
| Female | 17 | 11.7 | 145.7 | (84.8-233.3) |

| EASTHAM | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 18 | 11.4 | 157.9 | (93.5-249.6) |
| Female | 6 | 3.5 | 170.7 | (62.3-371.5) |

| FALMOUTH | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 67 | 56.2 | 119.2 | (92.4-151.4) |
| Female | 16 | 20.3 | 78.8 | (45.0-128.0) |

| HARWICH | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 27 | 26.3 | 102.7 | (67.7-149.5) |
| Female | 13 | 10.1 | 129.3 | (68.8-221.2) |

| MASHPEE | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 30 | 19.9 | 150.8 | (101.8-215.4) |
| Female | 5 | 6.8 | 73.9 | (23.8-172.5) |

| ORLEANS | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 30 | 16.5 | 181.7 | (122.6-259.4) |
| Female | 11 | 5.9 | 187.3 | (93.4-335.2) |

| PROVINCETOWN | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 11 | 5.1 | 217.3 | (108.3-388.8) |
| Female | 2 | 1.7 | nc | (nc-nc) |

| SANDWICH | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 35 | 23.3 | 150.3 | (104.7-209.1) |
| Female | 11 | 8.4 | 131.1 | (65.3-234.5) |

| TRURO | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 3 | 3.2 | nc | (nc-nc) |
| Female | 0 | 1.1 | nc | (nc-nc) |

| WELLFLEET | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 8 | 4.9 | 163.7 | (70.5-322.6) |
| Female | 3 | 1.6 | nc | (nc-nc) |

| YARMOUTH | | | | |
|---|---|---|---|---|
| | **Obs** | **Exp** | **SIR** | **95% CI** |
| **Bladder, Urinary** | | | | |
| Male | 75 | 52.9 | 141.7 | (111.4-177.6) |
| Female | 23 | 19.7 | 116.9 | (74.1-175.4) |

**Source:-**

Mass.gov. "The Official Website of the Office of Health and Human Services (EOHHS)." *Cancer Incidence in Massachusetts - City/Town Supplement 2000-2004.* 2009.

## APPENDIX C

Town Hall Contact sheet and information

| TOWN | ADDRESS | PHONE # TOWN HALL | TOWN POPULATION | PUBLIC | GEOLOGY | PRIVATE | GEOLOGY | REFERENCE |
|---|---|---|---|---|---|---|---|---|
| Acton | 472 Main St | 978-264-9612 | 23,000 | 99% | Gravel Packed wells | 1% | Unknown, likely bedrock | Rick Linde, Foreman of the Water Dept. |
| Ashburnham | 32 Main Street | 978-827-4104 | 5,546 | 43% | Gravel Packed | 57% | Likely bedrock | Water Department |
| Ashland | 101 Main Street | 508-881-0100 | 16,340 | 99.9% | Gravel Packed wells | 0.10% | | Deborah Mercer, Business Manager, DPW, Ashland |
| Berlin | 12 Wood-ward Avenue | 978-838-2931 | 2,880 | 0% | | 100% | Unknown, likely bedrock | Eloise Salls, Town Clerk |
| Boxborough | 29 Middle Road | 978-263-1116 | 53,305 | 0% | | 100% | Mostly bedrock | Elizabeth Hughes, Town Planner |
| Boylston | 221 Main Street | 508-869-2234 | 4,300 | 50% | MWRA, Surface Water | 50% | Unknown, likely bedrock | Boylston Town Water Supply |
| Carlisle | 66 Westford Street | 978-369-6155 | 5,320 | 0% | | 100% | Mostly bedrock | Department of Public Works |
| Clinton | 242 Church Street | 978-365-4119 | 13,435 | 99% | Surface water | 1% | Likely bedrock | Lisa Prophet, Secretary, DPW |
| Framingham | 150 Concord St | 508-532-5520 | 64,786 | 98% | MWRA | 1% | Likely bedrock | Jane, DPW |
| Gardner | 95 Pleasant Street | 978-630-4008/9 | 20,000 | 85% | Surface and Groundwater | 15% | Unknown, likely bedrock | Department of Public Works |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Groton | 173 Main St | 978-448-1100 | 10,563 | 0 | Surface water and wells, Merrimack Basin | 60% | Bedrock and unconsolid-ated | Patricia Dufresene, Business Manager |
| Harvard | 13 Ayer Road | 978-456-4100 X 16 | 5,741 | 2.70% | Bedrock | 97% | Bedrock and Artesian | Rich Nota, Director DPW |
| Hopkinton | 18 Main Street | 508-497-9710 | 12,000 | 80% | Groundwat-er, gravel pack | 20% | Unknown, likely bedrock | Eric Carty, DPW |
| Hudson | 78 Main Street | 978-568-9615 | 18,600 | 85% | Surface water and gw | 15% | Unknown, likely bedrock | Anthony Marques, Director DPW |
| Lancaster | 695 Main Street | 978-365-2542 | 8,200 | 6000 | Groundwat-er, gravel pack | 2200 | Mostly bedrock | Robert Pelletier, Water Department |
| Lunenberg | | 978-582-4130 | 10,000 | 37% | Groundwat-er, gravel packed | 63% | Bedrock | Fran McNamara, Superintendent Lunenberg |
| Northborough | 63 Main street | 508-393-5001 | 15,000 | 80% | Purchased from MWRA | 20% | Bedrock | Kara Buzanoski, Director, DPW |
| Pepperell | One Main Street | 978-433-0333 | 12,200 | 80% | Groundwat er, gravel packed, | 20% | Bedrock | Bob Lee Director DPW |
| Shirley | 7 Keady Way | 978-425-2600 x205 | 6,000 | 50% | Gravel Packed | 50% | Mostly bedrock | Rhonda Caissie, Treasurer, Water Department |
| Shrewsbury | 100 Maple Avenue | 508-841-8507 | 34,000 | 99% | Gravel Packed | 1% | Unknown, likely bedrock | Robert Moore, Sanitarian Health Department |
| Southborough | 17 Common street | 508-485-0710 | 10,000 | 80% | MWRA, Surface Water | 20% | Unknown, likely bedrock | Jane Johnson, Administrative Secretary, Water Department |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Sterling | 1 Park St. | 978-422-8111 | 7,257 | 80% | Gravel Packed and Surface Water | 20% | Unknown, likely bedrock | Website:- http://www.sterling-ma.gov/Pages/SterlingMA_DPW/water |
| Stow | 380 Great Road | 978-897-4514 | 6,300 | 10% | Gravel packed | 90% | Mostly bedrock | Wallace, Health Agent, Board of Health |
| Sudbury | 278 Old Sudbury Road | 978-639-3381 | 14,900 | 95% | Gravel Packed | 5% | Mostly bedrock | Renee Adams, Customer Service Manager, Water District Sudbury |
| Townsend | 272 Main Street | 978-597-1704 | 9,501 | 50% | Gravel Packed & Tubular well | 50% | Unknown, likely bedrock | Micheal Maccearchern, Water Tech 1, Townsend Water Commission |
| Tyngsborough | 25 Bryants Lane | 978-649-2300 | 11,800 | 50% | Gravel Packed | 50% | Likely Bedrock | Joan Ferrari, Health Administrator, Board of Health |
| West Boylston | 127 Hartwell Street | 508-835-6240 | | 99% | Sand and gravel pack | 1% | Unknown, likely bedrock | Micheal Coveney, Superintendent of Water District |
| Westborough | 34 West Main Street | 508-366-3020 | 18,000 | 90% | Gravel Pack and MWRA | 10% | Unknown, likely bedrock | John Walden, Manager, Department of Public Works |
| Westford | 55 Main Street | 978-692-5500 | 23,000 | 25% | Gravel Packed | 75% | Mostly bedrock | Rae Dick, Health Agent, Board of Health |
| Westminster | 11 South Street | 978-874-7406 | 7,000 | 40% | Gravel Packed | 60% | Mostly bedrock | Rita McConville, Assistant Health Agent, Board of Health |

## Appendix D

Risk Calculation

| County of Concern | EPC | RAF | Intake | Freq | Duration | Exp. Period | CF | BW | AP | LADD | SF | ELCR |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | |
| | µg/L | | L/day | day/wk | wk/yr | yr | | kg | days | mg/kg*day | (mg/kg*day)^1 | |
| | | | | | | | | | | | | |
| Middlesex | 0.2 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 2.4E-06 | 1.5E+00 | 3.5E-06 |
| | 1 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 1.2E-05 | 1.5E+00 | 1.8E-05 |
| | 5 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 5.9E-05 | 1.5E+00 | 8.9E-05 |
| | 10 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 1.2E-04 | 1.5E+00 | 1.8E-04 |
| | 15 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 1.8E-04 | 1.5E+00 | 2.7E-04 |
| | 20 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 2.4E-04 | 1.5E+00 | 3.5E-04 |
| | 25 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 3.0E-04 | 1.5E+00 | 4.4E-04 |
| | 26 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 3.1E-04 | 1.5E+00 | 4.6E-04 |

| | EPC | RAF | Intake | Freq | Duration | Exp. Period | CF | BW | AP | LADD | SF | ELCR |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | |
| **Worcester** | µg/L | | L/day | day/wk | wk/yr | yr | | kg | days | mg/kg*day | (mg/kg*day)^1 | |
| | | | | | | | | | | | | |
| | 0.2 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 2.4E-06 | 1.5E+00 | 3.5E-06 |
| | 1 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 1.2E-05 | 1.5E+00 | 1.8E-05 |
| | 5 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 5.9E-05 | 1.5E+00 | 8.9E-05 |
| | 10 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 1.2E-04 | 1.5E+00 | 1.8E-04 |
| | 12 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 1.4E-04 | 1.5E+00 | 2.1E-04 |

| Probabilities of concern | EPC | RAF | Intake | Freq | Duration | Exp. Period | CF | BW | AP | LADD | SF | ELCR |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | |
| | µg/L | | L/day | day/wk | wk/yr | yr | | kg | days | mg/kg*day | (mg/kg*day)^1 | |
| | | | | | | | | | | | | |
| less than 0.2µg/L -10 µg/L | 0.2 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 2.4E-06 | 1.5E+00 | 3.5E-06 |
| | 1 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 1.2E-05 | 1.5E+00 | 1.8E-05 |
| | 5 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 5.9E-05 | 1.5E+00 | 8.9E-05 |
| | 10 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 1.2E-04 | 1.5E+00 | 1.8E-04 |
| less than 0.2µg/L -22 µg/L | 0.2 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 2.4E-06 | 1.5E+00 | 3.5E-06 |
| | 1 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 1.2E-05 | 1.5E+00 | 1.8E-05 |
| | 5 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 5.9E-05 | 1.5E+00 | 8.9E-05 |
| | 10 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 1.2E-04 | 1.5E+00 | 1.8E-04 |
| | 15 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 1.8E-04 | 1.5E+00 | 2.7E-04 |
| | 20 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 2.4E-04 | 1.5E+00 | 3.5E-04 |
| | 22 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 2.6E-04 | 1.5E+00 | 3.9E-04 |
| less than 0.2µg/L -26 µg/L | 0.2 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 2.4E-06 | 1.5E+00 | 3.5E-06 |
| | 1 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 1.2E-05 | 1.5E+00 | 1.8E-05 |
| | 5 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 5.9E-05 | 1.5E+00 | 8.9E-05 |
| | 10 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 1.2E-04 | 1.5E+00 | 1.8E-04 |
| | 15 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 1.8E-04 | 1.5E+00 | 2.7E-04 |
| | 20 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 2.4E-04 | 1.5E+00 | 3.5E-04 |
| | 25 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 3.0E-04 | 1.5E+00 | 4.4E-04 |
| | 26 | 1 | 2 | 7 | 50 | 30 | 0.001 | 65 | 27375 | 3.1E-04 | 1.5E+00 | 4.6E-04 |