Geographic Exposure and Risk Assessment for Food Contaminants in Canada

by

Roslyn Cheasley
B.Sc., University of Victoria, 2010

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Supervisory Committee

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Abstract

The purpose of this thesis is to explore differences in lifetime excess cancer risk (LECR) for Canadians from intake of contaminants in food and beverages based on geographic location, gender and income levels. A probabilistic risk assessment approach (Monte Carlo simulation) was used to estimate the range and frequency of possible daily contaminant intakes for Canadians, and associate these intake levels with lifetime excess cancer risk. Monte Carlo risk simulation was applied to estimate probable contaminant intake and associated lifetime excess cancer risk from arsenic, benzene, lead, polychlorinated biphenyls (PCBs) and tetrachloroethylene (PERC) in 60 whole foods from the dietary patterns of 34,944 Canadians from 10 provinces, as derived from Health Canada's Canadian Community Health Survey, Cycle 2.2, Nutrition (2004)[1]. These results were compared to the current Health Canada guideline that suggests that 10 extra cancers per one million people is a negligible risk. Of the 5 contaminants tested in my model arsenic showed the greatest difference between urban and rural estimated lifetime excess cancer risk, although extra cancers in both rural and urban Canada were predicted from exposure to PCB and benzene. Lifetime excess cancer risk is estimated to be higher for men in Canada for all five contaminants, with an emphasis on males in British Columbia compared to females from the dietary intake of arsenic. When based on income level, my model predicts extra cancers higher for low and middle incomes from dietary exposures to arsenic, benzene, lead and PERC, however, high income populations are more likely to have extra cancers from dietary intake of PCBs.

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Acknowledgments

I extend my heartfelt gratitude to my committee members, whose insightful questions and comments allowed me to probe deeper into the analysis results and assessment outcomes for a greater, in-depth understanding of the process and procedures of conducting risk assessments.

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1.0 Introduction

1.1 Research Context

We often hear about acute health issues related to food and beverages (i.e., e coli outbreaks; salmonella poisoning), but less is known about the incidence and prevalence of adverse impacts due to the long term intake of low levels of contaminants, including known carcinogens. This may be due, in part, to the challenging nature of assessing dietary exposure over time.

The most accurate assessments of dietary exposure to carcinogens over time would use a direct approach, recording every day each food item and the amount consumed, and analyzing a duplicate sample for contaminant concentrations, for every individual. This may be realistic for a short period of time for a very small study group. However, the more people involved in the study, and the longer the time period of interest, the more such an approach becomes unfeasible.

Many dietary exposure studies for large populations therefore rely on an indirect approach incorporating a number of assumptions that may not reflect the actual variability in contamination of food and amount of foods consumed. They usually capitalize on and combine existing datasets, collected by different agencies, to estimate dietary intake of contaminants and the associated health risks. Indirectly estimating dietary exposure (and risk) can be achieved by either a deterministic or a probabilistic methodology. Deterministic, also known as 'point estimate' assessment[2], uses single values for ingested amounts and contaminant concentrations to represent exposure. This approach is typically used in screening-level assessments with maximum levels for ingestion and concentrations (i.e., 'worst-case' scenario), as the results produce a conservative, high-end risk estimate and are simple, inexpensive to produce, and relatively easy to communicate[3]. Probabilistic assessments utilize probability theory and sampling to generate risk estimates, often combining distributions of data from multiple

sources[2,3]. One probabilistic model is Monte Carlo simulation, which is used to repeatedly draw random dietary records and contaminant values from distributions of measured carcinogen concentration levels and recorded dietary patterns to produce a distribution of probable intake levels[4–6].

1.2 Research Objectives

This research began in 2009 as part of the CAREX Canada project, which focuses on compiling publically-available data for selected known and suspected carcinogens to develop national indicators of possible exposures via air, water and food and beverages[7]. A deterministic approach of risk assessment was used in the calculation of intake and exposure to contaminants. When updating the information in 2013, a probabilistic risk methodology was used to estimate contaminant exposure in food and beverages producing results that are likely more realistic than the conservative, deterministic values.

The goal of this thesis was to explore such a probabilistic effort. Research reported here therefore summarizes preliminary probabilistic assessments of lifetime excess cancer risk in Canada for a selected group of substances which have been classified as known carcinogens and detected in North American foods. These include arsenic[8], benzene[9], lead[10], polychlorinated biphenyls (PCBs)[11] and tetrachloroethylene (PERC)[12]. The assessments are considered preliminary due to data limitations encountered; however, the results produced here are useful to inform next steps for more detailed modelling.

Food consumption data are for a representative sample population based on a 2004 national survey on nutrition conducted by Health Canada and published as the Canadian Community Health Survey (CCHS), Cycle 2.2, Nutrition[1]. This survey recorded the daily dietary intake of approximately 35,000 participants distributed across Canada's ten (10) provinces (territories

were excluded). The CCHS data include variables that allow for risk assessments based on gender for each province; national income level (low; middle; high); and urban vs. rural inhabitants. These dietary patterns include the daily intake, in grams (g), of all foods consumed over a 24-hour period. It does not give any information about the contaminant content of ingested foods.

Contaminant content and concentration level data for the various foods were obtained from the Canadian Food Inspection Agency's (CFIA)[13] National Chemical Residue Monitoring Program (NCRMP), the US-Food & Drug Administration (US FDA) Total Diet Study (TDS) Elements Summary 2006-2011[14] and the US-FDA TDS results from 1991-2006[15]. CFIA's National Chemical Residue Monitoring Program tests for residues of metals, including arsenic and lead, in domestic and imported dairy products, eggs, honey, meat products, fresh fruit and vegetables[13]. The US FDA Total Diet Study results from 1991-2006 reported residue levels for benzene, PCBs and PERC in a wide variety of food and beverages[15]. The US FDA (TDS) Elements Summary 2006-2011 published results for arsenic and lead found in various food and beverages[14].

For this research, the above data on consumption patterns and distributions of measure levels in commonly consumed foods were analysed using a Monte Carlo simulation risk model developed with Palisade Corporation's @RISK Monte Carlo simulation software to yield estimates of probable lifetime dietary contaminant exposures.

1.3 Thesis organization

This thesis is presented in three sections:

Section one provides reviews of key components of the research, including brief overviews of health risk assessment; probabilistic approaches to risk assessment; dietary risk assessment for food consumption in general, including a review of data availability for dietary risk assessment in Canada and the US', an explanation of the contaminants selected for study in this thesis and detailed descriptions of the methodological approach, data used and assumptions made for this study.

Section two is made up of two separate papers presenting results, formatted for submission to scientific journals. The first of these papers focusses on the differences between urban and rural lifetime excess cancer risk from food and beverages for the five named substances; the second on the differences between arsenic intake and potential lifetime excess cancer risk for several sample groups including gender by province, and income level.

The final section of the thesis brings the two papers together presenting concluding remarks and recommendations for future dietary exposure endeavours.

2.0 Dietary Health Risk Assessment Overview

2.1 Overview of Health Risk Assessment

The Industrial Revolution, beginning in the mid-nineteenth century, brought many advances, socially, technologically, and economically, to our way of living around the world, and with these advances, numerous toxic substances have been introduced to our planet. Although we have been studying chemical compounds for centuries[16,17], we continue to investigate and discover new possible harmful implications of chemical compounds to human health[17].

The United States has been a North American leader in the development of regulatory health risk assessment. The United States created federal laws in 1906 mandating control over substances including pesticides that were additives or contaminants to foods. Epidemiological studies and toxicology testing were the early drivers of change in assessing exposure to industrial chemicals and other pollutants as evidence of adverse health effects to certain contaminants began to materialize in the workplace and elsewhere[16,17].

In the latter half of the twentieth century, a significant shift occurred in the traditional ways of assessing exposure to both environmental and industrial contaminants in food, water, air, and soil, etc., and evaluating any adverse health effects[16–19]. This shift is sometimes associated with Rachel Carson's publication of "*Silent Spring*" (1962) where she described the potential health hazards regarding widespread use of the pesticide DDT[20]. Before the publication of Carson's book the notion of '*exposure assessment*' did not really exist[21,22]. In the early 1970s the Environmental Protection Agency (EPA) was established by the US Federal Government, with one of its mandates to regulate the use of pesticides like DDT[17]. In 1983 the National Academy of Sciences (NAS) established standards and practices for conducting risk assessments published in what has become known as the "Red Book", and subsequently in 2008 in the "Silver Book"[17].

These standards are now widely adopted, and the US-EPA has emerged as a world leader in environmental monitoring, risk assessment and risk management practices[21].

Following the recommendations laid out in the "Red Book", the US-EPA has established a *4-Step Risk Assessment Process* consisting of following fundamental steps: 1) Hazard Identification; 2) Dose-Response Assessment; 3) Exposure Assessment; and 4) Risk Characterization (Figure 1). The following section reviews each of these four basic steps as they pertain to risk assessment of carcinogens in food and beverages[3].

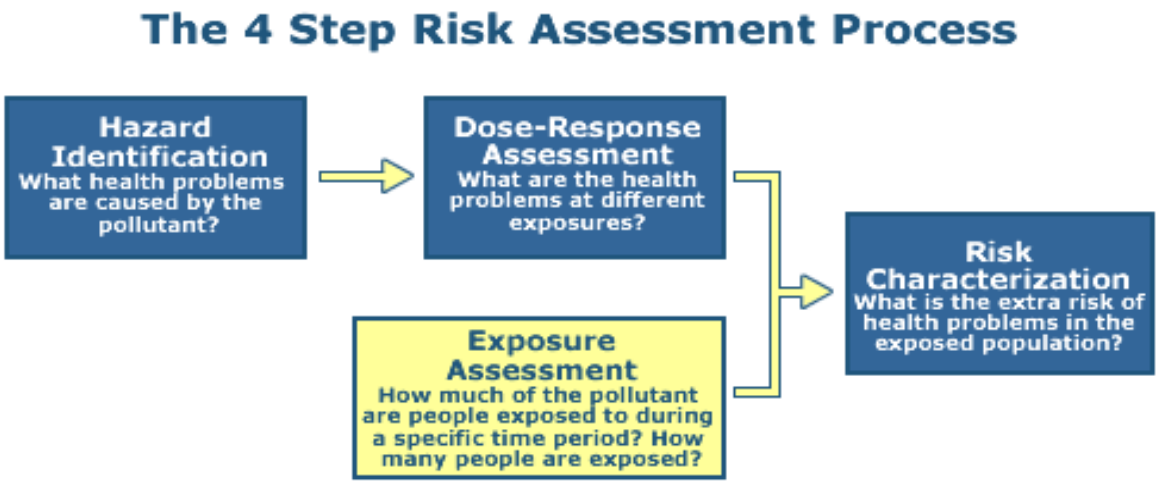


Figure 1: Risk Assessment Process from US EPA

2.1.1 STEP 1: Hazard Identification

The US EPA defines hazard identification as "the process of determining whether exposure to a stressor can cause an increase in the incidence of specific adverse health effects (e.g., tumor formation, organ distress/failure, birth defects) and whether the adverse health effect is likely to occur in humans"[23].

Hazard identification may use a variety of study methods to evaluate health risks (either cancer or non-cancer outcomes) to humans due from exposure to a chemical or other type of stressor. In practice, this is typically accomplished via toxicological and/or epidemiological studies (Figure 2).

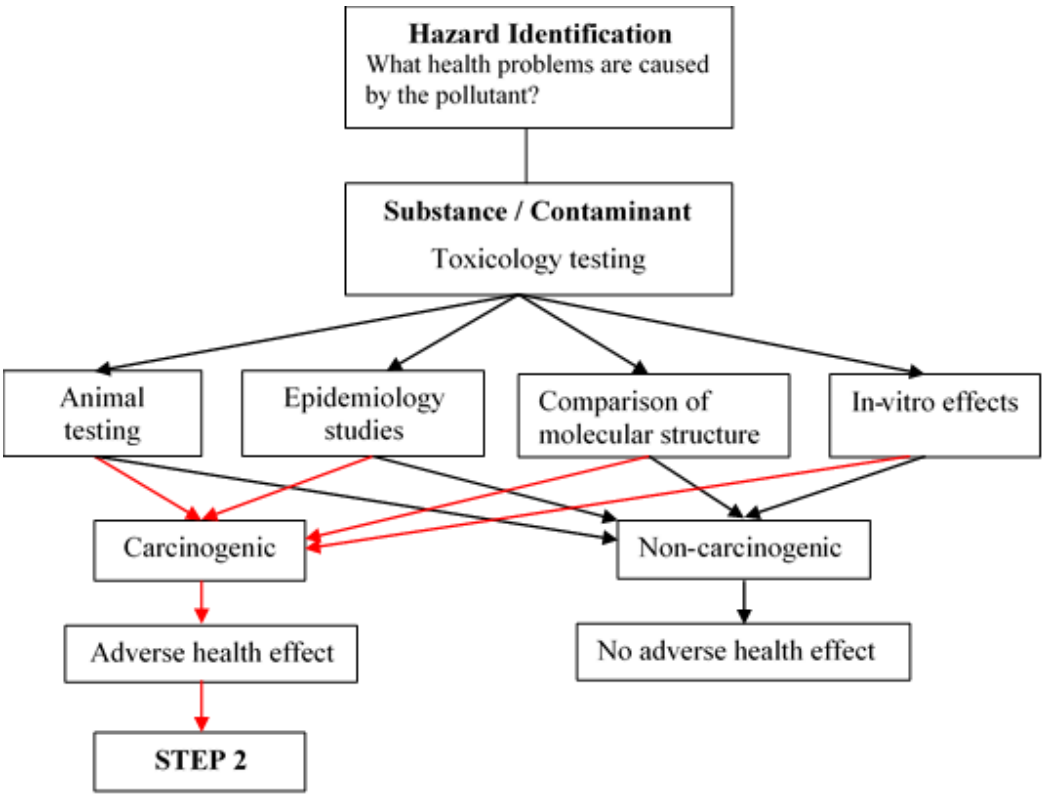


Figure 2: Hazard Identification Process

According to the National Academy of Science, four classes of information may be used in hazard identification: epidemiologic data, animal-bioassay data, data on in-vitro effects and comparisons of molecular structure[22]. For ethical and economic reasons, most evidence in the past has come from toxicological studies involving animals rather than humans, although some evidence comes from epidemiological studies of humans exposed in workplaces or who live in polluted areas[17,19].

Animal experimentation dates back to 1915, when Japanese scientists used skin painting studies in rabbits to detect carcinogenicity[24]. In the 1940s, to better understand how exposure to contaminants in food could potentially lead to wide-spread exposure-related health issues, the US-FDA initiated animal testing as the primary method of detection. This was for ethical reasons, and also because studies could be targeted, controlled and were then less costly to conduct[17,25]. The FDA published its "Procedures for the Appraisal of the Toxicity of Chemicals in Food" in 1949 as a guide for food producers and manufacturers where "FDA scientists pioneered the use of animal studies to predict potential chemical hazards (including carcinogenicity) in humans, and laid the early foundation for the use of animal data in human health risk assessment"[25]. In the 1970s the use of results from animal studies to evaluate carcinogenicity in humans gained worldwide acceptance[25], especially since using small, whole animals with relatively short life spans accommodated the testing of a much larger number of chemicals than human testing would ever allow[19].

An important limitation of using animals to test for chemicals regarding safety is the uncertainty of whether the effect observed in an animal (rodent, for example) will also be observed in humans[26,27]. Adverse effects in animals are sometimes not found in humans. For example, a recent study undertook toxicology testing for dietary intake of ochtravin A (OTA)

which is considered a "possible risk factor for adverse renal effects in humans"[26]. An increased incidence of kidney tumors in rat studies was indicated at high doses (50ug/kg/day) of OTA. Follow-up epidemiological studies, however, did not find a conclusive correlation between adverse effects in rats and a health hazard to humans[26]. Furthermore, other studies and reports have shown that many animal testing results are inadequate to substantiate claims of human carcinogenicity from the substances which produced tumors in animals[28]. Limitations notwithstanding, animal testing remains a preferred method in identifying potential human health hazards[25].

One of the most critical challenges to hazard assessment in the 21st century arises from the sheer number of chemicals in the environment. Currently, there is an effort to move from animal testing to the more high-throughput 'in vitro' testing strategies which would limit animal usage; increase the numbers of chemicals tested; and be more cost effective and timely[19,25,29]. Krewski (2009), details four approaches to toxicological testing, beginning with primarily animal-based testing, and moving to a human cell-based approach as a way to vastly increase the number of chemicals being evaluated (Table 1)[19].

Table 1: Proposed toxicological testing options

Option I	Option II	Option III	Option IV
In Vivo	Tiered In Vivo	In Vitro/In Vivo	In Vitro
Animal biology	Animal biology	Primarily human biology	Primarily human biology
High doses	High doses	Broad range of doses	Broad range of doses
Low throughput	Improved throughput	High and medium throughput	High throughput
Expensive	Less expensive	Less expensive	Less expensive
Time consuming	Less time consuming	Less time consuming	Less time consuming
Relative large number of animals	Fewer animals	Substantially fewer animals	Virtually no animals
Apical endpoints	Apical endpoints	Perturbations of toxicity pathways	Perturbations of toxicity pathways

Moving to high through put 'in vitro' testing, while providing many advantages in terms of finances, time-savings and reduction in animal usage, has important limitations. Just as one

cannot assume that health effects observed in animals will also be found in humans, it may also be difficult to relate changes at the cellular level under highly controlled conditions to the actual development of a disease in a person under real world conditions[28].

2.1.2 STEP 2: Dose-Response Assessment

The dose-response relationship is defined by the US-EPA as describing "how the likelihood and severity of adverse health effects (the responses) are related to the amount and condition of exposure to an agent (the dose provided)"[30]. Similar to hazard identification, dose-response relationships are established through conducting experiments via animal testing in a laboratory, clinical epidemiological studies, 'in vitro' analyses or from observational studies of humans exposed at work or in community settings (e.g., air pollution)[18,30–32]. In practice, establishing a dose-response relationship makes use of a wide array of advanced statistical techniques which are too complex to review here; however, some general considerations related to dose-response studies and the use of their results with respect to carcinogens are provided.

Dose-response is not necessarily a straight-line, linear relationship[30]. There exist curved, and even "U" shaped relationships, with sometimes significant differences in dose-response slopes when comparing observed, modelled and extrapolated data[33]. "U" shaped dose –responses generally are associated with the phenomenon of "hormesis" (Figure 3) where a small doses of a contaminant may have the opposite effect to that estimated for large doses[27]. What this means is that for any given substance, below a certain dose there may be no recognizable health effects, and in a U-shaped dose-response small doses may even have positive effect which turns harmful when the dose exceeds the U-shaped trough.

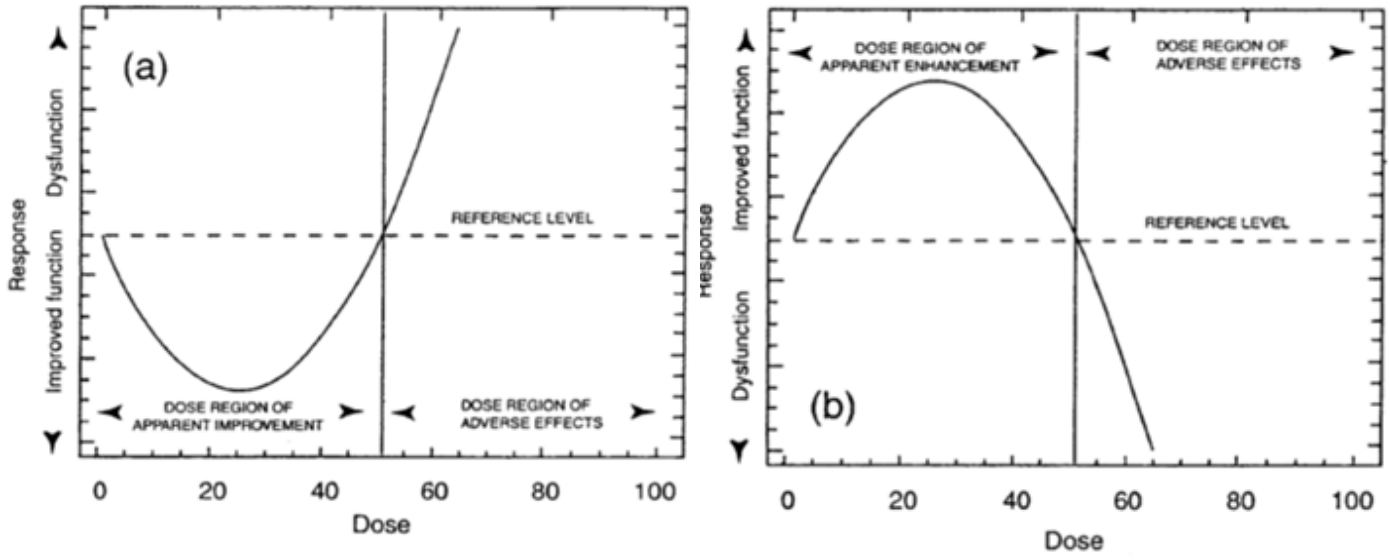


Figure 3: Dose responses to hermetic U-shaped curve

In order to set regulatory limits or guidelines, dose-response relationships are typically assumed either to have an identifiable threshold (non-carcinogenic substances), or to be linear with no threshold (carcinogenic subtances). For non-carcinogenic substances, the "no-observed effect level" (NOEL), the maximum dose where changes between test and control groups is indistinguishable, or the "lowest observed effect level" (LOAEL), which can be considered as the threshold for toxicity, are often used to set acceptable exposure levels (Figure 4)[29]. For carcinogenic substances the linear "no-threshold" hypothesis has been widely adopted, influenced in part by the incidences of radiation-induced cancers of the atomic bombings in 1945 and nuclear testing during the 1950s[17].

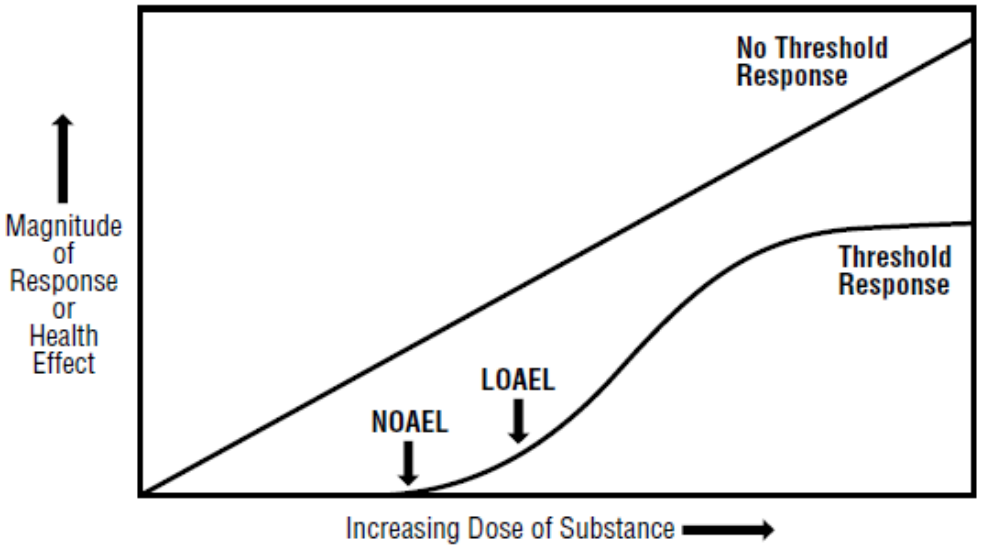


Figure 4: Threshold Response, Health Canada

The standard, straight-line relationship approach to cancer risk produces results that do not necessarily reflect effects at various levels of exposure and assumes that humans and animals are equally susceptible[27]. However, to be conservative regarding the thresholds established from animal data, an 'uncertainty factor' is typically factored in to account for humans' potential increased susceptibility to the substance being tested[28]. The linear 'no threshold' approach to carcinogens is considered conservative in establishing limits of contaminant intake and may over-estimate effects, resulting in regulatory limits that may have negative economic impacts[26]. Although there is mounting evidence that a hormetic model may better represent the dose-response relationship for some substances, changing current thinking and practices is a long and arduous process involving years of scientific evaluation and approval[27].

Once a dose-response relationship has been observed (or assumed) for carcinogenic substances, a 'cancer potency factor' or 'unit risk' factor can be derived. In extrapolating a linear relationship between risk and dose, a line is drawn from the point of departure (POD) (estimated dose that indicates a definable adverse health effect or toxic response) to the origin.

The slope of this line, aka, *slope factor* or *cancer potency factor* indicates the "upper-bound estimate of risk per increment of dose that can be used to estimate risk probabilities for different exposure levels"[33]. The 'unit risk' expresses the slope factor in terms of a standard intake rate derived for the various media of exposure[33].

2.1.3 STEP 3: Exposure Assessment

Exposure assessment has been defined as the qualitative evaluation and/or quantitative estimate of possible contaminants intake via various environmental media[16,34]. According to the US EPA, an exposure assessment, "measures the frequency, duration, and intensity of contact of an individual with the chemical or stressor"[35].

There are numerous pathways of exposure (Figure 5) including indoor- and outdoor air, drinking water and consumption of foods and beverages. Exposure routes include inhalation, ingestion and dermal absorption. The amount of exposure (also called intake) depends on various factors, such as activity engaged in, amounts consumed, or dermal absorption rates[16,18,32,36].

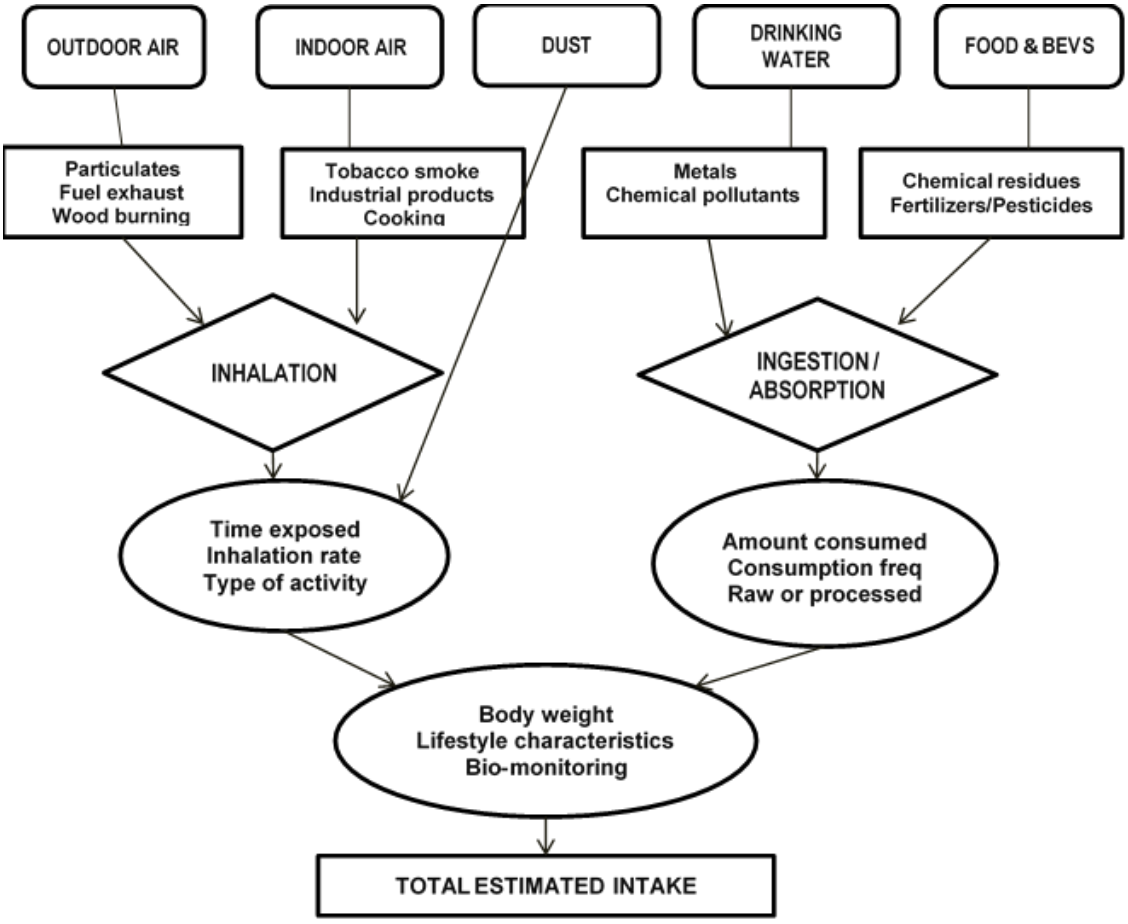


Figure 5: Exposure pathways and routes

Exposure assessments usually employ one of two main approaches: direct or indirect (Figure 6). A direct approach uses individual personal sampling and sometimes bio-monitoring, and is generally restricted to small study populations (several hundred to thousands) due to prohibitive costs. These studies are useful, however, as smaller population groups can be sampled, and the results generalized or used as a basis for modeling to a larger population[4–6]. The indirect approach uses data from various testing methods or sources, such as environmental monitoring (i.e., air quality measurements), contaminant monitoring (i.e., food and drinking water sampling results), or food frequency surveys (amount and type of foods consumed). The

indirect approach, which is based primarily around model building, can sometimes produce a wider range of possible outcomes and population cohorts at risk[37].

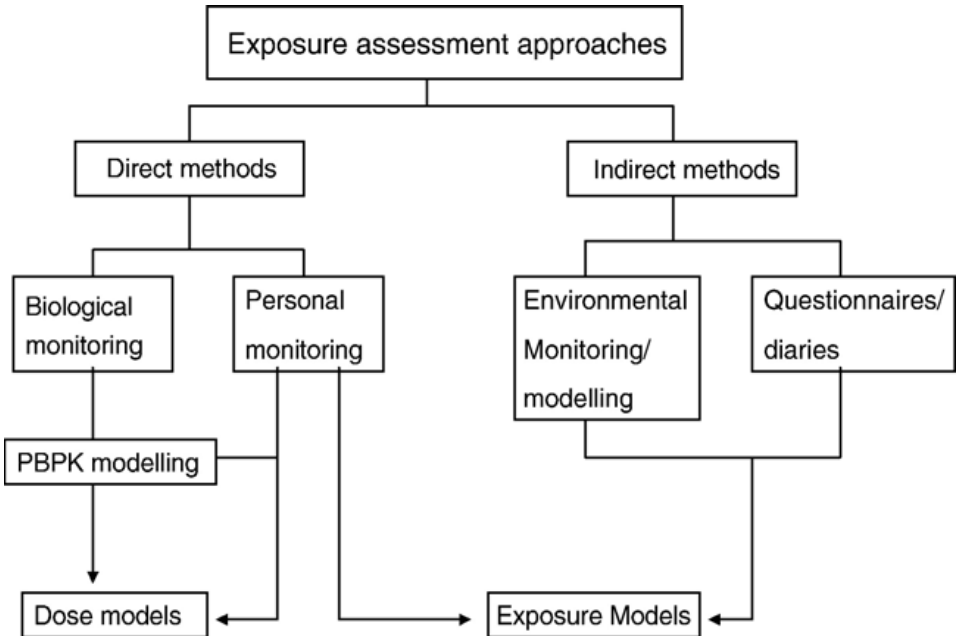


Figure 6: Exposure assessment methods

In its simplest conceptualization, dietary exposure is determined by:

Consumption frequency (g/d)	X	Chemical Residue (ug/g)	=	**Exposure (ug/d)**

Although it requires only two components (consumption frequency/amount and chemical residue levels in food items), there may be numerous variables; such as individual food items, individual substances, and sample population, in each component[7]. These may be much more complex to determine.

There are challenges in using a direct exposure approach for exposure via foods and beverages, with perhaps the most limiting being the logistics of obtaining and analyzing all the foods and beverages consumed over a period of time by each individual in the study. Not surprisingly Canadian studies using the direct exposure approach are typically those with a singular focus, for example, one or two contaminants in one or two food items/ groups[38–40], limited to one location[41–43], or based on the frequency of consumption, not ingested amounts[44,45]. Similarly, in the USA, studies using a direct approach are often targeted on a few contaminants[37,46,47], food items or locations[48–52].

The indirect exposure assessment approach is frequently used to model population exposure via foods and beverages. Food consumption recording methods may be automated and include pre-determined food lists, or require completing daily dietary diaries of all food items and amounts of each consumed. The result establishes the consumption frequency component of dietary exposure[53,54]. Data on contaminant levels in each of the foods consumed is also required. Total Diet Studies (TDS) are typically utilized to estimate contaminants in food and beverages among specific populations, and may be considered a form of exposure assessment[15,32,55–57]; however, in Canada they are narrow in scope as only selected foods from a single city for a limited number of substances are tested (e.g., since 2000 only radionuclides and some trace elements have been monitored)[58]. A more detailed review of indirect exposure assessment of dietary intake using probabilistic methods is included in Section 2.3, and a review of consumption and contaminant concentration data available for use in this thesis is provided in Section 2.4.

2.1.4 STEP 4: Risk Characterization

The fourth and final step in the overall risk assessment process is risk characterization[59]. Risk characterization combines information from the previous steps to produce an estimate of the level and likelihood of an increased health risk in a particular population. What kind of health impacts might occur is determined by the hazard identification step; how frequently they are expected to occur at a given dose is estimated by the dose/response information; dose levels for the study population are provided by the exposure assessment.

For non-carcinogenic health outcomes, the characterization of risk often includes a comparison of the estimated intake (dose) from the exposure assessment step with the NOAEL (no observed adverse effect level), or other similar threshold adopted by regulators. For example, Health Canada has used NOAELs as a basis for establishing tolerable daily intake (TDI) thresholds from various animal studies; for example, the pTDI (provisional TDI) of 25 ug/kg bw/day of bisphenol-A was based on a NOAEL of 5 mg/kg bw/day for observed toxic effects in rats and mice[60]. Although new studies and new NOAELs have been assessed since the establishment of the 1996 TDI level, the initial recommendation of 25 ug/kg bw/day continues to fall within prescribed limits[60].

For cancer outcomes, risk is typically expressed as lifetime excess cancer risk. This is calculated by multiplying the estimated exposure level (also called intake or dose) by the cancer potency factor derived in the dose/response step. There is not one universally-adopted set of cancer potency factors (CPFs) (or associated unit risk factors). The US EPA criteria for estimating cancer slope (potency) factors were established in the 1980s, when oral slope was defined as “an upper bound, approximating a 95% confidence limit, on the increased cancer risk from a lifetime oral exposure to an agent”[61]. Health Canada defines the ‘slope factor’ as the

"exposure dose that provides an upper bound estimate of the probability of occurrence of cancer or germ cell mutation in a chronically exposed population"[31]. The CA OEHHA characterizes 'cancer slope factor' as "the relationship between an applied dose of a carcinogen and the risk of tumor appearance in a human", usually expressed in units of reciprocal dose or unit risk[62]. Each agency adheres to basically the same criteria; however, they may differ in risk values reported for contaminants as their source data, usually based on animal bioassay data or human data, is neither universal, nor standardized. As a result, CPFs may differ between reporting agencies as evidenced in Table 2:

Table 2: Cancer Potency Factors

Cancer Potency Factors			
Substance	**Health Canada**	**CA OEHHA**	**US EPA**
Arsenic	1.8	1.5	1.5
Benzene	0.0834	-	0.055
Lead	-	0.0085	-
PCBs	-	2.0	2.0
PERC	-	0.051	0.0021

Risk characterization may also take other pertinent information and data into consideration to determine if, and where, risk of adverse health effects may occur. In a recent French study to characterize dietary risk of pesticide residues, a ranking and scoring method was developed integrating agricultural uses and food contamination data. The ranking levels were: "Levels 0 and 1 include substances which are not of concern in terms of chronic dietary exposure. Levels 2–6 include substances of concern (which should be sought), including priority substances (levels 4–6) which must be systematically sought in the major dietary contributors"[63]. The findings indicated that "of 336 substances analyzed in food in France, 70 pesticides (21%) of

concern (levels 2–5) must be closely monitored, including 22 (6%) as a matter of priority (levels 4 and 5)[63].

All in all, risk characterization provides a clearer understanding of the risk assessment findings and allows a vehicle to better communicate those results along with developing risk mitigation strategies to reduce potential risks to human health[64].

2.1.5 The role of the International Agency for Research on Cancer

While national governments may adopt different approaches to developing regulations or guidelines for contaminant levels in foods, many look to the International Agency for Research on Cancer (IARC) to identify contaminants known or suspected to cause cancer. IARC works closely with the scientific community to identify agents suspected of causing cancer using evidence of carcinogenicity and human exposure to prioritize further analysis and classification[65]. Working Groups of independent international experts are convened to conduct extensive evaluations for the agents suspected of causing cancer. The experts conduct rigorous analyses including a critical review of pertinent scientific evidence of cancers made up of epidemiological studies, animal testing data, and laboratory tests of how cancer develops in response to the agent[65]. Once the review is complete, a final assessment is made whether the agent causes cancer, and a classification is determined (Table 3).

Table 3: IARC Classification Groups

Group 1	Carcinogenic to humans	117 agents
Group 2A	Probably carcinogenic to humans	74 agents
Group 2B	Possibly carcinogenic to humans	287 agents
Group 3	Not classifiable as to its carcinogenicity to humans	503 agents
Group 4	Probably not carcinogenic to humans	1 agent

2.2 Probabilistic Methods in Exposure Assessment

In the absence of comprehensive data for the population of interest, for practical purposes regulators may adopt a 'screening level' approach to health risk assessment. This often takes the form of using a deterministic point-estimate model of 'worst-case' exposure, in which the highest consumption level possible is combined with the highest contaminant level observed to calculate intake. If the result falls below regulatory guidelines, it is assumed that no health impact will occur from usual intake and contaminant levels. A key issue with this approach is its conservative bias[6,18]. For example, if regulatory guidelines or thresholds are exceeded, further action is required (e.g., a more detailed exposure assessment) to establish more realistic exposure levels. Another issue is that neither the frequency nor variability of intake, or the combinations of contaminants, are reflected[6].

More complex probabilistic approaches to exposure address many of the limitations inherent in deterministic exposure assessments. Probabilistic models allow for the estimation of a range of likely exposure levels, quantifying uncertainties, and takes variability of the population sample into account[5,6]. One of the most common probabilistic techniques is Monte Carlo simulation, which was adapted in the early 2000s for the "development, validation and

application of stochastic modelling of human exposure to food chemicals and nutrients"[66]. It is a computerized mathematical technique that uses a probability distribution for factors that have inherent variability (or uncertainty)[67]. As defined by the US-FDA, the simulation process follows a standard procedure (Figure 7):

> "Rather than using a single value for such an input (e.g., a point estimate such as mean or 90th percentile food intake), the simulation selects a value at random from the distribution of possible values for that input, uses that value to calculate an outcome for the model, stores the result, and then repeats the procedure a predetermined number of times (or iterations). For each iteration, all data inputs, defined as probabilistic expressions, are randomly sampled such that each iteration is likely to produce a different outcome. Once a specified number of iterations has been completed, the set of results is collected and statistical measures (e.g., mean, standard deviation) are calculated"[68].

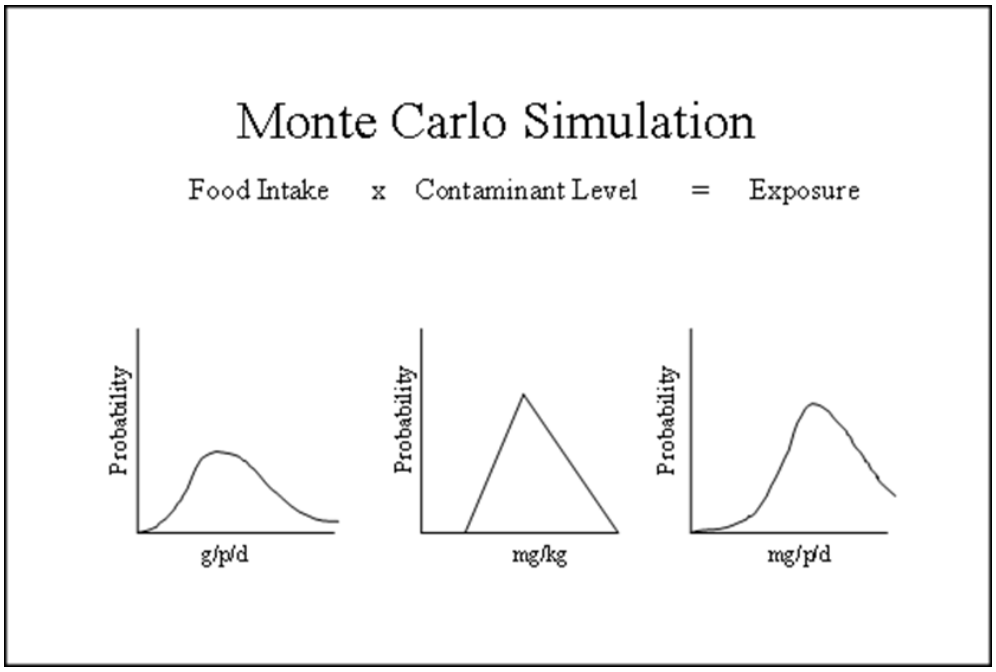


Figure 7: Distribution of variable inputs for a typical Monte Carlo simulation

Although more complex and data intensive, some of the advantages of a probabilistic risk assessment (i.e., Monte Carlo simulation) include a greater use of exposure data by using a

distribution of data rather than a single point to reflect key variables; providing a quantitative measure of uncertainty; and estimating a range of potential risks and their likelihood of occurrence[69]. However, when a distribution includes low probability outcomes, and when few iterations are selected, Monte Carlo simulation may not accurately sample the outliers[2]. To address this issue, a variation to the basic simulation model was developed: Latin Hypercube sampling (LHS), a quasi-Monte Carlo technique. LHS is a stratified sampling method when used in estimating dietary exposure to contaminants. LHS "divides the input distributions into intervals of equal probability and samples from each interval according the interval's probability distribution, so that the entire range of the distribution is sampled in an even consistent manner"[5]. This technique ensures that both the upper and lower ends of the distribution are accurately represented[2].

Regardless of the approach used, the simulation output will give a range of possible outcomes which can then be compared to safe intake threshold levels or combined with cancer potency factors.

2.3 Review of Available Food and Contaminant Data

To support the research conducted for this thesis, broad internet searches for data, information, scholarly articles, reports and relevant studies containing residue levels in food and/or consumption habits of Canadians in their daily lives were conducted. The search tools included Google Scholar, Google, academic search tools (e.g., Web of Science and Academic Search Complete), federal and provincial government websites and applicable scientific journals.

To narrow down these results of these searches, I scanned all titles and identified those with a national scope; a generalized population; and/or a varied diet or food supply. Thousands of article titles were scanned during the first analysis followed by a selection process with only a few hundred selected for further scrutiny. The second approach was to read through the abstracts of the chosen papers to determine the applicability of dietary patterns and/or contaminant residues in food items, preferably in Canada, or where unavailable, in the USA. Thus, the number of suitable articles was further reduced to less than 100. Finally, each paper and report in the final group was read for content and reviewed for measured data that fit our criteria of food-related databases with both consumption patterns and residue levels in a standard daily diet.

Similarly, federal government agency websites (Canadian and US), were scrutinized for reports, studies and databases relating to food dietary patterns and measured levels of contaminant residues. Of the many articles evaluated, those with data tended to have a singular focus, for example, one or two contaminants in one or two food items/ groups[38–40], based on the frequency of consumption, not ingested amounts[44,45], or limited to one location[41–43]. Results were similar in the USA where the topics were targeted on a few contaminants[37,46,47], food items or locations[48–52], and not a national, population-wide total diet perspective.

Initially a total of 20 publically available Canadian databases/studies were found, developed since 1969, with a specific focus on an examination of food and nutrition. Listed in Table 3, (with evaluation of characteristics), are the 6 databases selected as appropriate sources for calculating chemical or environmental contaminant exposures from food in Canada. None of these databases contained both residue and consumption data (only 4 contained consumption data (one dating back to 1970-72; one from 2004 - not publically available; while the remaining 2 had proxy data for food consumed). Two (2) data sources had limited residue data.

Table 4: Canadian Residue and Consumption Databases / Surveys

Databases / Surveys	**Year**	**Residue data**	**Consumption data**	**Nutrient data**	**Survey Method**	**Survey focus**
Nutrition Canada Survey	1970-72		X		24-hr recall	Large-scale study of consumption patterns
Food Consumption in Canada	2001-02		X (proxy)	X	Annual adjusted domestic retail sales	Per capita disappearance (general trends in consumption)
Canadian Community Health Survey, Cycle 2.2	2004		X	X	24-hr recall	Master File contains a large-scale study of dietary intake for ~35,000 Canadians
Statistics Canada	2006		X (proxy)		Annual supply - disposition tables (per capita)	Food available for consumption, adjusted for losses
Total Diet Studies	Since 1969 Latest 2009 (Calgary)	X		X	Analysis of 140 food composites prepared for consumption	Measures concentrations of contaminants in food composites
National Chemical Residue Monitoring Program (CFIA)	Since 1978 Latest 2008	X			Laboratory testing of random and targeted samples	Heavy metal residues in selected foods

2.3.1 Food Consumption Data

The *Nutrition Canada Survey* (1970-72) is a comprehensive large-scale, national study of detailed consumption habits of Canadians[70]. For the past forty plus years, these data have been used as the basis of Canadian consumption in most published literature regarding contaminant exposures[70]. This dataset is long outdated and has since been replaced by the CCHS data from 2004.

Food Consumption in Canada is a report produced in 2001-02 by Statistics Canada which includes the disappearance of food per capita for various food groups such as dairy and dairy by-products, beverages, eggs, pulses and nuts, sugar and syrups, cereals, meats and poultry, fruits, vegetables, juices, oils and fats, and fish. These data are used as a proxy for per capita food consumption[71,72]. This dataset does not indicate actual foods consumed, therefore not considered appropriate for this study.

In 2009, Statistics Canada released a new interactive program, *Canada Food Stats*, which provided access to a broad spectrum of food information and data. A report could be generated on the annual data collected regarding the quantity of food items available for consumption per capita (adjusted for losses) which acts as a proxy for food consumed per capita. This program was discontinued in 2010[73]. These data, customized into a report only indicated food available for consumption, not amounts consumed, therefore not suitable for this analysis.

The *Canadian Community Health Survey, Cycle 2.2, Nutrition* is a cross-sectional survey that, on a two-year collection cycle, gathers heath status and related information, such as dietary intake and nutritional well-being. The specific objectives of the CCHS 2.2 were to estimate the distribution of usual dietary intake in terms of foods, food groups, dietary supplements, nutrients and eating patterns among a representative sample of Canadians at national and provincial

levels[1]. This dataset compiled the dietary patterns of approximately 35,000 Canadians across ten provinces representing a national population; therefore, it is considered to be the most suitable for this assessment.

For comparison purposes, equivalent databases in the USA were evaluated. Of those considered as the most robust and compatible to the Canadian databases, none included both consumption and residue data. The most complete consumption data in the USA is compiled annually by the National Health and Nutrition Examination Survey[53] whose mandate includes vital and health statistics for the USA assessing health and nutritional status. The Continuing Survey of Food Intakes by Individuals (CFSII) was a nationwide food consumption survey from 1985 until 2002 when it was integrated with the NHANES program[74]. Both studies use the 2 non-consecutive days, 24-hr recall method of data gathering. Although these data surveyed a cross-section of American dietary patterns, it was estimated that the CCHS dataset was more representative of Canadian food consumption.

2.3.1.1 Consumption dataset – gaps & limitations:

According to a 2000 report, Canada has never had a systematic program of national food and nutrition surveillance[70]. Surveys published in food-related public databases have focused on either consumption frequency, or proxy for consumption levels. For example, differing consumption data can be found in the 1970-72 Nutrition Canada Survey[29]; Canadian Community Health Survey, Cycle 2.2[1]; Food Consumption in Canada[71,72]; and Canada Food Stats [73]. The 2004 Canadian Community Health Survey on Nutrition replaced the national approach of the 1970-72 survey for establishing average daily food intakes; however, the publically available data is based on 24-hr recall of food frequency in broad food groups (e.g., number of daily servings of fruit or vegetables) and not specific items or amounts ingested[1,75]. The full dataset is

only made available through an application process with Statistics Canada. If approved, access then is only possible via visit to an approved Research Data Centre, and final results are subject to a vetting procedure[1]. In the end, despite realization that access to these data would be cumbersome, and that publication of results would be subject to scrutiny and possible veto by a vetting process, this was the only Canadian consumption dataset considered adequate to represent national dietary intake, and is now a dozen years out of date.

Data on dietary intake is highly dependent on human recall and input of amounts consumed. These data therefore generally cannot be considered entirely accurate or completely comprehensive. Some dietary input studies rely on the memory of the participants eating habits over a prior period[45], others use a proxy amount for a typical serving[1], while still others rely on the 1972 Nutrition Canada Survey statistics[43]. There are several survey methods employed in gathering food data , including: 24-hr recall, 2 non-consecutive days; Food frequency diary, 1-7 consecutive days; Food availability, adjusted for losses (proxy); and Food disappearance, per capita (proxy), making it difficult to compare or cross-reference[76]. In many surveys, food intake is estimated from pictures or diagrams of portion sizes which are then translated into comparable weighted amounts rather than actual weighing of foods to be consumed[1]. Differing methodologies and approaches in measuring food consumption and residue levels in food make effective analysis problematic[53,77]. Sampling size, individual dietary habits, and seasonality also play an important role in determining the exposures from food; however, there is a lack of consistency in gathering and evaluating these data[38,39,43–45].

There are differences between governmental agencies – national, provincial, or international, regarding food descriptions and food list items. For example, the *Nutrition Canada Survey* lists 'beef' as 'beef, steak; beef, roast and stewing; beef, hamburg; and organ meats'[78]; whereas,

Canada Food Stats shows 'beef' as simply 'beef'[73]. This makes the usability and comparability of data challenging[74].

2.3.2 Food Contaminant Data

Total Diet Study surveys are targeted by substance and location; therefore, it is difficult to obtain a total picture of national trends or patterns in analyzing exposures from food. These studies have been conducted annually since 1969 in one or more major Canadian cities focusing on one or two substances per analysis. Since 2003 the emphasis has been to monitor radionuclides and trace elements in selected food composites[58]. These studies did not report concentration levels on the five targeted contaminants of this assessment; therefore, are not considered suitable.

The Canadian Food Inspection Agency's (CFIA) National Chemical Residue Monitoring Program (NCRMP) has been monitoring contaminants in the food supply since 1978 by producing annual reports on *Foods of Plant and Animal Origin*[13]. The results are displayed in a series of tables designed to show specific results and individual food items making it difficult to compare food elements with their inherent residues across a wider spectrum. However, as the data included heavy metals (arsenic and lead) measured in a select group of food items, these were used in our analysis.

Other considerations included proxy consumption data from the US Department of Agriculture for food availability per capita, adjusted for losses[79]. These data were not considered suitable, as they do not indicate dietary patterns. The US Environmental Protection Agency's exposure potential model, Dietary Exposure Potential Model (DEPM), developed for analysis purposes by integrating several databases comprising of 6700 food items with over 350 pesticide

and environmental contaminants[37,80]. This model has not been updated and was not considered useful for the current analysis.

The most current and comprehensive residue data were found in two sources: the US Food and Drug Administration's Total Diet Study (1991 – 2006), a compilation of 280 common foodstuffs, prepared for consumption and analyzed to measure the levels of over 700 selected contaminants[15] and the US FDA – Elements Results Summary - Market Baskets 2006 through 2011[14]. As these datasets reported concentration levels in food from the five named substances in this analysis; they were deemed the best fit.

2.3.2.1 Contaminant dataset – gaps & limitations:

Limited residue measurements are available via Canadian Total Diet Studies[58] and the National Chemical Residue Monitoring Program[13]. Canadian total diet studies, under the auspices of Health Canada and its Bureau of Chemical Safety, have been conducted since 1969; however, these surveys are very narrow in scope, usually focusing one or two cities per year targeting a specific substance[58]. For example, surveys conducted in the 1990s focused on pesticides, PCBs, dioxins and furans in various Canadian cities[58], with the last analysis conducted in 1998 in Whitehorse, NWT[43]. Since 2000, their focus has shifted to trace elements and radionuclides (the last survey was undertaken in Montreal in 2013 and was for radionuclides only), making it difficult to ascertain any level of known or suspected carcinogenic substances in the Canadian food chain or any substantive consumption amounts[58].

The random selection process basic to the probabilistic risk assessment method requires the residue data be reported with a range of values per occurrence – MIN, MEDIAN, MAX, as well as a detection frequency (DF). Regrettably, Canadian Total Diet Studies are publicly reported solely with median values of residues in food items; however, the CFIA does measure specific

metals in selected foods with a range of values and DFs. As neither source was entirely sufficient to conduct an effective risk assessment, and although partial CFIA data were utilized, additional reliable data resources had to be sought.

Several factors are necessary to be taken into considerations in evaluating data quality for residue content; food item selection, testing techniques, and amounts tested may all influence reported results. Although total diet study samples are tested in one laboratory location in Canada using standard techniques, food composites used in laboratory testing are not standardized from one city to the next, nor one year to the next[57]. American total diet studies are more representative of national exposures by selecting market baskets from three regional cities in each of four major sectors (Northeast, North Central, West, South)[81]. Each agency utilizes dedicated labs for testing, however, in Canada only one sample of each food item is analyzed for residues of specific contaminants, whereas the US_FDA tests between 20 and 44 samples of each market basket item for a wider range of chemical and pesticide residues.

2.3.3 Discussion

There are shortcomings inherent in any risk assessment, including gaps and limitations in the quantity and quality of data available in peer-reviewed literature, or government reports and studies. Ideally, both consumption and residue data would be available from a single source, however, this is not the case. Conducting a probabilistic risk assessment of food and beverages using strictly Canadian data is not possible as the data do not exist for both consumption and contaminant residue values at a national level. As a result of non-compatible and disparate data, any exposure assessment becomes a best-guesstimate of compiled information from non-related sources.

2.4 Overview of Contaminants

CAREX Canada has prioritized a number of known and suspected carcinogens, based on the potential for exposure to occur in Canada. Known carcinogens include arsenic and arsenic compounds, asbestos, benzene, benzo(a)pyrene, 1,3-butadiene, cadmium and cadmium compounds, hexavalent chromium, diesel engine exhaust, formaldehyde, nickel and nickel compounds, polychlorinated biphenyls, radon, and 2,3,7,8-tetrachlorodibenzo-para-dioxin (TCDD). Group 2A, probable carcinogens, include lead and lead compounds as well as tetrachloroethylene[7].

Only five substances listed above were chosen for analysis in this thesis. Asbestos, diesel engine exhaust, and radon are typically measured in indoor and outdoor air, and therefore are not of concern in foods and beverages. Formaldehyde, nickel and nickel compounds, and cadmium and cadmium compounds are not currently thought to be carcinogenic via ingestion. No suitable data were found for benzo(a)pyrene, 1,3- butadiene, hexavalent chromium, or TCDD in food and beverages. Therefore, arsenic and arsenic compounds, benzene, lead and lead compounds, polychlorinated biphenyls, and tetrachloroethylene were selected were selected for this study. Each compound is introduced in more detail below.

2.4.1 Arsenic (As)

Arsenic (As) is a chemical element that occurs in the environment both from natural and human sources. Natural occurrences are found in some rocks and occur during volcanic eruptions. Arsenic is also used by humans notably in mining and as a pesticide[82]. The International Agency for research on Cancer (IARC) has classified arsenic and its compounds as Group 1 (*carcinogenic to humans*) based on epidemiological studies establishing associations with various forms of cancer[8]. Exposure to and ingestion of arsenic has been associated with

adverse, long-term health effects including skin cancer, various cancers of the digestive tract, liver, bladder, kidney, prostate and lymphatic and hematopoietic systems[7]. Once in the environment, arsenic can enter the food chain. Food and water may contain two types of arsenic compounds: organic (most prevalent in food and not considered carcinogenic) and inorganic, which are absorbed from soil and groundwater contamination[82]. Inorganic arsenic is considered the more toxic form, and is found predominantly in water[83]. Studies from the 1980s indicate that arsenic intake from various foodstuffs was 75% organic and 25% inorganic[84,85]. Dietary sources of arsenic include rice, fruit juices and concentrates, shellfish, grain and dairy products[7,86]. Foods generally are only tested for total arsenic, not differentiating between organic and inorganic arsenic[13,82].

Health risk assessments conducted by Health Canada indicate that average concentrations of total arsenic in 10 surveyed food groups ranged from 0.46ug/L in drinking water to 0.0601ug/g in meat, fish and poultry[87]. Total daily intake of inorganic arsenic, based on an assumption that 37% of the arsenic content in food is inorganic, was estimated to range between <0.1 to 35 ug/bw/day[87]. However, these estimates were compiled from limited data on the relative proportion of inorganic arsenic in various foodstuffs[87]. Other estimates from the 1990s report the mean daily intake of total arsenic in food for adults to be 42 μg (range 22.5–78.7 μg) for adults 20–65+ years old in Canada[88], and 56 μg (range 27.5–92.1 μg) for adults 25–70+ years old in the United States[46].

The average lifetime excess cancer risk (LECR) calculated by CAREX Canada based on cancer potency factors (CPFs) from Health Canada is 59.43 extra cancers per million people and CPFs from the United States Environmental Protection Agency (US EPA) and the California Office of Environmental Health Hazard Assessment (CA OEHHA) is 49.53 per million people[7].

2.4.2 Benzene (C6H6)

Benzene (C6H6) is an organic compound that occurs naturally and human made in the environment at low levels. It is formed through the incomplete combustion of organic materials and occurs as a product of crude oil extraction, from volcanoes and forest fires as well as in cigarette smoke[89,90]. It permeates water and soil via "petroleum seepage and weathering of exposed coal-containing strata"[89]. Benzene has been classified as a Group 1 substance by IARC (*carcinogenic to humans*) and a 'non-threshold toxicant' with limited evidence linking exposure to some forms of leukemia and myeloma[7]. Although the primary route of benzene exposure is through inhalation from polluted air and cigarette smoke, there is limited exposure from the food chain[89,90]. Dietary sources for benzene ingestion have been found in beverages, predominantly soft drinks, as well as drinking water, dairy products, some fruits and vegetables, processed meats and packaged goods[90]. Benzene concentrations in foods in the USA have been detected to range between 0.001 ug/g to 0.19 ug/g[15], and in drinking water in Canada between 0.05 ug/l to 2 ug/l where the established maximum acceptable concentration is 5.0 ug/l[90]. The average lifetime excess cancer risk (LECR) has been estimated by CAREX using cancer potency factors (CPFs) from Health Canada at 1.91 extra cancers per one million people and CPF from the US EPA at 1.26 extra cancers per one million people[7].

Total Diet Studies, carried out regularly by the US Food & Drug Administration (US FDA), monitor benzene concentrations in food and beverages through laboratory testing; Canada does not include benzene in its Total Diet Study program[15,58].

2.4.3 Lead (Pb)

Lead (Pb) is an odourless lustrous metal that occurs naturally in rock and soil. It is widespread throughout the environment from anthropogenic use in the form of both soluble and insoluble compounds[91]. Although many industrial uses and practices using lead and lead compounds have been phased out or reduced over time, lead is still ubiquitous in the environment. Currently, the general population's predominant exposure to lead is via ingestion of food and drinking water, followed by inhalation [91]. IARC has classified inorganic lead compounds as Group 2A (*probably carcinogenic to humans*) and organic lead compounds as Group 3 (*not classifiable as to their carcinogenicity to humans*)[10]. Epidemiological studies have shown linkages between exposure, whether inhaled or ingested, and increased incidences of lung and stomach cancers, as well as, adverse health effects and cancers of the kidney, brain and nervous system[7]. Lead enters the food chain predominantly through uptake by crops grown in lead-bearing soils or fish and animals ingesting lead from water and sediments[92]. However, human exposure may also come as a result of food processing using lead-soldered cans (on the decline in food production), or the use of lead-contaminated water in food preparation[91]. Total Diet Studies in Canada monitored lead intake from the food supply between 1969 and 2007, showing a decline since 1981 due to the phasing out of lead-soldered cans for food storage[91]. Since 2004, the major contributor to lead intake for the Canadian population has been beverages (beer, wine, coffee, tea, and soft drinks), cereals and vegetables[91]. In 2011, Health Canada estimated the daily dietary intake of lead for Canadians of all ages to be 0.1ug/kg body weight[91]. LECR, using CPFs from the California Office of Environmental Health Hazard Assessment, are calculated to average 0.224 extra cancers per million people[7].

2.4.4 Polychlorinated Biphenyls (PCBs)

Polychlorinated Biphenyls (PCBs) represent a group of chemicals made up of 209 isomers. PCBs are used extensively in many industrial applications and products from sealing and caulking compounds, paint additives, to the production of transformers and capacitors. Although banned throughout North America since 1977, they are stable and persistent in the environment[93]. Human exposure can occur through inhalation of contaminated indoor air, ingestion of contaminated foods, and dermal contact[7]. PCBs are classified as Group 1 (*carcinogenic to humans*) by IARC based on linkages between PCBs exposure and increased risk of melanoma, non-Hodgkin lymphoma and breast cancer[11]. Additionally, there is evidence that long-term, high-level exposure may result in increased risk of liver and kidney cancers[93]. Dietary exposure and intake of PCBs comes from foods containing the highest concentrations of PCBs, mainly fish, meat and poultry[7]. Canadian Total Diet Studies conducted until 2002 have estimated the average daily dietary intake of PCBs to be less than half of one microgram (<0.5 ug)[93]. The average lifetime excess cancer risk (LECR) has been estimated by CAREX using cancer potency factors (CPFs) from the US EPA and CA OEHHA at 5.61 extra cancers per one million people[7]. Total Diet Studies, carried out regularly by the US FDA, monitor PCBs concentrations in food and beverages through laboratory testing; Canada no longer includes PCBs in its Total Diet Study program[15,58].

2.4.5 Tetrachloroethylene (PERC)

Tetrachloroethylene (PERC) is a synthetic chemical used primarily as a solvent in the dry cleaning industry. It is no longer produced in Canada, but continues to be imported[94]. It enters the environment from anthropogenic sources via volatilization, precipitation and adsorption affecting air, soil and water[94]. Exposure to PERC may occur from its presence in air, drinking water and possibly food. Supermarket proximity to dry cleaning establishments can affect the concentrations of PERC found in fatty food items such as butter or margarines[94]. IARC has classified PERC as Group 2A (*probably carcinogenic to humans*)[12], based on animal testing showing evidence of leukemia in rats, liver cancer in mice and kidney cancer in male rats[7]. Canada does not monitor for PERC in food surveys including its Total Diet Study (TDS) program[15,58]. Total Diet Studies carried out regularly by the US FDA monitor PERC concentrations in food and beverages through laboratory testing, and have found concentrations of PERC in dairy, meat, cereal, fruit, vegetable, fats and oil, and sugar composite food groups[15]. Average daily intakes of PERC from these studies indicate an ingestion of 8.4ug[15,94]. Health Canada suggests a maximum acceptable concentration (MAC) for PERC in drinking water of 0.010mg/L as the level protective of potential health effects[94].

2.5 Methods and Data

Preliminary probabilistic estimates of intake were produced using @RISK for each gender in each province, by three income levels nationally, and by place of residence nationally (urban vs rural), by combining consumption data from the CCHS, Cycle 2.2 survey, and measured levels of arsenic and arsenic compounds, benzene, lead and lead compounds, polychlorinated biphenyls, and tetrachloroethylene, from three sources: the Canadian Food Inspection Agency - National Chemical Residue Monitoring Program: 2012-2013 Annual Report[13]; the US Food and Drug Administration - Total Diet Study - Market Baskets 1991-3 through 2003-4 Report. Revision 3, 1991-2003, December 2006[15]; and the U.S. Food and Drug Administration - Total Diet Study - Elements results Summary Statistics – Market Baskets 2006 through 2011 report[14].

Intake of a substance for each individual food reported as being consumed was calculated as:

IF = CONS(g/d) * CONC (ug/g) * DF

Where:

IF = intake for an individual food item

CONS = amount reported as consumed in grams/day

CONC = randomly drawn value from distribution of concentration values for the food item

DF = the frequency of detection for the substance in the food item

Note: for beverages, consumption units are ml/d and concentration units are ppm (ug/g).

Total daily intake was calculated as the sum of all IF. Subtotals were also calculated by summing IF for all foods according to food group. Results were released as total daily intake and total food group intake for key percentile levels for analysis. These were converted to milligrams per kilogram of bodyweight (assuming a standard bodyweight of 70kg)[95,96] and multiplied by applicable cancer potency factors from Health Canada[97], the US Environmental Protection

Agency[61], and/or the California Office of Environmental Health Hazard Assessment[62] to produce indicators of lifetime excess cancer risk. Additional detail is provided in the following subsections.

2.5.1 Data

2.5.1.1 Consumption and demographic data:

Over 8,700 unique foods from the Nutrition Survey System (NSS) are reported as being consumed by 34,944 participants in the Canadian Community Health Survey, Cycle 2.2, Nutrition Survey[1]. Many of these are prepared, store-bought foods and include brand names in the description. Statistics Canada, for reasons of confidentiality regarding the use of brand name data, denied us its use, therefore, a more simplified food list was required. The CCHS Survey also includes a food system according to the Bureau of Nutritional Sciences (BNS) list[98,99], which includes approximately 232 individual foods in 78 food group codes without identifying specific brands. This was the only food data that was acceptable for release by Statistics Canada analysts. As defined by Statistics Canada and collected via survey questionnaires and interviews, the demographic data included: gender (male or female); province of residence (10 Canadian provinces, excluding the territories); urban ("continuously built-up areas that have a population concentration of 1,000 or more and a population density of 400 or more per km^2; all other areas are considered rural")[100] or rural location, and income range (CCHS defines household income as follows: Lowest is <$10,000 and <$15,000; Lower middle ranges between $10,000 to $29,999; Middle ranges between $15,000 and $59,999; Upper middle ranges between $30,000 and $79.999; Highest is between $60,000 and >$80,000)[100]. These data were provided in separate tables indexed by a unique respondent ID. A population weight variable for each

respondent was also provided in the CCHS. The population weight "corresponds to the number of persons in the entire population that are represented by the respondent"[98].

Developing an analysis-ready dataset required a number of steps:

- The consumption data were reported in 'vertically' for each respondent, i.e., multiple rows for respondent 1, each with a unique food consumed, producing over 1 million rows in total. This very large table was transposed so each row related to a unique respondent, with all foods reported consumed listed in columns.
- Demographic (gender, province of residence, urban/rural, and income) and population weight variables were linked to the transposed consumption table using the unique respondent ID.
- Data were exported from STATA into Excel, where the number of food items was reduced from 232 to 60 by removing all foods with less than 5 reported respondents or with brand names, as per confidentiality requirements by Statistics Canada, as well as prepared foods (134 items) which included multiple ingredients due to complexity of determining appropriate residue levels in these foods.
- In the final analysis, the 60 foods were categorized into eight food groups, and for which we had residue data, as shown in Table 5.

Table 5: Compiled food list from CCHS, Cycle 2.2, 2004

Group	**Individual Foods**
Meat	Bacon; Beef; Lean Beef, Chicken Meat; Cured Ham; Ground Beef; Lamb; Lean Lamb; Pork; Lean Pork; Lean Veal; Liver; Turkey with Skin; Turkey Meat
Fish	Fish
Dairy	Butters; Cottage Cheese; Eggs; Half & Half; Ice Cream; Lite Cheese; Regular Cheese; Sour Cream; Margarines;

	Whole Milk
Fruit	Apple; Banana; Cherries; Citrus fruits; Melons; Peaches; Pears; Plums; Raisins; Strawberries
Vegetables	Beans; Broccoli; Cabbage; Carrots; Celery; Corn; French Fries; Mushrooms; Onions; Peas; Peppers; Potatoes; Squashes; Tomatoes
Rice/ Cereals	Rice Cereals; Pasta; Rice; Wholegrain Cereals
Grains/ Nuts	Peanut Butter; White Breads; Whole Wheat Bread
Beverages	Tap & well water; Tea; Beers; Wines

2.5.1.2 Residue data:

As already justified in Sections 2.4.2, we used measured data from three sources: Canadian Food Inspection Agency - National Chemical Residue Monitoring Program: 2012-2013 Annual Report[13] tests for residues of metals, including total arsenic and lead, in numerous foods; the US FDA - Total Diet Study - Market Baskets 1991-3 and 2003-4: Revision Dec 2006[15] reported residue levels for benzene, PCBs and PERC in a wide variety of food and beverages; and the US FDA – Elements Results Summary - Market Baskets 2006 through 2011[14] published results for arsenic and lead found in various food products. The minimum, mean and maximum concentration of our selected contaminants for individual foods were matched to the CCHS food list to produce model inputs for amounts consumed with associated contaminant concentration. Table 6 lists the concentration data for each carcinogen in the foods included in our study.

Table 6: Concentration data

Food Group	Arsenic (ug/g)				Lead (ug/g)				Benzene (ug/g)				PCBs (ug/g)				PERC (ug/g)			
	MEAN	MIN	MAX	D F	MEAN	MIN	MAX	D F	MEAN	MIN	MAX	D F	MEAN	MIN	MAX	D F	MEAN	MIN	MAX	D F
MEAT																				
bacon					0.001	0.000	0.021	0.042	0.002	0.001	0.017	0.864					0.002	0.000	0.022	0.977
beef	0.002	0.000	0.014	0.125	0.001	0.000	0.018	0.083	0.020	0.001	0.099	0.455	0.020	0.020	0.020	1.000				
chicken meat	0.010	0.005	0.048	0.314	0.010	0.010	0.010	0.020	0.036	0.036	0.036	0.977	0.030	0.030	0.030	1.000				
cured ham					0.001	0.000	0.023	0.042												
ground beef									0.016	0.003	0.190	0.477					0.002	0.000	0.006	0.977
lamb					0.001	0.000	0.015	0.042					0.010	0.010	0.010	1.000				
lean beef	0.009	0.007	0.012	0.250	0.002	0.002	0.002	0.023					0.010	0.010	0.010	1.000	0.003	0.003	0.003	1.000
lean lamb					0.001	0.000	0.015	0.042					0.010	0.010	0.010	1.000				
lean pork	0.007	0.006	0.007	0.058	0.010	0.010	0.010	0.019	0.002	0.030	0.048	0.955	0.010	0.010	0.010	1.000				
lean veal	0.006	0.006	0.007	0.188	0.002	0.002	0.002	0.063					0.010	0.010	0.010	1.000				
liver					0.001	0.000	0.023	0.042												
pork													0.020	0.020	0.020	1.000				
turkey with skin	0.010	0.005	0.028	0.415	0.002	0.002	0.002	0.024	0.034	0.034	0.034	0.977								
turkey meat	0.010	0.005	0.028	0.415	0.002	0.002	0.002	0.024	0.034	0.034	0.034	0.977								
FISH																				
fish	0.305	0.000	0.436	0.958									0.024	0.009	0.055	0.375				
DAIRY																				
butter					0.002	0.000	0.031	0.083	0.003	0.001	0.022	0.795	0.003	0.020	0.120	0.977	0.009	0.003	0.102	0.432
cottage cheese					0.000	0.000	0.009	0.042												
egg	0.020	0.011	0.032	0.281	0.042	0.008	0.104	0.175												
half & half					0.001	0.000	0.024	0.042												
ice cream					0.000	0.000	0.009	0.042	0.001	0.002	0.014	0.932					0.002	0.000	0.006	0.977
lite cheese	0.001	0.000	0.022	0.042					0.001	0.000	0.009	0.955					0.002	0.002	0.002	1.000
margarines					0.001	0.000	0.033	0.042	0.003	0.001	0.030	0.818					0.003	0.002	0.042	0.886
regular cheese	0.026	0.015	0.047	0.429	1.704	1.139	2.221	0.857	0.003	0.001	0.047	0.886					0.000	0.002	0.008	0.977
sour cream					0.001	0.000	0.034	0.042	0.002	0.003	0.020	0.909					0.007	0.007	0.007	0.977
whole milk	0.011	0.010	0.020	0.143	0.012	0.010	0.020	0.024	0.000	0.001	0.008	0.977					0.003	0.003	0.003	1.000
FRUITS																				
apple	0.011	0.005	0.028	0.075	0.004	0.001	0.021	0.597	0.002	0.001	0.032	0.886								
banana									0.034	0.001	0.136	0.432								
cherries									0.016	0.016	0.016	0.971								
citrus fruits					0.001	0.000	0.021	0.083	0.001	0.001	0.015	0.886								
melons	0.006	0.000	0.024	0.500	0.000	0.000	0.010	0.042	0.013	0.013	0.013	0.977								
peaches	0.018	0.018	0.018	0.333					0.027	0.027	0.027	0.977								
pears					0.001	0.000	0.009	0.083	0.018	0.018	0.018	0.977								
plums									0.013	0.013	0.013	0.974								
raisins	0.007	0.000	0.031	0.250	0.005	0.000	0.023	0.333	0.005	0.001	0.097	0.795	0.010	0.010	0.010	1.000	0.011	0.011	0.011	0.977
strawberries	0.010	0.010	0.010	0.143	0.004	0.001	0.009	0.857	0.001	0.001	0.020	0.930					0.005	0.005	0.005	1.000
VEGETABLES																				
beans	0.007	0.007	0.007	0.200	0.008	0.002	0.024	0.800												
broccoli	0.002	0.000	0.010	0.042	0.003	0.001	0.005	1.000												
cabbage	0.004	0.004	0.004	0.200	0.002	0.001	0.003	0.600												
carrots	0.007	0.006	0.008	0.250	0.003	0.001	0.006	0.667												
celery	0.007	0.007	0.007	1.000	0.006	0.006	0.006	1.000												
corn	0.001	0.000	0.013	0.042																
french fries									0.004	0.002	0.058	0.773					0.002	0.000	0.008	0.932
mushrooms	0.014	0.005	0.030	0.889	0.002	0.001	0.004	0.556												
onions	0.009	0.009	0.009	0.250	0.005	0.002	0.009	0.500												
peas					0.005	0.002	0.012	1.000												
peppers	0.007	0.007	0.007	0.143	0.006	0.006	0.006	0.143												
potato	0.007	0.004	0.016	0.196	0.004	0.001	0.019	0.761	0.014	0.014	0.014	0.977								
squashes					0.006	0.004	0.007	1.000	0.014	0.014	0.014	0.977								
tomatoes					0.012	0.001	0.037	0.800	0.004	0.001	0.067	0.864								
RICE/CEREALS																				
rice	0.065	0.036	0.094	1.000																
rice cereal	0.161	0.000	0.505	0.958	0.001	0.000	0.013	0.083												
pasta					0.001	0.000	0.027	0.083												
wholegrain cereals	0.027	0.000	0.054	0.917	0.001	0.000	0.023	0.042												
GRAINS/NUTS																				
peanut butter	0.005	0.000	0.037	0.167					0.003	0.001	0.025	0.841					0.002	0.000	0.007	0.977
white bread					0.000	0.000	0.011	0.042	0.002	0.001	0.025	0.886					0.005	0.005	0.005	1.000
whole wheat breads	0.004	0.000	0.012	0.333	0.001	0.000	0.011	0.083												
BEVERAGES																				
beers					0.000	0.000	0.006	0.083												
tap and well water									0.003	0.005	0.006	0.750								
tea					0.000	0.000	0.010	0.042												
wine	0.008	0.000	0.018	0.750	0.007	0.000	0.029	0.875												

2.5.2 Software

The @RISK, version 6 software[67] was used to perform a Monte Carlo simulation using the INTAKE equation above, producing total and subtotal intakes and summary statistics. @RISK is a statistical software add-in to MS-Excel that performs risk analysis using Monte Carlo simulation to show many possible outcomes of a model, and how likely they are to occur. Working with a programmer at Palisade, a small dataset (1,000 rows) was used to develop and test the @RISK model. Once tested and updated to accommodate a dataset of ~35,000 rows, the simulations were run. The @RISK model uses 4 separate sheets in an MS-Excel workbook – **Data**; **Reference**; **Table**; and **Report**. The data within each sheet are organized to work together in the performance of the risk simulation.

The **Data** sheet (Table 7) contains the consumption data (in grams/day) of each respondent for the 60 designated foods. Also, the population weight associated with each individual and their corresponding demographic information including province; gender; income and urban/rural are indicated. *This data is used in establishing the selected sample population (as selected on the Table sheet).*

Table 7: @RISK model Data sheet

Sample ID	Population Weight	Province	Gender	Income	Rural/Urban	Apple	Bacon	Banana	Beans	Beef+Fat	Beers	Broccoli	Butters	Cabbage	Carrots	Cauliflower	Celery	Cherries	ChickenMeat	Citrus fruits	Corn	Cottage Cheese	CuredHam	Eggs
1	215.6	35	2	2	2	144.2		225.0	504.6		36.2	21.6	6.7			25.8	12.5	29.2	50.9				29.2	37.8
2	987.5	11	2	4	2		148.8		394.6	13.2		21.1	8.9							60.7	12.2		37.8	47.1
3	1,555.3	13	1	2	1		72.4		425.3				37.6		50.4	163.6			225.5				18.5	
4	355.7	24	1	2	1	227.9		250.0	501.0		40.2		9.5	255.0		42.5			70.9					
5	401.3	35	2	1	2					15.4		122.3	10.2							49.1		155.4		42.1
6	1,115.6	47	1	2	2		125.5		445.0				16.7				20.7		250.0				148.3	
7	2,577.4	35	1	1	2	288.5			650.5			124.1	9.6	100.5					325.6		23.6			37.8
8	877.6	35	1	4	2		155.2		305.0		45.6		27.4		46.9	145.0							123.3	
9	155.4	11	2	3	2	173.2	145.5		425.0			102.9						43.9	85.0	150.5				
10	654.1	46	1	1	1					19.4			28.2	175.5										155.9
11	580.5	59	1	2	1		155.9	117.5	401.5				9.1							78.0			144.0	
12	555.4	12	1	2	2	215.8			409.6			127.1	10.6	89.1	57.1		24.3	54.9	101.7		26.9			167.3
13	388.2	48	2	4	1		178.8	149.4	424.6			135.5	14.8	137.7	53.9		55.4		255.5			99.0	85.0	
14	1,050.6	47	2	4	2				350.0				25.5	255.5				160.8					135.0	
15	775.6	47	2	4	2		133.5				44.2	250.0	55.5				122.0		275.0			275.0	122.0	
16	422.3	13	2	2	2				325.0							274.5				88.3	129.1			145.5
17	501.4	35	2	1	1		187.0	125.0		27.0	55.0		45.5											
18	1,255.6	12	1	4	1		251.4		125.0	105.0	101.6	125.0	58.3	225.0			85.5			255.8				255.9
19	1,498.7	46	1	2	1	304.5			233.6								149.0							
20	254.6	12	2	2	1	352.1													154.2				122.0	
21	322.8	12	1	3	2			126.7	317.1	39.5	55.4	40.2	11.8	124.9	55.1	64.4	31.8	59.5	125.0	91.6			260.3	
22	1,622.1	35	1	1	1		105.2			54.2			68.5								30.3	100.8		
23	364.1	13	1	2	2						38.6			240.6	238.9						88.2			181.5
24	887.2	12	2	1	1				215.8	69.2	79.2	291.0	87.8						275.8					
25	244.8	46	2	2	1	207.1													357.3				189.0	

The **Reference** sheet (Table 8) contains concentration values for the contaminant (MEAN, MIN, MAX) and the detection frequency for each included food or beverage. The additional information in the Reference sheet are the codes for the food group of each food and beverage. *These codes are used in summarizing the dietary intakes in the Report sheet.*

Table 8: @RISK model Reference sheet

Food	Food Group	MEAN	MIN	MAX	Detection Freq	CONSUMPTION	MEAN CONTENT	MEAN RANK	Comp%
Apple	4	0.000	0.000	0.000	0.010	#NAME?	#NAME?	#NAME?	#NAME?
Bacon	1	0.020	0.010	0.050	0.500	#NAME?	#NAME?	#NAME?	#NAME?
Banana	4	0.001	0.001	0.001	0.020	#NAME?	#NAME?	#NAME?	#NAME?
Beans	5	0.008	0.005	0.016	0.513	#NAME?	#NAME?	#NAME?	#NAME?
Beef+Fat	1	0.007	0.007	0.007	0.150	#NAME?	#NAME?	#NAME?	#NAME?
Beers	8	0.008	0.005	0.010	0.176	#NAME?	#NAME?	#NAME?	#NAME?
Broccoli	5	0.001	0.001	0.001	0.020	#NAME?	#NAME?	#NAME?	#NAME?
Butters	3	0.006	0.006	0.006	0.250	#NAME?	#NAME?	#NAME?	#NAME?
Cabbage	5	0.007	0.007	0.007	0.150	#NAME?	#NAME?	#NAME?	#NAME?
Carrots	5	0.006	0.006	0.006	0.111	#NAME?	#NAME?	#NAME?	#NAME?
Cauliflower	5	0.007	0.007	0.007	0.150	#NAME?	#NAME?	#NAME?	#NAME?
Celery	5	0.006	0.006	0.006	0.111	#NAME?	#NAME?	#NAME?	#NAME?
Cherries	4	0.007	0.007	0.007	0.150	#NAME?	#NAME?	#NAME?	#NAME?
ChickenMeat	1	0.013	0.005	0.054	0.508	#NAME?	#NAME?	#NAME?	#NAME?
Citrus fruits	4	0.007	0.007	0.007	0.150	#NAME?	#NAME?	#NAME?	#NAME?
Corn	5	0.008	0.006	0.012	0.333	#NAME?	#NAME?	#NAME?	#NAME?
Cottage Cheese	3	0.001	0.001	0.001	0.010	#NAME?	#NAME?	#NAME?	#NAME?
CuredHam	1	0.135	0.081	0.201	1.000	#NAME?	#NAME?	#NAME?	#NAME?
Eggs	3	0.015	0.010	0.033	0.441	#NAME?	#NAME?	#NAME?	#NAME?

The CONSUMPTION column indicates the calculated values by food and beverage for the contaminant from the Table sheet. *These CONSUMPTION values are summed up by food group and indicated in the Summary table on the Report sheet.*

The **Table** sheet (Table 9) is the INTAKE calculation portion of the software. The PivotTable (centre box) allows the selection of the desired sample population by demographic category (Province; Gender; Income; Urban/Rural). *The risk simulation results for intake are shown in the 'ARSENIC CONSUMPTION' row (see table) once the simulation completes, along with the TOTAL intake value for the chosen sample population.*

Table 9: @RISK model Table sheet

ID	#NAME?	Apple	Bacon	Banana	Beans	Beef+Fat	Beers	Broccoli	Butters	Cabbage	TOTAL
FOOD CONSUMPTION	#NAME?	#NAME?	#NAME?	#NAME?	#NAME?	#NAME?	#NAME?	#NAME?	#NAME?	#NAME?	
ARSENIC CONTENT	#NAME?	#NAME?	#NAME?	#NAME?	#NAME?	#NAME?	#NAME?	#NAME?	#NAME?	#NAME?	
DETECTION FREQUENCY	#NAME?	#NAME?	#NAME?	#NAME?	#NAME?	#NAME?	#NAME?	#NAME?	#NAME?	#NAME?	
ARSENIC CONSUMPTION	#NAME?	#NAME?	#NAME?	#NAME?	#NAME?	#NAME?	#NAME?	#NAME?	#NAME?	#NAME?	#NAME?

Province	59	British Columbia
Gender	1	Male
Income	(All)	All Incomes
Rural/Urban	(All)	Urban

British Columbia Male All Incomes Urban

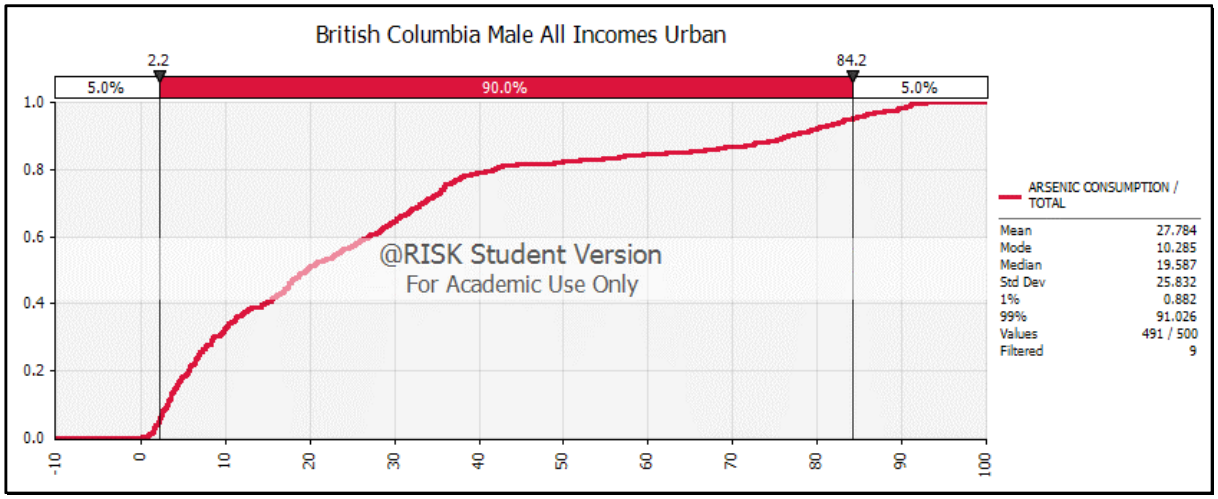
ID	Pop Weight
11	581
46	289
57	535
105	779
111	799
114	262
145	132
154	516
162	317
163	110
167	181

The **Report** sheet (Table 10) displays the results of the risk simulation by food group as generated by the Table sheet from the Data and Reference sheets:

- The Summary table is created from the Reference sheet (CONSUMPTION column).
- The TOTAL sample population chart is produced from the TOTAL cell in the Table sheet.

Table 10: @RISK model Report sheet

	British Columbia Male All Incomes Urban				
	Food Groups	Arsenic Consumption	Mean Consumption	MEAN RANK	Comp%
1	Meat	#NAME?	#NAME?	#NAME?	#NAME?
2	Fish / Seafood	#NAME?	#NAME?	#NAME?	#NAME?
3	Dairy	#NAME?	#NAME?	#NAME?	#NAME?
4	Fruit	#NAME?	#NAME?	#NAME?	#NAME?
5	Vegetables	#NAME?	#NAME?	#NAME?	#NAME?
6	Cereal / Rice	#NAME?	#NAME?	#NAME?	#NAME?
7	Grains / Nuts	#NAME?	#NAME?	#NAME?	#NAME?
8	Beverages	#NAME?	#NAME?	#NAME?	#NAME?
	TOTAL	#NAME?	#NAME?		#NAME?



The risk simulation process requires a few simple steps in the Table sheet:

1. Select the desired demographic categories in the PivotTable

Province	59	British Columbia
Gender	1	Male
Income	(All)	All Incomes
Rural/Urban	(All)	Urban

2. Select or type in the preferred number of iterations in the Iterations section of the @RISK ribbon
3. Click ‘Start Simulation’
4. Review the risk simulation results on the Report page. This procedure was repeated for each of the five (5) targeted substances - Arsenic; Benzene; Lead; Polychlorinated Biphenyls (PCBs); and Tetrachloroethylene (PERC). The dietary intake data remained consistent and unchanged for each substance.

A series of 25 risk simulations of 50,000 iterations each, using demographic information from the CCHS, Cycle 2.2 Master File, were conducted for each of the five substances as follows:

1. By province and gender – 10 simulations for Male; 10 simulations for Female
2. By 3 income levels – Low; Middle; High (nationally; all genders) – 3 simulations (1 for each level)
3. Urban and Rural (nationally; all genders) – 2 simulations (1 for Urban; 1 for Rural)

This was a lengthy process as each simulation took between 8 to 15 minutes each to run, with a total of 125 simulations to be conducted, totally over 20 computing hours. The Statistics Canada RDC is generally only accessible for use 15 hours a week (over a three-day period) which resulted in partial analysis and computing runtime during each visit. It took two weeks to complete all simulations and compile the results for release.

2.5.3 Approval for release of model results

The consumption data required Statistics Canada to vet and approve release of the final results. The release process necessitates working in conjunction with their analysts and vetting committee to assure respondent confidentiality, and acceptable sample population weighting. The final results, approved for release in summary tables, included total and subtotal (food group) intakes for each analysis population and the Mean intake at key percentile levels.

2.5.4 Cancer potency factors

LECR is calculated by multiplying the estimated intake by a cancer potency factor (CPF) which produces an estimate of the lifetime excess cancer risk. Using the intake values by percentile and cancer potency factors (CPFs) from Health Canada[97], US EPA[61] and CAOEHHA[62], this calculation was made separately for each substance and domain in MS Excel spreadsheets.

Table 11: Cancer Potency Factors for Ingestion

Substance	Health Canada	CA OEHHA	US EPA
Arsenic	1.8	1.5	1.5
Benzene	0.0834	--	0.055
Lead	--	0.0085	--
PCBs	--	2.0	2.0
PERC	--	0.051	0.0021

Health Canada[97]
US Environmental Protection Agency[61]
California Office of Environmental Health Hazard Assessment[62]

The results of these simulations of contaminant intake from food and beverages and calculations for LECR are presented as two separate papers in Section 3.0, each formatted for submission to academic journals for peer-review consideration of publication.

3.0 Results

3.1 Urban vs Rural Risk from Dietary Carcinogens

ABSTRACT

OBJECTIVES: To explore differences in urban vs rural lifetime excess risk of cancer from food and beverages.

METHODS: Monte Carlo risk simulation is applied to estimate probable lifetime contaminant intake and associated lifetime excess cancer risk from arsenic, benzene, lead, polychlorinated biphenyls (PCBs) and tetrachloroethylene (PERC) in 60 whole foods from the dietary patterns of 34,944 Canadians from 10 provinces as derived from Health Canada's Canadian Community Health Survey, Cycle 2.2, Nutrition (2004) (CCHS).

RESULTS: In the calculation of lifetime excess cancer risk from food and beverages for the five selected substances, two (lead and PERC), indicated no excess risk; whereas, the remaining three

(arsenic, benzene and PCBs) showed that at least 50% of the population were above 10 per million excess cancers. Arsenic residues, ingested via rice & rice cereal registered the greatest disparity between urban and rural intake with LECR/M levels well above 1000/M at the upper bound. Majority of PCBs ingestion comes from meat with values slightly higher for urban populations and LECR/M estimates between 50 and 400. Primary contributor of benzene intake in both urban and rural populations is from drinking water with LECR/M estimates of 35 extra cancers in the top 1% of sampled population.

CONCLUSION: Overall, there are few disparities between urban and rural lifetime excess cancer risk from food and beverages. Estimates could be improved with more complete Canadian dietary intake and concentration data in support of detailed exposure assessments in estimating lifetime excess cancer risk.

INTRODUCTION:

There is evidence that diets and health outcomes are related to geographic location; for example, there may be differences between urban versus rural populations. Some studies confirm that rural diets, with greater access to fresh, locally grown produce, contain more fruits and vegetables than urban counterparts[1]; although other studies report minimal differences[2], or the reverse showing that rural diets lack adequate nutrition to maintain good health[3]. Rural populations in the USA (23.3% compared to 20.5% for urban populations)[4] reportedly show increased incidences of obesity which have been ascribed by some to poor diet[5]. Monroe et al., report that cancer risk may be greater for urban populations due to life habits and urban environmental pollutants, however, rural populations are more vulnerable to contracting chronic diseases being “older, poorer and less educated” [6]. Other urban-rural health differences show

certain cancers (stomach and lung) have a higher rate of incidence for rural inhabitants; whereas, breast cancer and heart disease are more prevalent for urbanites[7,8].

The objective of this paper is to conduct probabilistic modelling of intake for five (5) known or suspected carcinogens (arsenic, benzene, lead, polychlorinated biphenyls (PCBs) and tetrachloroethylene (PERC) that have been detected in North American foods, with a specific focus on differences between Canadians living in urban versus rural areas. We hypothesize that rural residents, when compared to urban residents, consume different foods in different amounts, and therefore may have different associated intakes and risks. The importance in evaluating dietary health-related vulnerabilities between rural and urban populations can help in determining where health services would be most beneficial and where food security issues may exist leading to increased cancers within a community. The results of this study will serve to highlight important information gaps, identify potential priorities for more detailed exposure assessments or exposure reduction actions, and provide information useful for designing more rigorous epidemiological investigations related to urban versus rural differences in cancer incidence. This study is the first to look at dietary intake of carcinogens and lifetime excess cancer risk disparities between urban and rural populations in Canada.

METHODS:

We employ a probabilistic approach to estimate the range and frequency of possible daily contaminant intakes for urban versus rural Canadians, and associate these intake levels with lifetime excess cancer risk. We then compare our results to the current Health Canada guideline that suggests that 10 extra cancers per one million people is a negligible risk[9]. Typically, daily dietary intake is determined by:

$$\textbf{Intake} = \sum (F_1 \times C_1 \times DF_1) + (F_2 \times C_2 \times DF_2) + \ldots (F_n \times C_n \times DF_n) \quad \textbf{[Eq. 1]}$$

Where:
F = amount of specific food or beverage consumed in g/day
C = concentration of contaminant in ug/g
DF = detection frequency (# of detections / # of samples)
n = n^{th} food group

To estimate potential risk from long-term ingestion of carcinogens via diet, lifetime excess cancer risk (LECR) is used as an indicator of potential cancers occurring in a population. LECR assumes that the lifetime average daily intake is the same for 70 years. It is calculated by multiplying the estimated intake by a cancer potency factor (CPF) which produces an estimate of the lifetime excess cancer risk[9]:

LECR per million = 1,000,000/(ADI x CPF) **[Eq. 2]**

Where:
ADI = average daily intake in mg/kg of bodyweight
CPF = cancer potency factor (also called oral slope factor)

For this study, bodyweight is assumed to be 70kg, as per Health Canada's standards for exposure assessment[9]. LECR for each contaminant was generated using CPFs from Health Canada[10], the California Office of Environmental Health Hazard Assessment[11], and the US Environmental Protection Agency[12]. When more than one CPF was available, we used the highest, in order to produce a 'worst case' scenario, as shown in Table 1.

Table 1. Cancer Potency Factors (bold indicates used in analysis)

Substance	Health Canada	CA OEHHA	US EPA
Arsenic	**1.8**	1.5	1.5
Benzene	**0.0834**	--	0.055
Lead	--	**0.0085**	--
PCBs	--	**2.0**	2.0
PERC	--	**0.051**	0.0021

We used the most current Canadian consumption data (g/day) from the 24-hr dietary recall of representative populations from the Canadian Community Health Survey (CCHS), Cycle 2.2,

Nutrition (2004), a national canvassing of 34,944 respondents from ten (10) provinces[13]. Using data fields provided within the dataset (sample id; urban; rural; food items, grams consumed) and based on a 24-hr dietary recall survey, the records were coded as urban (n = 27,144; 77.7%) or rural (n = 7,800; 22.3%) and analysed separately. Urban and rural are defined in the CCHS by population concentration and density where urban is regarded as continuously built-up areas with a population concentration of 1,000+ and a population density of 400+ per square kilometre. All other areas are considered rural[14]. This split closely matches the Canadian Council on Social Development's finding that 79.6% of Canada's 2001 census population resided in urban centres, while 20.4% lived in rural locations[15].

The CCHS survey includes food lists from the Nutrition Survey System (NSS) (8700 food items) and the Bureau of Nutritional Sciences (BNS), with approximately 232 food products in 78 food groupings some whole (e.g., apples) and some prepared (e.g., vegetable soup). We were denied approval to use the NSS listing by Statistics Canada due to proprietary information contained within the dataset. We received clearance to use the BNS data. We do not include prepared foods (134 items) in our model, given the difficulties in establishing the ingredients and proportions thereof. We do include 60 commonly consumed whole foods, aggregated in the final analysis into eight food groups, and for which we had the most residue data, as shown in Table 2.

Table 2. Included Foods and Food Groups

Group	Individual Foods
Meat	Bacon; Beef; Lean Beef, Chicken Meat; Cured Ham; Ground Beef; Lamb; Lean Lamb; Pork; Lean Pork; Lean Veal; Liver; Turkey with Skin; Turkey Meat
Fish	Fish
Dairy	Butters; Cottage Cheese; Eggs; Half & Half; Ice Cream; Lite Cheese; Regular Cheese; Sour Cream; Margarines; Whole Milk

Fruit	Apple; Banana; Cherries; Citrus fruits; Melons; Peaches; Pears; Plums; Raisins; Strawberries
Vegetables	Beans; Broccoli; Cabbage; Carrots; Celery; Corn; French Fries; Mushrooms; Onions; Peas; Peppers; Potatoes; Squashes; Tomatoes
Rice/ Cereals	Rice Cereals; Pasta; Rice; Wholegrain Cereals
Grains/ Nuts	Peanut Butter; White Breads; Whole Wheat Bread
Beverages	Tap & well water; Tea; Beers; Wines

We used measured data from three sources: the Canadian Food Inspection Agency (CFIA) - National Chemical Residue Monitoring Program (NCRMP): 2012-2013 Annual Report[16]; the US Food and Drug Administration (US FDA) - Total Diet Study (TDS) - Market Baskets 1991-3 and 2003-4: Revision Dec 2006[17]; and the U.S. Food and Drug Administration – Elements Results Summary - Market Baskets 2006 through 2011[18]. The CIFA's NCRMP tests for residues of metals, including total arsenic and lead, in numerous foods[16]. The US FDA TDS results from 1991-2006 reported residue levels for benzene, PCBs and PERC in a wide variety of food and beverages[17]; whereas, the US FDA 2014 report published results for arsenic and lead found in various food and beverages[18]. The minimum, mean and maximum concentration of our selected contaminants for individual foods were matched to the CCHS food list to produce model inputs for amounts consumed with associated contaminant concentration. Table 3 lists the concentration data for each carcinogen in the foods included in our study.

Several factors are necessary considerations in evaluating data quality for residue content; food item selection, testing techniques, and amounts tested may all influence reported results. Canadian Total Diet Studies are publicly reported solely with mean values of residues in food items; however, the CFIA does measure specific metals in selected foods with a range of values

and DFs. As neither source was entirely sufficient to conduct an effective risk assessment, and although partial CFIA data was utilized, additional reliable data resources had to be sought. Canadian sourced contaminant data appropriate for this analysis was limited to arsenic and lead. The US total diet studies are more representative of national exposures by testing between 20 and 44 samples of each market basket item for a wide range of chemical and pesticide residues. Using datasets from the USA as proxies, although similar food items were analysed, may not be truly reflective of Canadian exposure to contaminants in food and beverages. In order to produce a Canadian risk assessment, more thorough monitoring of suspected carcinogens in food and beverages would provide a clearer understanding of who's at risk.

Table 3. Concentration data

Food Group	Arsenic (ug/g)				Lead (ug/g)				Benzene (ug/g)				PCBs (ug/g)				PERC (ug/g)			
	MEAN	MIN	MAX	DF	MEAN	MIN	MAX	DF	MEAN	MIN	MAX	DF	MEAN	MIN	MAX	DF	MEAN	MIN	MAX	DF
MEAT																				
bacon					0.001	0.000	0.021	0.042	0.002	0.001	0.017	0.864					0.002	0.000	0.022	0.977
beef	0.002	0.000	0.014	0.125	0.001	0.000	0.018	0.083	0.020	0.001	0.099	0.455	0.020	0.020	0.020	1.000				
chicken meat	0.010	0.005	0.048	0.314	0.010	0.010	0.010	0.020	0.036	0.036	0.036	0.977	0.030	0.030	0.030	1.000				
cured ham					0.001	0.000	0.023	0.042												
ground beef									0.016	0.003	0.190	0.477					0.002	0.000	0.006	0.977
lamb					0.001	0.000	0.015	0.042					0.010	0.010	0.010	1.000				
lean beef	0.009	0.007	0.012	0.250	0.002	0.002	0.002	0.023					0.010	0.010	0.010	1.000	0.003	0.003	0.003	1.000
lean lamb					0.001	0.000	0.015	0.042					0.010	0.010	0.010	1.000				
lean pork	0.007	0.006	0.007	0.058	0.010	0.010	0.010	0.019	0.002	0.030	0.048	0.955	0.010	0.010	0.010	1.000				
lean veal	0.006	0.006	0.007	0.188	0.002	0.002	0.002	0.063					0.010	0.010	0.010	1.000				
liver					0.001	0.000	0.023	0.042												
pork													0.020	0.020	0.020	1.000				
turkey with skin	0.010	0.005	0.028	0.415	0.002	0.002	0.002	0.024	0.034	0.034	0.034	0.977								
turkey meat	0.010	0.005	0.028	0.415	0.002	0.002	0.002	0.024	0.034	0.034	0.034	0.977								
FISH																				
fish	0.305	0.000	0.436	0.958									0.024	0.009	0.055	0.375				
DAIRY																				
butter					0.002	0.000	0.031	0.083	0.003	0.001	0.022	0.795	0.003	0.020	0.120	0.977	0.009	0.003	0.102	0.432
cottage cheese					0.000	0.000	0.009	0.042												
egg	0.020	0.011	0.032	0.281	0.042	0.008	0.104	0.175												
half & half					0.001	0.000	0.024	0.042												
ice cream					0.000	0.000	0.009	0.042	0.001	0.002	0.014	0.932					0.002	0.000	0.006	0.977
lite cheese	0.001	0.000	0.022	0.042					0.001	0.000	0.009	0.955					0.002	0.002	0.002	1.000
margarines					0.001	0.000	0.033	0.042	0.003	0.001	0.030	0.818					0.003	0.002	0.042	0.886
regular cheese	0.026	0.015	0.047	0.429	1.704	1.139	2.221	0.857	0.003	0.001	0.047	0.886					0.000	0.002	0.008	0.977
sour cream					0.001	0.000	0.034	0.042	0.002	0.003	0.020	0.909					0.007	0.007	0.007	0.977
whole milk	0.011	0.010	0.020	0.143	0.012	0.010	0.020	0.024	0.000	0.001	0.008	0.977					0.003	0.003	0.003	1.000
FRUITS																				
apple	0.011	0.005	0.028	0.075	0.004	0.001	0.021	0.597	0.002	0.001	0.032	0.886								
banana									0.034	0.001	0.136	0.432								
cherries									0.016	0.016	0.016	0.971								
citrus fruits					0.001	0.000	0.021	0.083	0.001	0.001	0.015	0.886								
melons	0.006	0.000	0.024	0.500	0.000	0.000	0.010	0.042	0.013	0.013	0.013	0.977								
peaches	0.018	0.018	0.018	0.333					0.027	0.027	0.027	0.977								
pears					0.001	0.000	0.009	0.083	0.018	0.018	0.018	0.977								
plums									0.013	0.013	0.013	0.974								
raisins	0.007	0.000	0.031	0.250	0.005	0.000	0.023	0.333	0.005	0.001	0.097	0.795	0.010	0.010	0.010	1.000	0.011	0.011	0.011	0.977
strawberries	0.010	0.010	0.010	0.143	0.004	0.001	0.009	0.857	0.001	0.001	0.020	0.930					0.005	0.005	0.005	1.000
VEGETABLES																				
beans	0.007	0.007	0.007	0.200	0.008	0.002	0.024	0.800												
broccoli	0.002	0.000	0.010	0.042	0.003	0.001	0.005	1.000												
cabbage	0.004	0.004	0.004	0.200	0.002	0.001	0.003	0.600												
carrots	0.007	0.006	0.008	0.250	0.003	0.001	0.006	0.667												
celery	0.007	0.007	0.007	1.000	0.006	0.006	0.006	1.000												
corn	0.001	0.000	0.013	0.042																
french fries									0.004	0.002	0.058	0.773					0.002	0.000	0.008	0.932
mushrooms	0.014	0.005	0.030	0.889	0.002	0.001	0.004	0.556												
onions	0.009	0.009	0.009	0.250	0.005	0.002	0.009	0.500												
peas					0.005	0.002	0.012	1.000												
peppers	0.007	0.007	0.007	0.143	0.006	0.006	0.006	0.143												
potato	0.007	0.004	0.016	0.196	0.004	0.001	0.019	0.761	0.014	0.014	0.014	0.977								
squashes					0.006	0.004	0.007	1.000	0.014	0.014	0.014	0.977								
tomatoes					0.012	0.001	0.037	0.800	0.004	0.001	0.067	0.864								
RICE/CEREALS																				
rice	0.065	0.036	0.094	1.000																
rice cereal	0.161	0.000	0.505	0.958	0.001	0.000	0.013	0.083												
pasta					0.001	0.000	0.027	0.083												
wholegrain cereals	0.027	0.000	0.054	0.917	0.001	0.000	0.023	0.042												
GRAINS/NUTS																				
peanut butter	0.005	0.000	0.037	0.167					0.003	0.001	0.025	0.841					0.002	0.000	0.007	0.977
white bread					0.000	0.000	0.011	0.042	0.002	0.001	0.025	0.886					0.005	0.005	0.005	1.000
whole wheat breads	0.004	0.000	0.012	0.333	0.001	0.000	0.011	0.083												
BEVERAGES																				
beers					0.000	0.000	0.006	0.083												
tap and well water									0.003	0.005	0.006	0.750								
tea					0.000	0.000	0.010	0.042												
wine	0.008	0.000	0.018	0.750	0.007	0.000	0.029	0.875												

A probabilistic risk model developed with @RISK software was used to conduct Monte Carlo simulation analysis for urban and rural intake. This technique selects values at random from input probability distributions. Each set of sample values is called an iteration. For our study, a dietary record was selected at random in each iteration, then for each food reported as being consumed, a random value for the concentration value was generated based on a PERT distribution, and finally **Eq 1** was calculated. Population weights provided by CCHS were used to guide the selection of the dietary record. We ran 50,000 iterations using the urban dietary records and 50,000 iterations using the rural dietary records, producing distributions of the resulting intake values. Finally, we calculated LECR for 16 percentile categories of each distribution, using available CPFs.

RESULTS:

Total intake (ug/day) for urban versus rural residents for each carcinogen is shown in Figure 1.

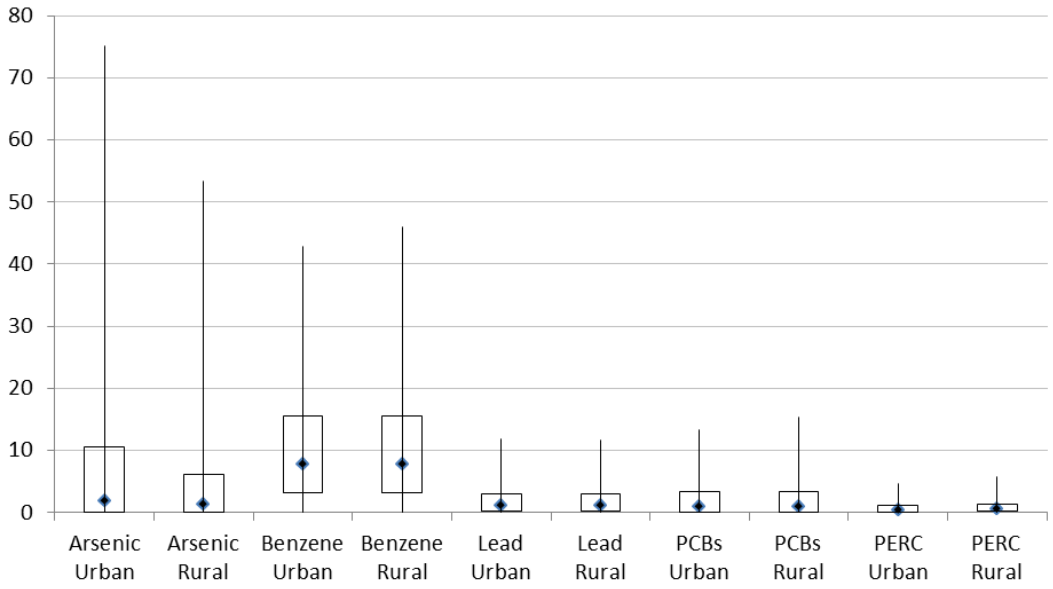


Figure 1. Intake (min, lower quantile, median, upper quantile, max) in ug/day

Arsenic intake levels show the greatest absolute disparity between urban and rural populations. The mean daily intake for urban was estimated at 7.44 ug/day compared to 4.82 ug/day for rural. The primary food group contributing to arsenic intake in both categories was rice & rice cereals (intake in ug/day; % of total intake), for urban = 4.96 ug/day (66.6%); rural = 2.48 ug/day (51.43%); followed by fish for urban = 1.11 ug/day (14.9%); rural = 0.98 ug/day (20.3%).

Benzene intake levels from food and beverages were similar for both urban and rural populations. The mean intake for urban residents was estimated at 10.10 ug/day and 10.19 ug/day for rural. The primary food group contributing to benzene intake in both categories was beverages for urban = 3.89 ug/day (38.56%); rural = 3.89 ug/day (38.13%); followed by meat for urban = 2.31 ug/day (22.93%); rural = 2.27 ug/day (22.3%).

Lead intake levels from food and beverages were the same for both urban and rural populations in all percentiles. The mean intake for urban was estimated at 1.91 ug/day and 1.93 ug/day for rural. The primary food group contributing to lead intake in both categories was vegetables for urban = 1.07 ug/day (55.85%); rural = 1.11 ug/day (57.32%); followed by dairy for urban = 0.31 ug/day (16.14%); rural = 0.34 ug/day (17.38%).

PCBs intake levels from food and beverages were the same for both urban and rural populations in all percentiles. The mean intake for urban was estimated at 2.01 ug/day and 2.02 ug/day for rural (Table 4). The primary food group contributing to PCBs intake in both categories was meat for urban = 1.72 ug/day (85.57%); rural = 1.71 ug/day (84.57%); followed by dairy for urban = 0.15 ug/day) (7.57%); rural = 0.18 ug/day (9.01%).

PERC intake levels from food and beverages were slightly higher for rural populations compared to urban populations. The mean intake for rural was estimated at 0.91 ug/day and 0.78

ug/day for urban. The primary food group contributing to PERC intake in both categories was dairy for rural = 0.37 ug/day (40.72%); urban = 0.32 ug/day (41.03%); followed by grains & nuts for rural = 0.20 ug/day (22.46%; urban = 0.16 ug/day) (20.72%). Although urban consumed a higher percentage of dairy (41.03% vs 40.72%), the overall intake from the other food categories was higher for rural.

LECR estimates for two carcinogens, lead and PERC suggest no excess cancer risk due to dietary intake, and no significant difference between urban and rural regions. LECR estimates for lead were calculated based on the CA OEHHA cancer potency factor (0.0085)[19]. The highest (99^{th} percentile) LECR value calculated for lead was 1.45 per million for urban dwellers and 1.41 per million for rural dwellers. Similarly, LECR estimates for PERC were calculated based on the CA OEHHA cancer potency factor (0.051). The 99^{th} percentile LECR values were 3.35 per million and 4.25 per million for urban and rural residents respectively.

Intakes of three carcinogens, arsenic, benzene and PCBs produced LECR estimates above 10 per million (Table 4). Between 60 and 70 percent of the estimated intakes for arsenic resulted in LECR values above 10 per million, based on Health Canada's cancer potency factor (1.8)[19]. Due to differences in daily arsenic intake estimated, the LECR values are on average 1.5 times higher at every percentile for urban dwellers than for rural dwellers, and reach 1,930 per million at the 99^{th} percentile for the urban sample. PCB LECR values based on cancer potency factors from CA OEHHA (2.0)[19] were above 10 per million at the 40^{th} percentile for both urban populations and rural populations, at approximately 15 extra cancers per million in both cases, and 99^{th} percentile LECRs of 378 to 440 per million. LECR estimates associated with benzene intake are based on Health Canada's cancer potency factor (0.0834)[19]. Fully fifty percent of

LECR estimates due to benzene intakes are above 10 per million, although 99th percentile level only reach 51 to 55 per million.

Table 4. Lifetime Excess Cancer Risk Estimates for Arsenic, PCBs and PERC

	Arsenic		PCBs		Benzene	
Percentile	Urban	Rural	Urban	Rural	Urban	Rural
1	0.0	0.0	0.0	0.0	0.1	0.1
5	0.0	0.0	0.0	0.0	0.9	0.9
10	0.0	0.0	0.0	0.0	1.9	1.9
20	2.7	1.6	0.0	0.0	3.7	3.7
30	**11.9**	8.2	5.1	5.3	5.5	5.3
40	**25.8**	**19.4**	**15.0**	**14.7**	7.2	7.1
50	**46.6**	**34.5**	**29.1**	**28.6**	9.2	9.2
60	**81.0**	**55.2**	**45.7**	**45.4**	**11.5**	**11.5**
70	**146.1**	**88.1**	**68.2**	**65.5**	**14.5**	**14.4**
80	**272.2**	**158.3**	**97.1**	**96.4**	**18.5**	**18.5**
90	**528.8**	**319.5**	**148.6**	**151.4**	**25.3**	**25.7**
95	**838.6**	**505.3**	**207.3**	**211.5**	**32.5**	**33.2**
96	**955.9**	**588.5**	**226.1**	**235.4**	**34.9**	**35.5**
97	**1137.7**	**724.1**	**252.0**	**252.4**	**38.2**	**39.3**
98	**1392.8**	**948.6**	**296.4**	**305.1**	**43.0**	**45.2**
99	**1930.5**	**1372.5**	**378.4**	**440.5**	**51.0**	**54.8**

DISCUSSION:

The objective of this paper was to compare urban vs rural LECR from food and beverages using a Monte Carlo probabilistic risk model to estimate contaminant intakes of arsenic, benzene, lead, PCBs and PERC. In our findings, the highest LECR was associated with arsenic intake. Arsenic was detected in 33 of the 60 foods listed. The major contributor to arsenic intake was rice & rice cereals. Arsenic intake was also associated with the largest difference between urban and rural residents.

Comparing our results to other studies is difficult due to differences in the number of foods being tested; consumption patterns used; differing testing, surveying, and reporting criteria between studies; and size of sample population.

For example, total arsenic daily intake values have been reported as ranging from 27.5 ug/day from 264 foods in a US study [20] to 77.0 ug/day from 300 foods in a study from Chile [21]. Both of these studies were deterministic, in that results were produced by assuming a hypothetical person consumed the population average amount of all foods tested, with the single level of total arsenic measured in each of those foods. Our study uses actual dietary patterns, which preserves more realistic consumption levels. Other studies reported results indicating that average daily intakes ranged between 0.25 – 0.36 ug/kg-bw [22], which becomes 17.5 – 25.2 ug/day respectively assuming the standard body weight of 70kg [9,23]. In this case, a very sophisticated probabilistic model was employed, and included 280 foods (whole and prepared), as well as drinking water which can be a significant source of arsenic. This suggests LECRs estimated in our study may be very conservative, highlighting the need for more detailed investigation of potential arsenic exposure in Canada.

The predominant route of exposure to benzene is via inhalation (cigarette smoke, air pollution) with previous studies reporting that food does not represent a significant source of human exposure[24]. Our study found that daily intakes ranged between a minimum of 0.04 ug/day (urban) and 0.09 ug/day (rural) to a maximum of 42.83 ug/day (urban) and 46.02 ug/day (rural) at the 99th percentile with a mean value of 7.70 ug/day for both urban and rural cohorts. While we could not find recent Canadian or American studies addressing human dietary intake of benzene,[24] a study from Belgium notes average benzene intake for all foods averaged 1.4 ug/day (0.020 ug/kg-bw/day) [25]. This probabilistic study focussed on processed, canned and bottled

foods known to contain some form of benzene (benzoic acid; added benzoate; etc.) where 455 food samples were tested for specific benzene content. Food consumption for the Belgian study, obtained from a national survey, involved 3,083 participants completing a 2-day 24-hr recall self-reporting food frequency questionnaire. This approach does not indicate gms/day consumed, only servings per day which may under-estimate actual intake. This variation in intake values may be attributable to differing approaches or methodologies in estimating dietary intake and differences in food surveys or contaminant quantification[25].

The daily dietary intake of lead was estimated to range from a minimum value of 0.00 ug/day for both urban and rural populations to a maximum of 11.90 ug/day and 11.62 ug/day (99^{th} percentile), with mean values of 1.08 ug/day and 1.13 ug/day respectively, suggesting negligible differences. Findings for lead reported here are significantly lower than have been reported in other recent studies. Turconi (2009), surveying 1,978 subjects in Northern Italy, estimated a range between 25.8 ug/day and 66.6 ug/day[27]. This study analysed 248 prepared and processed foods where consumption was based on frequency and general portion sizing, and exposure estimated on the average amount of food ingested, not actual amounts (gms/day). This approach may over-estimate intake. Munoz (2005), from a study in Chile involving 300 food items, estimated a daily intake of lead for adults from food at a maximum of 206.0 ug/day[21]. This deterministic study was based on food frequency and portion sizing rather than actual amounts of food consumed which may result in a conservative result. Health Canada, in the 2013 report, approximated the mean daily intake of lead from dietary sources to be 7.0 ug/day (0.1 ug/kg bw/d at 70 kg) based on average daily food intake and body weight of Canadians of all ages [28]. In our assessment, the average lead intake reached the equivalent that Health Canada

estimate at the 96th percentile (7.31 ug/day). Our study results are calculated on actual individual dietary patterns, providing a more realistic estimate of exposure and associated risk.

This study showed that PCBs intake ranged from the estimated minimum of 0.00 ug/day for both urban and rural populations to a maximum intake value (99th percentile) of 13.24 ug/day and 15.42 ug/day, respectively with averages at 1.02 ug/day (urban) and 1.00 ug/day (rural). Health Canada estimated adult PCBs dietary intake, based on 2002 TDS data, to vary between 0.08 – 0.19 ug/day (1.16 – 2.67 ng/kg bw/d at 70 kg)[29]. This is a deterministic result estimating the intake on average consumption of selected foods in one city in Canada which is difficult to compare. Our results include the dietary intake for ~35,000 respondents from across the ten provinces and actual daily food amounts consumed. A 2009 study based on a 7-day food consumption survey from France found the mean PCBs dietary intake from 22 food groups, including 1665 food samples tested, at 0.539 ug/day (7.7 ng/kg bw/d at 70 kg)[30]. This study included both whole and processed foods and actual body weights were used in assessing probable intake. The assessment approach employed to estimate intake was by combining actual individual consumption, average contaminant levels and actual body weights and using a simple equation to produce average intakes from food. In our assessment, the average intake to equate with some of these studies falls between the 30th and 50th percentiles at 0.18 ug/day and 0.53 ug/day respectively.

Human exposure to PERC is generally due to inhalation of polluted air or ingestion from contaminated waters and soil which may seep into the food chain; however, food is not considered a major route of PERC exposure[32]. This assessment, measured in 15 of 60 foods, found the major dietary contributors to PERC intake were from dairy, followed by grains and nuts. The minimum daily PERC intake was the same (0.00 ug/day) for urban and rural;

however, there were slight differences at the 99th percentile with 4.59 ug/day (urban) and 5.83 ug/day(rural); the daily average was 0.5 ug/day (urban) and 0.59 ug/day (rural). In a 1993 assessment report, Health Canada estimated that the adult average daily PERC intake from a composite of food groups to be 8.4 ug/day (0.12 ug/kg bw/d at 70 kg)[32]. These data are from studies and information from the 1980s and 1990s which may not be relevant today based on average levels ingested by average Canadians and not actual consumption. Our assessment was based on actual dietary patterns where maximum findings fell well below the level indicated by Health Canada.

There are limitations and biases that need to be taken into account regarding our analysis. We used data for 60 commonly consumed whole foods and beverages; however, using alternative food lists could produce different results. The concentration values measured in various foods could not be differentiated between urban and rural settings; whereas, consumption values were reported based on a consumer's locale. Limited residue measurements are available via Total Diet Studies[33] and the National Chemical Residue Monitoring Program (CFIA) (NCRMP, 2013). Canadian total diet studies, under the auspices of Health Canada and its Bureau of Chemical Safety, have been conducted since 1969; however, these surveys are very narrow in scope, usually focusing one or two cities per year targeting a specific substance[33]. For example, the 1990s surveys focused on pesticides, PCBs, dioxins and furans in various Canadian cities, with the last analysis done in 1998 in Whitehorse, NWT[33]. Since 2000, a shift has been made to detect trace elements and radionuclides (the latest taking place in Montreal in 2013, radionuclides only); thereby, making it difficult to ascertain any level of known or suspected carcinogenic substances in the Canadian food chain or any substantive consumption amounts[33].

More detailed exposure assessments would be better supported with more extensive and complete dietary intake and concentration data.

Future directions in improving health risk assessment for food and beverages in Canada may include establishing or adopting (from the USA or EU community) a standardized food item listing with clear and concise definitions. Establishing or adjusting a more robust food consumption survey system (from existing USA or EU systems) to suit Canadian criteria. Enhancing the existing Total Diet Study program of food contaminant residues to include known or suspected carcinogens and provide greater national coverage. Harmonizing databases between agencies and research groups. Developing and/or utilizing tools and technology to become proactive in the analysis of food safety and health risks from the accumulated effects of multiple exposures to chemicals and/or environmental contaminants in the food supply. Reliable data modelling can provide cancer prevention policy and decision makers with information regarding potential health risk areas allowing efforts to be prioritized in reducing exposure via ingestion.

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3.2 Lifetime Carcinogens in the Canadian Diet

ABSTRACT:

PURPOSE: To reveal differences in lifetime excess cancer risk from food and beverages for gender by province, and nationally, by income level from the dietary intake of arsenic.

METHODS: Monte Carlo risk simulation is applied to estimate probable lifetime contaminant intake and associated lifetime excess cancer risk from arsenic estimated in 60 whole foods for dietary patterns of 34,944 Canadians from 10 provinces as derived from Health Canada's Canadian Community Health Survey (CCHS) Cycle 2.2, Nutrition (2004) (Health Canada, 2007).

RESULTS: Assuming a 40% inorganic arsenic content, lifetime excess cancer risk (LECR) was shown to be above Health Canada guidelines of 10 extra cancers per million in 50 percent of the sampled population across Canada for both gender and income cohorts. In all provinces and most percentiles, male LECR values (range 0 to 1,148) were higher than female counterparts (range 0 to 874) based on Health Canada's cancer potency factor (CPF) of 1.8. The LECR estimated that high income earners were at lower risk for extra cancers (666 at the 99^{th} percentile). Low and middle incomes had similar results indicating higher risk of extra cancers in the 99^{th} percentile with 819 and 835 respectively.

CONCLUSIONS Lifetime excess cancer risk from dietary intake of arsenic is estimated to be higher for men in Canada, especially in British Columbia. Based on income level, extra cancers would be higher for low and middle incomes compared to high income from intake of arsenic from food and beverages.

Keywords: risk assessment; diet; organic arsenic; inorganic arsenic; gender; income

INTRODUCTION:

Arsenic, the 20th most common element in the earth's crust (IARC, 2012), occurs in the environment naturally and due to anthropogenic sources. Natural occurrences are found in specific rocks, especially associated with volcanic eruptions, while human activities associated occurrences are from industrial activities including mining, burning of fossil fuels and pesticide use, all contributing to environmental contamination (Health Canada, 1993; IARC, 2012; US FDA, 2005). Once in the environment, arsenic can enter the food chain. Arsenic has been found in a wide variety of foods and beverages, however, rice and fish/seafood have been found to predominate (Carlin et al., 2015; European Food Safety Authority, 2010; Health Canada, 1993; IARC, 2012). Ingestion of food and water is considered one of the primary routes of arsenic exposure where "daily intake of total arsenic from food and beverages is generally in the range of 20–300 μg/day" (IARC, 2012). Exposure to and ingestion of arsenic has been associated with adverse, long-term health effects including skin cancer, various cancers of the digestive tract, liver, bladder, kidney, prostate and lymphatic and hematopoietic systems (CAREX Canada, 2016). The International Agency for research on Cancer has classified arsenic and its compounds as Group 1, (*carcinogenic to humans*) based on epidemiological studies establishing associations with various forms of cancer (CAREX Canada, 2016; European Food Safety Authority, 2010; IARC, 2015).

Geographic location, along with socio-demographic factors, such as gender or household income may have an influence on our diet and health. In a Statistics Canada health report "How healthy are Canadians?", it is suggested that women are 80% more likely than men to consider food choice for maintaining overall good health (Statistics Canada, 2001a). In addition, a study

on factors leading to obesity indicates that along with diet, socio-economic status may also be causal; for example, those with lower income are shown to be at about 40% higher risk to incur health issues (Le Petit et al., 2006). A low-income model in the USA indicated that families with lower incomes to be at "high risk for poor eating habits and the associated chronic diseases of obesity, hypertension, hyperlipidemia, and diabetes", and that vegetables were the "least consumed food group" (McDermott and Stephens, 2010). One Canadian analysis showed that a higher income could be related to the purchasing of foods with higher nutritional value; such as fresh fruits and vegetables, lean meats and fish (Ricciuto and Tarasuk, 2007).

The objective of this paper is to conduct probabilistic modelling for intake of arsenic via foods and beverages, with a specific focus on differences between males and females across Canada, and differences based on income level. We hypothesize that men, when compared to women, consume different foods in different amounts, and therefore may have different associated intakes and risks. We hypothesize that dietary choices are impacted by income level, and therefore may have different associated intakes and health-related risks. The results of this study will serve to highlight important information gaps, identify potential priorities for more detailed exposure assessments or exposure reduction actions, and provide information useful for designing more rigorous epidemiological investigations related to differences in cancer incidence in various sectors of the Canadian population. This study is the first to look at dietary intake of arsenic and lifetime excess cancer risk disparities based on gender and income level across Canada.

MATERIALS & METHODS:

We employ a probabilistic approach to estimate the range and frequency of possible daily contaminant intakes for males versus females in Canada; as well as Canadians categorized into low, middle and high income brackets, and associate these intake levels with lifetime excess cancer risk. We then compare our results to the current Health Canada guideline that suggests that 10 extra cancers per one million people is a negligible risk (Health Canada, 2010). Typically, daily dietary intake is determined by:

$$\textbf{Intake} = \sum (F_1 \times C_1 \times DF_1) + (F_2 \times C_2 \times DF_2) + \ldots (F_n \times C_n \times DF_n) \quad \textbf{[Eq. 1]}$$

Where:
F = amount of specific food or beverage consumed in g/day
C = concentration of contaminant in ug/g
DF = detection frequency (# of detections / # of samples)
n = n^{th} food group

To estimate potential risk from long-term ingestion of carcinogens via diet, lifetime excess cancer risk (LECR) per million people is used as an indicator of potential cancers occurring in a population. LECR assumes that the lifetime average daily intake is the same for 70 years. It is calculated by multiplying the estimated intake by a cancer potency factor (CPF) which produces an estimate of the lifetime excess cancer risk (CAREX Canada, 2016):

$$\textbf{LECR per million} = 1{,}000{,}000/(ADI \times CPF) \quad \textbf{[Eq. 2]}$$

Where:
ADI = average daily intake in mg/kg of bodyweight
CPF = cancer potency factor (also called oral slope factor)

For this study, bodyweight is assumed to be 70kg, as per Health Canada's standards for exposure assessment (Health Canada, 1995). LECR for arsenic was generated using Health Canada's cancer potency factor of 1.8 (Health Canada, 2010b).

We use consumption data (g/day) from the 24-hr dietary recall of representative populations from the CCHS, Cycle 2.2, Nutrition (2004), a national canvassing of 34,944 respondents from Canada's ten (10) provinces (Health Canada, 2004): Newfoundland/ Labrador (NL), Prince Edward Island (PEI), Nova Scotia (NS), New Brunswick (NB), Quebec (PQ), Ontario (ON), Manitoba (MB), Saskatchewan (SK), Alberta (AB) and British Columbia (BC). Using data fields provided within the dataset (sample id; province; gender; income; food items (grams consumed), and based on a 24-hr dietary recall survey, the records were coded as Gender-Male (n = 16,461; 47.1%) or Gender-Female (n = 18,483; 52.9%); and Income <$19,999/yr-Low (n = 5,030; 14.4%); $20,000 - $59,999-Middle (n = 13,889; 39.7%); >$60,000-High (n = 11,990; 34.3%) and analysed separately. The CCHS includes household income in 11 brackets: we aggregated these into the three noted above. The gender split closely matches Statistics Canada's 2001 census for Age and Sex findings in a total population of 30,007,095 that 49.0% of Canada's population were males (Statistics Canada, 2001b), while 51.0% were female (Statistics Canada, 2001c). However, the 2001 census data (22.7 million income earners) for income levels in 2000 differ from this study's sample population (30,909 income earners) for Low (45.9% compared to 16.3%) and High (10.5% compared to 38.8%) income earners, while Middle income was close (43.6% compared to 44.9%) (Statistics Canada, 2001d). We attribute this difference to the CCHS sampling design which was stratified only by geographic location, age, and gender.

The CCHS survey lists approximately 232 food products in 78 food groupings as defined by the Bureau of Nutritional Sciences (BNS), some whole (e.g., apples) and some prepared (e.g., vegetable soup) (Health Canada, 2004). We do not include prepared foods (134 items) in our model, given the difficulties in establishing the ingredients and proportions thereof. We did

include 60 commonly consumed whole foods, aggregated in the final analysis into eight food groups as shown in Table 1. Arsenic data were only reported for 33 of the 60 foods listed (in **BOLD)**.

Table 12: Included Foods and Food Groups

Group	Individual Foods
Meat	Bacon; **Beef***; **Lean Beef***; **Chicken Meat**; Cured Ham; Ground Beef; Lamb; Lean Lamb; **Pork***; **Lean Pork***; **Lean Veal***; Liver; **Turkey with Skin***; **Turkey Meat***
Fish	**Fish**
Dairy	Butters; Cottage Cheese; **Eggs**; Half & Half; Ice Cream; **Lite Cheese***; **Regular Cheese***; Sour Cream; Margarines; **Whole Milk**
Fruit	**Apples**; Banana; Cherries; Citrus fruits; **Melons***; **Peaches**; Pears; Plums; **Raisins**; **Strawberries**
Vegetables	**Beans**; **Broccoli**; **Cabbage**; **Carrots**; **Celery**; **Corn**; French Fries; **Mushrooms**; **Onions**; Peas; **Peppers**; **Potatoes**; Squashes; Tomatoes
Rice/ Cereals	**Rice Cereals***; Pasta; **Rice***; **Wholegrain Cereals***
Grains/ Nuts	**Peanut Butter***; White Breads; **Whole Wheat Breads***
Beverages	Tea; Beers; **Wines***

* based on US data; otherwise from CFIA

We used the only available measured data: the Canadian Food Inspection Agency (CFIA) - National Chemical Residue Monitoring Program (NCRMP), 2012-2013 Annual Report (Canadian Food Inspection Agency, 2014) and the U.S. Food and Drug Administration – Elements Results Summary - Market Baskets 2006 through 2011 (US FDA, 2014). The CIFA's NCRMP tests for residues of metals, including total arsenic in numerous foods (Canadian Food Inspection Agency, 2014). The US FDA 2014 report published results for various elements including total arsenic found in various food and beverages (US FDA, 2014). The minimum,

mean and maximum concentration of our selected contaminant for individual foods were matched to the CCHS food list to produce model inputs for amounts consumed with associated contaminant concentration. Table 2 lists the concentration data for total arsenic in the foods included in our study.

Table 13: Concentration data

Food Group	Arsenic (ug/g) (ppm)			
	MEAN	MIN	MAX	D F
MEAT				
beef	0.002	0.000	0.014	0.125
chicken meat	0.010	0.005	0.048	0.314
lean beef	0.009	0.007	0.012	0.250
lean pork	0.007	0.006	0.007	0.058
lean veal	0.006	0.006	0.007	0.188
turkey with skin	0.010	0.005	0.028	0.415
turkey meat	0.010	0.005	0.028	0.415
FISH				
fish	0.305	0.000	0.436	0.958
DAIRY				
eggs	0.020	0.011	0.032	0.281
lite cheese	0.001	0.000	0.022	0.042
regular cheese	0.026	0.015	0.047	0.429
whole milk (ppm)	0.011	0.010	0.020	0.143
FRUITS				
apples	0.011	0.005	0.028	0.075
melons	0.006	0.000	0.024	0.500
peaches	0.018	0.018	0.018	0.333
raisins	0.007	0.000	0.031	0.250
strawberries	0.010	0.010	0.010	0.143
VEGETABLES				
beans	0.007	0.007	0.007	0.200
broccoli	0.002	0.000	0.010	0.042
cabbage	0.004	0.004	0.004	0.200
carrots	0.007	0.006	0.008	0.250
celery	0.007	0.007	0.007	1.000
corn	0.001	0.000	0.013	0.042
mushrooms	0.014	0.005	0.030	0.889
onions	0.009	0.009	0.009	0.250
peppers	0.007	0.007	0.007	0.143
potatoes	0.007	0.004	0.016	0.196
RICE/CEREALS				
rice	0.065	0.036	0.094	1.000
rice cereal	0.161	0.000	0.505	0.958
wholegrain cereals	0.027	0.000	0.054	0.917
GRAINS/NUTS				
peanut butter	0.005	0.000	0.037	0.167
whole wheat breads	0.004	0.000	0.012	0.333
BEVERAGES				
wines (ppm)	0.008	0.000	0.018	0.750

Although dietary sources of arsenic are generally reported as total arsenic (Canadian Food Inspection Agency, 2014; US FDA, 2014); food and water may contain two types (also called species) of arsenic compounds: organic (most prevalent in food and not considered carcinogenic) and inorganic, which can be absorbed from soil and groundwater contamination (European Food Safety Authority, 2010; US FDA, 2005). Inorganic arsenic, considered the more toxic form, is found predominantly in water and rice (European Food Safety Authority, 2010; Health Canada, 2006; Meacher et al., 2002). Studies from the 1980s indicate that arsenic intake from various foodstuffs was 75% organic and 25% inorganic (Hazell, 1985; US EPA, 1987). Analyses conducted by the Ontario Ministry of Environment and Energy estimated that between 20% and 40% of total arsenic intake from dietary sources was inorganic and mainly from cereals, rice and fish (Yost et al., 2010). Analysis of the US FDA's Total Diet Study (1991-1996) indicated that the inorganic arsenic contribution in total arsenic was 43% in rice, 49% in cereals, and 1% in marine fish (Tao and Bolger, 1999). Recently, Health Canada conducted a study of arsenic species in rice and pear products(Health Canada, 2014). They found that 70 to 80 percent of arsenic in white and brown rice was inorganic, and that pear products contained from 20 percent inorganic arsenic (pear juice) up to 55 percent (pear snacks, pear nectar and pear baby food). We present results assuming 40 percent of total arsenic consumed is inorganic.

A probabilistic risk model developed with @RISK software was used to conduct Monte Carlo simulation analysis for gender and income level intakes. This technique selects values at random from input probability distributions. Each set of sample values is called an iteration. For our study, a dietary record was selected at random in each iteration, then for each food reported as being consumed, a random value for the concentration value was generated based on a PERT distribution, and finally **Eq 1** was calculated. Population weights provided by CCHS were used

to guide the selection of the dietary record. We ran 50,000 iterations using the gender (male and female, separately) dietary records and 50,000 iteration using the income (low, middle, and high, separately) dietary records, producing distributions of the resulting intake values. Finally, we calculated LECR for key percentiles of each distribution, using Health Canada's cancer potency factor.

RESULTS:

Gender by Province: Total arsenic intake levels based on gender by province are shown in Figure 1. The 50^{th} percentile intake ranged from 1.3 ug/day (females in Newfoundland/Labrador) to 3.0 ug/day (males in British Columbia). Males and females in British Columbia had the highest 80^{th} percentile intake (19 ug/day and 14 ug/day respectively) and the highest 99^{th} percentile intake (112 ug/day and 85 ug/day respectively). In general, female intakes were lower than male intakes.

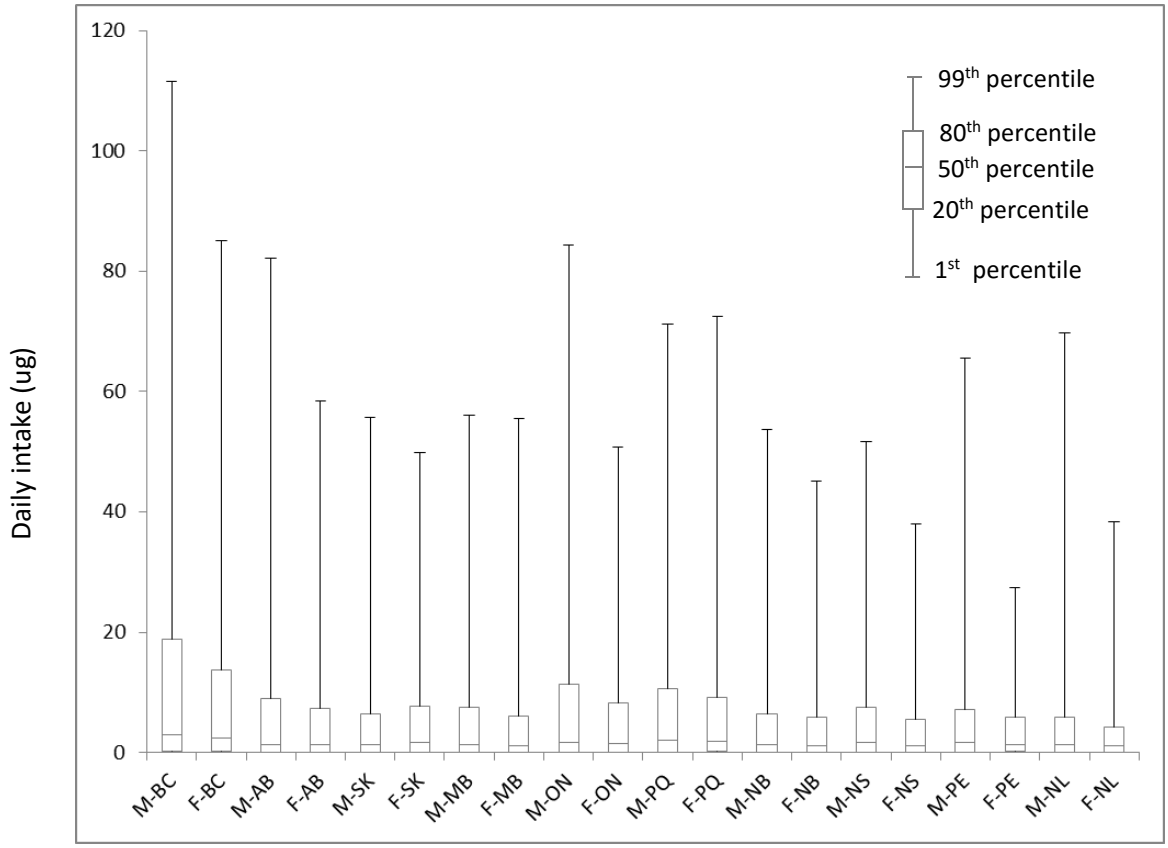

Figure 8: Total Arsenic intake - Gender by province

(BC = British Columbia; AB = Alberta; SK = Saskatchewan; MB = Manitoba; ON = Ontario; PQ = Quebec; NB = New Brunswick; NS = Nova Scotia; PE = Prince Edward Island; NL = Newfoundland/Labrador)

The primary food group contributing to arsenic intake was rice & rice cereals: at the 50th percentile, intake of arsenic from rice and rice cereals for males ranged from a low of 41.0% in NL to a high of 74.5% in MB; and for females ranging from a low of 54.3% in PQ to a high of 69.8% in ON. Fish was the second most contributing food for arsenic intake at the 50th percentile, with males ranging between 7.83% in MB to 32.3% in NL and females from 10.2% in AB to 21.6% in PQ. BC respondents registered the highest 50th percentile arsenic intake from cereal/rice for both males and females at 8.39 ug/day and 6.47 ug/day respectively; followed by fish, 2.04 ug/day (males) and 1.77 ug/day (females) for fish (Table 3). NL respondents were

estimated to have the lowest 50th percentile arsenic intake for males and females from cereal/rice at 2.01 ug/day and 2.00 ug/day respectively; however, for fish NL males had the lowest intake (0.28 ug/day), while SK females has the lowest intake (0.26 ug/day) (Table 3).

Table 14: 50th Percentile Arsenic intake (Percent) due to Rice/Cereal and Fish

	Cereal & Rice (ug/day)		Fish (ug/day)	
	M	**F**	**M**	**F**
NL	2.01 (41.0%)	2.00 (58.0%)	0.28 (4.9%)	0.60 (12.4%)
NS	2.71 (48.1%)	2.40 (59.3%)	0.60 (12.5%)	0.43 (10.1%)
NB	2.76 (57.7%)	2.70 (62.7%)	0.68 (14.1%)	0.61 (11.9%)
SK	2.76 (57.0%)	3.26 (62.8%)	0.84 (15.0%)	0.26 (6.55%)
PE	3.13 (56.2%)	2.32 (59.5%)	1.19 (14.7%)	0.58 (10.4%)
PQ	3.91 (55.6%)	3.57 (54.3%)	1.21 (17.7%)	0.55 (10.2%)
MB	4.26 (74.5%)	3.15 (64.9%)	1.31 (18.7%)	1.42 (21.6%)
AB	4.39 (63.9%)	3.66 (68.5%)	1.34 (23.7%)	0.52 (12.9%)
ON	5.69 (70.0%)	3.87 (69.8%)	1.58 (32.3%)	0.43 (12.4%)
BC	8.39 (68.7%)	6.47 (66.8%)	2.04 (16.7%)	1.77 (18.3%)

Assuming 40 percent of total arsenic intake is inorganic in form, LECR estimates were above the Health Canada guideline of 10 per million at the 50th percentile in every group. In other words, based on the included foods, consumption levels, and reported arsenic concentrations, we found there was a 50 percent chance that intake would be associated with a non-negligible excess cancer risk for Canadians, regardless of gender or province of residence. (Table 4). The highest LECRs at all percentiles were seen in BC males followed by BC females, reaching 1,148 per million and 874 per million respectively at the 99th percentile.

Table 4: LECR assuming 40% inorganic

%-ile	BC		AB		SK		MB		ON		PQ		NB		NS		PE		NL	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20	2	2	1	0	1	1	0	1	1	1	1	2	1	0	1	1	1	2	0	1
30	9	7	3	3	3	5	3	3	4	4	5	6	3	2	4	3	4	5	3	2
40	**17**	**14**	7	7	8	**10**	7	7	10	8	**12**	**12**	7	6	10	7	9	9	7	6
50	**30**	**25**	**14**	**13**	**14**	**17**	**14**	**12**	**18**	**15**	**21**	**20**	**13**	**11**	**18**	**13**	**17**	**15**	**13**	**11**
60	**56**	**45**	**24**	**22**	**23**	**28**	**24**	**20**	**32**	**25**	**36**	**32**	**22**	**19**	**29**	**20**	**27**	**23**	**21**	**18**
70	**110**	**85**	**41**	**38**	**38**	**47**	**42**	**34**	**59**	**45**	**63**	**53**	**35**	**32**	**46**	**32**	**43**	**37**	**33**	**27**
80	**194**	**141**	**92**	**75**	**66**	**80**	**77**	**63**	**116**	**85**	**109**	**94**	**66**	**60**	**77**	**57**	**74**	**60**	**60**	**44**
90	**363**	**291**	**201**	**150**	**128**	**135**	**156**	**133**	**233**	**163**	**190**	**170**	**128**	**118**	**147**	**119**	**151**	**110**	**119**	**89**
95	**550**	**434**	**314**	**248**	**203**	**205**	**263**	**239**	**369**	**262**	**290**	**262**	**206**	**195**	**264**	**192**	**252**	**168**	**178**	**141**
96	**615**	**476**	**359**	**278**	**232**	**240**	**313**	**279**	**426**	**289**	**324**	**311**	**232**	**231**	**300**	**215**	**284**	**187**	**202**	**159**
97	**728**	**533**	**428**	**316**	**275**	**286**	**385**	**337**	**498**	**329**	**380**	**417**	**265**	**271**	**342**	**243**	**324**	**210**	**239**	**188**
98	**908**	**641**	**546**	**403**	**361**	**366**	**465**	**437**	**624**	**394**	**500**	**557**	**339**	**344**	**404**	**289**	**392**	**240**	**324**	**250**
99	**1,148**	**874**	**845**	**601**	**574**	**513**	**576**	**572**	**867**	**522**	**733**	**746**	**552**	**464**	**531**	**391**	**675**	**282**	**717**	**394**

BOLD indicates higher than Health Canada guideline

Income Level: Arsenic intake based on income show the highest levels were for Low and Middle incomes (Figure 9) with the average measuring 7.64 ug/day and 7.40 ug/day respectively, compared with High income intake at 6.40 ug/day (Table 5).

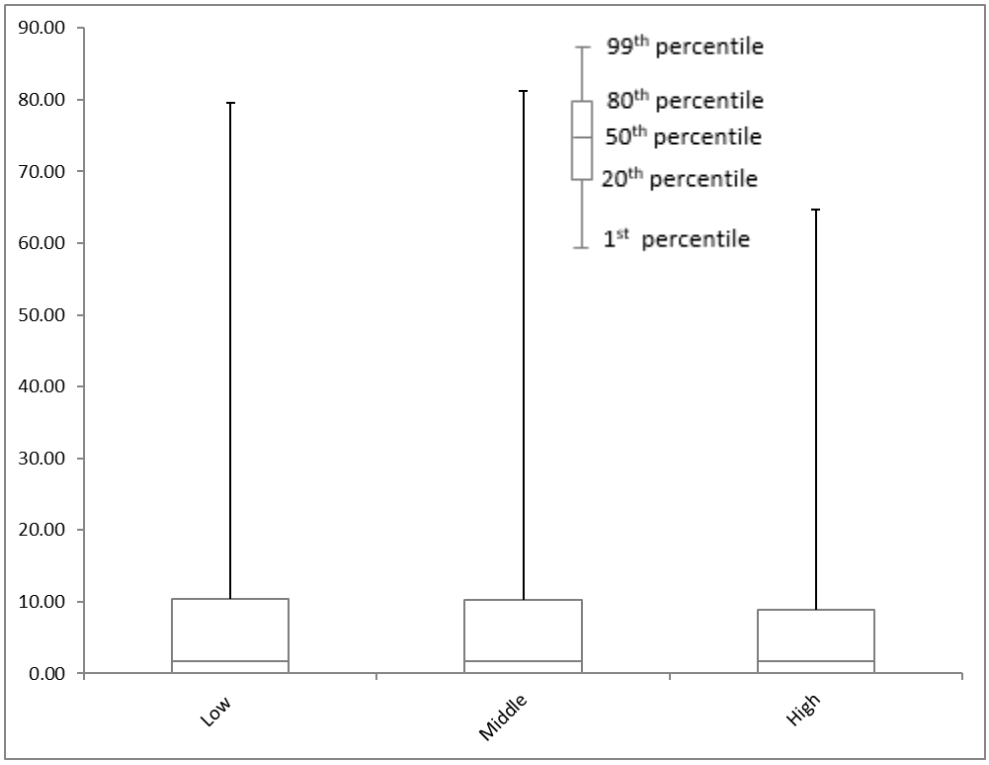

Figure 9: Arsenic intake by income level

The primary food group contributing to arsenic intake in all categories was rice & rice cereals (Table 5).

Table 5: MEAN Arsenic intake by income

Income Level	Arsenic intake (ug/day)		
	MEAN	Cereal/Rice	Fish
Low	7.64	5.38 (70.4%)	1.03 (13.5%)
Middle	7.40	4.80 (64.9%)	1.24 (16.8%)
High	6.40	3.99 (62.4%)	0.96 (15.0%)

Assuming 40 percent of total arsenic intake is inorganic in form, LECR estimates were above the Health Canada guideline of 10 per million at the 50th percentile in every group. In other words, based on the included foods, consumption levels, and reported arsenic concentrations, we found there was a 50 percent chance that intake would be associated with a non-negligible excess cancer risk for Canadian, regardless of gender of province of residence. (Table 6). The highest LECR at all percentiles was seen in Middle incomes reaching 835 per million; the lowest LECR was seen in High incomes at 666 per million, both at the 99th percentile.

Table 6: LECR assuming 40% inorganic

	LECR - Health Canada		
%-ile	**Low income**	**Middle income**	**High income**
1	0	0	0
5	0	0	0
10	0	0	0
20	1	1	1
30	4	5	5
40	10	10	10
50	**18**	**18**	**17**
60	**31**	**31**	**28**
70	**57**	**56**	**50**
80	**107**	**105**	**92**
90	**217**	**203**	**181**
95	**367**	**327**	**292**
96	**418**	**382**	**334**
97	**489**	**458**	**397**
98	**607**	**556**	**487**
99	**819**	**835**	**666**

BOLD indicates higher than Health Canada guideline

CONCLUSIONS:

We observed differences in arsenic intake and associated LECR among between males and females, among provinces and across income categories as hypothesized. Importantly, at least 50 percent of the provincial populations simulated had LECRs above the 10 per million, suggesting the potential for real increased cancer risks. Differences based on income shows at least 60 percent of the sample population above the 10 per million. This indicates more detailed exposure assessment is warranted to more fully understand the determinants of exposure. This could include more detailed dietary studies, for specific geographic regions, genders and income levels.

Our assumption of 40 percent inorganic arsenic content impacts the percentiles at which LECR exceeds 10 per million. For example, a more conservative assumption of 20 percent inorganic content would lower the chance of exceeding the Health Canada guideline from 50 percent to 30 or 40 percent in every group (Table 7).

Table 7: LECR assuming 20% inorganic (**BOLD** indicates higher than Health Canada guideline)

%-ile	BC		AB		SK		MB		ON		PQ		NB		NS		PEI		NL	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20	1	1	0	0	0	1	0	0	0	0	1	1	0	0	0	0	0	1	0	0
30	4	4	2	1	2	3	1	2	2	2	3	3	2	1	2	2	2	2	1	1
40	9	7	4	4	4	5	4	4	5	4	6	6	4	3	5	4	5	4	4	3
50	**15**	**13**	7	7	7	9	7	6	9	7	**10**	**10**	7	6	9	6	8	7	7	6
60	**28**	**23**	**12**	**11**	**11**	**14**	**12**	10	**16**	**13**	**18**	**16**	**11**	9	**15**	10	**13**	**12**	10	9
70	**55**	**42**	**20**	**19**	**19**	**24**	**21**	**17**	**29**	**23**	**32**	**27**	**18**	**16**	**23**	**16**	**22**	**19**	**17**	**14**
80	**97**	**71**	**46**	**37**	**33**	**40**	**38**	**31**	**58**	**42**	**55**	**47**	**33**	**30**	**39**	**28**	**37**	**30**	**30**	**22**
90	**182**	**146**	**101**	**75**	**64**	**67**	**78**	**67**	**116**	**82**	**95**	**85**	**64**	**59**	**74**	**59**	**76**	**55**	**60**	**45**
95	**275**	**217**	**157**	**124**	**102**	**102**	**131**	**119**	**185**	**131**	**145**	**131**	**103**	**98**	**132**	**96**	**126**	**84**	**89**	**70**
96	**308**	**238**	**180**	**139**	**116**	**120**	**156**	**140**	**213**	**144**	**162**	**155**	**116**	**115**	**150**	**107**	**142**	**93**	**101**	**80**
97	**364**	**267**	**214**	**158**	**137**	**143**	**193**	**169**	**249**	**165**	**190**	**209**	**132**	**135**	**171**	**121**	**162**	**105**	**119**	**94**
98	**454**	**321**	**273**	**201**	**180**	**183**	**232**	**219**	**312**	**197**	**250**	**279**	**169**	**172**	**202**	**144**	**196**	**120**	**162**	**125**
99	**574**	**437**	**422**	**301**	**287**	**257**	**288**	**286**	**433**	**261**	**367**	**373**	**276**	**232**	**266**	**196**	**337**	**141**	**359**	**197**

The differences we observed are strictly due to variation in consumption patterns. It may be that arsenic in foods differ among regions and between genders, as well as the percent inorganic content. More specific studies the focus on difference among regional foods and inorganic arsenic content would improve the accuracy of similar risk assessments. Similarly, additional research could determine how factors such as the cost of foods contribute – for example, do lower income people consume more rice and cereals due to economic factors?

Our results may differ from comparative studies on dietary intake of arsenic as the variables and methods used in each analysis may vary widely; such as, the number of foods being tested; consumption patterns used; differing testing, surveying, and reporting criteria between studies; and size of sample population. For example, total arsenic daily intake values have been reported as ranging from 27.5 ug/day from 264 foods in a US study (Tao and Bolger, 1999b) to 77.0 ug/day from 300 foods in a study from Chile (Munoz et al., 2005). Both of these studies were deterministic, in that results were produced by assuming a hypothetical person consumed the population average amount of all foods tested, with the single level of total arsenic measured in each of those foods. Our study uses actual dietary patterns, which preserves more realistic consumption levels. Other studies reported results indicating that average daily intakes ranged between 0.25 – 0.36 ug/kg-bw (Xue et al., 2010), which becomes 17.5 – 25.2 ug/day respectively assuming the standard body weight of 70kg (Health Canada, 1995; US EPA, 2011). In this case, a very sophisticated probabilistic model was employed, and included 280 foods (whole and prepared), as well as drinking water which can be a significant source of arsenic. This suggests LECRs estimated in our study may be very conservative, highlighting the need for more detailed investigation of potential arsenic exposure in Canada.

In conclusion, our study reveals geographic, gender and income differences in exposure to arsenic exist based differences in amounts of foods and wine., and that these result in LECRs above 10 per million in a significant proportion of the populations simulated. Given key gaps due to data availability, we believe we have underestimated the intake and associated risk, perhaps substantially. Improvements in our ability to accurately assess risks due to the ingestion of arsenic are clearly a critical next step.

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4.0 Conclusions and Recommendations

4.1 Data Issues

In the process of conducting this risk assessment for carcinogens in food and beverages, the complexities of establishing dietary intake became evident. Food data and information was widely diverse across government studies or reports, and academic literature making selection for analysis challenging and subject to uncertainty. Data availability and data quality from reliable sources remains an issue for producing credible results[18,36].

Although the Internet searches provided a wide variety of peer-reviewed articles and published reports on food and beverages covering a myriad of topics, narrowing the search became the issue in locating the most reliable and effective databases and information outlets to meet the requirements for this risk assessment. Once the selections had been made, using the information and data became the next challenge. Lack of standardized measurement methodologies and testing practices utilized between studies and agencies required interpretations and assumptions to be made, leading to more uncertainty and questionably reliable results[101]. Data terminology, such as standardized food naming, portion sizing, and units of measure, are some of the factors that remain inconsistent requiring interpretation and thereby adding uncertainty[34,102]. Food items consumed and food items tested for residues are rarely the same, causing additional interpretation and uncertainty[55–57]. Food sample selection, criteria for testing and techniques to be used may differ widely between reporting agencies or studies[57,81]. Intake thresholds or 'dose-response' levels where adverse health effects may materialize are not consistent between analytic groups or testing agencies[16,17,19,26].

The design and planning of the risk assessment model and which dietary intake approach would produce the most effective and useful results is an instrumental decision in risk assessment. Point estimates produce 'worst-case' scenario, conservative values, indicating that the entire sample population is similarly exposed which, in turn, leads to over-estimating potential health effects[2]. Probabilistic methods give a broader range of results allowing for greater flexibility in decision-making based on results. Variable selection play an important role in effecting a meaningful analysis by taking into consideration sample population demographics, sample size, food items to include/exclude, residues selection (quantity and quality), to name a few. Then comes the challenge in managing so many possible variations and still produce meaningful results. Building an effective model takes effort and patience, because even with today's sophisticated technologies, it can take significant time to run a model. Therefore, selecting good, reliable datasets and risk analysis software are key to usable results.

Regrettably, in Canada, when dietary intake surveys are only conducted every decade or so, and total diet studies do not measure a substantial number of potential carcinogenic substances in food items, good datasets are not readily available making effective risk assessment difficult. Any risk or exposure assessment is only as good as the data available for analysis which is deemed very low. Unfortunately, government agencies in Canada have adopted a reactionary approach to health issues regarding food, only taking action following an outbreak (e.g., e-coli, salmonella, listeria, etc.) or substantial finding (e.g., BPA in plastic containers)[103].

4.2 Recommendations

While estimating and analyzing dietary intake for the population at large is a complex and complicated matter, it is integral to humans' overall well-being where being informed and pro-active may lead to better food policies and practices from health agencies. The following recommendations may allow for that flow of information:

1. Establish or adopt (from the USA or EU community) a standardized food item listing with clear and concise definitions.
2. Establish or adjust (from existing USA or EU systems) to suit Canadian criteria, a more robust food consumption survey system.
3. Establish or expand the existing number of contaminant residues in food monitoring systems.
4. Conduct duplicate studies to test for contaminants in the same foods as consumed.
5. Harmonize databases between agencies and research groups.
6. Develop and/or utilize tools and technology to become proactive in the analysis of food safety and health risks from the accumulated effects of multiple exposures to chemicals and/or environmental contaminants in the food supply.

In the 21st century, considered the 'age of information' with a proliferation of emerging technologies and connectivity, there is an opportunity to make total diet studies and dietary intake surveys into effective and efficient tools in cancer prevention and proactive healthcare. Risk assessments, and specifically probabilistic models, among other analysis methods, allow decision and policy-makers to identify populations at risk for adverse health effects from dietary intake; thereby, enabling appropriate action(s).

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