An Assessment of the Burden of Disease Attributable to Ambient Air Toxics in Ontario: a Disability-Adjusted Life Year (DALY) Methodology

by

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Authors Declaration

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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Abstract

Hazardous air pollutants (HAP's) are assumed to act without threshold meaning any level of exposure can theoretically initiate the carcinogenic process. With approximately 57,000 new cancer diagnoses and 25,900 deaths predicted in Ontario in 2006, the implications of lifetime low dose cumulative exposure to HAP's in the etiology of cancer is unknown, yet may be significant. As such, this burden of disease (BoD) model was designed to provide a comprehensive assessment of the current and future BoD attributable to long term cumulative exposure to six carcinogenic HAP's in two highly exposed regions of Ontario, using a summary measure of population health, disability-adjusted life years (DALY's). Results indicated a total of 32,074 DALY's were lost in Toronto and Southwestern Ontario (SWO) from six cancer sites in 2001, with the largest burden from cancers of the lung, followed by lymphomas, then leukemia. Approximately 0.58% of the burden (187 DALY's) was attributable to current HAP exposures, with the largest health impacts associated with exposure to nickel refinery dusts in SWO (8.91 DALY's) and benzene in Toronto (46.30 DALY's). The model predicted 0.3% of the exposure attributable BoD (96 DALY's) could be avoided in the future if ambient exposures were reduced to a feasible distribution. If ambient exposures were further reduced to levels expected if there were no anthropogenic releases, the model predicts 147 DALY's could be avoided, such that only 0.12% of the total BoD would be attributable to natural sources of HAP's. Results of the sensitivity analysis support the notion of the DALY as a robust measure to estimate exposure attributable health impacts, as the incorporation of alternative value choices had negligible impact on the relative importance of cancer sites, or exposures to the total BoD. Results of the model can be used by decision makers to inform public health policy regarding abatement priorities of HAP's in Ontario, on the basis associated health impacts.

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1. INTRODUCTION

In developed societies that have undergone epidemiologic and demographic transitions, the contribution of the environment to the burden of disease (BoD) is an important public health concern. Economic prosperity following these transitions has resulted in industrialization, urbanization, and an aging population dominated by chronic disease (Melse & de Hollander, 2001; Smith & Ezzati, 2005).

The environment operates as a distal risk factor affecting virtually all diseases through complex pathways that are not always understood (Smith & Ezzati, 2005). Genetic, social, and economic factors interact with environmental risks, creating disparities in exposure among subgroups of the population (Kay et al, 2000; Kreuter et al, 2004; Melse & de Hollander, 2001). For example, neighbourhoods within the vicinity of industrial facilities, with elevated levels of toxics releases, are more likely to be of low income, poorer general health status, and have greater social distress and distrust of industry, compared to communities in rural or distant areas (Luginaah et al, 2002; Melse & de Hollander, 2001).

Recently in Ontario there has also been increased reliance on fossil fuels to meet increasing energy and transportation demands. Although the national average annual concentrations of hazardous air pollutants (HAP's) are generally below Health Canada's "acceptable risk" values, the National Air Pollution Surveillance (NAPS) system has consistently reported elevated concentrations within the vicinity of industrial and urban locations, reflecting concentrated point source emissions, traffic congestion, and population densities.

Despite inequalities in exposure to environmental air toxics, chronic toxicity studies in animal models and epidemiological studies in occupationally exposed workers have causally associated many HAP's with various types of cancers (IARC, 2007). Furthermore, since the

concentration-response function for carcinogenic substances in the environment is assumed to act linear without threshold (McColl, Hicks et al, 2000), it is theoretically possible that any level of exposure can initiate the carcinogenic process.

Since the 1980's the total number of individuals either being diagnosed or dying from cancer in Ontario has been on the rise. Over the past 12 years, the number of deaths and diagnoses has increased by 20-25% (CCDPC-PHAC, 2006). For example, in 1992 there were 42,886 incidence and 20,109 fatal cases (CCDPC-PHAC, 2006), compared to a best prediction of 57,200 new diagnoses and 25,900 deaths in Ontario in 2006 (Canadian Cancer Society, 2006), with less then 1% occurring in persons under 20 years. With an aging population structure, the statistics imply an increased risk of cancer in older ages may result from a lifetime of low dose cumulative exposure to risk factors such as ambient air toxics.

Previous studies have estimated between 1.5-4% of the total BoD in the Organization for Economic Co-operation and Development regions can be attributable to environmental factors (Melse & de Hollander, 2001). Historically, developed countries of the OECD have been held responsible for 80% of toxic pollutant emissions (CPHA, 1996). However, with recent economic and industrial advances in developing countries, such as China and India with populations in the billions, the potential global health burden associated with air toxics is in its infancy.

With uncertainty in current scientific knowledge regarding the contribution of HAP's to the BoD, this regional level assessment can provide valuable information on a potentially significant environmental health issue (Kay et al, 2000; Mathers et al, 2001). A better understanding of health impacts associated with long term exposure to ambient air toxics can aid in informed decision making and efficient policy development to reduce the exposure associated BoD, while supporting sustainable development and environmental protection.

2. BACKGROUND

2.1. Ambient Air Toxics[1]

With increased industrialization and urbanization, anthropogenic release of toxics into the ambient environment has been recognized as hazardous to human health (Burnett et al, 2000; Cohen et al, 2005; Campbell et al, 2004). Environmental health indicators, which quantify health impacts associated with environmental hazards, have increasingly been used by decision makers to inform discussion concerning control and mitigation policies (Cohen et al, 2005).

A decision making model to assess human health risks and to develop priorities for reductions in oil refinery emissions was produced by the Network for Risk Assessment and Management (NERAM) in 2003 (McColl, Hicks et al, 2003). The prototype HEIDI model (Health Effects Indicators Decision Index) was originally developed for the Canadian Council of Ministers of the Environment (CCME) to support the National Frameworks for Petroleum Refinery Emission Reductions (NFPRER). Fourteen substances have since been included in the updated HEIDI II; assumptions and uncertainties of the model are described elsewhere (McColl, Hicks et al, 2003). Of the 14 substances included in the model, six have been classified as carcinogenic by the International Agency for Research on Cancer (IARC) and will be briefly reviewed[2]. Table 2.1 outlines the physical and chemical properties of acetaldehyde, formaldehyde, benzene, 1,3-butadiene, ethylene oxide, and nickel (refinery dusts)

[1] The term ambient air toxics is synchronously used with the term hazardous air pollutants (HAP's)
[2] BaP/PAH was excluded because of known confounding relationship with environmental tobacco smoke (ETS)

Table 2.1: Physical and Chemical Properties of Six Carcinogenic Ambient Air Toxics

Chemical Identity:	Benzene[1]	1,3-Butadiene[1]	Ethylene Oxide[1]
CAS Registry	71-43-2	106-99-0	75-21-8
Synonyms	Anuleen, benzeen, benzole, benzol, coal naphtha, cyclohexatriene, fenzen, phene, phenol hydride, pyrobenzol, pyrobenzole	Butadiene, buta-1,3-diene, biethylene, bivinyl, vinylethylene, erythrene, pyrrolylene	Ethylene oxide oxirane, dihdydro oxirene, dimethylene oxide, epoxyethane, ethene oxide, ETO anaprolene
Physical Description	Clear, colorless liquid	Colorless gas	Colorless gas
Molecular Weight	78.11g/mol	54.09 g/mol	44.05g/mol
Molecular Formula	C_6H_6	C_4H_6	C_2H_4O
Boiling Point	80.1 degrees Celsius	-4.4 degrees Celsius	11 degrees Celsius
Melting Point	5.5 degrees Celsius	-108.9 degrees Celsius	-111 degrees Celsius
Density	0.8787	0.6211g/ml	0.8824
Vapor Pressure	75 mmHg	2100mmHg	1.095×10^3 mmHg
Odor recognition Threshold	$4.9mg/m^3$	1-1.6ppm	$787mg/m^3$
Solubility	Log Ko/w 2.13 Log Ko/c 1.8 – 1.9	Log o/c 1.99 Log Ko/c 2.46	Log Ko/w -0.22 Log Ko/c 0.342
Conversion	$1ppm = 3.24 mg/m^3$	$1ppm = 2.21mg/m^3$	$1ppm = 1.83mg/m^3$

Chemical Identity:	Acetaldehyde[2]	Formaldehyde[1]	Nickel (compounds)[3]
CAS Registry	75-07-0	50-00-0	NA-11
Synonyms	Ethanal, acetic aldehyde, acetylaldehyde, ethylaldehyde, methyl formaldehyde	Formic aldehyde, methanal, methyl aldehyde, methylene oxide	Inorganic nickel compounds: oxidic, sulfidic, soluble nickel
Physical Description	Colorless liquid with fruity odor at room temperature	Colorless gas	
Molecular Weight	44.05 g/mol	30.03 g/mol	
Molecular Formula	CH_3CHO	CH_2O	
Boiling Point	20.2-20.8 degrees Celsius	-21 degrees Celsius	
Melting Point	-123.5- -121 d. Celsius	-92 degrees Celsius	
Density	0.788 g/ml	0.815 g/ml	
Vapor Pressure	98.642 to 134.08 kPa	3,883 mmHg	
Odor Recognition Threshold	0.21ppm	0.5-1.0ppm	
Solubility	Log Ko/w 0.45 Log Ko/c 0.063	Log Ko/w 0.350 Log Ko/c 1.567	
Conversion Factor	$1ppm = 1.83mg/m^3$	$1ppm = 1.23mg/m^3$	

[1]ATSDR (Agency for Toxic Substances and Disease Registry) toxicological profile-physical and chemical properties
[2]Priority substance list profile
[3]N/A given nature of multiple compounds

2.1.1. Acetaldehyde

Acetaldehyde is released with the incomplete combustion of gasoline, diesel fuels, biomass combustion, and from industrial emissions (Health Canada, 2000). Preliminary data from the National Pollution Release Inventory (NPRI) reports 275.13 tonnes of acetaldehyde were emitted from industrial point sources in Ontario in 2005. Furthermore, stationary sources of acetaldehyde include emissions from wood burning stoves, fireplaces, furnaces, waste incinerators, coffee bean roasting and environmental tobacco smoke (ETS) (Health Canada, 2000). However, the largest contribution of acetaldehyde to ambient air concentrations (56%) likely results from secondary formation from precursor volatile organic compound (VOC's) oxidations (CARB, 1987; Health Canada, 2000). With an overall half-life of less then 10 hours (Health Canada, 2000), long range transport is unlikely, and acetaldehyde is not persistent nor bioaccumulative (Health Canada, 2000)

2.1.2. Formaldehyde

Similar to acetaldehyde, formaldehyde is released during anthropogenic activities, yet the largest contribution in ambient air results from secondary formation in the atmosphere (Health Canada, 2001). In urban areas during air pollution episodes, secondary formation can account for 70-90% of the urban ambient concentration (ATSDR, 1999; Health Canada, 2001). Formaldehyde reacts with hydroxyl radicals with a half-life pending atmospheric conditions, generally around 10 days (ATSDR, 1999). Despite large ambient concentrations from secondary production, the NPRI reports industrial point sources released 901.76 tonnes of formaldehyde in Ontario in 2005.

2.1.3. Benzene

Compared to emissions from anthropogenic sources, benzene is found at low concentrations naturally in the environment, released from bush fires, crude oil seeps, and plant volatiles (ATSDR, 2005; Health Canada, 1993). Preliminary data from the NPRI reports 405.80 tonnes of benzene were emitted from industrial sources in Ontario in 2005, yet the largest contribution of benzene to ambient air has historically resulted from on and off road vehicle emissions, accounting for approximately 76% of benzene release (Health Canada, 1993), prior to the implementation of new Canada-wide standards for benzene content in gasoline.[3] Benzene is degraded by photo-oxidation, with a short half-life limiting long range transport (ATSDR, 2005).

2.1.4. 1,3-Butadiene

1,3-butadiene, hereafter referred to as 1,3-BD, is released during petrochemical production, use, and transport, from vehicle exhaust, and naturally during biomass combustion (ATSDR, 1992; Health Canada, 2000). Upon release, 1,3-BD undergoes rapid photo-oxidation with hydroxyl radicals (Health Canada, 2000). The NPRI reports 41.76 tonnes of 1,3-BD were emitted from industrial point sources in Ontario in 2005. The highest environmental mean concentration in Ontario ($28\mu g/m^3$) has been recorded by the National Air Pollution Surveillance program (NAPS) 1km distance from a point source of 1,3-BD production (Health Canada, 2000).

2.1.5. Ethylene Oxide

Ethylene oxide, hereafter referred to as ETO, is released during herbicide fumigation, hospital equipment sterilization, vehicle exhaust, and ETS, with negligible contributions from

[3] The new CEPA vehicle emission reduction regulations for benzene content in gasoline has reduced the average benzene content in gasoline from 1.6% in 1995 to 0.7% in 1999. Such regulations have been followed by a reduction in annual mean ambient benzene concentrations in Canada by approximately 45% (Environment Canada, 2001)

natural releases (ATSDR, 1990; Health Canada, 2001). ETO is degraded by radical formation and hydrolysis, with an estimated atmospheric half-life of 69-149 days (ATSDR, 1990). Although the NPRI (2005) reports smaller quantities of emissions from industrial point sources in Ontario (13.59 tonnes) compared to other air toxics, exposure to ETO may occur in areas of petrochemical production of dense vehicle traffic from the oxidation of ethylene.

2.1.6. Nickel (Refinery Dusts)

Nickel exists naturally in the earth's crust generally bound in insoluble complexes with large diameter, not posing a human health hazard. However nickel refinery dusts, which include inorganic nickel compounds: oxidic, sulfidic, and soluble nickel, are able to penetrate the lungs and are hazardous to human health (Health Canada, 1994). Release of inorganic nickel into the ambient air occurs during primary bas metal production (mining, smelting, refining), fossil fuel combustion, alloy production, and scrap reprocessing. The NPRI reports 164.92 tonnes of nickel refinery dusts were emitted into the ambient air in Ontario in 2005.

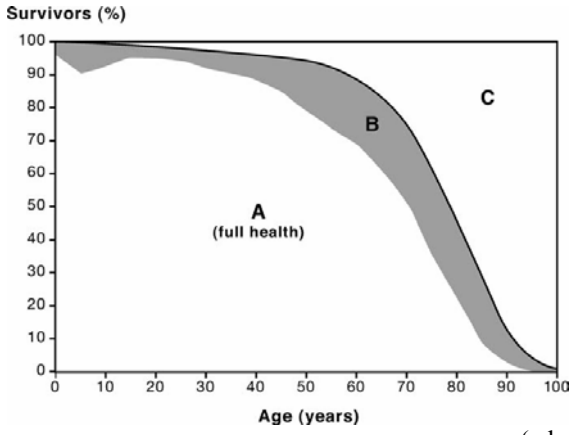
2.2. Summary Measures of Population Health

Exposure to environmental hazards has been shown to lead to premature death (Campbell et al, 2004; de Hollander et al, 1999; Krewski et al, 2000) and also to suboptimal quality of life (Luginaah et al, 2002; Melse & de Hollander, 2001). Summary measures of population health (SMPH) combine information on morbidity and mortality in an aggregate estimate of population health status, incorporating implicit and explicit social values (Kay et al, 2000; Mathers et al, 2001; Melse & de Hollander, 2001; Murray & Lopez, 1997; Murray & Lopez, 2000; Pruss-Usten

et al, 2003; Smith & Ezzati, 2005). Time lived in less then perfect health is combined with time lost due to premature death. SMPH are used to:

- Aggregate individual data to produce population health statistics
- Enable comparisons of health conditions between two or more populations, or the same population over time
- Quantify inequalities among subgroups in the population
- Ensure disabilities receive appropriate and balanced public health policy attention
- Provide baseline data to aid in priority setting, policy, health planning and research
- Inform policy and decision making regarding the magnitude of health impacts associated with selected risk factors
- Examine intervention benefits through cost effectiveness analysis

SMPH are divided into two broad classes: health expectancies and health gaps (Figure 2.1) (Mathers et al, 2001; Murray & Lopez, 2000; Smith & Ezzati, 2005).



(adapted from Smith & Ezzati, 2005)

Figure 2.1 Hypothetical Survivorship Curve. The line above 'B' depicts the proportion of people alive at each age and the line below 'B' depicts the proportion alive with optimal health. Thus, Area A is represents time lived with optimal health, Area B represents time lived in suboptimal health, and Area C represents time lost to due mortality. Life expectancy = A + B

Health expectancies extend the concept of life expectancy, providing a measure of the average time a person can expect to live in a health state, given by A + f(B) (Figure 2.1), where f( ) is a function of time lived in less then perfect health with condition B, weighted from 0(suboptimal) to 1(optimal) (Mathers et al, 2001; Murray & Lopez, 1997; Smith & Ezzati, 2005). International attempts to measure the BoD using health expectancy measures have generally been plagued by discrepant conceptual understandings, methodologies, and interpretations of the measures (Murray & Lopez, 1997). Examples of health expectancy measures include: disability-free life expectancy, active life expectancy, disability-adjusted life expectancy, and quality-adjusted life years (Mathers et al, 2001; Murray & Lopez, 2000).

Health gaps extend to concept of potential years of life lost (PYLL), to measure the difference between the actual health status and an ideal normative goal for a population, given by C + g(B), (Figure 2.1**),** where g( ) is a function that weights time lived in state B from 0(perfect health) to 1(death) (Mathers et al, 2001; Smith & Ezzati, 2005). The most well known measure of a health gap is the disability adjusted life year (DALY).

DALY's measure years of life lost due to mortality and years of life lost due to disability in a single estimate with explicit and transparent value choices and assumptions (Mathers et al, 2001; Melse & de Hollander, 2001). The DALY was originally developed by Murray & Lopez in the early 1990's to generate informed debate regarding the global burden of disease.

2.3. History of the Global Burden of Disease Study

The Global Burden of Disease (GBD) project was initiated by the World Bank in collaboration with the World Health Organization (WHO) in 1992 to establish comprehensive,

consistent, and unbiased estimates of global ill-health (Mathers et al, 2003; Murray & Lopez, 1997; Ezzati et al, 2006).

Cause of death and disability have been analyzed by 14 epidemiologic sub-regions in three broad disease classes (i) communicable, maternal, and perinatal, (ii) non-communicable, and (iii) injuries (Mathers et al, 2001; Murray & Lopez, 1997; Smith & Ezzati, 2005)[4]. Methods used to quantify the global BoD have been widely published (Ezzati et al, 2002; Ezzati et al, 2003; Mathers et al, 2003; Murray & Lopez, 1997; Murray & Lopez, 2000; RIVM, 2001; Smith & Ezzati, 2005; WHO, 2001).

Since the first study was published in 1996 (Murray & Lopez, 1997), there have been numerous publications on the original 1990 data, incorporating new data sources, with internally consistent estimates of incidence, prevalence, severity, case-fatality, duration and mortality for over 150 causes of death and disability, analyzed by sex and eight age groups, for 226 countries and territories (Ezzati et al, 2002; Ezzati et al, 2003; Murray & Lopez, 1997; Murray & Lopez, 1998; Lopez et al, 2006; Smith & Ezzati, 2005).

Furthermore, the Comparative Risk Assessment (CRA) module of the GBD analyzed the contribution of 26 important risk factors to population health (five environmental)[5] through a unified framework that enabled comparison of risk factors with various levels of causality (distal, proximal, environmental, physiological) (Mathers et al, 2001; Ezzati et al, 2003; Ezzati et al, 2003; Ezzati et al, 2006).

[4] Group 1 causes are divided into infectious, parasitic causes, respiratory infections, maternal causes, parinatal disorders, and nutritional deficiencies. Group 2 causes are divided into 14 categories of non-communicable disease. Group 3 is divided into intentional and non intention injuries (Murray & Lopez, 97)

[5] For environmental risk factors, the attributable burden of disease was calculated for (i) unsafe water, sanitation, hygiene, (ii) urban outdoor air pollution, (iii) indoor smoke from solid fuels, (iv) lead, and (v) global climate change (Ezzati et al, 2003)

Results of the GBD study indicated a total of 10% of global disease could be attributed to the environmental risks considered in the analysis (Pruss-Usten & Corvalan, 2006). In established marked economy (EME) regions, urban outdoor air pollution (the closest proxy to HAP's in the GBD study) contributed to 0.5% of the total BoD. Although a smaller determinant of health in the GBD study compared to independent behavioural risk factors such as tobacco use (11.7%) and alcohol abuse (10.3%), the contribution of environmental risk factors to disease has varied among other BoD studies, from 1.5-4% in high income OECD countries (Melse & de Hollander, 2001), to 5-12% in the Netherlands (de Hollander et al, 1999), to 25-33% globally (Smith et al, 1999). Inconsistencies in environmental BoD estimates reflect methodological and conceptual discrepancies at a global level concerning the definition of 'environmental risks', the causal linkage between environmental and health, and exposure and disease data collection procedures (Ezzati et al, 2003; Kay et al, 2000; Pruss-Usten et al, 2003). As such, the next section will describe standardized methods that have been proposed to causally attribute health impacts to environmental risk factors such as hazardous air pollutants.

2.4. Environmentally Attributable Burden of Disease

2.4.1. Causal Attribution

Traditionally, there have been two methods used to describe the causal attribution of environmental risk factors to the BoD: categorical attribution and counterfactual analysis (Ezzati et al, 2003; Ezzati et al, 2006; Kay et al, 2000; McMichael et al, 2001; Murray et al, 2003; Melse & de Hollander, 2001).

Categorical attributes death to a single cause of a group of causes based on a defined set of criteria (Ezzati et al, 2002; Kay et al, 2000; Mathers et al, 2001; Pruss-Usten, 2003), and thus

overlooks the multi-causal nature of many chronic diseases for which the environment usually operates distally in the causal chain.

Counterfactual analysis assesses the contribution of one or more risk factors to disease by comparing the current disease burden with the burden predicted under a hypothetical alternative scenario. Four 'hypothetical' exposure scenarios have been described in the literature (Kay et al, 2000; Murray & Lopez, 1999; Mathers et al, 2001; Murray et al, 2003; Pruss-Usten et al, 2003), the (i) theoretical minimum risk, (ii) plausible minimum risk, (iii) feasible minimum risk, and (iv) cost-effective risk.

The theoretical minimum risk corresponds with an exposure distribution of lowest possible risk *ceteris paribus* ie: zero exposure, whether or not attainable. The plausible minimum risk corresponds with an exposure distribution that is imaginable in the population. The feasible minimum risk corresponds to risk encountered with an exposure distribution that has been achieved in a population. Finally the cost-effective risk would consider the cost of reducing exposure when selecting an appropriate alternative scenario for the purposes of policy implementation.

Causal attribution of risk factors for disease can theoretically be done using either categorical attribution or counterfactual analysis. However, the CRA group of the GBD using counterfactual analysis and a theoretical minimum risk distribution of exposure consistently across risk factors, to estimate the reduction in disease if exposure to a risk factor were reduced to a counterfactual distribution[6] (Ezzati et al, 2003).

[6] For outdoor air pollution in the GBD study, the reference distribution of exposure for particulate matter was the World Health Organization Air Quality Guidelines

2.4.2. Attributable Fraction

Attributable risk describes the extent to which a risk factor causes disease. The most common measure of attributable risk is the population attributable fraction (PAF), which represents the magnitude of the current disease burden that would not have occurred in the absence of exposure (Hennekens & Buring, 1987; Melse & de Hollander, 2001; Murray et al, 2003; Steenland & Armstrong, 2006).

The PAF, also described as a population attributable risk (PAR), excess rate, or etiologic fraction, considers the population prevalence of exposure and the magnitude of the relative risk (RR) in an 'exposed' group compared to an 'unexposed' group (Husted, 2005).

Alternatively, the contribution of a risk factor to the burden of disease can be estimated by a population impact fraction (PIF), which compares the disease burden observed with the current exposure distribution in a population with that expected assuming an alternative hypothetical distribution, a counterfactual (Ezzati et al, 2003; Mathers et al, 2001). Similar to the PAF, the PIF considers the magnitude of the relative risk and the population distribution of exposure, with both equations described as follows,

$$\text{PIF} = \frac{\sum_{i=1}^{n} P_i \, RR_i - \sum_{i=1}^{n} P_i' \, RR_i}{\sum_{i=1}^{n} P_i \, RR_i} \qquad \text{PAF} = \frac{P_i \, (RR_i - 1)}{P_i \, (RR_i - 1) + 1} \quad \text{(Equation 1)}$$

where:
PIF = population impact fraction
PAF = population attributable fraction
RR_i = relative risk for disease i
P_i = prevalence of exposure i
P_i' = counterfactual prevalence of exposure i

3. TECHNICAL DESCRIPTION OF THE MODEL

3.1. Model Development and Conception Process

Evidence from environmental burden of disease (EBD) studies can provide detailed information on exposure associated health impacts, facilitate reliable and internally consistent data collection, and support the continuous development of harmonized methodologies, tools, and modelling techniques for population health impact assessments (Mathers et al, 2001; McMichael et al, 2001; Kay et al, 2000; Pruss et al, 2001; Pruss-Usten et al, 2003).

This model was envisioned to enable a novel analysis of the contribution of ambient air toxics to the burden of disease (BoD) in two suspected high risk geographic regions in Ontario, using descriptive epidemiological disease data and predicative risk assessment approaches. The model is designed to assess public health impacts associated with exposure in three stages:

- Quantification of the total burden of morbidity and mortality for selected diseases
- Determination of the magnitude of the BoD attributable to current hazardous air pollutant (HAP) exposures
- Quantification of the magnitude of the BoD that could be reduced with mitigated HAP exposures

Although exposure to ambient air pollution has been associated with a plethora of health effects, through three different routes of exposure (dermal, ingestion, inhalation) (de Hollander et al, 1999; Melse & de Hollander, 2001) the assessment is limited to quantifying carcinogenic outcomes from inhalation exposure to selected air toxics, under the assumption that each exerts independent and additive effects.

Many additional assumptions and simplifications were required to quantify and characterize exposure associated health impacts in the model. When specific disease and

environmental data was unavailable to model, the best alternative estimates are substituted in place; uncertainties and justification of simplifying assumptions are provided transparently to aid in informed decision making and policy in Ontario regarding abatement priorities for HAP's on the basis of the magnitude of associated health impacts.

The model is structured in a user-friendly MS Excel Workbook, version 2003. As modelling is an iterative process and accuracy is dependant upon the quality of the data (Pruss-Usten et al, 2003), the model can continuously be updated with recent epidemiological and risk data in the future to ensure complete, reliable, and comprehensive analyses of the BoD and exposure associated risk.

3.2. Model Overview

3.2.1. Graphic Description of the Model:

Broadly, the analysis involves modelling exposure associated health impacts in two phases (i) the DALY model, and (ii) the Risk model as depicted in Figure 3.1

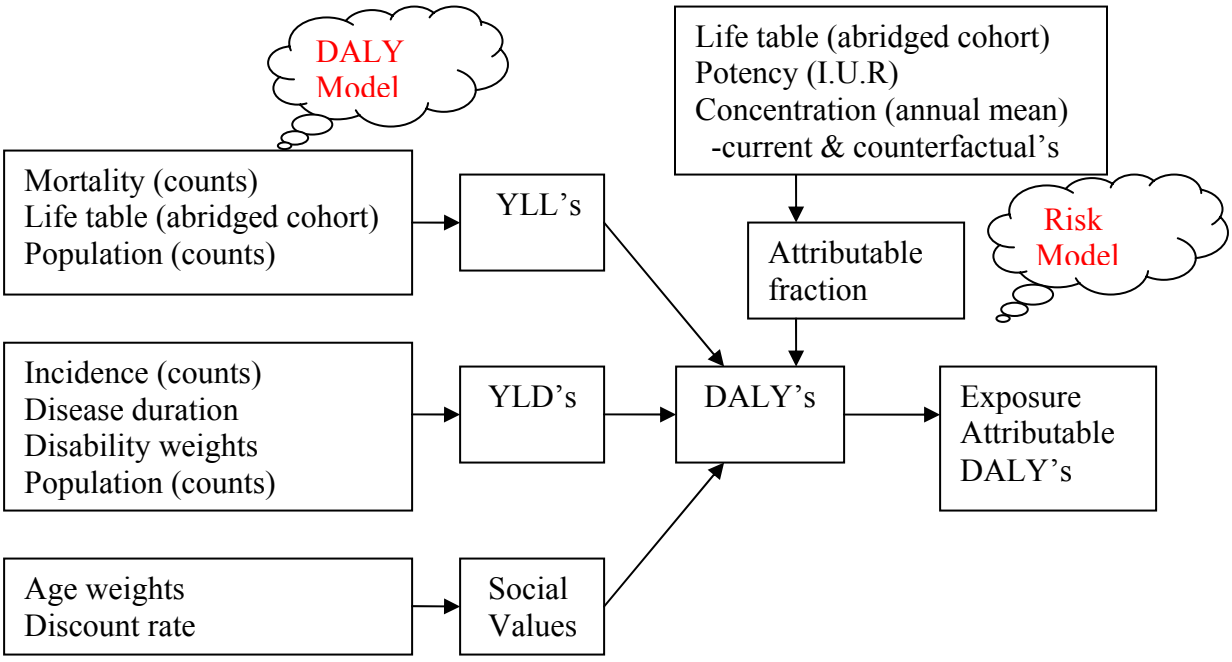


Figure 3.1 Graphical representation of the Model, Phase One and Phase Two

The first phase quantifies health impacts associated with selected disease endpoints as 'risk factor-independent' DALY's. Recall that DALY's are a time based SMPH that enables quantification of disease specific estimates of morbidity and mortality in an aggregate estimate of population health. The DALY model methodology has been adapted from the WHO GBD project (Murray & Lopez), and relies largely upon epidemiological methods.

The second phase incorporates risk assessment approaches to quantify exposure attributable health impacts in terms of DALY's derived by an attributable fraction. The exposure attributable BoD is modelled under an exposure based approach, using current knowledge of exposure and risk to predict current and future disease burdens (Pruss-Usten et al, 2003).

3.2.2. Selection of Exposures, Diseases, and the Reference Year of Analysis

The purpose of the model is to quantify the current and future burden of premature mortality and morbidity by age and sex, based on exposure estimates and dose response modelling, for six ambient air toxics in two high risk regions of Ontario, Toronto and the Chemical Valley of Southwestern Ontario (S.W.O).

Six carcinogenic air toxics were selected on the basis of their inclusion in the updated HEIDII II model, demonstrating evidence of disease causality and potential hazard, and availability of exposure and disease data. The air toxics selected for analysis have been described in detail in section 2.1 and include: acetaldehyde, formaldehyde, benzene, 1,3-butadiene (1,3-BD), ethylene oxide (ETO), and nickel refinery dusts

In accordance with Section 64 of the Canadian Environmental Protection Act, 1999, the aforementioned air toxics are considered "CEPA Toxic"[7] (CEPA, 1999). Furthermore, toxicological and epidemiological studies have provided evidence of a causal linkage between inhalation exposures and carcinogenic outcomes in humans following high dose inhalation exposures in animal models and occupational exposures in human populations. The carcinogenic potential of acetaldehyde, formaldehyde, benzene, 1,3-BD, ETO, and nickel refinery dusts has thus been evaluated by the International Agency for Research on Cancer (IARC).

The International Agency for Research on Cancer (IARC) consists of an interdisciplinary group of expert scientists who evaluate the weight of evidence for substance carcinogenicity following standardized protocols. Cancers associated with inhalation exposure to acetaldehyde, formaldehyde, benzene, 1,3-BD, ETO, and nickel refinery dusts are selected on the basis of IARC risk evaluations, and are listed in Table 3.1.

Table 3.1. Cancer Associations with Exposure to HAP's on the Basis of IARC and Health Canada Risk Evaluations

Air Toxic	Associated Cancer(s)	Reference	ICD-9 codes	IARC Class
Acetaldehyde	Oral Cavity & Pharynx Esophagus Ear, Nasal, & Larynx	Woutersen et al, 1986 Health Canada PSL	140-150, 160-161	2B *Possible Human Carcinogen*
Formaldehyde	Oral Cavity & Pharyx Ear, Nasal, & Larynx	Monticello et al, 1996 Health Canada PSL	140-149, 160-161	1 *Known Human Carcinogen*
1,3-Butadiene	Lymphomas Leukemias	Delzell et al, 1995 Health Canada PSL	200-203, 204-208	2A *Probable Human Carcinogen*
Benzene	Lymphomas Leukemias	Rinsky et al, 1987 Health Canada PSL	200-203, 204-208	1 *Known Human Carcinogen*
Ethylene Oxide	Lymphomas Leukemias	Snellings et al, 1984 Health Canada PSL	200-203, 204-208	1 *Known Human Carcinogen*
Nickel Refinery Dusts	Ear, Nasal, & Larynx Lung, Bronchus, & Trachea	Doll et al, 1990 Health Canada PSL	160-161, 162-165	1 *Known Human Carcinogen*

[7] substances enter the environment in amounts that have been or may have an immediate or long term effect on the environment or human health

Cancer endpoints are classified to three digit code in accordance with the International Classification of Disease, 9th Version (ICD9) (Appendix A). The ICD represents a global standard for disease diagnosis, standardizing the management of epidemiological data for the purpose of disease surveillance.

In the model, cancer endpoints are grouped at the organ level, under a presumed common mechanism (Mathers et al, 2001; Smith et al, 1999) thus include (i) oral cavity & pharynx, (ii) esophagus, (iii) middle ear, nasal, & larynx, (iv) lung, bronchus, & trachea, (v) lymphomas & multiple myeloma, and (vi) leukemia's.

Population data and epidemiologic indicators of disease (ie: incidence, mortality, duration, etc) are modelled for the reference year of 2001. The year 2001 was selected for analysis as having the most complete and reliable dataset. With stability in the population structure in recent years (Statistics Canada, 2001) it is reasonable to assume 2001 data is representative of the current population (Campbell et al, 2004).

The next section (section 3.3) will provide an overview of the technical requirements to model the BoD for the selected site-specific cancers, in terms of DALY's. The following section (section 3.4) will discuss methodology to assess the magnitude of the BoD that is attributable to the air toxics under analyses. Detailed descriptions of specific data sources, estimates, and assumptions of the modelling are presented following the technical description of the model (section 4.0)

3.3. Public Health Impacts: Disability-Adjusted Life Years (DALY's)

Public health impacts are most often characterized by measures of mortality, life expectancy, potential years of life lost (PYLL), and quality-adjusted life years (QALY's); however with increases in life expectancy and chronic disease in the Ontario population, such measures fail to provide a complete and comprehensive picture of population health (Melse & de Hollander, 2001; Thomas & Hrudey, 1997)

The DALY represents a time based measure of quantity and quality of life. DALY's quantify years of life lost due to premature mortality (YLL) and healthy years of life lost due to disability (YLD) as an aggregate estimate of population health (Anand & Hanson, 1997; Arnesen & Kapriri, 2004; Gold et al, 2002; Mathers et al, 2001; Melse & de Hollander, 2001; Murray & Acharya, 1997). One DALY represents the loss of a perfectly healthy year of life (Melse & de Hollander, 2001).

$$DALY = YLL + YLD \qquad \text{(Equation 2)}$$

Where:
YLL = Years of life lost
YLD = Years of life lived with disability

Quantification of health impacts in terms of DALY's requires a range of disease information including site-specific estimates of cancer incidence, mortality, age of diagnosis, and life expectancy. Additionally, DALY's require estimates of average disease duration and severity, provisional to disease staging.

In the model, epidemiological estimates of disease are input in terms of 'years' to ensure a comparable and consistent time scale to aggregate time lost due to fatal and non fatal health outcomes. Consistent with GBD study methodology, site specific cancer DALY's are quantified by sex and eight age groups: 0-4, 5-14, 15-29, 30-44, 45-59, 60-69, 70-79, and 80+ years.

By combining population disease data of diverse severity into a common unit, the DALY serves as a comparative measure, suitable to assess the relative disease burdens associated with different cancers between regions. The model thus quantifies the BoD as 'Total DALY's' and 'DALY's / 100,000 Persons' to enable BoD assessment between Toronto and S.W.O.

3.3.1. Years of Life Lost (YLL):

The mortality component of the DALY calculation, years of life lost due to premature death (YLL), is modelled as a function of age specific mortality and the remaining life expectancy at the age of death from site specific cancers

$$YLL_i = N X L \qquad \text{(Equation 3)}$$

where:
N =population estimates of mortality per age-sex group
L = remaining life expectancy at age of death

3.3.1.1. Mortality

Site specific estimates of mortality counts in the Toronto and S.W.O regions were ascertained by five year age interval, in accordance with ICD9 cause of death classification. For computational purposes, average age at death is assumed the midpoint of each age interval, and frequency counts are converted to a rate per 100,000 persons, considering the population count in each age category.

3.3.1.2. Life Expectancy

Life expectancy most commonly refers to the number of years an individual can expect to live on the basis of current death rates (Thomas & Hrudey, 1997). In the DALY, life expectancy is used to estimate the number of years of life a person has lost due to premature mortality. Four methods have been proposed to estimate years of life lost due to premature mortality: (i) cohort

life tables, (ii) period life table, (iii) standard life tables, and (iv) potential years of life lost (Murray, 1994), each with specific strengths and limitations, as described in Table 3.2

Table 3.2. Methods to Estimate Life Expectancy, Strengths, and Limitations

Method	Description	Strengths	Limitations
Cohort Life Expectancy	Provides an estimate of the mortality experience of an entire group of individuals from the first birth the last death (Mathers et al, 2001)	Most accurate description of mortality for national burden of disease assessments. Amendable to cost effectiveness analysis (Murray, 1994)	Data may be difficult to generate (Mathers et al, 2001) Not valid for GBD studies (Murray, 1994)[1]
Period Life Expectancy	Follows the mortality experience of a synthetic cohort, taken cross-sectionally in time, subject to current age-specific mortality rates (Brand, 2005; Ellison & Gibbons, 2006; Mathers et al, 1999; Murray, 1994)	Reflects the current survival experience and provides a better estimate for recently diagnosed cases (Ellison & Gibbons, 2006) Useful for national burden of disease studies (Murray, 1994)	Emphasizes premature death in wealthy countries. Use of local life expectancy is not suitable for GBD assessments (Murray, 1994)[1]
Standard Life Expectancy	Based on a West Level 26 table based and the highest observed life expectancy among Japanese to provide an ideal standard (Murray & Lopez, 1997; Murray, 1994)	Deaths at all ages contribute to estimates of premature mortality, and deaths at the same age contribute equally to the BoD (Murray, 1994)	Arbitrarily defined maximum expectation to life (Murray & Acharaya, 1997; Anand & Hanson, 1997)
Potential Years of Life Lost	Determined by subtracting age at death from an arbitrary defined upper limit to life, commonly set to 65 or 75 years	Ease of calculation Egalitarian treatment of deaths at the same age (Murray, 1994)	Deaths after age 65 do not contribute to the BoD, PYLL thus contradicts a fundamental principle of DALY (Murray, 1994)[2] Weight placed on death at younger ages & emphasizes disease that prevent longevity (Thomas & Hrudey, 1997)

1contradicts DALY principle of treating "like health outcomes as like"

2The DALY is based on the principles of fairness and egalitarianism, grounded upon a "common set of minimalist values that is need for societies" (Murray & Archarya, 1997, p.709).

The GBD study used a Standard West Level 26 life table to assess the standard expected years of life lost (SEYLL) in a comparable manner across nations with different life expectancies. However, for national and regional BoD assessments, local or cohort life expectancy is recommended as a normative goal to calculate DALY's, being amendable to cost-effectiveness analysis (Murray, 1994). As such, the model quantified premature mortality specific to the current Canadian cohort life expectancy of 78 years for males and 83 years for females on the basis of an abridged cohort life table (WHO, 2006)

3.3.2. Years of Life Lived with Disability (YLD)

Internally consistent YLD estimates require a clear definition of the disease under analysis in terms of severity and stage (Table 3.3) (Mathers et al, 2003). Referring to Figure 3.1 YLD estimates for site specific cancers require a more extensive and uncertain range of epidemiological data then the above YLL information including estimates of incidence, severity, duration, and age of onset distributed by stage, which in turn requires epidemiological estimates of remission and case-fatality (Mathers et al, 2001).

Table 3.3 Definitions of Malignant Neoplasm Disease Staging

Stage of Disease	Case Definition
Diagnosis	Period of medical diagnosis and tests
Primary Therapy	Chemotherapy, radiotherapy, surgery
Remission / Control & Waiting	Clinical observation during control/remission phase
Metastasis	Dissemination of the disease
Terminal	Terminal stage prior to death

(As adapted from WHO GBD study, Mathers et al, 2001)

The morbidity component of the DALY calculation, years of life lived with less then perfect health, is modelled as a function of estimates of site specific incidence, and the average disability weighting and duration of cancer.

$$YLD = I \; X \; DW \; X \; D \qquad \text{(Equation 4)}$$

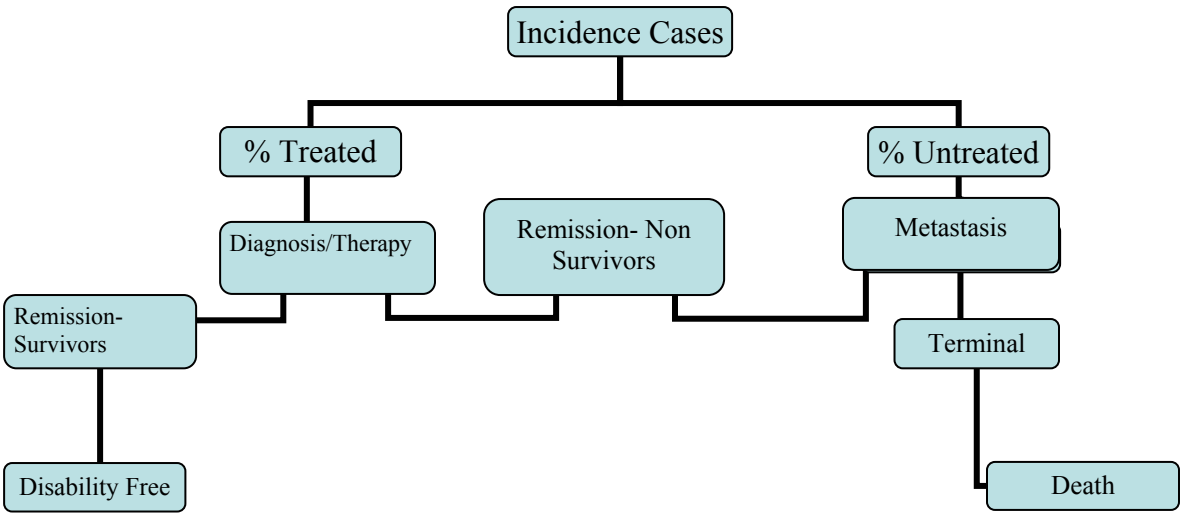
where:
I = age and sex specific estimates of incidence
DW = disability weight of cancer
D = average duration (years)

3.3.2.1. Incidence:

Although the population frequency of cancer can be estimated either as an indicator of incidence or prevalence, YLD's are quantified on the basis of incidence counts. Incidence provides a direct estimate of *new diagnosis*, equivalent to the mortality incidence indicator for YLL's, and is most sensitive to recent epidemiologic trends (Mathers et al, 2001; Melse et al, 2000; Murray, 1994; Pruss-Usten et al, 2003). Like mortality, site-specific frequency counts are converted in the DALY model to a rate per 100,000 persons.

3.3.2.2. Disease Model:

The GBD (WHO, 2000) and Dutch study (Essink-Bot et al, 2002) disease model has been adapted, with provisional disability weights and durations for the cancer stages, to ensure internally consistent epidemiological modelling of disease estimates (Figure 3.2)



(Figure 3.2 Cancer Survival Model)

Based on Figure 3.2 a newly diagnosed case is assumed to follow one of three disease paths,

(i) Incidence cases that are eventually cured of cancer undergo a period of diagnosis, treatment, and remission prior to being considered *disability-free*.

(ii) Incidence cases that are diagnosed but are not cured of cancer enter a period of treatment, remission, metastasis, and finally a terminal stage prior to death.

(iii) Incidence cases untreated are assumed to pass through the stages of diagnosis, metastasis, and a terminal period prior to death.

3.3.2.3. Disease Duration:

Average duration of disease was considered separately for survivors and non-survivors, for the stages of disease, stratified by age and sex, for site-specific cancers. Consistent with GBD study methods (Murray & Lopez, 1997), it is accepted that 90% of cases in EME regions[8] are treated and 10% are untreated. Survivorship, the cure rate, is taken as the five year relative survival rate (RSR), describing the percent of cases alive five years after diagnosis, without adjustment for background all-cause mortality.

Survivors are considered disability-free five years from the initiation treatment. For the non-survivors that eventually die of cancer, the average time to death (LNS) is assumed to follow an exponential distribution and is estimated from the one, three, and ten year RSR (Essink-Bot et al, 2002; WHO, 2000) as follows:

[8] The established market economy consists of the high income countries of the Organization for Economic Cooperation and Development

$$LNS = \frac{1}{\lambda}\{\frac{\gamma+1}{\gamma}\} \qquad \text{(Equation 5)}$$

Where:
LNS = duration of survival for non-survivors

$$\gamma = \ln(\frac{\ln\sigma 3}{\ln\sigma 1}) / \ln 3$$

$$\lambda = [-\ln\sigma 1]^{1/\gamma}$$

$$\sigma 1 = \frac{RSR(1yr) - RSR(10yrs)}{1 - RSR(10yrs)}$$

$$\sigma 3 = \frac{RSR(3yr) - RSR(10yrs)}{1 - RSR(10yrs)}$$

The duration of the primary diagnosis, therapy, remission, metastasis, and terminal stages were determined through literature review of expert opinion. The durations for the stages of diagnosis, metastasis, and terminal periods are assumed constant for all cancers; however, since diagnosis at an earlier stage (as in medical severity) considerably influences disease outcome, duration for primary therapy and remission stages varied pending treatment regime and/or survivorship.

Duration of the primary therapy stage for site-specific cancers is derived independent of survivorship, as a function of the distribution of cases undertaking various treatment regimes and the time to complete the regime, considering medical severity at the time of diagnosis. The model assumes treatment regimes progress from: surgery (in-patient, out-patient), chemotherapy (mild, moderate, severe), and/or radiotherapy (curative, palliative), and that cancer severity is diagnosed as local, regional, or distant (Flanagan et al, 2005).

Remission is considered separately for survivors and non-survivors and is estimated by subtracting the duration of all other stages from a defined average disease length, described at five years for survivors and LNS for non-survivors. As such, for survivors the average remission duration for site-specific cancer is calculated as 5-D_{TR}, with cases assumed disability-free five

years after diagnosis (WHO, 2000). In contrast, for non-survivors average remission duration is derived as follows: (WHO, 2000)

$$LNS - (D_{TR} + D_M + D_T) \quad \text{(Equation 6)}$$

Where:
LNS = mean survival duration non survivors
D_D = duration of diagnosis
D_{TR} = duration of treatment
D_M = duration of metastasis
D_T = duration of terminal phase

Calculations to derive average disease duration across cancer staging and pathway are reviewed in Table 3.4. Based on the case-fatality rate (ie: the 5 year RSR) and the distribution of cases by disease path, durations are combined to generate a single estimate of the average site-specific disease duration (stratified by age and sex) in the YLD model (WHO, 2000; Essink-Bot et al, 2002)

Table 3.4 Derivation of disease duration based on survivorship

Disease Path	Disease Duration	Assumptions
(i) diagnosis, treatment, remission, *'disability-free'*	$D_D + D_{TR} + (5\text{-}D_{TR})$	Cases assumed 'cured' experience negligible disability following initial diagnosis, treatment, remission durations (WHO, 2000)
(ii) diagnosis, treatment, remission, metastasis, '*death'*	$D_D + D_{TR} + (LNS - D_{TR} + D_M + D_T) + D_M + D_T$	Average survival duration can be derived from 1,3,10 year RSR's Survivorship assumed to follow an exponential Weibull distribution
(iii) diagnosis, metastasis, terminal, '*death'*	$D_D + D_M + D_T$	Duration of diagnosis, metastasis, and terminal phases are set to 6 weeks, 5 months, and 1 month respectively, for all cancers (Flanagan et al, 2005; WHO, 2000)

Where: LNS = average survival duration non survivors, DD = duration of diagnosis, DTR = duration of treatment, DM = duration of metastasis, and DT = duration of terminal phase (WHO, 2000).

3.3.2.4. Disability Weights:

Disability weights of cancer severity (distinct from duration) are incorporated in the calculation of YLD's to standardize epidemiologic estimates of time lived with morbidity to time lost from premature mortality. The weights range from zero, indicating a state equivalent to perfect health, to one, indicating a state equivalent to death, and were determined for the GBD project by person trade-off method and expert opinion of social preferences for disease states (Mathers et al, 2001; Murray & Acharya, 1997; Reidpath et al, 2003).

Person trade-off is a deliberative and iterative process whereby individuals are given the option of curing a certain number of people with a particular health state versus curing a certain number in a different health state. Disability weights are elicited when individuals are indifferent between the two options (Mathers et al, 2001; Murray & Acharya, 1997; Reidpath et al, 2003). As such, a weight of zero indicates indifference between a health state and full health, and a weight of one indicates indifference between the health state and death.

Supporting a principle of egalitarianism in the DALY, disability weights are constant across social, environmental, and cultural contexts (Reidpath et al, 2003). For malignant neoplasms, disability weights have been determined for the states of disease: diagnosis/therapy, waiting (remission), metastasis, and terminal, constant across gender and age groups, and are listed in Table 3.5

Table 3.5 GBD Disability Weights for Malignant Neoplasm

Site & GBD Cause	ICD 9	Diagnosis/Therapy	Waiting	Metastasis	Terminal
A1.Mouth & Oropharynx cancers	140-149	0.09	0.09	0.75	0.81
A2.Oesophagus cancer	150	0.20	0.20	0.75	0.81
A7.Trachea, bronchus, and lung cancers	162-165	0.15	0.15	0.75	0.81
A15.Lymphomas	200-203	0.06	0.06	0.75	0.81
A16.Leukemias	204-208	0.09	0.09	0.75	0.81
Other Malignant Neoplasms	160-161	0.09	0.09	0.75	0.81

To calculate YLD's, the disability weights across cancer stages must be derived into one disability weight associated site-specific cancer in the DALY model (Essink-Bot et al, 2002; Melse et al, 2000). As such, the average disability weight is calculated on the basis of the prevalence distribution across diagnosis, therapy, control, metastasis, and terminal stages, and the stage specific disability weight used in the GBD study.

3.3.3. Social Value Choices:

The DALY creates a common currency to estimate morbidity and mortality by explicitly incorporating numerous social value choices such as: a maximum expectation of life, a 'like' valuation for 'like' health outcomes, severity weighting for non fatal health states, a discount rate for future healthy life, and unequal valuation of time lived at different ages (Anand & Hanson, 1997; Arnesen & Kapiriri, 2004; Melse & de Hollander, 2001; Murray & Acharya, 1997). Table 3.6 provides a complete overview of the value choices incorporated in the DALY, arguments for and against, and introduces some limitations. The following paragraph reviews two of the most controversial value choices of the DALY, discounting and age weighting.

Table 3.6. Value Choices & Assumptions of the DALY

Value Choice	Argument For…	Argument Against…
Standard expectancy of life of 80 years for men & 82.5 years for females[1]	Equality: all individuals have the same standard life expectation despite income, geography, etc	Arbitrarily determined (Anand & Hanson, 1997; Arnesen & Kapiriri, 2004)
	Male female differences reflect biological differences in survival potential (Murray et al, 1997)	Male-female survival differences reflect differences in risk behaviours, modifiable through future public health interventions (Murray & Acharya, 1997)
		Sex differences reflect genetic determinism, compelling risk behaviours in males (Anand & Hanson, 1997)
		Murray & Acharya, (1997) argue for the same survival norm incorporated in the DALY
		80 years of life for males and 82.5 years for females is unachievable in developing countries (Anand & Hanson, 1997)
Disability Weights[2] determined by PTO method[3]	Elicited by social preferences for different health states (Murray & Acharya, 1997)	Severity rating of a health state may change with adaptation/coping (Murray & Acharya, 1997) Anand & Hanson (1997) describe 'compensated' &'uncompensated' DW
	Based on 'expert' preferences & knowledge (Murray & Acharya, 1997)	Health state preferences vary between individuals (Murray & Acharya)
	Weights vary for treated and untreated forms of disability (Murray & Acharya, 1997)	DW do not take into account quality of life, social resources, or the context in which life is lived (Anand & Hanson, 1997)
	Disability weights vary among age groupings, reflecting the BoD	DW do not reflect impacts of co-morbidities; weights could add to greater then 1 (death) (Anand & Hanson, 1997)
Discounting[4]	Consistent with economic principles & health policy	3% discount rate arbitrary (Murray & Acharya, 1997), reflects a compromise between economics and excessive sacrifice (r=0)
	Eradication-research paradox & excessive sacrifice[6] (Murray & Acharya, 1997)	Time of illness: weighted more severe if experienced today, then if in a years time
	"Time Paradox" (Murray & Acharya, 1997) Delay investments in health until the future	Discounting DALYs, reduces the value of life to a monetary value.
		Argument for discounting rests on assumption the world may end which is an infinitely small chance (not 3% or even 1%) (Anand & Hanson, 1997)
		Discounting compounds criticisms of age weights[7] (Anand&Hanson, 1997;

		Arnesen&Karpiriri,1997)
Age weighting[8]	Differential value assigned to time lived at different ages is a reflection of social roles in society[9] (Murray & Acharya, 1997)	Differential age valuation inequitably is a reflection of human capital principles & differential productivity (Murray & Acharya, 1997), thus assigning a monetary value to life
	Ethically justified because all individuals pass through the same life cycle	Social value of life may differ among occupation, sex, income bracket (Anand & Hanson, 1997)
	Instrumental justification, as ill health in middle ages indirectly impacts the health of young and elderly (interdependence) (Anand & Hanson, 1997)	Principle of Universalism- same value of life no matter age (Anand & Hanson, 1997)

[1]For maximum life expectation, 82.5 years for females was determined based on the Japanese female life expectancy, the country with the highest life expectancy globally. Male life expectancy was determined by incorporating recognized differences in survival of 1.9-3.2 years using modelling techniques (Murray & Acharya, 1997)
[2]Disability weights: life years assigned different value pending the health state in which they are lived (Arnesen & Kapiriri, 2004) Ranging from 0=perfect health to 1=death
[3]PTO = Person Trade-off method
[4]Discounting: future years of life are assigned less value then years lived today (Arnesen & Kapiriri, 2004) if applied, discounting 3%
[5]Discounting future life justifies current environmental degradation, benefiting the current generation at the expense of future generations
[6]For example, if r=0, the possibility of improved health technologies, care, and treatment, could eliminate disease in the future, justifying significant sacrifice ie: 100% research and resources, for future health benefits
[7]The combined impact of age weights and discounting is a lower value of morbidity and mortality at younger ages; for example: the life of a 20 year old should be valued and saved more then an infant
[8]Age weights: assign different value to life at different ages (Anand & Hanson, 1997; Arensen & Kapiriri, 2004; Murray & Acharya, 1997) Maximum DALYs are prevented at 24.5 years of age.
[9]Social roles at some groups include caring for the well-being of other age groups (the young and old), providing physical, emotional, and financial support, and helping society flourish (Murray and Acharya, 1997)

3.3.3.1. Discounting

Discounting future time is a traditional concept in economic and social policy. In BoD assessments, a discount rate places less value on future healthy life to estimate the net present value of life (Murray & Acharya, 1997; Murray et al, 1994). Although a discount rate of 5% is standard in economic analysis, the World Bank Disease Control Priorities study and the GBD study have established a lower discount rate of 3% for BoD studies (Murray, 1994; Pruss-Usten et al, 2003), believed consistent with long term yield on investments. A 3% discount rate implies a year of healthy life gained in ten years time is worth 24% less then one gained this year. A discount rate is justified in BoD assessments to avoid placing excessive emphasis on childhood

deaths and intervention investments at the health expense of the current generation, ie: excessive sacrifice (Murray & Acharya, 1997).

3.3.3.2. Age-weighting

Studies have indicated social preferences for the value of life lived during young adulthood over life lived during childhood or the later years (Murray & Lopez, 1997; Murray et al, 1994). Age-weighting (K=1) places less value on healthy life during the younger and older ages, with peak valuation at age 24.5. Age-weights have been justified as an attempt to capture the instrumental value of time lived at different ages through the life cycle (Anand & Hanson, 1997; Mathers et al, 2001; Melse & de Hollander, 2001; Murray & Acharya, 1997; Murray, 1994). Since discounting and age-weighting have been widely criticized on conceptual, ethical, and empirical grounds (Anand & Hanson, 1997; Reidpath et al, 2003), the model has been developed to enable sensitivity analysis of the impacts of incorporating discounting and age-weighting on BoD estimates. With the inclusion of the social value choices, the complete computational formulas for the YLL and YLD calculations can be described as,

$$YLL = \frac{KCe^{ra}}{(r+\beta)^2}\left[e^{-(r+\beta)(L+a)}\left[-(r+\beta)(L+a)-1\right]-e^{-(r+\beta)a}\left[-(r+\beta)a-1\right]\right]+\frac{1-K}{r}\left(1-e^{-rL}\right)$$

(Equation 7)

$$YLD = DW\left\{\frac{KCe^{ra}}{(r+\beta)^2}\left[e^{-(r+\beta)(L+a)}\left[-(r+\beta)(L+a)-1\right]-e^{-(r+\beta)a}\left[-(r+\beta)a-1\right]\right]+\frac{1-K}{r}\left(1-e^{-rL}\right)\right\}$$

(Equation 8)

where:
a = age of death
r = discount rate
β = age weighting constant
K = age-weighting modulation constant
C = adjustment constant for age-weights
L = standard life expectancy at age of death or duration of disability
DW = disability weight

3.4. Exposure Attributable Disease Burden

3.4.1. Burden Attributable to Current Ambient Concentrations:

A measure of attributable risk is required to estimate the health impacts associated with exposure to current concentrations of ambient air toxics. Modelling the environmentally attributable BoD requires: (i) an assessment of the population distribution of exposure for each of the air toxics, (ii) a quantitative estimate of the exposure-disease associations, and (iii) characterization of the risk (DeHollander et al, 1999; Pruss-Usten et al, 2003).

For ambient air toxics, there has been little or no epidemiological work concerning the magnitude of associated cancer risk from environmental concentrations. Furthermore, with a ubiquitous population distribution of exposure, air quality is not a risk factor amendable to traditional 'exposure' 'no exposure' PAF categorization.

As such, for carcinogenic substances that are assumed to act linear with no threshold on the concentration-response curve, the fraction of disease burden attributable to environmental exposures is estimated as, (de Zwart et al, 2006)

$$AF_{x.e} = \frac{IUR_x}{LE} x C_x x F_{\exp.x.e.} x N_{pop} \qquad \text{(Equation 9)}$$

where:
$AB_{x.e.}$ *= population attributable burden of disease e*
$IUR_{x.}$ *= inhalation unit risk value of HAP x (ug/m3)*
LE *= average life expectancy (years)*
$C_{x.}$ *= concentration of HAP x (ug/m3)*
$F_{exp.x.e.}$ *= fraction of population exposed*
$N_{pop.}$ *= population count*

Similar to the PAF, the attributable fraction in Equation 9 requires information on the population distribution of exposure and a quantitative estimate of risk. For carcinogenic air toxics, quantitative risk estimates associating exposure and disease are based on potency estimates rather then relative risks. The carcinogenic potency of the six air toxics at

environmental concentrations is estimated as a slope factor (q*1) which predicts lifetime cancer risk assuming constant low dose cumulative exposure.

Concentrations of the selected air toxics are determined specific for the Toronto and S.W.O regions through extensive literature review. As mentioned, the concentration-response function for carcinogenic substances is assumed to act linear non threshold such that it is theoretically possible any level of exposure can initiate the carcinogenic process. As such, annual mean concentrations, representative of chronic low dose cumulative exposure (Campbell et al, 2004) are modelled, assuming dose-rate independence and the absence of ceiling or threshold effects.

For consistency with the calculation of risk factor independent DALY's, an abridged cohort life table estimates current Canadian life expectancy of 78 years for males and 83 years for females (WHO, 2006). The fraction of the population exposed is assumed equal to one, and the population count is standardized to 100,000 to enable comparison of the attributable disease burden between Toronto and S.W.O regions.

Finally, to characterize the public health impacts attributable to exposure to current concentrations of ambient air toxics in terms of DALY's, attributable fractions are multiplied by estimates of site-specific DALY's per 100,000 persons (phase one) in Toronto and S.W.O, describe as follows, (DeZwart et al, 2006; Lopez et al, 2006; Murray et al, 2003; Steenland & Armstrong, 2006)

$$BoD_{AB.DALYs} = \sum_{x} \sum_{e} AF_{x.e.} xDALY_{e} \qquad \text{(Equation 10)}$$

where:
$BoD_{AB.DALYs}$ *= attributable DALY BoD*
$AB_{x.e.}$ *= population attributable BoD e to exposure x*
$DALY_{e.}$ *= DALY's lost to disease e*

3.4.2. Counterfactual Analysis

To inform policy and decision making in Ontario regarding abatement priorities for hazardous air pollutants, projection scenarios of future exposure distributions were developed and modelled in a counterfactual analysis. Counterfactual analysis enables a comparison of the burden of morbidity and mortality experienced under current exposure distributions to be compared with the burden predicted under alternative exposure distributions, termed counterfactuals (Ezzati et al, 2006; Lopez et al, 2006; Mathers et al, 2001; Murray et al, 2003; Pruss-Usten et al, 2003; Smith & Ezzati, 2005). As mentioned in section 2.4 counterfactual exposure distributions include theoretical minimum risk, plausible minimum risk, and feasible minimum risk levels.

The impact of reducing ambient air toxics exposures on BoD estimates in Toronto and S.W.O is modelled for a plausible minimum risk and a feasible minimum risk level. The concentrations of the selected air toxics associated with plausible and feasible minimum risk distributions have been determined through literature review and are modelled by substituting the alternative counterfactual concentration (ug/m^3) in place of the current concentration component of Equation 9

The plausible minimum risk is modelled as the cancer risk expected assuming an exposure distribution if there were no anthropogenic releases of air toxics. The feasible minimum risk is modelled as the cancer risk expected under an exposure distribution that has been observed in the population with minimal vehicle or industrial emissions. Since natural sources of air toxics exist in the environment, zero risk to human health is not achievable for linear acting carcinogenic substances, such that a theoretical minimum risk level is not included in the model.

4. DATA SOURCES, ESTIMATES & UNCERTAINTIES

4.1. Population Demographics

Geographic regions were selected as representative high risk from exposure to ambient air toxics in Ontario; Toronto from motor vehicle emissions and S.W.O from industrial releases of the Chemical Valley. The Toronto area includes the municipal counties of Durham, Peel, York, and the City of Toronto, and S.W.O includes the counties of Chatham-Kent, Windsor-Essex, and Lambton.

Baseline population profiles were ascertained for the regions of interest by 5-year age and sex grouping from the 2001 Canadian Census, the most recent published census at the initiation of the project (Community Profiles, Statistics Canada, 2001). Detailed population counts can be found in Appendix B

Census data is collected every five years and provides a valid and reliable source of demographic information on 98% of households in Canada. However, specific subgroups including children less then one, transient young males, and immigrants are more likely to be under reported in data collection. Under-representation would produce uncertainty in estimates of specific-rates if the subgroups differ on characteristics associated with either exposure or disease outcomes (Husted, 2005), biasing estimates of risk.

4.2. Cancer Incidence & Mortality

Incidence and mortality counts were ascertained from the Ontario Cancer Registry (OCR), Cancercare Ontario, and can be found in Appendix C. Cancercare Ontario is the principle advisory organization for the provincial government responsible for coordinating surveillance, care, prevention, and developing evidence based guidelines. Data was collected

from the SEER*Stat 6.2.4 CD software package (2006), upon request from Cancercare. SEER*Stat is a database updated annually with aggregate information on cancer incidence (1964-2003), mortality (1950-2003), survival, prevalence rates, crude and adjusted rates, and frequency data, with standard errors and confidence intervals.

Data was ascertained at the municipal level and aggregated for regional analysis. Incidence and mortality counts were collected by sex and age group, for the reference year 2001. When cell counts smaller then five were noted but not disclosed by OCR to protect patient confidentiality, counts were averaged over a 5-year period (1999-2003) to produce a best estimate; when cell counts remained less then five over this period, the count was assumed one.

As mentioned, cancer endpoints were classified to three digit code in accordance with the International Classification of Disease, 9th Version (ICD9) (Appendix A). The ICD represents a global standard for disease diagnoses, standardizing the management of epidemiological data for disease surveillance. Consistent with GBD and National Burden of Disease (NBD) study methodology (Mathers et al, 1999; Mathers et al, 2003; WHO, 2001), cancers diagnosed under "other" or "ill-defined" sites: 149 and 165, have been redistributed across primary sites, ie: 140-147 and 162-164. Since ill-defined classifications typically include less then 1% of coding classifications (Mathers et al, 2001), pro-rata re-distribution was not expected to introduce parameter uncertainty to the model.

4.3. Life Expectancy:

As mentioned, the remaining life expectancy at death in the YLL calculation, and life expectancy in the calculation of the lifetime risk of the attributable fraction was ascertained from an abridged cohort life table, obtained from the World Health Organization (WHO, 2006), found

in Appendix D. Life expectancy was based upon the current Canadian life expectancy of 83 years for females and 78 years for males (WHO, 2006), and deaths were assumed to occur at the midpoint of the age interval.

4.4. Average Disease Duration:

Average disease duration was derived for site-specific cancers on the basis of descriptive epidemiological estimates ascertained from Statistics Canada (Flanagan et al, 2005) and the World Health Organization (Mathers et al, 2001; WHO, 2000).

Statistics Canada provided a rich source of site-specific data on stage distribution[9], duration, and medical severity in the form of a treatment algorithm, reviewed by medical expert (Flanagan et al, 2005). The Statistics Canada database was published as part of the Public Health Impact of Disease in Canada research program, with limitations and methodologies of the primary data described further by Flanagan et al, (2005).

Average duration of *primary therapy* for site-specific cancers was derived in two stages. First, considering a patients medical severity at diagnosis and typical treatment regimes (Appendix E1), and second considering medical severity at diagnosis and the age distribution of cases (Appendix E2). The modeled estimates of average duration for primary therapy for site-specific cancers, disaggregated by age and sex interval are described in Appendix E3

The average duration for the *remission* stage was derived separately for survivors and non-survivors based on relative survival rates at one, three, five, and ten years (methods described in section 3.3.2.3). The RSR's, stratified by age and sex for each cancer site, can be found in Appendix F. The RSR's were ascertained in accordance with ICD9 coding from the

[9] The Ontario Cancer Registry currently does not collect data on stage of cancer (medical severity) at diagnosis. With greater uncertainty in epidemiological disease data parameters (ie: duration, medical severity), the estimates of YLD's are likely associated with greater uncertainty then estimates of YLL's.

SEER*Stat 6.2.4 database. Recall, the average duration of disease for survivors is set to five years, and for non-survivors the average duration of disease, stratified by age and sex for site-specific cancers is found in Appendix G. The average duration of the *remission* stage for survivors can be found in Appendix H1 and for non-survivors in Appendix H2

The duration of the stages of *diagnosis*, *metastasis*, and *terminal* periods has been set to six weeks (0.1 years), five months (0.417 years), and one month (0.083 years) respectively for all cancers and age groupings, regardless of survivorship (Flanagan et al, 2005; Mathers et al, 2001; WHO, 2000). On the basis of estimates of survival duration, cure rates, as well as stage durations for diagnoses, treatment, remission (survivors & non-survivors), metastasis, and terminal periods, estimates of average disease duration are listed in Table 4.1**.**

Table 4.1 Average Duration of Disease by ICD9 Coding (age & sex disaggregated)[1]

Cancer site	Age	Males	Females	Cancer Site	Age	Males	Females
140-149 Oral Cavity & Pharynx	0-4	0	0	162-165 Lung, Bronchus, & Trachea	0-4	4.35	4.65
	5-14	0	4.55		5-14	4.13	0
	15-29	4.58	4.64		15-29	3.50	3.92
	30-44	4.58	4.70		30-44	2.45	2.84
	45-59	4.68	4.71		45-59	2.41	2.83
	60-69	4.72	4.83		60-69	2.34	2.73
	70-79	4.51	4.75		70-79	1.97	2.25
	80+	4.57	3.76		80+	1.48	1.61
150 Esophagus	0-4	0	0	200-203 Lymphomas & Multiple Myeloma	0-4	0	3.99
	5-14	0	0		5-14	4.61	4.56
	15-29	0	0		15-29	4.71	4.70
	30-44	2.52	0		30-44	4.88	5.04
	45-59	2.36	2.72		45-59	5.62	5.50
	60-69	2.21	2.54		60-69	5.40	5.26
	70-79	2.09	2.31		70-79	4.66	4.77
	80+	2.05	1.69		80+	3.10	3.43
160-161 Middle Ear, Nasal, & Larynx	0-4	0	0	204-208 Leukemias	0-4	4.44	4.11
	5-14	0	4.68		5-14	4.44	4.33
	15-29	0	4.64		15-29	3.91	3.99
	30-44	4.74	4.65		30-44	4.60	4.42
	45-59	4.76	5.18		45-59	5.58	4.49
	60-69	4.88	5.03		60-69	5.12	5.06
	70-79	5.14	5.10		70-79	3.93	4.23
	80+	3.84	4.06		80+	2.49	2.54

[1] determined as a weighted average of case distribution and treatment by stage

4.5. Disability Weights

The GBD disability weights for malignant neoplasm were ascertained online from the WHO for the stages of malignant neoplasm as listed in Table 3.5. The weights have been well validated[10] amongst a global representation of experts, demonstrating little empirical evidence of cross-cultural variability, with Pearson and Spearman rank coefficients for 22 indicator conditions >0.9, as described elsewhere (Essink-Bot et al, 2002; Mathers et al, 1999; Murray & Acharya, 1997; Schwarzinger et al, 2003).

The average disability weight was calculated in the model by means in which the stage specific disability weight contributed in accordance with its fraction of its share of the prevalence. As an example, assume 90% of females age 15-29 with oral cancer are treated, the five-year RSR is 51.4%, 38.6% will be treated and not survive, such that the average disability weight is derived as:

Stage	Disability Wt.	% Cases	Fraction Cases / Stage	
Diagnosis	0.09	100	1	0.09
Treatment	0.09	90	0.9	0.081
Remission	0.09	90	0.9	0.081
Metastasis	0.75	48.6	0.486	0.365
Terminal	0.81	48.6	0.486	0.394
			Average Disability Weight:	0.202

As such, the average disability weight is calculated, stratified by age and sex, as the sum of the fraction of cases undergoing each state multiplied by the associated stage disability weight for site specific cancers (Flanagan et al, 2005; Melse et al, 2000). Average disability weights for site specific cancers, stratified by age and sex interval, in the model are listed in Table 4.2.

[10] Disability weights in GBD were originally estimated among 10 different expert groups (4 multinational groups of health care practitioners) using multi-measure approaches (ie: time trade offs, standard gamble, visual analogue scales, and person trade-off methods PTO) with groups from various parts of the world: USA, Mexico, Brazil, Morocco, Japan, Netherlands, etc. This approach for health valuation served as the foundation for the Disability Weights Project for Diseases in the Netherlands, and continuation of the European Disability Weights Project. Correlation coefficients of the 10 studies resulted in a Pearson product correlation coefficient of 0.954. Therefore, disability valuations appear quite stable universally despite heterogeneity of respondents (Murray & Lopez, 2000)

Table 4.2 Average Disability Weights, by ICD9 Code, disaggregated by age & sex

ICD9 Code	140-149	150	160-161	162-165	200-203	204-208
Males						
0-4	n/a	n/a	n/a	0.148	n/a	0.187
5-14	n/a	n/a	n/a	0.194	0.108	0.199
15-29	0.108	n/a	n/a	0.237	0.102	0.249
30-44	0.132	0.372	0.137	0.327	0.136	0.226
45-59	0.179	0.384	0.152	0.343	0.171	0.206
60-69	0.189	0.387	0.157	0.350	0.210	0.233
70-79	0.178	0.388	0.176	0.361	0.240	0.259
80+	0.176	0.396	0.194	0.370	0.263	0.290
Females						
0-4	n/a	n/a	n/a	0.115	0.171	0.177
5-14	0.112	n/a	0.095	n/a	0.099	0.188
15-29	0.085	n/a	0.111	0.207	0.073	0.227
30-44	0.119	n/a	0.099	0.314	0.108	0.222
45-59	0.157	0.353	0.142	0.328	0.151	0.220
60-69	0.175	0.373	0.158	0.339	0.189	0.219
70-79	0.183	0.372	0.177	0.351	0.226	0.252
80+	0.190	0.392	0.183	0.359	0.259	0.282

n/a: average disability weight could not be calculated b/c no cases diagnosed in this age group

4.6. Risk Potency Estimates

Risk potency values for of the each ambient air toxics are obtained from the International Toxicity Estimates for Risk (ITER) database, maintained by the organization for Toxicology Excellence and Risk Assessment (TERA). ITER is an electronic database containing quantitative and qualitative estimates of human health risk estimates for more then 600 carcinogenic environmental substances of health concern to organizations such as the United States Environmental Protection Agency (U.S. EPA), RIVM, and Health Canada.

The potency values (slope factors) for the six carcinogenic air toxics were derived on the basis of TC05 and TC01 estimates (tumorigenic concentration) from Health Canada risk evaluations, representing exposure concentrations associated with either a 5% of 1% increased risk of cancer in human populations, and are consistent with values in the HEIDI II model as listed in Table 4.3

Table 4.3 Health Canada Inhalation Unit Risk (I.U.R) Cancer Potency Estimates

Substance	CAS #	Risk Value	Type of Value (ug/m3)	IARC Class
Acetaldehyde	75-07-0	5.88E-07	I.U.R	2B
Formaldehyde	50-00-0	5.30E-06	I.U.R	2A
Benzene	71-43-2	3.50E-06	I.U.R	1
1,3-Butadiene	106-99-0	5.88E-06	I.U.R	2A
Ethylene Oxide	75-21-8	2.27E-05	I.U.R	1
Nickel (dusts)	NA-11	1.25E-03	I.U.R	1

Slope factors derived from Health Canada TC values are based on a measure of central tendency directly from the dose response curve, and thus express 'best fit' estimates of risk in contrast to the 'upper bound' estimates of risk commonly employed by the US EPA, which require additional conservative assumptions (McColl, Hicks et al, 2000).

4.7. Concentrations of Ambient Air Toxics

4.7.1. Current Concentrations

Annual mean ambient concentrations of acetaldehyde, formaldehyde, benzene, 1,3-BD, ETO, and nickel refinery dusts were ascertained for the S.W.O Toronto regions as secondary data from the City of Toronto Board of Health reports, Ontario Air Quality Reports, the National Air Pollution Surveillance (NAPS) system, Canadian Environmental Protection Agency Priority Substance List Profiles, and the HEIDII II model. Annual mean ambient concentrations (ug/m^3) in Toronto and S.W.O of the six carcinogenic air toxics, along with the reference source, are provided in Table 4.4. Annual mean concentrations were ascertained between the years 2000 to 2004 for each of the toxics, assumed representative of current concentrations with little fluctuation in long term chronic exposures.

Table 4.4 Current Concentrations of Ambient Air Toxics in Toronto and S.W.O

Substance	Concentration (ug/m3)	Reference Source(s)
Toronto		
Acetaldehyde	2.000	CEPA (2000) PSL Report Acetaldehyde
Formaldehyde	3.300	CEPA (2000) PSL Report Formaldehyde
Benzene	1.400	Gower, McColl (2007) HEIDI II (data_background); Tom Dann, NAPS Annual Data Summary (2003)
1,3-Butadiene	0.200	NAPS Annual Data Summary (2003)
Ethylene Oxide	0.059	Ontario Air Quality Report (2004): Ethylene = 1.197ug/m3, assume 5% as oxide
Nickel (dusts)	0.00142	Gower, McColl (2007) HEIDI II (data_background); NAPS Annual Report (2002)
S.W.O		
Acetaldehyde	2.400	CEPA (2000) PSL Report Acetaldehyde; Ambient concentration in Windsor
Formaldehyde	2.605	Ontario Air Quality Report (2001), Windsor value
Benzene	1.311	Ontario Air Quality Report (2004); NAPS Annual Data Summary (2001)
1,3-Butadiene	0.343	Ontario Air Quality Report (2004); NAPS Annual Data Summary (2001)
Ethylene Oxide	0.175	Ontario Air Quality Report (2004). Ethylene in Sarnia = 3.5ug/m3, assume 5% as oxide
Nickel (dusts)	0.00162	Gower, McColl (2007) HEIDI II (data_background); NAPS Annual Report (2002)

4.7.2. Counterfactual Concentrations

Counterfactual concentrations of each of the ambient air toxics were ascertained from Health Canada PSL reports, Ontario Air Quality Reports, ATSDR, and the US EPA Air Toxics Network. The parametric estimates and reference source of concentrations corresponding to plausible and feasible minimum risk distributions are provided in Tables 4.5a,b.

Feasible minimum risk concentrations are generally represented by concentrations that have been achieved in rural communities, with minimal air emissions of toxics from either industrial or motor vehicle releases. As emissions modelling was beyond the scope of the project, it was accepted that feasible minimum risk concentrations generally corresponded to a reduction in current concentrations by approximately 50%.

Concentrations of the six air toxics corresponding to plausible minimum risk levels were ascertained from the US EPA Air Toxics Network as 'background' concentrations. Background concentrations express contributions to ambient concentrations from natural sources, and persistent emissions from past and distant sources. Plausible minimum risk concentrations are representative of ambient levels expected if there were no anthropogenic releases of the air toxics, corresponding approximately with a 75% reduction in current concentrations.

Table 4.5a Concentrations of air toxics associated with feasible minimum risk levels

Substance	Concentration (ug/m3)	Reference Source
Acetaldehyde	1.000	Health Canada PSL Report, average concentrations in rural Canada recorded <1ug/m3
Formaldehyde	1.240	Ontario Air Quality Report (2001), annual mean concentration in Windsor 1.24ug/m3
Benzene	0.600	Health Canada PSL Report (1993), mean concentrations of benzene in rural Canada range 0.6 to 1.2ug/m3
1,3-Butadiene	0.100	Health Canada PSL, mean ambient concentrations of 1,3-BD in rural Canada recorded at 0.1ug/m3
Ethylene Oxide	0.029	Remote locations in California, ETO ranged in concentration from 0.029 to 0.36ug/m3 (ATSDR)
Nickel Refinery Dusts	0.001	Health Canada PSL Report (Tom Dann, 1991), mean concentrations in 11 Canadian cities ranged 0.001 to 0.02ug/m3

Table 4.5b Concentrations of air toxics associated with a plausible minimum risk levels

Substance	Concentration (ug/m3)	Reference Source
Acetaldehyde	0.511	US EPA Air Toxics Network (1996) Nationwide Assessment Acetaldehyde (background concentration)
Formaldehyde	0.755	US EPA Air Toxics Network (1996) Nationwide Assessment Formaldehyde (background concentration)
Benzene	0.395	US EPA Air Toxics Network (1996) Nationwide Assessment Benzene (background concentration)
1,3-Butadiene	0.050	US EPA Air Toxics Network (1996) Nationwide Assessment 1,3-Butadiene (background concentration)
Ethylene Oxide	0.0062	Health Canada Priority Substance List Report
Nickel Refinery Dusts	0.0002	US EPA Air Toxics Network (1996), rural Michigan mean concentration of area & other =0.00019

5. RESULTS

Estimates of the burden of disease from six cancer outcomes in Toronto and S.W.O will be presented in two sections: (i) the total BoD analyses, which presents baseline DALY estimates, independent of attributable exposure (section 5.1), and (ii) the counterfactual analyses, which presents exposure attributable DALY's, assuming current and counterfactual scenarios (section 5.2).

5.1. Phase One Results: DALY Burden of Disease

The following subsections will present estimates of the disease burden in terms of DALY's from six cancers in the S.W.O and Toronto regions as absolute estimates of site specific BoD (section 5.1.1.), and as site-specific rank order based on absolute estimates (5.1.2). Results are presented as both crude estimates, and as age and sex stratified estimates to examine the impact of alternative social value choices (age weighting and discounting) of the relative importance of the six cancers through sensitivity analyses (section 5.1.3.). Although DALY's were calculated with and without the inclusion of age weighting and discounting for the sensitivity analysis, the discussion and result tables will assume the inclusion of age weights an discounting at a rate of 3%, unless otherwise noted.

5.1.1. Absolute Estimates of the BoD

A combined total of 32,074.10 DALY's were lost from six cancer endpoints in the Toronto and S.W.O regions in 2001 (84% in Toronto and 16% in S.W.O). Table 5.1 summarizes crude estimates of the BoD from cancers of the (i) oral cavity and pharynx, (ii) esophagus, (iii) ear, nasal, and larynx, (iv) lung, bronchus, and trachea, (v) lymphomas and multiple myelomas,

and (vi) leukemias, in Toronto and S.W.O regions as estimates of Total DALY's lost and DALY's lost per 100,000 persons.

Table 5.1 Estimates of the Total BoD and BoD / 100,000 Persons, age & sex aggregated

	Total DALY's			DALY's / 100,000 Persons		
TORONTO	**YLL**	**YLD**	**DALY's**	**YLL**	**YLD**	**DALY's**
Oral, Pharynx	1,205.49	260.00	1,465.49	50.73	11.17	31.14
Esophagus	1,357.54	67.98	1,425.53	56.94	2.93	30.29
Ear, Nasal, Larynx	513.51	66.69	580.20	22.27	2.89	12.33
Lung, Bronchus, Trachea	14,782.75	1,169.66	15,952.41	631.56	49.95	338.94
Lymphoma, Multiple Myeloma	4,103.53	811.59	4,915.12	173.80	34.58	104.43
Leukemias	2,352.25	364.30	2,716.55	99.39	15.59	57.72
S.W.O						
Oral, Pharynx	186.13	53.07	239.20	68.24	19.92	44.33
Esophagus	185.67	14.46	200.12	68.04	5.42	37.09
Ear, Nasal, Larynx	114.58	15.05	129.62	43.38	5.62	24.02
Lung, Bronchus, Trachea	3,164.93	256.72	3,391.65	1,166.72	95.35	628.58
Lymphoma, Multiple Myeloma	473.70	97.38	571.09	174.57	36.21	105.84
Leukemias	432.94	54.19	487.13	160.09	20.21	90.28

For the six cancer endpoints, results indicate the BoD associated with mortality exceedingly outweighs the BoD associated with long term disability, with the YLL component dominating the total BoD by approximately nine-fold in S.W.O (4,557.95 YLL's / 490.87 YLD's) and Toronto (24.315.07 YLL's / 2,740.22 YLD's)[11], consistent with relatively high case fatality rates for malignant neoplasm, notably lung and esophagus cancers (CCS, 2006).

In accordance with a Torontonian population seven and a half times the size of S.W.O (Appendix B) the BoD associated with each cancer site in Toronto is expectedly larger then S.W.O; however with a standardized population size, the total BoD in S.W.O (930 DALY's) nearly doubles the BoD in Toronto (575 DALY's), a pattern consistently demonstrated among each of cancer site.

[11] Results did not involve statistical analysis of association and/or uncertainty

Estimates of the disease burdens of the selected cancer sites are presented separately for males and females in Tables 5.2a and 5.2b for Toronto and S.W.O. In both the Toronto and S.W.O, females experience a greater BoD for all cancer sites excluding middle ear, nasal, and larynx; and lung, bronchus, and trachea, yet the total BoD from all sites combined is slightly greater among males in both S.W.O (998.73 DALY's vs. 865.03 DALY's) and Toronto (617.53 DALY's vs. 534.26 DALY's) when comparing the DALY rates per 100,000 persons.

Table 5.2a Site-specific DALY's lost in Toronto, disaggregated by sex

Males	Total DALY's	DALY's / 100,000 Persons
Oral cavity & Pharynx	536.22	23.38
Esophagus	365.61	15.94
Middle Ear, Nasal, & Larynx	518.79	22.62
Lung, Bronchus, & Trachea	9,460.02	412.43
Lymphomas & Multiple Myeloma	2,173.08	94.74
Leukemias	1,110.92	48.43
Females		
Oral cavity & Pharynx	929.27	38.51
Esophagus	1,059.92	43.93
Middle Ear, Nasal, & Larynx	61.41	2.55
Lung, Bronchus, & Trachea	6,492.39	269.08
Lymphomas & Multiple Myeloma	2,742.04	113.64
Leukemias	1,605.63	66.55

Table 5.2b Site-specific DALY's lost in S.W.O, disaggregated by sex

Males	Total DALY's	DALY's / 100,000 Persons
Oral cavity & Pharynx	90.45	34.42
Esophagus	59.64	22.69
Middle Ear, Nasal, & Larynx	113.09	43.03
Lung, Bronchus, & Trachea	1,907.48	725.79
Lymphomas & Multiple Myeloma	230.65	87.76
Leukemias	223.50	85.04
Females		
Oral cavity & Pharynx	148.75	53.75
Esophagus	140.49	50.76
Middle Ear, Nasal, & Larynx	16.53	5.97
Lung, Bronchus, & Trachea	1484.17	536.27
Lymphomas & Multiple Myeloma	340.44	123.01
Leukemias	263.63	95.26

Absolute estimates of site specific DALY's lost, disaggregated by sex and age grouping, are presented in Tables 5.3a through 5.3f. Results may better be presented in Figures 5.1a

through 5.6d providing an illustration of the age distribution of DALY's lost due to site-specific cancers throughout the life cycle, with estimates of rates per population size of 100,000 persons.

When stratified by age group (0-4, 5-14, 15-29, 30-44, 45-59, 60-69, 70-79, and 80+), results indicate the BoD associated with cancer in both Toronto and S.W.O regions is relatively small prior to the age of 30 and dominate in individuals ages 60+. Interestingly, despite a larger Torontonian population, S.W.O experiences a greater absolute burden of lung, bronchus, and trachea cancers among females aged 0-4; leukemia's among males aged 15-29; and middle ear, nasal, and larynx cancer among females aged 15-29 and 60-69. Results likely reflect small cell sizes with few numbers of incidence and fatal cases among particular age groups. With small numbers of incidence and mortality counts, DALY estimates of site specific cancers may be easily skewed. Analysis of the BoD between the two regions reveals an inconsistent pattern regarding regional dominance cancer site by age distribution, with inconsistent patterns among males and females.

Table 5.3a Estimates of Total DALY's and DALY's / 100,000: The Burden of Disease from Cancers of the Oral Cavity & Pharynx in Toronto and S.W.O Regions, disaggregated by age and sex

	Total DALY's						DALY's / 100,000					
	Males		Females		Total		Males		Females		Total	
Age	S.W.O	Toronto	S.W.O	Toronto	S.W.O	Toronto	S.W.O	Toronto	S.W.O	Toronto	S.W.O	Toronto
0-4	0	0	0	0	0	0	0	0	0	0	0	0
5-14	0	0	0	1.18	0	1.18	0	0	0	0.38	0	0.19
15-29	0.70	33.04	0.56	2.80	1.26	35.85	1.31	6.99	1.05	0.59	1.18	3.77
30-44	1.52	68.55	26.71	77.11	28.23	145.66	2.45	11.46	42.60	12.31	22.64	11.89
45-59	39.86	170.81	39.07	353.19	78.93	524.00	76.33	39.45	73.90	77.01	75.11	58.77
60-69	30.74	135.49	60.74	288.23	91.47	423.73	144.43	82.31	263.33	159.07	206.28	122.53
70-79	11.58	79.28	16.72	158.50	28.30	237.78	73.40	72.11	81.03	110.99	77.72	94.08
80+	6.05	49.05	4.95	48.26	11.00	97.31	106.76	118.33	41.75	63.04	62.76	82.46

Table 5.3b Estimates of Total DALY's and DALY's / 100,000: The Burden of Disease from Cancers of the Esophagus in Toronto and S.W.O Regions, disaggregated by age and sex

	Total DALY's						DALY's / 100,000					
	Males		Females		Total		Males		Females		Total	
Age	S.W.O	Toronto	S.W.O	Toronto	S.W.O	Toronto	S.W.O	Toronto	S.W.O	Toronto	S.W.O	Toronto
0-4	0	0	0	0	0	0	0	0	0	0	0	0
5-14	0	0	0	0	0	0	0	0	0	0	0	0
15-29	0	0	0	0	0	0	0	0	0	0	0	0
30-44	0	27.69	0	123.44	0	151.13	0	4.63	0	19.71	0	12.34
45-59	5.46	50.85	35.49	398.63	40.94	449.49	10.45	11.74	67.12	86.92	38.96	50.41
60-69	31.74	134.89	45.54	298.99	77.28	433.88	149.17	81.95	197.43	165.01	174.27	125.47
70-79	16.69	115.71	47.04	177.38	63.73	293.08	105.76	105.24	227.97	124.21	175.01	115.96
80+	5.74	36.47	12.42	61.48	18.17	97.95	101.39	87.99	104.73	80.31	103.65	83.01

Table 5.3c Estimates of Total DALY's and DALY's / 100,000: The Burden of Disease from Cancers of the Middle Ear, Nasal, and Larynx in Toronto and S.W.O Regions, disaggregated by age and sex

	Total DALY's						DALY's / 100,000					
	Males		**Females**		**Total**		**Males**		**Females**		**Total**	
Age	**S.W.O**	**Toronto**	**S.W.O**	**Toronto**	**S.W.O**	**Toronto**	**S.W.O**	**Toronto**	**S.W.O**	**Toronto**	**S.W.O**	**Toronto**
0-4	0	0	0	0	0	0	0	0	0	0	0	0
5-14	0	0	0	0.51	0	0.51	0	0	0	0.17	0	0.08
15-29	0	0	0.73	0	0.73	0	0	0	1.37	0	0.68	0
30-44	0.81	47.13	2.89	27.04	3.70	6.06	1.31	7.88	4.60	4.32	2.97	6.06
45-59	45.02	194.38	0	16.34	45.02	23.63	86.22	44.89	0	3.56	42.84	23.63
60-69	48.70	179.58	11.63	1.67	60.33	52.41	228.86	109.10	50.42	0.92	136.05	52.41
70-79	17.93	81.07	0.97	8.65	18.90	35.50	113.62	73.74	4.70	6.06	51.90	35.50
80+	0.63	16.63	0.31	7.20	0.94	20.19	11.08	40.11	2.62	9.40	5.36	20.19

Table 5.3d Estimates of Total DALY's and DALY's / 100,000: The Burden of Disease from Cancers of Lung, Bronchus, and Trachea in Toronto and S.W.O Regions, disaggregated by age and sex L

	Total DALY's						DALY's / 100,000					
	Males		**Females**		**Total**		**Males**		**Females**		**Total**	
Age	**S.W.O**	**Toronto**	**S.W.O**	**Toronto**	**S.W.O**	**Toronto**	**S.W.O**	**Toronto**	**S.W.O**	**Toronto**	**S.W.O**	**Toronto**
0-4	0	0.38	0.32	0	0.32	0.38	0	0.26	2.06	0	1.00	0.13
5-14	0	0.93	0	0	0	0.93	0	0.28	0	0	0	0.15
15-29	1.20	1.20	1.17	32.57	2.36	33.77	2.23	0.25	2.18	6.80	2.20	3.55
30-44	46.23	244.48	75.53	449.29	121.76	693.76	74.59	40.86	120.47	71.74	97.66	56.66
45-59	495.10	2969.40	453.16	1941.28	948.25	4910.68	948.10	685.79	857.11	423.29	902.33	550.77
60-69	702.83	3459.62	456.12	1865.20	1158.95	5324.82	3302.78	2101.77	1977.52	1029.39	2613.48	1539.86
70-79	535.34	2182.74	401.21	1678.93	936.55	3861.67	3392.53	1985.39	1944.30	1175.68	2571.88	1527.89
80+	126.78	601.28	96.68	525.12	223.45	1126.40	2237.93	1450.61	815.14	685.98	1275.06	954.58

Table 5.3e Estimates of Total DALY's and DALY's / 100,000: The Burden of Disease from Lymphoma's and Multiple Myelomas in Toronto and S.W.O Regions, disaggregated by age and sex

	Total DALY's						DALY's / 100,000					
	Males		**Females**		**Total**		**Males**		**Females**		**Total**	
Age	**S.W.O**	**Toronto**	**S.W.O**	**Toronto**	**S.W.O**	**Toronto**	**S.W.O**	**Toronto**	**S.W.O**	**Toronto**	**S.W.O**	**Toronto**
0-4	0	0	0	1.18	0	1.18	0	0	0	0.83	0	0.41
5-14	0.58	76.54	1.04	40.61	1.62	117.16	1.63	23.55	2.86	13.22	2.25	18.53
15-29	2.73	15.69	0.49	89.81	3.22	105.49	5.07	3.32	0.91	18.76	2.99	11.09
30-44	5.79	263.81	33.83	306.97	39.63	570.78	9.35	44.09	53.96	49.02	31.78	46.61
45-59	48.43	539.01	122.60	849.79	171.03	1388.80	92.74	124.48	231.90	185.30	162.75	155.76
60-69	68.23	602.12	59.31	669.91	127.54	1272.03	320.63	365.80	257.12	369.72	287.60	367.85
70-79	91.20	451.81	95.51	582.21	186.71	1034.02	577.96	410.96	762.84	407.70	512.73	409.12
80+	13.69	224.10	27.66	201.56	41.34	425.66	241.62	540.66	233.20	263.30	235.92	360.73

Table 5.3f Estimates of Total DALY's and DALY's / 100,000: The Burden of Disease from Leukemia in Toronto and S.W.O Regions, disaggregated by age and sex

	Total DALY's						DALY's / 100,000					
	Males		**Females**		**Total**		**Males**		**Females**		**Total**	
Age	**S.W.O**	**Toronto**	**S.W.O**	**Toronto**	**S.W.O**	**Toronto**	**S.W.O**	**Toronto**	**S.W.O**	**Toronto**	**S.W.O**	**Toronto**
0-4	1.48	5.92	0	3.38	1.48	9.30	8.90	3.98	0	2.39	4.59	3.20
5-14	1.02	131.76	2.82	45.01	3.84	176.76	2.89	40.53	7.73	14.65	5.35	27.96
15-29	64.67	51.92	0	143.06	64.67	194.98	120.06	10.98	0	29.89	60.21	20.49
30-44	27.33	256.35	75.29	321.62	102.62	577.98	44.09	42.85	120.09	51.36	82.31	47.20
45-59	39.89	184.80	45.46	340.40	101.56	560.10	76.39	42.68	85.99	74.22	81.22	58.90
60-69	28.59	203.53	72.97	356.57	101.56	560.10	134.34	123.65	316.37	196.79	229.02	161.97
70-79	41.28	180.73	48.86	304.82	90.14	485.55	261.57	164.39	236.80	213.45	247.53	192.11
80+	19.25	95.92	18.22	90.77	37.47	186.69	339.79	231.41	153.63	118.58	213.80	158.21

Figure 5.1a

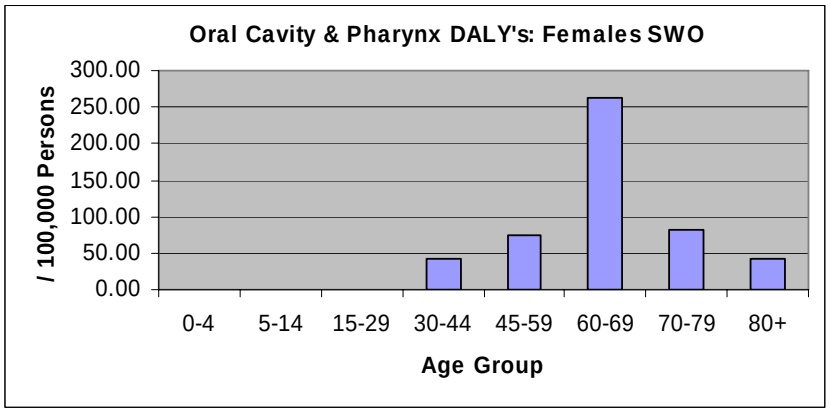


Figure 5.1b

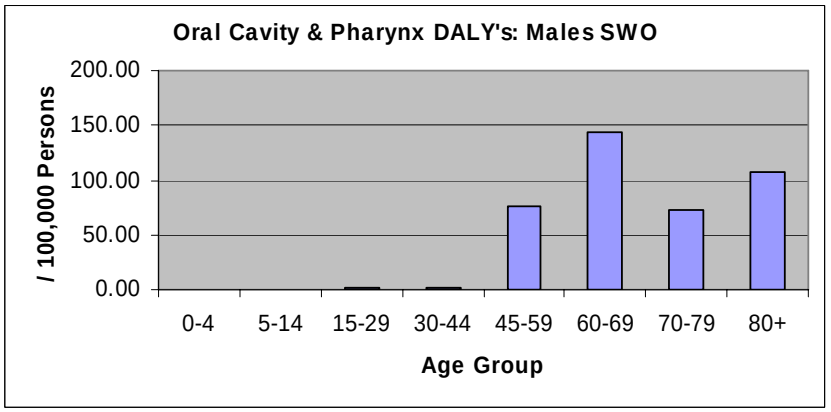


Figure 5.1c

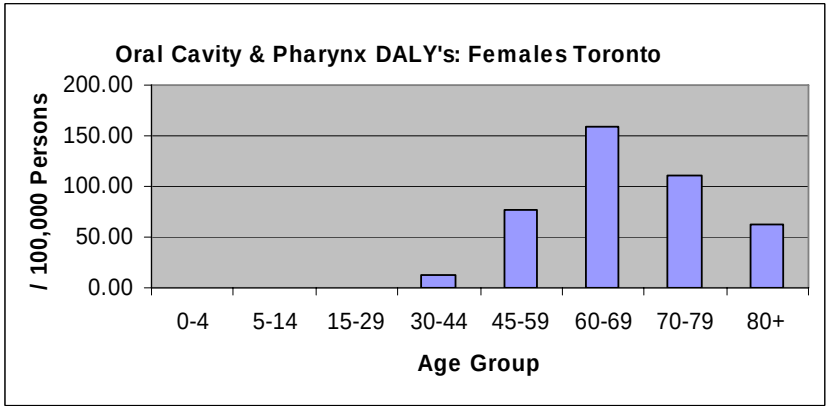


Figure 5.1d

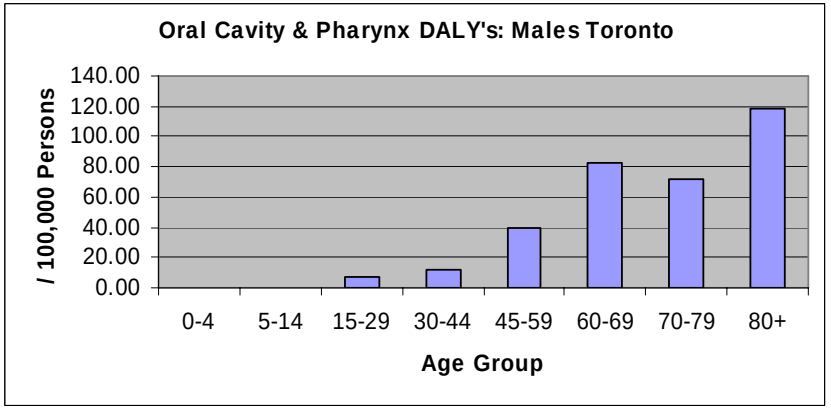


Figure 5.2a

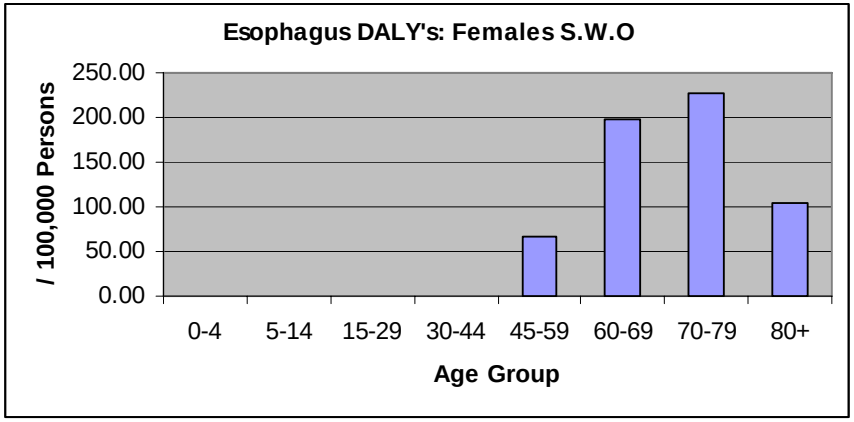


Figure 5.2b

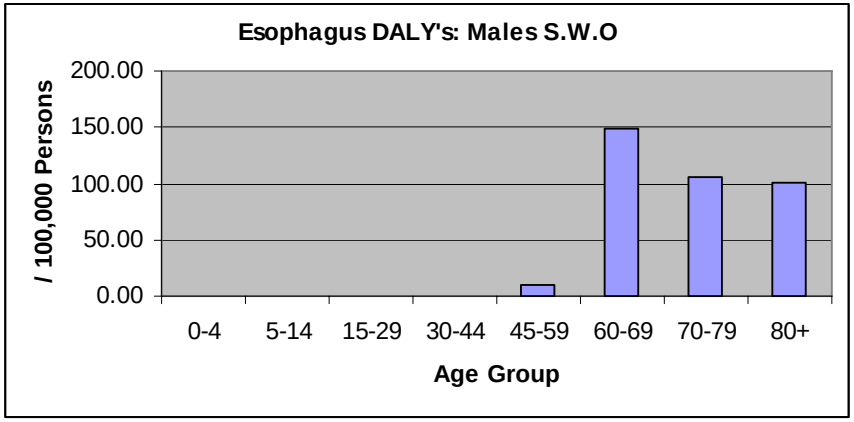


Figure 5.2c

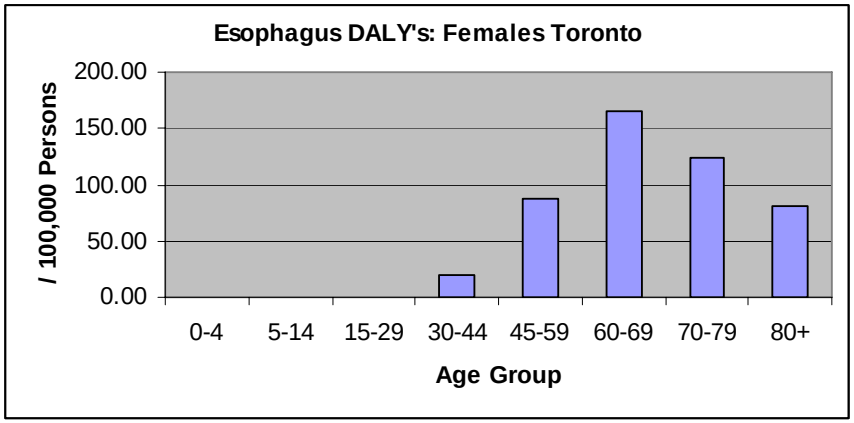


Figure 5.2d

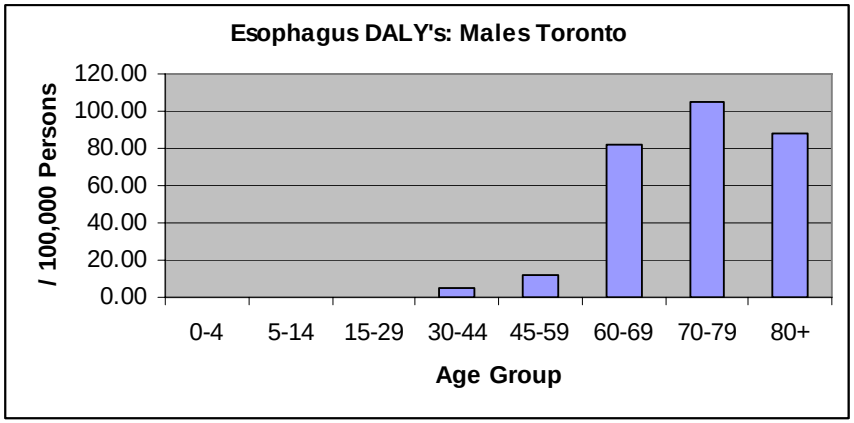


Figure 5.3a

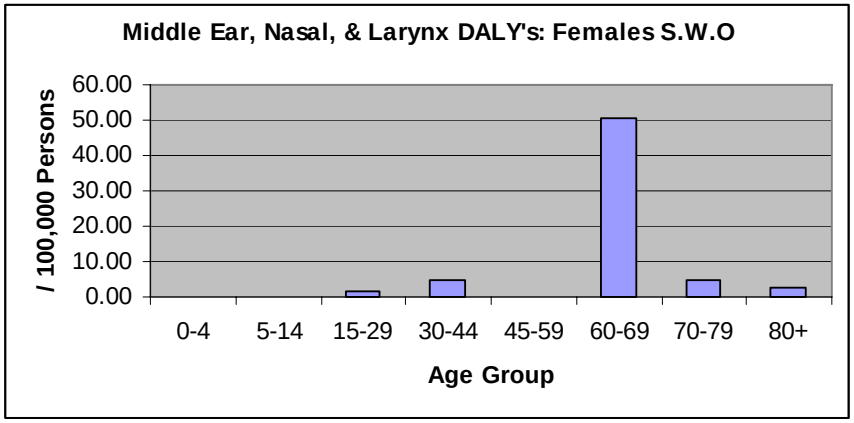


Figure 5.3b

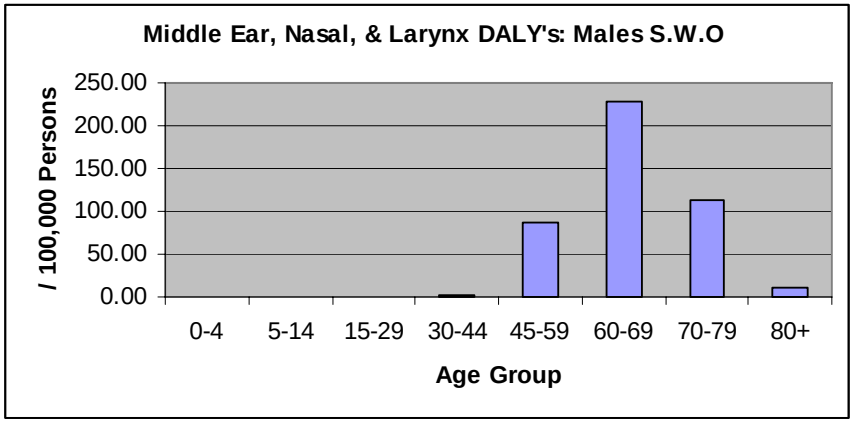


Figure 5.3c

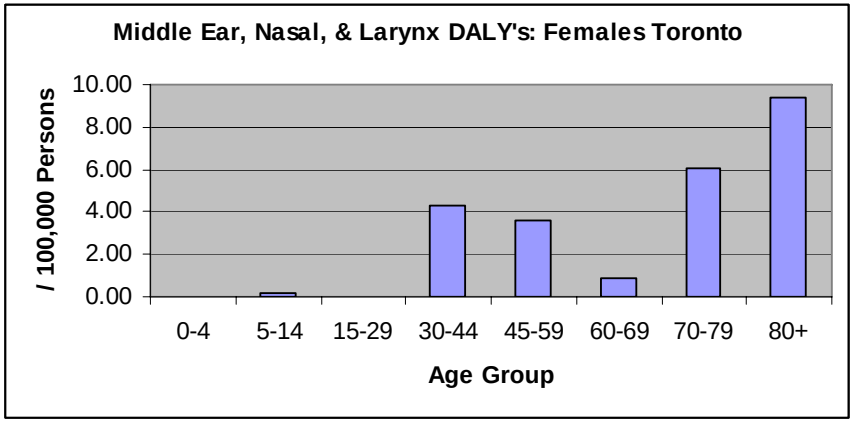


Figure 5.3d

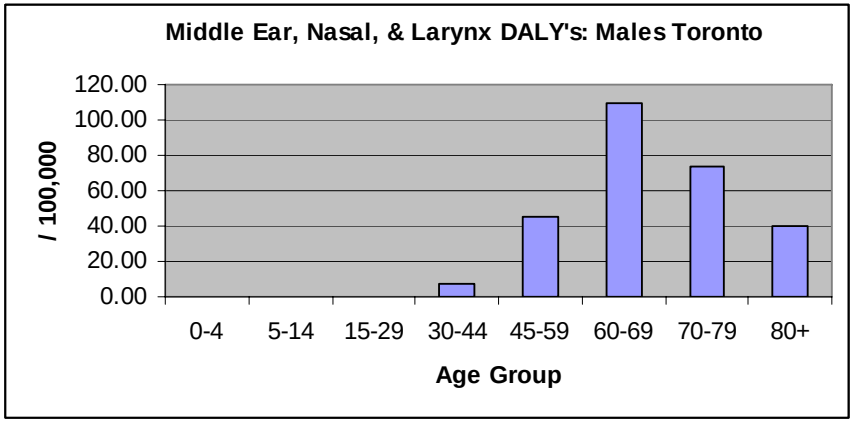


Figure 5.4a

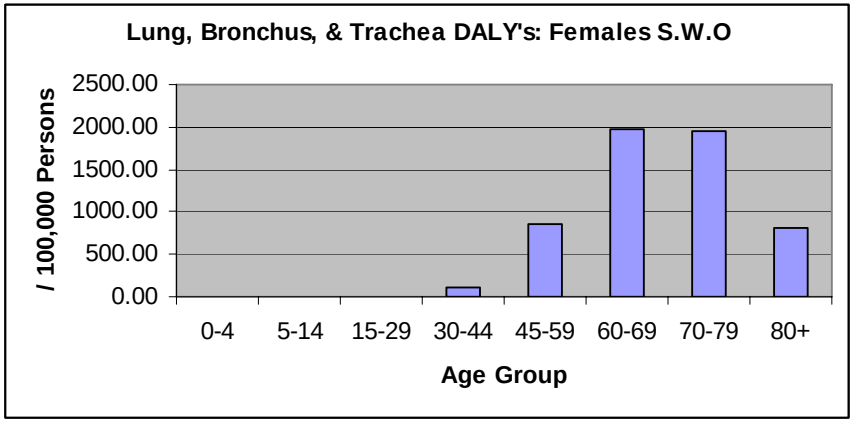
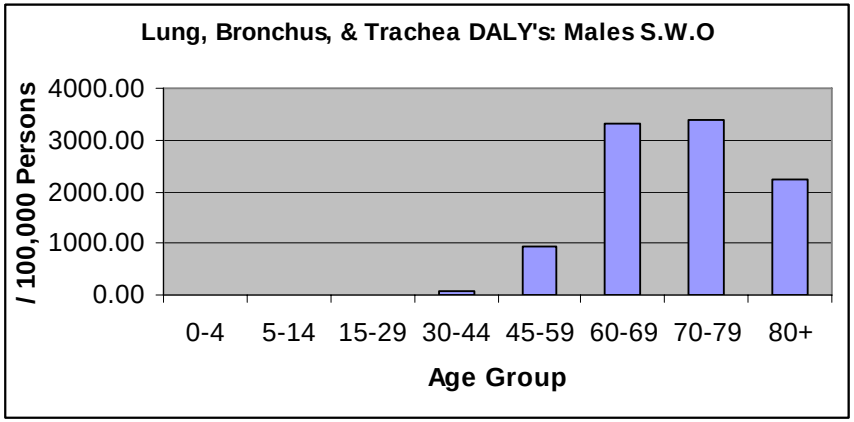


Figure 5.4b



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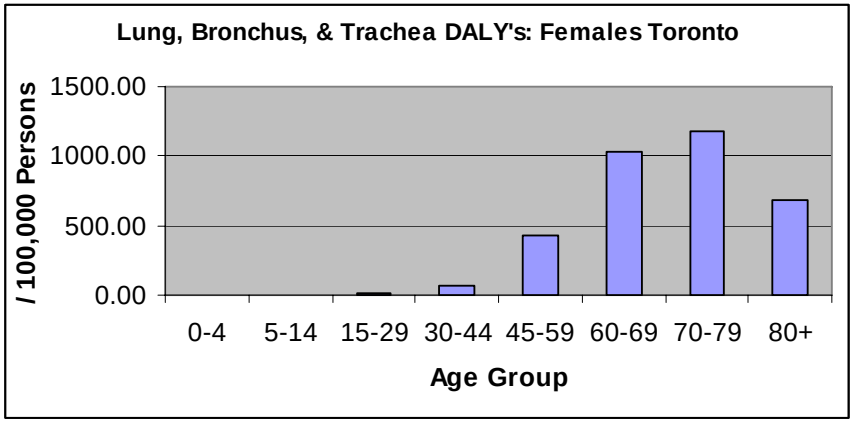


Figure 5.4d

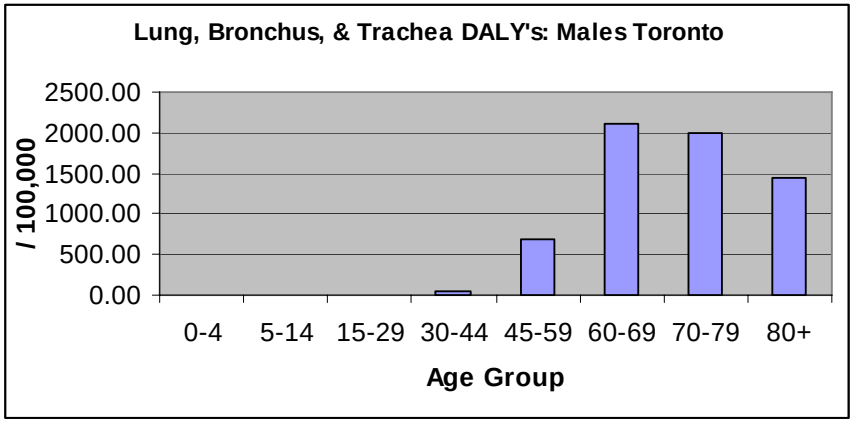


Figure 5.5a

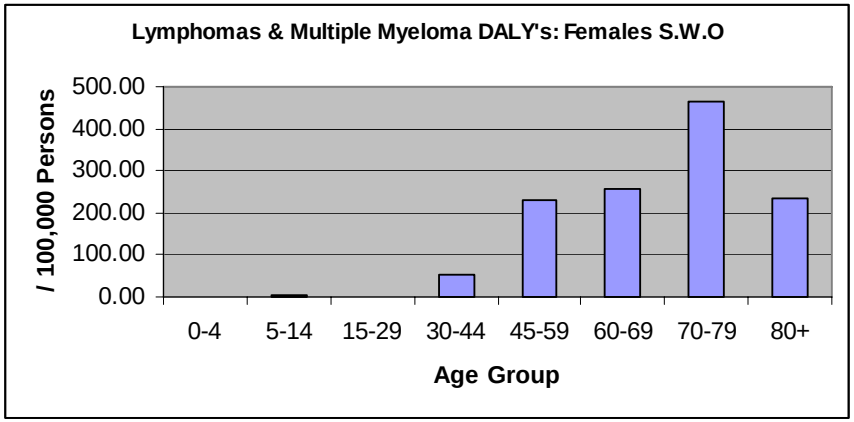


Figure 5.5b

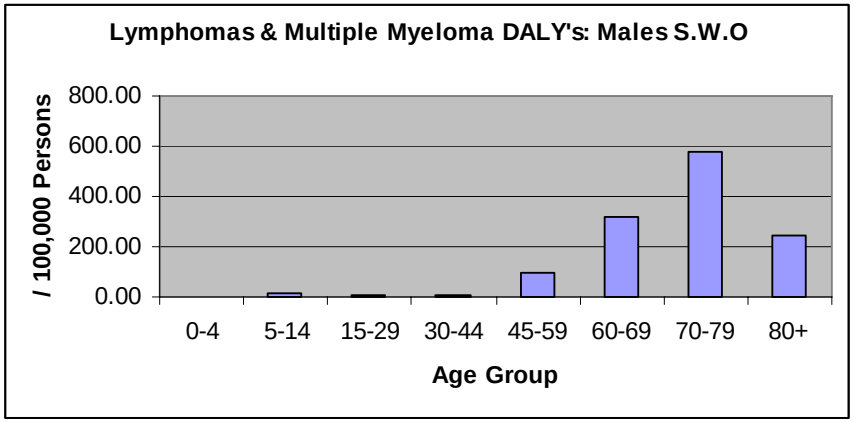


Figure 5.5c

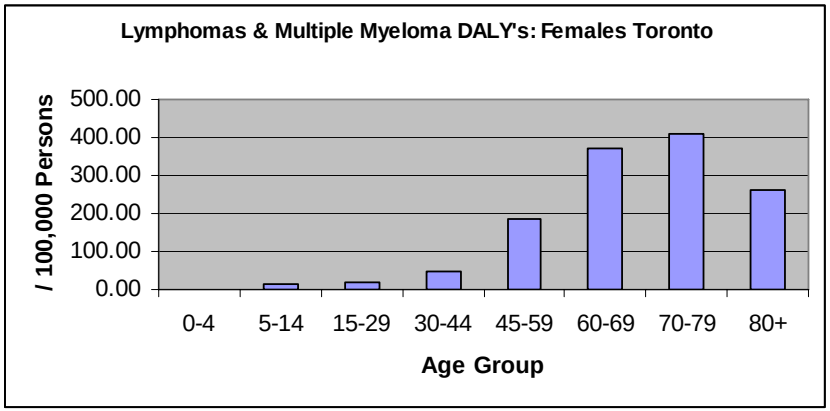


Figure 5.5d

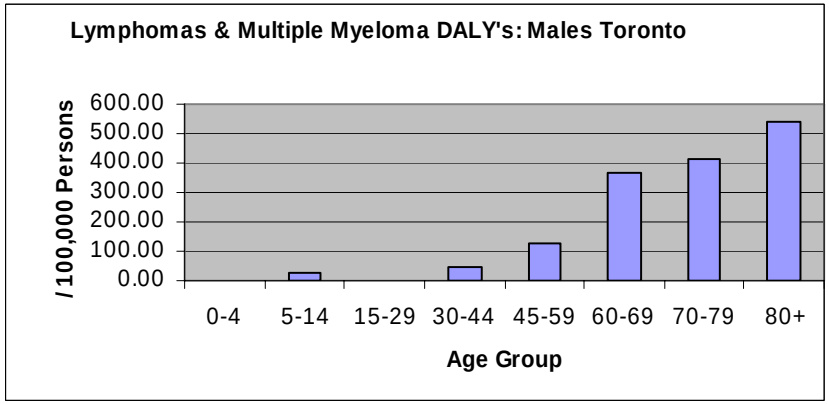


Figure 5.6a

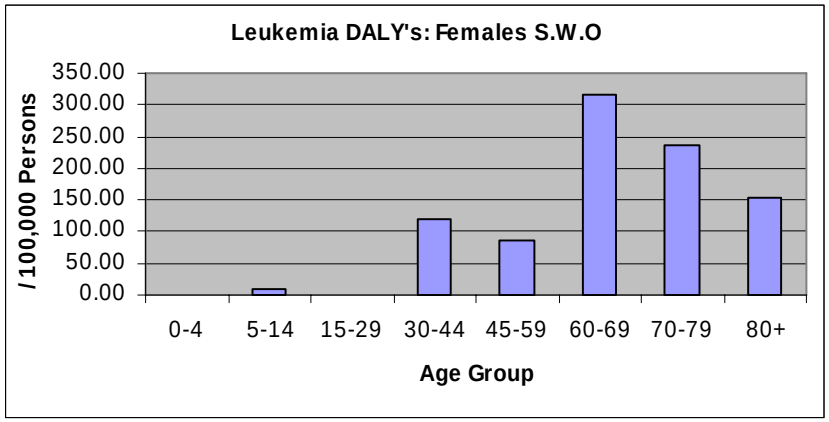


Figure 5.6b

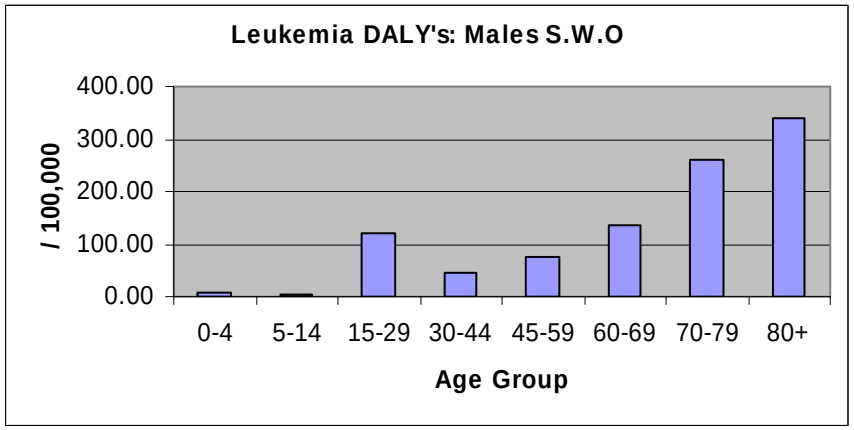


Figure 5.6c

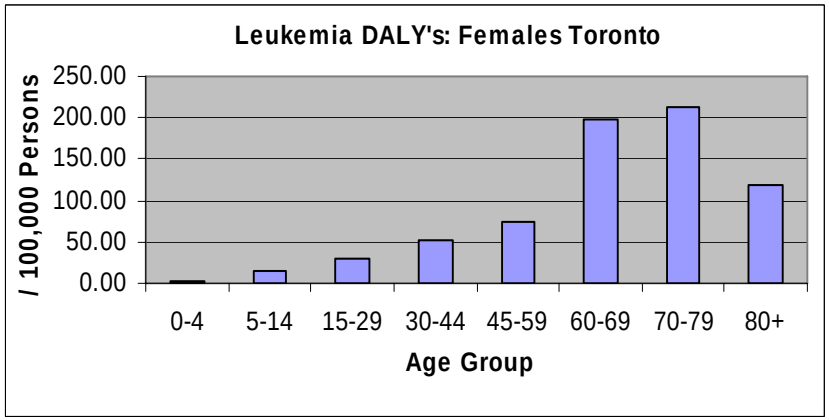
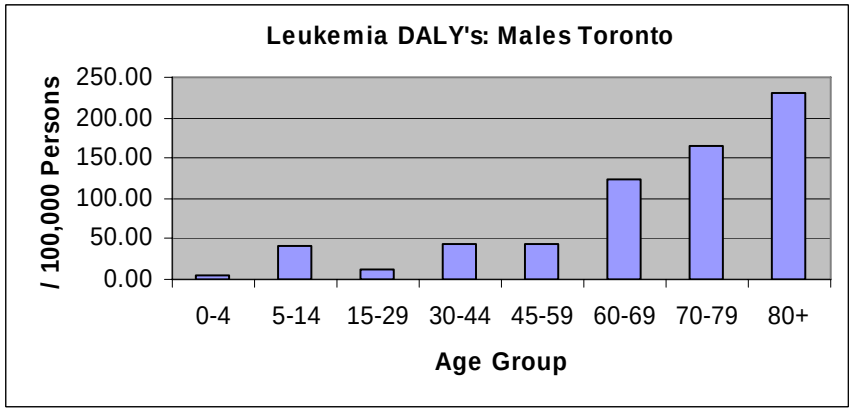


Figure 5.6d



5.1.2. Disease Burden Rankings

The DALY model serves as a useful tool for ranking the relative importance of cancer sites to the total BoD in Toronto and S.W.O to inform resource allocation and priorities, such that disease control strategies and interventions focus on the largest public health issues.

In both Toronto and S.W.O regions, cancers of the lung, bronchus, and trachea are the leading cause of morbidity and mortality, followed by lymphomas and multiple myelomas, and leukemia's. Table 5.4 describes the leading causes of DALY's in the two regions in rank order, with absolute estimates of total DALY's [K=1, r=0.03] provided for reference in parenthesis. Results clearly indicate identical disease burden rankings between the two regions, despite large discrepancies in DALY estimates on an absolute scale.

Table 5.4 Ranking of the BoD for Site-specific Cancer, age & sex aggregated

S.W.O	Toronto
Lung, Bronchus, Trachea (3391.62)	Lung, Bronchus, Trachea (15952.41)
Lymphoma's & Multiple Myeloma (571.09)	Lymphoma's & Multiple Myeloma (4915.12)
Leukemia's (487.13)	Luekemia's (2716.55)
Oral Cavity & Pharynx (239.20)	Oral Cavity & Pharynx (1465.49)
Esophagus (200.12)	Esophagus (1425.53)
Middle Ear, Nasal, and Larynx (129.62)	Middle Ear, Nasal, and Larynx (138.30)

Tables 5.5a and 5.5b present the leading cause of disease in descending order, separately for males and females by age distribution. Absolute quantities of DALY estimates were provided in Tables 5.3a through 5.3f for reference.

The rankings of the disease burden from all cancer sites during younger age groups (0-29) demonstrate inconsistent patterns between males and females in Toronto and S.W.O regions, again reflecting the small disease burden during youth. Among individuals aged 30-44 years, males and females in S.W.O experience identically ranked disease burdens from the six cancer sites; Toronto generates different relative rankings among this age group, however the three sites with the largest burdens are consistent with both S.W.O, and the age and sex aggregated ranks

(Table 5.4). Relative rankings in Toronto and S.W.O during the ages 45-59 are also consistent with age and sex aggregated BoD rankings (Table 5.4), with the exception of middle ear, nasal, and larynx cancers among males. During the oldest age groups when cancer is most prominent, individuals aged 60-69 and 70-79 consistently rank lung, bronchus, and trachea cancers; lymphomas and multiple myeloma; and leukemia's as the leading cause of morbidity and mortality in both regions. Similarly in the oldest age group (80+), individuals experience the largest health impacts from the aforementioned cancers with a reversal of the 2nd and 3rd rankings of lymphomas and leukemia's between the two regions.

Table 5.5a Ranking of Site-specific BoD in Toronto, sex and age disaggregated[1]

Age		Males	Females
0-4	1	Luekemias	Leukemia's
	2	Lung, Bronchus, Trachea	Lymphoma's
	3	Oral Cavity & Pharynx; Esophagus; Middle Ear, Nasal, & Larynx; Lymphomas	Oral Cavity & Pharynx; Esophagus; Middle Ear, Nasal, &Larynx; Lung, Bronchus, & Trachea
5-14	1	Leukemias	Leukemia's
	2	Lymphomas & Multiple Myelomas	Lymphoma's & Multiple Myelomas
	3	Lung, Bronchus, & Trachea	Oral Cavity & Pharynx
	4	Oral Cavity & Pharynx; Esophagus; Middle Ear, Nasal, & Larynx	Middle Ear, Nasal, & Larynx
	5		Esophagus; Lung, Bronchus, & Trachea
15-29	1	Leukemia's	Leukemia's
	2	Oral Cavity & Pharynx	Lymphoma's & Multiple Myeloma's
	3	Lymphomas & Multiple Myelomas	Lung, Bronchus & Trachea
	4	Lung, Bronchus, & Trachea	Oral Cavity & Pharynx
	5	Esophagus; Middle Ear, Nasal, & Larynx	Esophagus; Middle Ear, Nasal, & Larynx
30-44	1	Lymphoma's & Multiple Myeloma's	Lung, Bronchus, & Trachea
	2	Leukemia's	Leukemia's
	3	Lung, Bronchus, & Trachea	Lymphoma's & Multiple Myeloma's
	4	Oral Cavity & Pharynx	Esophagus
	5	Middle Ear, Nasal, & Larynx	Oral Cavity & Pharynx
	6	Esophagus	Middle Ear, Nasal, & Larynx
45-59	1	Lung, Bronchus & Trachea	Lung, Bronchus, & Trachea
	2	Lymphoma's & Multiple Myeloma's	Lymphoma's & Multiple Myeloma's
	3	Middle Ear, Nasal, & Larynx	Esophagus
	4	Leukemia's	Oral Cavity & Pharyx
	5	Oral Cavity & Pharynx	Leukemia's
	6	Esophagus	Middle Ear, Nasal, & Larynx
60-69	1	Lung, Bronchus, & Trachea	Lung, Bronchus, & Trachea
	2	Lymphoma's & Multiple Myeloma's	Lymphoma's & Multiple Myeloma
	3	Leukemia's	Leukemia's
	4	Middle Ear, Nasal, & Larynx	Esophagus
	5	Oral Cavity & Pharynx	Oral Cavity & Pharynx
	6	Esophagus	Middle Ear, Nasal, & Larynx
70-79	1	Lung, Bronchus, & Trachea	Lung, Bronchus, & Trachea
	2	Lymphoma's & Multiple Myeloma	Lymphomas & Multiple Myeloma
	3	Leukemias	Luekemias
	4	Esophagus	Esophagus
	5	Middle Ear, Nasal, & Larynx	Oral Cavity & Pharynx
	6	Oral Cavity & Pharynx	Middle Ear, Nasal, & Larynx
80+	1	Lung, Bronchus, & Trachea	Lung, Bronchus, & Trachea
	2	Lymphomas & Multiple Myeloma	Lymphoma's & Multiple Myeloma
	3	Leukemia's	Leukemia's
	4	Oral Cavity & Pharynx	Esophagus
	5	Esophagus	Oral Cavity & Pharynx
	6	Middle Ear, Nasal, & Larynx	Middle Ear, Nasal, & Larynx

1 Absolute quantities can be found in Tables 5.3a through 5.3f

Table 5.5b Ranking of Site-specific BoD in S.W.O, sex and age disaggregated[1]

Age		Males	Females
0-4	1	Luekemias	Lung, Bronchus, & Trachea
	2	Oral Cavity & Pharynx; Esophagus; Middle Ear, Nasal & Larynx; Lung, Bronchus, & Trachea; Lymphoma's & Multiple Myeloma	Oral Cavity & Pharynx; Esophagus; Middle Ear, Nasal, & Larynx; Lymphomas & Multiple Myeloma; Leukemia's
5-14	1	Leukemia's	Leukemia's
	2	Lymphomas & Multiple Myeloma	Lymphoma's & Multiple Myeloma
	3	Oral Cavity & Pharynx; Esophagus; Middle Ear, Nasal, & Larynx; Lung, Bronchus & Trachea	Oral Cavity & Pharynx; Esophagus; Middle Ear, Nasal & Larynx; Lung, Bronchus & Trachea
15-29	1	Leukemia's	Lung, Bronchus, & Trachea
	2	Lymphoma's	Middle Ear, Nasal, & Larynx
	3	Lung, Bronchus, & Trachea	Oral Cavity & Pharynx
	4	Oral Cavity & Pharynx	Lymphomas
	5	Esophagus; Middle Ear, Nasal & Larynx	Leukemia's; Esophagus
30-44	1	Lung, Bronchus, & Trachea	Lung, Bronchus & Trachea
	2	Leukemia's	Leukemia's
	3	Lymphoma's	Lymphoma's
	4	Oral Cavity & Pharynx	Oral Cavity & Pharynx
	5	Middle Ear, Nasal, & Larynx	Middle Ear, Nasal, & Larynx
	6	Esophagus	Esophagus
45-59	1	Lung, Bronchus, & Trachea	Lung, Bronchus, & Trachea
	2	Lymphoma's	Lymphoma's
	3	Middle Ear, Nasal, & Larynx	Leukemia's
	4	Leukemia's	Oral Cavity & Pharynx
	5	Oral Cavity & Pharynx	Esophagus
	6	Esophagus	Middle Ear, Nasal, & Larynx
60-69	1	Lung, Bronchus, & Trachea	Lung, Bronchus, & Trachea
	2	Lymphoma's	Leukemia's
	3	Middle Ear, Nasal, & Larynx	Oral Cavity & Pharynx
	4	Esophagus	Lymphoma's
	5	Oral Cavity & Pharynx	Esophagus
	6	Leukemia's	Middle Ear, Nasal, & Larynx
70-79	1	Lung, Bronchus, & Trachea	Lung, Bronchus, & Trachea
	2	Lymphoma's	Lymphoma's
	3	Leukemia's	Leukemia's
	4	Middle Ear, Nasal, & Larynx	Esophagus
	5	Esophagus	Oral Cavity & Pharynx
	6	Oral Cavity & Pharynx	Middle Ear, Nasal, & Larynx
80+	1	Lung, Bronchus, & Trachea	Lung, Bronchus, & Trachea
	2	Leukemia's	Lymphoma's
	3	Lymphoma's	Leukemia's
	4	Oral Cavity & Pharynx	Esophagus
	5	Esophagus	Oral Cavity & Pharynx
	6	Middle Ear, Nasal, & Larynx	Middle Ear, Nasal, & Larynx

1 Absolute quantities can be found in Tables 5.3a through 5.3f

5.1.3. Sensitivity Analysis

The impacts of incorporating social value choices in the DALY model (age weighting K=1, and discounting r=0.03) on site-specific disease burden rankings, and absolute estimates of DALY's was examined through sensitivity analysis. Tables 5.6a and 5.6b present the disease ranks in S.W.O and Toronto regions assuming four alternative value choice scenarios: (i) without age weighting or discounting, (ii) with age weights, no discount rate, (iii) discounting, no age weights, and (iv) both age weighting and discounting.

Results in S.W.O demonstrate no difference on the relative order of health impacts from site-specific cancers when alternative value assumptions are included in the analysis. In Toronto, the age-weight reverses the relative importance of health impacts from esophagus and oral cancers, between fourth and fifth ranks when a discount rate is not applied to counter balance the impact; however, the three leading causes of DALY's remain unchanged.

Table 5.6a BoD Rankings in S.W.O with Alternative Value Choices, age-weights and discount rate

K=0, r=0	K=1, r=0	K=0, r=0.03	K=1, r=0.03
Lung, Bronchus, & Trachea (6678.94)	Lung, Bronchus, & Trachea (4192.25)	Lung, Bronchus, & Trachea (5193.91)	Lung, Bronchus & Trachea (3391.65)
Lymphomas & Multiple Myeloma (1119.35)	Lymphomas & Multiple Myeloma (716.02)	Lymphomas & Multiple Myeloma (872.44)	Lymphomas & Multiple Myeloma (571.09)
Leukemia's (934.42)	Leukemia's (666.90)	Leukemia's (674.45)	Leukemia's (487.13)
Oral Cavity & Pharynx (438.13)	Oral Cavity & Pharynx (308.55)	Oral Cavity & Pharynx (326.27)	Oral Cavity & Pharynx (239.20)
Esophagus (411.24)	Esophagus (248.67)	Esophagus (321.02)	Esophagus (200.12)
Middle Ear, Nasal, & Larynx (227.71)	Middle Ear, Nasal, & Larynx (156.16)	Middle Ear, Nasal, & arynx (173.93)	Middle Ear, Nasal, & Larynx (129.62)

Table 5.6b BoD Rankings in Toronto with Alternative Value Choices, age-weights and discount rate

K=0, r=0	K=1, r=0	K=0, r=0.03	K=1, r=0.03
Lung, Bronchus, & Trachea (31166.05)	Lung, Bronchus, & Trachea (19857.16)	Lung, Bronchus, & Trachea (24060.50)	Lung, Bronchus, & Trachea (15952.41)
Lymphomas & Multiple Myeloma (9443.16)	Lymphomas & Multiple Myeloma (6376.62)	Lymphomas & Multiple Myeloma (7132.76)	Lymphomas & Multiple Myeloma (4915.12)
Leukemia's (5180.09)	Leukemia's (3797.91)	Leukemia's (3683.44)	Leukemia's (2716.55)
Esophagus (2868.95)	Oral Cavity & Pharynx (1909.45)	Esophagus (2123.10)	Oral Cavity & Pharynx (1465.49)
Oral Cavity & Pharynx (2802.42)	Esophagus (1865.71)	Oral Cavity & Pharynx (2103.67)	Esophagus (1425.53)
Middle Ear, Nasal, & Larynx (261.13)	Middle Ear, Nasal, & Larynx (159.69)	Middle Ear, Nasal, & Larynx (211.17)	Middle Ear, Nasal, & Larynx (138.30)

A graphical display of impacts associated with age-weighting and discounting on DALY estimates throughout the life cycle are provided for S.W.O and Toronto in Figures 5.7a through 5.12b. The charts illustrate the estimates of DALY's calculated as rates per population of 100,000. Absolute estimates are found in Appendix I for reference.

Results clearly demonstrate the application of age weights has a greater impact on DALY estimates compared to the time preference of a positive discount rate of three percent. Age weights produce DALY estimates giving greater weight to disease during young adulthood (ages 5-14 and 15-29) and less weight to disease in the youngest and oldest ages (0-4, 30-44, 45-59, 60-69, 70-79, 80+), without consideration of discounting.

Figure 5.7a

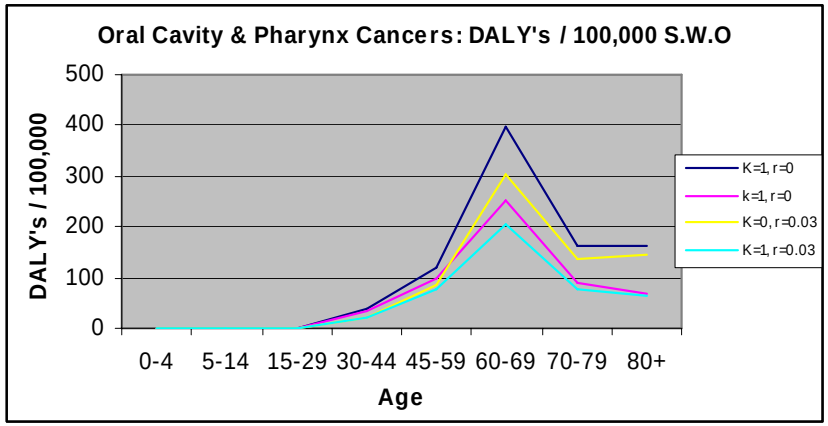


Figure 5.7b

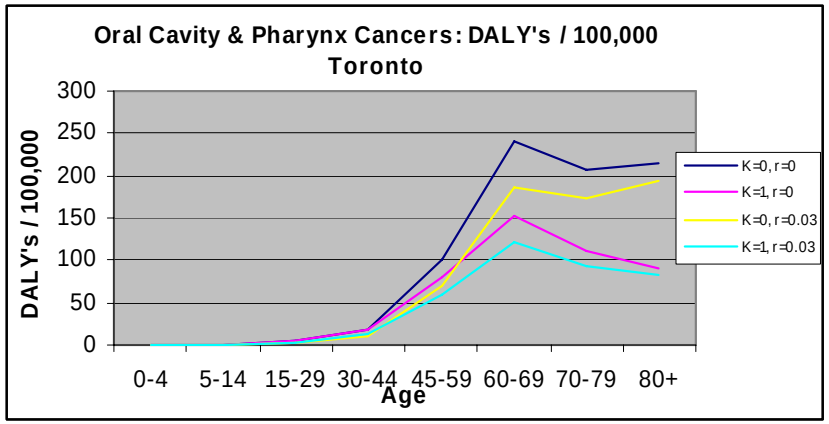


Figure 5.8a

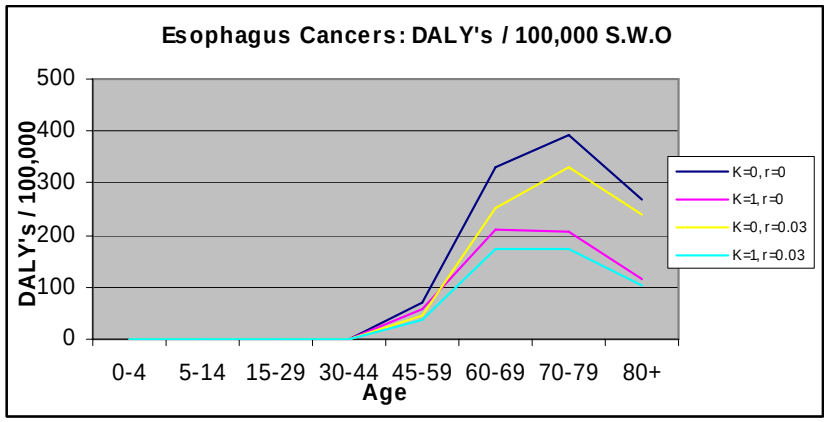


Figure 5.8b

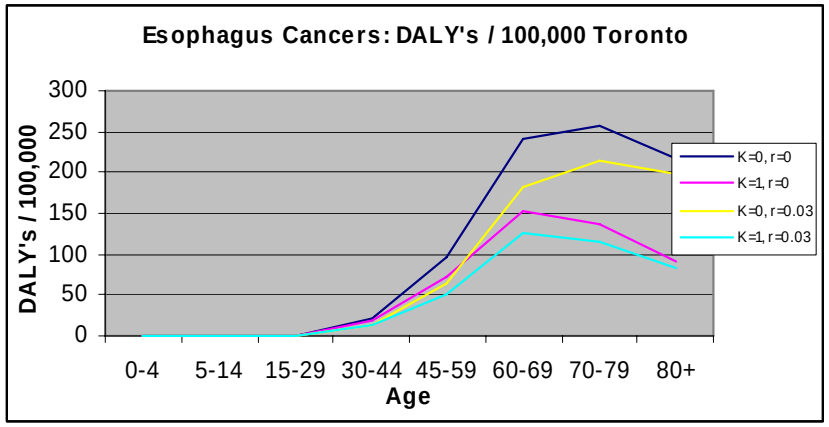


Figure 5.9a

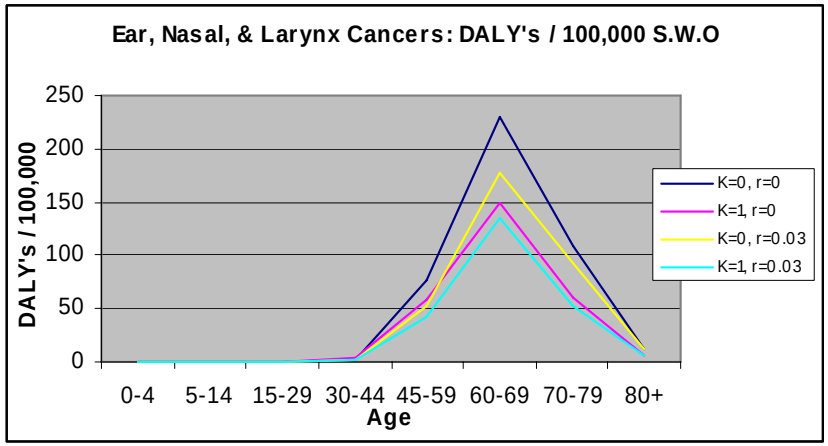


Figure 5.9b

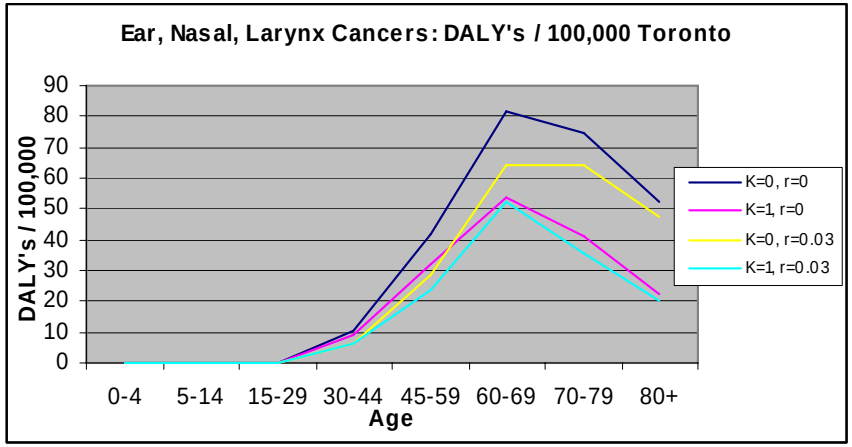


Figure 5.10a

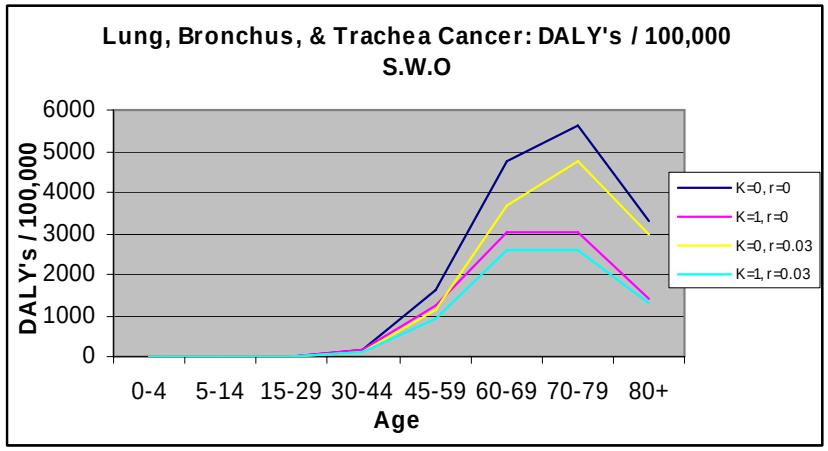


Figure 5.10b

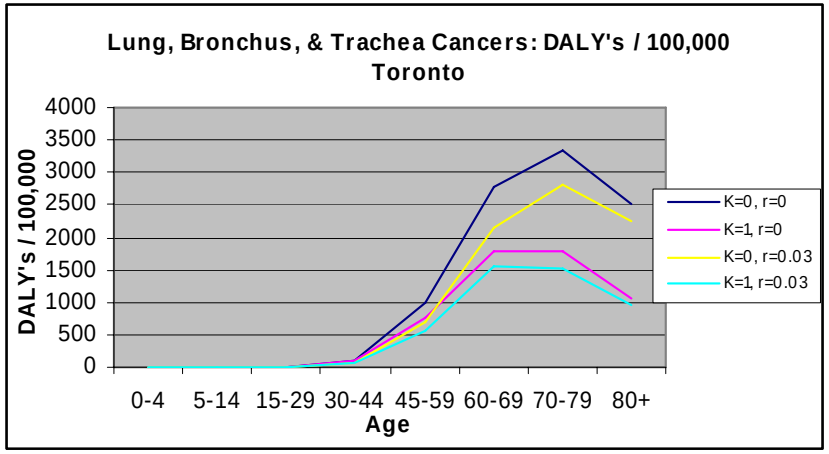


Figure 5.11a

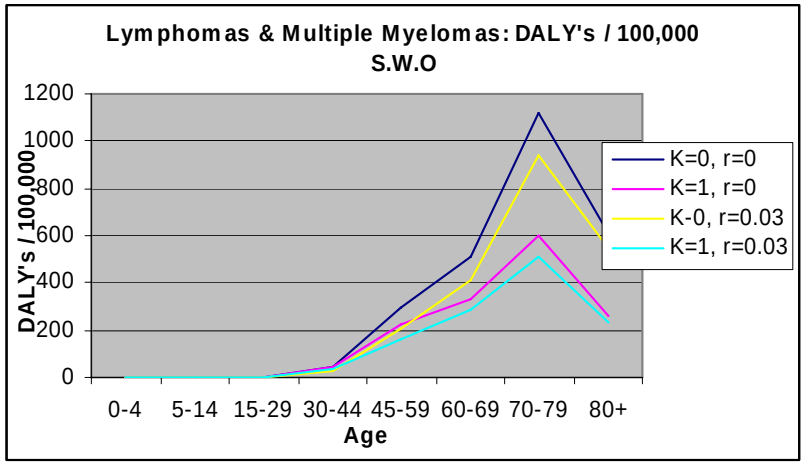


Figure 5.11b

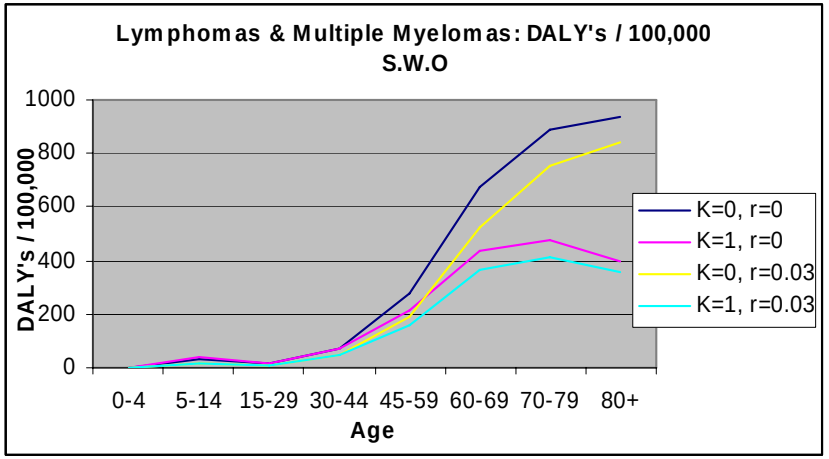


Figure 5.12a

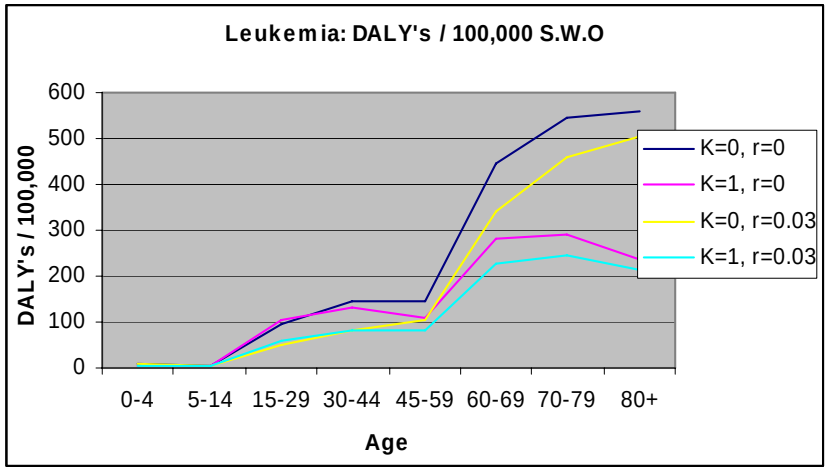
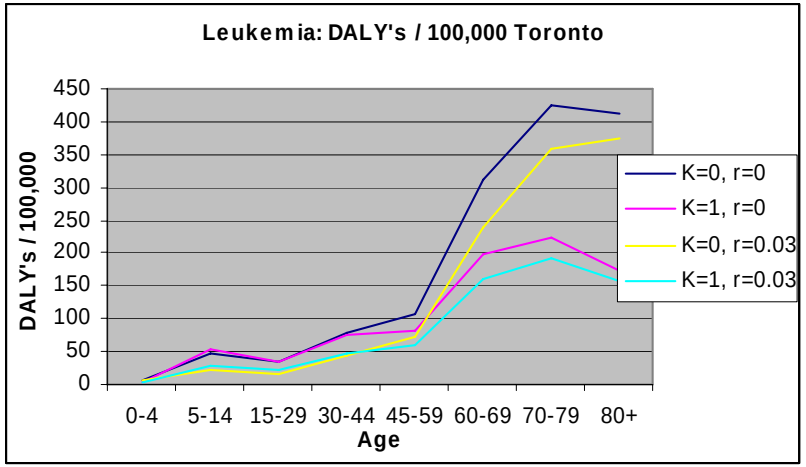


Figure 5.12b



5.2. Phase Two Results: Exposure Attributable Health Impacts

Results of the attributable BoD model are presented as crude estimates of the cancer burden in Toronto and S.W.O attributable to chronic inhalation exposure to current (section 5.2.1) and alternative reduced concentrations (section 5.2.2) of acetaldehyde, formaldehyde, benzene, 1,3-butadiene, ethylene oxide, and nickel refinery dusts. Sensitivity analysis of the attributable BoD results with alternative DALY value choices (age weighting and discounting) on the relative importance of current and alternative ambient exposures to the total BoD is presented in sub-sections 5.2.1.3 and 5.2.2.2.

Results are presented as crude estimates of the exposure attributable BoD separately for males and females without stratifying by age, since risk was assumed constant through life. The exposure attributable BoD tables and discussion are again presented with the application of age weighting and a 3% discount rate, unless otherwise noted.

5.2.1. Exposure Attributable Disease Burden (Current Concentrations)

The disease burden attributable to exposure to current environmental concentrations of acetaldehyde, formaldehyde, benzene, 1,3-BD, ETO, and nickel refinery dusts in Toronto and S.W.O was quantified in terms of DALY's by means of attributable fractions (A.F) (Equation 9). The attributable fractions listed in Table 5.7 were derived as estimates of the proportion of disease attributable to current long term annual mean ambient concentrations in Toronto and S.W.O, on the basis of I.U.R potency estimates derived from Health Canada risk evaluations.

Table 5.7 Attributable fraction of DALY's for related Cancers associated with current concentrations (annual ambient mean ug/m3) of each of the air toxics

	Substance					
Region	**Acetaldehyde**	**Formaldehyde**	**Benzene**	**1,3-BD**	**ETO**	**Nickel (dusts)**
Toronto						
Males	1.49E-03	2.24E-02	6.28E-03	1.51E-03	1.72E-03	2.28E-03
Females	1.40E-03	2.11E-02	5.90E-03	1.42E-03	1.61E-03	2.14E-03
S.W.O						
Males	1.78E-03	1.80E-02	5.88E-03	2.59E-03	5.09E-03	2.60E-03
Females	1.68E-03	1.69E-02	5.53E-03	2.43E-03	4.79E-03	2.44E-03

As males have a lower life expectancy then females (Appendix D) but assumed exposed to the same ubiquitous concentrations of air toxics, the fraction of disease attributable to each exposure is constantly higher among males then females within each of the regions. Between the two regions, S.W.O has larger A.F's for disease associated with current exposure to four of the air toxics: acetaldehyde, 1,3-BD, ETO and nickel refinery dusts; whereas Toronto has larger A.F's for males and females from exposure to formaldehyde and benzene, reflecting the predominant toxics concentrations in the regions (Table 4.4). The largest discrepancy in the A.F's between Toronto and S.W.O results from exposure to ETO, reflecting the difference in the environmental concentration (ug/m^3) between the regions. The toxic with the largest A.F for cancer (formaldehyde) reflects its elevated concentration in both S.W.O and Toronto (Table 4.4), and the toxic with the lowest attributable fraction (acetaldehyde), reflects a lower potency value and classification of a *possible* rather then *probable or known* human carcinogen.

5.2.1.1. Absolute Estimates of the Exposure Attributable BoD

Absolute estimates of the BoD attributable to current environmental concentrations of acetaldehyde, formaldehyde, benzene, 1,3-BD, ETO, and nickel refinery dusts in Toronto and S.W.O regions are presented in Tables 5.8a (total) and 5.8b (standardized), on the basis of site-specific cancer associations as determined through literature review (Table 3.1)

Overall, current exposures to the six carcinogenic air toxics in Toronto and S.W.O are responsible for 0.58%[12] of the total BoD from the six cancer endpoints. Consistent with a greater total DALY BoD in S.W.O (Phase 1) the exposure attributable BoD in S.W.O (5.60 DALY's) is again nearly double that in Toronto (3.30 DALY's) when calculated as a rate per 100,000 persons. The exposure attributable BoD was also slightly greater among males then females in both Toronto (5.91 DALY's vs. 5.30 DALY's) and S.W.O (3.48 DALY's vs. 3.18 DALY's) per 100,000 persons.

Table 5.8a Estimates of the Exposure Attributable BoD: Absolute DALY Estimates in S.W.O and Toronto, disaggregated by sex

		S.W.O			*Toronto*		
Substance	**Site-specific Cancers**	**Males**	**Females**	**Total**	**Males**	**Females**	**Total**
Acetaldehyde	Oral Cavity & Pharynx	0.161	0.249	0.411	0.797	1.299	2.096
	Esophagus	0.106	0.236	0.342	0.544	1.481	2.025
	Ear, Nasal, & Larynx	0.202	0.028	0.230	0.772	0.086	0.857
	Total	*0.470*	*0.513*	*0.982*	*2.113*	*2.866*	*4.979*
Formaldehyde	Oral Cavity & Pharynx	1.629	2.517	4.416	12.024	19.582	31.606
	Ear, Nasal, & Larynx	2.036	0.280	2.316	11.633	1.294	12.927
	Total	*3.665*	*2.797*	*6.642*	*23.657*	*20.876*	*44.532*
Benzene	Lymphomas & Multiple Myeloma	1.357	1.882	3.239	13.651	16.188	29.839
	Leukemia's	1.315	1.457	2.772	6.979	9.479	16.458
	Total	*2.672*	*3.339*	*6.011*	*20.630*	*25.667*	*46.297*
1,3-Butadiene	Lymphoma's & Multiple Myeloma	0.596	0.827	1.424	3.276	3.885	7.161
	Leukemia's	0.578	0.641	1.219	1.657	2.275	3.950
	Total	*1.174*	*1.468*	*2.642*	*4.951*	*6.160*	*11.111*
Ethylene Oxide	Lymphoma's & Multiple Myeloma	1.175	1.629	2.804	3.731	4.425	8.156
	Leukemia's	1.138	1.262	2.400	1.908	2.591	4.498
	Total	*2.313*	*2.891*	*5.204*	*5.639*	*7.015*	*12.654*
Nickel (dusts)	Lung, Bronchus, & Trachea	4.952	3.621	8.573	21.528	13.884	35.412
	Ear, Nasal, Larynx	0.294	0.040	0.334	11.810	0.131	1.312
	Total	*5.246*	*3.661*	*8.907*	*22.708*	*14.016*	*36.724*

[12] Attributable percent calculated as follows: total exposure attributable DALY's / total baseline DALY's X 100% (ie: 187 DALY's / 32,074 DALY's X 100% = 0.58% of disease is attributable to current exposures)

Table 5.8b Estimates of the Exposure Attributable BoD: DALY's / 100,000 persons in S.W.O and Toronto, disaggregated by sex

		S.W.O			*Toronto*		
Substance	**Site-specific Cancers**	**Males**	**Females**	**Total**	**Males**	**Females**	**Total**
Acetaldehyde	Oral Cavity & Pharynx	0.061	0.090	0.076	0.035	0.054	0.045
	Esophagus	0.040	0.085	0.063	0.024	0.061	0.043
	Ear, Nasal, & Larynx	0.077	0.010	0.043	0.034	0.004	0.018
	Total	0.179	0.185	0.182	0.092	0.119	0.106
Formaldehyde	Oral Cavity & Pharynx	0.620	0.910	0.768	0.524	0.812	0.672
	Ear, Nasal, & Larynx	0.775	0.101	0.429	0.507	0.054	0.275
	Total	1.395	1.011	1.198	1.031	0.865	0.946
Benzene	Lymphomas & Multiple Myeloma	0.516	0.680	0.600	0.595	0.671	0.634
	Leukemia's	0.500	0.527	0.514	0.304	0.393	0.350
	Total	1.017	1.207	1.114	0.899	1.064	0.984
1,3-Butadiene	Lymphoma's & Multiple Myeloma	0.227	0.299	0.264	0.143	0.161	0.152
	Leukemia's	0.220	0.231	0.226	0.073	0.094	0.084
	Total	0.447	0.530	0.490	0.216	0.255	0.236
Ethylene Oxide	Lymphoma's & Multiple Myeloma	0.447	0.589	0.520	0.063	0.183	0.173
	Leukemia's	0.433	0.456	0.445	0.083	0.107	0.096
	Total	0.880	1.045	0.964	0.246	0.291	0.269
Nickel (dusts)	Lung, Bronchus, & Trachea	1.884	1.308	1.589	0.939	0.575	0.752
	Ear, Nasal, Larynx	0.112	0.015	0.062	0.051	0.005	0.028
	Total	1.996	1.323	1.651	0.990	0.58	0.780

5.2.1.2. Rankings of the Exposure Attributable BoD

The rank order of relative importance of the six carcinogenic air toxics contributions to the total BoD is presented in descending order in Table 5.9 disaggregated by sex, to inform public health policy regarding the exposures of highest priority for reduction on the basis of the magnitude of associated health impacts. Absolute estimates of exposure attributable DALY's can be found in Tables 5.8a for reference.

Table 5.9 Rank ordering of the importance of the six ambient air toxics to the BoD in Toronto and S.W.O on the basis of associated health impacts, disaggregated by sex

S.W.O			**Toronto**		
Males	Females	Total	Males	Females	Total
Nickel	Nickel	Nickel	Formaldehyde	Benzene	Benzene
Formaldehyde	Benzene	Formaldehyde	Nickel	Formaldehyde	Formaldehyde
Benzene	Ethylene Oxide	Benzene	Benzene	Nickel	Nickel
Ethylene Oxide	Formaldehyde	Ethylene Oxide	Ethylene Oxide	Ethylene Oxide	Ethylene Oxide
1,3-Butadiene	1,3-Butadiene	1,3-Butadiene	1,3-Butadiene	1,3-Butadiene	1,3-Butadiene
Acetaldehyde	Acetaldehyde	Acetaldehyde	Acetaldehyde	Acetaldehyde	Acetaldehyde

In S.W.O results indicate that the current environmental concentration of nickel refinery dust is clearly the priority for reduction among both males and females, on the basis of the current *total* attributable health impacts, 8.91 DALY's. In Toronto, the foremost air toxic of priority for exposure reduction is less evident with inconsistency between males and females, and relatively similar contributions to the total BoD from ambient concentrations of benzene (46.30 DALY's) and formaldehyde (44.53 DALY's). In both regions, the top three priorities for exposure reduction are formaldehyde, benzene, and nickel refinery dusts; whereas current concentrations of ETO, 1,3-BD, and acetaldehyde appear of lesser public health concern, with minor inconsistencies in rank orders between the sexes.

5.2.1.3. Sensitivity Analysis

As presented in Table 5.10a and 5.10b, the rank order of air toxics for priority reduction, based on the BoD attributable to current environmental concentrations, is relatively insensitive to the impact of incorporating alternative value choices (age-weight or discount rate) in the DALY estimates. The only exception is a reversed order of importance of benzene and formaldehyde in S.W.O between the 2nd and 3rd rank priority for exposure reduction, pending the application of age weights. Tables 5.10a and 5.10b present the ranks of air toxics ranks in descending order of health impacts in S.W.O and Toronto, with total attributable DALY's presented for reference in parenthesis.

Table 5.10a Ranking of Exposure Attributable Health Impacts under Alternative Value Choices (age-weights and discount rate) in S.W.O

K=0, r=0	K=1, r=0	K=0, r=0.03	K=1, r=0.03
Nickel (17.44)	Nickel (10.98)	Nickel (13.57)	Nickel (8.91)
Benzene (11.65)	Formaldehyde (8.12)	Benzene (8.78)	Formaldehyde (6.46)
Formaldehyde (11.64)	Benzene (7.85)	Formaldehyde (8.76)	Benzene (6.01)
Ethylene Oxide (10.08)	Ethylene Oxide (6.80)	Ethylene Oxide (7.60)	Ethylene Oxide (5.20)
1,3-Butadiene (5.12)	1,3-Butadiene (3.45)	1,3-Butadiene (3.86)	1,3-Butadiene (2.64)
Acetaldehyde (1.86)	Acetaldehyde (1.23)	Acetaldehyde (1.42)	Acetaldehyde (0.98)

Table 5.10b Ranking of Exposure Attributable Health Impacts under Alternative Value Choices (age-weights and discount rate) in Toronto

K=0, r=0	K=1, r=0	K=0, r=0.03	K=1, r=0.03
Benzene (88.56)	Benzene (61.66)	Benzene (65.56)	Benzene (46.30)
Formaldehyde (83.20)	Formaldehyde (57.18)	Formaldehyde (62.53)	Formaldehyde (44.53)
Nickel (71.39)	Nickel (45.65)	Nickel (55.10)	Nickel (36.72)
Ethylene Oxide (24.21)	Ethylene Oxide (16.85)	Ethylene Oxide (17.92)	Ethylene Oxide (12.65)
1,3-Butadiene (21.26)	1,3-Butadiene (14.80)	1,3-Butadiene (15.74)	1,3-Butadiene (11.11)
Acetaldehyde (9.59)	Acetaldehyde (6.44)	Acetaldehyde (7.16)	Acetaldehyde (4.98)

5.2.2. Counterfactual Scenarios:

Hypothetical exposure scenarios of the six carcinogenic air toxics were modeled for concentrations associated with plausible and feasible minimum risk levels to predict the magnitude of the BoD that could be avoided in the future if present ambient concentrations are reduced, fitting with the relevant latency time lag between the exposure and the cancer.

Attributable fractions associated with feasible and plausible minimum risk concentrations of the six carcinogenic air toxics are presented in tables 5.11a and 5.11b for males and females,

based on alternative chronic exposure concentrations determined through literature review (Tables 4.5a,b) and risk potency values as derived from Health Canada risk evaluations.

Table 5.11a Attributable fraction of DALY's for related Cancers, associated with a feasible minimum risk concentration of each air toxic

	Substance					
	Acetaldehyde	**Formaldehyde**	**Benzene**	**1,3-BD**	**ETO**	**Nickel (dusts)**
Males	7.44E-04	8.43E-03	2.69E-03	7.54E-04	8.44E-04	1.60E-03
Females	6.99E-04	7.92E-03	2.53E-03	7.08E-04	7.93E-04	1.51E-03

Table 5.11b Attributable fraction of DALY's for related Cancers, associated with a plausible minimum risk concentration of each air toxic

	Substance					
	Acetaldehyde	**Formaldehyde**	**Benzene**	**1,3-BD**	**ETO**	**Nickel (dusts)**
Males	3.80E-04	5.13E-03	1.77E-03	3.77E-04	1.80E-04	3.21E-04
Females	3.57E-04	4.82E-03	1.67E-03	3.54E-04	1.70E-04	3.01E-04

As the alternative ambient concentrations for the plausible and feasible exposure distributions were the same (ug/m^3) for the Toronto and S.W.O regions, the A.F's for site-specific disease for males and females were also the same for the two regions.

5.2.2.1. Estimates of the Avoidable Disease Burden

The attributable BoD (DALY's / 100,000 persons) from the six cancer sites, associated with alternative reduced ambient concentrations of each of the six air toxics, are presented in Tables 5.12a,b (feasible minimum risk concentrations) and 5.13a,b (plausible minimum risk concentrations) for males and females in Toronto and S.W.O. Tables 5.12 and 5.13 also summarize the percent reduction in the current *attributable* disease burden if current concentrations were reduced to the counterfactual levels.

Table 5.12a Attributable BoD / 100,000 Persons in S.W.O, assuming concentrations associated with feasible minimum risk distributions

Substance	Site-specific Cancers	Males	Females	Total	Reduction	% Reduce
Acetaldehyde	Oral Cavity & Pharynx	0.026	0.038	0.032	0.044	
	Esophagus	0.017	0.035	0.026	0.037	
	Ear, Nasal, & Larynx	0.032	0.004	0.018	0.025	
	Total	0.074	0.077	0.076	0.106	58.33
Formaldehyde	Oral Cavity & Pharynx	0.290	0.426	0.360	0.409	
	Ear, Nasal, & Larynx	0.363	0.047	0.201	0.228	
	Total	0.653	0.473	0.560	0.637	53.21
Benzene	Lymphomas & Multiple Myeloma	0.236	0.311	0.275	0.326	
	Leukemia's	0.229	0.241	0.235	0.279	
	Total	0.465	0.552	0.510	0.604	54.23
1,3-Butadiene	Lymphoma's & Multiple Myeloma	0.066	0.087	0.077	0.187	
	Leukemia's	0.064	0.067	0.066	0.160	
	Total	0.130	0.155	0.143	0.347	70.85
Ethylene Oxide	Lymphoma's & Multiple Myeloma	0.074	0.098	0.086	0.434	
	Leukemia's	0.072	0.076	0.074	0.371	
	Total	0.146	0.173	0.160	0.805	83.43
Nickel (dusts)	Lung, Bronchus, & Trachea	1.163	0.808	0.981	0.608	
	Ear, Nasal, Larynx	0.069	0.009	0.038	0.024	
	Total	1.232	0.817	1.019	0.632	38.27

Table 5.12b Attributable BoD / 100,000 Persons in Toronto assuming concentrations of air toxics associated with a feasible minimum risk distribution

Substance	Site-specific Cancers	Males	Females	Total	Reduction	% Reduce
Acetaldehyde	Oral Cavity & Pharynx	0.017	0.027	0.022	0.022	
	Esophagus	0.012	0.031	0.022	0.022	
	Ear, Nasal, & Larynx	0.017	0.002	0.009	0.009	
	Total	0.046	0.060	0.053	0.053	49.95
Formaldehyde	Oral Cavity & Pharynx	0.197	0.305	0.252	0.419	
	Ear, Nasal, & Larynx	0.191	0.020	0.103	0.171	
	Total	0.388	0.325	0.356	0.591	62.42
Benzene	Lymphomas & Multiple Myeloma	0.255	0.288	0.272	0.362	
	Leukemia's	0.130	0.168	0.150	0.200	
	Total	0.385	0.456	0.422	0.562	57.14
1,3-Butadiene	Lymphoma's & Multiple Myeloma	0.071	0.081	0.076	0.076	
	Leukemia's	0.037	0.047	0.042	0.042	
	Total	0.108	0.128	0.118	0.118	50.00
Ethylene Oxide	Lymphoma's & Multiple Myeloma	0.080	0.090	0.085	0.088	
	Leukemia's	0.041	0.053	0.047	0.049	
	Total	0.121	0.143	0.132	0.137	50.85
Nickel (dusts)	Lung, Bronchus, & Trachea	0.661	0.405	0.530	0.223	
	Ear, Nasal, Larynx	0.036	0.004	0.020	0.008	
	Total	0.697	0.409	0.549	0.231	29.58

Table 5.13a Attributable BoD / 100,000 Persons in S.W.O, disaggregated by sex, assuming concentrations associated with a Plausible minimum risk distribution

Substance	Site-specific Cancers	Males	Females	Total	Reduction	% Reduce
Acetaldehyde	Oral Cavity & Pharynx	0.013	0.020	0.017	0.059	
	Esophagus	0.009	0.018	0.013	0.050	
	Ear, Nasal, & Larynx	0.016	0.002	0.009	0.033	
	Total	0.038	0.041	0.039	0.143	78.36
Formaldehyde	Oral Cavity & Pharynx	0.177	0.259	0.219	0.549	
	Ear, Nasal, & Larynx	0.211	0.029	0.122	0.307	
	Total	0.397	0.288	0.341	0.856	71.51
Benzene	Lymphomas & Multiple Myeloma	0.156	0.205	0.181	0.419	
	Leukemia's	0.151	0.159	0.155	0.359	
	Total	0.306	0.364	0.336	0.778	69.87
1,3-Butadiene	Lymphoma's & Multiple Myeloma	0.033	0.044	0.038	0.225	
	Leukemia's	0.032	0.034	0.033	0.193	
	Total	0.065	0.077	0.071	0.418	85.42
Ethylene Oxide	Lymphoma's & Multiple Myeloma	0.016	0.021	0.018	0.501	
	Leukemia's	0.015	0.016	0.016	0.429	
	Total	0.031	0.037	0.1034	0.930	96.46
Nickel (dusts)	Lung, Bronchus, & Trachea	0.233	0.162	1.96	1.393	
	Ear, Nasal, Larynx	0.014	0.002	0.008	0.054	
	Total	0.246	0.163	0.204	1.447	87.65

Table 5.13b Attributable BoD / 100,000 Persons in Toronto, disaggregated by sex, assuming concentrations of air toxics associated with a Plausible minimum risk distribution

Substance	Site-specific Cancers	Males	Females	Total	Reduction	% Reduce
Acetaldehyde	Oral Cavity & Pharynx	0.009	0.014	0.011	0.033	
	Esophagus	0.006	0.016	0.011	0.032	
	Ear, Nasal, & Larynx	0.009	0.001	0.005	0.014	
	Total	0.024	0.030	0.027	0.079	74.45
Formaldehyde	Oral Cavity & Pharynx	0.120	0.186	0.154	0.518	
	Ear, Nasal, & Larynx	0.116	0.012	0.063	0.212	
	Total	0.263	0.198	0.216	0.730	77.12
Benzene	Lymphomas & Multiple Myeloma	0.168	0.189	0.179	0.455	
	Leukemia's	0.086	0.118	0.102	0.247	
	Total	0.254	0.307	0.281	0.702	71.71
1,3-Butadiene	Lymphoma's & Multiple Myeloma	0.036	0.040	0.038	0.144	
	Leukemia's	0.018	0.024	0.021	0.063	
	Total	0.054	0.064	0.059	0.177	75.00
Ethylene Oxide	Lymphoma's & Multiple Myeloma	0.017	0.019	0.018	0.155	
	Leukemia's	0.009	0.011	0.010	0.086	
	Total	0.026	0.031	0.028	0.241	89.49
Nickel (dusts)	Lung, Bronchus, & Trachea	0.132	0.081	0.106	0.646	
	Ear, Nasal, Larynx	0.007	0.001	0.004	0.024	
	Total	0.139	0.082	0.110	0.670	85.92

If current concentrations of each of the six toxics were reduced to concentrations associated with a feasible minimum level of risk, results indicate a total of 3.13 DALY's per 100,000 persons in S.W.O, and 1.63 DALY's per 100,000 persons in Toronto could be avoided in the future, such that the exposure attributable BoD would be reduced to 0.28%[13] of the total burden.

Reducing ambient concentrations of ethylene oxide in S.W.O and formaldehyde in Toronto to feasible concentrations would predict the greatest reduction in the BoD from lymphohematopoeitic cancers S.W.O (0.81 DALY's per 100,000), and head and neck cancers in Toronto (0.59 DALY's / 100,000 persons). Ambient concentrations of nickel would be responsible for the largest BoD of all the exposures under a feasible distribution (1.02 DALY's per 100,000 persons in S.W.O and 0.55 DALY's per 100,000 persons in Toronto), associated with lung and respiratory cancers.

If ambient concentrations of the six air toxics were further reduced to a plausible level of risk (ie: if there were no anthropogenic releases of toxics into the environment), the model predicts a total of 4.57 DALY's per 100,000 persons in S.W.O and 2.60 DALY's per 100,000 persons in Toronto would be avoidable in the future, such that only 0.12% of the total BoD would be attributable to natural sources of air toxics in the ambient environment (a total reduction of 0.46%[14] from the BoD from current exposures). The greatest reduction in the exposure attributable BoD would occur by reducing the burden from lung and respiratory cancers associated with ambient nickel concentrations in S.W.O (1.45 DALY's / 100,000 persons) and head and neck cancers associated with ambient formaldehyde in Toronto (0.730 DALY's / 100,000 persons).

[13] 96 DALY's avoidable. Therefore: 96 DALY's / 32,074 DALY's X 100% = 0.30% of BoD avoidable.
[14] 147 DALY's avoidable. Therefore: 147 DALY's / 32,074 DALY's X 100% = 0.46% of the BoD is avoidable

Assuming plausible minimum risk concentrations of each of the air toxics, ambient exposure to formaldehyde in S.W.O (0.34 DALY's / 100,000 persons) and benzene in Toronto (0.28 DALY's / 100,000 persons) would be associated with the largest health impacts. The complete rank order of the relative importance of the six carcinogenic air toxics to the BoD, assuming the counterfactual distributions is reviewed in Table 5.14 with absolute estimates of the total attributable DALY's found in Tables 5.12 and 5.13 for reference

Table 5.14 Ranked order of the air toxics contributing to the disease burden in S.W.O and Toronto, assuming concentrations associated with feasible and plausible minimum risk levels

Feasible Minimum Risk		Plausible Minimum Risk	
SWO	Toronto	SWO	Toronto
Nickel	Nickel	Formaldehyde	Benzene
Formaldehyde	Benzene	Benzene	Formaldehyde
Benzene	Formaldehyde	Nickel	Nickel
Ethylene Oxide	Ethylene Oxide	1,3-Butadiene	1,3-Butadiene
1,3-Butadiene	1,3-Butadiene	Acetaldehyde	Ethylene Oxide
Acetaldehyde	Acetaldehyde	Ethylene Oxide	Acetaldehyde

6.2.2.2. Sensitivity Analysis with Counterfactual Exposures

If ambient concentrations of each of the six carcinogenic air toxics are independently reduced to concentrations associated with plausible or feasible minimum risk distributions, the incorporation of alternative value choices (age weights or time preference) has no impact on the relative order of exposures contributing the largest disease burden in each of the regions, as described in Tables 5.15a and 5.15b

Table 5.15a Ranking of the BoD under alternative value choices, assuming a feasible minimum risk concentration

Toronto			S.W.O		
K=0, r=0	K=1, r=0	K=0, r=0.03	K=0, r=0	K=1, r=0	K=0, r=0.03
Nickel (50.27)	Nickel (32.15)	Nickel (38.80)	Nickel (10.77)	Nickel (6.78)	Nickel (8.38)
Benzene (37.96)	Benzene (26.43)	Benzene (28.10)	Formaldehyde (5.45)	Formaldehyde (3.80)	Formaldehyde (4.10)
Formaldehyde (31.26)	Formaldehyde (21.49)	Formaldehyde (23.50)	Benzene (5.33)	Benzene (3.59)	Benzene (4.02)
Ethylene Oxide (11.90)	Ethylene Oxide (8.28)	Ethylene Oxide (8.81)	Ethylene Oxide (1.67)	Ethylene Oxide (1.13)	Ethylene Oxide (1.26)
1,3-Butadiene (10.63)	1,3-Butadiene (7.40)	1,3-Butadiene (7.87)	1,3-Butadiene (1.49)	1,3-Butadiene (1.00)	1,3-Butadiene (1.13)
Acetaldehyde (4.80)	Acetaldehyde (3.22)	Acetaldehyde (3.59)	Acetaldehyde (0.773)	Acetaldehyde (0.51)	Acetaldehyde (0.59)

Table 5.15b Ranking of the BoD under alternative value choices, assuming plausible minimum risk concentrations

Toronto			S.W.O		
K=0, r=0	K=1, r=0	K=0, r=0.03	K=0, r=0	K=1, r=0	K=0, r=0.03
Benzene (25.33)	Benzene (17.64)	Benzene (18.74)	Benzene (3.51)	Benzene (2.37)	Benzene (2.65)
Formaldehyde (19.04)	Formaldehyde (13.08)	Formaldehyde (14.31)	Formaldehyde (3.32)	Formaldehyde (2.23)	Formaldehyde (2.49)
Nickel (10.06)	Nickel (6.43)	Nickel (7.76)	Nickel (2.15)	Nickel (1.36)	Nickel (1.68)
1,3-Butadiene (5.31)	1,3-Butadiene (3.70)	1,3-Butadiene (3.93)	1,3-Butadiene (0.746)	1,3-Butadiene (0.50)	1,3-Butadiene (0.56)
Ethylene Oxide (2.54)	Ethylene Oxide (1.77)	Ethylene Oxide (1.88)	Acetaldehyde (0.402)	Acetaldehyde (0.27)	Acetaldehyde (0.31)
Acetaldehyde (2.45)	Acetaldehyde (1.65)	Acetaldehyde (1.83)	Ethylene Oxide (0.357)	Ethylene Oxide (0.24)	Ethylene Oxide (0.27)

6. DISCUSSION:

The burden of disease (BoD) model was specifically designed to enable systematic and comprehensive analysis of the environmentally attributable health impacts associated with long term inhalation exposure to six ambient air toxics in two highly exposed regions of Ontario. Methods and model templates were adapted from the World Health Organization (WHO), the National Risk Institute for Public Health and the Environment (RIVM), and Statistics Canada to meet the requirements of the novel and multidisciplinary assessment (Flanagan et al, 2005; Mathers et al, 1999; Mathers et al, 2001; DeZwart et al, 2006).

The model estimated the BoD attributable to carcinogenic hazardous air pollutants (HAP's) in two phases. The first phase quantified the total BoD in Toronto and S.W.O regions in terms of DALY's (disability-adjusted life years). DALY's are a time based measure enabling comparative evaluation of risk factors and disease burdens between regions, cancer sites, and ambient exposures. The second phase estimated the BoD specifically attributable to ambient exposures by multiplying site-specific DALY's (phase one) by attributable fractions in a counterfactual analysis. Explicitly comparing the DALY BoD between current and counterfactual HAP exposure scenarios can facilitate informed decision making and priority setting in Ontario concerning abatement of HAP emissions based on health benefits anticipated with reduced exposures.

Although the model has drawn upon the best available evidence, many simplifying assumptions have been required, such that the model should be regarded as a relative tool to evaluate exposure reduction priorities, rather then an absolute quantitative assessment of the exposure attributable BoD. The following sections of the discussion will review the validity of the model to accurately quantify and characterize both the total BoD and the exposure

attributable BoD, examine uncertainties, strengths and limitations of the model, and finally explore the policy implications of the results and future work.

6.1. Validity of the DALY Model (as a Robust Measure of the Burden of Disease)[15]

6.1.1. Overview of Phase One Results

In Toronto and S.W.O regions results revealed a total of 32,704 DALY's were lost from cancers of the head and neck (ICD9 codes 140-149; 150; 160-161), respiratory system (162-165), and lymphohematopoeitic system (200-203; 204-108) during the reference year 2001 (27,055 in Toronto and 5,019 in S.W.O). When analysis was standardized to a population of 100,000 persons, S.W.O experienced nearly double the BoD compared to Toronto. Years of life lost due to premature mortality dominated the years of life lived with disability, consistent with high case-fatality rates for many cancer sites, and greater uncertainty in the YLD estimates. In both the Toronto and S.W.O regions the leading causes of the BoD were from (i) lung, bronchus, and trachea cancers, followed by (ii) lymphomas and multiple myelomas, and (iii) leukemia's. Subgroup analysis revealed the disease burden associated with the six selected cancers to be rare prior to the age of 30 and dominant in individuals 60 years and older. The incorporation of alternative value choices (age weighting and discounting) had a negligible impact on the relative order of cancer sites to the BoD based on the magnitude of absolute DALY estimates.

To provide a useful measure of the BoD from the selected cancer endpoints within each of the regions, the DALY estimates must be internally consistent, that is reflect the epidemiological characteristics of disease (incidence, mortality, duration, severity), specific to each region. The following subsections will thus discuss the validity of the DALY in estimating

[15] Murray & Acharaya (1997) have argued DALY's as a robust measure of population health status "not terribly sensitive to many of the assumptions underlying them, and are based on clearly articulated and debateable ethical principles"

the BoD including the use of time as a metric for analysis, the disability weights for cancer severity, and the impacts of age weights and discounting future health on the DALY estimates, independent from the process of causal attribution of cancer to ambient exposures.

6.1.2. Time as the Unit of Analysis

The DALY uses time as the metric of analysis to incorporate data on years of life lost (premature mortality), years lived with disability, and average disease duration for survivors and non survivors, into a comparable time unit to provide an aggregate indicator of the BoD. The model quantified the BoD in the Toronto and S.W.O regions on the basis of site specific incidence and mortality estimates ascertained for the defined reference year 2001. With new diagnosis and fatal events modelled for the year 2001, the analysis was thus cross sectional in time, such that estimates of site specific incidence and mortality counts will show variability from year to year. Annual variation in disease estimates is especially likely as data was ascertained by age and sex grouping at the level of the municipality, producing relatively small, sometimes negligible cell counts for many sites. Particularly in S.W.O, with a population size approximately seven and a half times smaller then Toronto, absolute estimates of the BoD from head and neck cancers (ICD9 sites 140-149, 150, 160-161), which are rarer then cancers of the lung or lymphatic organs, will be dependent on the reference year for which estimates were analyzed. Although estimates of smaller disease burdens and populations will be more likely to vary between neighbouring years, it is unlikely variation from the choice of a reference year of analysis would dramatically affect the disease burden rankings.

However differences in the size and structure of the population over time from population aging, immigration, or emigration, could cause the DALY estimates (and possibly ranks) of the

BoD from site-specific cancers to vary over time, when cancer *counts* are modelled rather then age-standardized *rates*. The impacts of immigration would likely be less of a concern in S.W.O with a relatively homogeneous, 87% Canadian born population (Statistics Canada, 2007). However in Toronto with approximately 52% of residents born outside of Canada in 2001 (Statistics Canada, 2007), the impacts of migration on the BoD from cancer could be significant if new immigrants differ on genetic factors (ie: glutathione-s-transferase allelic subtype) or lifestyle factors (dietary) which could increase or decrease their underlying cancer susceptibility. Furthermore, rates of disease may be lower in Toronto then S.W.O as a result of the 'healthy immigrant effect', similar to the 'healthy worker effect', whereby individuals who migrate are more likely to be of better health status, then those who do not migrate, which could partially account for differences in disease patterns.

Finally with the BoD assessment cross-sectional in time, differences in epidemiological estimates of site-specific staging, severity, and duration with improvements in treatment therapies or earlier detection will influence the transferability of disease estimates as representative in the future. Incorporating disease estimates into DALY's for the defined reference year of 2001 thereby provides public health officials with a baseline for the purpose of future disease surveillance and comparison of epidemiological disease characteristics.

6.1.3. The Disability Weights:

The severity weighting for time lived with disability has been extensively debated in the literature on DALY's (Essink-Bot et al, 2002; Murray & Acharya, 1997; Anand & Hanson, 1997; Murray, 1994). Although the inclusion of an 'average' weight for cancer sites supports the egalitarian foundation of DALY's as a SMPH (Murray & Acharya, 1997), the weights fail to

consider the influence of the social environment, infrastructure, or the impact of co-existing health conditions on quality of life[16].

Regional variations in the distribution of social and environmental conditions have not only been found to influence the risk of developing cancer, but also the severity associated with its impact (CCS, 2006; Reidpath et al, 2003). A socially supportive environment may reduce the overall severity associated with disease by decreasing stress and pain during the treatment stage, in particular chemotherapy, enhance the overall response to treatment, and thus the cancer outcome (whether an individual will experience the metastasis and terminal stages). With individuals in lower SES more likely to have lower levels of social support, and also be exposed to a plethora of cancer risk factors, uniform disability weights for site specific severity across all social and cultural contexts may underestimate disability among disadvantaged and high risk subgroups.

The average disability weights for site specific cancers were derived in the model ranging between 0.085 and 0.396. Weights towards to the more 'mild' end of the severity scale for publicly dreaded diagnoses, with high case fatality rates, reflects the derivation of average weights, based on GBD stage associated severity. For all cancer sites, the stage specific disability weights associated with the diagnosis, therapy, and remission phases of disease are rated less then 0.2 on the severity scale, such that only the cases that eventually die of cancer (based on the 5-year RSR) were more heavily weighted by the 0.75 to 0.81 severity associated with the metastasis and terminal stages. Disability weights disaggregated by age and sex reflect lower five-year RSR's (or high case fatality rates) for cancers of the esophagus (ICD9 site 150) and

[16] Global Burden of Disease Disability Weights may thus be especially likely to underestimate the 'true' BoD, with disability rated lower compared to more individualistic or self-rated health scales such as the Health Utilities Index or QALY weighting scales

lung, bronchus, and trachea (ICD9 sites 162-165), and decreasing rates of survival from all cancers with increasing age.

Variations in the GBD disability weights on the 'mild' end of severity may have a larger impact on the BoD estimates then variation in weights towards the more 'severe' end of the scale because the lower the disability weights are, the more sensitive they are to variation (de Hollander et al, 1999; Melse et al, 2000). With disability weights generally derived less then 0.3, the relative impact of a 0.1 change in severity with the introduction of a new treatment or change in the case fatality rate may have a large impact on the BoD estimates, suggesting the weights provide an estimate of site specific severity most useful for comparison purposes rather then as stable epidemiological parameters.

Furthermore the disability weights failed to account for the impact of co-morbidity since adding disability weights for different diseases could in theory sum to more then one (death). As more then 60% of the total BoD (19,242.60 DALY's) was lost from cancers in persons 60 years and older, who are most likely to experience multiple chronic conditions, the *true* BoD may have been underestimated in the model. The number, type, and severity of co-morbid conditions could influence the selection of therapy and survival outcome of patients, since some types of co-morbidities could exacerbate the morbidity associated with aggressive chemotherapy or radiotherapy treatments (cardiac, renal), or compliance to therapeutic regimes (mental, psychiatric) (Yates, 2001).

6.1.4. Sensitivity of the DALY Estimates to Social Value Choices:

Sensitivity of the DALY estimates to a positive discount rate for future healthy life, and differential value of time lived throughout the lifecycle were examined through sensitivity

analysis. Consistent with extensive sensitivity analyses of the GBD estimates (Murray et al, 1994), results in S.W.O indicated the incorporation of alternative value choices [K=1, r=0] [K=0, r=0.03] [K=0, r=0], altered the absolute estimates of the BoD, but had no effect on the rank order or the share contribution of site specific cancers to the total BoD. Sensitivity analysis of the BoD estimates in Toronto also support the notion of the DALY as a robust measure of the BoD, relatively insensitive to the impacts of alternative social value choices, with changes in the absolute estimates but unaltered rank estimates with one exception. When DALY's in Toronto were estimated with age weights but no discount rate, the site specific rankings of esophageal and oral cavity cancers were reversed between fourth and fifth ranks reflecting similar share contributions (5-6%) of each cancer site to the total BoD under all value choice scenarios.

Contrasting two extreme approaches, the classic [K=0, r=0] and development economist [K=1, r=0.03], the application of unequal age weights and a 3% discount rate reduced the total BoD by approximately half, 51.2% in S.W.O and 51.5% in Toronto, of the BoD with equal age weights and no discounting for future health.

In general, the application of unequal age weights (K=1) placed greater emphasis on disease among young individuals in ages groups 0-4, 5-14, 15-29, and 30-44. In contrast, the application of a 3% discount rate exerts a counter effect, shifting the disease burden from the two youngest age groups (0-4, 5-14), to increase the share of the burden among the age groups 45 years and older. Since the disease burden from cancer is relatively rare in the youngest age groups, and the largest burden is concentrated in the oldest (60+ years), insensitivity of the DALY estimates to a time preference or age weights is not surprising. However, the sensitivity analysis does support the idea that the incorporation of age-weighting places a double BoD

among the elderly by shifting the disease burden away from later life, a population which naturally experiences a larger disease burden.

6.2. Validity of the Risk Model (in Causally Attributing the BoD to Ambient Exposures)

6.2.1. Overview of the Results

Of the total BoD from six cancer endpoints (32,074 DALY's), a total of 187 DALY's or 0.58% was attributable to inhalation exposure to current ambient concentrations of acetaldehyde, formaldehyde, benzene, 1,3-butadiene, ethylene oxide, and nickel refinery dusts in Toronto (156 DALY's) and S.W.O (30 DALY's), assuming each of the air toxics exerts independent and additive effects. When calculated as a rate per 100,000 persons, S.W.O was found to experience nearly double the exposure attributable BoD (5.6 DALY's) compared to Toronto (3.3 DALY's). In S.W.O, current environmental exposure to nickel refinery dusts, followed by formaldehyde, and benzene made the largest contributions to ill health of the six carcinogenic toxics. In Toronto, the largest health impacts resulted from current environmental exposure to benzene, followed by formaldehyde, then nickel refinery dusts. Current concentrations of ethylene oxide, 1,3-BD, and acetaldehyde appear to be of lesser public health concern based on the magnitude of their associated health impacts. Further subgroup analysis by gender suggested the relative impact of each of the air toxics to the total disease burden in each region varied among males and females.

The counterfactual analysis predicted that reducing long term concentrations of the six carcinogenic air toxics in the Toronto and S.W.O regions to lower levels that have been recorded in other regions (feasible minimum risk levels), would reduce the exposure attributable BoD in the future by 96 DALY's (17 DALY's in S.W.O and 79 DALY's in Toronto), fitting with the

relevant latency periods of the site-specific cancers. Feasible distributions of the six air toxics would thereby reduce the BoD attributable to ambient air toxics exposures to 0.28% of the total BoD. Although the rank order of exposures causing the largest health impacts would remain unchanged from the current rank order in S.W.O, the relative importance of nickel, benzene, and formaldehyde is reversed from the current order in Toronto.

If concentrations of the six air toxics were further reduced from current concentrations to concentrations expected if there were no anthropogenic releases of the air toxics (a plausible distribution), a total of 147 DALY's could be avoided, again fitting with the relevant latency period of the associated cancers (25 DALY's in S.W.O and 122 DALY's in Toronto). Independently mitigating release of each of the six air toxics from anthropogenic sources would predict that only 0.12% of the total BoD in Toronto and S.W.O would be attributable to natural sources of the air toxics in the environment. Under the plausible exposure distribution, environmental concentrations of benzene in Toronto and formaldehyde in S.W.O would be responsible for the largest BoD from cancer endpoints included in the model.

However as a result of both the nature of the disease and the risk factor, there are inherent difficulties in modelling the BoD from cancer attributable to long term cumulative air toxics exposures. The following subsections will discuss the attributable fraction calculations, the multicasual nature of cancer, the temporal dimension of the exposure-cancer relationship, and the impacts of aggregating small population health effects, as related to the validity of the model in predicting the BoD attributable to environmental exposures.

6.2.2. The Attributable Fractions:

The attributable fractions in the counterfactual analysis were calculated on the basis of a lifetime risk estimate, considering the ambient concentration (ug/m^3) and potency of each toxic, divided by the current Canadian life expectancy for males and females to derive an annual risk, which was thus assumed constant through each year of life.

Although analyses did not derive exposure attributable fractions by age subgroup, or assess the impacts of age weighting and discounting on the exposure attributable BoD through the lifecycle, the greater exposure attributable BoD in S.W.O may at least partially be a reflection of differences in the population age structure between the two regions, with 18% of the population 60 years or older in S.W.O compared to 15% in Toronto, and dominance of baseline DALY's among the elderly (phase 1).

As the exposure attributable BoD was derived by multiplying the baseline DALY's from phase one, by the attributable fractions relating exposure to disease, the exposure attributable BoD in each region represents both the magnitude of the attributable risk and the baseline prevalence of disease. For example in S.W.O, ambient nickel was the leading cause of the exposure attributable BoD, however as the attributable fraction of the current environmental concentration was ranked fourth highest, the impact of nickel to the BoD results from its association with the large baseline burden of lung cancer, approximately 68% of the total share of the disease burden in S.W.O (phase one).

Contrary to a situation with low attributable risk but high prevalence of disease, current exposure to ambient formaldehyde was associated with the highest attributable fractions for disease in Toronto and S.W.O, however a less prevalent form of cancer (head and neck), but was responsible for the second largest attributable BoD in both areas, thus demonstrating the

attributable BoD analysis requires assessment of both the baseline prevalence of disease and the magnitude of associated risk.

Evidently describing the BoD to ambient exposures is more ambiguous then many other risk factor-disease relationships in public health (Doll & Peto, 1981), requiring consideration of many complexities when modelling the exposure attributable BoD, as discussed further in the next section.

6.2.3. Multicausality:

The BoD attributable to exposure to ambient air toxics is difficult to characterize, but easy to underestimate, as a result of the multifactoral nature of cancer. The ambient environment operates distally in the etiology of cancer, with the exposure-cancer relationship mediated through a number of more proximal and intermediate risk factors. Rather then fitting with the traditional 'necessary' and/or 'sufficient' criteria of the causal web,[17] air toxics act as component causes in cancer causality. Component causes act in conjunction with other component causes to create a sufficient cause of cancer (Schwartz & Carpenter, 1999) which alone can produce disease (Husted, 2005) as graphically illustrated in Figure 6.1

[17] most risk factors for chronic disease are neither necessary nor sufficient

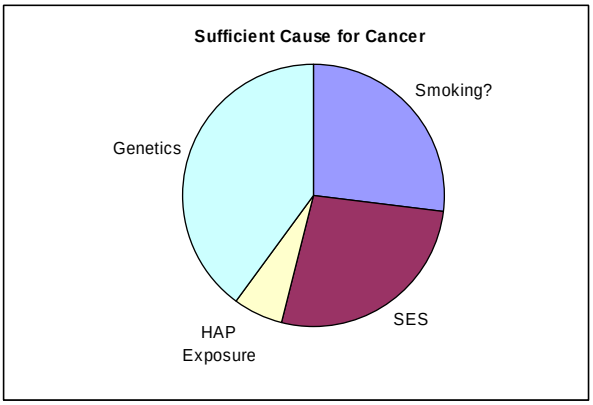


Figure 6.1 Sufficient Cause of Cancer. The figure describes ambient air toxics as a component cause of cancer, within a sufficient cause. Genetic susceptibility (DNA repair mechanisms), Age (exposure duration), and Behavioural factors influencing the exposure (smoking, occupation), also act as component causes.

As annual mean concentrations of the six air toxics were assumed homogenous throughout the S.W.O and Toronto regions, the BoD attributable to this normative exposure can easily go unrecognized, without differentiating inter-individual risk in each region; contrasting with risk factors such as smoking or occupation for which risk can more easily be identified through dichotomous 'exposed' and 'not exposed' categories.

Additionally, because individual risk factors for cancer (including ambient exposures) overlap and interact, the upper limits of the attributable fractions for cancer are theoretically unbounded and can thus exceed 100%. When cancer is a result of multiple risk factors, it is avoidable by eliminating any of the factors, especially important as multiple risk factors are often correlated and concentrated among subgroups as 'clusters' acting to increase cancer susceptibility and vulnerability. For example, cancer risk in Canada has been strongly associated with socioeconomic and demographic conditions (CCS, 2006), which themselves are strongly linked to environmental quality (Kay et al, 2000), suggesting individuals in neighbourhoods closer in proximity to industrial facilities (S.W.O) or traffic-dense highways (Toronto) may be at

greater cancer risk from exposure to a plethora of risk factors, including low SES and elevated air toxics emissions (Figure 6.2).

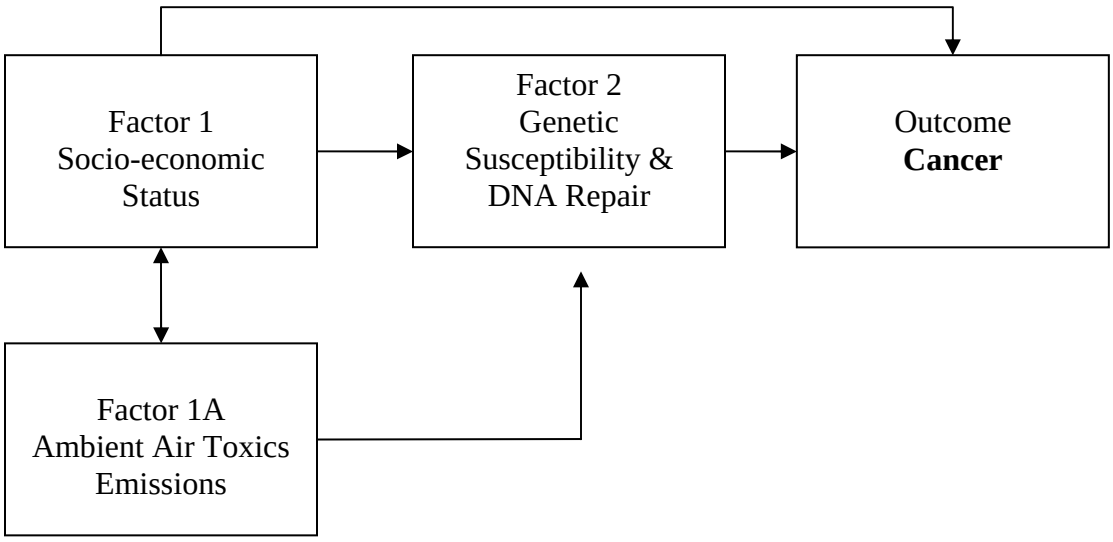


Figure 6.2: Example of a causal pathway relating exposure to ambient air toxics to cancer

The BoD attributable to current ambient air toxics exposures in S.W.O was estimated 1.68 times larger then the exposure attributable BoD in Toronto, consistent with higher ambient concentrations of four of the air toxics. However, comparisons of the disease burden attributable to exposure to ambient air toxics between the Toronto and SWO regions may not be especially accurate as a result of dramatic differences in the baseline DALY estimates, reflecting differences in ethnic origins and demographics between the two regions. Furthermore, with the baseline BoD in S.W.O, independent of risk factor attribution, also 1.62 times greater then the baseline BoD in Toronto, a greater total BoD (phase one) in S.W.O would be suggestive of risk factor clusters for cancer in this region, potentially occupational. Failure to consider differential risk of exposure attributable cancer as a result of exposure to co-risks or competing risk factors may have lead to a biased estimate of the exposure attributable BoD and oversight of potentially

cost effective intervention strategies to reduce the exposure attributable BoD in the Toronto and S.W.O regions by reducing co-risks simultaneously.

6.2.4. Temporal Dimension of the Exposure-Cancer Relationship

The BoD attributable to ambient air toxics exposures was assessed as a function of life long cumulative exposure, with annual mean ambient concentrations from a defined reference year assumed representative of current and past exposure distributions. Murray et al, (2003) has distinguished between the concepts of the 'attributable' and 'avoidable' disease, graphically illustrated in Figure 6.3.

The attributable burden refers to the BoD which retrospectively could have been avoided or prospectively could be reduced if *previous exposure* was reduced to a counterfactual distribution. Whereas, the avoidable burden refers to the future BoD which prospectively can be avoided if *current or prospective exposure* is reduced to a counterfactual exposure distribution.

However as the counterfactual analysis was ecological in design, the temporal dimension of the exposure-cancer relationship was not considered in the assessment. The purpose of the model was to derive a rough estimate of the BoD from selected cancers 'attributable' to chronic exposure to current concentrations of ambient air toxics in Toronto and S.W.O, in order to predict the BoD which prospectively could be avoided (T1) if present concentrations (T0) were reduced to counterfactual distributions, fitting with the relevant latency period of the associated cancer sites, and otherwise assuming no competing health risks and business-as-usual (B.A.U) trends in emissions.

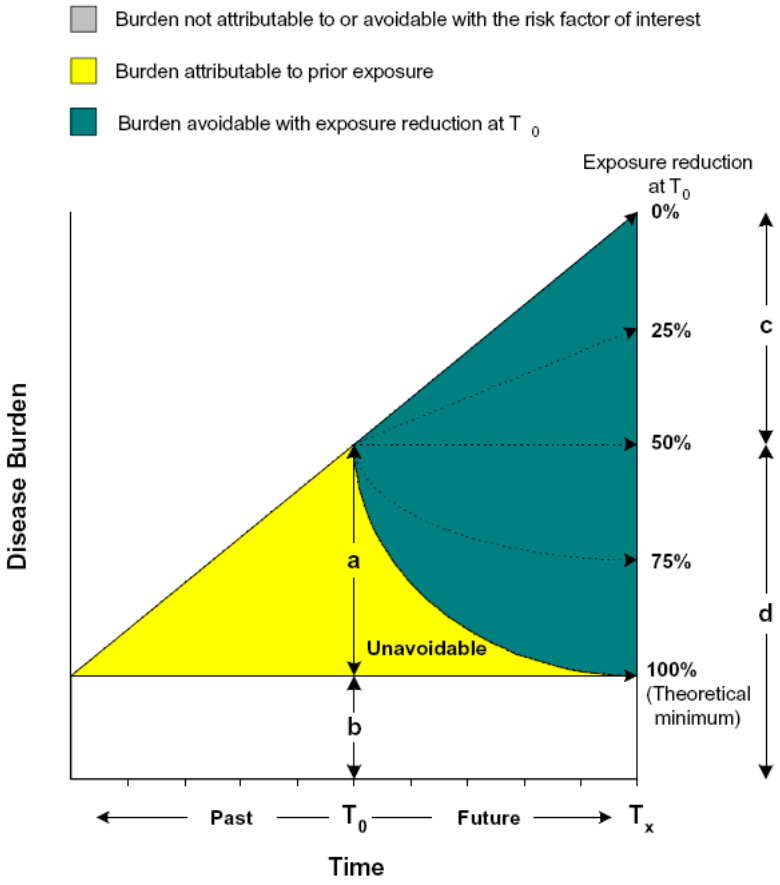


Figure 6.3 Distinction between the "Avoidable" and the "Attributable" Burden of Disease Adapted from Mathers et al, (2003) a = disease burden at t0 attributable to past exposure. The burden not attributable to the exposure of interest (yellow) may be reducing, constant, or increasing over time. b= disease burden at t0 not attributable to the exposure of interest (ie: attributable to another risk factor). The dashed lines represent the burden of cancer following at reduction in exposure at t0. c = the burden of disease avoidable at Tx with a 50% reduction in exposure (to a feasible distribution) at t0. d = remaining BoD at Tx after the 50% reduction in exposure.

Although results of the counterfactual analysis were insensitive to a time preference failure to consider the temporal dimension of the long latency period of cancer whereby exposure occurs years or decades prior to clinical manifestation of disease, may limit the models ability to predict the avoidable BoD in the future as a result of the changing population demographics in Canada. The Ontario Ministry of Finance (2007) predicts the proportion of the Ontario population over 65 will double by the year 2031; as the BoD associated with cancer dominates during the elderly years, a more accurate analysis of the exposure attributable BoD assessment

requires modelling assuming a projected population age structure. Furthermore, as the carcinogenic risk associated with exposure to ambient air toxics is a function of cumulative exposure, small health benefits associated with mitigating exposures would be more likely to accumulate in the future, accruing to the future generations rather then the current cohort.

6.2.5. Aggregating Small Exposure Attributable Impacts in the Population

Attributable fractions associating current chronic exposures to selected ambient air toxics and site specific cancers in Toronto and S.W.O regions, were relatively small ranging between 0.0014 and 0.0063[18] (representing 0.14% to 0.63% of the disease burden). However, as cancer is the leading cause of premature mortality in Canada (Canadian Cancer Society, 2006), and ambient air quality is a ubiquitous risk factor to which everyone is exposed, small attributable fractions relating exposure and disease have summed to hundreds (187) of DALY's in two risk regions with elevated exposures in Ontario (156 in Toronto and 30 in S.W.O).

Furthermore, when larger public health risks for cancer, such as cigarette smoking, have been discovered, intervened, and dominate health research priorities and resource allocation, more subtle risks causing hundreds of DALY's should also be considered as large public health concerns,[19] likely being concentrated among high risk subgroups and potentially modifiable with existing technologies and interventions.

Evidently if concentrations of all the air toxics in the two highly exposed regions of Ontario were individually reduced to concentrations associated with levels that have been observed in less polluted rural communities (approximately a 50% reduction in toxics

[18] 0.14% of the burden of oral, esophagus, ear, and nasal cancers among Toronto females is attributable to exposure to current concentrations of acetaldehyde; whereas 0.63% of the burden of leukemia and lymphomas among males in S.W.O is attributable to current ambient concentrations of benzene

[19] It would be useful to compare exposure attributable DALY's with DALY's lost from other risk factors in a comparative risk analysis

concentrations), the model predicted 96 DALY's per year could be avoidable (16 in S.W.O and 79 in Toronto). Furthermore, if there were no anthropogenic emissions of the air toxics in Toronto and S.W.O, an estimated 147 DALY's would be avoided per year, representing a reduction of 79% of the current exposure attributable BoD, and a 0.46% of the total disease burden (phase one results) associated with six cancer sites in Toronto and S.W.O.

Although the assessment suggests exposure attributable health impacts may be considerable, there are inherent uncertainties in the estimates as a result of the predicative nature of health impact assessment, and are critical to convey to decision makers weighing disease and exposure reduction priorities. As such, the next section will discuss in further detail the inherent uncertainty introduced using indirect evidence and predicative inference in the BoD model.

6.3. Uncertainty

Uncertainty deals with gaps in knowledge when estimating the baseline and exposure attributable BoD, and is reflected in the model by inaccurate and imprecise estimates of input parameters (Finkel, 1990; McColl, Hicks et al, 2000; Thomas & Hrudey, 1997).

Finkel (1990) describes three main forms of uncertainty in risk assessment models: (i) model uncertainty, which results from a lack of information on the structural or functional form of the model, (ii) parameter uncertainty, which results from measurement, systematic, or random errors, and (iii) decision-rule uncertainty, which results from the selection of health outcome measures, statistics, and value judgments in the model.

Uncertainty is distinguished from variability. Variability exists in the model as a result of natural heterogeneity in the population on factors such as demographics, age, exposure, and

underlying susceptibility which can lead to differential risk, and create a range of estimates around the true value.

Improvements in scientific knowledge with more accurate data collection, measurement, and methodologies will in theory reduce uncertainty, however can only help better understand variability which itself is a natural occurrence and can't be reduced (Thomas & Hrudey, 1997).

Major sources of model, parameter, and decision-rule uncertainty in the BoD model are thoroughly presented in Table 6.1. Since the project did not involve the collection of primary epidemiologic or risk data, and the controversy surrounding the validity of the DALY and its social value choices, have been extensively discussed thus far, the following discussion will focus on the main sources of model and parameter uncertainty related to the ability of the BoD model to predict exposure attributable health impacts. Variability will be dealt with in the context of variability leading to uncertainty.

Most of the uncertainties are not specific to the model but rather typical of any health impact assessment (HIA) exercise as a result of the simplifying assumptions required to model aggregated health and environmental data. The following discussion will review uncertainty in determining the structure of the exposure-response relationship (linear, sub-linear, supra-linear; threshold, no threshold), uncertainty in risk extrapolation, and uncertainty in estimating population exposures.

Table 6.1 Sources of Uncertainty in the Model (Adapted from *Scoping Study on Information Gaps and Uncertainties in the IP/RP Compendium Documents*, NERAM 1999)

Sources	Subtypes	Examples
Parameter	Measurement Errors	*inaccuracies in exposure estimates of annual mean ambient concentrations for Toronto and S.W.O
		*use of ambient exposure as an indirect measure of internal dose
		*"representativeness" of the counterfactual scenario concentrations for the Toronto and S.W.O regions
		*variability in estimates of case distribution of cancer severity at diagnosis, not routinely collected information by Ontario Cancer Registry
		*transferability of the 5-year relative survival rates of site-specific cancer over time with advances in treatment and detection
		*use of 5-year RSR as case-fatality rate without consideration of death from competing causes
	Random Errors	*extrapolation of risk estimates from epidemiological studies with small sample sizes
		*small cell sizes from subgroup analysis by age and sex grouping, w.r.t. incidence and mortality counts at the census level
	Systematic Errors	*extrapolating risk estimates from epidemiological studies with inadequate adjustment for confounding factors, ie: failure to consider smoking in Doll et al, (1990) relating nickel and lung cancer; potential co-exposure to DTC in Delzell et al, (1996) relating 1,3-BD and leukemia; or co-exposures such as arsenic in Doll et al, (1990)
Model	Surrogate Variables	*use of ambient mean concentration as an indicator of long term cumulative exposures
		*assumption of 5% of ethylene concentration as an oxide
		*use of average incidence and mortality counts (over 5 year period) to estimate annual count when <5 cases not reported by Ontario Cancer Registry
	Excluded Variables	*co-exposures, ie: attributable disease burden calculation for leukemia in Toronto considering benzene, 1,3-BD, and ETO in the attributable fraction: $AF_{overall} = 1 - (1 - AF_{benz})(1- AF_{1,3\text{-}BD})(1-AF_{ETO})$ (Steenland & Armstrong, 2006)
		*competing risk factors (ie: increased risk of cancer in older ages from lifetime of cumulative exposure to various risks: dietary, low physical activity etc) (Doll & Peto, 1981)
		*Co-morbidities and co-existing health conditions in disability weight of DALY
		*disability weights don't consider quality of life
	Incorrect Model Form	*assumption of linear non-threshold dose response vs.

		demonstrated evidence of sublinear dose response curve for formaldehyde (Monticello et al, 1996) and ETO (Snellings et al, 1984)
		*mechanism: high level inhalation exposures and cancer associations may be inconsistent with cumulative low dose mechanisms (ie: saturable pathways)
		*cross-sectional / ecological consideration of exposure-disease in study design
Decision-Rule	Measure to Describe Risk	*use of DALY's (vs. QALY's or PYLL or other Value of Statistical Life methods ie: willingness-to-pay)
		*presentation of BoD estimates, and attributable BoD predictions to 2 decimal places in tables displays a false sense of accuracy in the estimates
		*life expectancy based on cohort life expectancy vs. period or standard life tables
		*calculation of the A.F. as constant throughout life, ie: exposure attributable cancer risk likely varies at different ages
	Summary Statistic to Summarize Risk	*absolute quantities vs. relative rankings
	Definition of "acceptable risk"	*de-minimis risk level *consideration of risk perception (ignorance)
	Immediate vs. Delayed Health Consequences	*discounting future time at a rate of 3%

6.3.1. Assumption of Linearity and No-Threshold in Dose-Response

The exposure attributable BoD was modeled under the assumption that carcinogens act linear without threshold on the dose-response curve. Linearity is based on the concept of proportionality, whereby reducing an exposure concentration by 50% would predict a 50% reduction in tumor induction. No-threshold is based on the hypothesis that any level of non-zero exposure can produce enough DNA damage to initiate the carcinogenic process through a 'one-hit' genotoxic mechanism. Exposure leads to a cascade of cellular changes by means of biological amplification with hyperplasia, genotoxicity, cytotoxicity, and DNA cross-linking activity, prior to metastasis and potentially terminal disease (Thomas & Hrudey, 1997).

The linear non-threshold hypothesis implies that any level of non-zero exposure to carcinogenic air toxics possess some cancer risk, which may be small but non-zero (McColl,

Hicks et al, 2000; Thomas & Hrudey, 1997), such that zero risk to human health is not achievable assuming the non-threshold hypothesis, with natural sources of air toxics in the environment. However, this does not imply that there is not a safe level of exposure, or acceptable level of risk to which the population is willing to be exposed, since the absence of risk does not equate with safety (Thomas & Hrudey, 1997)

In the model, risk values for the six carcinogenic air toxics were derived on the basis of TC05 and TC01 (tumorigenic concentration) estimates from Health Canada, representing exposure concentrations associated with either a 5% or 1% increased risk of site specific cancers in human populations (Table 6.2).

Table 6.2 Health Canada derived quantitative cancer risk estimates and reference studies

Substance	Value Name	Risk Value	Target Organ	Species	Study
Acetaldehyde	TC05	8600ug/m^3	Nasal	Rat	Woutersen et al, 1986
Formaldehyde	TC05	9500ug/m^3	Nasal	Rat	Monticello et al, 1996
Benzene	TC05	1500ug/m^3	Blood	Human	Rinsky et al, 1987
1,3-Butadiene	TC01	1700ug/m^3	Blood	Human	Delzell et al, 1995
Ethylene Oxide	TC05	2200ug/m^3	Blood	Rat	Several, Snellings et al, 1984
Nickel, dusts	TC05	40-100ug/m^3	Lung	Human	Doll et al, 1990

The TC risk values for all six air toxics were derived by Health Canada assuming the default linear modeling approach for carcinogens, despite suggestions from chronic toxicity studies that the dose-response function for two of the toxics, formaldehyde and ethylene oxide, may act sub-linear (Health Canada, 2001; Health Canada, 1999), with the dose response slope becoming steeper with increasing dose. Significant increases in cell proliferation and DNA-protein cross links have been most frequently observed at or above formaldehyde concentrations of 4.8mg/m^3 (Monticello et al, 1996), and cytogenic damage has been most frequently observed at or above ETO concentrations of 9.2mg/m^3 (Snellings et al, 1984), implying the existence of a threshold. Thus if the dose-response for formaldehyde and ETO is indeed sublinear, assuming

the default linear non-threshold approach in the model may have actually overestimated the BoD in Toronto and S.W.O associated with low dose cumulative exposures. However, with uncertainties in mechanistic understandings of the dose-response functions, the model predicted the exposure attributable BoD under the protective and precautionary approach to avoid making a type-II error (false negative) in the interest of public safety.

Furthermore, assuming a single molecule of genotoxic air toxic carries some small (but non zero) risk for cancer argues against the phenomenon of 'hormesis' in which low dose chemical stimulations have been suggested as adaptive and beneficial to human health (Cook & Calabrese, 2006). With uncertainty in the dose-response relationships, setting permissible limits to environmental carcinogens on the basis of a biphasic or hormetic dose-response curve may unjustifiably impose greater involuntary risks on the two highly exposed populations included in the analysis.

The controversy regarding the shape of the dose-response curve in estimating population health impacts is further complicated by additional uncertainties of extrapolating risk estimates from studies in experimental animals and occupationally exposed workers to human populations and real world conditions, which will be further discussed in the next section.

6.3.2. Uncertainties in Inferring Population Risk from Epidemiology and Toxicology

The two main sources of evidence to evaluate cancer risk from environmental exposures come from epidemiological and toxicological studies. Epidemiological studies infer population cancer risk using indirect evidence from human populations exposed to environmental toxics unintentionally (McColl, Hicks, 2000), most often in the workplace (ie: benzene, 1,3-butadiene,

nickel). Whereas, toxicology infers risk in humans using predicative inference from experimental animals (ie: acetaldehyde, formaldehyde, and ethylene oxide).

Although there is no strict formula to judge cancer causality, the IARC and Health Canada classify carcinogenicity based on a weight-of-evidence approach considering elements such as the strength of the association (RR), dose-response gradient, consistency, temporality, specificity, biological plausibility, and coherence (Hill's Criteria of Causality) provided by epidemiological and toxicology studies.

There are trade-offs in the strengths and limitations of inferring population cancer risk from epidemiological and toxicology studies, however both types of evidence introduce uncertainty to the model in the need to extrapolate risk estimates between populations and from high to low exposures.

6.3.2.1. Uncertainties in Epidemiology

The ability to extrapolate quantitative cancer risk estimates from primary epidemiological studies is dependant on both the study design (cohort vs. case-control vs. ecological) and quality (control for random and systematic errors).

As a result of poor sensitivity to detect small or subtle cancer risks in populations from low and ubiquitous environmental exposures (Hrudey & Thomas, 1997; McColl, Hicks et al, 2000), epidemiological studies are most often conducted in the occupational setting among workers exposed to elevated concentrations of contaminants (Table 6.3). Extrapolating quantitative cancer risk estimates downwards from high concentrations in the workplace introduces a degree of uncertainty to the capability of the model to predict attributable health impacts encountered at lower environmental concentrations. For example, in the model leukemia

risk from chronic exposure to 1,3-BD in Toronto and S.W.O at concentrations of approximately 0.3mg/m^3 required low dose extrapolation from the TC01 value of 1.7mg/m^3 derived by Health Canada from the Delzell et al, (1996) cohort, which demonstrated evidence of elevated cancer risk among workers occupational exposed to concentrations of approximately 2mg/m^3.

Table 6.3. Uncertainties in Inferring Population Risk from Health Canada reference studies for benzene, 1,3-butadiene, and nickel refinery dusts on the basis of excess cancer risks among individuals exposed to elevated concentrations in the workplace

Criteria	Benzene	1,3-Butadiene	Nickel refinery dust
Reference	Rinsky et al, 1987	Delzell et al, 1996	Doll et al, 1990
Study Design	Cohort	Cohort	Cohort
Dose-response	Elevated risk with cumulative exposure (<10ppm over a 40-year work period)	Increased risk with cumulative exposure	Increased risk with length of exposure
Power	Limited by small sample size	Sample size >15,000 workers	Sample size >54,000 workers
Temporality	Demonstrated latency effect; sufficient follow-up	Demonstrated latency effect; 49 years of follow up	Demonstrated latency effect 20 years post exposure
Exposure estimates	Historical air sampling data	Potential exposure misclassification	Uncertainty in exposure estimates and measurements
Confounds	Few co-exposures in the workplace	Potential confounding with DTC exposure; study conducted in the BD polymer industry; Controlled for benzene exposure	Potential confounding with co-exposure to arsenic; failure to consider information on smoking status

In addition to the uncertainty introduced to the model with high to low concentration extrapolation, epidemiological studies are often plagued by a number of methodological problems such as confounding (Delzell et al, 1996; Doll et al, 1990) and poor exposure characterization (Delzell et al, 1996; Doll et al, 1990; Rinsky et al, 1987), which limit the ability to extrapolate risk estimates from the occupational setting to the general population with a high degree of confidence.

Confounds are factors that are independent risk factors for disease, are associated with the exposure of interest, but are not in the same causal pathway linking the exposure and disease (Husted, 2005). Simultaneous exposure to DTC with 1,3-BD in Delzell et al, (1996), arsenic with nickel in Doll et al (1990), and failure to stratify the analysis of nickel and lung cancer by smoking status in Doll et al (1990), suggest potentially confounded risk associations in the primary epidemiological studies which serve the basis of the Health Canada exposure-cancer associations. Extrapolating risk estimates from epidemiological studies based on spurious exposure-disease relationships may have lead to biased estimate of the BoD attributable to ambient air toxics exposures since potentially confounding factors may increase or decrease cancer susceptibility.

6.3.2.2. Uncertainties in Toxicology

Chronic toxicity studies in experimental animal models are most useful in risk assessment in their ability to establish biologically plausible mechanistic information on organ susceptibility and to evaluate the cumulative effects of site specific toxicity in a rigorously controlled laboratory environment. Table 6.4 reviews chronic toxicity studies for acetaldehyde, formaldehyde, and ethylene oxide from which HC risk potency values have been derived.

Table 6.4 Uncertainty in population risk inference from acetaldehyde, formaldehyde, and ethylene oxide on the basis of Health Canada reference toxicology studies

Criteria	Acetaldehyde	Formaldehyde	Ethylene Oxide
Reference Study	Woutersen et al, 1986	Monticello et al, 1986	Several, notably Snellings et al, 1984
Animal	Rats	Rats	Rats & Mice
Biological Plausible Mechanism	Genotoxic mechanism, with evidence of cell proliferation, mutagenic, and cytotoxic effects	Cytotoxicity, cellular proliferation, and DNA-protein crosslinks	Cytotoxicity, genotoxic action, potent alkylating activity
Dose-response	Concentration related increase in squamous cell carcinomas and adenocarcinomas in nasal and larynx	Pathology most correlated with exposure concentration rather then cumulative exposure	Exposure related increased risk of leukemias
Largest source of uncertainty	No lesions observed in other organs tested; lack of information on cytotoxicity, proliferation, DNA-protein cross-link induction; difficulties inferring dose response to the general population	Lack of certainty about the shape of the dose response curve; linear vs. sublinear?	Some evidence of brain tumors and peritoneal mesotheliomas with elevated concentrations Inadequate interspecies information on variations in metabolism and kinetic differences

Toxicology studies are in theory more sensitive then epidemiologically studies to detect cancer risks however, extrapolating risk estimates from animal models to human populations requires consideration of a number of modifying effects.

Interspecies extrapolation involves extrapolating risk estimates from the lowest dose demonstrating pathology in chronic toxicity tests to a corresponding risk in humans at environmental concentrations. Species differences in body surface area, anatomy, metabolism, and physiology are adjusted using allometric conversion factors (McColl, Hicks et al, 2000). Extrapolating risk estimates between species is associated with enormous uncertainty, especially as the technique may not adequately account for species differences in underlying susceptibility for site specific cancer risks; for example, mice and rats which are obligate nasal breathers may be especially susceptible to nasal and upper respiratory cancers from high dose inhalation

exposures of acetaldehyde and formaldehyde administered in the lab to intentionally overwhelm natural metabolic and detoxification mechanisms.

Like epidemiological studies, risk estimates from toxicology studies require extrapolation from higher then environmental doses administered in the lab to risk estimates corresponding with environmental concentrations. Unlike occupational exposures which occur on a continuum and are often confounded by co-exposures, animal models are administered a limited number of doses (usually four non-zero exposures) of a single substance in a controlled environment, which may not be representative of real world human exposure conditions.

Unfortunately, the lowest end of the dose-response curve, which is of greatest relevance for environmental exposures, is associated with the greatest degree of uncertainty for risk extrapolations from chronic toxicity studies (McColl, Hicks et al, 2000). Difficulty in accurately quantifying and characterizing disease at the lowest administered doses suggests some site-specific carcinogenic outcomes may go unrecognized in laboratory studies.

As the model derived the exposure attributable BoD on the basis of site-specific effects, failure to uncover site-specific risk in toxicity studies (type-II error), or selective exclusion of site specific risks from analyses, could have lead to an underestimate of the exposure associated BoD. For example, exposure to ETO in rats has been associated with a biologically plausible risk of brain tumors, however assessment was limited to estimates of leukemia and lymphoma outcomes on the basis of Health Canada's risk evaluation, thus potentially underestimating the BoD associated with chronic ETO exposure.

6.3.3. Uncertainty in Estimating Environmental Exposures in the Population

Exposure estimates contribute to a large amount of the uncertainty in the BoD model. With limited or poor quality data on ambient exposures, many oversimplifications were required to model the exposure attributable health impacts in Toronto and S.W.O regions.

A common assumption in risk assessment is that all individuals within a defined geographic boundary are exposed to the same concentrations of contaminants. However, individuals residing closer in proximity to the Chemical Valley in S.W.O or freeways in Toronto more likely experience elevated chronic exposure from industrial and motor vehicle releases, compared to more distant or rural areas, such that variability in the population distribution of exposure leads to uncertainty in the model when exposure is assumed homogeneous. Thus, modeling annual mean ambient concentrations as constant throughout each region may misrepresent true differences in exposure concentrations between cities, neighbourhoods, or subgroups. Without stratifying levels of ambient exposures in each region (ie: high, medium, low exposure), the exposure attributable BoD may be biased, pending the representiveness of the proxy point estimate to characterize the exposures (McColl, Hicks et al, 2000).

In addition to spatial variability, differences in individual micro-environments and time-activity patters including behaviour, occupation, age, co-risks, and genetic polymorphisms, act to increase or decrease susceptibility to exposure, and therefore lead to uncertainty in the exposure estimates among individuals in the population (McColl, Hicks et al, 2000; NERAM, 1999).

Furthermore, estimating health impacts associated with independent exposures, without consideration of multiple low dose co-exposures in the ambient environment also introduces significant uncertainty to the model. Unlike chronic toxicity studies, in real world conditions air toxics exposures cannot be easily isolated, such that four types of interaction (effect

modification) are possible: (i) additivity, in which the effects of two toxics arithmetically sum (ii) potentiation, whereby an exposure associated effect occurs with enhancement from another toxic (iii) synergism, whereby an effect associated with simultaneous exposures to two or more toxics is greater then the arithmetic sum, ie: multiplicative, and (iv) antagonism, in which an effect associated with simultaneous exposures of two or more toxics is less then the arithmetic sum, ie: protective (Thomas & Hrudey, 1997). With little known about the shape of the concentration response curve at low environmental concentrations, the effects of the six carcinogenic air toxics were assumed independent and additive.

Finally, the ability of the model to predict the BoD that could be reduced or avoided by mitigating current exposures to plausible or feasible exposure distributions is limited by temporal considerations of the latency period in the exposure-disease relationships. The time lag between exposure abatement and disease reduction would be influenced by the time frame over which mitigation occurs; for example, whether exposure mitigation occurs as a snap shot intervention or a gradual phase out over a defined time period. The longer the time lag between exposure and disease, the greater the uncertainty in the counterfactual analysis.

Although there are uncertainties in the ability of the model to predict health impacts attributable to exposure, cost-effective intervention shouldn't be postponed with evidence of a sizeable and potentially modifiable health burden. Assessing the BoD which could be avoided using hypothetical exposure distributions aids policy in mapping intervention strategies and exposure reduction priorities with minimal environmental data requirements. As such, the next section will further explore the policy implications of the BoD model and results for disease and exposure reduction priorities in the Toronto and S.W.O regions.

6.4. Policy Implications

The magnitude of the BoD that could be avoided, or the health benefits that could be anticipated, by modifying current environmental exposures in two highly exposed regions, to alternative reduced levels has profound implications on policy regarding emission reduction priorities.

Consistent with a larger population size, results indicated the BoD attributable to long term concentrations of acetaldehyde, formaldehyde, benzene, 1,3-BD, ETO, and nickel refinery dusts was greater in Toronto then S.W.O; however on a per capita basis, the BoD associated with six cancers in S.W.O exceed that of Toronto. Differences in exposure attributable disease rates per 100,000 persons suggests disparities between the two regions reflect broader social structures, that is the sources of release, infrastructure, and regulations governing emissions which in turn leads to the ubiquity of the ambient exposures in each region (Schwartz & Carpenter, 1999).

Chronic inhalation exposure to nickel refinery dusts contributed to the largest proportion of the exposure attributed cancer burden in S.W.O, proving to be a clear priority for exposure reduction among both males and females. Interestingly, according to the National Pollutant Release Inventory in 2001, one facility in S.W.O released more nickel (and compounds) to the environment then any other facility in Ontario outside the Chemical Valley or Copper Cliff-Falconbridge nickel belt by approximately 30-fold[20] (NPRI, 2001). A reduction in the environmental concentration of nickel in SWO to levels achieved in other Canadian cities predicts a reduction in the BoD attributable to nickel by 0.632 DALY's / 100,000 persons.

[20] Imperial Oil in Sarnia released 30.334 tonnes of nickel and compounds (NPRI, 2001)

However, assuming a feasible distribution of each of the six air toxics in SWO (Table 4.5a), the greatest reduction in the BoD (0.805 DALY's / 100,000 persons) would be predicted with reducing ETO exposure.

The ambient concentration of ethylene oxide was modeled assuming a 5% conversion of ambient ethylene to the oxide. With four facilities in the Chemical Valley[21] responsible for the largest industrial releases of ethylene in Ontario (NPRI, 2001), 83.4% of the BoD from lymphomas and leukemia's that is currently attributable to ambient ETO concentrations in SWO, could be avoided in the future with the mitigation of ethylene release from industry (assuming 5% conversion to oxide).

As mitigating release of the six HAP's to concentrations associated with plausible minimum risk levels (zero anthropogenic emissions) may not be a realistic policy option considering local employment and economy, decision makers should consider the ALARA principle '*as low as reasonably achievable'* in developing regulatory guidelines to reduce emissions with cost-effective interventions including best available control technologies (BACT) or best practicable control technologies (BPCT) (McColl, Hicks et al, 2000). Furthermore, as exposure to hazardous air pollutants is involuntarily imposed on individuals, an acceptable or 'de-minimis' level of public risk is especially essential to consider in policy development regarding mitigation of ubiquitous exposure to carcinogenic toxics, acting without threshold.

As mentioned, in Toronto the air toxic of foremost priority for exposure reduction is more ambiguous then S.W.O, with relatively similar attributable disease burdens associated with current chronic exposure to formaldehyde and benzene, and variability in the rank order of importance between the sexes. As new Canada-wide standards governing benzene content in gasoline have corresponded with 45% reductions in average Canadian ambient benzene

[21] Bayer, DOW, Imperial Oil, Nova Chemical

concentrations (ug/m^3) since 1995 (Environment Canada, 2001), policies governing heavy duty motor vehicle emissions (diesel) or the implementation of additional alternative transportation initiatives may result in the largest health benefits in Toronto. However, this may not be entirely feasible in Toronto as some studies have suggested that attempts to improve air quality with better fuel quality have been offset by increased driving frequency and coal based power production (Campbell et al, 2004).

As the largest contribution of urban ambient formaldehyde (70-90%) results from secondary formation of the combustion of volatile organic compounds (ATSDR, 1999; Health Canada, 2001), there may be limited ability to regulate natural sources of formaldehyde in Toronto. However, as formaldehyde is an off-gas product of benzene photo-oxidation, and vehicular emissions account for the largest anthropogenic release of ambient formaldehyde, the most practical strategy to reduce the burden of head and neck cancers associated with chronic formaldehyde exposure may be policy aimed to decrease ambient benzene and precursor VOC's.

Multicausality offers the opportunity to tailor policy and interventions to cost-effectively reduce the BoD attributable to multiple exposures and diseases. Although this assessment was limited to quantifying carcinogenic outcomes, policy or intervention to reduce the BoD from site-specific cancers by mitigating exposure may also reduce the BoD from other chronic conditions, such as cardiovascular events or asthma, or the BoD from co-exposures simultaneously. For example, in Toronto reducing benzene release with cleaner emission standards for heavy duty vehicles or alternative transportation planning, may act to reduce the BoD from lymphomas and leukemia's from benzene itself, but also by reducing emissions of 1,3-BD and ETO from motor vehicles in the process. Whereas in Sarnia, standards regulating benzene emissions from industrial processes at the Chemical Valley may not only be associated

with fewer cases of leukemia and lymphomas, but also secondary benefits such as improved environmental quality for local residents and less stigma associated with living in the local community, potentially serving to increase tourism and the local economy in the process.

As such, exposure reduction policy should be guided by the DPSEEA framework (Driving Force – Pressure – State – Exposure – Effect – Action) which considers the linkages between each of the components of the framework, distal and proximal factors, and recognizes action to reduce the exposure attributable BoD should occur at various levels with intersectoral collaboration (Kay et al, 2000; Pruss et al, 2001) .

6.5. Strengths & Limitations of the Model:

6.5.1. Strengths

Comprehensive and objective environmental BoD models support informed decision making and policy development to protect and promote public health (Cohen et al, 2005; Kay et al, 2000). Assessing the BoD associated with current and reduced HAP exposures in two highly exposed regions of Ontario aids in examining inequalities in exposure between geographic boundaries, and is important for health planning, surveillance, and priority setting. By incorporating community specific estimates of cancer morbidity and mortality with transparent value choices, the DALY serves as a useful indicator of both population health status and also facilitates resource allocation, amendable to cost-effectiveness analysis. Sensitivity analysis allows judgment of the impact of alternative value choices (severity weighting, life expectancy, discount rate, age weights) on the BoD and exposure attributable BoD results (Fox-Rusby & Hanson, 2001; Pruss-Usten et al, 2003). Furthermore, modeling the exposure attributable BoD doesn't require new data collection, rather purposeful analysis of key environmental and health

indicators, thereby providing a valuable baseline to compare future disease trends and monitor exposures (De Hollander et al, 1999).

With uncertainty in the current scientific knowledge regarding the contribution of hazardous air pollutants to the BoD, this regional level assessment provides valuable information on a difficult to quantify environment-health relationship, and thereby contributes to an improved understanding of HAP associated health impacts. Assumptions and uncertainties have been provided transparently to aid in fully informed decision making and policy development to reduce exposure attributable health impacts in Ontario, with a goal to support sustainable development and environmental protection.

6.5.2. Limitations

Many of the limitations are the result of the predicative nature of the model and simplifying assumptions required when aggregating disease and exposure data in the population, as previously discussed. One issue that has yet to be discussed in detail concerns risk characterization. An accurate characterization of true risk requires consideration of the public risk perception. As risk perception was not considered in the quantitative estimates of the BoD, an 'acceptable' level of exposure associated cancer risk should be considered by policy makers in setting mitigation priorities for exposures often regarded as 'externalities' (Pruss-Usten et al, 2003; Sexton, 2006).

Additionally, the analysis also failed to provide a range of estimates around the DALY estimates and the counterfactual analysis. A more comprehensive characterization of the BoD and the uncertainty around the results would involve 95^{th} percentiles around point estimates. Furthermore, with uncertainty in population exposure estimates, modeling an annual mean concentration for each region fails to capture the variability in the population distribution of

exposure among subgroups, and serves as a proxy for estimates of internal dose. As individuals have different micro-environments, and the body has natural physiological defense mechanisms including muccocilliary clearance and DNA repair, biomarkers of exposure and spatial analysis would serve as a more reliable tool for exposure estimation, however was beyond the scope of this model.

Furthermore, pending the trans-boundary contribution of air toxics from boarding states of the U.S.A, there may be limited ability for Canadian regulatory actions to reduce health impacts associated with ambient exposures as air quality is not confined to geographic borders.

Finally, the model was limited to quantifying carcinogenic endpoints associated with chronic inhalation exposure to six ambient air toxics in two high risk regions of Ontario. Results should thus be considered as an underestimate of the *total* BoD associated with exposures, failing to consider the initiation or exacerbation of other chronic conditions such as asthma, respiratory, and cardiovascular events. Furthermore, as SWO and Toronto were selected as highly exposed regions in Ontario on the basis of local emissions from industry and urbanization, results and implications should not be generalized to other industrial or urban areas outside of Canada or rural areas within Canada.

6.6. Future Work:

To better inform public health policy it would be useful to examine regional variability in the BoD by exposure and age distribution. Stratifying on the basis of exposure levels (high, medium, low) or subgroup (occupation, age, smoking status) may aid in differentiating variability in exposure associated cancer risk. Furthermore, examining the role of risk factor clusters for cancer, predisposing, and enabling factors, may be of particular public health policy

interest in SWO, and display the need to focus policy towards protecting highly vulnerable subgroups. Such modelling may require a collaborative effort among environmental and health organizations such as Environment Canada and Health Canada, to provide better estimates of the exposure attributable BoD using spatial analysis methods including probability density functions or monte carlo simulations.

In addition to the counterfactual concentrations in the analysis, future work should analyze the reduction in the BoD associated with the implementation of more comprehensive, policy oriented hypothetical scenarios, such as the BoD which could be avoided with the implementation of a particular policy or technology. For example, it would be interesting to examine the reduction in the BoD expected with the implementation of a particular transportation policy, assuming modified long term concentrations. In SWO, it would be interesting to predict the avoidable BoD if one of the four petrochemical plants in the Chemical Valley were to close; potentially of particular relevance for the nickel associated BoD. Such work requires emission and distribution modelling, however would enable cost-effective emission reduction priority setting.

Finally, with the globalization of environmental health, ambient exposures and chronic disease rates are expected to double or triple over the next two decades in some developing countries (Yach et al, 2004), such that it would be useful to extend this model internationally, to estimate exposure attributable health impacts in developing countries such as China and India where the health and environmental implications of urbanization and industrialization are only beginning to be realized.

7. CONCLUSIONS

Results of the BoD model indicated 0.58% of the total burden of morbidity and mortality from six cancer endpoints in S.W.O and Toronto is attributable to current exposure to six hazardous air pollutants. Although the attributable fractions relating air toxics exposures to disease were independently small, the attributable burden of disease summed to hundreds of DALY's lost as a result of the ubiquitous nature of the 'involuntary' risk factor. Furthermore, because of the pressures demographic, economic, and social development put on the environment, there is a need to develop informed and efficient policy that supports economic growth, while supporting sustainable development and healthy environmental quality for current and future generations.

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Abbreviations

1,3-BD	1,3-Butadiene
AF	Attributable Fraction
ATSDR	Agency for Toxicological Substance Disease Registry
B.A.U	Business-As-Usual (trends)
BoD	Burden of Disease
CCME	Canadian Council of Ministers of the Environment
CCS	Canadian Cancer Society
CEPA	Canadian Environmental Protection Agency
CEYLL	Cohort Expected Years of Life Lost (cohort life expectancy)
CRA	Comparative Risk Assessment
DALY	Disability Adjusted Life Year
D_D	Duration of Diagnosis Stage
D_M	Duration of Metastasis Stage
D_T	Duration of Terminal Stage
D_{TR}	Duration of Treatment Stage
DTC	Dithiocarbamate
DW	Disability Weight
EBD	Environmental Burden of Disease
EME	Established Market Economies
ETO	Ethylene Oxide
ETS	Environmental Tobacco Smoke
GBD	Global Burden of Disease

HAP	Hazardous Air Pollutants
HEIDI	Health Effects Indicator Decision Index
HIA	Health Impact Assessment
IARC	International Agency for Research on Cancer
ICD9	International Classification of Disease, Version 9
ITER	International Toxicity Estimates for Risk
I.U.R	Inhalation Unit Risk (potency)
K	Age weighting
LNS	Average time to death for cancer patients who eventually die
NAPS	National Air Pollution Surveillance (system)
NBD	National Burden of Disease
NERAM	Network for Risk Assessment and Management
NFPRER	National Frameworks for Petroleum Refinery Emission Reductions
NPRI	National Pollutant Release Inventory
OCR	Ontario Cancer Registry
OECD	Organization of Economic Developed (countries)
PHI	Public Health Impact of Disease in Canada (research program)
PSL	Priority Substance List (report)
PTO	Person Trade Off (method)
QALY	Quality Adjusted Life Years
PAF	Population Attributable Fraction
PAR	Population Attributable Risk
PEYLL	Period Expected Years of Life Lost

PIF	Population Impact Fraction
PYLL	Potential Years of Life Lost
r	Discounting
RIVM	Institute for Public Health and the Environment
RR	Relative Risk
RSR	Relative Survival Rate
SES	Socioeconomic Status
SEYLL	Standard Expected Years of Life Lost
SMPH	Summary Measure of Population Health
t0	Present (time period)
T1	Future (time period)
TC	Tumorigenic Concentration (1% or 5%)
TERA	Toxicology Excellence and Risk Assessment
S.W.O	Southwestern Ontario
U.S. EPA	United States Environmental Protection Agency
VOC’s	Volatile Organic Compounds
WHO	World Health Organization
YLD	Years of Life Lived with Disability
YLL	Years of Life Lost

Appendix A

International Classification of Disease Coding System, Version Nine: Malignant Neoplasm

Code	Cancer
140-149	**Oral Cavity & Pharynx**
140	Malignant neoplasm of the lip
141	Malignant neoplasm of the tongue
142	Malignant neoplasm of the major salivary glands
143	Malignant neoplasm of the gum
144	Malignant neoplasm of the floor of the mouth
145	Malignant neoplasm of other unspecified parts of the mouth
146	Malignant neoplasm of oropharynx
147	Malignant neoplasm of nasopharynx
148	Malignant neoplasm of hypopharynx
149	Malignant neoplasm of other and ill-defined sties within lip, oral cavity
150	**Esophagus**
160-161	**Middle Ear, Nasal, & Larynx**
160	Malignant neoplasm of nasal cavities, middle ear, and accessory sinuses
161	Malignant neoplasm of larynx
162-165	**Lung, Bronchus, Trachea**
162	Malignant neoplasm of trachea, bronchus, and lung
163	Malignant neoplasm of pleura
165	Malignant neoplasm of other and ill-defined sites within the respiratory and interthoracic organs
200-203	**Lymphomas and Multiple Myeloma**
200	Lymphomasarcoma and reticulosarcoma
201	Hodgkin's disease
202	Other malignant neoplasms of lymphoid and histiocytic tissue
203	Multiple myeloma and immunoproliferative neoplasms
204-208	**Leukemia**
204	Lymphoid leukemia
205	Myeloid leukemia
206	Monocytic leukemia
207	Other specified leukemia
208	Leukemia of unspecified cell type

Appendix B

Population Demographics by 5-year age interval

Toronto

	Males					Females				
Age	Toronto	Durham	Peel	York	Total	Toronto	Durham	Peel	York	Total
0-4	73,450	16,675	35,025	23,420	148,570	70,065	16,355	33,090	22,135	141,645
5-9	77,080	21,015	39,200	27,320	164,615	72,550	20,075	36,835	25,880	155,340
10-14	72,455	21,100	37,600	29,275	160,430	68,210	20,345	35,540	27,685	151,780
15-19	73,515	18,955	36,295	28,585	157,350	69,765	18,150	34,540	26,200	148,625
20-24	80,760	14,845	33,815	23,785	153,205	84,380	14,420	33,475	23,090	155,365
25-29	94,175	13,640	33,145	21,355	162,315	102,290	14,320	35,665	22,375	174,650
30-34	105,545	16,965	38,780	24,705	185,995	111,000	18,690	41,905	27,295	198,890
35-39	113,140	23,760	46,030	30,805	213,735	112,900	25,610	47,225	34,040	219,775
40-44	99,940	23,540	42,925	32,145	198,550	103,880	24,130	44,085	35,490	207,585
45-49	85,215	19,505	36,485	28,975	170,180	93,140	19,975	38,135	31,360	182,610
50-54	75,620	17,045	33,025	27,050	152,740	83,490	17,005	33,725	26,745	160,965
55-59	55,795	11,935	24,130	18,210	110,070	62,180	11,615	23,770	17,475	115,040
60-64	47,575	8,605	17,905	13,945	88,030	55,525	8,960	17,820	13,615	95,920
65-69	44,635	7,310	13,370	11,260	76,575	51,800	8,005	14,155	11,315	85,275
70-74	39,640	6,050	9,865	8,390	63,945	49,100	7,315	11,330	9,445	77,190
75-79	29,990	4,280	6,285	5,440	45,995	42,990	6,225	9,045	7,355	65,615
80-84	16,845	2,265	3,215	2,785	25,110	26,570	3,695	5,235	4,540	40,040
85+	11,165	1,345	1,955	1,875	16,340	25,095	3,175	4,350	3,890	36,510
Total	1,196,540	248,835	489,050	359,325	2,351,456	1,284,930	258,065	499,895	369,930	2,412,820

Southwestern Ontario

	Males				Females			
Age	Lambton	Kent	Essex	Total	Lambton	Essex	Kent	Total
0-4	3,315	3,145	10,160	16,620	3,215	3,005	9,375	15,595
5-9	4,230	3,605	10,850	18,685	4,040	3,585	10,380	18,005
10-14	4,810	4,020	10,895	16,725	4,570	3,845	10,075	18,490
15-19	4,910	4,210	10,335	19,455	4,705	4,060	10,110	18,875
20-24	3,740	3,290	10,710	17,740	3,730	3,090	10,570	17,390
25-29	3,030	2,825	10,810	16,665	3,205	2,935	11,135	17,275
30-34	3,440	3,145	11,695	18,280	3,515	3,265	11,650	18,430
35-39	4,290	4,135	13,070	21,495	4,755	4,335	12,935	22,025
40-44	5,090	4,515	12,600	22,205	5,300	4,530	12,410	22,240
45-49	5,005	4,000	10,780	19,785	5,125	3,935	11,115	20,175
50-54	4,660	3,670	9,945	18,275	4,680	3,675	10,170	18,525
55-59	3,765	2,805	7,590	14,160	3,655	2,935	7,580	14,170
60-64	2,960	2,395	5,920	11,275	3,140	2,550	6,315	12,005
65-69	2,745	2,075	5,185	10,005	3,055	2,285	5,720	11,060
70-74	2,505	1,910	4,730	9,145	2,860	2,265	5,640	10,765
75-79	1,810	1,410	3,415	6,635	2,540	2,135	5,195	9,870
80-84	980	770	1,780	3,530	1,645	1,480	3,185	6,130
85+	590	505	1,040	2,135	1,355	1,380	2,815	5,550
Total	61,875	52,430	151,500	265,805	65,100	55,280	156,380	276,760

Appendix C

Mortality Counts in Toronto for Site Specific Cancer (disaggregated by age & sex)

Oral Cavity & Pharynx (ICD9 codes 140-149)

	Males					Females				
Age	Toronto	Durham	Peel	York	Total	Toronto	Durham	Peel	York	Total
0-4	0	0	0	0	0	0	0	0	0	0
5-9	0	0	0	0	0	0	0	0	0	0
10-14	0	0	0	0	0	0	0	0	0	0
15-19	0	0	0	0	0	0	0	0	0	0
20-24	0	0	0	0	0	0	0	0	0	0
25-29	1	0	0	0	1	0	0	0	0	0
30-44	1	0	0	0	1	0	0	0	0	0
35-39	1	0	0	0	1	0	0	0	0	0
40-44	0	0	0	0	0	2	1	0	0	3
45-49	0	0	1	0	1	6	0	0	1	7
50-54	1	0	1	0	2	2	1	2	0	5
55-59	1	1	0	0	2	5	1	2	0	8
60-64	1	0	1	0	2	8	1	2	0	11
65-69	8	1	0	0	9	13	2	1	1	17
70-74	3	0	1	1	5	11	1	1	1	14
75-79	4	1	0	1	6	10	0	0	1	11
80-84	6	1	1	0	8	7	0	1	0	8
85+	5	1	1	1	8	4	1	1	1	7

Esophagus (ICD9 code 150)

	Males					Females				
Age	Toronto	Durham	Peel	York	Total	Toronto	Durham	Peel	York	Total
0-4	0	0	0	0	0	0	0	0	0	0
5-9	0	0	0	0	0	0	0	0	0	0
10-14	0	0	0	0	0	0	0	0	0	0
15-19	0	0	0	0	0	0	0	0	0	0
20-24	0	0	0	0	0	0	0	0	0	0
25-29	0	0	0	0	0	0	0	0	0	0
30-44	0	0	0	0	0	0	1	0	0	1
35-39	0	0	0	0	0	1	0	0	1	2
40-44	1	0	0	0	1	1	1	0	0	2
45-49	0	0	0	0	0	3	0	1	1	5
50-54	0	0	0	0	0	7	1	2	0	10
55-59	2	1	0	0	3	7	2	0	1	10
60-64	4	1	1	1	7	8	2	2	2	14
65-69	2	1	0	0	3	9	2	3	2	16
70-74	7	1	2	0	10	10	2	2	2	16
75-79	7	1	2	0	10	7	2	2	2	13
80-84	2	1	1	0	4	7	2	1	1	11
85+	9	1	1	0	11	6	2	2	1	11

Appendix C continued:
Mortality Counts in Toronto for Site Specific Cancer (disaggregated by age & sex)

Middle Ear, Nasal, & Larynx (ICD9 codes 160-161)

	Males					Females				
Age	Toronto	Durham	Peel	York	Total	Toronto	Durham	Peel	York	Total
0-4	0	0	0	0	0	0	0	0	0	0
5-9	0	0	0	0	0	0	0	0	0	0
10-14	0	0	0	0	0	0	0	0	0	0
15-19	0	0	0	0	0	0	0	0	0	0
20-24	0	0	0	0	0	0	0	0	0	0
25-29	0	0	0	0	0	0	0	0	0	0
30-44	0	0	0	0	0	0	0	0	0	0
35-39	0	0	0	0	0	0	0	1	0	1
40-44	1	0	0	1	0	0	0	0	0	0
45-49	3	0	0	0	3	0	0	0	0	0
50-54	2	0	1	0	3	0	0	0	0	0
55-59	5	0	0	1	6	0	0	1	0	1
60-64	5	1	2	0	8	0	0	0	0	0
65-69	5	0	1	0	6	0	0	0	0	0
70-74	7	0	0	0	7	0	1	0	0	1
75-79	5	0	1	0	6	0	0	0	0	0
80-84	2	0	0	0	2	1	0	0	1	2
85+	3	1	0	0	4	0	0	0	0	0

Lung, Bronchus & Trachea (ICD9 codes 162-165)

	Males					Females				
Age	Toronto	Durham	Peel	York	Total	Toronto	Durham	Peel	York	Total
0-4	0	0	0	0	0	0	0	0	0	0
5-9	0	0	0	0	0	0	0	0	0	0
10-14	0	0	0	0	0	0	0	0	0	0
15-19	0	0	0	0	0	0	0	0	0	0
20-24	0	0	0	0	0	0	0	0	0	0
25-29	0	0	0	0	0	0	0	1	0	1
30-44	1	0	0	0	1	1	0	1	0	2
35-39	2	0	0	0	2	1	0	0	2	3
40-44	2	1	1	2	6	5	3	3	2	13
45-49	13	3	5	5	28	13	2	6	5	26
50-54	35	7	11	5	58	16	8	5	4	33
55-59	57	7	19	23	106	29	6	10	11	56
60-64	55	21	25	18	119	33	12	8	15	67
65-69	131	18	25	25	199	74	17	10	11	112
70-74	126	19	36	28	209	75	19	14	18	126
75-79	115	28	28	14	185	87	23	20	12	142
80-84	72	11	16	17	116	55	13	9	12	89
85+	390	7	15	12	73	73	10	11	6	100

Appendix C continued:
Mortality Counts in Toronto for Site Specific Cancer (disaggregated by age & sex)

Lymphomas and Multiple Myeloma (ICD9 codes 200-203)

	Males					Females				
Age	Toronto	Durham	Peel	York	Total	Toronto	Durham	Peel	York	Total
0-4	0	0	0	0	0	0	0	0	0	0
5-9	1	0	0	0	1	0	0	0	0	0
10-14	1	0	0	0	1	1	0	0	0	1
15-19	0	1	0	0	1	0	0	1	0	1
20-24	0	0	0	0	0	1	0	0	0	1
25-29	0	0	0	0	0	0	0	0	0	0
30-44	2	1	0	0	3	1	0	0	0	1
35-39	2	0	1	0	3	5	1	0	0	6
40-44	2	0	0	0	2	3	1	0	0	4
45-49	3	0	1	1	5	4	0	2	1	7
50-54	6	2	2	0	10	10	5	1	3	19
55-59	7	1	3	1	12	14	2	5	2	23
60-64	8	2	5	5	20	14	3	6	3	26
65-69	17	3	4	3	27	18	4	6	6	34
70-74	22	3	7	0	32	24	5	4	9	42
75-79	27	8	4	4	43	25	8	7	7	42
80-84	24	3	4	5	36	27	2	5	1	35
85+	25	2	7	3	37	15	2	4	2	23

Leukemia's (ICD9 codes 204-208)

	Males					Females				
Age	Toronto	Durham	Peel	York	Total	Toronto	Durham	Peel	York	Total
0-4	0	0	0	0	0	0	0	0	0	0
5-9	1	1	0	0	2	0	0	0	0	0
10-14	1	0	0	0	1	1	0	0	0	1
15-19	1	0	0	0	1	0	0	1	1	2
20-24	1	0	0	0	1	0	0	0	0	0
25-29	0	0	0	1	1	2	0	0	0	2
30-44	2	0	1	0	3	3	0	1	0	4
35-39	2	1	0	0	3	3	0	0	0	3
40-44	2	0	1	0	3	3	1	1	0	5
45-49	2	0	0	0	2	4	0	0	0	4
50-54	2	1	1	0	4	4	1	1	1	7
55-59	0	0	2	1	3	6	0	2	1	9
60-64	4	0	0	1	5	12	1	2	1	16
65-69	9	1	1	0	11	11	2	2	2	17
70-74	9	0	1	2	12	12	3	2	2	19
75-79	12	1	3	1	17	19	2	4	6	31
80-84	9	1	2	2	14	7	2	2	1	12
85+	23	2	3	2	19	13	2	2	2	19

Appendix C continued:
Mortality counts in SWO for Site Specific Cancer (disaggregated by age & sex)

Oral Cavity & Pharynx (ICD9 codes 140-149)

	Males				Females			
Age	Lambton	Essex	Kent	Total	Lambton	Essex	Kent	Total
0-4	0	0	0	0	0	0	0	0
5-9	0	0	0	0	0	0	0	0
10-14	0	0	0	0	0	0	0	0
15-19	0	0	0	0	0	0	0	0
20-24	0	0	0	0	0	0	0	0
25-29	0	0	0	0	0	0	0	0
30-44	0	0	0	0	0	0	0	0
35-39	0	0	0	0	0	1	0	1
40-44	0	0	0	0	0	0	0	0
45-49	1	0	0	1	0	1	0	1
50-54	0	0	0	0	0	0	0	0
55-59	0	0	0	0	0	1	0	1
60-64	0	0	1	1	1	2	0	3
65-69	0	0	1	1	1	2	0	3
70-74	1	0	0	1	1	1	0	2
75-79	0	0	0	0	0	0	0	0
80-84	0	1	0	1	0	0	1	1
85+	0	1	0	1	0	0	0	0

Esophagus (ICD9 code 150)

	Males				Females			
Age	Lambton	Essex	Kent	Total	Lambton	Essex	Kent	Total
0-4	0	0	0	0	0	0	0	0
5-9	0	0	0	0	0	0	0	0
10-14	0	0	0	0	0	0	0	0
15-19	0	0	0	0	0	0	0	0
20-24	0	0	0	0	0	0	0	0
25-29	0	0	0	0	0	0	0	0
30-44	0	0	0	0	0	0	0	0
35-39	0	0	0	0	0	0	0	0
40-44	0	0	0	0	0	0	0	0
45-49	0	0	0	0	0	0	1	1
50-54	0	0	0	0	0	1	0	1
55-59	0	0	0	0	0	0	0	0
60-64	1	0	0	1	1	1	1	3
65-69	0	1	1	2	0	0	1	1
70-74	0	1	0	1	0	2	2	4
75-79	1	1	0	2	0	3	1	4
80-84	0	0	1	1	1	2	0	3
85+	0	1	0	1	1	0	0	1

Appendix C continued:
Mortality counts in SWO for Site Specific Cancer (disaggregated by age & sex)

Middle Ear, Nasal, & Larynx (ICD9 codes 160-161)

	Males				Females			
Age	Lambton	Essex	Kent	Total	Lambton	Essex	Kent	Total
0-4	0	0	0	0	0	0	0	0
5-9	0	0	0	0	0	0	0	0
10-14	0	0	0	0	0	0	0	0
15-19	0	0	0	0	0	0	0	0
20-24	0	0	0	0	0	0	0	0
25-29	0	0	0	0	0	0	0	0
30-44	0	0	0	0	0	0	0	0
35-39	0	0	0	0	0	0	0	0
40-44	0	0	0	0	0	0	0	0
45-49	0	0	0	0	0	0	0	0
50-54	1	1	0	2	0	0	0	0
55-59	0	1	0	1	0	0	0	0
60-64	1	0	1	2	0	1	0	1
65-69	0	1	1	2	0	0	0	0
70-74	0	1	1	2	0	0	0	0
75-79	0	1	0	1	0	0	0	0
80-84	0	0	0	0	0	0	0	0
85+	0	0	0	0	0	0	0	0

Lung, Bronchus, & Trachea (ICD9 codes 162-165)

	Males				Females			
Age	Lambton	Essex	Kent	Total	Lambton	Essex	Kent	Total
0-4	0	0	0	0	0	0	0	0
5-9	0	0	0	0	0	0	0	0
10-14	0	0	0	0	0	0	0	0
15-19	0	0	0	0	0	0	0	0
20-24	0	0	0	0	0	0	0	0
25-29	0	0	0	0	0	0	0	0
30-44	0	0	0	0	0	0	0	0
35-39	0	0	0	0	0	1	0	1
40-44	0	2	0	2	1	1	0	2
45-49	1	2	0	3	1	1	1	3
50-54	2	5	1	8	2	6	2	10
55-59	8	9	5	22	3	9	2	14
60-64	6	13	5	24	7	9	3	19
65-69	12	21	7	40	5	16	3	24
70-74	16	31	9	56	14	15	4	33
75-79	12	21	7	40	6	20	5	31
80-84	9	15	0	24	8	9	3	20
85+	5	10	3	18	2	5	3	10

Appendix C continued:
Mortality counts in SWO for Site Specific Cancer (disaggregated by age & sex)

Lymphomas & Multiple Myelomas (ICD9 codes 200-203)

	Males				Females			
Age	Lambton	Essex	Kent	Total	Lambton	Essex	Kent	Total
0-4	0	0	0	0	0	0	0	0
5-9	0	0	0	0	0	0	0	0
10-14	0	0	0	0	0	0	0	0
15-19	0	1	0	1	0	0	0	0
20-24	0	0	0	0	0	0	0	0
25-29	0	0	0	0	0	0	0	0
30-44	0	0	0	0	0	1	0	1
35-39	0	0	0	0	0	0	0	0
40-44	0	0	0	0	0	0	0	0
45-49	0	1	1	2	0	0	0	0
50-54	0	0	0	0	2	2	0	2
55-59	0	0	0	0	2	3	1	6
60-64	0	2	0	2	1	0	0	1
65-69	1	1	1	3	1	3	0	4
70-74	1	7	0	8	2	4	2	8
75-79	0	5	2	7	2	2	2	6
80-84	0	1	1	2	2	3	1	6
85+	1	2	0	3	1	1	0	2

Leukemia's (ICD9 codes 204-208)

	Males				Females			
Age	Lambton	Essex	Kent	Total	Lambton	Essex	Kent	Total
0-4	0	0	0	0	0	0	0	0
5-9	0	0	0	0	0	0	0	0
10-14	0	0	0	0	0	0	0	0
15-19	0	0	0	0	0	0	0	0
20-24	0	0	0	0	0	0	0	0
25-29	1	1	0	2	0	0	0	0
30-44	0	0	0	0	0	0	1	1
35-39	0	1	0	1	0	0	0	0
40-44	0	0	0	0	1	1	0	2
45-49	0	0	0	0	0	0	0	0
50-54	0	1	0	1	0	0	0	0
55-59	0	1	0	1	1	1	1	3
60-64	0	1	0	1	1	1	1	3
65-69	0	1	0	1	2	2	0	4
70-74	1	2	1	4	0	2	0	3
75-79	0	2	1	3	1	3	1	5
80-84	0	1	2	3	0	1	2	3
85+	1	2	1	4	0	2	1	3

Appendix C continued:
Site Specific Cancer Incidence counts in Toronto (disaggregated by age & sex)

Oral Cavity & Pharynx (ICD9 codes 140-149)

	Males					Females				
Age	Toronto	Durham	Peel	York	Total	Toronto	Durham	Peel	York	Total
0-4	0	0	0	0	0	0	0	0	0	0
5-14	0	0	0	0	0	0	0	1	1	2
15-29	3	0	0	0	3	3	0	1	1	5
30-44	5	5	5	6	21	3	2	8	2	15
45-59	67	10	27	17	121	30	2	6	3	41
60-69	36	2	10	10	58	18	6	1	4	29
70-79	34	6	7	9	56	16	2	3	1	22
80+	15	1	2	0	18	19	0	1	7	27

Esophagus (ICD9 codes 150)

	Males					Females				
Age	Toronto	Durham	Peel	York	Total	Toronto	Durham	Peel	York	Total
0-4	0	0	0	0	0	0	0	0	0	0
5-14	0	0	0	0	0	0	0	0	0	0
15-29	0	0	0	0	0	0	0	0	0	0
30-44	3	2	0	0	5	0	0	0	0	0
45-59	6	2	4	2	14	3	1	0	0	4
60-69	10	6	0	4	20	1	0	3	1	5
70-79	19	3	5	4	31	8	0	2	2	12
80+	6	2	2	2	12	10	2	1	0	13

Middle Ear, Nasal, & Larynx (ICD9 codes 160-161)

	Males					Females				
Age	Toronto	Durham	Peel	York	Total	Toronto	Durham	Peel	York	Total
0-4	0	0	0	0	0	0	0	0	0	0
5-14	0	0	0	0	0	0	0	1	0	1
15-29	0	0	0	0	0	0	0	0	0	0
30-44	2	3	0	0	5	1	0	2	0	3
45-59	14	1	6	3	24	2	1	1	0	4
60-69	21	2	5	9	37	2	0	1	0	3
70-79	20	4	2	4	30	1	1	2	0	4
80+	4	0	4	1	9	0	0	0	1	1

Lung, Bronchus, & Trachea (ICD9 codes 162-165)

	Males					Females				
Age	Toronto	Durham	Peel	York	Total	Toronto	Durham	Peel	York	Total
0-4	1	0	0	0	1	0	0	0	0	0
5-14	0	0	0	1	1	0	0	0	0	0
15-29	1	0	0	0	1	0	0	0	1	1
30-44	29	1	3	3	36	11	5	5	3	24
45-59	128	35	48	41	252	77	29	26	24	156
60-69	221	36	58	42	357	118	28	27	31	204
70-79	251	53	74	36	414	186	38	34	34	292
80+	116	19	17	18	170	97	15	21	17	150

Appendix C continued:
Site Specific Cancer Incidence counts in Toronto (disaggregated by age & sex)

Lymphomas & Multiple Myeloma (ICD9 codes 200-203)

	Males					Females				
Age	Toronto	Durham	Peel	York	Total	Toronto	Durham	Peel	York	Total
0-4	0	0	0	0	0	1	0	2	0	3
5-14	2	0	5	2	4	2	2	0	2	6
15-29	8	3	6	6	23	17	2	10	10	40
30-44	40	8	17	11	76	23	12	12	9	56
45-59	82	19	35	21	157	63	17	19	22	121
60-69	84	10	27	17	138	78	12	16	15	121
70-79	76	21	21	17	135	106	19	23	12	160
80+	61	6	12	3	82	76	11	10	8	105

Leukemia's (ICD9 codes 204-208)

	Males					Females				
Age	Toronto	Durham	Peel	York	Total	Toronto	Durham	Peel	York	Total
0-4	9	0	0	3	12	2	0	2	4	8
5-14	6	2	1	6	20	4	0	0	4	8
15-29	9	2	2	2	15	0	0	4	2	6
30-44	15	2	6	3	26	6	2	4	5	17
45-59	29	5	10	6	45	10	5	5	9	29
60-69	33	10	6	7	56	22	9	5	5	39
70-79	49	3	6	10	68	27	6	6	3	42
80+	24	7	7	3	41	35	3	5	6	49

Site-specific Cancer Incidence Counts in S.W.O (disaggregated by age & sex)

Oral Cavity & Pharynx (ICD9 codes 140-149)

	Males				Females			
Age	Lambton	Essex	Kent	Total	Lambton	Essex	Kent	Total
0-4	0	0	0	0	0	0	0	0
5-14	0	0	0	0	0	0	0	0
15-29	0	1	0	1	0	1	0	1
30-44	0	1	1	2	0	1	1	2
45-59	8	17	2	27	2	5	2	9
60-69	2	10	2	14	0	2	0	2
70-79	0	9	4	13	1	5	1	7
80+	0	1	1	2	1	4	0	5

Esophagus (ICD9 code 150)

	Males				Females			
Age	Lambton	Essex	Kent	Total	Lambton	Essex	Kent	Total
0-4	0	0	0	0	0	0	0	0
5-14	0	0	0	0	0	0	0	0
15-29	0	0	0	0	0	0	0	0
30-44	0	0	0	0	0	0	0	0
45-59	1	4	1	6	0	0	0	0
60-69	0	3	0	3	1	1	3	5
70-79	0	3	2	5	0	1	0	1
80+	1	0	0	1	0	1	0	1

Appendix C continued:
Site-specific Cancer Incidence Counts in S.W.O (disaggregated by age & sex)

Middle Ear, Nasal, & Larynx (ICD9 codes 160-161)

	Males				Females			
Age	Lambton	Essex	Kent	Total	Lambton	Essex	Kent	Total
0-4	0	0	0	0	0	0	0	0
5-14	0	0	0	0	0	0	0	0
15-29	0	0	0	0	0	1	0	1
30-44	0	0	1	1	2	3	0	5
45-59	0	1	1	2	0	0	0	0
60-69	2	5	2	9	0	0	1	1
70-79	0	3	1	4	0	1	1	2
80+	2	0	0	2	1	0	0	1

Lung, Bronchus & Trachea (ICD9 codes 162-165)

	Males				Females			
Age	Lambton	Essex	Kent	Total	Lambton	Essex	Kent	Total
0-4	0	0	0	0	0	1	0	1
5-14	0	0	0	0	0	0	0	0
15-29	0	1	0	1	0	1	0	1
30-44	0	1	2	3	2	3	0	5
45-59	13	19	12	44	6	27	13	46
60-69	17	45	20	82	11	28	12	51
70-79	15	47	27	89	9	25	25	59
80+	1	16	10	27	12	18	8	38

Lymphomas & Multiple Myeloma (ICD9 codes 200-203)

	Males				Females			
Age	Lambton	Essex	Kent	Total	Lambton	Essex	Kent	Total
0-4	0	0	0	0	0	0	0	0
5-14	0	1	0	1	0	2	0	2
15-29	0	3	1	4	0	1	0	1
30-44	1	4	2	7	0	7	1	8
45-59	1	11	1	13	0	9	2	11
60-69	7	8	6	21	2	10	7	19
70-79	7	11	6	24	4	15	2	21
80+	1	2	1	7	2	5	2	9

Leukemias (ICD9 codes 204-208)

	Males				Females			
Age	Lambton	Essex	Kent	Total	Lambton	Essex	Kent	Total
0-4	0	1	2	3	0	0	0	0
5-14	0	1	0	1	0	2	1	3
15-29	1	1	0	2	0	0	0	0
30-44	0	1	1	2	0	1	1	2
45-59	3	8	0	11	2	3	0	5
60-69	1	5	2	8	2	4	0	6
70-79	1	8	0	9	2	3	2	7
80+	2	2	1	5	1	5	2	8

Appendix D

Current Canadian Cohort Life Expectancy for Males and Females: by 5-year age group

Age Group	Males	Females
0	**77.8**	**82.6**
1-4	**77.2**	**81.9**
5-9	**73.3**	**78.0**
10-14	**68.3**	**73.0**
15-19	**63.4**	**68.1**
20-24	**58.6**	**63.2**
25-29	**53.8**	**58.3**
30-34	**49.0**	**53.4**
35-39	**44.2**	**48.5**
40-44	**39.4**	**43.6**
45-49	**34.7**	**38.8**
50-54	**30.1**	**34.2**
55-59	**25.7**	**29.6**
60-64	**21.5**	**25.2**
65-69	**17.6**	**21.0**
70-74	**14.0**	**17.0**
75-79	**10.8**	**13.3**
80-84	**8.1**	**10.1**
85-89	**5.9**	**7.3**
90-94	**4.2**	**5.1**
95-99	**2.9**	**3.4**
100+	**2.1**	**2.4**

Appendix E1

Derivation of Average Duration of Primary Therapy considering medical severity at diagnosis and duration of treatment regime

Site-specific Cancer	Severity at Diagnosis	Treatment Regime Progression (% cases x duration)[1]	Duration (years)
Oral Cavity & Pharynx	Local	In-patient surgery (70% x 0.077) + mild chemo (3% x 0.5) + moderate chemo (13% x 0.346) + radiotherapy (4% x 0.096)	0.118
	Regional	Inpatient surgery (70% x 0.077) + mild chemo (18% x 0.5) + moderate chemo (22% x 0.346) + curative radiotherapy (2% x 0.077)	0.221
	Distant	Inpatient surgery (41% x 0.077) + moderate chemo (15% x 0.5) + severe chemo (28% x 0.192) + palliative radiotherapy (9% x 0.067)	0.169
Esophagus	Local	In-patient surgery (62% x 0.077) + mild chemo (12% x 0.5) + moderate chemo (13% x 0.375) + radiotherapy (25% x 0.077)	0.177
	Regional	In-patient surgery (40% x 0.077) + mild chemo (17% x 0.167) + moderate chemo (36% x 0.25) + radiotherapy (46% x 0.077)	0.184
	Distant	In-patient surgery (10% x 0.077) + mild chemo (14% x 0.5) + moderate chemo (31% x 0.375) + palliative radiotherapy (25% x 0.064)	0.210
Middle Ear, Nasal, & Larynx	Local	In-patient surgery (70% x 0.077) + mild chemo (3% x 0.5) + moderate chemo (13% x 0.346) + radiotherapy (4% x 0.096)	0.118
	Regional	In-patient surgery (70% x 0.077) + mild chemo (18% x 0.5) + moderate chemo (22% x 0.346) + radiotherapy (2% x 0.077)	0.221
	Distant	In-patient surgery (41% x 0.077) + moderate chemo (15% x 0.5) + severe chemo (28% x 0.192) + palliative radiotherapy (9% x 0.067)	0.167
Lung, Bronchus, & Trachea	Local	In-patient surgery (65% x 0.077) + moderate chemo (8% x 0.25) + radiotherapy (23% x 0.096)	0.092
	Regional	In-patient surgery (16% x 0.077) + moderate chemo (56% x 0.25) + radiotherapy (59% x 0.096)	0.210
	Distant	Chemo (49% x 0.25) + palliative radiotherapy (47% x 0.058)	0.150
Lymphomas & Multiple Myeloma[2]	Local	NHL: Inpatient surgery (13% x 0.096) + moderate chemo (39% x 0.346) + radiotherapy (13% x 0.096) HL: Inpatient surgery (33% x 0.077) + outpatient surgery (42% x 0.077) + moderate chemo (12% x 0.417) + radiotherapy (29% x 0.089) MM: Inpatient surgery (62% x 0.077) + mild chemo (12% x 0.5) + moderate chemo (13% x 0.375) + radiotherapy (25% x 0.077)	0.158
	Regional	NHL: in/out-patient surgery (21% x 0.077) + moderate chemo (65% x 0.346) + radiotherapy (3% x 0.096) HL: inpatient surgery (54% x 0.077) + outpatient surgery (54% x 0.077) + moderate chemo (28% x 0.417) + radiotherapy (33% x 0.089) MM: inpatient surgery (40% x 0.077) + mild chemo (17% x 0.5) + moderate chemo (36% x 0.375) + radiotherapy (46% x 0.077)	0.245
	Distant	NHL: inpatient surgery (15% x 0.077) + severe chemo (61% x 0.346) + palliative radiotherapy (4% x 0.096) HL: inpatient surgery (20% x 0.077) + outpatient surgery (19% x 0.077) + moderate chemo (28% x 0.417) + curative radiotherapy (16% x 0.115) + palliative radiotherapy (15% x 0.077) MM: inpatient surgery (10% x 0.077) + mild chemo (14% x 0.5) + moderate chemo (31% x 0.375) + palliative radiotherapy (25% x 0.064)	0.204
Leukemias	Local	In-patient surgery (10% x 0.077) + mild chemo (100% x 0.5)	0.5077
	Regional	In-patient surgery (10% x 0.077) + mild chemo (100% x 0.5)	0.5077
	Distant	No cases diagnosed at this stage	0

[1] Treatment regime is assumed to progress from: (in, out patient) surgery, (mild, moderate, severe) chemotherapy, (curative, palliative) radiotherapy.

[2] Lyphomas and Multiple Myelomas: considered different treatment regimes for Non-hodgkins (NHL), Hodgkins (HL), and Multiple Myeloma (MM). Duration of primary therapy by severity is an average of the three cancers treatment progressions.
Local: NHL/HL/MM averaged = (0.164+0.133+0.176/3) 0.158
Regional: NHL/HL/MM averaged = (0.244+0.205+0.286/3) 0.245
Distant: NHL/HL/MM averaged = (0.226+0.177+0.21/3) 0.204

Appendix E2

Derivation of Average Duration of Primary Therapy considering age distribution of stage at diagnosis

		Males			Females		
Disease	Age	Local	Regional	Distant	Local	Regional	Distant
ICD 140-149	0-4	31.8	56.5	11.8	45.9	45.9	8.2
	5-14	31.8	56.5	11.8	45.9	45.9	8.2
	15-29	31.8	56.5	11.8	45.9	45.9	8.2
	30-44	31.8	56.5	11.8	45.9	45.9	8.2
	45-59	30.5	57.5	12.1	41.2	49.8	9.1
	60-69	29.9	58	12.2	38.8	51.7	9.5
	70-79	36.8	51.2	12	44.8	45.1	10.1
	80+	36.8	51.2	12	44.8	45.1	10.1
ICD 150	0-4	23.2	33	43.8	14	38	48
	5-14	23.2	33	43.8	14	38	48
	15-29	23.2	33	43.8	14	38	48
	30-44	23.2	33	43.8	14	38	48
	45-59	24.6	35.3	40.1	24	37.3	38.7
	60-69	25.3	36.4	38.3	29	37	34
	70-79	34.5	33.7	31.8	39.7	33.6	26.8
	80+	34.5	33.7	31.8	39.7	33.6	26.8
ICD 160-161	0-4	43.4	52.9	3.7	36.6	57.4	5.9
	5-14	43.4	52.9	3.7	36.6	57.4	5.9
	15-29	43.4	52.9	3.7	36.6	57.4	5.9
	30-44	43.4	52.9	3.7	36.6	57.4	5.9
	45-59	44.6	51.2	4.4	38.7	57.9	3.3
	60-69	45.2	50.4	4.4	39.8	58.2	2
	70-79	51.8	45.2	2.9	43.9	51.9	4.2
	80+	51.8	45.2	2.9	43.9	51.9	4.2
ICD 162-165	0-4	11.9	35.7	52.5	16.1	35.1	48.8
	5-14	11.9	35.7	52.5	16.1	35.1	48.8
	15-29	11.9	35.7	52.5	16.1	35.1	48.8
	30-44	11.9	35.7	52.5	16.1	35.1	48.8
	45-59	13.3	38.7	48	18	36.8	45.1
	60-69	14	40.2	45.8	18.9	37.7	43.3
	70-79	18.2	44.1	37.8	20.9	43	36.1
	80+	18.2	44.1	37.8	20.9	43	36.1
ICD 200-203	0-4	23.7	17.9	58.4	21.5	24	54.5
	5-14	23.7	17.9	58.4	21.5	24	54.5
	15-29	23.7	17.9	58.4	21.5	24	54.5
	30-44	23.7	17.9	58.4	21.5	24	54.5
	45-59	22	13.7	64.2	22.8	18.4	58.8
	60-69	21.2	11.7	66.1	23.5	15.6	61
	70-79	20.2	13.8	66.1	21.6	15	63.5
	80+	20.2	13.8	66.1	21.6	15	63.5
ICD 204-208	0-4	44	56	0	44	56	0
	5-14	44	56	0	44	56	0
	15-29	44	56	0	44	56	0
	30-44	44	56	0	44	56	0
	45-59	44	56	0	44	56	0
	60-69	44	56	0	44	56	0
	70-79	44	56	0	44	56	0
	80+	44	56	0	44	56	0

Appendix E3

Average Duration of Primary Therapy (age & sex disaggregated)[1]

Site-Specific Cancer	Age Group	Males	Females	Site-Specific Cancer	Age Group	Males	Females
140-149 Oral Cavity & Pharynx	0-4	0.182	0.169	162-165 Lung, Bronchus, & Trachea	0-4	0.165	0.163
	5-14	0.182	0.169		5-14	0.165	0.163
	15-29	0.182	0.169		15-29	0.165	0.163
	30-44	0.182	0.169		30-44	0.165	0.163
	45-59	0.183	0.174		45-59	0.166	0.162
	60-69	0.184	0.176		60-69	0.166	0.162
	70-79	0.176	0.170		70-79	0.160	0.164
	80+	0.176	0.170		80+	0.160	0.164
150 Esophagus	0-4	0.194	0.196	200-203 Lymphomas & Multiple Myeloma	0-4	0.200	0.204
	5-14	0.194	0.196		5-14	0.200	0.204
	15-29	0.194	0.196		15-29	0.200	0.204
	30-44	0.194	0.196		30-44	0.200	0.204
	45-59	0.193	0.192		45-59	0.199	0.201
	60-69	0.192	0.191		60-69	0.197	0.199
	70-79	0.190	0.188		70-79	0.201	0.201
	80+	0.190	0.188		80+	0.201	0.201
160-161 Middle Ear, Nasal, & Larynx	0-4	0.174	0.180	204-208 Leukemias	0-4	0.508	0.508
	5-14	0.174	0.180		5-14	0.508	0.508
	15-29	0.174	0.180		15-29	0.508	0.508
	30-44	0.174	0.180		30-44	0.508	0.508
	45-59	0.173	0.179		45-59	0.508	0.508
	60-69	0.172	0.179		60-69	0.508	0.508
	70-79	0.166	0.174		70-79	0.508	0.508
	80+	0.166	0.174		80+	0.508	0.508

[1] determined as a weighted average of case distribution and treatment by stage

Appendix F

1, 3, 10 Year Relative Survival Rates for Site-specific Cancer, disaggregated by sex

Oral Cavity & Pharynx (ICD9 codes 140-149)

	Males				Females			
Age	1-yr	3-yr	5-yr	10-yr	1-yr	3-yr	5-yr	10-yr
0-4	85.6	60.1	54.6	43.7	87.8	75.3	69.1	69.1
5-14	97.2	91.1	89.7	82.0	95.3	82.9	76.9	76.9
15-29	92.2	83.5	81.6	78.3	95.4	90.0	86.4	86.4
30-44	89.9	77.3	73.8	68.1	93.3	82.5	72.7	72.7
45-59	83.6	64.8	58.7	49.1	86.6	70.8	57.0	57.0
60-69	80.0	62.4	55.5	46.4	82.6	65.8	49.2	49.2
70-79	79.5	64.7	59.0	52.7	77.4	92.6	47.4	47.4
80+	75.4	64.8	59.9	52.9	69.7	56.9	51.4	51.4

Esophagus (ICD9 code 150)

	Males				Females			
Age	1-yr	3-yr	5-yr	10-yr	1-yr	3-yr	5-yr	10-yr
0-4	n/a	n/a	n/a	n/a	100	100	100	100
5-14	n/a	n/a	n/a	n/a	50.0	50.0	50.0	50.0
15-29	52.7	47.4	47.4	47.4	66.7	66.7	66.7	66.7
30-44	44.9	20.0	16.6	14.0	48.2	44.7	44.7	42.2
45-59	40.1	16.3	12.9	9.6	25.5	22.6	22.6	19.6
60-69	36.7	15.5	12.0	9.0	20.0	16.3	16.3	11.7
70-79	35.1	15.2	11.6	9.4	19.6	16.6	16.6	13.1
80+	25.7	11.4	9.1	9.0	11.2	10.1	10.1	8.2

Middle Ear, Nasal, & Larynx (ICD9 codes 160-161)

	Males				Females			
Age	1-yr	3-yr	5-yr	10-yr	1-yr	3-yr	5-yr	10-yr
0-4	87.6	43.9	43.9	43.9	75.1	50.1	50.1	25.1
5-14	69.2	69.2	61.1	61.1	85.7	85.7	85.7	85.7
15-29	91.4	81.2	78.2	76.8	93.7	82.9	80.6	80.6
30-44	90.9	77.7	72.4	65.5	94.5	85.9	84.3	79.1
45-59	88.4	73.4	67.3	59.5	88.7	76.9	70.7	59.8
60-69	87.6	71.1	65.8	55.2	86.5	73.1	65.6	57.0
70-79	82.7	66.3	59.9	46.6	80.1	66.1	59.4	48.6
80+	75.0	59.2	54.1	53.7	69.8	59.7	57.6	50.7

Lung, Bronchus, & Trachea (ICD9 codes 162-165)

	Males				Females			
Age	1-yr	3-yr	5-yr	10-yr	1-yr	3-yr	5-yr	10-yr
0-4	86.5	81.2	79.5	79.5	100	98.0	92.9	92.9
5-14	85.2	69.0	64.8	64.8	87.9	81.1	74.4	74.4
15-29	66.7	53.5	51.0	49.7	75.5	62.3	60.6	58.1
30-44	43.2	24.8	22.1	20.0	49.8	29.2	26.3	22.7
45-59	40.3	20.4	16.9	13.5	47.5	26.1	21.8	17.5
60-69	37.8	18.4	14.6	10.7	43.9	23.2	18.4	13.6
70-79	32.3	14.8	11.3	8.8	36.5	18.9	14.5	11.2
80+	24.7	10.4	8.2	8.0	27.8	15.2	12.0	11.1

Appendix F continued:
1, 3, 10 Year Relative Survival Rates for Site-specific Cancer, disaggregated by sex

Lymphoma's and Multiple Myeloma (ICD9 codes 200-203)

	Males				Females			
Age	1-yr	3-yr	5-yr	10-yr	1-yr	3-yr	5-yr	10-yr
0-4	79.1	70.2	68.3	66.1	75.1	62.9	55.9	55.9
5-14	87.8	78.9	76.3	71.3	89.5	81.3	79.0	75.7
15-29	90.0	81.8	78.2	73.6	95.2	89.9	87.3	83.4
30-44	83.3	72.1	67.2	59.1	90.7	81.4	76.2	67.8
45-59	80.3	65.1	56.1	42.4	85.0	71.0	62.4	49.8
60-69	73.0	54.3	43.8	30.1	78.0	59.7	50.2	37.3
70-79	62.3	43.9	33.7	23.5	67.2	48.1	38.2	27.8
80+	49.6	34.4	26.6	23.1	52.1	35.8	27.9	22.4

Leukemia's (ICD9 codes 204-208)

	Males				Females			
Age	1-yr	3-yr	5-yr	10-yr	1-yr	3-yr	5-yr	10-yr
0-4	84.2	64.1	56.1	51.4	80.1	63.3	59.4	56.5
5-14	80.6	60.8	52.5	47.2	83.1	62.5	55.8	51.0
15-29	69.0	45.1	36.2	32.1	73.3	48.6	43.5	36.8
30-44	70.7	51.3	43.8	33.3	69.5	51.5	45.0	35.7
45-59	73.4	58.1	50.2	35.3	68.1	52.0	45.8	35.9
60-69	64.7	49.9	41.5	29.0	66.7	52.7	46.0	33.0
70-79	53.4	40.0	33.1	23.5	56.7	43.1	35.4	25.7
80+	42.9	31.3	24.7	21.8	41.9	30.4	23.1	21.0

Appendix G

Mean Survival Duration for Non-Survivors (LNS) by Site-specific Cancer

	Oral Cavity & Pharynx	Esophagus	Middle Ear, Nasal, & Larynx	Lung, Bronchus, & Trachea	Lymphomas & Multiple Myeloma	Leukemia
Males						
0-4	4.52	n/a	n/a	2.1	2.54	4.37
5-14	8.78	n/a	n/a	2.95	4.73	4.43
15-29	4.16	n/a	3.60	2.04	5.50	3.62
30-44	4.59	2.09	5.50	1.76	5.96	4.89
45-59	5.09	2.03	5.49	1.94	7.86	7.34
60-69	5.19	1.87	5.93	1.93	6.61	5.94
70-79	4.55	1.74	6.62	1.59	5.02	3.73
80+	4.74	1.79	2.75	1.13	2.55	1.77
Females						
0-4	3.73	n/a	5.69	n/a	3.08	3.24
5-14	4.04	n/a	n/a	4.74	4.15	4.08
15-29	4.07	n/a	3.03	2.48	6.72	3.58
30-44	5.44	2.81	5.02	2.15	7.81	4.48
45-59	5.25	2.14	7.75	2.33	8.07	4.64
60-69	5.61	2.14	6.57	2.32	6.55	5.93
70-79	5.30	1.81	6.47	1.82	5.24	4.24
80+	2.45	1.29	3.18	1.11	3.04	1.71

n/a because no diagnosed incidence cases in the specific age-sex grouping

Appendix H1

Average Duration of Remission Stage for Survivors for Site-specific Cancer (disaggregated by age & sex)[1]

Site-Specific Cancer	Age Group	Males	Females	Site-Specific Cancer	Age Group	Males	Females
140-149 Oral Cavity & Pharynx	0-4	4.818	4.831	162-165 Lung, Bronchus, & Trachea	0-4	4.835	4.837
	5-14	4.818	4.831		5-14	4.835	4.837
	15-29	4.818	4.831		15-29	4.835	4.837
	30-44	4.818	4.831		30-44	4.835	4.837
	45-59	4.817	4.826		45-59	4.834	4.838
	60-69	4.816	4.824		60-69	4.834	4.838
	70-79	4.824	4.830		70-79	4.840	4.836
	80+	4.824	4.830		80+	4.840	4.836
150 Esophagus	0-4	4.806	4.804	200-203 Lymphomas & Multiple Myeloma	0-4	4.800	4.796
	5-14	4.806	4.804		5-14	4.800	4.796
	15-29	4.806	4.804		15-29	4.800	4.796
	30-44	4.806	4.804		30-44	4.800	4.796
	45-59	4.807	4.808		45-59	4.801	4.799
	60-69	4.808	4.809		60-69	4.803	4.801
	70-79	4.810	4.812		70-79	4.799	4.799
	80+	4.810	4.812		80+	4.799	4.799
160-161 Middle Ear, Nasal, & Larynx	0-4	4.826	4.820	204-208 Leukemia's	0-4	4.492	4.492
	5-14	4.826	4.820		5-14	4.492	4.492
	15-29	4.826	4.820		15-29	4.492	4.492
	30-44	4.826	4.820		30-44	4.492	4.492
	45-59	4.827	4.821		45-59	4.492	4.492
	60-69	4.828	4.821		60-69	4.492	4.492
	70-79	4.834	4.826		70-79	4.492	4.492
	80+	4.834	4.826		80+	4.492	4.492

[1] Remission Survivors = (5 years – duration of primary therapy)

Appendix H2

Average Duration Remission Stage of Site-specific Cancer for Non-survivors (disaggregated by age & sex)[1]

Site-Specific Cancer	Age Group	Males	Females	Site-Specific Cancer	Age Group	Males	Females
140-149 Oral Cavity & Pharynx	0-4	3.834	3.060	162-165 Lung, Bronchus, & Trachea	0-4	1.435	4.810
	5-14	8.094	3.366		5-14	2.284	4.180
	15-29	3.482	3.397		15-29	1.379	1.837
	30-44	3.904	4.770		30-44	1.092	1.500
	45-59	4.406	4.580		45-59	1.270	1.667
	60-69	4.509	4.934		60-69	1.265	1.655
	70-79	3.869	4.633		70-79	0.934	1.156
	80+	4.048	1.780		80+	0.469	0.446
150 Esophagus	0-4	n/a	n/a	200-203 Lymphomas & Multiple Myeloma	0-4	1.835	2.371
	5-14	n/a	n/a		5-14	4.035	3.446
	15-29	n/a	n/a		15-29	4.810	6.012
	30-44	1.398	2.110		30-44	5.295	7.107
	45-59	1.341	1.450		45-59	7.156	7.369
	60-69	1.181	1.450		60-69	5.917	5.834
	70-79	1.049	1.122		70-79	4.316	4.534
	80+	1.097	0.607		80+	1.848	2.334
160-161 Middle Ear, Nasal, & Larynx	0-4	n/a	5.010	204-208 Leukemia's	0-4	3.361	2.229
	5-14	n/a	5.010		5-14	3.425	3.068
	15-29	2.930	2.346		15-29	2.616	2.568
	30-44	4.827	4.336		30-44	3.885	3.474
	45-59	4.822	7.068		45-59	6.326	3.636
	60-69	5.262	5.893		60-69	4.934	4.919
	70-79	5.955	5.797		70-79	2.720	3.229
	80+	2.085	2.510		80+	0.762	0.706

[1] Median survival time Non-survivors = LNS - D_{TR} - D_M - D_T; where LNS = average survival time for non-survivors, D_{TR} = duration of primary therapy, D_M = duration of metastasis, D_T = duration of terminal period

Appendix I

Estimates of DALY's / 100,000 with Alternative Value Choices by Age-Distribution

Oral Cavity & Pharynx Cancers (DALY's per 100,000)				
	K=0, r=0	**K=1, r=0**	**K=0, r=0.03**	**K=1, r=0.03**
S.W.O				
0-4	0	0	0	0
5-14	0	0	0	0
15-29	0.83	1.26	0.77	1.18
30-44	38.80	36.11	21.76	22.61
45-59	119.49	100.02	84.59	75.11
60-69	396.50	252.05	302.25	206.28
70-79	162.63	90.72	137.68	77.72
80+	161.14	69.96	144.04	62.76
Toronto				
0-4	0	0	0	0
5-14	0.16	0.20	0.15	0.19
15-29	5.77	6.24	3.09	3.77
30-44	19.03	18.01	11.10	11.89
45-59	101.09	80.16	69.83	58.77
60-69	241.37	152.01	186.06	122.53
70-79	207.16	110.71	174.09	94.08
80+	215.21	91.67	193.02	82.46

Esophagus Cancers (DALY's per 100,000)				
	K=0, r=0	**K=1, r=0**	**K=0, r=0.03**	**K=1, r=0.03**
S.W.O				
0-4	0	0	0	0
5-14	0	0	0	0
15-29	0	0	0	0
30-44	0	0	0	0
45-59	70.26	55.90	45.64	38.96
60-69	330.93	211.95	251.38	174.27
70-79	394.38	207.57	328.82	175.01
80+	268.38	116.10	238.73	103.65
Toronto				
0-4	0	0	0	0
5-14	0	0	0	0
15-29	0	0	0	0
30-44	21.82	19.83	12.27	12.34
45-59	96.77	72.16	63.90	50.41
60-69	241.03	151.97	181.44	125.47
70-79	256.56	136.97	214.93	115.96
80+	217.79	91.54	197.06	83.01

Appendix I continued:
Estimates of DALY's / 100,000 with Alternative Value Choices by Age-Distribution

Middle Ear, Nasal, & Larynx Cancers (DALY's per 100,000)				
	K=0, r=0	**K=1, r=0**	**K=0, r=0.03**	**K=1, r=0.03**
S.W.O				
0-4	0	0	0	0
5-14	0	0	0	0
15-29	0.48	0.73	0.45	0.68
30-44	2.37	3.18	2.21	2.97
45-59	76.93	59.21	53.35	42.84
60-69	228.86	149.53	177.17	136.05
70-79	108.95	60.14	93.27	51.90
80+	12.74	5.67	12.02	5.36
Toronto				
0-4	0	0	0	0
5-14	0.07	0.09	0.07	0.08
15-29	0	0	0	0
30-44	10.19	9.34	6.04	6.06
45-59	41.52	32.44	28.93	23.63
60-69	81.53	53.91	64.32	52.41
70-79	74.94	41.03	64.31	35.50
80+	52.51	22.42	47.16	20.19

Lung, Bronchus, & Trachea Cancers (DALY's per 100,000)				
	K=0, r=0	**K=1, r=0**	**K=0, r=0.03**	**K=1, r=0.03**
S.W.O				
0-4	1.66	1.08	1.55	1.00
5-14	0	0	0	0
15-29	1.53	2.33	1.45	2.20
30-44	167.97	150.82	99.12	97.66
45-59	1646.94	1243.88	1137.00	902.33
60-69	4759.18	3031.41	3681.77	2613.48
70-79	5615.65	3020.53	4732.04	2571.88
80+	3316.34	1426.34	2953.23	1275.06
Toronto				
0-4	0.22	0.14	0.21	0.13
5-14	0.13	0.16	0.12	0.15
15-29	6.04	6.19	3.01	3.55
30-44	96.23	87.83	56.33	56.66
45-59	1000.02	764.89	685.21	550.77
60-69	2784.13	1770.67	2159.15	1539.86
70-79	3337.43	1789.05	2821.21	1527.89
80+	2499.82	1065.14	2232.68	954.58

Appendix I continued:
Estimates of DALY's / 100,000 with Alternative Value Choices by Age-Distribution

Lymphomas & Multiple Myeloma's (DALY's per 100,000)				
	K=0, r=0	**K=1, r=0**	**K=0, r=0.03**	**K=1, r=0.03**
S.W.O				
0-4	0	0	0	0
5-14	1.95	2.42	1.82	2.25
15-29	2.11	3.21	1.97	2.99
30-44	48.09	48.96	27.65	31.78
45-59	299.39	226.31	204.13	162.75
60-69	514.82	331.97	409.03	287.60
70-79	1115.56	600.70	942.42	512.73
80+	608.14	262.52	544.75	235.92
Toronto				
0-4	0.71	0.43	0.66	0.41
5-14	35.52	38.07	15.52	18.53
15-29	15.89	18.19	8.38	11.09
30-44	74.54	71.48	43.87	46.61
45-59	276.73	213.48	190.90	155.76
60-69	676.73	433.84	525.45	367.85
70-79	891.93	477.37	756.71	409.12
80+	934.82	400.44	839.44	360.73

Leukemia (DALY's per 100,000)				
	K=0, r=0	**K=1, r=0**	**K=0, r=0.03**	**K=1, r=0.03**
S.W.O				
0-4	7.73	4.95	7.24	4.59
5-14	4.63	5.72	4.34	5.35
15-29	97.53	103.49	50.50	60.21
30-44	143.73	132.06	81.01	82.31
45-59	143.96	108.21	102.88	81.22
60-69	443.89	280.71	338.96	229.02
70-79	545.17	290.20	460.29	247.53
80+	559.32	236.92	503.35	213.80
Toronto				
0-4	5.44	3.44	5.10	3.20
5-14	47.80	54.71	22.05	27.96
15-29	33.05	35.75	16.46	20.49
30-44	79.05	74.75	45.10	47.20
45-59	105.82	81.77	72.09	58.90
60-69	310.63	197.73	239.22	161.97
70-79	424.93	244.71	359.52	192.11
80+	413.60	174.38	374.27	158.21