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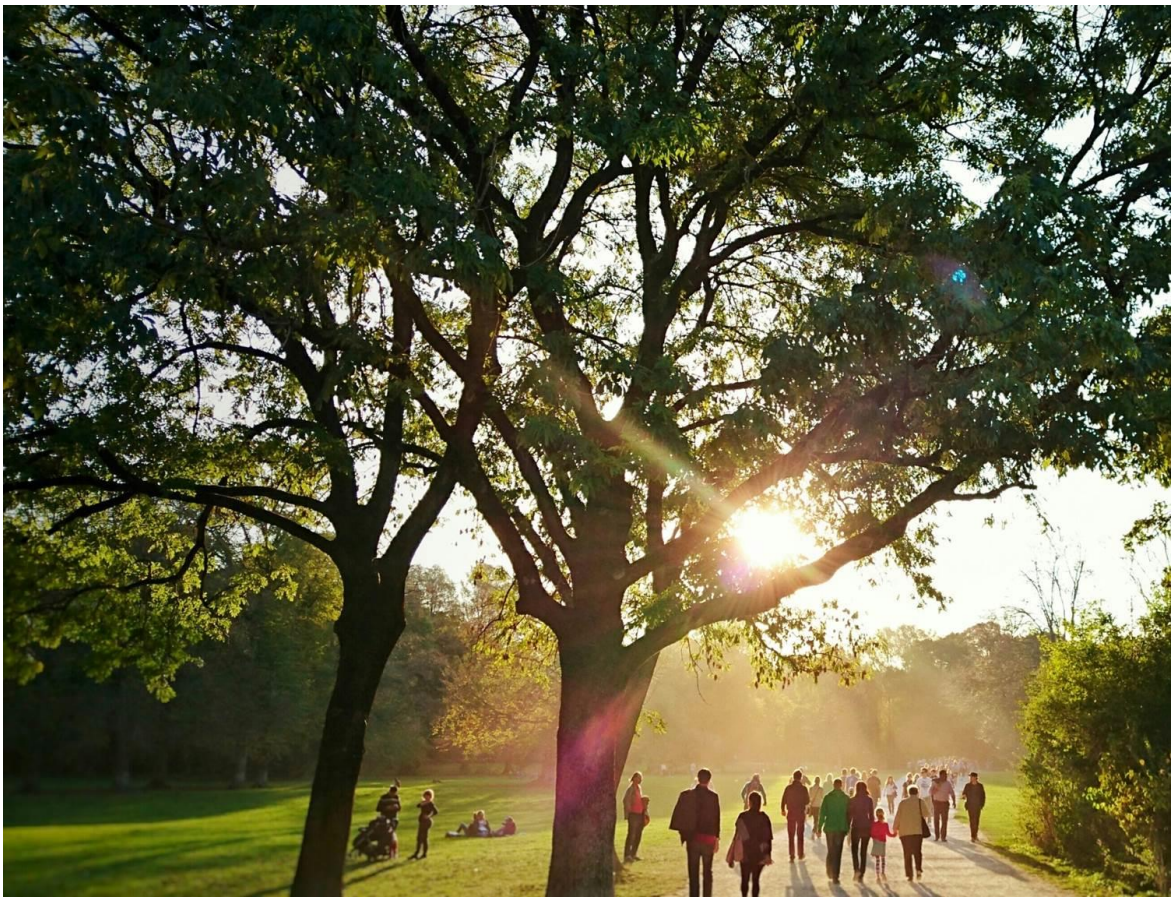

Environmental Burden of Cancer in Ontario

Technical Supplement
August 2016

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Disclaimer

This document was developed by Public Health Ontario (PHO). PHO provides scientific and technical advice to Ontario's government, public health organizations and health care providers. PHO's work is guided by the current best available evidence.

PHO assumes no responsibility for the results of the use of this document by anyone.

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Foreword

This technical supplement includes the concentration inputs and specifies the equations to estimate the *Environmental Burden of Cancer in Ontario*. An external Advisory Committee provided input on the development of the report, and researchers from the McLaughlin Centre reviewed the details on the probabilistic estimation.

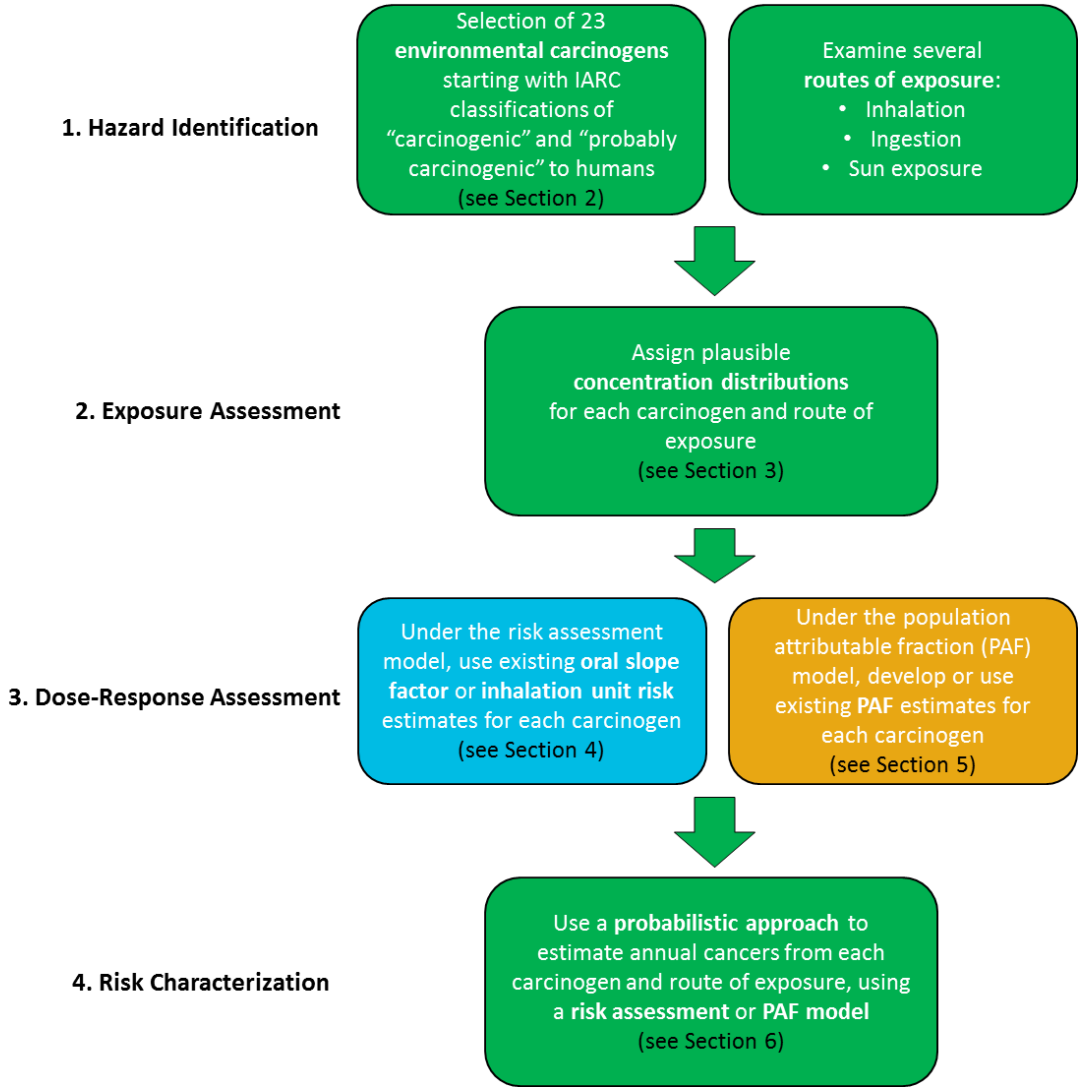
This document contains the methods and inputs used to estimate the environmental burden of cancer from 23 carcinogens in Ontario. We employed a probabilistic, rather than deterministic, approach to estimate a plausible range for the burden using a risk assessment (RA) or population attributable fraction (PAF) model, as appropriate. The main inputs were plausible ranges for concentration (in air, food, drinking water, and dust) and cancer potency (for the inhalation or ingestion routes of exposure), as well as point estimates for population or cancer incidence.

The Environmental and Occupational Health team of Public Health Ontario provides scientific and technical advice and support to the health care system and the Government of Ontario. For more information related to this technical supplement, please email eoh@oahpp.ca.

1. Overview of Approach

This section provides a high-level overview of the approach to estimate the environmental burden of cancer for Ontario. We followed a four-step risk assessment framework (see Figure 1).

Figure 1. Overview of risk assessment framework applied to estimate the environmental burden of cancer in Ontario



Hazard identification: Carcinogen selection and routes of exposure

The final list of environmental carcinogens for consideration was developed starting with the 188 Group 1 and 2A carcinogens classified by the International Agency for Research on Cancer (IARC). Carcinogens were excluded when exposure was deemed: unlikely to occur through environmental sources, not relevant to the general Ontario population, or unable to be quantified.

We categorized the final list of 23 environmental carcinogens into five chemical groupings for ease of presentation:

Combustion by-products
- fine particulate matter ($PM_{2.5}$)†
- diesel engine exhaust† (DEE, one component of $PM_{2.5}$)
- second-hand tobacco smoke (SHS) †
- polycyclic aromatic hydrocarbons (PAHs)
- 2,3,7,8-tetrachlorodibenzo-para-dioxin (TCDD)

Radiation
- radon†
- ultraviolet (UV) radiation†

Metals
- arsenic (As)
- cadmium (Cd)
- chromium (Cr)
- nickel (Ni)

Volatile Organic Compounds
- 1,2-dichloropropane (DCP)
- 1,3-butadiene
- alpha-chlorinated toluenes
- benzene
- dichloromethane (DCM)
- formaldehyde
- trichloroethylene (TCE)
- tetrachloroethylene (PCE)
- vinyl chloride (VC)

Other
- acrylamide
- asbestos
- polychlorinated biphenyls (PCBs)

† indicates a population attributable fraction (PAF) method was applied (otherwise a risk assessment (RA) method was applied)

We considered three routes of exposure:

- Inhalation of indoor air and outdoor air
- Ingestion of food, drinking water, and indoor dust
- Dermal contact of sunlight

See Section 2 for the description of the carcinogen selection process.

Exposure assessment: Assigning concentration distributions

Based on government-collected monitoring data or specific studies, we developed concentration distributions to help characterize exposure to the carcinogens in indoor air, outdoor air, food, drinking water, or dust. Examples of distribution types are: normal, log-normal, and discrete probability. Point estimates were also employed when indicated by the data (e.g., all measured levels for a carcinogen were the same value).

See Section 3 for a description of the concentration data sources and how the distributions were assigned to the concentration data.

Dose-response assessment: Identifying slope factors and relative risks

Dose-response estimates relate the risk (response) of developing cancer with the exposure (dose) to the carcinogen. They provide an indication of the cancer potency of the substance. Examples are oral slope factors and relative risks. These values were obtained from credible institutions and published studies.

See Section 6 for the slope factor and relative risk inputs

Risk characterization: Probabilistic approach applying two models

We employed a probabilistic approach that estimates a distribution (plausible range) of burden results. The results distribution can be summarized by a mean (or central) estimate, along with lower and upper bounds, such as the 5^{th} and 95^{th} percentile estimates. This is in contrast to a deterministic approach, which provides just one point estimate.

See Section 6 for a description of the probabilistic approach and inputs.

Our preference was to apply a risk assessment (RA) model to all carcinogens. However, we were able to locate suitable data for this approach for only 18 of the 23 carcinogens. Therefore, we applied another model -- population attributable fraction (PAF) – to the remaining 5 carcinogens.

Risk assessment model

The RA model, widely used by HC and US EPA to estimate cancer risk from lifetime exposure to carcinogens, is conceptually displayed below. It was applied to 18, as indicated in Hazard identification: Carcinogen selection and routes of exposure.

$$\text{Annual Excess Cancers} = \frac{\text{Concentration} \cdot \text{Potency} \cdot \text{Population}}{\text{Lifetime}}$$

Where
Concentration = Probabilistic estimate of concentration
Potency = Estimate of inhalation unit risk or oral slope factor
Population = Ontario population aged 80 and under (census year 2011)
Lifetime = 80 years

See Section 4 for a description of the risk assessment model and the specific equations employed.

Population Attributable Fraction model

In the PAF model, the PAF is calculated from relative risk (RR) estimates, and then applied to cancer incidence to reflect the cancer burden. The concentration (or exposure) is incorporated into the RR estimates. This approach is similar to that employed in the Global Burden of Disease analysis[1] led by the Institute for Health Metrics and Evaluation. The PAF model was applied to five carcinogens -- UV, radon, PM (including DEE), and SHS -- as shown conceptually below.

$$\text{Annual Attributable Cancers} = \text{PAF} \cdot \text{Annual Cancer Incidence}$$

Where
PAF = population attributable fraction (and may encompass a relative risk, prevalence, slope, and concentration)

Annual Cancer Incidence = estimate for a specific type of cancer associated with carcinogen exposure from the Ontario Cancer Registry (year 2011)

See Section 5 for the description of the population attributable fraction model and equations that were applied to the five carcinogens.

2. Carcinogen Selection, Chemical Groupings, and Cancer Sites

This section describes the approach we took to select the 23 carcinogens and defines the chemical groupings we used, as well as provides some context for the cancer types/sites that have been associated with exposure to the agent as noted by IARC.

Carcinogen selection

We took several steps to select environmental carcinogens for this report (see Figure 2). First, we consulted the International Agency for Research on Cancer (IARC) on March 10, 2015 to obtain the listing of 188 agents they classified as "carcinogenic to humans" (i.e., Group 1) or "probably carcinogenic to humans" (i.e., Group 2A). Second, we focused on the 52 Group 1 and 2A carcinogens where we deemed the exposure category to be "environmental" (excluding 136 carcinogens from other exposure categories, related to items like occupation, behavior, or diet; see Table 1 and below for these excluded exposure categories and carcinogens). Third, we then grouped some related carcinogens together (e.g., different wavelengths of UV radiation; see Table 2 for the groupings), reducing the number of carcinogens to 38. Fourth, we determined that the average Ontarian would be unlikely to be exposed to 14 carcinogens during normal daily activities, leaving 24 carcinogens. Fifth, we deemed there to be insufficient data to classify exposure to the general public to one carcinogen (silica). Ultimately, we included the 23 carcinogens most relevant to the Ontario population in our assessment. Table 2 provides a listing of the 52 environmental carcinogens and how the final list of 23 carcinogens included in the analysis was reached.

Figure 2. Overview of carcinogen selection process for inclusion in the report

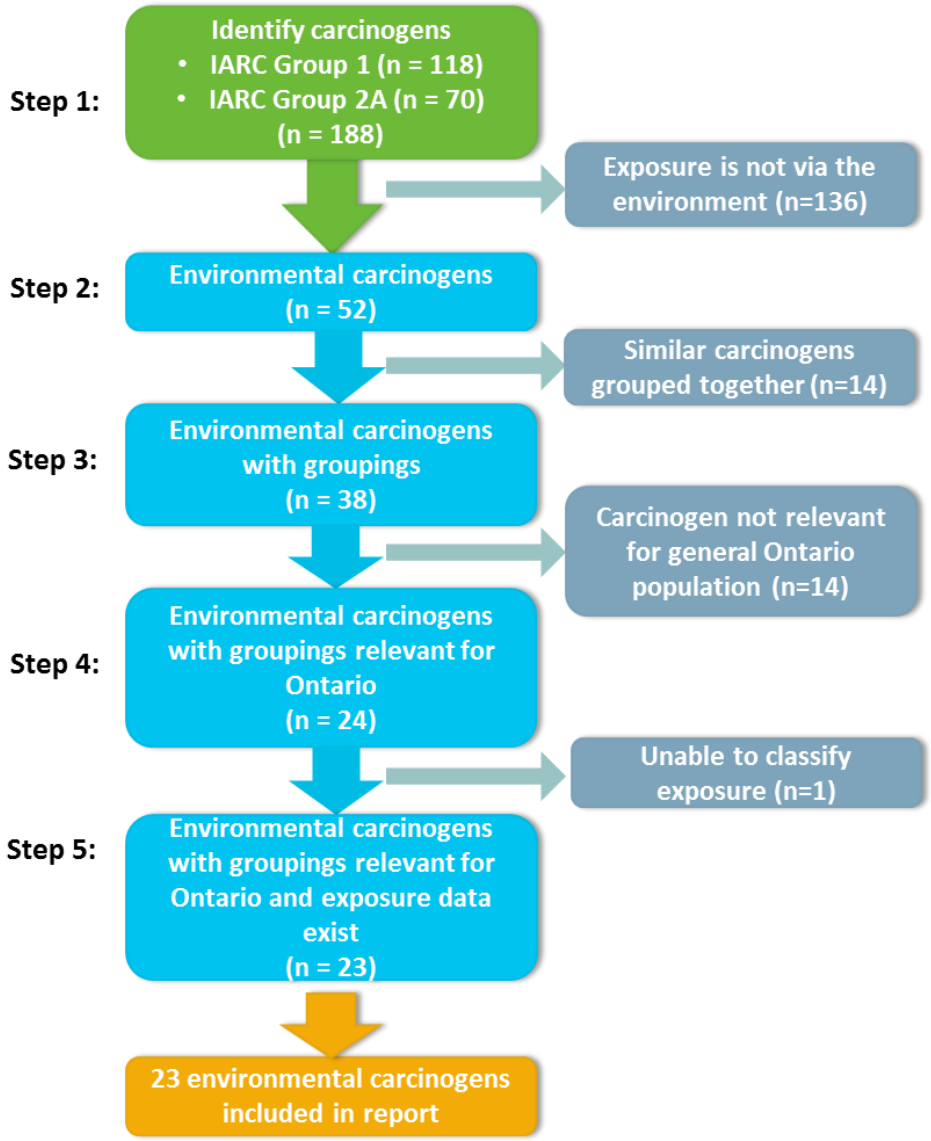


Table 1. Number and percentage of IARC Group 1 and 2A carcinogens by exposure category

	Group 1		***Group 2A***		***Total***	
Exposure Category	*n*	*%*	*n*	*%*	*n*	*%*
Behavioural	2	*1.7*	0	*0*	2	*1.1*
Dietary Agents	8	*6.8*	3	*4.3*	11	*5.9*
Environmental	32	*27.1*	20	*28.6*	52	*27.7*
Hormones	6	*5.1*	1	*1.4*	7	*3.7*
Microbiological Agents	12	*10.2*	3	*4.3*	15	*8.0*
Occupational	29	*24.6*	27	*38.6*	56	*29.8*
Pharmacologic Agents	22	*18.6*	16	*22.9*	38	*20.2*
Radionuclides	7	*5.9*	0	*0*	7	*3.7*
Total	**118**	**100%**	**70**	**100%**	**188**	**100%**

BEHAVIOURAL (n=2)

1. Tobacco smoking
2. Ultraviolet-emitting tanning devices

DIETARY AGENTS (n=11)

1. Acetaldehyde associated with consumption of alcoholic beverages
2. Alcoholic beverages
3. Areca nut
4. Betel quid with tobacco
5. Betel quid without tobacco
6. N'-Nitrosonornicotine (NNN) and 4-(N-Nitrosomethylamino)-1-(3-pyridyl)-1-butanone (NNK)
7. Salted fish, Chinese-style
8. Tobacco, smokeless
9. IQ (2-Amino-3-methylimidazo[4,5-f]quinoline)
10. Mate, hot
11. Nitrate or nitrite (ingested) under conditions that result in endogenous nitrosation

HORMONES (n=7)

1. Diethylstilbestrol
2. Estrogen-only menopausal therapy
3. Estrogen therapy, postmenopausal (see Estrogen-only menopausal therapy)
4. Estrogen-progestogen menopausal therapy (combined)
5. Estrogen-progestogen oral contraceptives (combined)
6. Ethanol in alcoholic beverages
7. Androgenic (anabolic) steroids

MICRBIOLOGICAL AGENTS (n=15)

1. Aflatoxins
2. Clonorchis sinensis (infection with)
3. Epstein-Barr virus
4. Helicobacter pylori (infection with)
5. Hepatitis B virus (chronic infection with)
6. Hepatitis C virus (chronic infection with)
7. Human immunodeficiency virus type 1 (infection with)
8. Human papillomavirus types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59
9. Human T-cell lymphotropic virus type I
10. Kaposi sarcoma herpesvirus
11. Opisthorchis viverrini (infection with)
12. Schistosoma haematobium (infection with)
13. Human papillomavirus type 68
14. Malaria (caused by infection with Plasmodium falciparum in holoendemic areas)
15. Merkel cell polyomavirus (MCV)

RADIONUCLIDES (n=7)

1. Fission products, including strontium-90
2. Neutron radiation
3. Phosphorus-32, as phosphate
4. Plutonium
5. Radioiodines, including iodine-131
6. Radionuclides, alpha-particle-emitting, internally deposited
7. Radionuclides, beta-particle-emitting, internally deposited

PHARMACEUTICAL AGENTS (n=38)

1. Aristolochic acid
2. Aristolochic acid, plants containing
3. Azathioprine
4. Busulfan
5. Chlorambucil
6. Chlornaphazine
7. Cyclophosphamide
8. Cyclosporine (see ciclosporin)
9. Etoposide
10. Etoposide in combination with cisplatin and bleomycin
11. Melphalan
12. Methoxsalen (8-methoxypsoralen) plus ultraviolet A radiation
13. Methyl-CCNU
14. MOPP and other combined chemotherapy including alkylating agents
15. Phenacetin
16. Phenacetin, analgesic mixtures containing
17. Semustine (see Methyl-CCNU)
18. Sulfur mustard
19. Tamoxifen
20. Thiotepa
21. Thorium-232 and its decay products
22. Treosulfan
23. Adriamycin
24. Azacitidine
25. Bischloroethyl nitrosourea (BCNU)
26. Chloramphenicol
27. 1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU)
28. Chlorozotocin
29. Cisplatin
30. 5-Methoxypsoralen
31. N-Methyl-N´-nitro-N-nitrosoguanidine (MNNG)
32. Nitrogen mustard
33. Procarbazine hydrochloride
34. Teniposide
35. Chloral
36. Chloral hydrate
37. N-Methyl-N-nitrosourea
38. Pioglitazone

OCCUPATIONAL (n=56)

Group 1

1. Acheson process, occupational exposure associated with
2. Acid mists, strong inorganic
3. Aluminium production
4. 4-Aminobiphenyl
5. Auramine production
6. Benzidine
7. Benzidine, dyes metabolized to
8. Bis(chloromethyl)ether; chloromethyl methyl ether (technical-grade)
9. Coal gasification
10. Coal-tar distillation
11. Coal-tar pitch
12. Coke production
13. Erionite
14. Ethylene oxide
15. Fluoro-edenite fibrous amphibole
16. Haematite mining (underground)
17. Iron and steel founding (occupational exposure during)
18. Isopropyl alcohol manufacture using strong acids
19. Leather dust
20. Magenta production
21. 4,4'-Methylenebis(2-chloroaniline) (MOCA)
22. Mineral oils, untreated or mildly treated
23. 2-Naphthylamine
24. Painter (occupational exposure as a)
25. 2,3,4,7,8-Pentachlorodibenzofuran
26. Rubber manufacturing industry
27. Shale oils
28. Soot (as found in occupational exposure of chimney sweeps)
29. ortho-Toluidine

Group 2A

30. Art glass, glass containers and pressed ware (manufacture of)
31. Carbon electrode manufacture
32. 4-Chloro-ortho-toluidine
33. Cobalt metal with tungsten carbide
34. Diethyl sulfate
35. Dimethylcarbamoyl chloride
36. 1,2-Dimethylhydrazine
37. Dimethyl sulfate
38. N-Ethyl-N-nitrosourea (ENU)
39. Hairdresser or barber (occupational exposure as a)
40. Indium phosphide
41. Petroleum refining (occupational exposures in)
42. Shiftwork that involves circadian disruption
43. Silicon carbide whiskers
44. Vinyl bromide
45. Vinyl fluoride
46. Glycidol
47. Methyl methanesulfonate
48. 6-Nitrochrysene
49. N-Nitrosodiethylamine
50. N-Nitrosodimethylamine
51. 2-Nitrotoluene
52. Non-arsenical insecticides (occupational exposures in spraying and application of)
53. 1,3-Propane sultone
54. Tetrafluoroethylene (TFE)
55. 1,2,3-Trichloropropane
56. Tris(2,3-dibromopropyl) phosphate

Table 2. Listing of IARC Group 1 and 2A carcinogens for the environmental exposure category (n=52), as well as whether the carcinogen appears in the report's final list or the reason for exclusion

IARC Agent	IARC Group	Report final list (or reason for exclusion)
Outdoor air pollution, particulate matter in	1	$PM_{2.5}$
Outdoor air pollution	1	
Biomass fuel, indoor emissions from household combustion of	2A	
Radon-222 and its decay products	1	Radon
Radium-224 and its decay products	1	
Radium-226 and its decay products	1	
Radium-228 and its decay products	1	
Benzo[*a*]pyrene	1	PAH
Cyclopenta[*cd*]pyrene	2A	
Dibenz[*a,j*]acridine	2A	
Dibenz[*a,h*]anthracene	2A	
Dibenzo[*a,l*]pyrene	2A	
Polychlorinated biphenyls	1	PCB
3,4,5,3',4'-Pentachlorobiphenyl (PCB-126)	1	
Polychlorinated biphenyls, dioxin-like, with a Toxicity Equivalency Factor (TEF) according to WHO	1	
Engine exhaust, diesel	1	DEE
1-Nitropyrene	2A	
Solar radiation	1	UV
Ultraviolet radiation	1	
Ionizing radiation (all types)	1	*Excluded (see note A)*
X- and Gamma-Radiation	1	
2,3,7,8-Tetrachlorodibenzo-*para*-dioxin	1	Dioxin
Arsenic and inorganic arsenic compounds	1	Arsenic
Asbestos	1	Asbestos
Benzene	1	Benzene
1,3-Butadiene	1	1,3-Butadiene
Cadmium and cadmium compounds	1	Cadmium
Chromium (VI) compounds	1	Chromium
Formaldehyde	1	Formaldehyde
1,2-Dichloropropane	1	Dichloropropane
Nickel compounds	1	Nickel
Tobacco smoke, second-hand	1	SHS
Trichloroethylene	1	TCE
Vinyl chloride	1	VC
Acrylamide	2A	Acylamide
alpha-Chlorinated toluenes (benzal chloride, benzotrichloride, benzyl chloride) and benzoyl chloride (combined exposures)	2A	Chlorinated Toluenes
Tetrachloroethylene (Perchloroethylene)	2A	PCE
Dichloromethane (Methylene chloride)	2A	DCM
Coal, indoor emissions from household combustion of	1	*Excluded (see note B)*
Beryllium and beryllium compounds	1	*Excluded (see note B)*

IARC Agent	IARC Group	Report final list (or reason for exclusion)
Wood dust	1	*Excluded (see note B)*
Silica dust, crystalline, in the form of quartz or cristobalite	1	*Excluded (see note C)*
Ethyl carbamate (Urethane)	2A	*Excluded (see note B)*
Bitumens, occupational exposure to oxidized bitumens and their emissions during roofing	2A	*Excluded (see note B)*
Captafol	2A	*Excluded (see note B)*
Creosotes	2A	*Excluded (see note B)*
Epichlorohydrin	2A	*Excluded (see note B)*
Lead compounds, inorganic	2A	*Excluded (see note D)*
Polybrominated biphenyls	2A	*Excluded (see note B)*
Styrene-7,8-oxide	2A	*Excluded (see note E)*
Frying, emissions from high-temperature	2A	*Excluded (see note B)*
Ethylene dibromide	2A	*Excluded (see note B)*

Notes:

A. Excluded because difficult to assess exposure and solar and ultraviolet radiation has a bigger impact than ionizing radiation.
B. Not relevant for general population environmental exposure in Ontario
C. Insufficient data to assess general population exposure in Ontario
D. Excluded because exposure to inorganic lead in the general Ontario population is unlikely and there is no way to estimate this given available exposure data sources. (We do not include general lead exposure since that is classified by IARC as Group 2B.)
E. Excluded because general population is exposed to styrene (which is IARC Group 2B) not this short-lived metabolite.

Chemical groupings

We categorized the carcinogens into five chemical groupings for ease of presentation:

1. **Radiation**: UV and radon
2. **Combustion by-products**: PM2.5, DEE, SHS, PAHs, and dioxins
3. **Metals**: As, CrVI, Cd, and Ni
4. **Volatile Organic Compounds (VOCs)**: DCP, butadiene, toluenes, benzene, DCM, formaldehyde, TCE, PCE, and VC
5. **Other**: acrylamide, asbestos, and PCBs

Cancer types/sites associated with exposure to carcinogens

IARC provides information on the cancer type or cancer site associated with an agent having limited or sufficient evidence of causing cancer in humans. This information is summarized in Table 3. Lung is a common cancer site, associated (limited or sufficient evidence) with exposure to over half of the carcinogens included in the report. Other common cancer sites/types were liver (associated with five carcinogens), bladder (associated with four carcinogens), and leukaemias (associated with three carcinogens).

Table 3. Summary of environmental carcinogens and associated cancer sites for which there is sufficient or limited evidence of cancer risk in humans, as classified by the International Agency for Research on Cancer (IARC)

Environmental carcinogen	Cancer site(s)	
	Sufficient evidence	Limited evidence
alpha-Chlorinated toluenes and benzoyl chloride		Lung
Arsenic	Lung, urinary bladder, skin (primarily squamous cell carcinoma)	Liver, prostate, kidney
Asbestos	Larynx, lung, mesothelioma, ovary	Pharynx, stomach, colon and rectum
Benzene	Acute myeloid leukaemia, acute non-lymphocytic leukaemia	Other leukaemias and lymphomas
1,3-Butadiene	Haematolymphatic organs	
Cadmium	Lung	Prostate
Chromium (VI)	Lung	Nasal cavity and paranasal sinus
Dichloromethane		Liver, non-Hodgkin lymphoma
1,2-Dichloropropane	Liver (cholangiocarcinoma)	
Diesel engine exhaust	Lung	Urinary bladder
Formaldehyde	Nasopharynx, leukemia	Nasal cavity and paranasal sinus
Nickel	Nasal cavity and paranasal sinus, lung	
Outdoor air pollution	Lung	Urinary bladder (soot)
Polychlorinated biphenyls	Melanoma	Breast, non-Hodgkin lymphoma
Radon and other alpha-particle emitters	Lung	Leukaemia
2,3,7,8-Tetrachlorodibenzo-para-dioxin	All sites (combined)	Lung, soft-tissue sarcoma, non-Hodgkin lymphoma
Tetrachloroethylene		Urinary bladder
Tobacco smoke, second-hand	Lung	Pharynx, larynx
Trichloroethylene	Kidney	Liver, non-Hodgkin lymphoma
Solar ultraviolet radiation	Skin (melanoma, squamous cell carcinoma, basal cell carcinoma)	Lip, eye
Vinyl chloride	Liver (angiosarcoma and hepatocellular carcinoma)	

Note: IARC did not provide any human cancer site/type information for acrylamide or PAHs (either individual PAHs, such as benzo[a]pyrene, or as a group) due to inadequate evidence from studies of cancer in humans. (These agents are classified as carcinogenic to humans because of strong mechanistic evidence in exposure humans.)

3. Concentration Distributions

We characterized concentration for inhalation of indoor air and outdoor air and ingestion of food, drinking water, and indoor dust following the guidelines in this section. We also outline our approaches to treating samples with concentrations below the limit of detection, zero values in lognormal distributions, and carcinogens that demonstrate a threshold, but for the most part, did not implement the approaches because of low occurrence of these issues in the data sets.

Concentration data sources

We fit concentration distributions to the strongest secondary sources we could locate (from the year 2010 and in Ontario, if possible), including data from governmental websites and the peer-reviewed literature. The availability of environmental concentration data varied by carcinogen and environmental source. Data from monitoring campaigns or studies with larger sample sizes, robust sampling protocols, and Ontario-specific information were preferred. The concentration data sources are summarized in Table 4, where the grey shading indicates that we did not obtain or use concentration data due to inapplicability to the Ontario population or a lack of data.

Table 4. Routes of exposure and environmental sources for each carcinogen assessed

GROUP / Carcinogen *(see note A)*	**Exposure Route / Environmental Source**				
	Inhalation		*Ingestion*		
	Outdoor Air	**Indoor Air**	**Indoor Dust**	**Drinking Water**	**Food**
COMBUSTION BYPRODUCTS					
Outdoor air pollution ($PM_{2.5}$)	OAMS[2]				
Diesel engine exhaust (DEE)	CARB[3]				
Polycyclic Aromatic Hydrocarbons (PAHs)	NAPS[4]	Li (2005)[5]	Maertens (2008)[6]	DWSP[7]	Kazerouni (2001)[8]
2,3,7,8-Tetrachlorodibenzo-para-dioxin (TCDD)	NAPS[4]				CTDS[9]
METALS					
Arsenic	NAPS[4]	Bari (2015)[10]	CHDS[11]	DWSP[7]	CTDS[9]
Cadmium	NAPS[4]	Bari (2015)[10]	CHDS *(see note B)*	DWSP *(see note B)*	CTDS *(see note B)*
Chromium (VI)	NAPS[4]	Bari (2015)[10]	CHDS[11]	DWSP[7]	
Nickel	NAPS[4]	Bari (2015)[10]	CHDS *(see note C)*	DWSP *(see note C)*	CTDS *(see note C)*

GROUP / Carcinogen *(see note A)*	Exposure Route / Environmental Source				
	Inhalation		*Ingestion*		
	Outdoor Air	**Indoor Air**	**Indoor Dust**	**Drinking Water**	**Food**
ORGANIC COMPOUNDS					
Alpha-chlorinated toluenes	NAPS[4]	Health Canada (2010)[12]		*(see note D)*	*(see note D)*
Benzene	NAPS[4]	Zhu (2013)[13]		DWSP[7]	
1,3-Butadiene	NAPS[4]	Health Canada (2010)[12]		*(see note D)*	*(see note D)*
Dichloromethane	NAPS[4]	Health Canada (2010)[12]		DWSP[7]	
1,2-Dichloropropane	NAPS[4]	Zhu (2013)[13]		DWSP[7]	
Formaldehyde	NAPS[4]	Heroux (2010)[14]			
Tetrachloroethylene (PCE)	NAPS[4]	Zhu (2013)[13]		DWSP[7]	
Trichloroethylene (TCE)	NAPS[4]	Zhu (2013)[13]		DWSP[7]	*(see note D)*
Vinyl chloride	NAPS[4]	Health Canada (2010)[12]		DWSP[7]	
OTHER					
Acrylamide				*(see note D)*	AMP[15]
Asbestos	Lee (2008)[16]	Lee (2008)[16]	*(see note D)*	*(see note D)*	
Polychlorinated biphenyls (PCBs)	NAPS[4]	Harrad (2009)[17]	Harrad (2009)[17]	*(see note D)*	CTDS[9]

Notes:

A. Concentration data were not collected for radon (results of a published article were used) or UV (since the estimation model is not based on concentration), so these are not shown in the table. For second-hand smoke, concentration data were also not used, but prevalence estimates from the CCHS were employed.

B. Although cadmium concentration data were located for the ingestion route of exposure (food, drinking water, and dust), most agencies (other than Cal EPA) did not classify cadmium to be carcinogenic by the ingestion route of exposure. Therefore, cancer burden estimates for cadmium via ingestion are not provided.

C. Although nickel concentration data were located through the ingestion route of exposure (food, drinking water, and dust), none of the agencies consulted for potency estimates provided one for nickel via ingestion. Therefore, cancer burden estimates for nickel via ingestion are not provided.

D. No data were available to characterize this route of exposure; other grey boxes represent routes of exposure that were not deemed relevant for the general population of Ontario.

AMP: Acrylamide Monitoring Program; CARB: California Air Resources Board; CCHS: Canadian Community Health Survey; CHDS: Canadian House Dust Study; CTDS: Canadian Total Diet Study; DWSP: Drinking Water Surveillance Program; NAPS: National Air Pollution Surveillance Program; OAMS: Ontario Air Monitoring Stations.

Procedures to characterize input distributions

We modelled the concentrations using an appropriate distribution type. Environmental exposure and monitoring data often follow a log-normal (right skew) distribution, with the bulk of the samples measuring low concentrations (but left-censored at zero) and some of the samples measuring higher concentrations (the tail). Other distribution types that might be applicable to environmental settings include the standard normal, individual discrete probability, and uniform (which is a case of individual discrete probability). See rules of thumb summarized in Table 5.

To determine the most suitable distribution type, we first examined a histogram of the raw data (or searched the published article or report to determine the evaluation made by the authors). In articles and reports, when the distribution type is not explicitly stated, it may be implied through the summary measures the authors chose to present. For example, if the arithmetic mean (AM) and standard deviation (ASD) are reported, a normal distribution may be assumed. If a geometric mean (GM) and geometric standard deviation (GSD) are reported, a log-normal distribution may be assumed.

Once we determined the most suitable distribution type, we then calculated or obtained the parameters required to characterize the exposure distribution. For a log-normal distribution, only two parameters are required: a measure of central tendency (the GM) and of spread (the GSD). For a normal distribution, the AM and ASD are required. For a discrete probability distribution, the range (x-axis) and probability (y-axis) of each bin are required (e.g., there are 5 ranges and 5 probabilities associated with 5 bins). In some cases, a point estimate was used in lieu of a distribution of values.

The concentration distributions are provided in Section 6.

Table 5. Rules of thumb for assigning distribution types to concentration data

Distribution Type	Description
Log-normal	- Histogram of logged concentrations follows a "bell-shaped" probability density function (PDF) - Authors report GM or median - AM > GM - GM ~50th percentile $$90\%\ \text{CI (range 95th to 5th)} \sim \left(\frac{\text{GM}}{\text{GSD}^{1.645}}, \text{GM} \cdot \text{GSD}^{1.645}\right)$$ $$\text{GSD} = \left(\frac{\text{GM}}{\text{5thPCT}}\right)^{1/1.645} = \left(\frac{\text{95thPCT}}{\text{GM}}\right)^{1/1.645} = \left(\frac{\text{95thPCT}}{\text{5thPCT}}\right)^{1/(2\cdot 1.645)}$$ Notes: Replace 1.645 with 1.96 for a 95% CI, 2.575 for a 99% CI, and 3 for min and max. Take the harmonic mean of both GSD estimates. To model zero values, create two distributions: (1) for the 0s and (2) with the lognormal fit to the remaining data.
Normal	- Histogram follows a "bell-shaped" PDF - Authors report AM, mean, or average - AM ~ 50th percentile $$90\%\ \text{CI(range 95th to 5th)} \sim (\text{AM} - 1.645 \cdot \text{ASD}, \text{AM} + 1.645 \cdot \text{ASD})$$ $$\text{ASD} = \frac{(95PCT - 5PCT)}{2 \cdot 1.645}$$ Notes: Replace 1.645 with 1.96 for a 95%CI, 2.575 for a 99% CI, and 3 for min and max. Must left truncate distribution at zero to avoid negative concentrations.
Discrete probability	- Histogram will be "choppy", having only specified concentration ranges that are possible, with different levels of probability associated with each.

Central concentration estimates

Table 6 illustrates the central estimate for the concentrations for the various environmental sources. These may be useful to help interpret the LOD information. The probabilistic inputs are presented in Section 6.

Table 6. Central concentration estimates by carcinogen and environmental source

Carcinogen	Environmental Source				
Combustion by-products	**Outdoor Air**	**Indoor Air**	**Drinking Water**	**Food**	**Dust**
UNITS	**µg/m^3**				
Outdoor air pollution ($PM_{2.5}$)	5.737				
Diesel engine exhaust (part of PM2.5)	0.684	0.456			
UNITS	**pg/m^3**			**pg/kg-d**	
2,3,7,8-Tetrachlorodibenzo-para-dioxin (TCDD)	0.010			0.670	
UNITS	**ng/m^3**	**ng/m^3**	**ng/L**	**ng/d**	**µg/g**
Polycyclic Aromatic Hydrocarbons (PAHs)	0.038	0.200	1.000	55.400	0.963
Metals and metalloids	**Outdoor Air**	**Indoor Air**	**Drinking Water**	**Food**	**Dust**
UNITS	**ng/m^3**	**ng/m^3**	**µg/L**	**µg/kg-day**	**µg/g**
Arsenic	0.458	0.125	0.393	0.568	13.100
Cadmium	0.081	0.025	0.112	0.223	6.000
Chromium (VI)	0.314	0.830	0.204		117.000
Nickel	0.349	0.385			
Volatile organic compounds (VOCs)	**Outdoor Air**	**Indoor Air**	**Drinking Water**	**Food**	**Dust**
UNITS	**µg/m^3**	**µg/m^3**	**µg/L**	**µg/kg-day**	
1,2-Dichloropropane	0.015	0.010	0.050		
1,3-Butadiene	0.019	0.141			
UNITS	**µg/m^3**	**µg/m^3**	**µg/L**	**µg/kg-d**	
Alpha-Chlorinated toluenes	0.009	0.004			
Benzene	0.389	1.040	0.050		
Dichloromethane (methylene chloride)	0.319	5.997	0.200		
Formaldehyde	1.337	26.692			
UNITS	**µg/m^3**	**µg/m^3**	**µg/L**		
Tetrachloroethylene (PCE)	0.063	1.940	0.051		
Trichloroethylene (TCE)	0.022	0.210	0.052		
Vinyl chloride (chloroethene)	0.002	0.010	0.050		
Other	**Outdoor Air**	**Indoor Air**	**Drinking Water**	**Food**	**Dust**
UNITS	**µg/m^3**	**µg/m^3**	**µg/L**	**µg/kg-d**	
Acrylamide				0.281	
UNITS	**fibres/mL**	**fibres/mL**			
Asbestos	2.0E-05	8.0E-05			
UNITS	**pg TEQ/m^3**	**pg ΣPCB/m^3**		**ng/kg-d**	**ng ΣPCB/g**
Polychlorinated biphenyls (PCBs)	0.002	6900.000		2.290	290.000

Limit of detection

For environmental data, a common approach to treat concentration estimates below the limit of detection (LOD), also known as non-detects, is substitution (e.g., by replacing the non-detects by concentrations of 0, the LOD/2, the LOD/$\sqrt{2}$, or the LOD). Substituting values below the LOD is consistent with exposure assessment practices elsewhere (e.g., Health Canada, US Centers for Disease Control and Prevention) and was employed in our analyses.

We use the following guidelines when we are calculating summary parameters *from raw data*:

1. We ascertained the LOD of the provided data (inquiring about the LOD if it was not stated in the documentation accompanying the data).
2. If the entity providing the data (i.e., the data steward) reported a result, we used it, even if the result was below the stated LOD.
3. If the entity providing the data reported a result as "<LOD" or "<DL" or "ND" or "<MRL", we substituted this value with the LOD/$\sqrt{2}$ (approximately 0.7071×LOD).

For journal articles, we ascertained how the authors treated samples below the LOD based on information provided in the manuscript and supplementary material (if applicable).

The LOD levels are presented in Table 7.

Table 7. Limit of detection (LOD) information by carcinogen and environmental source

11	Environmental Source	LOD	Units	Sample Size	Percent reported (%)^	Percent below LOD (%)^
Combustion by-products						
Outdoor air pollution ($PM_{2.5}$)	Outdoor Air	NR	µg/m^3	12122	100%	
2,3,7,8-Tetrachlorodibenzo-para-dioxin (TCDD)	Outdoor Air	NR	pg of TEQ/m^3	79	100%	
	Food and Beverages[x]	NR	pg of TEQ/kg-day			
Polycyclic Aromatic Hydrocarbons (PAHs)	Outdoor Air	NR	ng/m^3	198	100%	0%
	Indoor Air					
	Indoor Dust	0.051	µg/g		100%	
	Drinking Water	1	ng/L	68	100%	
Metals and metalloids						
Arsenic	Outdoor Air	0.02-0.06	ng/m^3	384	100%	2%
	Indoor Air	NR	ng/m^3	502	99%	1%
	Indoor Dust	0.1	µg/g	1025	100%	
	Drinking Water	1	µg/L	277	100%	92%
Cadmium˅	Outdoor Air	0.02-0.06	ng/m^3	384	100%	6%
	Indoor Air	NR	ng/m^3	502	74%	26%
	Indoor Dust	0.1	µg/g	1025	100%	
	Drinking Water	0.5	µg/L	277	100%	100%
Chromium (VI)	Outdoor Air	0.19-0.34	ng/m^3	384	100%	21%
	Indoor Air	NR	ng/m^3	502	57%	43%
	Indoor Dust	0.5	µg/g	1025	100%	
	Drinking Water	5	µg/L	277	100%	100%
Nickel˅	Outdoor Air	0.09-0.24	ng/m^3	384	100%	21%
	Indoor Air	NR	ng/m^3	502	48%	52%
	Indoor Dust	0.5	µg/g	1025	100%	
	Drinking Water	2	µg/L	277	100%	95%
Volatile organic compounds (VOCs)						
1,2-Dichloropropane	Outdoor Air	NR	ng/m^3	661	100%	100%
	Indoor Air	0.02	ng/m^3	3857	4%	96%
	Drinking Water	0.05	µg/L	342	100%	100%
1,3-Butadiene	Outdoor Air	NR	ng/m^3	1076	100%	100%
	Indoor Air	0.043-0.055	ng/m^3	884	100%	7%
Alpha-chlorinated toluenes	Outdoor Air	NR	ng/m^3	283	100%	0%
	Indoor Air	0.018-0.050	ng/m^3	845	100%	97%

11	Environmental Source	LOD	Units	Sample Size	Percent reported (%)^	Percent below LOD (%)^
Benzene	Outdoor Air	NR	µg/m^3	1174	100%	0%
	Indoor Air	0.07	µg/m^3	3857	100%	0%
	Drinking Water	0.05	µg/L	342	100%	100%
Dichloromethane	Outdoor Air	NR	µg/m^3	1122	100%	0%
	Indoor Air	0.081-0.089	µg/m^3	884	100%	0%
	Drinking Water	0.2	µg/L	342	100%	100%
Formaldehyde	Outdoor Air	NR	µg/m^3	164	100%	0%
	Indoor Air	NR	µg/m^3	215	100%	
Tetrachloroethylene (PCE)	Outdoor Air	NR	µg/m^3	1174	100%	0%
	Indoor Air	0.01	µg/m^3	3857	99%	1%
	Drinking Water	0.05	µg/L	342	100%	0%
Trichloroethylene (TCE)	Outdoor Air	NR	µg/m^3	1161	100%	0%
	Indoor Air	0.01	µg/m^3	3857	75%	25%
	Drinking Water	0.05	µg/L	342	100%	0%
Vinyl chloride (chloroethene)	Outdoor Air	NR	µg/m^3	844	100%	0%
	Indoor Air	0.110-0.115	µg/m^3	884	100%	
	Drinking Water	0.05	µg/L	342	100%	100%
Other						
Acrylamide	Food and Beverages	10	µg/kg of food			
Asbestos	Outdoor Air	0	f/mL	1678	100%	
	Indoor Air	0	f/mL	3979	100%	
Polychlorinated biphenyls (PCBs)	Outdoor Air	NR	pg TEQ/m^3	78	100%	
	Indoor Air	NR	pg ΣPCB/m^3	10	100%	
	Indoor Dust	NR	ng ΣPCB/g	10	100%	

LOD: limit of detection; NR: not reported.

Note: Except for acrylamide, no LOD information was provided for the food intakes.

^The percent reported refers to the fraction of samples where a value was provided by the data steward. Percent below limit of detection (LOD) refers to the percent of samples that were below the stated LOD. In our analysis, we used all values provided by the data steward (even if they were below the stated LOD). When the data steward listed a value as below the LOD, we performed substitution

Treatment of zero values in a lognormal distribution

Where a lognormal distribution is chosen as the best fit, we used the following procedure whenever zero values occurred. We specified two different distributions: (1) one for the zero values and (2) another for the lognormal fit of the non-zero data. For example, if 5% of the values in the concentration dataset were zero, then the PRA concentration model was: 0.05x[0] + 0.95x[lognormal distribution characterized by GM and GSD of non-zero concentration data].

Other commonly used approaches to deal with zero values in lognormal distributions were considered but not chosen due to their limitations. These approaches included:

1. Discarding the zero samples (limitation: this discards meaningful data that provide information about concentration levels);
2. Substituting the zeros with small values, such as the LOD or a fraction of it (limitation: the GM and GSD calculated using this approach are heavily influenced by the value used for the substitution); and
3. Shifting the raw concentration data by a constant, then fitting the lognormal distribution to these shifted data and removing the constant from the generated concentrations in the PRA (limitation: the value of the constant used for the shift influences the estimated GM and GSD).

There were zeros for the following carcinogens, but always less than 2% of samples, so we did not apply the zero correction.

Threshold levels for carcinogens

It is beyond the scope of this project to ascertain whether each of the 23 carcinogens (1) has a threshold and (2) if so, what the threshold should be, as there is known variability in individual-level thresholds. Thus, we did not consider thresholds in our exposure assessment approach. At least two of the carcinogens we examined (formaldehyde and 2,3,7,8-TCDD) have reported thresholds.

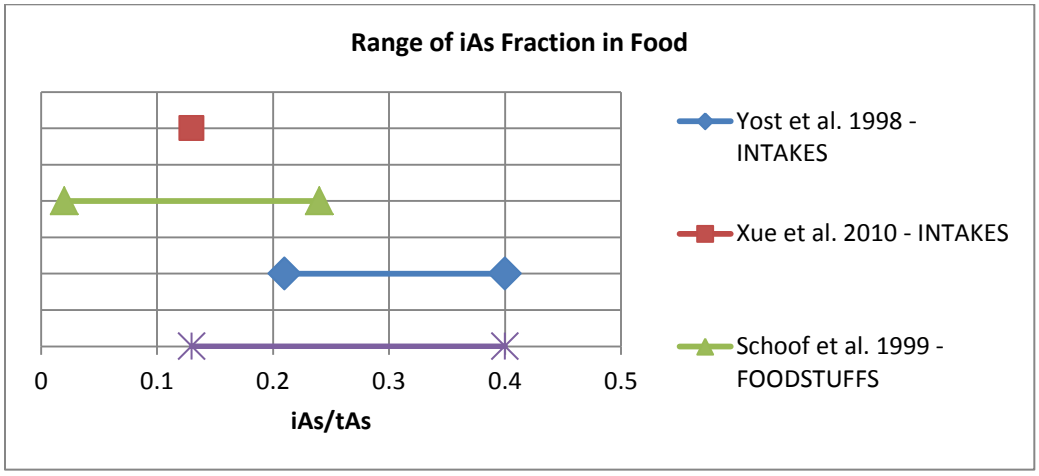
Carcinogen-specific information

We compiled additional information related to the concentration estimation for several of the carcinogens, as listed below.

Arsenic

For food ingestion, we model the fraction of food that is inorganic As versus organic by a uniform distribution, with range of 0.13 and 0.40 based on three studies[18-20] summarized in Figure 3.

Figure 3. Range of arsenic in food that is inorganic



Chromium

For Cr, we applied the fraction that is carcinogenic – that is the Cr(VI) fraction. We modelled this using a uniform distribution with a range of 0.1 to 0.5. We developed this range by evaluating information from a number of studies.[21-27]

Cadmium

While Cal EPA OEHHA lists a slope factor for cadmium ingestion, it is based on the inhalation unit risk. The WHO and USEPA do not classify cadmium as a carcinogen by the ingestion route of exposure. While IARC does not make a determination on the route of exposure, their association of cadmium with lung and prostate cancer is based on occupational studies where the primary route of exposure is inhalation. For this study, we estimated the cadmium cancer burden by inhalation and not ingestion.

Diesel PM

No exposure estimates for diesel PM exist for Ontario. Such estimates are difficult to obtain for any region because of the measurement and modeling challenges. Instead, we derived a diesel PM distribution using data from a California Air Resources Board (CARB) report on identifying diesel exhaust as a toxic air contaminant.[3] For the year 1990, the CARB report estimated a statewide California population-weighted diesel PM_{10} concentration of 3.0 µg/m^3, and projected this to decline to 1.7 µg/m^3 by the year 2010 (see Figure V-2 from CARB report). In other words, the 2010 diesel PM_{10} level was 0.5667 times the 1990 level. In Table V-2 of the same CARB report, there are 1990 diesel PM_{10} levels for 15 counties in California. We effectively converted these 1990 diesel PM_{10} estimates to 2010 estimates by applying the 0.5667 factor. Next, we applied a diesel $PM_{2.5}/PM_{10}$ ratio of 0.94 (taken from another CARB report on the same issue, "The Report on Diesel Exhaust, Findings of the Scientific Review Panel On The Report on Diesel Exhaust") to effectively convert the diesel PM_{10} estimates to diesel $PM_{2.5}$. Finally, we estimated an outdoor 2010 diesel $PM_{2.5}$ GM of 0.68 µg/m^3 (GSD of 2.35 µg/m^3) using the information above as applied to the 15 counties (Table 8).

Another approach to estimating the diesel PM levels would be to determine the fraction of $PM_{2.5}$ levels in Ontario that are of diesel exhaust origin. We did not locate any published values for this for Ontario. However, for six air basins in California, we have the 2010 diesel $PM_{2.5}$ estimates, along with monitored values for $PM_{2.5}$. For these six air basins, the fraction of $PM_{2.5}$ that was diesel ranged from 8% to 14%, with a mean value of 11% (median 11%; see Table 8). Applying 11% to the mean $PM_{2.5}$ level in Ontario (5.7 $\mu g/m^3$) gives an estimate of 0.57 $\mu g/m^3$, which is close to the modeled mean we employed of 0.67 $\mu g/m^3$. CAREX Canada has previously applied an estimate of 12% of $PM_{2.5}$ that is diesel $PM_{2.5}$, which is in line with our calculated estimate of 11%.

Furthermore, since the California Air Resources Board (CARB) report also stated that indoor levels of diesel are ⅔ of outdoor levels, we calculated an indoor level of 0.46 $\mu g/m^3$ (GSD of 2.35 $\mu g/m^3$) for the RA model.

Table 8. Lognormal 2010 diesel concentration distribution, fit to levels from 15 air basins

Air Basin	Estimated Outdoor Diesel $PM_{2.5}$ ($\mu g/m^3$)	Measured Outdoor $PM_{2.5}$ ($\mu g/m^3$)	Diesel fraction (%)
Great Basin Valley	0.11		
Lake County	0.16		
Lake Tahoe	0.53		
Mojave Desert	0.43		
Mountain Counties	0.32		
North Central Coast	0.75		
North Coast	0.64		
Northeast Plateau	0.59		
Sacramento Valley	1.33	10.9	12%
Salton Sea	1.38		
San Diego	1.54	10.8	14%
San Francisco Bay Area	1.33	10.6	13%
San Joaquin Valley	1.38	17.1	8%
South Central Coast	0.96	10.0	10%
South Coast	1.92	17.9	11%
GM ($\mu g/m^3$)	0.68	AM	11%
GSD ($\mu g/m^3$)	2.35	Range	8% - 14%

AM: arithmetic mean; GM: geometric mean; GSD: geometric standard deviation

Nickel

While we were able to calculate exposure concentrations from Ni in food, drinking water, and dust, there was no existing OSF. As such, we were unable to estimate the cancer burden by Ni ingestion. (We do estimate the cancer burden by Ni inhalation.)

PAHs

PAHs represent a class of compounds. We used benzo[a]pyrene as a surrogate for total PAH exposure. While there are many other PAHs, benzo[a]pyrene is the most toxic. Health Canada, US EPA, and Cal EPA developed OSF and IUR estimates for benzo[a]pyrene, which we applied in our analysis.

PCBs

PCBs are a class of compounds, consisting of many different congeners. There are two ways to treat this class of compound. One is to sum the individual PCB measurements and apply the PCB slope factor to this sum. Another is to weight the PCBs by their toxicities, summing the weighted values to obtain a toxic equivalency, or TEQ, then apply the dioxin slope factor to the TEQ. We applied the TEQ approach in our analysis.

4. Risk Assessment Model

In estimating the environmental burden of cancer in Ontario, we followed general human health risk assessment frameworks. Risk assessment-specific inputs and the equations are provided in this section. The actual inputs to the probabilistic modeling are provided in Section 6.

Risk assessment-specific inputs

Risk assessment-specific inputs, such as slope factors, exposure factors, and carcinogen-specific information are described in this section. The actual inputs to the probabilistic modeling are provided in Section 6.

Slope factor identification

We require a “dose-response” estimate, which provides a relationship between lifetime excess cancer risk and exposure for our analysis. For the RA, this takes the form of an OSF or IUR.

An **oral slope factor (OSF)** is an estimate of the increased cancer risk from oral exposure to a dose of, for example, 1 mg/kg-day for a lifetime. (*In our analysis, the OSF will be employed in the cancer EBD estimates for food, drinking water, and indoor dust ingestion.*) While a drinking water unit risk (DWUR) could be applied to the concentration in water directly to estimate lifetime risk to a carcinogen, we decided not to employ it in our analysis since DWURs are often calculated from OSFs, using default assumptions of 70 kg bodyweight and 2 L/day ingestion of water. Since we have exposure factors specific to the Canadian population in six age bins, we will apply these to the OSF for drinking water risks

An **inhalation unit risk (IUR)** is an estimate of the increased cancer risk from inhalation exposure to a concentration of, for example, 1 mg/m^3 for a lifetime. (*In our analysis, the IUR was employed in the cancer EBD estimates for the indoor and outdoor air inhalation.*)

The OSF and the IUR can be multiplied by an estimate of lifetime exposure (of dose in mg/kg-day or air concentration in mg/m^3, respectively) to estimate lifetime cancer risk. The slope factors are generally determined from fitting statistical models to animal or human occupational dose-response data, making assumptions, and using upper rather than mean model estimates of the relationship between dose and response.

We have collected OSFs and IURs for environmental pollutants derived and reported by the following agencies:

- Health Canada (HC)
- U.S. Environmental Protection Agency (USEPA)
- California EPA, Office of Environmental Health Hazard Assessment (OEHHA)

Generally, one particular study ("the critical effect study") forms the basis of the dose-response relationship where the oral slope factor or inhalation unit risk is derived. This study relates exposure to a particular carcinogen with the risk of developing a particular type of cancer. Details on this study (e.g., study population and cancer type) are provided along with the slope factor estimates in Section 6. A central estimate of the OSF or IUR is presented in Table 9.

Table 9. Central estimate of oral slope factors and inhalation unit risks by carcinogen

Carcinogen*	Inhalation Unit Risk† (per µg/m^3)	Oral Slope Factor† (per mg/kg-day)
Combustion by-products		
Diesel engine exhaust	3.0E-04	
2,3,7,8-Tetrachlorodibenzo-para-dioxin (TCDD)	3.8E+01	1.3E+05
Polycyclic Aromatic Hydrocarbons (PAHs)	5.7E-04	4.2E+00
Metals and metalloids		
Arsenic	4.7E-03	4.3E+00
Cadmium	5.3E-03	
Chromium (VI)	7.9E-02	5.0E-01
Nickel	2.6E-04	
Volatile organic compounds (VOCs)		
1,2-Dichloropropane	1.0E-05	3.6E-02
1,3-Butadiene	1.0E-04	6.0E-01
alpha-Chlorinated toluenes	4.9E-05	1.7E-01
Benzene	1.3E-05	7.9E-02
Dichloromethane (methylene chloride)	3.4E-07	5.4E-03
Formaldehyde	9.5E-06	
Tetrachloroethylene (PCE)	3.1E-06	2.7E-01
Trichloroethylene (TCE)	2.2E-06	1.8E-02
Vinyl chloride (chloroethene)^	4.3E-05	6.8E-01
Other		
Acrylamide	7.0E-04	2.5E+00
Asbestos˟	1.1E+00	
Polychlorinated biphenyls (PCBs)‡	3.4E-04	2.0E+00

*The burden for these carcinogens was estimated using the risk assessment model. The potency estimates for the carcinogens using the population attributable fraction model are presented separately.
†The average of the Health Canada, U.S. Environmental Protection Agency, and California Environmental Protection Agency values (when available) are presented here. Where one agency presented a range for the inhalation unit risk or oral slope factor, the high range was used.
^The "from birth" value was selected from the U.S. Environmental Protection Agency Integrated Risk Information System.
˟The inhalation unit risk units for asbestos are per fibres/mL
‡For PCBs, the toxic equivalents (TEQ) for concentration were determined, so the dioxin inhalation unit risk and oral slope factor were applied instead of those for PCBs.

Exposure factors

We used exposure factors in the RA model when the OSF was applied to the drinking water and indoor dust concentration estimates. Additionally, for PAH food ingestion, we also make use of the body weight exposure factor. We obtained age-resolved estimates of central tendency and spread for the following exposure factors:

- Drinking water ingestion rate[28]
- Indoor dust ingestion rate[29]
- Bodyweight[29]

We have adopted the six age group bins for a life expectancy of 80 years. (The age bins are the same as those reported in Section 1 of this technical supplement.)

These dust ingestion rates are based on 50% hard and 50% soft surface results (last column).[30]

Time aspect of analysis

For the environmental burden of cancer estimates generated by the RA method, we assume that individuals are exposed 100% of the time. We also assumed an 80 year lifespan. Our base year is 2010, so we tried to obtain environmental concentration data for this year. For population data, we used the nearest Census year: 2011.

We calculated the lifetime risk of cancer (per carcinogen per environmental source) for one individual over an 80 year lifespan. Then, we multiplied this risk by the Ontario population that is under 80 years of age. We assume that all Ontario residents under 80, regardless of their age, are exposed for 80 years. We assume that the exposure concentrations calculated using 2010 data (or available data that was closest to 2010) are applicable to past and future exposures.

Fraction of time spent indoors

Additionally, we refer to the Canadian Exposure Factors Handbook (2013) to estimate the fraction of time spent indoors (see their Table 8.1). This was employed for indoor and outdoor air inhalation in the RA model. Our mean estimate of 95.76% was calculated from an estimate of adult total time indoors of 1379 minutes per day. (There are 24*60 = 1440 total minutes in a day.)

Population

We calculated the 2011 Ontario population that is younger than 80 years to be: 12,745,163.[31]

Risk assessment equations to estimate excess cancers

Excess Cancers from Environmental Carcinogen Exposure from All Environmental Sources - RA (Series 1)

Equation 1-A. Excess Lifetime Cancer Cases from Environmental Carcinogen Exposure from All Environmental Sources

$$\text{Lifetime Cases} = \text{Lifetime Cases}_{\text{Air}} + \text{Lifetime Cases}_{\text{Drinking Water}} + \text{Lifetime Cases}_{\text{Dust}} + \text{Lifetime Cases}_{\text{Food}}$$

$$\text{Unit} = [\text{cases}]$$

Equation 1-B. Excess Lifetime (Individual) Risk from Environmental Carcinogen Exposure - General

$$\text{Lifetime Risk} = \text{Concentration} \cdot \text{Slope Factor}$$

$$\text{Unit} = [\text{risk}] = [\text{concentration}] \frac{[\text{risk}]}{[\text{concentration}]}$$

Equation 1-C. Excess Lifetime Cancers (in Ontario) from Environmental Carcinogen Exposure – General

$$\text{Lifetime Cases} = \text{Lifetime Risk} \cdot \text{Population}$$

$$\text{Unit} = [\text{cases}] = [\text{risk}]\,[\text{people}]$$

Equation 1-D. Excess Annual Cancer Cases (in Ontario) from Environmental Carcinogen Exposure from All Environmental Sources – General

$$\text{Annual Cases} = \frac{\text{Lifetime Cases}}{\text{Lifetime of 80 years}} = \frac{\text{Concentration} \cdot \text{Slope Factor} \cdot \text{Population}}{\text{Lifetime of 80 years}}$$

$$\text{Unit} = \frac{[\text{cases}]}{[\text{year}]}$$

Excess Cancer for the Inhalation Route of Exposure - RA (Series 2)

Equation 2-A. Lifetime Excess Cases from Inhalation

$$\text{Lifetime Cases}_{\text{Air}} = \text{Lifetime Cases}_{\text{Indoor Air}} + \text{Lifetime Cases}_{\text{Outdoor Air}}$$

$$\text{Unit} = [\text{cases}]$$

Equation 2-B. Lifetime Excess Cases for *Indoor* Air Inhalation

$$\text{Lifetime Cases}_{\text{Indoor Air}} = \{\text{fraction of time}_{\text{Indoors}} \cdot \text{Concentration}_{\text{Indoor Air}} \cdot \text{ Inhalation Unit Risk}\} \cdot \text{ Population}$$

$$\text{Unit} = [\text{cases}] = \left[\frac{\mu g}{m^3}\right] \left[\frac{\text{risk}}{\frac{\mu g}{m^3}}\right] [\text{people}]$$

Equation 2-C. Lifetime Excess Cases for *Outdoor* Air Inhalation

$$\text{Lifetime Cases}_{\text{Outdoor Air}} = \{\ (1 - \text{fraction of time}_{\text{Indoors}}) \cdot \text{Concentration}_{\text{Outdoor Air}} \cdot \text{ Inhalation Unit Risk}\} \cdot \text{ Population}$$

$$\text{Unit} = [\text{cases}] = \left[\frac{\mu g}{m^3}\right] \left[\frac{\text{risk}}{\frac{\mu g}{m^3}}\right] [\text{people}]$$

Excess Cancer for the Ingestion Route of Exposure - RA (Series 3)

Equation 3-A. Lifetime Excess Cases from Ingestion

$$\text{Lifetime Cases}_{\text{Air}} = \text{Lifetime Cases}_{\text{DrinkingWater}} + \text{Lifetime Cases}_{\text{Dust}} + \text{Lifetime Cases}_{\text{Food}}$$

$$\text{Unit} = [\text{cases}]$$

Equation 3-B. Lifetime Excess Cases - Drinking Water Ingestion

$$\text{Lifetime Cases}_{\text{Drinking Water}} = \sum_{i=1}^{6} \text{F}_i \frac{\text{Ingestion Rate}_{\text{DrinkingWater}_i}}{\text{Bodyweight}_i} \cdot \left\{\text{Concentration}_{\text{Drinking Water}} \cdot \text{Oral Slope Factor} \cdot \text{Population}\right\}$$

$$\text{Unit} = [\text{lifetime cases}] = \left[\frac{\text{mg}}{\text{L}}\right]\left[\frac{\text{risk}}{\frac{\text{mg}}{\text{kg}-\text{d}}}\right]\left[\frac{\frac{\text{L}}{\text{d}}}{\text{kg}}\right][\text{people}]$$

Equation 3-C. Lifetime Excess Cases - Dust Exposure Ingestion

$$\text{Lifetime Cases}_{\text{Dust}} = \sum_{i=1}^{6} \text{F}_i \frac{\text{Ingestion Rate}_{\text{Dust}_i}}{\text{Bodyweight}_i} \cdot \{\text{Concentration}_{\text{Dust}} \cdot \text{Oral Slope Factor} \cdot \text{Population}\}$$

$$\text{Unit} = [\text{lifetime cases}] = \left[\frac{\text{mg}}{\text{mg}}\right]\left[\frac{\text{risk}}{\frac{\text{mg}}{\text{kg}-\text{d}}}\right][\frac{\frac{\text{mg}}{\text{d}}}{\text{kg}}][\text{people}]$$

Equation 3-D. Lifetime Excess Cases - Food Exposure Ingestion

$$\text{Lifetime Cases}_{\text{Food}} = \{\text{Intake}_{\text{Food}} \cdot \text{Oral Slope Factor}\} \cdot \text{ Population}$$

$$\text{Unit} = [\text{lifetime cases}] = \left[\frac{\text{mg}}{\text{kg}-\text{d}}\right]\left[\frac{\text{risk}}{\frac{\text{mg}}{\text{kg}-\text{d}}}\right][\text{people}]$$

F_i represents the fraction of the lifespan spend in one of i=6 age bins with cut points at 1, 4, 12, 20, 65, and 80 years of age. Exposure factors for inhalation rate, drinking water ingestion rate, indoor dust ingestion rate, and bodyweight are available for the six age bins.

Note: We assume the bioavailability of carcinogens in food/dust/water is 100%.

Risk assessment assumptions

We made several assumptions in estimating excess annual cancers from exposure to the carcinogens. These are listed below, along with the potential bias resulting from the assumption.

- Ontario residents are exposed 100% of the time to all carcinogens in the analysis for 80 years.
    - Upward bias expected, since exposure is likely less than 24 hours a day, 7 days a week for the lifetime.
- The lifespan of all Ontarians is 80 years.
    - No upward or downward bias expected from this lifespan assumption which was required to estimate annual risks from lifetime risks. In Ontario (for those born in 2007 to 2009), the life expectancy of males is 79 and females is 84, which are both in line with our estimate.
- The bioavailability of carcinogens in food/dust/water is 100%.
    - Upward bias expected, since the bioavailability of carcinogens may be less than 100%. Note, we attempted to quantify the toxic components of arsenic and chromium in our analysis.
- The IUR or OSF values that we selected and created distributions from are applicable to the Ontario population.
    - Upward bias expected, since IURs and OSFs generally represent upper bounds on excess lifetime risk of cancer from lifetime exposure.
- The IUR or OSF values that we employed were developed using data from a specific study on a particular species (e.g., human - occupational, animal) and cancer endpoint, but are applicable to the Ontario population to estimate general “excess cancers”.
    - Bias could be upward or downward, since the species may be sensitive or the carcinogens may result in more than one cancer and IURs and OSFs only capture one.
- When one agency reported a range for an OSF or IUR, the upper end of the range was selected for the analysis (e.g., EPA IRIS for benzene).
    - Upward bias expected.
- When an OSF or IUR estimate was provided for a specific lifespan, the lifetime value was applied if possible (e.g., VC the “from birth” value was selected).
    - No downward or upward bias expected, but this demonstrates that our approach does not account for critical periods of exposure for some of the carcinogens.

5. PAF Models for Select Carcinogens

Originally, we planned to apply a RA model to all 23 carcinogens. However, we did not locate potency information in the form suitable (e.g., oral slope factor, inhalation unit risk) to apply the RA model for five carcinogens: UV, radon, PM (and its subset, DEE), and SHS. For these carcinogens, we were able to locate potency information of another form (e.g., relative risk) to estimate the population attributable fraction (PAF). With an estimate of PAF, the cancers attributable to exposure to the carcinogen can be calculated as the product of the PAF and the observed cancer incidence (see Box 3). This approach is often employed for environmental burden of disease estimates for health endpoints other than cancer and is similar to the approach to generate the Global Burden of Disease (GBD) estimates (e.g., see Lim et al. (2013)).

For the RA model, the potency estimates are derived from fitting models to dose-response data (generated in animal or human studies). However, for the PAF model, the cancer type is specified in the relative risk relationship or in the derivation of the PAF by comparing "expected" and "observed" cancers.

This section outlines the development of the PAF for the five carcinogens where we employed the PAF model: UV, radon, PM (and its subset, DEE), and SHS.

UV

There are several challenges in estimating how much melanoma skin cancer is attributable to solar ultraviolet (UV) radiation exposure, including the lack of population-based data on duration and patterns of exposure, and the absence of a truly non-exposed population. Previous epidemiological studies have used various approaches to define a non-exposed population in order to estimate the cancers attributable to UV. We reviewed the literature and, based on the nature of melanoma incidence data available in Ontario, selected two PAF approaches that were suitable. We focused solely on melanoma, the most fatal form of skin cancer. The Ontario Cancer Registry (OCR) does not contain information about the more common basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) skin cancers diagnosed in Ontario, and no other reliable source of information on non-melanoma skin cancers exists in the province.

UV PAF Method 1: Classifying 1913 birth cohort as unexposed

The first approach was based on a method[32] that estimated UV-attributable cases as the difference between the observed number of cases and the number expected with a theoretical minimum-risk exposure distribution. For our calculation, the minimum-risk exposure distribution was based on historical data: the estimated incidence rates for Ontarians born in 1913. This allowed us to fit an age-cohort model to the data to recreate age-specific incidence rates for age groups without observations in the OCR. (High-quality melanoma incidence data is available in the OCR beginning in 1980.) This was done by sex (male, female) and age group (15–24, 25–34, 35–49, 50–64 and 65+ years).

We selected the cohort born in 1913 as the reference (non-exposed) population. Using the estimated incidence rates for this cohort, we calculated the expected number of cases in 2011 if sun exposure was the same as it had been in the 1913 birth cohort. The difference between this number and the number of observed melanoma cases in Ontario in 2011 is the estimated number of UV-attributable melanoma cases (i.e., attributable cases). The observed melanoma cases in 2011, the attributable cases, and the PAF estimates are shown in Table 10.

Table 10. Melanoma cases diagnosed in 2011 in Ontario and those estimated to be attributable to UV exposure with corresponding PAF, based on Method 1

	Males		Females		Both sexes	
Age (years)	**Observed cases**	**Attributable cases (PAF)**	**Observed cases**	**Attributable cases (PAF)**	**Observed cases**	**Attributable cases (PAF)**
15-24	13	7.2 (55.1)	32	22.0 (68.8)	45	29.2 (64.8)
25-34	47	27.5 (58.5)	82	51.8 (63.2)	129	79.3 (61.5)
35-49	227	152.1 (67.0)	282	188.6 (66.9)	509	340.7 (66.9)
50-64	544	376.5 (69.2)	423	284.3 (67.2)	967	660.8 (68.3)
65+	946	590.8 (62.5)	588	337.7 (57.4)	1.534	928.5 (60.5)
Total	1,777	1,154.0 (64.9)	1,407	884.4 (62.9)	3,184	2,038.4 (64.0)

PAF: population attributable fraction (calculated as the attributable cases divided by the observed cases)

UV PAF Method 2: Classifying an African-American population as unexposed

The second approach was based on a method[33] that used melanoma incidence in the African-American population in the U.S. as a proxy for incidence in the non-exposed white population. Because the source of our observed melanoma estimates, the OCR, does not contain information on race or ethnicity, we used incidence data for the U.S. black population from the SEER (Surveillance, Epidemiology and End Results) 18 registries as a proxy for incidence in the non-exposed Ontario population. The SEER program of the National Cancer Institute in the U.S. provides cancer incidence data from population-based cancer registries covering approximately 30 per cent of the population. SEER 18 melanoma incidence rates for 2011 were extracted by sex (male, female) and age group (15–24, 25–34, 35–49, 50–64 and 65+) and applied to the Canadian 2011 postcensal estimates of the Ontario population to obtain the expected number of melanoma cases if incidence rates for the SEER 18 black population were observed in Ontario. The difference between this number and the number of observed melanoma cases in Ontario in 2011 was taken as the estimated number of UV-attributable melanoma cases (i.e., attributable cases). The observed melanoma cases in Ontario in 2011, the attributable cases, and the PAF estimates are shown in Table 11.

Table 11. Melanoma cases diagnosed in 2011 in Ontario and those estimated to be attributable to UV exposure with the corresponding PAF, based on Method 2

	Males		Females		Both sexes	
Age (years)	Observed cases	Attributable cases (PAF)	Observed cases	Attributable cases (PAF)	Observed cases	Attributable cases (PAF)
15-24	13	13.0 (100.0)	32	31.0 (97.0)	45	44.0 (97.9)
25-34	47	45.8 (97.5)	82	80.9 (98.6)	129	126.7 (98.2)
35-49	227	222.8 (98.2)	282	274.4 (97.3)	509	497.3 (97.7)
50-64	544	528.6 (97.2)	423	398.4 (94.2)	967	927.0 (95.9)
65+	946	907.3 (95.9)	588	536.5 (91.2)	1.534	1,443.8 (94.1)
Total	1,777	1,717.6 (96.7)	1,407	1,320.4 (93.8)	3,184	3,037.9 (95.4)

PAF: population attributable fraction (calculated as the attributable cases divided by the observed cases)

Modeling the PAF for UV in the probabilistic assessment

Based on the two methods outlined above, we modeled the PAF for UV and skin cancer as a uniform distribution with a range of 0.640 to 0.954.

Assumptions for estimating the UV PAF

- The cancer burden of UV radiation can be quantified by examining melanoma skin cancer, for which IARC has deemed there to be sufficient evidence in humans; other cancers including those with sufficient evidence (non-melanoma skin cancers) but with not enough information and those with limited evidence in humans (e.g., lip and eye) were not examined
- The 1913 birth cohort in Ontario and the African-American population covered in the SEER 18 registries are reflective of the "non-exposed" Ontario population.
- All of the observed attributable melanoma cases are due to solar UV radiation exposure.
- Accounting for non-melanoma skin cancers (such as basal cell carcinoma and squamous cell carcinoma) would increase the number of skin cancers attributable to UV exposure. Non-melanoma skin cancers are also associated with UV exposure, however they are not included in these estimates of melanoma skin cancers since there is not a readily available non-melanoma skin cancer incidence estimate for Ontario (these typically treatable cancers are not tracked and it is difficult to develop an incidence estimate).

Radon

The impact of radon exposure in homes on the lung cancer burden in Ontario was recently estimated.[34] This study applied the method developed by Brand et al. who made use of an exposure-age-concentration model called BEIR-VI[35] to estimate the lung cancer burden of radon

in Canada. Peterson et al. (2013) estimated the PAF[36] using Ontario data, separately for never- and ever-smokers to reflect the influence of smoking on lung cancer incidence.

The data sources and methods for Peterson et al. are reviewed in brief below and are described in more detail in the above references. To estimate radon exposure, the authors used Health Canada's Cross-Canada Survey of Radon Concentrations in Homes. This survey was conducted from 2009 to 2011 and sampled 3,891 homes across Ontario. Radon exposure in Ontarians was found to follow a log-normal distribution with a GM of 43 Bq/m^3 and GSD of 3.1 Bq/m^3. (The radon exposure detection limit was 15 Bq/m^3.) The authors gathered data on factors that would influence radon exposure and lung cancer incidence, including the presence of apartment buildings (from Statistics Canada) and on smoking status (from Canadian Community Health Survey). The all-cause and lung cancer mortality information was derived from intelliHEALTH Ontario (year 2007).

As outlined in Brand et al., the BEIR-VI model was used to calculate the excess risk ratio (ERR) of lung cancer mortality (using a Monte Carlo simulation to assess uncertainty). Separately, life-table calculations were performed to determine the lifetime risk of lung cancer (LR) for ever- and never-smokers. The ERRs were used in the life-table calculations in order to determine the lifetime risk (LR_E) in radon-exposed individuals. Finally, the PAF was calculated using $PAF = (LR_E - LR) / LR_E \times 100$.

Modeling the PAF for radon in the probabilistic assessment

From Table 1 of Peterson et al. (2013), the mean PAF estimate for radon and lung cancer in Ontario (combined for never- and ever-smokers) was 13.6% (median 13.5%), with a 95%CI of 11.0% to 16.7%. We modeled the PAF in @RISK using a normal distribution with mean of 13.6% and standard deviation of 1.45%. (We left-truncated this distribution at 0 and right-truncated it at 1.0 to avoid implausible results.)

Assumptions for estimating the radon PAF

- The cancer burden of radon can be quantified by examining lung cancer, for which IARC has deemed there to be sufficient evidence in humans; other cancers with limited evidence in humans (e.g., leukaemia) were not examined.
- The exposure to radon for each public health unit in Ontario could be adequately modeling using data from Health Canada's Cross-Canada Survey of Radon Concentration in Homes, even though radon levels are known to vary widely from home to home and in some health units less than 100 samples were available.
- The estimated radon exposure is constant over a lifetime, though residential mobility is known to exist.
- The ever-smoker category (which included current, occasional, and previous smokers) to be the appropriate categorization for smoking risk, though this may be an oversimplification of the risk in this group. (It was employed to be consistent with the BEIR-VI model, a model used in the analysis.)

$PM_{2.5}$

We employed a PAF approach for $PM_{2.5}$ because there was no slope factor reported by the agencies we consulted. The PAF for $PM_{2.5}$ exposure (assuming 100% exposure prevalence) and lung cancer is:

$$\mathrm{PAF}_{\text{Outdoor Air,PM}} = \left\{\frac{\mathrm{RR}-1}{\mathrm{RR}}\right\} = \left\{1 - \mathrm{e}^{-\beta \cdot \mathrm{Concentration}_{\text{Outdoor Air,PM}}}\right\}$$

Where

RR is the relative risk where $\mathrm{RR} = \mathrm{e}^{\beta \cdot \mathrm{Concentration}_{\text{Outdoor Air,PM}}}$

β is the slope derived from the study RR as $\frac{\ln(\mathrm{RR})}{\Delta X}$

$\mathrm{Concentration}_{\text{Outdoor Air,PM}}$ is the ambient $PM_{2.5}$ concentration

For the RR, we used the results from a recent analysis that was specifically designed to develop a quantitative estimate to accompany the IARC classification of $PM_{2.5}$ as a Group 1 carcinogen. Based on seven studies in North America (one of which was conducted in Canada), Hamra et al. (2014)[37] conducted a random effects meta-analysis and reported a RR relating lung cancer incidence and $PM_{2.5}$ exposure of 1.11 (95% CI: 1.05, 1.16) per 10 $\mu g/m^3$ increase in $PM_{2.5}$. This RR corresponds to a β of 0.0104 (95% CI: 0.0049, 0.0148) per $\mu g/m^3$.

Modeling the PM PAF in the probabilistic analysis

For PM, the PAF was modeled using β in order to relate the potency with the PM levels. We modelled the β as a normal distribution in @RISK© with a mean of 0.0104 and a standard deviation of 0.0025 per $\mu g/m^3$, left-truncating the distribution at zero to avoid implausible estimates. The $PM_{2.5}$ concentration distribution is provided in Section 6.

Assumptions for the $PM_{2.5}$ PAF approach

Assumptions for this approach include:

- The cancer burden of $PM_{2.5}$ can be quantified by examining lung cancer, for which IARC has deemed there to be sufficient evidence in humans; other cancers with limited evidence in humans (e.g., urinary bladder) were not examined
- Prevalence of exposure to $PM_{2.5}$ is 100%
- There is no threshold in the model (no PM level below which adverse effects would not occur); PM levels are compared to a level of 0 $\mu g/m^3$
- Annual average $PM_{2.5}$ concentrations from outdoor monitors reflect the appropriate concentration metric
- DEE is a subset of $PM_{2.5}$ and can be modeled using a RR developed for $PM_{2.5}$
- The RR from a meta analysis of $PM_{2.5}$ environmental epidemiology studies is applicable to the Ontario population

Diesel $PM_{2.5}$

Diesel $PM_{2.5}$ is one component of ambient $PM_{2.5}$. As such, these estimates should be considered a portion of the ambient $PM_{2.5}$ estimates, and not added to them. Ambient PM is made up of primary PM (directly emitted) and secondary PM (formed from SO_2, NO_2, NH_3, and organics in the atmosphere) and has many sources (including natural – like volcanoes; and anthropogenic – like high temperature combustion from cars, trucks, buses, and power plants).

While we can also analyze diesel PM using a RA model, in the report we presented results using the PAF model to be consistent with the assessment model for $PM_{2.5}$. We did, however, compare the PAF model and RA model-derived estimates. We found that application of the PAF model for diesel PM resulted in a three-fold higher burden estimate than the RA model. This demonstrates that the two models will likely produce different estimates, but the same difference cannot be expected for other carcinogens even if the application of both models were possible.

SHS

We apply a PAF approach to estimate the proportion of incident lung cancer cases that can be attributed to exposure to environmental tobacco smoke (ETS)/second-hand smoke (SHS). Levin's standard formula was used:

$$\mathrm{PAF}_{\mathrm{SHS}} = \frac{\mathrm{P}_{\mathrm{SHS}}(\mathrm{RR}_{\mathrm{SHS}} - 1)}{1 + \{\mathrm{P}_{\mathrm{SHS}}(\mathrm{RR}_{\mathrm{SHS}} - 1)\}}$$

Where
$\mathrm{PAF}_{\mathrm{SHS}}$ is the proportion of incident lung cancer cases attributable to second-hand smoke exposure
$\mathrm{P}_{\mathrm{SHS}}$ is the prevalence of second-hand smoke exposure at home among non-smokers and
$\mathrm{RR}_{\mathrm{SHS}}$ is the relative risk of lung cancer for non-smokers exposed to second-hand smoke at home vs. non-smokers unexposed to second-hand smoke exposure at home.

Since the relative risk and prevalence estimates are based on non-smokers only, we needed to first estimate the number of new lung cancers among non-smokers as these statistics are not available from the Ontario Cancer Registry. To do this, we used the following method[38]:

Step 1. We calculated the proportion of new lung cancers attributable to current smoking (PAF_{CS}) using the following version of Levin's formula:

$$\mathrm{PAF_{CS}} = \frac{\mathrm{P_{CS}(RR_{CS} - 1)}}{1 + \{\mathrm{P_{CS}(RR_{CS} - 1)}\} + \{\mathrm{P_{FS}(RR_{FS} - 1)}\}}$$

Where
$\mathrm{P_{CS}}$ = prevalence of current smokers,
$\mathrm{P_{FS}}$ = the prevalence of former smokers,
$\mathrm{RR_{CS}}$ = relative risk for current smokers vs. never smokers, and
$\mathrm{RR_{FS}}$ = relative risk for former smokers vs. never smokers.

Step 2. We calculated the number of lung cancer cases among non-smokers ($\mathrm{Lung\ Cancers_{NS}}$) by first subtracting the number of lung cancers attributable to current smoking from the total number of lung cancers diagnosed in Ontario during 2011 and then partitioning the resulting number of cancers according to the prevalence of non-smoking:

$$\mathrm{Lung\ Cancers_{NS}} = \{\mathrm{Total\ lung\ cancers} - (\mathrm{PAF_{CS}} \cdot \mathrm{Total\ lung\ cancers})\} \cdot \{1 - \mathrm{P_{CS}}\}$$

Once the number of lung cancers among non-smokers was estimated, we calculated the number of lung cancers due second-hand smoke exposures using the following equation:

$$\mathrm{Lung\ Cancers_{SHS}} = \mathrm{PAF_{SHS}} \cdot \mathrm{Lung\ Cancers_{NS}}$$

- The above steps were carried out and the PAF_{SHS} was calculated by sex (male, female) and age group (20-29, 30-44, 45-64, and 65+). The lung $cancers_{SHS}$ were summed for each age and sex group to get the total lung cancers attributable to SHS in Ontario.

- Prevalence data for second-hand smoke exposure at home among non-smokers and for current smoking was obtained from the 2009-2010 Canadian Community Health Survey (CCHS). Prevalence of exposure to second-hand smoke at home among non-smokers, as well as prevalence of current and former smoking, was calculated for Ontario by sex and age group. See Table 12.

Table 12. Prevalence (and standard deviation) of smoking for current and former smokers, as well as exposure to second-hand smoke in the home, by sex and age

	P_{CS}		P_{FS}		P_{SHS}	
	Prevalence	s.d.	Prevalence	s.d.	Prevalence	s.d.
Males						
20–29	0.3097	0.0169	0.0877	0.0079	0.1055	0.0126
30–44	0.2691	0.0117	0.2012	0.0093	0.0279	0.0074
45–64	0.2569	0.0101	0.3398	0.0109	0.0459	0.0060
65+	0.0938	0.0073	0.5357	0.0116	0.0328	0.0036
Females						
20–29	0.2203	0.0130	0.0981	0.0075	0.0566	0.0074
30–44	0.1640	0.0079	0.1717	0.0085	0.0352	0.0073
45–64	0.1761	0.0085	0.2758	0.0092	0.0379	0.0045
65+	0.0901	0.0051	0.3000	0.0085	0.0245	0.0034
Both sexes						
20–29	0.2651	0.0110	0.0929	0.0054	0.0796	0.0072
30–44	0.2157	0.0073	0.1862	0.0063	0.0319	0.0052
45–64	0.2161	0.0065	0.3074	0.0071	0.0416	0.0039
65+	0.0917	0.0042	0.4058	0.0070	0.0282	0.0025

P_{CS}: prevalence of current smokers; P_{FS}: prevalence of former smokers; P_{SHS}: prevalence of exposure to second-hand smoke in the home; s.d.: standard deviation
Data source: Canadian Community Health Survey 2009-10 (Statistics Canada)

- Relative risk estimates for the association between lung cancer and second-hand smoke exposure among non-smokers and for the association between lung cancer and current and former smoking were obtained from the literature. These estimates and their associated sources are outlined in Table 13. The relative risks for a second-hand smoke exposure among non-smokers and for former smoking vs. never smoking were assumed to be the same for males and females and for all age-groups. Sex-specific relative risks were used for current smoking vs. never smoking but within each sex the relative risks were assumed to be the same for all age-groups.

Table 13. Summary of relative risks employed in the second-hand smoke PAF Approach

Exposed Population vs. Referent Population	Relative Risk (95% CI)	
	Males	Females
Second-hand smoke at home among non-smokers vs. non -smokers unexposed at home(RR_{SHS})[38]	1.21† (1.13, 1.30)	1.21† (1.13, 1.30)
Current smoking vs. never smoking (RR_{CS})[39]	9.87 (6.85, 14.24)	7.58 (5.36, 10.73)
Former smoking vs. never smoking (RR_{FS})[39]	3.85† (2.77, 5.35)	3.85† (2.77, 5.35)

CI: confidence interval; RR_{CS}: relative risk for current smokers; RR_{FS}: relative risk for former smokers; RR_{SHS}: relative risk for those exposed to second-hand smoke

† No difference in estimate of relative risk by sex

Modeling the SHS PAF in the probabilistic analysis

The prevalence estimates were modeled as normal distributions with the corresponding means and standard deviations in Table 12. The RRs were modeled as normal distributions, with the means as shown in Table 13 and the standard deviations calculated from the 95% CI as in Section 6. The mean estimates of the PAF for SHS ranged from 0.5% to 2.2% across the age and sex subgroups and was 0.6% overall (Table 14).

Table 14. Inputs and outputs of second-hand smoke PAF approach

Age (years)	Total lung cancers	Lung cancers$_{NS}$	Lung cancers$_{SHS}$ (PAF$_{SHS}$)†
			Mean estimates
Males			
20–29	6	1	0 (2.2%)
30–44	48	14	0 (0.6%)
45–64	1,307	450	4 (1.0%)
65+	3,623	2,470	17 (0.7%)
Total, males	4,984	2,936	21 (0.7%)
Females			
20–29	6	2	0 (1.2%)
30–44	71	34	0 (0.7%)
45–64	1,423	711	6 (0.8%)
65+	3,175	2,190	11 (0.5%)
Total, females	4,674	2,937	17 (0.6%)
Both sexes			
20–29	12	3	0 (1.6%)
30–44	119	48	0 (0.7%)
45–64	2,730	1,161	10 (0.9%)
65+	6,798	4,660	28 (0.6%)
Total	9,658	5,872	38 (0.6%)

†Lung cancers$_{SHS}$ are calculated as the product of the Lung cancers$_{NS}$ and the PAF$_{SHS}$ and rounded to the nearest whole number for the age and sex subgroups. For the total, the Lung cancers$_{SHS}$ are the sum of the age subgroup Lung cancers$_{SHS}$ and the PAF$_{SHS}$ is estimated from the Lung cancers$_{SHS}$ divided by the Lung cancers$_{NS}$.

Data sources: Total lung cancers for year 2011 from Ontario Cancer Registry, 2015 (Cancer Care Ontario); Lung Cancers$_{NS}$, Lung Cancers$_{SHS}$, and PAF$_{SHS}$ estimated from equations above, using prevalence data in Table 12 and relative risks from Table 13.

Assumptions for SHS PAF approach

Assumptions for this approach include:

- The cancer burden of SHS can be quantified by examining lung cancer, for which IARC has deemed there to be sufficient evidence in humans; other cancers with limited evidence in humans (e.g., pharynx, larynx) were not examined
- Exposure to smoking in the home (rather than in "any location") is the relevant metric to capture the prevalence of exposure to SHS indoors
- Second-hand smoke exposure among the non-smoking population has not changed over time. Therefore, prevalence estimates from 2009-2010 assumed to be representative of past exposure.
- There is no lag time between exposure to second-hand smoke and the development of lung cancer.
- The study populations from which the relative risk estimates are derived are representative of the Ontario population and reflect the risk of lung cancer associated with second-hand smoke exposure at the present time.
- Second-hand smoke exposure does not influence the risk of developing lung cancer among current smokers and therefore no lung cancers among current smokers are attributable to second-hand smoke exposure.

Our assumptions related to current second-hand smoke prevalence being representative of past exposures and no lag time between exposure and disease are consistent with the assumptions we made for the other carcinogens and allow comparison across carcinogens. However, we acknowledge that exposure to second-hand smoke at home has declined significantly over the past decade and a lag time of 10 to 20 years between exposure and the development of lung cancer is more realistic. To examine the potential influence of these simplifying assumptions, we calculated the burden using prevalence estimates from 2000/01 (instead of 2009/10), thereby introducing an 11 year lag and found a central estimate of 68 cancers attributed to SHS compared to 38, or 1.8 times higher estimates.

6. Probabilistic Analysis

In this section, we describe the general probabilistic approach for the RA and PAF methods, as well as list the inputs.

Approach

We employed a probabilistic, approach to estimate a plausible range for the burden using a risk assessment (RA) or population attributable fraction (PAF) model, as appropriate. In a probabilistic analysis, essentially, point estimate inputs into equations are replaced with distributional inputs, so the result is also a range of plausible values. The main inputs in this analysis were plausible ranges for concentration (in air, food, drinking water, and dust) and cancer potency (for the inhalation or ingestion routes of exposure). We conducted the analysis using @RISK software. This section describes the analysis and inputs.

The following definitions are helpful for understanding probabilistic analyses:

- **Variability**: Refers to true differences in attributes due to heterogeneity. Not usually reduced by further measurement/study, though it can be better characterized.
- **Uncertainty**: Lack of information. Uncertainty analysis attempts to describe the degree to which a calculated value may differ from a true value.
- **Sensitivity**: The degree to which the outputs of a quantitative assessment are affected by changes in the selected input parameters or assumptions.

A probabilistic analysis incorporates the variability and uncertainty in the inputs. In our analysis, we characterized variability and uncertainty to the extent possible. Sensitivity of the estimated results to the inputs could be assessed using the standard output from the @RISK model (e.g., tornado plots). Table 15 indicates the variability and uncertainty for each parameter, and if or how it was characterized in the analysis.

Table 15. Variability and uncertainty in probabilistic inputs

Input	Model	Variable?	Uncertain?
Concentration	RA & PAF	Yes, concentration was characterized by a distribution in this analysis. The distribution may not reflect the entire spectrum of possible concentrations, only what was captured in the data source.	Yes, but did not have information to characterize it for this analysis.
Oral slope factor (OSF) or inhalation unit risk (IUR)	RA	Yes, in that different institutions can determine different values. The different values were used in this analysis.	Yes, generally OSFs and IURs represent an upper bound estimate. We did not attempt to obtain the underlying dose-response data for each carcinogen/route of exposure to estimate some of the uncertainty in each OSF or IUR estimate in this analysis.
Relative risks (RR)	PAF	Yes, the RR could differ by sub-populations (e.g., by sex or age group), though we generally did not have this information in this analysis.	Yes, the 95% confidence intervals of the RR or the slopes calculated from the RRs (reflecting statistical uncertainty) were employed in this analysis.
Exposure factors (EF; e.g., ingestion rate, bodyweight)	RA	Yes, EFs vary within and across age bins. We employed separate distributions for these parameters for each of the six age bins.	Yes, but did not have information to characterize it for this analysis.
Population	RA	No, one estimate for the province (from 2011 Census).	Yes, but uncharacterized. Expect this Census number to be robust.
Cancer Incidence	PAF	No, one estimate for the province (from 2011 Ontario Cancer Registry).	Yes, but uncharacterized. Expect this Ontario Cancer Registry estimate to be robust.

PAF: population attributable fraction; RA: risk assessment

Probabilistic modeling and simulation settings

We conducted the probabilistic modeling using software that runs in a spreadsheet called @RISK (@RISK for Excel: Risk Analysis Add-In for Microsoft Excel, Professional Edition, version 6.3.1, Pallisade Corporation, 2014). The @RISK add-in performs risk analysis using Monte Carlo simulation, showing a range of plausible outcomes, along with estimates of how likely the outcomes are to occur. It has been used to analyze risk and uncertainty in a wide variety of industries, such as finance, insurance, oil and gas, and the environment. Output can be presented as probability distribution functions, summary statistics, and tornado plots (which reflect the sensitivity of the model to input parameters).

We followed these steps to estimate the cancer burden:

1. **Specify the equations (RA and PAF models) to estimate the annual cancer burden**. After specifying the equations, we noted whether each input was treated as a variable, uncertain, or constant (point) estimate.

See Sections 4 and 5 for the RA and PAF equations

2. **Define the distributions corresponding to each of the input variables in the equations**. We assigned the appropriate distributional (e.g., normal, discrete probability) or point estimate to each input. There were 143 inputs in our analysis.

See Tables 18 to 22 for the input distributions.

3. **Designate the output cells as such in the spreadsheet**. After inserting the appropriate equation, the output cells in @RISK were designated as such.

    - There were 155 outputs in our analysis. (Many of these were interim outputs.)

4. **Define the settings for the simulations**. We set the number of simulations to 1 and the number of iterations to 10,000. We selected Latin hypercube sampling (rather than Monte Carlo sampling) for our analysis.

Note: Monte Carlo sampling techniques are random, meaning a sample value may fall anywhere within the range of the input distribution. By contrast, Latin Hypercube sampling stratifies the input probability distributions which more closely matches the input distribution and results in faster convergence.

- We checked the sensitivity of our results to running 10 simulations instead of 1 simulation. Since the model results converged well before the 10,000 iterations were completed in a simulation, using 10 simulations had no impact on the result

(i.e., there was no difference in the results whether the number of simulations was set to 1 or 10).

- We checked the sensitivity of our results to using Monte Carlo sampling instead of Latin hypercube sampling. This had only a minimal impact on the results: the Monte Carlo sampling generally produced higher estimates than the Latin Hypercube sampling, with the means between 0% and 5% higher.

5. **Run the simulation**. Once the equations are specified, the inputs were defined, and the simulation settings are set, it was straightforward to run the simulation in @RISK.

6. **Analyze the results**. The standard @RISK output included a probability density function, a cumulative probability density function, a tornado plot (showing the influence of all inputs), and summary statistics (e.g., 5/10/…90/95 percentiles, mean, min, max). There are several built-in tools that facilitate viewing the results in multiple formats in @RISK.

    - For this analysis, we summarized the results using the mean (as central tendency estimate) and a range consisting of the 5^{th} percentile and 95^{th} percentile estimates.

    - We visually examined the tornado plots to understand the influence of the input variables on the burden estimate.

Assumptions

Many of the assumptions we employed are specific to the model used. Therefore, RA model-specific and PAF model specific assumptions are listed under Sections 4 and 5, respectively. There are other general assumptions we employed, including:

- It is valid to present the environmental cancer burden estimates from different calculation methods (RA and PAF) together and to compare them.
- The bioavailability of carcinogens in air/food/dust/water is 100%.
- The exposure concentration did not vary across life stages. (In other words, we were not able to account for critical developmental periods associated with each carcinogen.)
- The exposure concentrations calculated using 2010 data (or available data that was closest to 2010) are applicable for this analysis (and do not reflect potentially higher concentrations in the past or potentially lower concentration in the future). Furthermore, potentially highly exposed individuals were not accounted for in this analysis.
- There is no lag between the onset of exposure and the onset of disease

Inputs

Prior to conducting the probabilistic modeling, we defined all inputs as distributions or point estimates. All inputs are presented below.

Concentration distributions

We developed concentration inputs following the approach and data sources outlined in Section 3. These are presented below in Table 16 and Table 17.

Table 16. Concentration inputs for probabilistic modeling by carcinogen and environmental source (presenting central estimates for food intakes)^

Carcinogen	Environmental Source	Distribution type	Mean (AM/ GM)[x]	Standard deviation (ASD/GSD) [x]	Units
Combustion by-products					
Outdoor air pollution (PM2.5)	Outdoor Air	lognormal	5.7367	1.2563	µg/m^3
Diesel PM2.5	Outdoor Air	lognormal	0.6837	2.3477	µg/m^3
2,3,7,8-Tetrachlorodibenzo-para-dioxin (TCDD)	Outdoor Air	lognormal	0.0104	2.2481	pg of TEQ/m^3
	Food^	point estimate	0.7935		pg of TEQ/kg-day
Polycyclic Aromatic Hydrocarbons (PAHs)	Outdoor Air	lognormal	0.0376	4.0223	ng/m^3
	Indoor Air	lognormal	0.1000	3.4256	ng/m^3
	Indoor Dust	lognormal	0.9630	3.1347	µg/g
	Drinking Water	point estimate	1.0000		µg/L
	Food^	point estimate	55.400		ng/d
Metals and metalloids					
Arsenic	Outdoor Air	lognormal	0.4584	2.4808	ng/m^3
	Indoor Air	lognormal	0.1166	2.5735	ng/m^3
	Drinking Water	lognormal	0.3927	1.8307	µg/L
	Indoor Dust	normal	13.1000	14.3000	µg/g
	Food^	point estimate	0.5676		µg/kg-day
Cadmium	Outdoor Air	lognormal	0.0814	2.2453	ng/m^3
	Indoor Air	lognormal	0.0245	2.1153	ng/m^3
Chromium (VI)	Outdoor Air	lognormal	0.3142	2.0196	ng/m^3
	Indoor Air	lognormal	0.5916	2.8576	ng/m^3
	Indoor Dust	normal	117.0000	112.0000	µg/g
	Drinking Water	lognormal	0.2038	2.2686	µg/L
Nickel	Outdoor Air	lognormal	0.3491	2.4067	ng/m^3
	Indoor Air	lognormal	0.3776	4.1270	ng/m^3

Carcinogen	Environmental Source	Distribution type	Mean (AM/ GM)[x]	Standard deviation (ASD/GSD) [x]	Units
Volatile organic compounds (VOCs)					
1,2-dichloropropane	Outdoor Air	lognormal	0.0149	1.5952	µg/m^3
	Indoor Air	logormal	0.0100	1.5985	µg/m^3
	Drinking Water	point estimate	0.0500		µg/L
1,3-butadiene	Outdoor Air	lognormal	0.0192	3.8044	µg/m^3
	Indoor Air	lognormal	0.1089	2.1914	µg/m^3
Alpha-chlorinated toluenes	Outdoor Air	lognormal	0.0092	2.0990	µg/m^3
	Indoor Air	lognormal	0.0156	1.0791	µg/m^3
Benzene	Outdoor Air	lognormal	0.3894	2.0649	µg/m^3
	Indoor Air	lognormal	1.0400	2.9308	µg/m^3
	Drinking Water	point estimate	0.0500		µg/L
Dichloromethane	Outdoor Air	lognormal	0.3189	1.7592	µg/m^3
	Indoor Air	lognormal	1.3828	2.1914	µg/m^3
	Drinking Water	point estimate	0.2000		µg/L
Formaldehyde	Outdoor Air	lognormal	1.3373	2.3582	µg/m^3
	Indoor Air	lognormal	26.9622	1.6380	µg/m^3
Tetrachloroethylene (PCE)	Outdoor Air	lognormal	0.0633	2.2631	µg/m^3
	Indoor Air	lognormal	0.3100	5.2528	µg/m^3
	Drinking Water	lognormal	0.0513	1.3143	µg/L
Trichloroethylene (TCE)	Outdoor Air	lognormal	0.0216	2.9063	µg/m^3
	Indoor Air	lognormal	0.0400	2.7346	µg/m^3
	Drinking Water	lognormal	0.0516	1.2511	µg/L
Vinyl chloride	Outdoor Air	lognormal	0.0022	1.9162	µg/m^3
	Indoor Air	lognormal	0.0245	1.1357	µg/m^3
	Drinking Water	point estimate	0.0500		µg/L
Other					
Acrylamide	Food^	point estimate	0.2807		µg/kg-day
Asbestos	Outdoor Air	normal	0.0000	0.0003	f/mL
	Indoor Air	normal	0.0001	0.0003	f/mL
Polychlorinated biphenyls (PCBs)	Outdoor Air	lognormal	0.0019	2.6430	pg of TEQ/m^3
	Indoor Air	lognormal	0.1470	2.0189	pg of TEQ/m^3
	Indoor Dust	normal	0.0087	0.0060	ng of TEQ/g
	Food^	point estimate	2.7000		ng/kg-day

Note: Environmental concentration estimates were not used for the UV, second-hand smoke, or radon PAF models.

Carcinogen	Environmental Source	Distribution type	Mean (AM/ GM)[x]	Standard deviation (ASD/GSD) [x]	Units

[x]Arithmetic or geometric means and standard deviations are presented for normal (AM and ASD) and lognormal (GM and GSD) distributions, respectively.

^Discrete probability distributions were used to model intake by food ingestion (see table below for more detail); point estimates are provided here as a summary.

Food intake details

The food intakes (in units of μg/kg-d) were obtained from the Total Diet Study as mean values for approximately 11 age bins. When male and female mean intakes were provided separately for each age bin, we averaged them. In an effort to attempt to characterize variability associated with the food intake estimates, we used the spread of measures from the ten age bins, noting this will underestimate true variability. For PAH, we obtained an estimate of intake (in ng/d) converted it to intake units of ng/kg-d by dividing by bodyweight.

Table 17. Food intake discrete probability distributions for dioxin, acrylamide, arsenic, PCBs, and PAHs

2,3,7,8-tetrachlorodibenzo-para-dioxin (TCDD)		Acrylamide		Arsenic		Polychlorinated biphenyls (PCBs)		Polycyclic aromatic hydrocarbons (PAHs)	
Exposure (pg of TEQ/kg-day)	Probability	Exposure (µg/kg-day)	Probability	Exposure (µg/kg-day)	Probability	Exposure (ng/kg-day)	Probability	Exposure (ng/d)	Probability
0.440	0.188	0.157	0.113	0.365	0.188	1.625	0.188	10.000	0.030
0.535	0.313	0.187	0.250	0.420	0.002	1.950	0.313	30.050	0.265
0.710	0.250	0.211	0.013	0.440	0.002	2.545	0.250	50.050	0.310
0.890	0.100	0.248	0.250	0.490	0.003	2.920	0.100	70.050	0.265
1.520	0.088	0.288	0.150	0.530	0.250	4.820	0.088	90.050	0.080
1.880	0.002	0.356	0.063	0.545	0.100	5.180	0.002	110.050	0.040
1.930	0.002	0.442	0.063	0.575	0.313	5.240	0.002	130.050	0.000
2.100	0.003	0.597	0.063	0.630	0.003	5.500	0.003	150.050	0.010
2.390	0.050	0.609	0.038	0.830	0.050	7.160	0.003		
2.450	0.002			0.940	0.088	7.410	0.050		
2.710	0.003			2.920	0.002	7.940	0.002		

Carcinogenic potency

Slope factors and unit risks (risk assessment model)

We used a discrete uniform probability distribution to model the IURs and OSFs in @RISK. In other words, if one agency provided an estimate for the IUR (or OSF) for a carcinogen, we applied that estimate (weighting it by 100%). If two agencies provided an estimate, we weighted each estimate by 0.5. In the few cases that three agencies provided an estimate, we weighted each estimate by 0.33. See Table 18 and Table 19 for the IUR and OSF estimates, as well as the cancer sites associated with each carcinogen, as defined by IARC. (The RR estimates for the carcinogens that were evaluated using a PAF approach are contained in Section 5.)

Table 18. Oral slope factors (by agency) and summary of cancer site associated with carcinogen exposure in critical effect study

Carcinogen*	Oral Slope Factor (per mg/kg-day)					
	Health Canada	Cancer/ Species	US EPA	Cancer/ Species	CalEPA	Cancer/ Species
Combustion by-products						
Diesel engine exhaust						
2,3,7,8-Tetrachlorodibenzo-para-dioxin (TCDD)					1.3E+05	liver / mouse
Polycyclic Aromatic Hydrocarbons (PAHs)	2.3E+00	gastric / mice	7.3E+00	gastric / mice	2.9E+00	gastric / mice
Metals and metalloids						
Arsenic	1.8E+00	bladder, lung, liver / human	1.5E+00	skin / human	9.5E+00	skin / human
Cadmium[x]						
Chromium (VI)					5.0E-01	stomach / mice
Nickel						
Volatile organic compounds (VOCs)						
1,2-Dichloropropane					3.6E-02	liver / mice
1,3-Butadiene					6.0E-01	lung / mice
alpha-Chlorinated toluenes			1.7E-01	thyroid / rats	1.7E-01	thyroid / rats
Benzene[#]	8.3E-02	lymphoma / rats, mice	5.5E-02	leukemia / human, occupational	1.0E-01	leukemia / human, occupational
Dichloromethane (methylene chloride)	7.9E-05	lung / rats, mice	2.0E-03	liver / mice	1.4E-02	lung / mice

Carcinogen*	Oral Slope Factor (per mg/kg-day)					
	Health Canada	Cancer/ Species	US EPA	Cancer/ Species	CalEPA	Cancer/ Species
Formaldehyde						
Tetrachloroethylene (PCE)			2.1E-03	liver / mice	5.4E-01	liver / mice
Trichloroethylene (TCE)	8.1E-04	renal / rats	4.6E-02	renal, liver, non-hodgkin's lymphoma / humans	5.9E-03	liver, lymphoma / mice
Vinyl chloride (chloroethene)^	2.6E-01	liver / rats	1.5E+00	liver / rats	2.7E-01	lung / mice
Other						
Acrylamide			5.0E-01	thyroid, tunica vaginalis mesotheliomas / rats	4.5E+00	central nervous system, thyroid, breast, uterus, oral / rats
Asbestos						
Polychlorinated biphenyls (PCBs)			2.0E+00	liver, bile ducts / rats	2.0E+00	liver / mice

[#]Where one agency presented a range for the slope factor, the high range from that agency was used.

^The "from birth" value was selected from US EPA IRIS.

*The burden for these carcinogens was estimated using the RA model. The potency estimates for the carcinogens using the PAF model are presented separately.

[x]While CalEPA presented an OSF for cadmium we did not employ it.

Table 19. Inhalation unit risk (by agency) and summary of cancer site associated with carcinogen exposure in critical effect study

Carcinogen*	Inhalation Unit Risk (per µg/m^3)					
	Health Canada	Cancer/ Species	US EPA	Cancer/ Species	CalEPA	Cancer/ Species
Combustion by-products						
Diesel engine exhaust					3.0E-04	Lung / humans, occupational
2,3,7,8-Tetrachlorodibenzo-para-dioxin (TCDD)					3.8E+01	
Polycyclic Aromatic Hydrocarbons (PAHs)	3.1E-05	Respiratory tract / hamsters			1.1E-03	Respiratory tract / hamsters
Metals and metalloids						
Arsenic	6.4E-03	Lung / humans	4.3E-03	Lung / humans, occupational	3.3E-03	Lung / humans, occupational
Cadmium	9.8E-03	Lung / humans	1.8E-03	Lung, trachea, bronchus / humans, occupational	4.2E-03	Lung / humans, occupational
Chromium (VI)	7.6E-02	Lung / Human	1.2E-02	Lung / Human	1.5E-01	Lung / Human
Nickel					2.6E-04	Lung /Human, occupational
Volatile organic compounds (VOCs)						
1,2-Dichloropropane					1.0E-05	hepatocellular adenoma, carcinomas /mice
1,3-Butadiene			3.0E-05	leukemia / humans, occupational	1.7E-04	lung / mice
alpha-Chlorinated toluenes					4.9E-05	thyroid / rats
Benzene[#]	3.3E-06	leukemia / human, occupational	7.8E-06	leukemia / human, occupational	2.9E-05	leukemia / human, occupational
Dichloromethane (methylene chloride)	2.3E-08	lung, liver / rats, mice	1.0E-08	lung, liver / mice	1.0E-06	lung / mice
Formaldehyde			1.3E-05	squamous cell carcinoma/ rats	6.0E-06	nasal squamous carcinoma / rats
Tetrachloroethylene (PCE)			2.6E-07	liver / mice	5.9E-06	liver / mice

Carcinogen*	Inhalation Unit Risk (per µg/m^3)					
	Health Canada	Cancer/ Species	US EPA	Cancer/ Species	CalEPA	Cancer/ Species
Trichloroethylene (TCE)	6.1E-07	testes (leydig cells) / rats	4.1E-06	renal, liver, non-Hodgkin's lymphoma / humans	2.0E-06	lung, liver, lymphoma / mice
Vinyl chloride (chloroethene)^			8.8E-06	liver / rats	7.8E-05	lung / mice
Other						
Asbestos[x]			2.3E-01	lung, mesothelioma / humans, occupational	1.9E+00	lung, mesothelioma / humans, occupational
Polychlorinated biphenyls (PCBs)			1.0E-04	liver, bile ducts / rats	5.7E-04	liver / rats

[#]Where one agency presented a range for the slope factor, the high range from that agency was used.

^The "from birth" value was selected from US EPA IRIS.

*The burden for these carcinogens was estimated using the RA model. The potency estimates for the carcinogens using the PAF model are presented separately.

[x]The units for the asbestos IUR are per fibres/mL

Estimated population attributable fractions, relative risks, and slopes (PAF model)

The potencies for the PAF model are either from PAFs directly (radon and UV), from RRs (SHS), or from calculated measures from RRs ($PM_{2.5}$). See Table 20, which also notes the cancer site associated with the study for each carcinogen.

Table 20. Probabilistic inputs for the potencies for the PAF model

Carcinogen	Cancer site	Note	Metric	AM	ASD
$PM_{2.5}$[#]	Lung	Units: per µg/m^3	slope	0.0104	0.0025
UV[^]	Skin	Method 1	PAF	0.640	NA
		Method 2	PAF	0.954	NA
Radon	Lung		PAF	0.136	0.015
Second-hand smoke[†]	Lung	SHS	PAF	0.006	NA
		SHS	RR	1.21	0.04
		CS/male	RR	9.87	1.89
		CS/female	RR	7.58	1.37
		FS	RR	3.85	0.66

AM: arithmetic mean; ASD: arithmetic standard deviation; CS: current smoker; FS: former smoker; RR: relative risk; NA: not applicable; PAF: population attributable fraction; SHS: second-hand smoke
$PM_{2.5}$ slope also applied to diesel $PM_{2.5}$; units are per µg/m^3
^ The UV PAF was modeled as a uniform distribution, with the range as the AMs from Method 1 and 2
[†] See Section 5 for the equations in which these RRs are applied, along with the corresponding prevalence estimates

Other inputs

The rest of the inputs for the RA and PAF models are described here.

Exposure factors (RA model only)

The sources for the exposure factors are listed in Section 4. The drinking water ingestion rate was lognormally distributed with GM and GSD shown in Table 21. The dust ingestion rate and bodyweight were normally distributed with AM and ASD shown in Table 21. The normal distributions were left-truncated at zero in @RISK to avoid generating implausible (negative) input parameters.

Table 21. Exposure factor distributions for ingestion and bodyweight, by age group

		Drinking Water ingestion rates (L/d)		Dust Ingestion Rate (mg/d)		Bodyweights (kg)	
Age Group	**Fraction of Lifespan**	*GM*	*GSD*	*AM*	*ASD*	*AM*	*ASD*
Infant	0.013	0.25	1.84	36	130	8.1	2
Toddler	0.038	0.5	1.84	41	71	15.3	2.3
Child	0.100	0.72	1.49	32	59	35.2	14.9
Teen	0.100	0.86	1.73	2.2	3.6	65.2	14.5
Adult	0.563	1.32	1.65	2.6	4.2	76.5	15.8
Senior	0.188	1.49	1.43	2.6	4.2	73.6	13.9

AM: arithmetic mean; ASD: arithmetic standard deviation; GM: geometric mean; GSD: geometric standard deviation

Time spent indoors (RA model only)

The source for the fraction of time spent indoors is specified in Section 3. This normal distribution, with AM of 0.96 (and ASD of 0.08), was constrained between the values of 0 (all time spent outdoors) and 1.0 (all time spent indoors) to avoid generating implausible inputs. This fraction was applied to indoor air inhalation in the RA and (1 – this fraction) was applied to outdoor air inhalation in the RA, as specified in the RA equations shown in Section 4.

Point estimates

We applied several point estimates in our probabilistic analysis, as defined in Table 22.

Table 22. Point estimates in probabilistic analysis

Parameter	Model	Value	Unit
Lifetime	RA	80	years
Population of Ontario, less than 80 years old (2011)†	RA	12,745,163	persons
Incident melanoma cases (2011)^	PAF	3,184	cases
Incident lung cancer cases (2011)^	PAF	9,663	cases

PAF: population attributable fraction; RA: risk assessment

†Data Source: Pop Est Summary (Statistics Canada, Ontario Ministry Finance), Fall 2014 release, based on the 2011 Census

^Data Source: CCO SEER*Stat Package Release 10 - OCR (Aug. 2015).

7. Good Analytical Practices

We have tried to follow good analytical practices in this project. Some notable ones are listed below.

Following written standard operating procedures

Team members were asked to familiarize themselves with and follow the latest standard operating procedures (SOPs) in performing analyses related to this project.

Avoiding transcription errors

It is best to avoid manual transcription whenever possible. So, calculations performed using a statistical program were output directly to a results table, if at all possible. If manual transcription was unavoidable, standard double-checking techniques, such as having another person double check select results or re-typing results to ensure they match with original results, were used.

Quality Assurance (QA)/Quality Control (QC)

There were several levels of QA/QC.

1. Project team members assisted in developing and were asked to follow the SOPs.
2. A risk assessment practitioner reviewed the risk assessment equations and spot-checked several of the results. (December 2015)
3. We employed double-checking for the slope factor and concentration inputs, and did spot checking of several results. (January to March 2016)
4. We developed a spreadsheet containing point cancer burden estimates and compared these results with the mean estimates from the probabilistic analysis and investigated any areas of discrepancy.
5. The advisory committee reviewed the SOP and preliminary results (January 2016).
6. Risk assessors from the McLaughlin Centre reviewed our probabilistic approach (April 2016).
7. Several additional topic-area specific reviewers examined specific aspects of the report (e.g., technical supplement, food results, air results).

8. References

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