



Estimates of future cancer mortality attributable to modifiable risk factors in Canada

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Abstract

Objectives Modifiable lifestyle, environmental, and infectious risk factors associated with cancer impact both cancer incidence and mortality at the population level. Most studies estimating this burden focus on cancer incidence. However, because these risk factors are associated with cancers of disparate mortality rates, the burden associated with cancer incidence could differ from cancer mortality. Therefore, estimating the cancer mortality attributable to these risk factors provides additional insight into cancer prevention. Here, we estimated future cancer deaths and the number of avoidable deaths in Canada due to modifiable risk factors.

Methods The projected cancer mortality data came from OncoSim, a web-based microsimulation tool. These data were applied to the methodological framework that we previously used to estimate the population attributable risks and the potential impact fractions of modifiable risk factors on Canadian cancer incidence.

Results We estimated that most cancer deaths will be attributed to tobacco smoking with an average of 27,900 deaths annually from 2024 to 2047. If Canada's current trends in excess body weight continue, cancer deaths attributable to excess body weight would double from 2786 deaths in 2024 to 5604 deaths in 2047, becoming the second leading modifiable cause of cancer death. Applying targets to reduce these risk factors, up to 34,600 cancer deaths could be prevented from 2024 to 2047.

Conclusion Our simulated results complement our previous findings on the cancer incidence burden since decreasing the overall burden of cancer will be accelerated through a combination of decreasing cancer incidence and improving survival outcomes through improved treatments.

Résumé

Objectifs Les facteurs de risque modifiables associés au cancer (liés au mode de vie, à l'environnement, aux maladies infectieuses) ont des effets à la fois sur l'incidence du cancer et sur la mortalité par cancer à l'échelle de la population. La plupart

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des études qui estiment ce fardeau portent sur l'incidence du cancer. Cependant, comme les facteurs de risque susmentionnés sont associés à des cancers dont les taux de mortalité sont disparates, le fardeau associé à l'incidence du cancer pourrait différer de la mortalité par cancer. En conséquence, l'estimation de la mortalité par cancer imputable à ces facteurs de risque pourrait éclairer la prévention du cancer. Nous estimons ici les décès futurs par cancer et le nombre de décès évitables au Canada dus à des facteurs de risque modifiables.

Méthode Les données projetées sur la mortalité par cancer proviennent d'OncoSim, un outil de microsimulation en ligne. Elles ont été appliquées au cadre méthodologique que nous avons déjà utilisé pour estimer les risques attribuables dans la population et les fractions de l'incidence potentielle des facteurs de risque modifiables sur l'incidence canadienne du cancer.

Résultats Selon nos estimations, entre 2024 et 2047, la plupart des décès par cancer seront imputés au tabagisme, qui causera en moyenne 27 900 décès par année. Si les tendances actuelles au Canada en matière de surpoids se maintiennent, les décès par cancer attribuables au surpoids doubleraient, passant de 2 786 décès en 2024 à 5 604 en 2047, et le surpoids deviendrait la deuxième cause modifiable de décès par cancer. En appliquant des cibles de réduction de ces facteurs de risque, jusqu'à 34 600 décès par cancer pourraient être évités entre 2024 et 2047.

Conclusion Les résultats de notre simulation confirment nos constatations antérieures sur le fardeau de l'incidence du cancer, car la diminution du fardeau global du cancer sera accélérée par une combinaison de la diminution de l'incidence du cancer et de l'amélioration des résultats de survie grâce à l'amélioration des traitements.

Keywords Cancer prevention · Cancer mortality · Risk factors · Microsimulation

Mots-clés Prévention du cancer · mortalité par cancer · facteurs de risque · microsimulation

Introduction

With an estimated 83,300 projected deaths due to cancer in Canada in 2020, cancer is the leading cause of death in Canada accounting for approximately 30% of all deaths among Canadians (Brenner et al. 2020). Cancer mortality rates vary across cancer sites, largely due to differences in cancer incidence and also in differences in cancer control activities such as screening, diagnosis, treatment, and follow-up care, and spatial differences in the many risk factors for cancer such as tobacco smoking, alcohol use, diet, sun exposure, body size, and physical activity (Canadian Cancer Society's Advisory Committee 2017). With cancer a leading cause of mortality and morbidity, preventive efforts to reduce the cancer burden are a top priority globally (Bray and Soerjomataram 2018). Understanding the incidence and subsequent preventable mortality burden of cancer due to modifiable risk factors is an important step towards focusing preventive efforts and prevention resources. Reducing cancer mortality involves efforts to control the disease across the cancer continuum from incidence (primary prevention) to screening and treatment (secondary prevention) and survival (tertiary prevention).

Cancer etiologic research over the past six decades has elucidated risk factors for which there is moderate to strong evidence that they are associated with an elevated risk of different cancer sites. Systematic reviews and syntheses of this evidence have been conducted by the International Agency for Research on Cancer (IARC) and the World Cancer Research Fund (WCRF), as two of the leading organizations focused on cancer prevention (World Cancer Research Fund/American Institute for Cancer Research 2011, 2018a, 2018b). Some of the leading

risk factors that have been identified through these evidence synthesis activities include factors that are both modifiable and non-modifiable (International Agency for Research on Cancer (IARC) 2004, 2010, 2016). In our previous work on the main modifiable risk factors for cancer incidence (Poirier et al. 2019a), we focused on tobacco smoking, inadequate physical activity, excess body weight, sedentary behaviour, alcohol consumption, low fruit and vegetable intake, red and processed meat consumption, air pollution, residential radon, ultraviolet radiation, *Helicobacter pylori* (*H. pylori*), human papillomavirus, Epstein-Barr virus, and hepatitis B and C viruses as key risk factors for which there were population-level exposure prevalence data available. Our study examined the current and future burden of cancer incidence that could be prevented if exposures to these modifiable risk factors were reduced or eliminated. The study was limited to examining only the burden of cancer associated with cancer incidence and did not consider the resulting decreased burden of cancer mortality that would ensue with decreases in cancer incidence, because we previously did not have reliable projections of cancer mortality data. We estimated that up to 70,000 (or 37%) of all cancers diagnosed in Canada in 2015 could be attributed to 16 modifiable risk factors, where this figure could rise to 102,000 cases in 2042. By achieving modest to aspirational intervention targets in all risk factors (such as 10% to 50% reduction in exposure prevalence), about 10,700 to 39,700 cancer cases could be prevented annually by 2042.

OncoSim, a suite of microsimulation models developed with Canadian population-level data by the Canadian Partnership Against Cancer and Statistics Canada, is a modeling analysis tool that can be used to project cancer incidence,

mortality, and cancer management costs to inform policy and decision-making in regard to cancer care, treatment, and prevention (Gauvreau et al. 2017). The OncoSim framework supports cancer policies and decision-making across Canada because its suite of models can simulate the health and economic impacts of current, future, and past cancer control interventions in the Canadian population using Canadian health care costs (Ruan et al. 2021). Specifically, OncoSim has projected cancer deaths in Canada up to 2051 based on validated models (Gauvreau et al. 2017). We have also validated the OncoSim mortality projections against historical mortality data in Canada. These mortality projections present an opportunity to apply our methodological approach for estimating preventable incidence in estimating the number of future cancer deaths attributable to modifiable risk factors. The objective of these analyses was to estimate the attributable cancer mortality due to modifiable risk factors, and to estimate the preventable cancer mortality with various intervention targets in Canada.

Methods

Projected cancer mortality

The projected cancer mortality was retrieved from the OncoSim microsimulation model (version 3.2.7), which is based on death data from the Canadian Vital Statistics Death Database. The OncoSim model, previously known as the Cancer Risk Management Model (CRMM), is a publicly accessible, web-based tool consisting of four in-depth cancer models (lung, colorectal, cervical, and breast) and a generalized all-cancer model (an additional 27 other cancers). The development, validation, and application of the OncoSim model have been extensively documented (Coldman et al. 2018; Gauvreau et al. 2017; Popadiuk et al. 2016). In this study, we used the cancer mortality projections of 31 cancer types diagnosed among Canadians 35 years of age and over, from the years 2024 to 2047. This time window corresponds to the period of estimates for the population attributable risk (PAR) and potential impact fraction (PIF) from the Canadian Population Attributable Risk of Cancer study, or ComPARE (2019 to 2042). Here, we assumed a five-year latency between cancer incidence and death.

Risk factor selection and risk estimates

We included risk factors where we had previously estimated the future burden of their associated cancers and preventable fractions (Brenner et al. 2018, 2019). This included active and passive tobacco smoking exposure, excess body weight, physical inactivity, leisure-time sedentary behaviour, alcohol use, low fruit and vegetable consumption, red and processed meat

consumption, ultraviolet radiation risk behaviours, air pollution (PM_{2.5}), residential radon, *H. pylori*, and hepatitis B and C viruses. We applied the same relative risks for each exposure-cancer association that were used in the ComPARE study (Table S1) (Brenner et al. 2018, 2019). We assumed that the relative risk of cancer incidence for each exposure was approximately equal to the relative risk of cancer death for the same exposure. These risk estimates were extracted from the WCRF continuous update project, from high-quality systematic reviews and meta-analyses published up to August 2017, or through our own meta-analyses when a summary estimate of interest was not available (Brenner et al. 2018, 2019).

Exposure prevalence projection and intervention scenarios

The specific methods to project the future prevalence of exposures have been previously described (Brenner et al. 2018). Briefly, when historical repeated prevalence measures were available (i.e., active and passive smoking, body mass index (BMI), inadequate physical activity, leisure-time sedentary behaviour, alcohol use, low fruit and vegetable intake, air pollution, and hepatitis C virus (HCV)), we projected future prevalence up to 2032 (2036 for air pollution) based on the assumption that the observed past trend would continue into the future. For most risk factors, the time period of exposure up to 2032 corresponds to the projected mortality up to 2047, accounting for a 15-year latency period between exposure and death. When historical prevalence measures were limited (e.g., only one measure for ultraviolet radiation risk behaviours, radon, hepatitis B virus (HBV), *H. pylori*, and red and processed meat), we assumed constant future prevalence at the value of the past prevalence measure. We used the same intervention scenarios as in the ComPARE study, which are described in detail elsewhere (Poirier et al. 2019b) and summarized in Table 1. When evidence-based intervention targets were not available, we included “benchmark” targets for the risk factors, such as 10%, 25%, and 50% relative reductions in the exposure prevalence.

Estimation of preventable future cancer deaths

We used the same PIF framework employed in the ComPARE study to estimate the number of preventable cancer deaths in Canada up to 2047 based on the intervention scenarios. First, we calculated the PIF (the fraction of cancer deaths that could be prevented) of each scenario using the specific approach for each given exposure (Table 1). We then estimated the number of avoidable cancer deaths by multiplying the projected future cancer deaths with the PIF for each exposure-cancer association. We assumed a 15-year latency period between the

Table 1 Risk factors, associated cancers, intervention targets or scenarios, and the method to estimate potential impact fractions

Risk factor	Associated cancers	Intervention targets/scenarios	Method to estimate PIF
Active smoking	Lung, oral cavity, larynx, esophagus, stomach, liver, pancreas, colon and rectum, kidney, bladder, ureter, ovary, cervix, breast, acute myeloid leukemia	10% reduction in smoking by 2032 25% reduction in smoking by 2032 50% reduction in smoking by 2032 Price increases reduced smoking by 3.7% in 2018 Reduce smoking prevalence to 5% by 2035 WHO 2020 goal: 30% relative reduction in current smoking by 2020	Proportions shift $PIF = \sum_c P_c \frac{RR_c - \sum_c P_c RR_c}{\sum_c P_c RR_c}$
Passive smoking	Lung, colon and rectum, cervix, breast	10% reduction in secondhand smoking by 2032 25% reduction in secondhand smoking by 2032 50% reduction in secondhand smoking by 2032	Proportions shift
Excess weight (as measured by body mass index)	Esophagus (ADC), stomach (cardia), liver, pancreas, colon, rectum, kidney, gallbladder, multiple myeloma, thyroid, breast (post-menopausal), ovary, endometrium, prostate (advanced)	Population BMI held at 2018 level Population BMI reverted to 1994 distribution Population mean BMI reduced by 1.0 Prevalence of overweight and obesity reduced by 5% by 2032 Prevalence of overweight and obesity reduced by 10% by 2032 Prevalence of overweight and obesity reduced by 25% by 2032	Distribution shift $PIF = \frac{\int RR(x)P(x)dx - \int RR(x)P^*(x)dx}{\int RR(x)P(x)dx}$
Inadequate physical activity	Breast (post-menopausal), lung, endometrium, colon, rectum, kidney, bladder, esophagus (ADC), stomach, liver, small intestine, myeloid leukemia, multiple myeloma, head and neck, non-Hodgkin lymphoma	Breast, colon and rectum, endometrium, ovary	Proportions shift
Sedentary behaviour	Breast, colon and rectum, oral cavity, larynx, liver, esophagus (SCC), pancreas, stomach	10% reduction in sedentary time by 2032 25% reduction in sedentary time by 2032 50% reduction in sedentary time by 2032	Proportions shift
Alcohol	Pancreas, bladder, lung, colon and rectum, breast, stomach, esophagus (SCC)	Alcohol drinking prevalence decreases by 10% by 2032 Alcohol drinking prevalence decreases by 25% by 2032 Alcohol drinking prevalence decreases by 50% by 2032 Everyone who drinks > 1/day reduces 1 drink each day WCRF guideline	Proportions shift Relative risk shift $PIF = \sum_c P_c RR_c - \sum_c P_c \frac{P_c RR_c}{\sum_c P_c RR_c}$
Low fruit	Pancreas, bladder, lung, colon and rectum, breast, stomach, esophagus (SCC)	Canadian guideline Everyone increases fruit intake by 1 serving/day Everyone increases fruit intake by 2 servings/day A relative 50% reduction in the prevalence of low fruit intake by 2032	Relative risk shift Proportions shift
Low vegetable	Pancreas, bladder, lung, colon and rectum, head and neck, ovary, liver, esophagus (ADC)	Everyone increases vegetable intake by 1 serving/day Everyone increases vegetable intake by 2 servings/day A relative 50% reduction in the prevalence of low vegetable intake by 2032	Relative risk shift Proportions shift
Processed meat	Colon and rectum, pancreas, stomach (non-cardia), esophagus (SCC)	Everyone reduces processed meat by 0.2 servings/week Everyone reduces processed meat by 0.5 servings/week Everyone reduces processed meat by 1 serving/week	Relative risk shift

Table 1 (continued)

Risk factor	Associated cancers	Intervention targets/scenarios	Method to estimate PIF
Red meat	Colon and rectum, pancreas, stomach	Everyone reduces red meat by 0.5 servings/week Everyone reduces red meat by 1 serving/week Everyone reduces red meat by 2 servings/week	Relative risk shift
Ultraviolet radiation risk behaviours (indoor tanning, sunburn, sunbathing)	Melanoma	10% reduction in UVR risk behaviours by 2037 25% reduction in UVR risk behaviours by 2037 50% reduction in UVR risk behaviours by 2037	Proportions shift
PM _{2.5}	Lung	Declining trend 50% reduction off stabilized levels by 2036	Distribution shift
Radon	Lung	Radon mitigation of above 100 Bq/m ³ to 50 Bq/m ³ by 2036	Distribution shift
Hepatitis B virus	Hepatocellular carcinoma	Radon mitigation of above 200 Bq/m ³ to 50 Bq/m ³ by 2036 10% reduction in the prevalence of HBV infection by 2027 25% reduction in the prevalence of HBV infection by 2027 50% reduction in the prevalence of HBV infection by 2027	Proportions shift
Hepatitis C virus	Hepatocellular carcinoma, non-Hodgkin lymphoma	10% reduction in the prevalence of HCV infection by 2027 25% reduction in the prevalence of HCV infection by 2027 50% reduction in the prevalence of HCV infection by 2027	Proportions shift
<i>Helicobacter pylori</i>	Stomach (non-cardia)	10% reduction in the prevalence of <i>H. pylori</i> infection by 2027 25% reduction in the prevalence of <i>H. pylori</i> infection by 2027 50% reduction in the prevalence of <i>H. pylori</i> infection by 2027	Proportions shift

ADC, adenocarcinoma; Bq/m³, becquerels per cubic metre; HBV, hepatitis B virus; HCV, hepatitis C virus; HCC, squamous cell carcinoma; SCC, squamous cell carcinoma; UVR, ultraviolet radiation; WCRF, World Cancer Research Fund; WHO, World Health Organization

recorded exposure to lifestyle and environmental risk factors (2009–2032) and cancer death (2024–2047), and a 20-year latency period for the infectious agents (HBV, HCV, and *H. pylori*) (2004–2027).

Results

Projected cancer mortality

From 2024 to 2047, we projected that the deaths from all cancers among Canadians aged 35 and over would rise from around 89,850 in 2024 to 112,920 in 2047. In 2047, the five highest projected mortality cancers were lung (25,400), colorectal (11,280), pancreas (8190), prostate (6970), and breast (5510) (Fig. 1). Colorectal, pancreatic, prostate, and breast cancers all showed a slight increase in the number of deaths over time, while lung cancer peaked at 28,530 deaths in 2034 and declined thereafter (Fig. 1).

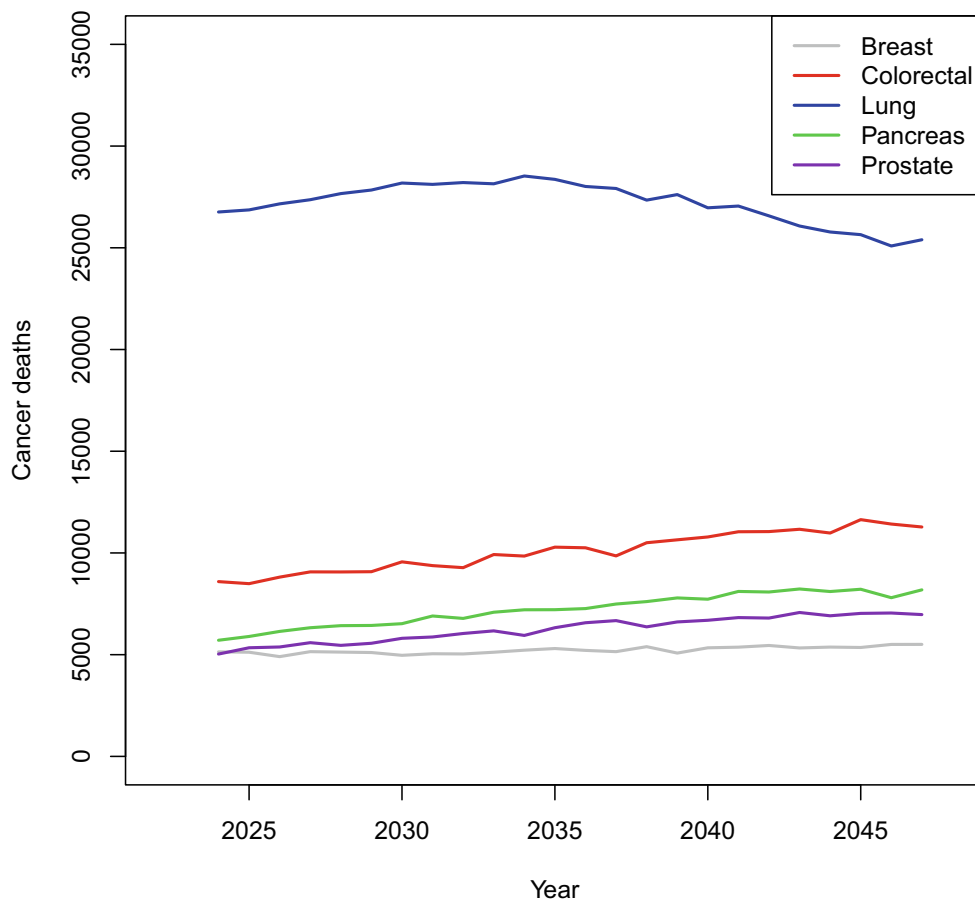
More cancer deaths were projected in males than in females (average of years 2024–2047, males: 54,500/year, females: 49,800/year). Among males, lung remained as the cancer with the highest mortality; however, annual lung cancer deaths

started declining after 2034 (Fig. S1). The second to fifth highest mortality cancers in males were prostate, colorectal, pancreatic, and bladder. Similarly for females, lung cancer also had the highest mortality, with a peak number of annual deaths reaching 15,380 in 2034 that is projected to decrease to 14,180 in 2047. For females, the next leading cancers with the highest mortality were breast, colorectal, pancreatic, and ovarian. The number of deaths due to breast cancer remained steady during this projected time period, while a slight increase in deaths from colorectal, pancreatic, and ovarian cancers was estimated to occur over the modeling period.

Attributable cancer mortality

We projected the attributable cancer deaths due to 10 lifestyle, three environmental, and three infectious agent risk factors (Table S2). Active tobacco smoking was associated with the most cancer deaths between 2024 and 2047, leading to an average of 27,900 cancer deaths each year. Excessive body weight would be attributed to a projected 2790 cancer deaths in 2024, which is estimated to double to 5600 deaths by 2047, the largest increase among all the risk factors under study.

Fig. 1 Projected breast (females), colorectal, lung, pancreatic, and prostate (males) cancer deaths in Canadians 35 years of age and over from 2024



Preventable cancer mortality

We further projected the number of cancer deaths that could be prevented if certain intervention targets could be achieved. Reducing the prevalence of active smoking by 10%, 25%, or 50% by 2032 could potentially prevent 6370, 15,920, or 31,870 cancer deaths from 2024 to 2047, respectively (Table 2). If we were able to achieve the World Health Organization (World Health Organization 2013) goal of reducing smoking by 30% by 2020 (World Health Organization 2012), as many as 34,601 cancer deaths from 2024 to 2047 would be prevented. In addition to the preventable deaths due to active tobacco smoking, 10%, 25%, or 50% reductions in the exposure to passive smoking by 2032 could additionally prevent 280, 690, or 1380 cancer deaths, respectively. Lung cancer deaths would be the most preventable cancer deaths from smoking intervention. A 10%, 25%, or 50% reduction in both active and passive smoking could prevent a cumulative 4950, 12,370, or 24,740 lung cancer deaths, respectively (Tables S3–S4).

In 2047, 2648 cancer deaths were attributed to alcohol consumption. If the drinking prevalence was decreased by 10%, 25%, or 50%, a cumulative 4310, 10,780, or 21,560 cancer deaths could be prevented from 2024 to 2047, respectively. In addition, if all Canadians were to drink within the WCRF or Canadian drinking guideline (WCRF: no more than 2 drinks a day for males and 1 drink a day for females; Canada: no more than 3 drinks a day for males and 2 drinks a day for females) (Butt et al. 2011; World Cancer Research Fund/American Institute for Cancer Research 2007), a cumulative 13,240 or 5760 cancer deaths could be prevented (Table 2). More than half of these preventable cancer deaths were from colorectal and oral cancers. For example, there were 4140 colorectal cancers and 3106 oral cancers among the 13,240 preventable cancer deaths due to not meeting the WCRF guideline (Table S5).

If we were able to halt the increasing trend of excess weight at the population level by holding the population BMI distribution at 2018 levels, 9030 cancer deaths could be prevented (Table 2). More aspirational intervention targets, such as reverting the population BMI to its distribution as of 1994, or reducing mean BMI by 1.0, would prevent 22,500 or 13,790 cancer deaths, respectively. Finally, a reduction in the prevalence of Canadians with a BMI over 25.0 by 5%, 10%, or 25% would prevent 8560, 14,950, or 27,230 cancer deaths, respectively (Table 2, Table S6). A 10%, 25%, or 50% reduction in the prevalence of inadequate physical activity could prevent 3310, 8270, or 16,540 cancer deaths. Likewise, the same percent reductions in the percentage of people classified as sedentary could prevent 1440, 3600, or 7190 cancer deaths (Table 2, Tables S7–S8).

We found that increasing fruit or vegetable consumption by one serving per day could prevent 5350 or 2638 colorectal

cancer deaths by 2047 (Tables S9–S10). If all convincing, probable, and suggestive associations between cancers and low fruit or vegetable consumption were considered, a total of 43,500 (fruit) or 37,010 (vegetable) cancer deaths could be prevented by 2047 (Table 2). Reducing processed meat or red meat consumption by one serving per week could prevent 7010 or 3370 colorectal cancer deaths, respectively (Tables S11–S12). If the suggestive association with pancreatic and stomach cancers were included, reducing processed or red meat consumption by one serving per week could prevent 15,070 or 9960 cancer deaths by 2047, respectively (Table 2).

We examined the preventable lung cancer deaths due to outdoor air pollution (PM_{2.5}) and residential radon exposure and the melanoma deaths due to UVR risk behaviours (Table 3, Table S13). Achieving a 50% reduction off the stabilized PM_{2.5} levels by 2036 could prevent 2920 lung cancer deaths by 2047. Mitigation of radon exposure in homes above 100 becquerels per cubic metre (Bq/m³; WHO guideline) or 200 Bq/m³ (Canadian guideline) to 50 Bq/m³, 2830 or 1840 lung cancer deaths could be prevented by 2047, respectively. Reduction in UVR risk behaviours such as sunbathing, sunburn, and indoor tanning by 10%, 25%, or 50% would prevent 410, 1050, or 2230 melanoma deaths by 2047, respectively.

Finally, we estimated the preventable cancer deaths due to infectious agents including HBV, HCV, and *H. pylori* (Table 3, Tables S14–S16). A 50% reduction in HBV or HCV infection could prevent 510 or 910 cancer deaths by 2047, respectively. Reducing *H. pylori* infection prevalence by 10%, 25%, or 50% by 2027 would prevent 610, 1530, or 3060 non-cardia stomach cancer deaths by 2047, respectively.

Discussion

We previously estimated the current and future burden of incident cancers in Canada due to modifiable risk factors as part of the ComPARE study (Brenner et al. 2019; Poirier et al. 2019c). The ComPARE study results on cancer incidence were incorporated within the OncoSim framework to estimate future cancer mortality and estimate preventable cancer mortality from years 2024 to 2047. Using validated projections of cancer mortality from OncoSim, we estimated the future burden of cancer deaths due to a selection of lifestyle, environmental and infectious agent risk factors, based on the methodological framework and hierarchy of evidence developed for the ComPARE study. Our projections suggest that deaths from all cancers in those aged 35 and over would increase by approximately 23,000 cases from 2024 to 2047 in Canada. At the end of this time period that we used, the OncoSim model projected that the greatest number of cancer deaths in 2047 would be for lung, colorectal, and pancreas cancers as well as prostate cancer in men and breast cancer in women. The

Table 2 Projected cancer deaths, attributable or preventable cancer deaths, and cumulative preventable cancer deaths of selected lifestyle factors that are associated with cancers in Canada from 2024 to 2047 estimated using the OncoSim all-cancer model

Exposure	Intervention targets/scenarios	Projected cancer deaths*	Preventable/attribution deaths**	Cumulative preventable deaths†
Active smoking	Base	72,934	26,446	6373
	10% reduction in smoking by 2032	72,200	734	15,934
	25% reduction in smoking by 2032	71,098	1836	31,869
	50% reduction in smoking by 2032	69,262	3672	28,461
	Price increases reduced smoking by 3.7% in 2018	71,016	1918	33,158
	Reduce smoking prevalence to 5% by 2035	69,103	3831	34,601
Passive smoking	WHO 2020 goal: 30% relative reduction in current smoking by 2020	70,731	2203	
	Base	23,453	278	
	10% reduction in secondhand smoking by 2032	23,425	28	276
	25% reduction in secondhand smoking by 2032	23,384	70	690
	50% reduction in secondhand smoking by 2032	23,314	139	1379
	Base	34,405	2809	
Alcohol	Alcohol drinking prevalence decreases by 10% by 2032	34,124	281	4312
	Alcohol drinking prevalence decreases by 25% by 2032	33,703	702	10,780
	Alcohol drinking prevalence decreases by 50% by 2032	33,000	1405	21,557
	Everyone who drinks > 1/day reduces 1 drink	33,062	1343	21,526
	WCRF guideline	33,584	822	13,240
	Canadian guideline	34,060	345	5756
Excess body weight	Base	49,241	5604	
	Population BMI held at 2018 level	47,978	1264	9030
	Population BMI reverted to 1994 distribution	46,199	3042	22,495
	Population mean BMI reduced by 1.0	47,333	1909	13,792
	Prevalence of overweight and obesity reduced by 5% by 2032	48,044	1198	8561
	Prevalence of overweight and obesity reduced by 10% by 2032	47,180	2061	14,951
Inadequate physical activity	Prevalence of overweight and obesity reduced by 25% by 2032	45,612	3630	27,234
	Base	53,266	4898	
	10% reduction in inadequate physical activity by 2032	52,862	405	3309
	25% reduction in inadequate physical activity by 2032	52,255	1012	8271
	50% reduction in inadequate physical activity by 2032	51,243	2023	16,543
	Base	21,114	1975	
Sedentary behaviour	10% reduction in sedentary time by 2032	20,926	188	1438
	25% reduction in sedentary time by 2032	20,643	471	3595
	50% reduction in sedentary time by 2032	20,172	942	7191
	Base			

Table 2 (continued)

Exposure	Intervention targets/scenarios	Projected cancer deaths**	Preventable/attributional deaths**	Cumulative preventable deaths†
Low fruit consumption	Base	58,821	5647	
	Everyone increases fruit intake by 1 serving/day	56,594	2227	43,500
	Everyone increases fruit intake by 2 servings/day	54,849	3973	78,740
	A relative 50% reduction in the prevalence of low fruit by 2032	55,998	2823	22,692
Low vegetable consumption	Base	59,410	4297	
	Everyone increases vegetable intake by 1 serving/day	57,555	1855	37,012
	Everyone increases vegetable intake by 2 servings/day	56,217	3192	65,959
	A relative 50% reduction in the prevalence of low vegetable by 2032	57,262	2148	17,824
Processed meat	Base	22,397	1094	
	Everyone reduces processed meat by 0.2 servings/week	22,226	170	3068
	Everyone reduces processed meat by 0.5 servings/week	21,974	423	7629
	Everyone reduces processed meat by 1 serving/week	21,563	834	15,065
Red meat	Base	23,288	1849	
	Everyone reduces red meat by 0.5 servings/week	23,006	282	5012
	Everyone reduces red meat by 1 serving/week	22,728	560	9958
	Everyone reduces red meat by 2 servings/week	22,184	1104	19,655

BMI, body mass index; *WCRF*, World Cancer Research Fund; *WHO*, World Health Organization

*Projected cancer deaths from all cancer sites associated with the risk factor in 2047

**Attributable cancer deaths of base scenario in 2047, or preventable cancer deaths of interventions in 2047

†Cumulative preventable deaths from 2024 to 2047

Table 3 Projected cancer deaths, attributable or preventable cancer deaths, and cumulative preventable cancer deaths of selected environmental factors and infections that are associated with cancers in Canada from 2024 to 2047 estimated using the OncoSim all-cancer model

Exposure	Intervention targets/scenarios	Projected cancer deaths*	Preventable/attributionable deaths:**	Cumulative preventable deaths†
Air pollution (PM _{2.5})	Base	25,395	1360	
	Declining trend	25,145	250	2288
	50% reduction off stabilized levels by 2036	25,032	363	2916
Radon	Base	25,395	1735	
	Radon mitigation of above 100 Bq/m ³ to 50 Bq/m ³ by 2036	25,064	331	2832
	Radon mitigation of above 200 Bq/m ³ to 50 Bq/m ³ by 2036	25,175	220	1841
UVR risk behaviours	Base	2028	1190	
UVR risk behaviours	10% reduction in UVR risk behaviours by 2037	1985	43	408
UVR risk behaviours	25% reduction in UVR risk behaviours by 2037	1916	112	1053
UVR risk behaviours	50% reduction in UVR risk behaviours by 2037	1784	244	2232
HBV	Base	2484	219	
HBV	10% reduction in the prevalence of HBV infection by 2027	2462	22	101
HBV	25% reduction in the prevalence of HBV infection by 2027	2429	55	253
HBV	50% reduction in the prevalence of HBV infection by 2027	2374	110	507
HCV	Base	7223	385	
HCV	10% reduction in the prevalence of HCV infection by 2027	7184	38	182
HCV	25% reduction in the prevalence of HCV infection by 2027	7127	96	453
HCV	50% reduction in the prevalence of HCV infection by 2027	7031	192	907
<i>H. pylori</i>	Base	2361	1406	
<i>H. pylori</i>	10% reduction in the prevalence of <i>H. pylori</i> infection by 2027	2221	141	611
<i>H. pylori</i>	25% reduction in the prevalence of <i>H. pylori</i> infection by 2027	2010	352	1528
<i>H. pylori</i>	50% reduction in the prevalence of <i>H. pylori</i> infection by 2027	1658	703	3056

Bq/m³, becquerels per cubic metre; HBV, hepatitis B virus; HCV, hepatitis C virus; *H. pylori*, *Helicobacter pylori*; PM_{2.5}, particulate matter with a diameter of less than 2.5 µm; UVR, ultraviolet radiation

*Projected cancer deaths from all cancer sites associated with the risk factor in 2047

**Attributable cancer deaths of base scenario in 2047, or preventable cancer deaths of interventions in 2047

†Cumulative preventable deaths from 2024 to 2047

model also projected that cases would be higher among males than among females. This projected ranking is similar to the current situation in Canada, except that there are more breast cancer deaths than prostate cancer deaths (Brenner et al. 2020).

Depending on the intervention scenario used in these analyses, between 6370 and 34,600 cancer deaths could be prevented by 2047 with reductions in active smoking prevalence. By reducing the prevalence of overweight and obesity, between 8560 and 27,230 cancer deaths could be prevented by 2047, and with reductions to alcohol intake, between 4310 and 21,560 deaths could be prevented. Increasing the prevalence of leisure-time physical activity could prevent between 3310 and 16,540 cancer deaths by 2047. Population-level modifications to diet, UVR exposure, air pollution levels, radon exposure, and infections could also reduce thousands of cancer deaths. Tens of thousands of cancer deaths could be prevented if various population-level changes to modifiable cancer risk behaviours were made, highlighting the importance of prioritizing the development and implementation of cancer prevention strategies at the population level.

We used a similar methodological framework as the ComPARE study (Brenner et al. 2018). We obtained the same PARs and PIFs for individual risk factor-cancer associations and, therefore, the findings that we estimated for cancer mortality were generally similar to those found for cancer incidence. Nevertheless, there were some differences in the findings for all associated cancers. For example, we previously reported that in 2042, active smoking will be attributed to 31.8% and 20.1% of associated incident cancer cases in males and females, respectively (Poirier et al. 2019a). For cancer mortality, we estimated here that 40% and 32% of associated cancer deaths in males and females were attributable to active tobacco smoking, respectively, in 2047 (Table S2). This difference in percentages of cancers that can be attributed to active smoking for cancer incidence versus cancer mortality can likely be explained by the low survival rates for smoking-associated cancers (e.g., lung, esophageal, pancreatic, and liver cancer) (Canadian Cancer Society's Advisory Committee 2019). This observation reinforces the urgency of taking immediate actions on tobacco smoking.

Our study had notable strengths as we were able to conduct a comprehensive assessment of the attributable and preventable cancer deaths associated with several lifestyle, environmental, and infectious agent risk factors using novel methods. Specifically, we demonstrated an approach to incorporating the information from two sources, i.e., the PAR and PIF results from the ComPARE study and the cancer mortality data from the OncoSim platform, and how such collaborations can lead to new findings that provide more evidence on cancer prevention. Both the ComPARE data and the OncoSim platform are very accessible because they are freely available to the public and consequently can be accessed to investigate any number of

related questions. As with any projection or simulation modeling framework, OncoSim has limitations. OncoSim requires ongoing updates with newer input data (incidence and mortality) and calibration for accuracy. As access and ongoing updates to more recent data are needed, there is a time lag for incorporating the latest data into the tool. There were also limitations specific to this study. First, we assumed that the relative risk of cancer incidence and that of cancer death for each exposure were the same. This assumption only holds when the cancer prognosis is independent of the past exposure to a risk factor. Although it is reasonable for most risk factors, the prognosis could be affected by certain other risk factors. For example, post-menopausal breast cancers attributable to excess body weight were shown to be associated with poorer prognosis (Sun et al. 2018). Ideally, our study should have used risk estimates for cancer deaths due to the specific exposures. However, risk estimates on cancer deaths are not consistently available for most exposures as they are for risk and are subject to substantial heterogeneity related to study design and case heterogeneity. Second, we used a five-year average latency period between cancer diagnosis and cancer death. This is an oversimplification, as in reality, the median survival of cancers varies by cancer type. We carried out a sensitivity analysis with different latency periods from 0 to 10 years (Table S17). The influence on the number of attributable cancer deaths by the length of latency varies by risk factors. The variation is determined by the projected trend of risk factor prevalence. Latency period has no influence on the attributable cancer death if risk prevalence is constant. In contrast, larger annual changes in risk factor prevalence lead to higher sensitivity to the latency period. Finally, because this study was an extension of the ComPARE study, most of the ComPARE study limitations (Brenner et al. 2018) were also present in this study. For example, the prevalence data of all lifestyle risk factors were from self-reported surveys that are subjected to measurement errors and self-report bias. Some risk estimates, although from high-quality meta-analyses, might not be adequately adjusted for confounding factors. In addition, we did not include any cancer risk factors that were not included in the ComPARE study such as hormone therapy and occupational exposures.

This study is a supplement to the ComPARE study, in which we outlined the most impactful interventions by risk factor that would contribute to reductions in Canadian cancer mortality (Poirier et al. 2019b). The interventions examined in this study were either evidence-based scenarios or aspirational targets that were taken into consideration for the Canadian population (Brenner et al. 2018, 2019). Our results are aimed to inform health policies and decision-makers regarding the potential effectiveness of these interventions in reducing population exposures to various cancer risk factors, and in lowering cancer incidence and mortality. For active smoking in Canada, we previously suggested a hypothetical scenario of increasing cigarette prices to reduce smoking prevalence (Poirier et al. 2019b). Past

systematic reviews concluded that a price increase on tobacco products should be prioritized as a method to reduce the prevalence of smoking (Hoffman and Tan 2015). For excess body weight, physical inactivity, and sedentary behaviour, our future estimates relied on population reductions to all three risk factors. Achieving those reduction targets through public health interventions may come from overlapping interventions. For example, systematic reviews on interventions for reducing adult obesity showed that targeting physical activity and the built environment had reduced overall weight and BMI (Tseng et al. 2018). Technological interventions delivered through multiple information channels have also demonstrated greater weight loss compared to control groups (Hutchesson et al. 2015). Interventions that target obesity and excess body weight often also impact physical inactivity and sedentary behaviour. Similar effects have also been observed in randomized control trials (RCTs) of nutrition and diet, which led to increased vegetable and fruit consumption and decreased meat intake (Hawkes et al. 2012; Sacerdote et al. 2006). Feasibility studies which can have several areas of focus, such as acceptability, adaptation, integration, practicality, and efficacy, can be used to evaluate health intervention programs (Bowen et al. 2009). RCTs of health interventions have also been used to determine the efficacy and effectiveness of health interventions (Jelsma et al. 2019; Song and Baicker 2019). Both feasibility studies and RCTs have found some low-cost work-place, school-based, and home-based interventions to be effective in changing unhealthy behaviours (Brown et al. 2018; Djuric et al. 2010; Eather et al. 2019; Jelsma et al. 2019; Song and Baicker 2019). As with any implementation of an intervention, even evidence-based approaches may prove less effective in real-world settings. The scenarios included in this manuscript are presented as a spectrum of potential interventions ranging in cost and feasibility. To make meaningful progress in cancer prevention, considerable up-front investment will be required, preferably starting with those interventions that are most feasible with the shortest intervention window, e.g., vaccination and exposure remediation, progressing to those that require long-term effort and investment.

Conclusion

We utilized the OncoSim modeling and projection framework to extend our previous analyses of modifiable cancer incidence to include cancer mortality. The findings of relative cancer burden were similar between OncoSim and the ComPARE study. With the OncoSim model, we projected that deaths from all cancers among those aged 35 and over would increase by approximately 23,000 cases from 2024 to 2047 in Canada. The highest number of preventable cancer deaths was estimated to be attributable to active tobacco smoking. We also projected preventable cancer deaths related to various cancer intervention targets, which provided additional evidence in support of intervention programs for

cancer control. The results from our microsimulation modeling echo the previous findings on the modifiable cancer incidence burden from the ComPARE study (Poirier et al. 2019c) that over 100,000 cancer deaths could potentially be avoided through ambitious cancer prevention targets. These results provide additional data to inform cancer prevention strategies for governments, policymakers, and health promotion programs.

Contributions to knowledge

What does this study add to existing knowledge?

- Models used in this study suggest that by 2047 the highest cancer deaths in Canada would be from lung, colorectal, pancreas, prostate and breast cancers.
- By 2047, active tobacco smoking and excess body weight are projected to be the leading modifiable risk factors for preventable cancer mortality.
- About 34,600 cancer deaths associated with active tobacco smoking could be prevented from 2024 to 2047 if a 30% relative reduction in smoking prevalence was achieved by 2020.
- About 27,200 cancer deaths associated with excess body weight could be prevented from 2024 to 2047 if a 25% reduction in the prevalence of overweight and obesity is achieved by 2032.

What are the key implications for public health interventions, practice or policy?

- The results of our study provide additional information to support cancer prevention strategies through intervention targets for governments, policy makers and health promotion programs.
- Our results projected preventable cancer deaths related to various cancer intervention targets, which provides further evidence in support of intervention programs for cancer control.
- Noteworthy interventions from our study included meeting reduction targets for smoking, obesity, and inadequate physical activity and increasing vegetable and fruit intake to prevent cancer mortality in Canada.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.17269/s41997-020-00455-7>.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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