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CANADIAN CANCER RISK MANAGEMENT MODEL: EVALUATION OF CANCER CONTROL

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Objectives: The aim of this study was to develop a decision support tool to assess the potential benefits and costs of new healthcare interventions.
Methods: The Canadian Partnership Against Cancer (CPAC) commissioned the development of a Cancer Risk Management Model (CRMM)—a computer microsimulation model that simulates individual lives one at a time, from birth to death, taking account of Canadian demographic and labor force characteristics, risk factor exposures, and health histories. Information from all the simulated lives is combined to produce aggregate measures of health outcomes for the population or for particular subpopulations.
Results: The CRMM can project the population health and economic impacts of cancer control programs in Canada and the impacts of major risk factors, cancer prevention, and screening programs and new cancer treatments on population health and costs to the healthcare system. It estimates both the direct costs of medical care, as well as lost earnings and impacts on tax revenues. The lung and colorectal modules are available through the CPAC Web site (www.cancerview.ca/cancerrriskmanagement) to registered users where structured scenarios can be explored for their projected impacts. Advanced users will be able to specify new scenarios or change existing modules by varying input parameters or by accessing open source code. Model development is now being extended to cervical and breast cancers.

Keywords: Cancer, Simulation model, Policy tool

Governments and health system leaders are continually faced with investment decisions that could improve cancer control. Typically, these decisions involve individual strategies such as prevention initiatives, screening programs and the introduction of new treatments. Understanding how these often competing opportunities interact while estimating which approach might produce the greatest benefit to the health of the population is challenging.

The Canadian Partnership Against Cancer (CPAC) was established in April 2007 by Canada's federal government to address long-standing limitations and gaps within the cancer control system (1). As a priority project, the Partnership initiated the development of a Cancer Risk Management Model (CRMM) to enable users to simulate the impact of different policies on the future health of Canadians.

The current work builds on population health microsimulation work undertaken by Statistics Canada in the 1990s (2). The CRMM was planned to incorporate up-to-date Canadian cancer incidence, prevalence and case fatality rates, as well as current prevention, screening, diagnostic and therapeutic interventions. The CRMM was designed to enable users to estimate and evaluate the implications of various cancer control strategies in terms of their potential clinical benefit and impact on healthcare expenditures. The CRMM was developed to be Web-enabled to support direct and easy use by cancer control and health policy decision makers in Canada and elsewhere.

The first modules to be developed were lung and colorectal cancer. These tumors were selected because of their major contribution to the cancer burden in developed countries (3–5) and the potential to reduce that burden by new effective cancer control interventions. In the case of lung cancer, the burden could potentially be reduced through policy interventions to reduce exposure to known carcinogens (6), low dose CT screening (7), the adoption of post-operative chemotherapy for surgically resected lung cancer (8) and the introduction of palliative drug treatments for metastatic disease (9). Similarly, for colorectal cancer, the burden of illness might be reduced by prevention strategies, introducing population-based screening programs (10), the adoption of pre- and postoperative adjuvant therapies (11) and the use of new systemic therapies for advanced disease (12).

This study describes how the CRMM was developed from available data sources and how the model has been validated. It also illustrates some of the CRMM's potential by presenting outputs from several cancer control scenarios of current relevance to policy makers.

Development of the Cancer Risk Management Model

The CRMM was developed by a team from Statistics Canada building on their prior experience with the POpulation HEalth Microsimulation model (POHEM) (2). POHEM contained modules for lung, colon and breast cancer (13–16) and had been used to address a variety of health policy questions (17–21). The Statistics Canada team was expanded to include health economists and clinical leaders knowledgeable of lung and colorectal cancer.

The CPAC provided oversight to the CRMM development through an Advisory Committee comprised of senior health and cancer system leaders, and experts in biostatistics, health economics, epidemiology, public and private sector finance, and clinical care. This Committee set the overall direction for the initiative, helped to identify questions likely to be of policy relevance in the near future and advised on knowledge transfer to the cancer control community (Supplementary Table A, which can be viewed online at www.journals.cambridge.org/thc2013084). A Technical Committee was also established to advise on the validity and accuracy of the modeling work, to ensure transparency of the methods and to facilitate knowledge transfer to others involved in microsimulation modeling (Supplementary Table B, which can be viewed online at www.journals.cambridge.org/thc2013084).

Conceptual Framework of the Cancer Risk Management Model

The CRMM is based on a conceptual framework as shown in Figure 1. It incorporates risk factors, where known, that contribute to the incidence of cancer according to age, sex and province of residence. For example, the incidence of lung cancer within the model is determined by cumulative smoking and radon exposure according to a risk-incidence equation de-

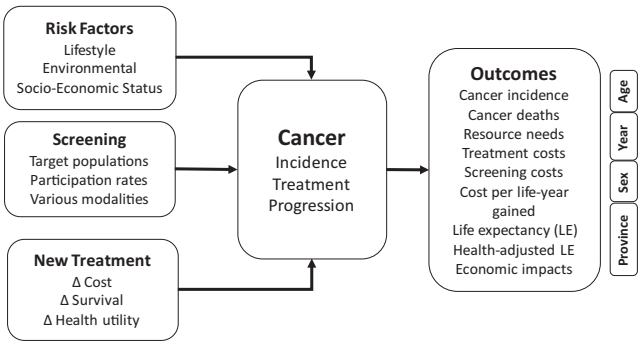

Figure 1. Cancer risk management conceptual framework. Source: Cancer Risk Management Model 1.3.

rived from the literature (22). The conceptual framework for the model enables different screening approaches to be examined, including scenarios for alternative screening frequency, modalities, age ranges, and participation rates. Effective screening has been shown to shift the stage of the detected cancers to earlier and more treatable stages and to reduce the incidence of advanced cancer. In the case of colorectal cancer screening, the detection of early stage cancers by fecal occult blood testing (FOBT) and the removal of polyps, which are a precursor to cancer, contribute to a reduction in colorectal incidence and mortality (23–26). The model produces estimates of the cancer incidence and related treatment by tumor stage. These three components—risk factors, screening interventions and treatment—influence the outputs of the model which include projections of cancer incidence and death, the costs of screening and treatment, estimates of cost-effectiveness (cost per life-year gained; cost per quality-adjusted life-year gained) and the impact on taxes and transfers.

Components of the CRMM

The CRMM synthesizes a representative sample of the entire Canadian population focusing on their demographic and labor force characteristics, risk factor exposures and health histories. The simulation process creates millions of individual biographies for a range of birth cohorts and includes population migrations. These biographies unfold in a continuous time, discrete event Monte Carlo microsimulation with explicit competing risks. The result is similar to a comprehensive longitudinal health, demographic and economic survey of the population, which includes future years, and to the extent possible reflects both the heterogeneity of the actual population, the relationships observed among key variables and their dynamics, and the risk of developing or dying from cancer or other causes. Death from other causes is based on multi-cohort life tables that have been adjusted to remove lung and colorectal cancer-specific mortality.

Once the CRMM synthesizes this representative population, the results are presented as cross tabulations. For example, adding up all the new cancer cases each year, within sex and age groups, produces a time series for cancer incidence. These incidence patterns are then benchmarked against the observed

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rates from the Canadian Cancer Registry. The characteristics of the individuals simulated by the CRMM include age, sex, province of residence, income quintile, health-related quality of life, lung cancer status, colorectal cancer status, and screening status. In the lung cancer example, each individual in the population is aged from birth to death and their cumulative exposure to smoking and radon is factored into the risk of developing lung cancer. If and when lung cancer is "diagnosed", patients are assigned a tumor type and stage according to their distribution in lung cancer cases in Canada. They then receive a diagnostic workup and treatment appropriate for that stage, and the costs of the diagnostic workup, treatment interventions, follow-up and supportive/palliative care are then assigned to the individual. The impact of smoking on mortality from other causes was also modeled.

Health-related quality of life is estimated for both the general population and for cancer patients. Health utilities (preference scores) range from 1 (full health) to 0 (death). As a person ages, their health status generally declines. For the general population, health status was assigned based on the average Health Utilities Index (27) reported on the National Population Health Survey (for ages 4–14) (28) and the Canadian Community Health Survey (for ages 15 and older) (29). For cancer patients, the Classification and Measurement System of Functional Health (CLAMES) was used to assign preference scores to various health states related to the stage of cancer at diagnosis, treatments administered (surgery, radiotherapy, chemotherapy), remission, relapse and end-of-life care (30;31). As a simulated individual is diagnosed and undergoes treatment, their health status is adjusted. For example, a person diagnosed with stage I colorectal cancer would have their health status adjusted by a factor of 0.85 (the preference score for this state) which is equivalent to a loss of 15 percent of their current health state. The impact of living with multiple health conditions is calculated according to a multiplicative rule (32). For example, a person aged 35 who does not have cancer would have an assigned health status of 0.90, the average for the population for this age. If this individual is then diagnosed with stage I colorectal cancer, the health status would be further lowered by 15 percent and the new health status would be 0.765 calculated as 0.90×0.85. The simulated individual's life is thus made up of a series of values associated with each health state that they experience, starting from full health at birth (value of 1) through to death (value of 0). The sum across their life is their health-adjusted life expectancy, although typically this is estimated as the average across the entire population.

Data Sources

Multiple data sources were required for the CRMM development. The Canadian Cancer Registry provided data on incidence and staging, while Vital Statistics and Census data were the source of information on births, deaths, immigration and population projections. The Canadian Community Health Survey (29), the National Population Health Survey (28), the General Social Survey (33), and the Canadian Health Survey (34) were used to obtain Canadian smoking rates, population health utilities, and time use data to estimate time spent in the basement of a home as opposed to the rest of the home to estimate radon exposure, respectively. The literature was extensively used to determine the impact of screening on cancer stage, frequency of treatment by stage, complications of treatment, and survival.

Healthcare costs were obtained predominantly from Ontario sources and included the Ontario Health Insurance Plan Schedule of Benefits for physician fees, the Ontario Case Costing Initiative for hospital costs and Cancer Care Ontario's New Drug Funding Program (drug costs). The Juravinski Cancer Center at Hamilton Health Sciences was the source of information on the cost of chemotherapy administration. Data was obtained from the province of Manitoba on the cost of palliative therapy following the completion of active treatment (35). Some key costs are shown in Supplementary Table C, which can be viewed online at www.journals.cambridge.org/thc2013084. Census data (36) and the Social Policy Simulation Database and Model (37) were used for earnings, transfers and taxes.

A "bottom up" approach was used to cost health care. Typical treatment patterns were mapped based on known practice patterns, practice guidelines or expert opinion and costs for each component of cancer management—diagnosis, surgery, radiotherapy, or chemotherapy—were estimated in detail to arrive at a cost per person per type of treatment. More detail on the methodology used to build the model can be obtained from the CPAC Web site (38).

The Lung Cancer Module and Its Potential Uses

Development of the lung cancer treatment algorithms was led by two clinical experts (W.K.E., J.G.) and modified on the basis of discussion in focus groups involving thirteen Canadian lung cancer oncologists. The module describing lung cancer management is shown schematically in Figure 2 and reasonably reflects current practice. In the CRMM, symptomatic patients are evaluated by a family physician and referred for specialist investigation and treatment appropriate to the tumor type [(non-small cell lung cancer (NSCLC) or small cell lung cancer (SCLC)] and stage of disease. The proportion of patients receiving treatment by stage reflects the current stage distribution of lung cancer in Canada, adjusted by knowledge of the proportion of patients who are not candidates for treatment due to poor performance status, age and/or co-morbidities. The proportion of patients receiving adjuvant chemotherapy for early-stage NSCLC and combined modality therapy for stage III NSCLC was obtained from Cancer Care Ontario data. The proportion of patients receiving first-line, second line and third line therapy was determined from Cancer Care Ontario's New Drug Funding Program. Survival by stage was extracted from the literature, according to stage and tumor type (8;39–46). Follow-up practice was based on generally accepted guidelines in use by Ontario thoracic surgeons and oncologists.

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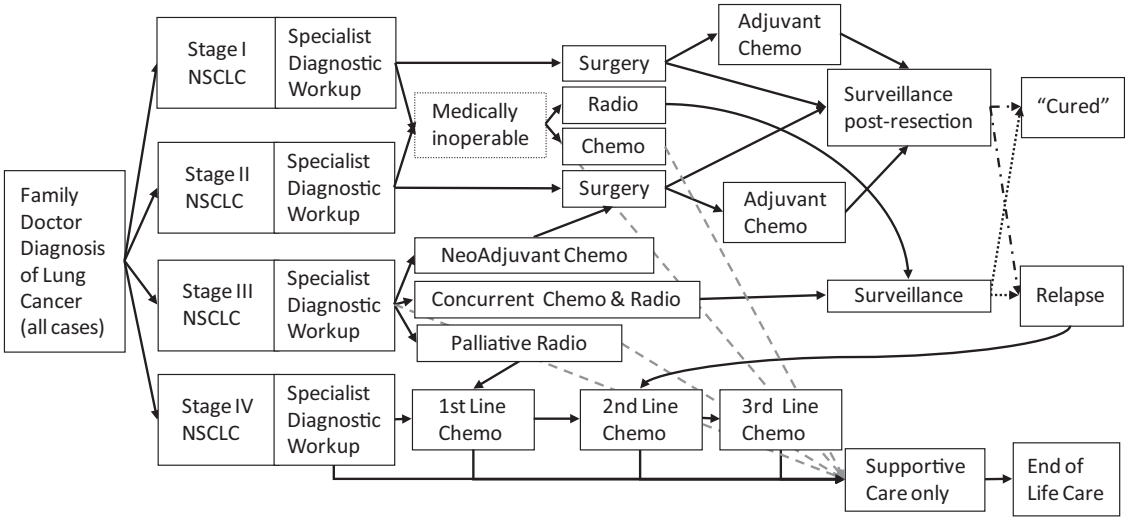

Figure 2. The model of management for non-small cell lung cancer in the Canadian Partnership Against Cancer (CPAC) Cancer Risk Management model. The dotted lines after surveillance represent competing risk of disease progression versus cure (i.e., "cured" if disease-free at 10 years and no longer at risk of progression). Source: Cancer Risk Management Model 1.

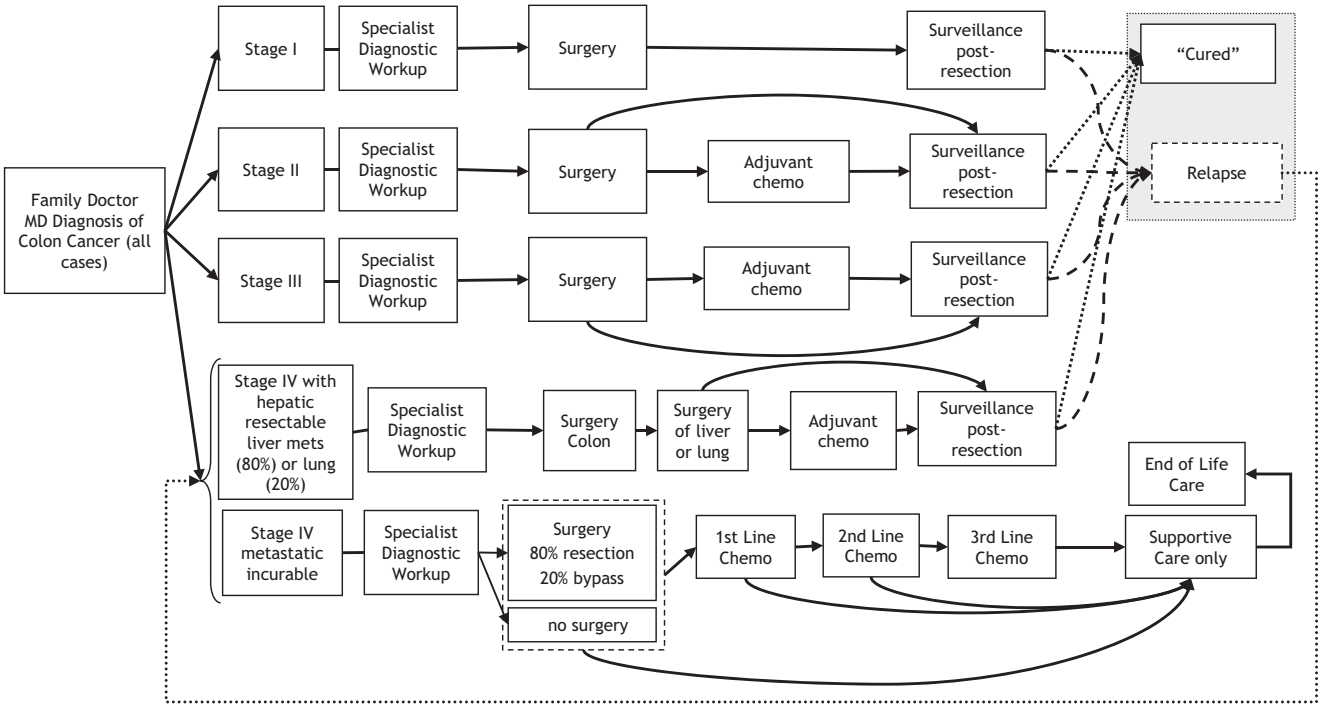

Figure 3. The model of management for colon cancer in the Canadian Partnership Against Cancer (CPAC) Cancer Risk Management Model. The dashed and dotted lines after surveillance represent competing risk of progression of disease versus cure, i.e., disease-free at 5 years and no longer at risk of progression. Source: Cancer Risk Management Model 1.3.

The lung cancer module can be used to address several questions of relevance to the prevention of lung cancer. For example, the CRMM can estimate the likely incidence of lung cancer given current provincial prevention policies projected out over the next 20 years. Incidence can be modeled by age, sex and province for alternative smoking and/or radon exposures. The CRMM can demonstrate how lung cancer mortality rates would change with the introduction of smoking policies designed to reduce the frequency of smoking in the population. The CRMM can also show the overall impact of changes in prevention policy on aggregate healthcare costs, earnings, total income and net changes to government due to changes in taxes and transfers.

Colorectal Cancer Model and Possible Uses

Figure 3 for colon cancer is similar to Figure 2 for lung cancer and illustrates the stage-specific treatment algorithms. Rectal cancer (not shown) has also been modeled and its treatment is similar in most respects, with the exception of the management of localized disease where radiation plays a significant role.

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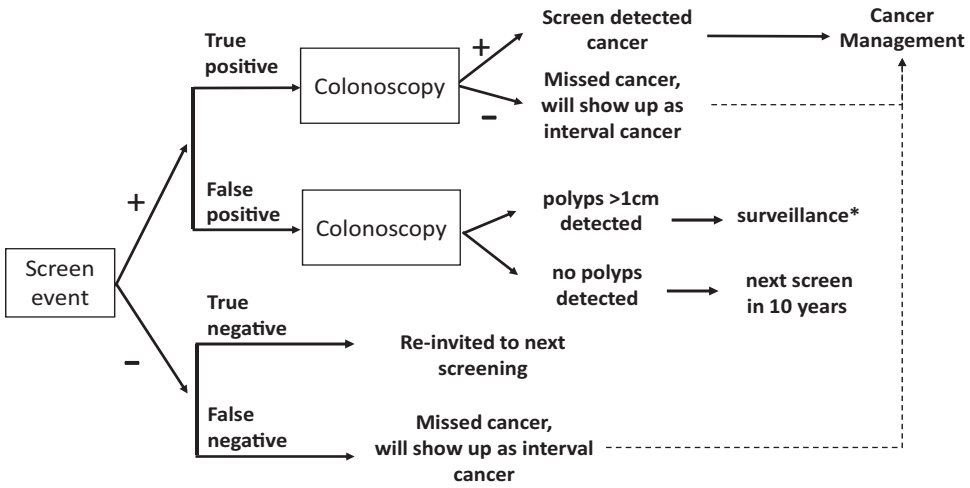

Figure 4. Screening protocol for fecal occult blood testing (guaiac or immunological). *Surveillance protocol after large polyps (>1cm) detected: colonoscopy at 3, 5, and 10 years if no polyps or cancer detected at subsequent follow-up;—dashed arrow indicates that interval cancer will occur if the patient does not die and would begin cancer management after clinical detection. Source: Cancer Risk Management Model 1.3.

Risk factors for colorectal have not been considered so far. The development of the treatment algorithms was led by colorectal cancer experts (J.G., C.E.) and vetted with nine gastrointestinal oncologists through focus groups. These treatment algorithms reasonably represent current practice in the management of colorectal cancer. Data sources similar to those described above for lung cancer were used to determine stage distribution, diagnostic work-up, therapeutic interventions and palliative care.

Colorectal screening has been built into the CRMM as the potential impact of colorectal screening was one of the priority questions driving the CRMM development. As FOBT has been demonstrated to reduce colorectal cancer mortality (24;26), patients who test positive with FOBT in the model are directed to colonoscopy to distinguish between a true positive or false positive test (Figure 4). Polyps may be removed, if present at colonoscopy, and the modeled patient would enter surveillance. A negative FOBT results in the modeled patient being followed up by further screening (true negative) or as a false negative which will show up as an interval cancer.

Parameters for the costs of the FOBT (both guaiac and immunologic (FIT), consultation fees and procedure costs) have been built into the model. However, the overhead and promotion of a provincial screening program and the costs of physician recruitment have not been included.

The colorectal cancer model can be used to address several policy relevant questions, such as the likely incidence of colorectal cancer if the current screening policies are continued over the next 20-years. Incident cases by stage, sex, age, and province, as well as cost of treatment can be displayed. Of importance to policy makers, it can show the impact on cancer incidence, mortality and costs of increasing the proportion of the population that is screened. For example, the impact of screening on colorectal cancer mortality has been modeled assuming that an organized screening program increased enrollment by 50 percent gradually over a 2-year period and maintained it from 2010/11 onward with 93 percent adherence to follow-up screens. Under this scenario, the CRMM projects a decline in mortality by as many as 1,344 cases per year in Canada or the avoidance of a total of 26,855 deaths over the next 20 years.

Model Validation

The CRMM was subjected to internal and external validation to ensure that all components, including population demographics, risk factors, screening interventions, cancer incidence, treatment, healthcare costs and cause-specific mortality reproduced observed levels in the Canadian population over recent years. The demographic characteristics of the population synthesized by the CRMM reproduce the Canadian population as observed in the Census from 1971 to 2006 by age, sex, and province. The provincial population totals were reproduced by age groups and sex; age-sex specific smoking patterns were calibrated to data from 1956 up to 2008 using a variety of surveys, and externally validated against tobacco manufacturer's data; radon exposure was verified against Health Canada published data (47); colorectal cancer screening was externally validated by reproducing randomized controlled trial results (24;26); cancer treatment pathways and costs were verified through consultation with experts; lung and colorectal cancer incidence and mortality were compared with data in the Canadian Cancer Registry and the Canadian mortality database, respectively, over recent years to ensure reasonable fit of the risk and survival equations.

DISCUSSION

The burden of cancer has been increasing significantly in developed countries in large measure due to the aging of the population (3–5). In Canada, this burden is also increasing because of an increase in the size of the population. Heavy investment in research over the past several decades has resulted in better cancer control measures across the spectrum from prevention to end of life care, resulting in a decline in the incidence and mortality

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Table 1. Colon Cancer

Treatment type	Cost per treatment
Surgical resection (Stages I, II, & III)	22,786
Adjuvant chemotherapy (Stage III)	15,777
1st line chemotherapy for metastatic cancer	31,521
Surveillance (1st year, Stage I)	1,127
End of life care (3 months before death)	2,053
End of life care (2 months before death)	4,105
End of life care (1 months before death)	7,526

Note. Source, CRMM Colon cancer management workbook version 1.4.0.7. Costs shown above include diagnostics, hospital, physician, drug, radiotherapy, other institutional care, other professional (e.g. nursing, pharmacy) and other (e.g., supplies) costs, wherever applicable.

from several cancers (48). However, these increasingly sophisticated cancer control strategies come at a significant price, such as monoclonal antibody therapy in non-small cell lung cancer (49). It was estimated by the Economist Intelligence Unit that the global cost of new cancer cases in 2009 was at least US $289 B of which medical costs made up more than half (50). The economic cost of new cases in the United States was estimated to be $142.8 billion (US) compared with $6.5 billion in Canada (population 33.6 million in 2010). As the healthcare budgets of governments are increasingly strained by these costs, there is a need for information to support decision making and, in particular, to ensure that taxpayer dollars are spent in ways that yield the greatest health benefit.

The CRMM provides decision makers with a tool that will allow them to estimate the net impacts of a variety of new cancer control measures. For example, as evidence emerges on the value of new screening programs, the CRMM can support the decision maker in looking at the interplay between the uptake of the screening intervention and the downstream requirements for treatment. Although the evidence that screening using FOBT can reduce colorectal cancer mortality is compelling, the introduction of population-based screening programs is complex and costly and these factors can be a barrier to the implementation of screening in a publicly funded system. Screening programs should detect cancer at an earlier stage of disease when cure rates are highest and there is the potential to avoid expensive palliative treatments for metastatic disease. The CRMM allows the policy maker to see the interplay between expansion of a screening program against other opportunities, such as the introduction of a new therapy for advanced disease. The CRMM will provide policy makers with quantitative estimates enabling them to determine where the next dollar could be spent most effectively.

A common challenge faced by policy makers is the introduction of new and expensive anticancer drugs. The CRMM can be used to evaluate the cost of the new drug therapy based on where it is introduced into therapy (adjuvant, palliative first-line, second-line, etc.) and its impact on cancer survival, cost per life-year gained, health adjusted person-years saved and total cost to the jurisdiction introducing the drug, as well as estimate the lost earnings and revenues to government from disease-related disability. This ability to estimate the impact of cancer control strategies on earnings and tax revenues is a unique feature of the CRMM.

It must be realized that any model is just that—a model—and as such, it is limited by the accuracy of the available data, as well as the assumptions that are included in model development. Nonetheless, the CRMM has been constructed by individuals knowledgeable of cancer control interventions for lung and colorectal cancer; it has been validated by peers across the country and it has been built on a detailed analysis of Canadian statistical and administrative data sets to the maximum extent possible. Where data were either not available or limited, the best judgment of clinical and other experts has been used. For these reasons, we believe the CRMM is a robust reflection of current cancer control interventions for the tumor types included in the model.

The CRMM will continue to be developed using a similar framework and methods as the developers work toward the goal of a comprehensive cancer model for Canada. The next phase of CRMM development will be focused on cervical and breast cancer. These two cancers have been selected because of current policy questions related to cervical screening programs and the introduction of human papillomavirus (HPV) vaccination, controversies over screening, and the introduction of new therapies for the treatment of breast cancer.

The CRMM has capitalized on the modeling strength of Statistics Canada and engagement with selected clinical experts from across the country to build the cancer specific modules. This approach enables all cancer sites modeled to be included within one comprehensive modeling platform, increasing the accessibility of the models to users and enabling the testing of more complex policy scenarios that would affect more than one type of cancer, such as an intervention to modify exposure to risk factors like smoking or obesity.

The CRMM has been introduced to the cancer control community in Canada through a series of webinars followed by training workshops for users. Access to the CRMM and a User Guide is by means of a link on CPAC Web site www.cancerview.ca/cancerriskmanagement (38). Users can construct their own scenarios in a run mode by altering the set of default parameters and running the model to produce projections on the Web site. Advanced users are invited to contact CPAC to request the microsimulation source code if they wish to create additional output tables or implement new features. The intent is to enable as many users as possible to benefit from the CPAC investment. At present, access to the CRMM requires an initial training session followed by registration with CPAC.

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CPAC's goal is to train users in provincial governments and cancer agencies so that CRMM is used directly by those who have to answer cancer control policy questions.

In conclusion, the CRMM has been developed to enable a broad group of users across Canada and beyond to be able to assess the impact of potential decisions on cancer control strategies. It is anticipated that the introduction of this new health policy analysis tool will enable CPAC and other decision makers to examine the interplay between a variety of potential cancer control initiatives and provide new perspectives on their impact, ultimately leading to better quality, evidence-informed decisions.

SUPPLEMENTARY MATERIAL

Supplementary Table A:
www.journals.cambridge.org/thc2013084
Supplementary Table B:
www.journals.cambridge.org/thc2013084
Supplementary Table C:
www.journals.cambridge.org/thc2013084

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CONFLICTS OF INTEREST

John Goffin reports having no potential conflicts of interest. Nicole Mittmann reports a grant to her institution from Statistics Canada. All other authors report funding to themselves, their institutions, or both from Canadian Partnership Against Cancer.

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