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Colorectal cancer deaths attributable to nonuse of screening in the United States

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ABSTRACT

Purpose: Screening is a major contributor to colorectal cancer (CRC) mortality reductions in the United States but is underused. We estimated the fraction of CRC deaths attributable to nonuse of screening to demonstrate the potential benefits from targeted interventions.
Methods: The established microsimulation screening analysis colon model was used to estimate the population attributable fraction (PAF) in people aged ≥50 years. The model incorporates long-term patterns and effects of screening by age and type of screening test. PAF for 2010 was estimated using currently available data on screening uptake. PAF was also projected assuming constant future screening rates to incorporate lagged effects from past increases in screening uptake. We also computed PAF using Levin's formula to gauge how this simpler approach differs from the model-based approach.
Results: There were an estimated 51,500 CRC deaths in 2010, about 63% (N ~ 32,200) of which were attributable to nonscreening. The PAF decreases slightly to 58% in 2020. Levin's approach yielded a considerably more conservative PAF of 46% (N ~ 23,600) for 2010.
Conclusions: Most of the current United States CRC deaths are attributable to nonscreening. This underscores the potential benefits of increasing screening uptake in the population. Traditional methods of estimating PAF underestimated screening effects compared with model-based approaches.

Introduction

Colorectal cancer (CRC) is the second leading cause of cancer deaths in the United States and is estimated to cause 50,310 deaths in 2014 [1]. Both the absolute number of cases and the incidence and mortality rates have declined over the last three decades despite a high prevalence of risk factors, in contrast to trends observed in some other countries [2]. Evidence indicates that the increasing use of CRC screening has been the major contributor to the declining incidence and mortality rates in the United States [3,4]. However, screening remains underused, suggesting that a substantial proportion of current CRC deaths in the United States are avoidable. This has galvanized public action on increasing the uptake of screening [5]; however, lack of clarity persists regarding the proportion of current CRC deaths occurring as a result of nonuse of screening, and thus the potential public health benefits from increasing screening uptake.

The population attributable fraction (PAF) proposed by Levin [6] in 1953 has been widely used to assess the proportion of a disease outcome that occurs as a result of exposure to a risk factor, and thus the potential benefits from public health interventions to eliminate that exposure. This concept, which is a function of the level of exposure to the risk factor and the size of the effect of exposure on

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the disease outcome, has been previously applied to assess the impact of underuse of CRC screening on disease mortality [7]. Using this approach, Stock et al. reported that about 28% to 44% of deaths from CRC in the United States in 2005 may be attributable to nonuse of colonoscopy. However, this study used somewhat conservative estimates for the effect of colonoscopy screening that may not be applicable for the United States [8–10]. In addition, the study did not consider specific features of CRC epidemiology that are important for valid estimation of PAF. First, apart from colonoscopy, flexible sigmoidoscopy or fecal occult blood tests are also used for screening in the United States and therefore need to be considered in estimating PAF. Second, CRC is a heterogeneous disease characterized by a long latency between risk factor exposure and outcome. Mortality benefits from screening are derived not only from cancer detection but also from the detection and treatment of precursor or early more curable invasive lesions. Thus, valid estimates of PAF require the consideration of benefits of screening that are realized over long time periods after the test date. Finally, patterns of exposure to CRC screening have evolved since the 1980s. According to data from the National Health Interview Survey (NHIS), the proportion of the United States population recently exposed to CRC screening tests increased from about 39% in 2000 to 58% in 2010 [11,12].

In the present study, we used microsimulation modeling to estimate the PAF of United States CRC deaths from nonscreening. We compared this to estimate of PAF using Levin's formula to gauge how this simpler more accessible approach may differ from the microsimulation approach.

Methods

Population attributable fraction

The PAF for CRC is defined as the proportion of CRC deaths in adults who are aged ≥50 years which is due to nonreceipt of screening as recommended by national guidelines. Analogous to the first definition discussed by Rockhill et al. [13], a short treatise on the most common definitions used for PAF, this is expressed algebraically as:

$$PAF = \frac{R_T - R_0}{R_T} = \frac{RR_{T/0} - 1}{RR_{T/0}}, \quad (1)$$

where R_T is the observed CRC mortality risk within the population per year, R_0 is the risk in those screened (unexposed) per year, and $RR_{T/0}$ is the ratio. We used a microsimulation screening analysis (MISCAN) model to generate the entries R_T and R_0 in definition (1). To compare the model approach and simple approach, the risk in the absence of screening, R_1, was also assessed. Because the use of screening, disease incidence and mortality, and risk of death from competing causes change over a person's lifetime, we derived PAF according to three age strata (ages 50–64, 65–74, and ≥75 years). It was first derived for calendar year 2010 on the basis of observed patterns of exposure to nonscreening from national survey data up to 2010, and then extended to 2030 assuming a constant rate of exposure to screening after 2010, to explore the lagged effects from recent increases in screening uptake. (See the Supplementary Appendix for more precise definitions of PAF according to stratum and calendar year.)

This study was conducted within the National Cancer Institute's (NCI) Cancer Research Network and as part of the NCI-funded Population-based Research Optimizing Screening through Personalized Regimens consortium that aims to conduct multisite, coordinated, transdisciplinary research to evaluate and improve cancer screening processes.

MISCAN colon microsimulation population

The MISCAN colon microsimulation model was used to stochastically generate a virtual population similar to the United States population in terms of the life expectancy and the natural history and occurrence of CRC. This model was defined for the period from 1980 to 2030 to cover both historical and possible future patterns of screening use and the corresponding CRC mortality effects. Simulated births and all-cause mortality in the United States were based on United States Census Bureau population estimates from 2000 [14] and generational mortality tables from the Berkeley Mortality Database [15], respectively. Cancers were assumed to develop along the adenoma-carcinoma sequence, that is, originate from small adenomatous lesions (≤5 mm) which first slowly grow to become medium (6–9 mm in diameter) or large adenomas (≥10 mm) before turning malignant [16]. The size-specific prevalence of adenomas by age was based on autopsy and colonoscopy data from before the era of CRC screening [17–20]. The stage- and location-specific incidences of CRC by age were based on Surveillance Epidemiology and End Results (SEER) program data from the pre-screening era [21]. The model was developed by the Department of Public Health at the Erasmus Medical Center in Rotterdam, the Netherlands, as part of the NCI-funded Cancer Intervention and Surveillance Modeling Network and has been described more extensively elsewhere [22,23].

Exposure to nonscreening

To derive PAF, we simulated two scenarios on the uptake of screening in the United States. First, we closely replicated age- and test-specific screening patterns for the United States as observed in eight waves of NHIS from 1987 to 2010 (Fig. 1). The NHIS is a cross-sectional survey with a complex design on a nationally representative sample of the United States population [24]. Questions regarding the use of CRC screening tests were asked during the following survey years: 1987, 1992, 1998, 2000, 2003, 2005, 2008, and 2010. The estimated overall screening rate in 2010 (ages 50–100 years) was 59%. We assumed screening rates leveled off at ~60% (i.e., a 40% nonscreening rate) after 2010. Screening as measured in the NHIS comprises home-based fecal occult blood testing (FOBT) and endoscopy (particularly flexible sigmoidoscopy or optical colonoscopy).

In the second scenario, to assess the mortality risk from CRC that persisted despite complete screening of the population, after 1980

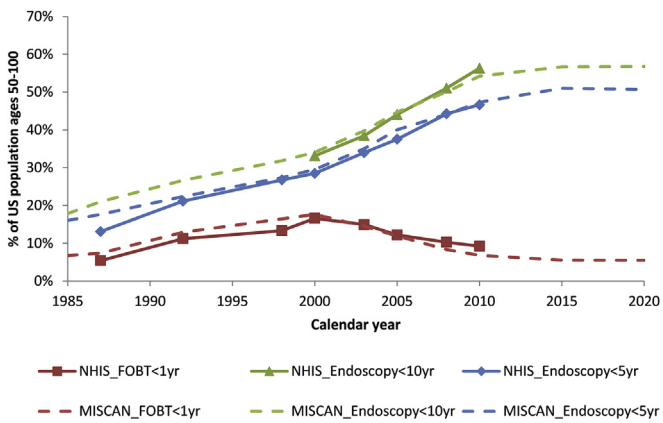

Fig. 1. Colorectal cancer screening trends in National Health Interview Survey (NHIS) data and MISCAN. The red line plots the proportion of the U.S. population which had a home FOBT in the previous year, the blue and green lines plot the proportions which had an endoscopy in the previous 5 or 10 years, respectively. (For interpretation of references to color in this figure legend, the reader is referred to the Web version of this article.)