

Estimating the Remaining Lifetime Risk of Colorectal Cancer Based on the Current Age and Screening History

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Received: 25 Sep 2026; **Accepted:** 30 Sep 2026; **Published:** 05 Oct 2026

Citation: Dongfeng Wu. Estimating the Remaining Lifetime Risk of Colorectal Cancer Based on the Current Age and Screening History. *J Women's Health Res Rev.* 2026; 1(1), 01-08.

Abstract

The remaining lifetime risk of colorectal cancer (CRC) for both males and females was estimated according to an individual's current age and screening history using a recently developed probability-based method and data from the annual screening cohort of the Minnesota Colon Cancer Control Study (MCCCS). The remaining lifetime risk is determined by three key parameters: the screening sensitivity, the transition probability density from the disease-free state to the preclinical state, and the sojourn time in the preclinical state. These parameters were estimated from the MCCCS data and subsequently incorporated into the probability model to calculate the remaining lifetime risk of CRC. The results show that, before age 44, males have a higher remaining lifetime risk of CRC than females of the same age. However, this pattern reverses after age 45, with females exhibiting a higher remaining lifetime risk. Overall, the remaining lifetime risk declines gradually with increasing age in both genders. The clinical incidence of CRC reaches its peak at age 74 in males and age 80 in females.

Keywords: Risk; Sensitivity; Sojourn Time; Transition Density; Colorectal Cancer

1. Introduction

Colorectal cancer (CRC) remains a major global public health challenge, ranking as the third most commonly diagnosed cancer and the second leading cause of cancer-related mortality worldwide [1]. According to the American Cancer Society, an estimated 158,850 new cases of colon and rectal cancer and 55,230 related deaths are expected in 2026 [2]. In recent years, the incidence of colorectal cancer has also increased among younger adults, raising growing public health concerns [3]. Because colorectal cancer typically develops over many years, it is well suited for screening and early detection. Early diagnosis can substantially improve patient outcomes, and the overall 5-year relative survival rate is approximately 65.4% [4].

A review of the literature shows that extensive research has been conducted on the risk factors for colorectal cancer, including age, sex, lifestyle, family history, and chronic inflammatory diseases of the gastrointestinal tract [5–7]. Several studies have also developed models for predicting colorectal cancer risk [8, 9]. However, much of the existing research is based on observational studies or descriptive statistical analyses rather than probability modeling.

Current estimates of lifetime risk typically refer to the probability of developing colorectal cancer over the entire lifespan, from birth to death. This lifetime risk is approximately 4%, with males having a slightly higher risk than females [10]. Other approaches estimate the probability of developing colorectal cancer over a fixed time horizon, such as a specific age interval [11]. In contrast, we propose a probability-based approach that estimates an individual's remaining lifetime risk from their current age until death while incorporating their screening history.

For an individual who is currently healthy, several important questions arise: What is the probability of developing colorectal cancer from the current age until death? How is this risk influenced by previous negative screening results? At what age does the risk of colorectal cancer reach its peak? To address these questions, we apply a recently developed probability framework that treats human lifetime as a random variable rather than a fixed quantity. Under this framework, the lifetime risk of developing colorectal cancer is defined as the probability of experiencing clinical symptoms before death, for which we have derived general probability formulas [15]. A key advantage of this approach is that it estimates an individual's remaining lifetime risk of colorectal cancer from the current age onward, rather than restricting the assessment to a fixed time horizon such as five or ten years. We apply this method to data from the Minnesota Colon Cancer Control Study (MCCCS).

We will adopt the commonly used disease progression model, in which clinical symptoms are assumed to develop through three stages [19]: $S_0 \rightarrow S_p \rightarrow S_c$. Here, S_0 represents the disease-free state, or the condition in which the disease cannot be detected by any available technology. S_p refers to the preclinical state, where an asymptomatic individual unknowingly has the disease, but it can be detected through screening. Finally, S_c is the clinical state, in which the disease manifests through clinical symptoms.

The paper is organized as follows: In Section 2, we will provide a brief overview of the Minnesota Colon Cancer Control Study and outline the recently developed probability method for calculating cancer incidence for an asymptomatic individual based on their current age and projected lifespan, under two scenarios: with and without prior screening. In Section 3, we will apply these methods to estimate the risk of colorectal cancer using parameters derived from the MCCCS screening data. Finally, we will conclude with a discussion in Section 4.

2. Materials and Methods

2.1 Materials

The Minnesota Colon Cancer Control Study was conducted between 1976 and 1982. It employed a non-invasive screening tool known as the Fecal Occult Blood Test (FOBT), which checks stool samples for hidden (occult) blood that could indicate gastrointestinal bleeding and serve as an early sign of colorectal cancer before symptoms manifest.

Approximately 46,000 asymptomatic males and females were randomized into three groups: Group 1 received five annual FOBTs, Group 2 received three biennial FOBTs, and Group 3 underwent no screening at all. Each test comprised six hemoccult slides, with about 83% of the slides being rehydrated. If any of the slides tested positive, the screening was deemed positive, leading to a definitive follow-up exam that included a colonoscopy.

Due to a lower than anticipated death rate among the control group, the investigators resumed screenings from 1986 to 1992. We will utilize the data obtained from the original study group that underwent five annual screenings, which were published as Table 1 and Table 2 in the paper [14], and are available online at: <https://pmc.ncbi.nlm.nih.gov/articles/PMC2773467/>.

2.2 Methods

We briefly review the probability method to estimate the remaining lifetime risk based on one's current age and screening history [15].

We let T_1 be the time duration in the S_p , with probability density function (PDF) $T_1 \sim w(t)$, and T_2 be the time duration in the S_c , i.e., the sojourn time, and $T_2 \sim q(x)$; $Q(z) = P(T_2 > z) = \int_z^\infty q(x)dx$ is the survival function of the sojourn time. T_1 and T_2 are assumed to be independent random variables. We let the screening sensitivity $\beta_i = \beta(t_i)$, where t_i represents an individual's age at the exam.

Suppose a woman at her current age a_0 has never taken any screening exam and she looks healthy (i.e., asymptomatic), then the PDF of her clinical incident time/age $Y = T_1 + T_2$ (i.e., Y is the age when symptoms appear) would be:

$$I_Y(y) = \int_0^y w(x)q(y-x)dx. \quad (1)$$

If the lifetime $T = t(> a_0)$ is fixed, the probability of incidence in (a_0, t) is [13]:

$$\begin{aligned} P(a_0 < Y < T | T = t) &= P(a_0 < Y < t | T = t) \\ &= \int_{a_0}^{a_0} w(x)[Q(a_0 - x) - Q(t - x)]dx + \int_{a_0}^t w(x)[1 - Q(t - x)]dx. \end{aligned} \quad (2)$$

When the lifetime T is random, the probability of having clinical symptoms after age a_0 and before her death is:

$$P(a_0 < Y < T | T > a_0) = \int_{a_0}^{\infty} P(a_0 < Y < T | T = t) f_T(t | T > a_0) dt, \quad (3)$$

where $f_T(t | T > a_0)$ the conditional PDF of human lifetime:

$$f_T(t | T > a_0) = \begin{cases} \frac{f_T(t)}{P(T > a_0)} = \frac{f_T(t)}{1 - F_T(a_0)}, & \text{if } t > a_0; \\ 0, & \text{otherwise.} \end{cases} \quad (4)$$

And $f_T(t)$ can be estimated by transforming the actuarial life table of the United States Social Security Administration [16].¹

If she has taken $K(\geq 1)$ screening exams with negative results at her ages $t_0 < t_1 < \dots < t_{K-1}$, and she is asymptomatic at her current age $a_0(\geq t_{K-1})$. The probability of having clinical symptoms after age a_0 and before her death is [15]:

$$P(I_K | T > a_0) = \int_{a_0}^{\infty} P(I_K | T = t) f_T(t | T > a_0) dt, \quad (5)$$

where,

$$\begin{aligned} P(I_K | T = t) = & \sum_{i=0}^{K-1} (1 - \beta_i) \dots (1 - \beta_{K-1}) \int_{t_{i-1}}^{t_i} w(x) [Q(a_0 - x) - Q(t - x)] dx \\ & + \int_{t_{K-1}}^{a_0} w(x) [Q(a_0 - x) - Q(t - x)] dx \\ & + \int_{a_0}^t w(x) [1 - Q(t - x)] dx, \end{aligned} \quad (6)$$

and $\beta_i = \beta(t_i)$ is the screening sensitivity at age t_i .

3. Results

We apply the method to estimate the risk of colorectal cancer for both genders using the MCCC five annual screen group data [14]. This risk or the probability of having a specific cancer from one's current age until death is a function of the three key model parameters: the sensitivity $\beta(t)$, the transition density $w(t)$, and the survival function $Q(x)$ of the sojourn time. Estimation of the three key parameters $\beta(t)$, $w(t)$, and $Q(x)$ were obtained using a likelihood function and the parametric link functions as below [14]:

$$\begin{aligned} \beta(t) &= \frac{1}{1 + \exp\{-b_0 - b_1(t - m)\}}, \\ w(t | \mu, \sigma^2) &= \frac{0.1}{\sqrt{2\pi\sigma^2}} \exp\left\{-\frac{(\log t - \mu)^2}{2\sigma^2}\right\}, \quad \sigma > 0, \\ Q(x) &= \frac{1}{1 + (x\rho)^\kappa}, \quad \kappa > 0, \quad \rho > 0, \end{aligned} \quad (7)$$

where $\beta(t)$ was the sensitivity, t was one's age at the exam, and m was the mean age at the first exam. The $w(t)$ is a sub-PDF, i.e. $\int w(t) dt < 1$, as not all people would enter the preclinical state in their lifetime.

There were 6 unknown parameters $\theta = (b_0, b_1, \mu, \sigma, \kappa, \rho)$ in this model. Using noninformative priors, the likelihood function, and Markov Chain Monte Carlo simulation, 1000 posterior samples of θ were obtained after the burn-in and thinning steps for males and females respectively. For more details on the multiple chain simulation and convergence diagnostics, see Wu et al 2009 [14].

3.1 Colorectal Cancer Risk without any Screening History

For males and females without any screening history of colorectal cancer, the estimation of remaining lifetime risk is relatively straightforward. Each of the 1000 posterior samples was plugged into equation (1) to derive an estimated probability

density function of the incidence age ranging from 0 to 119. Similarly, Each set of the posterior samples was incorporated into equations (2) and (3) to estimate the probability of developing colorectal cancer after the current age (a_0) but before death, with a_0 changing from 0 to 119. Since there are 1000 posterior samples, the point-wise median and the 95% highest probability density (HPD) credible interval for the PDF of incidence age and the risk of colorectal cancer can be obtained. These are plotted in Figure 1.

The left two panels of Figure 1 illustrate the lifetime risk as a function of current age for males and females. The risk remains stable before age 45 for men and before age 50 for women. Beyond these ages, the lifetime risk gradually decreases for both genders as they grow older. The right two panels display the PDF of the incidence age of colorectal cancer for males and females. Males have the highest density of incidence around age 74, while females have the highest density around age 80. These ages correspond to the periods when males and females are most likely to experience clinical symptoms of colorectal cancer.

The simulation results are summarized in Table 1. The first three columns present the current age (0 to 100 years) and the corresponding projected median remaining lifetime risk of CRC, together with the 95% HPD credible intervals (expressed as percentages), for females and males.

The results indicate that females have a lower remaining lifetime risk of CRC than males up to age 44. After age 45, however, this pattern reverses, with females exhibiting a higher remaining lifetime risk. This reversal is likely attributable to the longer life expectancy of females compared with males. Additional ages (45, 55, 65, 75, and 85 years) are included in Table 1 to facilitate comparisons with individuals who have different screening histories, which are presented later.

The last three columns report the probability density function of the age at clinical incidence over the age interval of 70-85 years, with the corresponding curves shown in

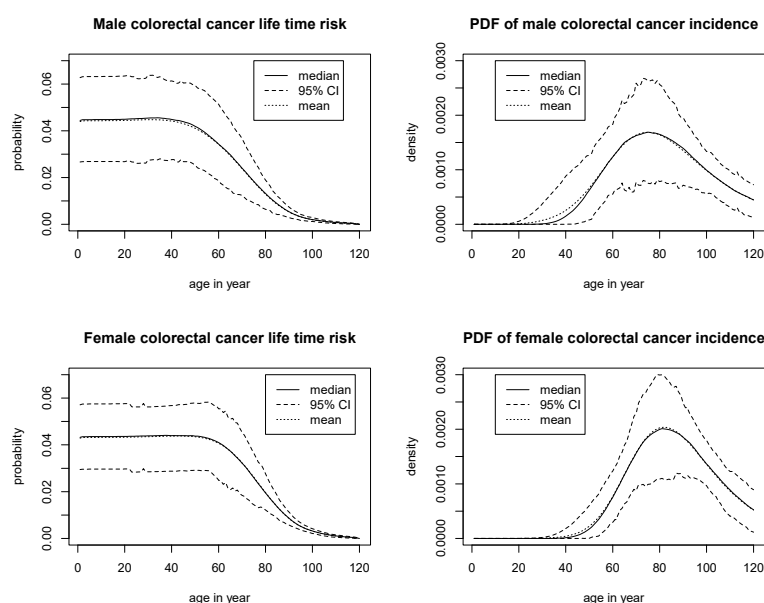


Figure 1: Lifetime risk and clinical incidence distribution for colorectal cancer using the MCCCS data

Figure 1. The estimated incidence age is most likely to be 74 years for males and 80 years for females.

3.2 Colorectal cancer risk with a screening history

Because CRC typically develops over many years and its clinical incidence increases with age, the U.S. Preventive Services Task Force (USPSTF) recommends routine CRC screening for adults between 50 and 75 years of age using FOBT, sigmoidoscopy, or colonoscopy at the recommended screening intervals. For individuals at increased risk, such as those with a family history of CRC, the USPSTF recommends initiating screening at age 45 and continuing through age 85 [12].

Following the USPSTF recommendations, we conducted simulation studies to estimate the remaining lifetime risk of CRC. Specifically, for an individual with a previous history of FOBT screening who has remained asymptomatic and has not been diagnosed with CRC, we estimated the remaining lifetime risk under the following scenarios:

- past screening ages: $[t_0, t_{K-1}] = [45, 55], [55, 65], [65, 75]$;
- past screening interval: $\Delta = 1$ or 2 years.

Table 1: Estimated colorectal cancer risk (in percentage) and the estimated median probability density at different incidence age using the MCCC data

age a_0	risk in percentage		age	density in 10^{-3}	
	Female	Male		Female	Male
0	4.33 (2.94, 5.71)	4.44 (2.67, 6.27)	70	1.635	1.640
10	4.35 (2.96, 5.75)	4.48 (2.69, 6.32)	71	1.705	1.652
20	4.36 (2.97, 5.76)	4.50 (2.71, 6.36)	72	1.764	1.667
30	4.39 (2.85, 5.63)	4.55 (2.75, 6.37)	73	1.814	1.678
40	4.40 (2.88, 5.69)	4.47 (2.77, 6.10)	74	1.859	1.690
45	4.39 (2.89, 5.73)	4.36 (2.68, 6.05)	75	1.894	1.685
50	4.38 (2.91, 5.78)	4.14 (2.42, 5.83)	76	1.926	1.674
55	4.27 (2.89, 5.83)	3.78 (2.15, 5.51)	77	1.952	1.672
60	4.04 (2.46, 5.54)	3.35 (1.75, 4.97)	78	1.975	1.662
65	3.64 (2.16, 5.14)	2.86 (1.35, 4.21)	79	1.997	1.647
70	3.11 (1.79, 4.41)	2.29 (1.15, 3.47)	80	2.012	1.632
75	2.46 (1.37, 3.45)	1.73 (0.86, 2.56)	81	2.006	1.609
80	1.82 (1.14, 2.55)	1.22 (0.61, 1.76)	82	2.000	1.592
85	1.24 (0.76, 1.63)	0.80 (0.42, 1.12)	83	1.992	1.567
90	0.78 (0.52, 1.01)	0.49 (0.26, 0.66)	84	1.982	1.544
100	0.29(0.19, 0.38)	0.19 (0.11, 0.26)	85	1.963	1.516

- current age: $a_0 = t_{K-1}, t_{K-1} + 1, t_{K-1} + 2, \dots, 119$;

Please note that the number of exams K in the past depends on the past screening interval. If the past screening interval Δ was 1 year, then $K = 11$; If the past screening interval Δ was 2 years, then $K = 6$. We estimated the probability of colorectal cancer risk from one's current age until death, using equations (5) and (6) and the 1000 posterior samples for both genders. The simulation results were summarized in Table 2 for both females and males.

The first column in Table 2 represents the current age a_0 . We observe that the estimated risk of cancer remains nearly constant across different past screening intervals for a given age, though with slightly varying 95% HPD intervals. As the current age a_0 increases, the estimated risk gradually decreases. Comparing results for the same age group with those in Table 1, we find that asymptomatic individuals with a screening history tend to have a slightly lower risk than those without prior screening. However, after a few years, the risk converges for both groups; in other words, if the last examination was conducted three or four years ago, it has no appreciable effect on the remaining cancer risk.

Figure 2 presents the projected remaining lifetime risk of CRC as a function of the current age, a_0 , for individuals with and without a screening history. Because the projected risks are nearly identical for individuals with a screening interval of $\Delta = 1$ and $\Delta = 2$, only the results for $\Delta = 1$ are shown.

The figure shows that individuals with a previous screening history have a slightly lower projected risk than those without prior screening during the first few years after the most recent screening. However, this difference gradually disappears, and after approximately 2 to 3 years, the projected risks become nearly identical. These results

Table 2: Estimated colorectal cancer risk from the current age a_0 to death

age a_0	$(t_0, t_{K-1}) = (45, 55)$			
	Female		Male	
	$\Delta = 1$	$\Delta = 2$	$\Delta = 1$	$\Delta = 2$
55	4.19 (2.73, 5.72)	4.19 (2.72, 5.70)	3.62 (1.93, 5.47)	3.63 (1.95, 5.45)
65	3.64 (2.04, 5.03)	3.64 (2.04, 5.03)	2.86 (1.42, 4.34)	2.86 (1.38, 4.30)
75	2.46 (1.37, 3.45)	2.46 (1.37, 3.45)	1.73 (0.86, 2.59)	1.73 (0.86, 2.59)
85	1.24 (0.76, 1.63)	1.24 (0.76, 1.63)	0.80 (0.41, 1.12)	0.80 (0.41, 1.12)
95	0.47 (0.33, 0.60)	0.47 (0.33, 0.60)	0.29 (0.16, 0.39)	0.29 (0.16, 0.39)
105	0.17(0.09, 0.23)	0.17 (0.09, 0.23)	0.12 (0.06, 0.16)	0.12 (0.06, 0.16)
age a_0	$(t_0, t_{K-1}) = (55, 65)$			
	Female		Male	
	$\Delta = 1$	$\Delta = 2$	$\Delta = 1$	$\Delta = 2$
65	3.41 (1.77, 4.78)	3.41 (1.78, 4.78)	2.63 (1.16, 4.04)	2.64 (1.19, 4.04)
75	2.46 (1.36, 3.46)	2.46 (1.36, 3.45)	1.72 (0.84, 2.60)	1.72 (0.84, 2.60)
85	1.24 (0.76, 1.63)	1.24 (0.76, 1.63)	0.80 (0.40, 1.12)	0.80 (0.40, 1.12)

95	0.47 (0.33, 0.60)	0.47 (0.33, 0.60)	0.29 (0.16, 0.39)	0.29 (0.16, 0.39)
105	0.17 (0.09, 0.23)	0.17 (0.09, 0.23)	0.12 (0.06, 0.16)	0.12 (0.06, 0.16)
$(t_0, t_{K-1}) = (65, 75)$				
age a_0	Female		Male	
	$\Delta = 1$	$\Delta = 2$	$\Delta = 1$	$\Delta = 2$
75	2.13 (1.18, 3.11)	2.14 (1.18, 3.09)	1.48 (0.62, 2.30)	1.49 (0.64, 2.28)
85	1.24 (0.80, 1.67)	1.24 (0.80, 1.67)	0.80 (0.39, 1.13)	0.80 (0.39, 1.13)
95	0.46 (0.33, 0.60)	0.46 (0.33, 0.60)	0.29 (0.16, 0.39)	0.29 (0.16, 0.39)
105	0.17 (0.09, 0.23)	0.17 (0.09, 0.23)	0.12 (0.06, 0.16)	0.12 (0.06, 0.16)

suggest that a negative screening result has only a limited effect on the remaining lifetime risk of CRC, primarily reducing the risk during the first few years following the most recent screening. Similar findings have also been reported for breast cancer [15].

4. Discussion

We applied a recently developed probability-based method to estimate the remaining lifetime risk of CRC from an individual's current age until the end of life using data from the annual screening cohort of the MCCCS. The results indicate that the remaining lifetime risk for both males and females remains relatively stable from birth until middle age and then gradually declines with increasing age.

One might intuitively expect the remaining lifetime risk of cancer to remain constant throughout life or even increase with age. However, our simulation results suggest a different pattern. This finding is reasonable because, as individuals age, their remaining life expectancy decreases. In addition, reaching a given age without clinical evidence of CRC provides information that the individual has remained free of clinically detectable disease up to that point, resulting in a lower projected remaining lifetime risk. Furthermore, the estimated age at clinical incidence is most likely

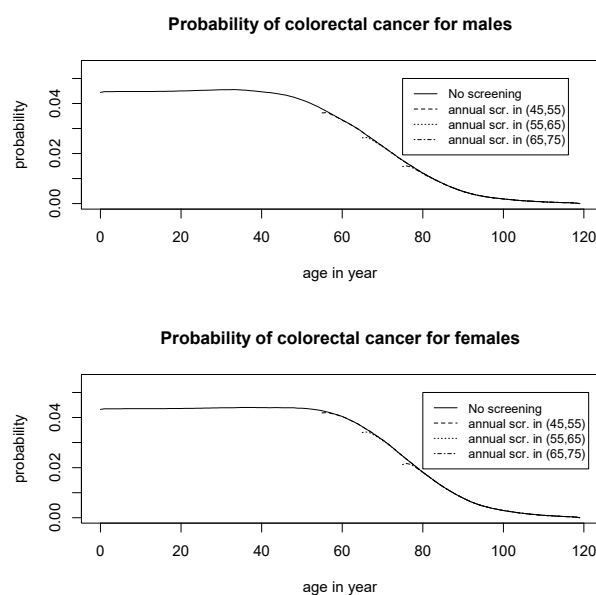


Figure 2: Lifetime risk for colorectal cancer

to be approximately 74 years for males and 80 years for females. These findings provide further insight into the natural history and age-specific development of colorectal cancer.

The findings of this study underscore the importance of evaluating CRC from the perspective of remaining lifetime risk, as this measure captures epidemiological patterns that may not be apparent from conventional age-standardized incidence rates alone. Our analysis shows that the remaining lifetime risk of developing CRC is relatively stable at approximately 4%-5% from birth until middle age, after which it gradually declines with increasing age. At the same time, this overall pattern contrasts with the well-documented increase in early-onset CRC, with the incidence among individuals younger than 50 years increasing by approximately 1.5% per year [17]. These findings highlight the complexity of current CRC epidemiology and the need to consider both age-specific incidence and remaining lifetime risk when assessing disease burden.

An online CRC risk calculator is available through the National Cancer Institute (NCI) website [18]. The calculator estimates an individual's 5-year and lifetime risks of developing CRC based on personal characteristics, including lifestyle factors, medical history, and other risk factors. The underlying methodology is based on the widely used Gail model or its extensions [11],

in which risk estimates are derived from epidemiological studies and survival analysis.

Our approach differs in that it directly estimates the remaining lifetime risk using a probability-based framework. In principle, the proposed method can be extended to incorporate additional risk factors, such as family history, medical history, and lifestyle characteristics. Such an extension would require estimating the three key model parameters: screening sensitivity, the sojourn time distribution, and the transition probability density, for different risk groups using screening data. Future work will focus on developing these extensions and applying the proposed method to populations at elevated risk of CRC.

Acknowledgements: All simulations was carried out in the University of Louisville HPC.

Declarations

- Funding: This project was not funded.
- Conflict of interest/Competing interests: There is no conflict of interest/competing interests.
- Data availability statement: All data supporting the findings of this study are available within the paper. The MCCC annual screening group data are human-related data for both genders without personal identification, and all human-related data used in the present study were extracted directly from the previously published article (Tables 1 and 2) [14], rather than obtained from a separate dataset.
- Ethical approval statement: The project is a secondary data analysis; it involves applying a statistical method to the existing MCCC data, without any personal identifiers. All methods were carried out in accordance with relevant guidelines and regulations.

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