Assessing the Impact of Screening Colonoscopy on Mortality in the Medicare Population

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BACKGROUND: Some have recommended against routine screening for colorectal cancer (CRC) among patients ≥75 years of age, while others have suggested that screening colonoscopy (SC) is less beneficial for women than men. We estimated the expected benefits (decreased mortality from CRC) and harms (SC-related mortality) of SC based on sex, age, and comorbidity.

OBJECTIVE: To stratify older patients according to expected benefits and harms of SC based on sex, age, and comorbidity.

DESIGN: Retrospective study using Medicare claims data.

PARTICIPANTS: Medicare beneficiaries 67–94 years old with and without CRC.

MAIN MEASURES: Life expectancy, CRC- and colonoscopy-attributable mortality rates across strata of sex, age, and comorbidity, pay-off time (i.e. the minimum time until benefits from SC exceeded harms), and life-years saved for every 100,000 SC.

KEY RESULTS: Increasing age and comorbidity were associated with lower CRC-attributable mortality. Due to shorter life expectancy and CRC-attributable mortality, the benefits associated with SC were substantially lower among patients with greater comorbidity. Among men aged 75–79 years with no comorbidity, the number of life-years saved was 459 per 100,000 SC, while men aged 67–69 with ≥3 comorbidities had 81 life-years saved per 100,000 SC. There was no evidence that SC was less effective in women. Among men and women 75–79 with no comorbidity, number of life-years saved was 459 and 509 per 100,000 SC, respectively; among patients with ≥3 comorbidities, there was no benefit for either men or women.

CONCLUSIONS: Although the effectiveness of SC was equivalent for men and women, there was substantial variation in SC effectiveness within age groups, arguing against screening recommendations based solely on age.

Received December 20, 2010
Revised April 19, 2011
Accepted July 1, 2011
Published online August 13, 2011

KEY WORDS: screening colonoscopy; colorectal cancer screening; medicare.
J Gen Intern Med 26(12):1441–9
DOI: 10.1007/s11606-011-1816-4

BACKGROUND

Screening colonoscopy (SC) is advocated by many professional organizations and is increasingly common in clinical practice[2–6]. However, there are important concerns about how age, sex, and comorbidity moderate the effectiveness of SC. Some speculate that SC is not as effective in women compared to men because of women's lower incidence of adenomas and colorectal cancer (CRC)[7]. However, because women have longer life expectancies, they may experience equal or greater benefits from screening and prevention. Similarly, the United States Preventive Services Task Force (USPSTF) recently cautioned against routine screening of patients 76–85-years-old[1]. Yet age should not be considered in isolation, as a "healthy" 80-year-old might benefit from preventive care that would not help a 70-year-old with multiple comorbidities.

Incorporating age, sex, and comorbidity into a refined assessment of the risks and benefits of screening has been challenging[8–10]. Prior analyses have not considered that the impact of cancer on a patient's risk of death may be diminished among patients with higher comorbidity[11,12]. Further, while prior work has stratified patients into life expectancy groups, comorbidity was not incorporated into the approach[13–18]. Finally, prior work has not accounted for the fact that increasing age and declining health would increase one's susceptibility to the risk of SC-associated complications[11,12].

Recognizing that SC is becoming increasingly common, but is still associated with benefits as well as harms, it is important to generate data that will enable physicians and patients to make informed decisions about screening. We used cancer registry and Medicare claims data to incorporate sex, age, and comorbidity into a framework that quantified and weighed the harm of screening in terms of SC-related mortality and the benefit of screening in terms of reduced mortality from CRC. We then created a decision rule that allowed us to evaluate two specific issues; among older

persons who are eligible for SC (i.e. who have not had a SC within the prior 10 years and do not have a history of polyps): whether the USPSTF recommendation against routine screening among patients ≥75 years is substantiated and whether SC is less effective in women than men.

METHODS

We used the Surveillance, Epidemiology, and End Results (SEER)-Medicare database[19–23]. All incident cancer patients reported to the SEER registries are cross-matched with Medicare enrollment and claims files[24]. We selected patients 67–94-years-old diagnosed with initial invasive primary CRC from 1993 through 2002 (Appendix 1). We only included patients who had fee-for-service and Part B coverage in the 24 months preceding diagnosis.[20]. To construct our non-cancer sample, we randomly selected a subset of 50,000 non-cancer patients who met the same age and administrative criteria as the cancer patients for each year from 1993–2002. Many patients were eligible in more than 1 year; we removed these duplicate patients by randomly selecting one of the years. We then randomly selected a month during that year to serve as the patient's index date, which served as "time zero" for subsequent survival analyses. Follow-up lasted through December 2007. This study was approved by the Yale Human Investigations Committee.

Construction of Variables

Chronic conditions were identified by searching Medicare claims during the 24 through 3 months prior to cancer diagnosis/index date[23,25]. We used the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9) codes recommended by Elixhauser[26] to identify chronic conditions, with the exception of specific ICD-9 codes for CRC and blood loss anemia, which could be associated with CRC or serve as an indication for colonoscopy[23,25]. We constructed a multivariable Cox proportional hazards model including all Elixhauser conditions in the non-cancer patients, adjusted for sex and age. Conditions that had a hazard ratio >1.0 and were significantly associated with survival were retained in the final model. The hazard ratios for all conditions included in the model were between 1.0 and 2.0, with the exception of AIDS/HIV (prevalence of 0.01% in the study sample). As such, the weighting for nearly all the conditions was similar.

We used a standard life table approach to estimate life expectancy. Annual mortality rates for each sex/age/comorbidity stratum were derived from our non-cancer sample (ages 67–94) and the U.S. Census (ages 95–119). Based on trends observed in our data, we transitioned patients toward increasing comorbidity with increasing age: as patients progressed from one age category to the next (i.e. 67–69 to 70–74), 20% of the surviving sample moved up to the next comorbidity category (i.e. from 0 conditions to 1–2 conditions).

In order to estimate the mortality risk associated with undergoing a screening, rather than diagnostic, colonoscopy, we used the Medicare claims to identify patients who had undergone an outpatient colonoscopy[27,28]. We searched for the HCPCS codes specifically created for this procedure (G0105, G0121) and all other colonoscopies that were not preceded by claims that were consistent with gastrointestinal symptoms (abdominal pain, weight loss, gastrointestinal bleeding, anemia, altered bowel habits, positive FOBT) during the previous 90 days (HCPCS codes 44388–44389, 44392–4, 45378, 45379, 45380, 45382–45385; ICD-9 codes 45.23, 45.25, 45.41-45.43, 48.36)[29].

Estimating the Colorectal Cancer-Attributable Risk of Death

We determined the CRC-specific case fatality rate by subtracting the 5-year mortality rate of the non-cancer sample from that of the cancer sample within each sex/age/comorbidity stratum , applying the validated Declining Exponential Approximation of Life Expectancy (DEALE) approach[30–32]. We then estimated the CRC-attributable mortality rate by multiplying the CRC-specific case fatality rate by age- and sex-specific incidence rates (based on prior published SEER data).

We also estimated the expected benefit of SC among patients who had received a negative SC in the past 10–15 years. Prior studies have suggested that the "protective effect" of a negative SC in terms of decreased CRC mortality lasts for more than 10 years[33–37]. Based on estimates from this literature, we reduced the CRC mortality rate by 50% and replicated the analysis to estimate how these patients would benefit from SC.

Estimating the Benefit and Harms of Screening Colonoscopy

We quantified the benefit of SC as the reduction in CRC-attributable mortality. We estimated this benefit by assuming that the procedure reduces the CRC-attributable mortality by 70%, which is the median estimate from the USPSTF summary[38]. Consistent with published trials, we assumed that the annual reduction in CRC mortality would not begin until 5 years after receipt of SC, since screening improves mortality by removing early stage lesions, which can take 5+ years to result in death[39–41].

We quantified the harm of SC as mortality related to the procedure. While we recognize that there are important complications other than mortality, we were unable to reliably assess them using our data. To estimate mortality attributable to SC, rather than other causes, we used a two-step approach. First, we calculated the 30-day mortality among patients who had undergone SC in our non-cancer sample. We then used an internal control group by selecting the patients in this sample who survived 90 days after SC and calculating the 30-day mortality starting from day 91. Subtracting the latter mortality rate from the former yielded an overall SC-attributable mortality estimate that was distinct from the overall risk of death. Because stratum-specific outcomes were so rare that reliable estimates of stratum-specific SC-related mortality were not feasible, we used estimates of the relative risk of SC mortality associated with increasing age and comorbidity derived from prior studies[42,43]. Specifically, we estimated that the relative risks for the group with 1–2 and ≥3 comorbidities were 1.5 and 3 times that of the zero comorbidity group, respectively[43].

Similarly, we estimated that the relative risk of mortality for patients 75–79 years and ≥80 years were 1.5 and 2 times the risk in patients 67–74 years, respectively[42,43].

We then estimated "pay-off time" for each stratum. Pay-off time is defined as the minimum elapsed time until the cumulative incremental benefits of an intervention (i.e. reduced CRC mortality due to SC) exceed the cumulative incremental harms (i.e. death from SC-related complications). Each stratum had a minimum pay-off time of 5 years, since prior data from randomized trials suggest a 5-year lag between initiating cancer screening and observed mortality reduction. Pay-off time was equal to 5 years plus the ratio of the mortality increase due to SC over the mortality decrease due to SC[44]. We then compared the pay-off time to life expectancy estimates to determine whether it was likely that patients would live long enough for benefits to exceed harms. When life expectancy is shorter than pay-off time, harm is likely to exceed benefit.

Decision Rule

To create a decision rule, each sex/age/comorbidity stratum was categorized according to the number of life-years saved by SC. For strata in which life expectancy did not exceed pay-off time, harm exceeded benefit and the decision rule advised against screening. If life expectancy exceeded the pay-off time, the number of life-years saved per person screened was calculated by multiplying the reduction in mortality rate attributable to SC (Table 3, Col. B) by the number of years a patient would live past the pay-off time (Table 3, Col. F).

Table 1. Patient Characteristics

	Cancer sample (N=68,073)		Non-cancer sample (N=226,868)	
	N (%)	% survived 5-years	N (%)	% survived 5-years
Age at diagnosis/ index date				
67-69	8,004 (11.8)	57.7	52,846 (23.3)	90.7
70-74	16,301 (24.0)	53.4	66,591 (29.4)	87.0
75-79	17,259 (25.4)	47.7	48,305 (21.3)	78.3
80-84	14,351 (21.1)	38.5	32,388 (14.3)	64.5
85-94	12,158 (17.9)	25.2	26,738 (11.8)	42.9
Race/ethnicity				
White	59,819 (87.9)	44.7	193,147 (85.1)	77.5
Black	5,006 (7.4)	35.2	16,158 (7.1)	75.3
Other	3,248 (4.8)	50.7	17,563 (7.7)	80.9
Sex				
Male	30,672 (45.1)	42.9	82,119 (36.2)	75.4
Female	37,401 (54.9)	45.4	144,749 (63.8)	78.9
# of conditions*				
0	35,200 (51.7)	50.5	125,748 (55.4)	87.1
1-2	23,459 (34.5)	42.7	74,685 (32.9)	73.1
≥3	9,414 (13.8)	25.2	26,435 (11.7)	45.4
Colorectal cancer stage				
1	17,353 (25.5)	64.0	–	–
2	21,181 (31.1)	54.5	–	–
3	15,699 (23.1)	40.6	–	–
4	10,612 (15.6)	4.2	–	–
Missing	3,228 (4.7)	20.9	–	–

**Conditions used to create comorbidity categories included congestive heart failure, cardiac arrhythmias, valvular disease, pulmonary circulation disorders, peripheral vascular disorders, paralysis, other neurological disorders, chronic pulmonary disease, diabetes, renal failure, lver disease, AIDS/HIV, lymphoma, metastatic cancer, solid tumor without metastasis, rheumatoid arthritis/collagen, coagulopathy, weight loss, fluid and electrolyte disorders, deficiency anemia, alcohol abuse, drug abuse, psychoses, depression*

RESULTS

Patients in both the cancer and non-cancer samples who were older or had greater comorbidity were less likely to survive 5 years (Table 1). Age alone was an insufficient predictor of both overall survival and CRC-specific case fatality rate. For instance, among men who were 75–79-years-old with zero conditions, the 5-year survival for patients with CRC was 49.3%, compared to 82.9% for those without cancer, yielding a CRC-specific case fatality rate of 33.6% (Table 2, Col. D). Among men in the same age group who had ≥3 conditions, the CRC-specific case fatality rate was only 16.4%, due to a smaller difference in survival between the cancer (27.3%) and non-cancer (43.7%) patients. Similarly, the CRC-specific case fatality rate for patients diagnosed at age 75–79 years was 32.9% for women with zero conditions, compared to 21.3% for women with ≥3 conditions (Table 3, Col. D). As a result, the annual CRC mortality rate (incidence x CRC-specific case fatality) was lower for patients with a greater comorbidity burden (Table 2, Col. D-F).

Women tended to have lower CRC incidence, but a slightly higher life expectancy. For men without cancer, life expectancy ranged from a high of 15.1 years in the youngest, healthiest cohort to a low of 3.5 years in the oldest, least healthy cohort (Table 4). For women without cancer, life expectancy ranged from a high of 17.5 years to a low of 3.8 years (Table 5). The life expectancy of both men and women aged 75–79 years with zero conditions (10.3 and 11.9 years) exceeded that of patients age 67–69 years with ≥3 conditions (7.4 and 8.8 years, respectively).

Among the non-cancer patients who received SC, the 30-day mortality rate was 0.10%. Among those who survived 90 days past SC, the 30-day mortality rate was 0.07%, resulting in a colonoscopy-attributable mortality rate of 0.03% or 30 deaths per 100,000 persons screened. The stratum-specific mortality rates ranged from 15.4 deaths per 100,000 for patients 67–74 with zero conditions to 92.2 deaths per 100,000 for patients aged 80–94 with ≥3 conditions.

The magnitude of benefit of SC (reduction in CRC mortality) was lower among patients with more comorbid conditions. For example, among men aged 75–79 years with no comorbidity, the number of life-years saved was 459 per 100,000 SC. In contrast, men who were younger (67–70 years old) but had ≥3 comorbidities had a benefit of only 81 life-years saved per 100,000 SC (Table 4, Col. G). The number of life-years saved for women 75–79-years-old with no comorbidity versus 67–70 years old with ≥3 comorbidities was 509 and 130 per 100,000 SC, respectively (Table 5, Col. G).

Decision Rule

For most strata, pay-off time was in the range of 5–7 years. Among those who were expected to outlive pay-off time, there was substantial variation in the magnitude of SC benefit. For

Table 2. Colorectal Cancer-Attributable Mortality Rates for Men

Age	Comorb-idities	A N (Non-cancer)	B 5-year survival: Cancer sample (%)	C 5-year survival: Non-cancer sample (%)	D Colorectal cancer- specific case fatality rate	E Colorectal cancer incidence (per 100,000)	F Colorectal cancer mortality rate (per 100,000 patients/year)
67-69							
	0	14,217	59.0	92.8	33.8	264.0	89.1
	1-2	5,878	53.4	84.7	31.3	264.0	82.7
	≥3	1,735	38.5	56.8	18.3	264.0	48.2
70-74							
	0	15,587	54.5	89.9	35.4	359.7	127.3
	1-2	7,950	49.5	80.0	30.5	359.7	109.8
	≥3	2,572	31.6	52.6	21.0	359.7	75.4
75-79							
	0	8,937	49.3	82.9	33.6	464.7	156.0
	1-2	5,982	42.9	70.6	27.6	464.7	128.4
	≥3	2,346	27.3	43.7	16.4	464.7	76.4
80-84							
	0	4,620	41.2	70.2	29.0	577.0	167.0
	1-2	3,856	34.0	54.5	20.5	577.0	118.5
	≥3	1,816	19.8	31.4	11.6	577.0	66.9
85-94							
	0	2,567	26.8	48.6	21.8	593.5	129.3
	1-2	2,640	20.4	35.3	14.8	593.5	88.0
	≥3	1,416	12.3	21.0	8.7	593.5	51.5

D. 5-year survival of the cancer sample subtracted from the 5-year survival of the non-cancer sample
E. Based on SEER data from1989-1993
F. Colorectal cancer-attributable mortality rate multiplied by colorectal cancer incidence rate

example, women aged 70–74 years with ≥3 comorbidities were expected to outlive their pay-off time by only 1.7 years, while women of the same age with zero comorbidities were expected to outlive pay-off time by nearly 10 years. The number of life-years saved (Table 3, Col. G) reflected the variation in the time expected to live past pay-off time (Table 3, Col. F) as well as variation in SC benefit (Table 3, Col. B). Among men who were expected to receive some benefit from SC, the number of life-years saved ranged from 12 to 1,128 years per 100,000 patients screened (Table 4). For women, the range was from 34 to 989 years per 100,000 patients screened (Table 5). The life-years saved were very similar for both sexes among the lower comorbidity strata for all age groups (Fig. 1).

Table 3. Colorectal Cancer-Attributable Mortality Rates for Women

Age	Comorb-idities	A N (Non-cancer)	B 5-year survival: Cancer sample (%)	C 5-year survival: Non-cancer sample (%)	D Colorectal cancer- specific case fatality rate	E Colorectal cancer incidence (per 100,000)	F Colorectal cancer mortality rate (per 100,000 patients/year)
67-69							
	0	20,003	62.4	96.9	34.5	165.5	57.1
	1-2	8,813	62.0	90.8	28.7	165.5	47.6
	≥3	2,200	37.2	64.0	26.9	165.5	44.4
70-74							
	0	24,406	60.5	94.8	34.3	235.6	80.8
	1-2	12,648	56.6	86.8	30.2	235.6	71.2
	≥3	3,428	36.1	61.5	25.4	235.6	59.7
75-79							
	0	16,645	56.3	89.2	32.9	319.5	105.1
	1-2	10,770	49.8	77.7	27.9	319.5	89.3
	≥3	3,625	32.0	53.3	21.3	319.5	68.0
80-84							
	0	10,523	47.0	79.1	32.1	400.3	128.7
	1-2	8,180	40.2	64.8	24.6	400.3	98.4
	≥3	3,393	24.8	39.9	15.1	400.3	60.2
85-94							
	0	8,243	32.6	57.0	24.5	444.9	108.8
	1-2	7,968	27.3	41.7	14.4	444.9	64.2
	≥3	3,904	13.4	24.6	11.2	444.9	49.9

D. 5-year survival of the cancer sample subtracted from the 5-year survival of the non-cancer sample
E. Based on SEER data from1989-1993
F. Colorectal cancer-attributable mortality rate multiplied by colorectal cancer incidence rate

Table 4. Benefits and Harms of Screening Colonoscopy for Men

Age	Comorb-idities	A Life expectancy (years)	B Reduction in colorectal cancer mortality from screening (per 100,000/year)	C Colonoscopy mortality rates (per 100,000)	D Pay-off time (years)	E Will average person live past pay-off time?	F Number of years alive past pay-off time	G Number of life-years saved (per 100,000 patients screened)
67-69								
	0	15.1	62.4	15.4	5.2	Yes	10.0	1128
	1-2	11.1	57.9	23.1	5.3	Yes	5.8	519
	≥3	7.4	33.8	46.1	5.9	Yes	1.5	81
70-74								
	0	13.1	89.1	15.4	5.1	Yes	8.0	852
	1-2	9.7	76.9	23.1	5.3	Yes	4.5	382
	≥3	6.5	52.8	46.1	5.9	Yes	0.6	28
75-79								
	0	10.3	109.2	23.1	5.2	Yes	5.1	459
	1-2	7.7	89.9	34.6	5.4	Yes	2.3	139
	≥3	5.3	53.4	69.2	6.5	No	–	0
80-84								
	0	7.9	116.9	30.7	5.3	Yes	2.6	232
	1-2	5.9	83.0	46.1	5.7	Yes	0.2	12
	≥3	4.3	46.9	92.2	7.6	No	–	0
85-94								
	0	6.1	90.5	30.7	5.3	Yes	0.7	65
	1-2	4.6	61.6	46.1	5.7	No	–	0
	≥3	3.5	36.0	92.2	7.6	No	–	0

A. Average life expectancy determined using life table approach
B. Colorectal cancer mortality rate among non-screened minus colorectal cancer mortality rate among screened patients; assumed to start 5 years after screening occurs
C. Estimated from Gatto et al.[43]
D. Number of years until the benefits of SC outweigh the risks
E. Does life expectancy exceed pay-off time?
F. Life expectancy minus pay-off time—indicates the number was not estimated because life expectancy does not exceed pay-off time

Table 5. Benefits and Harms of Screening Colonoscopy for Women

Age	Comorb-idities	A Life expectancy (years)	B Reduction in colorectal cancer mortality from screening (per 100,000/year)	C Colonoscopy mortality rates (per 100,000)	D Pay-off time (years)	E Will average person live past pay-off time?	F Number of years alive past pay-off time	G Number of life-years saved (per 100,000 patients screened)
67-69								
	0	17.5	40.0	15.4	5.3	Yes	12.2	989
	1-2	13.1	33.3	23.1	5.5	Yes	7.6	549
	≥3	8.8	31.1	46.1	6.1	Yes	2.7	130
70-74								
	0	15.1	56.6	15.4	5.2	Yes	9.9	823
	1-2	11.3	49.8	23.1	5.4	Yes	6.0	388
	≥3	7.7	41.8	46.1	6.0	Yes	1.7	73
75-79								
	0	11.9	73.6	23.1	5.3	Yes	6.7	509
	1-2	8.9	62.5	34.6	5.5	Yes	3.4	151
	≥3	6.2	47.6	69.2	6.6	No	–	0
80-84								
	0	9.2	90.1	30.7	5.4	Yes	3.8	287
	1-2	6.8	68.9	46.1	6.0	Yes	0.7	34
	≥3	4.8	42.2	92.2	7.6	No	–	0
85-94								
	0	6.9	76.1	30.7	5.4	Yes	1.5	111
	1-2	5.0	44.9	46.1	6.0	No	–	0
	≥3	3.8	34.9	92.2	7.6	No	–	0

A. Average life expectancy determined using life table approach
B. Colorectal cancer mortality rate among non-screened minus colorectal cancer mortality rate among screened patients; assumed to start 5 years after screening occurs
C. Estimated from Gatto et al.[43]
D. Number of years until the benefits of SC outweigh the risks
E. Does life expectancy exceed pay-off time?
F. Life expectancy minus pay-off time—indicates the number was not estimated because life expectancy does not exceed pay-off time

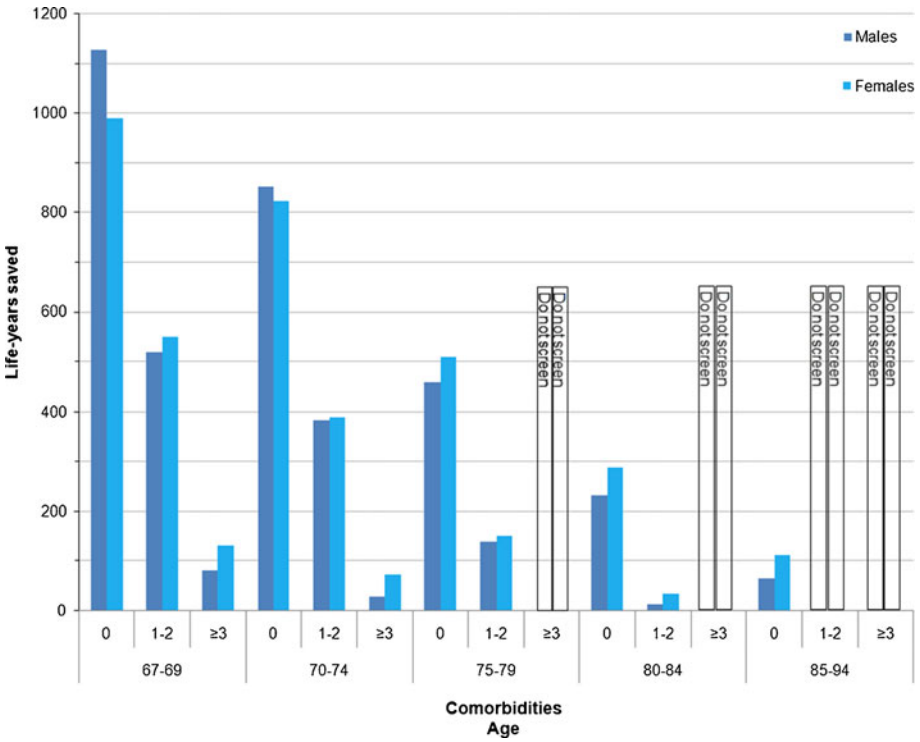


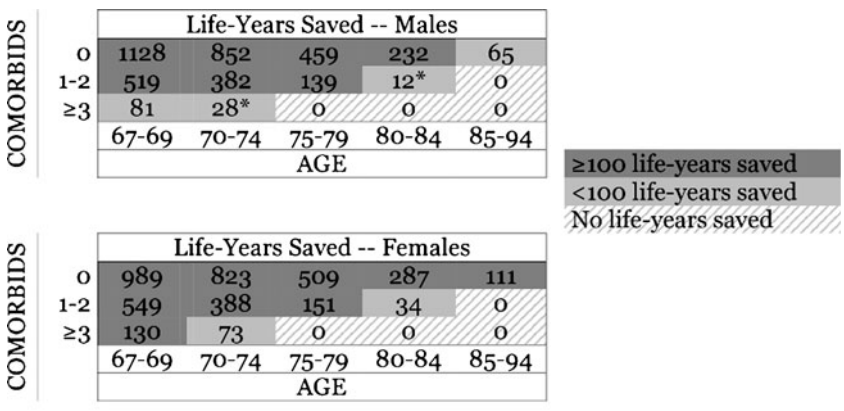
Figure 1. Number of life-years saved by sex, age, and comorbidity strata.

The number of life-years saved was greater than 100 per 100,000 patients screened for men and women aged 67–84 years with zero comorbidities and aged 67–79 years with 1–2 comorbidities, and for women aged 67–69 with ≥3 comorbidities or 85–94 with zero comorbidities. No life-years were saved, indicating no benefit from SC, for all patients ≥75 with ≥3 comorbidities or 85–94 with 1–2 comorbidities (Fig. 2).

In our sensitivity analysis, in which we reduced the CRC mortality rate by 50% to account for prior negative SC, the categories remained the same for 23 of the 30 strata (Appendix 2). However, there were three strata (males and females ages 80–84 with 1–2 comorbidities, males ages 70–74 with ≥3 comorbidities) for which there was an expected benefit of SC in the main analysis but no benefit in the sensitivity analysis. Additionally, the number of life years saved was substantially lower in many of categories.

DISCUSSION

We analyzed population-based data and used a decision analytic model to develop a straightforward approach that



*Indicates that colonoscopy was not found to be beneficial for patients in this stratum, if they had undergone prior colonoscopy (see Appendix Table 2 for full results of sensitivity analysis)

Figure 2. Screening colonoscopy decision rule.

clinicians can use when making decisions about CRC screening using colonoscopy. Our results do not support previous statements that SC may be more effective in men than women[7]. While we found that the higher CRC incidence rates in men resulted in a greater annual reduction in CRC mortality due to SC, the longer life expectancy of women counteracted this effect.

Earlier iterations of cancer screening guidelines have been criticized for a lack of an upper age limit. The USPSTF guidelines issued in 2008 were a notable departure, recommending against routine CRC screening in patients 76-85-years-old because of "moderate or high certainty that the net benefit is small" [1]. They did not recommend screening of any type in adults >85 years. While this approach acknowledges the diminishing benefit of screening with increasing age, the guidelines failed to recognize that factors other than age could affect the benefits and harms of CRC screening. We found that comorbidity had a substantial impact on the expected benefit of SC. In fact, for both men and women who were 75–79-years-old but had fewer than three comorbid conditions, SC was likely to be beneficial. For patients without comorbid conditions, SC was beneficial even up to 84 years. Conversely, among patients with ≥3 conditions, the expected benefits of SC were uncertain for patients as young as 67–69 years, and there was no expected benefit above the age of 75.

In general, our estimates of the benefits of SC tended to be lower than those reported in a prior analysis[12]. Although our life expectancy and CRC incidence rates were similar, our CRC-specific case fatality rates were much lower than previously estimated. The reason for this difference is twofold; first, we accounted for the impact of competing risks on CRC-specific case fatality by allowing for variation in CRC-specific case fatality rates, which decrease with increasing comorbidity. It is also notable that we found that the benefits were even lower when we revised our estimates to account for the lower CRC incidence that would be expected among patients with a prior colonoscopy that was negative. Second, we accounted for the baseline mortality rate among the non-cancer sample. This is preferable to calculating risk based on age-specific mortality rates reported by SEER[11,12]. SEER mortality data is obtained from death certificates, which tend to over-report cancer as the cause of death[45,46].

There are several limitations to our study. Comorbid conditions are not always reliably recorded in administrative claims. However, we used an algorithm for identifying conditions that required diagnosis codes to appear on at least one inpatient claim or ≥2 outpatient claims billed more than 30 days apart[23]. Additionally, SEER-Medicare data do not include important measures of health status such as functional disability or geriatric syndromes. Future work should incorporate more refined clinical data to determine whether our decision rule is applicable in different settings. Second, more detailed information about variation in SC effectiveness as well as colonoscopy-associated death rates and non-fatal health outcomes, including quality of life and patient preferences, should be explored[47,48]. Third, future work should incorporate other determinants of cancer risk as well as alternate screening modalities, given evidence suggesting the benefits of flexible sigmoidoscopies in particular may be comparable to SC[49–51]. Fourth, our categorization of patients into the three benefit categories (higher, lower, and no expected benefit) was likely subject to some misclassification, as we were not able to account for all relevant factors. Future validation of these categories is warranted. Fifth, although life-years saved can be a useful metric for assessing the benefit-to-harm ratio of screening, it is not a definitive rule for or against screening. Screening decisions are also influenced by clinical judgment, patient preferences, and cost, among other things. Our results indicate that there are few sex differences in the likelihood of risk and benefit from SC. Additionally, age and comorbidity are important considerations when making screening decisions, calling for reconsideration of guidelines which are based solely on age[1]. Particularly in cases where number of life-years saved is low, data-driven decision tools may help patients and healthcare providers make more informed screening decisions.

Acknowledgements: *This study used the linked SEER-Medicare database. The interpretation and reporting of these data are the sole responsibility of the authors. The authors acknowledge the efforts of the Applied Research Program, NCI; the Office of Research, Development and Information, CMS; Information Management Services (IMS), Inc.; and the Surveillance, Epidemiology, and End Results (SEER) Program tumor registries in the creation of the SEER-Medicare database.*

This work was supported by funding from by the National Institutes of Health (grant number 1 R21 HS017624-01).

Conflict of Interest: *None disclosed.*

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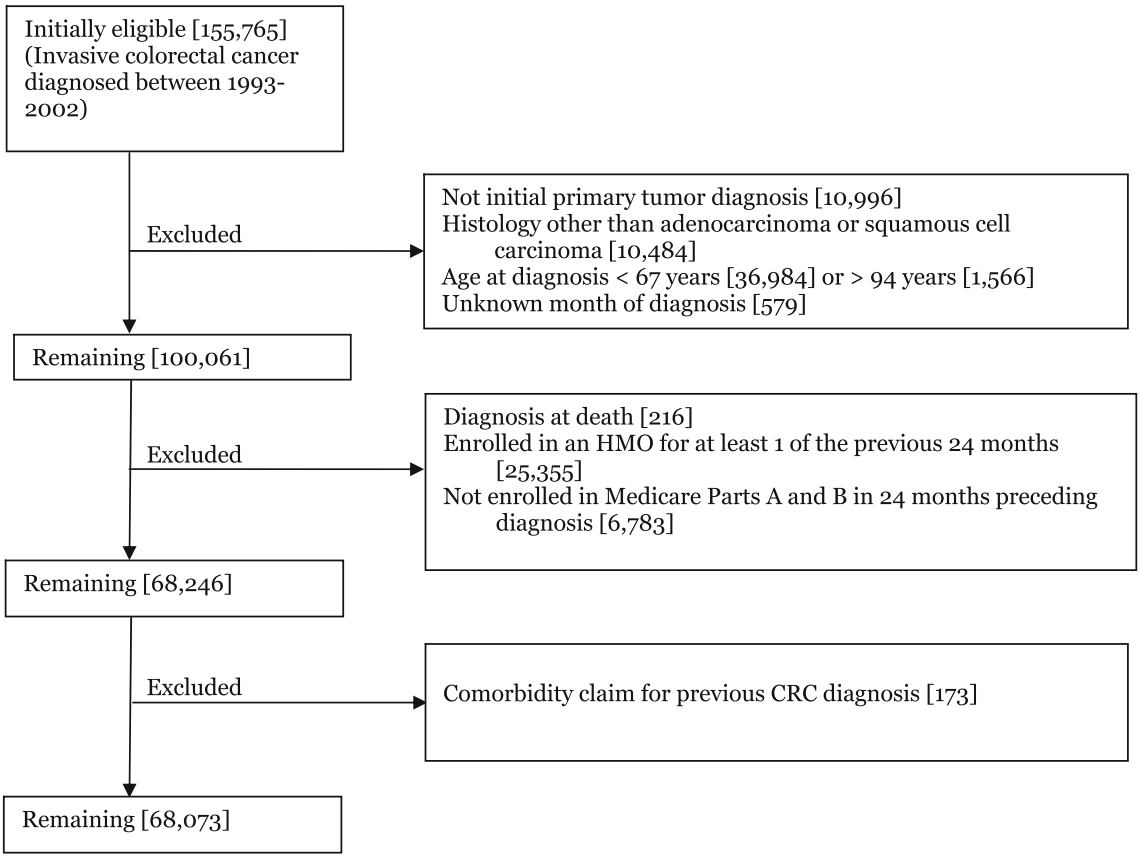
APPENDIX 1

Selection of cancer sample



APPENDIX 2

Decision rule figure for sensitivity analysis, assessing life-years saved for patients who had undergone a negative colonoscopy during 10–15 years prior