

Screening Colonoscopy in Very Elderly Patients

Prevalence of Neoplasia and Estimated Impact on Life Expectancy

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CURRENT GUIDELINES FOR colorectal cancer (CRC) screening do not specify an age limit above which screening is not recommended. The number of screening colonoscopies in elderly US patients has increased dramatically since Medicare coverage was approved in 2001.¹ However, some clinicians may have concerns with regard to screening extremely elderly patients, especially when an invasive modality such as colonoscopy is used. Colonoscopy in very elderly patients is associated with lower procedural completion rates, higher complication rates, and higher risk of inadequate bowel preparation.²⁻⁶ Other theoretical concerns yet to be rigorously evaluated include a potentially higher incidence of logistical problems (eg, transportation) and higher probability of informed consent difficulties because of cognitive impairment. In addition, very elderly patients have shorter life

See also pp 2366 and 2411.

Context Current guidelines do not include an upper age cutoff for colorectal cancer screening with colonoscopy. Although the prevalence of colonic neoplasia increases with age, life expectancy decreases. Thus, the benefit of screening colonoscopy in very elderly patients may be limited.

Objective To compare estimated life-years saved with screening colonoscopy in very elderly vs younger persons.

Design, Setting, and Participants Cross-sectional study conducted among 1244 asymptomatic individuals in 3 age groups (50-54 years [n = 1034], 75-79 years [n = 147], and ≥80 years [n = 63]) who underwent screening colonoscopy at a US teaching hospital and clinic.

Main Outcome Measures Prevalence of various types of colon neoplasia; estimated gain in life expectancy, calculated as life expectancy – (life expectancy during polyp lag time + life expectancy after colorectal cancer diagnosis); and comparison of mean gain in life expectancy across the 3 groups. Life expectancy and mortality data were derived from life tables, previous studies, and national databases.

Results The prevalence of neoplasia was 13.8% in the 50- to 54-year-old group, 26.5% in the 75- to 79-year-old group, and 28.6% in the group aged 80 years or older. Despite higher prevalence of neoplasia in elderly patients, mean extension in life expectancy was much lower in the group aged 80 years or older than in the 50- to 54-year-old group (0.13 vs 0.85 years). In sensitivity analysis, with longer polyp lag times the mean extension in life expectancy decreased more in the elderly than in the younger patients; alternatively, if it was assumed that a smaller proportion of adenomas progress to colorectal cancer, the mean extension in life expectancy decreased less in the elderly than in the younger patients.

Conclusions Even though prevalence of neoplasia increases with age, screening colonoscopy in very elderly persons (aged ≥80 years) results in only 15% of the expected gain in life expectancy in younger patients. Screening colonoscopy in very elderly patients should be performed only after careful consideration of potential benefits, risks, and patient preferences.

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expectancies, potentially limiting the benefits of screening procedures. The objective of this study is to estimate

the mean extension in life expectancy in very elderly vs younger patients using cross-sectional data

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collected from patients undergoing screening colonoscopy.

METHODS

Institutional review board approval at Virginia Mason Medical Center, Seattle, Wash, and oral informed consent were obtained.

Participants

Consecutive asymptomatic patients undergoing screening colonoscopy at Virginia Mason Medical Center from January 2002 to January 2005 were categorized by age: 50 to 54 years, 75 to 79 years, and 80 years or older. Race was self-described by the participants. Patients were interviewed by a nurse using a standard questionnaire and were excluded if they had gastrointestinal symptoms, including but not limited to bleeding, persistent or severe diarrhea, change in bowel habits, or abdominal pain. Additional exclusion criteria included previous history of CRC or adenomas, inflammatory bowel disease, hereditary nonpolyposis CRC, or familial adenomatous polyposis syndrome. Patients who had undergone colonoscopy or sigmoidoscopy within the past 5 years were excluded, as were patients who had an incomplete colonoscopy or suboptimal bowel preparation. Family history of CRC was not considered because the prevalence of neoplasia was directly measured in our cohort. Twelve board-certified gastroenterologists performed all colonoscopies.

Screening Procedures

Bowel preparation was performed with polyethylene glycol lavage (Schwarz Pharma, Milwaukee, Wis) using a standard protocol identical to that used for diagnostic colonoscopy. Colonoscopy was performed as an outpatient procedure, with patients under conscious sedation using intravenous midazolam and fentanyl. During colonoscopy, the location and size of all polyps were recorded, and the polyps were removed if technically possible. A complete examination was defined as the endoscope reaching the cecum, as documented in a photograph of the cecal pole. Polyp specimens

were classified according to criteria established by the World Health Organization. An advanced neoplastic lesion was defined as an adenoma with more than 25% villous features or at least 1 cm in size (not including adenomas with high-grade dysplasia or frank malignancy, which were considered separately for this study). In the case of patients with multiple polyps, patients were classified according to the most precancerous lesion. Procedure-related complications and hospitalizations were documented for 30 days following each colonoscopy.

Outcomes

The following outcomes were measured or imputed and compared across the 3 age groups: (1) prevalence of neoplasia, advanced neoplasia, high-grade dysplastic lesions, and CRC; (2) estimated mean extension of life expectancy (expressed as life-years saved); (3) adjusted mean extension of life expectancy (expressed as percentage); (4) percentage of patients who benefited from colonoscopy; and (5) number of colonoscopies per life-year saved.

Data Analysis

Statistical analysis was performed using Excel XP (Microsoft Inc, Redmond, Wash) and SPSS, version 11.0 (SPSS Inc, Chicago, Ill).

For our calculations, we used the following definitions for each patient:

$LE_{no\ neoplasia}$: life expectancy if no neoplasm is found on colonoscopy

$LE_{removed}$: life expectancy if a neoplasm is removed by colonoscopy

$LE_{neoplasia}$: life expectancy if a neoplasm is found but not removed at colonoscopy

$LE_{extension}$: extension of life expectancy due to screening colonoscopy

YL_{lag} : expected number of years lived during polyp lag time

LE_{CRC} : life expectancy after CRC diagnosis (with standard treatment)

The $LE_{extension}$ for each patient was calculated using the following formulas:

1. $LE_{removed} = LE_{no\ neoplasia}$
2. $LE_{neoplasia} = YL_{lag} + LE_{CRC}$
3. $LE_{extension} = LE_{removed} - LE_{neoplasia}$
 $= LE_{removed} - (YL_{lag} + LE_{CRC})$

4. To calculate mean $LE_{extension}$ for each group: mean $LE_{extension} = \text{sum of } LE_{extension} \text{ in group} / \text{number of patients in group}$

The $LE_{neoplasia}$ is the sum of the YL_{lag} and LE_{CRC} . The polyp lag time was defined as the estimated mean interval between discovery of an adenomatous polyp and the development of CRC if the polyp were left alone; this is thought to vary according to polyp size and histologic characteristics.⁷ We based our assumptions of polyp lag time on the results of previous studies on the natural history of adenomatous polyps. For our base case, we assumed the following average polyp lag times: 0 years for a polyp containing cancer; 1 year for neoplasia with high-grade dysplasia; 3 years for advanced neoplasia; 6 years for nonadvanced neoplasia sized 5 to 9 mm; and 8 years for nonadvanced neoplasia smaller than 5 mm. The YL_{lag} was derived by calculating the area under the age- and sex-specific survival probability curve during the polyp lag time. This survival curve was created using baseline age-, race-, and sex-specific annual mortality rates, μ_{age} , from 2001 US life tables (see BOX for examples of calculations for 2 representative patients).

The LE_{CRC} was estimated from the annual total mortality using the Declining Exponential Approximation of Life Expectancy (DEALE) principle.⁸ For patients who developed CRC, the annual total mortality is the sum of the age-, race-, and sex-specific CRC mortality, μ_{CRC} , and the baseline age-, race-, and sex-specific mortality, μ_{age} . The annual CRC mortality is obtained by applying the DEALE principle to national 1991-2000 cancer survival data from the US Surveillance, Epidemiology and End Results (SEER) program of the National Cancer Institute. The SEER program collects cancer survival data from 14 population-based cancer registries covering approximately 26% of the US population, considered to be representative of the country as a whole. The SEER database gives us the relative 5-year survival rate for CRC, stratified by age and sex. The rela-

tive survival for a group of cancer patients is the ratio between observed and expected survival, where expected survival is based on the survival probability curve of the general population, as described in US life tables. The DEALE principle is a mathematical model by which the effect of a medical condition on the life expectancy of a patient can be calculated. By using the DEALE principle, complex contributions of multiple mortality influences can be represented by a summation of individual mortality rates. The DEALE technique is based on the assumption that with the advancement of time, survival of a population cohort may be described by an exponential decline: $S(t) = S_0 \times e^{-\mu(\text{total}) \times \text{time}}$. The $S(t)$ is defined as the number of survivors as a function of time, the S_0 is the initial size of the population, and the μ_{total} is the total mortality rate, which represents the separate influences of age and CRC:

$$\mu_{\text{total}} = \mu_{\text{age}} + \mu_{\text{CRC}}$$

Therefore, this validated model allows one to estimate, with a relatively high degree of precision, the CRC-specific annual mortality rate, μ_{CRC} , from the relative survival rate, $R(t)$.⁹

In accordance with the DEALE principle, the LE_{CRC} is simply the reciprocal of the total annual mortality rate pertaining to the age at which CRC develops for a particular patient:

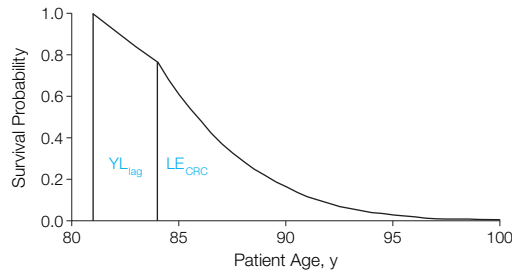
$$LE_{\text{CRC}} = \frac{1}{\mu_{\text{CRC}} + \mu_{\text{age}}}$$

Patients with no neoplastic findings were assumed to have zero life-years saved (ie, $LE_{\text{extension}} = 0$). Assuming some type of bell-curve distribution for life spans and polyp lag times, some patients might have an actual life span longer than their polyp lag time, even though their life expectancy is less than the average polyp lag time. This can be represented by the overlapping areas between the bell curves for life span and polyp lag time. However, it is impossible to accurately calculate this area because the bell curve is unlikely to be symmetric and the standard deviation and other parameters that define the bell

Box. Examples of Survival Curve Calculations for 2 Representative Patients

Example 1: An 81-year-old white man with a 1.2-cm tubulovillous adenoma found at colonoscopy

1. If his tubulovillous adenoma is removed, his LE_{removed} is 7.3 years (from US life tables).
2. If the patient's tubulovillous adenoma were not removed, his polyp lag time is 3 years under base conditions for an advanced neoplasm. The FIGURE is a schematic representation of the patient's survival probability curve if the tubulovillous adenoma were not removed. The area under the survival curve corresponds to life expectancy. YL_{lag} indicates number of years lived during polyp lag time; LE_{CRC} , life expectancy after colorectal cancer diagnosis.



3. The baseline annual mortality is 0.080467, 0.082817, and 0.094767 for men aged 81, 82, and 83 years, respectively. His YL_{lag} is thus $1.0 \times (1 - 0.080467) + [1.0 \times (1 - 0.080467) \times (1 - 0.082817)] + [1.0 \times (1 - 0.080467) \times (1 - 0.082817)] \times (1 - 0.094767) = 2.5264$ years.
4. At the end of this 3-year period, when he is 84 years old, he is assumed to have a 75% chance of developing colorectal cancer.
5. Assuming that this patient is randomly selected as one of the 75% of patients with advanced neoplasms who develop colorectal cancer, then using the Declining Exponential Approximation of Life Expectancy (DEALE) technique (based on age-, race-, and sex-specific Surveillance, Epidemiology and End Results 5-year relative survival data), his annual colorectal cancer-specific mortality is 0.09755. His baseline annual mortality at age 84 years is 0.103118 (from 2001 US life tables).
6. $LE_{\text{CRC}} = \text{probability of surviving to age 84} \times \text{reciprocal of } 0.09755 + 0.103118 = 0.7635 \times 4.98 = 3.8$ years.
7. $LE_{\text{extension}} = LE_{\text{removed}} - YL_{\text{lag}} - LE_{\text{CRC}} = 0.974$ years.

Example 2: An 84-year-old white man with a 4-mm tubular adenoma removed at colonoscopy

1. His LE_{removed} is 6.1 (from US life tables).
2. He has an adenoma of less than 5 mm, so his polyp lag time is 8 years under base case conditions.
3. Because the polyp lag time is more than his life expectancy by less than 2 years, his $LE_{\text{extension}}$ is assumed to be $0.5 \times 1 \text{ year} = 0.5$ years.

curve are unknown. Therefore, we made the simplifying assumption that if the polyp lag time was longer than the patient's $LE_{\text{no neoplasia}}$ by 2 years or less, then the patient would have a 50%

chance that he or she would gain 1 year of life expectancy. Patients in whom the polyp lag time was longer than their $LE_{\text{no neoplasia}}$ by more than 2 years were assumed to have zero life-years saved.

Table 1. Outcomes Under Base Case Assumptions for 1244 Individuals Who Underwent Screening Colonoscopy, January 2002 to January 2005

Outcomes*	Age Group, y		
	50-54 (n = 1034)	75-79 (n = 147)	≥80 (n = 63)
Patients with adenoma(s) <5 mm, No. (%)	66 (6.4)	16 (11)	4 (6.3)
Patients with adenoma(s) 5-9 mm, No. (%)	44 (4.3)	16 (11)	5 (7.9)
Patients with advanced neoplasia, No. (%)	33 (3.2)†	7 (4.7)	9 (14)‡
Life expectancy, mean (SD), y	28.87 (2.82)	10.37 (1.15)	7.59 (1.13)
Polyp lag time, mean (SD), y§	5.23 (2.27)	5.44 (1.95)	3.58 (2.43)
Y _{Lag} , mean (SD), y§	4.78 (2.12)	4.17 (1.32)	2.55 (1.44)
LE _{CRC} , mean (SD), y§	9.53 (1.53)	4.50 (1.33)	3.62 (1.48)
LE _{extension} , mean (SD), y	0.85 (3.40)	0.17 (0.49)	0.13 (0.30)
Adjusted LE _{extension} , %¶	2.94	1.64	1.71

Abbreviations: LE_{CRC}, life expectancy after colorectal cancer diagnosis; LE_{extension}, extension of life expectancy due to screening colonoscopy; Y_{Lag}, life expectancy during polyp lag time.
 *Classification is according to the most advanced lesion for each patient.
 †Includes 1 patient with high-grade dysplasia and 2 patients with cancer.
 ‡Includes 2 patients with high-grade dysplastic polyps and 1 with cancer.
 §These values were calculated only for patients with neoplastic findings, not the entire group.
 ||LE_{extension} was calculated as LE_{removed} - (Y_{Lag} + LE_{CRC}).
 ¶Adjusted LE_{extension} was calculated as (LE_{extension}/LE) × 100.

Furthermore, in our base case, we assumed that only a random 25% of adenomas smaller than 5 mm, 50% of adenomas sized 5 to 9 mm, 75% of advanced neoplasia, and 100% of high-grade dysplastic lesions would progress to CRC (even if given unlimited time). Our assumption was based on the fact that it is uncertain if nonadvanced neoplasia (in particular, small tubular adenomas <5 mm in size) will necessarily progress to CRC even if left untreated for very long periods of time.¹⁰ Some studies have shown that instead of progressing, small adenomas may regress, and even advanced neoplasia may not inevitably progress to CRC. Computerized random selection of patients who would go on to develop CRC was performed according to medical record numbers.

The LE_{no neoplasia} was derived from 2001 US life tables based on the age, sex, and race of each patient. Since life expectancies in US life tables already take into account mortality from all types of cancers (including CRC), the LE_{no neoplasia} was defined as the life expectancy without mortality due to CRC. According to the DEALE principle, this is equal to the reciprocal of the annual mortality rate without CRC, which is itself equal to the annual age-, race-, and sex-specific mortality rate (obtained from US life tables)

minus the annual CRC mortality rate for the US population (from the SEER database).

The number of screening colonoscopies per life-year saved for each group was calculated as the total number of colonoscopies divided by the total number of life-years gained in the group (ie, the sum of the gains in life expectancy).

The adjusted mean extension of life expectancy (expressed as a percentage) for each group was defined as (mean LE_{extension}/mean LE) × 100.

Patients in whom the LE_{extension} was zero were assumed not to have benefited from screening colonoscopy. Thus, the percentage of patients who benefited from colonoscopy was:

$$\frac{\text{Number of patients with a positive value for LE}_{\text{extension}}}{\text{Number of patients in group}} \times 100.$$

Sensitivity Analysis

Polyp Lag Time. Because there is considerable uncertainty about polyp progression rates, we analyzed scenarios in which the polyp lag times were either significantly shorter or longer than those used for our base case. The short lag time scenario used the following lag times: 0 years for a polyp containing cancer; 1 year for neoplasia with high-grade dysplasia; 2 years for advanced

neoplasia; 3 years for nonadvanced neoplasia sized 5 to 9 mm; and 5 years for nonadvanced neoplasia smaller than 5 mm. The long lag time scenario used the following lag times: 0 years for a polyp containing cancer; 1 year for neoplasia with high-grade dysplasia; 5 years for advanced neoplasia; 9 years for nonadvanced neoplasia sized 5 to 9 mm; and 14 years for nonadvanced neoplasia smaller than 5 mm.

Progression to Colorectal Cancer. In sensitivity analysis, we included an inevitable progression scenario, whereby all neoplastic lesions would inevitably progress to CRC if allowed enough time. We also included a limited progression scenario, whereby 5% of adenomas smaller than 5 mm in size, 33% of adenomas sized 5 to 9 mm, 67% of advanced neoplasia, and 100% of high-grade dysplastic lesions would progress to CRC. We applied these different progression scenarios to short, base case, and long polyp lag times.

RESULTS

Participants

A total of 1244 participants were included. The 50- to 54-year-old group consisted of 488 men and 546 women with a mean age of 51.7 [SD, 1.4] years; the 75- to 79-year-old group had 69 men and 78 women (mean age, 76.8 [SD, 1.4] years); and the group aged 80 years or older had 33 men and 30 women (mean age, 82.0 [SD, 2.1] years). No procedural complications were reported.

Prevalence of Neoplasia

As expected, the prevalence of neoplasia increased with age (TABLE 1). Participants aged 80 years or older had a significantly higher prevalence of advanced neoplasia than the 50- to 54-year-old group (14% vs 3.2%; P<.001). Overall, men had a significantly higher prevalence of neoplasia than women (18.5% vs 13%; P=.008); however, stratifying the data by sex did not result in any changes in our life expectancy outcomes (data not shown). There were 3 cases of CRC, 2 in those aged 50 to 54 years and 1 in those aged

80 years or older. There were also 3 large adenomas with high-grade dysplasia, one in those aged 50 to 54 years and 2 in those aged 80 years or older.

Mean Extension of Life Expectancy

As expected, the baseline mean life expectancy was lower in the 2 older age groups vs the 50- to 54-year-old group. Because of this, despite the higher prevalence of advanced neoplasia in elderly patients, the mean extension of life expectancy was lower in the 2 elderly groups (Table 1). The group aged 80 years or older had a mean extension of life expectancy of only 0.13 years, compared with 0.85 years for the 50- to 54-year-old group, a 6.5-fold difference.

The number of colonoscopies per life-year saved was much lower for the 50- to 54-year-old group than for the 2 older groups (1.18 vs 5.77 and 7.95, respectively).

The adjusted mean extension of life expectancy was also lower in the 2 elderly groups, although the difference was less pronounced (Table 1). The 2 elderly groups had an adjusted mean extension of life expectancy of 1.6% to 1.7% compared with 2.9% for the 50- to 54-year-old group.

Patients Who Benefited From Screening Colonoscopy

TABLE 2 shows that because of the lower prevalence of advanced neoplasia, in the base case the percentage of patients who benefited from screening colonoscopy in the 50- to 54-year-old group was lower than that for the 2 older groups (6% vs 12.2% and 15.9%, respectively).

Multiway Sensitivity Analysis

Polyp Lag Time. As expected, longer polyp lag times lead to a decrease in the mean extension in life expectancy across all groups (Table 2). This phenomenon is more pronounced in older patient groups; in other words, longer lag times favor screening in younger patients more than very elderly patients because the latter are much more likely to die of “natural” causes before an adenoma turns into cancer, thus negat-

ing any potential benefits of colonoscopy and polypectomy.

Progression to CRC. If it is assumed that there is inevitable progression from adenomas to CRC, then compared with the base case, the mean extension in life expectancy is increased in all groups. Inevitable progression leads to larger increases in life

expectancy extension in younger patients than older patients because the polyp lag time will always be shorter than the baseline life expectancy in younger patients, a fact that is not always true in very elderly patients. Conversely, if progression to CRC is very unlikely (the limited progression scenario), then the mean extension in

Table 2. Sensitivity Analysis Outcomes for 1244 Individuals Who Underwent Screening Colonoscopy, January 2002 to January 2005

Progression of Polyp to Colorectal Cancer by Polyp Lag Time	Age Group, y*		
	50-54 (n = 1034)	75-79 (n = 147)	≥80 (n = 63)
LE_{extension}, Mean, y†			
Inevitable			
Short	2.09	0.41	0.23
Base	1.84	0.32	0.18
Long	1.35	0.10	0.09
Base			
Short	0.94	0.21	0.15
Base	0.85	0.17	0.13
Long	0.66	0.08	0.07
Limited			
Short	0.62	0.15	0.11
Base	0.57	0.12	0.10
Long	0.47	0.06	0.06
Patients Benefiting, %			
Inevitable			
Short	13.6	26.5	27.0
Base	13.6	26.5	22.2
Long	13.6	12.9	12.7
Base			
Short	6.0	12.2	17.5
Base	6.0	12.2	15.9
Long	6.0	9.5	11.1
Limited			
Short	3.9	8.2	12.6
Base	3.9	8.2	12.6
Long	3.9	6.8	9.5
No. of Colonoscopies per Life-Year Saved‡			
Inevitable			
Short	0.48	2.41	4.29
Base	0.54	3.10	5.64
Long	0.74	10.6	11.6
Base			
Short	1.07	4.70	6.64
Base	1.18	5.77	7.95
Long	1.51	12.9	13.4
Limited			
Short	1.60	6.65	9.46
Base	1.74	8.08	10.5
Long	2.11	17.3	15.8

*Mean life expectancies were as follows: age 50 to 54 years, 28.87 years; age 75-79 years, 10.37 years; and 80 years or older, 7.59 years.

†Extension of life expectancy due to screening colonoscopy (LE_{extension}) was calculated as LE_{removed} - (Y_{Lag} + LE_{CRC}).

‡Number of screening colonoscopies per life-year saved was calculated as total number of colonoscopies/total number of life-years gained.

life expectancy is decreased in all groups. This phenomenon is more pronounced in younger patients because small adenomas that develop into CRC always cause a mean extension in life expectancy in younger patients, whereas they do not always cause a mean extension in life expectancy in older patients, who are much more likely to die of “natural” causes before the polyp turns into cancer. Thus, changing the probability of small adenomas turning into cancer has a disproportionate impact on younger patients.

The difference in extension in life expectancy between participants aged 50 to 54 years and those aged 80 years or older can range from a 5.6-fold to a 15-fold difference (using the least and most favorable assumptions for polyp lag time and polyp progression probability).

COMMENT

Currently, CRC screening is recommended for all patients aged 50 years or older¹¹; colonoscopy is advocated as a “preferred” screening method by some groups.¹² However, as physicians consider screening in elderly patients, they have to consider whether the morbidity, risk, and cost of screening colonoscopy can be justified by the declining potential benefits that occur with increasing age. Screening for many other types of cancer, such as breast cancer, focuses on identifying early-stage cancers. In contrast, colonoscopic screening derives much of its benefit from the identification and removal of precancerous lesions, thus preventing CRC. Because the main target of colonoscopic screening is the adenoma, the lag time before this precancerous lesion can develop into cancer and cause death is unusually long. This feature suggests that the potential benefit of colonoscopic screening in very elderly patients may be smaller than what can be expected for other types of cancer screening because elderly patients are more likely to die of “natural” causes before the adenoma develops into cancer. Currently, very elderly patients and their physicians are using individual

judgment to decide whether to undergo screening. These decisions are based on scant data regarding the impact of screening colonoscopy on life expectancy. The results reported here show that even though the prevalence of colonic neoplasia increases with age, screening colonoscopy in very elderly patients results in only 15% of the expected gain in life expectancy achieved in younger patients. However, it is not the purpose of this study to establish any firm cutoff age beyond which screening should not be recommended or offered.

Previous studies of colonoscopy in symptomatic and asymptomatic elderly patients have consistently shown a high prevalence of colorectal neoplasia.^{2,4,13,14} However, cecal intubation rates are lower,^{2,3,14} procedure times are longer,⁴ perforation risks are higher,⁶ and suboptimal bowel preparation is more likely in very elderly patients.^{3,5} Most of the studies included substantial numbers of patients with symptoms, such as abdominal pain, changes in bowel habits,¹³ or gastrointestinal tract bleeding.^{2-5,14-17} Most previous controlled studies have not reported an increase in complication rates with age.^{2,15,17} However, because colonoscopic complication rates are very low (about 0.1%-0.5%),¹⁸ even if there were a 5-fold increase in complication rates in elderly vs younger patients, one would need a sample size of more than 5000 to demonstrate a statistically significant difference (with a statistical power of 80%). Thus, most previous studies were underpowered to detect differences in complication rates because most included fewer than 1000 participants. Nevertheless, 1 large study was able to demonstrate a higher risk of perforation in elderly patients.⁶

To assess the impact of screening colonoscopy on life expectancy, a randomized trial or longitudinal observational study that follows every screened participant until death would be ideal, but this would require a 30- to 40-year follow-up period, making such a study impractical. The only available research on this topic have been model-

ing studies using decision analysis. One study used the DEALE technique to assess the impact of colonoscopic screening on the entire 50- to 74-year-old US population.¹⁹ The model evaluated the relationship between age and extension of life expectancy but did not focus on very elderly patients. It concluded that colonoscopic screening would lead to a 170-day extension in life expectancy for patients aged 50 to 54 years vs a 41-day extension in those aged 70 to 74 years; this was mainly due to the fact that CRC caused a much smaller reduction in life expectancy in the older group than in the younger group (70 vs 292 days). Another modeling study estimated the risks and benefits of screening colonoscopy in elderly patients²⁰ and found that the number needed to screen to prevent 1 CRC death was 227 for 80- to 84-year-old men and 140 for 80- to 84-year-old women, compared with 61 to 63 in 50- to 54-year-old controls. Men aged 85 years or older and women aged 90 years or older would not benefit from CRC screening at all, while in several patient subgroups the risk of a colonoscopy-related complication was higher than the probability of preventing CRC death. This study did not attempt to assess extension in life expectancy as an end point. Other groups have used microsimulation models to assess the cost-effectiveness of CRC screening using sigmoidoscopy. However, these models focused on cost-effectiveness rather than life expectancy and did not explicitly target screening colonoscopy in elderly patients.^{21,22}

Our study extends the findings of this prior work by using a novel and more individualized method to estimate gains in life expectancy. Instead of trying to model large hypothetical populations, we measured the prevalence of precancerous lesions in 3 groups of patients of different ages and estimated the extension in life expectancy on an individual level. Because we estimated gains in life expectancy from cross-sectional data, this necessarily involved making predictions about what

happens to patients in the future. To estimate life expectancy gains, we compared the life expectancy of each screened patient with the life expectancy of that same patient if he or she had not been screened, then averaged the gains for each of the 3 age groups. While the life expectancy of patients without colon neoplasia can be obtained directly from US life tables, the life expectancy of patients with a known precancerous lesion was calculated by summing life expectancies during the polyp lag time and after CRC diagnosis. Compared with traditional decision analysis, our method requires fewer assumptions. Traditional decision analysis requires making assumptions about the prevalence and distribution of lesions in a hypothetical screened cohort at a certain point in time, as well as assumptions about the natural history of lesions and prognosis of patients over time. Often, such models resort to using a homogeneous hypothetical cohort of patients of the same age, a percentage of whom are assumed to develop lesions. Furthermore, the benefit from screening colonoscopy is assumed to be a fixed proportional reduction in the baseline CRC mortality rate. For screening colonoscopy, the value of this mortality reduction is based on 1 case-control study on colonoscopy,²³ with supporting evidence from 2 case-control studies on sigmoidoscopy,^{24,25} and is assumed to be the same in older and younger patients. Our method is based on a real-life screening population, giving us actual data on the age, sex, and colonoscopic findings of each individual patient. Our assumptions involve only the natural history of lesions and prognosis of patients over time, and we explicitly take into account differences in CRC mortality reduction from screening in younger vs older patients because older patients are much more likely to die of "natural" causes before an adenoma turns into cancer, thus negating any potential benefits of colonoscopy and polypectomy.

Because there is uncertainty regarding some of our assumptions, we performed extensive sensitivity analysis.

One of the main uncertainties concerns the duration of the polyp lag time, defined as the interval between discovery of an adenomatous polyp and development of CRC if the polyp were left alone; this is assumed to be somewhat shorter than the length of the polyp dwell time, defined as the interval between the development of an adenomatous polyp and the development of CRC. Our knowledge of the natural history of adenomas is mostly based on indirect evidence^{7,26} because adenomas are generally removed at the time of discovery. Some studies have tried to estimate polyp progression rates by comparing differences in the mean ages of patients with adenomas vs those with CRC. For example, the National Polyp Study found that the mean age of patients with adenomas was 7 years younger than that of patients with CRC,²⁷ while an analogous Japanese study concluded that it took up to 11 years for a small adenoma to become cancer.²⁸ Other studies have used mathematical models, based on case cohort data, to estimate polyp dwell times of 7.75 years for small adenomas (6-10 mm) and 5.27 years for large adenomas (>1 cm).²⁹ Tumor volumetric doubling time studies have suggested that it takes 2 to 3 years for adenomas smaller than 5 mm to grow to larger than 1 cm, and 2 to 5 years for a 1-cm polyp to become cancer.^{30,31} Finally, a few older studies have followed small adenomas left in place for up to 3 years using serial barium studies or endoscopy; in general, they have found that polyp growth and progression was slow,^{32,33} and the risk of CRC development was only 2.5%, 8%, and 24% at 5, 10, and 20 years, respectively.³⁴ Life expectancy is also affected by the fact that adenomas may not always progress to CRC, even if given unlimited time. In our base case, we have assumed that only a random proportion of adenomas will progress to CRC. There is evidence to suggest that small adenomas are not associated with any increased risk of subsequent CRC¹⁰ and that some small adenomas remain stable or even regress.^{35,36} Conversely, other studies

have shown premalignant changes at the cellular level even in very small adenomas.³⁷ Because of these uncertainties, we have performed extensive sensitivity analysis, using wide ranges for polyp lag times and risks for progression to CRC (ranging from inevitable progression to limited progression).

Reliable data on life expectancy after CRC diagnosis for the general US population are not currently available. However, the SEER database provides detailed age-specific mean 5-year survival data after CRC diagnosis, taking into account the distribution of stages at which CRC is diagnosed and the impact of cancer treatment. Using the DEALE principle, we can estimate life expectancy using survival data. The DEALE principle has been validated by comparing its results with those of more sophisticated survival analyses using the Gompertz law.⁸ This showed that the DEALE principle underestimates absolute life expectancy by only a small amount; it is especially accurate in the setting of older patients and high disease-specific mortality. For example, the discrepancy was only about 0.3 years in 60-year-old patients who had a disease associated with a 15% excess annual mortality. More importantly (with respect to our study), it has been shown to accurately estimate the difference in life expectancy gains between competing interventions or different patient populations.³⁸ In fact, modeling studies have shown that basing intervention decisions on the DEALE method vs the Gompertz method leads to discrepancies only 0.2% of the time (consisting of extreme scenarios).⁸

Several other assumptions in our methods require discussion. First, for patients found to have CRC on screening colonoscopy, screening can detect cancer at an earlier stage (ie, a stage shift) and, thus, result in better prognosis. Three pivotal fecal occult blood test trials give a rough estimate of the CRC mortality reduction due to this stage-shift effect.³⁹⁻⁴¹ All 3 studies showed a stage shift in the distribution of diagnosed CRC, while none demonstrated a reduction in CRC in-

cidence within the study time frames. Thus, their reported annual CRC mortality rate reductions of 15% to 33% are mostly due to the stage-shift effect and not prevention of CRC. We have taken the weighted mean CRC mortality reduction in the 3 trials and applied it our study to reflect the stage-shift effect. Patients with precancerous lesions who are assumed to develop CRC in the future will not be affected by the stage-shift effect.

Second, we assumed that $LE_{no\ neoplasia}$ equaled $LE_{removed}$. However, $LE_{no\ neoplasia}$ is not completely equivalent to $LE_{removed}$ because there is a higher risk of metachronous neoplasia in patients who have had neoplastic lesions removed on colonoscopy. Currently, there are almost no available data on life expectancy differences between persons with colorectal neoplasias that are removed and demographically matched controls with no neoplasia. We assumed that the increased risk of metachronous neoplasia in someone with removed neoplasia would be negated by more frequent surveillance colonoscopies in the future. This assumption is supported by data showing that subsequent CRC incidence is not increased in patients who had colonic neoplasia removed compared with matched controls.⁴²

Third, we did not include patients aged 55 to 74 years in our study because of space limitations. We selected 50- to 54-year-old patients as the control group because they represent the youngest age at which CRC screening is recommended for average-risk individuals. We felt that this control group would provide the greatest contrast compared with very elderly patients and that by comparing the extremes of the age spectrum in the screened population, we could best illustrate the impact of age on estimated gain in life expectancy for colonoscopic screening.

Fourth, the SEER data that we used reflect treatment advances only up to 2000. However, the impact is likely to be small because new treatments introduced since 2000 have been approved only for patients with advanced CRC and

result in only a modest extension in life expectancy. The methods that we used also take into account competing mortality because life expectancy values from US life tables incorporate the effects of competing mortality.

Fifth, even though the sizes of our 2 elderly patient groups were small, our study was still able to demonstrate statistically significant differences in neoplasia prevalence, as well as life expectancies, between the 2 elderly groups and the control group. Thus, for the purpose of answering our study question on life expectancy, our study was adequately powered. However, demonstrating differences in complication rates between very elderly and younger patients was not the purpose of our study, and our study was inadequately powered to demonstrate such differences.

Finally, we did not address quality-of-life reductions due to CRC or its treatment, morbidity of colonoscopy, and polyp miss rates during colonoscopy. We chose not to address these issues because there is no evidence that they affect younger and older patients to different degrees⁴³⁻⁴⁵; therefore, they should not markedly affect the differences in life expectancy gain among the 3 age groups. We felt that we could simplify our calculations without detracting from the validity of our results.

In conclusion, even though the prevalence of colonic neoplasia increases with age, screening colonoscopy in very elderly patients results in smaller gains in life expectancy compared with younger patients, even when adjusted for life expectancy. Depending on the assumptions made, the difference can be as much as 15-fold. These data suggest that the benefit of screening colonoscopy in very elderly patients may be smaller than what is commonly believed. This should help individual patients and clinicians decide whether screening colonoscopy should be performed and help avoid its use in patients who are unlikely to benefit substantively.

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Study concept and design: Lin, Rabeneck.

Acquisition of data: Lin.

Analysis and interpretation of data: Lin, Kozarek, Schembre, Ayub, Gluck, Drennan, Soon, Rabeneck.

Drafting of the manuscript: Lin.

Critical revision of the manuscript for important intellectual content: Kozarek, Schembre, Ayub, Gluck, Drennan, Soon, Rabeneck.

Statistical analysis: Lin, Kozarek, Soon.

Study supervision: Kozarek, Schembre, Ayub, Rabeneck.

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The supreme end of education is expert discernment in all things—the power to tell the good from the bad, the genuine from the counterfeit, and to prefer the good and the genuine to the bad and the counterfeit.
—Samuel Johnson (1709-1784)