
Colorectal Cancer Screening

Health Impact and Cost Effectiveness

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Background: Colorectal cancer is the second leading cause of cancer-related death in the United States, yet recommended screenings are not delivered to most people. This assessment of colorectal cancer screening's value to the U.S. population is part of the update to a 2001 ranking of recommended clinical preventive services found in the accompanying article. This article describes the burden of disease prevented and cost-effectiveness as a result of offering patients a choice of colorectal cancer screening tools.

Methods: Methods used were designed to ensure consistent estimates across many services and are described in more detail in the companion articles. In a secondary analysis, the authors also estimated the impact of increasing offers for colorectal cancer screening above current levels among the current cross-section of adults aged 50 and older.

Results: If a birth cohort of 4 million were offered screening at recommended intervals, 31,500 deaths would be prevented and 338,000 years of life would be gained over the lifetime of the birth cohort. In the current cross-section of people aged 50 and older, 18,800 deaths could be prevented each year by offering all people in this group screening at recommended intervals. Only 58% of these deaths are currently being prevented. In year 2000 dollars, the cost effectiveness of offering patients aged 50 and older a choice of colorectal cancer screening options is \$11,900 per year of life gained.

Conclusions: Colorectal cancer screening is a high-impact, cost-effective service used by less than half of persons aged 50 and older.

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Introduction

Colorectal cancer (CRC) is the second leading cause of cancer death in the United States.¹ An estimated 56,290 CRC deaths occurred in 2005.¹ The U.S. Preventive Services Task Force (USPSTF) recommends that clinicians screen men and women aged 50 years and older for CRC.² The USPSTF found good direct evidence for the effectiveness of fecal occult blood testing (FOBT), fair direct evidence for the effectiveness of sigmoidoscopy, and indirect evidence for the combined use of FOBT and sigmoidoscopy, colonoscopy alone, and double barium enema.

The majority of people at risk of CRC are not being screened.³ Although more than half of adults aged 50 and older in the United States have ever received a colorectal test, only 35% received tests for screening purposes at recommended intervals.⁴ Noncompliance with clinician recommendations to receive screening do not account entirely for the shortfall. About 25% of

adults aged 50 and older do not recall a physician recommending a CRC screening test.^{5,6}

This assessment of the health impact and cost effectiveness of CRC screening and the accompanying articles are part of the update to Partnership for Prevention's 2001 ranking of 30 clinical preventive services recommended by the USPSTF.⁷ The National Commission on Prevention Priorities (NCPP) guided the development of the updated ranking. The NCPP chose to prioritize services based on the same criteria used previously: (1) clinically preventable burden (CPB) as a measure of health impact, and (2) cost effectiveness.

This article describes new estimates of CPB and cost effectiveness for CRC screening. It also provides an estimate of the potential impact of increasing screening rates among the current cross-section of adults aged 50 and older.

Colorectal cancer screening was among the eight highest-ranking services with the lowest delivery rates identified in the 2001 ranking. However, the estimates for CRC screening in the 2001 ranking were limited to the impact of FOBT and flexible sigmoidoscopy screening due to limited use and data availability for other screening options. Increasing use of colonoscopy for screening purposes and improved data availability have

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made it necessary and possible to update these estimates to include colonoscopy.

The cost-effectiveness literature on CRC screening focuses on the incremental value of one service relative to others in order to inform decisions regarding which screening test is best. The USPSTF recommended that patients be offered a choice of screening strategies. The cost-effectiveness estimate presented here focuses on the average value of offering patients a choice of CRC screening tools rather than the incremental value of each screening tool relative to the others. Also, two methods were used to derive consistent cost-effectiveness estimates across the 25 services and groups of services included in the updated ranking of clinical preventive services presented in the companion article.⁸ This article provides an example of the second, less-common method—adjustment to the results of an existing, high-quality cost-effectiveness study.

Methods

A more detailed description of the study methods appears in the companion article.⁸ The methods were designed primarily to ensure consistency in estimating CPB and cost effectiveness across services that differ substantially from one another, while managing an enormous volume of evidence. This report summarizes key aspects of the methods used to evaluate all services and the methods specific to the evaluation of CRC screening.

Screening Tools and Intervals

Estimates of CPB and cost effectiveness were based on the delivery of FOBT, flexible sigmoidoscopy (“sigmoidoscopy” hereafter), and colonoscopy because the vast majority of screening is currently performed by one of these tests. Since the optimal screening intervals for FOBT, sigmoidoscopy, and colonoscopy were uncertain, estimates were based on intervals most commonly recommended by other organizations for average-risk people aged ≥ 50 years: annual FOBT, sigmoidoscopy every 5 years, or colonoscopy every 10 years.⁹

In addition to these tests, the USPSTF found indirect evidence that FOBT combined with sigmoidoscopy every 5 years and contrast barium enema are also effective screening options. These are excluded from estimates due to lack of data on the extent of their use for screening purposes and their effectiveness. Less than 1% of adults aged ≥ 50 are up-to-date on both FOBT and sigmoidoscopy.⁴ National data are not collected on the use of contrast barium enema. Computed tomography (CT) colography has also been excluded because the USPSTF found insufficient evidence to support its use for screening.

Evidence Gathering

Two sets of standardized search strategies were developed for the overall prioritization study (one for effectiveness and cost-effectiveness data and a second for burden of disease and cost data).⁸ Each strategy included four levels, where Level 1 included the most current literature and data sources, and

each subsequent level extended to less-current sources and sources less likely to yield useful data. For effectiveness and cost-effectiveness literature, Level 1 includes a PubMed search for English-language articles dating from 1992, a search of the Cochrane Collaboration Reviews, and a search of bibliographies for related work back to 1987.⁸

The searches identified 23 articles reporting the effectiveness of CRC screening in preventing CRC mortality.^{10–32} Eight of these studies were excluded either because participants were not compared to a no-screening group^{10,30} or because a more recent article on the same study with longer follow-up was available.^{11,13,15,16,19,32} After this literature was reviewed, modeled estimates of the mortality reduction obtainable with screening from sigmoidoscopy and colonoscopy^{33–35} were added to the evidence base due to the scarcity of direct evidence for these screening tools.

Estimating Clinically Preventable Burden

Clinically preventable burden was defined as the proportion of disease and injury prevented by the service in typical practice if the service were offered to 100% of the target population at recommended intervals. This model for estimating CPB was analogous to a simplified cost-effectiveness model. The results of algebraic calculations performed at base-case (i.e., “best”) estimates of each variable were reported. The details of the algebraic models used to derive CPB are available online in each service’s technical report (prevent.org/ncpp). Although the models differ for each service and are more detailed in practice, conceptually CPB was the product of burden of disease and effectiveness.

For CRC screening, CPB was measured in life years saved (LYS). Adjustments for quality-of-life effects were not included in the base-case estimates due to important data limitations. To gauge the importance of this, hypothetical quality-of-life adjustments were performed in sensitivity analyses as reported below.

Clinically preventable burden was based on the delivery of the service to a 1-year U.S. birth cohort (the size of which is defined consistently in this study as 4 million) over the age range that the service was recommended by the USPSTF. Because all CPB estimates were based on effectiveness in typical practice, patient adherence to offers to accept the service and to follow-up treatment or changes in behavior was considered for every service. The primary distinction that was made between efficacy and effectiveness is adherence,⁸ so that:

$$\% \text{ effectiveness} = \% \text{ adherence} \times \% \text{ efficacy.}$$

Clinically preventable burden was estimated independent of current delivery rates to indicate a service’s total value, rather than the value of improving delivery rates over current levels for the U.S. population, in order to compare services fairly with widely varying current delivery levels.⁸

Table 1 shows the values used to estimate CPB for CRC screening. The “base case” column shows the best available estimate for each variable, and the “range” column shows the range over which the point estimates were varied in this sensitivity analysis.³⁶

Burden of disease. Surveillance, Epidemiology, and End Results (SEER) cancer statistics were used for cancer mortality data. There would be 78,965 CRC deaths among persons

Table 1. Data used in estimating clinically preventable burden

Variable	Base case	Source	Range for sensitivity analysis
Number of life years above age 50 per 4 million birth cohort	112,057,600	Arias (2002) ³⁸	
Weighted average annual risk of colorectal cancer death	0.000810	National Cancer Institute (2003) ³⁷	±20%
Weighted life expectancy at death	10.7	See text	±20%
Delivery rate for any recommended screening in 1992	17.6%	Nadel (2002) ³⁹	15–25%
Percent of screening that was FOBT in 1990s	47.8%	Subramanian (2005) ⁴⁰	30% to 70%
Percent of screening that was sigmoidoscopy in 1990s	19.1%	Subramanian (2005) ⁴⁰	15% to 30%
Percent of screening that was colonoscopy in 1990s	33.1%	Subramanian (2005) ⁴⁰	Calculated: residual of FOBT and sigmoidoscopy
Percent of screening that was FOBT in 2003	48.4%	CDC (2003) ⁴	30% to 70%
Percent of screening that was sigmoidoscopy in 2003	8.7%	CDC (2003) ⁴	5% to 15%
Percent of screening that was colonoscopy in 2003	42.8%	CDC (2003) ⁴	Calculated: residual of FOBT and sigmoidoscopy
Efficacy of FOBT in preventing CRC mortality	38%	Faivre (1999) ¹² , Jorgensen (2002) ¹⁴ , Lamah (2001) ¹⁷ , Lazovich (1995) ¹⁸ , Mandel (1999) ²⁰ , Niv (2002) ²³ , Saito (1995) ²⁴ , Scheitel (1999) ²⁵ , Scholefield (2002) ²⁶ , Selby (1993) ²⁸ , Wahrendorf (1993) ²⁹ , Zappa (1997) ³¹	25% to 60%
Efficacy of sigmoidoscopy in preventing CRC mortality	50%	Muller (1995) ²¹ , Newcomb (1992) ²² , Scheitel (1999) ²⁵ , Selby (1992) ²⁷ , Khandker (2000) ³³ , Vigan (2001) ³⁴ , Song (2004) ³⁵	25% to 75%
Efficacy of colonoscopy in preventing CRC mortality	70%	Muller (1995) ²¹ , Khandker (2000) ³³ , Vigan (2001) ³⁴ , Song (2004) ³⁵	40% to 85%
Weighted efficacy of screening in 1990s	50.8%	Calculated	
Weighted efficacy of screening in 2003	52.6%	Calculated	
Adherence with screening offers	60%	Faivre (1999) ¹² , Hardcastle (1996) ¹³ , Jorgensen (2002) ¹⁴ , Niv (2002) ²³ , Rasmussen (1999) ⁴⁴ , Kewenter (1994) ⁴⁵ , Myers (1993) ⁴⁶ , Hardcastle (1980) ⁴⁷ , Thrasher (2002) ⁴⁸ , Ore (2001) ⁴⁹ , Hart (1998) ⁵⁰ , Grazzini (2000) ⁵¹ , Brevinge (1997) ⁵² , Hart (1997) ⁵³ , Church (2004) ⁵⁴ , Verne (1998) ⁵⁵ , Thiis-Evensen (2001) ⁵⁹ , Bretthauer (2002) ⁶¹ , Blom (2002) ⁶⁵	40% to 75%

CDC, Centers for Disease Control and Prevention; CRC, colorectal cancer; FOBT, fecal occult blood testing.

aged ≥ 50 in a U.S. birth cohort of 4 million individuals given current rates of CRC screening, current CRC mortality rates,³⁸ and current life expectancy.³⁷ Average life expectancy at death was calculated as the weighted average of life expectancy in 5-year age groups from life tables³⁸ and the age of death for CRC.³⁷

Delivery rates. Delivery rates were used to calculate a weighted average of the benefits of FOBT, sigmoidoscopy, and colonoscopy in the calculation of predicted deaths in the absence of screening, which required adjusting currently observed burden for current delivery rates and efficacy of the service.³⁶ Earlier delivery rates were used to determine what

the total mortality attributable to CRC would have been in the absence of screening in 2000 because the largest impact of screening on mortality is realized in the years following screening. Using data reported by Nadel,³⁹ 17.6% of the U.S. population aged ≥ 50 years was up-to-date on recommended screening for CRC in 1992. This estimate was based on the reported use of home FOBT kits for screening purposes in 1992, the reported use of proctoscopy (sigmoidoscopy or colonoscopy) for any purpose in 1992, and the portion of proctoscopy that was performed for screening purposes in 1998, as such data were not available for 1992. Because only the most recent National Health Interview Survey (NHIS)

questions distinguished between sigmoidoscopy and colonoscopy, the relative portion of screening by home FOBT (47.8%), sigmoidoscopy (19.1%), and colonoscopy (33.1%) recently reported by Subramanian et al.⁴⁰ from the 2000 NHIS were used.

To estimate the impact of screening in the future, recent delivery rates were tabulated from the 2003 NHIS survey.⁴ Approximately 35% of the U.S. population aged ≥ 50 years was up-to-date on recommended screening in 2003. Of these, 48.4% were screened by home FOBT, 8.7% by sigmoidoscopy, and 42.8% by colonoscopy.⁴

Effectiveness. The efficacy of a series of FOBT screens was approximated by dividing effectiveness by adherence reported in three randomized controlled trials (RCTs)^{14,20,26} and one quasi-randomized trial.²³ Similar approximations were made using the results of eight case-control studies^{12,17,18,24,25,28,29,31} by assuming that people who had at least one screen were 80% adherent with recommended screening intervals.¹² One estimate was excluded because it was based predominately on office sample collection rather than home kits.²² This produced a range of efficacy for FOBT of 13% to 60%. The base-case estimate was the mean of this range (38%). The calculation included estimates of annual screening, biennial screening, and screening of undefined intervals. One RCT compared annual with biennial screening and found the annual screening to be more effective.²⁰ However, little difference was found between these screening frequencies in the larger body of evidence in this review. The subgroup means were 37%, 40%, and 36% for annual, biennial, and undefined frequency, respectively. Therefore, all studies were included in calculating the mean efficacy of FOBT.

The evidence base for quantifying the effectiveness of sigmoidoscopy was comparatively scarce. Four case-control studies^{21,22,25,27} yielded estimates of 5%, 11%, 35%, and 79% reductions in all CRC mortality (from proximal and distal cancers) with the use of sigmoidoscopy for screening purposes. The lowest estimates (5% and 11%) were based on odds ratios that were not statistically different from zero. Due to the nature of retrospective case-control studies, the use of sigmoidoscopy is defined as having at least one screen. These case-control studies provided reasonable estimates of efficacy, because false negatives are less common compared to FOBT, and therefore previous missed screening opportunities would not greatly affect the estimate of efficacy.

Due to the small number and wide range of these four estimates, modeled estimates were also considered for which the efficacy of screening was determined from the incidence of polyps, probabilities of cancers developing from polyps and independently of polyps, the sensitivity of screening in detecting polyps and cancers, and survival rates at various stages of treatment. Three cost-effectiveness studies have estimated reductions in deaths with the use of sigmoidoscopy every 5 years of 53%,³⁴ 66%,³⁵ and 68%,³³ assuming 100% compliance.

Among both case-control studies and modeled estimates, reductions in CRC mortality were 5%, 11%, 35%, 53%, 66%, 68%, and 77%, with a mean and median of 45% and 53%, respectively. It is difficult to define a base-case estimate for the effectiveness of sigmoidoscopy because this range is wide, there is no obvious cluster of estimates within the range, and

each estimate has moderate limitations. A base-case estimate of 50% efficacy of sigmoidoscopy in preventing CRC deaths was assigned. Data from case-control studies that did not report mortality outcomes⁴¹⁻⁴³ indicate that similar reductions in cancer cases can be expected when using odds ratios to approximate relative risk and assuming that 55% of cancers are distal.

The base-case estimate of 50% seems to imply nearly 100% efficacy in the prevention of mortality from cancers within reach of the sigmoidoscope. However, efficacy of 50% and higher is feasible because follow-up colonoscopy detects and treats polyps outside the reach of the sigmoidoscope. Both Selby et al.²⁷ and Newcomb et al.²² report non-statistically significant reductions in mortality from cancers outside the reach of the sigmoidoscope.

Only one observational estimate—and no controlled trials—of the efficacy of colonoscopy in preventing mortality was identified. In a case-control study among Veterans Administration (VA) patients, Muller and Sonnenberg²¹ reported adjusted odds ratios of 0.45 for CRC death associated with the use of colonoscopy without tissue removal as the most recent colorectal procedure. The results imply an effectiveness of 55% in reducing CRC mortality. As noted by the authors, incomplete data capture outside the VA system and the categorization of patients by most recent type of endoscopic procedure are limitations of both the mortality and case-reduction estimates from these reports.^{21,41} As with sigmoidoscopy, modeled estimates were considered, due to the scarcity of direct estimates. The same cost-effectiveness studies that reported modeled estimates of the efficacy of sigmoidoscopy screening reported 68%,³⁴ 78%,³⁵ and 90%³³ reductions in mortality with screening by colonoscopy in 10-year intervals with 100% compliance.

The overall mean and median of the four estimates for reductions in CRC deaths from the single case-control study and three modeled estimates were 73% and 74%, respectively. Because there was only one direct estimate, these summary measures were heavily influenced by the three modeled estimates. A base-case estimate of 70% was assigned. Because colonoscopy views approximately 85% of the colon, this estimate implied that colonoscopy screening is roughly 83% effective in preventing deaths from cancers within reach of colonoscopy.

An overall efficacy of screening was estimated by calculating a weighted average of the efficacy of FOBT, sigmoidoscopy, and colonoscopy, where the weights correspond to the approximate portion of each screening tool used in practice. This was calculated twice: once for efficacy in the 1990s to estimate the number of mortalities that would have occurred in the absence of screening, and again for 2003 to estimate the current efficacy of screening.

Patient adherence. The intention-to-treat effectiveness estimates from the randomized trials were unlikely to reflect adherence with invitations for screening in typical practice. In case-control studies, effectiveness estimates reflected the odds of CRC death with or without at least one screen, and thus did not fully reflect nonadherence. Therefore, to estimate the effectiveness of offering screening in typical practice, the efficacy estimates summarized above were multiplied by adherence.

Sixteen studies^{12–14,23,44–55} identified in the literature review provided estimates of adherence with offers for FOBT screening among unselected populations. Most were from outside the United States, where attitudes toward screening may be different, reported adherence with one screen rather than a series of screens, and reported adherence with offers to screen that were sent by mail rather than offers made in a clinical setting. The vast majority of these mailed invitations included an FOBT kit, and nonresponders usually received reminder calls. The mean adherence and median adherence to these offers were 50% and 47%, respectively. The minimum and maximum values for these estimates were 20% and 75%, where the highest estimates reflect the probability of getting at least one screen after three or four opportunities.

Sixteen estimates of adherence with sigmoidoscopy were identified,^{30,44,52,55–67} six of them among unselected populations.^{44,52,55,59,61,65} As with FOBT screening, a large portion (three of six) were from other countries, and they reported adherence with a mailed invitation for a single screen. The mean and median adherence levels were 54% and 46%, respectively, and the minimum and maximum values for these estimates were 39% and 81%, respectively.

One recent estimate of adherence with referrals for colonoscopy in an unselected population found that 50% of individuals completed screening.⁶⁸ Three studies in selected populations (high risk, consented to randomization, or scheduled an initial screen) reported acceptance of screening at >60%.^{66,67,69}

This evidence suggests that average adherence with either FOBT or sigmoidoscopy is about 50%. Offering more than one test may increase acceptance of screening because those who reject one type of screening may accept an alternative.⁷⁰ The literature showed some evidence of this,^{52–54} but provided insufficient data to accurately quantify the incremental increase in adherence over offering a single type of screening.^{44,55} Church et al.⁵⁴ reported 72% utilization of any screening following mailings of home FOBT kits and information on other screening options for those at increased risk. However, the offers for screening were not initiated in a clinic, and the study was conducted in a single county within a state (Minnesota) with very high CRC screening rates.^{3,71} Based primarily on 50% acceptance of an offer for a particular type of screening, a base-case estimate of 60% was assigned for the national average acceptance of offers among a choice of screening alternatives, and a range of 40% to 75% was used in sensitivity analysis. Only two estimates of adherence with repeated offers for screening in unselected populations were identified.^{12,13} When compared to the body of evidence on adherence with a single screen, it was not possible to conclude that adherence with repeated offers is substantially different. Therefore, the base-case adherence was assumed to be equally applicable to one-time and repeated screening. Additional data on adherence with repeated screening might have led to a different conclusion.

Estimating Cost Effectiveness

Cost effectiveness was measured as the net cost of the preventive service divided by the number of quality-adjusted life years (QALYs) saved, where net costs are the value of resources used in providing the preventive service plus any follow-up services, minus the resource savings from averted

Table 2. Data used in calculating adjusted CE

	Base case	Range for sensitivity analysis (%)
FOBT		
Discounted days of gained life expectancy	8.0	±25%
Discounted net costs	170	±40%
Original average CE	7,756	
Personal time costs of screening	109	±75%
Sigmoidoscopy		
Discounted days of gained life expectancy	10.7	±25%
Discounted net costs	430	±40%
Original average CE	14,668	
Personal time costs of screening	90	±75%
Colonoscopy		
Discounted days of gained life expectancy	15.6	±25%
Discounted net costs	300	±40%
Original average CE	7,019	
Personal time costs of screening	55	±75%

CE, cost effectiveness; FOBT, fecal occult blood testing.

disease or injury. Thus, the conceptual cost-effectiveness formula was:

$$\text{cost effectiveness} = (\text{costs of prevention} - \text{cost averted}) / \text{QALY saved}$$

The standards recommended for the “reference case” of the Panel on Cost Effectiveness in Health and Medicine (PCEHM)⁷² were followed to produce comparable estimates of cost effectiveness across preventive services in the accompanying ranking. A societal perspective and a 3% discount rate were used for both costs and benefits. The PCEHM recommendation on including the value of patient time losses resulting from illness, injury, and treatment in the societal perspective varies with the source of the quality of life data. In most cases, these disease costs should be excluded; they were excluded from all cost-effectiveness estimates in the ranking to provide consistency. All cost-effectiveness ratios were standardized to year 2000 dollars.

For each service, the cost effectiveness of providing the service as recommended relative to no provision of the service was estimated. Cost-effectiveness estimates from the literature were used when available, and adjustments were made to ensure consistency across services.⁸ For CRC screening, it was not possible to develop an appropriate cost-effectiveness estimate by making minor adjustments to a high-quality published cost-effectiveness study.³⁴ Using a Level-1 search for cost-effectiveness articles,⁸ seven studies^{33–35,70,73–75} were identified and abstracted that estimated the cost per life year saved of FOBT screening, sigmoidoscopy, or colonoscopy screening for a birth cohort of adults aged ≥50 years to ≥80 years. No studies were identified that estimated cost effectiveness using QALYs. As with the CPB estimate, health benefits were measured by life years saved.

Table 2 shows the data points that enter into the calculation of cost effectiveness. The cost-effectiveness estimate was based on a study by Vijan et al.³⁴ that best modeled two potentially important variables: adherence and the costs of

Table 3. CPB for birth cohort of 4 million

Colorectal cancer deaths with current screening practices	90,785
Predicted deaths in the absence of screening	99,668
Weighted effectiveness of FOBT, sigmoidoscopy, and colonoscopy	31.6%
Deaths prevented	31,481
Life years saved (CPB)	337,556

CPB, clinically preventable burden.

screening. The costs of screening tools used by Vijan et al.³⁴ were carefully chosen and were near the mean of the costs used in the seven abstracted studies noted above. After adjustment to year 2000 dollars, the procedure costs used in Vijan et al.³⁴ were \$18, \$234, \$250, \$572, and \$796, for FOBT, sigmoidoscopy, sigmoidoscopy with biopsy, colonoscopy, and colonoscopy with tissue removal, respectively. Vijan et al.³⁴ presented estimates with varying levels of hypothetical adherence. They did model the 60% adherence level that was assigned based on the literature review. Therefore, the adjusted cost-effectiveness ratios were based on their estimates with 75% adherence. Based on the varying levels of adherence reported by Vijan et al.,³⁴ it was found that changing the level of adherence by 25 percentage points changed the adjusted cost-effectiveness ratio by <\$1000/QALY.

The net costs from Vijan et al.³⁴ shown in Table 2 included the costs of screening and follow-up and cost offsets from early treatment. To make the estimate consistent with the PCEHM reference case, net costs were adjusted to reflect the cost of patient time for screening and follow-up. For this portion of costs, the more detailed results on the frequency of follow-up diagnostics provided by Sonnenberg et al.⁷⁴ were used. They reported estimates of the number of screening and follow-up diagnostic and therapeutic procedures per 100,000 screened. These rates were reduced to account for incomplete adherence. For each procedure, average hourly earnings plus benefits in 2000⁷⁶ were used to estimate the value of patient time. For FOBT, 30 minutes of patient time were assigned to discussing screening and using the home kit. For sigmoidoscopy and colonoscopy, 2 hours of preparation, travel, and visit time for a visit devoted to the procedure were assumed. From these data and assumptions, the lifetime value of patient time spent for screening and follow-up was estimated to be \$109, \$90, and \$55 per targeted individual for annual FOBT, 5-year sigmoidoscopy, and 10-year colonoscopy, respectively (where the estimates are expressed in year 2000 dollars and discounted to the present value at the first year of screening). These time costs were added to the per-person net costs reported for each type of screening by Vijan et al.³⁴ Adjusted cost-effectiveness ratios were then calculated as average per person net costs divided by average gains in life expectancy (also from Vijan et al.³⁴).

Results

Clinically Preventable Burden

Table 3 shows the results of the CPB calculation. Given current screening practices, there would be 90,800 deaths from CRC among persons aged ≥ 50 in a birth cohort of 4 million individuals. In the absence of

screening, there would be about 99,700 deaths from CRC in the same population. About 32% of these 99,700 deaths (31,500 deaths) could be prevented if screening were offered to 100% of the target population. With an average life expectancy at death of 10.7 years, CPB is estimated to be 338,000 life years saved.

Table 4 shows the potential increment in prevented deaths by improving delivery rates. These estimates are presented for the birth cohort of 4 million and, from the secondary analysis, for the current cross-section of individuals aged ≥ 50 . For the cross-section of 72.6 million adults aged 50 to 84 in 2000, some 31,300 deaths could be prevented each year if all eligible individuals were offered screening at recommended intervals and all individuals accepted screening (with 48%, 9%, and 43% choosing FOBT, sigmoidoscopy, and colonoscopy, respectively). Given current delivery rates and adherence, only 10,900 of the 31,300 clinically preventable deaths (35%) are being prevented. If screening were offered to the entire population, while adherence remained at the estimated rate of 60%, 18,800 deaths would be prevented, an increment of 7900. Only 58% of these 18,800 deaths are currently being prevented. The final column of Table 4 indicates how these missed opportunities will increase without improvements in screening rates as birth cohorts of 4 million reach the ages of high risk.

Cost Effectiveness

Table 5 shows the results of the calculation of adjusted average cost-effectiveness ratios based on the work of Vijan et al.³⁴ Readers interested in the incremental analysis of the various screening tools, costs, and effectiveness are referred to their original work. The net costs and cost-effectiveness ratios reported by Vijan et al.³⁴ increase by 7.7% when adjusted to year 2000 dollars. The cost of time to receive screening and follow-up services adds approximately \$5000 per life year saved (\$/LYS) to the cost effectiveness of annual FOBT screening, \$4000/LYS to that of 5-year sigmoidoscopy screening, and \$1300/LYS to that of colonoscopy. This additional cost increased the cost-effectiveness ratios to \$13,300/LYS, \$18,900/LYS, and \$8800/LYS,

Table 4. Deaths currently and potentially prevented

	Today's cross-section	Cohort of 4 million
Total preventable deaths	31,299	52,468
Colorectal cancer deaths prevented at current delivery and adherence rates	10,917	18,301
Preventable deaths if offered to 100% of target population	18,779	31,481
Additional deaths prevented if offered to 100% of target population	7,862	13,180

Table 5. Adjusted cost-effectiveness ratio

	FOBT	Sigmoidoscopy	Colonoscopy	Weighted average
Discounted net costs adjusted to year 2000 dollars	183	463	323	
Inflation adjusted average cost effectiveness	8,355	15,801	7,561	
Discounted net costs with addition of time costs	292	553	378	
Adjusted cost effectiveness	13,334	18,869	8,840	11,947

FOBT, fecal occult blood testing.

respectively. The base-case estimate of \$11,900/LYS is a weighted average of these three estimates, where the weights reflect the current relative delivery of FOBT (48%), sigmoidoscopy (9%), and colonoscopy (43%) in 2003.

Sensitivity Analysis

In single-variable sensitivity analysis, CPB was most sensitive to the number of deaths attributable to CRC, life expectancy at death, efficacy of colonoscopy in preventing deaths, and adherence with screening. Following these methods for sensitivity analysis,³⁶ three of these variables were changed simultaneously in the same direction to produce lower and upper CPB estimates of 134,000 and 623,000 LYS. If all other preventive services in the accompanying ranking remained at their base-case CPB estimate, the CPB score of CRC would not change using the lower estimate, and would increase 1 point (from 4 to 5 of 5 possible) if using the higher estimate.

The estimate excluded complications from screening and adjustments for quality of life. Major complications as a result of FOBT or sigmoidoscopy are rare. Data on the frequency of events, quality of life, and duration of impaired or improved quality of life are insufficient to estimate QALYs saved in manner that would clearly improve this estimate of CPB. To gauge the potential impact of excluding quality-of-life adjustments, an estimate was created using readily available estimates of the frequency of events and assumptions on the quality-of-life impact of screening, treatment, and adverse events. It was estimated that these adjustments would increase the CPB estimate by about 2.0% (from 338,000 life years saved to 344,000). The complete underlying calculations are available in the technical report (prevent.org/ncpp), based on the complication rates used by Sonnenberg et al.⁷⁴ The small impact is consistent with this experience, that changes in the quality-of-life assumptions have minimal impact on the CPB estimate when a substantial number of deaths are prevented by the service.³⁶

For cost effectiveness, the range for sensitivity analysis was based on changes in the two most influential “aggregate variables.”³⁶ Using the results of Vijan et al.,³⁴ the impact of independent changes in discounted years of life gained, discounted net costs, the mix of screening tools used in weighting, and an alternative

estimate of adherence with screenings and follow-up (50% rather than the 75% used in the base case) were explored. Adherence and the mix of screening tools were found to be less influential than gains in life expectancy and net costs. Therefore, a range was calculated for cost effectiveness based on simultaneous changes to life expectancy and net costs and obtained \$5700 to \$22,000/LYS. Neither the low nor high estimate would change the cost-effectiveness score of CRC in the accompanying ranking of clinical preventive services.

Cost-effectiveness studies were not consistent in their determination of which screening strategy is the most cost effective.^{77,78} Although Song et al.³⁵ did not model incomplete adherence, they, like Vijan et al.,³⁴ used cost estimates based on a thorough review of available data. While Vijan et al.³⁴ found colonoscopy to be the most cost effective of the three strategies included in this weighted estimate, Song et al.³⁵ found annual FOBT to be the most cost effective. However, when the adjusted, weighted cost-effectiveness ratio was recalculated based on the estimates of Song et al.,³⁵ it changed by only \$200/LYS (\$12,100 based on Song et al.³⁵ compared to \$11,900 based on Vijan et al.³⁴).

Discussion

These updated methods and new evidence produced a small net change in the CPB estimate from the previous effort (338,000 compared to 325,000 LYS) and a small increase in the cost-effectiveness ratio in nominal terms (\$11,900/LYS in year 2000 dollars compared to \$11,800/LYS in 1995 dollars). Colorectal cancer screening continues to be a high-impact, cost-effective service utilized by fewer than half of the group aged 50 and older. It remains an important missed opportunity for improving health at a reasonable cost. Ten thousand additional deaths would be prevented each year if screening were offered to the entire target population, and an additional 12,000 would be prevented if all individuals accepted screening.

Other than the previous study,⁷ there is no direct comparison in the literature for an estimate of CPB. This CPB estimate is based on a weighted estimate of effectiveness of 32%. A 1998 meta-analysis of four RCTs of FOBT reported an effectiveness of 16% in reducing CRC mortality and a 23% reduction in mortality using

a measure conceptually similar to the measure of efficacy (i.e., controlling for nonadherence). The efficacy estimate for FOBT (38%) was based on a different body of evidence, including updated RCT results and case-control studies.^{12-14,17,18,20,24,25,28,29,31} Although higher than the 23% estimate suggested by the earlier meta-analysis of RCTs, this base-case estimate for FOBT is lower than estimates produced by cost-effectiveness models that reported the following percent reductions in mortality: 44%,³⁴ 69%,³⁵ and 80%.³³

This algebraic model of CPB is likely to be less precise than most published cost-effectiveness models of CRC screening. However, we more carefully considered adherence, systematically reviewed and abstracted the literature on effectiveness, and used data on the direct link from screening to CRC mortality reduction. A limitation of this model is that it cannot provide the detailed incremental analysis of various screening options that the advanced cost-effectiveness models provide. The purpose is to provide comparable estimates across a wide range of preventive services, and therefore to produce estimates of their average value compared to no provision of the service. The comparatively simple model of CPB meets this need and the sensitivity analysis showed that the CPB score in the ranking of clinical preventive services is stable over a wide range of CPB estimates.

Six of the seven studies identified in the Level-I search for cost effectiveness reported annual FOBT screening and sigmoidoscopy every 5 years.^{33-35,70,73,75} Each study either reported the cost effectiveness of screening relative to no screening or reported the results in sufficient detail to allow this calculation. The range of base-case estimates in these six studies, adjusted to year 2000 dollars, was \$6300/LYS to \$19,700/LYS for FOBT and \$13,600/LYS to \$36,300/LYS for sigmoidoscopy. All seven studies^{33-35,70,73,75,79} reported or allowed calculation of the cost effectiveness of screening by colonoscopy every 10 years compared to no screening. Adjusted to year 2000 dollars, the range of base-case estimates in these studies was \$7300/LYS to \$22,000/LYS for colonoscopy. By comparison, after adjusting the estimates of Vijan et al.³⁴ to reflect patient costs, and weighting cost-effectiveness ratios for different screening options according to current delivery rates, this base-case estimate is \$11,900/LYS. This provides a single estimate of the cost effectiveness of offering CRC screening for use in making decisions about its relative priority among recommended preventive services.

The secondary analysis on the health consequences of foregone screening in the current U.S. cross-section of all individuals aged 50 and older is limited by the underlying assumption that individuals who are currently being screened are at equal risk for developing CRC as those who are not being screened. Available evidence suggests that CRC screening is associated with

predictors of better health (higher socioeconomic status, use of preventive services, being a never smoker, more physical activity, higher self-reported health status), but also with having a family history of CRC.^{39,79-88} Therefore, those who are currently receiving screening may or may not have a higher or lower risk of CRC on average.

These results demonstrate the impact and value of the current mix of CRC screening and the lives lost as a result of less-than-optimal delivery and adherence to these services. Decisions about where to start improving the delivery of preventive services require comparable information on the value of other clinical preventive services. This may be found in the reports for other services and the accompanying ranking.^{8,89-91}

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