ONLINE FIRST

Long-term Outcomes Following Positive Fecal Occult Blood Test Results in Older Adults

Benefits and Burdens

Christine E. Kistler, MD, MASc; Katharine A. Kirby, MS; Delia Lee, BS; Michele A. Casadei, BS; Louise C. Walter, MD

Background: In the United States, older adults have low rates of follow-up colonoscopy after a positive fecal occult blood test (FOBT) result. The long-term outcomes of these real world practices and their associated benefits and burdens are unknown.

Methods: Longitudinal cohort study of 212 patients 70 years or older with a positive FOBT result at 4 Veteran Affairs (VA) facilities in 2001 and followed up through 2008. We determined the frequency of downstream outcomes during the 7 years of follow-up, including procedures, colonoscopic findings, outcomes of treatment, complications, and mortality based on chart review and national VA and Medicare data. Net burden or benefit from screening and follow-up was determined according to each patient's life expectancy. Life expectancy was classified into 3 categories: best (age, 70-79 years and Charlson-Deyo comorbidity index [CCI], 0), average, and worst (age, 70-84 years and CCI, ≥4 or age, ≥85 years and CCI, ≥1).

Results: Fifty-six percent of patients received follow-up colonoscopy (118 of 212), which found 34 significant adenomas and 6 cancers. Ten percent experienced complications from colonoscopy or cancer treatment (12 of 118). Forty-six percent of those without follow-up colonoscopy died of other causes within 5 years of FOBT (43 of 94), while 3 died of colorectal cancer within 5 years. Eighty-seven percent of patients with worst life expectancy experienced a net burden from screening (26 of 30) as did 70% with average life expectancy (92 of 131) and 65% with best life expectancy (35 of 51) ($P=.048$ for trend).

Conclusions: Over a 7-year period, older adults with best life expectancy were less likely to experience a net burden from current screening and follow-up practices than are those with worst life expectancy. The net burden could be decreased by better targeting FOBT screening and follow-up to healthy older adults.

Arch Intern Med. 2011;171(15):1344-1351.
Published online May 9, 2011.
doi:10.1001/archinternmed.2011.206

Author Affiliations: Department of Family Medicine, University of North Carolina at Chapel Hill (Dr Kistler); Division of Geriatrics, San Francisco Veterans Affairs Medical Center, and University of California, San Francisco (Mss Kirby and Casadei and Dr Walter); and University of Arkansas School of Medicine (Ms Lee).

In many real-world settings, fewer than 60% of patients receive a colonoscopy within 1 year of a positive FOBT result.[1-4] A recent study found that many older patients without follow-up are in poor health or decline follow-up, which suggests that they should not have been screened in the first place.[5] In addition,

See also pages 1332 and 1335

rates of follow-up have shown minimal improvement over the last decade.[3,4,6,7] Despite persistently low rates of follow-up colonoscopy in older adults with positive FOBT results, the long-term outcomes of these real-world screening and follow-up practices have not been described.[3,4,8]

The benefit of finding asymptomatic cancer or precancerous polyps that would have caused symptoms years later must be weighed against immediate burdens of follow-up procedures and treatments stemming from a positive screening result.[9]

See Editor's Note at end of article

Randomized trials of FOBT suggest that a person should have a life expectancy of at least 5 years to derive survival benefit from screening; otherwise they are only subject to the potential burdens.[9,10] We are not aware of any studies of real-world practices that observe older patients for more than 3 years after a positive FOBT result to determine whether patients lived long enough to potentially benefit from detecting large adenomas or early stage colorectal cancer, or whether they only experienced burdens from follow-up procedures

and treatments (eg, false-positive results, repeated testing, complications).[3,4] Such information about the benefits and burdens experienced by older adults with positive FOBT results would help to guide individualized screening and follow-up decisions in clinical practice.

We describe 7-year outcomes following a positive FOBT result in older adults in real-world clinical practice. We took a novel approach of combining VA and Medicare claims and medical chart review to follow the downstream outcomes after a positive FOBT result among patients 70 years or older screened at 4 geographically diverse VA facilities. Downstream outcomes included follow-up testing, polypectomies, cancer diagnoses and treatments, procedural complications, and overall mortality. Net benefit or burden resulting from these screening and follow-up practices was determined according to each patient's predicted life expectancy.[11] The goal was to inform how clinical practice could improve to maximize the net benefit of FOBT screening and follow-up in older adults.

METHODS

DATA SOURCES AND PATIENTS

We conducted a longitudinal cohort study of 212 adults aged 70 years or older who had a positive FOBT result during 2001 at 4 VA facilities (Minneapolis, Minnesota; Durham, North Carolina; Portland, Oregon; and West Los Angeles, California) and observed them for 7 years to determine downstream outcomes. We chose to focus on positive FOBT results as the FOBT is the most common colorectal cancer screening test within the VA.[12] To identify our cohort, we used outpatient claims from the VA National Patient Care Database to identify all patients 70 years or older who had a FOBT between January 1, 2001, and December 31, 2001, at the 4 facilities and met our inclusion and exclusion criteria (n=2410).[5] All patients had continuous enrollment in Medicare Parts A and B and fee-for-service coverage from January 1, 2000, through December 31, 2002. Patients were excluded if they had a history of colorectal cancer or polyps, inflammatory bowel disease, colectomy, or colostomy, or were not due for screening.[5] We used claims from 6 months before their FOBTs and medical chart review to exclude patients with signs or symptoms that would justify performance of FOBT for nonscreening purposes (eg, iron-deficiency anemia, gastrointestinal bleeding, abdominal pain, change in bowel habits, unexplained weight loss).[5] Two hundred twelve of 2410 patients had positive FOBT results (9%), which were extracted from the Veterans Health Information Systems and Technology Architecture (VISTA) laboratory package. If any FOBT cards indicated a positive finding for occult blood, the FOBT result was considered positive.

We used National VA Data Systems as well as inpatient and outpatient Medicare claims through December 31, 2002, to capture follow-up testing within 1 year of a positive FOBT result inside and outside the VA system.[5] Patient age was determined on the date of the FOBT. Comorbidity was measured using the Deyo adaptation of the Charlson Comorbidity Index (CCI), derived from administrative data.[13,14] Charlson-Deyo scores were calculated from VA and Medicare inpatient and outpatient claims during the 12 months before the date of the FOBT. Race and sex were obtained from both VA and Medicare data.

Next, 3 of us (C.E.K., M.A.C., and L.C.W.) reviewed VA medical records to determine the long-term outcomes of screening and follow-up through December 31, 2008. The VA computerized medical records system contains notes from all inpatient and outpatient visits. These notes contain information about follow-up that occurs outside the VA per patient report to their VA clinician.[15]

OUTCOMES OF SCREENING

First, we categorized patients as having received follow-up colonoscopy related to their positive FOBT result or not. Patients who did not receive colonoscopy over the 7 years or had a colonoscopy for gastrointestinal (GI) tract bleeding or other symptoms unrelated to their positive FOBT result were categorized with the "no follow-up colonoscopy" group. Patients with follow-up colonoscopy were categorized according to whether they were diagnosed as having cancer, significant adenoma, or nonsignificant or normal findings. Significant adenoma was defined as 1 or more large adenomas (≥1 cm), 3 or more small adenomas (<1 cm), or any adenoma with villous pathologic characteristics based on standard GI guidelines.[16] Nonsignificant or normal findings included findings of diverticula, fewer than 3 small adenomas (<1 cm), angiodysplasia, hyperplastic polyps, and normal mucosa.

Next, we determined downstream outcomes over 7 years in those with and without follow-up colonoscopy. Outcomes included cancer diagnoses, complications from treatment, frequency of follow-up testing, and 5-year mortality. Cancer diagnoses included cancer stage and treatment. Complications included those documented in the medical chart as being related to colonoscopy or cancer treatment (eg, pain and/or discomfort, gastrointestinal bleeding, infection, death). Frequency of follow-up testing included the number of repeated FOBTs, sigmoidoscopies, barium enemas, and/or colonoscopies patients received during the 7 years. Five-year mortality was determined from the VA Vital Status File.[17]

Next, 2 of us (C.E.K. and L.C.W.) reviewed each patient's outcomes to determine whether they experienced net benefit or net burden from screening and follow-up. Patients were considered to have experienced net benefit if they had a significant adenoma and/or colorectal cancer found on follow-up and lived at least 5 years, even if they had complications or repeated procedures.[18,19] Net benefit or burden was indeterminate for (1) patients with 1 or 2 small adenomas who lived at least 5 years because some clinicians believe that this group potentially benefitted from screening[20-22]; or (2) patients who had a colonoscopy outside of the VA without an available pathology report and lived at least 5 years. All other patients, including those with normal findings on follow-up colonoscopy (ie, false-positive FOBT results), those without follow-up colonoscopy (ie, had a positive FOBT result that was not worked up), and those who died within 5 years of their FOBT (ie, subjected to tests for an asymptomatic disease that would never have affected them), were defined as experiencing net burden. While net burden may be small in some cases (eg, those without follow-up who did not develop cancer), some older adults experience embarrassment and discomfort from performing FOBTs,[23,24] and a positive test result may be anxiety provoking.[25]

STATISTICAL ANALYSIS

To determine downstream outcomes, we observed patients from the date of their positive FOBT result until death or the end of the study period (December 31, 2008). To examine the association between life expectancy and net benefit from screening, we stratified patients into 3 life expectancy subgroups a priori: best—the youngest and healthiest patients (age 70-79 years; CCI, 0) who were expected to live more than 10 years; average—the younger patients with increasing comorbidity and the oldest healthiest patients (age 70-84 years; CCI, 1-3 or age,

Table 1. Characteristics of Patients Aged 70 Years or Older With a Positive FOBT Result

Characteristic	Patients, No. (%) (n=212)
Age, y	
70-74	75 (35.4)
75-79	93 (43.9)
≥80	44 (20.8)
Men	211 (99.5)
Race/ethnicity	
White	180 (84.9)
Black	30 (14.2)
Other	2 (0.9)
Married	145 (68.4)
CCI categories[a]	
0	66 (31.1)
1-3	119 (56.1)
≥4	27 (12.7)
VA site	
A	57 (26.9)
B	119 (56.1)
C	21 (9.9)
D	15 (7.1)
Lived in ZCTA where ≥25% of adults had a college education[b]	56 (26.4)
Undergoing warfarin sodium therapy for anticoagulation	26 (12.3)
History of CRC screening	117 (55.2)
Life expectancy group	
Best (age 70-79 y; CCI, 0)	51 (24.1)
Average (age 70-84 y; CCI, 1-3 or age ≥85 y; CCI, 0)	131 (61.8)
Worst (age >70 y; CCI, ≥4 or age, >85 y; CCI, ≥1)	30 (14.2)

Abbreviation: CCI, Charlson-Deyo comorbidity index; CRC, colorectal cancer; FOBT, fecal occult blood test; LE, life expectancy; VA, Veterans Affairs health care center; ZTCA, zip code tabulation areas

[a] Fewer than 1% of the patients in our cohort had dementia at the time of their FOBT.

[b] The median (range) income of this ZCTA was $22 378 ($9810-$75 050).

≥80 years; CCI, 0) who were expected to live 5 to 10 years; and worst—the sickest and oldest patients (age 70-84 years; CCI, ≥4 or age ≥85 years; CCI, ≥1) who were expected to live less than 5 years.[13] Differences between patients receiving net burden and net benefit were determined according to worsening life expectancy using the Cochran-Armitage χ^2 test for trend. We used SAS software, version 9.1 (SAS Institute, Cary, North Carolina) and and Stata/SE, version 10.0 (StataCorp, College Station, Texas) for all analyses.

The committee on human research at the University of California, San Francisco; the committee for research and development at the San Francisco VA Medical Center; and the institutional review board at the Minneapolis VA Medical Center approved this study.

RESULTS

PARTICIPANT CHARACTERISTICS

The mean age of the 212 patients was 76.4 years (age range, 70-89 years). Consistent with the elderly veteran population, 99.5% were men (211 of 212), and 84.9% were white (180 of 212) (**Table 1**). Sixty-six of 212 patients died within 5 years of their FOBT result (31.1%). Five-year mortality was 5.9% for patients with best life expectancy (3 of 51); 38.2% for patients with average life expectancy (50 of 131), and 46.7% for patients with worst life expectancy (14 of 30), which equates to a life expectancy of 5.4 years.

OUTCOMES OF SCREENING

Patients With Follow-up Colonoscopy

Among the 118 patients who had follow-up colonoscopy over the 7-year period, 6 patients had cancer (5.1%), 34 had significant adenoma (29%), and 70 had neither cancer nor significant adenoma (59%) (**Figure 1**). One patient with a normal colonoscopy finding developed an interval colorectal cancer 5 years later that was successfully treated, but he died a year later of congestive heart failure. Eight patients had colonoscopies outside the VA without an available pathology report, so it is unclear if they had a significant adenoma. No subsequent notes indicated that any of these patients were ever diagnosed as having colorectal cancer. Seventeen percent of these patients died within 5 years of causes other than colorectal cancer (20 of 118). We also assessed complications of follow-up. Ten percent of patients who underwent colonoscopy or cancer treatment experienced complications (12 of 118), as illustrated in Figure 1. Three of the 6 patients with cancer had complications from surgical treatment of their cancer (**Table 2**), although all eventually recovered and survived more than 5 years after their positive FOBT result. Finally, 29% of patients with significant adenomas had 3 or more follow-up tests over the 7 years (10 of 34), compared with 20% of patients with nonsignificant or normal colonoscopy results (14 of 70).

Patients With No Follow-up Colonoscopy

Among the 44.3% of patients who had no follow-up colonoscopy over the 7-year study period (94 of 212) (Figure 1), 6% were eventually diagnosed as having colorectal cancer (6 of 94), of whom 4 died within a few months of treatment (Table 2). A total of 46% of patients who did not get a follow-up colonoscopy died within 5 years of causes other than colorectal cancer (43 of 94). A total of 57% of patients underwent some form of follow-up other than colonoscopy (54 of 94), such as repeat FOBT or sigmoidoscopy, and 59% of those patients had more than 1 follow-up test over the study period (32 of 54) but never a colonoscopy.

Benefits and Burdens

A total of 15.6% of patients were diagnosed as having cancer or significant adenomas on follow-up colonoscopy (33 of 212) and lived at least 5 years and were defined as receiving net benefit (**Table 3**). Since it is controversial whether the 22 patients with nonsignificant adenomas (<1 cm) who lived at least 5 years benefitted from screening, we categorized them as receiving indeterminate benefit, as we categorized the 8 patients for whom we did not have pathology reports from their colonoscopy. The remaining 149 patients were defined as re-

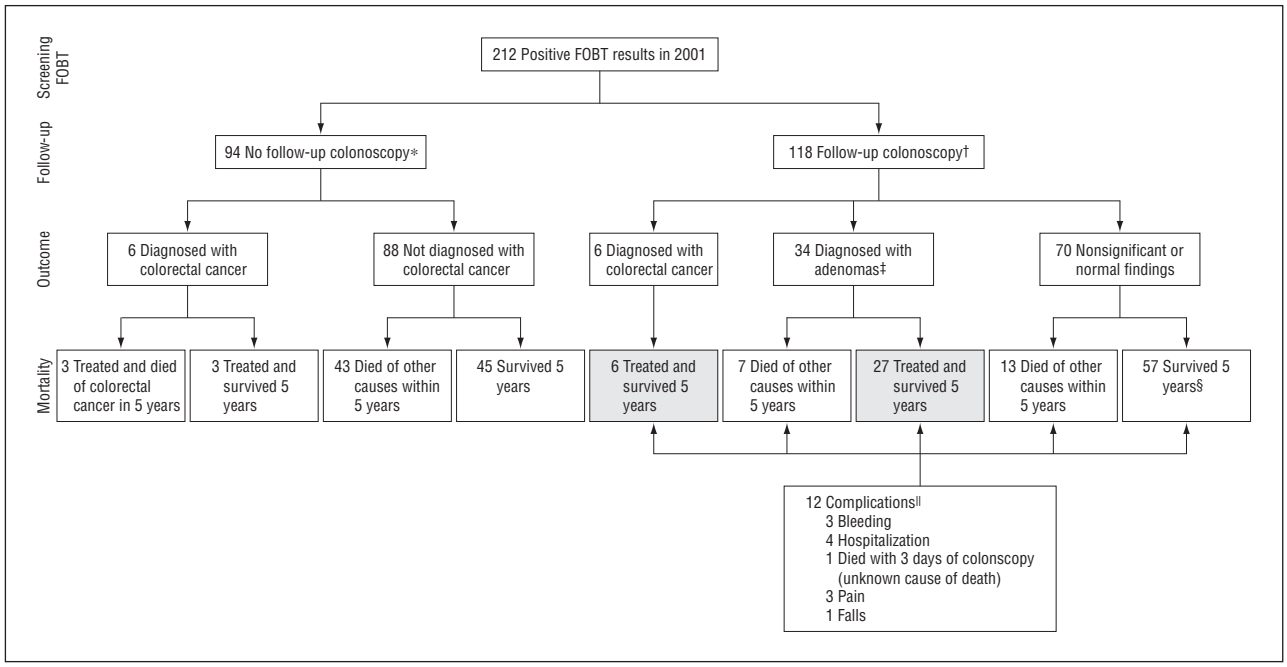

Figure 1. Flowchart of the long-term outcomes following a positive fecal occult blood test (FOBT) result. *Among the 94 patients who did not have a follow-up colonoscopy related to their positive FOBT result, 10 ultimately underwent colonoscopy for symptoms that developed over the 7-year study period (eg, hematochezia, unexplained weight loss, anemia), and 2 patients underwent screening colonoscopy many years later without any mention of their positive FOBT result from 2001. The 3 patients in the no–follow-up colonoscopy group who died of colorectal cancer within 5 years of their FOBT all had refused follow-up colonoscopy.[5] †Eight patients did not have a pathology report available from their colonoscopy performed outside of the Veterans Affairs (VA) health system to determine size or type of polyps detected. Therefore, we were unable to definitively classify them as "significant adenoma" vs "nonsignificant or normal findings." None of these 8 patients had any evidence in their medical records that they ever were diagnosed as having colorectal cancer. Overall, 17% of patients received follow-up colonoscopy outside the VA health care system (35 of 212). ‡*Significant adenoma* was defined as an adenoma of 1 cm or larger, 3 or more adenomas, and/or any adenoma with villous features. §One patient was diagnosed as having an incidental colorectal cancer and survived more than 5 years. ||Twelve patients had complications from colonoscopy: 3 of the 34 patients with significant adenomas had notable bleeding following polypectomy; of these, the first required hospital admission; the second had a vasovagal episode following epinephrine treatment for bleeding; and the third had the procedure aborted and required another colonoscopy. Two patients had complications from other testing after their colonoscopy; of these, the first had a fall after a barium enema and required transfer to the emergency department but was otherwise unharmed; the second had a sigmoidectomy to treat a large adenoma complicated by a hypoxic event and a 3-week hospitalization. Three of the 45 patients with normal colonoscopy findings had discomfort with the colonoscopy. Finally, colonoscopy may have contributed to the death of 1 patient who died within 3 days of his colonoscopy, although the exact cause of death was unknown, per the medical records. Gray shading indicates patients who potentially benefited from screening.

ceiving net burden, including 10 patients who had adenomas removed but died within 5 years; 45 patients with no adenomas of any kind found on colonoscopy (ie, unequivocal false positives); and 94 patients who did not have a follow-up colonoscopy. The magnitude of net burden varied, ranging from false-positive results in patients without cancer to cancers not found because patients declined follow-up (6.4%).

Also, the net burden of these screening and follow-up practices varied across the 3 prognostic groups (**Figure 2**). A total of 87% of those with worst life expectancy experienced net burden compared with 70% of those with average life expectancy and 65% of those with best life expectancy ($P=.048$ for trend). Conversely, 20% of patients with best life expectancy experienced net benefit (10 of 51) vs 15.3% of those with average life expectancy (20 of 131) and 10% of those with worst life expectancy (3 of 30) ($P=.25$ for trend.).

COMMENT

Even over 7 years after a positive FOBT result, only a little over half of older adults received follow-up colonoscopy. Among those who received follow-up colonoscopy, more than a quarter had significant adenomas or cancer detected and treated and lived more than 5 years, potentially benefitting from screening, while approximately 59% had no significant findings on follow-up (70 of 118), and 10% experienced complications from colonoscopy or cancer treatment. Among patients who did not receive follow-up colonoscopy, nearly half died of other causes within 5 years, while 3% died of colorectal cancer. Patients with worst life expectancy (5.4 years) were more likely to experience net burden than were patients with average or best life expectancy. As current guidelines from the US Preventive Services Task Force[26] and other groups encourage individualized decision making in patients older than 75 years,[16] our study provides data about the consequences following the choice to pursue or forego follow-up of a positive FOBT result.

The low rate of follow-up colonoscopy found in this study (56%) is similar to that of other studies in older adults, even though the follow-up period in other studies ranged from only a few months to 3 years, whereas we extended the follow-up period to 7 years.[1-4,7,8] Patients may not get follow-up colonoscopy because of the risks of colonoscopy and treatment and other competing causes of mortality, as perceived either by the physician[27] or the patient.[5] We found that nearly half of those without follow-up colonoscopy died of causes other than

Table 2. Outcomes of Patients Diagnosed as Having Colorectal Cancer According to Whether They Received Follow-up Evaluation After Their Positive FOBT Result

Life Expectancy Group	Clinical Course (n=13)
	Patients Who Had a Follow-up Colonoscopy (n=7)
Best	A 74-year-old active man, CCI, 0, had a follow-up colonoscopy that revealed T2N1M0 colorectal cancer in 2002. He underwent curative hemicolectomy without complications and subsequently underwent 2 more colonoscopies with normal findings. At last follow-up, he was alive and healthy.
	A 73-year-old healthy man, CCI, 0, had follow-up colonoscopy with normal findings. In 2006, he suddenly developed hematochezia, and colonoscopy revealed T1N0M0 colorectal cancer for which he underwent curative hemicolectomy. He remained healthy until 2007, when he was diagnosed as having congestive heart failure and died later that year from heart failure.
	A 71-year-old healthy man, CCI, 0, had a follow-up colonoscopy that revealed rectal cancer. He underwent curative right hemicolectomy complicated by recurrent colostomy leakage. He remained relatively healthy until 2007, when he was diagnosed as having lung cancer, and he died shortly thereafter.
Average	A 72-year-old man with emphysema had a follow-up colonoscopy that revealed T1N0M0 colorectal cancer for which he underwent curative hemicolectomy without complications. He had 3 follow-up colonoscopies during the study period with normal findings. He developed renal failure in 2008 and at last follow-up remained alive.
	An 81-year-old man with chronic obstructive pulmonary disease had a follow-up colonoscopy that revealed a 3-cm colorectal cancer without metastases. He underwent curative hemicolectomy, developed delirium requiring prolonged hospitalization, and eventually recovered. He had progressive functional decline since surgery but at last follow-up remained alive.
	An 81-year-old man with diabetes and mild heart failure had a follow-up colonoscopy that revealed nearly obstructing colorectal cancer. He was referred for surgery but became unresponsive and required emergency colectomy. He recovered from surgery but developed progressive renal failure. At last follow-up, he remained alive in a nursing home.
Worst	A 74-year-old man with emphysema, prostate cancer, and severe rheumatoid arthritis treated with long-term steroid therapy had a follow-up colonoscopy that revealed a T1N0M0 colorectal cancerous polyp, which was removed. Owing to a possibly inadequate resection, he subsequently underwent a subtotal colectomy complicated by repeated hospitalizations for recurrent wound infections and bowel obstruction. His chronic obstructive pulmonary disease worsened, but at last follow-up, he remained alive.
	Patients Who Did Not Have a Follow-up Colonoscopy (n=6)
Best	A 77-year-old active man with prostate cancer treated with androgen deprivation therapy (this comorbidity was missed by claims data) had a positive FOBT result in 2001. He was sent to the GI clinic, but knowing that he had prostate cancer, he did not want to know if he had colon cancer, and so he adamantly refused a colonoscopy. He agreed to repeat the FOBT 4 years later, the results of which were positive, and at that time, he was persuaded to have a colonoscopy that revealed T3N0M0 colon cancer. He underwent curative hemicolectomy 2006 and remained alive at last follow-up.
	A 79-year-old healthy man, CCI, 0, had a positive FOBT result in 2001 but repeatedly declined colonoscopy over the next 6 years as his hematocrit concentration slowly fell. In 2007, he developed hematochezia, and a colonoscopy revealed 2 obstructing colorectal cancers. The colonoscopy was complicated by aspiration requiring intubation delaying surgery for several weeks. He underwent a hemicolectomy in 2007, which was complicated by renal failure and sepsis, and he died soon afterwards in the ICU as a result of his late-stage colorectal cancer.
Average	A 75-year-old active man with diabetes had a positive FOBT result in 2001, and his VA physician recommended colonoscopy. Instead, he had a sigmoidoscopy performed outside the VA system in 2001, and the findings were normal, per patient report. He felt well until he developed hematochezia in 2006, and a colonoscopy revealed stage 3 colorectal cancer, which was treated with resection, chemotherapy, and irradiation. At last follow-up, he remained alive without recurrence.
	A 76-year-old man with a history of a myocardial infarction and coronary stents had a positive FOBT result in 2001 and was referred for colonoscopy. Instead, he had a barium enema and sigmoidoscopy owing to his heart disease, both of which revealed an obstructing colorectal cancer. Further evaluation revealed widely metastatic disease. He underwent palliative hemicolectomy in 2001 complicated by a myocardial infarction, abdominal abscesses, and delirium requiring prolonged hospitalization. He enrolled in hospice in 2002 and died shortly afterwards of metastatic colorectal cancer.
	A 79-year-old obese man with diabetes undergoing treatment with warfarin sodium for atrial fibrillation had a positive FOBT result in 2001 and was scheduled for colonoscopy, but he suddenly developed abdominal pain and narrow-caliber stools, so he had a barium enema in 2001 that revealed T3N1M0 colorectal cancer. He was treated with hemicolectomy and declined adjuvant therapy. He was diagnosed as having metastatic disease in 2001 and died shortly afterwards of metastatic colorectal cancer.
Worst	An 81-year-old man with stage III congestive heart failure, emphysema, and diabetes with end-organ damage had a positive FOBT result in 2001 but refused colonoscopy. He had one in 1987 and said that he never wanted another. Nevertheless, when he developed progressive anemia in 2002 and had a colonoscopy in that revealed stage 2 colorectal cancer. He underwent hemicolectomy complicated by pneumonia, and he died shortly afterwards in the hospital.

Abbreviations: CCI, Charlson-Deyo comorbidity index; FOBT, fecal occult blood test; GI, gastrointestinal tract; ICU, intensive care unit.

colorectal cancer within 5 years, which suggests that the decision to forego follow-up colonoscopy was appropriate for those patients. It also suggests that such decisions are occurring after FOBT results are known rather than following recommendations to avoid the FOBT screening if there is no intention to follow up a positive result with colonoscopy. As the use of screening colonoscopy increases, colonoscopy decisions will be made up front and will need to be better targeted than the FOBT, or the number of colonoscopies performed in people who die within 5 years will increase.

Among our patients with follow-up colonoscopy, about a third had colorectal cancer or significant adenomas, on par with other studies.[10,28,29] Strul et al[30] found the overall adenoma rate in older adults to be 26%. Our study indicates that older patients without follow-up had a 3%

Table 3. Downstream Outcomes Classified According to Benefits and Burdens From Screening and Follow-up Practices for All 212 Study Patients Aged 70 Years or Older With a Positive FOBT Result

Downstream Outcome	Sample Case Report	Net Benefit or Net Burden
	Follow-up Colonoscopy (n=118)	
Cancer (n=6)		
FOBT result led to diagnosis of CRC, and patient lived 5 or more years (n=6)	A 74-year-old man, status post–coronary artery bypass graft, otherwise healthy, underwent a curative resection for rectal cancer. Two more colonoscopies showed negative findings for recurrence. He remained healthy at last follow-up.	Net benefit
Significant adenoma (n=34)		
FOBT led to diagnosis of a significant adenoma, and patient lived 5 or more years (n=27)	A 79-year-old man who was relatively healthy with a large adenoma (1.5 cm) discovered on colonoscopy had 4 more colonoscopies over 7 years that revealed adenomas. He remained healthy at last follow-up.	Net benefit
FOBT led to diagnosis of a significant adenoma, and patient died within 5 years (n=7)	A 74-year-old man with severe heart disease, an implanted cardiac defibrillator, dependent in several instrumental activities of daily living, and a history of multiple falls had 2 adenomas, one large (2 cm), found on colonoscopy. He broke a hip in 2003 and died in early 2004.	Net burden
Insignificant/normal findings (n=78)		
FOBT revealed 1 or 2 small nonvillous adenomas or indeterminate disease and patient lived 5 or more years (n=30)	A 76-year-old man who was independent in instrumental activities of daily living had 2 small adenomas (3 and 8 mm) found on colonoscopy. He had several additional procedures: repeated FOBTs in 2002 and 2004 and repeated colonoscopy in 2005. All results were negative. He remained healthy at last follow-up.	Indeterminate
FOBT revealed no adenoma, and patient lived 5 or more years (n=35)	A 76-year-old man with peripheral neuropathy had 2 hyperplastic polyps found on colonoscopy. He had repeated testing with normal colonoscopy findings in 2006, and no further screening was recommended. He remained alive but quite ill at last follow-up.	Net burden
FOBT revealed no significant adenomas and patient died within 5 years (n=13)	A 75-year-old man with end-stage chronic obstructive pulmonary disease, home oxygen, and multiple emergency department visits for dyspnea had 1 hyperplastic polyp found on colonoscopy. He was diagnosed as having inoperable 3-vessel coronary disease and severe aortic stenosis in 2004 but had another colonoscopy, findings negative. His angina worsened, and he died in 2005.	Net burden
	No Follow-up Colonoscopy (n=94)	
No evaluation after positive FOBT result (n=40)	A 73-year-old man with chronic obstructive pulmonary disease, status post–stroke with aphasia and left hemiparesis, coronary disease status post–coronary artery bypass graft had screening at a preventive visit despite physician note not recommending screening, indicating that patient had less than 5 years' life expectancy. Physician recommended against further evaluation, and patient progressively declined and died in 2002 in hospice.	Net burden
Further evaluation after positive FOBT result (n=54)	An 80-year-old man with gout and arthritis had a positive FOBT result in 2001 followed by a negative FOBT result in 2004. He never had a follow-up colonoscopy. He moved to a VA nursing home in 2007 and remained alive at last follow-up	Net burden

Abbreviations: CCI, Charlson comorbidity index; FOBT, fecal occult blood test; GI, gastrointestinal tract; ICU, intensive care unit.

risk of dying of colorectal cancer in the next 5 years. On the other hand, undergoing follow-up procedures is not without risk. While prior studies have suggested minimal complications from colonoscopy in older adults, these studies only observed patients over a short period.[4,31-35] We found complications of follow-up encompassed more than immediate events. In our cohort, 4 of the 40 older patients with cancer or significant adenomas were hospitalized for several weeks as a result of complications from treatment. In addition, 23% of those with follow-up colonoscopy (24 of 104), excluding those with cancer, had 3 or more additional tests over 7 years. However, while older adults are often at greatest risk for complications from colonoscopy and colorectal cancer treatment owing to their increasing comorbidity,[36] they may be most likely to benefit from screening, especially if they have a substantial life expectancy.

While our study is not a randomized trial, the lengthy follow-up allows us to identify patients who most likely received net benefit from real-world screening and follow-up practices, ie, those with significant disease treated as a result of screening and who lived more than 5 years. The choice of a 5-year survival time to achieve benefit is based on the natural history of polyps[18] and on the findings of randomized trials that show survival benefit beginning around 5 years after the start of FOBT screening.[10] In addition, several of the cancers and adenomas found in our study were large (>3 cm) such that it is reasonable to expect that they would have caused symptoms within 5 years. As with all screening tests, FOBT does not benefit most patients because most do not have cancer or significant adenomas. However, more than 15.6% of our patients aged 70 years or older had colorectal cancer or significant adenomas successfully treated and lived more than 5 years (33 of 212), which suggests that a significant minority received net benefit from current practices.

It makes intuitive sense that patients with the best life expectancy are more likely to benefit from screening than those with the worst. This has been shown in cost-effectiveness analyses,[37,38] which are based on numerous methodologic assumptions, whereas our study uses real-world data to describe outcomes of screening according to life expectancy. We found that older patients with the

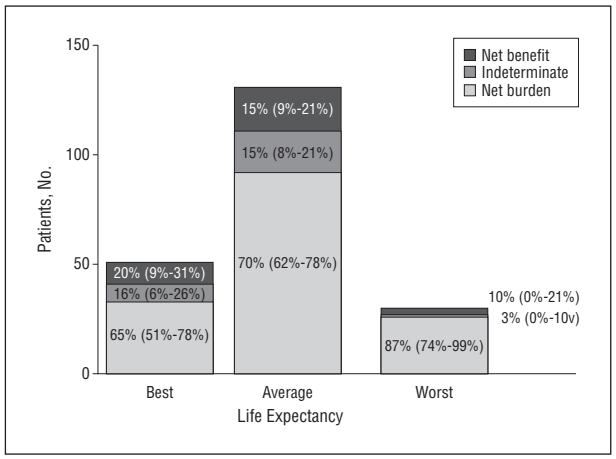

Figure 2. Benefits and burdens of screening and follow-up practices according to life expectancy among 212 patients aged 70 years or older with a positive fecal occult blood test (FOBT) result. Net benefit was assigned to those patients diagnosed as having a significant adenoma or colorectal cancer on follow-up colonoscopy who lived at least 5 years after screening, even if they experienced complications from screening or treatment. Net benefit or burden was indeterminate if (1) patients had 1 or 2 small adenomas and lived at least 5 years or (2) patients had a colonoscopy outside of the Veterans Affairs health system without an available pathology report and lived at least 5 years. Net burden was assigned to patients who failed to receive a colonoscopy after their positive FOBT result, who had a false-positive FOBT result (ie, nonsignificant findings on follow-up colonoscopy), or who had a significant adenoma detected but died within 5 years. Among patients with the best life expectancy who experienced a net burden, the most common reason was failure to undergo a follow-up colonoscopy (55%; 18 of 33); among patients with average or worst life expectancy, the most common reason for net burden was dying within 5 years of their FOBT (54%; 64 of 118). Five-year mortality was 6% for patients with best life expectancy (3 of 51), 38.2% for patients with average life expectancy (50 of 131), and 47% for patients with worst life expectancy (14 of 30), which equates to a life expectancy of 5.4 years. Numbers in parentheses are 95% confidence intervals.

best predicted life expectancy were less likely to experience net burden from screening than those with the worst. Our study supports guidelines that recommend using life expectancy to guide colorectal cancer screening decisions in older adults and argues against 1-size-fits-all interventions that simply aim to increase overall screening and follow-up rates.[16,26] We used the well-validated Charlson-Deyo comorbidity index because it strongly predicts long-term mortality.[14] In our cohort, it effectively stratified patients into groups with widely differing 5-year mortality rates, ranging from 6% for patients with best life expectancy to 47% for those with worst (life expectancy, 5.4 years) for whom most would not recommend screening.[36] However, more comprehensive prognostic indices (eg, incorporating functional status) over more than 5 years are needed to better guide physicians as they target screening and follow-up to those older adults with substantial life expectancies.[39,40]

This study has several limitations. First, our cohort is primarily composed of men who use VA medical centers, so the generalizability of our findings to nonwhite men, women, and persons who do not use VA medical centers is uncertain. However, the VA medical system is the largest health care system in the United States, so outcomes of screening and follow-up in this system are likely to have generalizable lessons for US health care. Second, our sample size was small because only 212 patients had positive FOBT results at the 4 participating facilities in 2001 (9%). Third, although we used Medicare claims data for the first year of follow-up, we relied on medical chart review for later outcomes, which might have missed some complications or tests that occurred outside the VA health system, and we were unable to find pathology results for 8 patients with a colonoscopy outside the VA system, although all 8 remained alive without colorectal cancer. Fourth, we defined patients as having benefitted from screening if they had colorectal cancer or significant adenomas detected on follow-up colonoscopy and were treated and survived more than 5 years. Others may argue for a longer or shorter survival length to define benefit in older adults.[10,41]

In conclusion, systematic reviews of colorectal cancer screening have called for more studies to assess the net benefit of real-world colorectal cancer screening practices to improve appropriate use and minimize burdens of screening.[39] Our study used a novel method of observing patients with a positive FOBT result for 7 years to determine the net benefit and burden of real-world screening and follow-up practices in older adults. We demonstrated that older adults with substantial life expectancies were less likely to experience net burden than those with limited life expectancies. Therefore, through individualized decision making, the percentage of patients experiencing net burden could be decreased by better targeting FOBT screening and follow-up to healthy older adults.

Accepted for Publication: March 3, 2011.
Published Online: May 9, 2011. doi:10.1001/archinternmed.2011.206
Correspondence: Christine E. Kistler, MD, MASc, Department of Family Medicine, University of North Carolina at Chapel Hill, 590 Manning Dr, CB 7595, Chapel Hill, NC 27599-7595 (Christine_Kistler@med.unc.edu).
Author Contributions: Drs Kistler and Walter had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Walter. *Acquisition of data:* Kistler, Lee, and Walter. *Analysis and interpretation of data:* Kistler, Kirby, Lee, Casadei, and Walter. *Drafting of the manuscript:* Kistler and Walter. *Critical revision of the manuscript for important intellectual content:* Kirby, Lee, Casadei, and Walter. *Statistical analysis:* Kistler and Kirby. *Obtained funding:* Walter. *Administrative, technical, and material support:* Casadei.
Financial Disclosure: None reported.
Funding/Support: Work for this research was supported by the VA Quality Scholars Program, National Institute on Aging grant T32 AG000212-16, Agency for Healthcare Research and Quality Mentored Career Development Program in Comparative Effectiveness Development grant K12 HS19468-01, the Cecil G. Sheps Center for Health Services Research, and the Lineberger Cancer Center at the University of North Carolina at Chapel Hill (Dr Kistler); and by VA Health Services Research and Development grant IIR-04-427 and National Cancer Institute grant 1R01CA134425 (Dr Walter).
Role of the Sponsors: The funding institutions had no role in the design, conduct, or analysis of this study or in the decision to submit the manuscript for publication.

REFERENCES

1. Myers RE, Balshem AM, Wolf TA, Ross EA, Millner L. Screening for colorectal neoplasia: physicians' adherence to complete diagnostic evaluation. *Am J Public Health*. 1993;83(11):1620-1622.
2. Levin B, Hess K, Johnson C. Screening for colorectal cancer: a comparison of 3 fecal occult blood tests. *Arch Intern Med*. 1997;157(9):970-976.
3. Fenton JJ, Elmore JG, Buist DS, Reid RJ, Tancredi DJ, Baldwin LM. Longitudinal adherence with fecal occult blood test screening in community practice. *Ann Fam Med*. 2010;8(5):397-401.
4. Lurie JD, Welch HG. Diagnostic testing following fecal occult blood screening in the elderly. *J Natl Cancer Inst*. 1999;91(19):1641-1646.
5. Carlson CM, Kirby KA, Casadei MA, Partin MR, Kistler CE, Walter LC. Lack of follow-up after fecal occult blood testing in older adults: inappropriate screening or failure to follow up? *Arch Intern Med*. 2011;171(3):249-256.
6. Morris JB, Stellato TA, Guy BB, Gordon NH, Berger NA. A critical analysis of the largest reported mass fecal occult blood screening program in the United States. *Am J Surg*. 1991;161(1):101-106.
7. Garman KS, Jeffreys A, Coffman C, Fisher DA. Colorectal cancer screening, comorbidity, and follow-up in elderly patients. *Am J Med Sci*. 2006;332(4):159-163.
8. Shields HM, Weiner MS, Henry DR, et al. Factors that influence the decision to do an adequate evaluation of a patient with a positive stool for occult blood. *Am J Gastroenterol*. 2001;96(1):196-203.
9. Walter LC, Covinsky KE. Cancer screening in elderly patients: a framework for individualized decision making. *JAMA*. 2001;285(21):2750-2756.
10. Hardcastle JD, Chamberlain JO, Robinson MH, et al. Randomised controlled trial of faecal-occult-blood screening for colorectal cancer. *Lancet*. 1996;348(9040):1472-1477.
11. Walter LC, Lindquist K, Nugent S, et al. Impact of age and comorbidity on colorectal cancer screening among older veterans. *Ann Intern Med*. 2009;150(7):465-473.
12. Fisher DA, Jeffreys A, Coffman CJ, Fasanella K. Barriers to full colon evaluation for a positive fecal occult blood test. *Cancer Epidemiol Biomarkers Prev*. 2006;15(6):1232-1235.
13. Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. *J Clin Epidemiol*. 1994;47(11):1245-1251.
14. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol*. 1992;45(6):613-619.
15. Singh H, Kadiyala H, Bhagwath G, et al. Using a multifaceted approach to improve the follow-up of positive fecal occult blood test results. *Am J Gastroenterol*. 2009;104(4):942-952.
16. Smith RA, Cokkinides V, Brawley OW. Cancer screening in the United States, 2009: a review of current American Cancer Society guidelines and issues in cancer screening. *CA Cancer J Clin*. 2009;59(1):27-41.
17. Sohn MW, Arnold N, Maynard C, Hynes DM. Accuracy and completeness of mortality data in the Department of Veterans Affairs. *Popul Health Metr*. 2006;4:2.
18. Winawer SJ, Zauber AG, O'Brien MJ, et al; The National Polyp Study Workgroup. The National Polyp Study: design, methods, and characteristics of patients with newly diagnosed polyps. *Cancer*. 1992;70(5)(suppl):1236-1245.
19. Loeve F, van Ballegooijen M, Boer R, Kuipers EJ, Habbema JD. Colorectal cancer risk in adenoma patients: a nation-wide study. *Int J Cancer*. 2004;111(1):147-151.
20. Brooks DD, Winawer SJ, Rex DK, et al; US Multi-Society Task Force on Colorectal Cancer; American Cancer Society. Colonoscopy surveillance after polypectomy and colorectal cancer resection. *Am Fam Physician*. 2008;77(7):995-1002.
21. Laiyemo AO, Murphy G, Albert PS, et al. Postpolypectomy colonoscopy surveillance guidelines: predictive accuracy for advanced adenoma at 4 years. *Ann Intern Med*. 2008;148(6):419-426.
22. Winawer SJ, Zauber AG, Fletcher RH, et al; US Multi-Society Task Force on Colorectal Cancer; American Cancer Society. Guidelines for colonoscopy surveillance after polypectomy: a consensus update by the US Multi-Society Task Force on Colorectal Cancer and the American Cancer Society. *Gastroenterology*. 2006;130(6):1872-1885.
23. Hoogewerf PE, Hislop TG, Morrison BJ, Burns SD, Sizto R. Health belief and compliance with screening for fecal occult blood. *Soc Sci Med*. 1990;30(6):721-726.
24. Beeker C, Kraft JM, Southwell BG, Jorgensen CM. Colorectal cancer screening in older men and women: qualitative research findings and implications for intervention. *J Community Health*. 2000;25(3):263-278.
25. Parker MA, Robinson MHE, Scholefield JH, Hardcastle JD. Psychiatric morbidity and screening for colorectal cancer. *J Med Screen*. 2002;9(1):7-10.
26. US Preventive Services Task Force. Screening for colorectal cancer: US Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2008;149(9):627-637.
27. Jimbo M, Myers RE, Meyer B, et al. Reasons patients with a positive fecal occult blood test result do not undergo complete diagnostic evaluation. *Ann Fam Med*. 2009;7(1):11-16.
28. Hewitson P, Glasziou P, Watson E, Towler B, Irwig L. Cochrane systematic review of colorectal cancer screening using the fecal occult blood test (hemoccult): an update. *Am J Gastroenterol*. 2008;103(6):1541-1549.
29. Mandel JS, Bond JH, Church TR, et al. Reducing mortality from colorectal cancer by screening for fecal occult blood. Minnesota Colon Cancer Control Study. *N Engl J Med*. 1993;328(19):1365-1371.
30. Strul H, Kariv R, Leshno M, et al. The prevalence rate and anatomic location of colorectal adenoma and cancer detected by colonoscopy in average-risk individuals aged 40-80 years. *Am J Gastroenterol*. 2006;101(2):255-262.
31. Warren JL, Klabunde CN, Mariotto AB, et al. Adverse events after outpatient colonoscopy in the Medicare population. *Ann Intern Med*. 2009;150(12):849-857, W152.
32. Zerey M, Paton BL, Khan PD, et al. Colonoscopy in the very elderly: a review of 157 cases. *Surg Endosc*. 2007;21(10):1806-1809.
33. Lukens FJ, Loeb DS, Machicao VI, Achem SR, Picco MF. Colonoscopy in octogenarians: a prospective outpatient study. *Am J Gastroenterol*. 2002;97(7):1722-1725.
34. Arora A, Singh P. Colonoscopy in patients 80 years of age and older is safe, with high success rate and diagnostic yield. *Gastrointest Endosc*. 2004;60(3):408-413.
35. Karajeh MA, Sanders DS, Hurlstone DP. Colonoscopy in elderly people is a safe procedure with a high diagnostic yield: a prospective comparative study of 2000 patients. *Endoscopy*. 2006;38(3):226-230.
36. Gross CP, McAvay GJ, Krumholz HM, Paltiel AD, Bhasin D, Tinetti ME. The effect of age and chronic illness on life expectancy after a diagnosis of colorectal cancer: implications for screening. *Ann Intern Med*. 2006;145(9):646-653.
37. Lin OS, Kozarek RA, Schembre DB, et al. Screening colonoscopy in very elderly patients: prevalence of neoplasia and estimated impact on life expectancy. *JAMA*. 2006;295(20):2357-2365.
38. Ko CW, Sonnenberg A. Comparing risks and benefits of colorectal cancer screening in elderly patients. *Gastroenterology*. 2005;129(4):1163-1170.
39. Holden DJ, Jonas DE, Porterfield DS, Reuland D, Harris R. Systematic review: enhancing the use and quality of colorectal cancer screening. *Ann Intern Med*. 2010;152(10):668-676.
40. Lewis CL, Griffith J, Pignone MP, Golin C. Physicians' decisions about continuing or stopping colon cancer screening in the elderly: a qualitative study. *J Gen Intern Med*. 2009;24(7):816-821.
41. Quanstrum KH, Hayward RA. Lessons from the mammography wars. *N Engl J Med*. 2010;363(11):1076-1079.

EDITOR'S NOTE

ONLINE FIRST

Colorectal Cancer Screening Protocols and Procedures

While it is well known that colorectal cancer screening has enormous potential to substantially reduce the incidence of colorectal cancer, how to do so in an optimal way remains elusive. Many questions about proper processes, who to screen, when to stop screening, and what defines the proper interval for screening have not been adequately studied. Two articles in this issue of the *Archives* indicate that there is much room for improvement in the way we measure proper utilization of screening colonoscopy, ensure

See also pages 1335 and 1344

adequate follow-up, and evaluate net benefit among those who screen positive.

Patrick G. O'Malley, MD, MPH