Background: Harms and benefits of cancer screening depend on age and comorbid conditions, but reliable estimates are lacking.

Objective: To estimate the harms and benefits of cancer screening by age and comorbid conditions to inform decisions about screening cessation.

Design: Collaborative modeling with 7 cancer simulation models and common data on average and comorbid condition level–specific life expectancy.

Setting: U.S. population.

Patients: U.S. cohorts aged 66 to 90 years in 2010 with average health or 1 of 4 comorbid condition levels: none, mild, moderate, or severe.

Intervention: Mammography, prostate-specific antigen testing, or fecal immunochemical testing.

Measurements: Lifetime cancer deaths prevented and life-years gained (benefits); false-positive test results and overdiagnosed cancer cases (harms). For each comorbid condition level, the age at which harms and benefits of screening were similar to that for persons with average health having screening at age 74 years.

Results: Screening 1000 women with average life expectancy at age 74 years for breast cancer resulted in 79 to 96 (range across models) false-positive results, 0.5 to 0.8 overdiagnosed cancer cases, and 0.7 to 0.9 prevented cancer deaths. Although absolute numbers of harms and benefits differed across cancer sites, the ages at which to cease screening were consistent across models and cancer sites. For persons with no, mild, moderate, and severe comorbid conditions, screening until ages 76, 74, 72, and 66 years, respectively, resulted in harms and benefits similar to average-health persons.

Limitation: Comorbid conditions influenced only life expectancy.

Conclusion: Comorbid conditions are an important determinant of harms and benefits of screening. Estimates of screening benefits and harms by comorbid condition can inform discussions between providers and patients about personalizing screening cessation decisions.

Primary Funding Source: National Cancer Institute and Centers for Disease Control and Prevention.

In 2008, the U.S. Preventive Services Task Force (USPSTF) recommended against routine breast and colorectal cancer screening after age 74 years (1, 2) because the average gain in life-years associated with extending screening beyond age 74 years was believed to be small compared with the harms. However, because comorbid conditions may shift the balance of harms and benefits toward cessation at ages younger or older than 74 years, the USPSTF and other groups recommended that screening cessation decisions be individualized based on health status (1–4).

More than 13 million persons in the United States are between ages 75 and 85 years, and this number is expected to increase to greater than 28 million by 2050 (5). Thus, clinicians will be caring for a large and growing number of persons affected by the uncertainty in how to assess health status and make recommendations about screening upper age limits. There is considerable heterogeneity in the health of these older persons, but none of the current guidelines provide clinicians with data to implement personalized approaches. Previous decision analyses that examined health benefits of different cancer screening cessation ages by life expectancy (6, 7) have limited clinical utility because they did not provide a framework for determining life expectancy.

To fill this gap, we estimated the harms and benefits of breast, prostate, and colorectal cancer screening by age based on individual comorbid conditions using 7 established, independently developed models from the Cancer Intervention and Surveillance Modeling Network.

Methods

We used microsimulation models to estimate the harms and benefits of having 1 more cancer screen in regularly screened cohorts aged 66 to 90 years by comorbid condition level. The harms and benefits for each cohort

See also:

Summary for Patients....................... I-22

Web-Only

Supplement
were compared with that of an average-health cohort having 1 more screen at age 74 years.

The Models

We used the Microsimulation Screening Analysis (MISCAN–Fadia) and Georgetown–Einstein models for breast cancer (8, 9); MISCAN-Prostate and the Fred Hutchinson Cancer Research Center (FHCRC) models for prostate cancer (10, 11); and MISCAN-Colon, Colorectal Cancer Simulated Population Model for Incidence and Natural History (CRC-SPIN), and Simulating Colorectal Cancer (SimCRC) models for colorectal cancer (12–14) models for this analysis. Each model simulates the life histories of persons from birth to death and tracks underlying disease in the presence and absence of screening. These models have previously been applied to inform the USPSTF recommendations for breast and colorectal cancer screening (15, 16) and to evaluate prostate cancer screening and treatment interventions (17, 18). The use of multiple models per cancer site provides a credible range of results and serves as a sensitivity analysis on the effect of variations in underlying model structure and assumptions (Table 1 of the Supplement and the Appendix Figure, both available at www.annals.org). In brief, screening extends life through detecting disease at an earlier stage or a smaller size when it may have better survival after treatment than without screening. Inputs were standardized across models within the cancer site, including test characteristics, screening and follow-up assumptions, treatment distributions, and cancer-specific and other-cause survival. Sources for the model inputs have been described in previous publications (15, 16, 19). Descriptions of each model have been published elsewhere (8–14); model profiles are available at http://cisnet.cancer.gov/profiles, and additional information about the models is available from the authors on request. The Cancer Intervention and Surveillance Modeling Network also includes procedures for external collaboration for interested investigators (http://cisnet.cancer.gov). Selected model outputs for persons aged 74 years who have average health (and life expectancy) and had been screened regularly before age 74 years are provided in Table 1.

Population

After assuming that all persons had regular screening starting at age 50 years with biennial mammography, biennial prostate-specific antigen (PSA) testing, or annual fecal immunochemical testing (FIT), the models began simulation for U.S. cohorts of persons aged 66 to 90 years in the year 2010 who had average risk for cancer and a specified comorbid condition level (none, mild, moderate, or severe) and followed them for their remaining lifetime.

Table 1. Selected Clinical Model Outputs for Persons Aged 74 Years Who Had Average Health and Life Expectancy and Had Been Screened Regularly Before Age 74 Years With and Without Screening at Age 74 Years*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Breast Cancer</th>
<th>Prostate Cancer</th>
<th>Colorectal Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lifetime probability of developing cancer</td>
<td>MISCAN-Fadia</td>
<td>MISCAN-Prostate</td>
<td>MISCAN-Colon</td>
</tr>
<tr>
<td>without screening at age 74 y</td>
<td>G-E Model</td>
<td>FHCRC Prostate</td>
<td>CRC-SPIN</td>
</tr>
<tr>
<td></td>
<td>6.9</td>
<td>7.9</td>
<td>1.9</td>
</tr>
<tr>
<td>Lifetime probability of developing cancer</td>
<td>7.2</td>
<td>9.8</td>
<td>1.8</td>
</tr>
<tr>
<td>with screening at age 74 y</td>
<td>8.2†</td>
<td>4.4</td>
<td>0.19</td>
</tr>
<tr>
<td>Prevalence of undiagnosed cancer immediately before screening at age 74 y</td>
<td>9.3†</td>
<td>1.0</td>
<td>0.06</td>
</tr>
<tr>
<td>Prevalence of undiagnosed cancer immediately after screening at age 74 y</td>
<td>8.2†</td>
<td>11.3</td>
<td>0.05</td>
</tr>
</tbody>
</table>

CRC-SPIN = Colorectal Cancer Simulated Population Model for Incidence and Natural History; Fadia = fatal diameter; FHCRC = Fred Hutchinson Cancer Research Center; G-E = Georgetown–Einstein; MISCAN = Microsimulation Screening Analysis; SimCRC = Simulating Colorectal Cancer.

* Values are percentages.
† The large difference in undiagnosed cancer between the models reflects differences in modeling approach. MISCAN-Fadia includes cancer from a very small tumor size (0.1 mm) not yet detectable by mammography.

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Original Research

Personalizing Age of Screening Cessation by Comorbid Conditions

Context

Decisions about cancer screening are based on the tradeoff between benefits (life-years gained) and harms (false-positive test results and overdiagnosed cancer cases).

Contribution

In simulation studies of mammography, prostate-specific antigen testing, and fecal immunochemical testing, the tradeoffs were roughly the same in persons aged 74 years with average health as in persons aged 76 years with no comorbid conditions, those aged 74 years with mild comorbid conditions, those aged 72 years with moderate comorbid conditions, and those aged 66 years with severe comorbid conditions.

Caution

Comorbid conditions affected only life expectancy.

Implication

Comorbid conditions should inform decisions about when to stop screening older persons for cancer.

—The Editors
For reference, we also simulated cohorts aged 74 and 76 years (75 years for colorectal cancer) with average health and corresponding average life expectancy. We assumed that comorbid conditions influenced noncancer life expectancy but not cancer risk or progression, treatment, or cancer-specific survival.

**Comorbid Condition–Specific Life Tables**

Noncancer life expectancy was derived from comorbid condition scores for 16 conditions derived from claims from a random 5% sample of noncancer beneficiaries continuously enrolled with Medicare Parts A and B from 1992 to 2005 and residing in the Surveillance, Epidemiology, and End Results areas (20–22). Cox proportional hazard methods were used to estimate noncancer, age-conditional life tables for each sex and age combination using comorbid conditions as a covariate. Comorbid conditions were then grouped into 4 levels: none, mild, moderate, and severe, each with its own life expectancy at a given age (Table 2). We used the weighted average of the comorbidity condition–specific life tables for the reference average-health cohorts. We extrapolated beyond the 13 years of available data by assuming that mortality rates converged abruptly to average U.S. rates after that period. This is a conservative assumption for personalizing age at screening cessation because life expectancy is overestimated for persons with moderate and severe comorbid conditions and underestimated for those with no or mild comorbid conditions.

**Analysis**

For each cohort, we estimated the benefits and harms of screening at their current age. Diagnostic follow-up was based on current recommendations (breast and colorectal) or practice (prostate). Screening benefits were expressed as the life-years gained (LYGs) and cancer deaths prevented (CDPs) for every 1000 persons screened at a given age. Harms were expressed as the false-positive test results and overdiagnosed cancer cases (that is, cancer that would not have caused symptoms during a person’s lifetime) per 1000 persons screened. The balance between harms and benefits was expressed as the number needed to screen per life-year gained (NNS/LYG). For reference, we also determined the age at which the harms and benefits of screening (NNS/LYG) were similar to screening the average-health population at age 74 years for each comorbid condition level.

**Sensitivity Analysis**

We varied our method for extrapolating comorbid condition–specific life tables by assuming that the hazard ratio between the average-health life table and the comorbid condition–specific life table at the 13th year of observation was maintained until death. For colorectal cancer, we also estimated the harms and benefits of colonoscopy screening by age and comorbid condition level.

**Role of the Funding Source**

The National Cancer Institute and Centers for Disease Control and Prevention funded this study. The funding source had no role in study design and conduct; collection, management, analysis, and interpretation of the data; or preparation, review, or approval of the manuscript.

**RESULTS**

**Screening Based on “Average” Comorbid Condition Level**

At age 74 years, the average life expectancy for women across all comorbid condition groups is 13.9 years. Screening 1000 women for breast cancer who have average health

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**Table 2. Overview of Comorbid Condition Levels, Associated Conditions, and Life Expectancies at Ages 68, 74, and 78 Years**

<table>
<thead>
<tr>
<th>Comorbid Condition Group</th>
<th>Population at Age 74 Years, %</th>
<th>Conditions Included*</th>
<th>HR†</th>
<th>Life Expectancy at Age 68 Years, y</th>
<th>Life Expectancy at Age 74 Years, y</th>
<th>Life Expectancy at Age 78 Years, y</th>
</tr>
</thead>
<tbody>
<tr>
<td>No comorbid conditions</td>
<td>69</td>
<td>None</td>
<td>1.00</td>
<td>15.6</td>
<td>19.3</td>
<td>13.1</td>
</tr>
<tr>
<td>Mild comorbid conditions</td>
<td>2</td>
<td>History of MI, acute MI, ulcer, or rheumatologic disease</td>
<td>1.01–1.38</td>
<td>15.4</td>
<td>17.1</td>
<td>12.5</td>
</tr>
<tr>
<td>Moderate comorbid</td>
<td>12</td>
<td>Cardiovascular disease; paralysis; diabetes; or combinations of diabetes with MI, ulcer, or rheumatologic disease</td>
<td>1.39–1.66</td>
<td>14.4</td>
<td>16.3</td>
<td>11.0</td>
</tr>
<tr>
<td>Severe comorbid conditions</td>
<td>17</td>
<td>AIDS, COPD, mild or severe liver disease, chronic renal failure, dementia, congestive heart failure, or combinations of aforementioned diseases not categorized under moderate comorbid conditions</td>
<td>≥1.67</td>
<td>10.8</td>
<td>13.3</td>
<td>8.1</td>
</tr>
</tbody>
</table>

Average health population 100 All 15.7 18.3 11.9 13.9 9.6 11.2

COPD = chronic obstructive pulmonary disease; HR = hazard ratio; MI = myocardial infarction.

* Any one of the conditions listed places a person in the associated comorbid condition level and its life expectancy at age 68, 74, or 78 y. Conditions included are those that affect life expectancy. See Tables 2 to 8 of the Supplement for life expectancies at other ages. See Table 9 of the Supplement for International Classification of Diseases, Ninth Revision, Clinical Modification, codes for the conditions.

† HR for all-cause mortality compared with no comorbid conditions for the conditions included in each level.
(and life expectancy) and had been screened regularly before age 74 years resulted in 79 to 96 false-positive test results (range across models) and 0.5 to 0.8 overdiagnosed cancer cases (Table 3). On the benefits side, screening at age 74 years resulted in 0.7 to 0.9 CDPs and 5.8 to 7.6 LYGs, corresponding to 132 to 173 women who need to be screened to gain 1 life-year.

Screening 1000 women aged 76 years or older for breast cancer yields increased harms and decreased benefits. Specifically, 146 to 198 women needed to be screened at age 76 years to gain 1 life-year. The balance of harms and benefits for prostate and colorectal cancer screening were mostly similar except for the rates of overdiagnosis, which were orders of magnitude (15 to ≥100 times, depending on the model) greater for prostate cancer versus breast or colorectal cancer screening.

### Screening by Comorbid Condition Level

In persons with no comorbid conditions (that is, persons with longer-than-average life expectancy), screening 1000 regularly screened women aged 74 years resulted in fewer overdiagnosed breast cancer cases (0.3 to 0.5) and more CDPs (0.8 to 1.0) and LYGs (6.6 to 8.5) compared with women the same age with average health. The NNS/LYG of 117 to 150 was lower than that for the average-health population (Tables 2 to 8 of the Supplement). In fact, women with no comorbid conditions could be screened until age 76 to 78 years and still yield an NNS/LYG similar to screening until age 74 years in the average-health population (Figures 1 and 2). A similar median age of 76 years was obtained for prostate and colorectal cancer screening (Tables 2 to 8 of the Supplement and Figure 1).

For the group with mild comorbid conditions, screening for all 3 cancer sites at age 74 years yielded harms and benefits similar to screening the average-health population (Tables 2 to 8 of the Supplement and Figures 1 and 2). In persons with moderate comorbid conditions, screening at age 74 years was considerably less favorable than in the average-health population at that age: Overdiagnosed cancer cases were up to 15% greater, whereas CDPs and LYGs were as much as 20% lower (Tables 2 to 8 of the Supplement). Screening persons with moderate comorbid conditions at a median age of 72 years (range, 68 to 74 years) resulted in harms and benefits similar to screening the average-health population at age 74 years (Tables 2 to 8 of the Supplement and Figures 1 and 2). Screening persons with severe comorbid conditions for breast cancer at age 74 years resulted in fewer overdiagnosed breast cancer cases (0.3 to 0.4) and more CDPs (6.2 to 6.5) and LYGs (161 to 162) compared with women the same age with average health. The NNS/LYG of 117 to 150 was lower than that for the average-health population (Tables 2 to 8 of the Supplement). In fact, women with no comorbid conditions could be screened until age 76 to 78 years and still yield an NNS/LYG similar to screening until age 74 years in the average-health population (Figures 1 and 2). A similar median age of 76 years was obtained for prostate and colorectal cancer screening (Tables 2 to 8 of the Supplement and Figure 1).

### Table 3. Benefits and Harms of Screening 1000 Regularly Screened Persons at Age 74 or 76 Years* With Average Health, by Cancer Site and Model

<table>
<thead>
<tr>
<th>Age at Screening, by Cancer Site and Model</th>
<th>Harm†</th>
<th>Incremental Benefit†</th>
<th>Balance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>False-Positive Test Results, n</td>
<td>Overdiagnosed Cancer Cases, n</td>
<td>LYS Gained, n‡</td>
</tr>
<tr>
<td>Breast cancer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MISCAN-Fadia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>74 y</td>
<td>79</td>
<td>0.8</td>
<td>7.6</td>
</tr>
<tr>
<td>76 y</td>
<td>77</td>
<td>1.0</td>
<td>6.9</td>
</tr>
<tr>
<td>G-E model</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>74 y</td>
<td>96</td>
<td>0.5</td>
<td>5.8</td>
</tr>
<tr>
<td>76 y</td>
<td>96</td>
<td>0.6</td>
<td>5.1</td>
</tr>
<tr>
<td>Prostate cancer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MISCAN-Prostate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>74 y</td>
<td>116</td>
<td>19.7</td>
<td>6.6</td>
</tr>
<tr>
<td>76 y</td>
<td>136</td>
<td>24.9</td>
<td>6.3</td>
</tr>
<tr>
<td>FHCRC prostate cancer model</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>74 y</td>
<td>242</td>
<td>14.5</td>
<td>6.1</td>
</tr>
<tr>
<td>76 y</td>
<td>268</td>
<td>16.2</td>
<td>5.1</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MISCAN-Colon</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>74 y</td>
<td>39</td>
<td>0.3</td>
<td>6.2</td>
</tr>
<tr>
<td>75 y</td>
<td>39</td>
<td>0.4</td>
<td>5.5</td>
</tr>
<tr>
<td>CRC-SPIN</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>74 y</td>
<td>37</td>
<td>0.0</td>
<td>4.4</td>
</tr>
<tr>
<td>75 y</td>
<td>37</td>
<td>0.0</td>
<td>3.7</td>
</tr>
<tr>
<td>SimCRC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>74 y</td>
<td>38</td>
<td>0.1</td>
<td>4.9</td>
</tr>
<tr>
<td>75 y</td>
<td>38</td>
<td>0.1</td>
<td>4.3</td>
</tr>
</tbody>
</table>

CDP = cancer deaths prevented; CRC-SPIN = Colorectal Cancer Simulated Population Model for Incidence and Natural History; Fadia = fatal diameter; FHCRC = Fred Hutchinson Cancer Research Center; G-E = Georgetown–Einstein; LY = life-year; MISCAN = Microsimulation Screening Analysis; NNS/CDP = number needed to screen to prevent 1 cancer death; NNS/LYG = number needed to screen to gain 1 life-year; SimCRC = Simulating Colorectal Cancer.

* Age 75 y for colorectal cancer.
† Results per 1000 persons screened according to guidelines (breast and colorectal) or current practice (prostate) since age 50 y.
‡ 1 LY gained per 1000 persons corresponds with 0.4 d gained per person.
years resulted in even more harms (1.3 to 1.9 overdiagnosed cancer cases) and fewer benefits (0.5 to 0.6 CDPs; 3.5 to 4.5 LYGs) (Tables 2 to 8 of the Supplement). In this group, screening at a median age of 66 years (range, 64 to 69 years) provided harms and benefits similar to screening the average-health population at age 74 years (Tables 2 to 8 of the Supplement and Figures 1 and 2).

**Sensitivity Analysis**

If noncancer mortality rates do not converge to average U.S. rates after the 13 years of observed data, persons with moderate and severe comorbid conditions could stop screening at even younger ages to have harms and benefits similar to screening the average-health population at age 74 years.

For colonoscopy, screening to age 70 years for those with no, mild, or moderate comorbid conditions provided harms and benefits similar to screening the average-health population at age 70 years (the last colonoscopy screening age for a person regularly screened since age 50 years); among those with severe comorbid conditions, the balance is similar at age 60 years (Tables 10 to 12 of the Supplement).

**DISCUSSION**

To our knowledge, this is the first study to use collaborative modeling to evaluate screening across 3 cancer sites. It systematically quantifies the balance of benefits and harms of screening older persons for breast, prostate, and colorectal cancer by comorbid condition level. The results are robust across models and cancer sites and indicate that comorbid conditions affect screening benefits and harms and decisions about ages of screening cessation. These outcomes can directly inform individualized decisions about screening. Approximately 70% of the current U.S. population aged 74 years has none of the comorbid conditions noted in recent analyses to influence life expectancy (20). Our results suggest that this group could continue to be screened until age 76 years and still have the same balance of benefits and harms expected from screening the average-health population until age 74 years. However, the 13% of the U.S. population aged 65 to 74 years with severe comorbid conditions should stop screening at age 66 years to have the same balance of benefits and harms as seen among average-health groups having screening from ages 50 to 74 years.
Our findings are consistent with and extend previous research addressing the upper age limits for cancer screening. For instance, Walter and Covinsky (7) found that screening for breast, cervical, and colorectal cancer until about age 60 years for persons in the lower quartile of population life expectancy has the same number needed to screen to prevent 1 cancer death as those with the median life expectancy at age 75 years. They also estimated that screening could be continued to age 85 years for those in the upper quartile of life expectancy (7). This range is consistent with but wider than our model projections of 66 to 76 years based on the NNS/LYG. When we used CDP rather than LYG, our ranges were closer to those of Walter and Covinsky, although our maximal upper age limit was still lower because we considered persons without comorbid conditions (70% of the population) and they used the upper quartile (25%) of life expectancy.

A recent analysis that examined time lag to benefit after screening for breast and colorectal cancer suggests that screening for breast and colorectal cancer is most appropriate for patients with a life expectancy greater than 10 years (23). However, that study and others (6, 7, 24–29) provide little guidance on applying this framework in clinical practice, leaving it to clinical judgment to estimate life expectancy and individualize screening decisions. Several studies have investigated the relationship between comorbid conditions and life expectancy (30–32) but do not address the question of how this relationship influences cancer screening. To date, only 2 analyses have directly related comorbid conditions to cancer screening recommendations. One focused only on diabetes-related comorbid conditions and colorectal cancer screening (33), and the other examined cardiovascular disease and breast screening (6). Our analysis is a multimodel collaborative analysis of 3 major cancer sites and includes a wider range of comorbid conditions than considered previously.

There is considerable debate about the value of PSA screening. The USPSTF recently concluded that PSA screening results in little or no reduction in prostate cancer–specific mortality rates while leading to substantial overdiagnosis of prostate cancer. On the basis of these findings, the USPSTF recommends against routine prostate cancer screening. However, similar to other national guidelines panels (such as the American Cancer Society, American Urological Association, and American College of Physicians), the USPSTF recognized a role for screening in the context of appropriate patient–physician decision making (34–37). Our modeling study provides clinicians with valuable information for such shared decision making. Recent modeling studies indicate that overdiagnosis and unnecessary biopsies could be reduced by cessation of prostate cancer screening at age 69 years, increasing the PSA threshold for biopsy referral for men older than this age, or restricting further screening to men at the low comorbid condition level (17, 18). Our findings confirm these results and underscore that overdiagnosed cancer cases detected with PSA screening are orders of magnitude greater than for breast or colorectal cancer screening. If personalized PSA screening strategies achieve a sufficiently favorable balance of outcomes, our results advocate tailoring screening...
cessation according to comorbid condition–based life expectancy.

Our results provide clinicians with data for use in informed decision-making discussions about who may consider continuing screening and for how long. For example, if a clinician is meeting with a regularly screened patient aged 70 years with chronic obstructive pulmonary disease, our results indicate that this person is in the severe comorbid condition level and, depending on patient preferences, the benefits of screening may no longer outweigh the potential harms. However, a person aged 76 years with no comorbid conditions may consider having another screening test. The final decision about screening should depend on individual patient preferences. Prevention of death from cancer is one outcome to consider, but some patients may be more concerned with influence on other outcomes, such as quality of life or functional independence. Persons may also prefer to have cancer detected at earlier stages when less intensive treatment may be needed, compared with somewhat later diagnosis and more aggressive therapy, even if survival is unchanged. In such a situation, for example, a healthy patient may choose to continue breast cancer screening up to age 80 years, where the mortality benefit is small but early detection can find the cancer early when less aggressive treatment is required.

The fact that comorbid condition–specific conclusions about age-specific benefits and harms differ meaningfully from those included in clinical guidelines highlights the tension between the need to provide public health recommendations for the general population and the potential advantages of using a more personalized approach. Our suggested approach of continuing screening in healthy persons and earlier cessation in the sickest persons does not increase the number of screens required in the population but rather leads to a more efficient allocation of resources, increasing the benefit and decreasing the harms to the growing older population (38). The age-, sex-, and comorbid condition–specific life expectancies used for these analyses also provide clinicians and the general screening-eligible population with a foundation for discussing preferences for benefits and harms, facilitating individual decision making.

The testing intervals for colorectal and breast cancer were chosen according to the latest USPSTF guidelines, but our conclusions can be generalized to other intervals. The screening cessation ages are determined in relation to screening the average-health population up to age 74 years. When choosing a different screening interval, such as an annual mammography for breast cancer, the benefits and harms will be different for screening the average-health population at age 74 years. The benefits and harms by comorbid condition level will change accordingly, such that the optimal screening cessation age by comorbid condition remains the same.

Despite the innovation and strengths of our approach, there are several caveats that should be considered in evaluating our results. First, we chose the balance of harms and benefits as our primary metric. We did not explicitly consider complications from screening and diagnostic follow-up as harms, but these would be proportional to the number of false-positive screening test results. Costs per quality-adjusted life-year gained are another common metric used in many countries, but this is not widely accepted in the United States (39–43). Second, we assumed that comorbid conditions influenced only life expectancy and not cancer risk or biology. Health conditions, such as diabetes, are known to be associated with obesity and other lifestyle factors (44) that, in turn, can be associated with improved mammography performance (45) and increased breast (46–48) or reduced prostate (49) cancer risk. Adverse events of screening, such as perforations with colonoscopy, are also associated with comorbid conditions (50). In the future, it will be important to extend our work to capture the known effect of specific comorbid conditions on other model variables. For now, competing noncancer mortality is the single most germane variable in screening decisions for the oldest age groups (27). Third, we only estimated harms and benefits of screening by comorbid conditions for persons aged 66 years or older because life expectancy estimates by comorbid condition were obtained from Surveillance, Epidemiology, and End Results–Medicare data.

Next, we only considered persons regularly screened since age 50 years to demonstrate how current screening recommendations could be adapted on the basis of comorbid conditions. In general, cessation ages are higher in persons who are unscreened or have skipped previous screening rounds because they have a greater risk for prevalent cancer. Further, the models used life tables based on noncancer cases and therefore do not include cancer-specific mortality rates for cancer other than the one targeted by screening. This underestimates the true rate of competing other-cause mortality rates and therefore the harm–benefit ratios but does not affect our internal comparisons of comorbid condition groups to the average-health population. We did not consider situations in which the comorbid condition level decreased (such as from severe to moderate level) after the age of screening cessation. Given the chronic nature of the comorbid conditions in older ages, this is a reasonable assumption.

Overall, the results across models and cancer sites were very robust and strongly suggest that the age of screening cessation based on comorbid conditions varies by nearly a 10-year interval around the age cut point of 74 years included in current recommendations on breast and colorectal cancer screening. Our data on common chronic health conditions and their associated comorbid condition level, together with model projections of screening benefits and harms at each of these comorbid condition levels, can inform discussions between providers and their older patients about personalizing decisions regarding when to stop cancer screening.
From Erasmus University Medical Center, Rotterdam, the Netherlands; Fred Hutchinson Cancer Research Center and Group Health Research Institute, Seattle, Washington; National Cancer Institute, Bethesda, Maryland; Albert Einstein College of Medicine, Yeshiva University, Bronx, New York; Massachusetts General Hospital, Boston, Massachusetts; University of Minnesota, Minneapolis, Minnesota; Memorial Sloan Kettering Cancer Center, New York, New York; and Georgetown University, Washington, DC.

Disclaimer: The content is solely the responsibility of the authors and does not represent the official views of the National Institutes of Health, the National Cancer Institute, or the Centers for Disease Control and Prevention.

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Appendix Figure. Observed and simulated cancer incidence rates, by calendar year of diagnosis (breast and prostate cancer) or age at diagnosis (colorectal cancer).

Panels show age-standardized breast cancer incidence rates per 100,000 women aged 30 to 79 y for MISCAN-Fadia and G-E models, age-standardized prostate cancer incidence rates per 100,000 men aged 50 to 84 y for MISCAN-Prostate and FHCRC models, and colorectal incidence rates per 100,000 persons for years 1975 to 1979 for MISCAN-Colon, CRC-SPIN, and SimCRC models. CRC-SPIN = Colorectal Cancer Simulated Population Model for Incidence and Natural History; Fadia = fatal diameter; FHCRC = Fred Hutchinson Cancer Research Center; G-E = Georgetown–Einstein; MISCAN = Microsimulation Screening Analysis; SEER = Surveillance, Epidemiology, and End Results; SimCRC = Simulating Colorectal Cancer.