

# Individualizing Cancer Screening in Older Adults: A Narrative Review and Framework for Future Research

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Older adults often have multiple chronic conditions that may decrease additional life expectancy. Research evaluating the benefits and harms of screening must include consideration of competing morbidities and patient heterogeneity (beyond age), potentially increased harms of screening, and patient preferences. Other areas in need of additional research include the lack of evidence for older adults on the harms of screening tests; the overdiagnosis of disease; the burden of disease labeling; the effects of inaccurate test results; the harms of disease treatment; and harms related to prioritization of healthcare (e.g., for a particular patient, lifestyle counseling may be more important than screening). Nontraditional outcomes, such as the effects on family caregivers, are also relevant. Studies comparing trajectories of quality-adjusted survival with and without screening to assess net benefit are typically lacking. There is little evidence on the preferences of older adults for deciding whether to be screened, the process of being screened, and the health states associated with being or not being screened. To enhance the quality and quantity of evidence, older adults need to be enrolled in screening trials and clinical studies. Measures of functional status and health-related quality of life (HRQL) need to be included in trials, registries, and cohort studies. This article addresses these challenges, and presents a framework for what research is needed to better inform screening decisions in older adults.

**KEY WORDS:** older adults; cancer screening; patient preferences.

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In the last 4 years, the United States Preventive Services Task Force (USPSTF) has issued recommendations for individualizing screening decisions for colon, breast, and cervical cancer in older adults, noting the importance of considering both quantity and quality of life in screening

decisions. In addition, the Task Force rating system has been revised to more explicitly reflect the balance of benefits and harms, utilizing “I” ratings (“Evidence that the service is effective is lacking, of poor quality, or conflicting and the balance of benefits and harms cannot be determined.”) and “C” ratings (“Clinicians may provide this service to selected patients depending on individual circumstances. However, for most individuals without signs or symptoms, there is likely to be only a small benefit from this service.”).<sup>1–3</sup> The Task Force has recently outlined a robust approach to geriatric topics, including “addressing the outcomes that are important to patients (including nontraditional outcomes, such as effect on caregivers),” as well as patient reported outcomes such as health related quality of life (HRQL) and function<sup>4</sup> that we will apply to cancer screening recommendations in older adults; reviewing the existing evidence for increased harms; the role of nontraditional outcomes; patient preferences in making screening recommendations; and presenting a framework for future research needs to better inform screening decisions (Fig. 1).

## CLINICAL EXAMPLES ILLUSTRATING CANCER SCREENING CHALLENGES IN OLDER ADULTS

Mr. A has a history of falls, mild cognitive impairment, and had a recent heart attack shortly after his wife died. He is 72 years old and lives alone; his only daughter lives 100 miles away. Today, he presents for an annual check-up; you note that he never had colorectal cancer screening. Although he qualifies for screening by age, his recent heart attack, falls, and cognitive impairment make you hesitate to mention this.

Mrs. B is a 74-year-old woman with congestive heart failure (CHF) and Parkinson disease. She uses a quad cane to ambulate, but is largely homebound due to poor mobility. Today she reminds you that it is time to order her mammogram, stating, “The last thing I want to die from is breast cancer.”

In each scenario, an older patient with chronic illnesses and functional impairment “qualifies” for cancer screening by published guidelines. However, you wonder if screening is in the patient’s best interest. Would Mr. A’s heart disease

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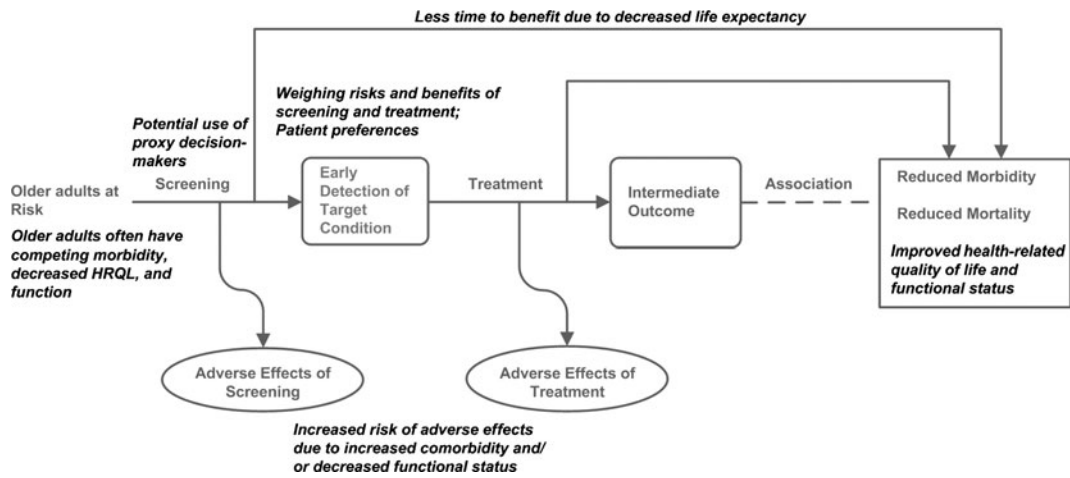


Figure 1. Incorporating considerations important to older adults into the USPSTF screening framework.

and memory problems put him at high risk for complications from colonoscopy? Could Mrs. B tolerate lumpectomy and hormone therapy in light her of CHF and Parkinson disease? How would her quality of life be impacted if you ignored her preference for screening? These questions highlight the complexity of screening decisions in patients with functional impairment and chronic illnesses, and the need to incorporate information on HRQL and function into screening decisions.

### CHALLENGES TO DEVELOPING SCREENING GUIDELINES

While it might be simpler to try to define age “cut-offs” for screening, this approach could underemphasize the value of screening for a hearty 80-year-old, or overemphasize the value of screening for the frail 60-year-old. A more comprehensive framework encompassing chronic illness, functional status, and HRQL must consider three major challenges: 1) patient heterogeneity; 2) appropriate patient-important benefits and harms; and 3) patient preferences.

#### Patient Heterogeneity

When considering screening adults at age 50 for colon cancer, most will be in good health, with a life expectancy of 20 years or more. When considering screening adults at age 80 for colon cancer, there will be marked heterogeneity in function and comorbidities, and life expectancy can range from months to over 10 years.<sup>5</sup> Older patients also follow varying health trajectories,<sup>6</sup> complicating prognostication. And older patients often have lower education level, language difficulties, decreased hearing, cognitive decline, and other challenges that make it more difficult to help them understand the magnitude of “net benefit” from screening and participate in shared decision making around screening.<sup>7</sup> A recent systematic review of prognostic

indices for mortality in older adults concluded that the currently available non-disease specific indices have insufficient evidence to support their use in general practice.<sup>8,9</sup> However, combining objective measures of prognosis (see e-prognosis.org for validated indices) with clinical judgment results in more accurate estimations of prognosis than either alone.<sup>10</sup>

#### Appropriate Patient-Important Benefits and Harms

It is a common assumption that prevention in general—and screening in particular—is always in the patient’s best interest.<sup>11</sup> In young healthy populations, benefits of early cancer detection and treatment are considered to outweigh harms. In older populations, mortality benefits may be less than for younger counterparts, screening tests themselves may pose a greater threat to health, and comorbid status may make treatment options untenable.

Screening harms that are more prevalent in older adults include those of the test itself, disease labeling, inaccurate test results, overdiagnosis of disease (finding a cancer that was unlikely to become clinically evident during the patient’s lifetime in the absence of screening), harms of treatment, and harms related to prioritization of medical care.

We must also recognize the constraints of current research to guide our discussion. First, many screening studies do not even consider harms of screening, so we do not know their extent. Second, older adults are underrepresented in screening trials, and subgroups by age are rarely reported, so harms specific to this population remain underappreciated. Third, most randomized trials are efficacy trials in all ages; subjects are chosen for lack of competing comorbidities and ability to follow screening protocols, and may not be similar to patients who present to clinicians for screening. Older adults who join trials likely have fewer screening complications than those in real-world practice.

Fourth, values and preferences change as we age, and these receive little consideration in most screening studies. These limitations increase the challenge of making screening recommendations in older adults with multiple chronic illnesses, functional impairments, and shorter life expectancy.

**Harms of Screening Tests.** Harms of screening tests relevant to older adults include those related to preparing for the test (discomfort or side effects of prep), testing harms (colon perforation, fatigue from a long testing day), and harms of procedure after-care (anesthesia side effects). A review of adverse events associated with colonoscopy found that most studies were retrospective reviews of immediate complications. A prospective study including a patient questionnaire administered 10 days after colonoscopy identified several additional complications, suggesting that record review may underestimate complication rates.<sup>1,12</sup> In the 2008 USPSTF review of colorectal screening, two of 16 studies suggested increased complications from colonoscopy (e.g., perforation, major bleeding) in persons 60 and older.<sup>13</sup> However, only half of the studies (9/16) included older adults; most did not provide outcomes by age subgroups and did not assess harms as subjects approached the extremes of age or had multiple comorbidities, declining function, and diminished HRQL.<sup>14</sup>

**Harms of Inaccurate Test Results.** The screening goal in an asymptomatic population is to detect disease (true positives) at a preclinical stage when it can be cured. But a true positive result is not always good. An 80-year-old man with a high prostate-specific antigen (PSA) and biopsy-proven prostate cancer (true positive) may have low-grade disease that would never have become clinically apparent, yet experience significant distress by being labeled with prostate cancer, and undergo unnecessary treatments. This harm of overdiagnosis is largely unstudied and difficult to quantify at an individual level. Recent cancer screening recommendations by the USPSTF have more explicitly tried to estimate rates of overdiagnosis through systematic review<sup>2,15</sup> or modeling, with an increased risk for overdiagnosis in breast cancer as women's age increases suggested through modeling.<sup>16</sup> Because life expectancy is limited in older adults, overdiagnosis is more likely and greatly needs further study.

The risks of false positive screening tests have been well described elsewhere,<sup>17</sup> and range from emotional distress, to lost work days, to post-biopsy infection and other complications of unnecessary follow-up. However, these risks have rarely been specifically described for older adults, so we can only speculate that complications might be worse in this population.

The main risk of a false negative screening is missed disease that could impact mortality. Screening for cervical

cancer illustrates the potential for higher false negative rates in older women; the transition zone moves further up the cervical canal, making a higher false negative rate possible. In women for whom cervical screening is recommended beyond age 65 (inadequate or no prior screening, history of cervical cancer) this could be important, but test characteristics are so poorly described that no firm conclusions can be drawn.<sup>18</sup> Even so, false negative results may be less critical in older adults with multiple competing comorbidities or if the disease has a more indolent natural history.

**Harms of Disease Treatment.** The impact of potential harms of treatment on overall health and function are of specific concern in older adults, when all organ systems have less reserve (a concept known as homeostenosis). For example, urinary urgency due to prostate resection may be inconvenient in a middle-aged man, but may cause falls and hip fracture in an older man trying to make it to the bathroom repeatedly during the night. Though a detailed review of cancer treatment harms is beyond the scope of this manuscript, it is important to recognize that for older adults with limited life expectancy, up front harms of treatment lend greater relative weight than downstream benefits of treatment. In an older Veterans Affairs population, Walter and colleagues found that 41 % of patients with severe comorbidity and life expectancies less than 5 years were screened for colon cancer, despite the low probability that they would receive benefit from screening.<sup>19</sup> Although not specifically discussed, these people would be expected to have the same (or greater) risk of complications, such as colonic perforation. So these older adults are likely to experience only harm, without benefit, from such screening (since it takes about 7 years for mortality benefits from colorectal screening to accrue).<sup>1</sup> Finally, many randomized trials of cancer treatment exclude older adults, so we are again left with inadequate data to make recommendations about treatment harms. And we risk overestimating benefit and underestimating harms when extrapolating from studies of younger people (similar to chronic-disease management, where, for example, recent data show that tight HbA1C control causes increased harm and less benefit in older people).<sup>20</sup>

**Harms in Healthcare Prioritization.** Older adults are seldom free of chronic illness; at least 65 % of people over 65 have multiple chronic conditions.<sup>21</sup> For most, primary care visits are crowded with disease management, lifestyle counseling, setting goals of care, and preventive services. Clinicians striving to practice evidence-based medicine attempt to follow guidelines for chronic-illness management, ensure well being and safety, and provide appropriate screening. In a constrained primary care environment, services must often be prioritized.<sup>6</sup> Little research is available to help clinicians with this task—is it

more important to discuss home safety or order colon cancer screening? Is it more important to assess caregiver burden or order a mammogram? One could argue that screening tasks are easier and more familiar to many clinicians—and may be the chosen task, even if they should not be the highest priority for that patient encounter.

Taking another perspective, there is evidence that behavior change can provide substantial life expectancy gains even in an older population. A recent USPSTF review found that counseling to improve diet or exercise changed health behaviors and was associated with small improvements in adiposity, blood pressure, and lipid levels at all ages.<sup>22</sup> Yates and colleagues found that men with a healthy lifestyle at age 70 had a better chance of reaching 90 years than those with a less healthy lifestyle (54 % if a man regularly exercised, didn't smoke, and didn't have obesity, diabetes or hypertension, versus 22–36 % if two factors were present and 4 % if all five were).<sup>23</sup> Khaw and colleagues studied exercise, moderate alcohol, eating enough fruits and vegetables, and not smoking and found that those who practiced all four compared to none added 14 years to their life expectancy. The impact of health behaviors on mortality was greater for those over 65 years than for those under 65.<sup>24</sup> These numbers are convincingly strong, and lend support to the recommendation that clinicians prioritize counseling about healthy lifestyle over cancer screening.

### The Importance of Assessing Net Benefit—Utilizing Nontraditional Outcomes to Assess Screening Effectiveness

Trade-offs between harms and longevity are well known in oncology and should be considered in all cancer screening. Given treatment harms, are the additional months of survival worthwhile to patients? As an example, Litwin and Talcott note that for patients with early-stage prostate cancer, the potential for impaired sexual, urinary, and bowel function is substantial, and may offset modest longevity benefits.<sup>25</sup>

Quality-adjusted survival—how long people live and how well they live while alive—is arguably the most important outcome of the provision of healthcare services.<sup>26–29</sup> Ideally, HRQL assessment would include preference-based measures providing a single summary HRQL score, thereby integrating all effects on mortality and morbidity. Preference-based HRQL measures use a conventional scale, with dead (the lack of health status)=0.00 and perfect health=1.00. Quality-adjusted life years (QALYs) estimated using preference-based measures are a prominent method for estimating quality-adjusted survival. In a simulation study, Stout and colleagues illustrate this approach in an evaluation of alternative mammography

screening programs.<sup>30</sup> More details about HRQL and which measures are good measures in older adults can be found in a companion article (Feeny DH, Eckstrom EN, Whitlock EP, Perdue LA. A primer for systematic reviewers on the measurement of functional status and health-related quality of life in older adults. In preparation). There is little evidence on the HRQL effects of screening, and even less evidence comparing HRQL associated with screening and not screening. People's personal ratings of their HRQL can vary widely based on their chronic illnesses, and don't always match their physician's perception.<sup>31</sup> Further research on the impact of patient-reported HRQL could critically inform discussions with older adults about their screening decisions.

### Considering Patients' Preferences about Screening

Early in the development of preventive services research, little attention was paid to patient preferences for screening. However, the population has aged and become more heterogeneous, screening complexities have increased, and in today's environment, patient preferences must play a critical role in screening decisions. In 2001, the USPSTF updated their grading recommendations framework, assigning a "C" recommendation to services thought to have small net population benefit, but where the net benefit might be larger for individual patients with personal preferences that differed from those of the panel.<sup>32</sup> The USPSTF highlighted that all "C" decisions are "likely to be sensitive to individual patient preferences."<sup>33,34</sup>

The Clinical Practice Subcommittee from the Program for All-Inclusive Care of the Elderly (PACE) offers a framework to address patient preferences about screening. PACE's program treats frail individuals who meet their states' definition of nursing-facility-eligible; median life expectancy for participants is 4 years. This framework is meant to help participants clarify their preferences for screening based on what is most important to them—longevity, function, or palliation. These three "trajectories" map approximately to life expectancies of 5–7 years (longevity trajectory), 2–5 years (functional trajectory), and 2 years or less (palliative trajectory). So for example, if a patient chooses the longevity trajectory and had not had a mammogram, one would be recommended. A mammogram would not be recommended for a person on the palliative trajectory. Though patient preferences might not always match their life expectancy, this type of framework approach could help clinicians and patients focus on the highest priority tasks for individual preferences (Kinosian B., personal communication).

However, older patients may not wish to base decisions on their additional life expectancy. Lewis and colleagues



conducted interviews with 116 retirement community residents 70 years of age or older. Of these, 62 % believed their life expectancy was not important for decision making; 48 % preferred not to discuss life expectancy. Most participants reported that they would continue screening throughout their lives, and 43 % would consider screening even if their doctor recommended against it. Only 13 % thought they would not live long enough to benefit from cancer screening. The authors concluded that this group held positive attitudes about cancer screening, and may have had unrealistic expectations.<sup>11</sup> In another analysis of this group, 64 % of subjects felt their physicians could not correctly estimate their life expectancy. Sixty-six percent wanted their physicians to talk with them about life expectancy, believing such discussions could help with future planning, maintain open communication, and provide knowledge about their medical conditions.<sup>35</sup> These conflicting results speak to the complexity of individualizing cancer screening discussions.

In semi-structured interviews with 23 family caregivers of women with dementia, caregivers of women with mild and moderate dementia valued screening mammograms, and planned to continue screening regardless of dementia stage. In contrast, caregivers of women with severe dementia did not consider mammograms important. Caregivers' views on appropriate treatment of breast cancer varied widely, except in the case of severe dementia, in which case a palliative approach was consistently preferred.<sup>36</sup>

One might ask "Can older adults understand screening complexities in the context of multi-morbid conditions?" Fried and colleagues asked a group of older adults about their treatment goals and perceptions about whether their illnesses and treatments interacted with each other. Patients were largely unaware that treating one condition could worsen another, and held misconceptions about their survival, preservation of function, and symptom relief. However, many had experienced adverse medication events and could use this experience to understand competing outcomes, enabling them to state a preference for the treatment that would allow the most desired outcome.<sup>37</sup> These few studies on patient preferences highlight the potential lack of awareness of screening effectiveness, as well as the potential discrepancy between their preferences and their healthcare provider's recommendations. There is little research to guide busy primary care providers and practices in effectively performing cancer screening. In a 2007 study, fewer than 10 % of physicians used a comprehensive set of systems strategies to support cancer screening.<sup>38</sup>

To improve patient understanding of screening value, decision aids have been developed to assist older adults in breast cancer and prostate cancer decision making. Mathieu and colleagues developed a decision aid outlining potential risks of breast cancer screening, using event rates per 1,000 women and including the possibility of resultant over-

detection and over-treatment. In this study, clearly presenting potential risks and benefits of mammography to 70-year-old women who have been regularly screened did not reduce their intentions to continue (95 % of women randomized to read the decision aid remained positive toward screening).<sup>39</sup> Results from these studies may imply that older adults believe screening is valuable and a marker for good quality of care. Indeed, that has been the public health message for decades, though it is largely based on screening outcomes in younger populations.

Yet another challenge to considering patient preferences is that older adults often involve proxy decision makers, such as a spouse or child—even if they have decisional capacity themselves. A systematic review of the accuracy of surrogate decision makers analyzed 19,526 patient-surrogate paired responses and found that patient-designated and next-of-kin surrogates incorrectly predict end-of-life preferences one-third of the time (sometimes surrogates recommended interventions the patient did not want, and sometimes the surrogate recommended withholding patient-preferred interventions).<sup>39</sup> Thus, lengthy conversations must often occur to ensure all engaged parties have a similar understanding and can reach a consensus decision.

## SUMMARY AND RECOMMENDATIONS FOR FUTURE RESEARCH

In summary, many challenges complicate cancer screening discussions in older adults—lack of evidence for screening effectiveness and harms, limited understanding of how screening ultimately impacts HRQL for older people, and limited understanding of patient preferences and goals, and how these might affect cancer screening decisions. In both our patient scenarios, Mr. A and Mrs. B, life expectancy, functional and cognitive impairment, patient preferences, goals of care, possible harms of screening, and attitudes toward screening should be considered with the patient in making shared screening decisions. Future research should look at large longitudinal population studies such as registries, cohort studies, or studies based on longitudinal medical records to better understand these issues. The CaPSURE database is a longitudinal, observational study of over 13,800 patients with all stages of biopsy-proven prostate cancer.<sup>40</sup> Publications from this registry confirm that age at diagnosis, time from treatment and primary treatment were significant predictors of HRQL in all domains; treatment had a greater impact on disease specific than general HRQL; and all treatments adversely affected urinary and sexual function.<sup>41</sup> This is an example of how using large registries to elucidate harms of treatment helps ensure that those who would have been rejected from a randomized controlled trial contribute data to harms assessments.<sup>42–44</sup> Further, focused HRQL studies will be required

to provide evidence on the HRQL of the temporary health states associated with screening. Because randomized controlled trials of screening tests are unlikely due to costs and preestablished preferences around screening, carefully controlled observational studies of screening need to compare similar older adults who continue to undergo screening to those who don't, to determine screening's true benefits. Harms (and benefits) of screening need to be expanded to HRQL outcomes. Comparative effectiveness studies need to help prioritize screening relative to lifestyle counseling, chronic illness management, and other patient care needs. Studies need to address better ways to imbed screening in newer person-centered, team-oriented health care. And much more work needs to be done on patient preferences, patient educational tools, and communication techniques to enhance the shared decision-making process for clinicians and their older patients.<sup>42</sup>

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