CLINICAL GUIDELINE

Screening for Cancer: Advice for High-Value Care From the American College of Physicians

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Background: Cancer screening is one approach to reducing cancer-related morbidity and mortality rates. Screening strategies vary in intensity. Higher-intensity strategies are not necessarily higher value. High-value strategies provide a degree of benefits that clearly justifies the harms and costs incurred; low-value screening provides limited or no benefits to justify the harms and costs. When cancer screening leads to benefits, an optimal intensity of screening maximizes value. Some aspects of screening practices, especially overuse and underuse, are low value.

Methods: Screening strategies for asymptomatic, average-risk adults for 5 common types of cancer were evaluated by reviewing clinical guidelines and evidence syntheses from the American College of Physicians (ACP), U.S. Preventive Services Task Force, American Academy of Family Physicians, American Cancer Society, American Congress of Obstetricians and Gynecologists, American Gastroenterological Association, and American Urological Association. "High value" was defined as the lowest screening intensity threshold at which organizations agree about screening recommendations for each type of cancer and "low value" as agreement about not recommending overly intensive screening strategies. This information is supplemented with additional findings from randomized, controlled trials; modeling studies; and studies of costs or resource use, including information found in the National Cancer Institute's Physician Data Query and UpToDate.

The ACP provides high-value care screening advice for 5 common types of cancer; the specifics are outlined in this article. The ACP strongly encourages clinicians to adopt a cancer screening strategy that focuses on reaching all eligible persons with these high-value screening options while reducing overly intensive, low-value screening.

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Cancer is a major health problem in the United States, causing 1 in 4 deaths (1). One approach to reducing cancer morbidity and mortality rates is screening. However, even full implementation of effective screening strategies would not eliminate cancer deaths.

Screening strategies vary in what we call "intensity" (2). Higher-intensity strategies screen broader populations more frequently or with more sensitive screening tests. Screening strategies also vary in value. As defined by the American College of Physicians (ACP) (3–5), value is determined by an intervention's health benefits versus its harms and costs. High-value strategies return large health benefits for the harms and costs incurred; low-value strategies return disproportionately small benefits for the harms and costs. Although high-intensity strategies aim to maximize cancer detection, value is optimized by finding the level of intensity that best balances benefits with harms and costs (2).

Regardless of value, cancer screening is popular among the U.S. public and is done more frequently than in other countries (6–8). Some aspects of our screening practices, especially overuse and underuse, are low value. A screening program is considered low value when persons in whom the benefits clearly outweigh the harms and costs are not being screened intensively enough (9, 10) or when persons are being screened overly intensively (11).

Improving cancer screening value requires overcoming 3 main challenges: increasing access to high-value screening for populations without adequate access to care; increasing high-value screening in persons with adequate care access; and reducing use of low-value screening strategies in everyone, with or without adequate access. This article focuses on the latter 2 challenges. It is the second of 2 papers commissioned by the ACP to define and encourage high-value, cost-conscious cancer screening. We note agreement among various organizations on the lowest-intensity screening threshold recommended for "average-risk individuals" for each type of cancer (high value) and whether they recommend against or do not recommend for more intensive screening strategies (low value). We provide information on use of overly intensive, low-value screening and end with evidence suggesting future directions to reduce overly intensive screening that may enhance cancer screening value.

See also:

Related article 712
Summary for Patients I-25

* This paper, authored by Timothy J. Wilt, MD, MPH; Russell P. Harris, MD, MPH; and Amir Qaseem, MD, PhD, MHA, was developed for the High Value Care Task Force of the American College of Physicians (ACP). Contributor committee members include Amir Qaseem, MD, PhD, MHA (*Chair*); John Biebelhausen, MD, MBA; Sanjay Desai, MD; Lawrence Feinberg, MD; Carrie A. Horwitch, MD, MPH; Linda L. Humphrey, MD, MPH; Robert M. McLean, MD; Tanveer P. Mir, MD; Darilyn V. Moyer, MD; Kelley M. Skeff, MD, PhD; Thomas G. Tape, MD; and Jeffrey Wiese, MD. Approved by the ACP Board of Regents on 15 November 2014.

METHODS

We focused on 5 common types of cancer: breast, cervical, colorectal, ovarian, and prostate. This article is intended to provide advice rather than to serve as a guideline. It is based on a narrative review of clinical guidelines and evidence syntheses from the American College of Physicians (ACP), U.S. Preventive Services Task Force, American Cancer Society, American Academy of Family Physicians, American Congress of Obstetricians and Gynecologists, American Urological Association, and American Gastroenterological Association. Because these organizations usually do not estimate costs in their recommendations, we searched the National Cancer Institute's Physician Data Query system, UpToDate, and modeling studies from the National Cancer Institute's Cancer Intervention and Surveillance Modeling Network for additional evidence from randomized, controlled trials (RCTs) or models of screening effectiveness, as well as national studies of the costs of various screening strategies for our target types of cancer. We searched MEDLINE for articles about the costs and resource use of cancer screening published within the past 5 years (1 January 2009 to 30 June 2014) in the following medical journals: *Annals of Internal Medicine*, *The Journal of the American Medical Association* (*JAMA*), *JAMA Internal Medicine*, *Journal of General Internal Medicine*, *The New England Journal of Medicine*, *BMJ*, *The Lancet*, *Journal of the National Cancer Institute*, *Obstetrics & Gynecology*, and *CA: A Cancer Journal for Clinicians*. We examined reference lists of articles to find further studies.

For each type of cancer, we listed the least intensive screening strategies that all organizations recommend (defined as high-value care) and strategies that organizations either did not recommend or recommended against (defined as low-value care). The ACP used this information to develop high-value care advice statements. We used articles identified previously to suggest future directions that might enhance screening value by reducing overuse of overly intensive screening. Although the ACP High Value Care Task Force does not include evidence about costs in its advice statements, cost is still an important part of the "value framework" developed by the authors (2). We provide examples from national studies about overuse of nonrecommended strategies.

We focus on screening average-risk, asymptomatic adults. We do not address surveillance in patients with previous abnormal screening results or high-risk populations. Our understanding of factors, beyond patient age or a history of cancer in multiple family members or in an immediate family member at an early age, that have both clinically important effects on cancer risk and health outcomes due to screening is limited. Value may differ for persons at higher or lower risk for cancer mortality. Value may also differ based on any individual patient (and physician) weighting of population estimates of benefits, harms, and costs.

This article was reviewed and approved by the High Value Care Task Force, whose members are physicians trained in internal medicine and its subspecialties and experts in evidence synthesis. The Task Force developed the high-value care advice statements on the basis of a narrative review of the literature. At each conference call, all members declared all financial and nonfinancial interests. The target audience for this paper is all clinicians. The target patient population is average-risk, asymptomatic persons.

RESULTS

Breast Cancer

On the basis of RCTs and corresponding modeling studies, all groups recommend mammography screening, or discussions about screening, at least every 2 years for women aged 40 to 74 years (**Table 1** and **Appendix Table 1**, available at www.annals.org) (9, 12–14). No group recommends regular systematic breast self-examination, magnetic resonance imaging (MRI), or tomosynthesis screening for average-risk women. Evidence is insufficient on the benefits of clinical breast examination beyond mammography alone (15). Reasons for not recommending more intensive strategies (such as annual screening, screening younger or older age groups, screening persons of any age with a life expectancy less than 10 years, and screening with more sensitive tests) include concerns that they would lead to few benefits but large increases in harms, such as false-positive screening test results and overdiagnosis and overtreatment of lesions that would never have progressed to cause clinical problems (16–20). Screening costs would also greatly increase (21).

High-value care advice 1: Clinicians should discuss the benefits and harms of screening mammography with average-risk women aged 40 to 49 years and order biennial mammography screening if an informed woman requests it.

High-value care advice 2: Clinicians should encourage biennial mammography screening in average-risk women aged 50 to 74 years.

High-value care advice 3: Clinicians should not screen average-risk women younger than 40 years or aged 75 years or older for breast cancer or screen women of any age with a life expectancy less than 10 years.

High-value care advice 4: Clinicians should not screen average-risk women of any age for breast cancer with MRI or tomosynthesis.

Cervical Cancer

On the basis of strong and consistent observational and modeling studies, all organizations recommend starting screening with cytology every 3 years at age 21 years, regardless of sexual history (**Appendix Table 1** and **Table 1**) (9, 13, 22, 23). At age 30 years, women have the choice of continuing cytology screening every 3 years or cotesting with cytology plus human papillomavirus (HPV) testing every 5 years. For women with previously negative test results, screening can be safely stopped at age 65 years. The reasons for not screening women younger than 21 years or older than 65 years

Table 1. High- and Low-Value Screening Strategies for 5 Types of Cancer*

Cancer Type	Least Intensive Recommended Cancer Screening Strategies (High Value)	Cancer Screening Strategies That Are Not Recommended (Low Value)
Breast	Women aged 40–49 y: Discuss benefits and harms with women in good health, and order screening with mammography every 2 y if a woman requests it Women aged 50–74 y in good health: Encourage mammography every 2 y	Women aged <40 y or ≥75 y and women of any age not in good health and with a life expectancy <10 y: Any screening Women of any age: Annual mammography, MRI, tomosynthesis, or regular systematic breast self-examination
Cervical	Women aged 21–29 y: Cytology testing every 3 y Women aged 30–65 y: Cytology testing every 3 y or cytology and HPV testing every 5 y	Women aged <21 y or >65 y with previous recent negative screening results: Any screening Women of any age without a cervix: Any screening Women aged 21–65 y: Cytology testing more frequently than every 3 y Women aged <30 y: HPV testing Women of any age: Pelvic examination
Colorectal	Adults aged 50–75 y: Encourage 1 of the 4 following strategies: High-sensitivity FOBT or FIT (every year); sigmoidoscopy (every 5 y); combined high-sensitivity FOBT or FIT (every 3 y) plus sigmoidoscopy (every 5 y); or optical colonoscopy (every 10 y)	Adults aged <50 y or >75 y or adults of any age not in good health and with a life expectancy <10 y: Any screening Adults aged 50–74 y: Repeated colonoscopy more frequently than every 10 y or flexible sigmoidoscopy every 5 y if results of previous colonic examination were normal (i.e., without adenomatous polyps) Any age: Interval fecal testing in adults having 10-y screening colonoscopy or more frequently than biennially in adults having 5-y screening flexible sigmoidoscopy
Ovarian	None	Women of any age: CA-125 screening, TVUS, or pelvic examination
Prostate	Men aged 50–69 y: Discuss benefits and harms of screening with men who inquire about PSA-based screening and are in good health with a life expectancy >10 y at least once (or more as the patient requests), order screening only if the informed man expresses a clear preference for screening, and order PSA testing no more often than every 2–4 y	Men aged 50–69 y who have not had an informed discussion and have not expressed a clear preference for testing after the discussion: PSA testing Men aged <50 y or >69 y and men of any age who are not in good health and have a life expectancy <10 y: Any testing

CA-125 = cancer antigen 125; FIT = fecal immunofluorescence testing; FOBT = fecal occult blood testing; HPV = human papillomavirus; MRI = magnetic resonance imaging; PSA = prostate-specific antigen; TVUS = transvaginal ultrasonography.
* This table provides information for persons at average risk for a specific cancer type who do not have severe competing risk for mortality from another condition. The least intensive recommended strategies are the minimal ones recommended by high-visibility medical groups and guideline organizations (high value). The strategies that are not recommended represent general agreement among groups and signify low-value screening. The rationale for not recommending strategies usually involves an unfavorable tradeoff between benefits and harms, a type of value calculation, but does not include costs. Strategies that are not recommended are more intensive than recommended strategies.

and for reducing screening frequency to every 3 to 5 years rather than every year include the concern that more intensive screening would lead to few benefits but many more harms, including increased psychological and physical complications from colposcopy follow-up of false-positive screening test results, overdiagnosis, overtreatment, and higher costs.

High-value care advice 5: Clinicians should not screen average-risk women younger than 21 years for cervical cancer.

High-value care advice 6: Clinicians should start screening average-risk women for cervical cancer at age 21 years once every 3 years with cytology (Papanicolaou [Pap] tests without HPV tests).

High-value care advice 7: Clinicians should not screen average-risk women for cervical cancer with cytology more often than once every 3 years.

High-value care advice 8: Clinicians may use a combination of Pap and HPV testing once every 5 years in average-risk women aged 30 years or older who prefer screening less often than every 3 years.

High-value care advice 9: Clinicians should not perform HPV testing in average-risk women younger than 30 years.

High-value care advice 10: Clinicians should stop screening average-risk women older than 65 years for cervical cancer who have had 3 consecutive negative cytology results or 2 consecutive negative cytology plus HPV test results within 10 years, with the most recent test done within 5 years.

High-value care advice 11: Clinicians should not screen average-risk women of any age who have had a hysterectomy with removal of the cervix for cervical cancer.

High-value care advice 12: Clinicians should not perform cervical cancer screening with a bimanual pelvic examination.

Colorectal Cancer

On the basis of results from RCTs of screening (fecal occult blood test [FOBT] and sigmoidoscopy) and consistent observational studies, all organizations recommend screening persons aged 50 to 75 years with 1 of 4 strategies: high-sensitivity FOBT or fecal immunochemical test (FIT) (every year); sigmoidoscopy (every 5 years); combined high-sensitivity FOBT or FIT (every 3 years) plus sigmoidoscopy (every 5 years); or optical colonoscopy (every 10 years) (**Appendix Table 1** and **Table 1**) (9, 13, 24–27). The U.S. Food and Drug Administration approved a new DNA stool test, Cologuard (Exact Sciences), for which more comparative effectiveness data are needed. More intensive screening strategies, such as starting at a younger age, continuing to an older age, screening more frequently than recommended, or screening with tests not yet recommended, would be of lower value because benefits would in-

crease only slightly while costs and harms would increase greatly, including complications due to more colonoscopies, overdiagnosis, and overtreatment (26, 28–30).

High-value care advice 13: Clinicians should encourage colorectal cancer screening by 1 of 4 strategies: high-sensitivity FOBT or FIT (every year); sigmoidoscopy (every 5 years); combined high-sensitivity FOBT or FIT (every 3 years) plus sigmoidoscopy (every 5 years); or optical colonoscopy (every 10 years) in average-risk adults aged 50 to 75 years.

High-value care advice 14: Clinicians should not screen for colorectal cancer more frequently than recommended in the 4 strategies mentioned previously.

High-value care advice 15: Clinicians should not conduct interval screening with fecal testing or flexible sigmoidoscopy in adults having 10-year screening colonoscopy.

High-value care advice 16: Clinicians should not screen for colorectal cancer in average-risk adults younger than 50 years or older than 75 years or those with an estimated life expectancy of less than 10 years.

Ovarian Cancer

Based on a large RCT of screening, all organizations recommend against pelvic examinations, cancer antigen 125 blood tests, and transvaginal ultrasonography for ovarian cancer screening (Appendix Table 1 and Table 1) (9, 13, 31–33). Screening would lead to no benefits and would increase harms and costs, including complications of invasive work-ups.

High-value care advice 17: Clinicians should not screen average-risk women for ovarian cancer.

Prostate Cancer

On the basis of RCT findings, no organization recommends prostate-specific antigen (PSA) testing for prostate cancer screening without a discussion of benefits and harms and a patient's expressed, clear preference for screening (Appendix Table 1 and Table 1) (9, 13, 34–36). The primary target group is men aged 50 to 69 years. More intensive screening, including widespread testing in the absence of a request from a well-informed patient to be screened or among men older or younger than the target group, would lead to small incremental benefits, at most, with a larger increase in costs and harms, especially from prostate biopsy and overdiagnosis and overtreatment (37–39). The role of screening digital rectal examinations by trained clinicians, either alone or with PSA cotesting if the digital rectal examination result is abnormal, has not been well-studied. This strategy would likely reduce overdiagnosis and overtreatment compared with broad-based PSA screening and may decrease mortality rates compared with no prostate cancer screening (34).

High-value care advice 18: Clinicians should have a 1-time discussion (more if the patient requests them) with average-risk men aged 50 to 69 years who inquire about PSA-based prostate cancer screening to inform them about the limited potential benefits and substantial harms of screening for prostate cancer using the PSA test.

High-value care advice 19: Clinicians should not screen for prostate cancer using the PSA test in average-risk men aged 50 to 69 years who have not had an informed discussion and do not express a clear preference for screening.

High-value care advice 20: Clinicians should not screen for prostate cancer using the PSA test in average-risk men younger than 50 years or older than 69 years or those with a life expectancy of less than 10 years.

Future Directions: Enhancing Cancer Screening Value by Reducing Overly Intensive Screening

An important step to improving cancer screening value is to increase implementation of underused strategies in which benefits clearly justify harms and costs. This is an important problem, especially in populations with inadequate access to care. We list 6 key principles that could enhance future cancer screening value by reducing overly intensive screening (Table 2). In Ap-

Table 2. Future Directions to Reduce Screening Intensity That May Further Enhance Cancer Screening Value

Future Direction	Evidence Findings Needed Before Implementation
Screen less frequently	Research consistently showing that less frequent screening leads to a small reduction in benefits for the targeted cancer with a larger reduction in harms and costs
Discontinue screening after previous negative screening results	Research consistently showing that persons with repeated negative results on screening tests have low probability of health problems from the target condition while continued screening leads to considerably greater harms and costs
Stop screening persons with a life expectancy of 15–20 y rather than 10 y	Research consistently showing that the probability of benefits from screening is small unless a person lives ≥15–20 y while the harms and costs would continue to increase rapidly with decreasing life expectancy Additional research to permit more accurate estimates of life expectancy beyond age, race, and sex More research to clearly define, discover, and deliver information related to the frequency of screening and harms about overdiagnosis and overtreatment
Start screening at an older age or for readily identifiable higher-risk subgroups	Research consistently showing that targeting screening to higher-risk groups on the basis of age, sex, or readily identifiable risk factors would achieve a large proportion of the benefit while avoiding a large degree of the harms and costs
Screen with less sensitive tests	Research consistently showing that screening with a less sensitive test reduces cancer mortality rates to a similar extent by nearly as much as higher-sensitivity tests with much fewer harms and lower costs
Use higher thresholds for defining positive results on a screening test	Research consistently showing that raising the threshold for defining abnormal results on a screening test decreases benefits to only a small degree while reducing harms and costs to a greater degree

pendix Table 2 (available at www.annals.org), we provide the types of additional evidence needed before widespread implementation, as well as selected preliminary evidence that supports these principles. The results of the presented studies should stimulate consideration for future research and implementation of strategies to enhance screening value by reducing overly intensive screening. The identified studies are not based on a systematic search and are not definitive. Findings are primarily based on single studies or modeling or cost analyses requiring several assumptions. Other suggestive evidence comes from subgroup results from randomized trials. Further research confirming these findings is needed before widespread implementation, but they may hold promise for future, higher-value strategies that involve less-intensive screening. Few studies considered by guideline developers or in our additional searches examined harms and costs to the same degree that they examined benefits. Thus, few studies and corresponding guideline developers could directly assess the value of the screening strategy they were investigating.

How Common Is Overly Intensive, Low-Value Screening?

Overly intensive, low-value screening is common. For example, 20% of women aged 30 to 39 years received a physician recommendation for mammography, and 23% to 35% in this age group had mammography (40). Most women having mammography receive it annually. One third of surveyed primary care physicians screen with ultrasonography and MRI, in addition to mammography, in women who are not at increased risk for breast cancer. Claims data demonstrate high use of screening MRI in women who are not at increased risk (41). Among women aged 80 years or older, cervical and breast cancer screening occurs in 38% and 50%, respectively (19). Cervical cancer screening is commonly done earlier and more frequently than recommended (42). Nearly 70% of women without a cervix received a Pap test for cervical cancer screening in 2002 (43). An estimated 1.2 million U.S. women have ovarian cancer screening (44). More than 40% of responding internists and nearly all gynecologists report performing annual pelvic examinations for ovarian or other gynecologic cancer screening (45).

Inappropriate colorectal cancer screening is also common. Sixty percent of adults had colonoscopies more frequently than guidelines recommend, and screening often occurs in adults with life expectancies of 5 years or less (46–48). Among persons having an FOBT screening test, 8% had a negative result less than 1 year before (49). One third of men having PSA testing do not recall being told that the test was ordered (50). Most persons having PSA testing received annual cancer screening, and one half of men aged 75 to 79 years had recent screening. More than 50% of men and women older than 75 years report that their physicians continue to recommend screening (51).

Discussion

The ACP strongly encourages considering value in making health care decisions (4). Our growing appreciation of the problems of overly intensive, low-value care, including unjustifiable harms and costs, should lead us to consider value in many areas of health care. Cancer screening is no exception.

We summarized cancer screening recommendations for 5 common types of cancer, finding much agreement about acceptable minimal screening strategies and not recommending overly intensive strategies. Guideline groups are increasingly considering value in terms of balancing benefits and harms in making cancer screening recommendations. This value consideration is associated with greater agreement on recommendations for screening for specific types of cancer. Although disagreement remains in some areas, such as annual (9) versus biennial (14) mammography screening for breast cancer, it is possible to develop a list of generally agreed-on, less intensive strategies that we define as high value. This consensus should be seen as a remarkable achievement.

In addition to generally acceptable, high-value screening strategies, we found much agreement about recommending against or not recommending overly intensive, low-value screening. Recommendations have trended toward less-intensive screening and may foreshadow further discussion about screening intensity and value. We believe that this trend enhances screening value, chiefly by forgoing the small incremental benefits of more intensive screening as not being justified by the increase in harms. Although these organizations do not make recommendations based on financial costs, less-intensive, high-value screening is less expensive than overly intensive screening. We also found evidence that overly intensive and thus low-value care is common. In addition, underutilization of high-value care exists, especially among persons with limited health care access. Thus, clinicians can markedly improve cancer screening value by adhering to the widely agreed-on, high- and low-value strategies recommended by the High Value Care Task Force.

Further enhancing value may be possible through implementation of less rather than more intensive screening. We provided preliminary evidence and a value framework suggesting additional strategies that could enhance value through less intensive screening for clinicians, researchers, policymakers, and patients to consider. However, implementation will require additional research consistently demonstrating that less-intensive screening leads to little loss in benefits and larger reductions in harms and costs. Guideline groups and researchers need to better clarify which screening strategies represent high or low value. Guideline developers can help clinicians determine the value of screening strategies by searching for evidence about health benefits, harms, and costs and then carefully analyzing tradeoffs. For some organizations, this would be a departure because they may not adequately consider evidence about harms and often do not assess costs. To

improve the value of screening (and health care in general), harms and costs should be considered equally with benefits to explicitly assess value. Clinicians should pay special attention to transparent recommendations from organizations that are rigorous in making these determinations.

Researchers play an essential role in determining and enhancing the value of screening strategies. For persons with repeated negative test results, research should consider the additional value of continued screening. Research should also consider how much benefit would be lost and how much harms and costs would be reduced by screening less frequently; using a higher test threshold to define abnormality; or screening a smaller, higher-risk population. It would be difficult to consider these questions under a "maximum cancer detection" framework, but they become priority questions under a value framework (2). Research must focus on the consequences of the full screening cascade, including a better understanding of what constitutes "overdiagnosed cancer" and how to reduce overdiagnosis and overtreatment (52). It should also focus on approaches clinicians can use to communicate the benefits, harms, and costs of screening to their patients and society, including ways of incorporating the concept of value.

Considering screening through the lens of value could change discussions between clinicians and patients. Rather than assuming that all screening is high-value, clinicians might start a conversation with the understanding that it always involves tradeoffs between benefits versus harms and costs and that some patients may reasonably decide that they would prefer less intensive screening. Further, considering the patient's situation and own weighting of benefits and harms may lead him or her to conclude that cancer screening is not the highest priority and that there may be other more pressing issues to discuss.

In conclusion, we advise clinicians to consider value when discussing cancer screening with their patients. Implementation of high-value strategies and avoidance of the overly intensive, low-value strategies that we outlined as widely agreed-on would increase cancer screening value. In addition, an emphasis on enhancing value by decreasing harms and costs while preserving most benefits may resonate with many patients. Low-value screening can result from strategies that are either too low or too high in intensity. We have focused on the problem of overly intensive strategies that lead to low value. Reducing overly intensive, low-value screening would not only reduce screening harms and costs but also release time and resources to increase intensity among underserved groups, thus further improving value.

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Appendix Table 1. Cancer Screening Recommendations of the ACP, USPSTF, AAFP, ACS, and Professional Societies

Population Considered	Test	Frequency
Breast cancer		
ACP		
Women 40-49 y	Film mammogram	Shared decision making
Women 50+ y	Film mammogram, clinical breast exam, digital mammogram, MRI, systematic regular breast self-exam	No recommendations
USPSTF		
Women 40-49 y	Film mammogram	Individual decision every 2 y
Women 50-74 y	Film mammogram	Every 2 y
Women 75+ y	Film mammogram	Insufficient evidence
Women any age	Clinical breast exam, digital mammogram, MRI	Insufficient evidence
	Systematic regular breast self-exam	Recommend against
AAFP		
Adult women	Film mammogram, clinical breast, digital mammogram, MRI, systematic regular breast self-exam	Discuss with each woman the potential benefits and harms of breast cancer screening tests and develop a plan for early detection of breast cancer that minimizes potential harms Refer to USPSTF recommendations
ACS		
Women 40 y or older in good health	Mammogram	Annual
Women 40 y or older with serious health problems or short life expectancies	Mammogram	Discuss whether to continue
Women in their 20s and 30s	Clinical breast exam	Every 3 y
Women 40 y or older and women in good health	Clinical breast exam	Annual
Women 20 y or older	Systematic regular breast self-exam	Optional
Women 40 y or older with lifetime risk <1%	MRI	Recommend against
ACOG		
Women 40 y or older	Mammogram	Annual
Women 75+ y	Mammogram: Discuss whether to continue	Not stated
Women 20-39 y	Clinical breast exam	Every 3 y
Women 40+ y	Clinical breast exam	Annual
Women 20+ y	Breast self-awareness	No specific interval or systematic examination technique
Women 40+ y	MRI	Not recommended
Cervical cancer		
ACP		
Women <21 y	Any test	Do not screen
Women 21-65 y	Cervical cytology (Pap test)	Every 3 y
Women 30-65 y	Pap and HPV testing	Alternatively, combination screening may be performed once every 5 y
Women >65 y for cervical cancer who are not at increased risk and have had prior normal screenings	Any test	Recommend against
Women of any age for cervical cancer who had a hysterectomy with removal of cervix and with no prior history of high-grade precancerous cervical lesions	Any test	Recommend against
USPSTF		
Women <21 y	Any test	Recommend against
Women 21-30 y	Cervical cytology	Every 3 y
Women <30 y	HPV	Recommend against
Women 30-65 y	Cervical cytology without HPV Cervical cytology with HPV	Every 3 y or Every 5 y
Women >65 y with adequate prior negative screens	Any test	Do not screen
Women who have had a hysterectomy with removal of the cervix and do not have a history of a high-grade precancerous lesion	Any test	Recommend against
AAFP	–	
Adult women	Cervical cytology with or without HPV	Refer to USPSTF recommendations

(*continued on following page*)

Appendix Table 1–Continued

Population Considered	Test	Frequency
ACS/ASCCP/ASCP		
Women 21-29 y	Conventional or liquid-based cytology tests	Every 3 y
Women 30-65 y	HPV and cytology (preferred)	Every 5 y
	Cytology alone (acceptable)	Every 3 y
Women 65+ y with ≥3 consecutive negative Pap or ≥2 consecutive negative HPV and Pap tests within the past 10 y and no history of CIN2+ within the past 20 y	Any test	Do not screen
Women who have had a total hysterectomy and no history of cervical cancer or serious precancer	Any test	Do not screen
Women who have been vaccinated against HPV	Any test	Follow screening recommendations for age group
Colorectal cancer		
ACP		
All adults	Perform individualized risk assessment	Once or more if indicated
Adults 50+ y	High-sensitivity FOBT or FIT	Annually
	Flexible sigmoidoscopy	Every 5 y
	Colonoscopy	Every 10 y
	Select any of the above tests based on benefits and harms and availability of the screening test and patient preferences	–
Adults >75 y with a life expectancy <10 y	–	Recommend against
USPSTF		
Adults 50-74 y	High-sensitivity FOBT	Annually
	Flexible sigmoidoscopy alone or in combination with FOBT/FIT	Every 5 y for flexible sigmoidoscopy; FOBT/FIT if performed every 3 y
	Colonoscopy	Every 10 y
	Computed tomographic colonography and fecal DNA testing	Insufficient to assess benefits and harms
Adults 75-84 y	–	Recommend against routine screening; there may be considerations that support colorectal cancer screening in an individual patient
Adults 85+ y	–	Recommend against
AAFP		
Adults	FOBT	Refer to USPSTF recommendations
	Sigmoidoscopy	
	Colonoscopy	
ACS, MSTF-CRC, and ACR		
Beginning at age 50 y	High-sensitivity FOBT or FIT	Annually
	Stool DNA with high sensitivity for cancer	Unknown interval
	Flexible sigmoidoscopy alone or in combination with FOBT/FIT	Every 5 y for flexible sigmoidoscopy or
	Colonoscopy	Every 10 y or
	Double-contrast barium enema	Every 5 y* or
	CT colonography	Every 5 y*
	All tests acceptable; tests designed to detect both early cancer and adenomatous polyps should be encouraged (i.e., colonoscopy, flexible sigmoidoscopy, double-contrast barium enema, or CT colonography) if resources are available and patients are willing to undergo an invasive test	–
Ovarian cancer		
ACP		
Adult women	CA-125 and TVUS	No recommendation
	Pelvic exam	Recommend against
USPSTF		
Adult women	CA-125 and TVUS	Recommend against
AAFP		
Adult women	CA-125 and TVUS	Refer to USPSTF recommendation
ACS		
Women 20+ y	CA-125 and TVUS	Recommend against
	Examine ovaries	On the occasion of a periodic health examination

(*continued on following page*)

Appendix Table 1–Continued

Population Considered	Test	Frequency
ACOG		
Adult women	No effective screening strategy	Not stated
Prostate cancer		
ACP		
Men 50-69 y	PSA: Inform men about the limited potential benefits and substantial harms of screening for prostate cancer; test only men who request screening after informed discussion	Discuss at least once Among men who request screening, frequency of screening not specified though increasing interval between tests may reduce harms
	DRE	No recommendation
Men who do not express a clear preference for screening	PSA	Recommend against
Men <50 y, >69 y, or with a life expectancy <10 y	Any test	Recommend against
USPSTF		
Asymptomatic men	PSA	Recommend against
	DRE	No recommendation
AAFP		
Adult men	PSA DRE	Refer to USPSTF
ACS		
Men ≥50 y with at least a 10-y life expectancy (African American men ≥45 y)	PSA with or without DRE: Opportunity to make informed decision with health care provider about whether to be screened	Discuss at least once every 2 y among men screened with baseline PSA <2.5 ng/mL; annually if PSA ≥2.5 ng/mL
Men not having informed decision making	Any test	Do not screen
AUA		
Men <40 y	PSA	Do not screen
Men 40-54 y	PSA	Do not recommend routine screening
Men 55-69 y	PSA: Shared decision making in men considering; proceed based on patient values and preferences	Every 2 y or more among men screened
	DRE	No recommendation
Men 70+ y or with a life expectancy of <10 to 15 y	PSA	Do not recommend routine screening

AAFP = American Academy of Family Physicians; ACOG = American Congress of Obstetricians and Gynecologists; ACP = American College of Physicians; ACR = American College of Radiology; ACS = American Cancer Society; ASCCP = American Society for Colposcopy and Cervical Pathology; ASCP = American Society for Clinical Pathology; AUA = American Urological Association; CA-125 = cancer antigen 125; CIN2+ = cervical intraepithelial neoplasia grade 2+; CT = computed tomography; DRE = digital rectal examination; FIT = fecal immunofluorescence testing; FOBT = fecal occult blood testing; HPV = human papillomavirus; MRI = magnetic resonance imaging; MSTF-CRC = Multisociety Task Force on Colorectal Cancer; Pap = Papanicolaou; PSA = prostate-specific antigen; TVUS = transvaginal ultrasonography; USPSTF = U.S. Preventive Services Task Force.

* If test is positive, colonoscopy should be done.

Appendix Table 2. Future Evidence Required Before Implementation of, and Selected Current Evidence Supporting, Reduced Screening Intensity That May Further Enhance Cancer Screening Value

Future Direction	Evidence Findings Needed Before Implementation	Selected Current Evidence
Screen less frequently	Research consistently showing that less frequent screening leads to a small reduction in benefits for the targeted cancer with a larger reduction in harms and costs.	Cervical cancer: Modeling studies suggest that cervical cancer screening for 5-7 rounds using intervals of >5 y and with primary HPV testing with cytology triage may provide better tradeoffs than current recommended strategies (53). Colorectal cancer: Modeling studies for the USPSTF suggest that screening colonoscopy at intervals of every 15 y rather than 10 y may reduce mortality benefits only minimally and result in fewer colonoscopies (54). Four large RCTs demonstrated that a single sigmoidoscopy between ages 55 and 64 y reduced colorectal cancer incidence by >20% and mortality by nearly 30% (55-58). Prostate cancer: One RCT demonstrated that annual PSA and DRE screening do not reduce prostate cancer mortality compared to less frequent screening. Another large RCT, modeling, and cost-effectiveness studies suggest that PSA screening intervals of every 2-4 y may reduce cancer mortality and would markedly lower harms and costs compared to annual testing (34, 38).
Discontinue screening after prior negative screens	Research consistently showing that people with repeated negative screening tests have low probability of developing health problems from the target condition, while continued screening leads to considerably greater harms and costs.	Cervical cancer: One model used found that the ICER for continuing to conduct every 3 y screening for women ages 45 to 59 y with 2 previously negative cytologies was high ($161 818). For older women or for women with 3 previously negative screens, the ICER was even higher (59). Colorectal cancer: One study found that among patients with a negative colonoscopy, no one developed colorectal cancer and only 1.3% developed an advanced adenoma after 5.3 y of follow-up (60). Prostate cancer: A population-based cohort study demonstrated that discontinuing PSA screening at age 60 y for men with a PSA level of <2 would have no negative impact on cancer mortality and would reduce screening harms and costs (61).
Stop screening people with life expectancy of 15-20 y rather than 10 y	Research consistently showing that the probability of benefit from screening is small unless an individual lives 15-20 y or longer while the harms and costs would continue to increase rapidly with decreasing life expectancy. Additional research to permit more accurate estimates of life expectancy beyond age, race, and gender. More research to clearly define, discover, and deliver information related to the frequency and harms regarding overdiagnosis and overtreatment.	Breast and colorectal cancer: A modeling study based on screening RCT data found that the probability of a person avoiding a colorectal cancer death reached 1-2 in 1000 only 15-16 y after screening. The probability for avoiding a breast cancer death was similar (20). Additional studies have shown that incorporating comorbid conditions into decisions about discontinuing cancer screening in older adults can alter the balance of screening benefits and harms. Discontinuing screening at a younger age among individuals with specified comorbid conditions would reduce screening harms with no negative impact on cancer mortality (27, 62). Prostate cancer: RCTs demonstrate that the probability of a person avoiding a death from prostate cancer due to PSA testing through 10-15 y is 1 in 1000 or less (33). All cancers: Current research demonstrates that intensive screening strategies result in overdiagnosis that is closely linked to overtreatment (63).
Start screening at an older age or for readily identifiable higher-risk subgroups	Research consistently demonstrating that targeting screening to higher-risk groups based on age, sex, or readily identifiable risk factors would achieve a large proportion of the benefit while avoiding a large degree of the harms and costs.	Breast cancer: A 25-year follow-up of a screening mammography RCT found no mortality benefit from screening women ages 40 to 59 y, while a meta-analysis for the USPSTF found a larger relative risk reduction for women ages 60-69 y than for women 40-59 y. Thus, one might consider targeting screening only at women ages 60-69 y (64, 65). Cervical cancer: Models have found that starting screening at age 25 y (especially in women having received HPV vaccination) rather than earlier loses little of the benefit of screening while markedly reducing harms and costs (66). Colorectal cancer: Thirty-year follow-up results from the Minnesota screening trial and a Norwegian flexible sigmoidoscopy trial indicate that relative and absolute cancer mortality reduction is larger for men than for women. Screening did not reduce colorectal mortality in women under age 60 y (67, 58).

(*continued on following page*)

Appendix Table 2–Continued

Future Direction	Evidence Findings Needed Before Implementation	Selected Current Evidence
Screen with less sensitive tests	Research consistently showing that screening with a less sensitive screening test reduces cancer mortality to a similar extent by nearly as much as higher-sensitivity tests with many fewer harms and lower costs.	Breast cancer: A 25-year follow-up of an RCT of screening mammography found that, for women ages 50 to 59 y, mammography did not add mortality benefit to a less sensitive well-conducted clinical breast examination (64). MRI, computer-aided mammography, and tomosynthesis have higher costs than mammography and provide little additional improvement in diagnostic accuracy for average-risk women (68-70). Prostate cancer: One RCT of radical prostatectomy vs. observation for men with prostate cancer detected primarily by DRE found a reduced all-cause and prostate cancer–specific mortality that was limited to men age <65 y (71). Another RCT of radical prostatectomy vs. observation for men with prostate cancer detected primarily by PSA testing did not find mortality differences through 12 y of follow-up, though benefits may exist among men with higher baseline PSA values (72). Findings from case-control studies of DRE are inconclusive. Screening with DRE (either alone or with PSA co-testing if DRE is abnormal) or using higher thresholds to indicate PSA abnormality would likely reduce overdiagnosis and overtreatment compared to routine annual PSA screening at thresholds of 4 ng/mL and may decrease mortality compared to no prostate cancer screening. The U.S. PLCO trial found that annual screening with DRE and PSA did not reduce mortality compared to usual care (34). Colorectal cancer: A model for the USPSTF found that colorectal cancer screening with sigmoidoscopy and a high-sensitivity fecal test gained as many life-years with many fewer colonoscopies than screening with a more sensitive primary colonoscopy (19). An RCT in a safety-net health care system in Texas found that screening with FIT found as many cancers as screening with colonoscopy, chiefly because of higher adherence in the FIT group (73).
Use higher thresholds for defining a positive screening test	Research consistently showing that raising the threshold for defining an abnormal screening test decreases benefit to only a small degree while reducing harms and costs to a greater degree.	Prostate cancer: One RCT of radical prostatectomy vs. observation for men with screen-detected prostate cancer found reduced all-cause mortality through 10 y among men with an initial PSA of >10 ng/mL but not for men with lower levels of PSA (72). SEER data indicate that increasing the threshold to define PSA abnormality as 6-10 ng/mL would markedly reduce the number of men labeled as abnormal with little if any impact on cancer mortality (74).

DRE = digital rectal examination; FIT = fecal immunofluorescence testing; HPV = human papillomavirus; ICER = incremental cost-effectiveness ratio; MRI = magnetic resonance imaging; PLCO = Prostate, Lung, Colorectal and Ovarian; PSA = prostate-specific antigen; RCT = randomized, controlled trial; SEER = Surveillance, Epidemiology, and End Results; USPSTF = U.S. Preventive Services Task Force.