Gaps in the Evidence Base for Clinical Cancer Prevention and Strategies for Improving the Evidence Base

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Disclaimers

Although I am a member of the U.S. Preventive Services Task Force (USPSTF), materials provided in this presentation reflect my individual views only and do not represent the views or recommendations of the USPSTF except where noted on individual slides. The overall presentation should not be attributed to the USPSTF.
Outline

• Brief Introduction to the USPSTF and the Methods
• Focus will be on Health Equity Evidence Gaps for the USPSTF Cancer Screening Recommendations
  • Analytic Framework
  • Evidence gaps
  • Strategies to fill the gaps
USPSTF Overview

- **Independent**, volunteer panel of 16 national experts in prevention and evidence-based medicine
- Makes evidence-based recommendations about clinical preventive services, including screening, counseling, and preventive medications
- Recommendations address only services offered in the primary care setting or services referred by a primary care clinician
- Recommendations apply to adults and children with no signs or symptoms (or unrecognized condition)
USPSTF Overview

• More than 80 preventive service recommendations across the lifespan
• Existing recommendations are regularly updated and new recommendations are developed
  - Listserv is available for email updates
  - Anyone can nominate a topic for the USPSTF to consider

www.uspreventiveservicestaskforce.org
USPSTF Recommendation Development Process

1. **Review Topic Nominations**
   - Anyone can nominate a new topic for review at any time.
   - USPSTF reviews nominated topics for relevance and impact on prevention, primary care, and public health.
   - USPSTF selects and prioritizes topics for review.

2. **Develop Draft Research Plan**
   - Once a topic is prioritized for review, USPSTF and an Evidence-based Practice Center (EPC) develop a research plan and seek expert input.
   - USPSTF posts the draft research plan to website for public comment.

3. **Review Public Comments & Finalize Research Plan**
   - USPSTF and EPC review all comments carefully and revise the research plan.
   - USPSTF posts the final research plan to website.

4. **Review Evidence & Develop Draft Recommendation**
   - EPC analyzes peer-reviewed evidence, develops a draft evidence review.
   - USPSTF assesses EPC-gathered evidence, weighs effectiveness and benefits/harms, and develops a draft recommendation statement.
   - USPSTF posts the draft recommendation statement and EPC evidence review to its website for public comment.

5. **Review Public Comments & Finalize Recommendation**
   - EPC and USPSTF consider all comments on the draft evidence review, then EPC finalizes.
   - USPSTF considers all comments on the draft recommendation statement, then finalizes.
   - USPSTF posts the final recommendation and evidence summary to website and publishes in a peer-reviewed journal.
Steps to Determine a Recommendation Grade

• Assess the evidence across the analytic framework
  ➢ Assess the **certainty** of the estimate of benefits and harms
  ➢ Assess the **magnitude** of both benefits and harms
  ➢ Determine the **balance** of benefits and harms: the **magnitude of net benefit**

• When evidence is not sufficient (low certainty), the USPSTF does not use “expert opinion”
  ➢ An “I” **statement** (not a recommendation) is issued
### What Grades Mean for Clinicians and Patients

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
<th>Suggestions for Practice</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>The USPSTF recommends the service. There is high certainty that the net benefit is substantial.</td>
<td>Offer or provide this service.</td>
</tr>
<tr>
<td>B</td>
<td>The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.</td>
<td>Offer or provide this service.</td>
</tr>
<tr>
<td>C</td>
<td>The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.</td>
<td>Offer or provide this service for selected patients depending on individual circumstances.</td>
</tr>
<tr>
<td>D</td>
<td>The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.</td>
<td>Discourage the use of this service.</td>
</tr>
<tr>
<td>I</td>
<td>The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.</td>
<td>Read the clinical considerations section of USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.</td>
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</table>
Policy Implications: Why focus on evidence gaps that are drivers of health disparities?

- Filling these gaps will help to improve the health of people nationwide, including populations disproportionately affected by health conditions.
- Future research may result in important new recommendations or help inform policy to improve access to and use of these preventive services, reduced disparities in healthcare, and increased health equity.
- Identifying evidence gaps and highlighting them as research priorities will inspire public and private researchers to collaborate and target their efforts to generate new knowledge, address important health issues, and improve health equity.
USPSTF “Generic” cancer screening analytic framework: places in the indirect chain of evidence most likely to have gaps.

Key questions:

1. Is there direct evidence that screening improves health outcomes?
2. What is the prevalence of disease in the target group? Can a high-risk group be reliably identified?
3. Are there accurate screening tests available that can detect the target condition?
4. Are effective treatments available that make a difference in intermediate outcomes when the disease is caught early, or detected by screening?
5. Does treatment improve health outcomes?
6. How strong is the association between the intermediate outcomes and final health outcomes?
7. What are the harms of the screening test?
8. What are the harms of the treatment?
Challenges when addressing systemic racism in preventive service recommendations

• Need to **extrapolate** to populations that are not in the RCTs – age, race/ethnicity, condition severity etc. Often, we have to assume that findings in international populations apply to US populations.

• Can you trust recommendations or parts of recommendations that are based on modeling? – modeling is required to identify screening intervals, initiation and stopping ages, applicable populations, etc.

• We cannot say with certainty who is high risk at the **patient level** when most of the tools to identify high risk persons are at the **population level**

• What if an evidence based screening threshold is contributing to a **health disparity**? The example of the thresholds chosen in the recently published Lung Cancer recommendation provides an example of how to mitigate this.
USPSTF Primary Prevention Recommendations

• Weight loss to Prevent Obesity-Related Morbidity and Mortality in Adults: Behavioral Interventions in Adults – B Grade

• Gaps:
  
  • Effects of interventions for obesity on longer-term weight and health outcomes, including data on older adults, racial/ethnic groups, or persons who are overweight.
  
  • Well-designed pragmatic trials and improved reporting of intervention characteristics to enable evaluation and dissemination of interventions in primary care settings are needed.
  
  • Comparative effectiveness trials would provide more evidence about the components of effective interventions.
USPSTF Primary Prevention Recommendations

• Tobacco Smoking Cessation in Adults, Including Pregnant Persons – A Grade

• The USPSTF concludes that the evidence on pharmacotherapy interventions for tobacco smoking cessation in pregnant persons is insufficient because few studies are available, and the balance of benefits and harms cannot be determined. – I Grade

• The USPSTF concludes that the evidence on the use of e-cigarettes for tobacco smoking cessation in adults, including pregnant persons, is insufficient, and the balance of benefits and harms cannot be determined. - I Grade

• Gaps: Lack of well-designed, randomized clinical trials on e-cigarettes that report smoking abstinence or adverse events as a critical gap in the evidence.
USPSTF Primary Prevention Recommendations

- BRCA-Related Cancer: Risk Assessment, Genetic Counseling, and Genetic Testing for women with a personal or family history of breast, ovarian, tubal, or peritoneal cancer or ancestry associated with BRCA ½ gene mutation – B Grade

- BRCA-Related Cancer: Risk Assessment, Genetic Counseling, and Genetic Testing for women whose personal or family history or ancestry not associated with BRCA ½ gene mutations – D Grade

- Gaps:
  - More research on mutation prevalence and effects on the general population
  - Research on how women with unknown family history should be assessed
  - Comparative effectiveness trials of screening and strategies to improve access to genetic counseling
USPSTF Primary Prevention Recommendations

• Breast Cancer: The USPSTF recommends that clinicians offer to prescribe risk-reducing medications, such as tamoxifen, raloxifene, pr aromatase inhibitors, to women at increased risk for breast cancer and at low risk for adverse medication effects - B Grade

• The USPSTF recommends against the routine use of risk-reducing medications, such as tamoxifen, raloxifene, pr aromatase inhibitors, in women who are not at increased risk for breast cancer - B Grade

• Gaps:
  • Better ways to identify high risk women
  • Given the higher mortality from breast cancer in Black women, we need studies of the effectiveness of risk reducing medications in this higher risk group
In its 2021 annual report, the USPSTF calls attention to high-priority research gaps related to health equity from recent recommendations on cardiovascular disease and cancer prevention.
Lung Cancer Screening: A Recommendation that is Increasing a Health Disparity

Figure 1. Distribution and Median Smoking Pack-Years at Diagnosis by Race for Incident Lung Cancer Cases

A Screening Recommendation that is Increasing a Health Disparity

Table 2. Reasons for USPSTF Lung Cancer Screening Ineligibility for SCCS Smokers With Lung Cancer

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>SCCS Smokers, No. (%)</th>
<th></th>
<th></th>
<th></th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>White</td>
<td>African American</td>
<td>Total</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All cancer cases</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>478</td>
<td>791</td>
<td>1269</td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Age &lt;55 y</td>
<td>91 (19)</td>
<td>192 (24)</td>
<td>283 (22)</td>
<td></td>
<td>.03</td>
</tr>
<tr>
<td>&lt;30 Pack-years</td>
<td>77 (16)</td>
<td>358 (45)</td>
<td>435 (34)</td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Smoking cessation &gt;15 y</td>
<td>43 (9)</td>
<td>47 (6)</td>
<td>90 (7)</td>
<td></td>
<td>.04</td>
</tr>
<tr>
<td>Ineligible lung cancer cases</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>208</td>
<td>536</td>
<td>744</td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Age &lt;55 y</td>
<td>91 (44)</td>
<td>192 (36)</td>
<td>283 (38)</td>
<td></td>
<td>.046</td>
</tr>
<tr>
<td>&lt;30 Pack-years</td>
<td>77 (37)</td>
<td>358 (67)</td>
<td>435 (58)</td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Smoking cessation &gt;15 y</td>
<td>43 (21)</td>
<td>47 (9)</td>
<td>90 (12)</td>
<td></td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Abbreviations: NA, not applicable; SCCS, Southern Community Cohort Study; USPSTF, United States Preventive Services Task Force.

a Categories are not mutually exclusive.
Summary of Review Findings - Screening Eligibility

• The NELSON trial enrolled 50-74 year-olds with a lighter smoking history, providing empiric evidence to support lung cancer screening in persons with lighter smoking histories and at an earlier age.

• Screening for lung cancer in persons with lighter smoking histories (i.e., 20 pack-years) and at an earlier age may help partially ameliorate racial disparities in screening eligibility.
  
  • Black persons who smoke have a higher risk of lung cancer compared with White persons. This risk difference is more apparent at lower levels of smoking intensity.
  
  • A screening program that starts at age 50 and 20 pack years would lead to a relative increase in the percentage of persons eligible for screening by 86% overall, 77% in non-Hispanic whites, and 105% in non-Hispanic Blacks compared with a program that starts at age 55 and 30 pack years.
Important Evidence Gaps for Lung Cancer Screening

• Research that assesses the benefits and harms of using risk prediction models to select patients for lung cancer screening, including whether the use of risk prediction models represents a barrier to lung cancer screening in primary care.

• Evaluations of how to increase the uptake of lung cancer screening discussions in clinical practice, particularly among people at higher risk of death from lung cancer and people who are socially and economically disadvantaged (for whom smoking prevalence and lung cancer incidence is higher).

Colorectal Cancer Evidence Gaps - Black Adults

**Higher burden of CRC:**
- Black adults have highest incidence of and mortality from CRC compared to other races/ethnicities across all age groups
- Most likely cause is inequities in implementation of screening and subsequent care due to systemic racism
- The recent increase in CRC among young adults has not been observed in Black adults, it is mainly seen in Whites & LatinX

**Little evidence on benefits/harms:**
- Few studies reported findings by race/ethnicity, and most found no or inconsistent differences by race/ethnicity
- But, modeling estimates similar balance of benefits and harms for Black adults

![CRC Incidence and Mortality by Race/Ethnicity](chart.png)

Data from SEER Cancer Statistics Review, 1975-2017
Most Important Evidence Gaps for Colorectal Cancer Screening

• Assess the factors that contribute to increased colorectal cancer incidence and mortality in Black adults, such as access to and availability of care and characteristics of systems providing healthcare. Once these factors are identified, more research is needed to evaluate interventions designed to mitigate these differences for Black adults.

• Evaluate the effectiveness of screening in adults younger than age 50 years and whether screening strategies should differ in younger versus older populations.

Breast Cancer Screening Evidence Gaps

• Most screening clinical trials and cohort studies were performed in Europe and predominately enrolled white women younger than age 70 years.

• **Direct evidence about differential effectiveness of breast cancer screening is lacking for subgroups of women, such as African American women, who are at increased risk for dying of breast cancer.**

• Older women, for whom balancing the potential benefits and harms of screening may become increasingly challenging with advancing age.

• Long-term randomized trials or longitudinal cohort studies are needed that compare screening outcomes in women with dense breasts who are not otherwise at increased risk for breast cancer who receive adjunctive screening versus those who do not and report important outcomes, such as breast cancer stage at diagnosis, breast cancer recurrence rates, rates of overdiagnosis, and most importantly, breast cancer mortality.

Evidence Gaps: Cancer Prevention and Screening

• Largely driven by lack of access to behavioral interventions, medications, screening and treatment with the highest risk populations having the poorest access

• Rigorous studies to identify best policy models, funding mechanisms, and practices for dissemination and implementation are needed for all cancer screening recommendations in primary care
Dissemination of Recommendations

• USPSTF Website
  • Subscribe to USPSTF Listserv
  • Prevention TaskForce app (formerly ePSS)
  • Clinician Summaries
    • News Bulletins
• JAMA
• Healthfinder.gov
• Podcasts
  • JAMA
  • The Curbsiders