

Engaging NIH and Extramural Investigators in Addressing Evidence Gaps in Clinical Prevention

NASEM Committee on Addressing Evidence Gaps in Clinical Prevention Recommendations: Meeting #1

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Presentation Outline

- Describe ODP activities to engage NIH and the extramural research community in addressing USPSTF-identified evidence gaps.
- Discuss challenges that we have experienced in this effort.
- Propose some solutions based on our experience.

NIH is a Federal Partner to the USPSTF Program

- NIH coordinates with AHRQ/USPSTF to ensure that:
 - USPSTF evidence reports and recommendations are informed by NIH-supported research.
 - AHRQ/USPSTF are users of scientific evidence.
 - NIH is a major generator of scientific evidence.
 - NIH Institutes, Centers, and Offices (ICOs) are aware of “Insufficient Evidence” (I) statements.
- ODP is the NIH liaison to the USPSTF:
 - Work with NIH ICOs to facilitate NIH scientific review and input on topics.
 - Monitor progress on active topics and I statements.
 - **Facilitate discussions about ways of addressing I statement evidence gaps.**



NIH Research Underpins USPSTF Recommendations

- ODP-led study of funding sources for articles included in the evidence reviews for 25 published recommendations of the USPSTF (January 2014 – February 2016) showed:
 - 21 NIH ICOs (78%) provided funding support for 420 research articles (25%).
 - **NIH was the largest single funder of the evidence cited in USPSTF reviews.¹**

¹Villani J, Ngo-Metzger Q, Vincent IS, Klabunde CN. Sources of funding for research in evidence reviews that inform recommendations of the U.S. Preventive Services Task Force. *JAMA*. 2018; 319: 2132-2133.

Shifting from I Statement to Definitive Recommendation

USPSTF Recommendation Grades	
I Statement	Not enough evidence Cannot assess net benefit. Evidence is lacking, conflicting, and/or low quality.
A	Recommended High certainty of substantial net benefit.
B	Recommended High (moderate) certainty of moderate (substantial) net benefit.
C	Selectively offer service Moderate certainty of small net benefit.
D	Not recommended Moderate/high certainty of no net benefit, or harms outweigh benefits.

Common evidence gaps

- ▶ High-quality RCTs
- ▶ Long-term effects on morbidity or mortality
- ▶ Effects stratified by baseline risk or subpopulations
- ▶ Effects of intervention components
- ▶ Evidence of harms

I Statements Upgraded Between 2010 and 2018

Recommendation Topic (I Statement Released)	Service Type	Upgraded to	Upgrade Year
Abnormal Blood Glucose & Type 2 Diabetes (2008)	Screening	B	2015
Aspirin Use for Preeclampsia (1996)	Preventive medication	B	2014
Gestational Diabetes (2008)	Screening	B	2014
Hepatitis C (2004)	Screening	B	2013
Intimate Partner Violence (2004)	Screening	B	2013
Lung Cancer (2004)	Screening	B	2013
Obesity in Children & Adolescents (2005)	Screening & counseling	B	2010
Prostate Cancer (2008)	Screening	D	2012
Skin Cancer Prevention (2003, 2012)	Counseling	B	2012
		C	2018
Tobacco Use in Children & Adolescents (2003)	Counseling	B	2013

NIH Research Has Contributed to I Statement Upgrades

- ODP-led study¹ showed, for 10 I statement topics that were upgraded in 2010-2018:
 - NIH provided funding support for:
 - 29% of all articles in the evidence reviews for the upgraded recommendations
 - 62% of articles with U.S. sponsorship
 - NIH support was leveraged through a wide range of funding mechanisms:
 - Research grants, center grants, contracts, intramural projects, NIH-industry partnerships

¹Klabunde CN, Ellis EM, Villani J, Neilson E, Schwartz K, Vogt EA, Ngo-Metzger Q. Closing evidence gaps and informing national recommendations about clinical preventive services. Submitted.

ODP Fosters/Facilitates NIH Activities to Close USPSTF I Statement Research Gaps

- Conduct the Annual I Statement Reporting Survey among NIH ICs:
 - Alert ICs to I statements that are relevant to their missions/priorities
 - Encourage and monitor progress toward building research portfolios for addressing I statements
- Host conference calls with AHRQ staff and EPC representatives to discuss I statement Research Needs and Gaps.
- Convene scientific meetings/workshops/conferences—
 - Develop a research agenda and discuss priorities
 - Example: **Trans-NIH Workshop on the Impact of Screening in Childhood on Health Outcomes** (May 2019)
- Issue Funding Opportunity Announcements.

Example of USPSTF-Identified Research Needs and Gaps: I Statement on Unhealthy Alcohol Use in Adolescents

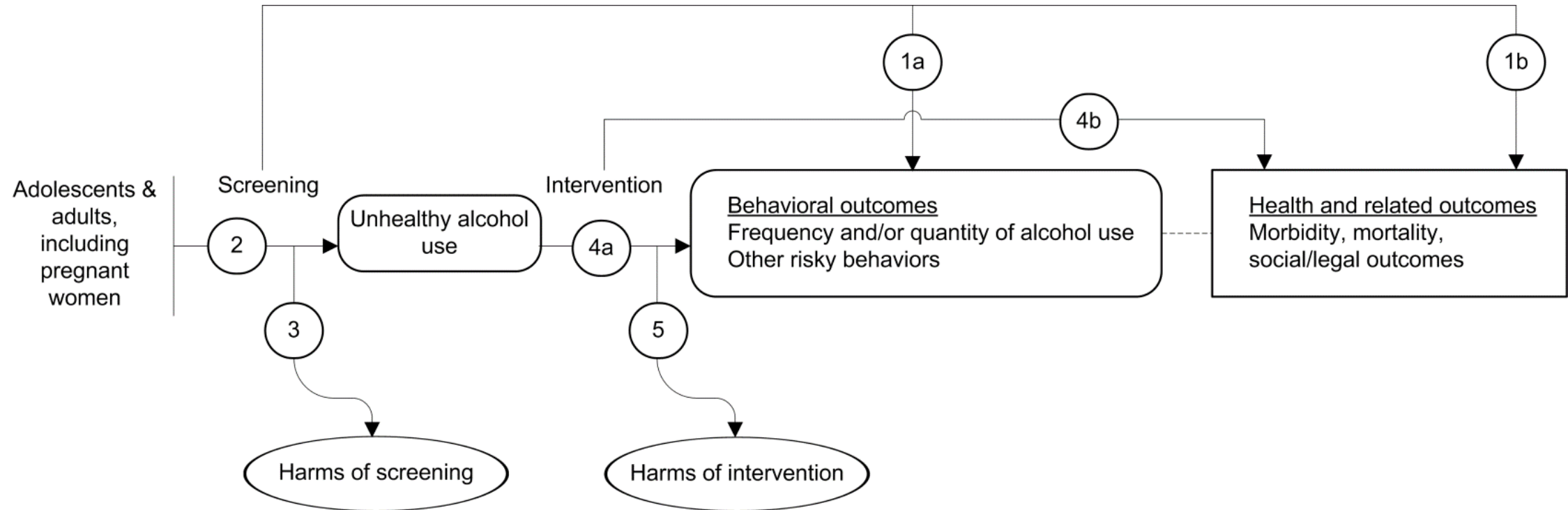
The current evidence is insufficient to assess the balance of benefits and harms of **screening and brief behavioral counseling interventions for alcohol use in primary care settings** in adolescents aged 12-17 years (2018).

- A trial with an unscreened comparison group to understand the population-level effects of screening in primary care settings.
- More direct evidence on the harms associated with screening and behavioral interventions.
- Further test performance studies on the USAUDIT and USAUDIT-C to confirm their accuracy in identifying unhealthy alcohol use in various populations.
- Evidence on important clinical outcomes, such as longer-term morbidity, mortality, health care utilization, and social and legal outcomes.
- Trials designed a priori to report subgroup effects in diverse populations (e.g., by age, sex, race/ethnicity, or baseline severity)
- High-quality studies to assess the effects of screening and behavioral counseling in adolescents
- In addition, studies in adolescents are often conducted in school settings, which may not translate to primary care settings. More studies of adolescents in primary care settings are needed.

Potential Gray Areas for Funders and Investigators Interested in Closing Evidence Gaps

- What is Direct vs. Indirect Evidence?
- What are Intermediate vs. Health Outcomes?
- What are “population-level effects of screening”?
- What does the USPSTF consider to be a “high-quality” study?
- What types of trials are most needed? What size?
- **Of the identified Research Needs and Gaps, which ones (if addressed) are most likely to move the topic or subgroup off of the “I”?**
- Where can I find more information about these Research Needs and Gaps?
 - Recommendation Statement
 - USPSTF Website for the Analytic Framework, Research Approach, and Procedure Manual
 - Full Evidence Report
 - Other?

Analytic Framework for Unhealthy Alcohol Use Topic (source: Recommendation Statement; Evidence Report)



1.
 - a. Does primary care screening for unhealthy alcohol use reduce alcohol use or improve other risky behaviors?
 - b. Does it reduce morbidity or mortality or improve other health, social, or legal outcomes?
2. What is the accuracy of commonly used instruments to screen for unhealthy alcohol use?
3.
 - a. Do counseling interventions to reduce unhealthy alcohol use, with or without referral, reduce alcohol use or improve other risky behaviors in screen-detected persons?
 - b. Do they reduce morbidity or mortality or improve other health, social, or legal outcomes in screen-detected persons?
4. What are the harms of interventions to reduce unhealthy alcohol use in screen-detected persons?
5. What are the harms of screening for unhealthy alcohol use?

Research Approach for the Unhealthy Alcohol Use Systematic Evidence Review (source: USPSTF Website)

Category	Features of Included Studies	Features of Excluded Studies
Aim	Screening and Interventions for unhealthy alcohol use	
Condition	Unhealthy alcohol use	
Population	Adolescents and adults	Treatment-seeking or persons with psychotic disorders
Screening	Brief standardized instruments are specified	Studies lacking screening instruments; laboratory tests
Interventions	Various counseling interventions	Pharmacotherapy
Comparators	No screening or usual care	Active intervention
Settings	Primary care or applicable to primary care	
Outcomes	Alcohol use, mortality, morbidity, QoL	Knowledge, attitudes, intentions
Study Design	Randomized and nonrandomized trials	Cohort, case-control, time-series, cross-sectional

Note: Populations, Screening, Comparators, Settings, Outcomes, and Study Design vary by KQ

Full Evidence Report¹ is Another Source of Information about Research Needs and Gaps

“Limitations of the Studies and Future Research Needs” section of the report:

- Provides a lengthy, 12-paragraph narrative.
- Considerably more detail here than in the brief Research Needs and Gaps section of the USPSTF Recommendation Statement.
- Caveat: reflects the assessment/interpretation of the Evidence-based Practice Center investigators who conducted the systematic review, not necessarily that of the USPSTF in reaching the Insufficient Evidence determination.

¹O'Connor EA et al. *Screening and Behavioral Counseling Interventions to Reduce Unhealthy Alcohol Use in Adolescents and Adults: An Updated Systematic Review for the U.S. Preventive Services Task Force.* Evidence Synthesis No. 171. Rockville, MD: Agency for Healthcare Research and Quality Report No. 18-05242-EF-1.

USPSTF Procedure Manual¹: Definitions and Explanations

Section 6: Methods for Arriving at a Recommendation

- Overview:
 - Direct and indirect evidence
 - Factors considered for evaluating adequacy of evidence for KQs
- Assessing evidence at the KQ and linkage levels
- Dealing with intermediate, secondary, and composite outcomes
- Metrics and data used to assess the magnitude of net benefit

¹<https://uspreventiveservicestaskforce.org/uspstf/procedure-manual>

Summary: Research Needs and Gaps Information Sources

Recommendation
Statement
[Research Needs &
Gaps List]

Analytic Framework
[Key Questions and
Evidence Chain]

Research Approach
[PICOTS; study
inclusion/exclusion
criteria]

Full Evidence Report
[EPC's narrative on
Future Research
Needs]

Procedure Manual
[Definitions and
Explanations]

Conclusions

- A taxonomy and structured approach to describe/report Research Needs and Gaps would help funders and investigators in efforts to act on them.
- Particular areas of information need:
 - Specific populations to target
 - Features/components of interventions and types of comparators
 - Specific outcomes to assess
 - Study designs: details/guidance on appropriate study features; sample sizes
- **PICOTS framework could be applied/adapted to characterize Research Needs and Gaps.**
- **Consolidating the information needed to understand Research Needs and Gaps would further assist funders and investigators.**

Potential Project Impact

- USPSTF recommendations and evidence reports often inform guidelines developed by other national and international expert groups and professional organizations.
- Some of these groups also review scientific evidence and comment on evidence gaps:
 - Example: Community Preventive Services Task Force (CPSTF) issues “Insufficient Evidence Findings”.
- Tools/approach developed in this project:
 - Will guide efforts by the USPSTF, AHRQ, and NIH to identify and address key evidence gaps.
 - May influence efforts by other expert groups such as the CPSTF to describe and disseminate evidence gaps.



Questions/Comments

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