Multicancer Detection Tests Guideline Development Perspective

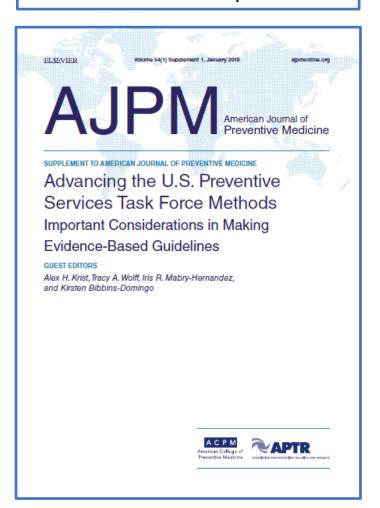
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National Cancer Policy Forum
Oct 28.2024

Disclosures

- No financial conflicts of interest
- Two viewpoints:
 - US Preventive Services Task Force (USPSTF)
 - Primary care
- I am speaking on my behalf. I am not serving as a USPSTF spokesperson and have not been involved with the USPSTF since 2022.

U.S Preventive Services Task Force Member and Chair (2014-2021)

Editor for methods special issue



Cowrote article on intermediate and health outcomes

American Journal of Preventive Medicine

SPECIAL ARTICLE

Update on the Methods of the U.S. Preventive Services Task Force: Linking Intermediate Outcomes and Health Outcomes in Prevention



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The U.S. Preventive Services Task Force (USPSTF) is an independent body of experts who make evidence-based recommendations about clinical preventive services using a transparent and objective process. Developing recommendations on a clinical preventive service requires evidence of its effect on health outcomes. Health outcomes are symptoms, functional levels, and conditions that affect a patient's quantity or quality of life and are measured by assessments of physical or psychologic well-being. Intermediate outcomes are pathologic, physiologic, psychologic, social, or behavioral measures related to a preventive service. Given the frequent lack of evidence on health outcomes, the USPSTF uses evidence on intermediate outcomes when appropriate. The ultimate goal is to determine precisely a consistent relationship between the direction and magnitude of change in an intermediate outcome with a predictable resultant direction and magnitude of change in the health outcomes. The USPSTF reviewed its historical use of intermediate outcomes, reviewed methods of other evidence-based guideline-making bodies, consulted with other experts, and reviewed scientific literature. Most important were the established criteria for causation, tenets of evidence-based medicine, and consistency with its current standards. Studies that follow participants over time following early treatment, stratify patients according to treatment response, and adjust for important confounders can provide useful information about the association between intermediate and health outcomes. However, such studies remain susceptible to residual confounding. The USPSTF will exercise great caution when making a recommendation that depends on the evidence linking intermediate and health outcomes because of inherent evidence limitations

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Helped define USPSTF approach to race, racism, sex-gender

Addressing Systemic Racism Through Clinical Preventive Service Recommendations From the US Preventive Services Task Force

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Wellness and disease prevention are the foundainually refined since 1982. This methodology was cited ng guidelines.1 in addition, the Patient Protection and Affordable Care Act mandated coverage by private Insurers without cost sharing for USPSTE grade A and B recommended clinical preventive services, reflecting

USPSTF often finds substantial data that potential lifetably available to Black, Indigenous, and Hispanic/Latino people. For instance, the 2020 systematic review to inform modeling for the USPSTF colorectal cancer screening recommendation found consistent evidence of inequlties across the screening-to-treatment continuum that encompassed access to screening, quality of screening. time from diagnosis to treatment, and quality of treatment.2 This underscores the need to Improve systems of care to ensure consistent delivery of highquality preventive and treatment services, with special at

As described in the 2003 institute of Medicine report Unequal Treatment: Confrontina Racial and Ethnic Disparities in Health Care, health inequities emerged from a "historic context in which healthcare has been differentially allocated on the basis of social class, race, and ethnicity and are sustained by systemic racism. The consistently found a limited evidence base for Black of societal and interpersonal practices within and out- ample, despite knowing for more than half a century that disproportionate risk, incidence, morbidity, or mortal- 3370 Black men in its 76 683 study sample. member of a racial ethnic minority group is associated with multiple dimensions of social disadvantage, which In turn is associated with worse health care access, af-

The 2018 Quality and Disparities Report from the tions of health. The US Preventive Services Task Force Agency for Healthcare Research and Quality, which (USPSTF) is congressionally mandated to make Included measures on healthy living (eg, receipt of evidence-based recommendations about clinical pre-smoking cessation counseling), patient-centeredness ventive services, which, if delivered equitably to the of care, care coordination (eg, for diabetes and asthma Intended population, can prevent many premature care), and effective treatment (eg, outcomes of cancer deaths. All USPSTF recommendations are based on a care), showed an improvement in the quality of health rigorous and objective methodology that has been concare from 2000 through 2017 on most, but not all. can Indian/Native American people 78.8 years for White saving benefits of recommended services are not equiyears for Asian people.5 These disparities are likely further exacerbated by the disproportionate effect of the COVID-19 pandemic in Black, Indigenous, and Hispanic Latino communities.

The USPSTF has sought to address health equity. As described in 2017, the evidence review for Recommenhave a higher prevalence or experience greater morbid-Ity or mortality from the condition.7 Evidence is then sought that can address the gaps identified in recommendations for groups disproportionately affected by the condition of the review. However, the same factors that affect unequal health outcomes (eg. access, affordability, and quality of health care) also influence inclusion in key clinical trials for prevention, in the development of recommendation statements, the LISPSTE has Black men are twice as likely to die from prostate cancer as White men, the US-based Prostate, Lung, Colo-

than White men for lung cancer at lower pack-years of screening, as the USPSTFIs now recommending, may re

US Preventive Services Task Force

- Makes recommendations on clinical preventive services to primary care clinicians
- The USPSTF scope for clinical preventive services include:
 - Screening tests
 - Counseling
 - Preventive medications
- Recommendations address only services offered in the <u>primary care setting</u> or services <u>referred by a primary care clinician</u>.
- Recommendations apply to adults & children with no signs or symptoms

USPSTF Methods

- All recommendations grounded in a rigorous systematic review with opportunities for public input at multiple steps of the process
- Consult with external subject matter experts through Evidence-based Practice Centers and Partners
- Procedure Manual available at: <u>http://www.uspreventiveservicestaskforce.org/Home/GetFile/6/7/proced</u> ure-manual 2016/pdf

USPSTF Steps: Brief and Generic

- The USPSTF assesses the evidence across the analytic framework:
 - Judges the certainty of the estimates of the potential benefits and harms
 - Judges the *magnitude* of the potential benefits and harms
 - The ultimate goal is to judge the balance of the benefits and harms, or the magnitude of the net benefit of the preventive service
 - When evidence is insufficient (low certainty), the USPSTF does not use "expert opinion"

Basic USPSTF Methods for Developing Recommendations: The Letter Grades

/	Certainty of Net Benefit		Magnitude of Net Benefit			
		Substantial	Moderate	Small	Zero/Negative	
	High	A	В	С	D	
	Moderate	В	В		D	
	Low	I—insufficient evidence				

Getting to Moderate Confidence (A, B, C, D)

- Requires studies with limited risk of bias demonstrating an improved health outcome. Usually randomized controlled trials.
- <u>Health Outcomes</u> include how long a person lives or the quality of life and are often described as conditions that a patient can feel or experience.
 - Harmful health outcomes: overdiagnosis, overtreatment, and false positives
- Intermediate Outcomes describe outcomes that may be influenced by a preventive service, but are not Health Outcomes in and of themselves.
 They are pathologic, physiologic, psychologic, social, or behavioral measures related to a preventive intervention.
 - Examples for cancer: stage shift, detection of precancers, interval cancers, biomarker changes

USPSTF Use of *COLLABORATIVE* Modeling

- Used for breast, cervical, colorectal, and lung cancer screening and aspirin, to
 - Understand lifetime effect of different screening programs (e.g. combinations of screening methods and intervals for screening)
 - Assess screening in specific populations (e.g. various ages for starting or stopping screening)
 - Combine benefits of service (e.g. cardiovascular and cancer prevention for aspirin)
- The USPSTF would not recommend a preventive service without primary evidence

American Journal of Preventive Medicine

SPECIAL ARTICLE

Collaborative Modeling: Experience of the U.S. Preventive Services Task Force



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Models can be valuable tools to address uncertainty, trade-offs, and preferences when trying to understand the effects of interventions. Availability of results from two or more independently developed models that examine the same question (comparative modeling) allows systematic exploration of differences between models and the effect of these differences on model findings. Guideline groups sometimes commission comparative modeling to support their recommendation process. In this commissioned collaborative modeling, modelers work with the people who are developing a recommendation or policy not only to define the questions to be addressed but ideally, work side-by-side with each other and with systematic reviewers to standardize selected inputs and incorporate selected common assumptions. This paper describes the use of commissioned collaborative modeling by the U.S. Preventive Services Task Force (USPSTF), highlighting the general challenges and opportunities encountered and specific challenges for some topics. It delineates other approaches to use modeling to support evidence-based recommendations and the many strengths of collaborative modeling compared with other approaches. Unlike systematic reviews prepared for the USPSTF, the commissioned collaborative modeling reports used by the USPSTF in making recommendations about screening have not been required to follow a common format, sometimes making it challenging to understand key model features. This paper presents a checklist developed to critically appraise commissioned collaborative modeling reports about cancer screening topics prepared for the USPSTF.

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INTRODUCTION

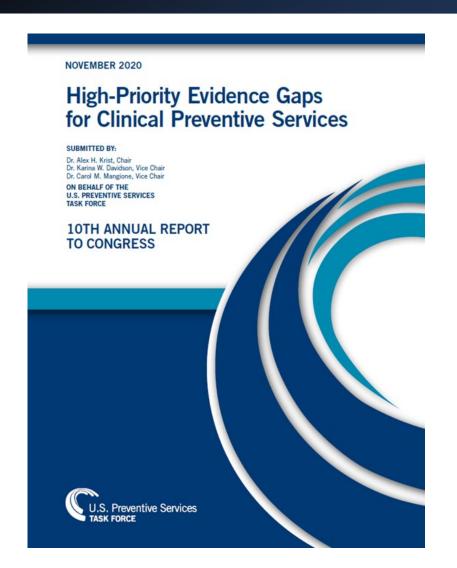
ecision models evaluate the effect of alternative intervention strategies on health outcomes. ^{1,2} Models, including but not limited to decision models, can be valuable tools for addressing uncertainty, trade-offs, and preferences when trying to understand the effects of interventions. ^{3,4} Models can bridge empiric evidence to inform decisions and help develop guide-lines. ^{2,3}: Zacharioudakis and colleagues ⁵ reported that mathematical models were used to support recommendations in 54% of the 100 most cited guidelines of the National Guideline Clearinghouse.

The U.S. Preventive Services Task Force (USPSTF) has used decision modeling in various capacities to inform its recommendations on a number of important topics 6-14 a comparison of results for multiple unique models evaluating the same questions (here called collaborative modeling, but also called comparative modeling in some publications)^{15–19} as well as alternatives to such collaborative modeling. Reporting of commissioned collaborative modeling and results is complex, and

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Knowledge Cycle: Annual Reports to Congress



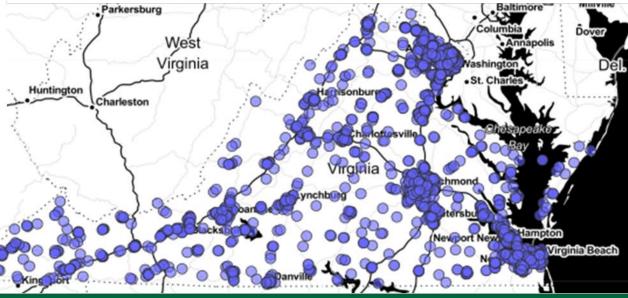
- 2020 Mental Health and Health Behaviors in Children
- 2019 Mental Health and Substance Use
- 2018 Cardiovascular Health
- 2017 Prostate Cancer Screening in African American Men
- 2016 | Statements
- 2015 Health of Women
- 2014 Health of Children and Adolescents
- 2013 Health of Older Adults





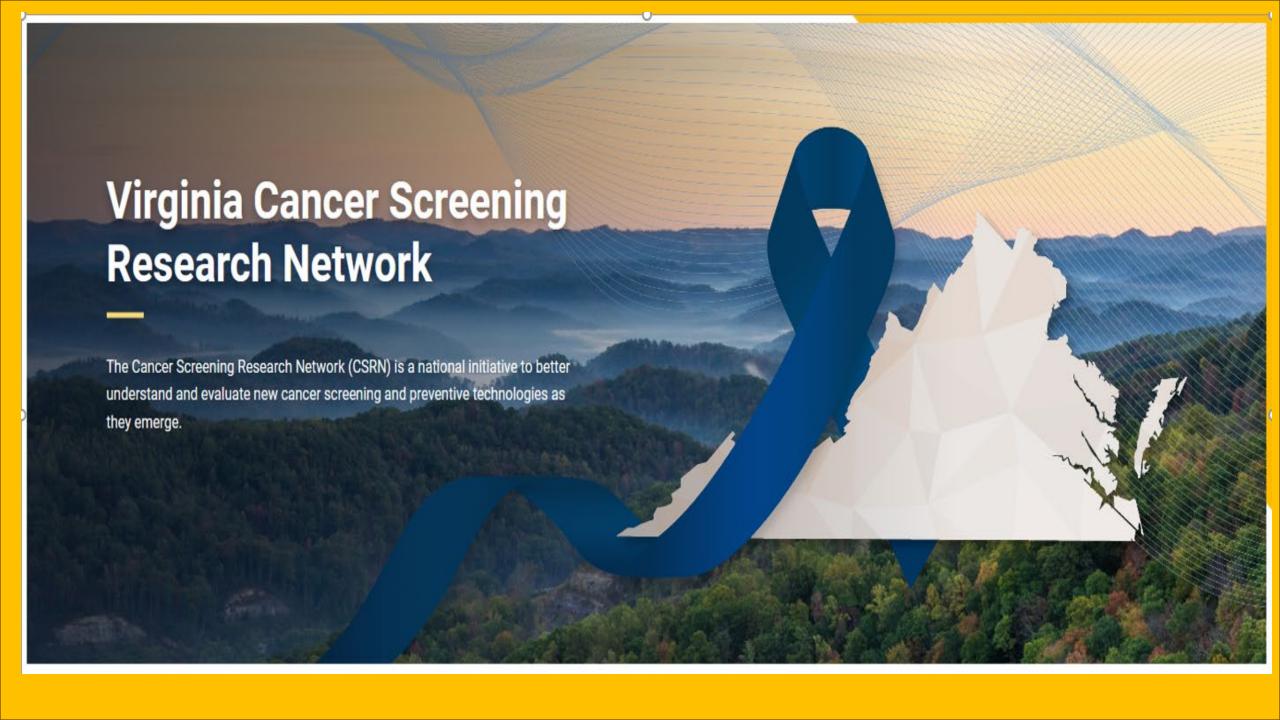












Virginia CSRN ACCESS Hub



^{*} The Virginia ACORN is a primary care-based research network, encompassing 526 practices throughout the state, and includes all primary care practices at VCU Health, Inova, Sentara, and EVMS.

Equitable and Inclusive Recruitment Methods



- EMR FOR PATIENT IDENTIFICATION
- LEVERAGE EXISTING PARTNERSHIP
- PRIMARY CARE NETWORKS



TARGETED RECRUITMENT

- APCD AS A RESOURCE
- EQUITABLE RECRUITMENT APPROACH
 - FLEXIBILITY IN RECRUITMENT SETTING



COMMUNITY OUTREACH RECRUITMENT

- COMMUNITY ADVISORY BOARDS
- ENGAGEMENT STUDIOS
 - PARTNER WITH COMMUNITY-BASED ORGANIZATIONS



VIRTUAL COMMUNITY OUTREACH RECRUITMENT

- ENGAGEMENT STUDIOS
 - PARTNER WITH ESTABLISHED CCTS INITIATIVES



58 Clinicians

17 Patients





69 Community
Advisory Board
Members

10 Community Members



Patients

"The fact that some of these cancers are so sneaky and you don't diagnose them until you're stage 4. The only answer is gonna lie in research and how to find it sooner and treat it more aggressively."

"If I had had this test, maybe [my cancer] would have been stage zero or one, as opposed to stage two. So, you know, I'm pleased as punch. I just think this is the greatest thing I've heard in my lifetime of 60 years."

Benefits of Early Detection

"For me, it is nice because you have the blood test once a year...so it's just a matter of getting it and the confirmation everything's still going well."

"I think it would help them feel better about their health to know and have additional screenings, because I do notice a lot of my newer and even younger patients, a big concern that they have is family history of cancer and what that means for them."

Clinicians

"A big trouble for me is getting patients to get their cancer screening, because of transportation issues and stuff. So, this would be a good thing, to just get a blood test."

"I see the convenience of this type of testing if we can just do a blood test and rule things out."

Patients

"I think it's important to make sure that we know the pros and cons. Because anybody who's had a family member go through cancer, just being told that you might have cancer is an earth-shattering moment, just right there. Though, I think that by doing this, we can actually build trust in the future for people, rather than rushing and getting it out."

"I would be concerned if maybe your insurance carrier if somehow they know about it, that they might drop you, or even your employer dropping you. I mean, people do that."

Concerns about MCDs

"I find it very odd that two companies, or maybe more companies, would be able to create this test and start marketing it, and general practitioners are putting it out there, without having done this study first. It seems a little bit cart, horse, chicken, egg situation...I would have liked to have seen this science go before the product and the marketing and the business."

Clinicians

"It may lead people to be overly optimistic about what it means for their health, meaning if they didn't see a doctor for ten years and can get one test."

"We need just as much research about how this impacts the patients and their providers as what is the predictive value of the tests."

"We're doing a blood test. We don't know what it means. We don't know what a positive means. We don't know what a negative means. The negative doesn't mean you're safe. The positive means you will probably get other scans and maybe procedures for what turns out to be nothing."

Diagnostic Work-ups for Positive Results

Clinicians

Patients

"So, you have a positive test, and you get further diagnostic testing, and nothing shows up. So, I guess that leaves you for the rest of your life wondering what's going to crop up in the future, and you just continue to follow up with the possibility that you have a slow growing cancer that's showing these cells."

'Say that it comes up positive and then after multiple tests, you've determined that you're actually negative. What creates that positivity and makes it false? So, like, now every time something goes wrong, like, 'Oh, is it cancer? Like, why did I show positive for cancer?"

"Not knowing the parameters or characteristics of the test, what do we actually do with an abnormal? Is it more imaging? Is it a specialist? What if the specialist does not know what to do with it? So that's a really important question. Not knowing what the test means, how do we know what evaluation would be needed?"

"What do we do with these results? And like, how do we follow them? What kind of scans do we do for positive tests? How often do you do the scans?

"A lot of times it's not just one additional test.

Sometimes that one test leads to other tests,
and then you're kind of chasing down the
rabbit hole trying to figure out what means
what, and what's really important, and how to
counsel the patient, and where to go from
there. ...and it becomes a huge process,
possibly for nothing, possibly for something,
but it's not just necessarily one follow-up test."

"Your PCP may not be knowledgeable of certain types of cancers to the degree that they feel comfortable talking about it."

Patients

"In addition to the anxiety and the chronic anxiety that comes with it, it's the cost, right? You have PET scans, you have to find your next oncologist, you have to find where you're going to get an infusion.

There's a huge financial cost to a

false diagnosis, as well."

"I think it will be a lot to put on the PCP. And also, you know, it can't be consistent because people see different PCPs all the time."

Financial Costs & Time Burden

"My question would be, do you think it would create more of a burden on an already overwhelmed healthcare system? I know it's sometimes hard to get an appointment even here at our clinics and I can only imagine what it's like in the hospitals."

"A lot of this anxiety and extra testing all happens outside of an office visit and through the inbox. And we only get compensated in RVUs when we see the patient in a visit ... A lot of this work in our current feefor-service [payment system] we're not compensated for.

Clinicians

"I have a lot of hesitation because until we prove that we're not just finding a bunch of latent early whatever cancers, I'm going to be the person that has to deal with all of the anxiety and all of the fallout when somebody has a positive test. And if it is a positive test that truly is going to change their life, great. But if it's something that is just going to make people more anxious and lead them down a path of more unnecessary testing...I'm not sure I want to be the person who's dealing with that."

"... how much time and work it takes to manage these things that we get very little benefit from."















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