

Research Priorities, Measures, and Recommendations for Assessment of Tobacco Use in Clinical Cancer Research

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Abstract

There is strong evidence that cigarette smoking causes adverse outcomes in people with cancer. However, more research is needed regarding those effects and the effects of alternative tobacco products and of secondhand smoke, the effects of cessation (before diagnosis, during treatment, or during survivorship), the biologic mechanisms, and optimal strategies for tobacco dependence treatment in oncology. Fundamentally, tobacco is an important source of variation in clinical treatment trials. Nevertheless, tobacco use assessment has not been uniform in clinical trials. Progress has been impeded by a lack of consensus regarding tobacco use assessment suitable for cancer patients. The NCI-AACR Cancer Patient Tobacco Use Assessment Task Force identified priority research areas and developed recommendations for assessment items and timing of assessment in cancer research. A cognitive interview study was conducted with 30

cancer patients at the NIH Clinical Center to evaluate and improve the measurement items. The resulting Cancer Patient Tobacco Use Questionnaire (C-TUQ) includes "Core" items for minimal assessment of tobacco use at initial and follow-up time points, and an "Extension" set. Domains include the following: cigarette and other tobacco use status, intensity, and past use; use relative to cancer diagnosis and treatment; cessation approaches and history; and secondhand smoke exposure. The Task Force recommends that assessment occur at study entry and, at a minimum, at the end of protocol therapy in clinical trials. Broad adoption of the recommended measures and timing protocol, and pursuit of the recommended research priorities, will help us to achieve a clearer understanding of the significance of tobacco use and cessation for cancer patients. *Clin Cancer Res*; 22(8); 1–7. ©2016 AACR.

Introduction

Ten years ago, Gritz and colleagues (1) raised awareness in the oncology research community of the significant omission of tobacco use measurement. The 2014 U.S. Surgeon General's Report provided compelling evidence of the need to address smoking by cancer patients (2). Cigarette smoking by cancer patients and survivors causes adverse outcomes, including increased overall mortality, cancer-specific mortality, and risk for a second primary cancer (2). Moreover, current smoking is strongly associated with an increased risk of cancer treatment

toxicity, poor quality of life, and comorbid conditions. Smoking increases adverse effects of cancer treatment for virtually all cancer disease sites and all cancer treatment modalities (3–8). Yet, studies have shown that 9.3% of all cancer survivors and 50% to 83% of cancer patients who are current smokers or recent former smokers at diagnosis continue to smoke or resume smoking after diagnosis (3, 9–12).

The American Association for Cancer Research (AACR) and the American Society of Clinical Oncology (ASCO) have recently

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recommended that all patients with cancer should be asked about their smoking status during clinical care and when participating in clinical research, and all current tobacco users should be provided with evidence-based tobacco cessation assistance (5, 13). Several other recent reviews and policy statements have also called for the inclusion of tobacco use history and current status in oncology clinical trials (1, 2, 6–8, 14–16). Most recently, the National Comprehensive Cancer Network (NCCN) developed and disseminated Clinical Practice Guidelines for Smoking Cessation (17).

The primary objective of cancer therapy trials is to advance therapeutic outcomes through improved overall survival, disease control, toxicity profiles, or a combination thereof. Recent emphasis has been placed on designing clinical trials that achieve clinically meaningful outcomes (18). The Institute of Medicine (IOM, now National Academy of Medicine) Committee on Improving the Quality of Cancer Care recommends using evidence-based care and improving translation of evidence into clinical practice to improve clinical outcomes (19). Because smoking can affect the primary endpoints of a clinical trial, the omission of routine tobacco use assessments introduces the risk of misinterpretation of results. Furthermore, important research questions about tobacco use after cancer diagnosis need to be addressed.

However, recent analysis of NCI-funded Cooperative Group clinical trials demonstrates that over two-thirds of actively accruing clinical trials do not capture any information on tobacco use, and the minority that ask about tobacco use frequently do not use standardized assessment approaches (20). The vast majority of prior work on the impact of tobacco use by cancer patients has relied on a wide variety of self-reported items used to classify patients as never, current, and former smokers (2, 12). The content and formatting of case report forms, data coding and annotation, data validation, and frequency of data collection vary greatly across studies (6–8, 12, 14, 20–22). Without adopting precise definitions and standardized measurement of tobacco use, findings in the literature may be difficult to compare or might appear contradictory, and pooling of data across studies is impeded. The current variability in defining and measuring tobacco use limits comparisons across studies and subgroups of the population, measurement of temporal trends, and estimation of exposure.

Several issues complicate the measurement of tobacco use among cancer patients. First, virtually all of the evidence of the adverse effects of tobacco on cancer treatment outcomes is based on cigarettes (7, 23), but there are a growing number of alternative tobacco and nicotine products, including large and small cigars, cigarillos, pipes, clove cigarettes/kretek, bidis, smokeless tobacco (chew, snuff, etc.), hookah, and electronic nicotine delivery systems (e.g., e-cigarettes; refs. 24, 25). Second, longitudinal assessment is necessary because of the chronic relapsing nature of tobacco use and dependence. Some research questions require that tobacco use be captured relative to specific milestones in the cancer continuum from screening through diagnosis, treatment, and survivorship. For example, if an analysis requires determining whether a patient smoked on the day of treatment initiation, an item with a 30-day recall might not be useful. Similarly, to compare clinical outcomes between patients who quit and those who continue smoking after diagnosis, it is important to have a thorough assessment of the timing of smoking cessation relative to diagnosis, and this is not typically captured with generic items currently used to assess smoking status and history.

In 2013, the National Cancer Institute (NCI) and AACR convened the NCI-AACR Cancer Patient Tobacco Use Assessment Task Force to develop recommendations for tobacco use measurement and research priorities in clinical cancer research. The present report advances the field by identifying the high priority research topics in this area, and by providing cognitively tested self-report items that can facilitate a standardized approach to capturing the necessary data about tobacco use in the oncology research setting.

Task Force Purpose and Membership

The charge for the Task Force was to employ a broad scientific and medical perspective, considering all cancer patients, to develop recommendations for the research agenda, tobacco measures, timing of assessment, breadth of assessment, and prioritization of tobacco use assessment across cancer populations and settings, as well as implementation of assessment in clinical research and/or clinical practice settings. The overall objective was to achieve consistency and breadth of tobacco use measures that could be used in clinical research without sacrificing precision or creating undue burden.

The members of the multidisciplinary Task Force provided a breadth of expertise in pre-specified domains as follows: tobacco use measurement, questionnaire item development, cancer, pharmacology, psychology/psychiatry, NCI-funded multicentered cancer clinical trials, oncology care, cancer surgery, the clinical practice setting, oncology nursing, health care systems, and payer systems. Members include representatives from the NCI's Division of Cancer Control and Population Sciences, Coordinating Center for Clinical Trials, and Cancer Therapy Evaluation Program; members of the AACR Subcommittee on Tobacco and Cancer; and additional experts from the academic research community. Detailed Task Force processes and methods of deliberation are described in the Supplementary Data that accompany this article.

Tobacco Use and Cancer Research Priorities

Task Force deliberations resulted in the detailed research priorities provided in Box 1. On the basis of our consideration of existing research, we suggest that high priority be given to clinical research focusing on cancer patients who continue to smoke cigarettes or use other tobacco products following diagnosis as well as those who recently quit (within 1 year before diagnosis). The Task Force also concluded that, although it is known that smoking causes adverse outcomes in cancer patients (23), significant work is needed to understand the specific effects of smoking and other forms of tobacco use and the potential for post-diagnosis smoking cessation to improve therapeutic and other clinical outcomes. The health effects of alternative tobacco products such as electronic nicotine delivery systems are essentially unknown, particularly in the cancer treatment setting (24). More evidence regarding the specific health implications of the dynamics of smoking cessation by cancer patients (including timing of cessation, reduction in smoking without abstinence, duration of cessation, and use of alternative tobacco products) is needed to guide cancer care guidelines and practice recommendations (e.g., advising cessation before cancer surgery). In addition, little research to

Box 1. Research priorities related to tobacco use by cancer patients

1. Determine the effects of tobacco and other forms of nicotine use or exposure on cancer patients as well as the effects of tobacco cessation (before diagnosis, during treatment, or during survivorship); research in this area could address the effects of tobacco/nicotine use/exposure and cessation on the following:
 - a. Tumor response, disease progression or recurrence, second primary cancer, survival, and mortality
 - b. Cancer treatment efficacy
 - c. Adverse effects and complications of cancer treatment, recovery from cancer treatment, and post-treatment comorbid disease (such as heart disease)
 - d. Needed dose, duration, and other characteristics of cancer treatment delivery
 - e. Symptoms, psychosocial outcomes, and behavioral factors, including quality of life, mental health, and adherence to cancer treatment and post-treatment procedures
2. Determine the effects of exposure or use of tobacco and its constituents in all products (tobacco, nicotine replacement therapy, e-cigarettes and other electronic nicotine delivery systems) on cancer biology including the following:
 - a. Carcinogenesis
 - b. Tumor proliferation
 - c. Angiogenesis
 - d. Migration/invasion and metastasis
 - e. Inflammation
 - f. Immune modulation
 - g. Tumor microenvironment
 - h. Viral carcinogenesis and effects of viruses on cancer therapy (such as HPV)
 - i. Metabolism of cytotoxic cancer agents
 - j. Response to surgery, chemotherapy, radiotherapy, and targeted systemic therapy
3. Determine optimal strategies for implementing tobacco dependence treatment and prevention within the cancer setting, including the following:
 - a. Evaluate the most effective platforms to promote system-wide identification of users of tobacco (and other forms of nicotine intake, such as e-cigarettes) and recent quitters using electronic health records and meaningful use criteria
 - b. Evaluate the most effective means of delivering tobacco dependence treatment to all such individuals, including motivational approaches for the ambivalent tobacco user and telemedicine for patients who live at a distance
 - c. Evaluate the effects of potential cessation treatment moderators, such as psychiatric comorbidities or genetic factors; develop focused approaches to ameliorate those effects
 - d. Assess the role of biochemical verification
 - e. Evaluate cost-effectiveness
 - f. Determine the optimal cancer and cessation treatment timing
 - g. Consider and inform provider behavior

date has investigated how the clinical outcomes of cancer patients are affected by secondhand exposure to tobacco smoke, which is classified as a known human carcinogen by the U.S. Environmental Protection Agency, the U.S. National Toxicology Program, the U.S. Surgeon General, and the International Agency for Research on Cancer (26–30). Similarly, the effect of other tobacco-derived products on clinical outcomes has received little research attention.

Additional areas identified by the Task Force as in need of examination include the effects of patients' smoking status on cost-effectiveness of cancer care, and evidence-based, scalable tobacco dependence treatment delivery models that are efficient, effective, and acceptable to patients in a broad range of cancer care settings.

Evidence indicates that widespread biologic effects of smoking on cancer cells lead to changes in tumor proliferation, angiogenesis, migration and invasion, and resistance to conventional cancer treatment (8, 31). However, little or no data currently exist on the effects of acute smoking cessation on cancer biology. These effects have implications for all forms of cancer treatment, including tumor vaccines, as well as for the need to develop animal/*in vivo* models of tobacco and cancer treatment/biology, as opposed to cellular models.

Assessing Patient-Reported Tobacco Use: Core and Extension Items

Candidate items for assessment of tobacco use by cancer patients were drawn from the National Health Interview Study (NHIS), National Survey on Drug Use and Health (NSDUH), Youth Risk Behavior Surveillance System, National Adult Tobacco Survey, and Health Information National Trends Survey; from previously published items (1); from the case report forms of MD Anderson Cancer Center, the University of Pittsburgh Cancer Institute, Roswell Park Cancer Institute, Memorial Sloan Kettering Cancer Center, and other Task Force member institutions; and from case report forms of the NCI-funded Cooperative Group clinical trials (8, 32, 33).

Upon examining these items, the Task Force found substantial variation in the manner in which current and past tobacco use has been assessed in both research and clinical practice. For example, since 2005, the Southwest Oncology Group (SWOG) included on the Pre-study Form in all lung cancer trials 1 smoking status item [current, former (defined as no smoking for 1 year or more), and never (defined as less than 100 cigarettes in lifetime)]. (D.R. Gandara, personal communication, November 2015). The Radiation Therapy Oncology Group collected information on smoking at least 100 cigarettes in a lifetime, age of smoking initiation, number of years smoked, average cigarettes smoked per day, and age at quitting. In many settings, assessments are limited to ever or current smoking status (23). The Task Force found that capturing tobacco use relative to cancer diagnosis, treatment, and survivorship had received limited attention. NHIS items and cancer-specific items previously developed at the University of Pittsburgh (D. Bovbjerg, personal communication, March 2013) served as a model for the development of new items to capture smoking during the year before diagnosis, during the period from diagnosis to the start of cancer treatment, and within several other clinically relevant epochs including from 2 days before to 2 days after cancer surgery, during the course of

Table 1. Recommended timing of tobacco use assessment in clinical cancer research

Time point	Rationale
Minimal, necessary assessments	
Study registration	Baseline history of use and exposure, and status at diagnosis and before start of treatment provide necessary analysis variables
End of protocol therapy	Registration is a feasible time point for assessment Change in tobacco use after/during treatment provides necessary analysis variables End of therapy is a feasible time point for assessment
Additional recommended assessments, as applicable	
Immediately before or after cancer surgery	These assessments are necessary for investigating the impact of tobacco use on surgical outcomes
Day 1 of every chemotherapy cycle, beginning and end of radiotherapy, beginning and end of other systemic therapy, or monthly	These assessments are necessary for investigating the impact of tobacco use on treatment efficacy; both tobacco use cessation and relapse are common during therapy
6–12 months after the end of therapy	Changes in tobacco use after the end of therapy are common and, for the analysis of long-term outcomes, should be captured as a predictor of subsequent continuation of use

treatment, and after treatment; as well as new items about tobacco cessation and other tobacco product use relative to cancer diagnosis.

Consensus was reached for the development of a short list of essential constructs ("Core") to be measured routinely across the cancer care continuum, plus a longer set of curated constructs ("Extension") for use when more detailed assessment is feasible. The draft item set was tested in a cognitive interviewing protocol with cancer patients (see Supplementary Data for brief details of the protocol methods and results). The full report of the cognitive interview study is published elsewhere (34).

The final Cancer Patient Tobacco Use Questionnaire (C-TUQ), with the Core and Extension items recommended for initial and follow-up assessments, is provided in Supplementary Fig. S1. The questionnaire formatted for paper-and-pencil administration is also available online at the NCI Grid-Enabled Measures Database (<https://www.gem-measures.org>; ref.35). The 4 Core items provide information about the respondent's status as an ever/never-smoker ["Have you smoked at least 100 cigarettes (5 packs=100 cigarettes) in your entire life?"], and the duration ["How many total years have you smoked (or did you smoke) cigarettes? Do not count any time you may have stayed off cigarettes."], the intensity ["On average when you have smoked, about how many cigarettes do you (or did you) smoke a day?"], and the recency of smoking ["How long has it been since you last smoked a cigarette (even one or two puffs)?"]. Core items enable the calculation of pack-years (i.e., the number of cigarette packs smoked per day multiplied by the number of years of smoking; for instance, smoking a pack per day for 20 years = 20 pack-years), a commonly used indicator of cumulative tobacco exposure.

One set of Extension items captures smoking during time frames relative to diagnosis and treatment: "During each of the following time frames, please indicate whether you smoked cigarettes every day, some days, or not at all." Reference periods are specified as: "The year before you were first told you had cancer," "after diagnosis, and before treatment started," "from 2 days before your last cancer surgery to 2 days after," "during the course of treatment," "after treatment ended," and "since your last visit to this clinic." Other Extension items capture current smoking (within 30 days, and frequency); age at smoking initiation; the use of alternative tobacco products (with time frames defined by diagnosis, past 30 days, or ever); longest quit interval after diagnosis; smoking cessation attempts and use of cessation products or assistance (during the time frame since diagnosis or past

30 days); advice from "cancer doctors" to quit smoking; and exposure to secondhand smoke (at home or work) or sharing a household with a smoker (current, past, and lifetime duration).

Timing of Tobacco Assessment in Cancer Clinical Trials

Cancer patients often quit smoking just before or at the time of diagnosis, but many patients also return to using tobacco after cancer treatment begins or concludes. There has been little scientific investigation of the ideal timing of tobacco use assessments in the oncology setting. The Task Force recommends that in cancer treatment trials, tobacco use be assessed at a minimum at study entry/registration and when the patient goes off protocol-specified treatment [either because the protocol-specified treatment regimen has been completed or the patient ends treatment early (e.g., due to toxicity, recurrence, or treatment futility)]. Assessment at these times (see schema in Table 1) is expected to minimize missing data based on the importance of these two time points in all cancer clinical trials data collection.

However, some research questions focus on the effects of smoking on the efficacy, toxicity, and outcomes of surgery, radiotherapy, and systemic therapy. Such questions may necessitate tobacco use assessments at the time of cancer diagnosis and at the beginning and end of each phase of treatment. A longer-term follow-up, 6 to 12 months after the end of therapy, is also warranted to evaluate the impact of continued smoking on long-term clinical outcomes. This scientific rationale for repeated assessments must also be balanced with feasibility and burden on the clinics and patients. An opt-out study with nearly 12,000 cancer patients demonstrated that mandatory assessments at every visit were met with significant resistance from clinical staff, but that repeated assessments scheduled once per month were feasible (33). Capturing tobacco use at critical junctures enables investigation of research questions regarding changes in tobacco use behavior and their impact on cancer outcomes.

Discussion

In this report, we identify high priority research topics and provide specific recommendations for valid, flexible, and clinically meaningful longitudinal assessment of tobacco use in clinical trials with cancer patients. These recommendations balance the need for greater standardization in the assessment of tobacco use with practical concerns about minimizing burden to patients

and clinical research staff. In compliance with the FDA's Patient-Reported Outcome guidelines (36), cognitive interviews were conducted to evaluate and improve patient understanding of the items and confirm content validity.

An emerging translational literature highlights tobacco use as a risk factor for adverse clinical outcomes and strongly supports the Task Force recommendation to include tobacco use assessment in the design of clinical cancer research (2). Given the significant gaps in knowledge about tobacco use and cancer presented in the 2014 U.S. Surgeon General's Report and identified in the Task Force Research Priorities (Box 1), it is critical to expand and harmonize the collection of tobacco use information in clinical trials to estimate the impact of tobacco use (and cessation) on clinical trial outcomes.

For some studies, it may be desirable to categorize patients as current, former, or never smokers at clinically relevant time points. The definition of a "never" cigarette smoker that is most accepted in the scientific literature is the one used in the NHIS: Whether an individual has smoked fewer than 100 cigarettes in his/her lifetime (Item 1 of C-TUQ). Typically, the category of "current smoker" is then defined as smoking at least 1 cigarette within the past 30 days. Less often, "current smoker" is defined as smoking within the past year. Item 6 (C-TUQ) provides both of these measures relative to the questionnaire completion date. Former and current smokers may also be distinguished on the basis of whether they have smoked cigarettes every day, some days, or not at all during a recent time frame. Item 7 provides that information for the year before cancer diagnosis and for other intervals relevant to cancer treatment. These new items will make it possible to distinguish patients who quit smoking after diagnosis from those who persisted during therapy, or who quit at diagnosis but resumed after therapy. Only by making these distinctions can the impact of smoking and the effect of smoking cessation during therapy be estimated (22). These distinctions are not always possible using existing items that employ 30-day or 7-day recall periods, which might not coincide with a time frame relevant to the cancer trajectory.

Measures of past cigarette smoking duration and dose have also varied across studies. Both categorical and quantitative measures have been used for duration, dose, or a combined duration and dose measure such as pack-years. The new C-TUQ items permit categorical, ordinal, or continuous scoring, thus allowing for comparisons with prior studies, including population-based samples.

In June 2014, the National Clinical Trials Network investigators activated five clinical trials that were part of the SWOG Lung Master Protocol: S1400—Phase II-III Intergroup. A Biomarker-Driven Master Protocol for Previously Treated Squamous Cell Lung Cancer (Lung-MAP) (ClinicalTrials.gov Registry Number: NCT02154490). These studies have now been redesigned as a result of the designation of a new standard-of-care agent for this disease (37), and two trials have been closed. A new phase III trial for patients with no matching biomarker was activated in December 2015, and other trials are currently in development for inclusion in this master protocol. The Smoking Status Assessment Form, which has 4 items that are essentially the Core C-TUQ items, continues to be included in the redesigned protocol for S1400. The form is being administered by research staff (Oncology Nurses or Clinical Research Associates; CRA) at study entry and when the patient goes off protocol therapy. All trials associated with the Lung Master Protocol will include the Smoking Status Assessment Form. Brief, informal phone calls with CRAs

who administered the Smoking Status Assessment Form in S1400 found that patients did not have difficulty completing this form; approximately 30 patient forms were addressed in this review (CMM, personal communication, March 2015).

The C-TUQ and recommended timing of data collection were developed specifically for use in clinical trials and other clinical research. Further attention is needed to standardize systematic screening of tobacco use in routine cancer care settings. Also needed are greater consistency in the assessment of tobacco use along with a clinical reminder system for screening all patients for smoking status and referring all current smokers for tobacco treatment (38). It is increasingly recognized that quality cancer care should include delivery of evidence-based treatment of tobacco dependence (5–8, 13, 39). Although generally included in social history recorded during routine clinical care, assessment and documentation of current smoking status in medical records are inconsistent (40) and may contain inaccuracies. Fortunately, the national landscape for clinical assessment of tobacco use is rapidly changing, and there are many quality of care policies and clinical compliance guidelines (e.g., Meaningful Use of Electronic Health Records, the Joint Commission, National Quality Forum, National Committee for Quality Assurance, and the Affordable Care Act) that are likely to improve the quality and consistency of tobacco use assessment in routine clinical care. Ongoing efforts to improve interoperability of electronic medical records will lead to improved exchange and interpretation of shared data that can be linked with clinical trial data.

Our recommendations should be interpreted in light of several limitations. First, although the cognitive interview study recruited a diverse group of cancer patients, the sample was restricted to adult patients who were fluent in English. Further effort is needed to develop items for pediatric patients or for patients with low English proficiency. Second, misreporting of past tobacco use might occur if patients find it difficult to recall the information being requested or prefer not to report accurately due to the stigma associated with persistent tobacco use (41–49), although the cognitive interview study did not reveal such difficulties. Prior studies in cancer patients have found mixed results, with misreporting rates as high as 29% in patients with repeated assessments during cancer treatment (50). Misreporting of tobacco use appears to be more of a problem for recent former smokers (51, 52). Nonetheless, in a large Veterans Affairs (VA) study of inpatient smokers with varying diagnoses, the sensitivity and specificity of self-report tobacco use were 97% and 93%, respectively (41). The issue of misreporting raises the question of whether biochemical verification of smoking status should be required in clinical trials (53). Self-reported smoking abstinence can be biochemically verified in several ways (e.g., exhaled carbon monoxide testing, cotinine assays) commonly used in tobacco cessation research. Although biochemical verification can add cost to clinical research and in some cases verification may be unnecessary (e.g., in self-identified smokers), we recommend that collection of biospecimens and biochemical verification be considered for use with study populations with high tobacco use (such as head/neck and lung cancer patients) when financially and logistically feasible. In all cases, improving the accuracy of patient reporting requires that smoking history and current status be assessed in an empathic, nonjudgmental manner so as to minimize patients' experience of guilt and self-blame (49, 54, 55).

In conclusion, the Task Force has developed a standardized assessment protocol and has outlined research priorities to improve our understanding of the effects of tobacco use on cancer

treatment efficacy and toxicity. On the basis of the initial review of the use of smoking status items in the Lung Master Protocol (S1400), and other trials conducted in the past, it appears feasible to incorporate tobacco use assessment in multicentered clinical trials. Given that smoking contributes to adverse outcomes across cancer disease sites and treatments, it is critical to implement tobacco use assessments for all disease sites and treatments (23). Standardized tobacco use assessment conducted with the C-TUQ in research across a range of disease sites and treatment modalities will permit data pooling and comparisons between populations. Researchers can benefit from the availability of a flexible and valid set of items designed to collect the requisite data for studies related to tobacco use by cancer patients, thus eliminating the need for researchers to investigate, create, and test suitable items. Reliable and valid measurement of tobacco use in clinical research will advance scientific knowledge in the areas identified in the Task Force Research Priorities.

Disclosure of Potential Conflicts of Interest

B.A. Toll reports receiving a commercial research grant from Pfizer. N.A. Rigotti and R.A. Schnoll report receiving commercial research grants from and are consultants/advisory board members for Pfizer. T. Brandon reports receiving commercial research support from Pfizer and is a consultant/advisory board member for Voxiva. S. Leischow reports receiving a commercial research grant from Johnson and Johnson. No potential conflicts of interest were disclosed by the other authors.

Disclaimer

The recommendations provided in this report reflect the consensus of the Task Force members. The recommendations do not represent an official position of the National Cancer Institute or the U.S. Government.

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