National Cancer Institute

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

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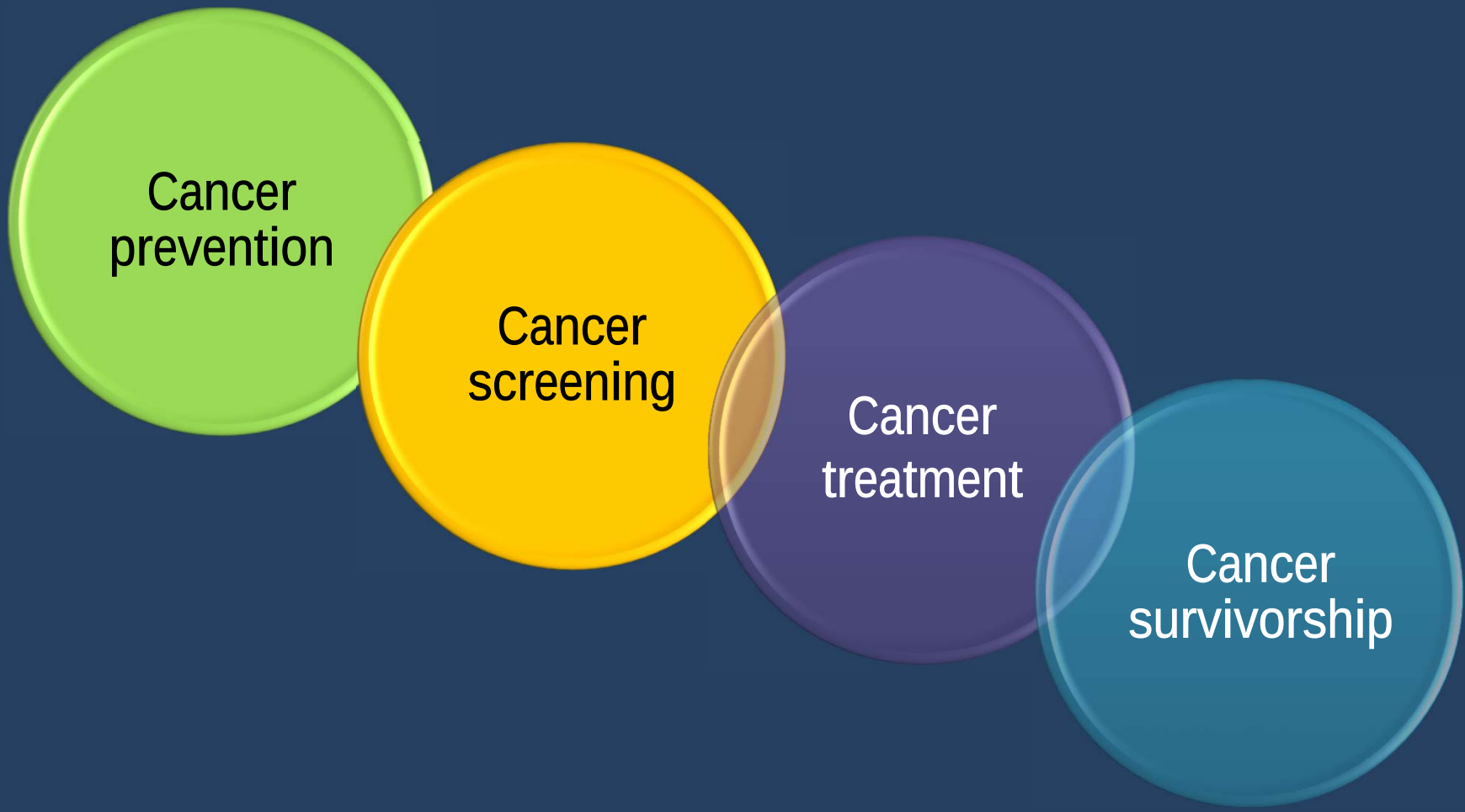
Formerly: Statistician, National Surgical Adjuvant Breast and Bowel Project (NSABP) and

University of Pittsburgh Cancer Institute (1999-2011)

Setting of tobacco's impact on cancer



Rationale for Assessing Tobacco Use in Cancer Clinical Trials

I. Tobacco use is both predictive & prognostic.

II. Scientific questions regarding tobacco use by cancer patients (examples):
   - When does tobacco diminish treatment efficacy?
   - What are the mechanisms of tobacco effects?
   - How much does prognosis improve with cessation after diagnosis?

Clinical Impact

Cancer patients and survivors who smoke cigarettes have worse health outcomes (including higher all-cause and cancer-specific mortality, and risk of tobacco-related second primary cancer).

Smokers may have higher risk of recurrence, poorer response to treatment, and increased toxicity.

Clinical Significance of Smoking by Cancer Patients

- Relative risk of all-cause mortality*
  - Current smokers 1.5 (relative to never smokers)
  - Former smokers 1.2
- Relative risk of cancer-specific mortality*
  - Current smokers 1.6 (relative to never smokers)
  - Former smokers 1.03

* U.S. Surgeon General's Report, 2014

Current approaches to data collection:

- Not widely assessed in trials or practice
- Inconsistent tobacco use assessment methods
- Little follow-up during/after treatment

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Patient reports 19-year
history of smoking,
starting at age 15, denies
alcohol, divorced,
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Land, JCO, 2012; Goldstein, NTR, 2012; Warren, IJC, 2012

2009: NCI Conference on Treating Tobacco Dependence at Cancer Centers

2013-present: NCI-AACR Cancer Patient Tobacco Use Assessment Task Force

Purpose: from the scientific and medical perspective, develop recommendations for

- patient-reported tobacco use measures
- timing of assessment
- research agenda

NCI-AACR Cancer Patient Tobacco Use Assessment Task Force

NCI	Stephanie Land (chair), Jeffrey Abrams, Sandra Mitchell, Sheila Prindiville
Moffitt Cancer Center	Thomas H. Brandon
Mayo Clinic	Jan C. Buckner, Scott J. Leischow
MD Anderson Cancer Center	Paul M. Cinciripini, Ellen R. Gritz
Medical U. of South Carolina	K. Michael Cummings, Graham Warren, Benjamin Toll
IASLC Smoking Cess. Tobacco Ctrl Cmte	Carolyn Dresler
Ohio State University	Sonia A. Duffy, Peter Shields
University of Wisconsin	Michael C. Fiore
University of Minnesota	Dorothy K. Hatsukami
Yale School of Medicine	Roy S. Herbst
Emory School of Medicine	Fadlo R. Khuri
Fred Hutchinson	Carol Moinpour
Memorial Sloan-Kettering	Jamie S. Ostroff
Harvard	Nancy Rigotti, K. (Vish) Viswanath
U. of California Los Angeles	Linda Sarna
University of Pennsylvania	Robert A. Schnoll
AACR	Shimere W. Sherwood

(Affiliations as of December, 2015)

Cancer Patient Tobacco Use Questionnaire (C-TUQ)

- Developed by the Task Force
- Tested in cognitive interview study (#NCT02233842)
- Posted to https://www.gem-measures.org
- Common Data Elements

Core: 4 items for broad use in trials and practice

Smoking status and history

Extension: Pool of items for comprehensive assessment

Baseline and follow-up items also include smoking history and status relative to diagnosis and treatment, other products, secondhand exposure, cessation

Land, Warren, Crafts, Hatsukami, Ostroff, Willis, Chollette, Mitchell, Folz, Gulley, Szabo, Brandon, Duffy, Toll. Cognitive testing of tobacco use items for administration to cancer patients and survivors in clinical research, *Cancer*, 2016

Task Force Recommendations

- Task Force recommends broad inclusion of C-TUQ items in cancer research
- Detailed research priorities (See Land et al, CCR, 2016* & handout)
- Timing of tobacco use assessment in clinical trials
    - Minimal: registration and end of protocol therapy
    - Before and after cancer surgery
    - Day 1 of each chemotherapy cycle
    - Beginning and end of radiation therapy
    - Beginning and end of other systemic therapy
    - 6-12 months after the end of cancer therapy

Or monthly

*Land, Toll, Moinpour, Mitchell, Ostroff, Hatsukami, Duffy, Gritz, Rigotti, Brandon, Prindiville, Sarna, Schnoll, Herbst, Cinciripini, Leischow, Dresler, Fiore, Warren. Research priorities, measures, and recommendations for assessment of tobacco use in clinical cancer research, *Clinical Cancer Research*, 2016

Administrative Supplements for Collection and Analysis of Tobacco Use Data via the Cancer Patient Tobacco Use Questionnaire (C-TUQ), among Participants in NCTN and NCORP Clinical Trials

NCI Goals

- Provide funding for scientific research using the C-TUQ
- Raise awareness of the C-TUQ
- Fund initial costs: systems changes that facilitate inclusion of C-TUQ in future trials (e.g. procedures to collect and manage data)
- Promote shared data
- Encourage tobacco use assessment as a routine, essential component in cancer clinical trials

Implementation

Three administrative supplements were funded:

- SWOG NCTN
- ECOG-ACRIN NCTN and NCORP

Other implementation:

- SWOG Lung Master Protocol (Lung-MAP)
- Other NCTN trials in development
- C-TUQ downloaded nearly 1000 times

ECOG-ACRIN NCTN and NCORP Supplements

- 8 diverse trials (disease sites & stages, regimens, patient populations)
- Core C-TUQ & several Extension C-TUQ items (including e-cigarette use)
- Baseline, 3-month and 6-month follow-ups

Aims: assess the effects of tobacco use on

- Treatment toxicity and symptom burden
- Treatment duration and dose intensity
- Therapeutic benefit

Discussion

- Tobacco use should be considered in cancer treatment comparisons.
- Many research questions remain regarding the impact of tobacco use on cancer patient outcomes.
- Standardized tobacco use assessment implemented in research across a range of disease sites and treatment modalities will permit data pooling and comparisons among populations.

(Extra slides follow)

Next steps

- Disseminate measures, timing recommendations, and research agenda
- Identify natural opportunities to increase the inclusion of tobacco use assessment in cancer clinical research

C-TUQ Core Constructs

- Ever smoked cigarettes
- Time since last cigarette
- Average number of cigarettes per day
- Total years smoked

(See handout.)

C-TUQ Extension Constructs

Age first smoked	Trying to quit in past 30 days
Age began smoking regularly	Smoking cessation products in past 30 days
Smoking frequency during time periods related to cancer diagnosis and treatment	Quit assistance methods in past 30 days
Regular use of other products* since cancer diagnosis	Regular use of other products* (ever)
Longest time stayed off cigarettes since cancer diagnosis	Other tobacco products in past 30 days
Smoking at all in past 30 days	Currently living with a smoker
Number of days smoked in past 30 days	Secondhand cigarette smoke exposure in home and work environments in past 30 days
Smoking cessation products since diagnosis	Secondhand cigarette exposure in home (ever) and total years
Quit assistance methods since diagnosis	Secondhand cigarette exposure in workplace (ever) and total years
Cancer doctors advised to quit	

* Other products include combustible, smokeless, and aerosol products, e.g., e-cigarettes

Item 7

- Capture smoking relative to diagnosis and treatment to address research questions related to impact of tobacco on surgical outcomes, toxicity, and treatment efficacy.

- Reference periods are specific to cancer experience.

Paragraph Styles

During each of the following time frames, please indicate whether you smoked cigarettes every day, some days, or not at all.

	Every day	Some days	Not at all	Don't know/ Not sure	Not Applicable
a. The year before you were first told you had cancer	☐	☐	☐	☐	☐ (I have not been diagnosed.)

(See handout.)

Questionnaire Development Methods

STEP 1: Task Force drafted recommendations based on literature review, existing tobacco use surveillance items, and consensus-building dialog via virtual and in-person workshops. (2013-2014)

STEP 2: Two survey methodologists modified item formats, applying question design best practices and results from cognitive testing of tobacco-related questions in other contexts. (2014)

STEP 3: Cognitive testing of tobacco use items

- NCI Center for Cancer Research (#NCT02233842)
- N=30 patients, variety of cancers, stage, tobacco use history, demographics
- 1-hour cognitive interviews conducted in clinic
- Interviews recorded, transcribed, analyzed
- Item revisions after each n=10 patients

Interview script for item 7 (example)

- How do Pts interpret the wording used for each of these time frames?
- What issues do Pts have, if they have had more than one type of cancer, or recurrence(s)?
- Are Pts able to remember and accurately report for each of these 6 different time frames?
- What factors do Pts consider when deciding how to answer each part?
- How accurate do Pts feel their answers are for each reference period?

How did you come up with your answer for part…a? b? c? d? e?

How easy or difficult was it to answer the parts of this question? [IF DIFFICULT]: What made it difficult?

In your own words, what does “during the course of treatment” mean to you?

Interview findings for item 7:

- Patients with recurrent or second primary cancer tended to answer with respect to first cancer.
- “Surgery” may be interpreted as including biopsy.
- “Treatment” has varied interpretations.

Note: Terms such as “treatment” can be replaced with specific term for the research.

Conclusions of cognitive interview study

- Numerous instrument improvements resulted in a final C-TUQ that performed well in terms of
  - patients' understanding of wording, response options, and reference periods;
  - navigation and ease of use.

- Interview results provide support for content validity of the English language, patient-administered C-TUQ.