National Cancer Institute

Tobacco Use by Cancer Patients in Clinical Trials

Stephanie Land, PhD

Tobacco Control Research Branch
Behavioral Research Program
Division of Cancer Control and Population Sciences

Formerly: Statistician, National Surgical Adjuvant Breast and Bowel Project (NSABP) and University of Pittsburgh Cancer Institute (1999-2011)

Purpose of today's presentation

- To inform CTAC of initiative
- To solicit early input

- Problem
- Scene
- Science
- Action
- Feedback

problem scene science action feedback

Problem (Clinical)

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 1.3
- Relative risk of cancer-specific mortality**
  - Current smokers 1.6 (relative to never smokers)
  - Former smokers 1.05

* Phipps, 2011 (colorectal cancer)
** Kenfield, 2011 (prostate cancer)

Problem (Scientific)

There are many scientific questions related to tobacco use in the cancer patient population.

Current approaches to data collection:

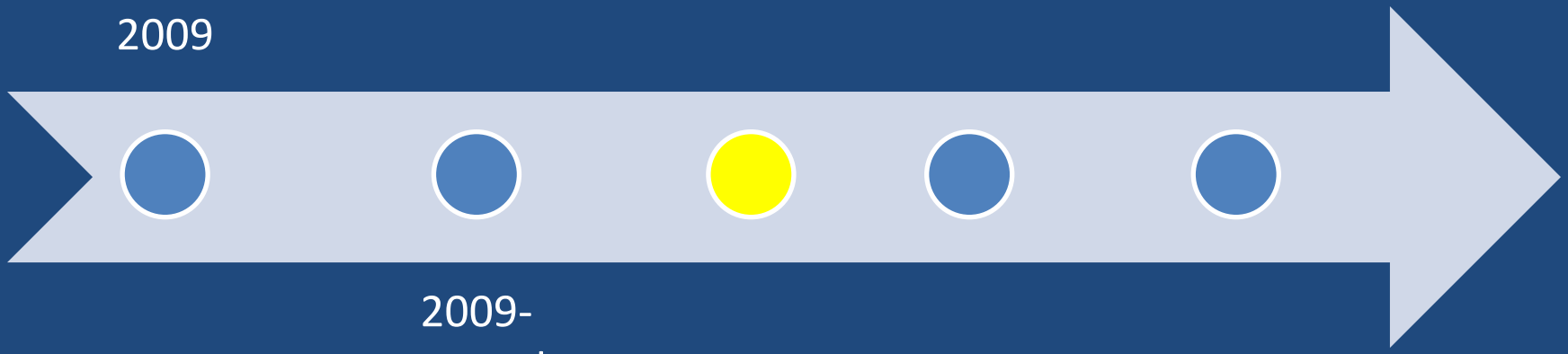
- Not widely assessed in trials or practice
- Inconsistent tobacco use assessment methods
- Little follow-up during/after treatment

Current practice

- NCI-Designated Cancer Centers
  - < 50% include tobacco use as a vital sign in the medical record
- NCI-funded phase III Cooperative Group trials
  - 22% record cigarette smoking status at enrollment, and
  - 4% during follow-up.

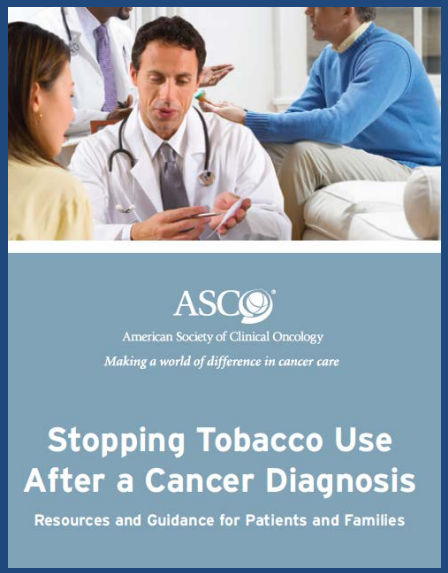
Goldstein, NTR, 2012; Warren, IJC, 2012

Action Timeline



problem **scene** science action feedback

Recent action and dissemination



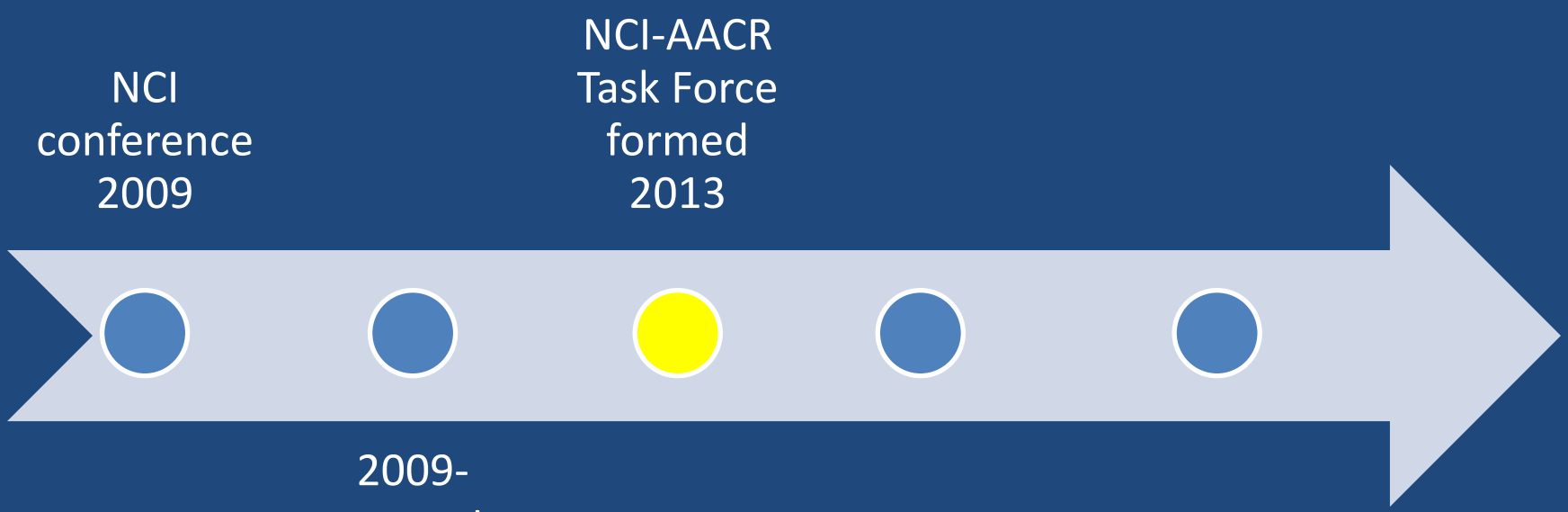
Land, JCO, 2012
Peters, JCO, 2012
Ganz, JCO, 2012
IOM, 2012
Warren, JOP, 2013
Warren, JTO, 2013
Toll,CCR, 2013
Hanna, JCO, 2013

“In the oncology setting, tobacco use should be addressed at presentation and throughout treatment.”

“If tobacco use data are systematically collected and analyzed, the information would provide clinicians and regulatory agencies with the data needed to understand the impact of existing and new tobacco products.”

Hanna, et al, Tobacco Cessation and Control a Decade Later: American Society of Clinical Oncology Policy Statement Update, *JCO*, 2013

Action Timeline



Scope and Purpose of NCI-AACR Cancer Patient Tobacco Use Assessment Task Force

From the scientific and medical perspective, develop recommendations for

- tobacco measures,
- timing of assessment,
- research agenda

Task Force Roster

Jeffrey S. Abrams, MD
Thomas H. Brandon, PhD
Jan C. Buckner, MD
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K. Michael Cummings, PhD, MPH
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Peter Shields, MD
Benjamin Toll, PhD
K. (Vish) Viswanath, PhD
Graham Warren, MD, PhD

See handout for titles and affiliations.

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Cooperative Group leadership and committee membership

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ASCO leadership and committee membership

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Cancer centers

NCCTG Phase III Trial N0147 (Alliance)

- 2686 resected stage III colon cancer randomized
- FOLFOX ± cetuximab
- Statistical power 90% to detect DFS HR=0.75 cetuximab
- No DFS benefit with cetuximab (Alberts, JAMA, 2012)
- Baseline smoking assessment (n=1968):
  - Smoked ≥100 cigarettes in lifetime
  - Currently smoker
  - Age initiation
  - Age quit
  - Average number of cigarettes smoked per day

Associations between Cigarette Smoking Status and Colon Cancer Prognosis among Participants in NCCTG Phase III Trial N0147 (Alliance)

- Phipps, Shi, Newcomb, Nelson, Sargent, Alberts, Limburg for the Alliance for Clinical Trials in Oncology *JCO Jun 1, 2013*
- Land, SR: New Evidence of the Clinical Significance of Cigarette Smoking by Colon Cancer Patients [podcast] , *JCO*
- 3-year DFS 70% for ever-smokers vs 74% never-smokers
- Current vs never-smokers (DFS HR=1.47; 95% CI 1.04 to 2.09)
- Former vs never-smokers (DFS HR=1.20; 95% CI 0.99 to 1.46)
- Interaction with BRAF mutation (P=.03):
  ever-smoking was associated with
  - shorter DFS in pts with BRAF wild-type (HR=1.36; 95% CI, 1.11 to 1.66)
  - not in BRAF mutated (HR=0.80; 95% CI, 0.50 to 1.29) colon cancer.

Scientific questions

- Cigarette smokers seem to have greater morbidity and poorer clinical outcomes, but:
  - Evidence needs to be strengthened
  - Is the association actually due to exposure history, use during cancer therapy, or continued accrual of risk after therapy?
  - What is the improvement in prognosis with cessation, for a given history of exposure?

Scientific questions (continued)

Does quitting smoking actually impact the outcome of cancer, or is the damage already done?

Peter Shields, Professor

The Ohio State University College of Medicine

Deputy Director, The Ohio State University Comprehensive Cancer Center (OSUCCC)

Scientific questions (continued)

Does tobacco use diminish treatment efficacy?

We need to understand the mechanisms by which tobacco could exacerbate the disease or dilute the efficacy of the treatment.

Vish Viswanath, Associate Professor
Harvard School of Public Health
and Department of Medical Oncology
Dana-Farber Cancer Institute

Scientific questions (continued)

"There are substantial opportunities to
identify better cancer therapeutics,
use smoking as a model of general therapeutic resistance, and
assess methods to improve outcomes."

Graham Warren, Associate Professor
Vice Chairman for Research in Radiation Oncology
Dept of Cell and Molecular Pharmacology and Experimental Therapeutics
Medical University of South Carolina
Alliance (Cooperative Group Prevention Committee)

Scientific questions (continued)

"Why does smoking affect virtually all disease sites for most treatment modalities?

Do we know of any other exposure that has this effect? If we can determine how tobacco causes these effects, we might have a spectacular opportunity to advance cancer treatment.

Costs of existing therapies are so high, maximizing the utility of these therapies could be a great investment."

K. Michael Cummings
Professor, Department of Psychiatry & Behavioral Sciences
Medical University of South Carolina

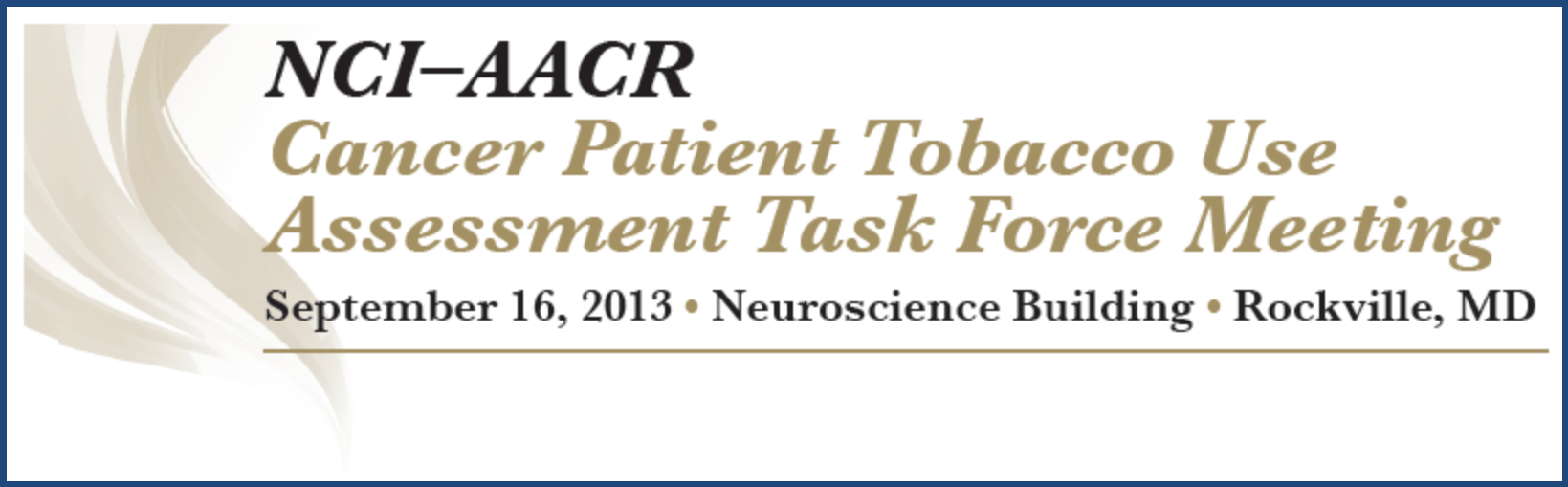
Scientific questions (continued)

- How does tobacco use affect tumor biology?
- Should cancer therapeutic agent dosing be modified for tobacco users?
- Optimal timing of cessation relative to therapy?
- What are the best approaches for cessation interventions in cancer patients?
- Can cessation improve adherence to cancer therapy?
- Can cessation improve quality of life?
- How does tobacco use interact with other behavioral and demographic factors?
- What is the clinical impact of other tobacco products?

Task Force Near Term Deliverables

- Recommended measures (online)
  - 3 tiers; Tier 1 is minimal set
- Protocol for tobacco use measurement (online)
  - Timing and procedures
- Research agenda (publication; see handout)

- June-present, 2013: Working groups and conference calls
- Sept 2013: In-person meeting facilitated by NCI Office of Science Planning and Assessment



Draft recommended measures Tier 1 (minimal) paraphrased

Baseline:

- Ever smoked 100+ cigarettes in lifetime?
- How long since smoked?
- How many years smoked?
- Average number of cigarettes per day?

Follow-up:

- How long since smoked?

Action Timeline

Next steps

- Finalize and promote measures and recommendations via scientific dialog
- Facilitate implementation of tobacco use assessment in National Clinical Trials Network
- Assessment in selected trials
- Develop NCI Guidance

Feedback

What are the barriers to incorporating tobacco use items in

- Selected clinical trials?
- All NCTN Phase III clinical trials?