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FDA-AACR-IASLC

Workshop to Address the Criticality of Tobacco Use Assessment in Oncology Therapeutic Trials

February 28, 2020 | Silver Spring, MD

@FDAOncology

@AACR

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Workshop Cochairs:

Michael E. Menefee, MD

Roy S. Herbst, MD, PhD

Matthew Steliga, MD



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SESSION I: Assessment Of Tobacco In Oncologic Therapeutic Trials: Introduction And Rationale

**Session Moderators: Carolyn M. Dresler, MD, MPA, and
Michael E. Menefee, MD**

Speakers:

Carolyn M. Dresler, MD, MPA

Paul A. Bunn, Jr. MD, FASCO

Graham Warren, MD, PhD

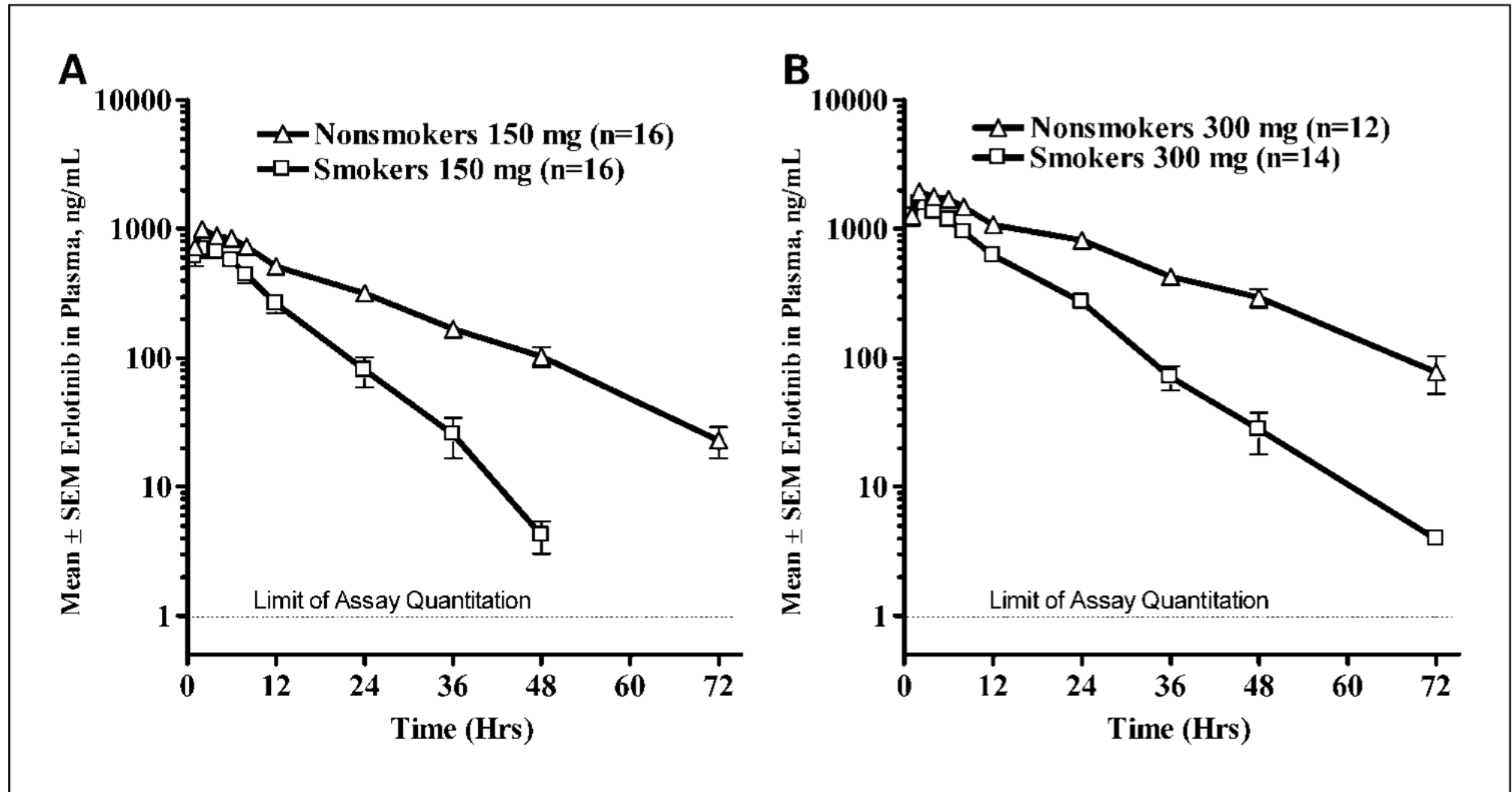
Stephanie Land, PhD

Addressing the Criticality of Tobacco Use Assessment In Oncology Therapeutic Trials

Overview

Carolyn Dresler, MD, MPA

Effects of smoking on the pharmacokinetics of erlotinib



Effects of smoking on the pharmacokinetics of erlotinib

Hamilton, et al. (from OSI Pharma)

Clin Cancer Res, 2006; 12(7pt1):2166-71

“In conclusion, this study supports that the decrease in erlotinib exposure obs

FDA dosing instructions - Erlotinib

7. Drug Interactions:

Cigarette smoking has been shown to reduce erlotinib AUC. Patients should be advised

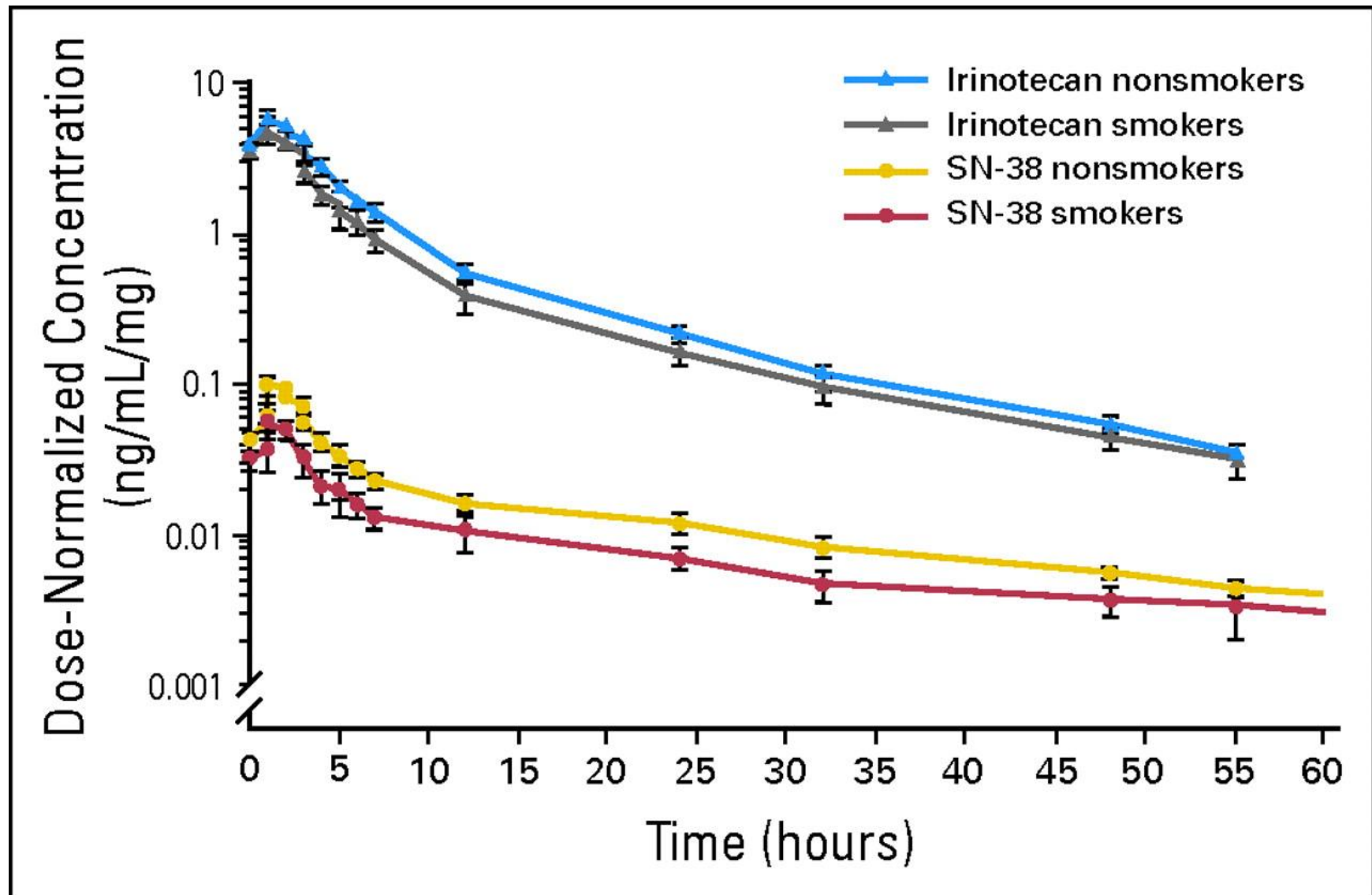
12.3 Metabolism:

“However, the exact dose to be recommended for patients who currently smoke is

17. Patient Counseling Information:

Smokers should be advised to stop smoking while taking TARCEVA as plasma conc

Mean dose-normalized plasma concentration–time curves ($\pm$ 95% CI) of irinotecan and SN-38 in smokers and nonsmokers (N = 190).

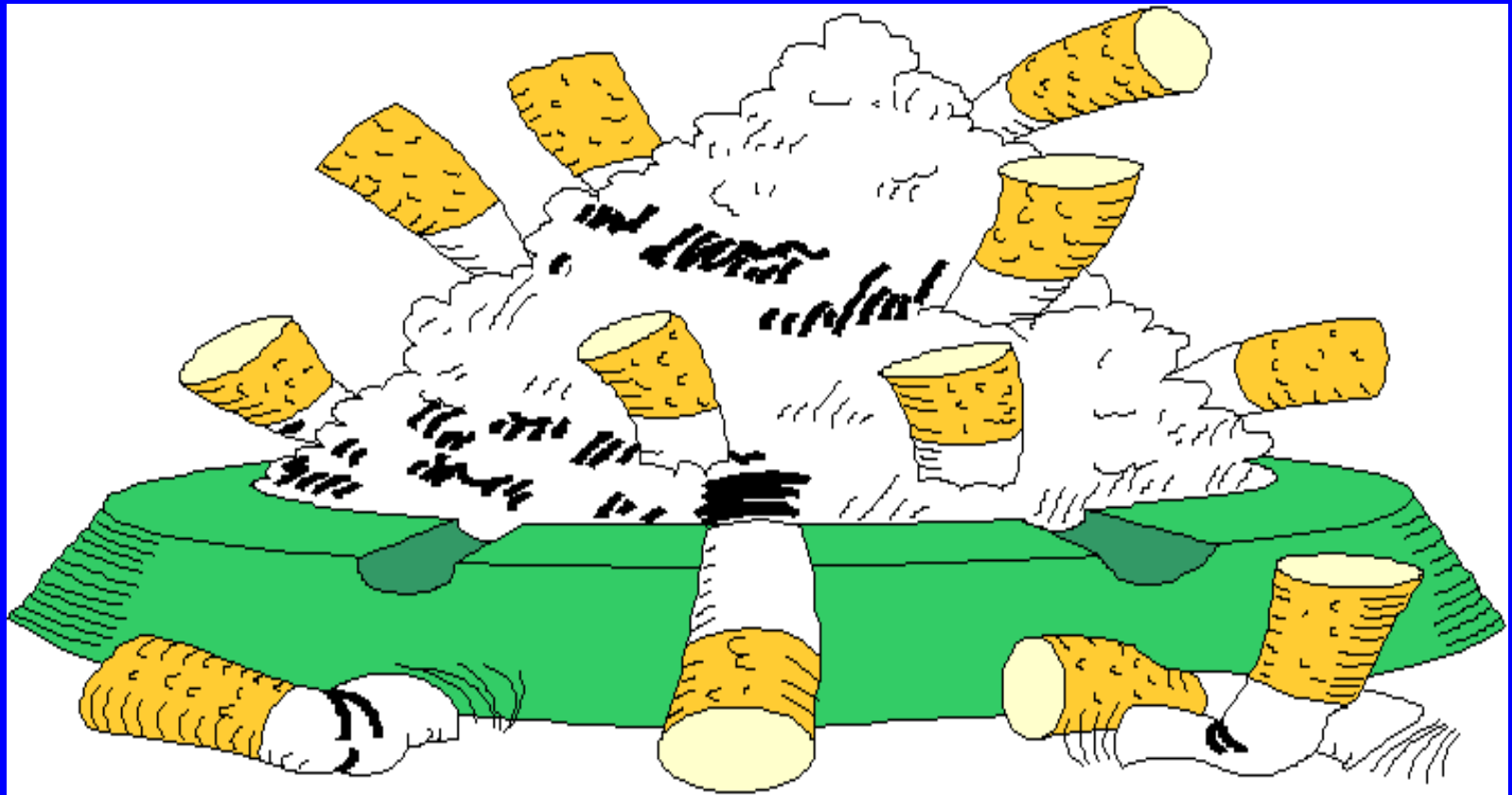


van der Bol J M et al. JCO 2007;25:2719-2726

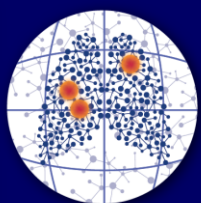
Awareness among patients with cancer of the harms of continued smoking

Responses from patients who were currently smoking at time of diagnosis

Question on Harms of Continued Smoking	Agree	Don't Know	Disagree
Smoking Increases Surgical Complications	29%	51%	20%
Smoking Increases Radiation Side Effects	20%	60%	19%
Smoking Reduces Quality of Life After Chemotherapy	28%	48%	24%
Smoking Reduces Efficacy of Chemotherapy/Radiation	26%	54%	20%
Smoking Increases Risk of Death	40%	35%	25%
Smoking Increases Risk of Second Primary Cancers	42%	31%	17%



Thank you!



2020 Targeted Therapies
of Lung Cancer Meeting

Tobacco/Nicotene Biology and Lung Cancer

Paul A. Bunn, Jr, MD, Distinguished Professor and Dudley Endowed Chair, Univ. of Colorado Cancer Center, Aurora, CO, USA

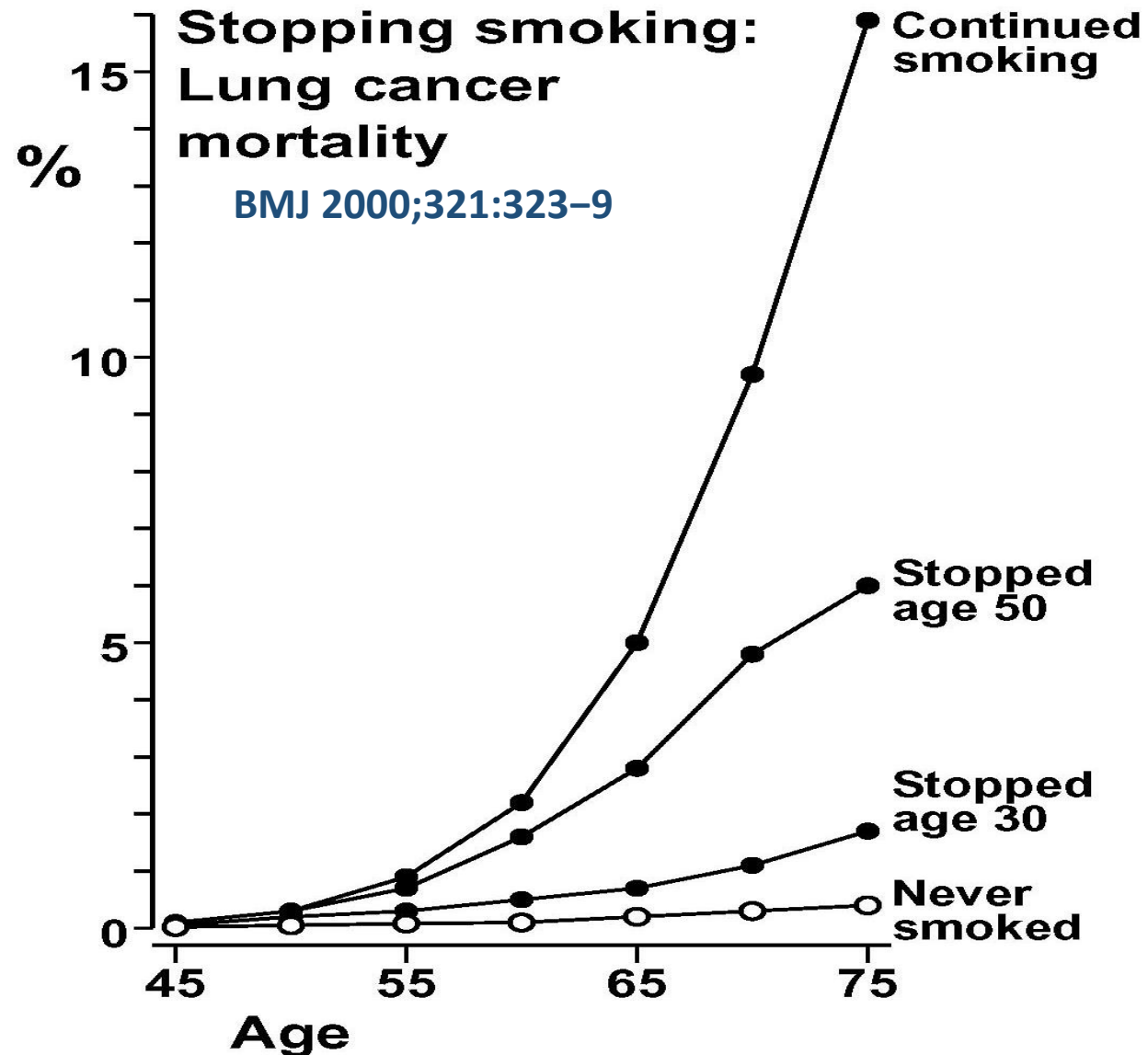


Consultant: Amgen, AstraZeneca, Bayer, BMS, Cellegene, Daiichi- Sankyo, Eli Lilly, Ipsen, Merck, Roche, C-Stone, Ascentage

Tobacco/Nicotine Biology and Lung Cancer

- 1. Does tobacco smoking cause lung and other cancers?**
- 2. Does tobacco cessation reduce cancer risk?**
- 3. Does tobacco smoke increase mutations and mutation burden and produce unique mutations?**
- 4. Do these tobacco induced mutations affect outcome from therapy?**
- 5. Does nicotine itself cause mutations and cancer and can e-cigarettes and vaping cause cancer or affect cancer treatment outcomes?**
- 6. Does smoking cessation after diagnosis affect outcome? From surgical resection?; From Radiation?; From Chemotherapy?; From immunotherapy?**

Cumulative Risk at UK Male 1990 Rates



- 1). Does tobacco smoking cause lung and other cancers? yes
- 2). Does tobacco cessation reduce cancer risk? yes

Causes of Death from tobacco smoke

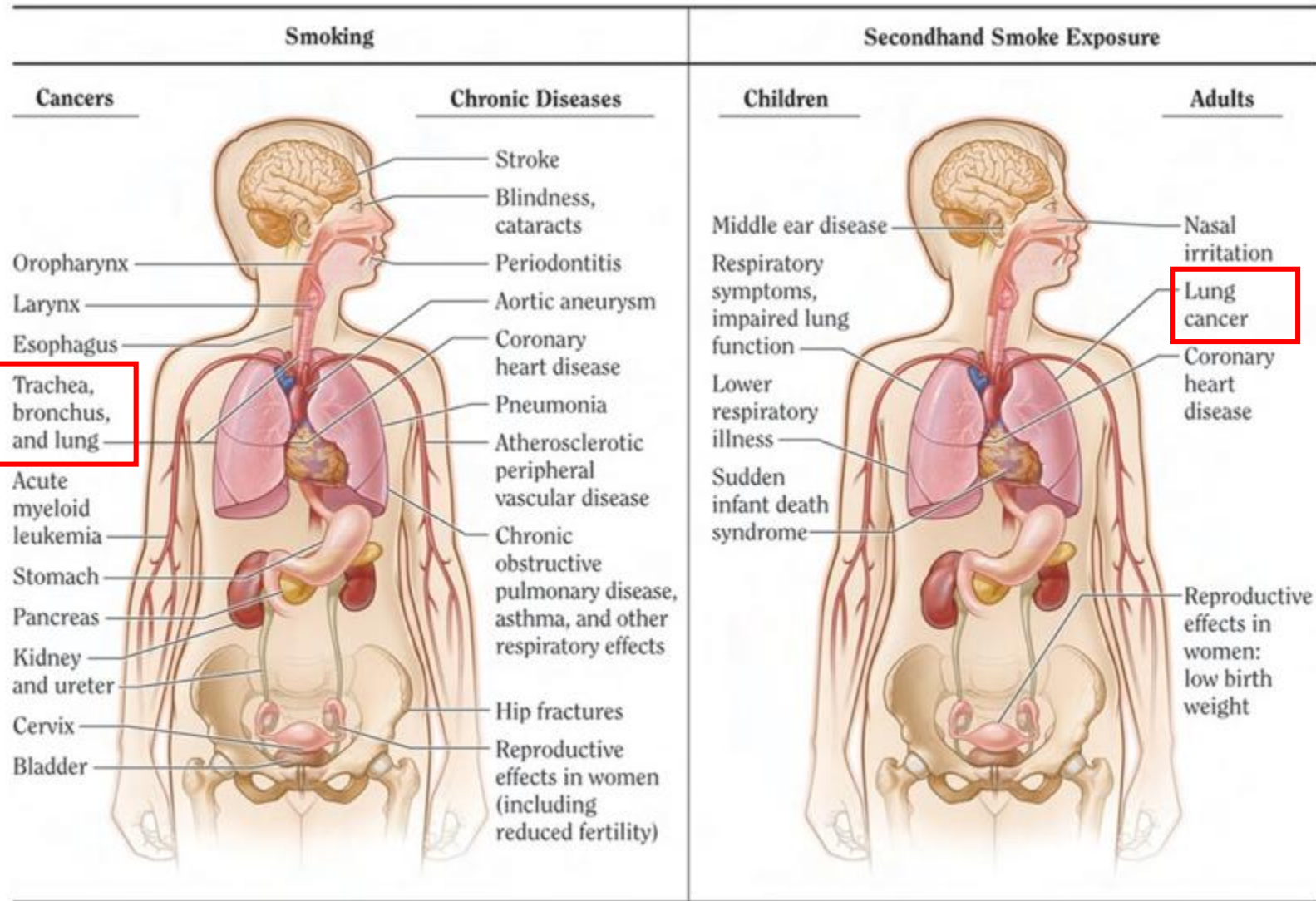
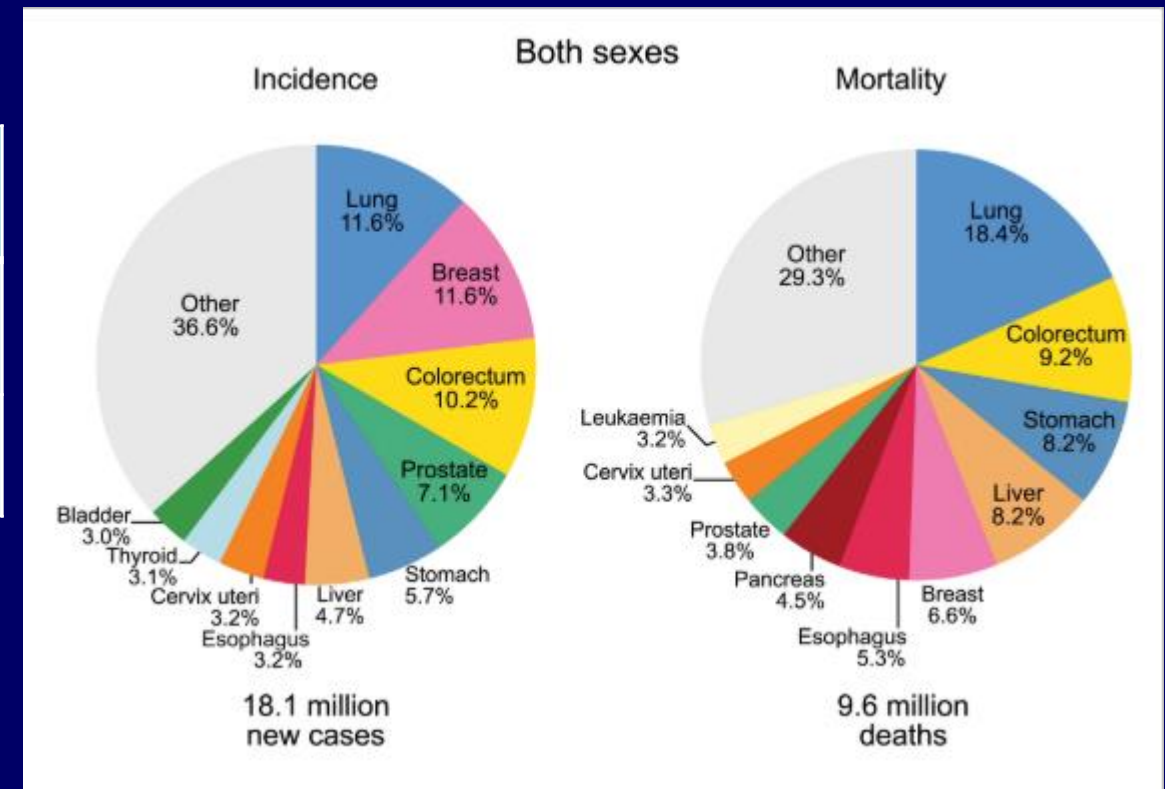


Figure 1.1 The health consequences causally linked to smoking and exposure to secondhand smoke

Source: [USDHHS 2004, 2006](#).

Global New cases and # of deaths from Lung Cancer 2015 and 2017

Cancer Site	# New cases (% of all)	# Deaths (% of all)	#China new Cases (%)	# China deaths (%)
Lung	2,093,876 (11.6)	1,761,007 (18.4)	733,300 (17.1)	610,200 (21.7%)
total	18,078,957 (100)	9,555,027 (100)	4,292,000	2,814,000

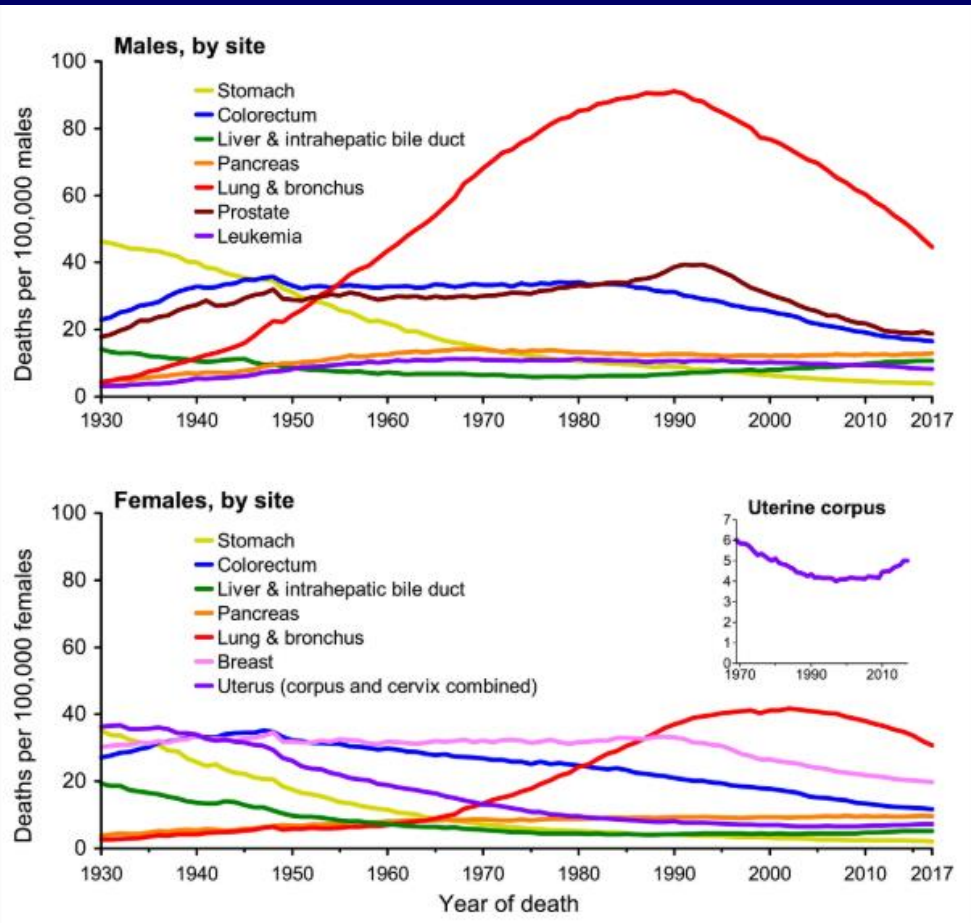


Bray F, et al Global Cancer Statistics 2018

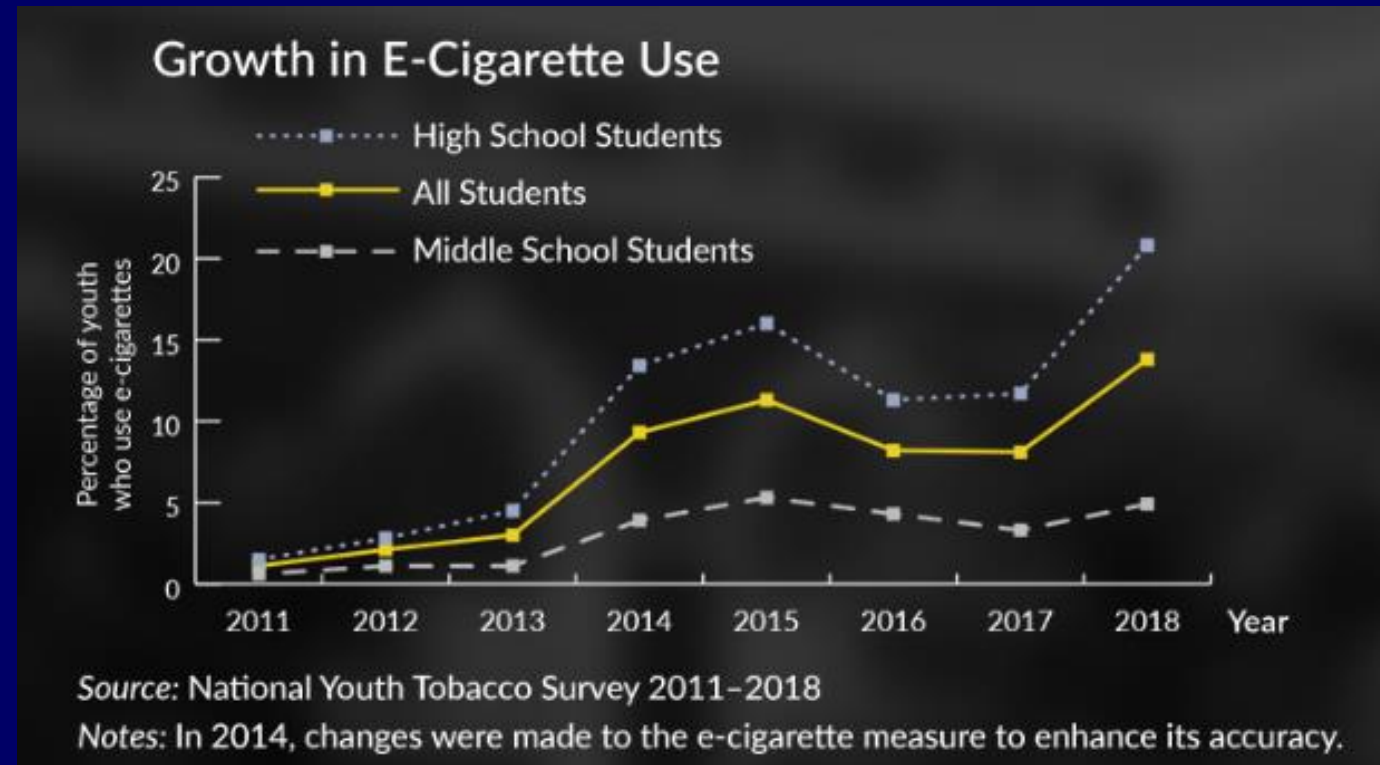
Ca Cancer J Clin 68:394-424,2018; Chen W et al Cancer Statistics in

China 2015, Ca Cancer J Clin 66:115-132, 2016

U.S. Cancer statistics and smoking trends, 2020



	New Cases	Rank	(%)	Deaths	Rank	(%)
Total	228,800	3	(13%)	135,700	1	(23.5%)
Male	116,300	2	(13%)	72,500	1	(23%)
Female	112,520	2	(12%)	63,220	1	(22%)



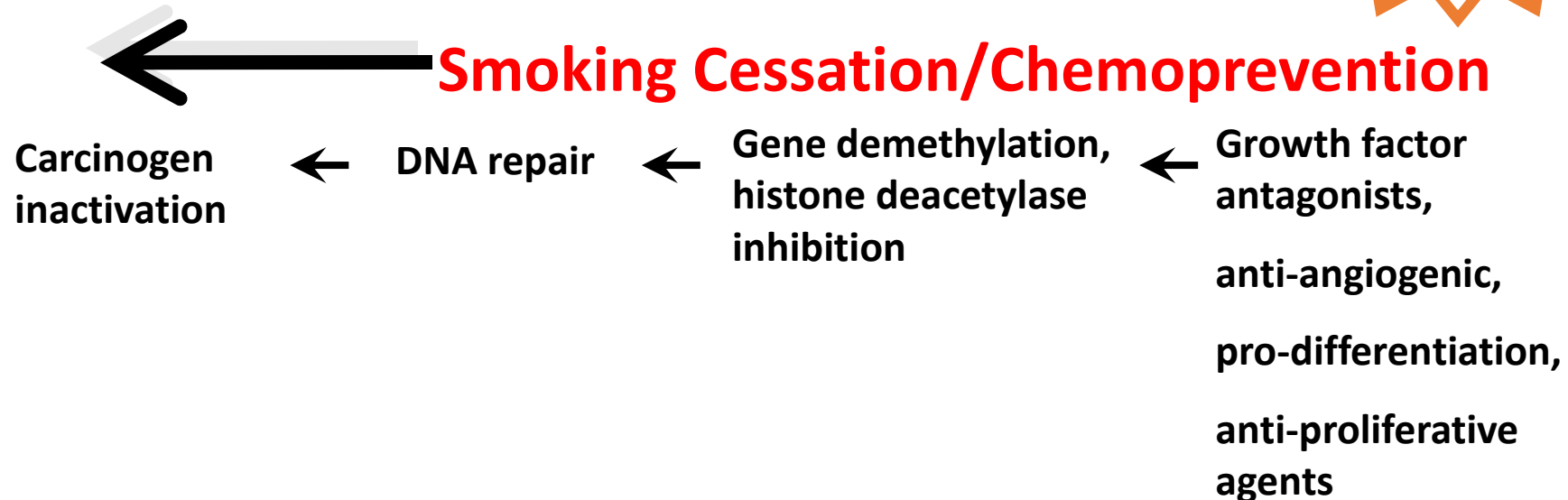
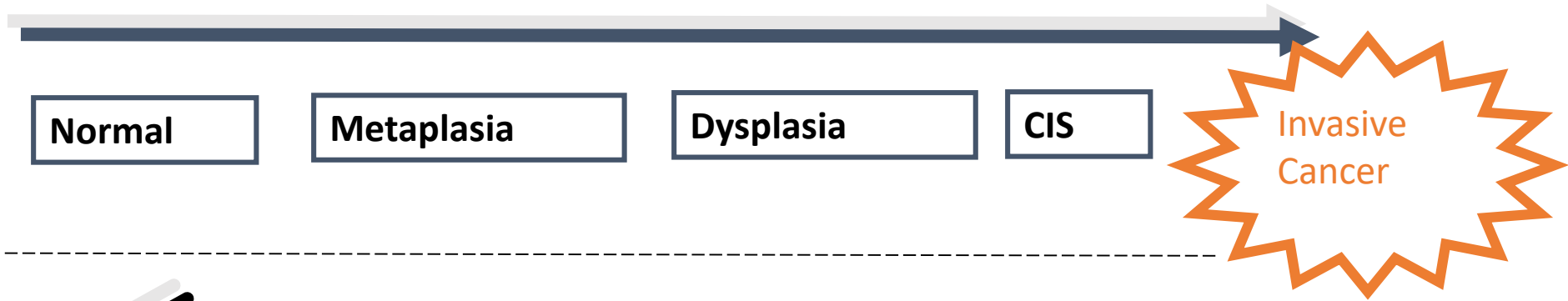
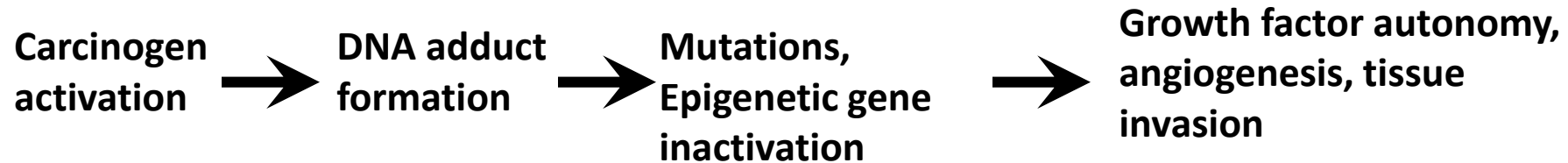
5-year survival = 19% (5% in 1964)

Tobacco/Nicotine Biology and Lung Cancer

- 1. Does tobacco smoking cause lung and other cancers? YES**
- 2. Does tobacco cessation reduce cancer risk? YES**
- 3. Does tobacco smoke increase mutations and mutation burden and produce unique mutations? Are stem cells affected? Are cells in the microenvironment affected?**

Tobacco Smoke Exposure/Carcinogenesis

Carcinogens, Oxidative stress, Inflammation



Carcinogens in tobacco

Table 1 | **Types of carcinogen in tobacco products***

Tobacco smoke			
Chemical class	Number of compounds[‡]	Representative carcinogens and typical amounts in mainstream smoke (ng per cigarette)[§]	
PAH	14	BaP	9
		Dibenz[a,h]anthracene	4
Nitrosamines	8	NNK	123
		NNN	179
Aromatic amines	12	4-Aminobiphenyl	1.4
		2-Naphthylamine	10
Aldehydes	2	Formaldehyde	16,000
		Acetaldehyde	819,000
Phenols	2	Catechol	68,000
Volatile hydrocarbons	3	Benzene	59,000
		1,3-Butadiene	52,000
Nitro compounds	3	Nitromethane	500
Other organic compounds	8	Ethylene oxide	7,000
		Acrylonitrile	10,000
Inorganic compounds	9	Cadmium	132
Total	61		
Unburned tobacco			
Chemical class	Number of compounds	Representative carcinogens and typical amounts in processed tobacco (ng g⁻¹)	
PAH	1	BaP	0.4–90
Nitrosamines	6	NNK	1,890
		NNN	8,730
Aldehydes	2	Formaldehyde	1,600–7,400
		Acetaldehyde	1,400–7,400
Inorganic compounds	7	Cadmium	1,300–1,6000
Total	16		

Table 2 | **Carcinogens and tobacco-induced cancers**

Cancer type	Likely carcinogen involvement *	References
Lung	PAH, NNK (major) 1,3-butadiene, isoprene, ethylene oxide, ethyl carbamate, aldehydes, benzene, metals	6,15,22,37,144,145
Laryngeal	PAH	5,6,15
Nasal	NNK, NNN, other nitrosamines, aldehydes	27,34–36
Oral cavity (smokers) (smokeless-tobacco users)	PAH, NNK, NNN NNK, NNN	6–8,18,21, 27,37,38,40
Oesophageal	NNN, other nitrosamines	6,27,39,40
Liver	NNK, other nitrosamines, furan	27,34,41
Pancreatic	NNK, NNAL	6,27,42,43
Cervical	PAH, NNK	26,44,45
Bladder	4-Aminobiphenyl, other aromatic amines	6,37,47–52
Leukaemia	Benzene	53

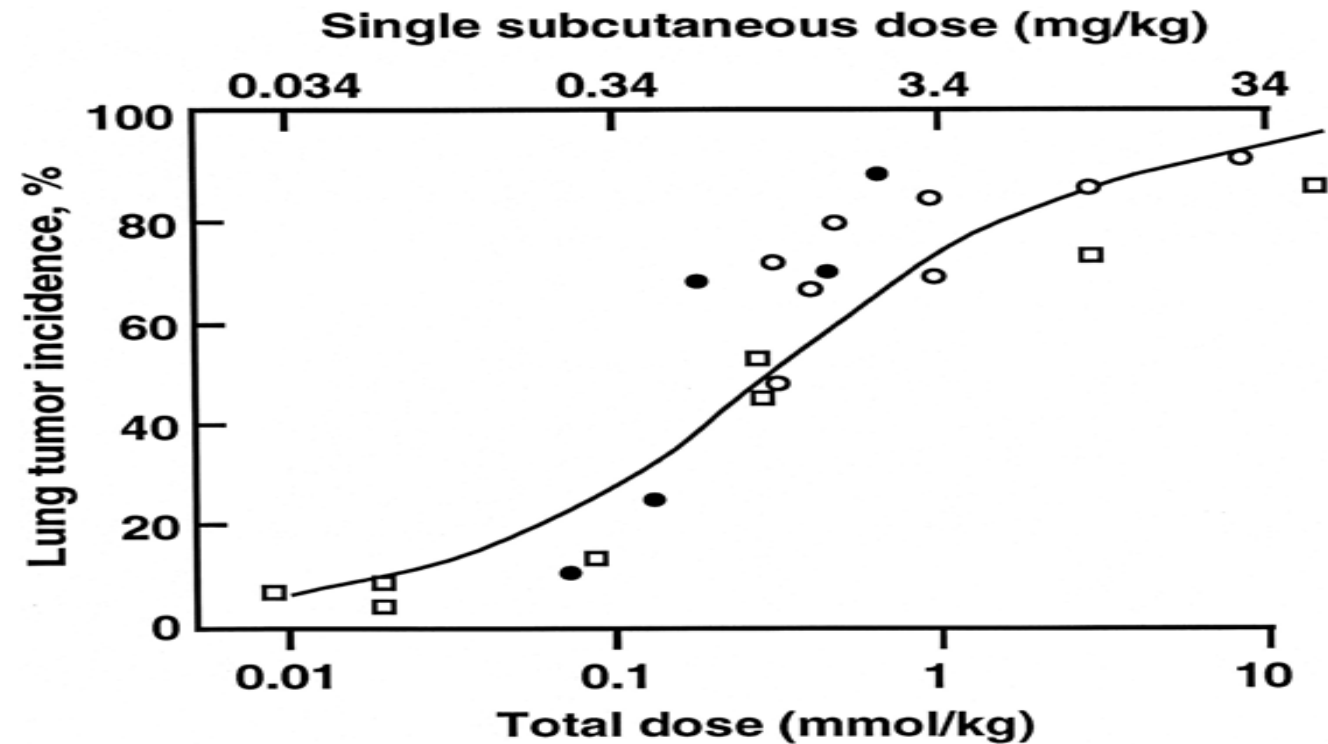
It has been established conclusively that DNA adducts derived from cigarette-smoke carcinogens cause miscoding — most frequently G–T and G–A mutations^{63,64,65}. If these permanent mutations occur in crucial regions of oncogenes such as [RAS](#) and [MYC](#), or in tumour-suppressor genes such as *TP53* and *CDKN2A* (which encodes p16), the result can be loss of normal cellular growth-control mechanisms and development of cancer.

Smoke carcinogens cause cancer in mice

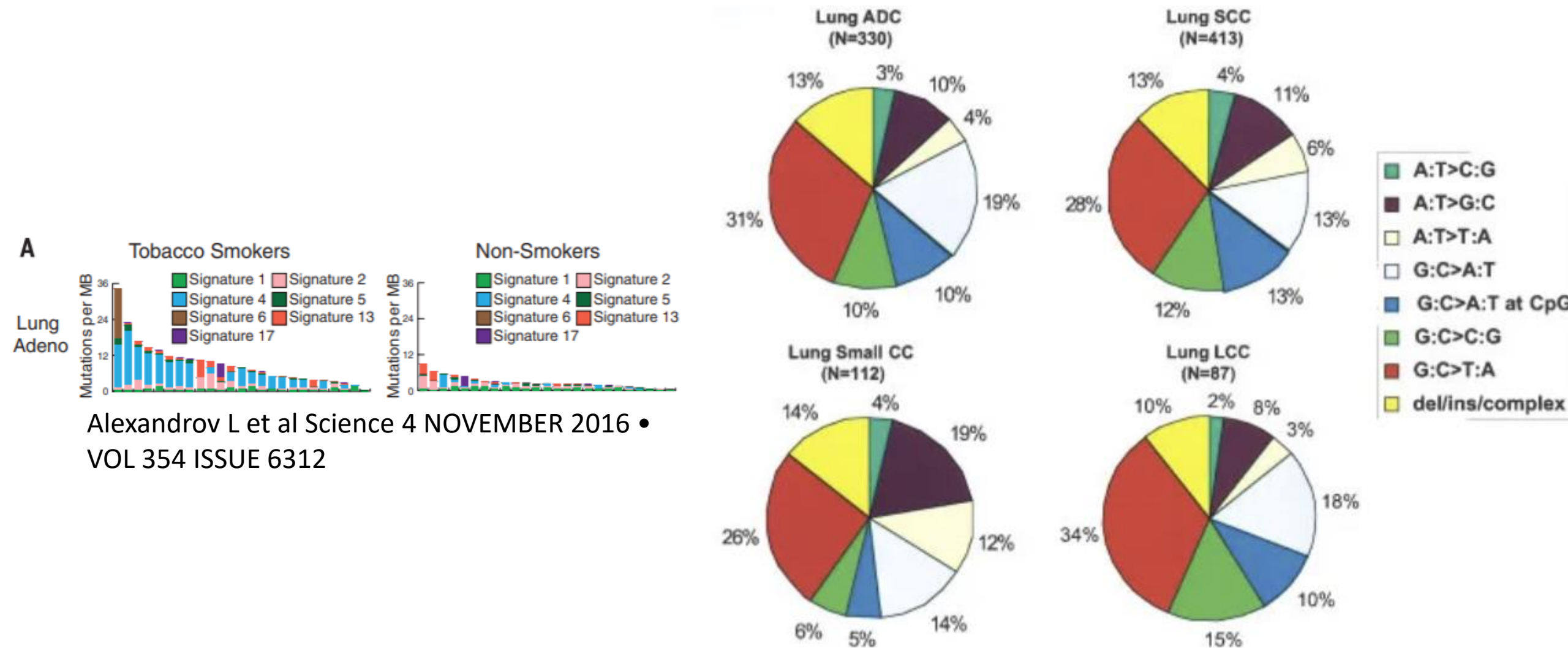
Fig. 3. Relationship between dose of

4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone and lung tumor incidence

in ...



Tobacco induced lung cancers have specific mutations and mutational signatures and higher TMB

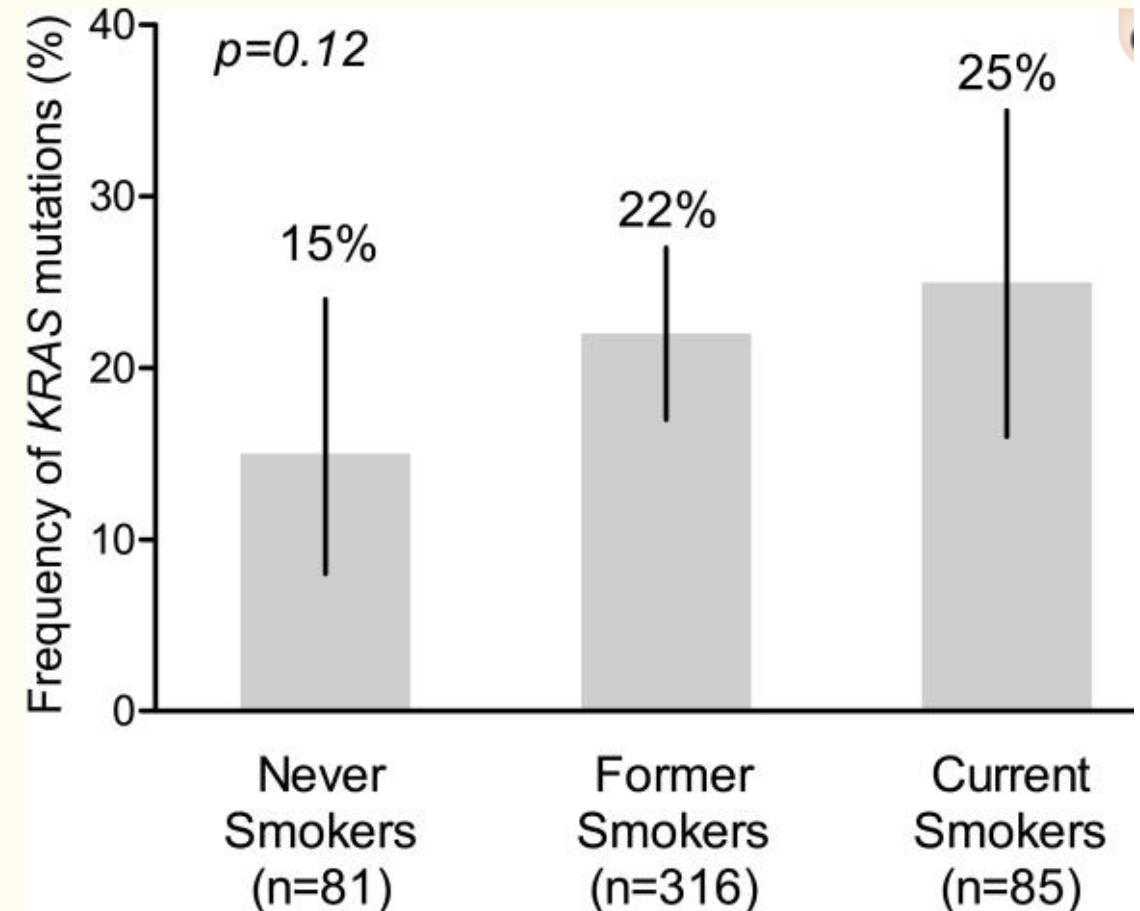


But do these mutations and signatures also affect the Tumor microenvironment and response to therapy?

KRAS mutation frequency and type by smoking status

KRAS mutation type as a function of smoking history

<i>KRAS</i>				
Mutation	Nucleotide	Former/current	Never	Total
G12A	GGT→GCT	13	0	13
G12C	GGT→TGT	38	0	38
G12V	GGT→GTT	20	1	21
G13C	GGC→TGC	2	0	2
G13D	GGC→GAC	1	0	1
G12D	GGT→GAT	15	10	25
G12S	GGT→AGT	1	1	2
Total		90	12	

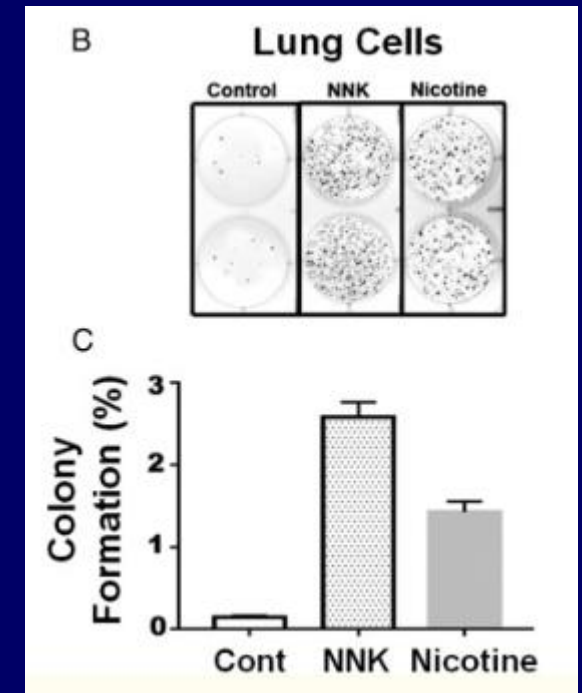


[Riely G et al](#) Frequency and Distinctive Spectrum of *KRAS* Mutations in Never Smokers with Lung Adenocarcinoma *Clin Cancer Res.* 2008 Sep 15; 14(18): 5731–5734. doi: [10.1158/1078-0432.CCR-08-0646](#) PMCID: PMC2754127
NIHMSID: NIHMS141466 PMID: [18794081](#)

Tobacco/Nicotine Biology and Lung Cancer

1. Does nicotine itself cause mutations and cancer and can e-cigarettes and vaping cause cancer or affect cancer treatment outcomes?

Unburned tobacco carcinogens			
Chemical class	Number of compounds	Representative carcinogens and typical amounts in processed tobacco (ng g ⁻¹)	
PAH	1	BaP	0.4–90
Nitrosamines	6	NNK	1,890
		NNN	8,730
Aldehydes	2	Formaldehyde	1,600–7,400
		Acetaldehyde	1,400–7,400
Inorganic compounds	7	Cadmium	1,300–1,6000
Total	16		

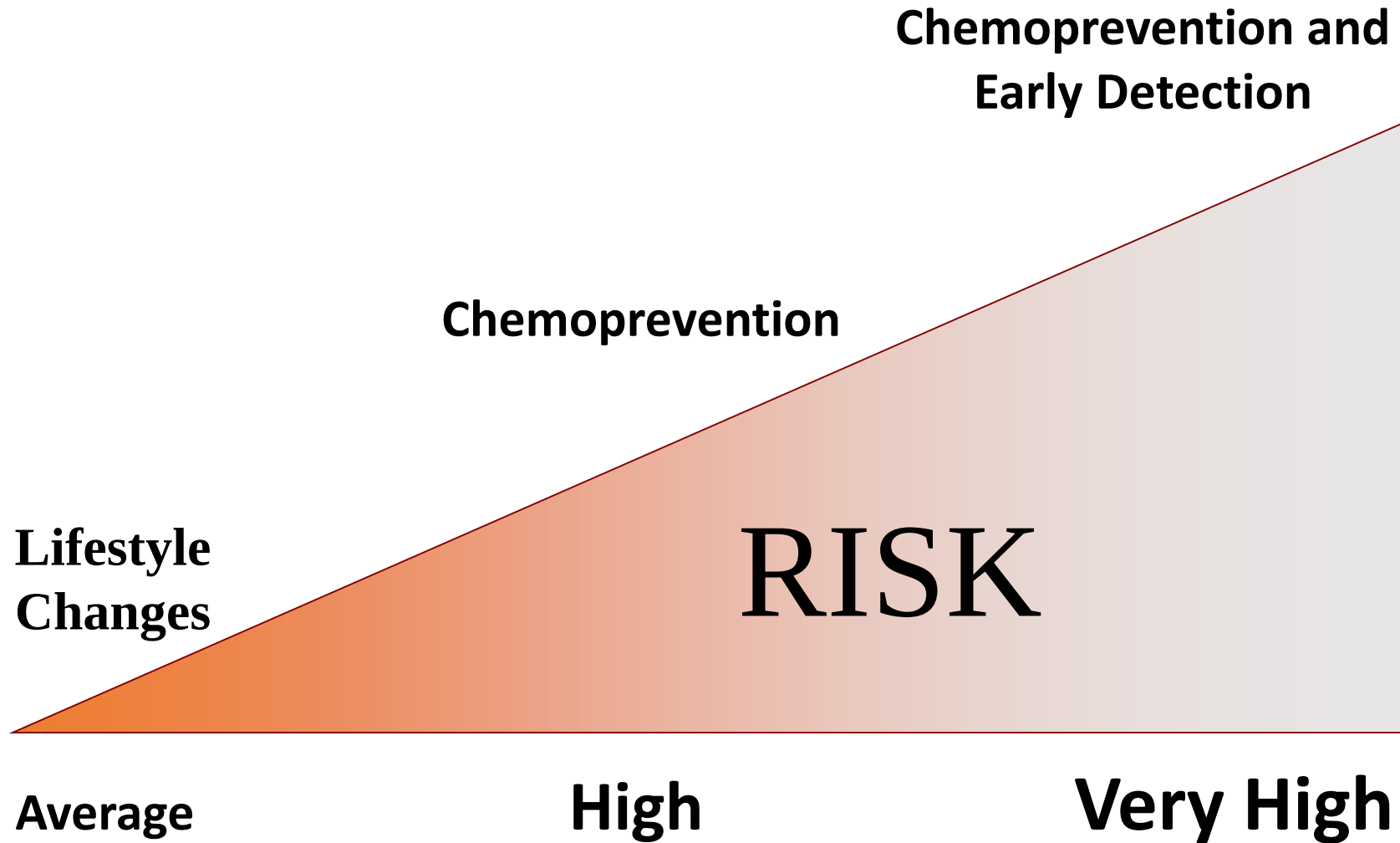


E-cigarette smoke (ECS) delivers nicotine through aerosols without burning tobacco. ECS is promoted as noncarcinogenic. We found that ECS induces DNA damage in mouse lung, bladder, and heart and reduces DNA-repair functions and proteins in lung. Nicotine and its nitrosation product 4-(methylnitrosamine)-1-(3-pyridyl)-1-butanone can cause the same effects as ECS and enhance mutations and tumorigenic cell transformation in cultured human lung and bladder cells. These results indicate that nicotine nitrosation occurs in the lung, bladder, and heart, and that its products are further metabolized into DNA damaging agents. We propose that ECS, through damaging DNA and inhibiting DNA repair, might contribute to human lung and bladder cancer as well as to heart disease, although further studies are required to substantiate this proposal.

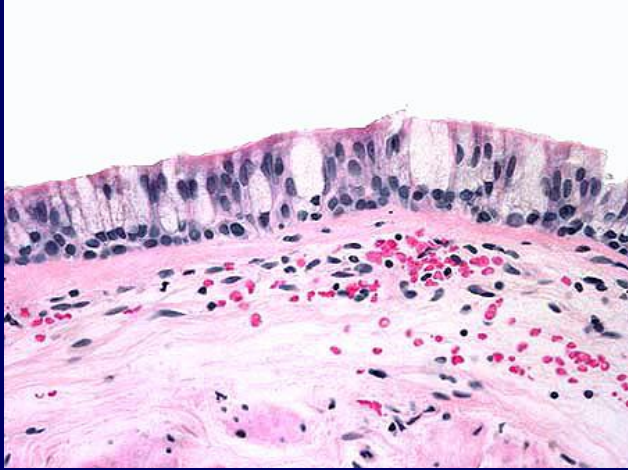
Tobacco/Nicotine Biology and Lung Cancer

- 1. Does smoking influence screening and prevention strategies?**

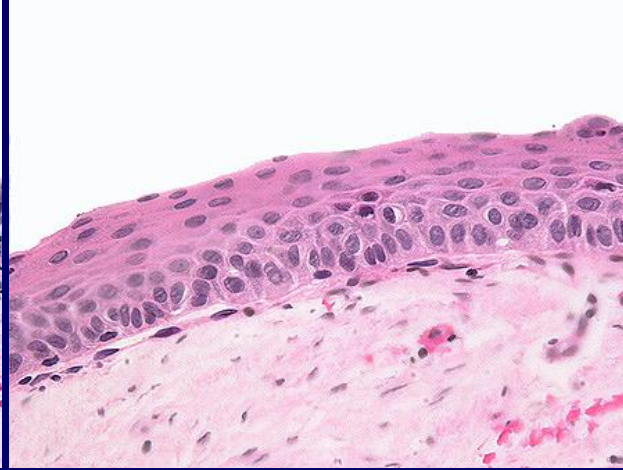
Intervention and Screening Strategies



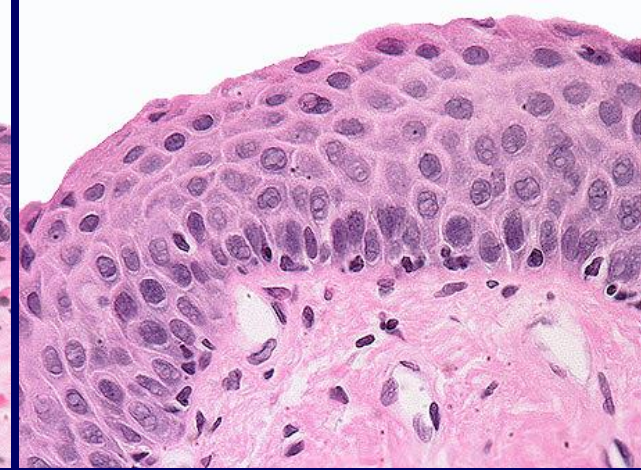
Histology of Bronchial Squamous Epithelium



**Normal
(Grade 1)**



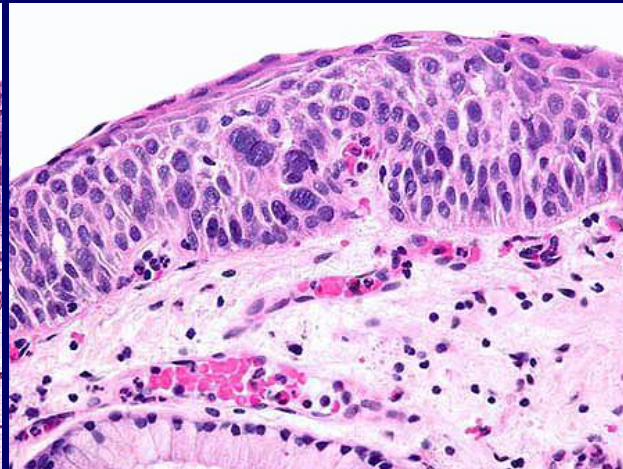
**Squamous Metaplasia
(Grade 3)**



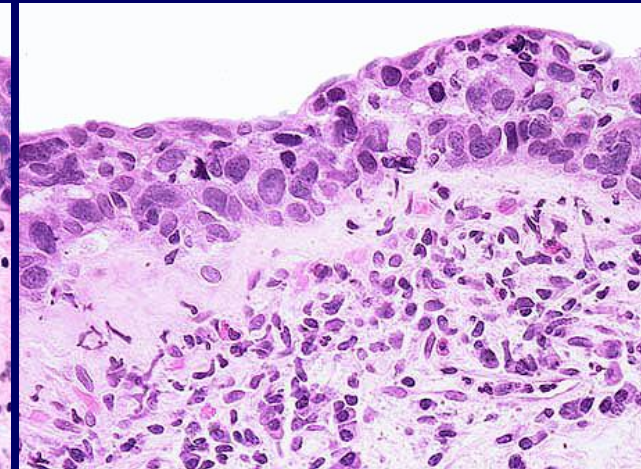
**Mild Dysplasia
(Grade 4)**



**Moderate Dysplasia
(Grade 5)**

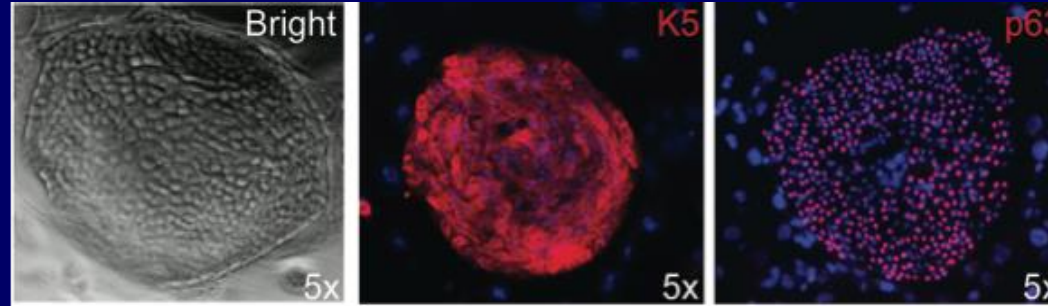


**Severe Dysplasia
(Grade 6)**

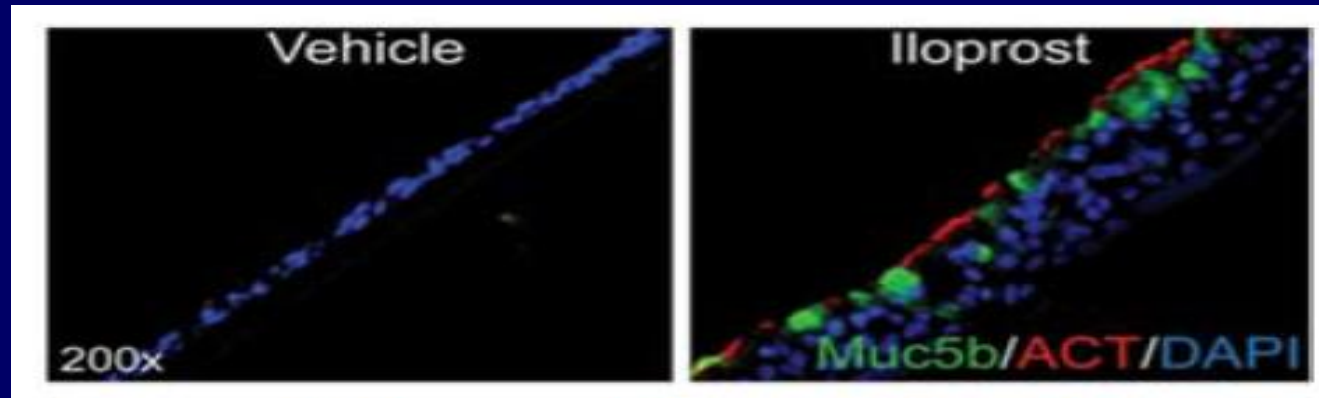


**Carcinoma *in situ*
(Grade 7)**

Organoid models from bronchial biopsies

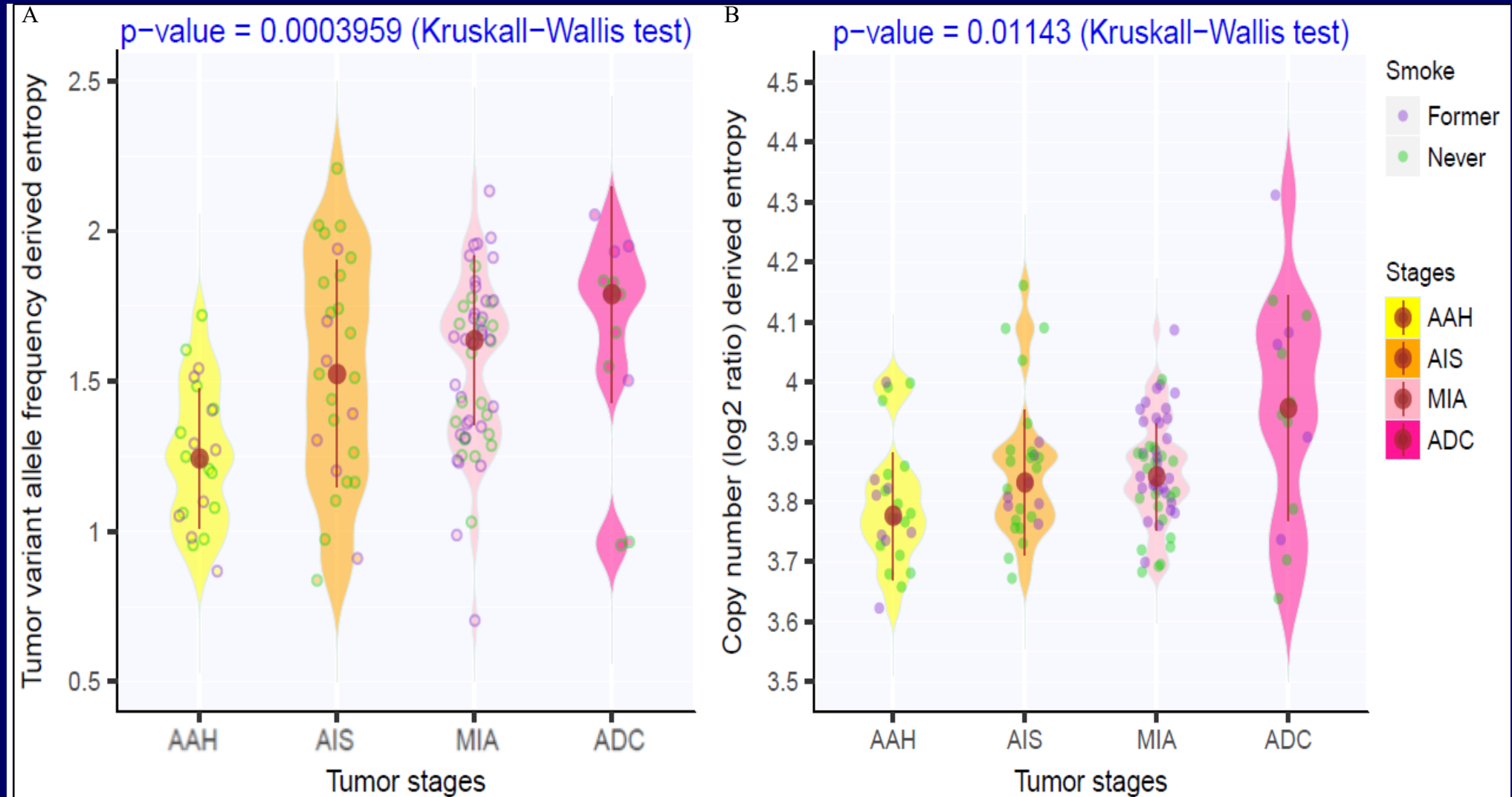


3-D organoid grown from a bronchial biopsy specimens: IF staining with airway basal epithelial cell markers keratin 5 (K5, red, middle, and p63 (red) (right).



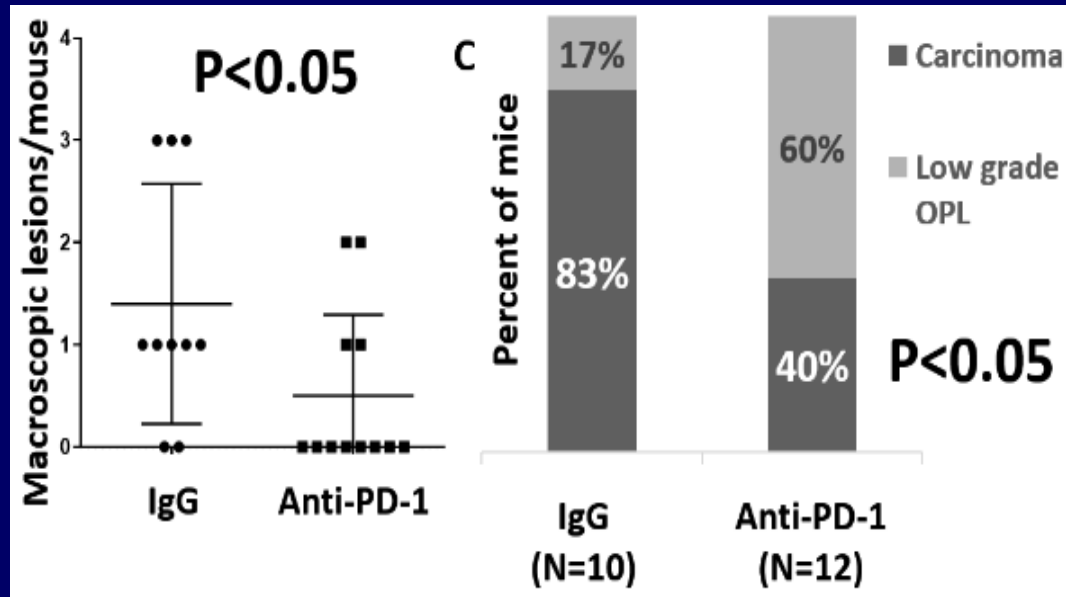
Organoid cultures from dysplastic bronchial biopsies treated with vehicle show only undifferentiated cells while cultures treated with iloprost show induction of differentiation

Evolution of Lung adenocarcinoma

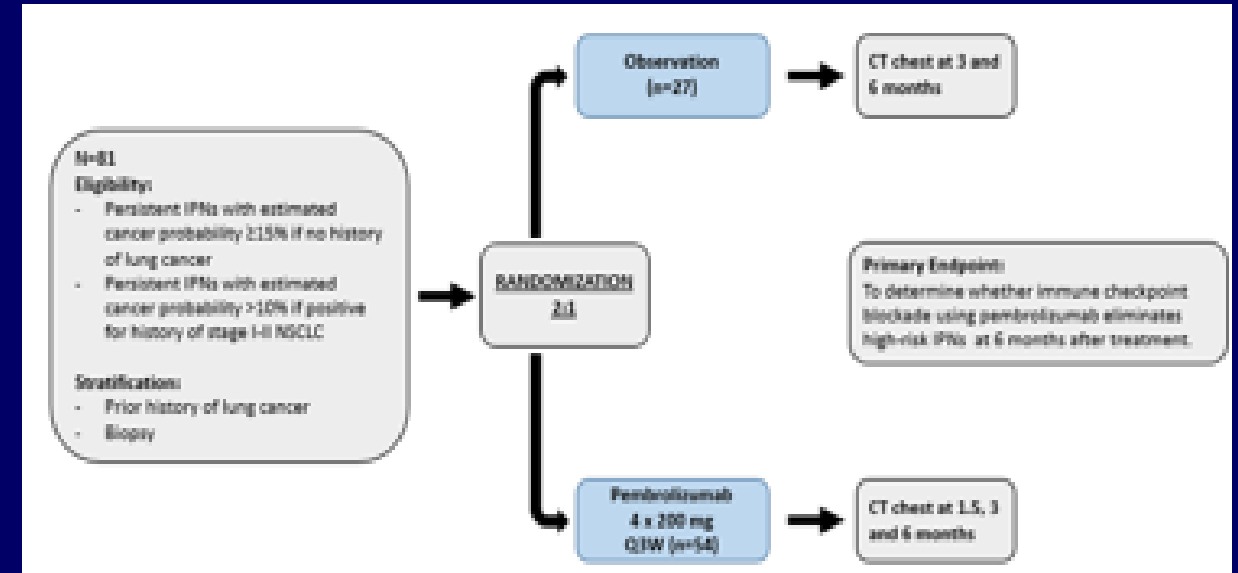


PD1 blockade decreases incidence of oral and lung cancers.

Murine model of carcinogen-induced cancers (4-NQO)



MD Anderson Nodule/Adenocarcinoma immuno-prevention study



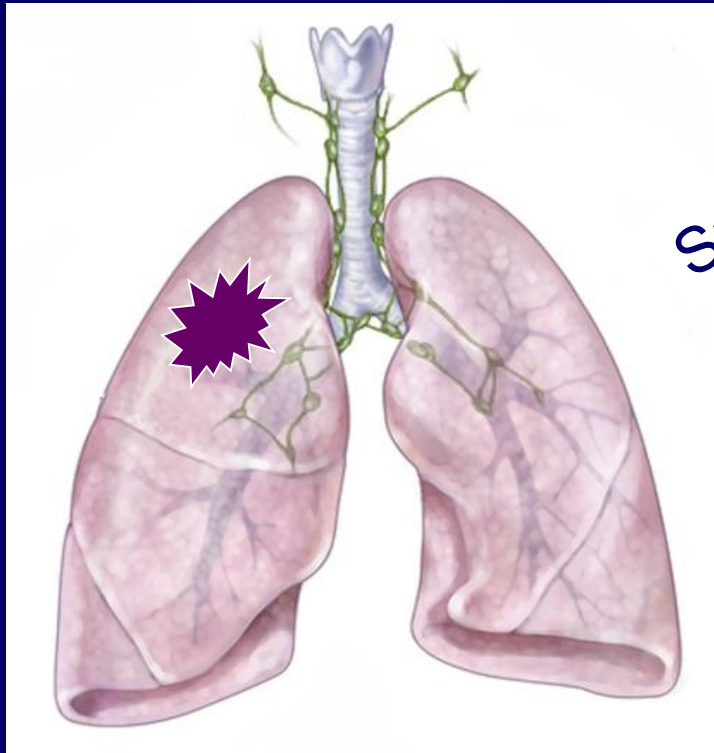
Treatment with PD1 blockade significantly decreases incidence of oral cancer compared to IgG control in 4-Nitroquinoline-1-oxide mouse model. (Adapted from Wang et al, 2017). Treatment with PD1 blockade decreases incidence of lung adenocarcinoma in KRAS mutant genetically engineered murine model.. Heymach Lab, unpublished data.

Should smoking status and tobacco cessation be included in study?

Chemo and immunoprevention studies

- **Prevention trials of high dose vitamins uniformly failed.**
- **Prevention trials in subjects with squamous dysplasia at high risk for squamous cancers using nivolumab (NCT03347838) and pulmonary nodules at high risk for adenocarcinomas using pembrolizumab (NCT03634241) are ongoing.**
- **The effects of smoking cessation on these trials will be critical.**
- **If positive, the effects of checkpoint inhibitors for tertiary prevention should be undertaken.**

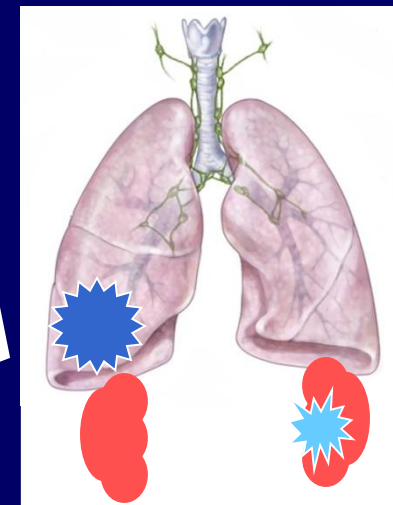
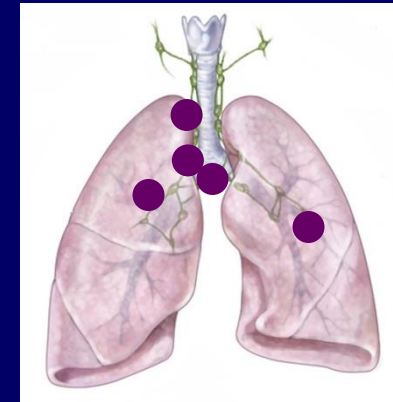
Tertiary Prevention: Stage I Lung Cancer: Recurrence vs Second Primary Tumor (SPT) ** in Lung or Elsewhere



Surgical Cure

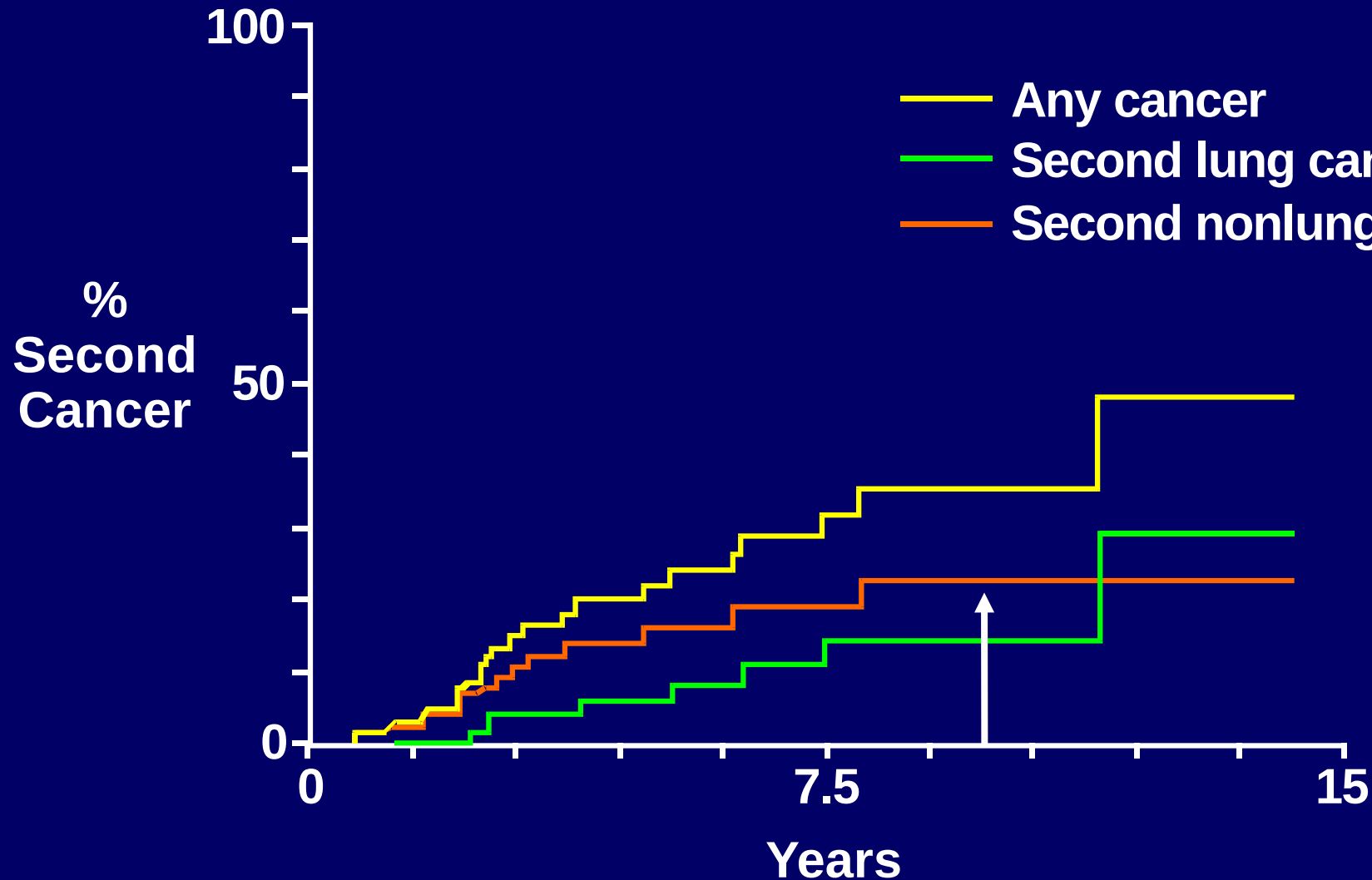
Recurrence

Second Primary Lung
(approx. 2% per yr)



** SPT = Cancer arising in different lobe or lung, different histology, or > 5 years later, or different site such as Kidney

Cumulative Incidence of Second Cancer

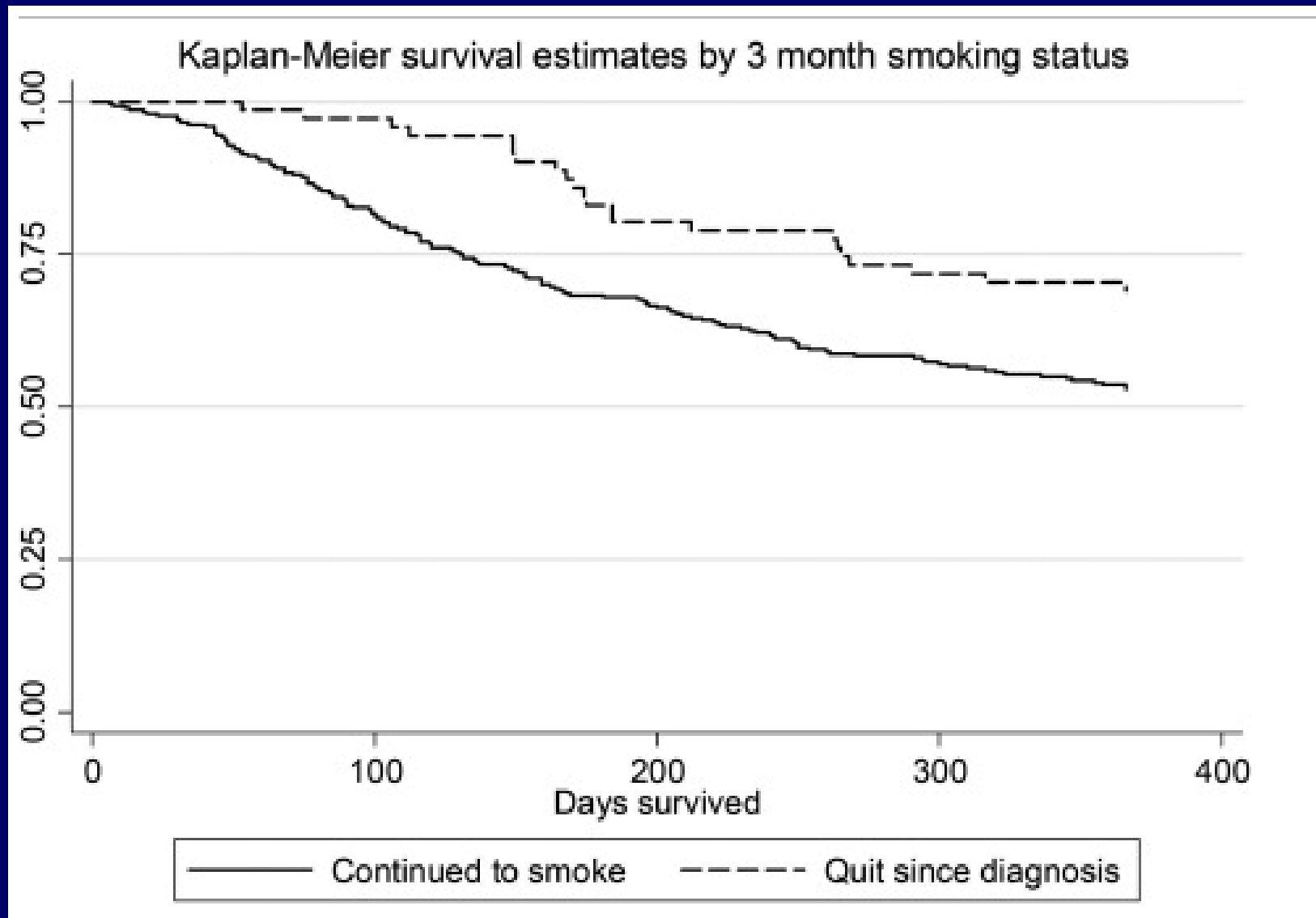


What are the effects of cessation vs continued smoking on these outcomes?
Collection of smoking status Over time should be part of any trial.

Tobacco/Nicotine Biology and Lung Cancer

- 1. Does smoking cessation after diagnosis affect outcome? From surgical resection?; From Radiation? From Chemotherapy? From immunotherapy?**

Effects of continued smoking on survival after lung cancer diagnosis: early stage

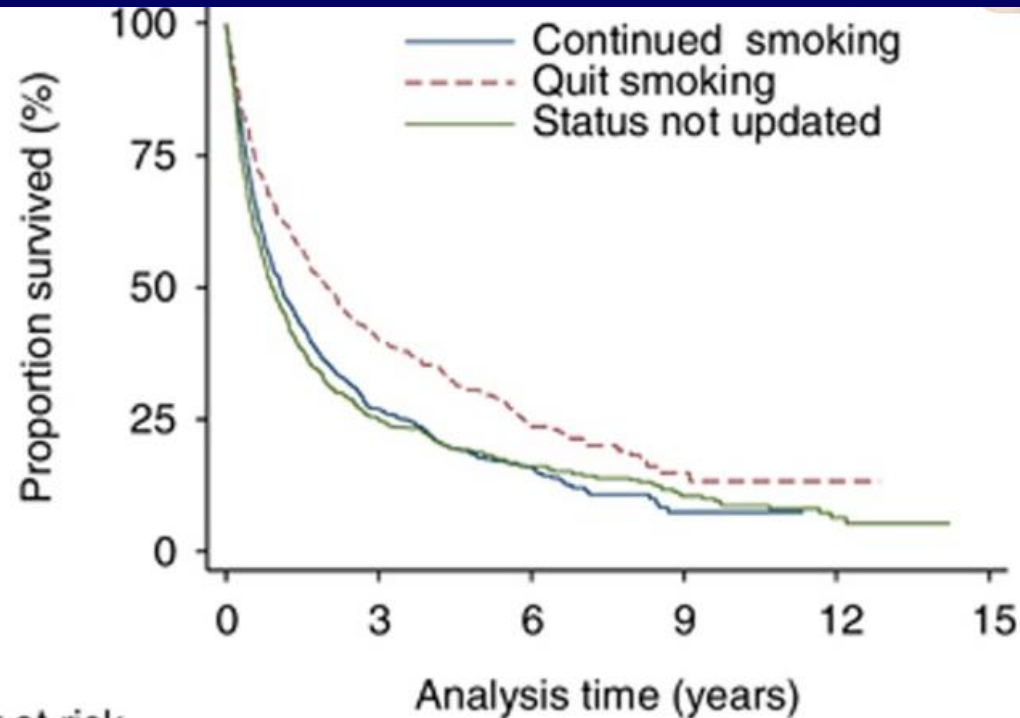


Longitudinal study to assess impact of smoking at diagnosis and quitting on 1-year survival for people with non-small cell lung cancer

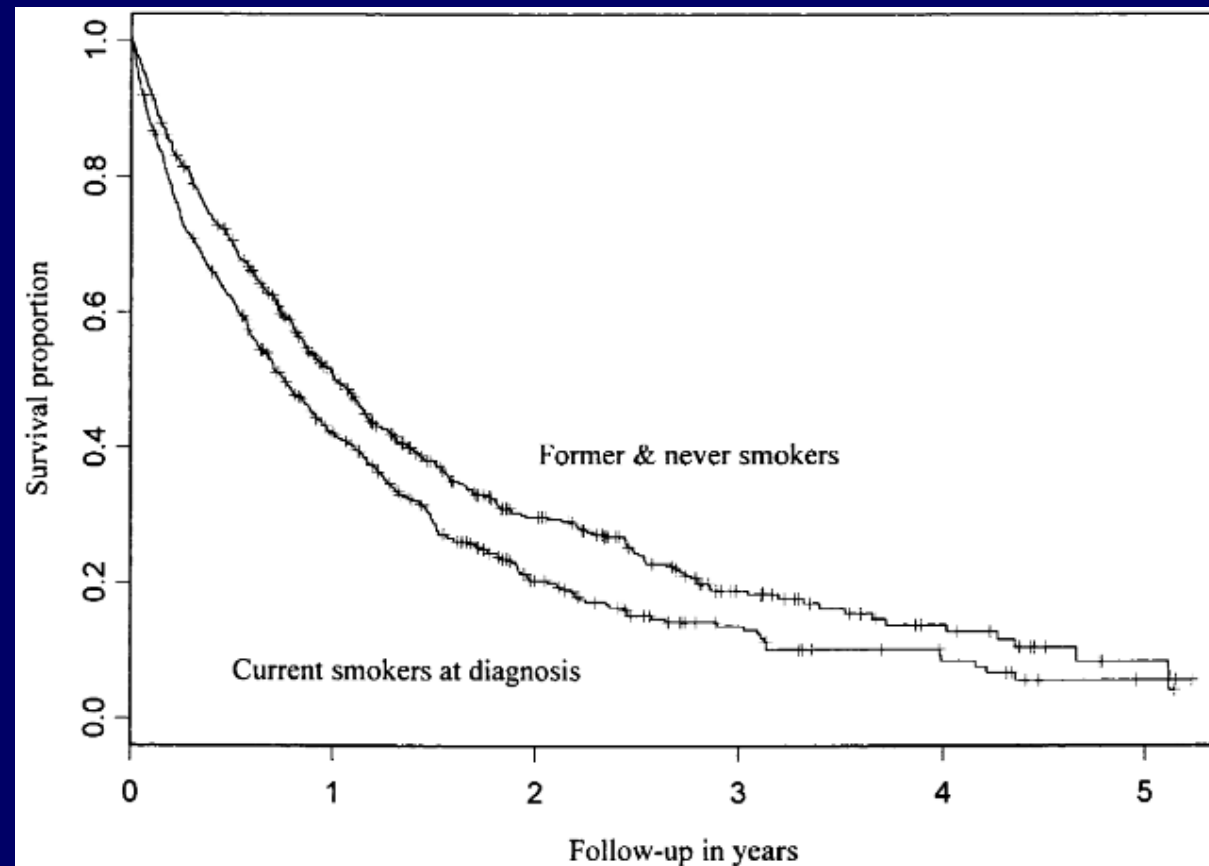
Author links open overlay panel Rachel E. Gemine^a Robin Ghosal^b Gareth Collier^b Diane Parry^b Ian Campbell^b Gareth Davies^b Kathryn Davies^b Keir E. Lewis^{a,b} on behalf of the LungCast Investigators

<https://doi.org/10.1016/j.lungcan.2018.12.028>

Effects of continued smoking on survival after lung cancer diagnosis



Number at risk	0	3	6	9	12	15
Continued smoking	1129	184	52	8	0	0
Quit smoking	784	187	54	9	1	0
Status not updated	969	178	74	24	7	0



[Br J Cancer](#). 2017 Oct 10;117(8):1224-1232. doi: 10.1038/bjc.2017.179. Epub 2017 Sep 12.
Smoking cessation and survival in lung, upper aero-digestive tract and bladder cancer:
cohort study.

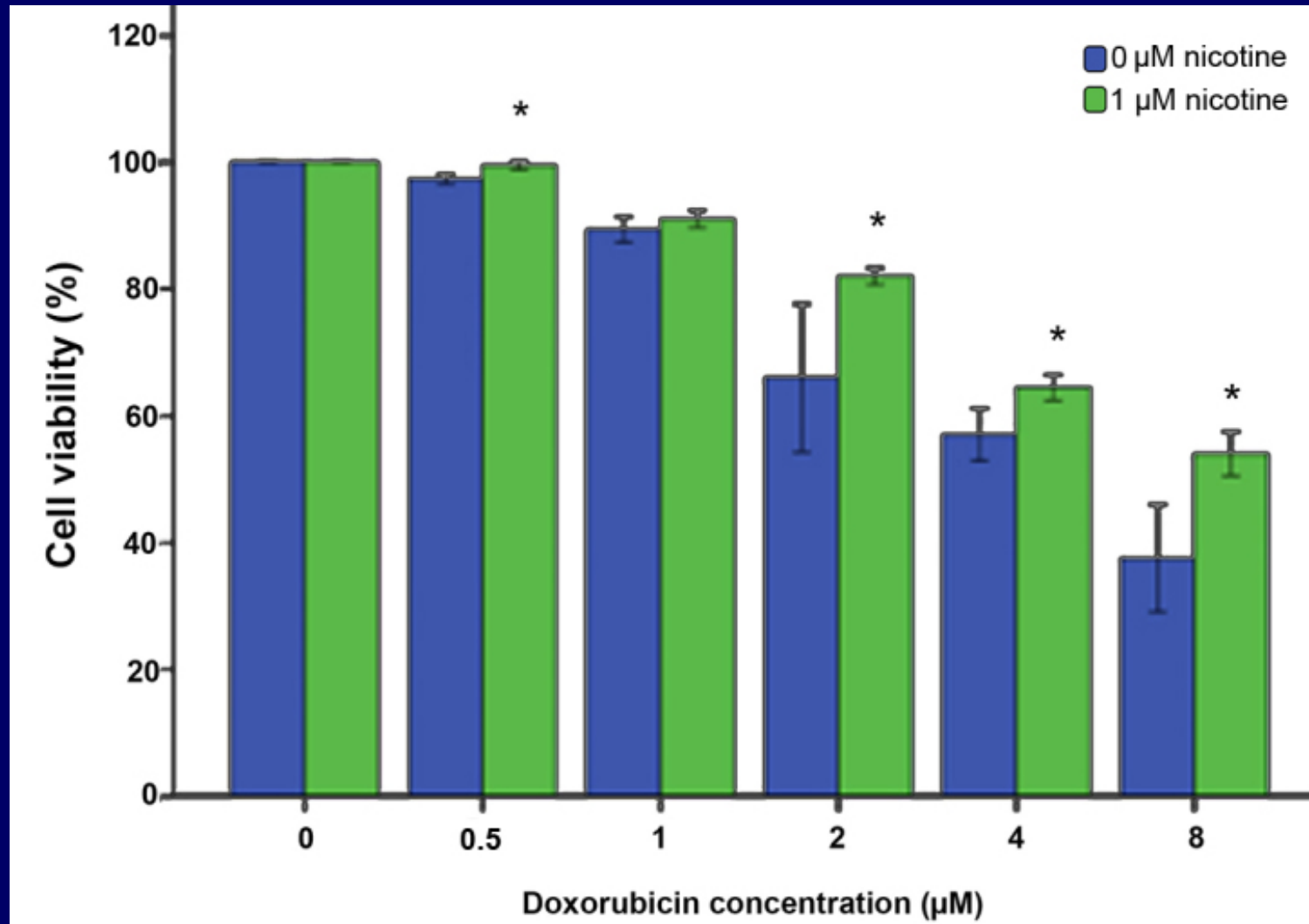
[Koshiaris C](#)¹, [Aveyard P](#)¹, [Oke J](#)¹, [Ryan R](#)², [Szatkowski L](#)³, [Stevens R](#)¹, [Farley A](#)²

[Chest](#). 2004 Jan;125(1):27-37.

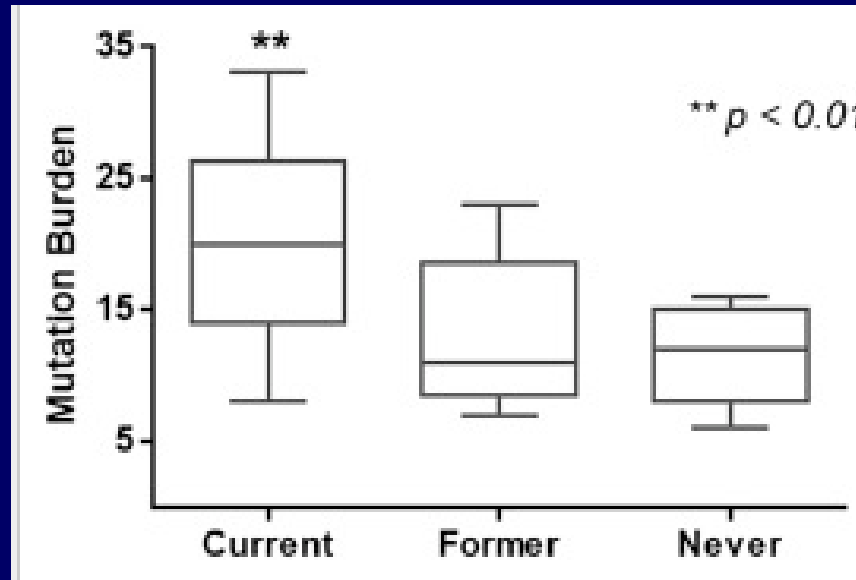
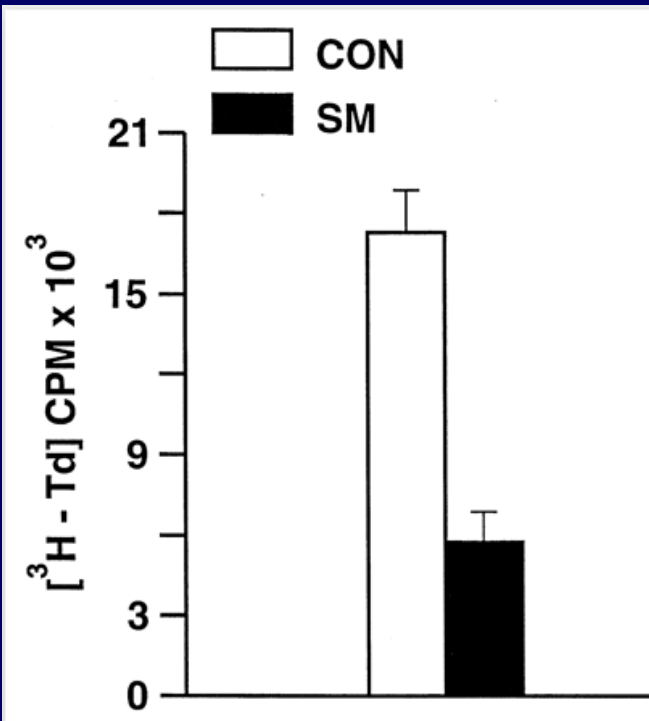
Smoking and lung cancer survival: the role of comorbidity and treatment.

[Tammemagi CM](#)¹, [Neslund-Dudas C](#), [Simoff M](#), [Kvale P](#)

Nicotine decreases Effectiveness of doxorubicin



Does continued smoking affect immunotherapy response?



Subgroup	No. of Events/ No. of Patients	Hazard Ratio for Disease Progression or Death (95% CI)	
Overall	189/305	0.50	(0.37–0.68)
Age			
<65 yr	91/141	0.61	(0.40–0.92)
≥65 yr	98/164	0.45	(0.29–0.70)
Sex			
Male	116/187	0.39	(0.26–0.58)
Female	73/118	0.75	(0.46–1.21)
Region of enrollment			
East Asia	21/40	0.35	(0.14–0.91)
Non-East Asia	168/265	0.52	(0.38–0.72)
ECOG performance-status score			
0	59/107	0.45	(0.26–0.77)
1	129/197	0.51	(0.35–0.73)
Histologic type			
Squamous	37/56	0.35	(0.17–0.71)
Nonsquamous	152/249	0.55	(0.39–0.76)
Smoking status			
Current	44/65	0.68	(0.36–1.31)
Former	133/216	0.47	(0.33–0.67)
Never	12/24	0.90	(0.11–7.59)
Brain metastases at baseline			
Yes	17/28	0.55	(0.20–1.56)
No	172/277	0.50	(0.36–0.68)
Platinum-based chemotherapy regimen			
Included pemetrexed	120/199	0.63	(0.44–0.91)
Did not include pemetrexed	69/106	0.29	(0.17–0.50)

Association of tumor mutational burden with smoking and mutation status in non-small cell lung cancer (NSCLC).

[Andrew A. Davis](#)

Keynote 024
: Pembrolizumab vs CT

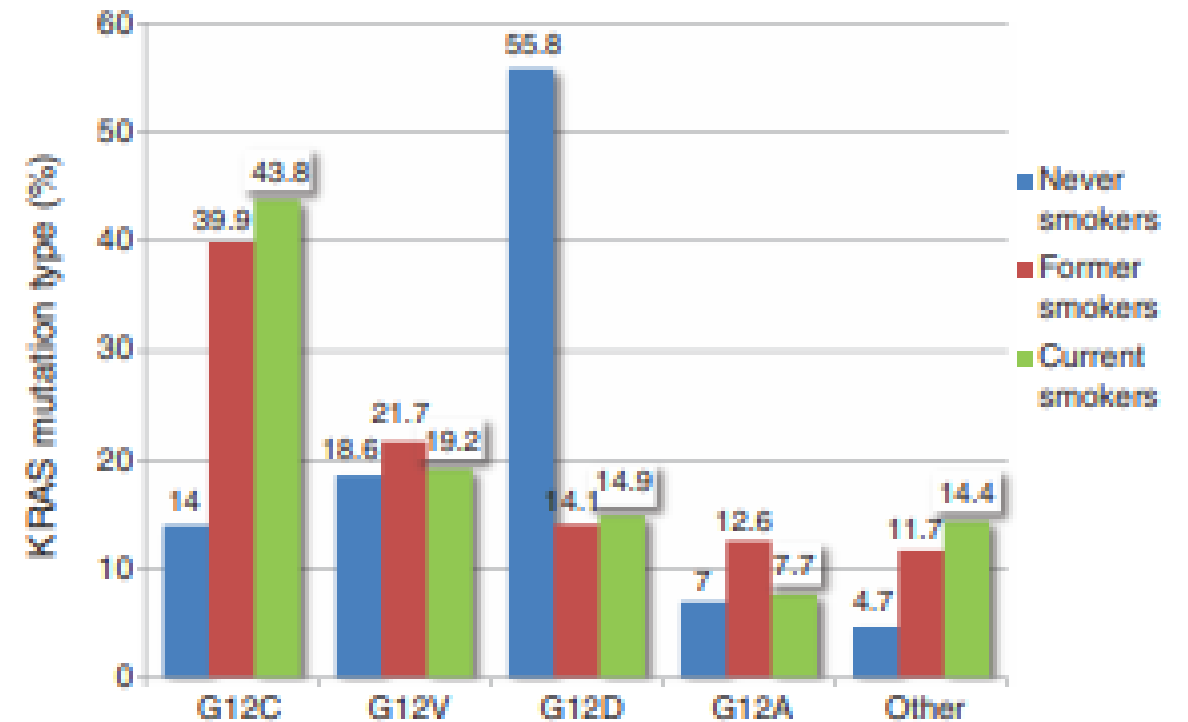
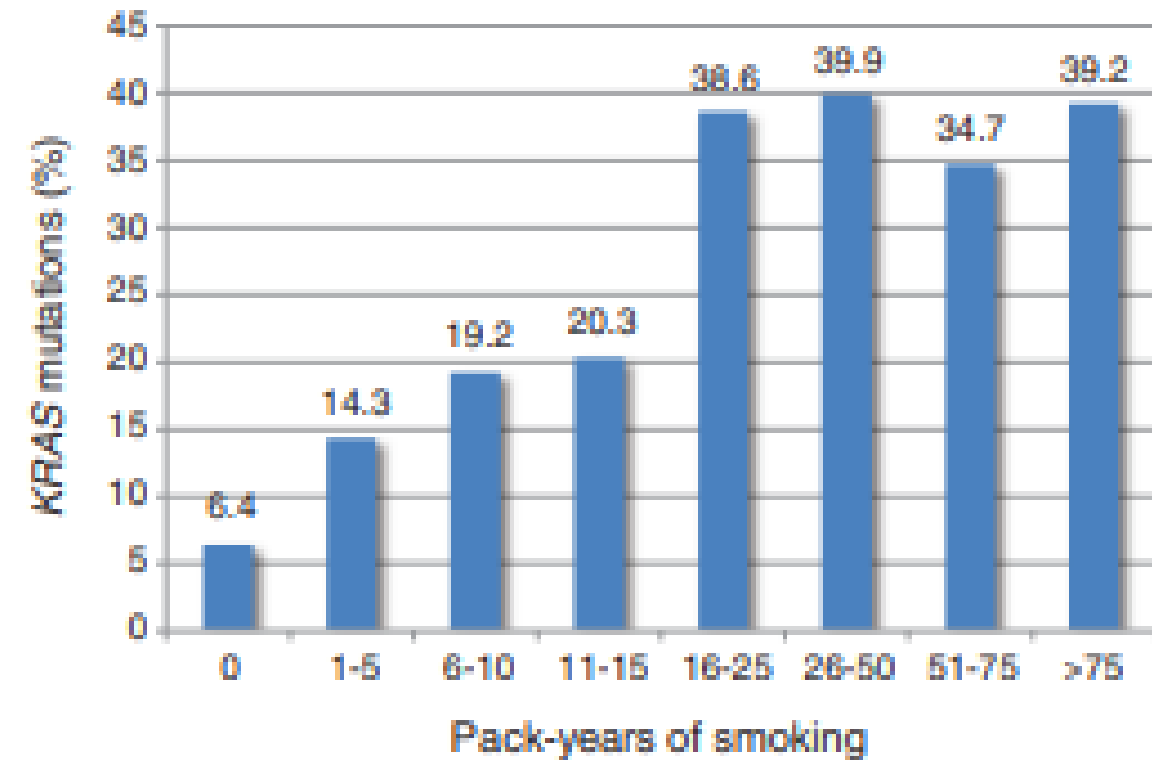
[Kalra R et al J Pharmacol Exp Ther.](#) 2000 Apr;293(1):166-71.

Effects of cigarette smoke on immune response: chronic exposure to cigarette smoke impairs antigen-mediated signaling in T cells and depletes IP3-sensitive Ca^{2+} stores.

An Alternative to Collecting Serial Smoking data: Insure Cessation in all patients

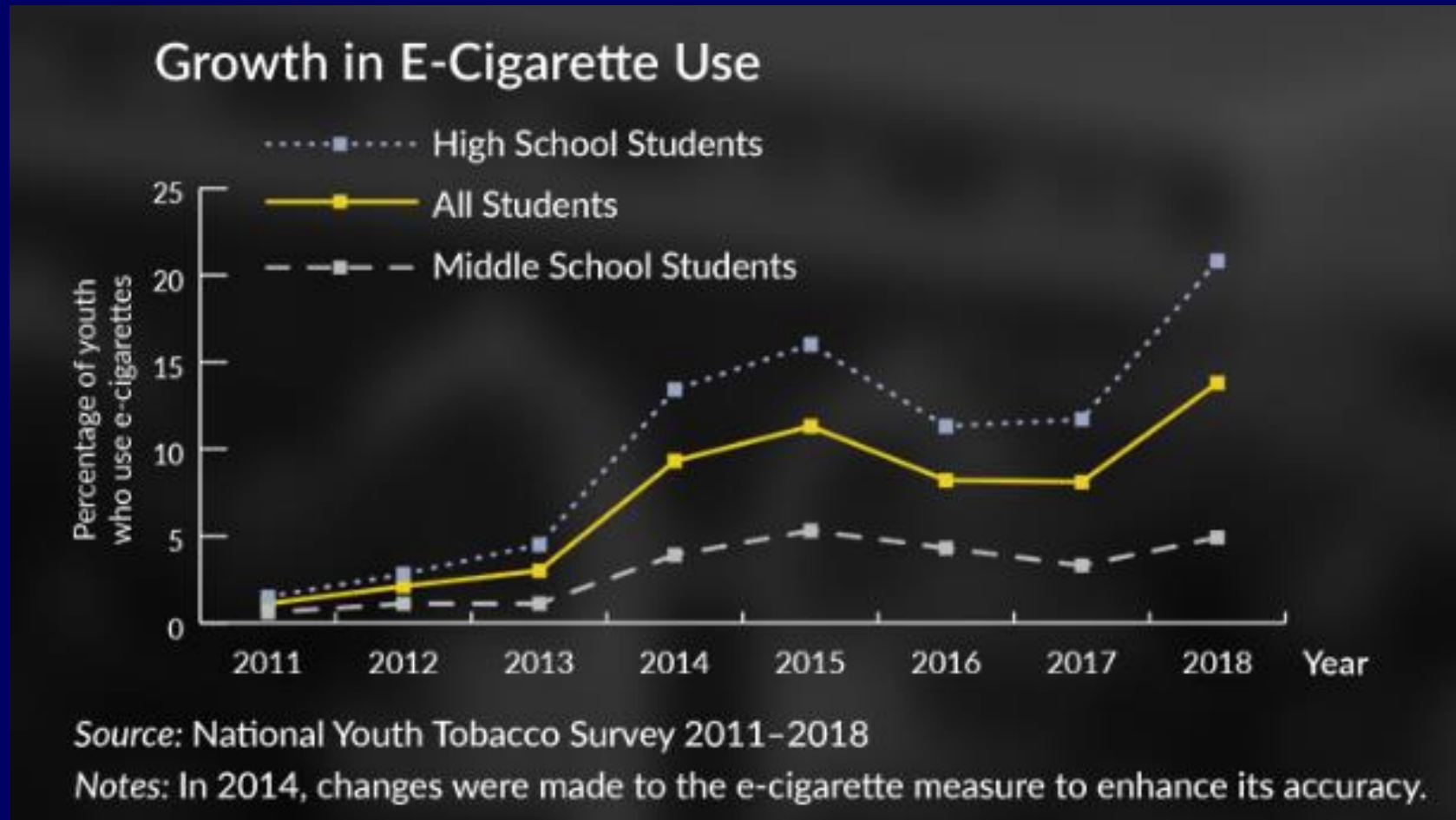


KRAS mutation frequency and type by smoking status



S. Dogan et al: Molecular Epidemiology of EGFR and KRAS Mutations in 3,026 Lung Adenocarcinomas: Higher Susceptibility of Women to Smoking-Related KRAS-Mutant Cancers, Clin Cancer Res; 1–9. 2012 AACR.

Increasing E-cigarette US in Students



Smoking affects TMB which may affect therapeutic outcomes from targeted and immunotherapies

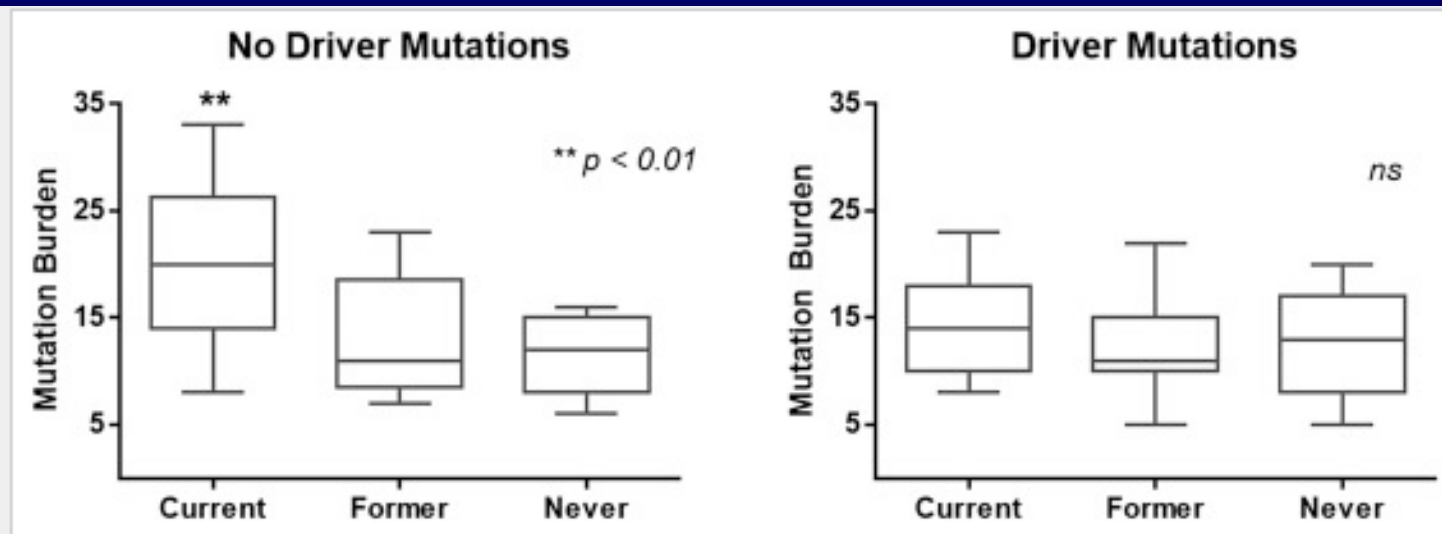


Fig. 2

Current smokers without driver mutations have the highest mutation burden in the Japanese cohort. The mutation burden was determined in the patients who were current smokers, former smokers, and never smokers in a group of patients with no driver mutations (left), and patients with driver mutations. Significance was determined by the Kruskal–Wallis test and a one-way ANOVA, **, $P < 0.01$.

Association of tumor mutational burden with smoking and mutation status in non-small cell lung cancer (NSCLC).

[Andrew A. Davis](#)

Health Benefits of Quitting Smoking

Major Conclusions of the Report

1. Smoking cessation is beneficial at any age. Smoking cessation improves health status and enhances quality of life.
2. Smoking cessation reduces the risk of premature death and can add as much as a decade to life expectancy.
3. Smoking places a substantial financial burden on smokers, healthcare systems, and society. Smoking cessation reduces this burden, including smoking-attributable healthcare expenditures.
4. Smoking cessation reduces risk for many adverse health effects, including reproductive health outcomes, cardiovascular diseases, chronic obstructive pulmonary disease, and cancer. Quitting smoking is also beneficial to those who have been diagnosed with heart disease and chronic obstructive pulmonary disease.
5. More than three out of five U.S. adults who have ever smoked cigarettes have quit. Although a majority of cigarette smokers make a quit attempt each year, less than one-third use cessation medications approved by the U.S. Food and Drug Administration or behavioral counseling to support quit attempts.
6. Considerable disparities exist in the prevalence of smoking across the U.S. population, with higher prevalence in some subgroups. Similarly, the prevalence of key indicators of smoking cessation—quit attempts, receiving advice to quit from a health professional, and using cessation therapies—also varies across the population, with lower prevalence in some subgroups.
7. Smoking cessation medications approved by the U.S. Food and Drug Administration and behavioral counseling are cost-effective cessation strategies. Cessation medications approved by the U.S. Food and Drug Administration and behavioral counseling

Quitting Smoking Saves Lives

Tobacco smoke contains a deadly mix of more than 7,000 chemicals; hundreds are harmful, and about 70 cause cancer. Extensive research has proven that smoking harms nearly every organ of the body, causes many diseases, and reduces health overall.

The 1990 Surgeon General's report was the first report to review the scientific evidence on the health benefits of quitting smoking. The report was clear – quitting smoking has major and immediate health benefits for men and women of all ages.

The current report expands on the findings of the 1990 report, reaching several important conclusions about the health benefits of quitting smoking, including:

- ▶ Quitting smoking reduces the risk of premature death, improves health, and enhances quality of life. Quitting can add as much as 10 years to life expectancy.
- ▶ Quitting smoking lowers the risk for many adverse health effects, including poor reproductive health outcomes, cardiovascular diseases, COPD, and 12 types of cancer.

QUITTING SMOKING LOWERS THE RISK

for many adverse health effects, including reproductive health outcomes, cardiovascular diseases, COPD, and 12 types of cancer.

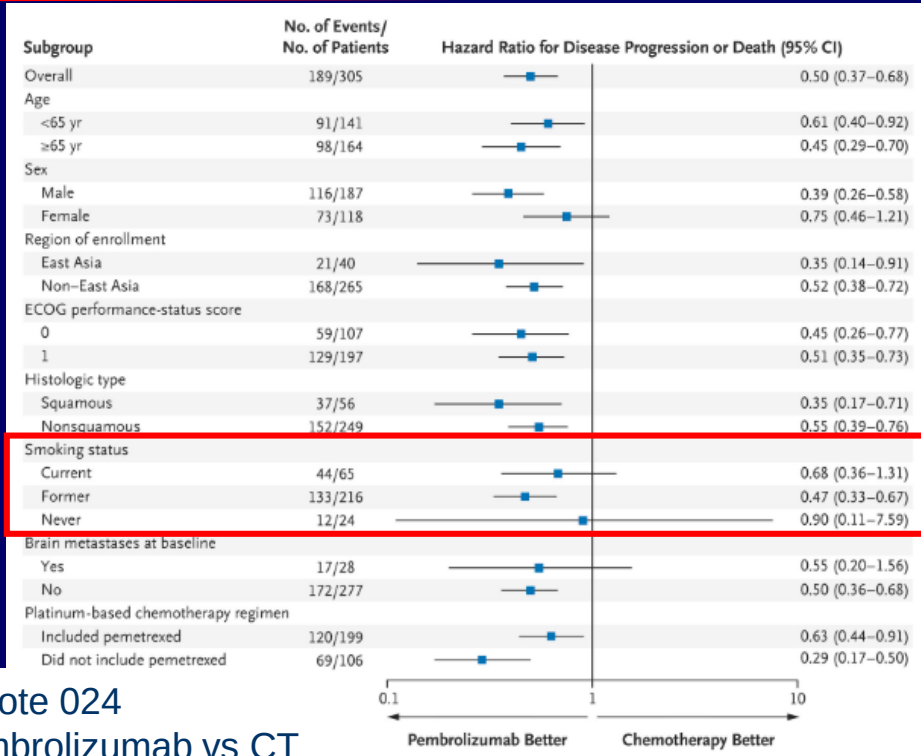
- ▶ Quitting smoking is also beneficial for people who have already been diagnosed with coronary heart disease or COPD.
- ▶ Quitting smoking reduces the costs of smoking for people who smoke, healthcare systems, and society.
- ▶ While quitting earlier in life yields greater health benefits, quitting smoking is beneficial to health at any age. Even people who have smoked for many years or have smoked heavily will benefit from quitting.

Smoking Cessation

A Report of the Surgeon General
Executive Summary

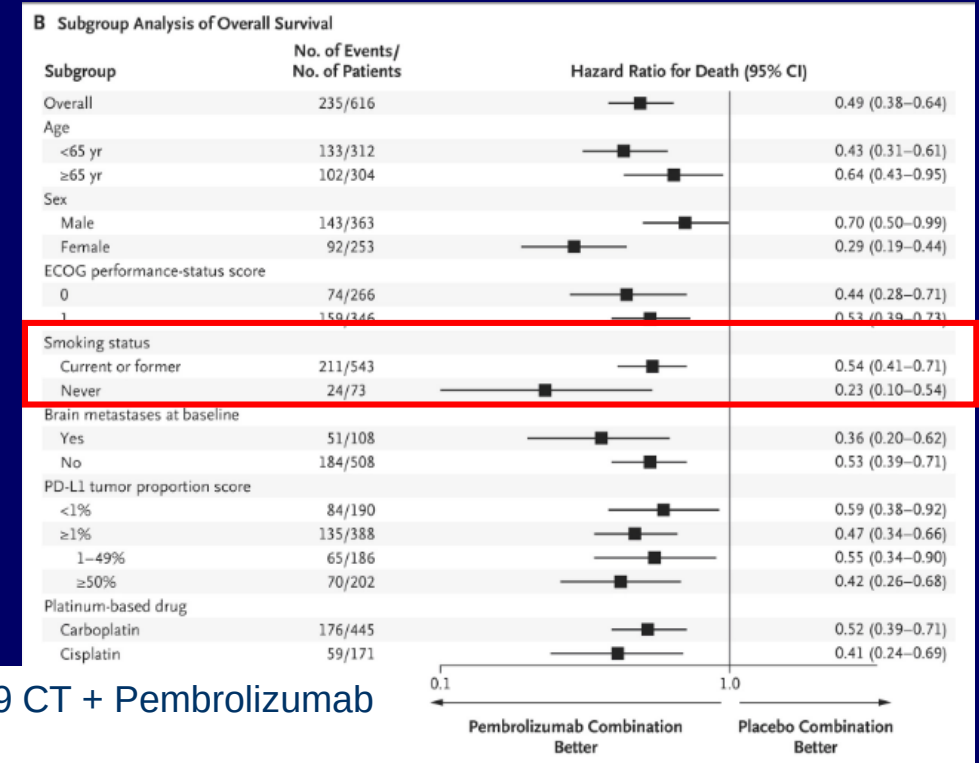


Effect of Smoking Status on Immunotherapy

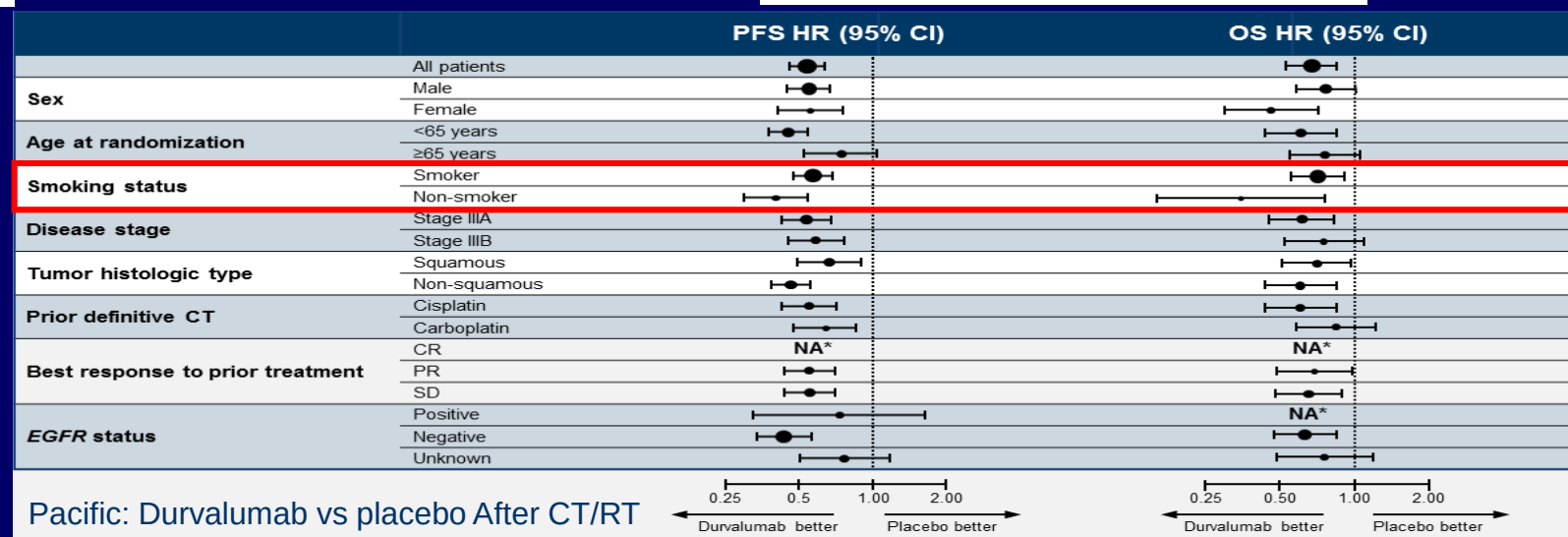


Keynote 024
: Pembrolizumab vs CT

In 024 former smokers had larger benefit from I/O than current or former smokers raising the question of whether cessation would help current smokers



Keynote 189 CT + Pembrolizumab
or Placebo



Pacific: Durvalumab vs placebo After CT/RT

In chemo + I/O trials no data on effects of cessation in current smokers

Addressing Tobacco Use by Cancer Patients: Clinical and Biologic Considerations

Graham Warren M.D., Ph.D.

Vice Chairman for Research

Department of Radiation Oncology

Department of Cell and Molecular Pharmacology

Cancer Prevention and Control Program

Hollings Cancer Center

Medical University of South Carolina

Disclosures

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- Member or Chair, ASCO, AACR, IASLC, SRNT Tobacco or Comorbidity Subcommittees
- Associate Editor/Editorial Board,
 - *Journal of Thoracic Oncology*
 - *Cancer Epidemiology Biomarkers & Prevention*
 - *Translational Lung Cancer Research*
- Advisor, Canadian Partnership Against Cancer (CPAC)
- No financial or educational disclosures, patents, royalties, payments, or tobacco industry support
- Views are mine and do not represent those of any parent or supporting organizations

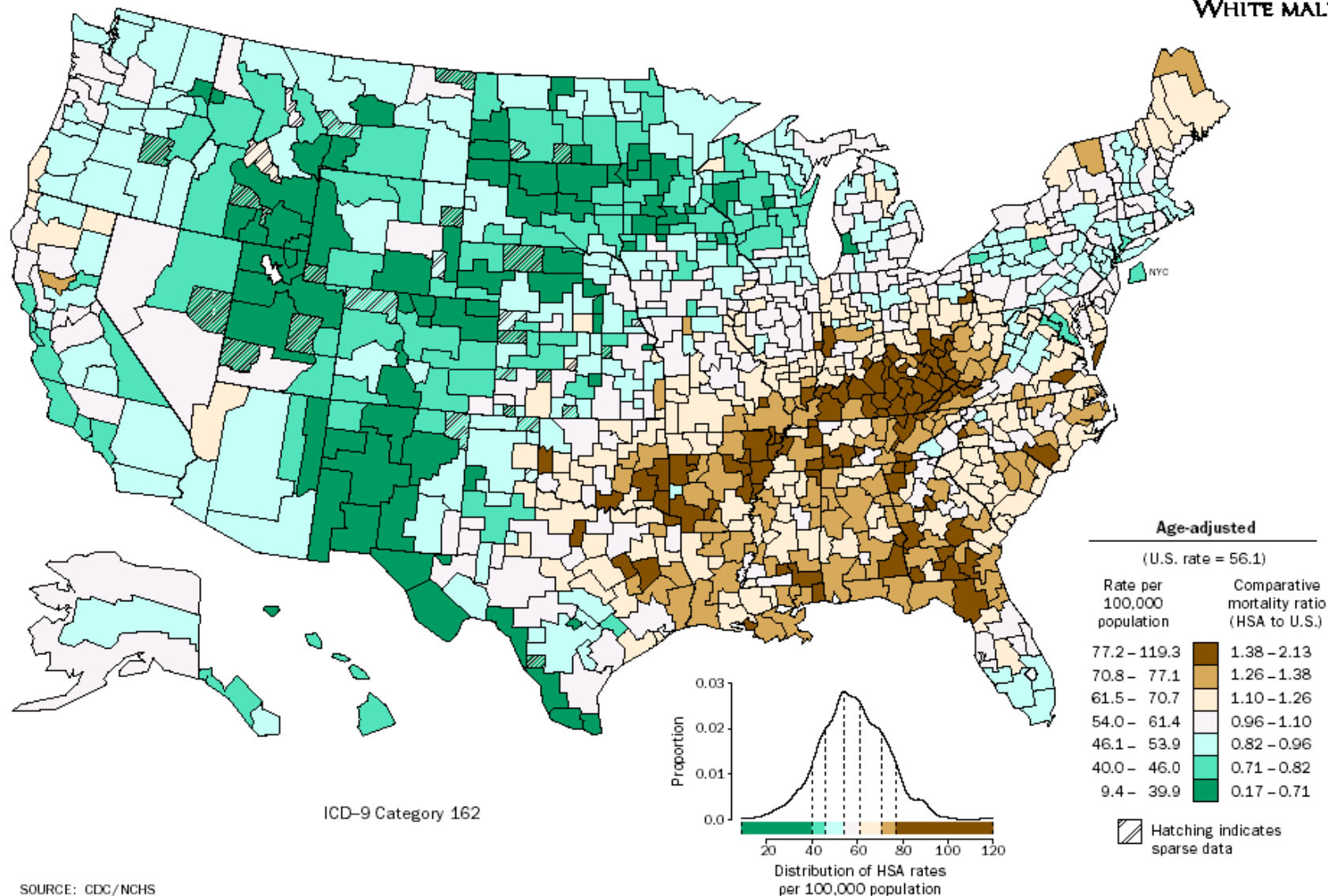
Cigarette Smoke

- Largest single contributor to cancer risk
 - Shifting views on largest contribution to preventable health risks as compared with obesity
- Over 7000 constituents in cigarette smoke
 - 60+ known carcinogens
 - Aldehydes
 - Benzene
 - Metals (cadmium, nickel, polonium)
 - Nicotine
 - Nitrosamines
 - Polyaromatic hydrocarbons
- Large number of additives
 - Enhance absorption
 - Increase flavor
 - Increase addiction

Lung Cancer Death Rates

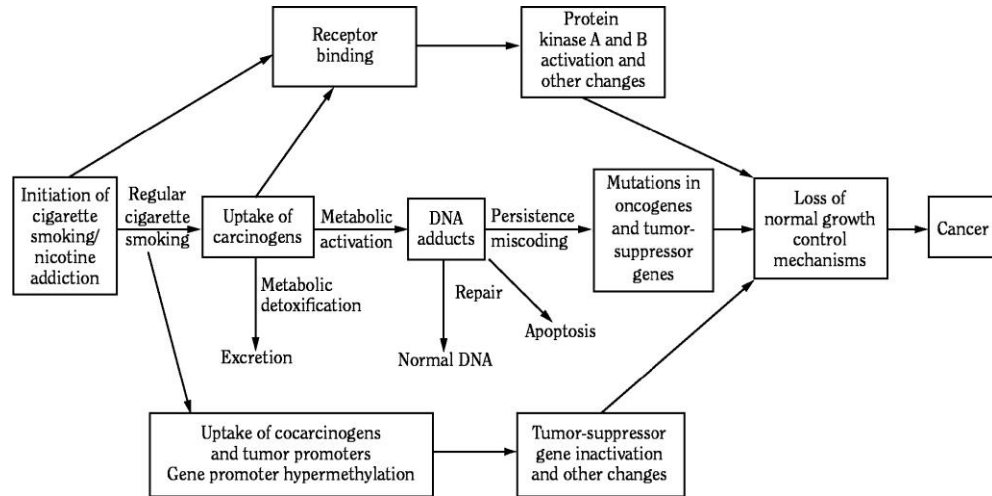
48 AGE-ADJUSTED DEATH RATES BY HSA, 1988-92

LUNG CANCER
WHITE MALE



Problem: We don't view Smoking in the Continuum of Cancer

The Established Carcinogenesis Model

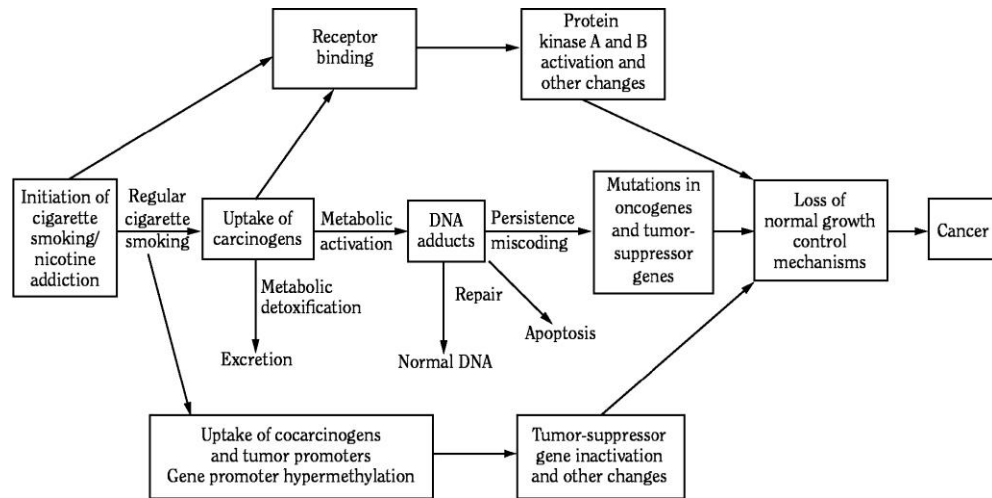


2010 Surgeon General's Report, Fig 5.1

Problem: We don't view Smoking in the Continuum of Cancer

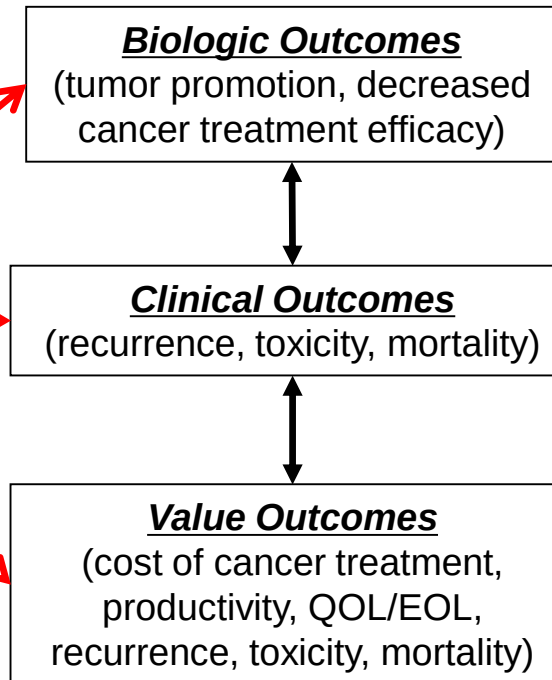
The Historical Disconnect

The Established Carcinogenesis Model

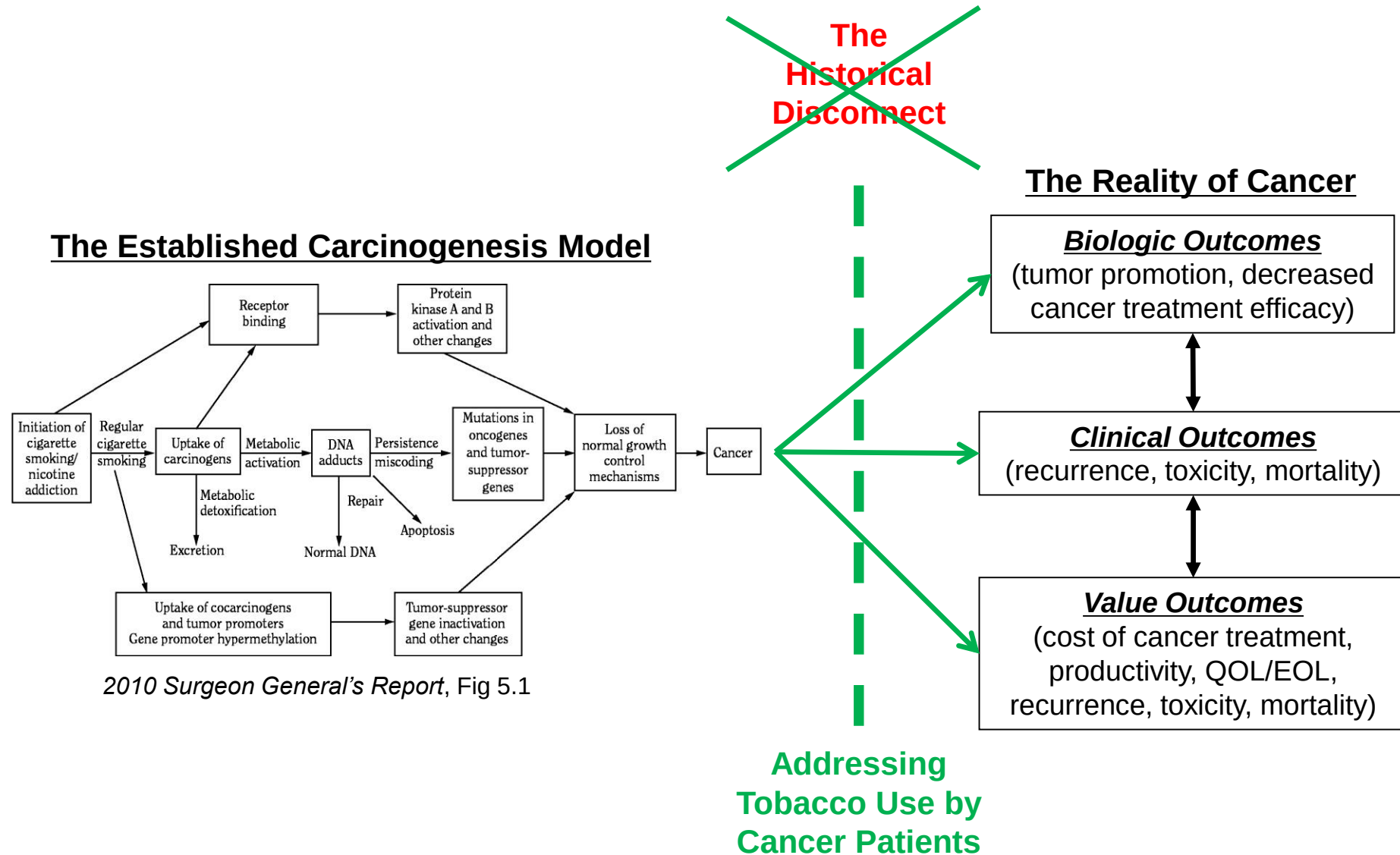


2010 Surgeon General's Report, Fig 5.1

The Reality of Cancer



Problem: We don't view Smoking in the Continuum of Cancer



The 2014 Surgeon General's Report

- Statistics:
 - Evidence for studies between 1990-2012
 - Studies with 100+ patients
 - ~400 studies reporting on over 500,000 patients
 - Effects of smoking on:
 1. Overall mortality/survival
 2. Cancer-specific mortality/survival
 3. Risk of second primary cancers
 4. Cancer recurrence/response to treatment
 5. Toxicity

U.S. Department of Health and Human Services. The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2014.

The 2014 Surgeon General's Report

- Conclusions:
 - In cancer patients and survivors, the evidence is sufficient to infer a **causal relationship** between cigarette smoking and **adverse health outcomes**. Quitting smoking improves the prognosis of cancer patients.
 - In cancer patients and survivors, the evidence is sufficient to infer a **causal relationship** between cigarette smoking and **increased all-cause mortality and cancer-specific mortality**.

The 2014 Surgeon General's Report

- Conclusions:
 - In cancer patients and survivors, the evidence is sufficient to infer a **causal relationship** between cigarette smoking and **increased risk for second primary cancers** known to be caused by cigarette smoking, such as lung cancer.
 - In cancer patients and survivors, the evidence is suggestive but not sufficient to infer a causal relationship between cigarette smoking and the risk of recurrence, poorer response to treatment, and increased treatment-related toxicity.

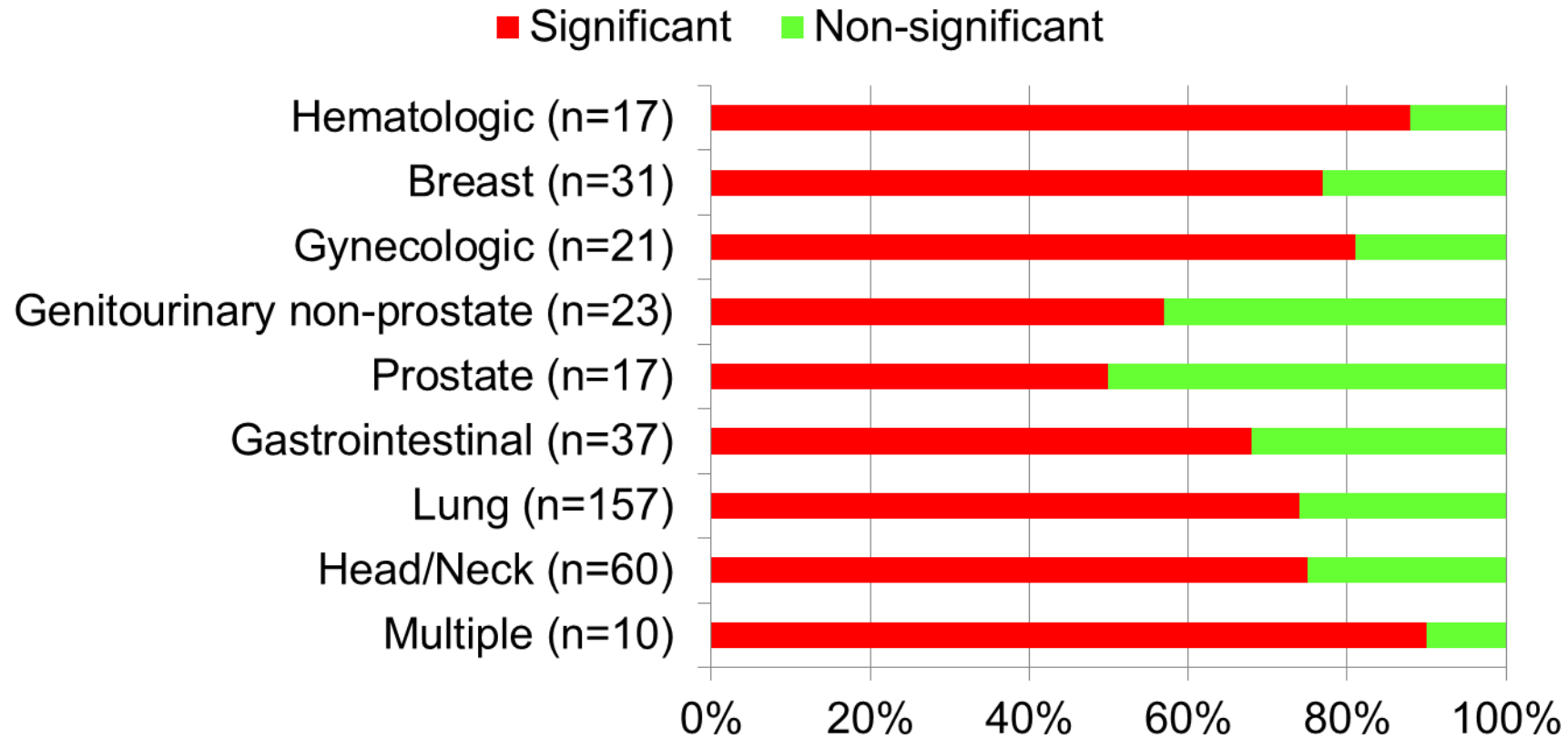
The 2014 SGR: Outcome Estimates

Effect	Studies	Associations (Significant)	RR Magnitude (median)
Overall Mortality	159	87% (62%)	Current: 1.51 Former: 1.22
Overall Survival	62	77% (42%)	
Cancer Related Mortality	58	79% (59%)	Current: 1.61 Former: 1.03
Second Primary	26	100% (100%)	
Recurrence	51	82% (53%)	Current:1.42 Former:1.15
Response	16	72%	
Toxicity	82	94% (80%)	

U.S. Department of Health and Human Services. The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2014.

Negative Associations of Smoking

(one or more negative association)

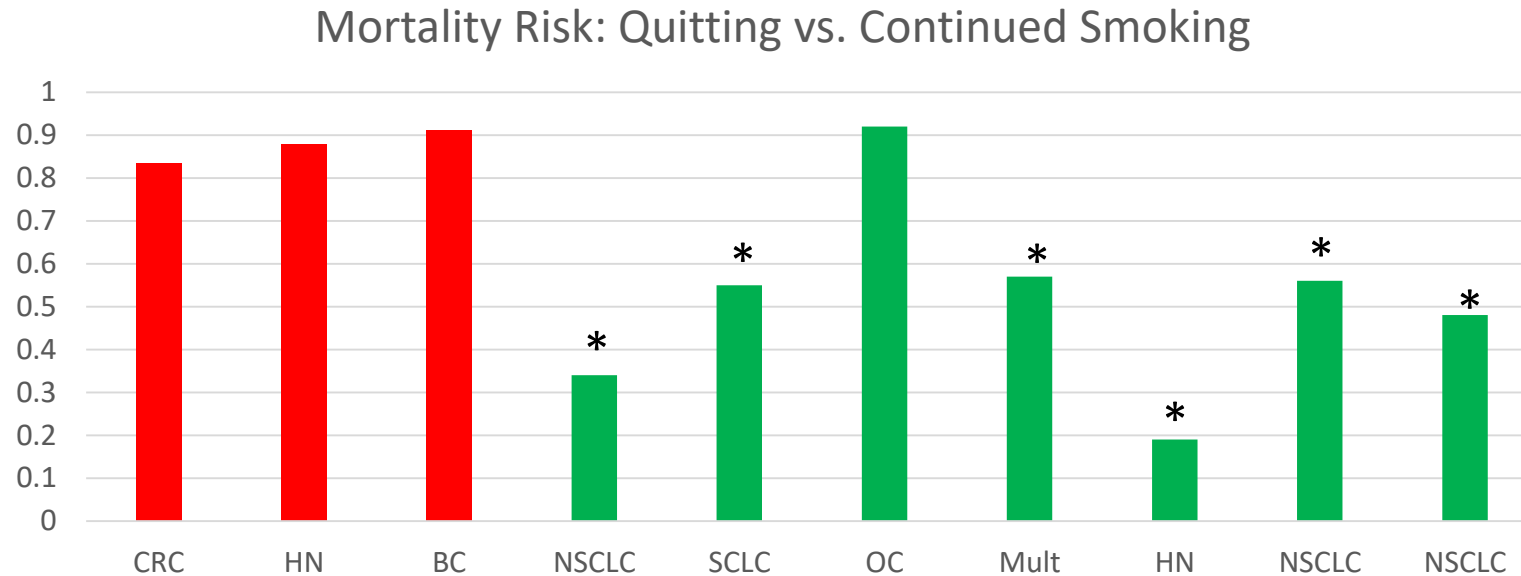


U.S. Department of Health and Human Services. The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2014.

The 2020 Surgeon General's Report

- Statistics:
 - 10 studies with ~11,000 patients, 2000-16
 - Evaluating effects of smoking cessation AFTER a cancer diagnosis on overall mortality
 - Smoking cessation associated with improved survival
 - The evidence is suggestive but not sufficient to infer a causal relationship between smoking cessation and improved all-cause mortality in cancer patients who are current smokers at the time of a cancer diagnosis.

The 2020 Surgeon General's Report



- 3 studies compared vs. never smoking
- In 7 studies comparing quitting vs. continued smoking
 - 6 showed significant reductions in mortality with quitting
 - Median 45% reduction in mortality

U.S. Department of Health and Human Services. Smoking Cessation: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2020.

Smoking and Prostate Cancer

Cause of Death	% of Total Deaths	HR for Current Smokers
Cardiopulmonary disease	50.3%	3.05
Other	15.5%	5.52
Gastrointestinal cancer	12.4%	4.09
Lung cancer	9.9%	
Other cancers	3.1%	
Prostate cancer	8.7%	

Treatment (surgery, radiotherapy, androgen deprivation and duration) all focus on optimizing a relatively low percentage of deaths

What about the larger percentage?

Current Smoking and Other Cancers

(35,000 pts from NHIS)

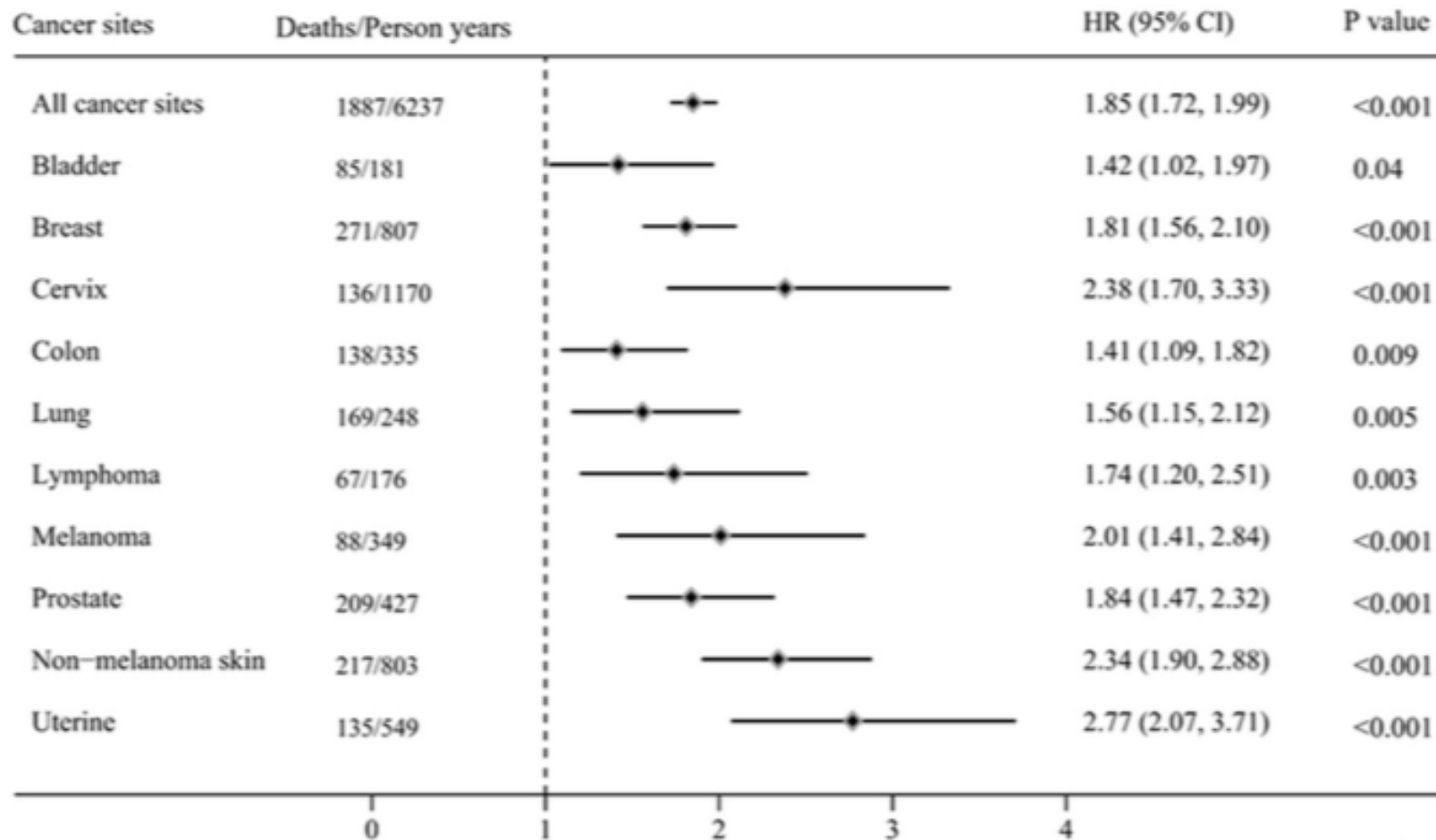


Figure 2. Current smoking and risk of all-cause mortality.

Former Smoking and Other Cancers

(35,000 pts from NHIS)

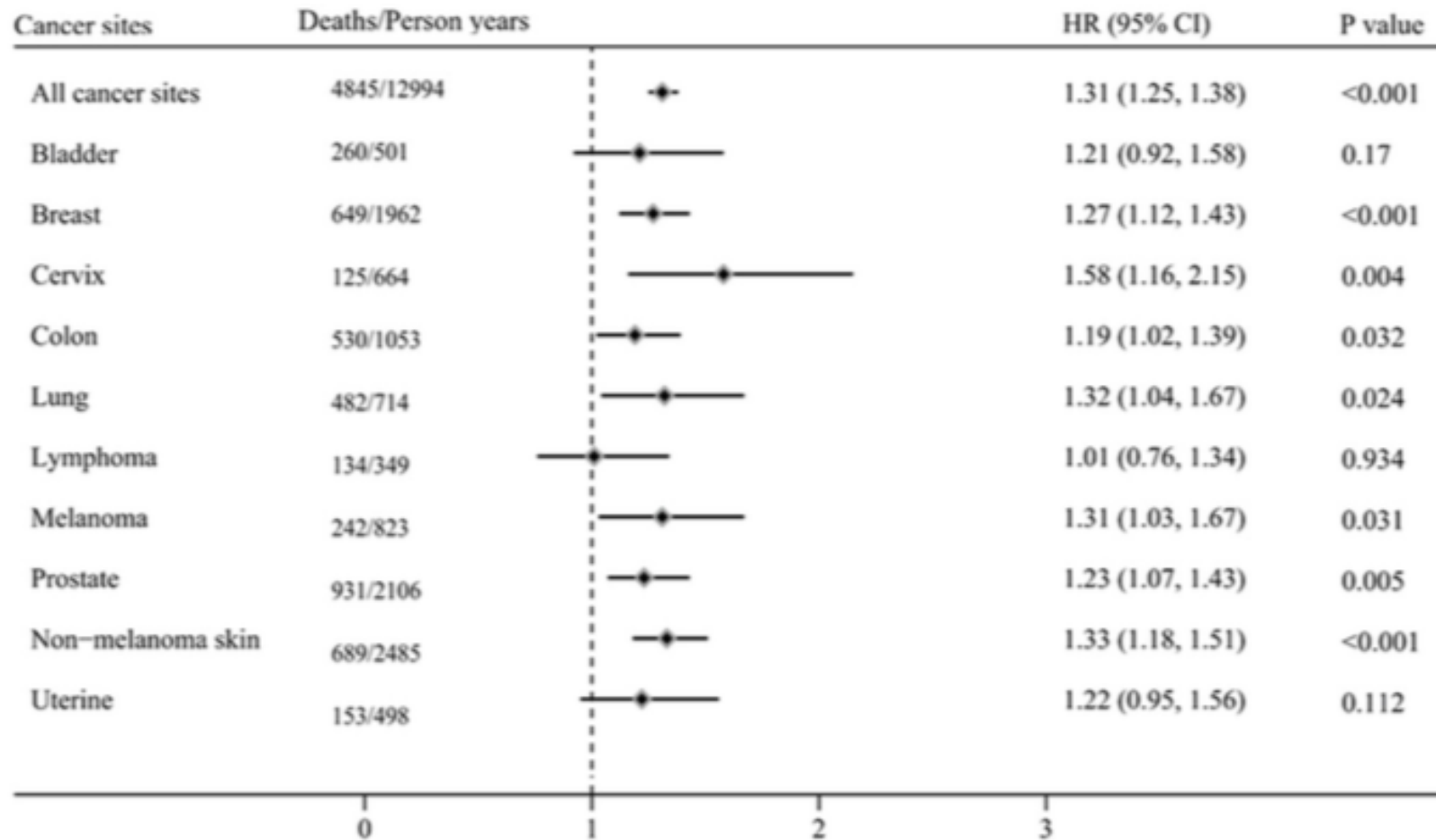


Figure 3. Former smoking and risk of all-cause mortality.

Smoking and Other Cancers

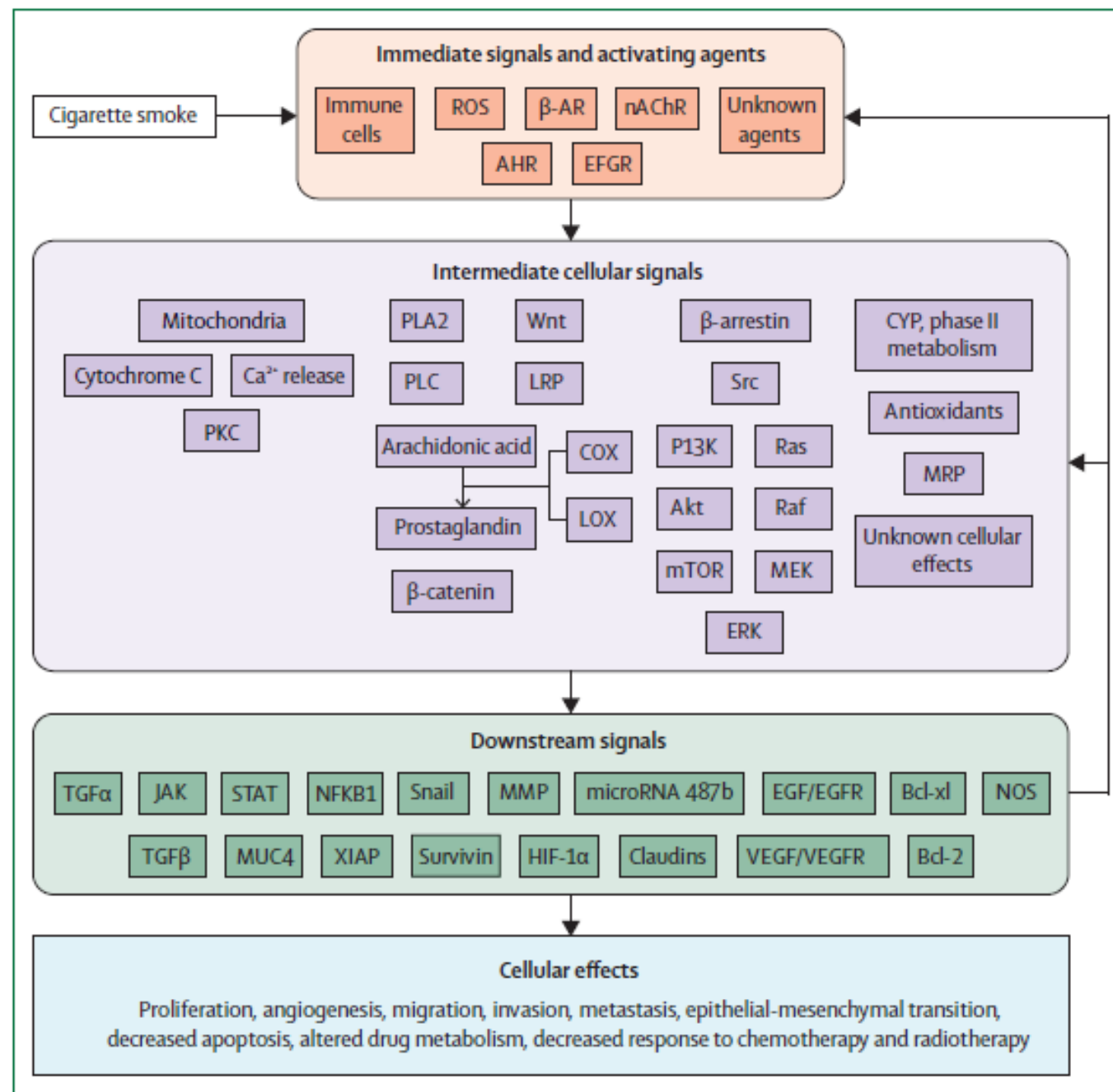
(35,000 pts from NHIS)

Smoking status	Subgroups	Cancer mortality				CVD mortality				Other mortality			
		Deaths	Person years	HR (95% CI)	P value ^a	Deaths	Person years	HR (95% CI)	P value ^a	Deaths	Person years	HR (95% CI)	P value ^a
Never smoking		1386	15862	1 (Reference)		941	15862	1 (Reference)		2007	15862	1 (Reference)	
Current smoking		825	6237	1.75 (1.57 to 1.95)	< 0.001	292	6237	1.73 (1.47 to 2.05)	< 0.001	770	6237	2.06 (1.83 to 2.33)	< 0.001
	< 10 cigarette per day			1.74 (1.50 to 2.03)	< 0.001			1.83 (1.42 to 2.37)	< 0.001			1.80 (1.50 to 2.16)	< 0.001
	≥ 10 cigarette per day			1.89 (1.67 to 2.14)	< 0.001			1.79 (1.47 to 2.18)	< 0.001			2.39 (2.09 to 2.75)	< 0.001
Former smoking		1768	12994	1.37 (1.25 to 1.49)	< 0.001	923	12994	1.08 (0.96 to 1.22)	0.194	2154	12994	1.38 (1.27 to 1.49)	< 0.001
	Quit smoking < 10 years			1.87 (1.66 to 2.10)	< 0.001			1.50 (1.23 to 1.83)	< 0.001			1.88 (1.65 to 2.14)	< 0.001
	Quit smoking 10-19 years			1.49 (1.31 to 1.68)	< 0.001			1.26 (1.07 to 1.48)	0.006			1.42 (1.27 to 1.60)	< 0.001
	Quit smoking ≥ 20 years			1.09 (0.98 to 1.21)	0.122			0.91 (0.79 to 1.05)	0.204			1.21 (1.11 to 1.33)	< 0.001
	P for trend				< 0.001				< 0.001				< 0.001

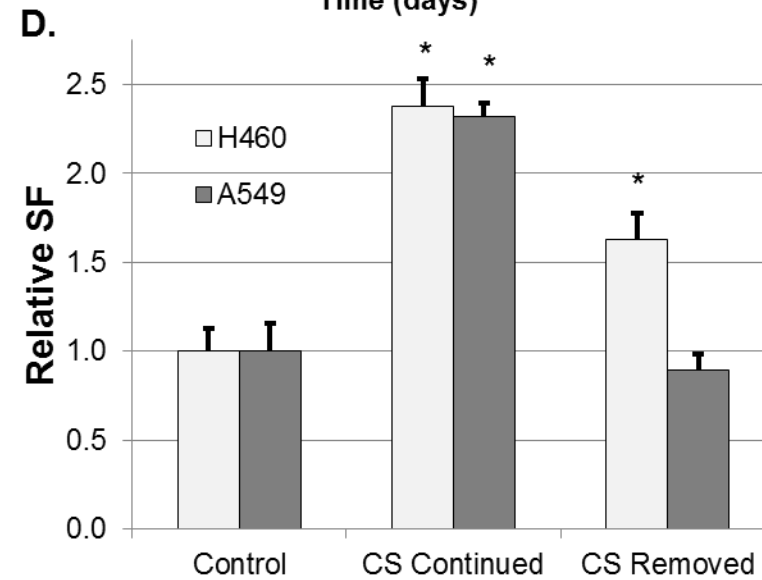
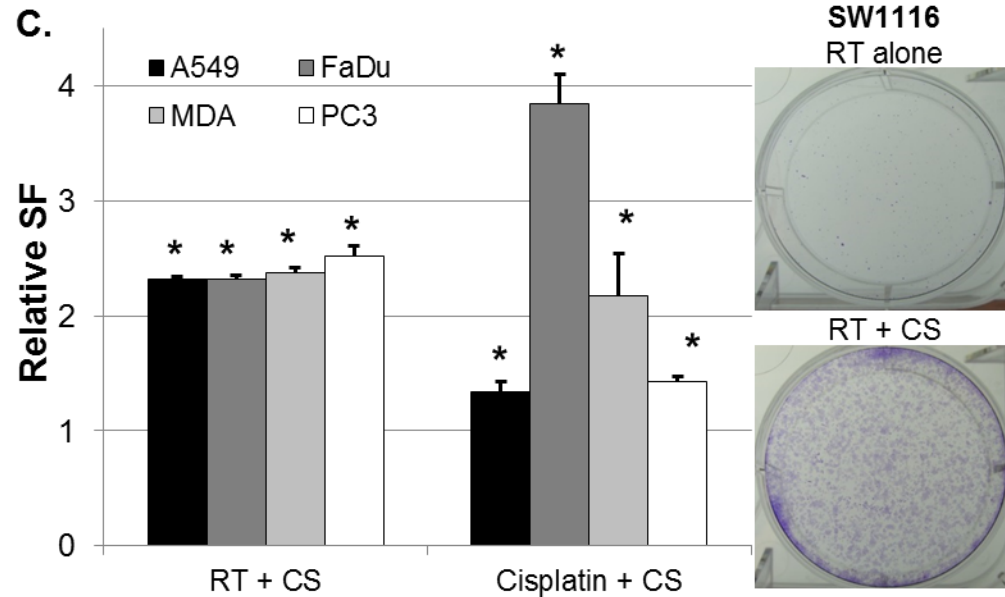
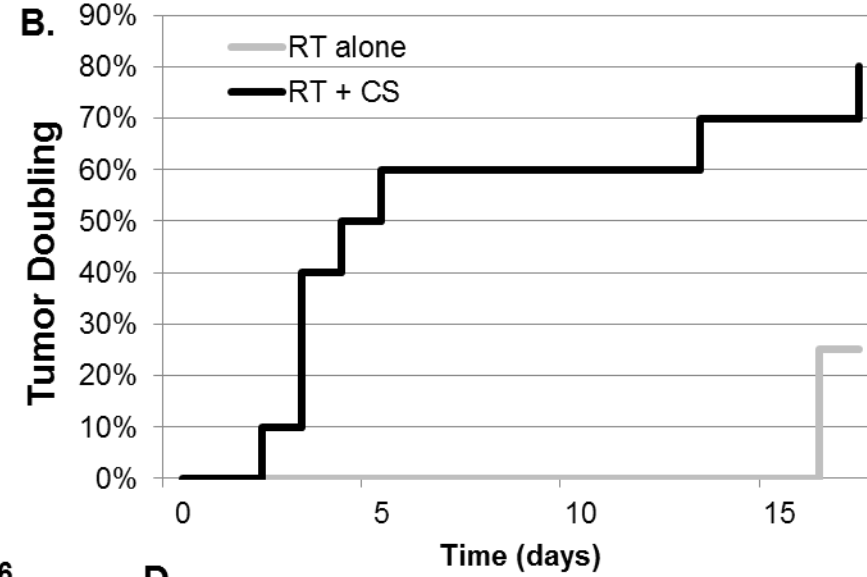
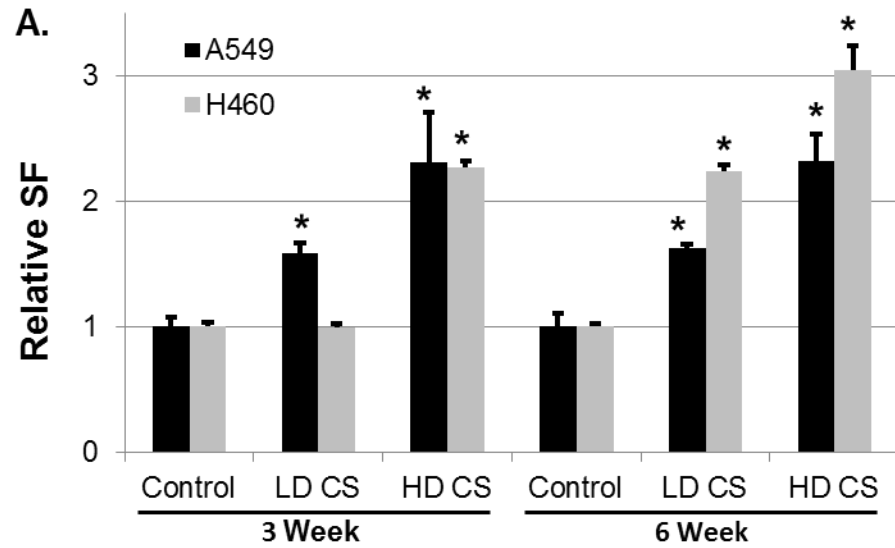
- Current smoking (all sites)
 - 75% increased risk for cancer mortality
 - 73% increased risk for CVD mortality
 - 106% increased risk for other mortality
- Former smoking (all sites)
 - 37% increased risk for cancer mortality
 - 8% (NS) risk for CVD mortality
 - 38% increased risk for other mortality

Clinical Trials and Smoking

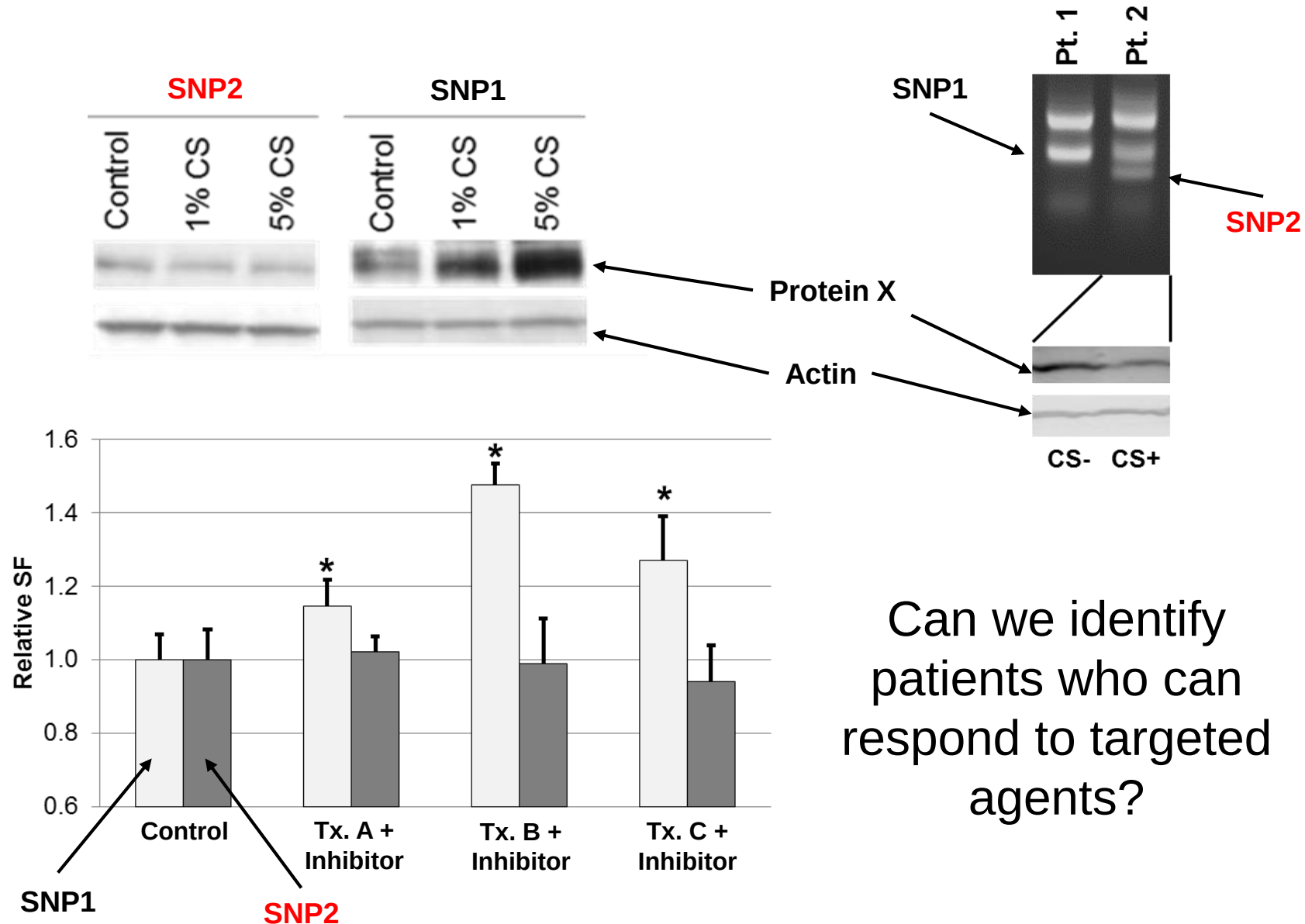
- Virtually all therapeutic trials have one or more of the following primary objectives
 - Overall survival
 - Cancer related survival (PFS, DFS, RFS)
 - Cancer treatment toxicity
- Smoking affects these primary objectives across disease sites and treatments
 - 50-60% median effects
 - Current smoking is different than former smoking
 - Smoking cessation can be an effect modifier
- How can we possibly justify the accuracy of clinical trial designs that ignore smoking



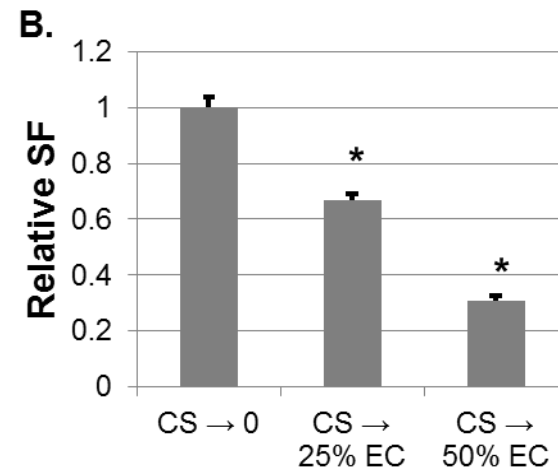
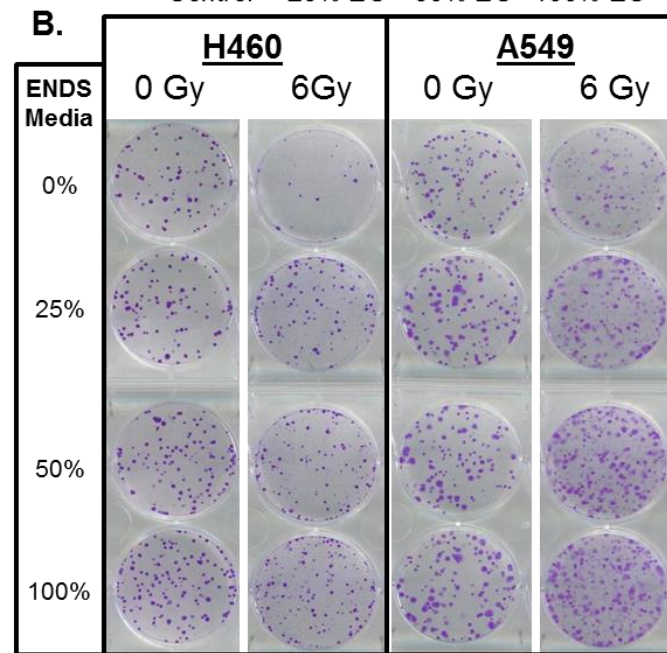
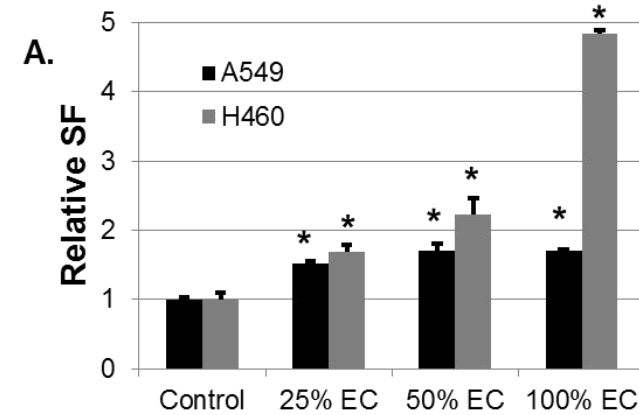
Smoking and Therapeutic Response



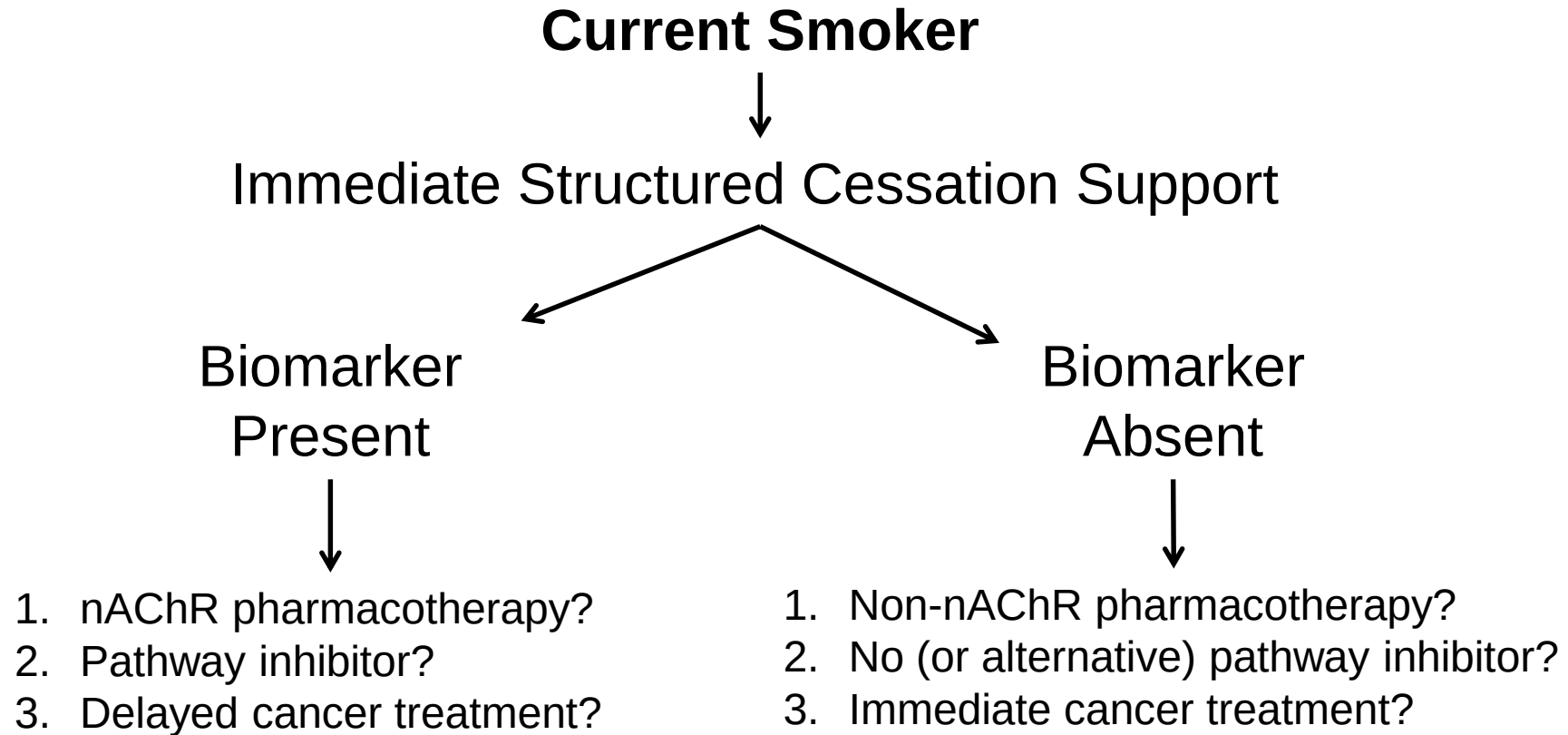
Smoking and Targeting Response



Smoking, ENDS and Response



Hypothetical Treatment Paradigm



Mitigating the Effects of Smoking

- **Patients** are limited to the ability to choose to quit smoking and comply with treatments
 - Message is clear as day: quitting smoking is the best thing they can do to improve cancer treatment
- **Providers** are tasked with knowing smoking is bad, assessing, advising, and providing support
 - Providers are limited by health systems resources
- **Health systems** have the opportunity to identify the best approaches to cancer treatment and cessation
 - Largest impact on how to support mitigation of tobacco use lies here

Mitigating the Effects of Smoking

System Level	Ability to Quit	Cancer Treatment	Cost of Treatment	Optimal Treatment
Patient	X			
Provider	X	X		
Institution	X	X	(x)	
Insurer	X	X	X	X
Health System	X	X	X	X
Regulatory Agencies		X	X	X

Assessment of Tobacco Use in Cancer Clinical Trials

Stephanie R. Land, PhD
Program Director and Statistician
Tobacco Control Research Branch
Division of Cancer Control and Population Sciences
National Cancer Institute

Formerly:
Associate Professor of Biostatistics, University of Pittsburgh &
Statistician, University of Pittsburgh Cancer Institute

Outline

- Rationale for assessing tobacco use in cancer clinical trials
- NCI-AACR Cancer Patient Tobacco Use Assessment Task Force
- How to assess tobacco use in cancer trials
 - Cancer Patient Tobacco Use Questionnaire (C-TUQ)
- Recommendations and discussion

The views expressed represent my own and not necessarily those of NCI.

Rationale for Assessing Tobacco Use in Cancer Clinical Trials

- I. Tobacco use is both predictive & prognostic.
- II. Scientific questions related to tobacco use in the setting of cancer therapy trials:
 - When and to what extent does tobacco diminish efficacy?
 - What are the mechanisms of tobacco's effects?
 - What are the implications of tobacco use for dosage, treatment regimen, and timing of therapy?
 - How do other tobacco products (including electronic cigarettes) change prognosis or treatment efficacy?

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).

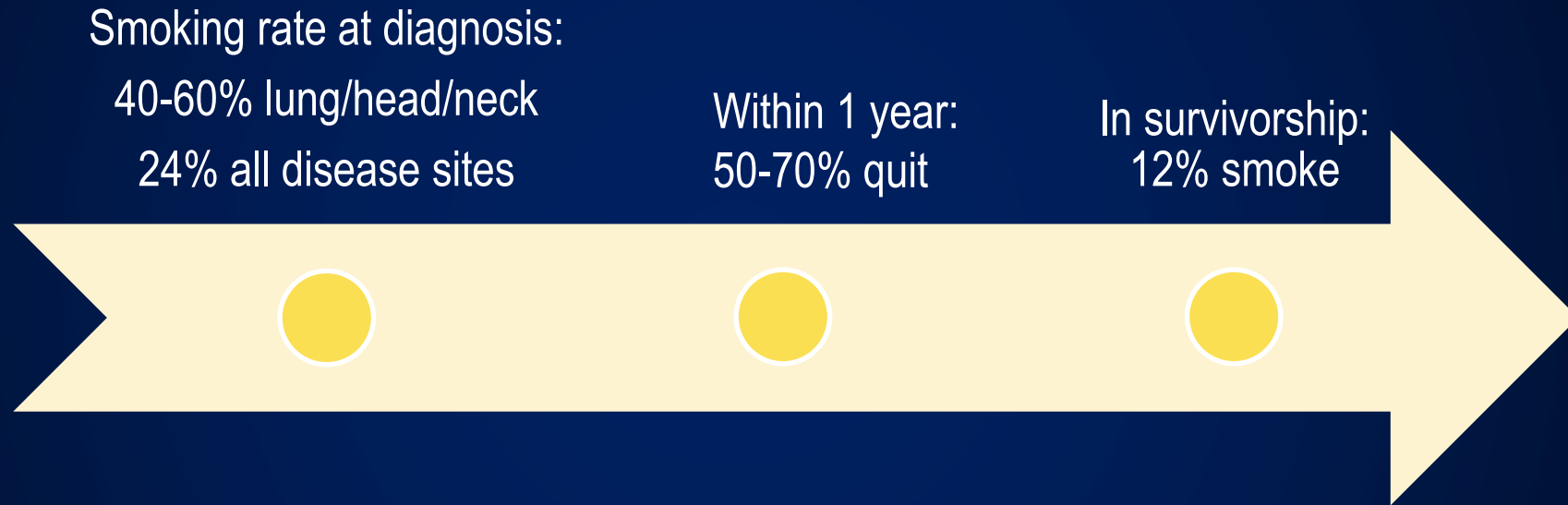
Studies indicate that smokers may have higher risk of recurrence, poorer response to treatment, and increased toxicity.

Conclusion: Tobacco use should be considered in the evaluation of new cancer therapies.

Mortality and 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
- The evidence is suggestive but not sufficient to infer a causal relationship between smoking cessation and improved all-cause mortality in cancer patients who are current smokers at the time of a cancer diagnosis.**

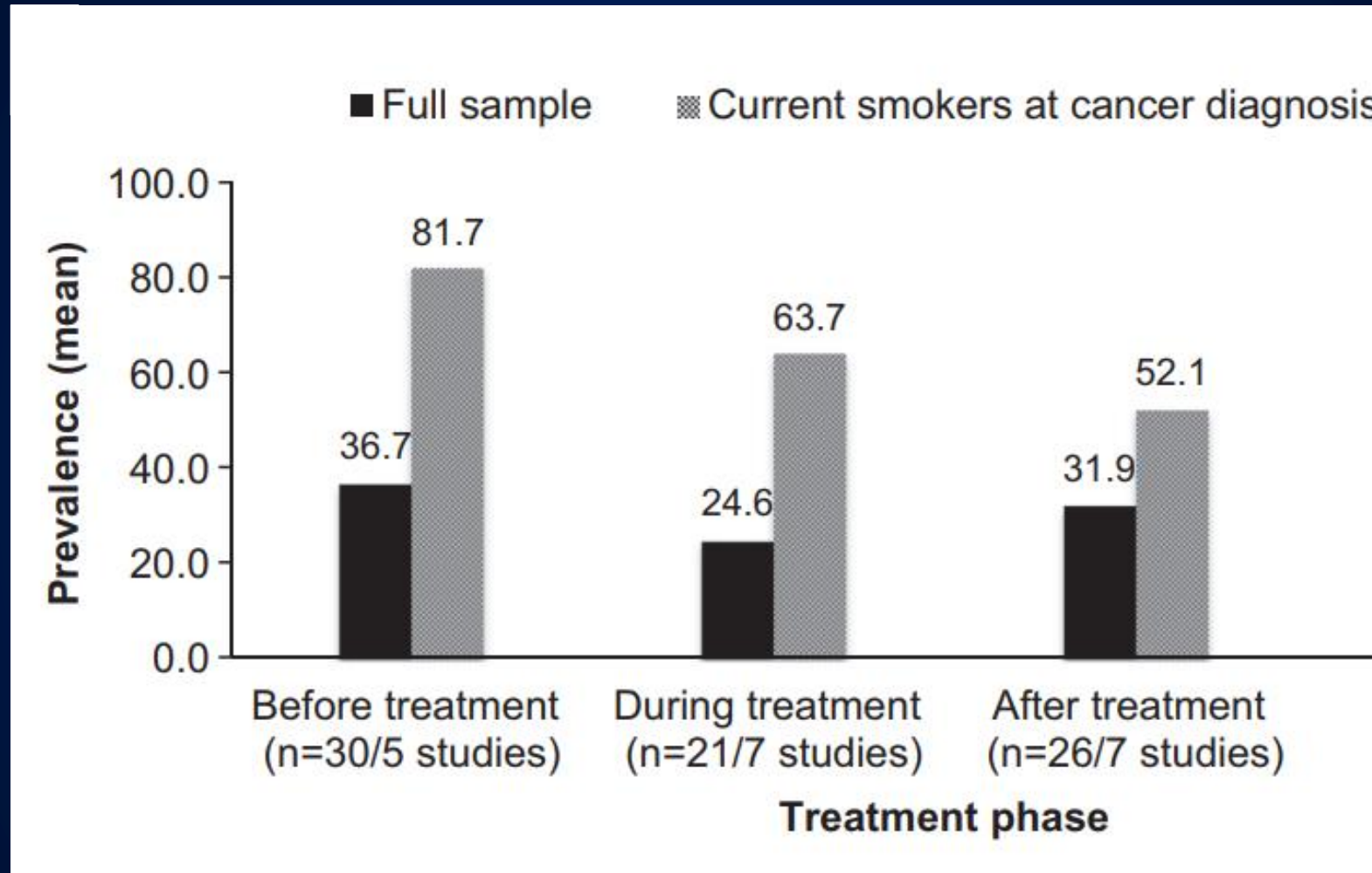
Rates of smoking and quitting after diagnosis



Note: retrospective studies subject to survivor bias
→ prevalence at diagnosis under-estimated

Gritz, 2005; Rock, MMWR, 2007; Burris, CEBP, 2015; Shoemaker, ONF, 2016; NCI, CTPR, 2018

Smoking by lung and head/neck cancer patients



Burris, CEBP, 2015 (systematic review)

Current Approaches to Data Collection

- Not widely assessed in trials or practice
- Inconsistent tobacco use assessment methods

Patient reports 19-year
history of smoking,
starting at age 15, denies
alcohol, divorced

- Little follow-up during/after treatment

Are associations due to exposure history, use during cancer therapy, or continued accrual of risk after therapy?

Land, JCO, 2012; Goldstein, NTR, 2012; Warren, IJC, 2012; Peters, Cancer, 2016

Assessing Tobacco Use by Cancer Patients and Facilitating Cessation: An AACR Policy Statement

Primary recommendations include:

- Evaluate the confounding effects of tobacco on cancer treatment, disease progression, comorbid events, and survival in all oncology clinical trials from registration to survival endpoints



ASSESSING AND TREATING TOBACCO USE BY CANCER PATIENTS: RECOMMENDATIONS FROM THE AACR
American Association for Cancer Research

It is never too late to quit. When diagnosed with cancer, patients can immediately make a meaningful positive impact on their health by stopping their tobacco use. The evidence is clear that tobacco use by patients with cancer decreases the effectiveness and safety of cancer treatments, decreases survival, decreases quality of life, increases treatment-related toxicity and increases risk of cancer recurrence and second primary tumors.

Evidence-based tobacco cessation interventions are infrequently offered in oncology settings despite data suggesting that tobacco cessation can improve outcomes and survival in patients with cancer.

Therefore, the American Association for Cancer Research suggests the following:

RECOMMENDATIONS

1 Patients with cancer from all clinical settings, including clinical trial participants and cancer screening patients, who use tobacco or have recently quit should be provided with evidence-based tobacco cessation assistance.

- Assistance should be provided to current users and recent quitters (past 30 days)
- Assistance should be provided within or associated with the oncology practice
- The oncology service provider should assume responsibility for ensuring that the patient receives appropriate care
- Oncology provider assistance can be supplemented with telephone quitline care by having patients call 1-800-QUIT-NOW

2 Researchers should evaluate the confounding effects of tobacco on cancer treatment, disease progression, comorbid events and survival in all oncology clinical trials, from registration to survival endpoints.

Implementation of these recommendations will require:

- Universal assessment and documentation of tobacco use by cancer patients in all clinical settings, including cancer clinical trials, and cancer screening patients
- Development of universal standards for measurement of tobacco use and exposure in clinical and research settings
- Incorporation of evidence-based tobacco interventions into review criteria used by research and health care quality and accreditation bodies
- Recognition and support of the value of tobacco cessation interventions by health systems, payers and research funders through provision of appropriate incentives for infrastructure development and intervention delivery

The full AACR policy statement can be accessed at:
tiny.cc/AACR2013Tobacco

Clinical Cancer Research, April 15, 2013 19; 1941

ASCO Policy Statement

“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.”

ASCO SPECIAL ARTICLES

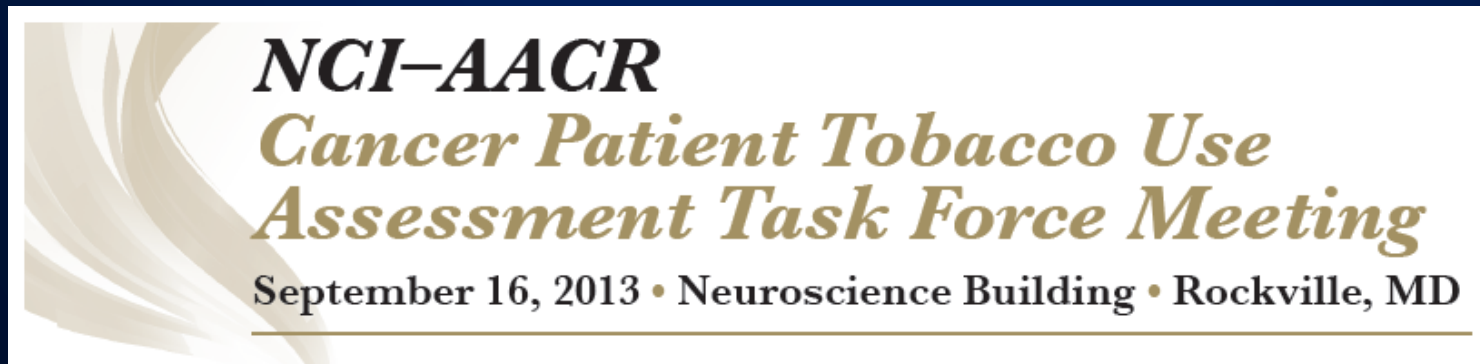
Tobacco Cessation and Control a Decade Later: American Society of Clinical Oncology Policy Statement Update

[Nasser Hanna](#) , [James Mulshine](#) , [Dana S. Wollins](#) , [Courtney Tyne](#) ,
[Carolyn Dresler](#)

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

NCI-AACR Cancer Patient Tobacco Use Assessment Task Force

- Established in 2013
- Purpose (from the scientific and medical perspective): to develop recommendations for
 - patient-reported tobacco use measures
 - timing of assessment
 - research priorities



NCI-AACR Cancer Patient Tobacco Use Assessment Task Force

NCI

Moffitt Cancer Center

Mayo Clinic

MD Anderson Cancer Center

Medical U. of South Carolina

IASLC Smoking Cess. Tobacco Ctrl Cmte

Ohio State University

University of Wisconsin

University of Minnesota

Yale School of Medicine

Emory School of Medicine

Fred Hutchinson

Memorial Sloan-Kettering

Harvard

U. of California Los Angeles

University of Pennsylvania

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Jamie S. Ostroff

Nancy Rigotti, K. (Vish) Viswanath

Linda Sarna

Robert A. Schnoll

Shimere W. Sherwood

Recommended Measures of Tobacco Use by Cancer Patients

- **Cancer Patient Tobacco Use Questionnaire (C-TUQ)**
 - Designed by Task Force
 - Validated in cognitive interview study
 - Posted to cancercontrol.cancer.gov/brp/tcrb/tobacco-after-cancer-diagnosis.html
- **C-TUQ Core:** SHORT FORM for broad use
- **C-TUQ Extension:** Pool of items for comprehensive assessment

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

C-TUQ Core Constructs

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

The Task Force concluded that these are the essential constructs for minimal assessment in cancer trials.

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

C-TUQ 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

Smoked every day, some days, not at all

- a. The year before you were first told you had cancer
- b. After diagnosis, and before treatment started
- c. From 2 days before your last cancer surgery to 2 days after
- d. During the course of treatment
- e. After treatment ended
- f. Since your last visit to this clinic

Task Force Recommendations

- Task Force recommends broad inclusion of C-TUQ items in cancer research

Standardized tobacco use assessment implemented in research across a range of disease sites and treatment modalities will permit data pooling and comparisons among populations.

- Detailed research priorities (See Land et al, CCR, 2016*)
- Timing of tobacco use assessment in clinical trials

*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

Task Force

Recommended Timing of Assessment

- Minimal: registration and end of protocol therapy
- Recommended:

- 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

Cancer Patient Tobacco Use Questionnaire (C-TUQ) Usage

NCI DCP-001—Use of a Clinical Trial Screening Tool to Address Cancer Health Disparities in the NCI Community Oncology Research Program (NCORP)

SWOG Lung Master Protocol: S1400—Phase II-III Intergroup. A Biomarker-Driven Master Protocol for Previously Treated Squamous Cell Lung Cancer (Lung-MAP) (NCT02154490)

Other SWOG and ECOG-ACRIN trials

Many projects of the Cancer Center Cessation Initiative (C3I)

Translated to Spanish

Downloaded over 2500 times

Discussion

- Integration of tobacco use assessment into electronic health records is an opportunity.*
- Other tobacco products increasingly used.
- Tobacco use is time varying, not necessarily a stratification factor.

Conclusion

- Tobacco use is an important prognostic and predictive factor in cancer treatment, with implications for regimen, morbidity, and disease outcomes.
- At a minimum, tobacco use should be assessed at trial registration and end of protocol therapy.

* Warren, Cancer, 2014; Giuliani, JMIR, 2019

Objectives for future discussions

- Share knowledge of the impact of tobacco use in clinical trials and its importance for regulatory review
- Identify joint priorities of FDA, cancer therapeutics industry, academic researchers, AACR, IASLC, ASCO, and NCI
- Identify barriers and best practices to assessing tobacco use in clinical trials
- Mechanisms for increasing accurate tobacco use assessment in clinical trials

The views expressed represent my own and not necessarily those of NCI.

Contact:

Stephanie.land@nih.gov

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ADMINISTRATION



American Association
for Cancer Research

FINDING CURES TOGETHER™



INTERNATIONAL
ASSOCIATION
FOR THE STUDY
OF LUNG CANCER
Conquering Thoracic Cancers Worldwide

SESSION II:

Assessment Of Tobacco In Oncology Therapeutic Trials: Implementation

Session Moderators: Roy S. Herbst, MD, PhD, and Stephanie Land, PhD

Speakers:

Roy S. Herbst, MD, PhD

Elyse Park, PhD

Cathy Pietanza, MD

THE IMPACT OF SMOKING ON LUNG CANCER TREATMENT

FEBRUARY 28, 2020

ROY S. HERBST, MD, PHD

Ensign Professor of Medicine

Professor of Pharmacology

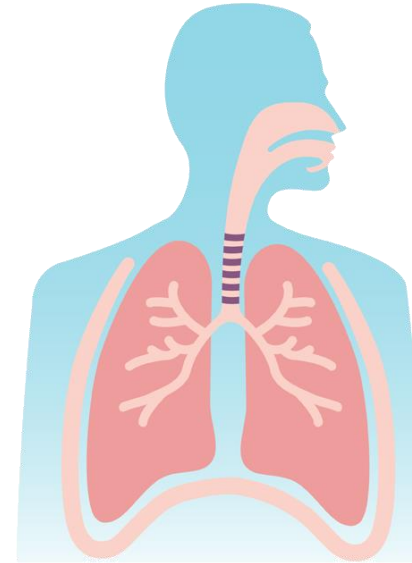
Chief of Medical Oncology

Director, Thoracic Oncology Research Program

Associate Cancer Center Director for Translational Research

The Burden of Lung Cancer

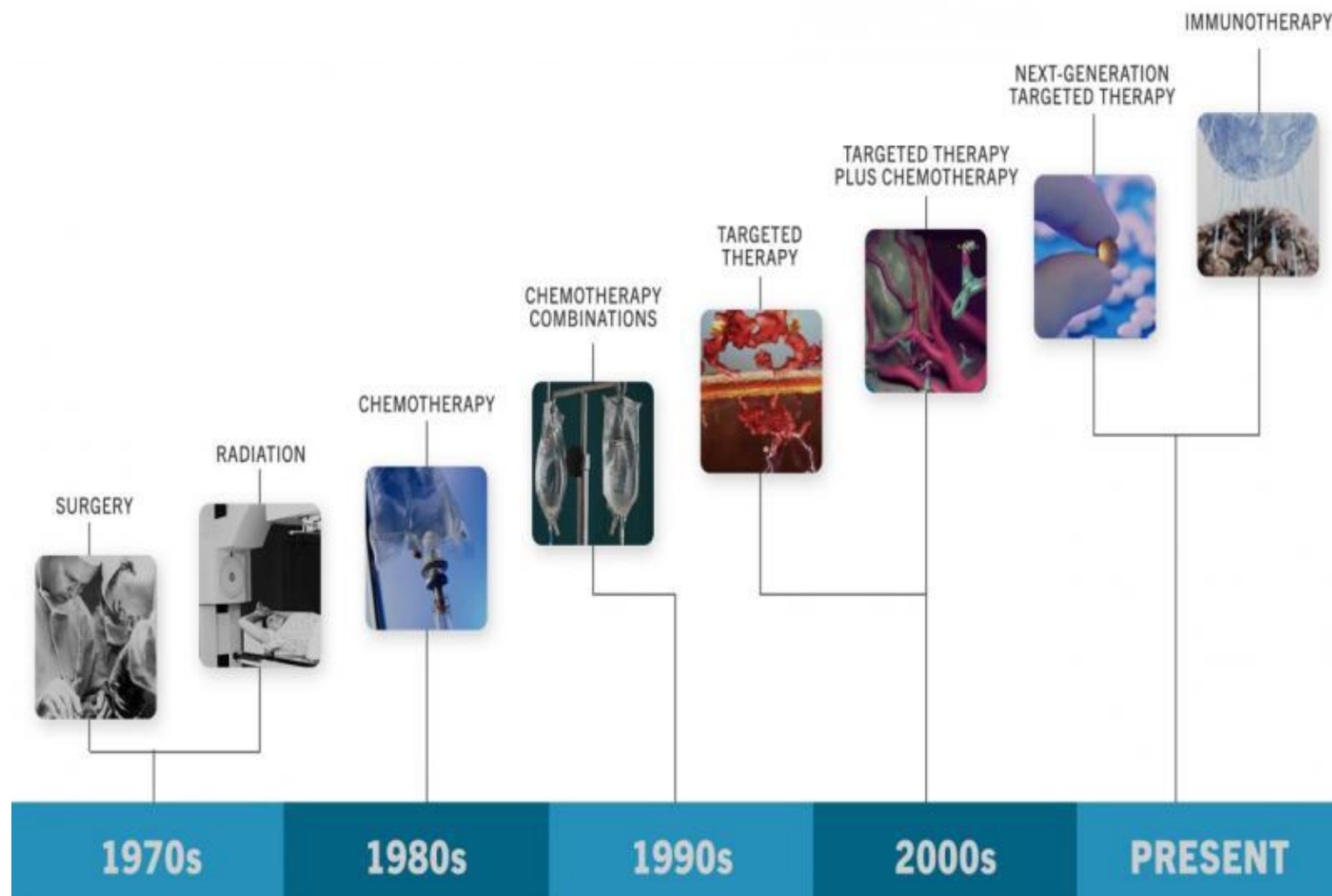
- The Leading Cause of Cancer Death in Most Countries
 - 1.8 M new cases, 1.6 M deaths ¹
- US Lung Cancer: ²
 - 234,030 new cases (13.5% of all cancer cases)
 - 154,050 deaths (25% of all cancer deaths)
- 85% of lung cancer is NSCLC (~15% small cell) ³
 - 40% Adenocarcinoma, 30% Squamous cell carcinoma



Tobacco use is the single largest preventable cause of cancer, leading to 30% of all cancer-related deaths

¹ Lung Cancer Fact Sheet, International Agency for Research on Cancer, WHO 2012; ² Cancer Facts and Figures, American Cancer Society 2018; ³ Lung Cancer (Non-small cell), American Cancer Society 2018; ⁴ Herbst et al Lancet 2016; 387:1540-50; ⁵ Herbst et al. Nature 2018: 553;446-454

Progress in Lung Cancer Treatment



Picture adapted; www.vaidam.com

- Advance therapeutic outcomes through improved overall survival, disease control, toxicity profiles, or a combination thereof.
- Designing clinical trials that achieve clinically meaningful outcomes using evidence-based care and improving translation of evidence into clinical practice to improve clinical outcomes.
- Smoking can affect the primary endpoints of a clinical trial, the omission of routine tobacco use assessments introduces the risk of misinterpretation of results.

2016

Special Report

Clinical
Cancer
Research

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

Stephanie R. Land¹, Benjamin A. Toll², Carol M. Moinpour³, Sandra A. Mitchell¹,
Jamie S. Ostroff⁴, Dorothy K. Hatsukami⁵, Sonia A. Duffy⁶, Ellen R. Gritz⁷, Nancy A. Rigotti⁸,
Thomas H. Brandon⁹, Sheila A. Prindiville¹⁰, Linda P. Sarna¹¹, Robert A. Schnoll¹²,
Roy S. Herbst¹³, Paul M. Cinciripini⁷, Scott J. Leischow¹⁴, Carolyn M. Dresler¹⁵,
Michael C. Fiore¹⁶, and Graham W. Warren^{2,17,18}

Impact of smoking

- Analysis of 4,200 patients from a prospective National Comprehensive Care Network database found that continued smoking decreased survival in advanced patients with lung cancer.
- Meta-analysis of smoking and cessation on patients with early-stage lung cancer confirmed that smoking significantly decreased disease-free survival and overall survival while increasing the risk for developing second primary tumors.
- Smoking by patients with cancer increases their risk of developing new cancers at other sites. (e.g., patients with Hodgkin disease who smoke have a substantially enhanced risk of developing lung cancer after chemotherapy and/or radiotherapy)

- Smoking cessation has immediate positive impact on health
- Improved treatment efficacy, survival, and quality of life
 - Smoking cessation may improve outcomes in patients with lung cancer and bladder cancer.
 - Study found that patients with lung or head and neck cancer who quit tobacco use within 12 months before a cancer diagnosis had improved survival as compared with current smokers

Full execution of evidence-based cessation interventions is infrequent in oncology settings

- Tobacco use should be comprehensively and repeatedly documented for all patients so that the confounding effects of tobacco on cancer treatment, disease progression, comorbid events, and survival can be evaluated in all oncology clinical trials, from registration to survival endpoints, and in all clinical cancer settings.

- Multiple Association statements (e.g., AACR, ASCO, etc.) suggest that oncology care should include tobacco cessation assistance



Assessing Tobacco Use by Cancer Patients and Facilitating Cessation: An American Association for Cancer Research Policy Statement

Benjamin A. Toll, Thomas H. Brandon, Ellen R. Gritz, Graham W. Warren, and Roy S. Herbst;
Writing Committee for the AACR Subcommittee on Tobacco and Cancer

1. Patients with cancer from all clinical settings, including clinical trial participants and cancer screening patients, who use tobacco or have recently quit should be provided with evidence-based tobacco cessation assistance.

- Assistance should be provided to current users and recent quitters (past 30 days)
- Assistance should be provided within or associated with the oncology practice
- The oncology service provider should assume responsibility for ensuring that the patient receives appropriate care
- Oncology provider assistance can be supplemented with telephone quitline care by having patients call 1-800-QUIT-NOW

Universal assessment and documentation of tobacco use as a standard of care

- improved provision of cessation assistance to all patients
- further study of the deleterious effects of tobacco use
- further study of the benefits of tobacco cessation

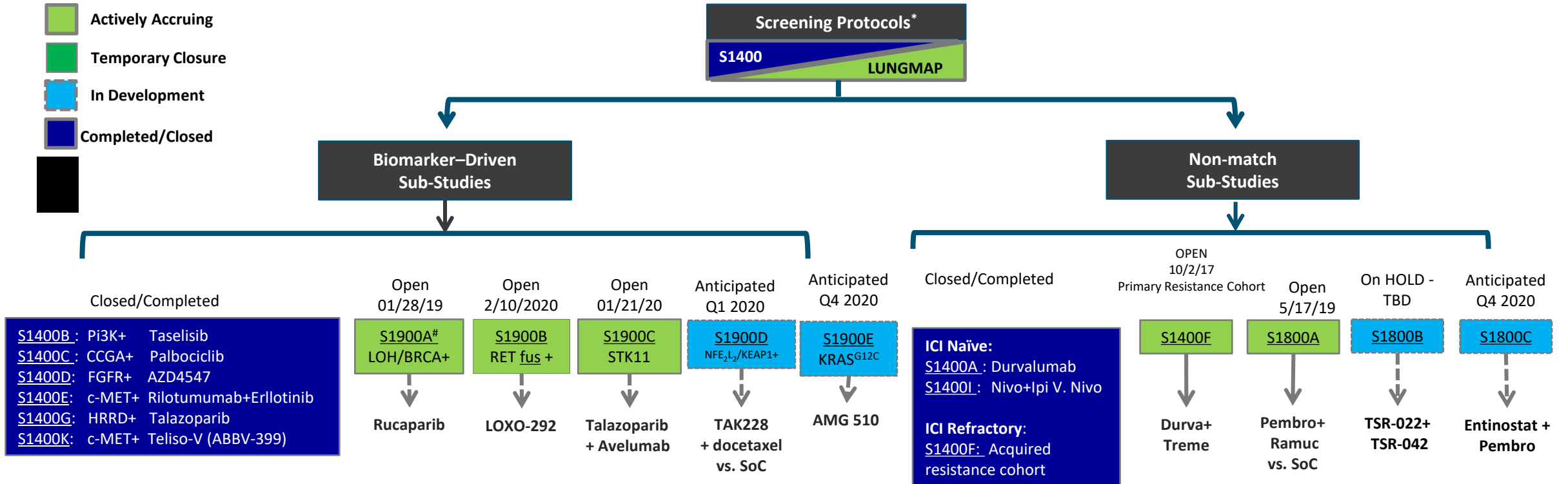
Oncology service provider assumes responsibility for evidence-based tobacco cessation assistance (including quitlines)

- cancer patients from all clinical settings
- participants in therapeutic cancer clinical trials
- cancer screening patients who use tobacco or have recently quit (past 30 days)

2. Researchers should evaluate the confounding effects of tobacco on cancer treatment, disease progression, comorbid events and survival in all oncology clinical trials, from registration to survival endpoints.

- Smokers receiving erlotinib or irinotecan exhibited rapid clearance, requiring higher dose to reach equivalent systemic exposure compared to nonsmokers

Lung-MAP Schema (Current: 02/26/20)



- S1400, the original screening/umbrella protocol included only squamous lung cancer.
- S1400 accrued patients between 6/16/2014 and 1/28/2019.
- LUNGMAP screening protocol (activated 1/28/19) allows all histologic types of NSCLC.
- Patients enrolled to S1400 may participate in sub-studies opened under LUNGMAP.

Smoking question asked during enrolment onto the Lung-MAP screening study (onstudy form)

Smoking history

- ☐ Current
☐ Former (no smoking for 1 year or more)
☐ Never (less than 100 cigarettes in lifetime)

Questionnaire
completed at baseline
and
off-treatment for
patients on Lung-MAP
sub-studies

1. Have you smoked at least 100 cigarettes in your ENTIRE LIFE?

- ☐ Yes ☐ No ☐ Don't know/Not sure ☐ Refused to answer

IF YES, PLEASE ANSWER THE FOLLOWING QUESTIONS:

2. How long has it been since you last smoked a cigarette (even one or two puffs)? Please check one of the following choices, either the number of days, weeks, months, or years, whichever applies to you.

- ☐ I smoked a cigarette today (at least one puff).
☐ Less than one week. Number of days:
☐ Less than 1 month. Number of weeks:
☐ Less than 1 year. Number of months:
☐ More than 1 year. Number of years:

3. How many total years have you smoked (or did you smoke) cigarettes? years

4. On average when you have smoked, about how many cigarettes do you (or did you) smoke a day?

Enter '1' if less than 1.
Enter '95' if 95 or more cigarettes.

Development of reliable, valid, and standard measures of tobacco use

- robust data collection allows later pooling of data and meta-analysis that may elucidate potential mechanisms of change and specific populations or conditions that are more or less amenable to treatment.

Include evidence-based procedures in quality and accreditation protocols ("5 A's")

- Ask about tobacco use at every clinic visit
- Advise to quit
- Assess interest in quitting
- Assist by providing counseling and pharmacotherapy
- Arrange follow-up

What is needed?

- Appropriate training, clinical infrastructure, and incentives for interventions

Lung SPORE Project Collaboration

PIP: Personalized Intervention Project for Tobacco Treatment

Co-PIs



Brenda Cartmel, PhD
Yale University

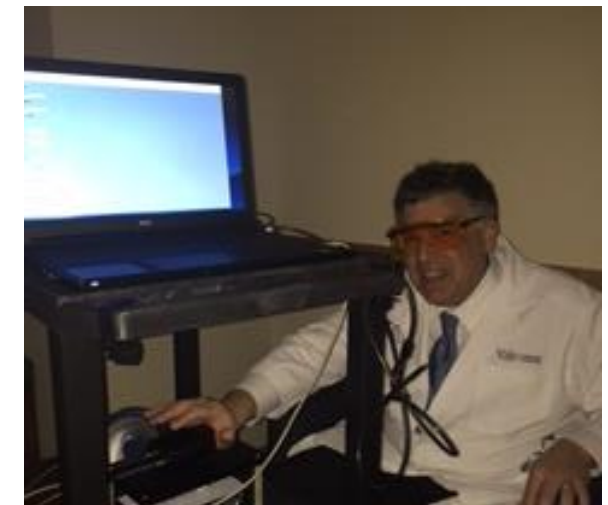


Ben Toll, PhD
Medical University
of South Carolina

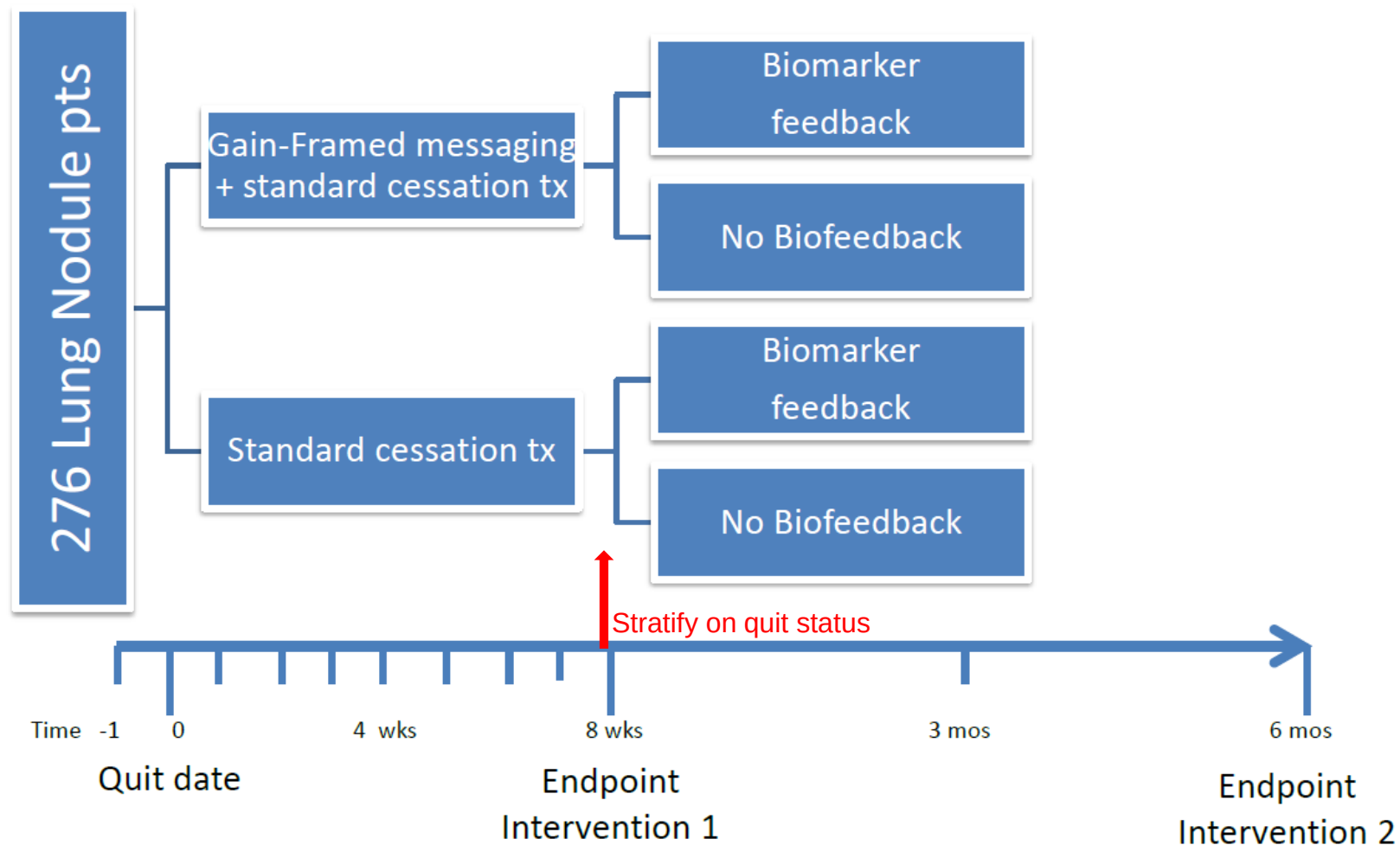


Objective

Randomized clinical trial that will test 2 different, sequential interventions in lung cancer screening population. Both involve personalized prevention and are based on gain-framed messaging



PIP: Study Design



Resonance Raman Spectroscopy (RRS): Method for Carotenoid Measurement

- Carotenoids are any of a class of mainly yellow, orange, or red pigments (including carotene) that give color to plants
- Well known that low concentrations of carotenoids in blood predict higher risk of various cancers including lung cancer
- Non-invasive method to objectively assess carotenoid status in human skin using a portable, rapid scanner, with visible light



Mayne et al. (2010). *American J of Clinical Nutrition*.
Mayne et al. (2013) *Archives Biochemistry Biophysics*.

What messages are most helpful for quitting?

Types of Framed Messages

Gain-framed

Benefits of
quitting
smoking

Loss-Framed

Costs of
continuing
smoking

Prospect Theory

- Nobel prize winning theory developed by Daniel Kahneman and Amos Tversky
- Prospect theory suggests:
 - Gains = people averse to risk
 - Losses = individuals seek risk



Prospect Theory and Smoking Cessation

- Smoking cessation is a prevention behavior with a fairly certain outcome
 - Quitting linked to reduced risk of health problems like cancer
- Prospect theory suggests:
 - Gain-framed messages would be more persuasive for encouraging smoking cessation
 - Several studies support this hypothesis

Examples of Framed Messages

Gain-framed Messages

If no one smoked, 430,000 lives would be saved in the United States each year.

In addition to the physical benefits of quitting smoking, it can also have a positive impact on one's social life.

Loss-framed Messages

Because people smoke, 430,000 lives are lost in the United States each year.

In addition to the negative physical effects of smoking, it can have a negative impact on one's social life.

Contact information

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Ensign Professor of Medicine

Professor of Pharmacology

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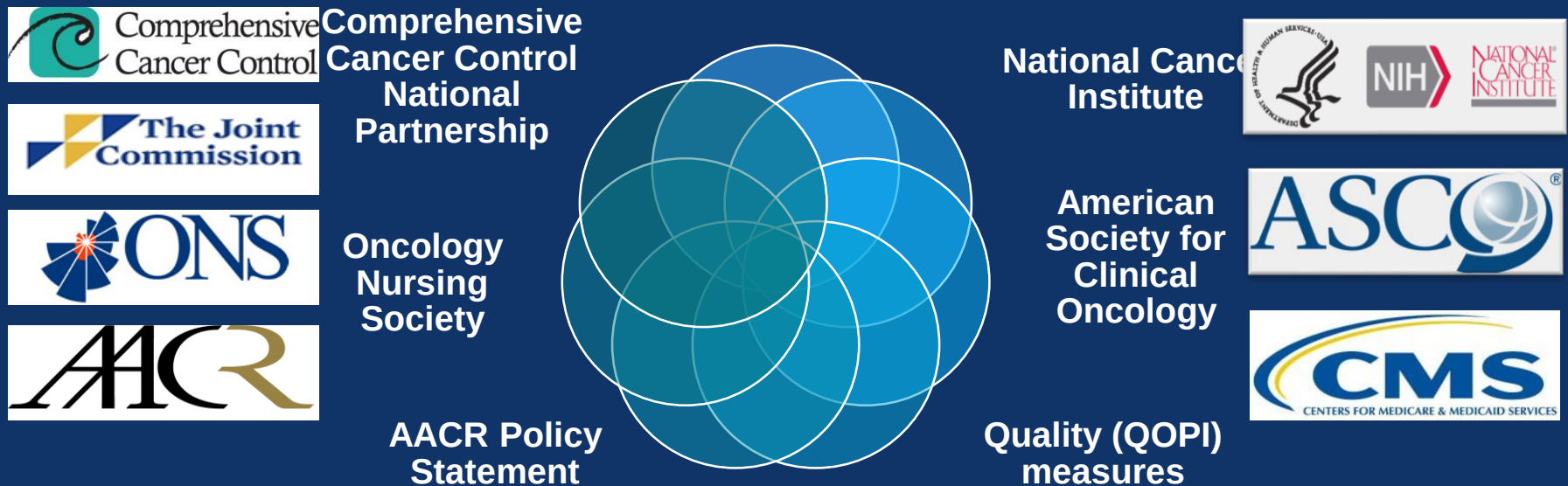
Implementing assessment of tobacco use in cooperative group cancer trials

Elyse R. Park, Ph.D., MPH

Massachusetts General Hospital/Harvard Medical
School

National Calls for Action

Tobacco Use Assessment and Treatment in Cancer Care



Rationale for Tobacco Use Assessment in Therapeutic Trials

The scope and patterns of tobacco use among cancer patients is limited

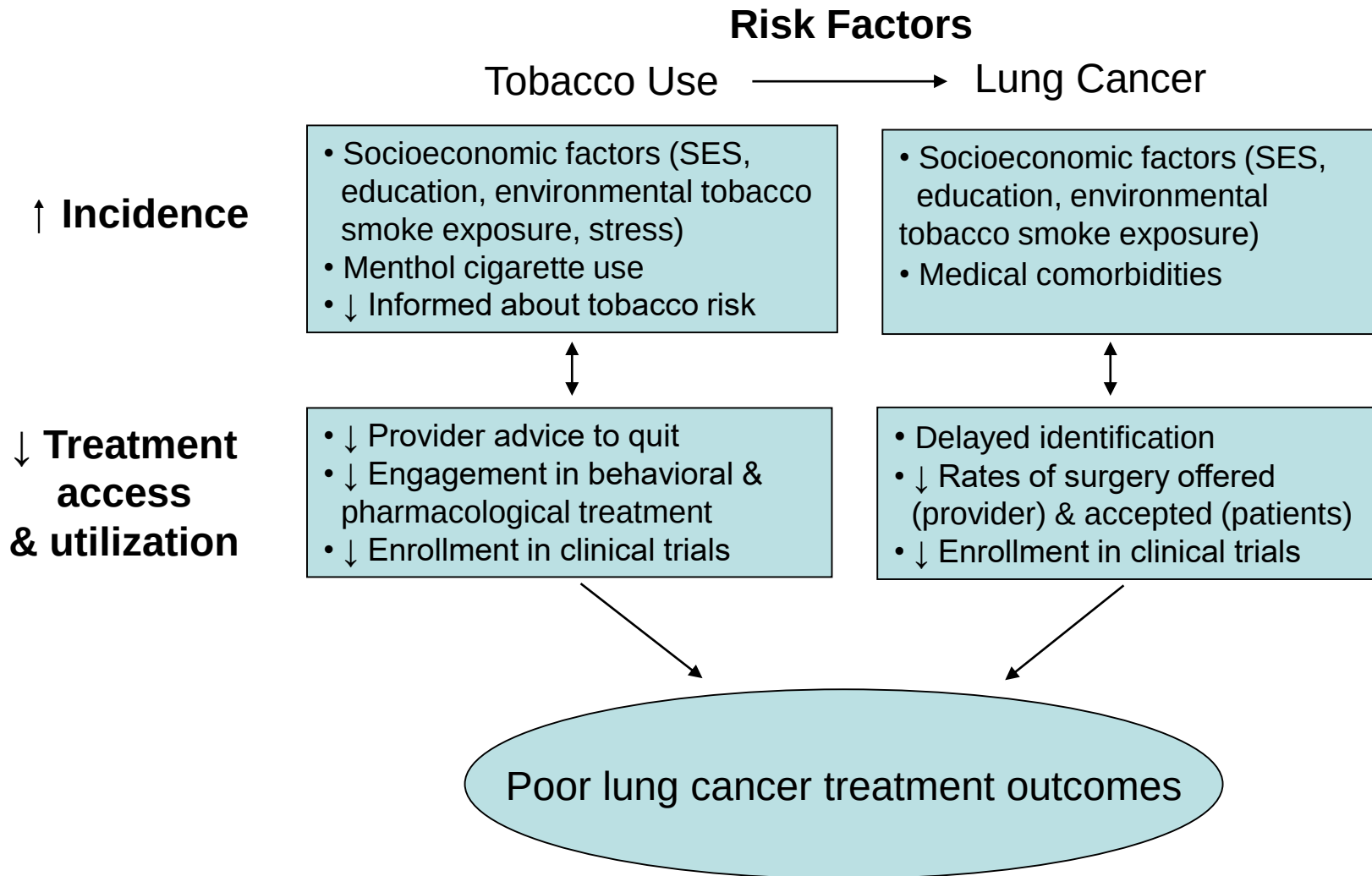
Tobacco use data collected in therapeutic trials vs. tobacco use data collected for smoking cessation trials

Information of the effects of tobacco use, among patients enrolled in clinical trials, is critically needed

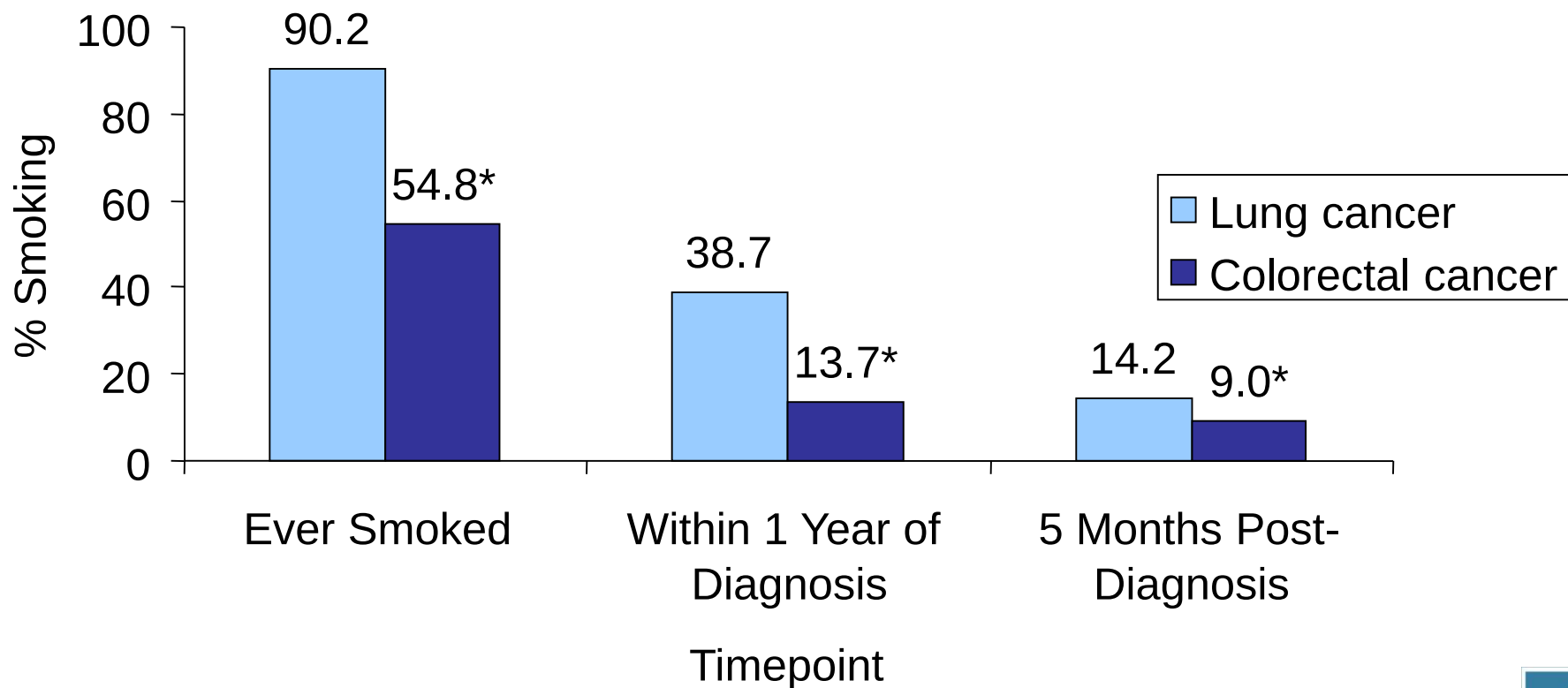
Without tobacco use assessment there is no opportunity for treatment



Risk factors for tobacco use and lung cancer among Black adults



Smoking Rates of Participants



NCI EAQ16T Supplement

- ▶ Among patients enrolled in Phase II and Phase III ECOG ACRIN (EA) therapeutic trials with varied cancers and cancer treatments, we are administering modified C-TUQ questions at trial enrollment and 3 and 6 month follow-up.

NCI Community Oncology Research Program (NCORP)



NCI

**Community Oncology
Research Program**

A program of the National Cancer Institute
of the National Institutes of Health

NCI

**Programa Comunitario de
Investigación Oncológica**

Un programa del Instituto Nacional del Cáncer
de los Institutos Nacionales de la Salud

C-TUQ initiative

Published OnlineFirst February 17, 2016; DOI: 10.1158/1078-0432.CCR-16-0104

Special Report

Clinical
Cancer
Research

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

Stephanie R. Land¹, Benjamin A. Toll², Carol M. Moinpour³, Sandra A. Mitchell¹, Jamie S. Ostroff⁴, Dorothy K. Hatsukami⁵, Sonia A. Duffy⁶, Ellen R. Gritz⁷, Nancy A. Rigotti⁸, Thomas H. Brandon⁹, Sheila A. Prindiville¹⁰, Linda P. Sarna¹¹, Robert A. Schnoll¹², Roy S. Herbst¹³, Paul M. Cinciripini⁷, Scott J. Leischow¹⁴, Carolyn M. Dresler¹⁵, Michael C. Fiore¹⁶, and Graham W. Warren^{2,17,18}

Abstract

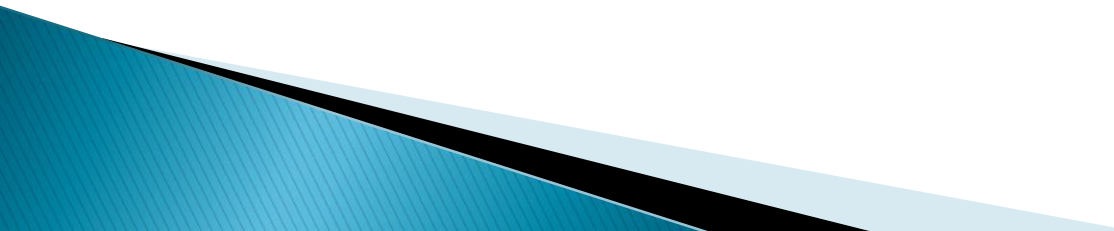
There is strong evidence that cigarette smoking causes adverse outcomes in people with cancer. However, more research is needed regarding those effects and the effects of alternative tobacco products and of secondhand smoke, the effects of cessation (before diagnosis, during treatment, or during survivorship), 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

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

RFA

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

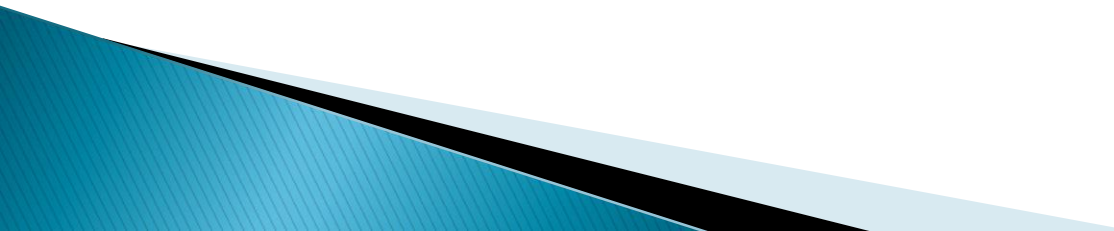
Purpose : The National Cancer Institute (NCI), Division of Cancer Control and Population Sciences (DCCPS) announces the opportunity for supplemental funding to support collection of new longitudinal data using the Cancer Patient Tobacco Use Questionnaire (C-TUQ) for participants enrolled to NCI Clinical trials Network (NCTN) and NCI Community Oncology Research Program (NCORP) clinical trials.



AIM 1: Treatment Toxicity

- ▶ To determine the associations of combustible tobacco use patterns (status and rate) to:
 - other forms of tobacco use
 - environmental tobacco exposure
 - provider-reported cancer-treatment toxicity (adverse events (both clinical and hematologic) and dose reductions and delays)
- 

Aim 2: Symptom Burden

- ▶ To determine the effects of tobacco use on patient-reported physical symptoms and psychological symptoms
 - Prevalence
 - Interference
- 

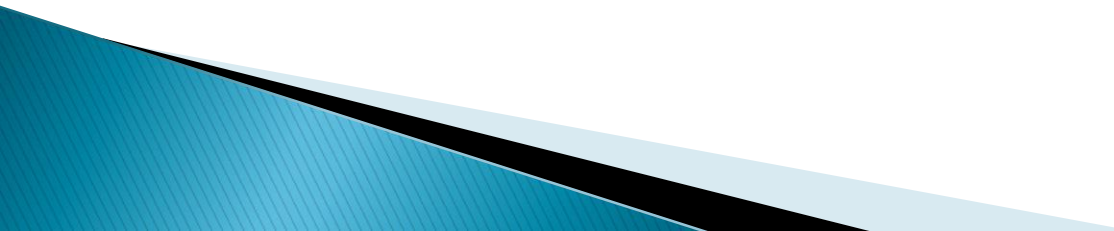
Aim 3: Cessation Patterns & Treatment

- ▶ To examine quitting behaviors and behavioral counseling/support and cessation medication utilization.

Aim 4: EA Trial Outcomes

- ▶ To explore the effect of tobacco use and exposure on treatment duration and dose intensity, and on therapeutic benefit, of EA trials.

Participant heterogeneity

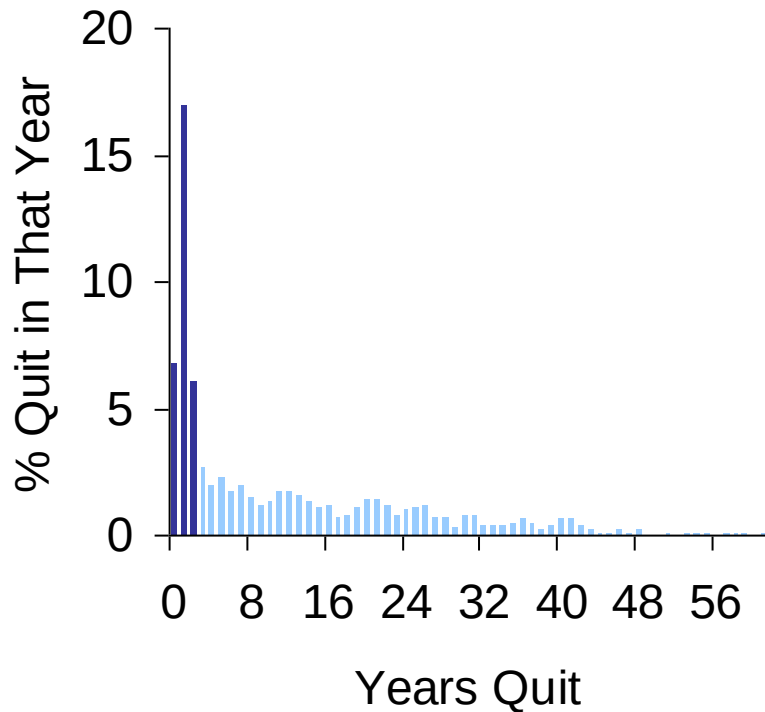
- ▶ Adjuvant trials (recurrence-free survival is a typical outcome) as well as advanced disease trials (assessing overall survival is primary endpoint).
 - ▶ Representation of cancer type, treatment regimen, tobacco-associated cancers, extent of disease, gender, and primary trial outcome (overall survival, disease-free survival, progression-free survival, recurrence-free survival).
- 

Smoking Status Categories

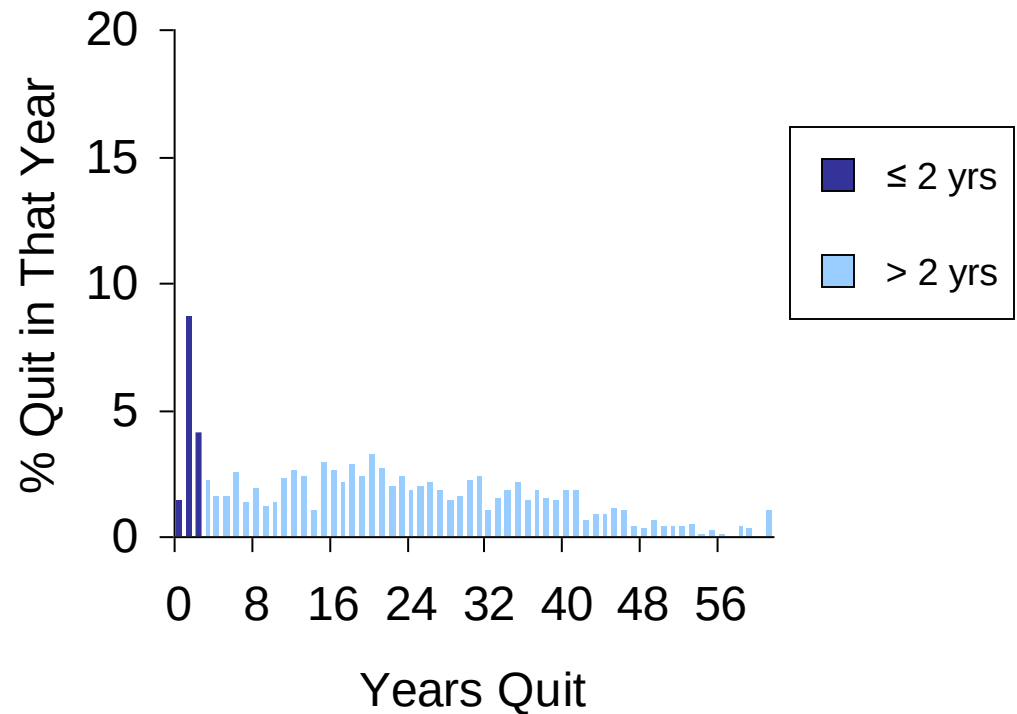
- ▶ Current Smokers
 - Any cigarette use in the past 30 days
 - Differentiating 7 vs 30 day use
 - ▶ Former Smokers
 - Smoked >100 cigarettes in lifetime
 - Differentiating use within past year vs greater than 1 year
 - ▶ Never Smokers
- 

Participants Reported Years Quit Prior to Diagnosis

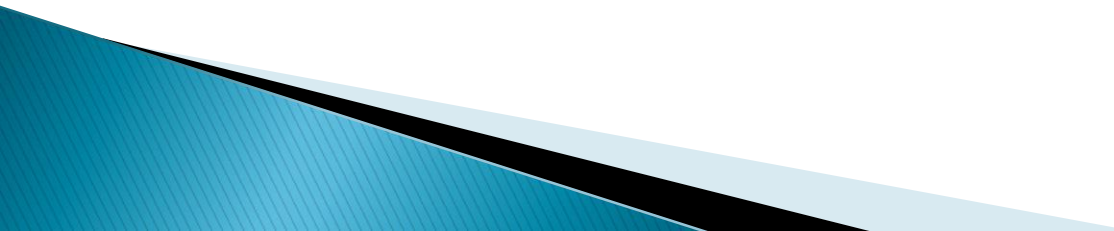
Lung Cancer



Colorectal Cancer



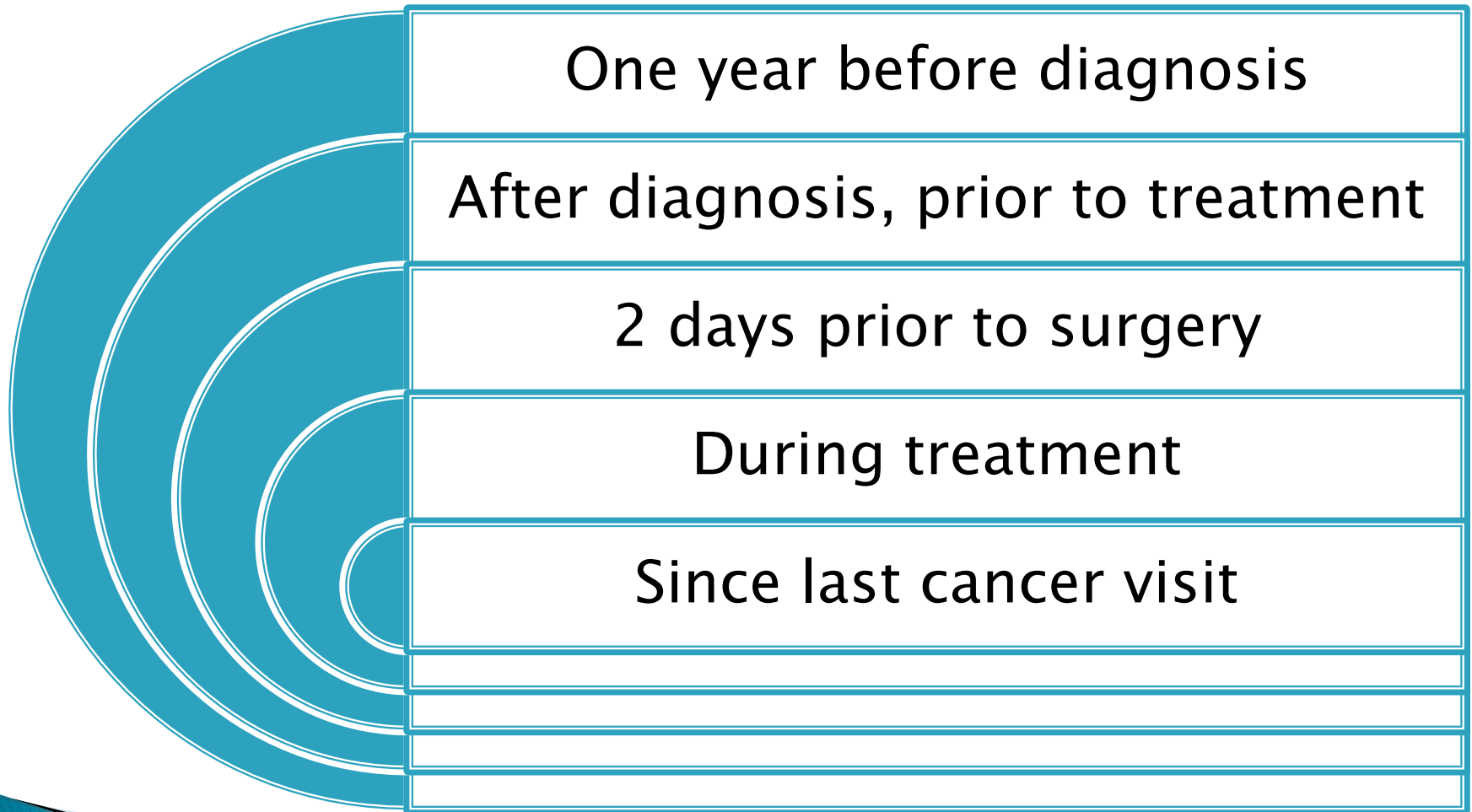
Analyses

- ▶ Analyses will be conducted across categories of smokers
 - ▶ Analyses will be conducted based on changes in smoking status
 - ▶ Effects of sociodemographic characteristics will be explored
 - ▶ Effects of cancer type and treatments will be explored
- 

Survey Tobacco Use

- ▶ Use of other forms of tobacco
 - ▶ Use of e-cigs
 - ▶ Use of FDA approved cessation aids
 - ▶ Use of behavioral support
-
- ▶ Timeframe: Ever AND 30 days

Patterns of Use by clinical timepoint



Survey Tobacco Use

- ▶ Psychological symptoms
- ▶ Stigma
- ▶ Physical and behavioral symptoms (PRO-CTCAE)
 - Nausea
 - Pain
 - Sleep difficulties
 - SOB
 - Coughing
 - Fatigue
- ▶ Perceived associations of symptoms with current/past tobacco use (prevalence & interference)

Integrating PROs into AE reporting for clinical trials

Development of the National Cancer Institute's Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE)

Ethan Basch, Bryce B. Reeve, Sandra A. Mitchell, Steven B. Clauser, Lori M. Minasian, Amylou C. Dueck, Tito R. Mendoza, Jennifer Hay, Thomas M. Atkinson, Amy P. Abernethy, Deborah W. Bruner, Charles S. Cleeland, Jeff A. Sloan, Ram Chilukuri, Paul Baumgartner, Andrea Denicoff, Diane St. Germain, Ann M. O'Mara, Alice Chen, Joseph Kelaghan, Antonia V. Bennett, Laura Sit, Lauren Rogak, Allison Barz, Diane B. Paul, Deborah Schrag

- ▶ JNCI 2014
- ▶ Clinician-rated CTCAE yield fewer, less severe symptomatic adverse events in comparison to patient-rated toxicities
 - More subjective symptoms (eg. fatigue, nausea) have greatest discrepancy between clinician- and patient-ratings
- ▶ <https://healthcaredelivery.cancer.gov/pro-ctcae/>

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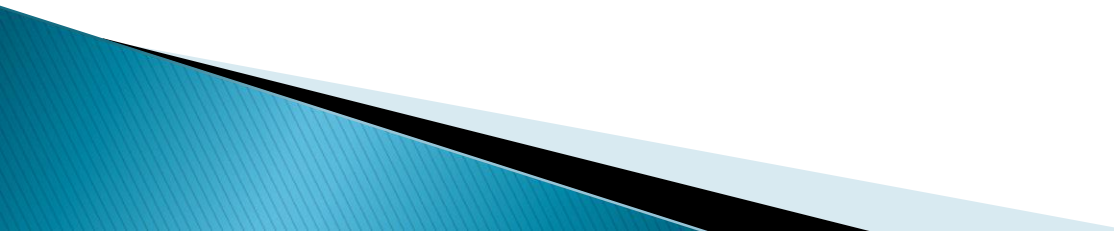
ORIGINAL REPORT

Feasibility of Implementing the Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events in a Multicenter Trial: NCCTG N1048

Ethan Basch, Amylou C. Dueck, Lauren J. Rogak, Sandra A. Mitchell, Lori M. Minasian, Andrea M. Denicoff, Jennifer K. Wind, Mary C. Shaw, Narre Heon, Qian Shi, Brenda Ginos, Garth D. Nelson, Jeffrey P. Meyers, George J. Chang, Harvey J. Mamon, Martin R. Weiser, Tatjana Kolevska, Bryce B. Reeve, Deborah Watkins Bruner, and Deborah Schrag

Perceived survey burden

Was completion of the tobacco use survey a burden to you?

- ☐ Not at all
 - ☐ A little bit
 - ☐ Somewhat
 - ☐ Quite a bit
 - ☐ Very Much
- 

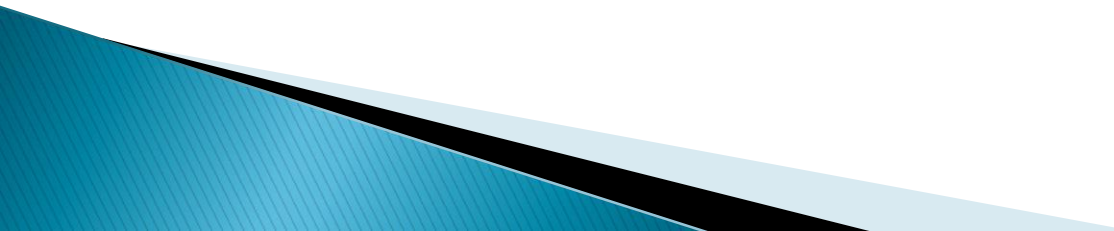
Participating Sites

- ▶ Activated 10 sites
- ▶ 7 currently active
 - Melanoma
 - Breast
 - Leukemia
 - H&N
 - GU
 - Lymphoma
 - Myeloma
 - Thoracic
- ▶ Tobacco use assessment must be included as part of overall trial data collection at trial activation

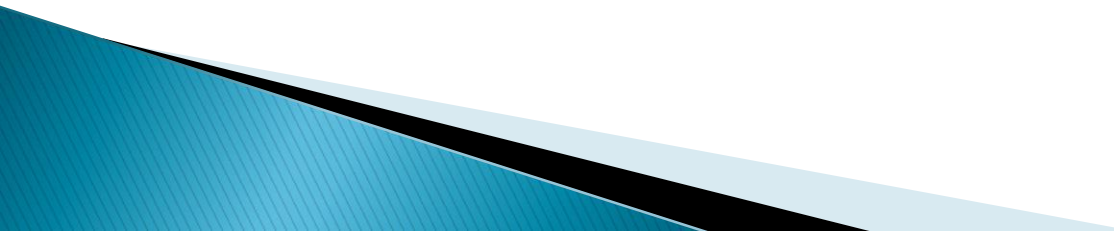
E/A TRIAL DATA COLLECTION TO DATE

# Eligible trial patients/# consented to tobacco study	1477/622 (42% of therapeutic trial patients)
# Eligible trial patients enrolled in tobacco study	603
# Tobacco study accounts activated	424 (70.3% enrolled patients activated)
# Baseline surveys completed	411 of activated completed BL survey (97% activated completed BL survey)
# 3-month follow-up surveys completed to date	271/371 (73.0%)

Data Sources

- ▶ Clinical data: Medidata Rave, used across the NCTN
 - Sociodemographics
 - Patient and disease characteristics
 - Treatment and toxicity
 - Clinical benefit and survival
 - ▶ Adverse events: CTEP–AERS system
 - ▶ Tobacco use questions: EASEEPRO, EA's system for PRO collection
- 

Tobacco Use Assessment in Therapeutic Trials: Recommendations

- ▶ Current and past combustible smoke use
 - ▶ Dose/timing of use
 - ▶ Exposure
 - ▶ Other forms of tobacco use
 - ▶ E-cig/vaping use
- 

Oncology Drug Development: Industry Perspective

Cathy Pietanza, MD
Executive Director
Oncology Clinical Research



Disclosures

- Employee of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA
- Hold shares in Merck & Co., Inc., Kenilworth, NJ, USA

Why Collect Tobacco History?

- Treatment outcomes are affected by continued cigarette smoking in patients with all malignancies
- In those patients with any cancer, continued smoking is strongly associated with:
 - Increased treatment-related complications
 - Lower QoL scores and greater symptom burden, including fatigue, weight loss, concentration problems, and depression
 - Poorer response to treatment and lower survival rates
 - Increased risk of developing recurrence and second primary tumors
- The metabolism of some cytotoxic agents is impacted by smoking, affecting efficacy (e.g. erlotinib, irinotecan)

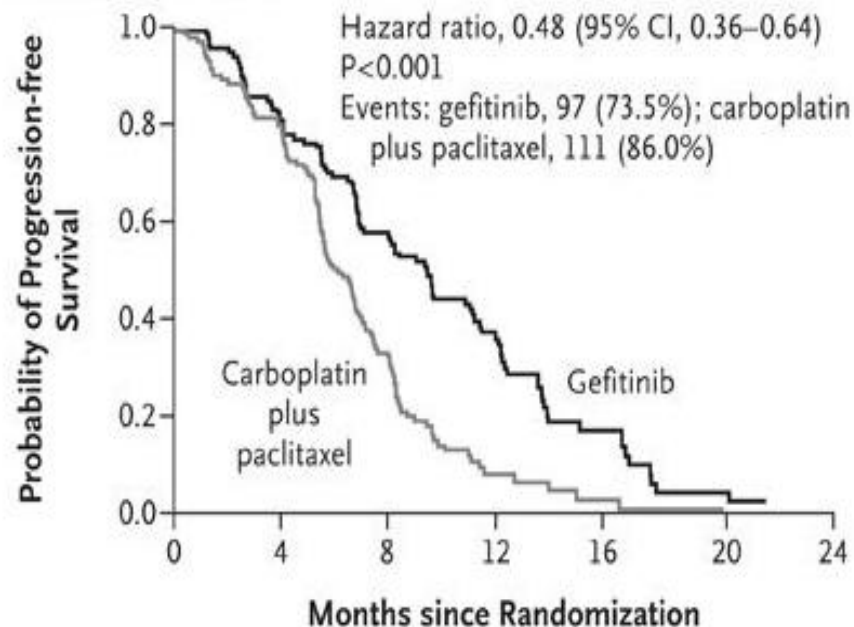
Importance of Tobacco History in Clinical Trials

- Early development of EGFR tyrosine kinase inhibitors first identified clinical characteristics that enriched for efficacy, including never-smoker status
- In 2004, three simultaneous studies reported that somatic mutations in the tyrosine kinase domain of EGFR (exon 19 deletions or L858R) exhibited significant tumor regressions when treated with gefitinib or erlotinib
- Between 2006 and 2008, numerous small, single-arm, prospective trials reported response rates of 55% to 91% utilizing gefitinib or erlotinib in patients with drug-sensitizing *EGFR* mutations

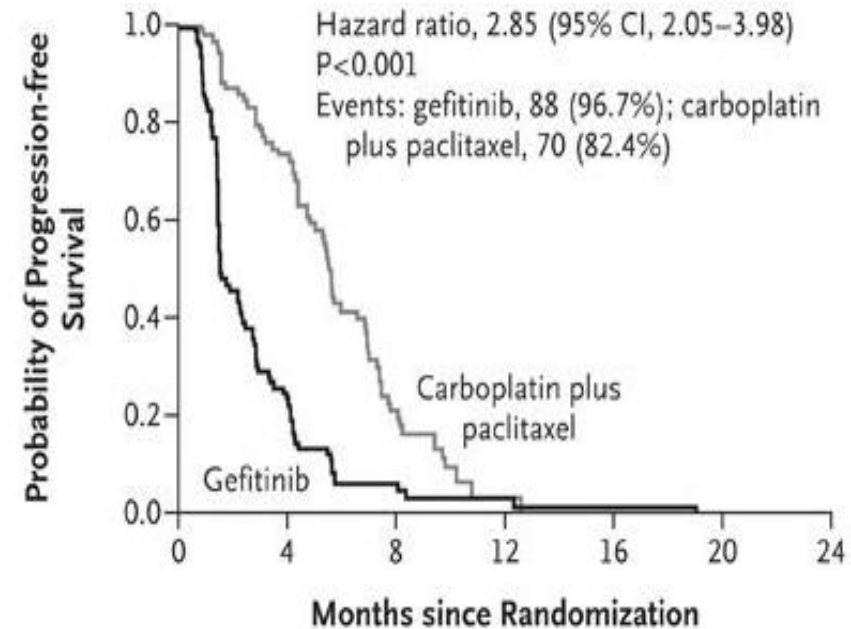
Importance of Tobacco History in Clinical Trials: iPASS

- The iPASS study evaluated gefitinib compared to carboplatin-paclitaxel as first line therapy in 1217 patients who were non-smokers or former light smokers in East Asia with adenocarcinoma of the lung
 - *Non-smokers* defined as patients who had smoked <100 cigarettes in their lifetime
 - *Former light smokers* defined as patients who had stopped smoking at least 15 years previously and had a total of ≤ 10 pack years of smoking
 - Study assessed role of *EGFR* mutation as a predictor of the efficacy of gefitinib or chemotherapy

EGFR mutation positive



EGFR mutation negative

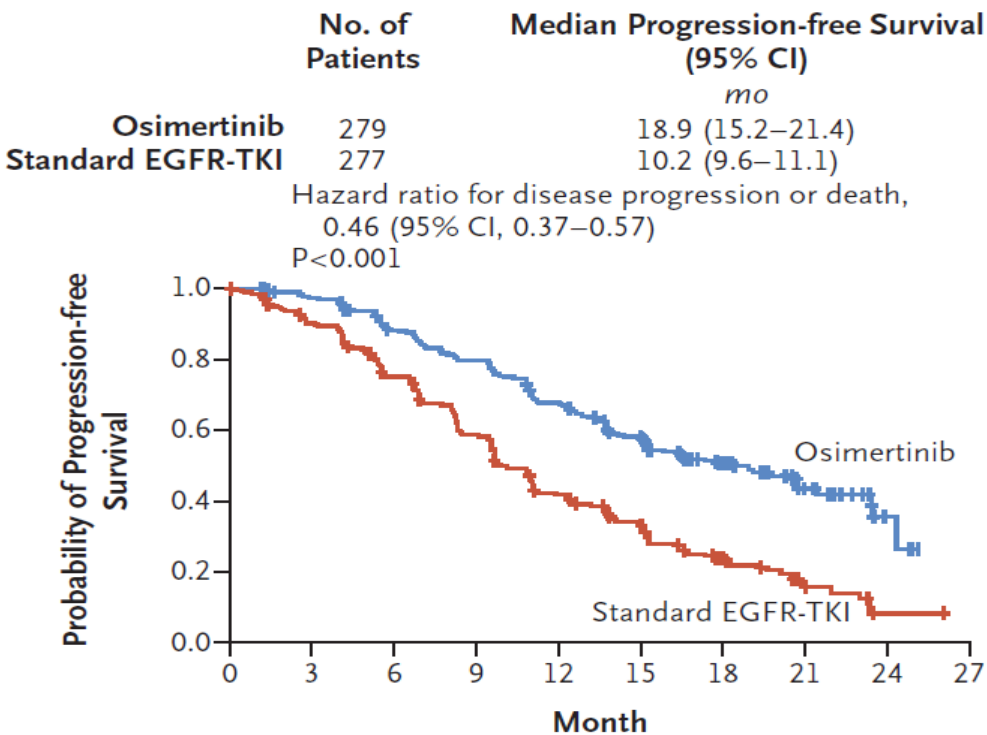


- Study confirmed the predictive value of *EGFR* mutations for the responsiveness of lung adenocarcinoma compared to chemotherapy

Importance of Tobacco History in Clinical Trials: FLAURA

- FLAURA compared osimertinib, the third generation, irreversible EGFR-TKI, to gefitinib or erlotinib in patients with untreated *EGFR*-mutation positive advanced NSCLC (exon 19 del or L858R)
 - Baseline characteristics included smoking history, although not defined in protocol

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*		
Characteristic	Osimertinib (N=279)	Standard EGFR-TKI (N=277)
Age — yr		
Median	64	64
Range	26–85	35–93
Male sex — no. (%)	101 (36)	105 (38)
Race — no. (%)†		
White	101 (36)	100 (36)
Asian	174 (62)	173 (62)
Other	4 (1)	4 (1)
Smoking status — no. (%)		
Never	182 (65)	175 (63)
Current	8 (3)	9 (3)
Former	89 (32)	93 (34)



- Study demonstrated improvement in PFS for osimertinib in patients with *EGFR* mutations, regardless of smoking status

Subgroup	No. of Patients	Hazard Ratio for Disease Progression or Death (95% CI)	
Overall	556	0.46 (0.37–0.57)	
Log-rank test: primary analysis		0.46 (0.37–0.57)	
Cox proportional-hazards model		0.46 (0.37–0.57)	
Sex			
Male	206	0.58 (0.41–0.82)	
Female	350	0.40 (0.30–0.52)	
Age at screening			
<65 yr	298	0.44 (0.33–0.58)	
≥65 yr	258	0.49 (0.35–0.67)	
Race			
Asian	347	0.55 (0.42–0.72)	
Non-Asian	209	0.34 (0.23–0.48)	
Smoking history			
Yes	199	0.48 (0.34–0.68)	
No	357	0.45 (0.34–0.59)	

Problems with Collecting Tobacco Use History

- Lack of consistent definitions in the literature/guidelines:
 - NCCN:
 - *Current smoker* (patient smoked within the past 30 days)
 - *Former smoker or recent quitter* (patient smoked more than 30 days to 1 year prior)
 - *Long term former smoker* (more than 1 year since patient last smoked)
 - *Never smoker*
 - Southwest Oncology Group (SWOG):
 - *Current smoker* (patient smoked within the past 1 year)
 - *Former smoker* (patient had not smoked for 1 year or more)
 - *Never smoker* (defined as less than 100 cigarettes in lifetime)
 - National Health Interview Study:
 - *Current smoker* (patient smoked at least 1 cigarette within the past 30 days OR patient smoked within the past year)
 - *Former smoker* (defined as no smoking for 1 year or more)
 - *Never smoker* (patient has smoked fewer than 100 cigarettes in his/her lifetime)

Problems with Collecting Tobacco Use History

- Inadequate or inconsistent assessment and documentation of smoking status
 - Dependent on patient recall and associated with stigma
- Information collected in data bases, and dependent on pre-specified rules and ability to clean data points regarding tobacco history effectively
 - Data collected at one timepoint (generally baseline) during clinical trials
- Individual protocols and manuscripts do not consistently provide definitions for current and former smokers

Collection of Tobacco Use History in Merck Sponsored Clinical Trials

- History of tobacco use collected within the pembrolizumab program for the following indications:
 - Lung (including small cell and mesothelioma)
 - Head and neck
 - Esophageal
 - Hepatocellular carcinoma and biliary tract
 - Renal cell carcinoma, urothelial and bladder (including non-muscle invasive and muscle invasive)

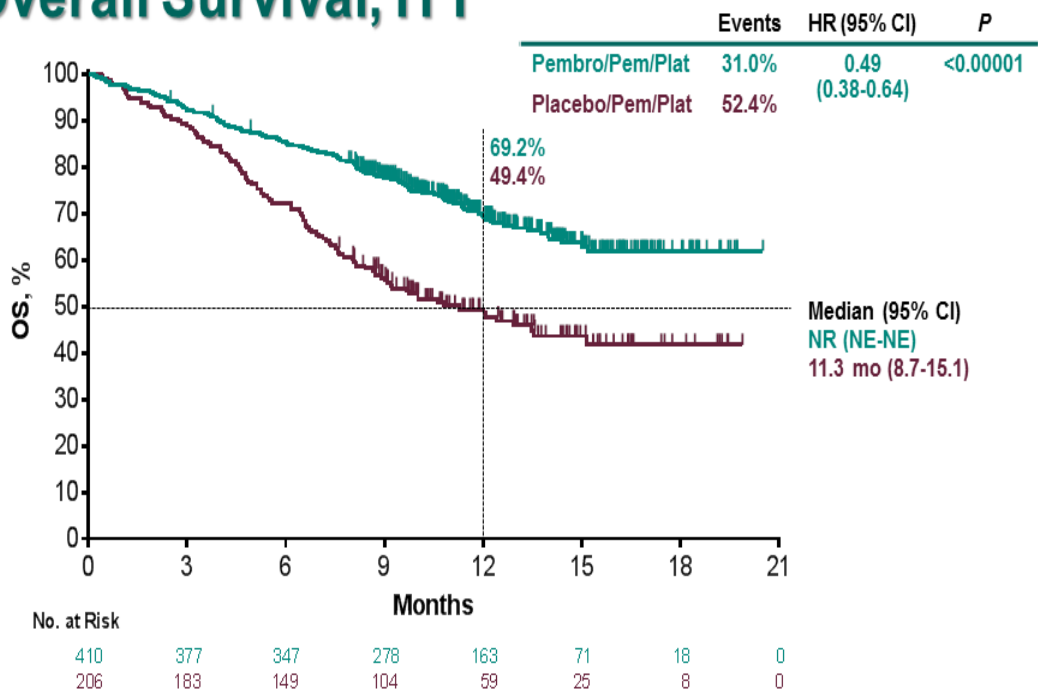
Merck Sponsored Clinical Trials: Electronic Case Report Form for Tobacco Use

Tobacco Use	
4.*	Substance Use Category <i>[read-only]</i>
5.	Has the subject ever used tobacco?
6.*	Cigarette
7.*	Start Date of Cigarette Use
8.*	Stop Date of Cigarette Use
9.*	Number of Cigarettes Smoked Per Day
10.*	Number of Years Smoked
11.*	Number of pack-years <i>[read-only]</i>
12.*	Cigarette Units <i>[read-only]</i>
13.*	Other Tobacco Use
14.*	Start Date of Other Tobacco Use
15.*	Stop Date of Other Tobacco Use

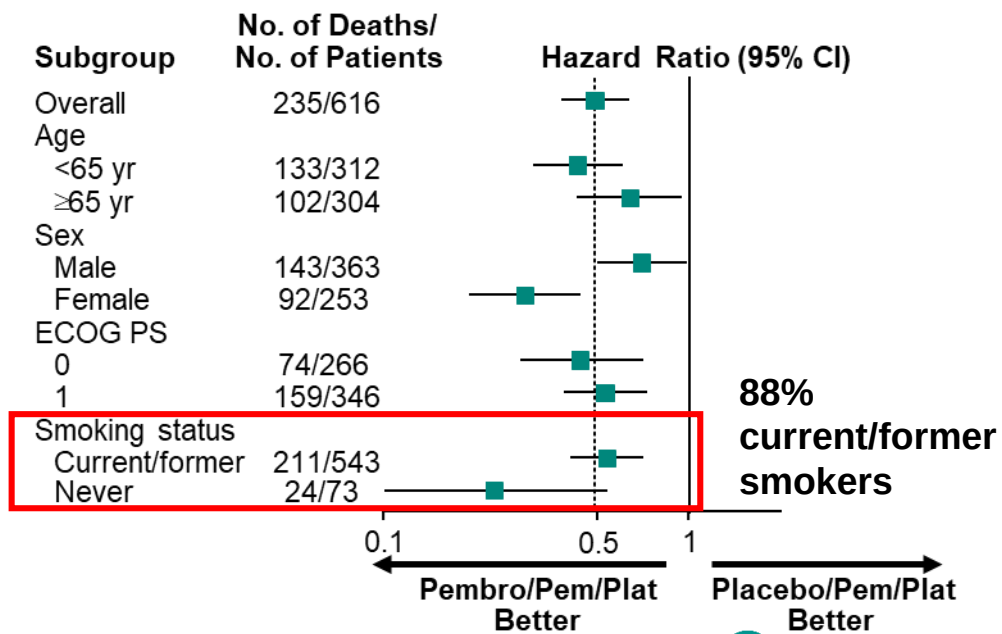
How Has Merck Used Tobacco History?

- KEYNOTE-189, the Phase III study evaluating Pembrolizumab or placebo plus pemetrexed and platinum as first-line treatment in metastatic NSCLC, utilized tobacco history as a stratification factor
 - Current/former smoker vs never smoker
 - PD-L1 expression (TPS <1% vs ≥1%)
 - Choice of platinum (cisplatin vs carboplatin)

Overall Survival, ITT



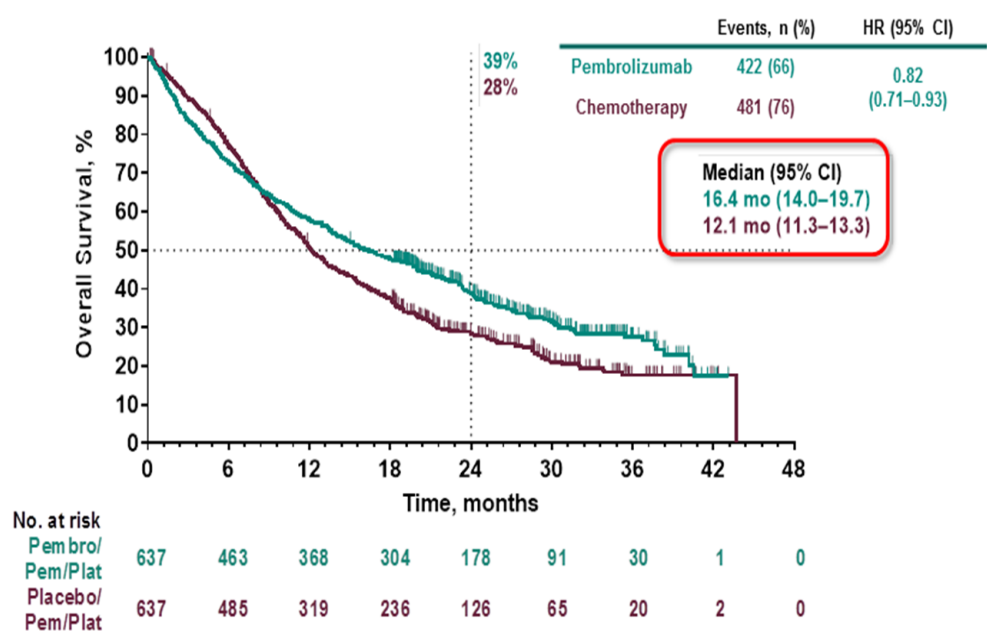
Overall Survival in Key Subgroups



How Has Merck Used Tobacco History?

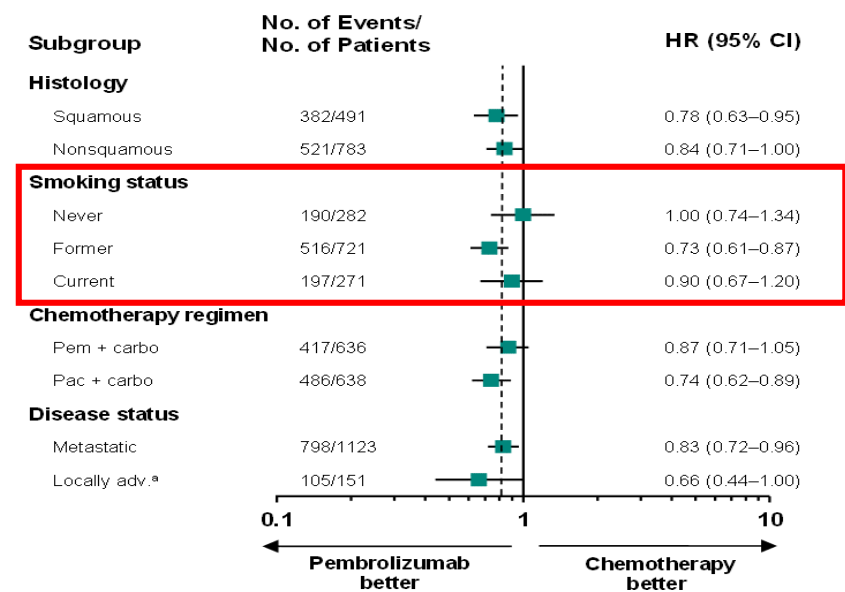
- Subgroup analyses, includes smoking status in trials where information collected
- In KEYNOTE-042, the Phase III study of pembrolizumab vs platinum-based chemotherapy as first-line therapy for patients with PD-L1 positive locally advanced or metastatic NSCLC, smoking status was evaluated

Overall Survival: TPS ≥1%^a



^aNo alpha was allocated, as the primary hypotheses for OS were met at the interim analysis.
Data cutoff date: September 4, 2018.

Overall Survival in Subgroups, TPS ≥1%



78%
current/
former
smokers

Dashed vertical line represents the hazard ratio in the total population.
^aIncludes stage III patients not eligible for definitive treatment.
Data cutoff date: September 4, 2018.



Conclusions

- Assessing tobacco history remains important in the context of large, Phase III randomized trials
- In industry-sponsored trials, obtaining tobacco history has been limited due to:
 - Lack of standardized definitions for current and former smokers
 - Difficulty obtaining precise information from patients
 - Absence of serial collection during treatment
- At Merck, we continue to obtain tobacco history and may add other indications
 - Such data will allow us to better interpret outcomes in never-smokers and former/current smokers
 - Further, with robust tobacco history and data from clinical trials evaluating pembrolizumab in combination with chemotherapy and other agents, we will be better able to interpret never-smoker data in the setting of monotherapy treatment



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American Association
for Cancer Research

FINDING CURES TOGETHER™



INTERNATIONAL
ASSOCIATION
FOR THE STUDY
OF LUNG CANCER
Conquering Thoracic Cancers Worldwide

SESSION III: Providing Tobacco Cessation Assistance To Cancer Patients

Session Moderators: Linda Bailey, JD, MHS, and
Matthew Steliga, MD

Speakers:

Linda Bailey, JD, MHS

Laura Bierut, MD

Matthew Steliga, MD

Community-based cessation services: What services exist and how do smokers access them?

Linda Bailey, JD, MHS
President & CEO
North American Quitline Consortium

FDA-AACR-IASLC Workshop
Silver Spring, Maryland
February 28, 2020

Outline

- ❖ Smokers' interest in quitting
- ❖ Types of community-based smoking cessation services
- ❖ Accessing quitlines and other cessation services
- ❖ Continuum of smoking cessation strategies

Adult smokers in the U.S.

- ❖ 68.0% are interested in quitting
- ❖ 55.4% attempted to quit in the past year
- ❖ 7.4% recent successful cessation

Source: Babb S, Malarcher A, Schauer G et al. Quitting Smoking Among Adults – United States, 2000-2015 MMWR 2017;65:1457-1464.

Evidence-base on smoking cessation treatment

Research-validated services

- ❖ Counseling (individual, group, quitline)
- ❖ 7 FDA approved medications

Other technology-based services

- ❖ Short text messages (sufficient evidence*)
- ❖ Web/Internet based interventions (can be effective*)
- ❖ Cessation apps (inadequate evidence*)

*SGR on Tobacco Cessation, 2020



Background on quitlines

- ❖ 53 state quitlines
- ❖ Funding - state and federal public health agencies
- ❖ 12 organizations that operate state quitlines (<http://map.naquitline.org/reports/operators/>)
- ❖ Each year state quitlines:
 - Receive ~ **one million** calls, 200K referrals*
 - Provide info to many friends, family and smokers
 - Enroll **over 300,000** tobacco users in treatment*
 - Achieve quit rates of 30% (7 months post tx)

*North American Quitline Consortium. 2017. Results from the 2017 NAQC Annual Survey of Quitlines. M. Rudie, editor. Available at <http://www.naquitline.org/?page=2017Survey>

Quitlines - Community-based service with national reach

- ❖ Phone counseling with trained tobacco treatment specialists (research-validated protocols)
- ❖ FDA-approved medications (research-validated)
- ❖ Other technology-based services (promising)
 - Text messaging
 - Web/online services and information
 - Cessation apps

Information on types of quitline services in each state



For detailed information on the types of quitline services offered by your state, go to <http://map.naquitline.org/> and click on the name of your state.

NAQC Quitline Profiles

South Carolina

Quitline Profile

United States

Quitline: South Carolina Tobacco Quitline

Began Operations: September 2004

Website: <http://www.scdhec.gov/quitforkeeps>

Standard Hours of Operation

Monday: 12:00 AM - 11:59 PM
Tuesday: 12:00 AM - 11:59 PM
Wednesday: 12:00 AM - 11:59 PM
Thursday: 12:00 AM - 11:59 PM
Friday: 12:00 AM - 11:59 PM
Saturday: 12:00 AM - 11:59 PM
Sunday: 12:00 AM - 11:59 PM
Closed on: Independence Day, Thanksgiving Day, 1/2 day Christmas Eve, Christmas Day, 1/2 day New Year's Eve, late open New Year's Day

Telephone Numbers

Line	Phone Number	Language/Subject
1	1-800-QUIT-NOW	English/Spanish
2	1-800-784-8669	English/Spanish
3	1-855-DEJELO-YA	Spanish
4	1-877-777-6534	Deaf/Hard of hearing

Supported Languages

Counseling offered in: English, Spanish

Third-party counseling:

Deaf/Hard of hearing: Direct TTY machine

**ENROLL IN ONLINE
CESSATION SERVICES**

Services Offered

Phone Counseling

Types:

- ☒ brief intervention
- ☒ multi-session (client-initiated)
- ☐ Text Msg to cell phone (two-way)
- ☒ single-session
- ☒ multi-session (counselor-initiated)
- ☒ Text Msg to cell phone (one-way)

Length of standard first session: 30 min

Length of standard follow-up session: 20 min

Counseling session topics:

- ☒ tobacco history
- ☒ setting a quit date
- ☒ relapse prevention
- ☒ use of cessation medication
- ☐ other
- ☒ developing a quit plan
- ☒ withdrawal symptoms
- ☒ weight gain
- ☒ stress management

Web-Based Services

- ☒ quitline information
- ☒ self-help tools
- ☒ interactive counseling
- ☒ cessation information
- ☒ automated e-mail messages
- ☒ chat rooms

Additional Info:

Also offer free combo NRT medications when indicated.

Cessation Medications

Free Medications

- ☒ patch
- ☒ lozenge
- ☐ inhaler
- ☐ bupropion
- ☒ gum
- ☐ nasal spray
- ☐ varenicline

Discounted Medications

- ☐ patch
- ☐ lozenge
- ☐ inhaler
- ☐ bupropion
- ☐ gum
- ☐ nasal spray
- ☐ varenicline

Distribution Methods

- ☐ voucher
- ☒ by mail

Other Services

- ☒ voicemail with callbacks
- ☒ referral to other health services
- ☒ recorded self-help messages
- ☒ mailed info or self-help resources

NAQC Quitline Profiles

Eligibility Criteria

To receive counseling: Single-call (1 session) offered to all enrollees. Readiness to quit desirable; not required. All enrollees must consent to services and call backs. Youth age 13-up, Uninsured, Medicare, Medicaid get multi-call (5 sessions). Pregnant/Postpartum get C-10 program (10 sessions) through post-delivery.

To receive medication: Registered participants who are uninsured, underinsured or have Medicare receive free medication. Pregnant/postpartum and under age 18 are not eligible for medication. Medicaid participants are referred to their provider for medication assistance.

Additional Info:

South Carolina is committed to removing all barriers to quitting by waiving some restrictions based on a participant's insurance coverage, maximum benefits, and inability to obtain effective medication support. We provide counseling support to all enrollees regardless of insurance status. We turn no one away.

Specialized Materials

Specialized Materials

- | | |
|--|---|
| ☐ youth, under 18 | ☐ youth, 18-25 |
| ☒ older tobacco users, 55+ | ☒ smokeless tobacco users |
| ☒ pregnant tobacco users | ☒ multiple addictions |
| ☒ racial/ethnic populations | ☒ lesbian, gay, bisexual or transgender |
| ☒ chronic health conditions | ☒ low socioeconomic status or Medicaid |
| ☒ low literacy | ☒ other |
| ☒ mental health disorders including psychiatric conditions | |

Additional Info:

SC's Quit Guide supports all of the specific audiences listed above with the purpose of addressing the universal dependency of tobacco and nicotine. The SC Quit Guide and Quitting Smokeless Tobacco Guide were updated in 2016. Youth under age 18 are no longer sent printed materials, but are given digital information, e.g. mobile apps, when they enroll for services. Also included in the standard mailed packet is a brochure about the QuitConnect online support community (www.quitconnect.org).

Provider Referral Program

Fax or electronic referral program: ☒ Yes

Person(s) eligible to refer patients: ☒

- ☒ certified or trained fax referral providers
- ☒ clinicians or non-clinicians in a healthcare setting
- ☒ clinicians or non-clinicians in a community-based organization
- ☐ other

Available referral methods: ☒

- ☒ faxed form
- ☐ e-mail or online
- ☒ EMR with electronic submission

Tobacco users can be referred if they: ☒

- ☒ are thinking about quitting
- ☒ indicate a readiness to quit within 30 days
- ☒ are ready to make a quit attempt
- ☒ are quit and seek help to stay quit

Referred patients contacted within: ☒ Within 48 hours

Other services available to referring providers: ☒

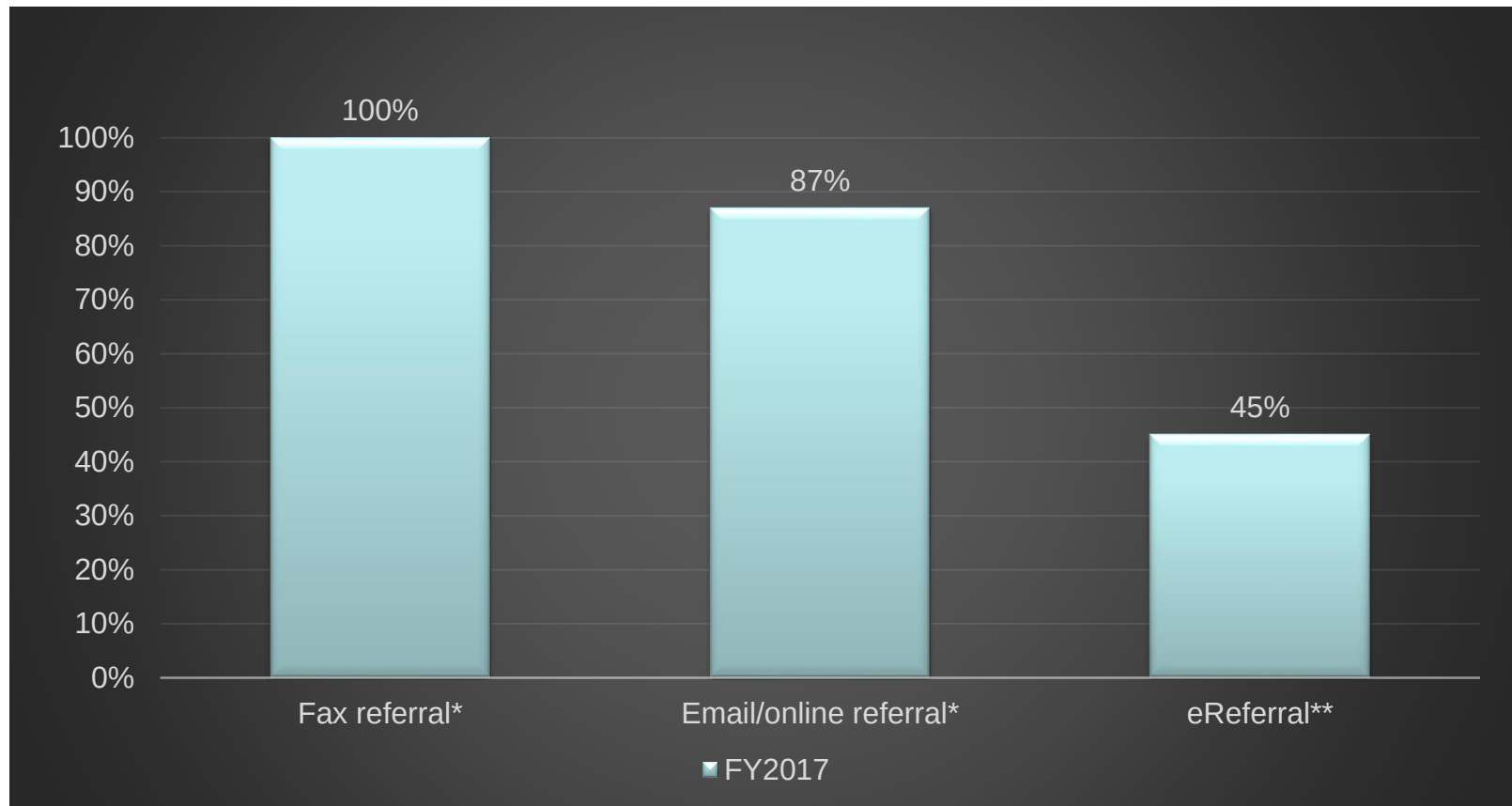
- ☒ quitline and/or referral brochures
- ☒ customized referral/consent forms
- ☒ patient progress reports
- ☐ customized provider feedback reports
- ☒ staff training
- ☐ quitline/referral program newsletter

Referral program contact: ☒ Dr. Katy L. Wynne
SC DHEC Division of Tobacco Prevention and Control
(803) 898-2285
wynnekl@dhec.sc.gov

Other information:

Free CME training at
<http://www.helppatientsquitsc.org> and eReferral
training at www.scoquitline.org

Quitlines accept fax, online and eReferrals



Continuum of strategies to encourage patients to seek cessation services

1. CDC's national media campaign, Tips from Former Smokers (no clinician involvement)

<https://www.cdc.gov/tobacco/campaign/tips/resources/index.html>

2. Patient resources -

CESSATION WORKS! cards for distribution to smokers in health care settings.



CDC videos “What is a quitline?”

https://www.cdc.gov/tobacco/campaign/tips/quit-smoking/quitline/index.html?s_cid=OSH_tips_A0001

Continuum of strategies to encourage patients to seek services (page 2)

3. “Direct referral” by clinician to quitline (use ACC pathway)

<https://doi.org/10.1016/j.jacc.2018.10.027> (higher level of clinician involvement)

Referral via fax, online or EMR

4. Tailored protocol that can be developed collaboratively by quitlines and clinicians to provide best cessation support while keeping clinician informed (high level of clinician involvement)

Ex. Quitline protocol for smokers with behavioral health conditions offers more counseling, more medications and keeps clinician informed of progress to ensure BH meds are adjusted as needed.

Other community-based cessation services with national reach

Group Counseling

Freedom from Smoking

American Lung Association

1-800-LUNG-USA

<https://www.lung.org/stop-smoking>

Hours: varies

Cost: varies

Languages: English and Spanish

Individual Counseling

ATTUD provider list

<https://www.attud.org/treatment-provider.php> to search for local

TTS-certified provider

Hours: varies

Cost: varies

Languages: varies

Other community-based cessation services with national reach

Smokefree.gov

www.smokefree.gov

Hours: 24/7

Cost: none

Languages: English and Spanish

Services: web counseling, chat, tools and info, text messaging, apps

Special services: Vet, women, teens, 60+

Become an Ex

www.becomeanex.org

Hours: 24/7

Cost: free for individuals (\$ for Emp/Health Plans)

Services: web chat, coach tools, info, email, txt msg

For more information on quitlines please
contact:

Linda Bailey, JD, MHS
President & CEO
Email: lbailey@naquitline.org

Integration of Tobacco Cessation in a Surgery Oncology Program

Matthew A. Steliga MD
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Disclosure

- Matthew A. Steliga MD
- No conflicts of interest
- No disclosures
- No off-label discussion

Points

- Why integrate cessation into clinical care
- Evolution of our program / lessons learned
- Different 'arms' of our programs
 - Lung Screening
 - Outpatient clinic
 - Inpatient



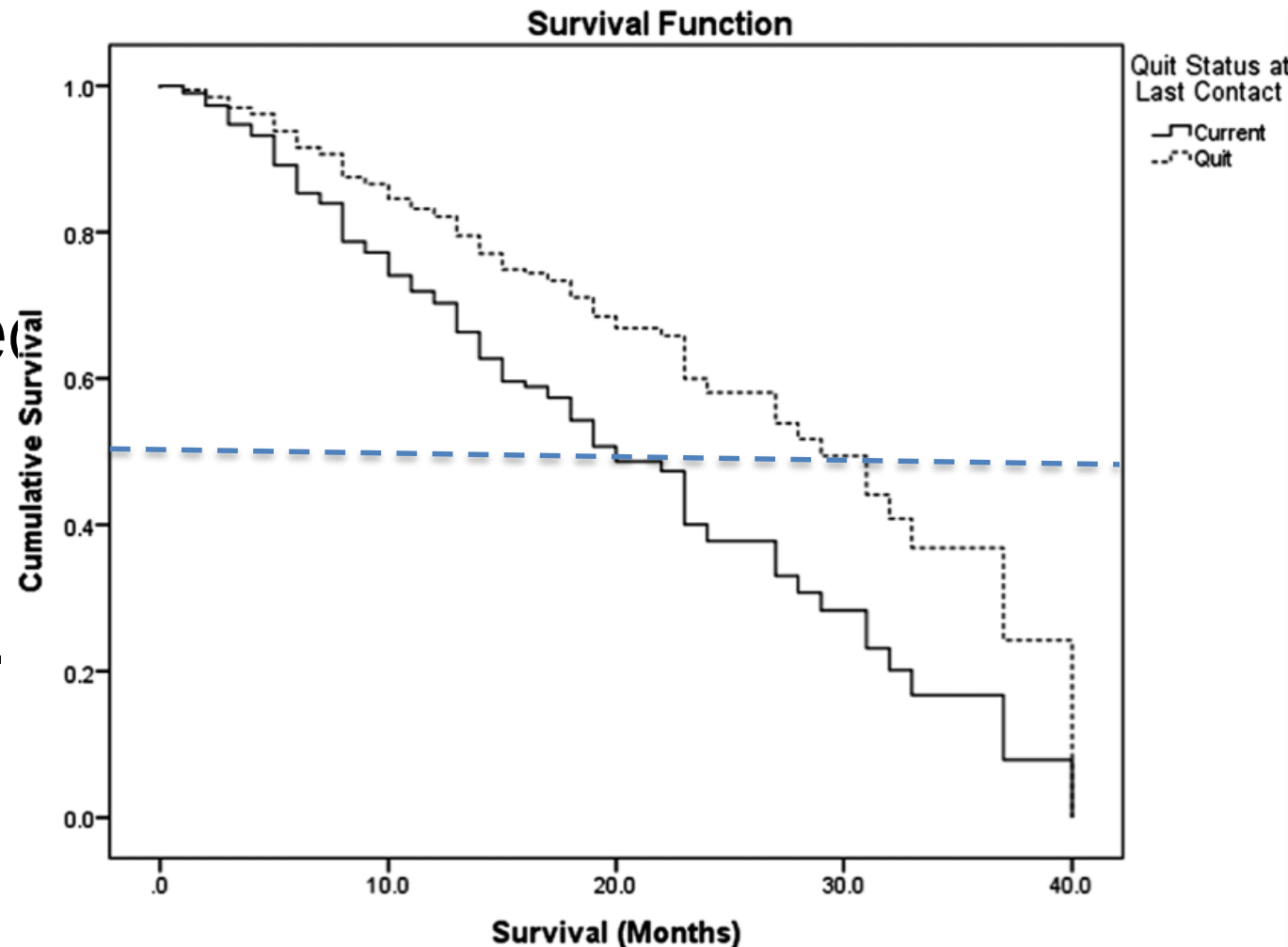
Importance of Integration of Tobacco Cessation

- High proportion of population smoking
- Smoking impacts treatment outcomes
- Cessation reduces risk
- Patients may be unfamiliar or reluctant to seek help
- Access to cessation resources can be a barrier

Specific examples:

Impact of tobacco on survival NSCLC

- Telephone survey of lung cancer patients who smoked
- Controlled for age, pack year history, stage, PS, etc.
- Current tobacco use associated with increase in death (HR 1.79)
- Median survival 20.0 vs 29.0 months.



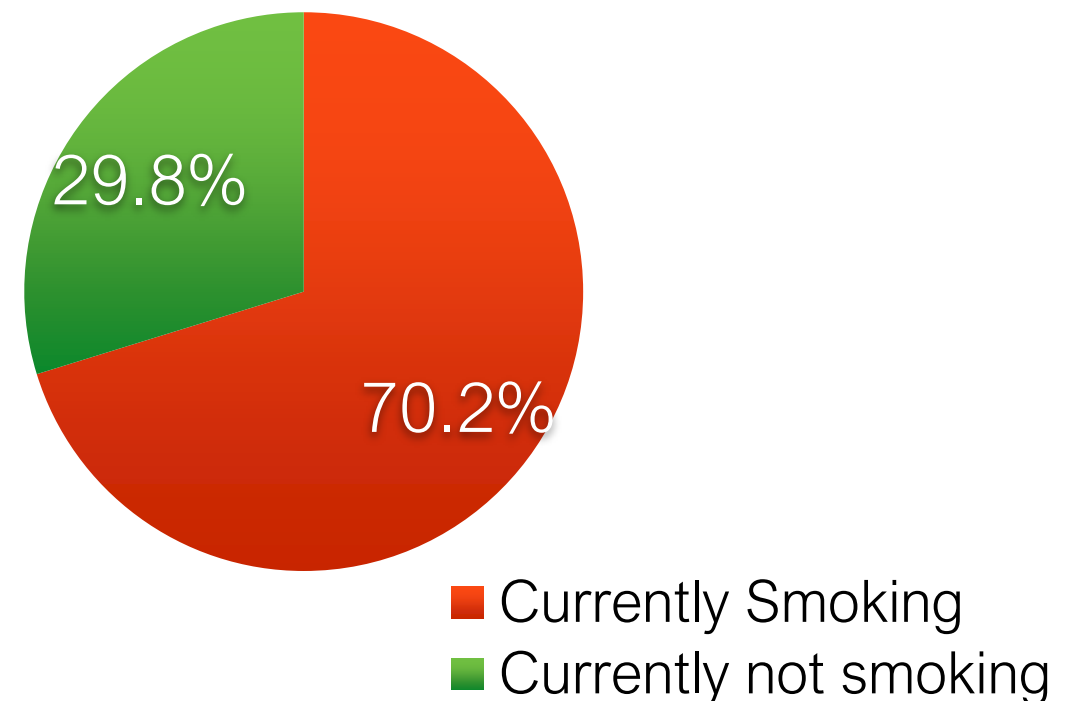
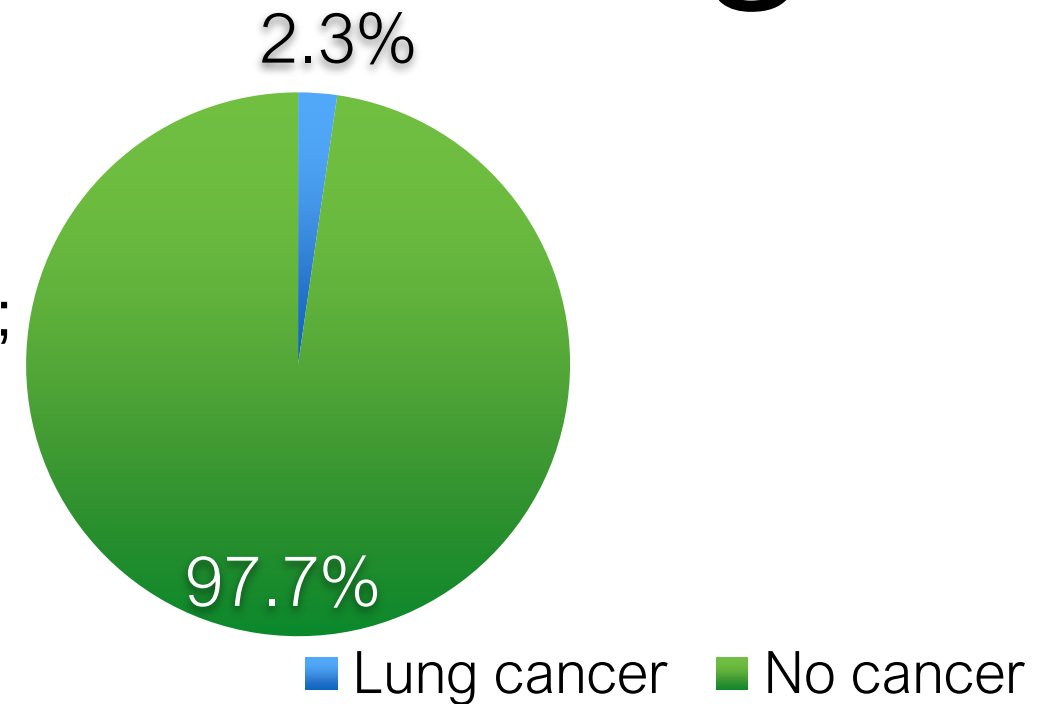
Dobson-Amato KA, J Thoracic Onc 2015.

Lessons learned

- Only giving patients print information for referral seemed to have minimal impact
- Referral to a counselor was often declined
- Sending them to the resources was not working
- Brought cessation to the patient
- Certified Tobacco Treatment Specialist (CTTS training)
 - MD, APRN, RN, RT, and others.
- Opt-Out is accepted

Lung Cancer Screening

- In our lung screening program:
 - Small minority may have lung cancer (2.3%; 10/440)
 - Well developed protocols to diagnose, stage and treat lung cancer
 - Large (potentially overlooked) proportion currently smoking. (70.2%; 309/440)
 - May be motivated to quit
 - “Teachable moment”
 - Delivery of cessation services may be lacking or quite variable

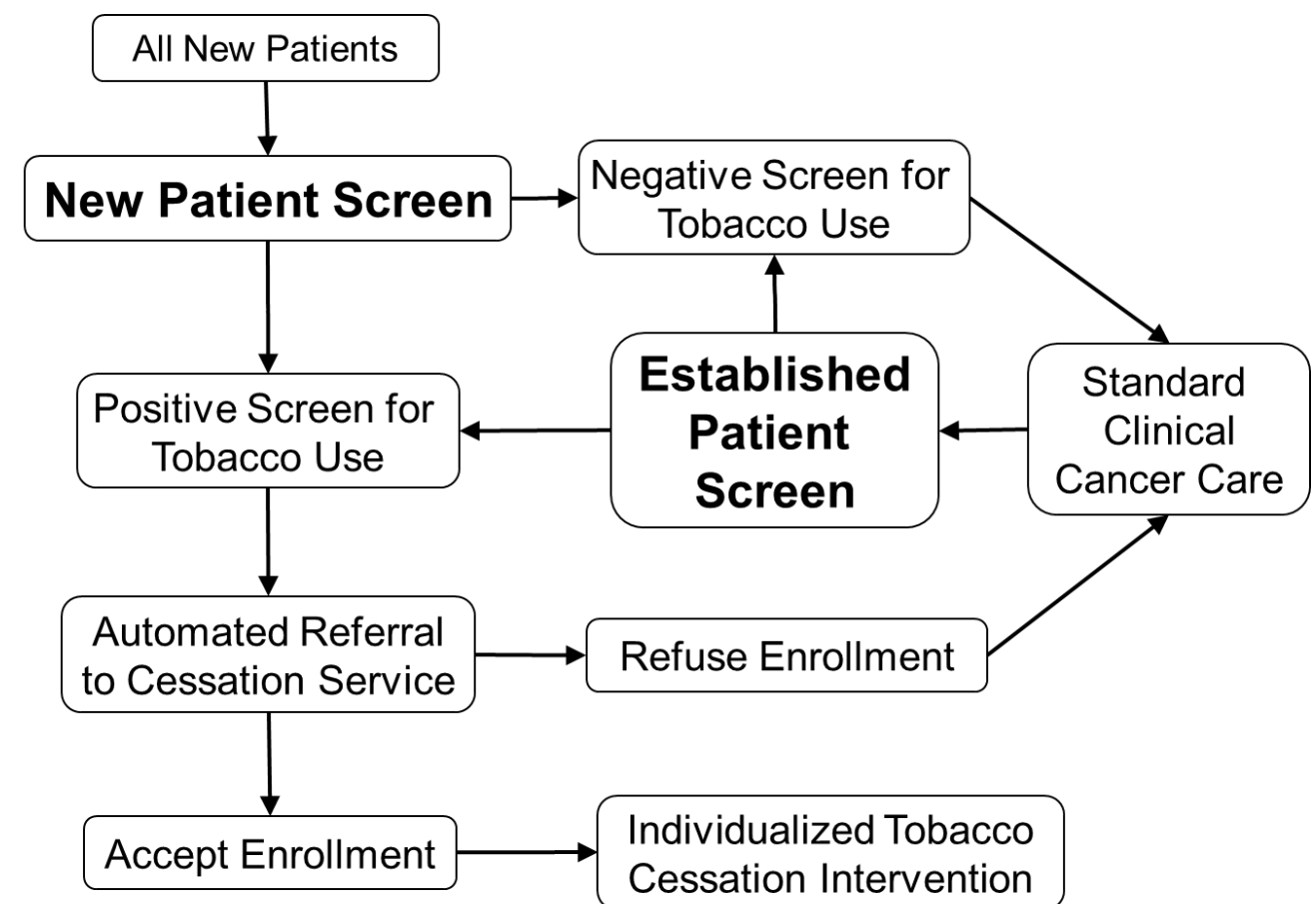


Tobacco Cessation in Lung Cancer Screening

- Tobacco assessment and cessation referral recommended for all lung screening patients
- Counseling & pharmacotherapy improve cessation rates
- The actual cessation resources can be variable and may be as minimal as printed material with a referral phone number.
- Delivering cessation resources to patients in a screening program may be challenging due to scheduling, cost, and patient compliance.

Automated Tobacco Assessment and Cessation for Cancer Patients

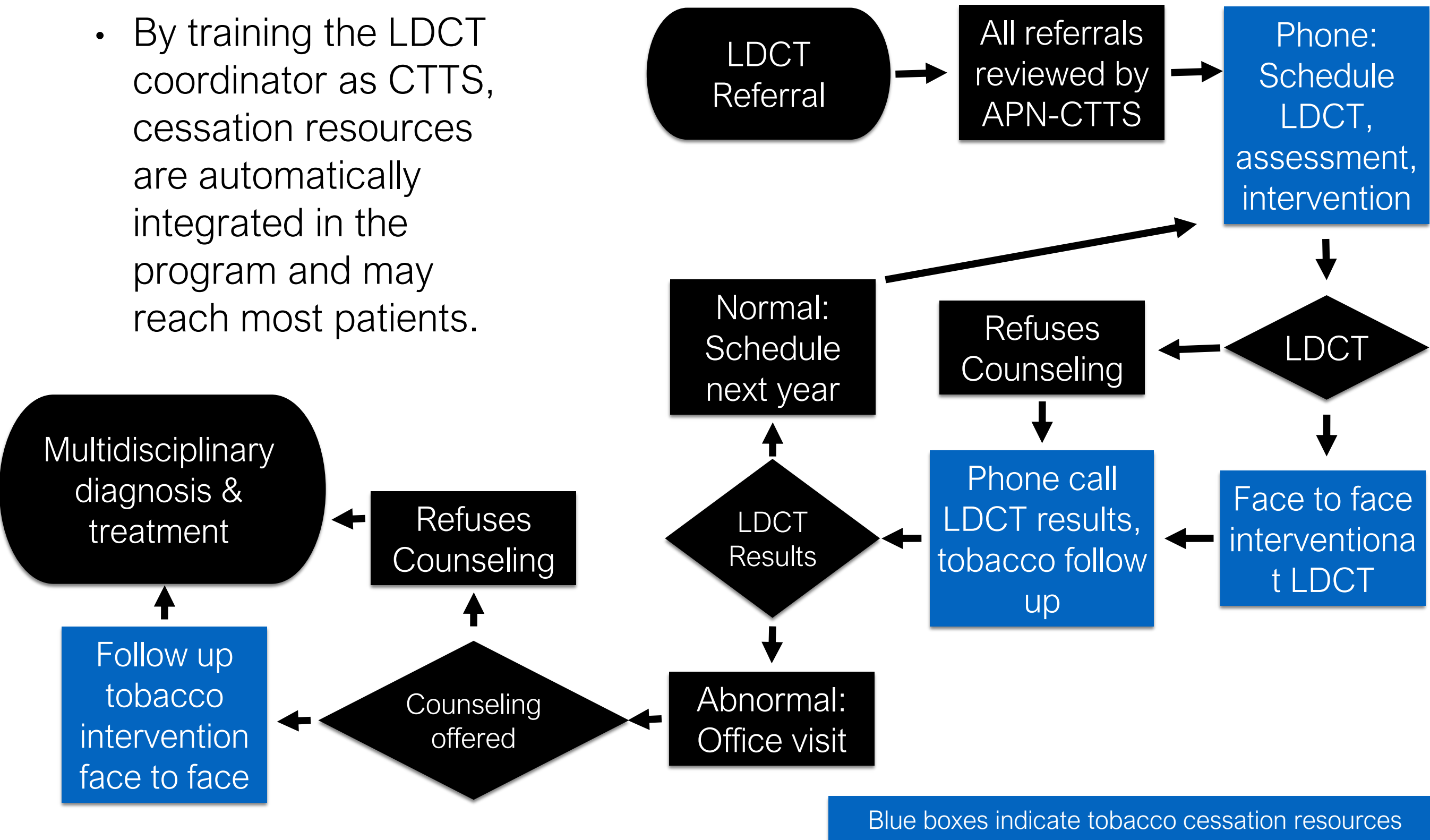
- Integration should be standard of care and part of treatment
- Patients may opt out, but default path includes cessation services for cancer patients
- This principle could be applied to screening programs.



From: Warren GW et al., *Cancer* 2014

Integration in Screening

- By training the LDCT coordinator as CTTS, cessation resources are automatically integrated in the program and may reach most patients.



Intake and Initial Phone Intervention

- Initial conversation:
 - Brief phone intervention for all active smoking (309/309; 100%)
 - Reinforce abstinence for those who have quit
 - Schedule LDCT
- ASK every patient about former and current tobacco use.
- ADVISE all patients to quit and discuss benefits of cessation
- REFER patients to evidence based cessation resources: Tobacco Cessation Specialist, Group Counseling, Phone Service (1-800-QUIT-NOW)

LDCT and Face-to-face Individual Intervention

- Coordinator :
 - Meets patient at the point of the LDCT
 - Initiates discussion of cessation resources and offers discussion while they are there for the LDCT
- ASK every patient about former and current tobacco use.
- ADVISE all patients to quit with a personalized message & discuss benefits of cessation
- ASSESS dependence on tobacco and willingness to quit
- ASSIST with behavioral counseling, pharmacotherapy
- ARRANGE follow up plan (in person, or if not possible- by telephone)

Lung Screening Cessation Outcomes

- 70.2% (309/440) of those referred for LDCT were actively smoking
- 100% (309/309) = Telephone intervention by a CTTS
- Of the 309 patients currently smoking:
 - 80.6% (249/309) were receptive to face-to-face counseling when provided at the point of service.
 - 18.4% (57/309) did not meet the CTTS due to: not going to the scan at their scheduled time, arriving after hours, or radiology not notifying the CTTS.
 - 1.0% (3/309) were offered counseling and refused.

Lung Screening Cessation Outcomes

- Patient's were receptive to counseling, and the counseling could be delivered in the workflow, but did it make a difference?
- 263 patients actively smoking at the time of the scan.
- 12.9% (34/263) quit at 1 year follow up.
- 87.1% (229/263) actively smoking at one year follow up.
- Of the 229 still smoking, follow up data about the amount was available for 156.
- Of those who were still smoking and we know the quantity, 50% (78/156) had reduced the amount smoked each day.

Lung Screening Cessation Outcomes

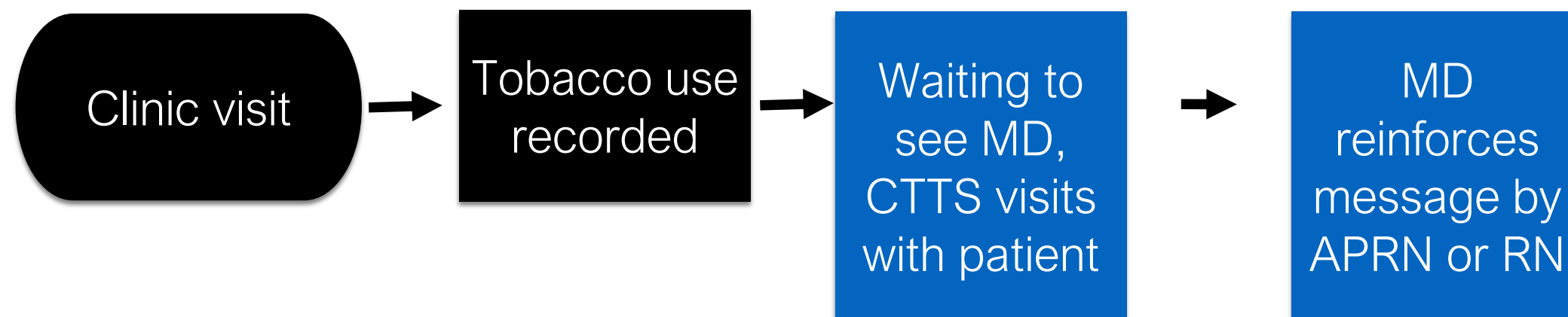
- Goals of screening-
 - Detect nodules?
 - Detect cancer?
 - Overarching goal is to improve health outcomes.
- Not assessing and addressing tobacco use ignores a great opportunity to measure risk factors and impact outcomes.

Tobacco Cessation in Thoracic Surgery Oncology Clinic

- Tobacco use impacts outcome
 - Smoking- linked with cancer progression.
 - Drug Interactions
 - Complications impacting care and survival
 - Long term risk- heart disease, cancer, etc.
- Counseling & pharmacotherapy improve cessation rates
- Referral to an outside resource may have poor uptake
- Much time in the physician's office is waiting, and an opportunity.

Outpatient Clinic Cessation

- By training the APRN, MD, and RNs, cessation resources are automatically integrated in the workflow
- Counseling in clinic
- Quitline enrollment
- Referral to on-campus group
- Individual phone follow up



Blue boxes indicate tobacco cessation resources

Outpatient Clinic Cessation Outcomes

- Patients are receptive to counseling, and the counseling is delivered in the workflow, but did it make a difference?
- 17 months: 275 patients actively smoking at the time of the visit.
- 87% (240/275) follow up data available.
- Of the 240 with follow up data:
 - 2.9% (7/240) increased the amount smoked
 - 23.3% (56/240) did not change
 - 29.2% (70/240) decreased the amount smoked
 - 44.6% (107/240) quit smoking

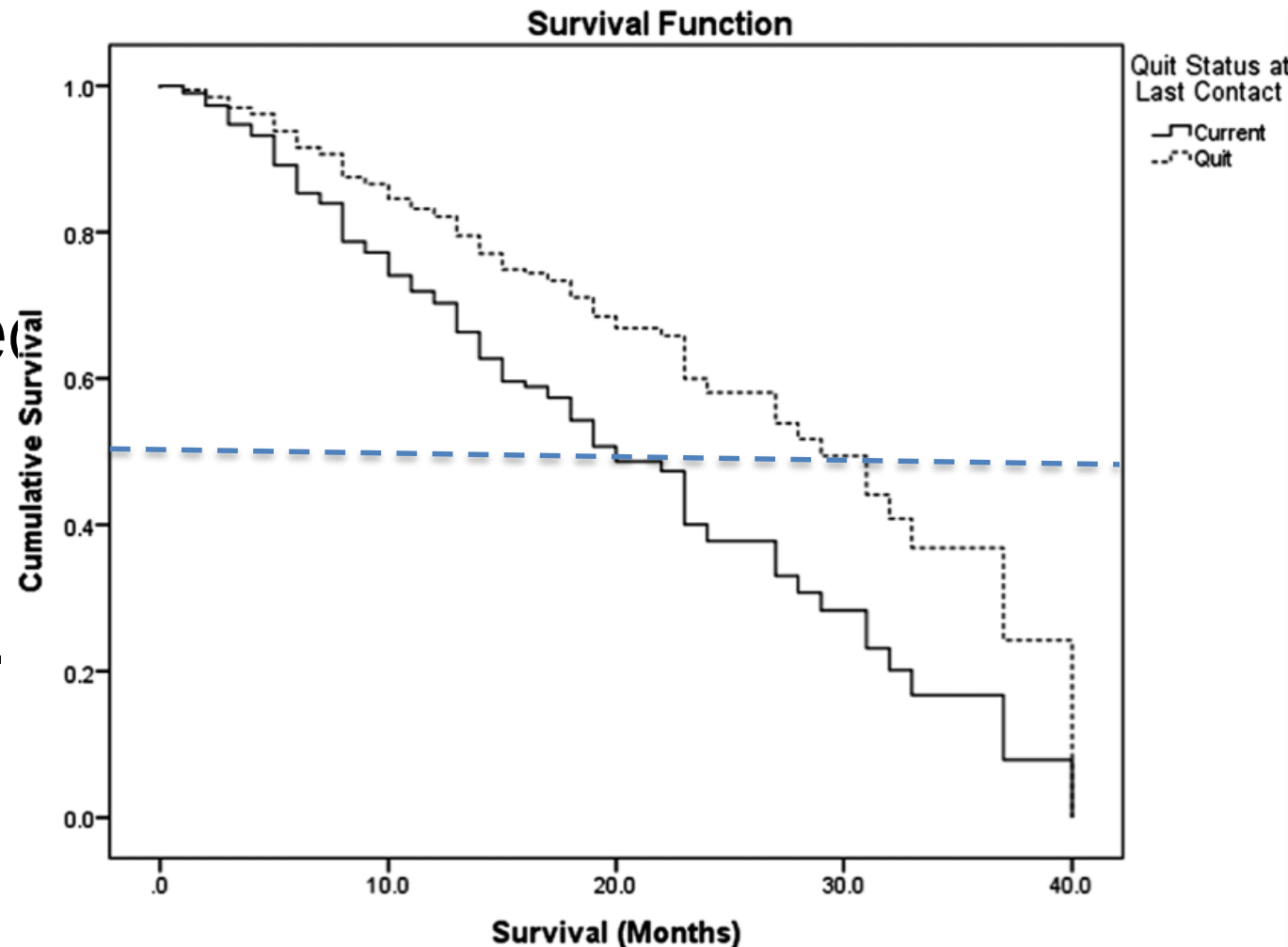
Tobacco Use in Cancer Care

- Goal not merely to do surgery, give drugs, or administer radiation, but the goal is to improve health.
- Ongoing use impacts outcomes and harms our mission
- Quitting improves outcomes
- Assessment should be automatic- with intake vital signs.
- Once assessed, patients can be targeted for cessation resources.
- Framing tobacco as an integral part of care is logical and accepted.
- Cessation resources are accepted and effective.
- Ignoring tobacco use in clinical care misses an opportunity for optimal care, and harms outcomes.

Specific examples:

Impact of tobacco on survival NSCLC

- Telephone survey of lung cancer patients who smoked
- Controlled for age, pack year history, stage, PS, etc.
- Current tobacco use associated with increase in death (HR 1.79)
- Median survival 20.0 vs 29.0 months.

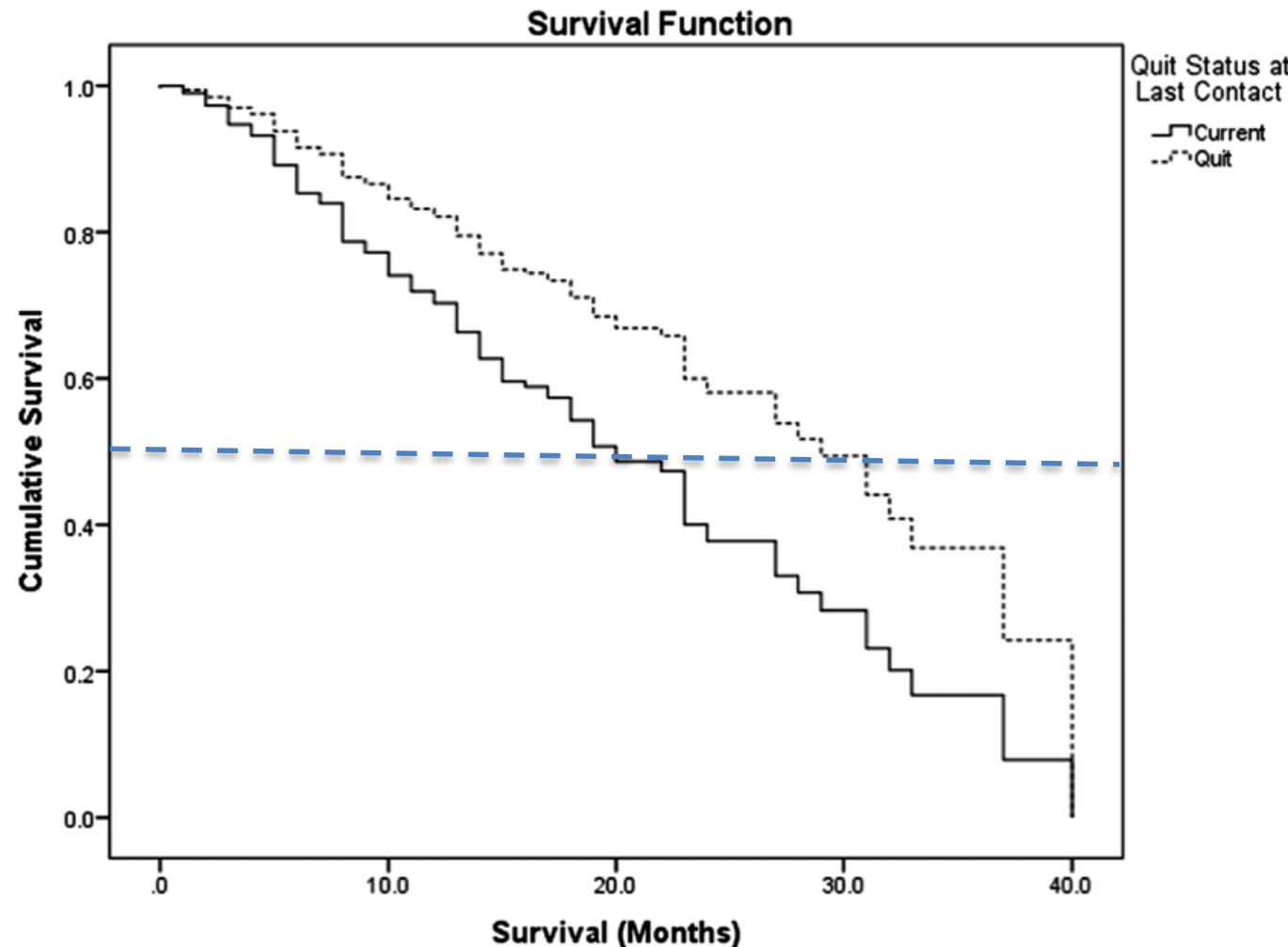


Dobson-Amato KA, J Thoracic Onc 2015.

Specific examples:

Impact of tobacco on survival NSCLC

- The impact of tobacco use on outcomes is significant and warrants assessment in order to provide an accurate understanding of outcomes in any cancer population undergoing treatment.



Dobson-Amato KA, J Thoracic Onc 2015.

Thank you

- MASteliga@uams.edu
- Twitter @SteligaMD

Smoking cessation and harm reduction in context of oncology clinical care: Clinical Guidelines

Laura Jean Bierut, MD
Alumni Endowed Professor of Psychiatry
February 2020



Washington University in St. Louis
SCHOOL OF MEDICINE

Quitting smoking is one of the most important things you can do for your health.



National Comprehensive
Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Smoking Cessation

Version 2.2019 — May 06, 2019

These guidelines are focused on smoking cessation recommendations for patients with cancer. There are health benefits to smoking cessation even after a cancer diagnosis, regardless of stage or prognosis, namely improvement in cancer treatment outcomes, primary cancer recurrence, and secondary cancers. **It is never too late for patients with cancer to stop smoking cigarettes and experience health benefits.**

Smoking – the 5th vital sign

Smoking status should be documented in the patient health record. Patient health records should be updated at regular intervals to indicate changes in smoking status, quit attempts made, and interventions utilized.

Have you smoking cigarettes in the last month?

How many cigarettes do you smoke per day?

Medications work, counseling works, both are best

Combining pharmacologic therapy and behavior therapy is the most effective approach and leads to the best results for smoking cessation.

- The two most effective pharmacotherapy agents are combination nicotine replacement therapy (NRT) and varenicline.
- High-intensity behavior therapy with multiple counseling sessions is most effective, but at least a minimum of brief advice is highly recommended.
- Quitlines may be used as an adjunct, especially in lower-resource settings. 1-800-QUIT-NOW

Evidence based care is not implemented

The New York Times

Smoking Cessation

A Report of the Surgeon General



U.S. Department of Health and Human Services

Surgeon General Says 'Shocking' Portion of People Aren't Told to Stop Smoking

In a new report, he cited a number of helpful smoking cessation methods but said that e-cigarettes haven't yet been proven to be an effective method.



"Far too many people who want to quit aren't getting access to the cessation treatments that we know work," said Dr. Jerome Adams, the surgeon general. Eric Baradat/Agence France-Presse — Getty Images



NATIONAL CANCER INSTITUTE'S 'MOONSHOT' TOBACCO INITIATIVE

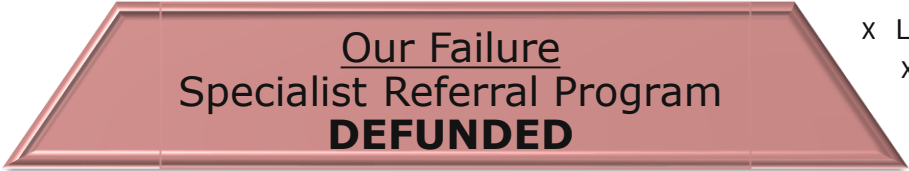
Posted on [December 4, 2017](#)



Siteman Cancer Center selected for the Cancer Moonshot Initiative to reduce tobacco to better prevent and treat cancer

LiShiun Chen, MD, MPH, ScD, Alex Ramsey, PhD, and Laura Bierut, MD

Implementation Science to Move from Specialist-Referral to Point-of-Care

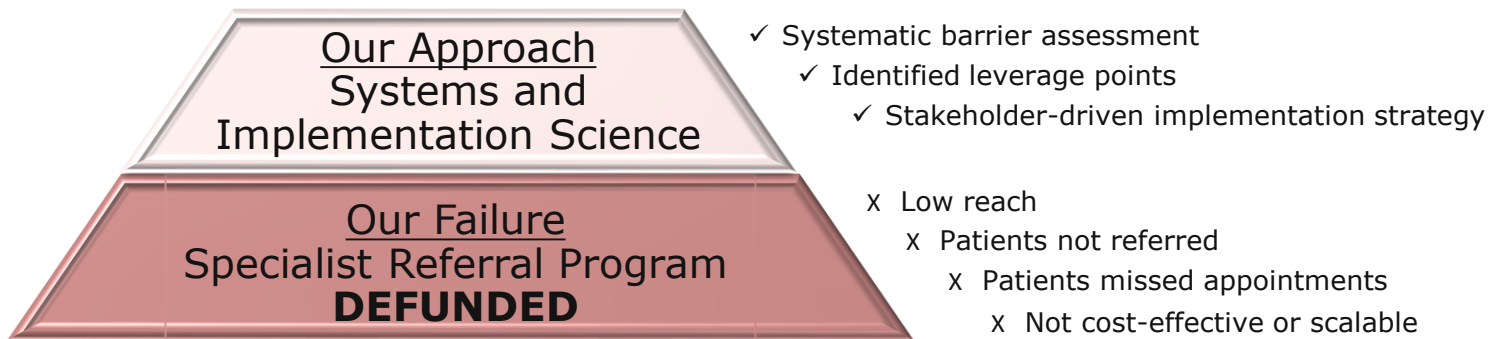


Our Failure
Specialist Referral Program
DEFUNDED

- x Low reach
- x Patients not referred
- x Patients missed appointments
- x Not cost-effective or scalable

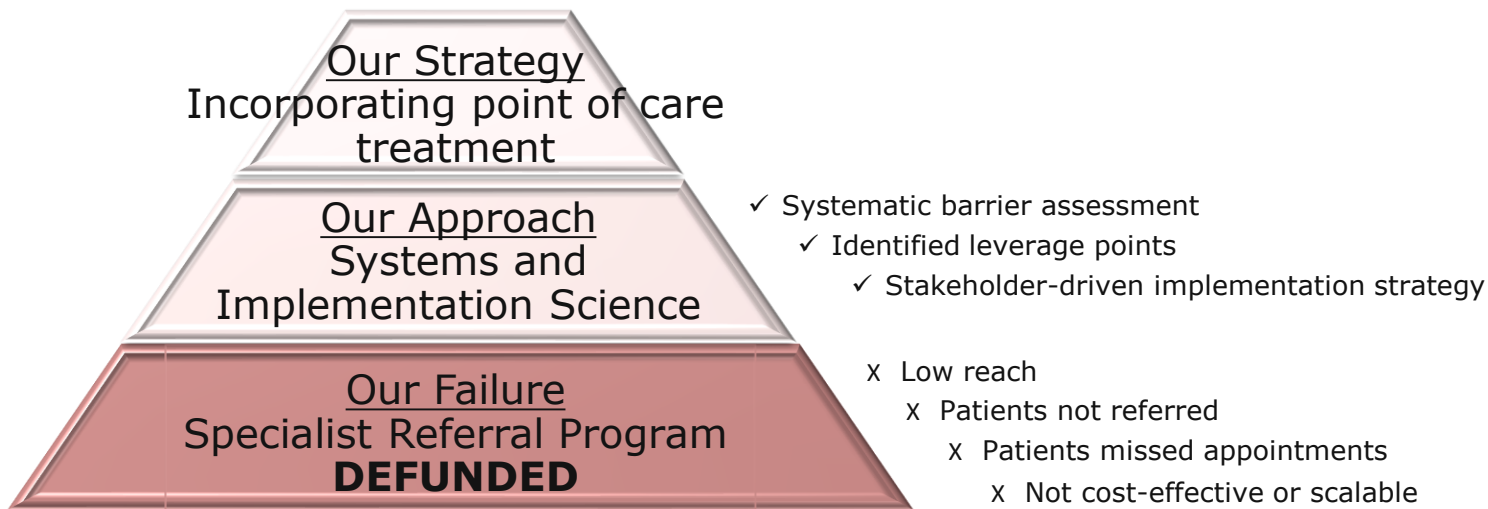
Patient: "You all asked me about smoking many times, but no one has offered any help! "

Implementation Science to Move from Specialist-Referral to Point-of-Care



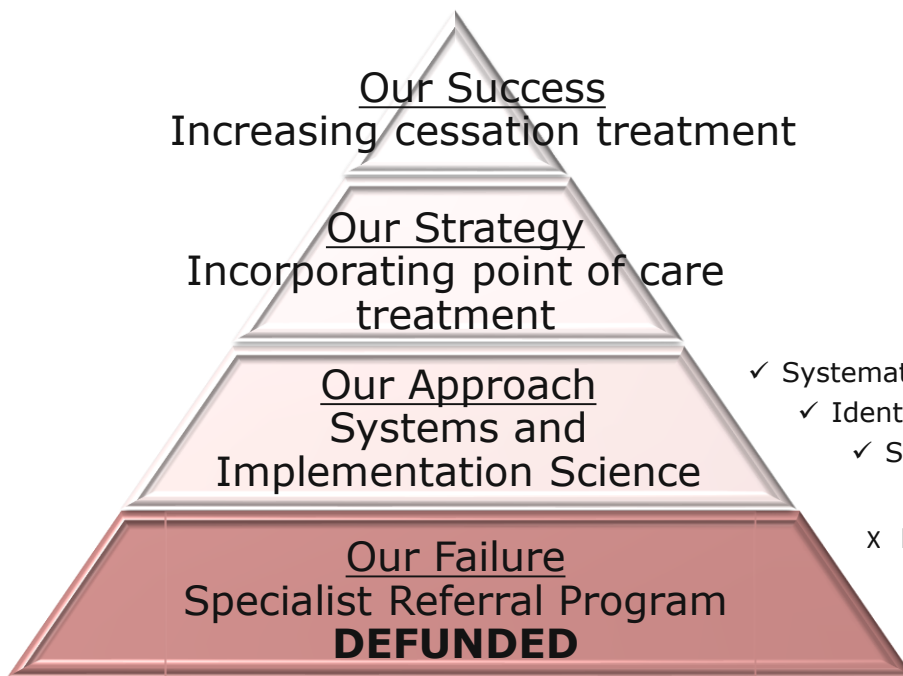
Patient: "You all asked me about smoking many times, but no one has offered any help! "

Implementation Science to Move from Specialist-Referral to Point-of-Care



Patient: "You all asked me about smoking many times, but no one has offered any help! "

Implementation Science to Move from Specialist-Referral to Point-of-Care



BMJ Open Leverage points to improve smoking cessation treatment in a large tertiary care hospital: a systems-based mixed methods study

Alex T Ramsey,¹ Donna Prentice,² Ellis Ballard,³ Li-Shiun Chen,¹ Laura J Bierut¹

- ✓ Systematic barrier assessment
- ✓ Identified leverage points
- ✓ Stakeholder-driven implementation strategy
- x Low reach
- x Patients not referred
- x Patients missed appointments
- x Not cost-effective or scalable

Patient: "You all asked me about smoking many times, but no one has offered any help! "

Point of Care increases Reach and Effectiveness

Goals

- Every patient is assessed
- Every smoker is offered treatment
- Increased smoking cessation

		June 2018		
				
		Refer to specialist	Point of Care	
		January-June 2018	July-December 2018	January-June 2019
	N patients	34,223	27,753	27,728
	Prevalence of smokers	--	11%	13%
Assessment	% patients assessed	48%	89%	93%
Reach	% received treatment	2%	28%	43%
Effectiveness	% smokers quit	12%	17%	Data being collected
			10% untreated 36% treated	Sustained!

A paradigm shift - point of care model within a learning health system

2x

More tobacco use
assessment
90% vs 48%

3x

More likely to quit smoking
if treated
36% vs 10%

5x

More patients treated with
medication
17% vs 3%

**Most Cost Effective
Program Among Cancer
Centers**

30x

More patients offered
counseling
21% vs < 1%

TBM

ORIGINAL RESEARCH

Care-paradigm shift promoting smoking cessation treatment
among cancer center patients via a low-burden strategy,
Electronic Health Record-Enabled Evidence-Based Smoking
Cessation Treatment

Alex T. Ramsey,² Amy Chiu,¹ Timothy Baker,^{2,3} Nina Smock,² Jingling Chen,¹ Tina Leston,⁴
Douglas E. Jorenby,^{2,3} Graham A. Colditz,^{2,4} Laura J. Bierut,^{2,4} Li-Shiun Chen^{1,2,5}

Change is the one constant

AUGUST 20, 2013

The Ambiguous Allure of the E-Cig

INTRODUCTION



Loic Venance/AFP/Getty Images

French actress Karole Rocher smokes an electronic cigarette at the 66th Cannes Film Festival in France earlier this year.

DEBATERS



What's Not to Like?

MICHAEL SIEGEL, BOSTON UNIVERSITY

Many anti-smoking groups oppose e-cigarettes because they find it difficult to endorse a behavior that looks like smoking, even though it is saving people's lives.



FDA Oversight Badly Needed

HAROLD P. WIMMER, AMERICAN LUNG ASSOCIATION

F.D.A. tests of e-cigs and their cartridges have revealed detectable levels of cancer-causing chemicals, including an ingredient used in anti-freeze.



Looser Rules for Life-Saving E-Cigs

LINDSAY FOX, BLOGGER, FORMER SMOKER



The Danger of Flavor

DELMONTE JEFFERSON, NATIONAL AFRICAN AMERICAN TOBACCO PREVENTION NETWORK

Electronic Nicotine Delivery Systems - E-cigarettes

E-cigarettes are not FDA-approved smoking cessation devices.

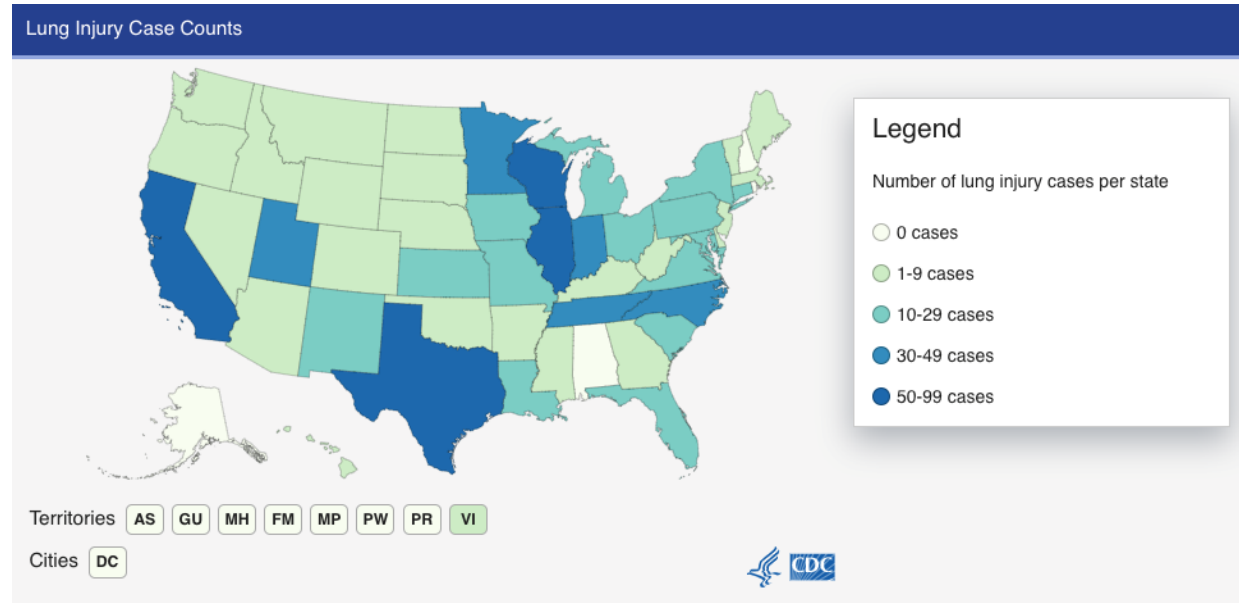
“There is substantial evidence that except for nicotine, under typical conditions of use, exposure to potentially toxic substances from e-cigarettes is significantly lower compared with combustible tobacco cigarettes.”

“There is conclusive evidence that completely substituting e-cigarettes for combustible tobacco cigarettes reduces users’ exposure to numerous toxicants and carcinogens present in combustible tobacco cigarettes.”

Public Health Consequences of E-Cigarettes

The National Academies of Sciences Engineering and Medicine 2018

An Outbreak of Lung Injury Associated with Vaping



Update: Interim Guidance for Health Care Providers Evaluating and Caring for Patients with Suspected E-cigarette, or Vaping, Product Use Associated Lung Injury — United States, October 2019

Weekly / October 18, 2019 / 68(41);919-927

Vaping Illnesses Are Linked to Vitamin E Acetate, C.D.C. Says

Samples of lung fluid from patients with the mysterious illness led to a breakthrough in finding a possible cause. More than 2,000 people have been sickened, many from illicit marijuana-based products.





PHILIP MORRIS
INTERNATIONAL

The New York Times

F.D.A. Permits the Sale of IQOS, a New Tobacco Device

OUR TOBACCO HEATING SYSTEM

IQOS

Tobacco Meets **Technology**

The enemy is combustible cigarettes

- Patients should be encouraged to use the most effective evidence based methods to quit combustible cigarettes.
- Not all tobacco products have the same risk.
- Many misperceptions exist about the dangers of tobacco products, both underestimating risk and overestimating risk.
- Smoking cessation after a cancer diagnosis extends life and reduces morbidity associated with treatment.

A harm reduction approach is also important!

It is never too late to stop smoking

There are health benefits to smoking cessation even after a cancer diagnosis, regardless of stage or prognosis, namely improvement in cancer treatment outcomes, disease recurrence, and secondary cancers.



U.S. FOOD & DRUG
ADMINISTRATION



American Association
for Cancer Research

FINDING CURES TOGETHER™



INTERNATIONAL
ASSOCIATION
FOR THE STUDY
OF LUNG CANCER
Conquering Thoracic Cancers Worldwide

SESSION IV:

Tobacco Cessation In Oncology Patients: Challenges And Lessons Learned

Session Moderator: Brenna VanFrank, MD, MSPH

Speakers:

Glen D. Morgan, PhD

Graham Warren, MD, PhD

Fumiko Chino, MD

TOBACCO CESSATION IN ONCOLOGY PATIENTS: CHALLENGES AND STRATEGIES

BRENNA VANFRANK, MD, MSPH | SENIOR MEDICAL OFFICER

FDA-AACR-IASLC WORKSHOP TO ADDRESS THE CRITICALITY OF TOBACCO USE ASSESSMENT IN ONCOLOGY THERAPEUTIC TRIALS • 2/28/2020



Centers for Disease Control and Prevention

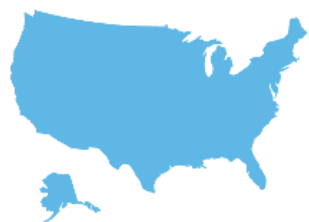
National Center for Chronic Disease Prevention and Health Promotion

Office on Smoking and Health



TOBACCO USE REMAINS A SIGNIFICANT PUBLIC HEALTH PROBLEM

Tobacco use is the leading cause of preventable disease, disability, and death in the US



34M

An estimated **34.2 million** U.S. adults smoked in 2018.



All Organs

Smoking impacts **nearly every organ system** in the body and causes **disease and death**.



480,000

Cigarette smoking and secondhand smoke exposure kill about **480,000** people in the U.S. each year.



1 vs. 30

For every one smoking-related death, **at least 30** people live with a serious smoking-related illness.



\$300B

Each year, cigarette smoking costs the United States more than **\$300 billion**, including \$170 billion in direct medical costs and \$156 billion in lost productivity.



What Are The Challenges?

- ✓ Disparities in tobacco use and cessation
- ✓ Underutilization of tobacco cessation treatment
- ✓ Evolving tobacco product landscape

TOBACCO-RELATED DISPARITIES PERSIST

Current Cigarette Smoking Among U.S. Adults – NHIS, 2018



Race/Ethnicity

22.6% American Indians/
Alaska Natives
15% White



Education Level

36% GED
3.7% Graduate degree



Annual Household Income

21.3% <\$35,000
7.3% ≥\$100,000



Health Insurance Coverage

23.9% Uninsured
23.9% Medicaid
10.5% Private
9.4% Medicare



Disability/Limitation

19.2% Yes
13.1% No



Sexual Orientation

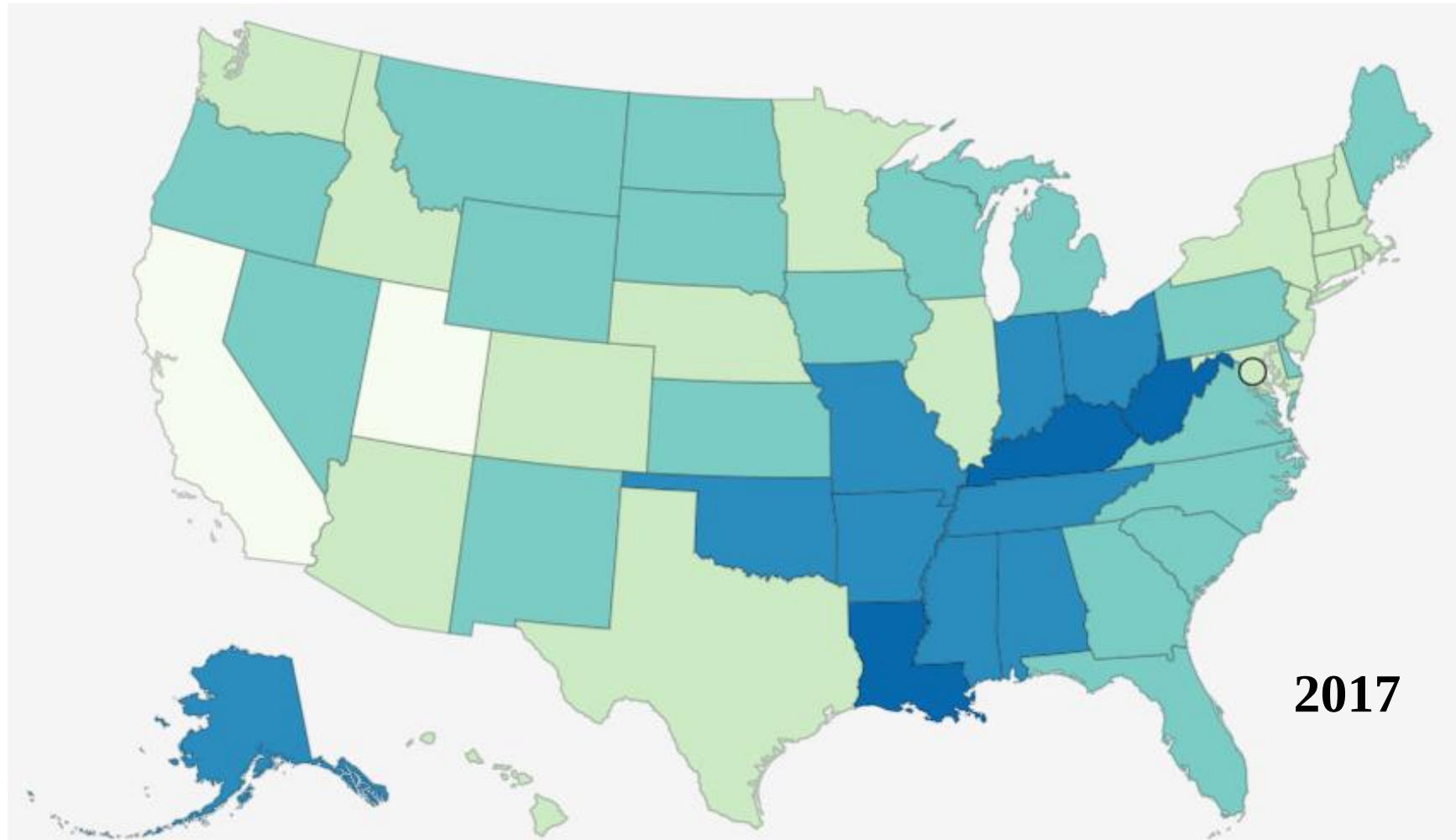
20.6% Lesbian/Gay/Bisexual
13.5% Heterosexual



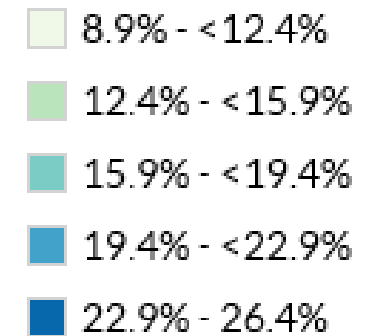
Serious Psychological Distress

31.6% Yes
13.0% No

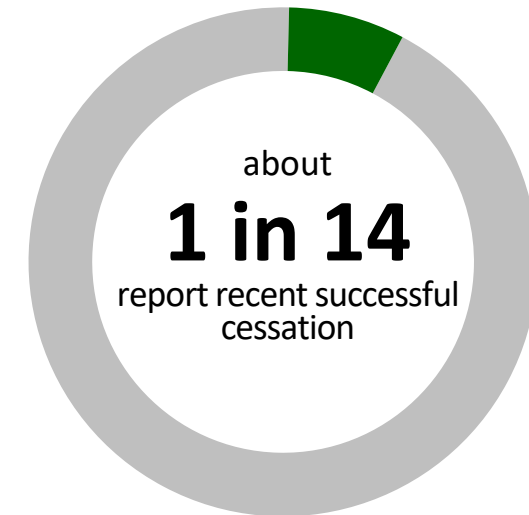
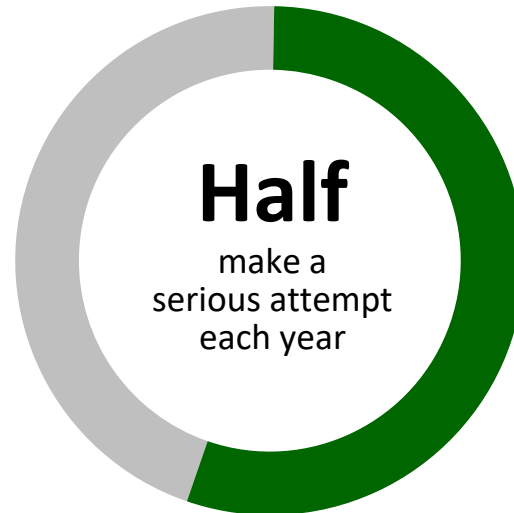
GEOGRAPHIC DISPARITIES EXIST



Adult Prevalence of Current Smoking, BRFSS



CESSATION REMAINS A CHALLENGE



Treatment can double the odds of success

Source: Babb S, Malarcher A, Schauer G, Asman K, Jamal A. Quitting smoking among adults — United States, 2000–2015. *MMWR Morb Mortal Wkly Rep* 2017;65:1457–1464; Fiore MC, Jaén CR, Baker TB, et al. *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline*. Rockville, MD: U.S. Department of Health and Human Services, Public Health Service, 2008.

WE KNOW WHAT WORKS FOR CESSATION

**Evidence-based
interventions that
increase quit rates:**

I'm Ready to QUIT!



**Advice to quit from
a health care
professional**



**Counseling: individual,
group, telephone, web,
text**



**7 FDA-approved
medications**



**Barrier-free
insurance coverage
of these treatments**



**Health systems changes
to integrate treatment
into routine care**

Tobacco Cessation Interventions Are Underutilized

How U.S. Adults Tried to Quit Smoking, 2015



57%
received
clinician
advice to
quit



69% did
NOT use
evidence-
based
cessation
treatment



Far more
used
medication
(29%) than
counseling
(6.8%)



< 5% used
BOTH
counseling
and
medication

DISPARITIES IN QUITTING

QUIT ATTEMPT

69.4%	Asian
63.4%	Black
53.3%	White

QUIT SUCCESS

9.4%	Private insurance
5.9%	Medicaid
5.2%	Uninsured

USE OF EVIDENCE-BASED TREATMENT

34.3%	White
20.5%	Asian
19.2%	Hispanic
31.7%	Straight
14.5%	LGB
32.1%	Private insurance
21.4%	Uninsured

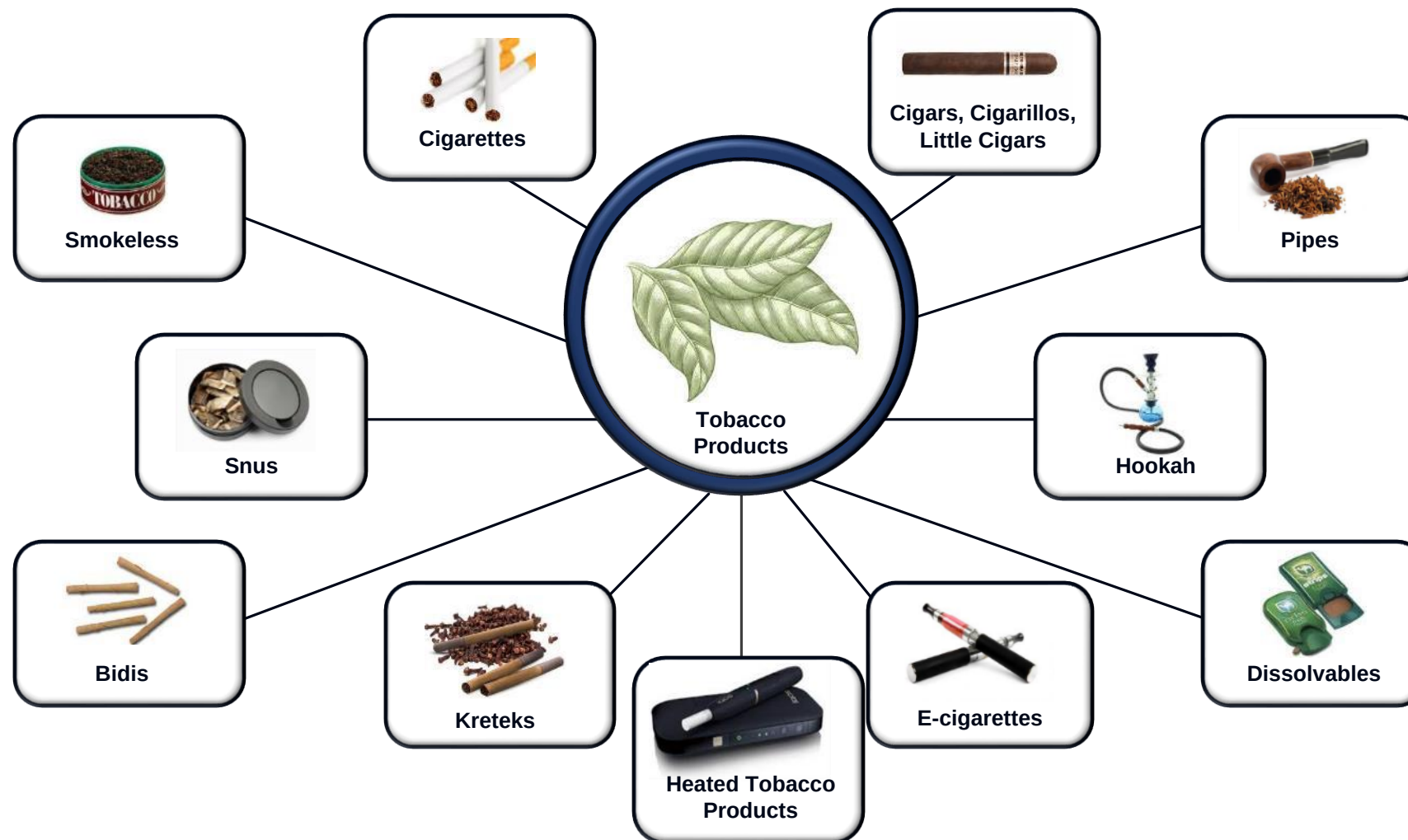
CLINICAL ADVICE

60.2%	White
42.2%	Asian
34.2%	Hispanic
32.1%	Private insurance
21.4%	Uninsured

U.S. Adults – NHIS, 2015



THE TOBACCO PRODUCT LANDSCAPE CONTINUES TO EVOLVE





What Are The Strategies?

- ✓ Contemporizing comprehensive treatment
- ✓ Clinical integration of treatment
- ✓ Comprehensive, barrier-free insurance coverage
- ✓ Population-level interventions

CONTEMPORIZING COMPREHENSIVE TREATMENT APPROACHES



Physical

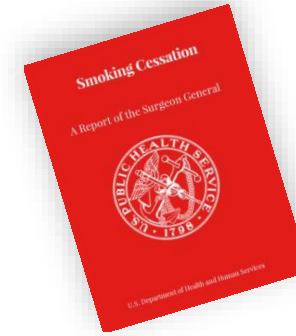
Tobacco dependence
is a chronic, relapsing
condition driven by
addiction to nicotine.



Behavioral



Psychological



2020 Surgeon
General's Report



*"Behavioral **counseling** and cessation **medications** are independently effective in increasing smoking cessation, and even more effective when used in **combination**."*

CLINICAL INTEGRATION: THE TOBACCO CESSATION CHANGE PACKAGE (TCCP)

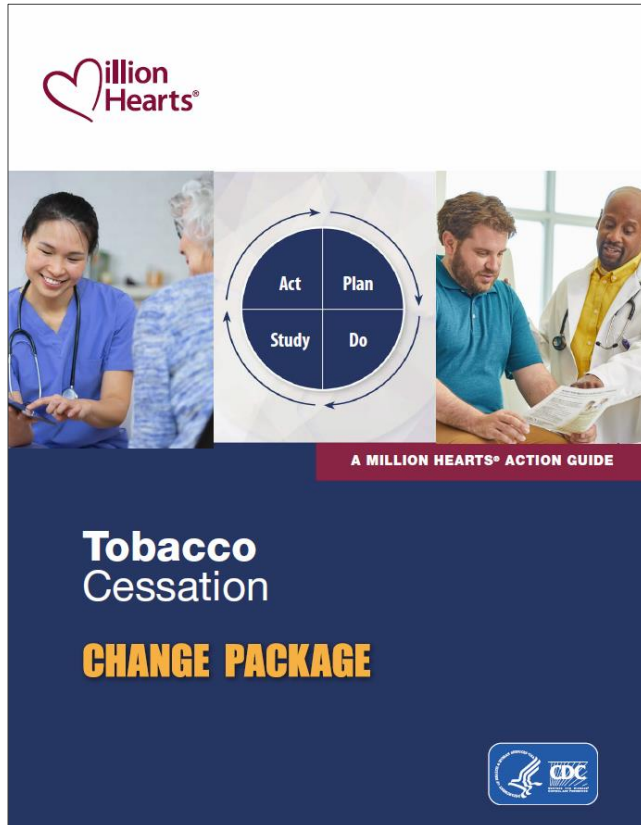
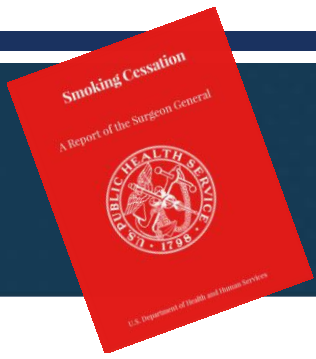


Table 1. Key Foundations			
Change Concept	Change Idea	Tools and Resources	Settings
Make Tobacco Cessation a Practice and System Priority	Identify one or two key champions and assemble a multidisciplinary team	Center of Excellence for Health Systems Improvement for a Tobacco-Free NY — Supporting Evidence-Based Tobacco Dependence Screening & Treatment (p. 155)	● ▲ ■

Table 3. Screening			
Change Concept	Change Idea	Tools and Resources	Settings
Make Tobacco Use a Vital Sign: Screen Every Patient for Tobacco Use at Every Visit	Adopt a tobacco use screening protocol	Million Hearts® — Protocol for Identifying and Treating Patients Who Use Tobacco NYC DOHMH and HealthyHearts NYC — ABCS Toolkit for the Practice Facilitator (p. 84) UW Health, UW-Madison SMPH, and UW-CTRI — Quit Connect Health: A Specialty Staff Protocol to Improve Referrals to Tobacco Quit Lines (p. 10) UW-CTRI — Treating Tobacco Use and Dependence in Hospitalized Patients: A Practical Guide (pp. 8, 13–14) UCSF SCLC — Destination Tobacco Free: A Practical Tool for Hospitals and Health Systems (pp. 6–7, Appendix N)	● ▲ ■ outpatient ● inpatient ▲ behavioral health
	Establish a workflow and determine roles for tobacco use screening and documentation	Center of Excellence for Health Systems Improvement for a Tobacco-Free NY — Supporting Evidence-Based Tobacco Dependence Screening & Treatment (pp. 148–153) ICSI — Tobacco Health Systems Change Starter Toolkit for Clinics (pp. 24–26) CU Anschutz Medical Campus — A Patient-	● ▲ ■ outpatient ● inpatient ▲ behavioral health



Access the Change Package at: https://millionhearts.hhs.gov/files/Tobacco_Cessation_Change_Pkg.pdf



SYSTEMS-LEVEL STRATEGIES PROMOTE SMOKING CESSATION



“Development and dissemination of **evidence-based clinical practice guidelines** increase the delivery of clinical interventions for smoking cessation.”



“With adequate promotion, **comprehensive, barrier-free, evidence-based insurance coverage** increases the availability and utilization of treatment services for smoking cessation.”



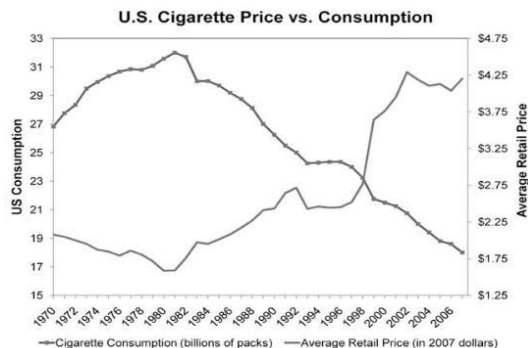
“Strategies that **link** smoking cessation-related **quality measures with payments** to clinicians, clinics, or health systems increase the rate of delivery of clinical treatments for smoking cessation.”



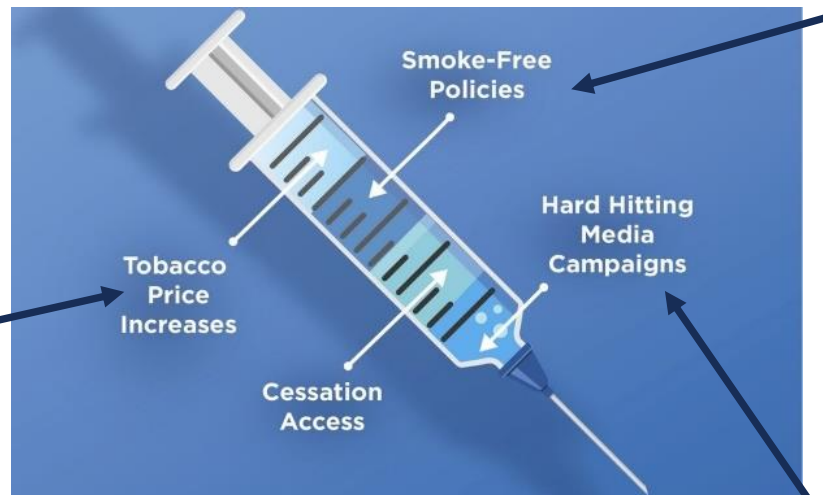
“Evidence is **suggestive**, but not sufficient, to infer that **electronic health record** technology increases the rate of delivery of smoking cessation treatments.”



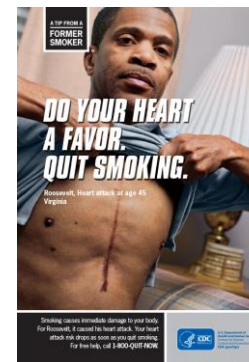
POPULATION-LEVEL STRATEGIES PROMOTE SMOKING CESSATION



“Increasing the price of cigarettes reduces smoking prevalence, reduces cigarette consumption, and increases smoking cessation.”



“Smokefree policies reduce smoking prevalence, reduce cigarette consumption, and increase smoking cessation.”



“Mass media campaigns increase the number of calls to quitlines and increase smoking cessation.”



“Comprehensive state tobacco control programs reduce smoking prevalence, increase quit attempts, and increase smoking cessation.”



KEY TAKEAWAYS

1

We know what works to treat tobacco use and dependence, but we need to integrate treatment into routine clinical care so that everyone has equal access.

2

Strategies to support and improve cessation exist at the clinical, systems, and population levels.

3

Contemporizing our approaches at all levels is needed to meet the shifting product landscape.

Thank You!

bvanfrank@cdc.gov



www.cdc.gov/tobacco

“
I wish I had known how much
strength I really had in me.
”

–Smokefree Michele

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.



Tobacco Cessation at Cancer Centers: Lessons Learned

FDA, February 28, 2020

Glen D. Morgan, Ph.D.

Clinical Psychologist

Vienna, VA

The Health Consequences of Smoking - 50 Years of Progress: A Report of the Surgeon General, 2014¹

The evidence is sufficient to infer a causal relationship between continued smoking among oncology patients:

- All-cause mortality is increased by 50%
- Cancer related mortality is increased by 60%
- Risk for second primary cancers is increased.
- Quitting improves the prognosis of cancer patients.

1. U.S. Department of Health and Human Services, Public Health Service, Office of the Surgeon General. *The Health Consequences of Smoking--*

The Health Consequences of Smoking - 50 Years of Progress: A Report of the Surgeon General, 2014¹

The evidence is suggestive but not sufficient to infer a causal relationship between continued smoking among oncology patients:

- The risk of recurrence is increased
- Poorer response to oncology treatment
- Increased oncology treatment-related toxicity

1. U.S. Department of Health and Human Services, Public Health Service, Office of the Surgeon General. *The Health Consequences of Smoking--50 Years of Progress: A Report of the Surgeon General*. Rockville, MD: DHSS, 2014.

Comprehensive Cancer Centers – A Need to Integrate Tobacco Cessation Treatment

In a 2009 survey of NCI-designated cancer centers:¹

- Only 38% recorded smoking status, and less than half have dedicated personnel to provide tobacco cessation clinical services.
- Tobacco cessation treatment delivery was not perceived as a core health care service by the majority of Comprehensive Cancer Centers (CCCs).

1. Goldstein AO, Ripley-Moffitt CE, Pathman DE, Patsakham KM. Tobacco use treatment at the U.S. national cancer institute's designated cancer centers. *Nicotine Tob Res* 2013;15:52–8.

NCI's (2009) Call to Action - Tobacco Dependence Tx at Cancer Centers¹

Enhancing the delivery of tobacco dependence treatment at cancer centers requires:

1. Refining electronic medical records to ensure universal identification and referral of smokers
2. Overcoming barriers to providing tobacco cessation treatment
3. Achieving institutional buy-in that treating tobacco use is an expected component of "Standard of Care."

1. National cancer institute conference on treating tobacco dependence at cancer centers. Morgan G1, Schnoll RA, Alfano CM, Evans SE, Goldstein A, Ostroff J, Park ER, Sarna L, Cox LS. J Oncol Pract. 2011 May;7(3):178-82.



The NEW ENGLAND JOURNAL of MEDICINE

Perspective

Addressing a Core Gap in Cancer Care — The NCI Moonshot Program to Help Oncology Patients Stop Smoking

Robert T. Croyle, Ph.D., Glen D. Morgan, Ph.D., and Michael C. Fiore, M.D., M.P.H., M.B.A.

Despite making great progress in caring for people with cancer, the oncology community has often neglected to capitalize on a highly feasible, readily available, and cost-effective

strategy for increasing the success of cancer treatment and rates of recovery — smoking cessation. Effective smoking-cessation treatments can double or triple a smoker's chances of quitting successfully, and new treatment innovations that further boost quit rates continue to emerge. But such treatments are infrequently provided to patients as part of their cancer care.

Our failure to effectively address smoking in patients with cancer exacts steep costs. Evidence shows that continued smoking after a cancer diagnosis increases post-treatment mortality as well as the risk of a new primary cancer, the risk of cancer recurrence, and rates of adverse side effects from cancer treatment.^{1,2} Con-

versely, quitting smoking after a cancer diagnosis is associated with longer survival and a reduced risk of new cancers.¹ The evidence is clear: for the approximately half of cancer patients who smoke at the time of their diagnosis, a cancer diagnosis signals an important and highly feasible opportunity to improve the effectiveness of cancer treatment and avert future cancers.

Despite recommendations (e.g., from the National Comprehensive Cancer Network) that all patients with cancer be offered effective treatment to help them quit smoking, such treatment is an often-neglected element of cancer care. For example, a 2009 survey of 58 National Cancer Institute (NCI)-designated clinical and

comprehensive cancer centers in the United States revealed that 21% offered no tobacco-use treatment services, only 62% routinely provided tobacco-education materials to patients, half reported having systems in place to identify which of their patients use tobacco, and less than half reported having a staff person dedicated to providing tobacco-treatment services or a commitment from center leadership to provide such services.³ Such inattention has had a predictable effect on the delivery of smoking-cessation interventions. Data show that just under half of cancer care providers consistently discuss cessation-medication options with their patients who smoke, and a similar proportion consistently treat their patients with cessation medications or refer them for treatment.⁴ Among people who have had cancer but continue to smoke, only about half report having received counseling or support to

Catalysts & steps

- Cancer center meeting Dec 2009
- Cancer moonshot 2016
- Focus group – 2016
- P30 supplements 2017 – 2020

NCI Cancer Center Cessation Initiative (P30 Supplement)

- \$250,000 total award per year for two years per center
- Funded NCI Cancer Moonshot Initiative plus NCI's Division of Cancer Control & Population Sciences
- Round 1 funded September 2017
- Round 2 funded September 2018
- Two meetings each year

NCI Cancer Center Cessation Initiative (P30 Supplement)

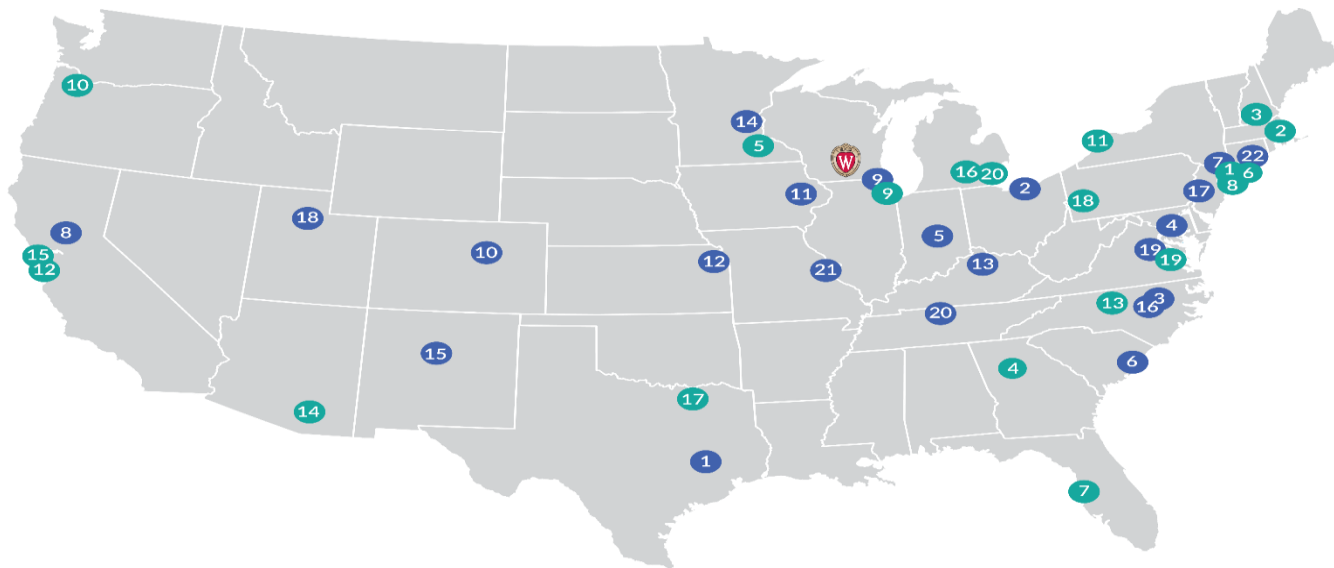
Goals:

- Short-term: Enhance capacity of Cancer Centers to address tobacco cessation with cancer patients.
- Long-term: Build and implement a sustainable tobacco cessation treatment program.

Funding Timeline

Sept. 2017	Sept. 2018	Sept. 2019	Sept. 2020
Cohort 1 – 22 cancer centers Sept 2017- Sept 2019		Continued (unfunded) participation	
	Cohort 1 – 22 cancer centers Sept 2018 - Sept 2020		Continued (unfunded) participation

Funded Centers



Cohort 1

1. Baylor College of Medicine
2. Case Western Reserve University
3. Duke University
4. Georgetown University
5. Indiana University
6. Medical University of South Carolina
7. New York University
8. University of California Davis
9. University of Chicago
10. University of Colorado
11. University of Iowa
12. University of Kansas
13. University of Kentucky
14. University of Minnesota
15. University of New Mexico
16. University of North Carolina at Chapel Hill
17. University of Pennsylvania
18. University of Utah
19. University of Virginia
20. Vanderbilt University
21. Washington University
22. Yale University

Cohort 2

1. Columbia University
2. Dana-Farber
3. Dartmouth College
4. Emory University
5. Mayo Clinic
6. Memorial Sloan Kettering
7. Moffitt
8. Mount Sinai
9. Northwestern University
10. Oregon Health and Sciences University
11. Roswell Park
12. Stanford University
13. Wake Forest University
14. University of Arizona
15. University of California San Francisco
16. University of Michigan
17. University of Texas Southwestern
18. UPMC Hillman
19. Virginia Commonwealth University
20. Wayne State University

Cancer Centers Cessation Intervention

– Leadership

- NCI – Stephanie Land, Ph.D
- Coordinating Center at the University of Wisconsin:
 - Michael Fiore, M.D. & Betsy Rolland, Ph.D.
- Panel of Experts:
 - Graham Warren, M.D., Ph.D.
 - Steven Bernstein, M.D.
 - Jamie Ostroff, Ph.D.
 - Paul Cinciripini, Ph.D.
 - Anne Joseph, M.D.
 - Monica Webb-Hooper, Ph.D.

Increasing capacity

- Utilize internal & external tx resources
- Hiring new staff vs. training existing
- referring externally
-

Delivery Channels

- Person to person (physician, NP, PA, TTS)
- Group interventions
- Web-based interventions (smokefree.gov)
- Text messaging
- Quitlines

Elements of intervention programs

- Identifying smokers
- Advising cessation
- Follow-up
- Monitoring progress of individual patients and patients collectively (refer to measures slide)

Measurement/ markers of success

- Baseline smoking rates
- Reach – engagement rates
- Effectiveness
- Abstinence rates 1, 6, & 12 months

Electronic Health Record

Health system IT adaptations

- Tobacco Registry
- Smoking Status documentation
- Order sets
 - Medications
 - Referral to internal treatment resources
 - Referral to external treatment resources

Cancer Center Leadership Support

Cancer Center Directors can:

- Assist in navigating the clinical environment
- Dedicate IT resources to this effort
- Provide support and put weight behind tobacco requests
- Ensure sustainability with specific, funded commitments

Lessons/ Keys to facilitating progress

- Seeing this as part of the mission
- Support of leadership
- Identification of a champion
- Buy-in across staff
- Significant I.T. engagement
- Persistence

Resources

Croyle RT, Morgan GD, Fiore MC. Addressing a Core Gap in Cancer Care - The NCI Moonshot Program to Help Oncology Patients Stop Smoking. N Engl J Med. 2019;380(6):512–515. doi:10.1056/NEJMp1813913

Video:

https://www.youtube.com/watch?time_continue=17&v=mH_Lot3PjR0

Thank you!

Glen Morgan

Glen.Morgan.PhD@gmail.com

Financial Considerations for Smoking and Cancer Treatment

Graham Warren M.D., Ph.D.

Vice Chairman for Research

Department of Radiation Oncology

Department of Cell and Molecular Pharmacology

Cancer Prevention and Control Program

Hollings Cancer Center

Medical University of South Carolina

The 2014 SGR: Outcome Estimates

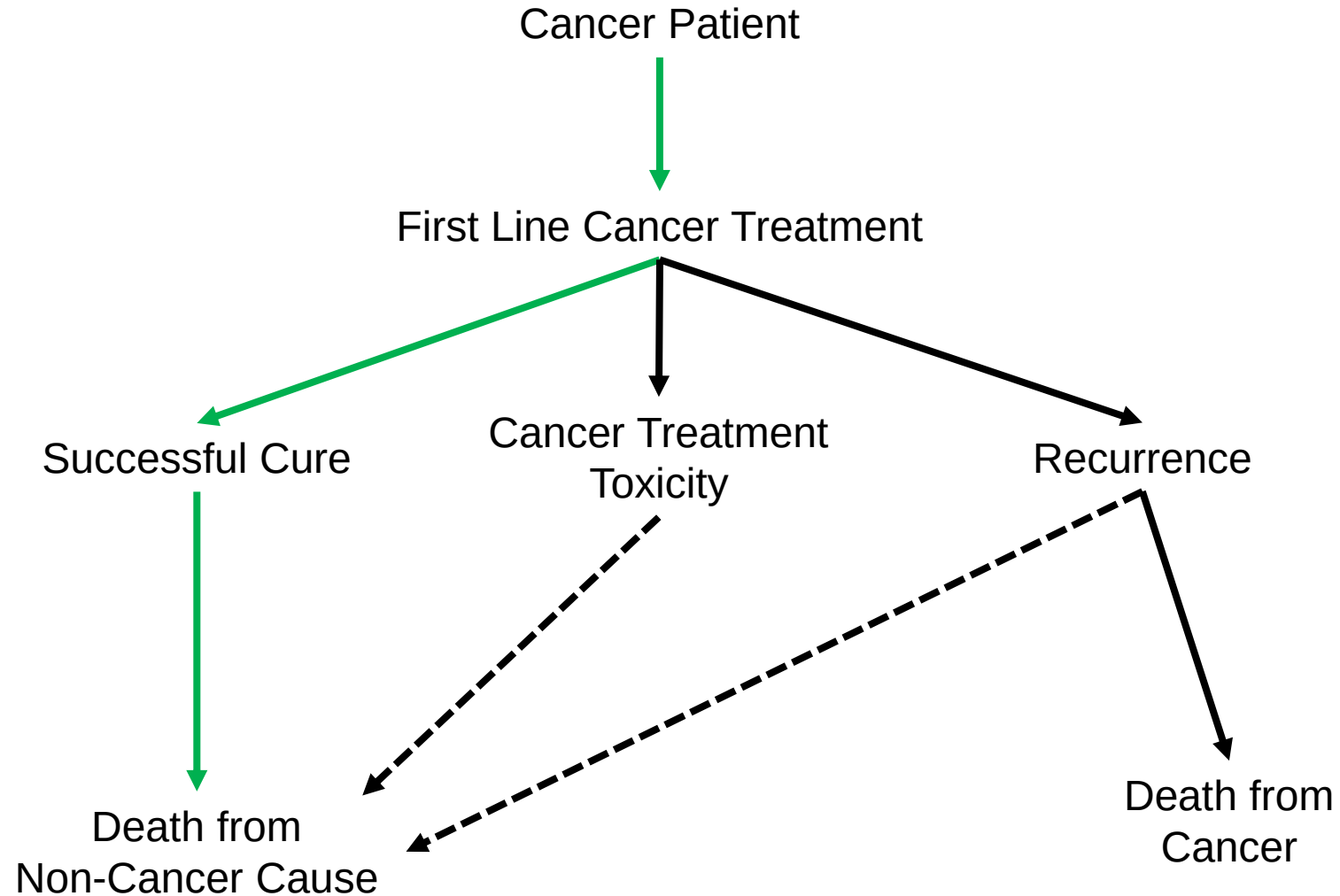
Effect	Studies	Associations (Significant)	RR Magnitude (median)
Overall Mortality	159	87% (62%)	Current: 1.51 Former: 1.22
Overall Survival	62	77% (42%)	
Cancer Related Mortality	58	79% (59%)	Current: 1.61 Former: 1.03
Second Primary	26	100% (100%)	
Recurrence	51	82% (53%)	Current:1.42 Former:1.15
Response	16	72%	
Toxicity	82	94% (80%)	

U.S. Department of Health and Human Services. The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2014.

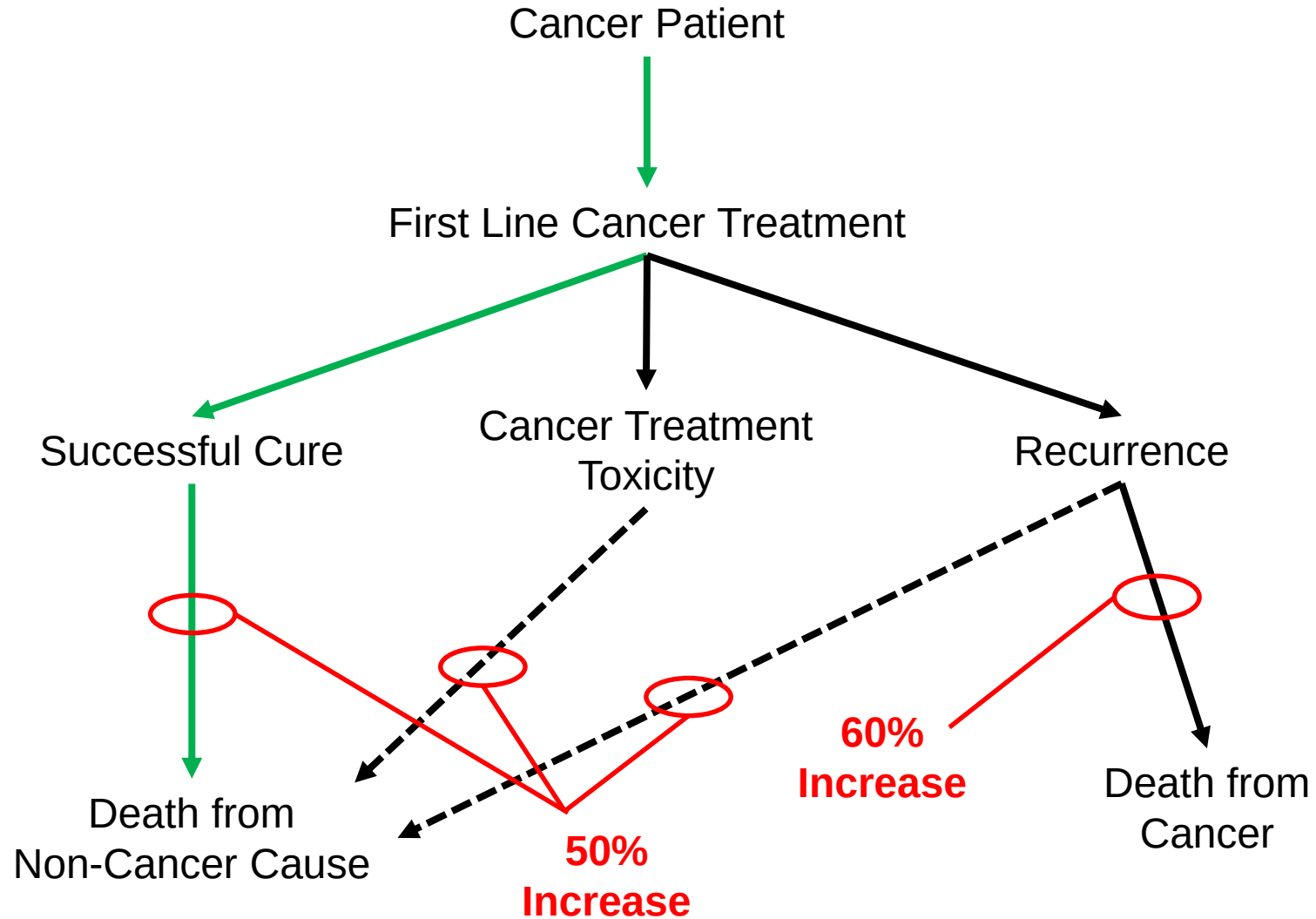
Staging Progress: Where are We?

- Stage I: clear evidence an adverse effect (2014 SGR)
- Stage II: identifying if addressing tobacco will produce meaningful benefits
- Stage III: development of cessation approaches that are clinically effective and efficient
 - Innovating to determine the best approach to cessation in an 'opt-out' setting
- Stage IV: identifying cancer treatment approaches (existing or new) optimized to reduce first line treatment failure

Conceptualizing Cancer Treatment



Conceptualizing **Smoking** in Cancer Treatment

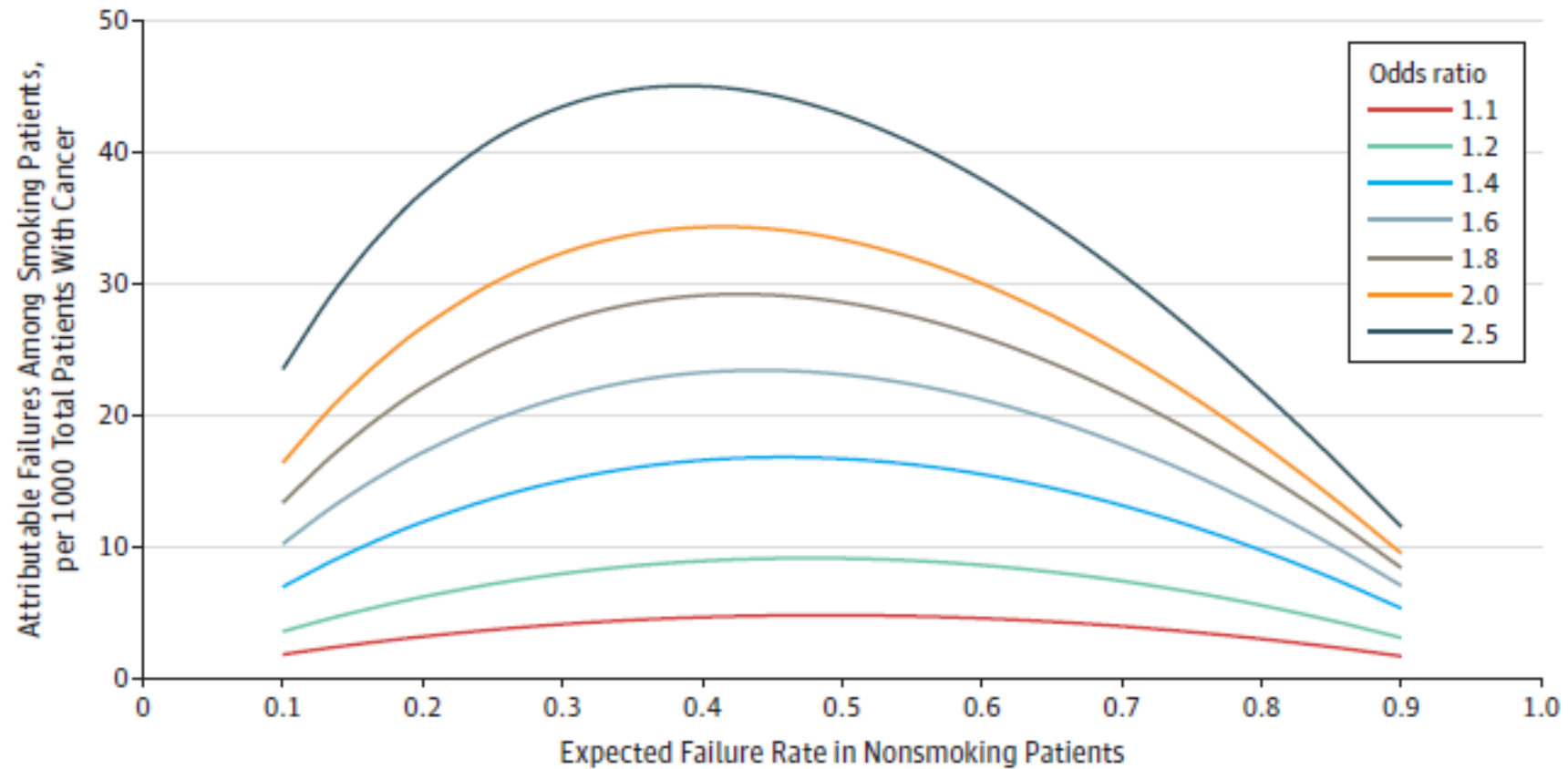


Magnitude of Smoking

- United States population: 328,000,000
 - Cancer incidence: 1.6 million
 - Reported smoking prevalence: ~15%
 - NOTE: ~30% of cancer patients who smoke misrepresent
 - Adjust to ~21% prevalence
 - US smoking cancer patient prevalence ~336,000
- Canadian population: 36,585,000
 - Canadian cancer incidence: 206,200
 - Smoking prevalence: 16.9% (adjust to 24%)
 - Canadian smoking cancer patient prevalence: ~49,500

Attributable Failure due to Smoking

Figure. Attributable Failure per 1000 Total Patients Due to Continued Smoking



Cost of Failure due to Smoking

Table 3. Mean Cost Associated With First-line Cancer Treatment Failure Attributed to Smoking per 1000 Total Patients With a 30% Failure Rate of First-line Cancer Treatment Among Nonsmoking Patients and 20% Smoking Prevalence

Odds Ratio ^a	Mean Individual Cost per Treatment Failure, \$			
	10 000	50 000	100 000	250 000
1.1	40 777	203 883	407 767	1 019 417
1.2	79 245	396 226	792 453	1 981 132
1.4	150 000	750 000	1 500 000	3 750 000
1.6	213 559	1 067 797	2 135 593	5 338 983
1.8	270 968	1 354 839	2 709 677	6 774 194
2.0	323 077	1 615 385	3 230 769	8 076 923
2.5	434 483	2 172 414	4 344 828	10 862 069
3.0	525 000	2 625 000	5 250 000	13 125 000

US Estimates (conservative): \$3.4 Billion Annually
\$10,678 per smoking patient

Pan-Canadian Estimates: \$239 Million Annually
\$5,795 per smoking patient

Magnitude Comparison

	Genome Driven Oncology¹	“Tobacco Cessation Adjuncted Oncology”
% of cancer patients who may benefit	5%	16.9%
Cost of sequencing	\$500 - \$3,000 (est. average \$1,500)	\$0
Cost of treatment	\$15,000 - \$250,000 (est. average \$80,000)	\$200 - \$1,500 (\$974: intensive + V + NRT) ²
Clinical benefit	54% response for 29.5 median months	~40% reduction in mortality
Cost per 1000 total patients	\$4.075 million	\$0.164 million
Cost ratio per 1000 total patients	~25:1	

1. Marquart J et al., *JAMA Oncol* 2018

2. CPAC Cost Estimates for Smoking Cessation 2017

How Can We Deal with Smoking

1. Smoking Cessation

- 2020 SGR suggests a 45% median reduction in overall mortality with cessation

2. Identifying cancer treatments that are not affected by smoking

- There may very well be existing treatments that are not affected by smoking
- Surgery (theoretically) would remove the nidus of recurrence vs. RT or chemo-RT

3. Identifying cancer treatments that target the effects of smoking

- PD-L1 based therapeutics appear to work better in patients with a smoking history (but not necessarily current smokers)

(1) Tobacco Assessment by Oncologists

(Always/Most of the time)

Parameter	IASLC (n=1507)	ASCO (n=1197)	NDCC (n=887)
Ask if use tobacco	90.2%	89.5%	90.2%
Advise to quit	80.6%	82.4%	83.3%
Actively treat	38.8%	38.6%	35.1%

- Predictive barriers by oncologists
 - Lack of education and experience in cessation
 - Lack of time
 - Lack of resources

Warren GW et al. *J Thorac Oncol* 2013

Warren GW et al. *J Oncol Pract* 2013

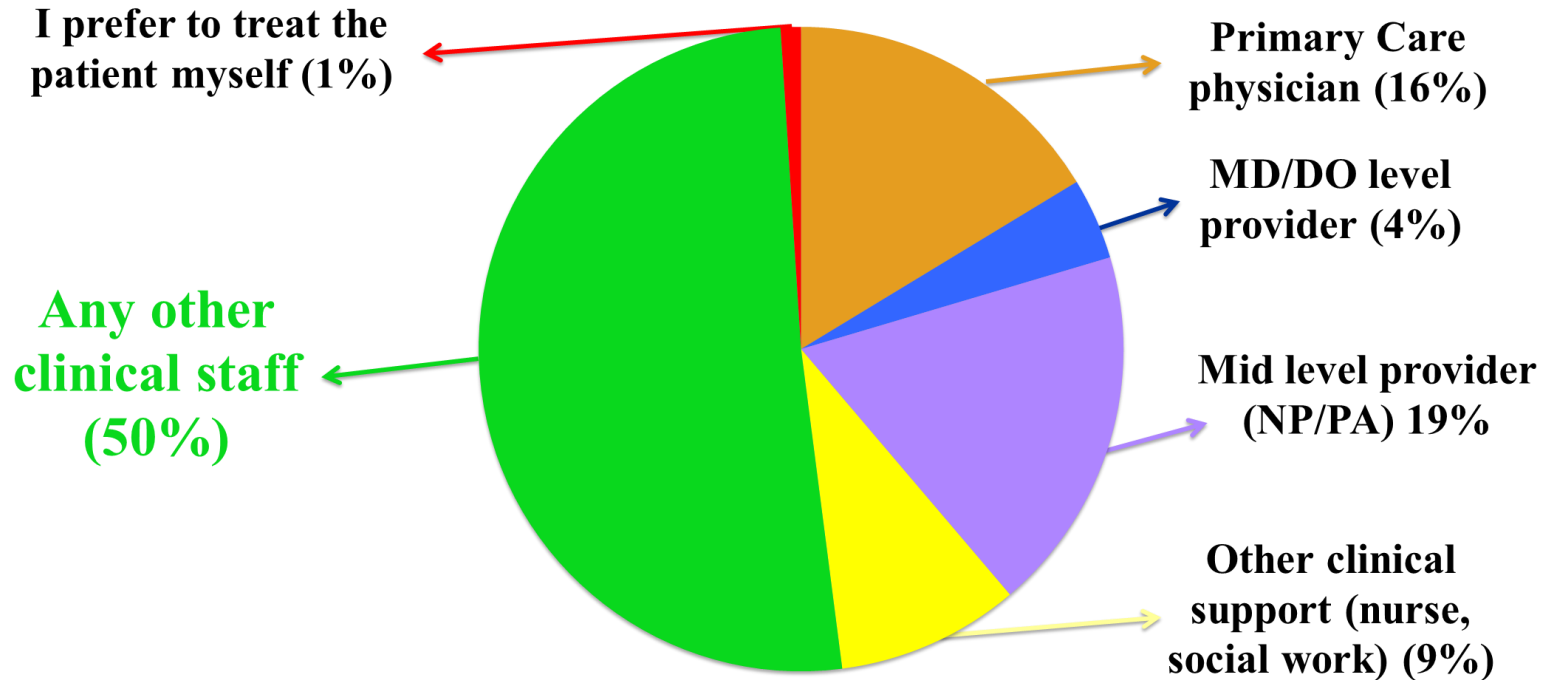
Pommerenke et al. *AACR 2014 Annual Meeting*

Warren et al. *J Thorac Oncol* 2015

(1) Who Should Provide Support?

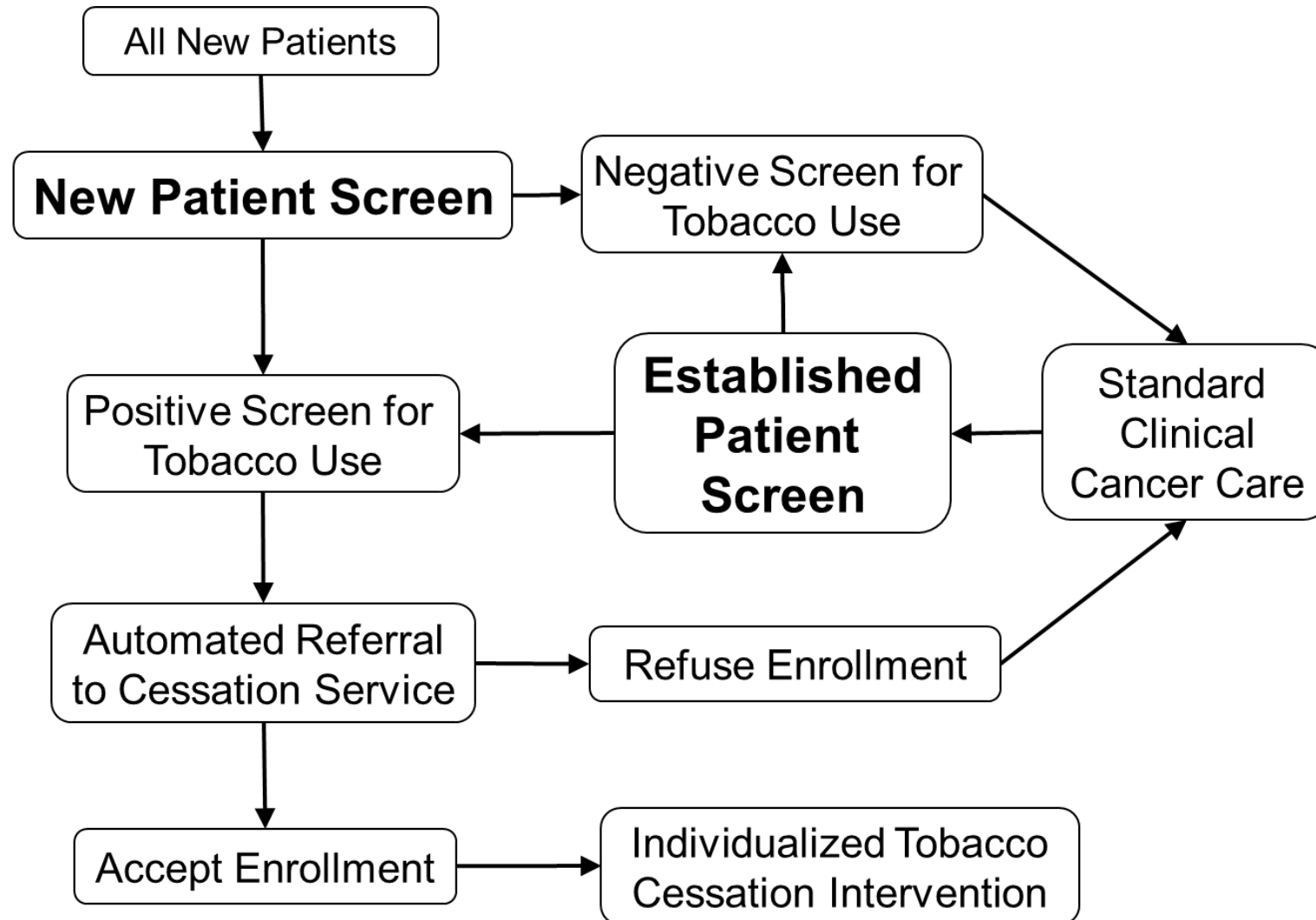
(NCI survey)

What provider do you prefer to provide cessation assistance?

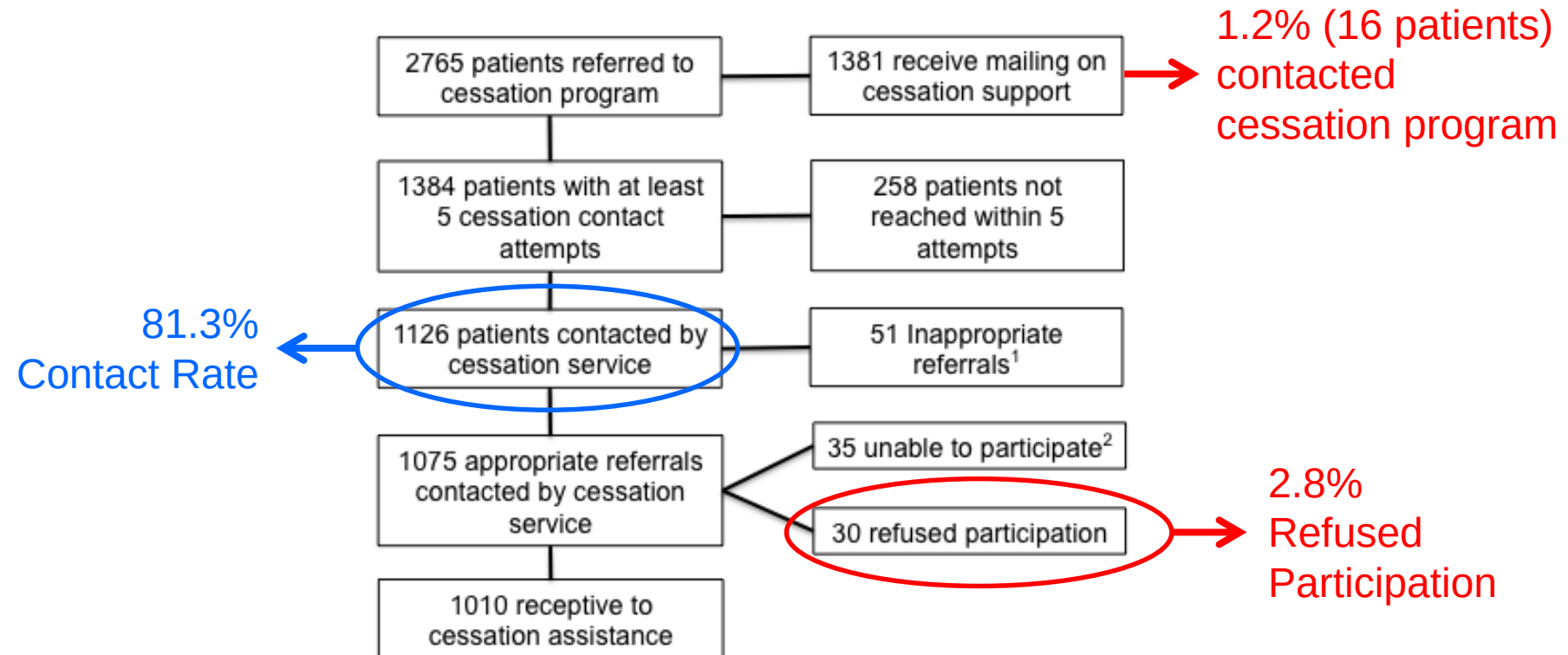


10% of respondents felt adequately trained
55% of respondents said train someone else in my clinic

(1) Opt-Out Screening and Treatment



(1) Participation at Cessation Contact



1. Includes 12 never smokers and 39 former smokers with no tobacco use in the past 30 days
2. Includes 12 patients in end-of-life situation and 23 patients in assisted living arrangement with contact by proxy

(1) New Patient Screen Yield

98.8% of patients captured with 3 questions

Referral Question	% of Total Referrals for Current Users	% of Total Referrals for Former Users	% of Total Referrals
Do you now smoke cigarettes everyday, some days, or not at all?	93.7%		83.1%
Do you currently use any other tobacco products such as cigars, pipes, chewing tobacco, snuff, dip, SNUS, clove cigarettes, kreteks, or bidis?	6.3%		5.6%
About how long has it been since you last smoked a cigarette, even a puff?		89.0%	10.1%
About how long has it been since you last smoked/used other tobacco products such as cigars, cigarillos, little cigars, pipe tobacco, or used chewing tobacco, snuff, dip, or SNUS even once?		1.4%	0.2%
Are you currently using any of the following methods or strategies to try to quit?		2.7%	0.3%
Are you interested in stopping tobacco use or speaking with our tobacco cessation specialist?		6.8%	0.8%

Extending assessment to every month delayed referral in only 3 of 428 cessation referrals (0.7%)

(1) Opt-Out Cessation and Mortality

Continuous Variables	N	Mean	Hazard Ratio	95% CI	p
Age at diagnosis (years)	224	61.9	1.04	1.02–1.06	0.001
Pack-years	224	59.7	1.00	0.99–1.01	0.495
Days between diagnosis and last contact	224	100.9	0.999	0.998–1.001	0.227
Categorical Variables	N	%	Hazard Ratio	95% CI	p
Sex					
Female	134	59.8	1.00	Ref.	0.051
Male	90	40.2	1.45	1.01–2.14	
Clinical stage					
Stage I/II	81	36.2	1.00	Ref.	<0.001†
Stage III	65	29.0	2.53	1.39–4.61	
Stage IV	78	34.8	8.72	4.93–15.40	
ECOG status					
0	127	56.7	1.00	Ref.	0.265
≥1	97	43.3	1.26	0.84–1.89	
Tumor histology					
NSCLC	197	87.9	1.00	Ref.	0.626
Other lung cancer	27	12.1	0.87	0.50–1.52	
Quit status at referral					
Quit	48	21.4	1.00	Ref.	0.393
Current	176	78.6	0.80	0.48–1.34	
Quit status at last contact					
Quit	95	42.4	1.00	Ref.	0.012†
Current	129	57.6	1.79	1.14–2.82	

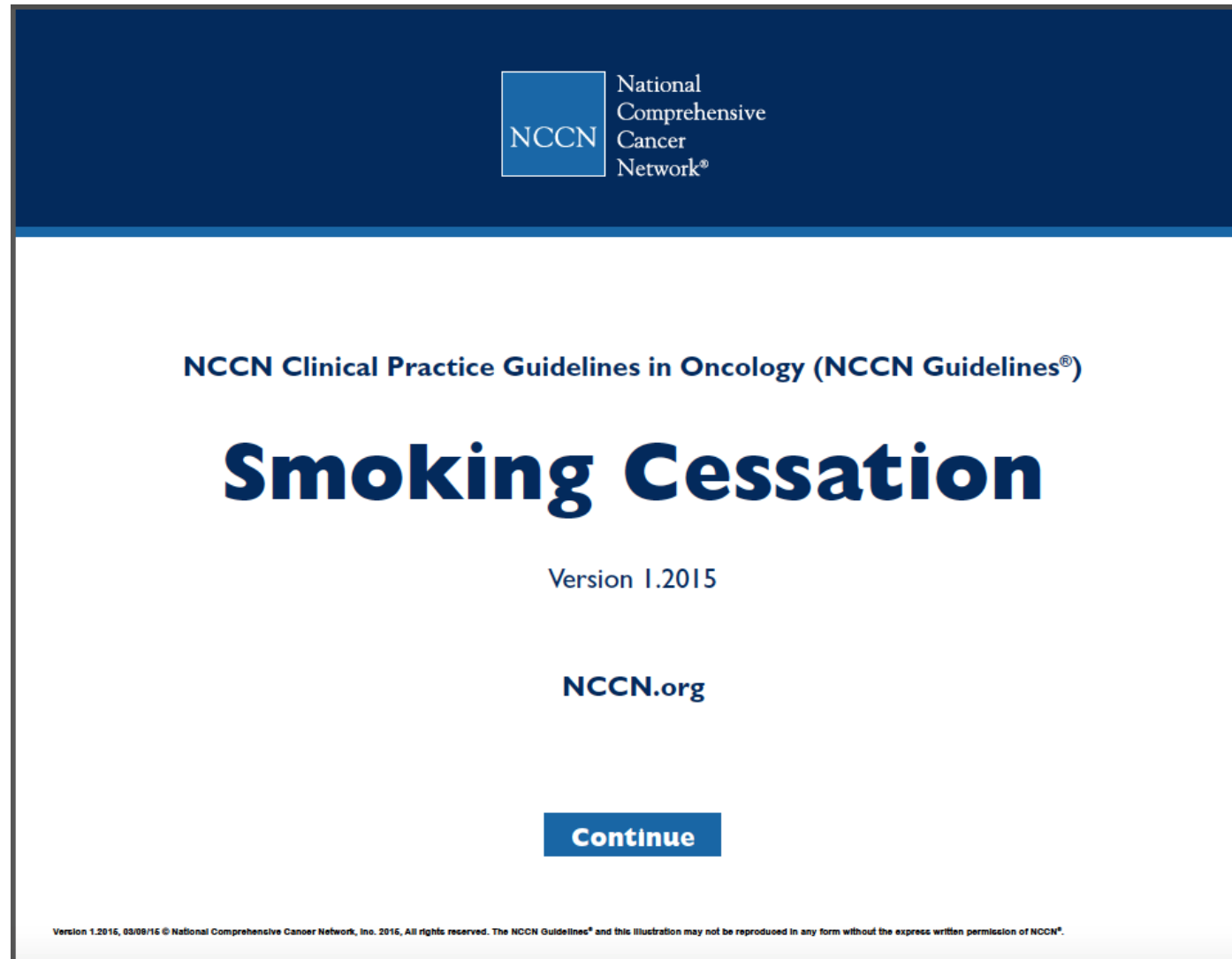
115 of 224 patients (51.3%) were deceased by the end of the follow-up period. The model is adjusted for all variables shown in this table based upon a Cox proportional hazards model.

*N = 224 of 250 due to 22 records missing clinical stage, two missing pack-years, and two missing both clinical stage and pack-years.

Bold indicates statistically significant at $p < 0.05$.

CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; NSCLC, non-small-cell lung cancer.

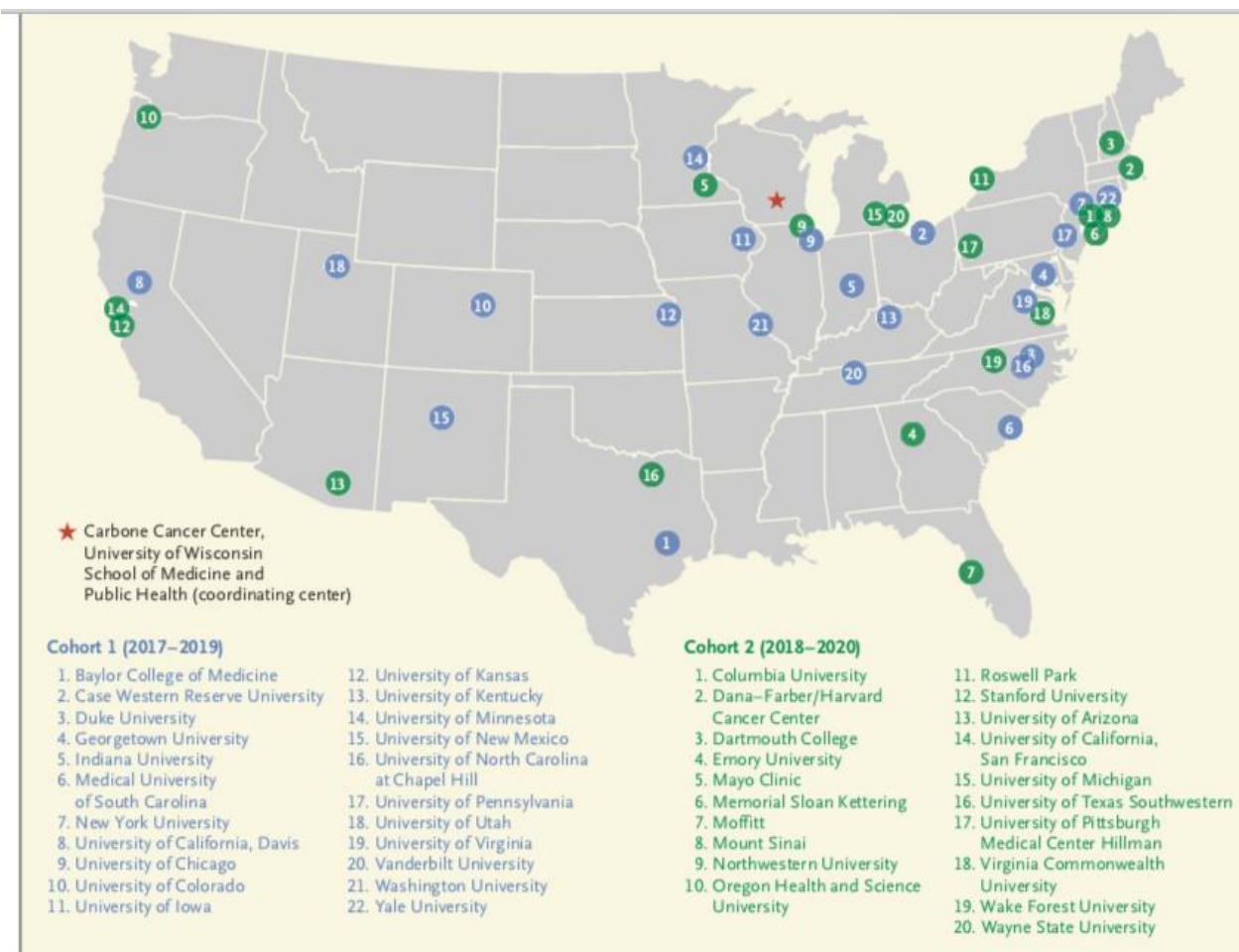
(1) NCCN Guidelines



Addressing a Core Gap in Cancer Care — The NCI Moonshot Program to Help Oncology Patients Stop Smoking

Robert T. Croyle, Ph.D., Glen D. Morgan, Ph.D., and Michael C. Fiore, M.D., M.P.H., M.B.A.

(1)



NCI-Designated Cancer Centers Selected as Part of the Cancer Center Cessation Initiative (C3I).

(1)

CANADIAN PARTNERSHIP
AGAINST CANCER



PARTENARIAT CANADIEN
CONTRE LE CANCER



Pan-Canadian Tobacco Cessation + Cancer Care Network



Ottawa, ON

January 16, 2019



(1)



A 10-YEAR ROADMAP FOR CANCER IN CANADA

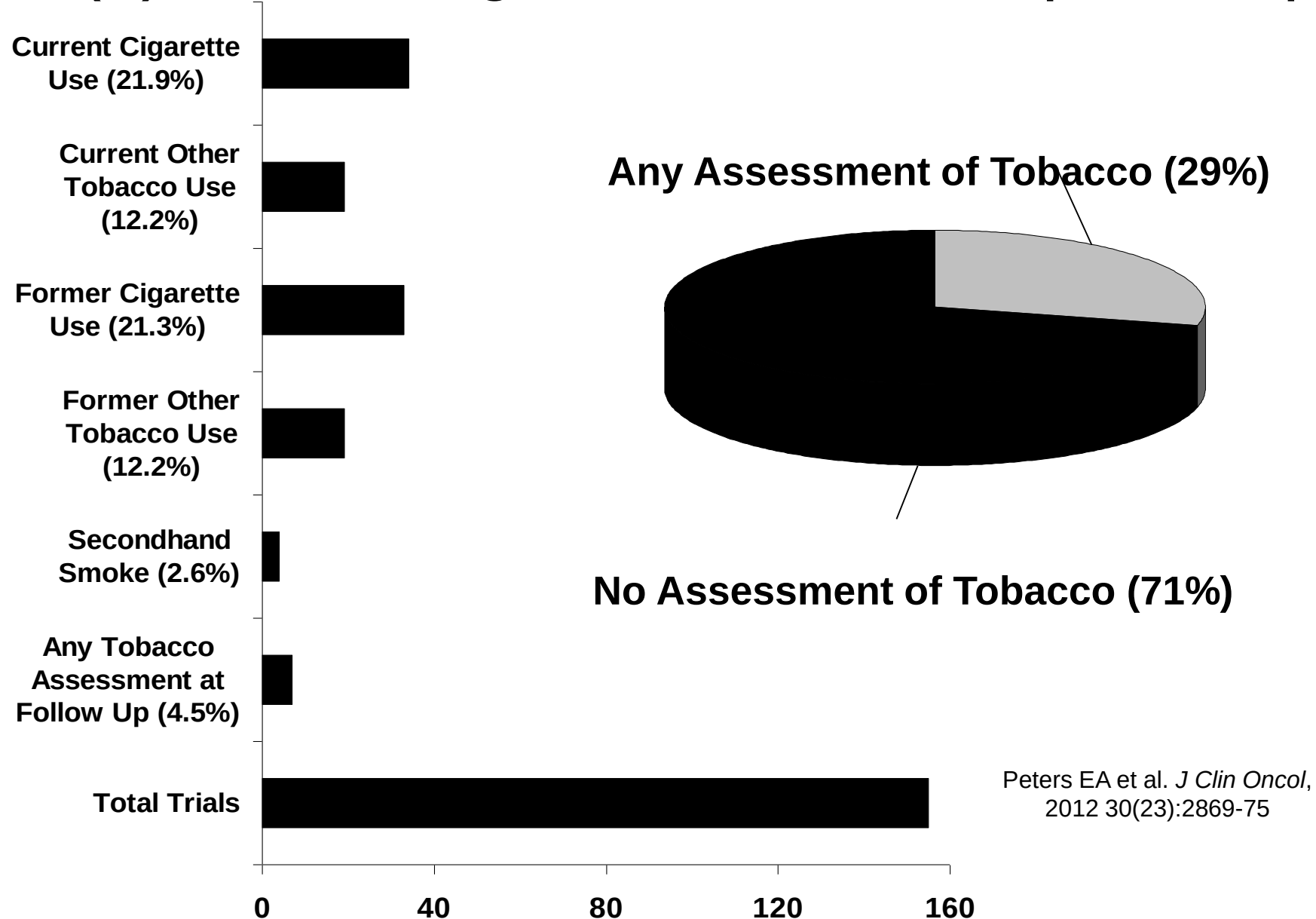


(1)

Pan-Canadian Vision Statement

“Our vision is that every patient with cancer across Canada receives support to quit smoking for the best treatment and quality of life.”

(2) Assessing Tobacco in Coop. Groups



(2) NCI/AACR Structured Questions

Published OnlineFirst February 17, 2016; DOI: 10.1158/1078-0432.CCR-16-0104

Special Report

Clinical
Cancer
Research

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

Stephanie R. Land¹, Benjamin A. Toll², Carol M. Moinpour³, Sandra A. Mitchell¹,
Jamie S. Ostroff⁴, Dorothy K. Hatsukami⁵, Sonia A. Duffy⁶, Ellen R. Gritz⁷, Nancy A. Rigotti⁸,
Thomas H. Brandon⁹, Sheila A. Prindiville¹⁰, Linda P. Sarna¹¹, Robert A. Schnoll¹²,
Roy S. Herbst¹³, Paul M. Cinciripini⁷, Scott J. Leischow¹⁴, Carolyn M. Dresler¹⁵,
Michael C. Fiore¹⁶, and Graham W. Warren^{2,17,18}

Cognitive Testing of Tobacco Use Items for Administration to Patients with Cancer and Cancer Survivors in Clinical Research

Stephanie R. Land, PhD^{1,2}; Graham W. Warren, MD, PhD^{3,4}; Jennifer L. Crafts, PhD⁵; Dorothy K. Hatsukami, PhD⁶;
Jamie S. Ostroff, PhD⁷; Gordon B. Willis, PhD²; Veronica Y. Cholleto, RN, MS²; Sandra A. Mitchell, PhD, CRNP, AOCN²;
Jasmine N. M. Folz, MA⁵; James L. Gulley, MD, PhD⁸; Eva Szabo, MD⁹; Thomas H. Brandon, PhD¹⁰;
Sonia A. Duffy, PhD, RN¹¹; and Benjamin A. Toll, PhD¹²

(2) Core Items

1. **Have you smoked at least 100 cigarettes (5 packs=100 cigarettes) in your entire life?**

- ☐ Yes
- ☐ No
- ☐ Don't know/Not sure

4. **How many total years have you smoked (or did you smoke) cigarettes? Do not count any time you may have stayed off cigarettes.**

_____ Years *If you smoked less than one year, write "1."*

5. **On average when you have smoked, about how many cigarettes do you (or did you) smoke a day?**

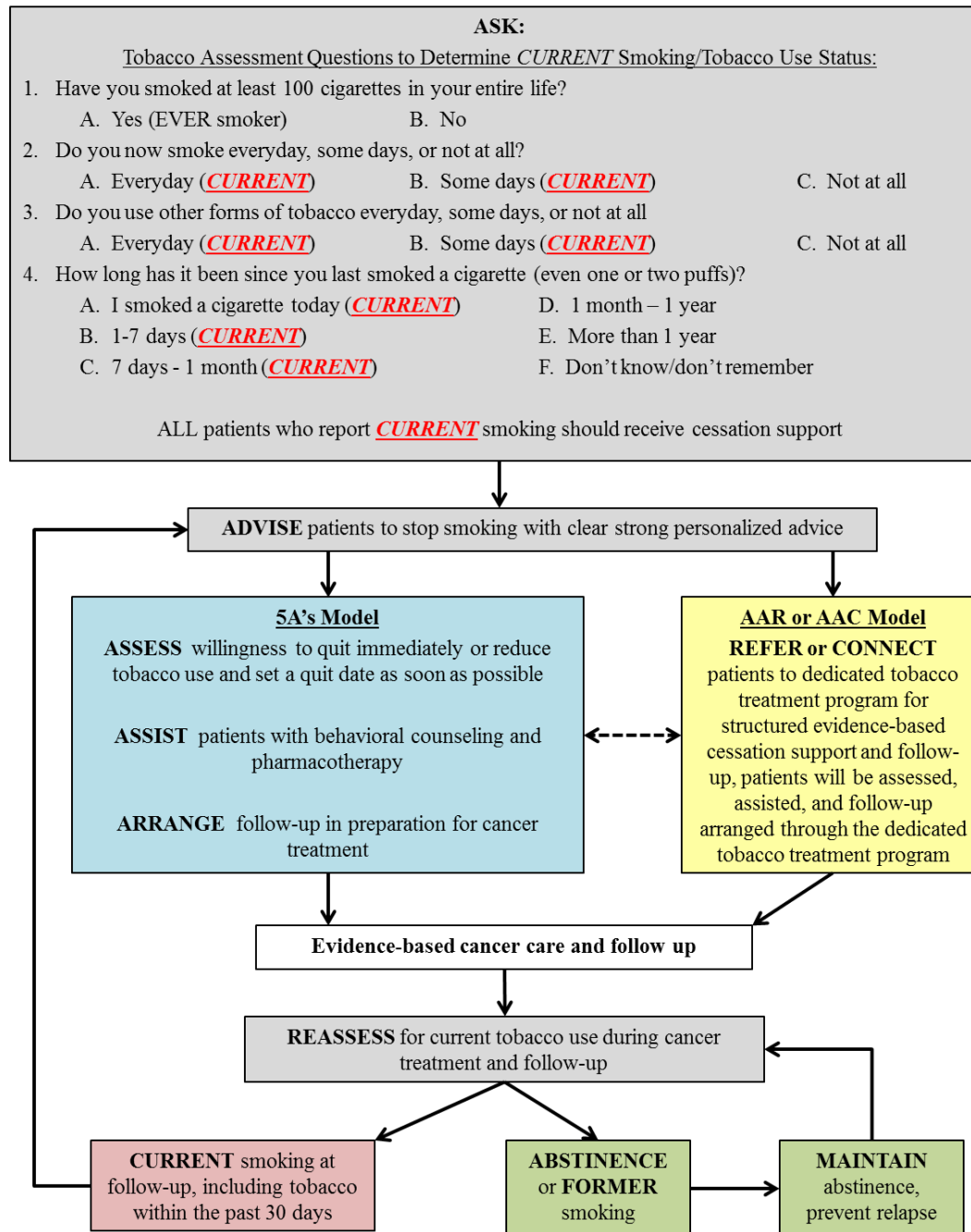
A pack usually has 20 cigarettes in it.

_____ Number of cigarettes per day

6. **How long has it been since you last smoked a cigarette (even one or two puffs)?**

First check which one of the following choices applies to you. Then, if applicable, write a number on the line for how many days, weeks, months, or years it has been since your last cigarette.

- ☐ I smoked a cigarette today (at least one puff).
- ☐ 1-7 days. ➡ Number of days since last cigarette: _____
- ☐ Less than 1 month. ➡ Number of weeks since last cigarette: _____
- ☐ Less than 1 year. ➡ Number of months since last cigarette: _____
- ☐ More than 1 year. ➡ Number of years since last cigarette: _____
- ☐ Don't know/Don't remember



(2) Implementing Cessation into Practice

- The 5 A' s Model
 - Ask
 - Advise
 - Assess
 - Assist
 - Arrange
- Implementing cessation into clinical care should consider new and follow-up approaches

(3) Targeted Strategies...

- Have you considered evaluating if targeted therapeutics could be used to treat patients with a smoking history or patients who smoke at the time of diagnosis?

(3) Targeted Strategies...

- Have you considered evaluating if targeted therapeutics could be used to treat patients with a smoking history or patients who smoke at the time of diagnosis?
- Have you considered if we figured this out, then maybe this is a way we could also improve second-line treatment for resistant cancers?

Urging Affordable Access to High-Value Cancer Drugs

Drug Costs Are a Burden on Cancer Patients



90% of Americans say cancer drugs are too expensive



Most new cancer drugs are priced higher than \$100,000 per patient per year

Financial Toxicity: Harmful Effects of Care Costs on Patients' Well Being

Financial toxicity can lead to:



Shortened survival



Skipped medication doses



Debt, depleted savings, and bankruptcy

Discussions About Cost and Value May Help Patients



Nearly 66% of cancer patients express interest in talking with their doctors about costs



27% of cancer patients and less than half of oncologists report having had cost-related discussions

President's Cancer Panel Recommendations

Critical actions to maximize the value and affordability of cancer drugs and to support investments in science and research that will drive future innovation:



The Imperative of Addressing Cancer Drug Costs and Value

- *“Promoting Value, Affordability, and Innovation in Cancer Drug Treatment”*
(President’s Cancer Panel)

1. Value based use
2. Communication
3. Minimize effects of drugs on financial toxicity
4. Stimulate competition
5. Adequate resources for FDA
6. Research



For full report text, including sources for data included here, read the President's Cancer Panel report *Promoting Value, Affordability, and Innovation in Cancer Drug Treatment* at PresCancerPanel.cancer.gov/report/drugvalue

Maximizing Value

- Smoking is an unequivocal effect modifier
- The cost of cessation (\$200-\$2000) is far less than the cost of cancer drugs (\$25,000-\$400,000)
- Current smoking affects over 300,000 cancer patients in the US every year
- Patients should be informed
- Providers should be informed
- FDA should be given resources
- Priority should be placed on identifying EVIDENCE-BASED CARE
- This can start by including brief structured smoking assessments into ALL clinical trials

Conclusions?

- Smoking after a cancer diagnosis is a broad EFFECT MODIFIER that affects more than 300,000 patients annually
 - STOP viewing smoking as a behavioral trait
 - Clinical trials MUST include tobacco as an effect modifier
 - Are we really going to continue to spend this much on ignoring a proven factor associated with recurrence and mortality
- Optimal treatment strategies likely exist for cancer patients who smoke at the time of diagnosis
 - Delay?
 - Surgery vs. RT/Chemo-RT?
 - Optimal systemic agents?
- Coherent prioritization to include funding and review



Financial Toxicity in Cancer Treatment in America



Memorial Sloan Kettering
Cancer Center

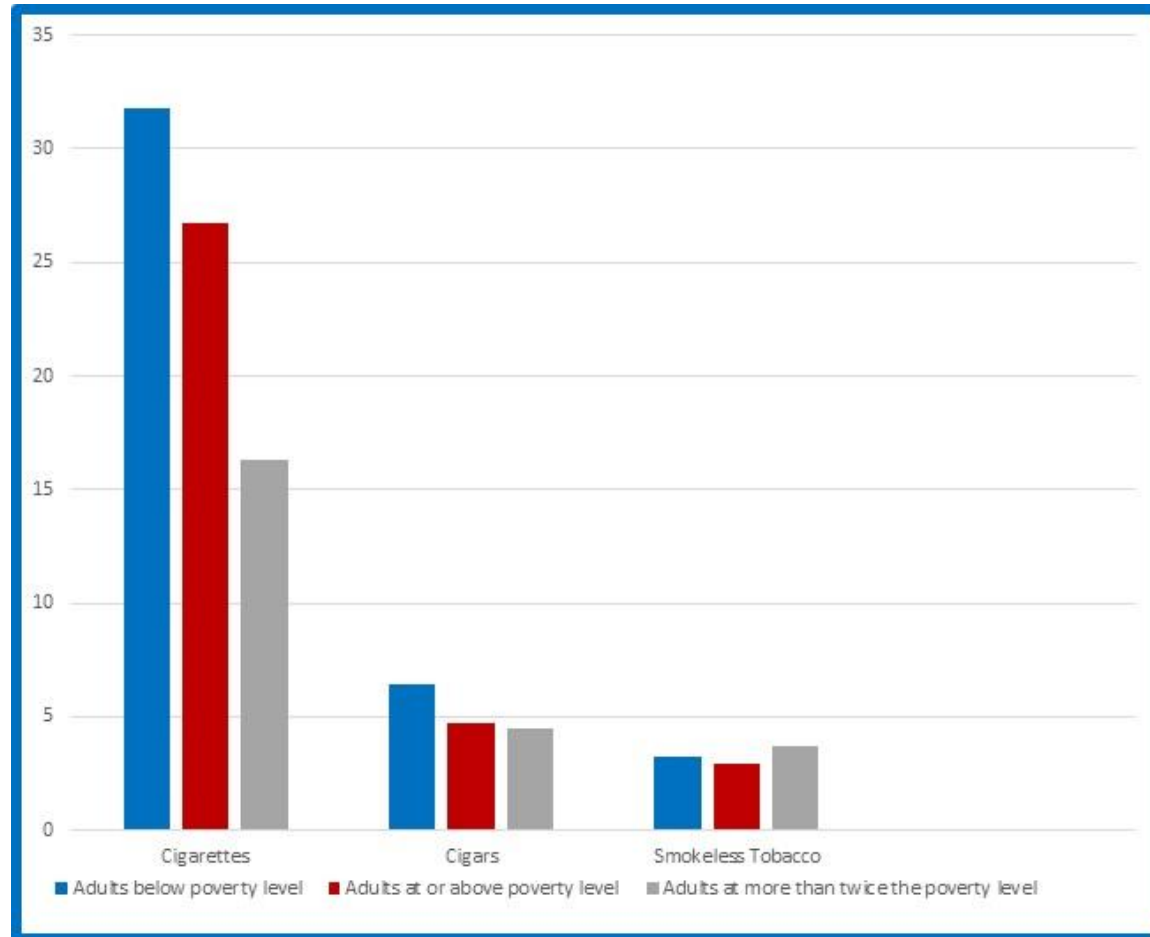
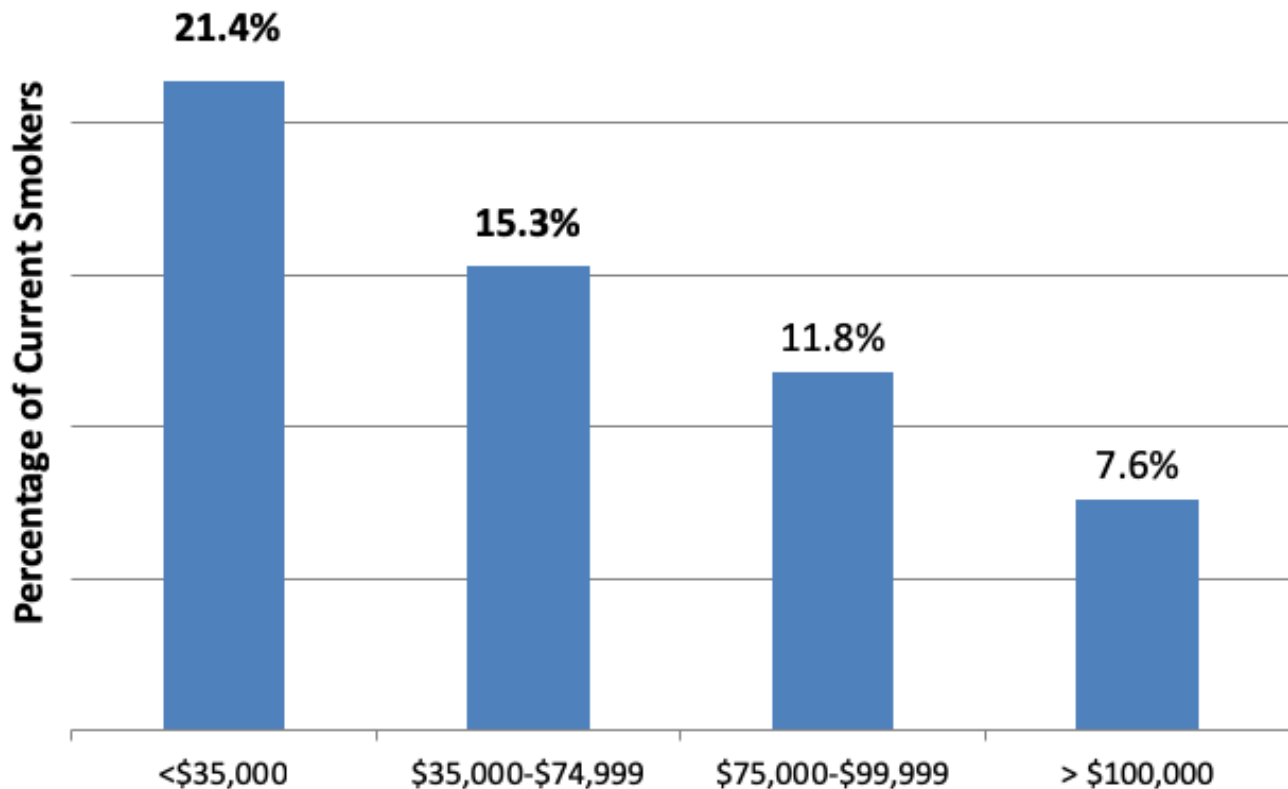
Fumiko Chino, MD
February 28, 2020



@fumikochino #OCETobaccoUse @AACR @IASLC @FDAOncology



Disparities in Smoking Rates by Household Income



Smokers who are diagnosed with cancer often have the LEAST financial resources to pay for their treatment or to engage in smoking cessation activities.

Financial Toxicity

“A new name for a growing problem”

NATIONAL CANCER OPINION SURVEY 2018 KEY FINDINGS

Cancer's Financial and Access Challenges

Just as many Americans are worried about **cancer's financial impact** as about **dying of cancer**



Financial
Burden



Death



61%

of **caregivers** say they or a loved one have taken at least one onerous step to **pay for cancer care** including:

35% dipped into **savings account**

23% worked **extra hours**

14% postponed **retirement**

13% took on an **additional job**

43%

of **cancer patients** experienced barriers to accessing the best possible care due to **health insurance coverage**



What is Financial Toxicity?

Financial Toxicity:

Problems a patient has related to the cost of medical care. Cancer patients are more likely to have financial toxicity than people without cancer.

-National Cancer Institute

“Even with health insurance, the high costs of cancer care are leaving some vulnerable American families adrift in debt. [...] Out-of-pocket costs can have real effects on quality of life and quality of care.”

-Chino, *JAMA Oncology*, 2018

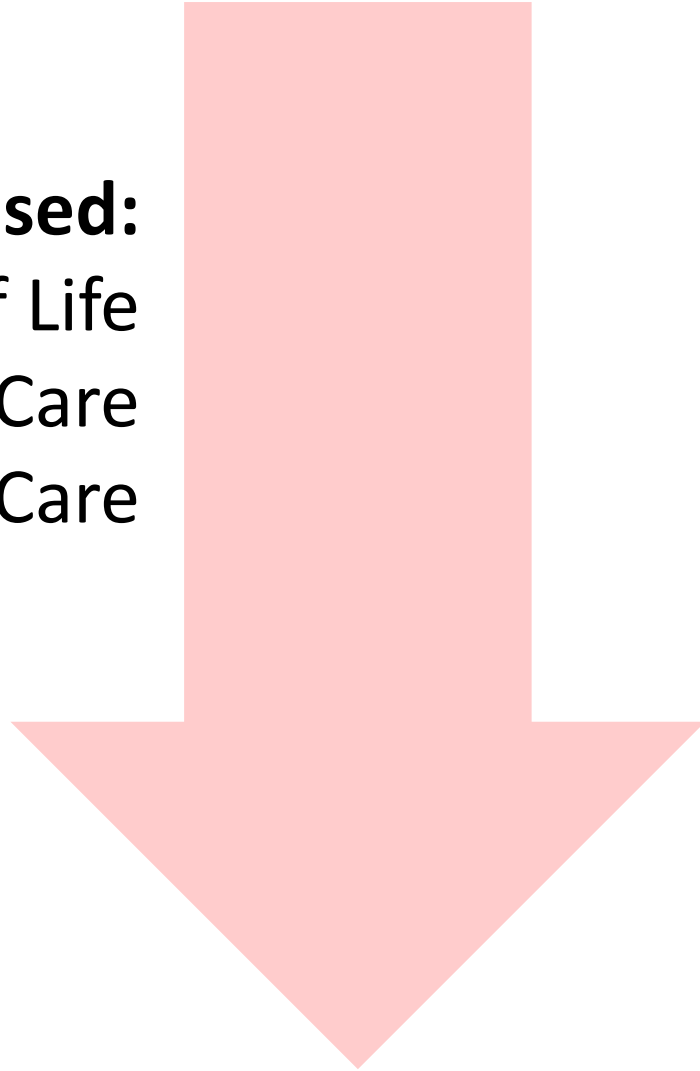
Why does Financial Toxicity Matter?

Decreased:

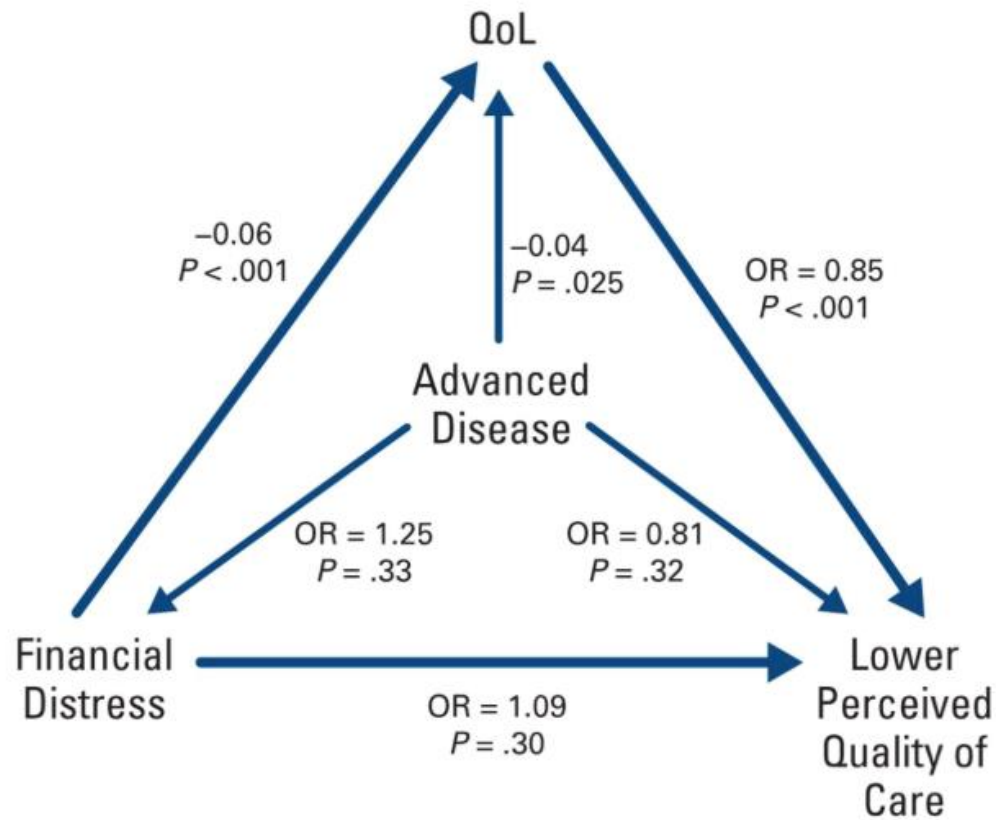
Quality of Life

Satisfaction with Care

Quality of Care



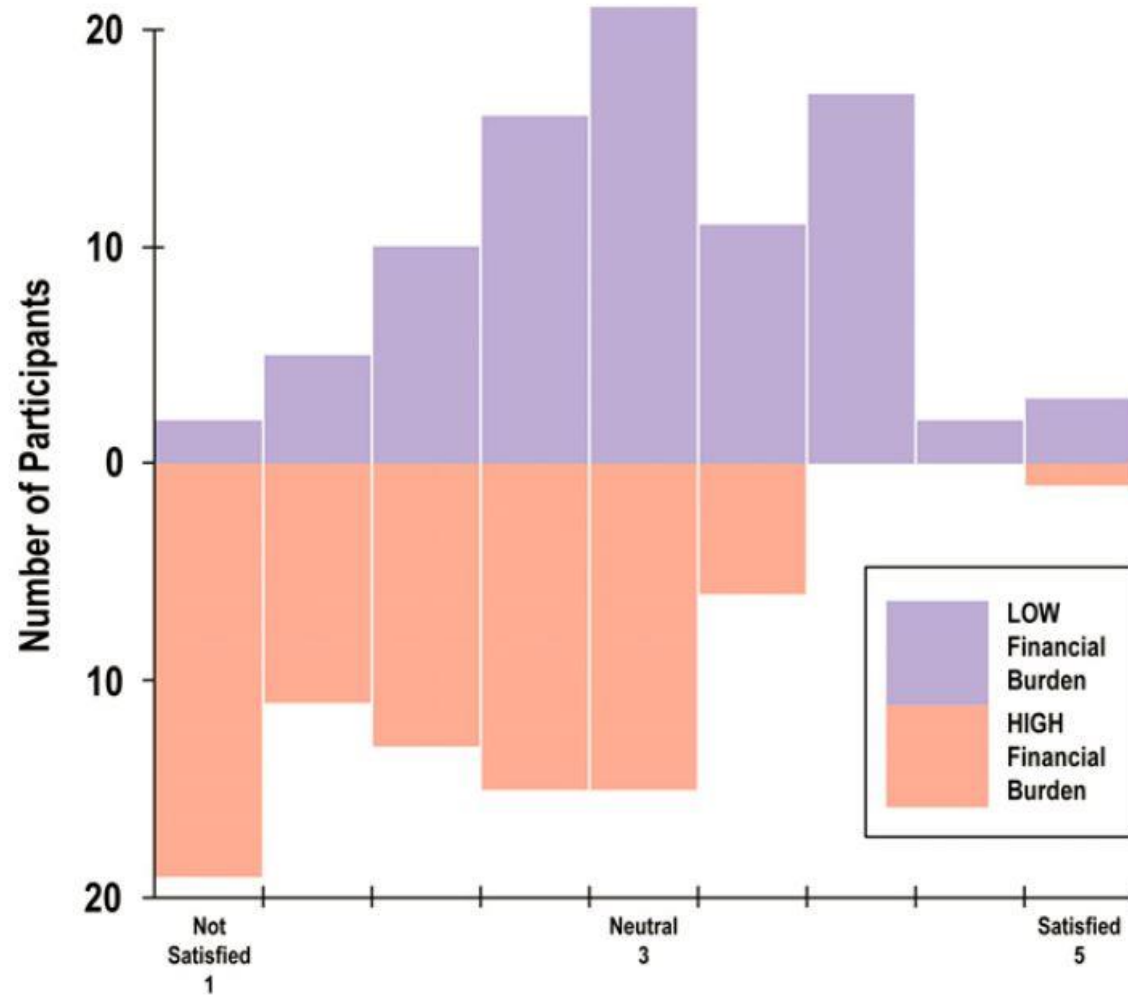
Decreased Quality of Life



Patients with “a lot” of financial problems were much less likely to rate their QOL as good (OR 0.24)

95% CI, 0.14-0.40

Decreased Satisfaction with Care



High financial burden decreases:

- General satisfaction with health care
(coefficient: -0.29; lower to upper bound: -0.57 to -0.01; $p=0.04$)
- Satisfaction with technical quality of care
(coefficient: -0.26; lower to upper bound: -0.48 to -0.03; $p=0.03$)

Decreased Quality of Care



Medication nonadherence = 27%

This included:

- 22% who didn't fill Rx due to cost
- 14% who skipped doses to make meds last longer
- 5% who skipped, took less, or didn't fill their chemotherapy prescriptions

Why does Financial Toxicity Matter?



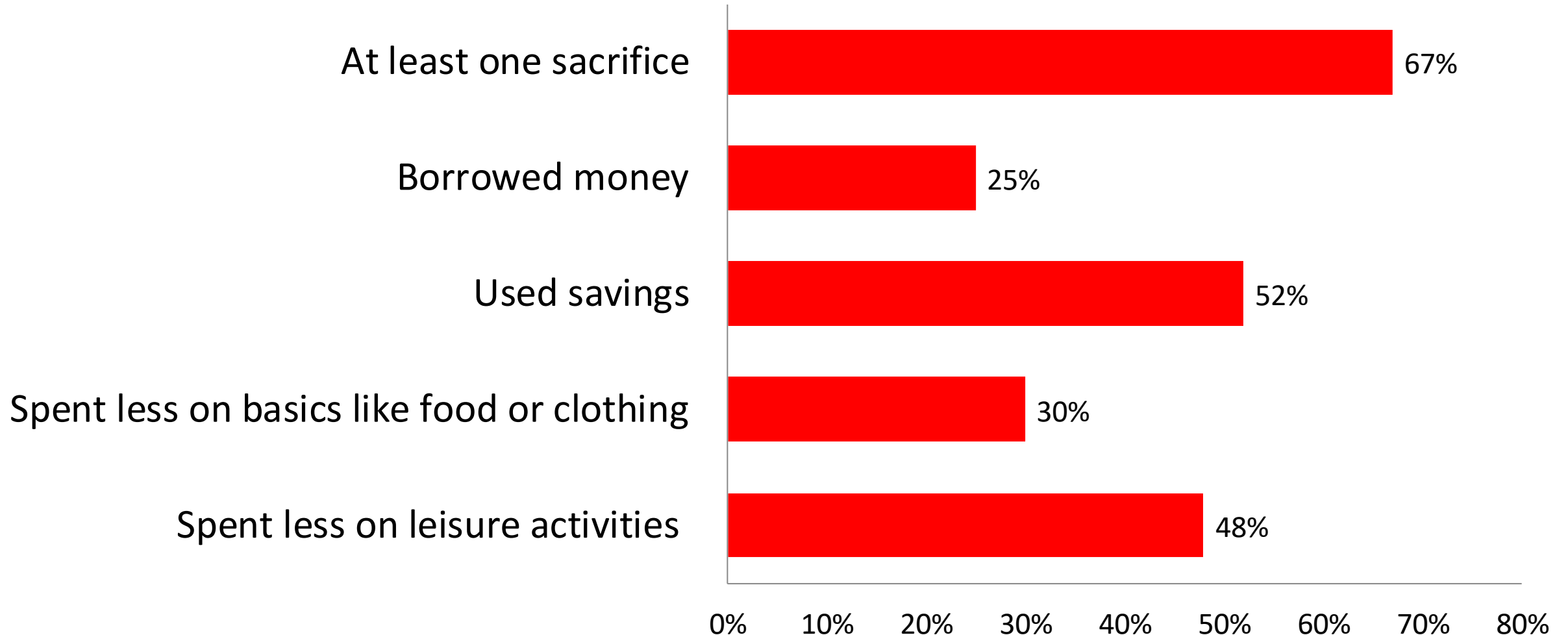
Increased:

Personal/Family Burden

Risk of Bankruptcy

Risk of Mortality

Increased Personal/Family Burden



Risk of Homelessness



1 in 20* Black or Latina women with early stage breast cancer **lost their home** due to the financial impact of their cancer treatment

*4.7% of black, 6.0% of Latinas

Increased Risk of Bankruptcy



In a study of 197,840 citizens,
4,408 had declared bankruptcy

2.65x

Risk of bankruptcy with
Cancer Diagnosis

Increased Risk of Death



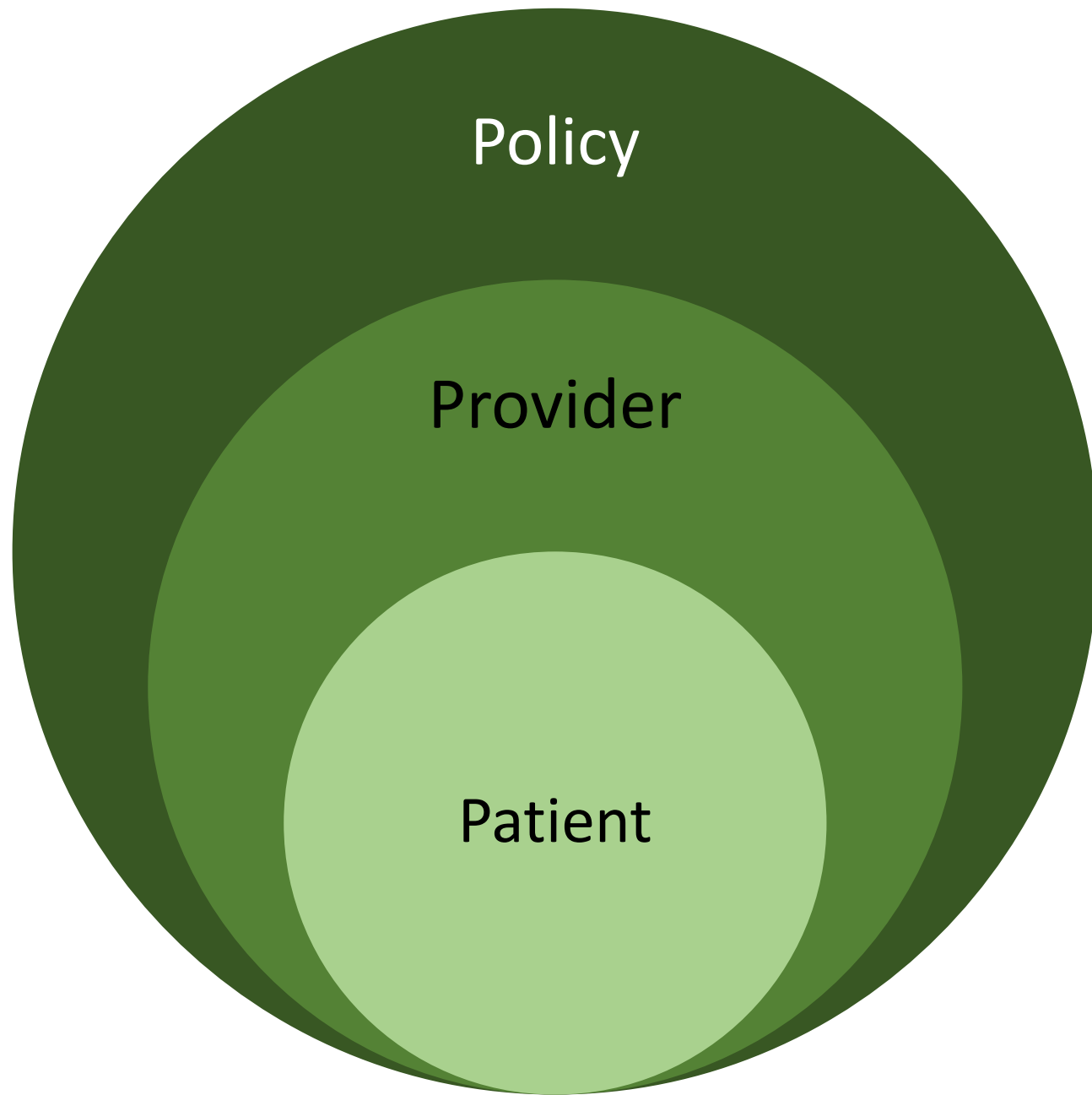
In a study of 7,570 matched patients,
bankruptcy was associated with

79%

increased mortality risk

HR 1.79 (1.64-1.96)

Where do we go from here?



Solutions exist
within systemic,
interpersonal,
and individual
frameworks

Policy Guidelines



Patients



Providers



Healthcare
Systems



Payers



Biopharmaceutical
Companies



Researchers



Society

*“A broad set of stakeholders must contribute to efforts to align cancer drug prices with their **value**, ensure **affordable access to cancer drugs** for all patients, and promote future **innovation** in cancer drug development.”*

De-escalation Research

VOLUME 36 · NUMBER 14 · MAY 10, 2018

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Prospective International Randomized Phase II Study of Low-Dose Abiraterone With Food Versus Standard Dose Abiraterone In Castration-Resistant Prostate Cancer

Russell Z. Szmulewitz, Cody J. Peer, Abiola Ibraheem, Elia Martinez, Mark F. Kozloff, Bradley Carthon, R. Donald Harvey, Paul Fishkin, Wei Walter M. Stadler, and M

Open access

Original research

ESMO *Open*
Cancer Horizons

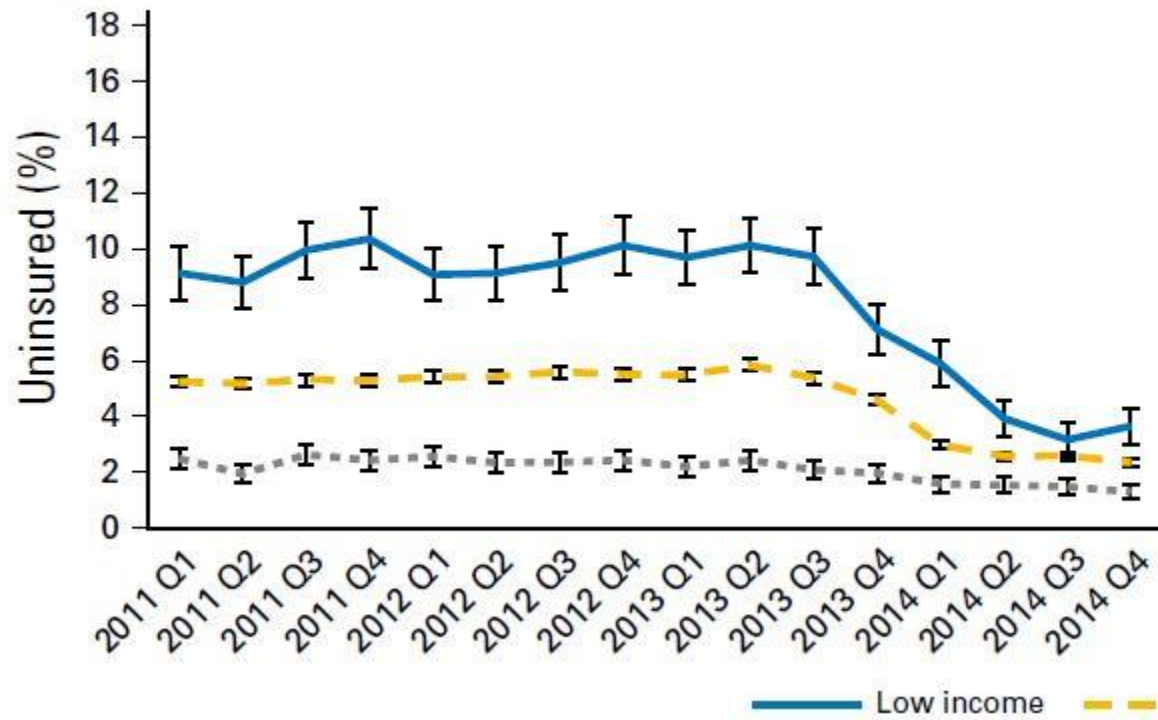


Low-dose nivolumab can be effective in non-small cell lung cancer: alternative option for financial toxicity

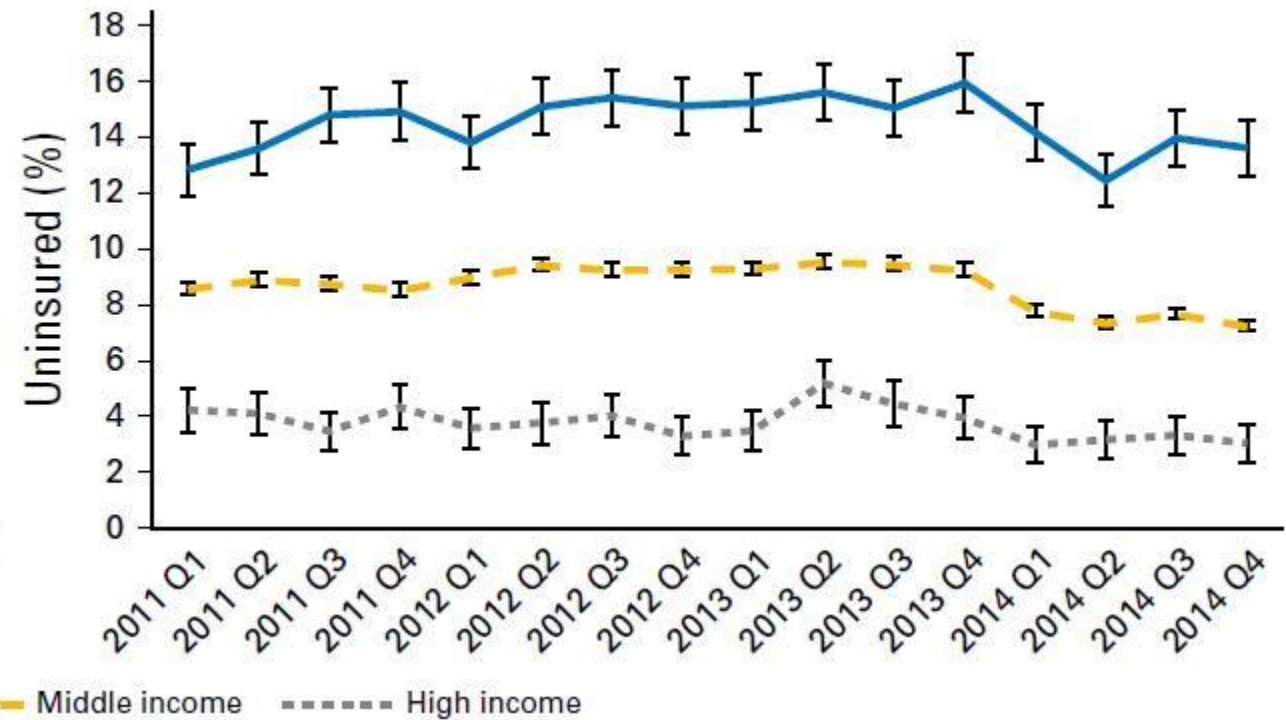
Shin Hye Yoo,¹ Bhumsuk Keam,^{1,2} Miso Kim,¹ Se Hyun Kim,³ Yu Jung Kim,³ Tae Min Kim,^{1,2} Dong-Wan Kim,^{1,2} Jong Seok Lee,³ Dae Seog Heo^{1,2}

National Health Care Initiatives: Affordable Care Act

Medicaid Expansion States



Medicaid Nonexpansion States

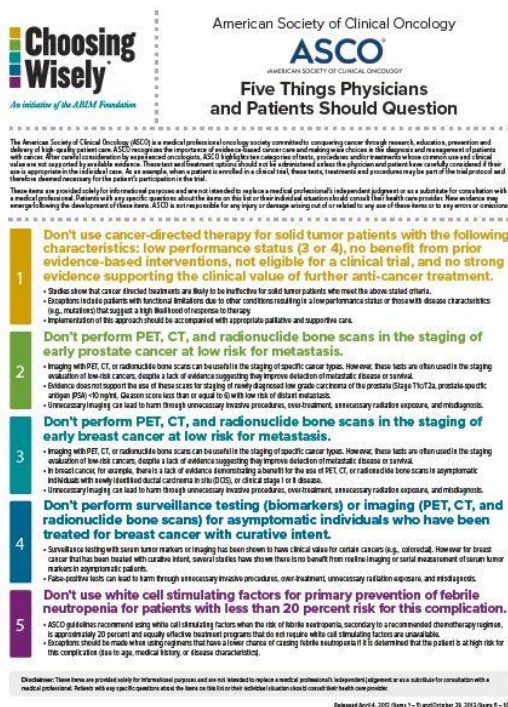


Affordable Care Act and Smoking Cessation



Tobacco cessation (individual counseling, group counseling, medications) must be provided at no cost as an “essential health benefit” under the ACA. Not all evidence-based cessation treatments are covered in all states.

Prior research has shown that NRT/counseling with **no cost sharing** increased quit rates by 5 percentage points over 12 months (13% -> 18%)



National Health Care Initiatives: ASCO Choosing Wisely

10 Cancer Tests and Treatments Routinely Performed Despite Lack of Evidence

“Opportunities to improve the quality and value of cancer care”

8

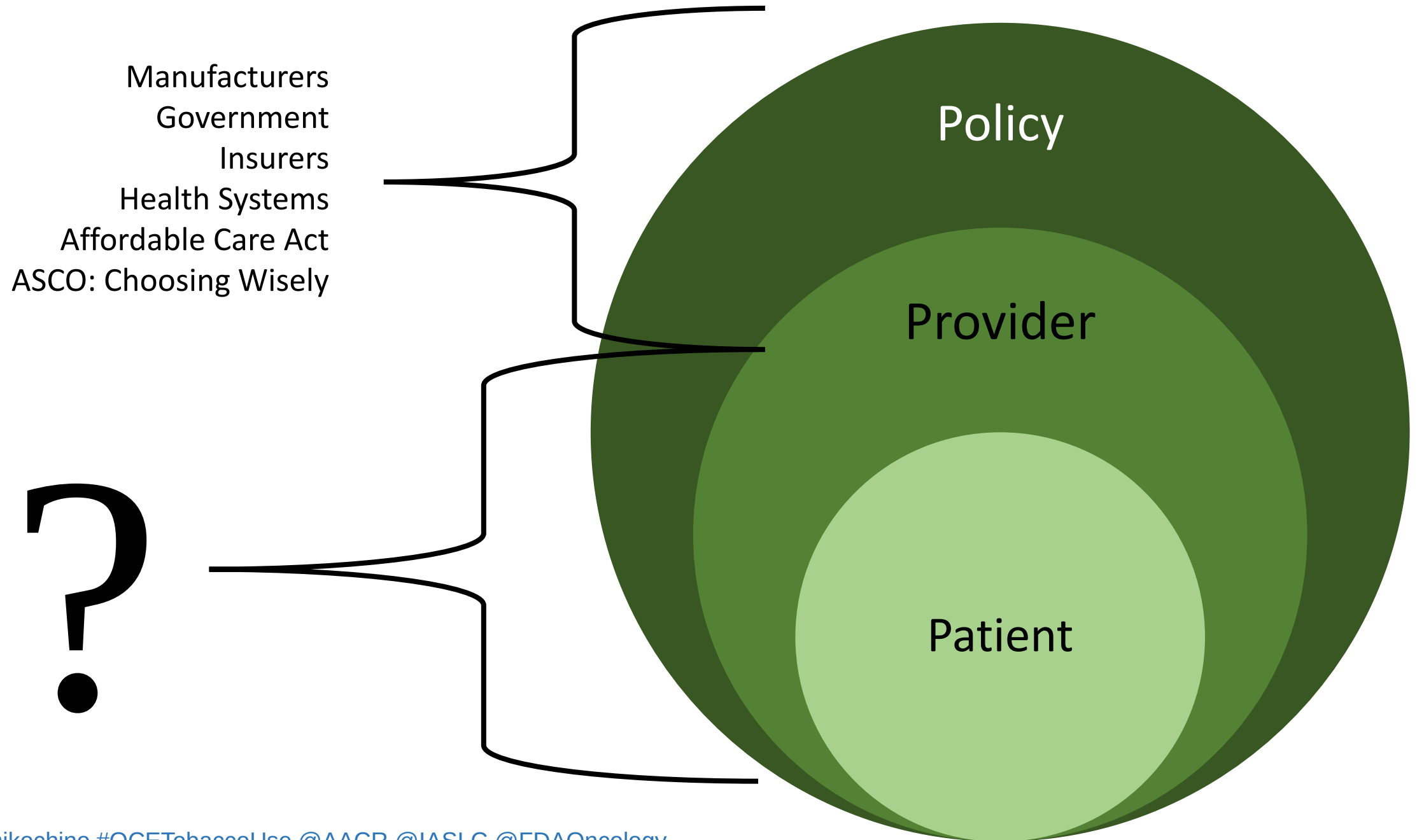
Avoid using PET or PET-CT scanning as part of routine follow-up care to monitor for a cancer recurrence in asymptomatic patients who have finished initial treatment to eliminate the cancer unless there is high-level evidence that such imaging will change the outcome.

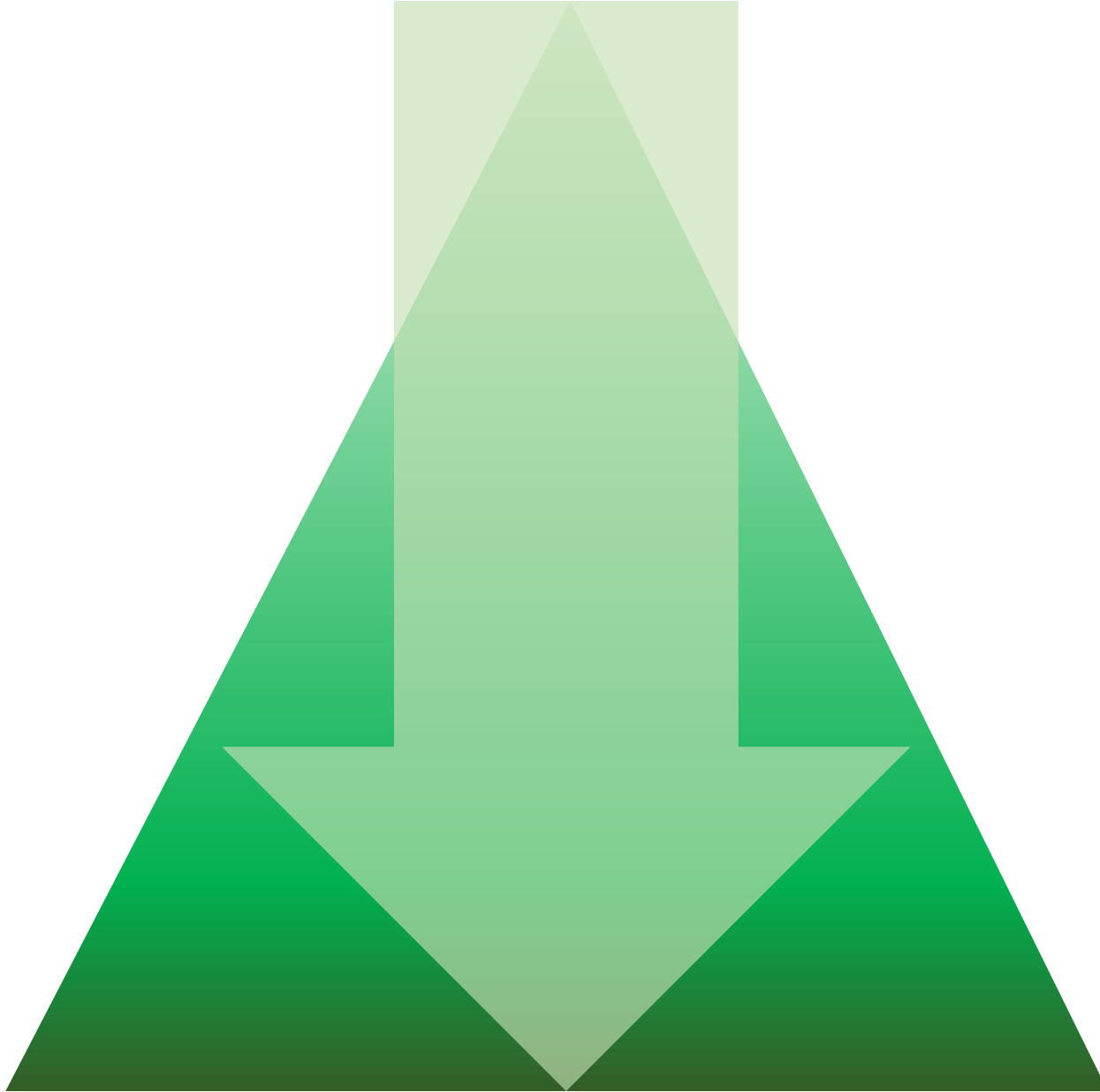
- PET and PET-CT are used to diagnose, stage and monitor how well treatment is working. Available evidence from clinical studies suggests that using these tests to monitor for recurrence does not improve outcomes and therefore generally is not recommended for this purpose.
- False positive tests can lead to unnecessary and invasive procedures, overtreatment, unnecessary radiation exposure and incorrect diagnoses.
- Until high level evidence demonstrates that routine surveillance with PET or PET-CT scans helps prolong life or promote well-being after treatment for a specific type of cancer, this practice should not be done.

10

Don't use a targeted therapy intended for use against a specific genetic aberration unless a patient's tumor cells have a specific biomarker that predicts an effective response to the targeted therapy.

- Unlike chemotherapy, targeted therapy can significantly benefit people with cancer because it can target specific gene products, i.e., proteins that cancer cells use to grow and spread, while causing little or no harm to healthy cells. Patients who are most likely to benefit from targeted therapy are those who have a specific biomarker in their tumor cells that indicates the presence or absence of a specific gene alteration that makes the tumor cells susceptible to the targeted agent.
- Compared to chemotherapy, the cost of targeted therapy is generally higher, as these treatments are newer, more expensive to produce and under patent protection. In addition, like all anti-cancer therapies, there are risks to using targeted agents when there is no evidence to support their use because of the potential for serious side effects or reduced efficacy compared with other treatment options.





1° Prevention:

Prevent disease or injury before it ever occurs

2° Prevention:

Reduce impact by detecting and treating disease or injury as soon as possible

3° Prevention:

Soften the impact of an ongoing illness or injury that has lasting effects

1° Prevention:

Prevent Financial Toxicity from Forming

Patient Level:

- Education
- Optimize Insurance (Financial Navigators)
- Improve Access (maintain work, health insurance)



Provider Level:

- Education
- Value Based Care (ASCO Value Framework)
- Cost aware prescribing patterns

2° Prevention:

Screen for Financial Toxicity Early and Often

PROBLEM LIST

Please indicate if any of the following has been a problem for you in the past week including today.

Be sure to check YES or NO for each.

YES	NO	<u>Practical Problems</u>	YES	NO	<u>Physical Problems</u>
-----	----	---------------------------	-----	----	--------------------------

- | | | | | | |
|--------------------------|--------------------------|---------------------|--------------------------|--------------------------|----------------------|
| ☐ | ☐ | Child care | ☐ | ☐ | Appearance |
| ☐ | ☐ | Housing | ☐ | ☐ | Bathing/dressing |
| ☐ | ☐ | Insurance/financial | ☐ | ☐ | Breathing |
| ☐ | ☐ | Transportation | ☐ | ☐ | Changes in urination |
| ☐ | ☐ | Work/school | | | |
| ☐ | ☐ | Treatment decisions | | | |

Family Problems

- | | | |
|--------------------------|--------------------------|--------------------------|
| ☐ | ☐ | Dealing with children |
| ☐ | ☐ | Dealing with partner |
| ☐ | ☐ | Ability to have children |
| ☐ | ☐ | Family health issues |

Emotional Problems

- | | | |
|--------------------------|--------------------------|------------|
| ☐ | ☐ | Depression |
|--------------------------|--------------------------|------------|

- | | | |
|--------------------------|--------------------------|----------------------|
| ☐ | ☐ | Getting things done |
| ☐ | ☐ | Indigestion |
| ☐ | ☐ | Memory/forgetfulness |
| ☐ | ☐ | Mouth problems |
| ☐ | ☐ | Nausea |

National Comprehensive Cancer Network (NCCN) Problem List

YES	NO	<u>Practical Problems</u>
-----	----	---------------------------

- | | | |
|--------------------------|--------------------------|---------------------|
| ☐ | ☐ | Child care |
| ☐ | ☐ | Housing |
| ☐ | ☐ | Insurance/financial |
| ☐ | ☐ | Transportation |
| ☐ | ☐ | Work/school |



The COmprehensive Score for Financial Toxicity (COST)

<http://www.facit.org/facitorg/questionnaires>

Cost of Cancer Care

 THE UNIVERSITY OF
CHICAGO

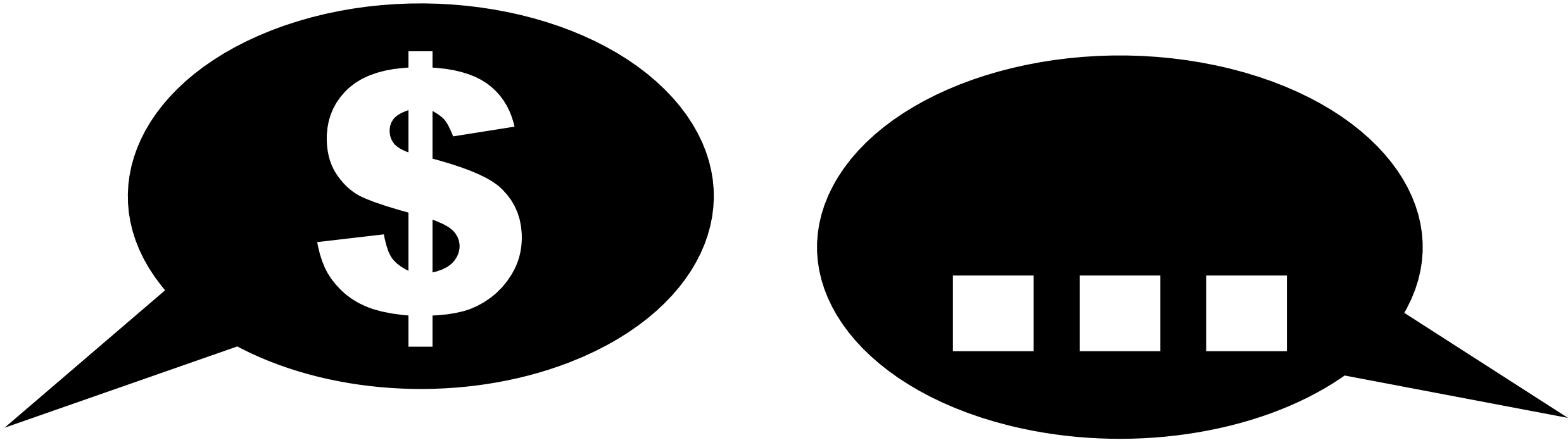
[Home](#) [Resources for You](#) [Understand Your Financial Toxicity](#) [Participate](#) [About](#) [Contact](#)

Below is a list of statements that other people with your illness have said are important. Please mark your response as it applies to you when considering the past 7 days.

	Not at all	A little bit	Somewhat	Quite a bit	Very much
I know that I have enough money in savings, retirement, or assets to cover the costs of my treatment.	☐	☐	☐	☐	☐
My out-of-pocket medical expenses are more than I thought they would be.	☐	☐	☐	☐	☐
I worry about the financial problems I will have in the future as a result of my illness or treatment.	☐	☐	☐	☐	☐
I feel I have no choice about the amount of money I spend on care.	☐	☐	☐	☐	☐
I am frustrated that I cannot work or contribute as much as I usually do.	☐	☐	☐	☐	☐
I am satisfied with my current financial situation.	☐	☐	☐	☐	☐
I am able to meet my monthly expenses.	☐	☐	☐	☐	☐
I feel financially stressed.	☐	☐	☐	☐	☐
I am concerned about keeping my job and income, including work at home.	☐	☐	☐	☐	☐
My cancer or treatment has reduced my satisfaction with my present financial situation.	☐	☐	☐	☐	☐
I feel in control of my financial situation.	☐	☐	☐	☐	☐

3° Prevention:

Soften the effects of Financial Toxicity



Simply **asking patients** if they have difficulty paying for their medical care is an important means for oncologists to ally themselves with patients. Talking about money is never easy. But when doctors are reluctant to talk about medical costs, a patient's health can be undermined.

Cost Conversations



50-80% cancer patients desire a cost conversation with oncologist

But only **19%** actually talked to their doctor

And only **28%** talked to ANY health care professional

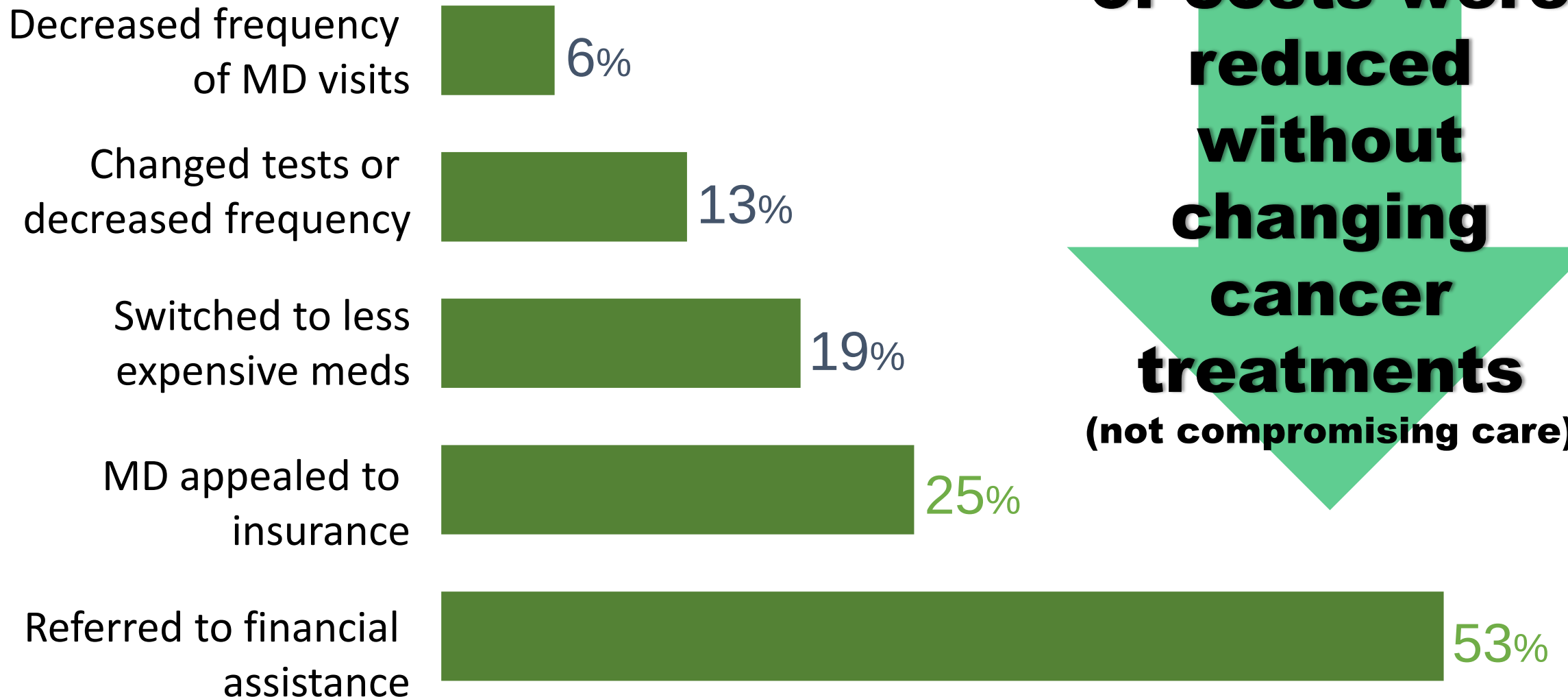


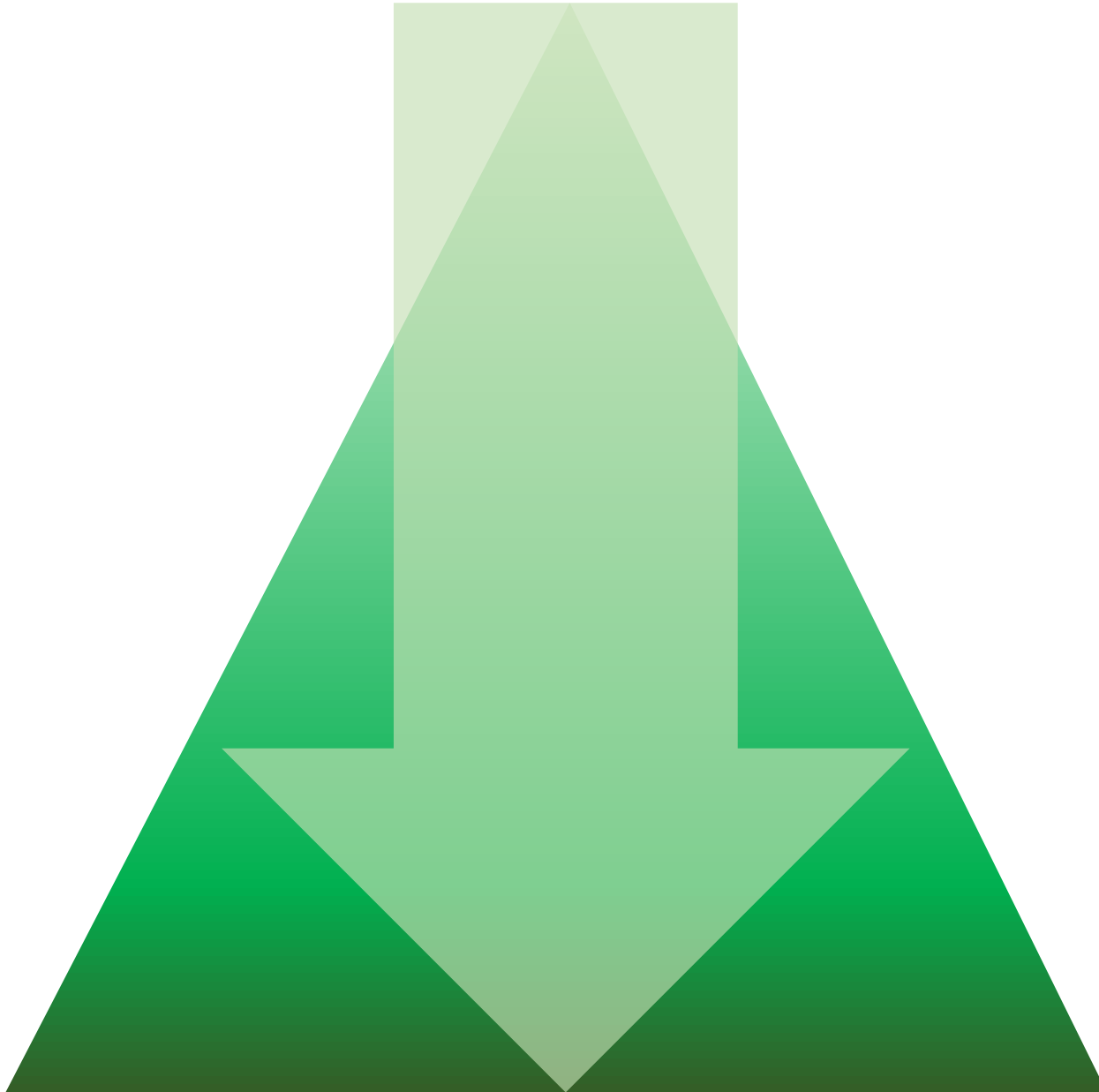
**Over
50%**

of those who discussed
their costs reduced them



How did cost conversations help?





1° Prevention:

Education, optimized insurance, value based care

2° Prevention:

Diagnose early by screening often

3° Prevention:

Normalize cost conversations, refer for assistance when appropriate



Next step: Flip the pyramid

1° Prevention:

Education, optimized insurance,
value based care

2° Prevention:

Diagnose early by screening often

3° Prevention:

Normalize cost conversations,
refer for assistance when
appropriate

Mitigating Financial Toxicity *is Possible*

... but Financial Toxicity *is Growing* in the US

... and Cancer Outcomes are *at Risk*



Thank you.

 [@fumikochino](#) [#OCETobaccoUse](#) [@AACR](#) [@IASLC](#) [@FDAOncology](#)



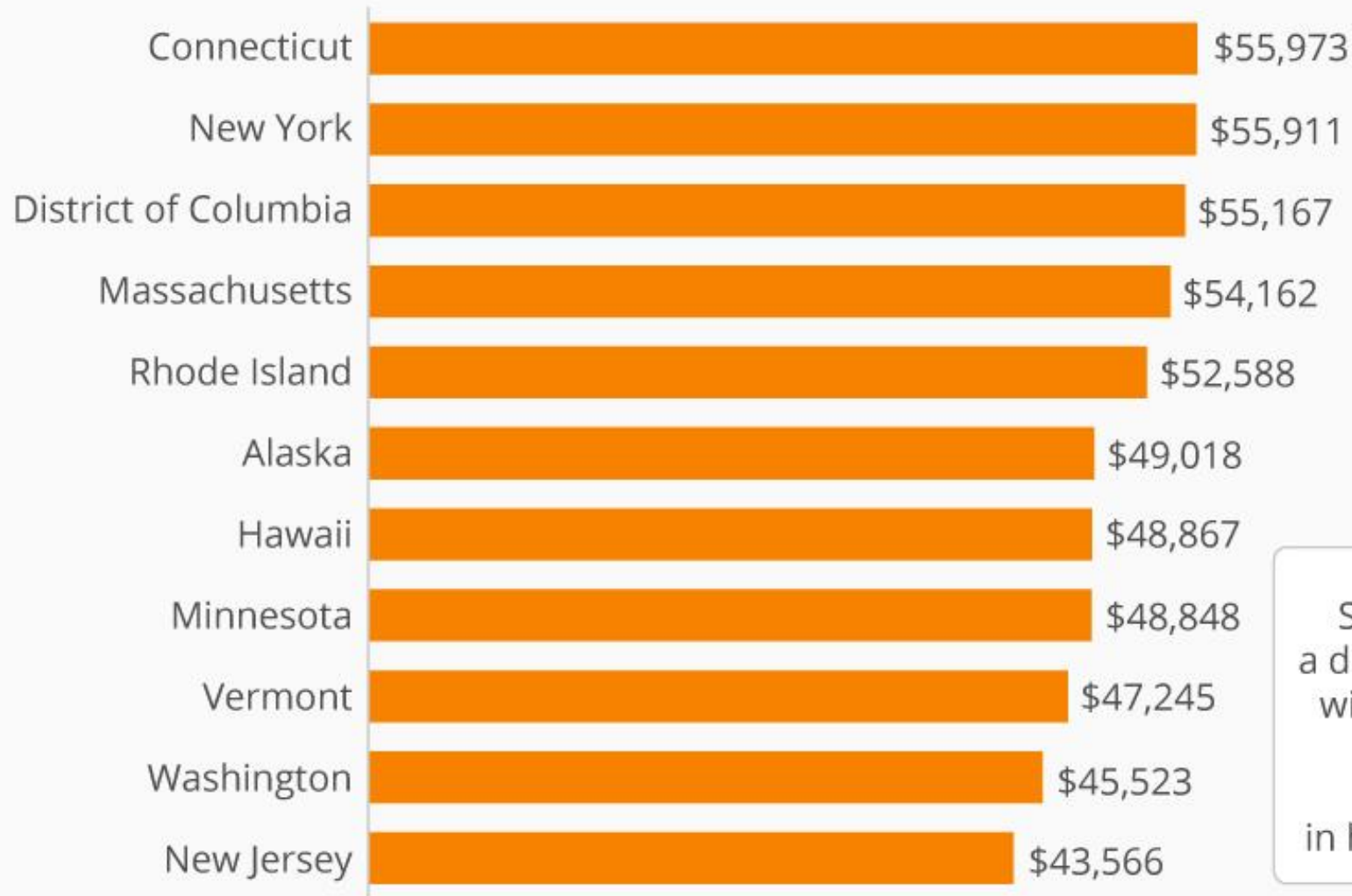


Extra Slides



Smoking Also Has Serious Financial Repercussions

Average cost per smoker associated with smoking one pack of cigarettes per day*



Smoking a pack a day in Connecticut will cost a smoker an average of **\$2.8 million** in his or her lifetime



@StatistaCharts

* 2019. Includes cost of a pack per day, health care expenditures, income losses and other costs.

Source: WalletHub

statista



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ADMINISTRATION



American Association
for Cancer Research

FINDING CURES TOGETHER™



INTERNATIONAL
ASSOCIATION
FOR THE STUDY
OF LUNG CANCER
Conquering Thoracic Cancers Worldwide

SESSION V:

Future Directions & Next Steps

Session Moderator: Stephanie Land, PhD

Speakers:

Srikumar Chellappan, PhD

Paul A. Bunn, Jr., MD, FASCO

Shakun Malik, MD

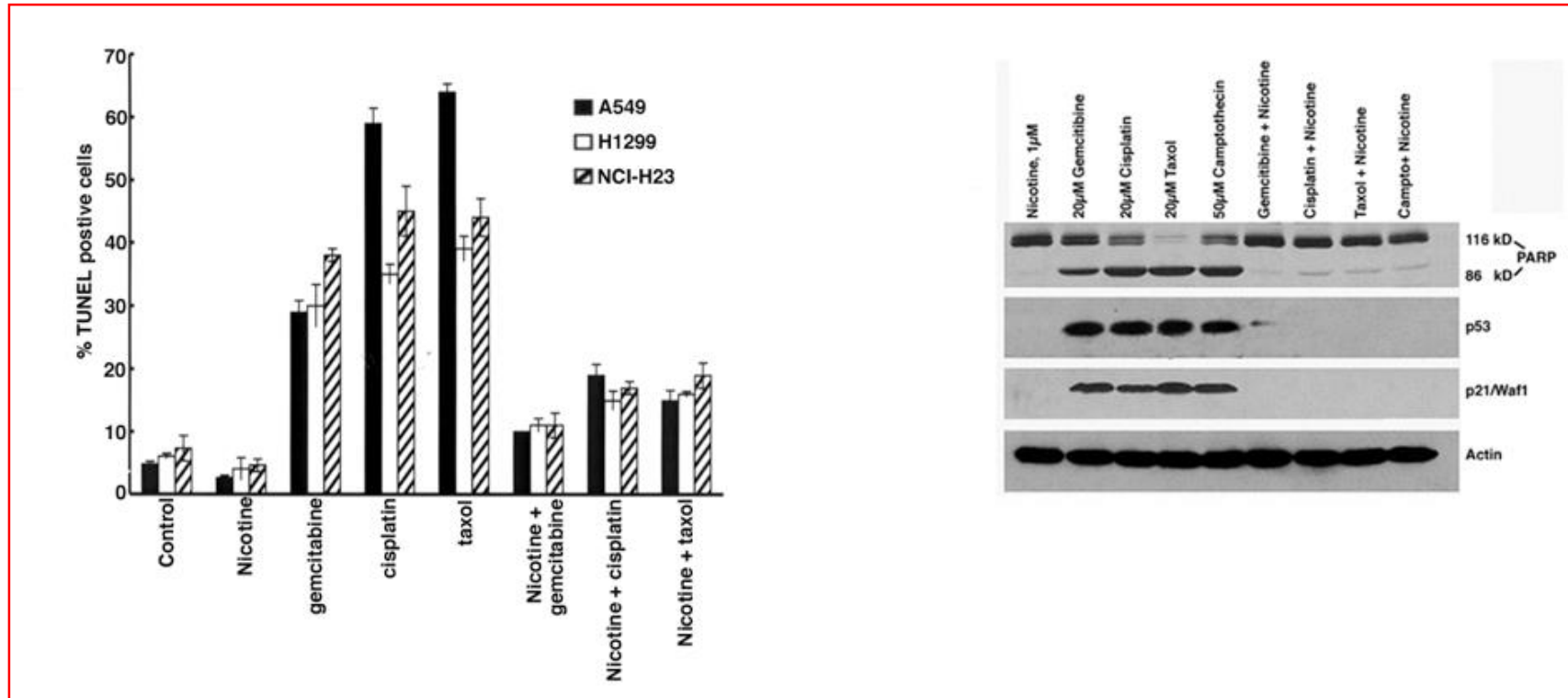
Nicotine, Smoking and Response to Therapy: Future Directions



Srikumar Chellappan, Ph.D.
Moffitt Distinguished Scholar
Chair, Dept. of Tumor Biology
H. Lee Moffitt Cancer Center and Research Institute
Tampa, FL 33612.

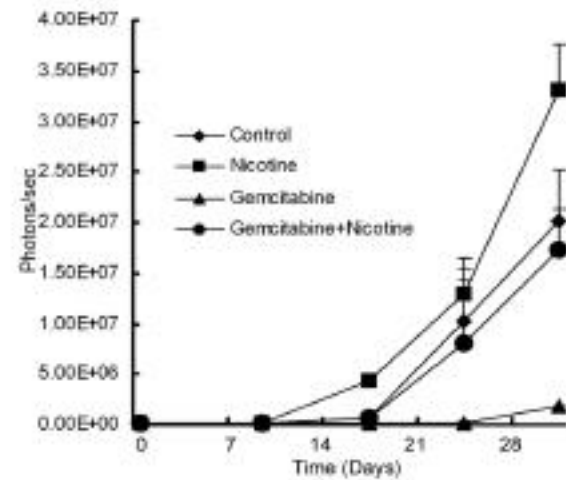
A. What we know:

- Patients who continue to smoke after cancer diagnosis have a worse outcome than non-smokers
- Smoking and exposure to nicotine confers resistance to chemotherapeutic agents

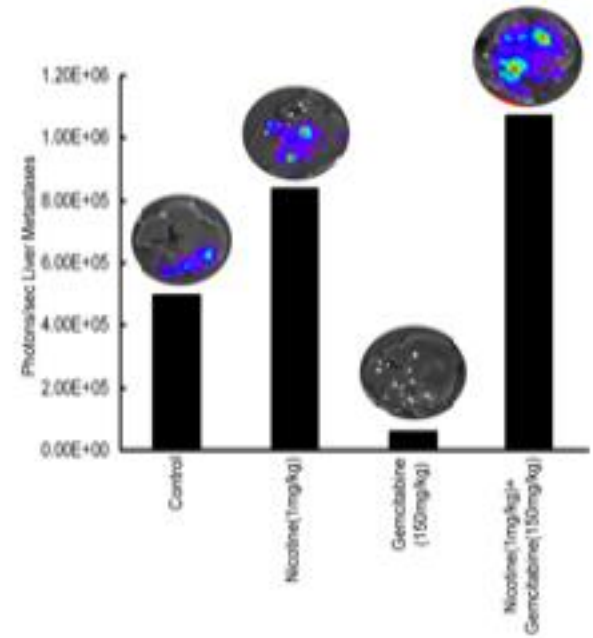
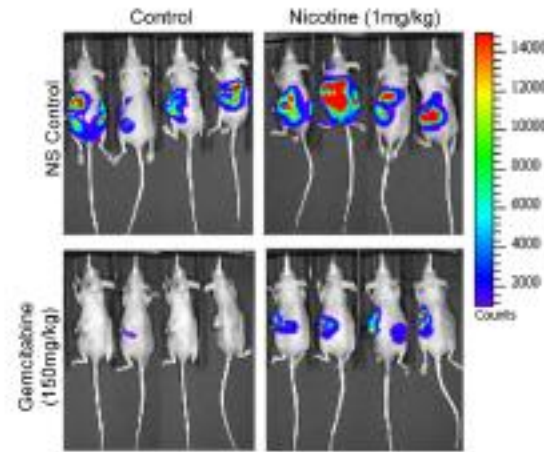


Nicotine can inhibit apoptosis induced by chemotherapeutic drugs in cultured cells: Dasgupta et al., PNAS, 2006.

Exposure to nicotine promotes PDAC growth and negates the effect of chemotherapy

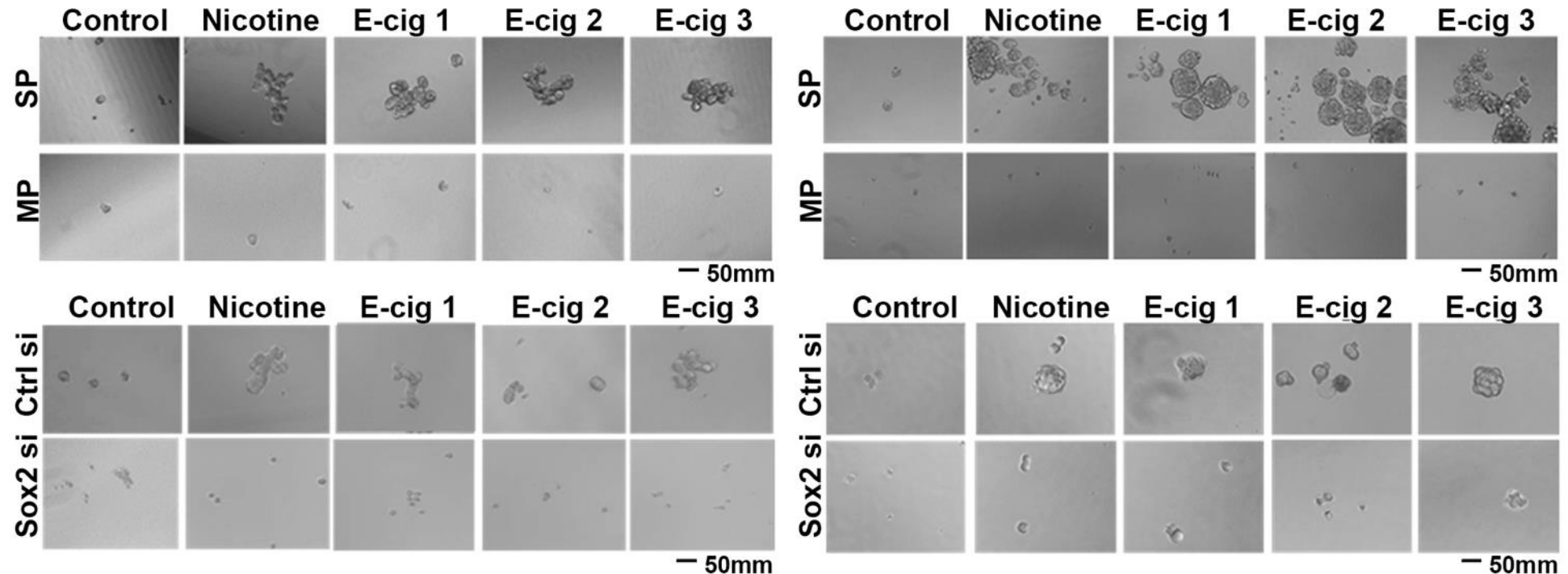
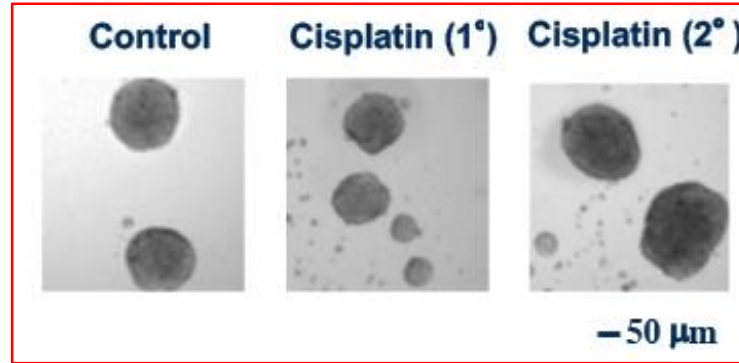


Tumor Growth



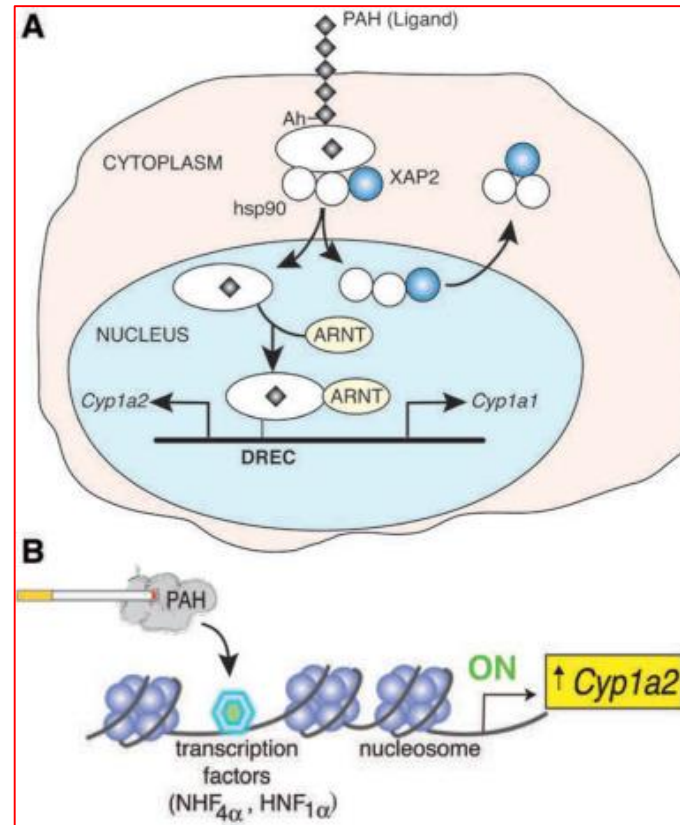
Liver metastasis

Nicotine and E-Cigarette extracts promote self-renewal of cancer stem-like cells



Smoking induces multiple proteins involved in drug metabolism

- Components of cigarette smoke induce drug metabolizing enzymes like cytochrome P450 and UDP-glucuronyltransferase



(O'Malley et al., JTO 9:917, 2014.)

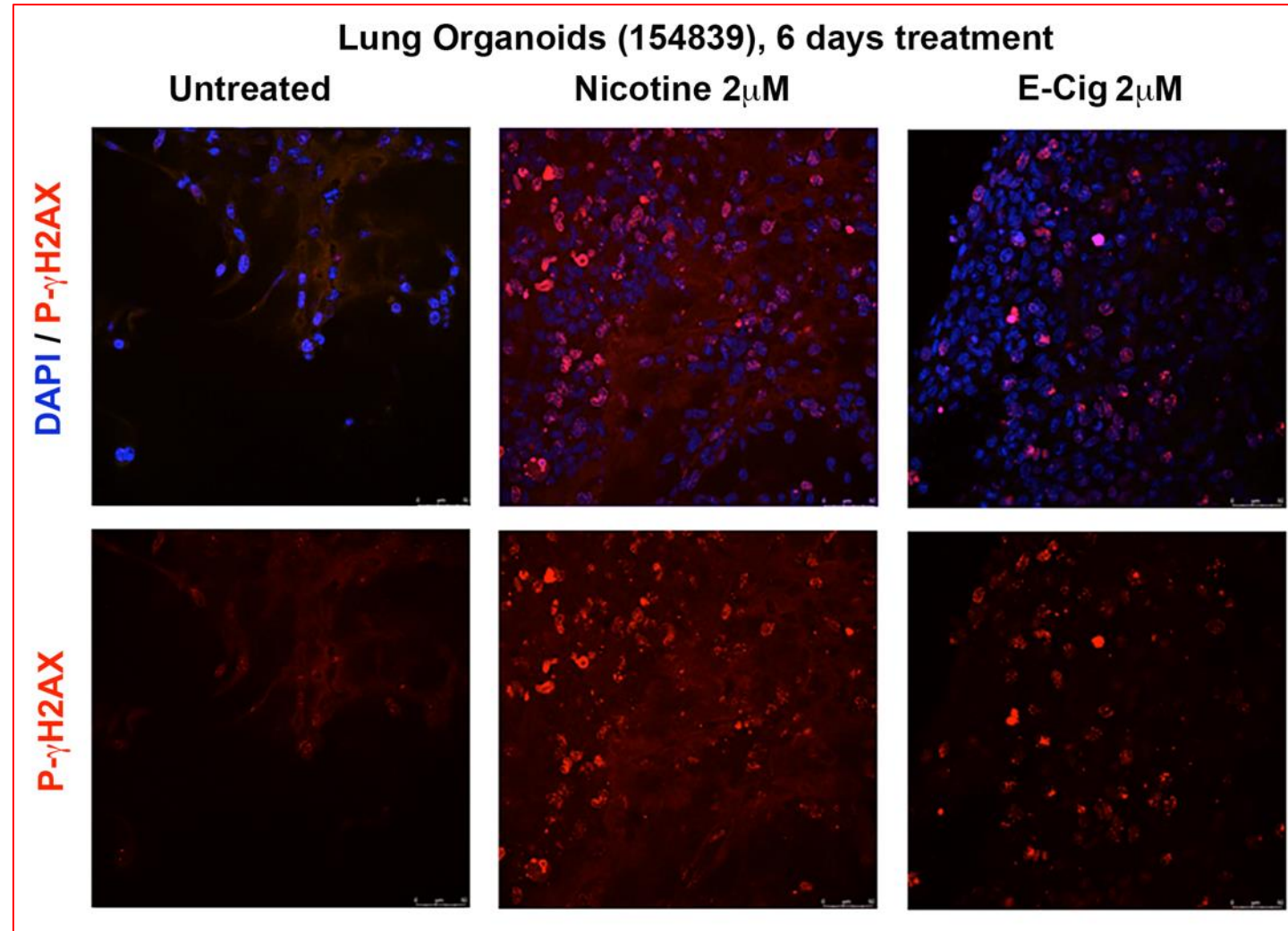
Tobacco smoke components facilitate the faster clearance of anti-cancer drugs

- Several chemotherapy drugs and targeted agents are metabolized and cleared through the action of these enzymes.
- Smoking can also affect the pharmacokinetics and pharmacodynamics of drugs, affecting their efficacy.
- Smokers receiving irinotecan or erlotinib showed rapid clearance of the drugs and required higher doses to obtain optimal systemic exposure.
- Thus, smoking status and exposure to tobacco smoke (and perhaps E-cigarettes) might affect the effective dose of the drugs in the body.

Tobacco smoke enhances the side effects of cancer treatment

- There is a statistically significant correlation between smoking and treatment-related toxicities (*Peppone et al., The Oncologist, 2011.*).
- One study on 947 patients showed that smokers had a markedly higher symptom burden than non-smokers. Smokers reported a higher symptom burden during six-month follow up as well.
- Quitting smoking before treatment reduced the symptom burden of the patients.
- Thus capturing smoking status/history would reveal the extent of side effects that are solely due to the drugs and if they can be eliminated by smoking cessation.

Nicotine and E-Cigarette contents enhance the levels of γ -H2AX foci in NSCLC organoids



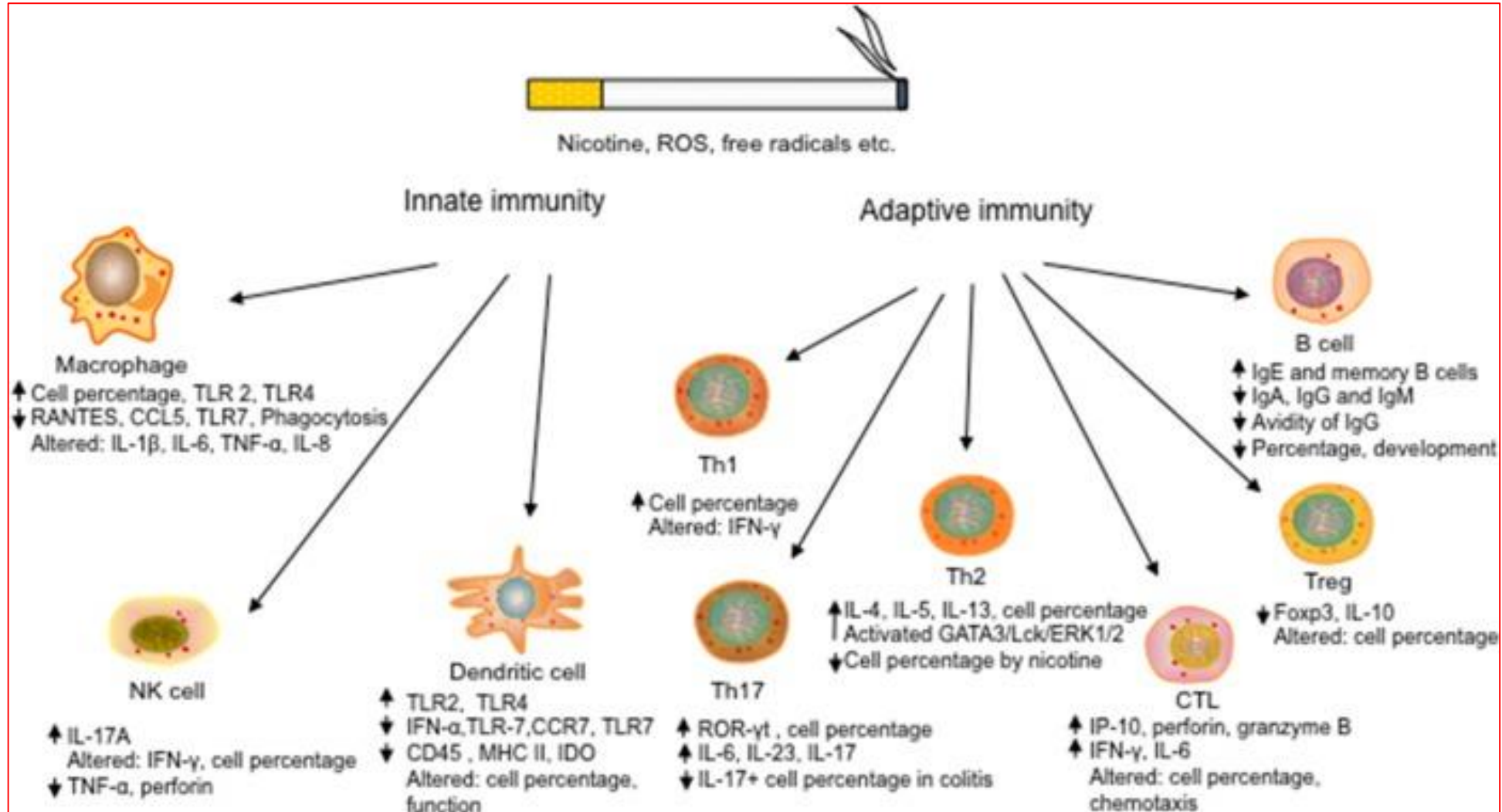
Tobacco smoke affects the response to radiotherapy

- It was reported more than 25 years ago that H&N cancer patients who continue to smoke while undergoing radiation therapy regimens had markedly lower rates of response (*Browman et al., NEJM, 1993*).
- Similarly, H&N cancer patients showed a significantly lower overall five-year survival rate compared to non-smokers who underwent radiation therapy
- Two year survival rates of smokers undergoing radiation or chemoradiation were lower than non-smokers, especially those with Stage I/II NSCLC.
- Not sufficient information on how NRT or E-cigarettes affect response to radiotherapy.

Smoking and response to immunotherapy

- A significant amount of information on how smoking affects the immune response and the tumor immune microenvironment
- Tobacco smoke components significantly reduce innate immunity. Smoking reduces NK cell activity and production of IFN γ , alters the ratio of T helper cells and Tregs, impairs phagocytic functions etc.
- Adaptive immune cells affected by smoking mainly include T helper cells (Th1/Th2/Th17), CD4+CD25+ regulatory T cells, CD8+ T cells, B cells and memory T/B lymphocytes while innate immune cells impacted by smoking are mostly DCs, macrophages and NK cells.

Immune cells affected by tobacco smoke



(Qiu et al., Oncotarget 8:268, 2017)

Smoking and response to immune checkpoint inhibitors

- Tumors with higher mutational burden generally respond better to immune checkpoint inhibitors
- Tumors in smokers have higher mutational burden; but this is counterbalanced by the immunosuppressive effects of tobacco smoke.
- Further, nicotine and other tobacco smoke components have been found to induce the expression of PD-L1 and similar immunosuppressive ligands to abrogate anti-tumor immunity.
- Substantially different results were obtained in different clinical trials as to how smoking status affects the response to immunotherapy.
- In certain studies, the smoking signature for gene expression predicted higher response than smoking history itself.

B. Unresolved Questions:

- It is not clear how smoking status and exposure to tobacco smoke affects the PK/PD and thus the effective systemic exposure of drugs. This would be vital in evaluating the efficacy of novel small-molecule inhibitors.
- It would be vital to assess how smoking status affects overall symptom burden, and side effects of new drugs.
- Smoking status is a confounding factor in the response to immunotherapy; a significant amount of additional data would be needed to assess how smoking affects immune checkpoint therapy.

C. Conclusion/Recommendation

- Capturing smoking history and smoking status would greatly enhance the ability to assess the efficacy of novel therapeutic strategies more accurately.
- Assessing smoking status would also enable the clinicians to encourage smoking cessation efforts, which would benefit the patients.
- Capturing the use of electronic cigarettes would also generate valuable information on how these newer nicotine delivery systems affect therapeutic agents.

Questions?

Future Directions in Tobacco Use Assessment in Oncology Therapeutic Trials

**Paul A. Bunn, Jr, MD, Distinguished and Dudley Professor,
Univ. of Colorado Cancer Center, Aurora, CO 80045**

Health Benefits of Quitting Smoking

Major Conclusions of the Report

1. Smoking cessation is beneficial at any age. Smoking cessation improves health status and enhances quality of life.
2. Smoking cessation reduces the risk of premature death and can add as much as a decade to life expectancy.
3. Smoking places a substantial financial burden on smokers, healthcare systems, and society. Smoking cessation reduces this burden, including smoking-attributable healthcare expenditures.
4. Smoking cessation reduces risk for many adverse health effects, including reproductive health outcomes, cardiovascular diseases, chronic obstructive pulmonary disease, and cancer. Quitting smoking is also beneficial to those who have been diagnosed with heart disease and chronic obstructive pulmonary disease.
5. More than three out of five U.S. adults who have ever smoked cigarettes have quit. Although a majority of cigarette smokers make a quit attempt each year, less than one-third use cessation medications approved by the U.S. Food and Drug Administration or behavioral counseling to support quit attempts.
6. Considerable disparities exist in the prevalence of smoking across the U.S. population, with higher prevalence in some subgroups. Similarly, the prevalence of key indicators of smoking cessation—quit attempts, receiving advice to quit from a health professional, and using cessation therapies—also varies across the population, with lower prevalence in some subgroups.
7. Smoking cessation medications approved by the U.S. Food and Drug Administration and behavioral counseling are cost-effective cessation strategies. Cessation medications approved by the U.S. Food and Drug Administration and behavioral counseling

Quitting Smoking Saves Lives

Tobacco smoke contains a deadly mix of more than 7,000 chemicals; hundreds are harmful, and about 70 cause cancer. Extensive research has proven that smoking harms nearly every organ of the body, causes many diseases, and reduces health overall.

The 1990 Surgeon General's report was the first report to review the scientific evidence on the health benefits of quitting smoking. The report was clear – quitting smoking has major and immediate health benefits for men and women of all ages.

The current report expands on the findings of the 1990 report, reaching several important conclusions about the health benefits of quitting smoking, including:

- ▶ Quitting smoking reduces the risk of premature death, improves health, and enhances quality of life. Quitting can add as much as 10 years to life expectancy.
- ▶ Quitting smoking lowers the risk for many adverse health effects, including poor reproductive health outcomes, cardiovascular diseases, COPD, and 12 types of cancer.

QUITTING SMOKING LOWERS THE RISK

for many adverse health effects, including reproductive health outcomes, cardiovascular diseases, COPD, and 12 types of cancer.

- ▶ Quitting smoking is also beneficial for people who have already been diagnosed with coronary heart disease or COPD.
- ▶ Quitting smoking reduces the costs of smoking for people who smoke, healthcare systems, and society.
- ▶ While quitting earlier in life yields greater health benefits, quitting smoking is beneficial to health at any age. Even people who have smoked for many years or have smoked heavily will benefit from quitting.

Smoking Cessation

A Report of the Surgeon General
Executive Summary



U.S. Department of Health and Human Services

But does quitting at the institution of therapy affect
The therapeutic outcome of cancer therapy including
Surgery, radiotherapy, chemotherapy, targeted therapy
And immunotherapy?

10 Potential Reasons collect continued Smoking status on lung cancer trials*

1	Quitting may improve Cancer Survival and Lower Recurrence
2	Quitting may lower the Risk of Death From Other Causes
3	Quitting may lower the Risk of Surgical Complications
4	Quitting may Lessen Complications and Makes Radiation Therapy Work Better
5	Smoking Can Decrease the Effect of Chemotherapy and Raise Complications
6	Smoking may lower the Effect of Targeted Therapies
7	Quitting may lower the Risk of a Second Cancer
8	Quitting Smoking Improves Quality of Life
9	Quitting Lowers Risk for Family and Friends
11	Quitting may improve the effect of immunotherapy

- But the only way to prove these reasons to quit are scientifically based is to require smoking status collection before and after institution of therapy

Tobacco Use in Oncology Therapeutic Trials: the Future

1. Tobacco Use Must be Assessed in Advanced Stage Therapeutic Trials before and after institution of therapy.

Should smoking status be a stratification factor?

2. Tobacco Use Must be Assessed in Locally Advanced Therapeutic Trials before and after institution of therapy.

Should smoking status be a stratification factor?

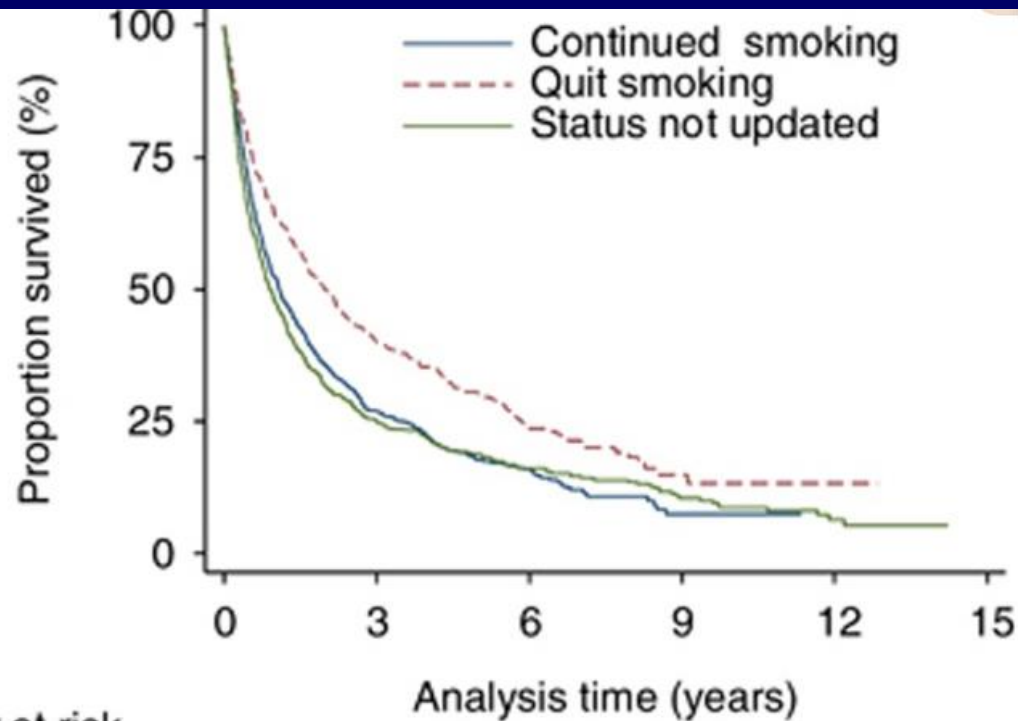
3. Tobacco Use Must be assessed in Early stage trials before and after institution of therapy.

Should smoking status be a stratification factor?

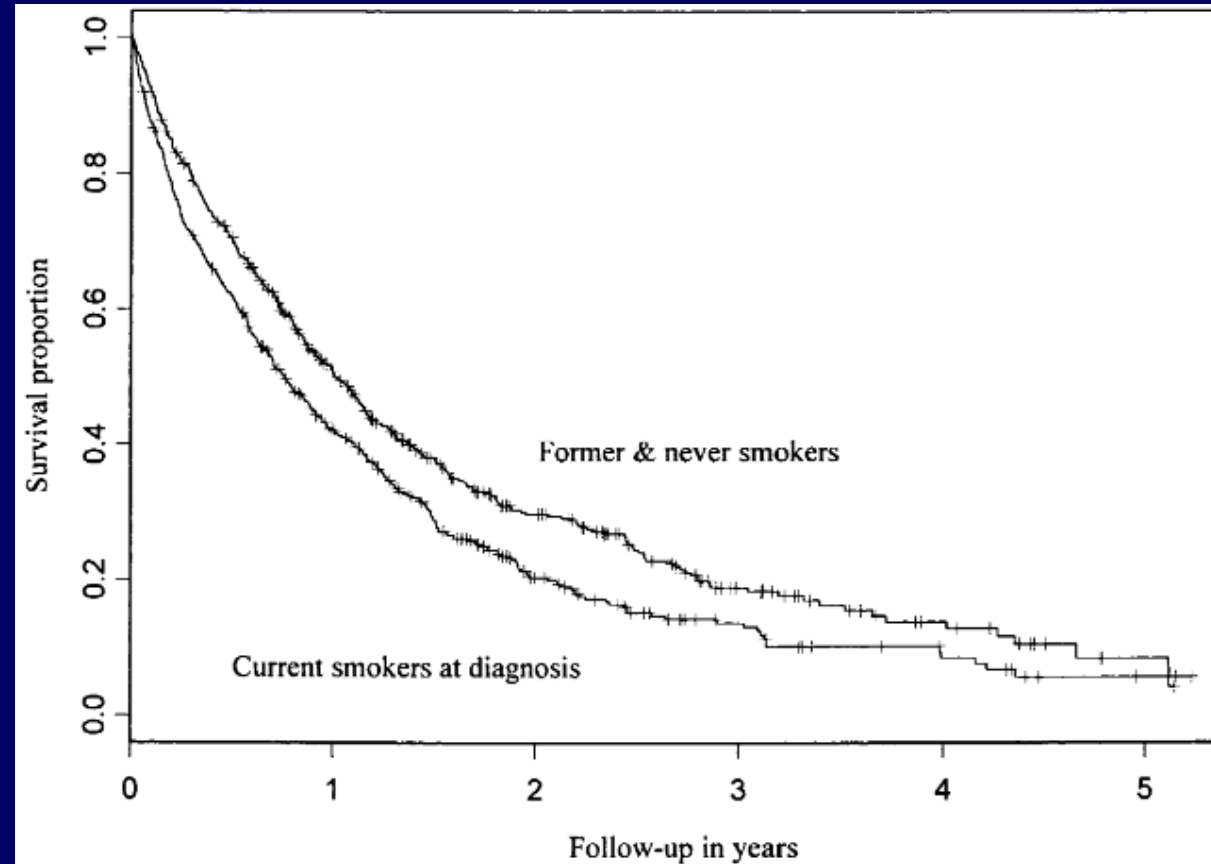
4. In prevention trials in patients at high risk for lung cancer is risk for adenocarcinoma different from squamous carcinoma? Does smoking cessation affect outcome? Should cessation be a stratification factor ,

5. Should tobacco cessation programs be a mandatory part of all trials?

Effects of continued smoking on survival after lung cancer diagnosis



Number at risk	0	3	6	9	12	15
Continued smoking	1129	184	52	8	0	0
Quit smoking	784	187	54	9	1	0
Status not updated	969	178	74	24	7	0



[Br J Cancer](#). 2017 Oct 10;117(8):1224-1232. doi: 10.1038/bjc.2017.179. Epub 2017 Sep 12.
Smoking cessation and survival in lung, upper aero-digestive tract and bladder cancer:
cohort study.

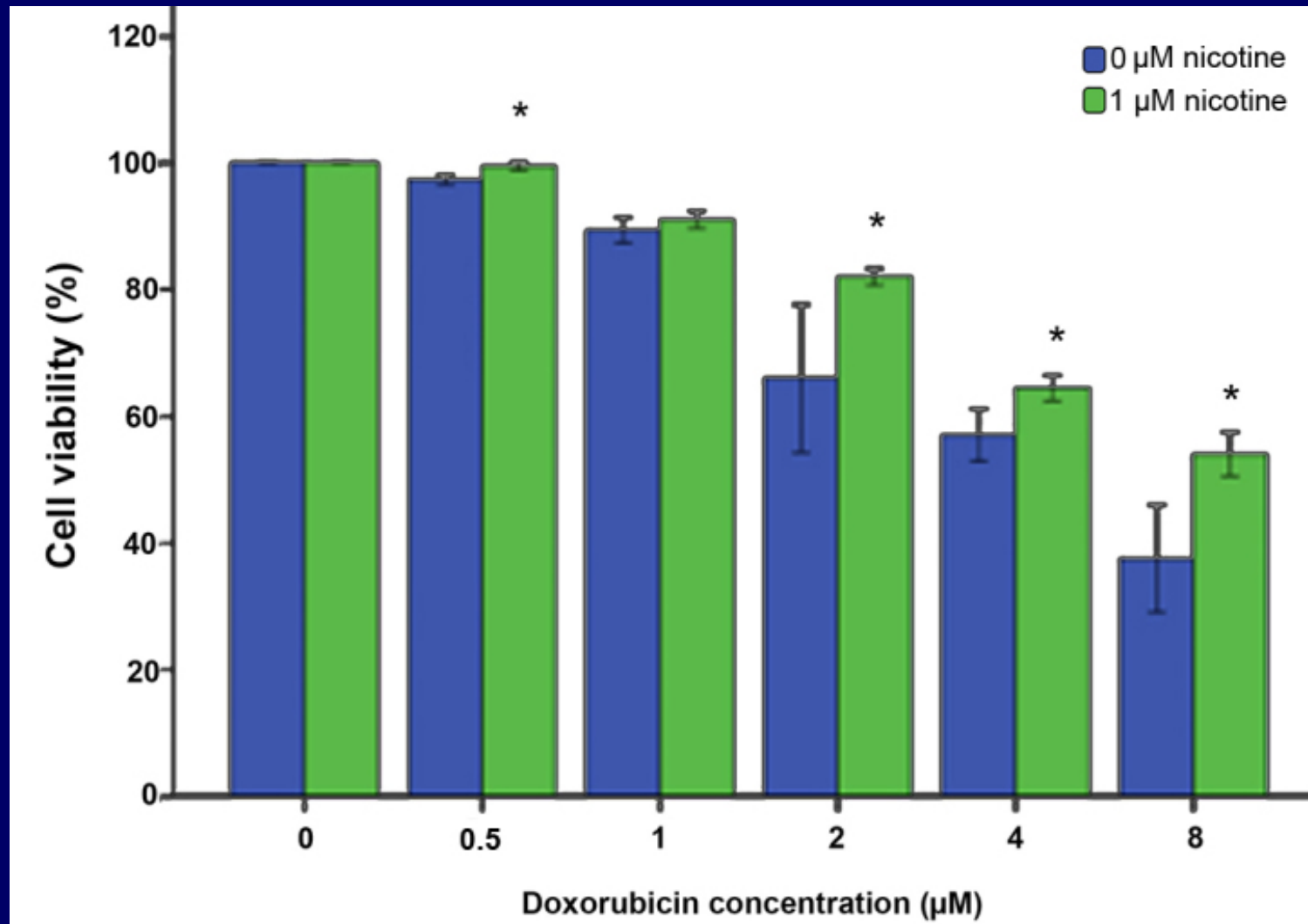
[Koshiaris C](#)¹, [Aveyard P](#)¹, [Oke J](#)¹, [Ryan R](#)², [Szatkowski L](#)³, [Stevens R](#)¹, [Farley A](#)²

[Chest](#). 2004 Jan;125(1):27-37.

Smoking and lung cancer survival: the role of comorbidity and treatment.
[Tammemagi CM](#)¹, [Neslund-Dudas C](#), [Simoff M](#), [Kvale P](#)

Tobacco Cessation appears to improve survival in advanced stages but data are too scarce to prove this.

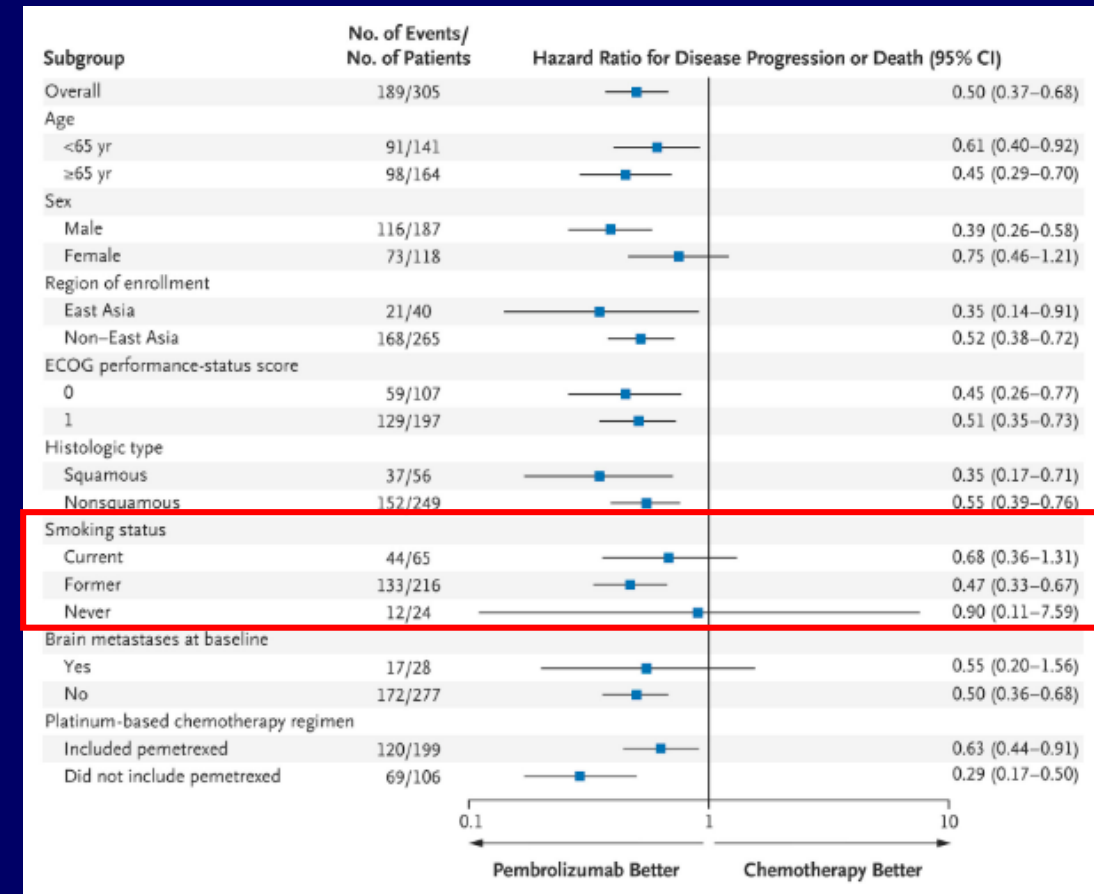
Nicotine decreases Effectiveness of doxorubicin



Does continued smoking affect immunotherapy response?

It appears that current smokers have higher PD-L1 expression and higher TMB than non-smokers and that they have higher objective response rates to checkpoint inhibitors. While there is insufficient evidence to draw firm conclusions, it appears that smokers who quit do better on checkpoint inhibitors than continuing smokers.

Thus, it is critical to collect this information in clinical trials and do multivariate analyses to determine if these smoking effects are independent of other variables



PACIFIC: Phase III, Randomized, Double-blind, Placebo-controlled, Multicenter, International Study in unresectable stage III NSCLC

- Patients with stage III, locally advanced, unresectable NSCLC who have not progressed following definitive platinum-based cCRT (≥2 cycles)
- 18 years or older
- WHO PS score 0 or 1
- Estimated life expectancy of ≥12 weeks
- Archived tissue was collected

All-comers population

1–42 days
post-cCRT

R

Durvalumab
10 mg/kg q2w for
up to 12 months
N=476

2:1 randomization,
stratified by age, sex,
and smoking history
N=713

Placebo
10 mg/kg q2w for
up to 12 months
N=237

Co-primary endpoints

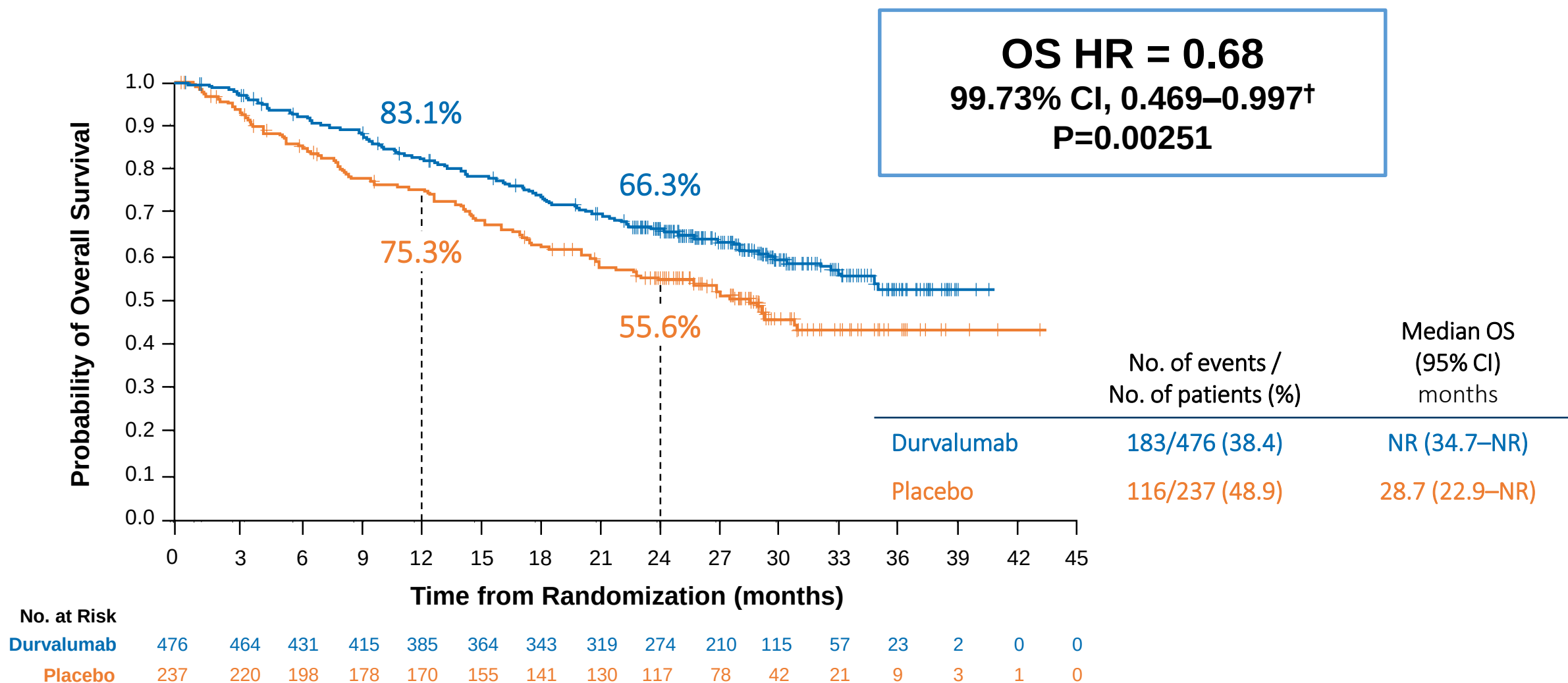
- PFS by BICR using RECIST v1.1*
- OS

Key secondary endpoints

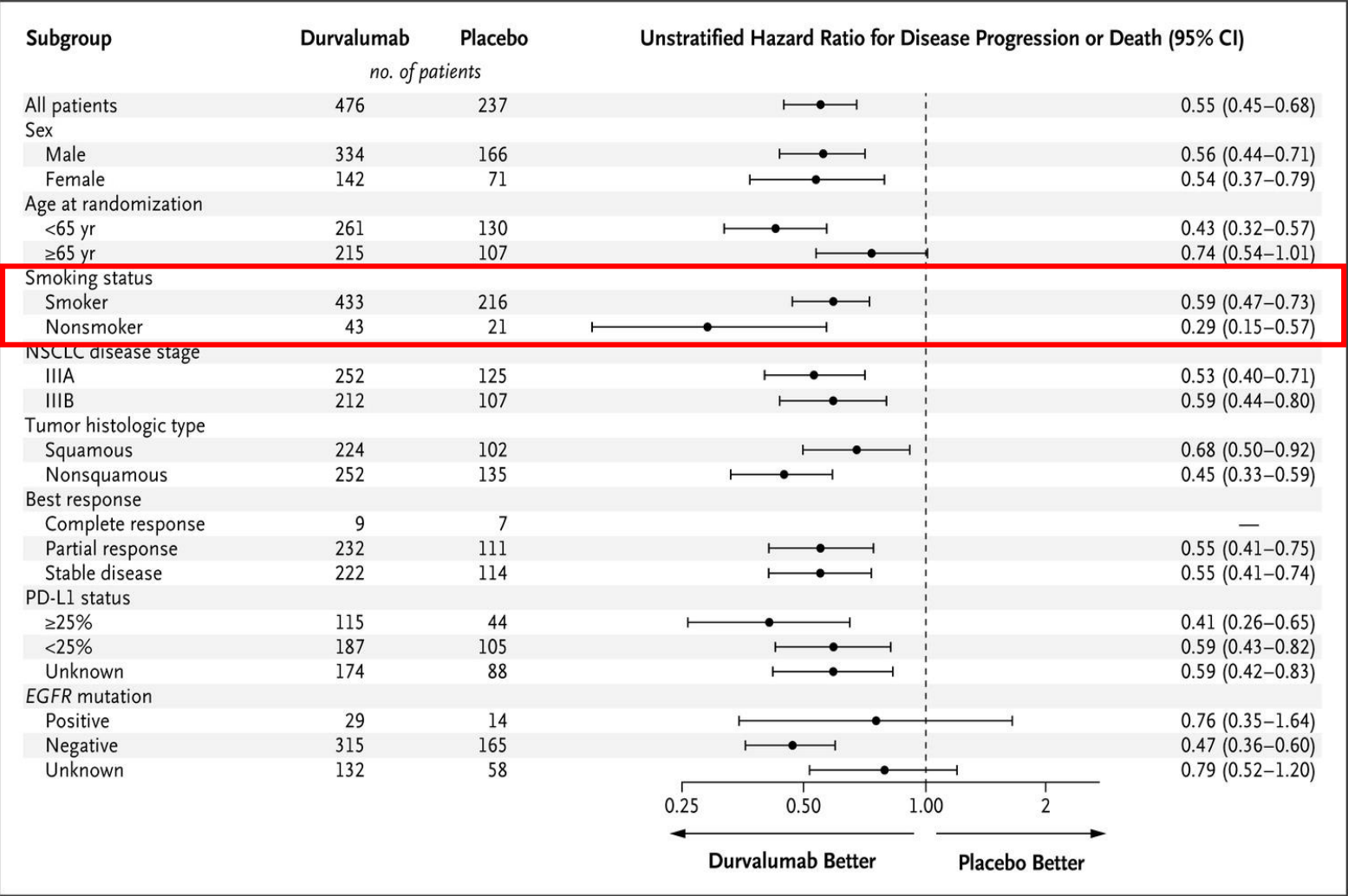
- ORR (per BICR)
- DoR (per BICR)
- Safety and tolerability
- PROs

*Defined as the time from randomization (which occurred up to 6 weeks post-cCRT) to the first documented event of tumor progression or death in the absence of progression.
ClinicalTrials.gov number: NCT02125461 BICR, blinded independent central review; cCRT, concurrent chemoradiation therapy; DoR, duration of response; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PROs, patient-reported outcomes; PS, performance status; q2w, every 2 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; WHO, World Health Organization

PACIFIC: Updated Overall Survival (ITT)

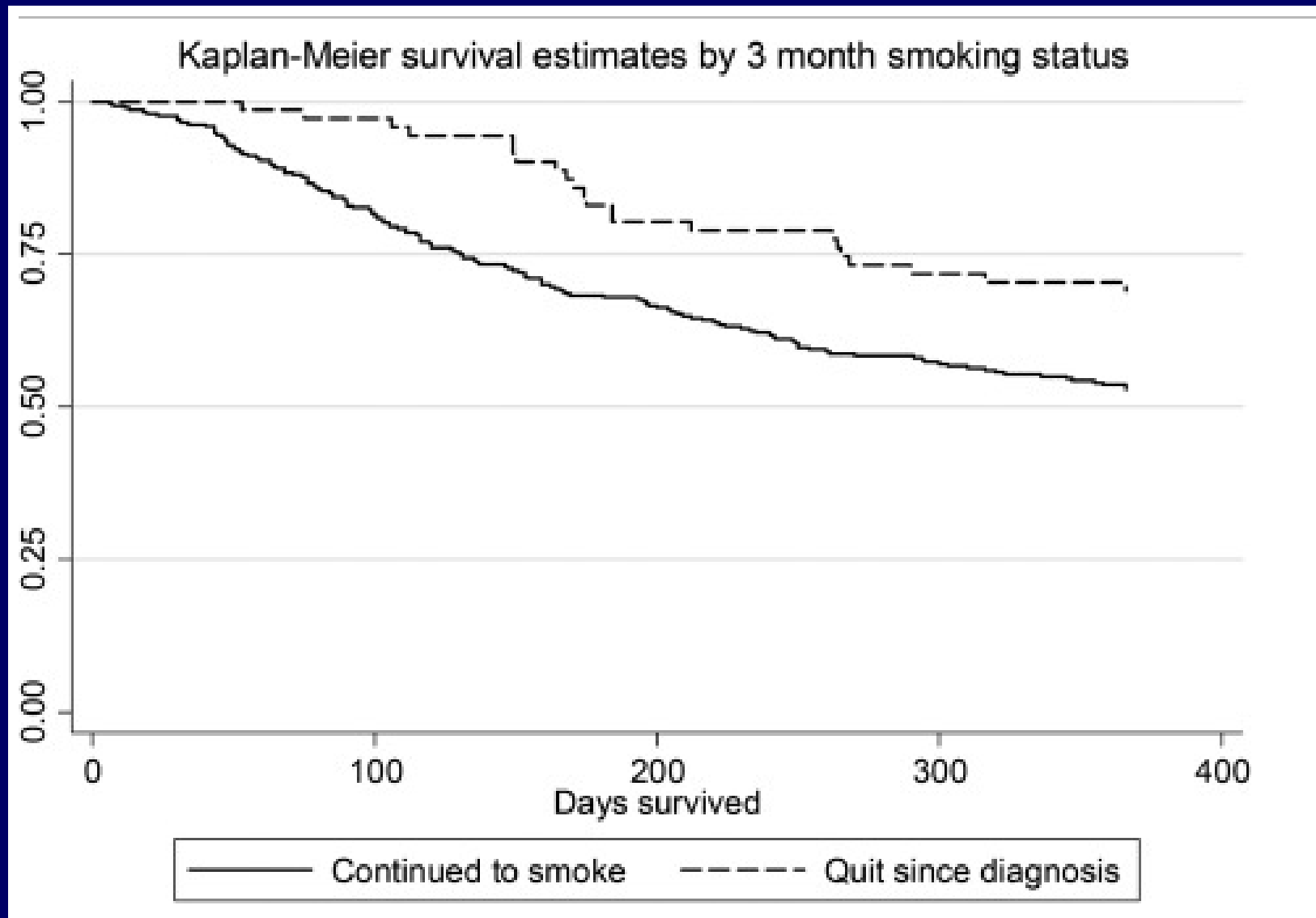


Pacific Trial of I/O Therapy in Stage 3 NSCLC: Subgroup Analysis of Prognostic Factors for Progression-free Survival in the Intention-to-Treat Population.



Both smokers and non-smokers benefitted from the durvalumab. While the benefit was greater in the never-smokers, and the survival differences were greatest in this subgroup, there are no data on whether smokers who quit had a better outcome than those who continued to smoke.

Effects of continued smoking on survival after early stage lung cancer diagnosis



Longitudinal study to assess impact of smoking at diagnosis and quitting on 1-year survival for people with non-small cell lung cancer

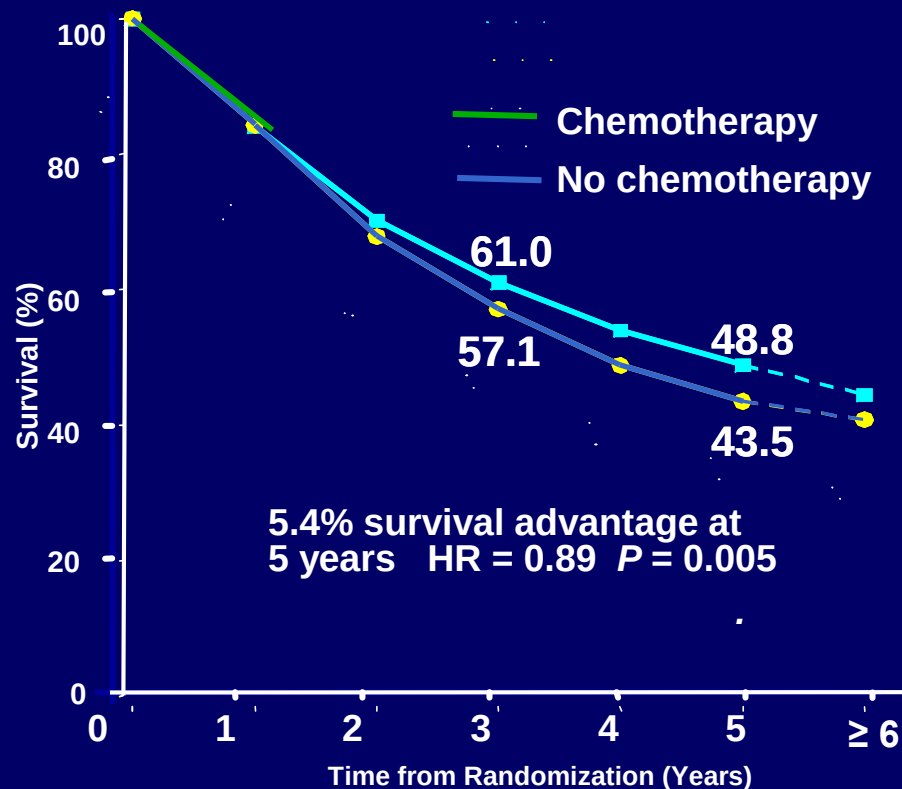
Author links open overlay panel Rachel E. Gemine^a Robin Ghosal^b Gareth Collier^b Diane Parry^c Ian Campbell^d Gareth Davies^e Kathryn Davies^f Keir E. Lewis^{g,h} on behalf of the LungCast Investigators

<https://doi.org/10.1016/j.lungcan.2018.12.028>

Meta-analyses of Adjuvant CT and Neoadjuvant CT

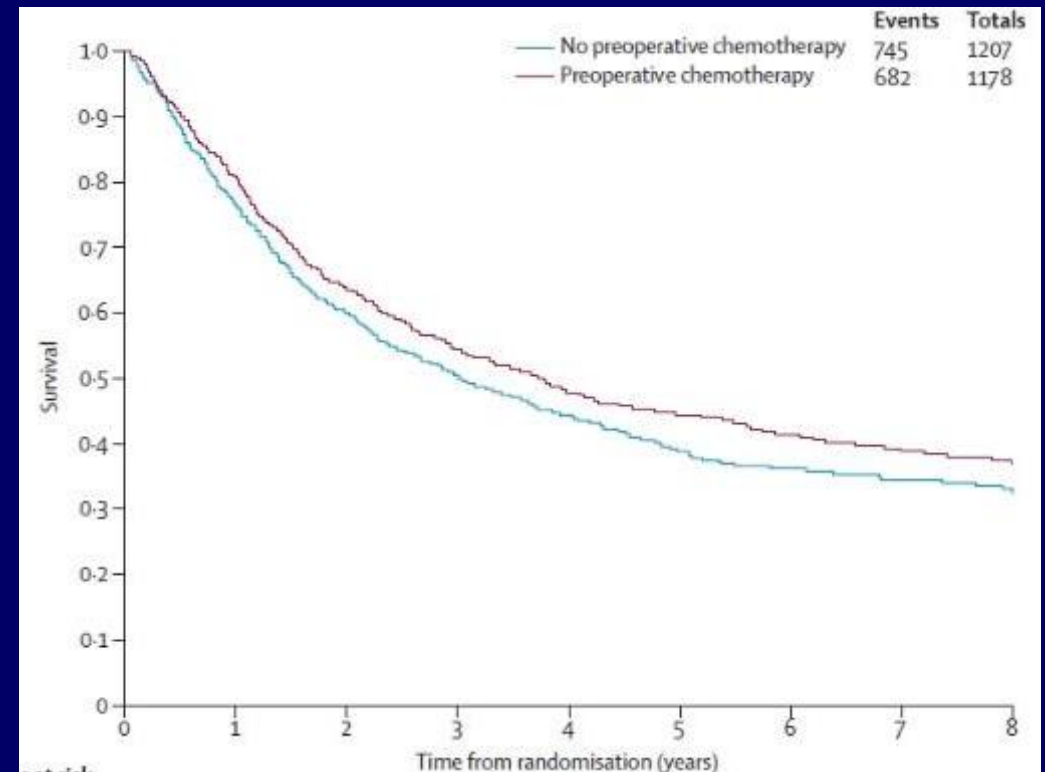
Platinum doublet chemotherapy has small but significant improvement in survival in both the adjuvant and neoadjuvant settings but there are no data on whether smoking cessation influences outcome.

LACE: Pooled Adjuvant Data Overall Survival



Pignon JP, et al. *J Clin Oncol.* 2008;26:3552-3559

NSCLC Neoadjuvant Collaborative Group meta-analysis



Lancet 2014;303:1561-71

Neoadjuvant I/O or I/O + CT Summary

Rx	N	mPR	pCR	ORR
Nivo	21	9 (43%)	NR	9.5%
Nivo or Nivo+Ipi	44	11/41 (25%)	8 (18%)	9 (20)
Atezo (LCMC3)	82	15 (18%)	4 (5%)	6 (7%)
Sintilimab	22	10 (45%)	3 (14%)	NR
Total I/O alone	169	45 (27%)	15/148 (10%)	24/147 (16%)
Nivo +CT	30	24 (80%)	18 (60%)	NR
Atezo +CT	14	7 (50%)	3 (21%)	8 (57%)
Total I/O + CT	44	31 (70%)	21 (48%)	8/14 (57%)

It appears that checkpoint inhibitors alone and with chemotherapy have higher mPR rates compared to chemotherapy alone, but there are no data on whether smoking status or smoking cessation influence outcomes.

NR=not reported

Ongoing Early Stage Randomized Immunotherapy Trials

Randomized Neoadjuvant Immunotherapy Trials			
Trial	Arms	# patients	SmokingStratification
Checkmate 816	Nivo/Ipi,plat doublet,nivo + plat. doublet	642	no
ImPower 030	Atezo+plat doublet vs plat doublet	302	no
Keynote 671	Pembro+placebo vs Pembro + plat. doublet	786	no
Canopy N	Canakinumab vs pembro vs canakinumab + pembro	110	No only stratification is histology

Adjuvant Immunotherapy Trials				
Trial	# Pts	Therapy	Endpoint	Smoking stratification
Pearls	1380	Pembro vs Placebo	DFS	No
BR31	1360	Durva vs placebo	DFS	No
IMPOWER 010	1127	Atezo vs placebo	DFS	No
ANVIL	714	Nivo vs placebo	OS/DFS	No; Stage, histology,other adj. rx,PD-L1
Canopy A	1500	Canikinumab vs placebo	OS/DFS	No

None of the trials stratify by smoking status nor track smoking cessation in smokers

Prior Task Force Recommended Timing of Assessment

- Minimal: registration and end of protocol therapy
- Recommended:

- 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

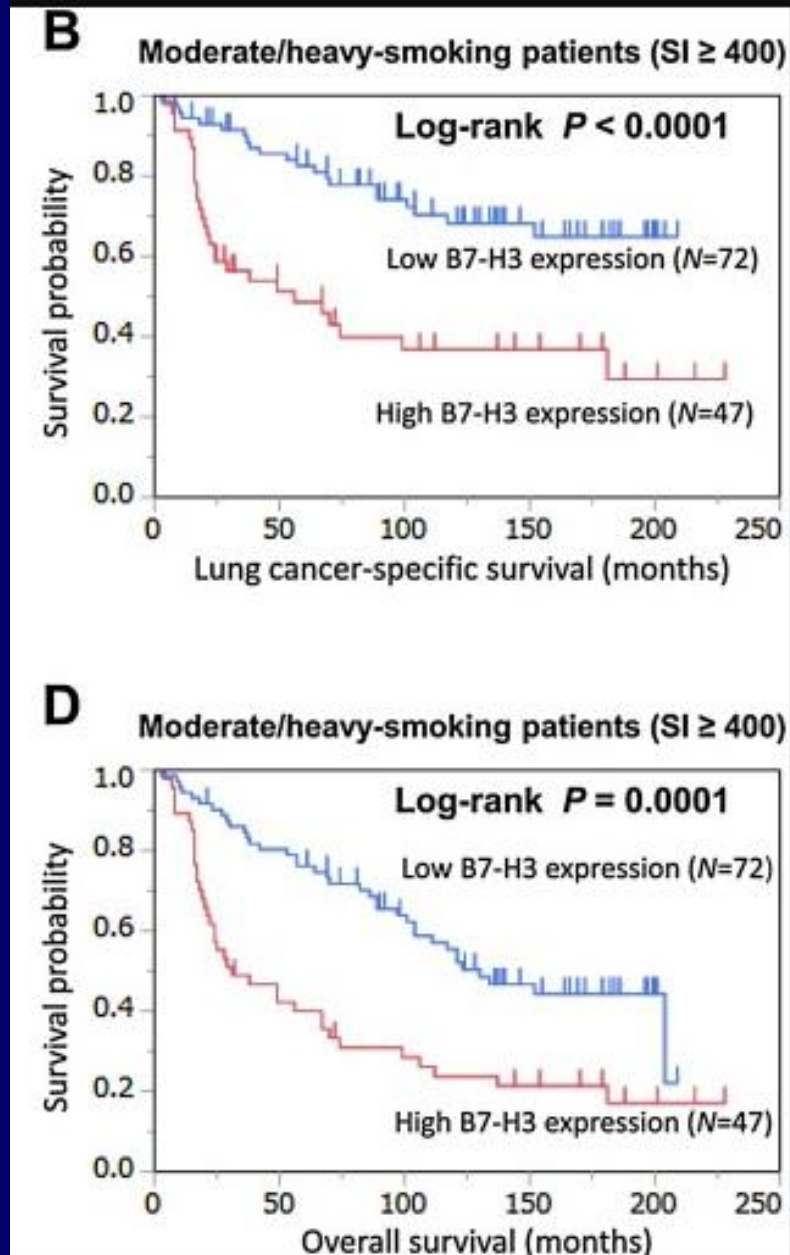


Or
monthly

Proposal

- **All Ongoing and Proposed therapeutic clinical trials in lung cancer include or be amended to include collection of smoking status before and after institution of therapy. Data on time of cessation should be included.**
- **Whether a stratification for smoking status before therapy should be included requires consideration.**
- **All of these trials should consider a smoking cessation program.**

Relationship of smoking to B7-H3 expression and survival in lung cancer



Conclusion Tobacco smoking patients with NSCLC generally have a higher PD-L1 tumour proportion score and experience a higher response rate in immunotherapy than non-smokers. There is little evidence on the effect of smoking during immunotherapy, but one study indicates better outcome for former smokers than for the current ones. Further studies are necessary to elucidate the negative effects of smoking during immunotherapy.

Effects of Smoking Status on Response to Immunotherapy

Table 1 An overview of the study characteristics, treatment and comparator, type of evaluation, perspective, year of value and time horizon of the selected studies

Reference	Study characteristics	Treatment and comparator	n	Key findings
24	Patients with NSCLC treated with nivolumab	Nivolumab monotherapy	50	Response to treatment before nivolumab associated with response to nivolumab. Smoking history had no significant influence (never vs current/former smoker ORR 5% vs 26%, p=0.1269).
16	Sequenced exons of NSCLCs	Pembrolizumab	34	Efficacy greater in tumours harbouring smoking signature (ORR 56% vs 17%, p=0.03)
25	EGFR and ALK rearrangements in NSCLC	PD-1/PD-L1 inhibitors	58	Smoking history had no significant influence (never/light vs heavy smokers ORR 4.2% vs 20.6%, p=0.123).
26	Adenocarcinoma of the lung	Testing PD-L1 tumour proportion score	71	Tumours with a PD-L1 TPS>50% were significantly associated with smoking status.
27	Patients with NSCLC in East Asia. 108 SCC and 221 LUAD.	PD-L1 expression/distribution	329	TPS>50% correlated with smoking history in both SCC (p=0.008) and adenocarcinoma (p=0.002).
17	Pembrolizumab in NSCLC. KEYNOTE-001.	Pembrolizumab 10 mg/kg every 2 weeks, 2 mg/kg every 3 weeks, 10 mg/kg every 3 weeks	495	Current/former smoking status was associated with increased ORR (10.3% vs 22.5% in never smokers).
15	Pembrolizumab or platinum-based CT. KEYNOTE-024.	Pembrolizumab 200 mg every 3 weeks Platinum	305	ORR 44.8% vs 27.8%. HR for progression/death among smokers 0.68 and former smokers 0.47.
18	Pemetrexed and platinum plus pembrolizumab or placebo in advanced NSCLC. KEYNOTE-189.	Pemetrexed, platinum and pembrolizumab or placebo every 3 weeks	616	88.1% current or former smokers. HR for death among current or former smokers 0.54 versus never smoker 0.23. Progression-free survival HR 0.54 and 0.43, respectively.
19	Nivolumab versus docetaxel in patients with NSCLC. Phase III study.	Nivolumab 3 mg/kg every 2 weeks versus docetaxel 75 mg/m ² every 3 weeks	582	79% were current/former smokers. HR was 0.70 and 1.02 in former/current smokers and never smokers, respectively.

ALK, anaplastic lymphoma receptor tyrosine kinase; CT, chemotherapy; EGFR, epidermal growth factor receptor; LUAD, lung adenocarcinoma; NSCLC, non-small cell lung cancer; ORR, overall response rate; PD-L1, programmed death ligand 1; SCC, squamous cell carcinoma; TPS, tumour proportion score.

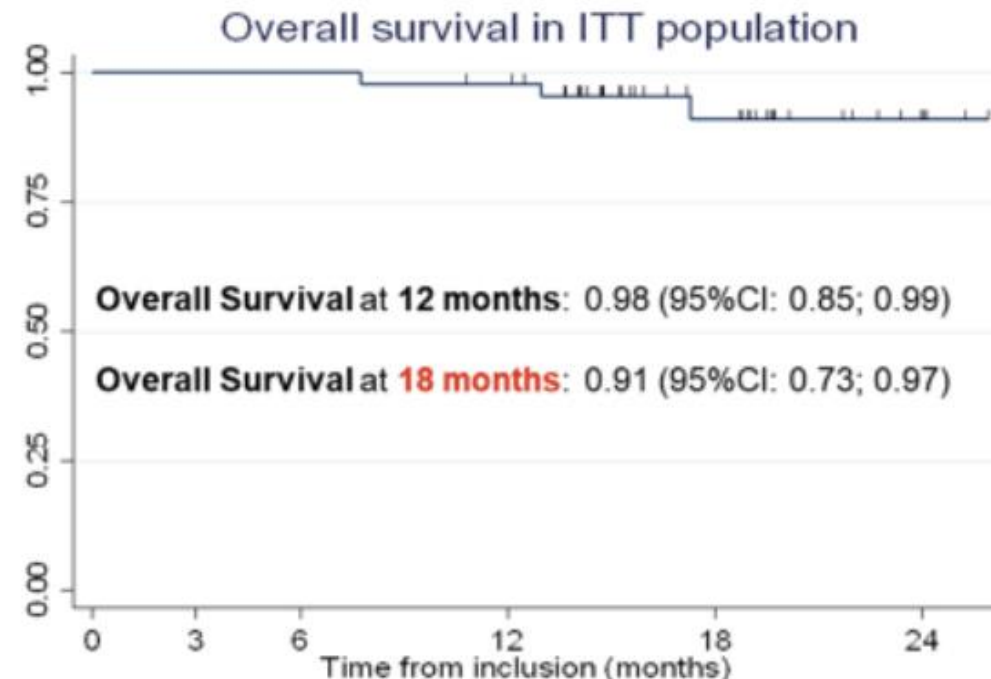
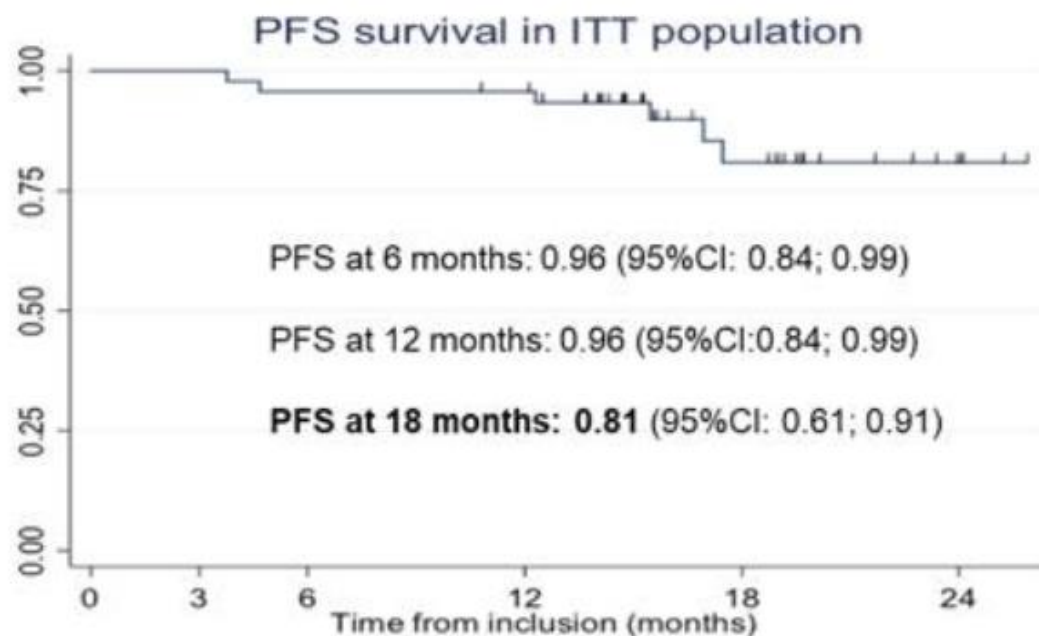
It appears that current smokers have higher PD-L1 expression and higher TMB than non-smokers and that they have higher objective response rates to checkpoint inhibitors. While there is insufficient evidence to draw firm conclusions, it appears that smokers who quit do better on checkpoint inhibitors than continuing smokers.

Thus, it is critical to collect this information in clinical trials and do multivariate analyses to determine if these smoking effects are independent of other variables

Neoadjuvant CT+I/O

Efficacy NADIM

	N (ITT/Evaluable)	cStage	R0	Morbidity/ Mortality	MPR/PCR
Nadim NIVO-CT x 3 Target: PD-1	46/41 (89%)	T3/4N1: 11% N2: 89%	100%	29%/0%	10/46 (22%) MPR 24/46 (52%) PCR



Future Directions & Next Steps: Perspective from NCI's Cancer Therapy Evaluation Program

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Cancer Therapeutics Evaluation Program (CTEP)

National cancer Institute, NIH



a National Cancer Institute program

February 28, 2020

- ❑ *People who smoke develop cancer*
- ❑ *Cancer patients who smoke have worse health outcomes*
 - ❑ Poor response to treatment,
 - ❑ higher risk of recurrence,
 - ❑ increased toxicity.

Smoking cessation interventions should be a part of standard oncologic treatment.

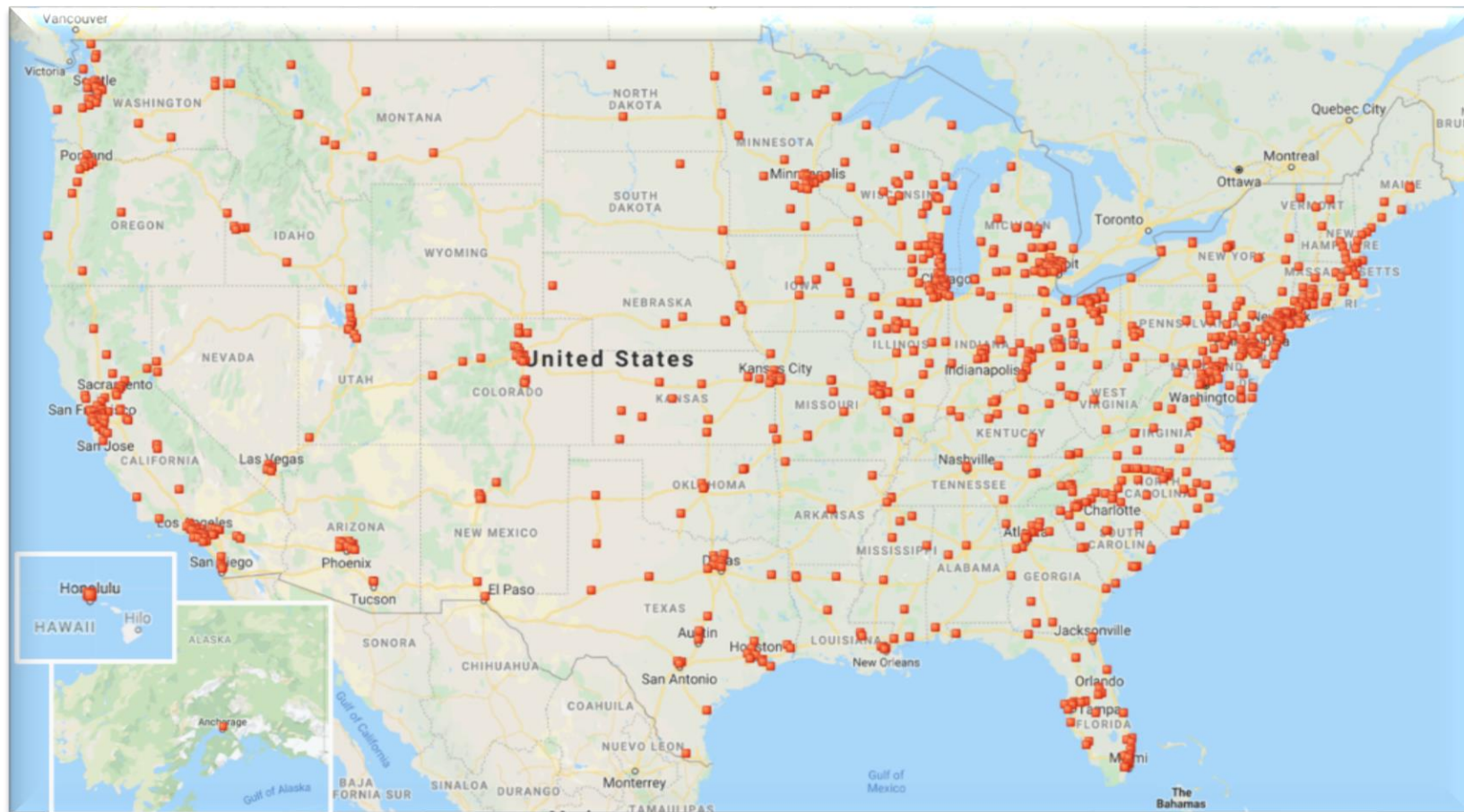
All patients should be screened for tobacco use and advised on the benefits of tobacco cessation.

In patients who continue smoking after diagnosis of cancer evidence-based tobacco cessation assistance should be integrated into multidisciplinary cancer care.

How such data is collected in NCI-Supported NCTN trials

Scope of the NCTN

- 2,000+ enrolling sites across North America (plus international sites)
- 190+ actively enrolling trials



How the NCTN Functions

- The NCTN is made up of 6 grant-funded clinical trials Groups, each of which develop and carry out clinical trials:
 - 4 US Adult Groups: Alliance, ECOG-ACRIN, NRG, and SWOG
 - 1 Pediatric Group: COG
 - 1 Canadian Collaborating Group
- Each NCTN group is a grantee of NCI
 - These are collaborative grants, so NCI is a partner in their work
 - However, each Group is independent and conducts itself differently, within the broad requirements of the network

NCI National Clinical Trials Network Structure



LEGEND

-  Centralized Functions:
 - Centralized Institutional Review Board
 - Cancer Trials Support Unit
 - Imaging and Radiation Oncology Core (IROC) Group
 - Common Data Management System Central Hosting
-  32 Lead Academic Participating Sites (LAPS)
-  Operations
-  Statistics & Data Management
-  Tissue Banks
-  Member Sites

cancer.gov

Tobacco Assessment in the NCTN

- NCTN Groups have implemented tobacco utilization assessment in their clinical trials in their own ways
 - Smoking history is collected in all trials conducted by some Groups
 - Smoking history is focused on tobacco-related cancers or other selected trials in some Groups
 - Some Groups do not have a universal policy so it depends on scientific needs of the trial
- There is no universal policy across the NCTN
- Moving forward, tobacco utilization questions will conform with the FDA requirement to use CDASH questions

American Society of Clinical Oncology Policy Statement Update

September 2013

Recommendations

*Include tobacco use status as a core data element in oncology clinical trials **where appropriate**.*

ASCO supports including tobacco use history and status as core data elements that are collected throughout the course of a clinical trial in which concomitant medications are routinely captured: at diagnosis, trial registration, and follow-up and during long-term survival or at death.¹²

ASCO also recognizes the importance of maximizing clinical trial resources and encourages the inclusion of tobacco-related data as concomitant medications in a strategic and nonburdensome manner.

Smoking data is normally collected in the demographic information of most lung cancer trials.

Perspective

- Important to distinguish between goals for clinical practice and goals for clinical research
 - Assessments should not be added to trials unless they have clear clinical research goals and a strong research plan

- Tobacco utilization assessments in clinical trials should:
 - Have a strong scientific justification for inclusion in the particular trial
 - Add minimal burden to enrolling sites and patients
 - Conform with CDASH questions
 - Have a clear research plan, including hypotheses and an appropriately-powered statistical plan, with analyses conducted and published promptly

NCI Cancer Moonshot: Cancer Center Cessation Initiative

- Launched in 2017 with the long-term goal to help cancer centers build and implement sustainable tobacco cessation treatment programs
- Plans include refining electronic medical records and clinical workflows to ensure the systematic identification and documentation of smokers and the routine delivery of evidence-based tobacco cessation treatment services = component of “Standard of Care”.
- Overcome patient, clinician, clinic, and health system barriers to providing tobacco cessation treatment services
- Create mechanisms to sustain tobacco cessation treatment services so that they continue beyond the funding period of the initiative

<https://cancercontrol.cancer.gov/brp/tcrb/cessation-initiative.html>

Panel Discussion on Next steps should focus on

Basic tobacco history (smoker, ex-smokers etc.) is part of demographics

1) If additional data is appropriate, what is the appropriate setting for collecting such data ?

Are clinical trials the ideal settings? (burden with experimental therapies, PRO's etc.)

Could this data be better collected outside clinical trials in oncology settings? In conjunction with projects like Moonshot initiatives?

If there is a specific hypothesis-driven objective with statistical analysis plan in a particular therapeutic clinical trial, these can be discussed with the NCI



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Thank You

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Join the conversation with #OCETobaccoUse