Tobacco, Cessation, and Cancer Survivors

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Disclosures

• Support from AHRQ and NCI/NIH
• Member or Chair, ASCO, AACR, IASLC, SRNT Tobacco or Comorbidity Subcommittees
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  – Cancer Epidemiology Biomarkers & Prevention
  – Translational Lung Cancer Research
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• Views are mine and do not represent those of any parent or supporting organizations
Problem: We don’t view Smoking in the Continuum of Cancer

The Established Carcinogenesis Model

- Receptor binding
- Protein kinase A and B activation and other changes
- Mutations in oncogenes and tumor-suppressor genes
- Loss of normal growth control mechanisms
- Cancer

Biologic Outcomes
(tumor promotion, decreased cancer treatment efficacy)

Clinical Outcomes
(recurrence, toxicity, mortality)

Value Outcomes
(cost of cancer treatment, productivity, QOL/EOL, recurrence, toxicity, mortality)

Addressing Tobacco Use by Cancer Patients

2010 Surgeon General’s Report, Fig 5.1
The 2014 Surgeon General’s Report

• Landmark SGR reviewing ~400 studies reporting on over 500,000 patients

• In cancer patients and survivors, the evidence is sufficient to infer a causal relationship between cigarette smoking
  – Adverse health outcomes
  – Increased all-cause mortality
  – Increased cancer-specific mortality
  – Increased risk for second primary cancers
  – Associated with increased risk of recurrence, poorer response to treatment, and increased treatment-related toxicity

The 2014 SGR: Magnitude Estimates

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

Breadth of Association across Cancer
(one or more negative association)

Smoking and Therapeutic Response

A. Relative SF

- **A549**
- **H460**

Control | LD CS | HD CS | Control | LD CS | HD CS

3 Week

6 Week

B. Tumor Doubling

- **RT alone**
- **RT + CS**

0% | 10% | 20% | 30% | 40% | 50% | 60% | 70% | 80% | 90%

0 | 5 | 10 | 15

C. Relative SF

- **A549**
- **FaDu**
- **MDA**
- **PC3**

RT alone | RT + CS

D. Relative SF

- **H460**
- **A549**

Control | CS Continued | CS Removed
Magnitude of Smoking in Cancer

• United States:
  • Annual cancer incidence: 1.6 million
  • Reported Smoking prevalence: ~15%
    • NOTE: ~30% of cancer patients who smoke misrepresent
    • Adjust to ~20% prevalence
  • US smoking cancer patient prevalence ~320,000

• Canada
  • Canadian cancer incidence: 206,200
  • Smoking prevalence: 16.9% (adjust to ~20%)
  • Canadian smoking cancer patient prevalence: ~41,240

https://www150.statcan.gc.ca/n1/pub/82-625-x/2018001/article/54974-eng.htm
Cost of Failure due to Smoking

<table>
<thead>
<tr>
<th>Odds Ratio³</th>
<th>Mean Individual Cost per Treatment Failure, $</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10000</td>
</tr>
<tr>
<td>1.1</td>
<td>40777</td>
</tr>
<tr>
<td>1.2</td>
<td>79245</td>
</tr>
<tr>
<td>1.4</td>
<td>150000</td>
</tr>
<tr>
<td>1.6</td>
<td>213559</td>
</tr>
<tr>
<td>1.8</td>
<td>270968</td>
</tr>
<tr>
<td>2.0</td>
<td>323077</td>
</tr>
<tr>
<td>2.5</td>
<td>434483</td>
</tr>
<tr>
<td>3.0</td>
<td>525000</td>
</tr>
</tbody>
</table>

**US Estimates:** $3.4 Billion Annually  
$10,678 per smoking patient

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

Warren et al., *JAMA Network Open*, 2019
Cessation and Overall Mortality

<table>
<thead>
<tr>
<th>Persistent versus Quit</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Al-Mamgani et al., 2014</td>
<td>5.25 (3.47-7.95) (calculated) (n=267, H/N, larynx)</td>
</tr>
<tr>
<td>Roach et al., 2016</td>
<td>2.07 (1.02-4.20) (n=119, lung)</td>
</tr>
<tr>
<td>Dobson Amato et al., 2015</td>
<td>1.79 (1.14-2.82) (n=224, lung)</td>
</tr>
<tr>
<td>Tao et al., 2013</td>
<td>1.76 (1.37-2.27) (n=411, male mult sites)</td>
</tr>
<tr>
<td>Passarelli et al., 2016</td>
<td>1.50 (RR 2.57 p vs. 2.34 q) (calc) (n=786, breast)</td>
</tr>
<tr>
<td>Browman et al., 2002</td>
<td>1.22 (0.79-1.87) (calculated) Comparison of smokers of &gt;1 cig/day vs. &lt;1 cig/day including nonsmokers</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Quit versus Persistent</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Nia et al., 2005</td>
<td>0.34 (0.16-0.71) (n=204, lung)</td>
</tr>
<tr>
<td>Chen et al., 2010</td>
<td>0.54 (0.37-0.77) (n=163, lung, SCLC)</td>
</tr>
<tr>
<td>Sandoval et al., 2009</td>
<td>0.77 (0.34-1.73) (n=85, H/N, oral cavity)</td>
</tr>
<tr>
<td>Choi et al., 2016</td>
<td>0.88 (RR 2.38 q vs. 2.71 p) (calc) (n=245, H/N)</td>
</tr>
</tbody>
</table>

Continued smoking increases risk ~1.6-1.7 as compared with quitting smoking

(smoking cessation can improve outcome?!?!)

## Magnitude Comparison

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

1. Marquart J et al., *JAMA Oncol* 2018
2. CPAC Cost Estimates for Smoking Cessation 2017
Assessing Tobacco in Cooperative Groups

- Current Cigarette Use (21.9%)
- Current Other Tobacco Use (12.2%)
- Former Cigarette Use (21.3%)
- Former Other Tobacco Use (12.2%)
- Secondhand Smoke (2.6%)
- Any Tobacco Assessment at Follow Up (4.5%)
- No Assessment of Tobacco (71%)
- Any Assessment of Tobacco (29%)

Tobacco Assessment by Oncologists
(Always/Most of the time)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>IASLC (n=1507)</th>
<th>ASCO (n=1197)</th>
<th>NDCC (n=887)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ask if use tobacco</td>
<td>90.2%</td>
<td>89.5%</td>
<td>90.2%</td>
</tr>
<tr>
<td>Advise to quit</td>
<td>80.6%</td>
<td>82.4%</td>
<td>83.3%</td>
</tr>
<tr>
<td>Actively treat</td>
<td>38.8%</td>
<td>38.6%</td>
<td>35.1%</td>
</tr>
</tbody>
</table>

- 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
Time: 4 Interesting Possibilities

• Multiverse:
  • Using the existence of an alternative universe to help deliver cessation support

• Quantum entanglement
  • Shrinking to quantum scale and messing with gluons to change addictive behavior in a patient's brain

• Simple time travel
  • Going back in time to speak to the patient, but meeting yourself and possible annihilation

• Getting administrative support to increase time spent with patients, and provide free medications
  • Probably the least likely option
Who Should Provide Support?
(NCI survey)

What provider do you prefer to provide cessation assistance?

- Primary Care physician (16%)
- MD/DO level provider (4%)
- Mid level provider (NP/PA) 19%
- Other clinical support (nurse, social work) (9%)
- Any other clinical staff (50%)
- I prefer to treat the patient myself (1%)

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

Pommerenke et al. AACR 2014 Annual Meeting
Resources: NCCN Guidelines

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Smoking Cessation

Version 1.2015

NCCN.org

Continue

www.nccn.org (v1, 2015)
Systemic Approaches: Expectations
(assuming ‘Opt-Out’ approach)

Phone
On site
70-80%
Contact/
Participate

In Person
On site
30-60%
Contact/
Participate

Phone
Off site
(quitline)
30-60%
Contact/
Participate

Smoking

Standardized
Screening

Interactive
Voice Recorder (IVR)
3-55% Contact/Participate
(little known)

In Person
Off site
<20%
Contact/
Participate
(unknown)
Opt-Out for Smoking Cessation

All New Patients

New Patient Screen

Positive Screen for Tobacco Use

Automated Referral to Cessation Service

Accept Enrollment

Negative Screen for Tobacco Use

Established Patient Screen

Refuse Enrollment

Standard Clinical Cancer Care

Individualized Tobacco Cessation Intervention

Warren GW et al., Cancer 2014
Participation at First Cessation Contact

2765 patients referred to cessation program
1384 patients with at least 5 cessation contact attempts
1126 patients contacted by cessation service
1075 appropriate referrals contacted by cessation service
1010 receptive to cessation assistance
1381 receive mailing on cessation support
258 patients not reached within 5 attempts
51 Inappropriate referrals
35 unable to participate
30 refused participation

81.3% Contact Rate

1.2% (16 patients) contacted cessation program
2.8% Refused Participation

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

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

Warren GW et al., Cancer 2014
# Automated Cessation and Mortality

<table>
<thead>
<tr>
<th>Continuous Variables</th>
<th>N</th>
<th>Mean</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis (years)</td>
<td>224</td>
<td>61.9</td>
<td>1.04</td>
<td>1.02–1.06</td>
<td>0.001</td>
</tr>
<tr>
<td>Pack-years</td>
<td>224</td>
<td>59.7</td>
<td>1.00</td>
<td>0.99–1.01</td>
<td>0.495</td>
</tr>
<tr>
<td>Days between diagnosis and last contact</td>
<td>224</td>
<td>100.9</td>
<td>0.999</td>
<td>0.998–1.001</td>
<td>0.227</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Categorical Variables</th>
<th>N</th>
<th>%</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>134</td>
<td>59.8</td>
<td>1.00</td>
<td></td>
<td>0.051</td>
</tr>
<tr>
<td>Male</td>
<td>90</td>
<td>40.2</td>
<td>1.45</td>
<td>1.01–2.14</td>
<td></td>
</tr>
<tr>
<td>Clinical stage</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage I/II</td>
<td>81</td>
<td>36.2</td>
<td>1.00</td>
<td></td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Stage III</td>
<td>65</td>
<td>29.0</td>
<td>2.53</td>
<td>1.39–4.61</td>
<td></td>
</tr>
<tr>
<td>Stage IV</td>
<td>78</td>
<td>34.8</td>
<td>8.72</td>
<td>4.93–15.40</td>
<td></td>
</tr>
<tr>
<td>ECOG status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>127</td>
<td>56.7</td>
<td>1.00</td>
<td></td>
<td>0.265</td>
</tr>
<tr>
<td>≥1</td>
<td>97</td>
<td>43.3</td>
<td>1.26</td>
<td>0.84–1.89</td>
<td></td>
</tr>
<tr>
<td>Tumor histology</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSCLC</td>
<td>197</td>
<td>87.9</td>
<td>1.00</td>
<td></td>
<td>0.626</td>
</tr>
<tr>
<td>Other lung cancer</td>
<td>27</td>
<td>12.1</td>
<td>0.87</td>
<td>0.50–1.52</td>
<td></td>
</tr>
<tr>
<td>Quit status at referral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quit</td>
<td>48</td>
<td>21.4</td>
<td>1.00</td>
<td></td>
<td>0.393</td>
</tr>
<tr>
<td>Current</td>
<td>176</td>
<td>78.6</td>
<td>0.80</td>
<td>0.48–1.34</td>
<td></td>
</tr>
<tr>
<td>Quit status at last contact</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quit</td>
<td>95</td>
<td>42.4</td>
<td>1.00</td>
<td></td>
<td>0.012†</td>
</tr>
<tr>
<td>Current</td>
<td>129</td>
<td>57.6</td>
<td>1.79</td>
<td>1.14–2.82</td>
<td></td>
</tr>
</tbody>
</table>

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.
Can this be Expanded?

- Michigan Quality Oncology Consortium (MOQC)
  - Initiative from 2012-17 to use Quitlines to provide cessation support for community oncology patients across Michigan
- Screening and fax referral with ‘opt-out’ approach
  - 38% contact rate (2015 assessment)
  - 28% opt-out
- Aggregate through 2017
  - 3,892 cancer patients enrolled in the Quitline
  - 58% participate in 1-2 calls
  - 2,064 unique patients made a quit attempt
  - 2,291 NRT samples
  - 26% 6 month self-reported quit rate
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.

Cohort 1 (2017–2019)
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 (2018–2020)
1. Columbia University
2. Dana-Farber/Harvard Cancer Center
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 Science University
11. Roswell Park
12. Stanford University
13. University of Arizona
14. University of California, San Francisco
15. University of Michigan
16. University of Texas Southwestern
17. University of Pittsburgh Medical Center Hillman
18. Virginia Commonwealth University
19. Wake Forest University
20. Wayne State University

NCI-Designated Cancer Centers Selected as Part of the Cancer Center Cessation Initiative (C3I).
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.”
1. Decrease the risk of people getting cancer

2. Diagnose cancer faster, accurately and at an earlier stage

3. Deliver high-quality care in a sustainable, world class system

4. Eliminate barriers to people getting the care they need

5. Deliver information and supports for people living with cancer, families and caregivers
PRIORITY AREAS

1. Decrease the risk of people getting cancer
2. Diagnose cancer faster, accurately and at an earlier stage
3. Deliver high-quality care in a sustainable, world class system
4. Eliminate barriers to people getting the care they need
5. Deliver information and supports for people living with cancer, families and caregivers
Effect Modification

What we are doing today will affect the outcome of over 1.6 million American and 200,000 Canadian cancer patients in the next 5 years

Get every cancer patient who smokes into a tobacco treatment program

Get everyone in as a priority for starting cancer treatment

Methods must be sustained long after we are done