Cost-effectiveness of the Prevention of Lung Cancer

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Chair, Cancer Care Ontario’s Smoking Cessation Advisory Committee
Smoking – the Principal Cause of Lung Cancer

• A global health problem
• Huge cost in human capital
• Estimated 450 million deaths worldwide in the next 50 years
• Reducing current smoking by 50% would avoid 20 -30 million premature deaths in the first quarter of the century; avoid 150 million in second quarter
Cigarette Smoke

• Over 4,000 constituents in cigarette smoke
• 250 known to be harmful: hydrogen cyanide, carbon monoxide, ammonia
• 69 known carcinogens in cigarette smoke, including
  Arsenic
  Benzene
  Metals (beryllium, cadmium, nickel, chromium, polonium-210)
  Ethylene oxide
  Nitrosamines
  Vinyl chloride
  Polyaromatic hydrocarbons

http://www.cancer.gov/cancertopics/factsheet/Tobacco/cessation
Smoking Directly Causes:

- 13 different types of cancer
  - 1 out of 3 cancer deaths are tobacco-caused
- ~30% of all cancers, including 90% of all lung cancers
- ~30% of all cardiovascular diseases
- ~90% of all COPD
Over 50+ years to learn what works to reduce tobacco dependence and to study the cost-effectiveness of interventions.
Major Conclusions from the 2014 Report

- Since the 1964 Surgeon General’s report, comprehensive tobacco control programs and policies have been proven effective for controlling tobacco use. Further gains can be made with the full, forceful, and sustained use of these measures.
Smoking Cessation

11.2 million hits!
Public Policy and Population-based Strategies

• Increase Price of Tobacco – Taxes
• Smoke Free Policies
• Health Promotion
  – Media Campaigns
  – School-based educational programs
Increasing the Tax on Cigarettes

• Single most effective policy to reduce the health and economic burden of smoking while generating higher revenue for government

• Quotes from internal tobacco industry documents:
  – Philip Morris: “When the tax goes up, industry loses volume and profits as many smokers cut back”
  – RJ Reynolds: “If prices were 10% higher, 12-17 incidence (youth smoking) would be 11.9% lower”
  – Philip Morris: It is clear that price has a pronounced effect on the smoking prevalence of teenagers and that the goals of reducing teenage smoking and balancing the budget would be served by increasing the federal excise tax on cigarettes”
Individual Interventions: Current Best Practice and Innovations

Best Practices:
• Combined counseling and pharmacotherapy
• Varenicline (Champix) and combination NRT are particularly effective options
• Using Quit lines as treatment extenders

Innovations:
• Pre-Quit use of NRT + Reduction Counseling
• Long-term NRT
NRT (long and short term) and Varenicline

<table>
<thead>
<tr>
<th>Medication</th>
<th>Number of arms</th>
<th>Estimated odds ratio (95% C. I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine Patch (reference group)</td>
<td>32</td>
<td>1.0</td>
</tr>
<tr>
<td>Varenicline (2 mg/day)</td>
<td>5</td>
<td>1.6 (1.3, 2.0)</td>
</tr>
<tr>
<td>Patch (long-term; &gt;14 weeks) + NRT (gum or spray)</td>
<td>3</td>
<td>1.9 (1.3, 2.7)</td>
</tr>
</tbody>
</table>
Medications in Combination with Counseling

Effectiveness of and estimated abstinence rates for the combination of counseling and medication versus medication alone (n = 18 studies)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number of arms</th>
<th>Estimated odds ratio (95% C.I.)</th>
<th>Estimated abstinence rate (95% C.I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication alone</td>
<td>8</td>
<td>1.0</td>
<td>21.7</td>
</tr>
<tr>
<td>Medication and counseling</td>
<td>39</td>
<td>1.4 (1.2, 1.6)</td>
<td>27.6 (25.0, 30.3)</td>
</tr>
</tbody>
</table>
How effective are the best smoking cessation strategies?
## Abstinence Rates for Various Interventions

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Average rate</th>
<th>Difference with usual care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual care</td>
<td>1.4%</td>
<td>—</td>
</tr>
<tr>
<td>Minimal or brief counseling</td>
<td>2.6%</td>
<td>1.2% ( -1.3% to 3.7%)</td>
</tr>
<tr>
<td>Intensive counseling ≥ 90 min.</td>
<td>6.0%</td>
<td>4.6% ( 1.8% to 7.4%)</td>
</tr>
<tr>
<td>Intensive counseling ≥ 90 min. with pharmacotherapy †</td>
<td>12.3%</td>
<td>10.9% ( 6.9% to 15.0%)</td>
</tr>
</tbody>
</table>

*Based on random effect meta-analysis performed on the absolute absence rates trial arms
† Pharmacotherapy consists of NRT and bupropion

Hoogendoorn M et al. Thorax 2010; 65:711 – 718
Nicotine Addiction

• True drug addiction, similar to that of other drugs of abuse (heroin, cocaine)
• Requires long-term, repeated clinical intervention
• Nicotine addiction needs to be viewed as a chronic disease
• Remission can be achieved with the proper interventions and treatments
• Relapse is common and is the nature of addiction, not the failure of the individual
Smoking Prevalence Among Adults 18 and Older United States 1965-2014

2014 = 17.0%
## Smoking Rates in Canada
*(12 years and older)*

<table>
<thead>
<tr>
<th></th>
<th>2001</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>28.2%</td>
<td>21.4%</td>
</tr>
<tr>
<td>Women</td>
<td>23.8%</td>
<td>14.8%</td>
</tr>
</tbody>
</table>

How cost-effective are these approaches?

For patient interventions
For population interventions
Cost and Cost-effectiveness of Smoking Cessation

1.38 million hits!
Assessing the Cost-effectiveness of an Intervention

Ideally, results from a randomized clinical trial
Determine the incremental benefit (Effectiveness) of the intervention compared to the standard approach
Determine the incremental cost of the intervention

Cost-Effectiveness = \[
\frac{\text{Cost}^1 - \text{Cost}^2 (\Delta C)}{\text{Effectiveness}^1 - \text{Effectiveness}^2 (\Delta E)}
\]
Defining Cost-effectiveness

• $\text{ICER} = \frac{\Delta C}{\Delta E}$ = cost/life-year gained

• $\text{ICUR} = \frac{\Delta C}{\Delta E}$ but $\Delta E$ adjusted for quality of life
cost/QALY gained

• Cost-effective: ICER $<$ Willingness to Pay (WTP)

• Cost-effective: $\frac{\Delta C}{\Delta E} < \text{WTP}$
  
  - \(\Delta C\) ↓ cost
  - \(\Delta E\) ↑ outcome
  - WTP: ↑ budget
Willingness to Pay

• Varies by
  – Geographical region/country
  – Health system
  – Payer
  – Disease cancer vs non-cancer; type of cancer

• Canada
  – < $100,000/ QALY (€69,000/ QALY)

• United Kingdom
  – ≈ £20-30,000/ QALY (€35- 44,000/QALY)
Challenges of undertaking cost-effectiveness studies on smoking cessation

Benefit of smoking cessation interventions (quit rate) determined from randomized trials
Large number of clinical trials involving NRT, therefore relative effect of NRT can be considered robust
Fewer trials for bupropion or varenicline
Short time horizons for quitting – 30 days to 12 months
Uncertainty of long term benefits on health and health care costs
Spontaneous quit rate has to be factored into effectiveness estimates (1-8%)
Estimating the Effectiveness of Smoking Cessation

- The difference in the total mortality between smokers and non-smokers is used to estimate of life years saved after smoking cessation.
- Typically derived from studies such as the cohort study of male doctors in England (Doll et al.) or the American Cancer Society 25 state Cancer Prevention Study.
- Estimation of life years saved depends on the age and gender of quitters, the number cigarettes smoke, the duration of smoking before cessation, the relapse rate and the diseases avoided.
Estimated Number of Life-years Saved per Lifetime Quitter*

<table>
<thead>
<tr>
<th>Age at which stopped smoking (years)</th>
<th>Undiscounted</th>
<th>Discounted (1.5%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 35</td>
<td>7.1</td>
<td>4.0</td>
</tr>
<tr>
<td>35 – 44</td>
<td>5.5</td>
<td>3.4</td>
</tr>
<tr>
<td>45 – 54</td>
<td>2.5</td>
<td>2.4</td>
</tr>
<tr>
<td>55 - 64</td>
<td>2.1</td>
<td>1.6</td>
</tr>
</tbody>
</table>

Average life years saved per quitter ranges from 0.28 to 2.4 years

*based on the total mortality of smokers and quitters; derived from the study by Doll et al. of male doctors in England

Health Tech Assessment 2002; v6: No.16 Chapter 5
Estimated Cost per Quitter

UK study of average cost per quitter

– Brief advice £ 172
– Advice plus self-help materials £ 218
– Advice plus self-help materials plus NRT £ 267
– Smoking cessation clinics £ 1997

Cost per life year saved (UK) \( \frac{\Delta C}{\Delta E} \)

- Brief advice £ 74 € 92
- Advice plus self-help material £ 221 € 273
- Advice plus self-help material plus NRT £ 269 € 333
- Special smoking cessation clinics £ 255 € 315

Objective: To determine the relative cost-effectiveness of 15 recommended smoking cessation interventions from the Agency for Health Care Policy and Research Clinical Practice Guideline on Smoking Cessation (1996) and then, using decision probabilities, combine the interventions into a global model of the guideline's overall cost-effectiveness
Methodology

- Effectiveness of interventions derived from 56 peer-reviewed publications
- Same interventions grouped together
- Assumed 75% of all smokers undertake an intervention during a year’s time
- Experts identified the likelihood of patients choosing one of the 5 counselling interventions +/- NRT
- Probabilities used to weight the costs and quit rates of the interventions

Cromwell J et al. JAMA 1997; 288:1759
### Expected Number of Quitters and Life-Years saved by Smoking Cessation Intervention (assumes 75% of smokers make one quit attempt during year)

<table>
<thead>
<tr>
<th>Interventions</th>
<th>Marginal Quit Rate, %</th>
<th>Life-years saved (No. in ‘000s)</th>
<th>Quality Life-Years Saved (No. in ‘000s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brief counseling alone</td>
<td>1.86</td>
<td>546</td>
<td>738</td>
</tr>
<tr>
<td>With patch</td>
<td>8.40</td>
<td>2467</td>
<td>3333</td>
</tr>
<tr>
<td>With gum</td>
<td>4.95</td>
<td>1454</td>
<td>1964</td>
</tr>
<tr>
<td>Full counselling</td>
<td>6.20</td>
<td>1821</td>
<td>2450</td>
</tr>
<tr>
<td>With patch</td>
<td>16.0</td>
<td>4700</td>
<td>6348</td>
</tr>
<tr>
<td>With gum</td>
<td>10.9</td>
<td>3202</td>
<td>4325</td>
</tr>
<tr>
<td>Intensive counseling alone</td>
<td>6.62</td>
<td>1945</td>
<td>2627</td>
</tr>
<tr>
<td>With patch</td>
<td>16.64</td>
<td>4888</td>
<td>6602</td>
</tr>
<tr>
<td>With gum</td>
<td>11.50</td>
<td>3378</td>
<td>4563</td>
</tr>
<tr>
<td>Combined intervention</td>
<td></td>
<td>2,439</td>
<td>3,294</td>
</tr>
</tbody>
</table>

## Cost-effectiveness of Smoking Cessation by Intervention

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Cost per quitter</th>
<th>Cost per Life-Year Saved, (3% discount)</th>
<th>Cost per Quality-Adjusted Life-Year (3% Discount)</th>
</tr>
</thead>
<tbody>
<tr>
<td>With NRT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimal counseling</td>
<td>4745</td>
<td>3248</td>
<td>2405</td>
</tr>
<tr>
<td>Brief counseling</td>
<td>4184</td>
<td>2864</td>
<td>2120</td>
</tr>
<tr>
<td>Full counseling</td>
<td>2715</td>
<td>1859</td>
<td>1376</td>
</tr>
<tr>
<td>Individual intensive counseling</td>
<td>2871</td>
<td>1969</td>
<td>1455</td>
</tr>
<tr>
<td>Group intensive counselling</td>
<td>2310</td>
<td>1581</td>
<td>1171</td>
</tr>
</tbody>
</table>

Summary Outcomes

- Average cost per quitter
  
  $3,779 US  (€3,317)

- Average cost per life-year saved
  
  $2,587 US  (€2,271)

- Average cost per quality-adjusted life year saved
  
  $1,915 US  (€1,682)
## Cost-Effectiveness of 1st Line Systemic Therapy Agents for Lung Cancer

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Erlotinib</td>
<td>mutation unknown</td>
<td>France, Germany, Italy</td>
<td>BSC</td>
<td>5 years</td>
<td>$16,038</td>
<td>0.30</td>
<td>$57,273/LYS</td>
</tr>
<tr>
<td>Pemetrexed</td>
<td>for mutation unknown</td>
<td>USA</td>
<td>BSC</td>
<td>3 years</td>
<td>$34,849</td>
<td>0.28</td>
<td>$133,500/LYS</td>
</tr>
<tr>
<td>Pemetrexed</td>
<td>Stage 1LM for mutation unknown</td>
<td>USA</td>
<td>Erlotinib</td>
<td>3 years</td>
<td>$26,700</td>
<td>0.18</td>
<td>$163,926/LYS</td>
</tr>
</tbody>
</table>

- 2013 US dollars
- Perspective: Public health care payer

## Cost-effectiveness of New Targeted Therapies (Canadian HTA Assessment)

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Indication</th>
<th>Country</th>
<th>Comparator</th>
<th>Time horizon</th>
<th>Δ cost</th>
<th>Δ effect (life years)</th>
<th>Cost-effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afatinib</td>
<td>1st Line advanced NSCLC</td>
<td>Canada</td>
<td>Pemetrexed-cisplatin</td>
<td>5 years</td>
<td>$4,387</td>
<td>.017</td>
<td>$25,069/QALY</td>
</tr>
<tr>
<td>Crizotinib</td>
<td>1st Line advanced NSCLC</td>
<td>Canada</td>
<td>Pemetrexed-cisplatin</td>
<td>4 years</td>
<td>$36,550</td>
<td>0.131</td>
<td>$285,300/QALY</td>
</tr>
</tbody>
</table>

Pan-Canadian Oncology Drug Review (pCODR)
Cost-effectiveness of Public Policy Initiatives
Cost-effectiveness of Smoking Cessation Interventions

• Estimating the costs in CDN $ of publically funded interventions to achieve an additional quality-adjusted life year through prevention of smoking related morbidity and mortality
  – Smoker’s Helpline operated by Canadian Cancer Society
  – Ottawa Model of smoking cessation for hospitals
Ontario Smoker’s Helpline

• Province-wide cessation service
• Operated by Canadian Cancer Society; funded by Ministry of Health
• Trained counsellors offer callers:
  – information
  – evidence-based behavioural counseling
  – referrals to local services
  – scheduled follow-up counseling
## Quitline Effectiveness

Effectiveness of and estimated abstinence rates for quitline counseling compared to minimal interventions, self-help or no counseling (n = 9 studies)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Number of arms</th>
<th>Estimated odds ratio (95% C.I.)</th>
<th>Estimated abstinence rate (95% C.I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal or no counseling or self-help</td>
<td>11</td>
<td>1.0</td>
<td>8.5</td>
</tr>
<tr>
<td>Quitline counseling</td>
<td>11</td>
<td>1.6 (1.4, 1.8)</td>
<td>12.7 (11.3, 14.2)</td>
</tr>
</tbody>
</table>
Smoker’s Help Line Cost-effectiveness

• Reported 30 day quit rate  15.%
• Expected quit rate (5.0 – 6.3%)
• Cost per additional quitter ranges from $900 - $ 1,650 CDN
• Highly cost-effective (ICUR < $20,000) at 4 years and dominant by 7 years
• Program provides good outcomes at low cost and is cost-effective
Ottawa Model of Smoking Cessation

- Evidence-based tobacco treatment in acute care-hospital setting
- Free counseling, self-help materials, pharmacotherapy offered
- After discharge, smokers contacted and offered assistance for 6-month period
- 2010-2011 3,870 patient –smokers treated from 14 regional hospitals
Ottawa Model for Smoking Cessation

- 30 day abstinence rate 47.1%
- Estimated cost per quitter including front-line staff $250 ($163 if staff excluded)
- Providing hospitalized patients with OMSC program is cost-effective and reached the $20,000 threshold by 2 years and dominance between 2 and 3 years
14 Hospitals Randomized to Usual Care vs OSCM Intervention

- **Usual Care Group**
  - n=641

- **Ottawa Model for Smoking Cessation Implementation**

- **Intervention Group**
  - n=726

- **2 year follow up**

**Outcomes:**
- all-cause readmissions (primary)
- smoking-attributable readmissions
- all-cause and smoking-related ER visits
- all-cause and smoking-related physician visits
- mortality
- cost
## Reductions in 30-day Healthcare Utilization

<table>
<thead>
<tr>
<th></th>
<th>Percent reduction</th>
<th>P-value</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause admissions</td>
<td>50</td>
<td>.0007</td>
<td>16</td>
</tr>
<tr>
<td>Smoking-related re-admissions</td>
<td>45</td>
<td>.0002</td>
<td>38</td>
</tr>
<tr>
<td>ER visits</td>
<td>30</td>
<td>.001</td>
<td>23</td>
</tr>
</tbody>
</table>

## Reductions in 2-year Healthcare Utilization and Risk of Death

<table>
<thead>
<tr>
<th></th>
<th>Percent reduction</th>
<th>P-value</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cause re-admissions</td>
<td>21</td>
<td>&lt;.0001</td>
<td>7</td>
</tr>
<tr>
<td>Smoking related re-admissions</td>
<td>21</td>
<td>&lt;.0001</td>
<td>10</td>
</tr>
<tr>
<td>ER visits</td>
<td>9</td>
<td>.04</td>
<td>25</td>
</tr>
<tr>
<td>Death</td>
<td>40</td>
<td>.0002</td>
<td>14</td>
</tr>
</tbody>
</table>
Reduction in Mean Healthcare Costs

Services included:
Inpatient admissions, ED visits, physician services, long term care, home care

Spend < $80
Save $4,100

Asthma ↓ 52%
>53 yrs ↓ 36%
COPD ↓ 35%
Diabetes ↓ 28%
3+ Chronic diseases ↓ 28%
Conclusions

• There is compelling evidence that treatment of tobacco dependence is both effective and cost-effective across a wide range of settings and interventions

• Screening for tobacco use and a brief intervention is one of the three most effective clinical preventive services

• Every healthcare encounter, including those with cancer patients should involve screening, advice to quit and referral for smoking cessation counseling and for therapy
Thank you

Questions?
CE of Smoking Cessation in LDCT Screening

• CE of annual screening no cessation
  – 130,000 LYG
  – 51,000 QALYs
  – Average ICER $52,000/QALY

• CE with smoking cessation (22.5% increase in quit rate; $440 per smoker)
  – 224,000 LYG
  – 117,000 QALYs
  – Average ICER $24,000/QALY

Cost-effectiveness of Smoking Cessation before Surgical Resection in Early NSCLC

- Slatore et al. 2009
- Decision analytic Markov model
- Intervention: NRT + 2 short and 2 long counselling sessions vs no program
- Perspective US health care providers
- Total program cost $199.96
- Abstinence rate reported at time of surgery (78%) and 3-month post-surgery (19%)
- Usual care rates 65% and 12%
- Yearly mortality 5.1% for recent quitters and 17.6% for current smokers
- At 1-year post-op, ICERs was $16,415 per QALY
- At 5 years, ICER was $2,609 per QALY