Lung Cancer Epidemiology & Prevention

A/Prof Fraser Brims
Introduction

Lung cancer burden
- Global, Australia, WA
- Current smoking rates
- Other risks and associations

Prevention
- Tobacco control
- E-cigarettes
Before the 20th century lung cancer was a rare disease

2012: Men >1.2-1.4m (17% of all cancers in the world)

58% of all lung cancers now occur in developing countries

Epidemiology is determined by tobacco use

Over the last 25 years: less squamous cell, more adenocarcinoma
Lung cancer – Australian Stats

2017:

5th most commonly diagnosed cancer in Australia
Most common cause of death from cancer
~10% of all new cancers
12,434 cases diagnosed


Source: AIHW [1].
Increasing risk with age

Estimated age-specific incidence and mortality rates for lung cancer, by sex, 2017

Source: AIHW [1].
Increasing incidence in females

Source: AIHW [2].
Increasing incidence in females

Australia

The Netherlands

United Kingdom

United States
Stages of the tobacco epidemic
Relative risk of lung cancer

ETS = environmental tobacco smoke

Cancer Australia, 2014
*dose dependent risk; raised risk with tobacco smoke

Occupational exposures – relative risk of lung cancer

- Radon*
- Aresenic*
- PAH
- Cadmium
- Asbestos*
- Silica*
- Iron & Steel*
- Nickel*
- Beryllium
- Painting
- Chromium VI
- Diesel

Cancer Australia, 2014
Never smokers and lung cancer

Up to 15% of men and 53% women

Genetics, ethnicity, occupational & environmental exposures

Histology – more adeno ++, few squamous and no small cell

Molecular – more EGFR & ALK mutations

Different disease
Stage at diagnosis

Very poor staging data for Australia & WA

Stage I  14-19%
Stage II  3.5-7.3%
Stage III 26.2-29.9%
Stage IV 46.8-55%

Walters, Thorax 2012

ORIGINAL ARTICLE
Lung cancer survival and stage at diagnosis in Australia, Canada, Denmark, Norway, Sweden and the UK: a population-based study, 2004–2007

Walters, Thorax 2012
Stage at diagnosis

Very poor staging data for Australia & WA

Stage I  14-19%  ) Surgery: 14-18%
Stage II  3.5-7.3%  )
Stage III  26.2-29.9%  )
Stage IV  46.8-55%

Original Article
Lung cancer survival and stage at diagnosis in Australia, Canada, Denmark, Norway, Sweden and the UK: a population-based study, 2004–2007

Walters, Thorax 2012
## Stage at diagnosis

<table>
<thead>
<tr>
<th>Stage</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>81.2</td>
<td>85.1</td>
</tr>
<tr>
<td>Stage II</td>
<td>66.3</td>
<td>68.7</td>
</tr>
<tr>
<td>Stage III</td>
<td>41.7</td>
<td>46.2</td>
</tr>
<tr>
<td>Stage IV</td>
<td>14.6</td>
<td>19.3</td>
</tr>
<tr>
<td>Stage Not Known</td>
<td>22.8</td>
<td>28.3</td>
</tr>
</tbody>
</table>

**Lung Cancer (C33-C34): 2014**

One-Year Net Survival (%) by Stage, Adults Aged 15-99, England
Global cigarette consumption

Tobacco use remains high in many countries, despite measures by some governments to curb smoking.

**Growth since 1950**

- **in billions of cigarettes smoked**
  - 1950: 1,686
  - 1960: 2,150
  - 1970: 3,262
  - 1980: 4,453
  - 1990: 5,328
  - 2000: 5,711
  - 2009: 5,884

**Top five consumers**

- 38% China
- 6.61 Russian Federation
- 3.96 Japan
- 4.42 Indonesia
- 5.35 United States

Sources: American Cancer Society, World Lung Foundation

* 2009 (latest data)
Tobacco control

WHO ‘Measures to assist with implementation with effective tobacco control’

M onitor tobacco use prevention policies
P rotect people from tobacco smoke
O ffer help to quit
W arn about the dangers of tobacco
E nforce bans on tobacco advertising, promotion and sponsorship
R aise taxes on tobacco
Death and taxes
Global

- Lung cancer death rates per 100,000 (divided by 4): men age 35–44
- Number per adult per day and death rates
- Cigarettes per adult per day
- Relative price

Plain packaging

Australia wins landmark WTO tobacco plain packaging case

Updated 5 May 2017, 2:11pm
Australian smoking rates are falling

Proportion of daily smokers in Australia (Persons aged 18–44 years)

2001: 28.2%
2014–15: 16.3%

Source: ABS

Teenage smoking habits in NSW, 1984–2008

- Never smoked
- Active smokers

Data source: New South Wales School Students Health Behaviours Survey 2008 (HOTS), NSW Ministry of Health

- Health warnings on packaging
- NSW campaign starts
- Ban on point-of-sale advertising
- National campaign starts
- Ban on all traditional advertising

1984: 32.1%
1992: 27.3%
2001: 8.6%
2005–2006: 74.7%

www.cancerinstitute.org.au/slides

Curtin University
Western Australian smoking rates are falling

**In 2014:**
- 58% of women and 49% of men were never smokers
- 12.3% current smokers (2004 = 19.4%)
- 4.8% school age students had smoked in the last week
- 96.6% homes smoke free

**In 2012/2013:**
- Aboriginal people x2.6 more likely to smoke than non-Aboriginal
- 41% Aboriginal and Torres Strait Islander people aged 15+
  current smokers


Peto, BMJ 2000
Nicotine/tobacco delivery: times are changing
Nicotine/tobacco delivery: times are changing

Pulmonary delivery of nicotine:

Cigarettes
Little cigars
Electronic nicotine delivery systems (ENDS)
Heat not burn (HNB)
Electronic Nicotine Delivery System
ENDS – e-cigarettes

Developed in China by a pharmacist
Varying policies or regulations around the world
Singapore, Australia, Canada have banned them
Canada and Australia are reconsidering
UK is overwhelming supportive of ENDS use
USA – conflicted – regulations moved off to 2022
Japan – cannot contain nicotine
E-cigarettes
E-cigarettes

Palm-sized, multiple colors
Leak-free, cute 18mg/ml of nicotine
E-cigarettes

Users can modify the settings on some products

Variable voltage
3.3-5 volts

Variable resistance
1.5-3 ohms

Build your own
"Smoking" machine data from 12 e-cigarettes

<table>
<thead>
<tr>
<th>Toxic compound</th>
<th>Conventional cigarette (µg in mainstream smoke)</th>
<th>Electronic cigarette (µg per 15 puffs)</th>
<th>Average ratio (conventional vs electronic cigarette)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formaldehyde</td>
<td>1.6–52</td>
<td>0.20–5.61</td>
<td>9</td>
</tr>
<tr>
<td>Acetaldehyde</td>
<td>52–140</td>
<td>0.11–1.36</td>
<td>450</td>
</tr>
<tr>
<td>Acrolein</td>
<td>2.4–62</td>
<td>0.07–4.19</td>
<td>15</td>
</tr>
<tr>
<td>Toluene</td>
<td>8.3–70</td>
<td>0.02–0.63</td>
<td>120</td>
</tr>
<tr>
<td>NNN</td>
<td>0.005–0.19</td>
<td>0.00008–0.00043</td>
<td>380</td>
</tr>
<tr>
<td>NNK</td>
<td>0.012–0.11</td>
<td>0.00011–0.000283</td>
<td>40</td>
</tr>
</tbody>
</table>

NNK, 4-(methylnitrosamo)-1-(3-pyridyl)-1-butanone; NNN, N'-nitrosonornicotine.

9-450 fold reduction in some toxic compounds relative to conventional cigarettes

Goniewicz et al. Tob Control; 2014
## Exposures

### Urinary Exposure Biomarker Levels*: E-Cigarette Users (n=28) vs. Cigarette Smokers

<table>
<thead>
<tr>
<th>Toxin of Interest</th>
<th>Biomarker</th>
<th>E-Cigarette User</th>
<th>Cigarette Smoker</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAH</td>
<td>1-hydroxypyrine</td>
<td>0.38</td>
<td>0.97</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>NNK</td>
<td>Total NNAL</td>
<td>0.02</td>
<td>1.21</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>NNN</td>
<td>Total NNN</td>
<td>0.005</td>
<td>0.073</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>acrolein</td>
<td>3-HPMA</td>
<td>1100</td>
<td>4040</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>crotononaldehyde</td>
<td>HMPMA</td>
<td>705</td>
<td>4990</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>propylene oxide</td>
<td>2-HPMA</td>
<td>141</td>
<td>399</td>
<td>p&lt;0.006</td>
</tr>
<tr>
<td>benzene</td>
<td>SPMA</td>
<td>0.29</td>
<td>2.85</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>nicotine</td>
<td>cotinine</td>
<td>1880</td>
<td>1930-3930</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Geometric means, pmol/ml urine

adapted from Hecht et al. Nicotine Tob Res; 2015.
BMJ – US cessation with ENDS

Zhu et al. BMJ 2017; 358:j3262
February 2018

Based on current evidence, the potential benefit of e-cigarettes on smoking cessation is not established, and there is increasing evidence of health harms. Accordingly, the undersigned health and medical organisations support a precautionary approach to the promotion and availability of e-cigarettes in Australia. This is in line with recommendations from the World Health Organization and the World Federation of Public Health Associations.
Statement on e-cigarettes in Australia

Additionally, the following health organisations support a precautionary approach to e-cigarettes:

- National Health and Medical Research Council
- Australian Medical Association
- Cancer Council Australia
- National Heart Foundation of Australia
- Public Health Association of Australia
- Royal Australasian College of Physicians
- Royal Australian College of General Practitioners
- Lung Foundation of Australia
- Australian Association of Smoking Cessation Professionals
- Australian Council on Smoking and Health
- Australian Competition & Consumer Commission
- Departments of Health in Australian states/territories
- World Health Organization
- World Medical Association
- World Heart Foundation
- World Federation of Public Health Associations
- Forum of International Respiratory Societies
- International Union Against Tuberculosis and Lung Disease
- British Medical Association
- Royal Pharmaceutical Society
- New Zealand Cancer Society
- Heart and Stroke Foundation, Canada
- American Association for Cancer Research
- American Society of Clinical Oncology
- US Surgeon General
- American Lung Association
- American Thoracic Society
- National Association of Attorneys General (USA)
- American College of Preventive Medicine
- American Medical Association
- American Society of Addiction Medicine
- American Osteopathic Association
- American Association of Clinical Endocrinologists
- American College of Cardiology
- American Academy of Family Physicians
- American Academy of Pediatrics
- Society of Thoracic Surgeons
- American College of Chest Physicians.
Heat not Burn

HNB – heats rather than combusts the tobacco
Still is pulmonary delivery
Still an aerosol
Is NOT ‘smokeless’
600 degrees Centigrade versus 800+
Heat not Burn: Philip Morris International

“Our goal for Japan is to switch every consumer we have to this. For me, it’s like a no-brainer. The biggest thing we know that smoking kills. If we’ve got an alternative to that, that’s a pretty good reason to switch.”

Launched in Japan 2014, ‘heat sticks’ “iQOS”
May 2017: 8.8% market share

“If you extrapolate the figures, then logically we could reach the tipping point in five years. That is when we could start talking to governments about phasing out combustible cigarettes entirely.”
iQOS: 5 days after smoking abstinence

Carbon monoxide

1,3-butadiene

Acrolein

Benzene

www.fda.gov/downloads/TobaccoProducts/Labeling/MarketingandAdvertising/UCM560044.pdf
% reduction day 90
iQOS vs smoking abstinence

In Japan

In USA

www.fda.gov/downloads/TobaccoProducts/Labeling/MarketingandAdvertising/UCM560044.pdf
Q2, 2017: Strong Sequential Growth Trend in RRP Net Revenues

($ millions)

<table>
<thead>
<tr>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1</td>
<td>55</td>
</tr>
<tr>
<td>Q2</td>
<td>123</td>
</tr>
<tr>
<td>Q3</td>
<td>212</td>
</tr>
<tr>
<td>Q4</td>
<td>343</td>
</tr>
</tbody>
</table>

Contribution to Total Net Revenues

<table>
<thead>
<tr>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.9%</td>
<td>8.9%</td>
</tr>
<tr>
<td>1.8%</td>
<td>7.2%</td>
</tr>
<tr>
<td>3.0%</td>
<td></td>
</tr>
<tr>
<td>4.9%</td>
<td></td>
</tr>
</tbody>
</table>

Note: "Reduced-risk products," or "RRPs," is the term PMI uses to refer to products that present, are likely to present, or have the potential to present less risk of harm to smokers who switch to these products versus continued smoking. Pack design and visual are for illustrative purposes only.

Source: PMI Financials or estimates

https://www.pmi.com/investor-relations/overview/event-details/?eventId=5246143
Key points

Lung cancer burden
– continues to increase
  - follows tobacco consumption trends

E-cigarettes / HNB - short term / long term

Prevention, prevention, prevention, screening?
Thoughts & Questions ?