The Global Burden of Alcohol-Attributable Cancers

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Alcohol and Cancer: Preview of Coming Attractions

Wednesday April 11, 2018
As required by the Alcohol Policy 18 Conference, I/we have signed a disclosure statement and note the following conflict(s) of interest:

None
# Modifiable risk factors for cancer

<table>
<thead>
<tr>
<th>Lifestyle factors</th>
<th>Occupational and Environmental factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>Occupation</td>
</tr>
<tr>
<td>Infections</td>
<td>Air pollution</td>
</tr>
<tr>
<td>Obesity</td>
<td>Chemical risks</td>
</tr>
<tr>
<td>Sedentary lifestyle</td>
<td>Radiation</td>
</tr>
<tr>
<td>Alcohol</td>
<td>Socio-economic status</td>
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<tr>
<td>Diet and vitamin D</td>
<td></td>
</tr>
<tr>
<td>Suboptimal breastfeeding</td>
<td></td>
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<tr>
<td>UV exposure</td>
<td></td>
</tr>
<tr>
<td>Exogenous hormone use</td>
<td></td>
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<tr>
<td>Aspirin</td>
<td></td>
</tr>
</tbody>
</table>

Approximately 40% of cancers are avoidable.

Some symbols were obtained from Cancer UK
A causal relationship between alcohol and the following cancers has been confirmed:

- Oral cavity and pharyngeal (excluding nasopharyngeal)
- Oesophageal (squamous cell carcinoma)
- Colorectal
- Liver
- Laryngeal
- Breast (female)

**Biological pathways:**

- Ethanol metabolism
- Inhibition of the one carbon metabolism pathway
- Modification of hormone levels and associated signaling pathways
Alcohol consumption and the risk of developing cancer by subtype

- Alcohol consumption (in terms of volume) is related to the overall risk of cancer incidence and mortality.

- Meta-analyses of epidemiological studies show that alcohol consumption increases the risk (incidence of and mortality from) various cancers.

<table>
<thead>
<tr>
<th>Site (number of included studies)</th>
<th>Alcohol intake</th>
<th>RR (95% CI)</th>
<th>I² (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral cavity and pharynx (52)</td>
<td>Light</td>
<td>1.13</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>1.85</td>
<td>72</td>
</tr>
<tr>
<td></td>
<td>Heavy</td>
<td>5.13</td>
<td>77</td>
</tr>
<tr>
<td>Oesophageal SCC (54)</td>
<td>Light</td>
<td>1.26</td>
<td>68</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>2.23</td>
<td>85</td>
</tr>
<tr>
<td></td>
<td>Heavy</td>
<td>4.95</td>
<td>91</td>
</tr>
<tr>
<td>Oesophagus AC and gastric cardia (25)</td>
<td>Light</td>
<td>0.86</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>0.97</td>
<td>46</td>
</tr>
<tr>
<td></td>
<td>Heavy</td>
<td>1.15</td>
<td>36</td>
</tr>
<tr>
<td>Stomach (39)</td>
<td>Light</td>
<td>0.99</td>
<td>55</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>0.97</td>
<td>48</td>
</tr>
<tr>
<td></td>
<td>Heavy</td>
<td>1.21</td>
<td>41</td>
</tr>
<tr>
<td>Small intestine (5)</td>
<td>Light</td>
<td>1.05</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>1.00</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Heavy</td>
<td>1.07</td>
<td>21</td>
</tr>
<tr>
<td>Colorectum (66)</td>
<td>Light</td>
<td>0.99</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>1.17</td>
<td>66</td>
</tr>
<tr>
<td></td>
<td>Heavy</td>
<td>1.44</td>
<td></td>
</tr>
<tr>
<td>Liver (36)</td>
<td>Light</td>
<td>1.00</td>
<td>47</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>1.08</td>
<td>45</td>
</tr>
<tr>
<td></td>
<td>Heavy</td>
<td>2.07</td>
<td>79</td>
</tr>
<tr>
<td>Gallbladder (8)</td>
<td>Light</td>
<td>1.23</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>0.88</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Heavy</td>
<td>2.61</td>
<td></td>
</tr>
<tr>
<td>Pancreas (39)</td>
<td>Light</td>
<td>0.95</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>1.03</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>Heavy</td>
<td>1.19</td>
<td>0</td>
</tr>
<tr>
<td>Larynx (41)</td>
<td>Light</td>
<td>0.87</td>
<td>39</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>1.44</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td>Heavy</td>
<td>2.65</td>
<td></td>
</tr>
<tr>
<td>Lung (84)</td>
<td>Light</td>
<td>0.84</td>
<td>44</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>0.98</td>
<td>57</td>
</tr>
<tr>
<td></td>
<td>Heavy</td>
<td>1.15</td>
<td>73</td>
</tr>
<tr>
<td>Melanoma (14)</td>
<td>Light</td>
<td>1.11</td>
<td>36</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>1.20</td>
<td>38</td>
</tr>
<tr>
<td></td>
<td>Heavy</td>
<td>Not evaluable</td>
<td></td>
</tr>
<tr>
<td>Female breast (118)</td>
<td>Light</td>
<td>1.04</td>
<td>63</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>1.23</td>
<td>54</td>
</tr>
<tr>
<td></td>
<td>Heavy</td>
<td>1.61</td>
<td>10</td>
</tr>
</tbody>
</table>

Bagnardi et al., 2015, *IJC*
Alcohol consumption and the risk of developing cancer

Cao et al., 2016, *BMJ*
Former drinkers and cancer risk

Laryngeal cancer

![Graph showing risk decline over time for laryngeal cancer after drinking cessation]

Pharyngeal cancer

![Graph showing risk decline over time for pharyngeal cancer after drinking cessation]

**Figure.** Risk decline of laryngeal and pharyngeal cancers over a forty year period after drinking cessation

Kiadaliri et al., 2013, *PLoS One*
Attributable fractions

Outcome data

*Cancer incidence and mortality by site:* Global Cancer Observatory

Exposure data

*Alcohol consumption data:* Adult per capita consumption of ethanol in 2002 - Global Information System on Alcohol and Health

*Drinking data:* Surveys on drinking status and consumption among drinkers globally for 2005

Relative Risks:

Site-specific meta-analyses [Bagnardi et al., 2015]

Population data:

United Nations Population Division

All data by country, age, and sex
Global alcohol consumption in 2002

Litres of pure alcohol per adult per year

- > 12.2
- > 10.0 to 12.2
- > 6.7 to 10.0
- > 4.9 to 6.7
- > 1.8 to 4.9
- > 0.2 to 1.8
- < 0.9
- No data (not estimated)
- Not applicable

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

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Trends in alcohol consumption in Europe

*Colors represent quartiles of per capita consumption of alcohol as of 2012*
Cancer cases in 2012 due to alcohol

769,400 Cases Per year
5.5% of all new Cancer cases

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Cancer cases in 2012

14,100,000 new cancer cases

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Source: IARC, 2017
Cancer deaths in 2012 due to alcohol

426,100 Deaths Per year
5.2% of all cancer deaths

World Health Organization
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Cancer deaths in 2012

Age-standardized new cancer deaths per 100,000 people

Source: IARC, 2017

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Source: IARC, 2017
Cancer cases in 2012 due to alcohol, by cancer site

- Oesophageal (SCC):
  - Former drinking: 2.1%
  - Light drinking: 5.8%
  - Moderate drinking: 13.1%
  - Heavy drinking: 14.7%

- Lip, oral cavity and pharynx:
  - Former drinking: 1.0%
  - Light drinking: 2.0%
  - Moderate drinking: 6.8%
  - Heavy drinking: 16.1%

- Larynx:
  - Former drinking: 1.6%
  - Light drinking: 2.2%
  - Moderate drinking: 7.1%
  - Heavy drinking: 12.5%

- Liver:
  - Former drinking: 2.6%
  - Light drinking: 1.5%
  - Moderate drinking: 3.5%
  - Heavy drinking: 3.3%

- Colorectal:
  - Former drinking: 2.8%
  - Light drinking: 1.3%
  - Moderate drinking: 3.1%
  - Heavy drinking: 3.6%

- Breast:
  - Former drinking: 2.8%
  - Light drinking: 1.5%
  - Moderate drinking: 2.8%
  - Heavy drinking: 2.5%

Percent (%) of new cancer cases attributable to alcohol
Cancer deaths in 2012 due to alcohol, by cancer site

- **Oesophageal (SCC)**
  - Former drinking: 2.0%
  - Light drinking: 5.9%
  - Moderate drinking: 13.5%
  - Heavy drinking: 15.3%

- **Lip, oral cavity and pharyngeal**
  - Former drinking: 1.1%
  - Light drinking: 2.3%
  - Moderate drinking: 7.9%
  - Heavy drinking: 17.0%

- **Laryngeal**
  - Former drinking: 1.6%
  - Light drinking: 2.4%
  - Moderate drinking: 7.6%
  - Heavy drinking: 13.0%

- **Colorectal**
  - Former drinking: 2.7%
  - Light drinking: 1.4%
  - Moderate drinking: 3.5%
  - Heavy drinking: 4.1%

- **Breast**
  - Former drinking: 2.8%
  - Light drinking: 1.8%
  - Moderate drinking: 3.6%
  - Heavy drinking: 3.0%

- **Liver**
  - Former drinking: 2.5%
  - Light drinking: 1.6%
  - Moderate drinking: 3.6%
  - Heavy drinking: 3.4%
Effects of a 10% reduction in consumption: Cancer cases

- Colorectal: Non-preventable - men: 128,000, Preventable - men: 9,600, Non-preventable - women: 2,300, Preventable - women: 21,800, Total: 151,500
- Liver: Non-preventable - men: 36,200, Preventable - men: 2,000, Non-preventable - women: 200, Preventable - women: 2,300, Total: 43,700
- Laryngeal: Non-preventable - men: 0, Preventable - men: 0, Non-preventable - women: 0, Preventable - women: 0, Total: 0
Effects of a 10% reduction in consumption: Cancer deaths

- Oesophageal (SCC):
  - Non-preventable - men: 105,500
  - Preventable - men: 8,200
  - Non-preventable - women: 19,000
  - Preventable - women: 1,400

- Liver:
  - Non-preventable - men: 63,700
  - Preventable - men: 3,200
  - Non-preventable - women: 18,000
  - Preventable - women: 800

- Colorectal:
  - Non-preventable - men: 49,500
  - Preventable - men: 2,200
  - Non-preventable - women: 25,500
  - Preventable - women: 1,500

- Lip, oral cavity and pharyngeal:
  - Non-preventable - men: 67,000
  - Preventable - men: 4,600
  - Non-preventable - women: 8,800
  - Preventable - women: 800

- Breast:
  - Non-preventable - men: 18,400
  - Preventable - men: 1,000
  - Non-preventable - women: 49,500
  - Preventable - women: 3,800

- Laryngeal:
  - Non-preventable - men: 18,400
  - Preventable - men: 1,000
  - Non-preventable - women: 49,500
  - Preventable - women: 3,800
Alcohol-attributable cancer burden, by Human Development Index
Alcohol-attributable cancer burden: The example of France in 2015

<table>
<thead>
<tr>
<th>Cancer site (ICD-10 code)</th>
<th>Total</th>
<th>Attributable cases</th>
<th>Population-Attributable Fraction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Causal evidence</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral cavity, oropharynx and hypopharynx (C01-C06, C09-C10, C12-C13)</td>
<td></td>
<td>5,679</td>
<td>54.6%</td>
</tr>
<tr>
<td>Oesophagus (SCC) (C16)</td>
<td></td>
<td>1,807</td>
<td>57.7%</td>
</tr>
<tr>
<td>Colorectum (C18-20)</td>
<td></td>
<td>6,664</td>
<td>16.7%</td>
</tr>
<tr>
<td>Liver (C22)</td>
<td></td>
<td>4,357</td>
<td>47.8%</td>
</tr>
<tr>
<td>Larynx (C22)</td>
<td></td>
<td>1,284</td>
<td>37.3%</td>
</tr>
<tr>
<td>Breast (C50)</td>
<td></td>
<td>8,104</td>
<td>15.1%</td>
</tr>
</tbody>
</table>

| **Insufficient evidence of causality** |       |                    |                                       |
| Stomach (C16)               |       | 444                | 6.2%                                  |
| Gallbladder (C23)           |       | 463                | 17.5%                                 |
| Pancreas (C25)              |       | 761                | 6.7%                                  |
| Prostate (C61)              |       | 2,663              | 5.8%                                  |
| Kidney (C64)                |       | (2,729)            | -22.3%                                |
| **Total (causal only)**     |       | 27,894             | 7.9%                                  |
| **Total (all sites)**       |       | 29,495             | 8.4%                                  |
Limitations and the critical need for further research

Biases in the data
– Relative risks: grouping of former drinkers and lifetime abstainers
– Survey biases: drinking status

Areas of future research
– Risk relationships by genotype
  o e.g. ‘Flushing gene’ ALDH2
– Interaction between alcohol and tobacco smoke
Alcohol consumption, smoking, and cancer

Cao et al., 2016, BMJ
Alcohol metabolism and the risk of cancer: The effects of genetic modifications

**Figure.** How genetic polymorphisms affect the risk relationship between alcohol and cancer incidence
**ALDH2 and the risk of esophageal cancer**

- **ALDH2** is characterized by a “flushing” phenotype.

- This genotype is found in Asian populations (e.g., in Japan, Korea, and China).

- The risk of cancer among people with a flushing response is much higher.

*Figure.* Cancer risk by alcohol consumption and genotype

P Brooks et al., 2009, *PLoS Med*
Alcohol-related cancers among American Indians

Moore et al., 2015, *Lancet Oncol*
Alcohol and tobacco use among American Indians / Alaskan Natives

Figure. Prevalence (%) of any past-year alcohol use disorder, nicotine dependence, and comorbid disorders, by race/ethnicity and gender in the United States, 2001–2002 NESARC. [Falk et al., 2006, Alcohol Res Health]
Alcohol-related cancers among American Indians (continued)

Moore et al., 2015, *Lancet Oncol*
The broader context of alcohol-attributable cancer harms

**SOCIETAL & POLITICAL FACTORS**
- Development and macro-economic profiles
- Culture & societal Value
- Public health policies
- Alcohol availability and marketing

**ALCOHOL CONSUMPTION**
- Volume (current and lifetime)
- Patterns (current and lifetime)
- Historical periods of alcohol consumption

**INDIVIDUAL VULNERABILITY FACTORS**
- Age and gender
- Genetics and familial factors
- Socio-economic status
- Smoking, diet, and other risk modifying factors

**OUTCOMES**
- Cancer incidence
- Social and economic harms
- Other causes of morbidity
- Cancer mortality
- Mortality from other causes