Modelling the effects of user exposure to harmful emissions across the spectrum of nicotine delivery

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Declaration: No conflicts of interest
Nicotine delivery by aerosol
Focus on cancer predictions based on emissions
Address questions such as “do different forms of nicotine delivery have less (or even more) carcinogenic potential than smoking cigarettes?”

6.4 million global tobacco-attributable deaths in 2015

From Tobacco Atlas, 4th edition
Model pathways of nicotine transfer by aerosol

**SOURCE** → **LIBERATION** → **MOBILISATION** → **INHALATION** → **FATE**

- **COMBUSTION**: Cigarettes, RYO, kretek
- **HEAT-NOT-BURN**: Waterpipe, iQOS, Glo
- **ATOMISING**: e-cigarettes

**Absorption** & circulation biomarkers → **Detoxification**

Toxicity: clinical epidemiology
Measuring emissions by machine

• Smoking machine collects particles and vapour using a set “puffing” protocol
• Emissions analysed off-line for “concentrations” of volatiles, particulate materials, metals, etc.
• US Food & Drug Administration (FDA) list 93 Harmful & Potentially Harmful Constituents (HPHC) in tobacco products
  ➢ 75 carcinogens
  ➢ 25 respiratory toxicants
  ➢ 12 cardiovascular toxicants
• Cigarettes well analysed, quality assurance
• Other products have less well developed protocols, reference standards etc.

<table>
<thead>
<tr>
<th></th>
<th>Canadian Intense</th>
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<tbody>
<tr>
<td>Puff volume (mL)</td>
<td>55</td>
</tr>
<tr>
<td>Puff frequency</td>
<td>30s</td>
</tr>
<tr>
<td>Ventilation holes</td>
<td>100% blocked</td>
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Methodology

- Inhalation **unit risk** is the increased cancer risk from inhalation exposure to 1 µg/m³ of a compound for a lifetime
- Unit risks for obtained from toxicological assessments by environmental protection agencies

**Cancer Potency** (individual compound) = Unit risk x Concentration

**Cancer Potency** (aerosol) = sum of individual potencies

\[ P_{sample} = U_1 C_{sample,1} + U_2 C_{sample,2} \ldots + U_n C_{sample,n} \]

**Cancer Risk** = Cancer Potency x Exposure

Proxies for exposure
- Nicotine: unit nicotine basis (=nicotine)
- Volume: daily aerosol intake (volume)
Comparison with Cigarette Smoke

“If I give up smoking cigarettes and get my nicotine from product X how would my health be affected in the longer term?”

Method not suitable for determining of absolute risk of cancer from product $i$ relative to the risk of cancer from smoking

Useful for comparing relative risks

$$R_{i/cig} = \frac{Cancer \ risk \ for \ product \ X}{Cancer \ risk \ for \ average \ cigarette \ smoke}$$

Average cigarette smoke based on data in peer reviewed publications from labs in public sector, independent consultancies and tobacco industry
Cancer potency: Context

Variable: Relative cancer potency
Source: Peer-reviewed literature
Symbols: Individual experiments

Cancer potency relative to tobacco smoke
Combustible tobacco

- Potency: Inhaler
- Risk (=nicotine): RYO, Kretek
- Risk (volume): RYO (roll your own)

Risk or potency relative to cigarette smoke

- Combustible tobaccos: Kretek (clove cigarette), RYO (roll your own), Pipes & cigars
Heated Tobacco: Resistance Heating Devices

- glo (BAT)
- iQOS (PMI)

### Potency
- Air
- Inhaler
- Heat not burn
- Cigarette smoke

### Risk

**Risk (=nicotine)**

**Risk (volume)**

- Risk or potency relative to cigarette smoke
- Heat not burn
- Cigarette smoke

- glo (BAT)
- iQOS (PMI)
Heated Tobacco: Waterpipe (Charcoal heating)

Potency

Risk (=nicotine)

Risk (volume)

Based on maximum in Shihadeh et al. (2015)

Risk or potency relative to cigarette smoke

Heat not burn

Cigarette smoke

10^{-6} 10^{-5} 10^{-4} 10^{-3} 10^{-2} 10^{-1} 10^{0} 10^{1}
Heated liquid vapourisers ("e-cigarettes")

Risk or potency relative to cigarette smoke

Risk (nicotine)

Risk (volume)

Potency

Pote
Risk 
Risk 
cigarette
smoke
inhaler
air
heat
not
burn
Cancer Potency of E-cigarettes by Generation

**GENERATION**

1st

2nd

3rd

4th

![Cigarettes with cancer potency indication](image)

**Cancer potency relative to tobacco smoke**

- 10^-1
- 10^-2
- 10^-3
- 10^-4
- 10^-5
- 10^0
- 10^1

**potency of tobacco smoke**
Farsalinos et al. Formaldehyde Aversion Experiments

V-formaldehyde relationship and effect on vapour acceptability

Formaldehyde (µg/mL) vs. Volts graph
- Total aversion
- Some aversion
- No aversion
(r² = 0.98)

Data from Farsalinos et al. (2017)

26 users

Risk or potency relative to cigarette smoke
- Potency
- Risk (=nicotine)
- Risk (volume)

Risk categories:
- Inhaler
- Heat
- Not burn
- Cigarette smoke

Risk and potency scale:
- 10⁻⁶ to 10⁻¹
- 10⁻¹ to 10⁰
Shortcomings and Unknowns

• Toxicological models
  More comprehensive models in advanced development with better constraints on uncertainties

• Metals
  E-cigarette devices are generally metallic
  Concentrations in vapour rarely measured
  Speciation, eg Cr(0), Cr(III) or Cr(VI), is largely unknown

• Particle size distributions
  Variation in distributions could be toxicologically relevant especially if large fraction of nanoparticles
Continuum of Risk for Nicotine Delivery by Aerosol

![Graph showing the potency of aerosol from different sources.]

- **Potency of aerosol average cigarette smoke**
- **Cigarette**
- **Kretek**
- **RYO**
- **Waterpipe**
- **HnB**
- **e-cig**
- **Inhaler**
- **Air**