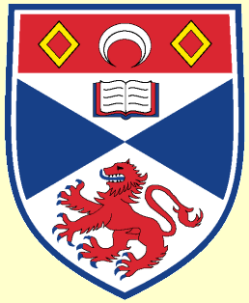
UK E-Cigarette Summit 2017

Relative risks of cancer posed by combustible and vapourising forms of nicotine delivery: Evidence from chemical exposures

Ed Stephens

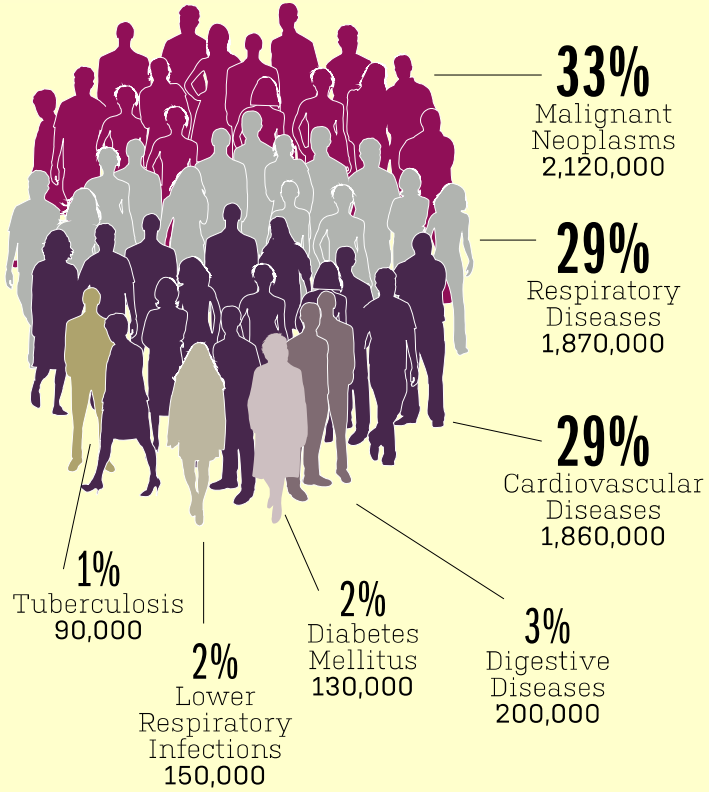


University of St Andrews

Scope of presentation

- Focus on cancer
- Carcinogenic potential of different nicotine aerosols assessed
- Use published data from many labs
- Aim to create a potency spectrum for comparing tobacco smoke, heat-not-burn emissions, e-cigarette vapour and other nicotine-delivering aerosols
- Convert potencies to risk via exposure
- Use tobacco smoke as basis for comparing relative risk

Projected global tobacco-attributable deaths in 2015

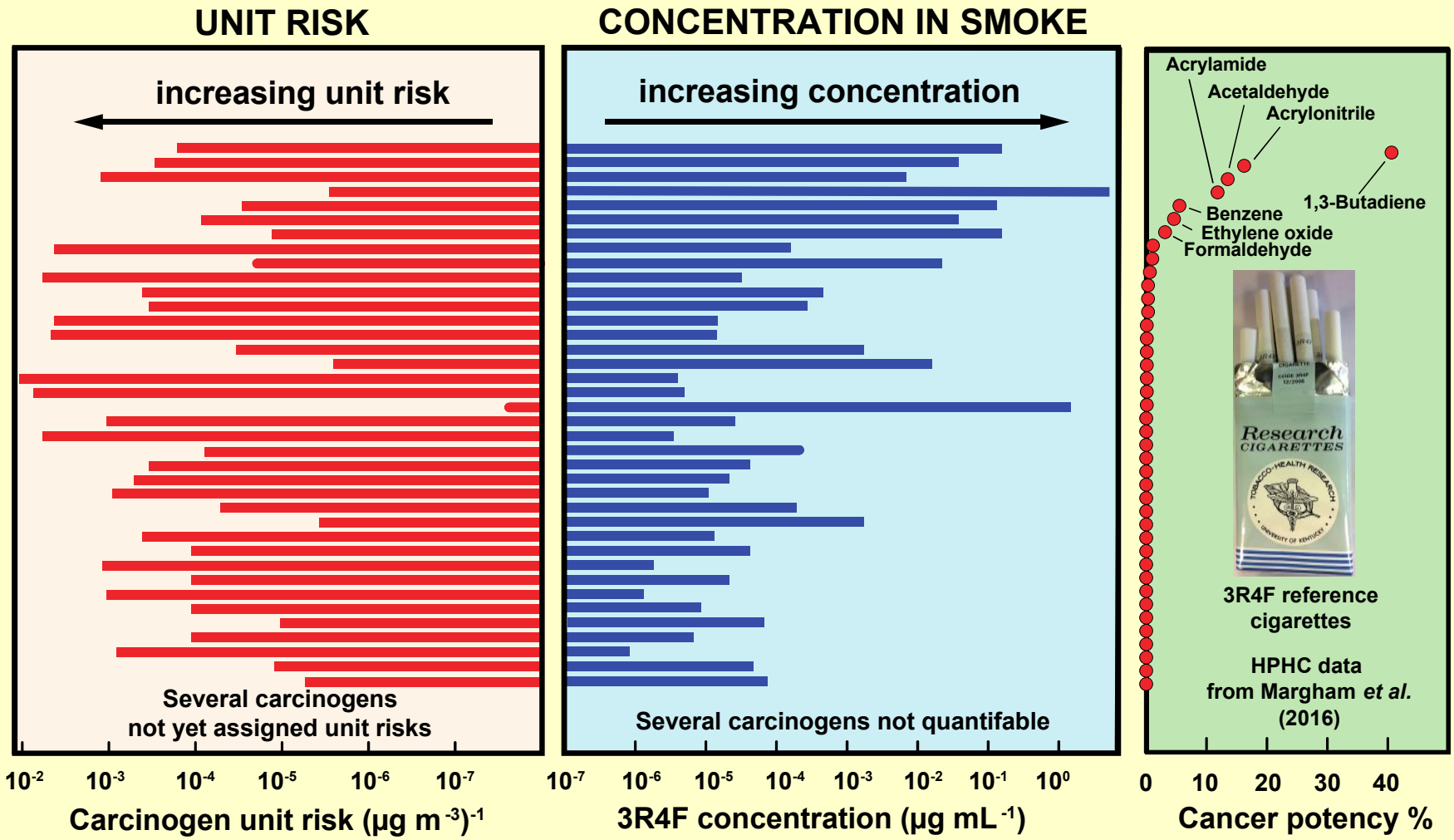


From Tobacco Atlas, 4th edition

Carcinogens in tobacco

- US Food & Drug Administration (FDA) list of Harmful & Potentially Harmful Constituents (HPHC) in tobacco products
- 93 chemical compounds in list, including
  - 75 carcinogens
  - 25 respiratory toxicants
  - 12 cardiovascular toxicants
- Others have added toxicants specifically for e-cigarettes (HPHC+)
- Full HPHC+ analysis well beyond the capability of most labs (>20 separate analytical procedures)
- Major tobacco companies use Labstat Inc. for independent analyses of HPHC or HPHC+ suite in their products, along with QA monitors (3R4F). Now publishing results in peer review journals
- Inhalation unit risk is the increased cancer risk from inhalation exposure to 1 $\mu g/m^3$ of a compound for a lifetime
- Unit risks for 44 HPHC carcinogens found in various sources

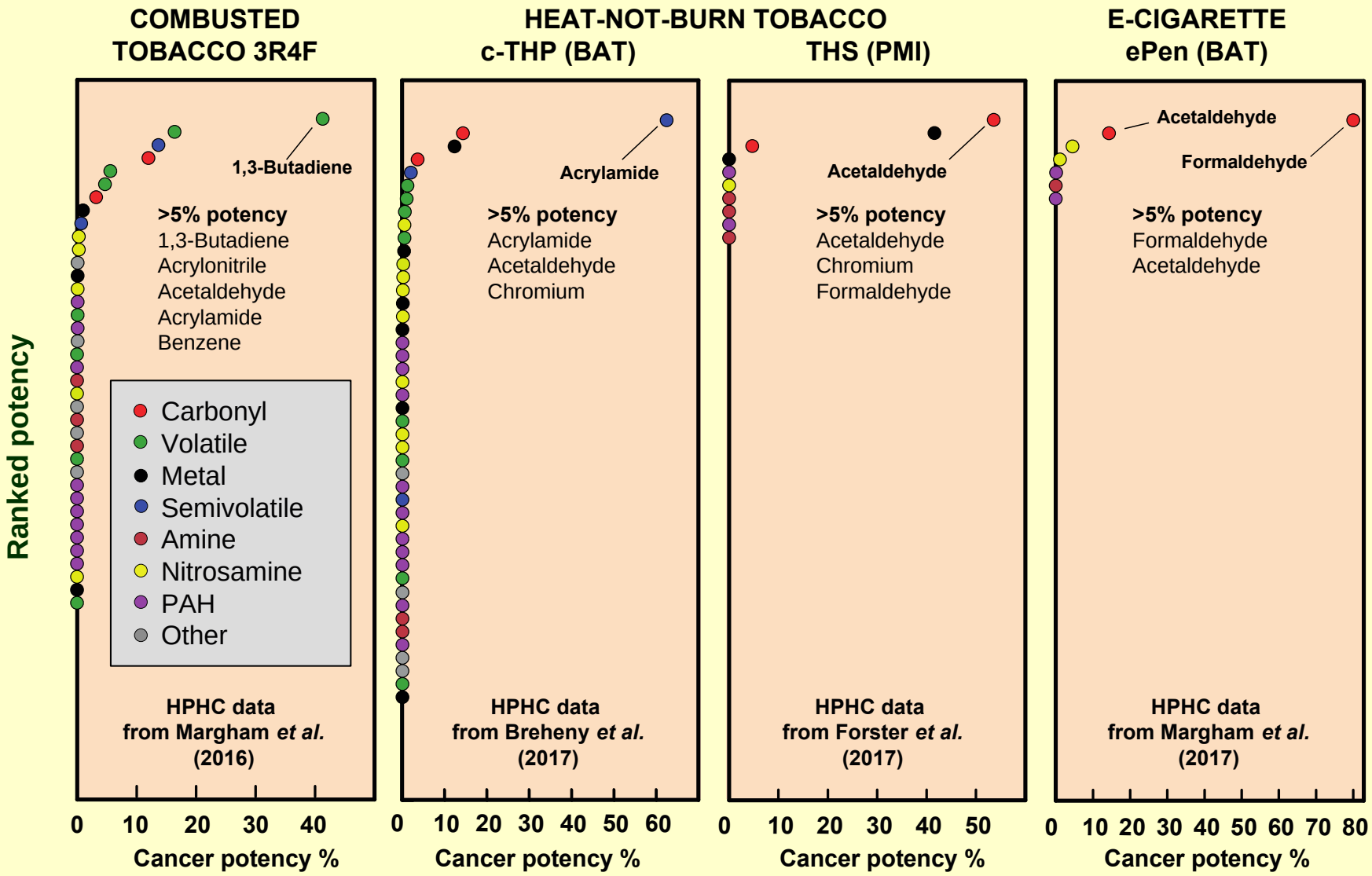
Prioritising Carcinogens



Cancer Potency (individual compound) = Unit risk x Concentration

Cancer Potency (aerosol) = sum of individual potencies

Comparing Priority Carcinogens



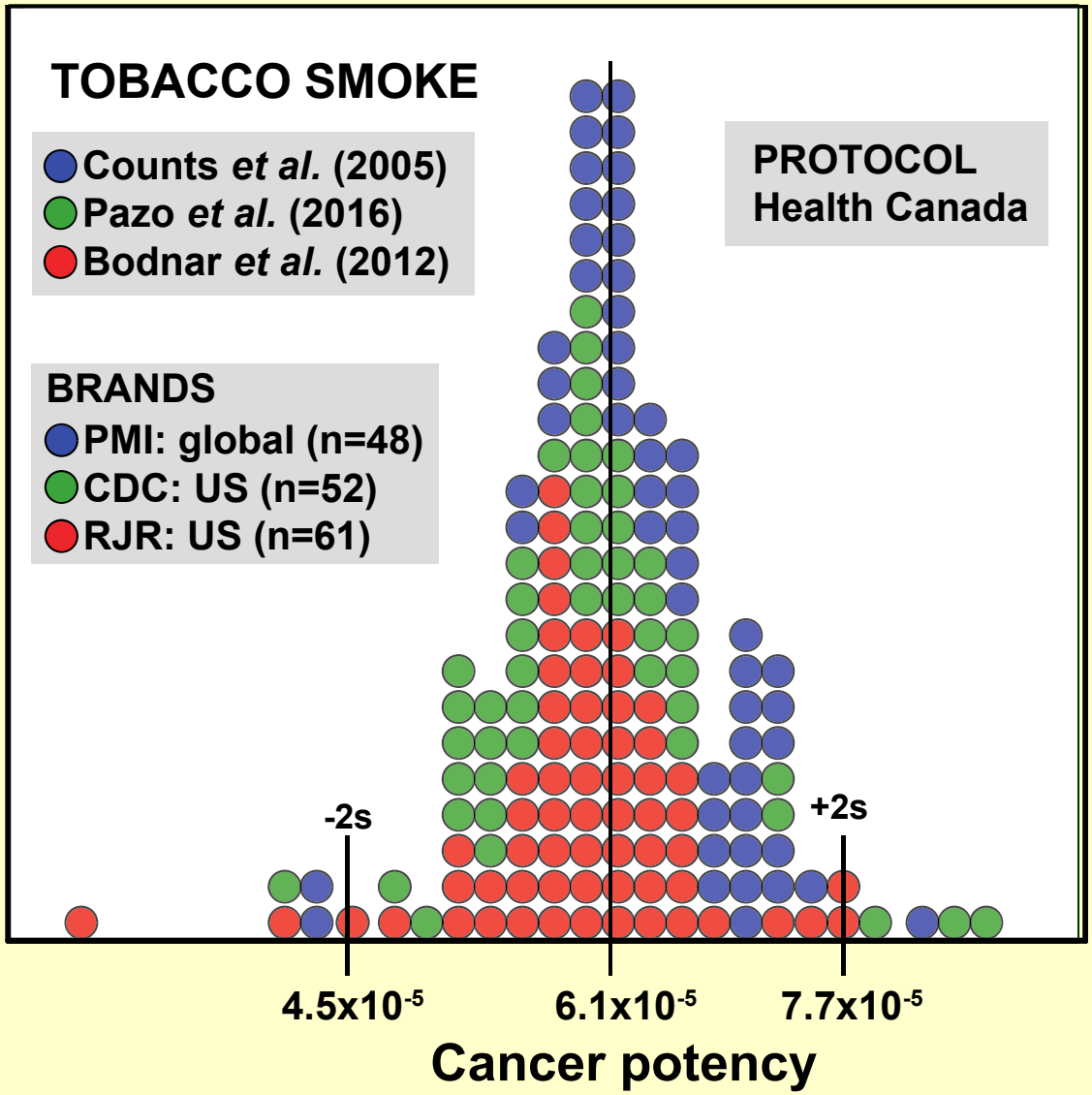
Range of Cancer Potency in Tobacco Smoke

Cancer potency calculated on basis of concentration, e.g. µg/mL

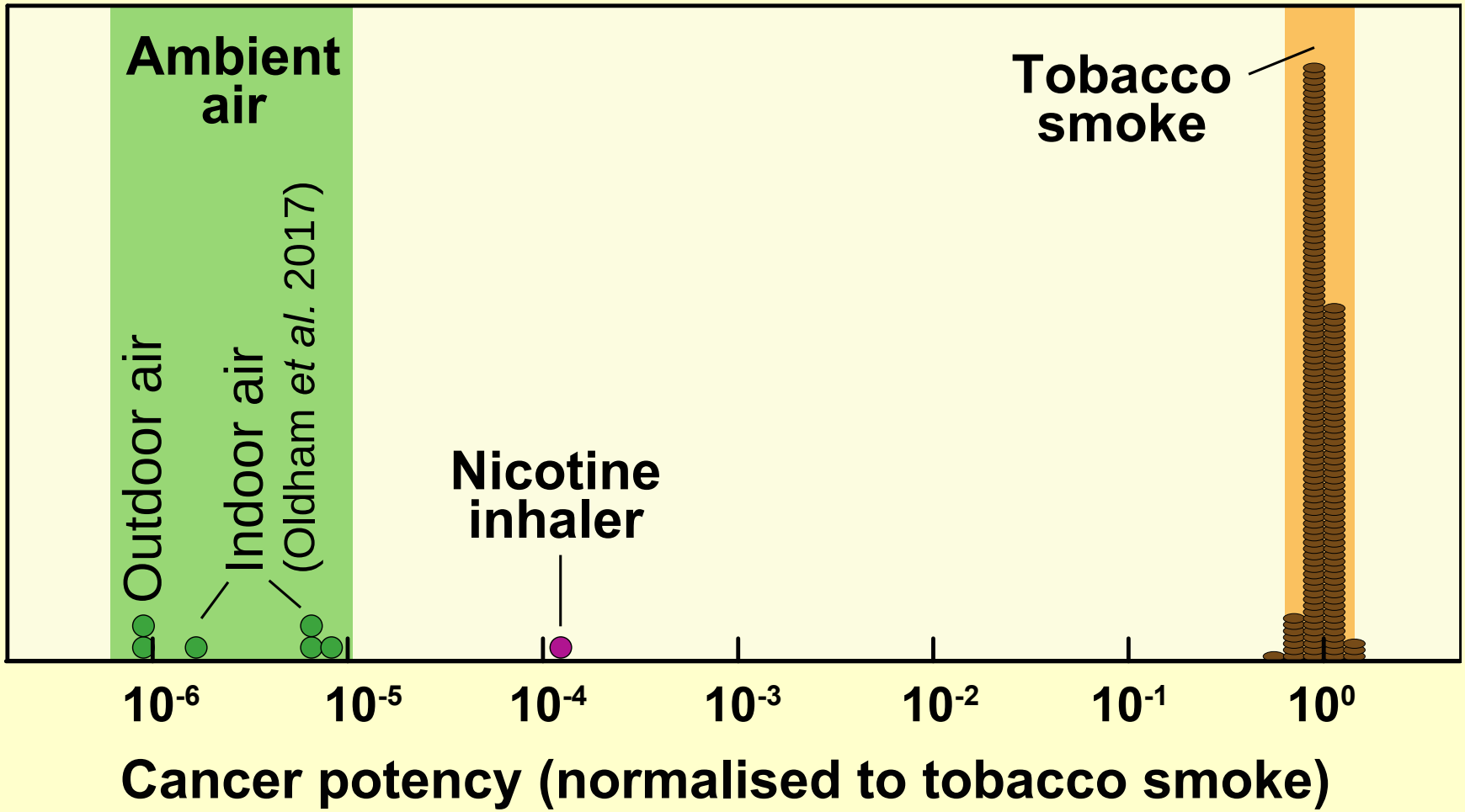
E-cigarettes usually reported as µg/N puffs of fixed volume

Tobacco smoke & HnB reported as µg/consumable

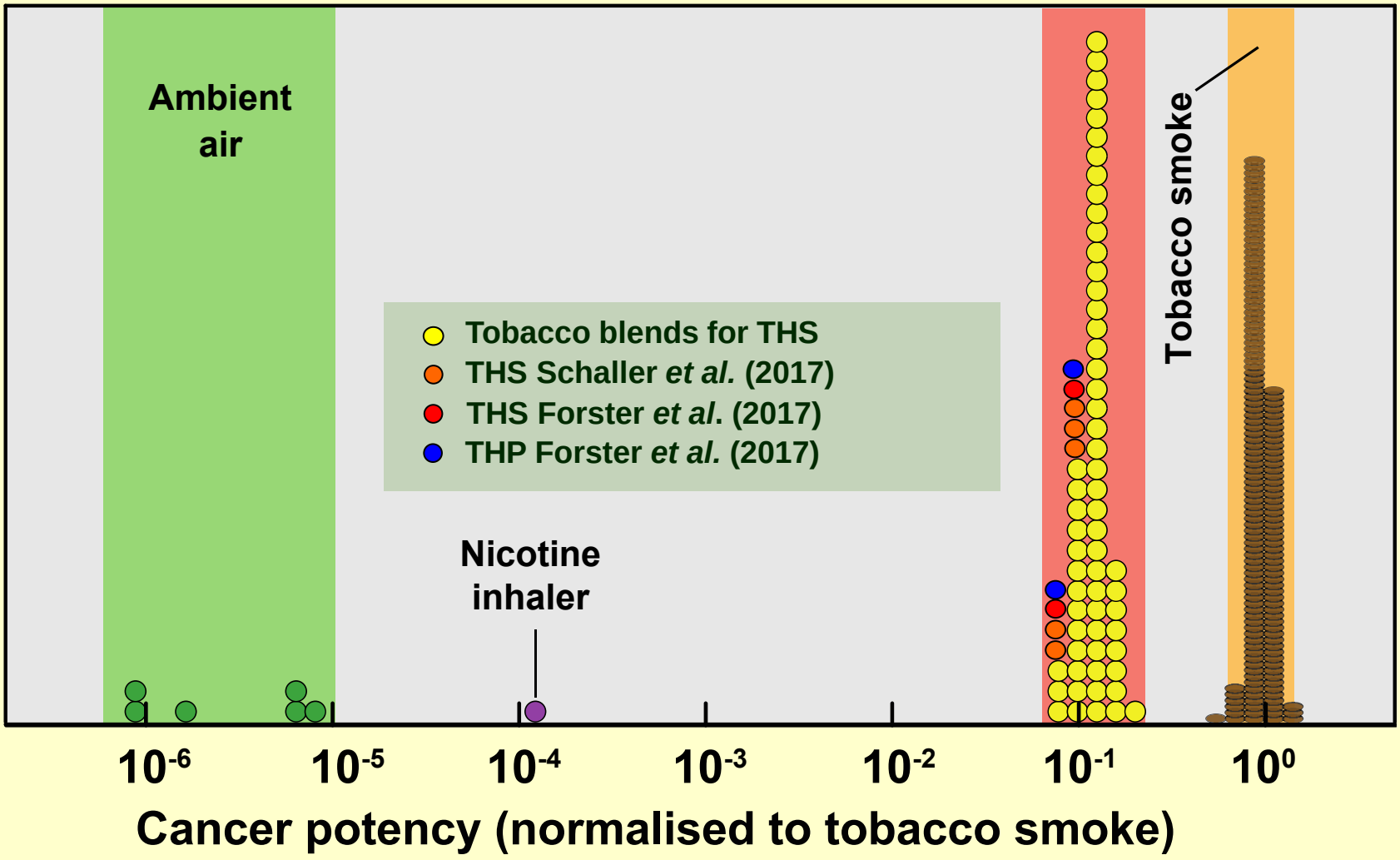
Detailed procedures for resolving incompatibilities and for calculating potency & risk described by Stephens, (2017) *Tobacco Control* (doi:10.1136/tobaccocontrol-2017-053808)



Cancer Potency Spectrum: From Fresh Air to Smoke

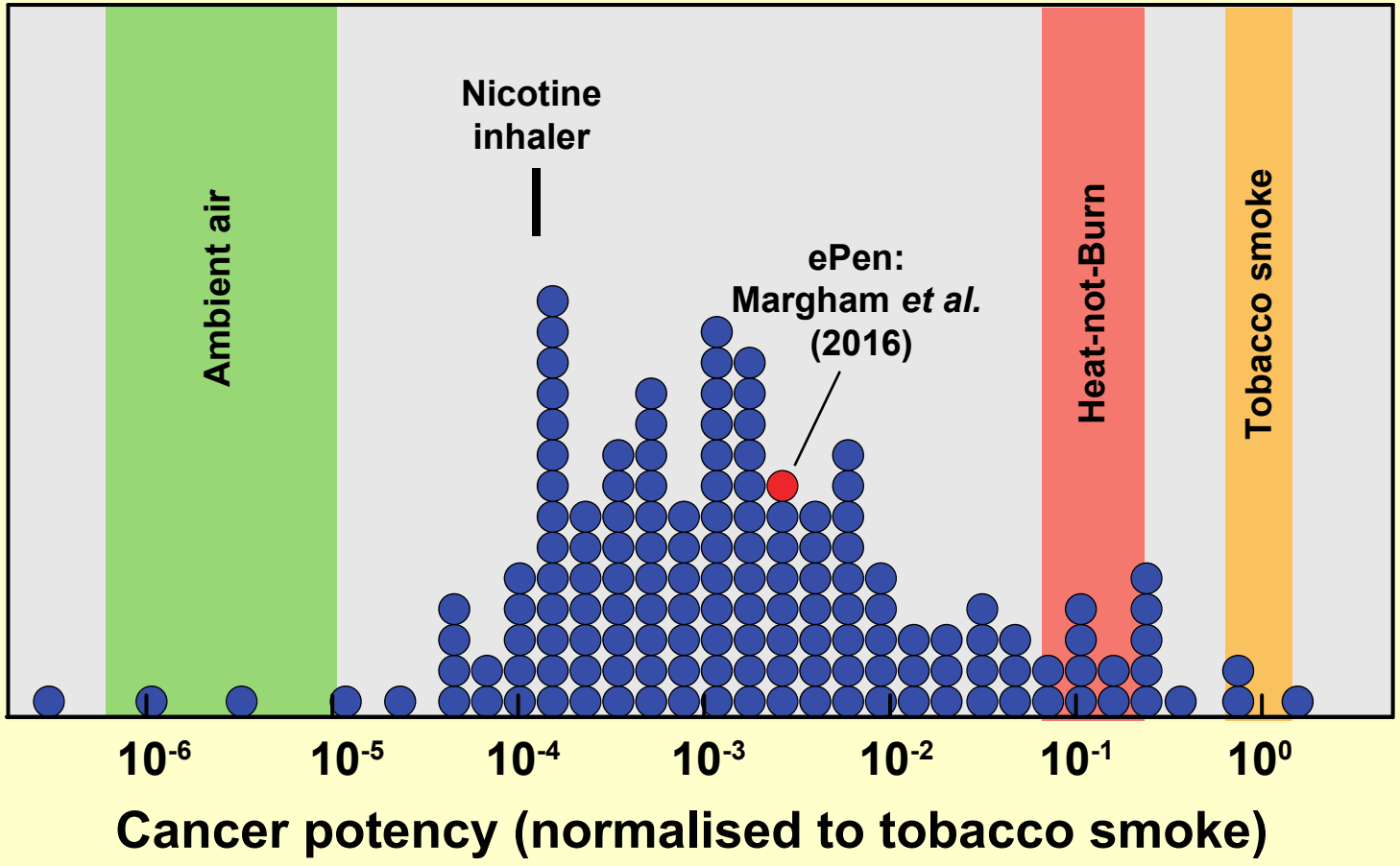


Cancer Potency Spectrum: Tobacco Products



Cancer Potency Spectrum: E-Cigarettes

Analyses of E-cigarette emissions collected from 16 publications
ePen has full HPHC, others have fewer analytes (mainly carbonyls)



Cancer Potency of E-cigarettes by Generation

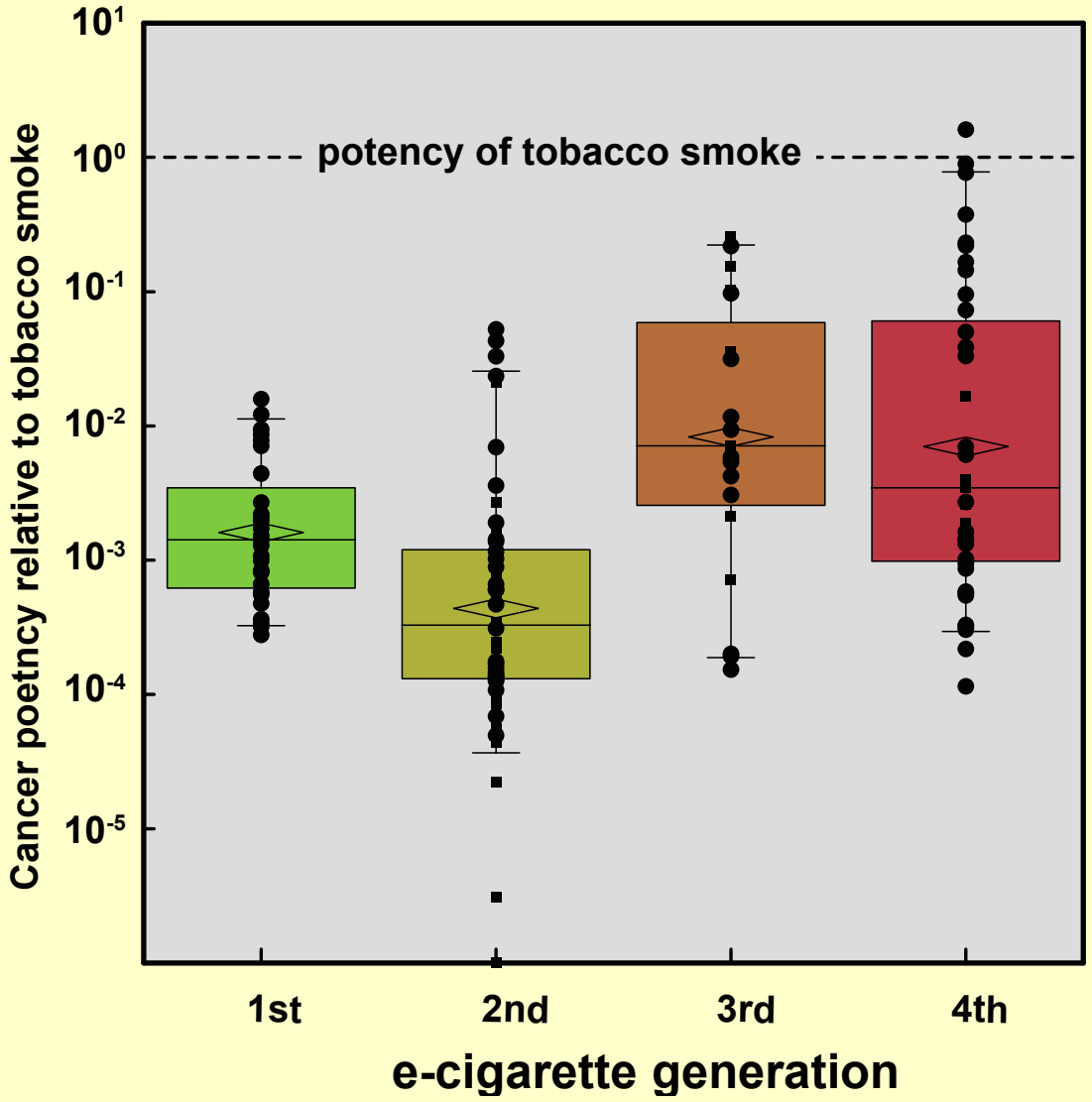
GENERATION

1st

2nd

3rd

4th

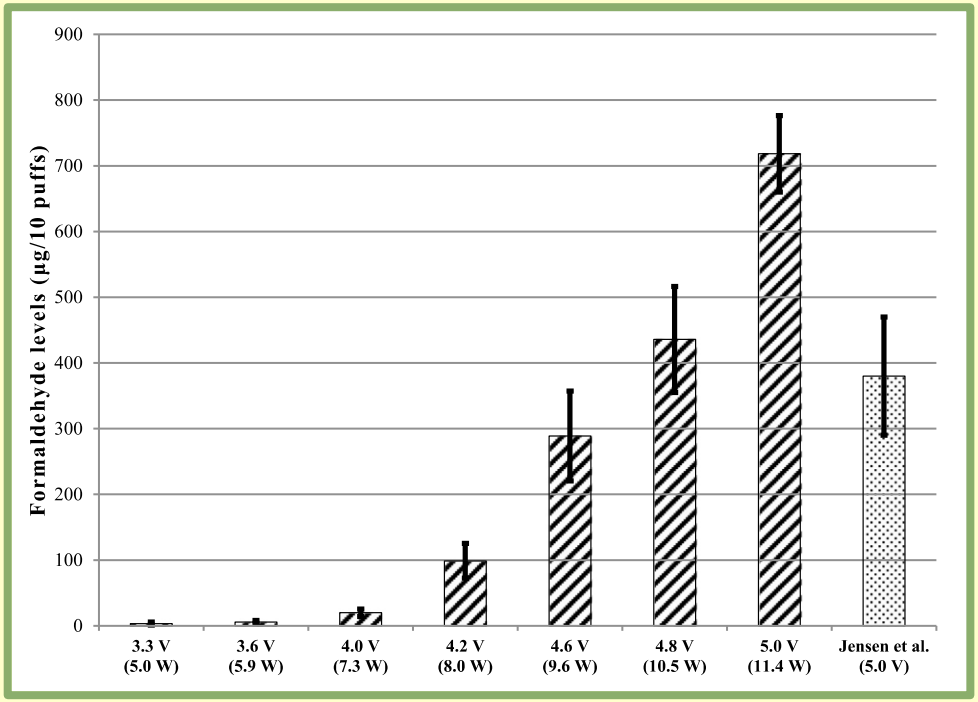


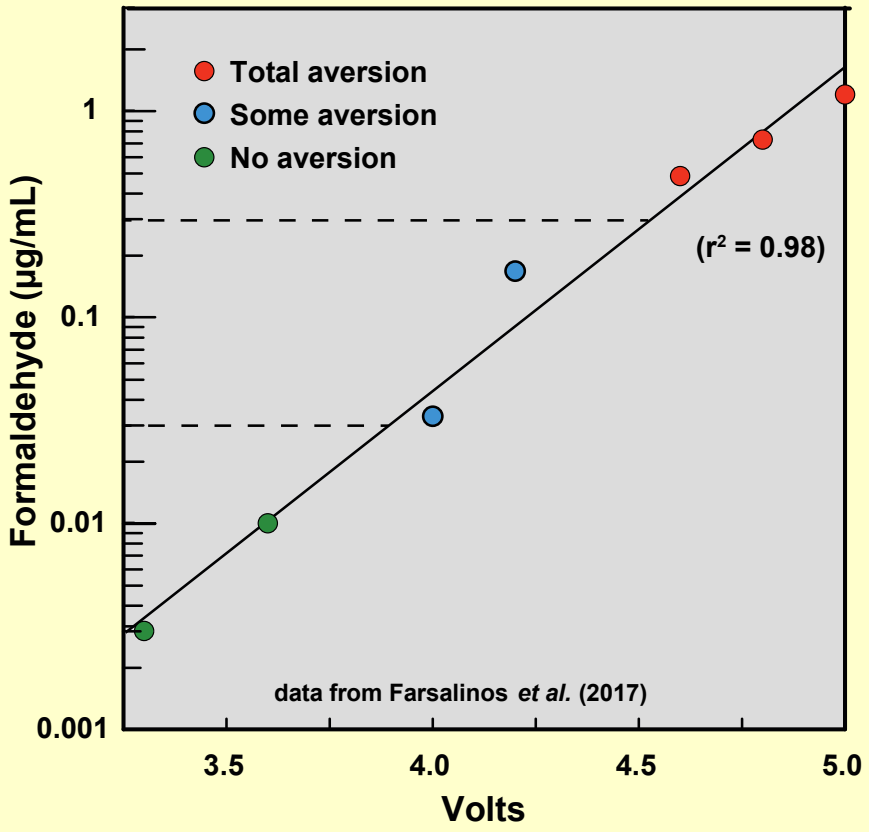
Formaldehyde–power–user experience 1

Experiment: 26 former smokers now e-cigarette users recruited

Same device & liquid vaped (CE4, Innokin iTaste VV, 6 mg/mL nicotine)

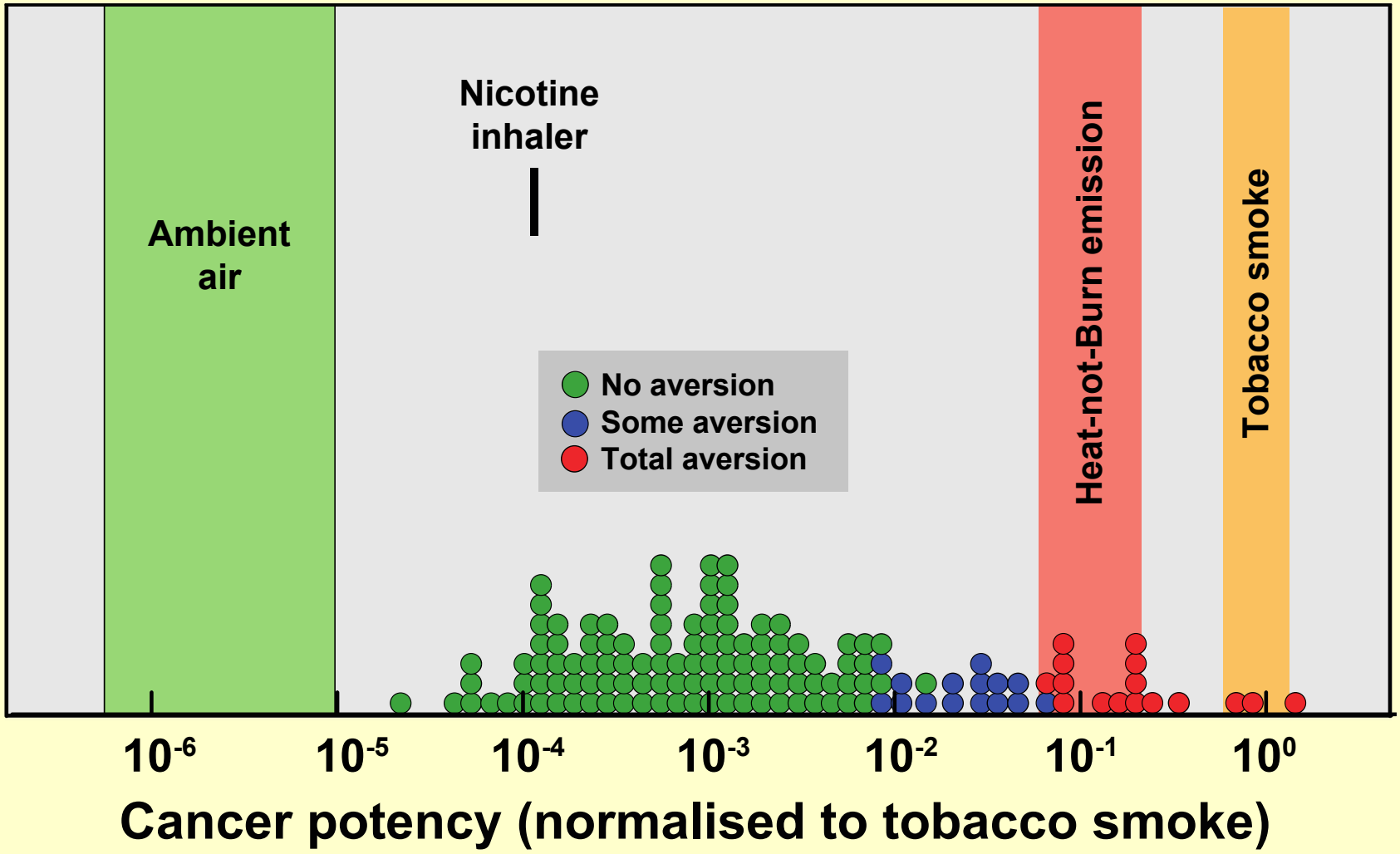
Voltage increased in steps and users reported taste responses





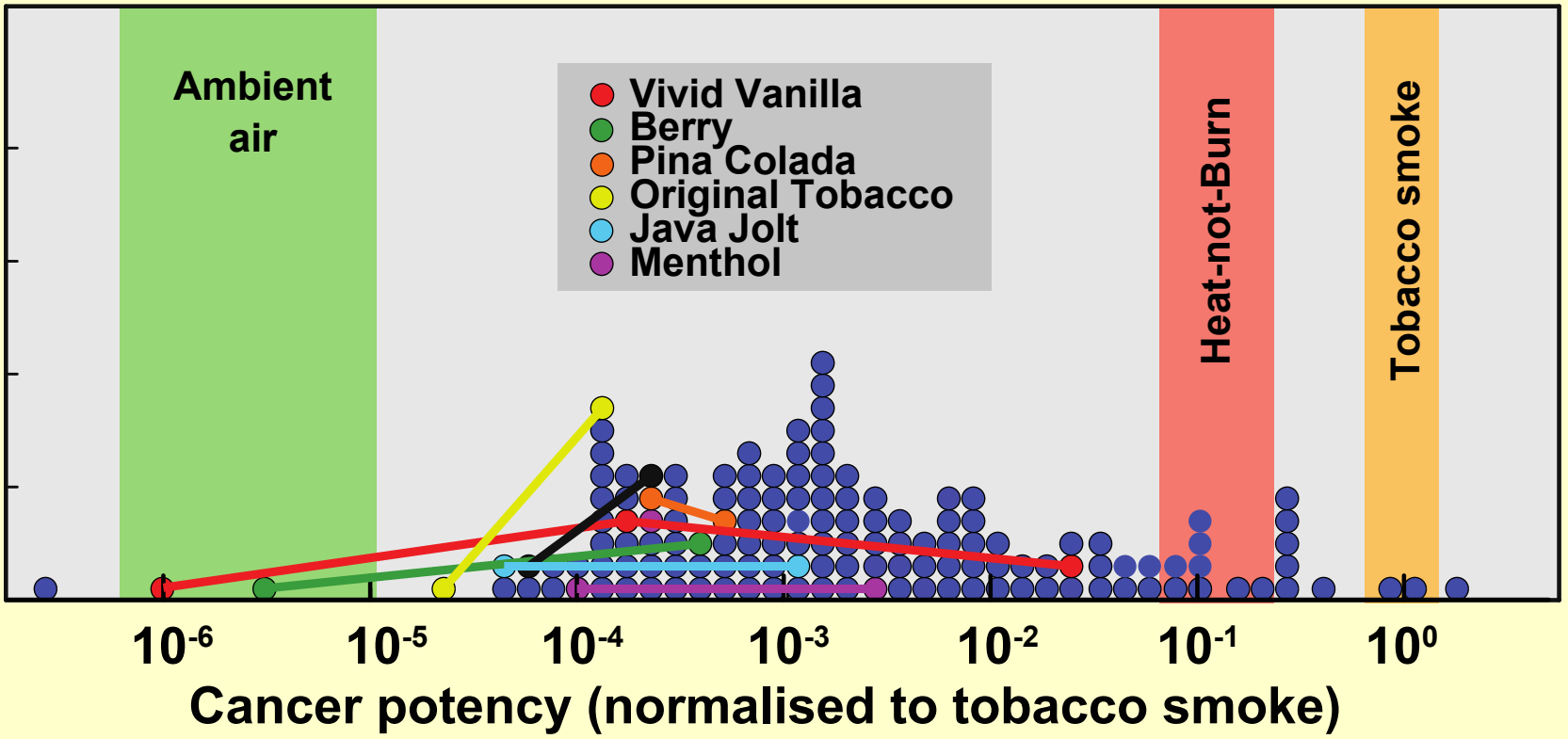
Farsalinos *et al.* (2017) Food and Chemical Toxicology 109, 90-94

Formaldehyde–power–user experience 2



Unexplained Potency Variation in Same Brand & Flavour

Solid lines connect the same brand & flavour in 2nd generation disposable cartomisers (US). Voltage/power was not varied. (data from Klager *et al.*, 2017)



Other factors?

METALS IN EMISSIONS

- **E-cigarette devices of all generations are largely constructed of metal**
- **Coils most commonly nichrome (NiCr alloy) or kanthal (FeAlCr)**
- **Very few measurements of metals in vapour**
- **No studies of metal speciation in e-cigarette emissions, e.g. $Cr^{(0)}$, $Cr^{(III)}$ & $Cr^{(IV)}$ have low toxicities whereas $Cr^{(VI)}$ is highly carcinogenic**

AEROSOL SIZE DISTRIBUTIONS

Mikheev *et al.* (2016) Real-Time Measurement of Electronic Cigarette Aerosol Size Distribution and Metals Content Analysis. *Nicotine & Tobacco Research* 18,1895-1902

Scungio *et al.* (2018) Measurements of electronic cigarette-generated particles for the evaluation of lung cancer risk of active and passive users. *Journal of Aerosol Science* 115, 1-11

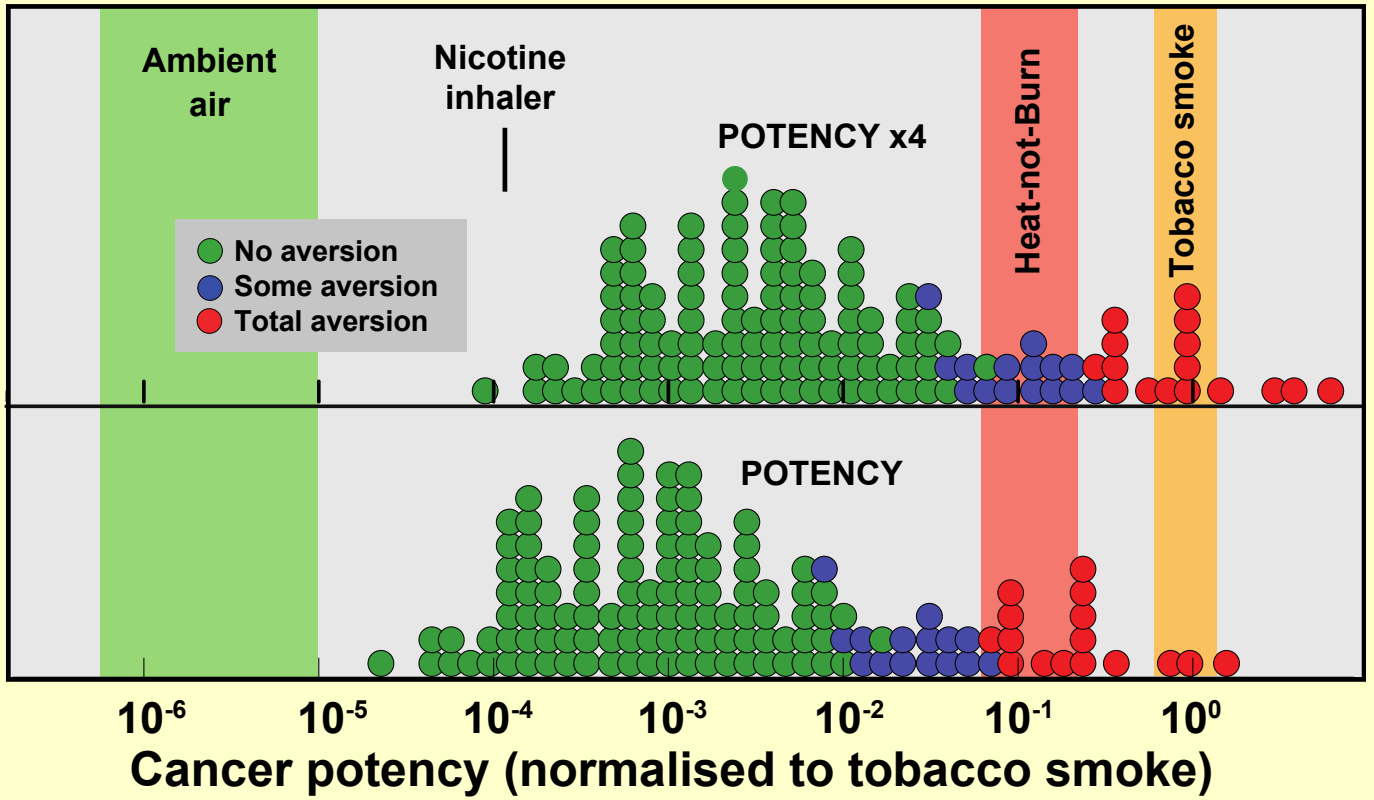
From Potency to Risk

Risk = Potency x Exposure

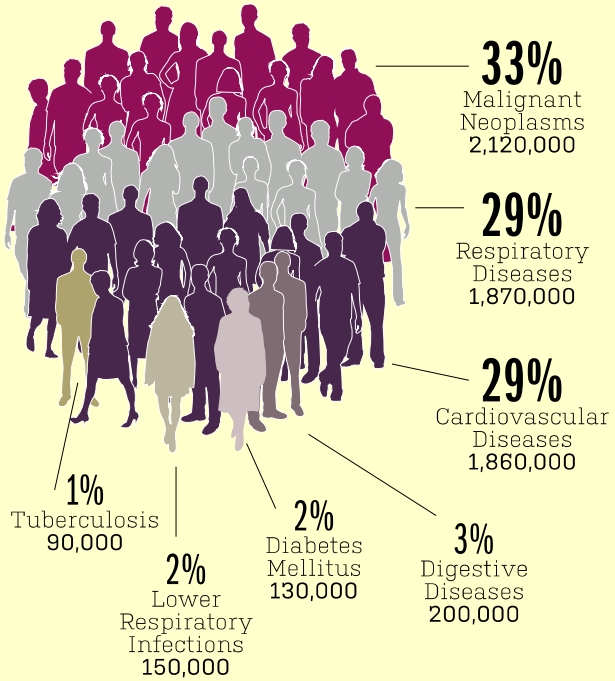
In this model exposure is a simple function of the volume of aerosol inhaled

Cigarettes: 15 cigs/day x 10 puffs x 50 mL/puff = 7.5 L smoke/day

e-cigarettes: Robinson *et al.* (2015) report 30L/day as the mean inhaled vapour across a sample (n=21) i.e. x4 greater exposure - consistent with Behar *et al*. (2014)



Effect of emissions on other medical conditions



RESPIRATORY & CARDIOVASCULAR DISEASE

Cancer potential appears to be dominated by carbonyls - most studies of emissions have focused on carbonyls (aldehydes)

Carbonyls are implicated in respiratory but not CV disease. Also volatiles (VOCs), metals, carbonyls, PAHs and other compounds involved

Applying analogous approaches to respiratory and cardiovascular diseases is currently limited by the very small number of studies with e-cigarette emissions data for the wider range of HPHC+ toxicants