

THE SPECTRUM OF HARM

Marcus Munafò

Disclosure

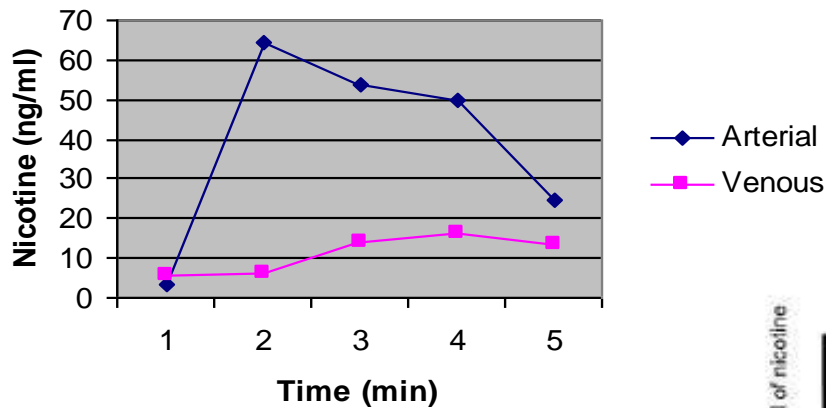
Received smoking cessation products (NRT, varenicline) for use in research from GlaxoSmithKline, Pfizer and Rusan Pharma, and honoraria for invited lectures GlaxoSmithKline, Pfizer, and Sepracor.

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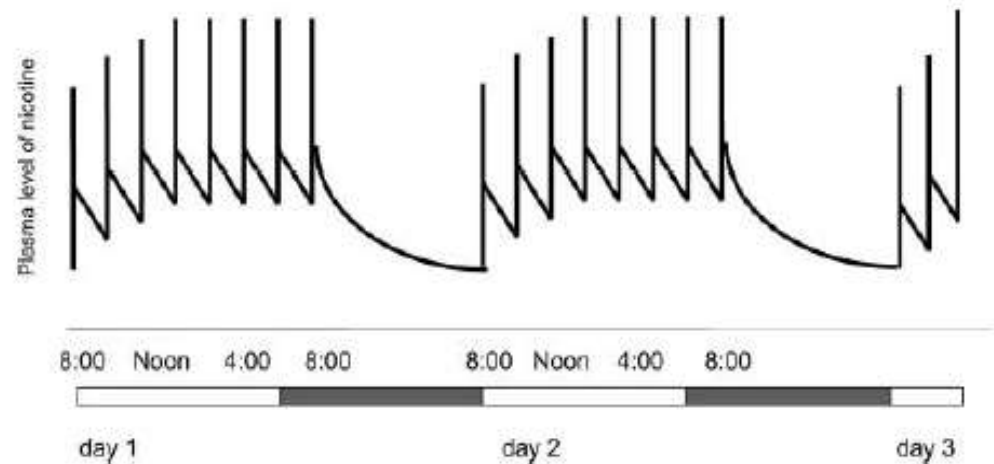
Tobacco Dependence

Time Course of Arterial and Venous Nicotine Concentrations



**“Smokers smoke for the nicotine,
but die from the tar”**

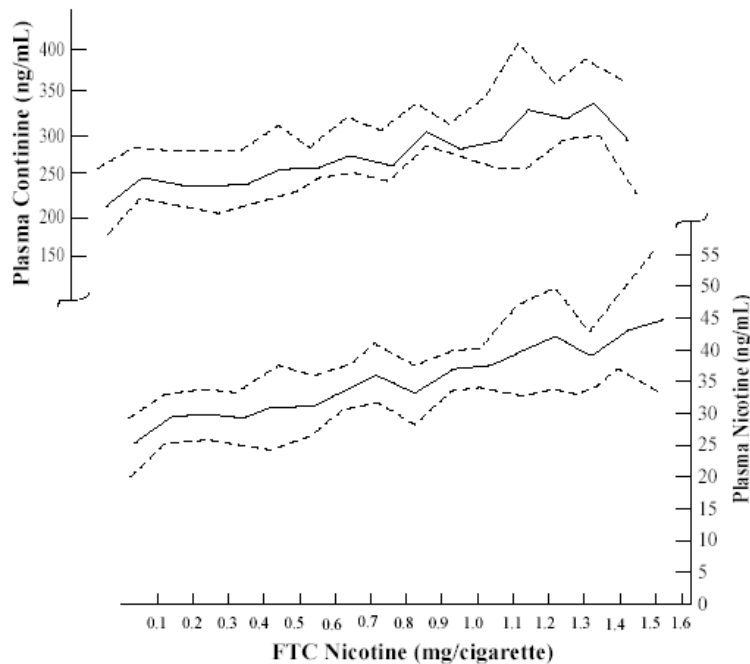
Mike Russell
Maudsley Smokers Clinic (1979)



Benowitz et al. (1982). Clin Pharmacol Ther, 32, 758-764.

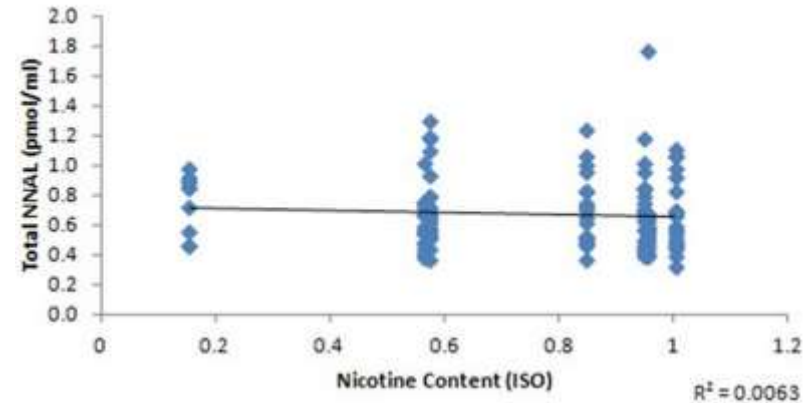
Tobacco Dependence

Plasma Cotinine and Nicotine Concentrations in Cigarette Smokers According to the FTC Nicotine Yield

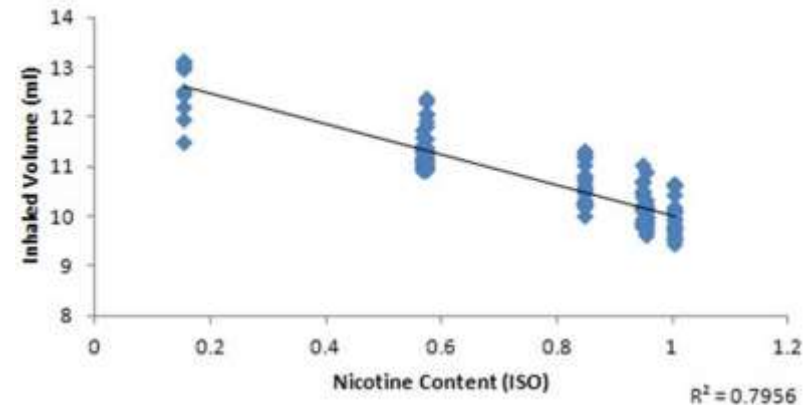


Note: Solid line indicates mean; dashed line indicates 95% confidence intervals (from Gori and Lynch, 1985).

Total NNAL

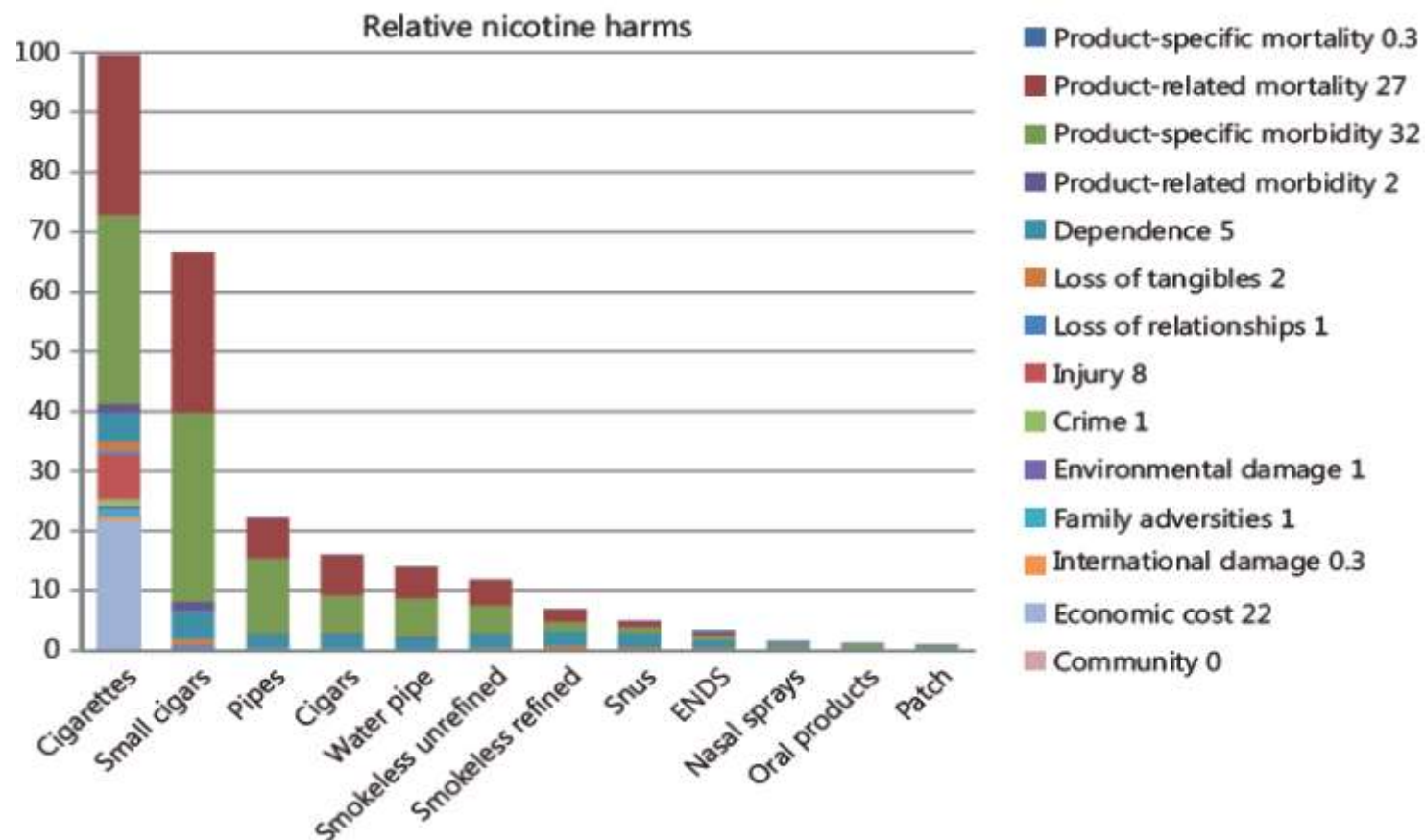


Inhaled Volume



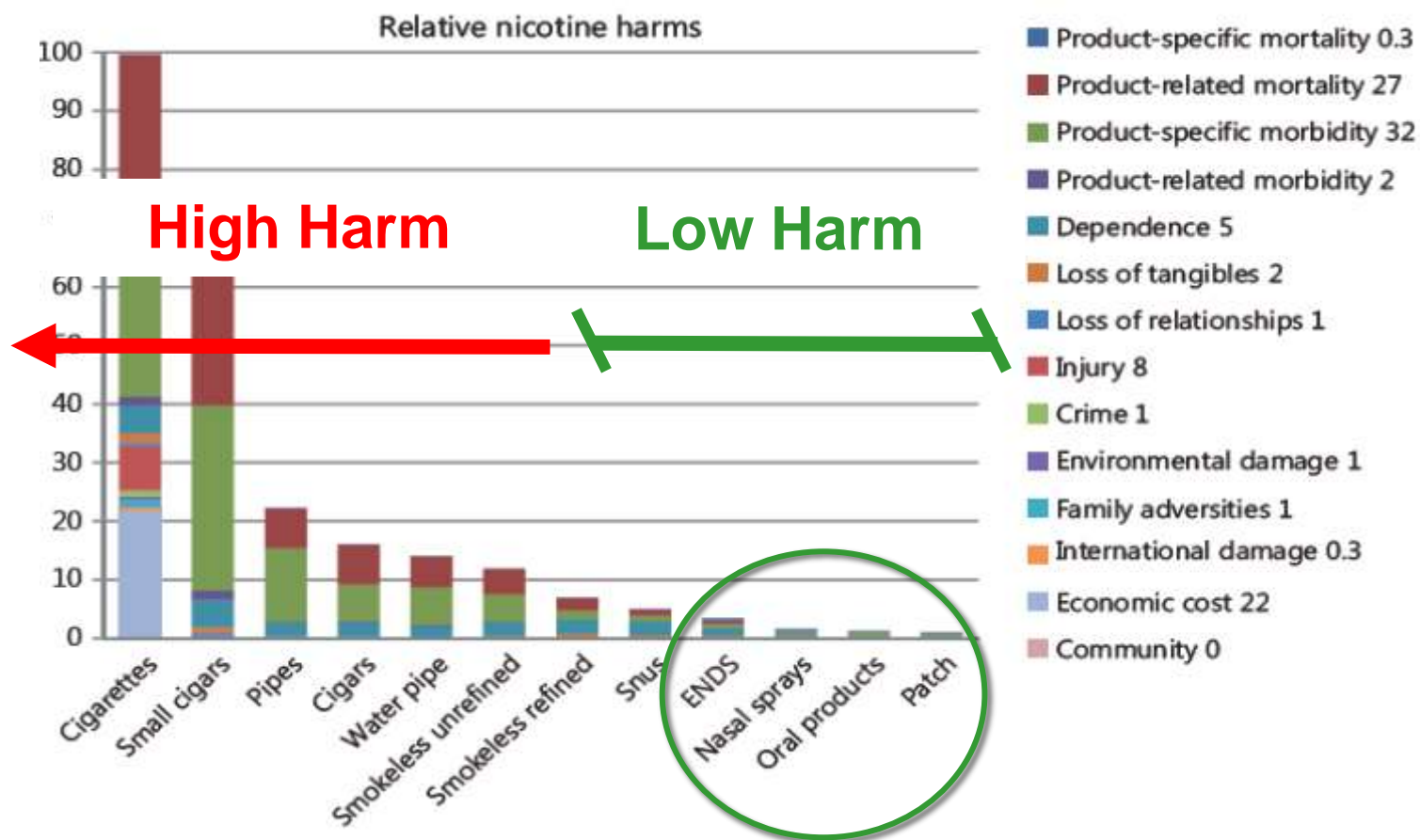
Munafò & McNeill (2013). J Psychopharmacol, 27, 13-18.

Harm Reduction



Nutt et al. (2014). Eur Addiction Res, 20, 218-225.

Harm Reduction



Nutt et al. (2014). Eur Addiction Res, 20, 218-225.

Estimating Harm

Table 4 Concentrations ($\mu\text{g}/\text{m}^3$) of selected compounds during the 8- m^3 emission test chamber measurement of e-cigarette A and conventional cigarette using Tenax TA and DNPH

Compounds	CAS	Participant blank	E-cigarette			Conventional cigarette
			Liquid 1	Liquid 2	Liquid 3	
1,2-Propanediol	57-55-6	<1	<1	<1	<1	112
1-Hydroxy-2-propanone	116-09-6	<1	<1	<1	<1	62
2,3-Butanedione	431-03-8	<1	<1	<1	<1	21
2,5-Dimethylfuran	625-86-5	<1	<1	<1	<1	5
2-Butanone (MEK)	78-93-3	<1	2	2	2	19
2-Furaldehyde	98-01-1	<1	<1	<1	<1	21
2-Methylfurane	534-22-5	<1	<1	<1	<1	19
3-Ethenyl-pyridine ^a	1121-55-7	<1	<1	<1	<1	24
Acetic acid	64-19-7	<1	11	13	14	68
Acetone	67-64-1	<1	17	18	25	64
Benzene	71-43-2	<1	<1	<1	<1	22
Isoprene	78-79-5	8	6	7	10	135
Limonene	5989-27-5	<1	<1	<1	<1	21
m,p-Xylene	1330-20-7	<1	<1	<1	<1	18
Phenol	108-95-2	<1	<1	<1	<1	15
Pyrrole	109-97-7	<1	<1	<1	<1	61
Toluene	108-88-3	<1	<1	<1	<1	44
Formaldehyde ^b	50-00-0	<1	8	11	16	86
Acetaldehyde ^b	75-07-0	<1	2	2	3	119
Propanal ^b	123-38-6	<0.2	<0.2	<0.2	<0.2	12

Schripp et al. (2013). *Indoor Air*, 23, 25-31.

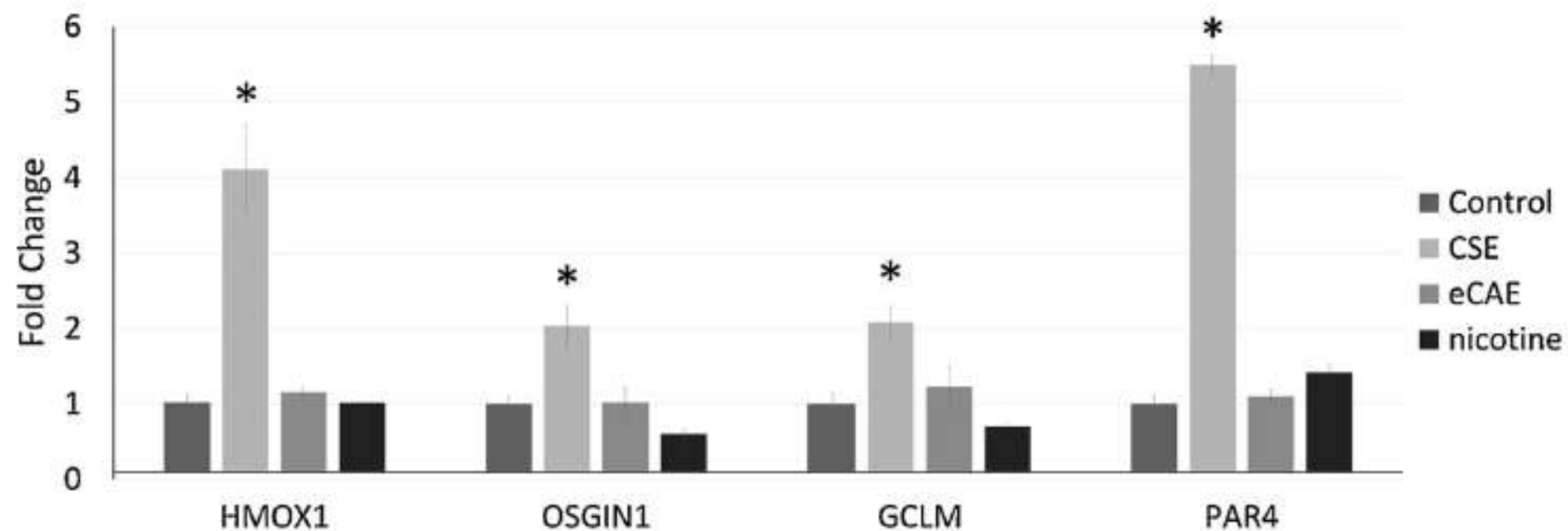
Estimating Harm

Toxic compound	Conventional cigarette [μg]	Electronic cigarette [μg per 15 puffs]	Conventional vs. electronic cigarette
Formaldehyde	1.6-52	0.20-5.61	9
Acetaldehyde	52-140	0.11-1.36	130
Acrolein	4.6-14	0.07-4.19	4
Toluene	6.4-9.0	0.02-0.63	23
NNN	0.012-0.37	0.00008-0.00043	145
NNK	0.009-0.08	0.00011-0.00283	30
Cd	0.03-0.35	0.001-0.022	16
Ni	0.003-0.60	0.011-0.029	15

Goniewicz et al. (2013). Tob Control, 23, 133-139.

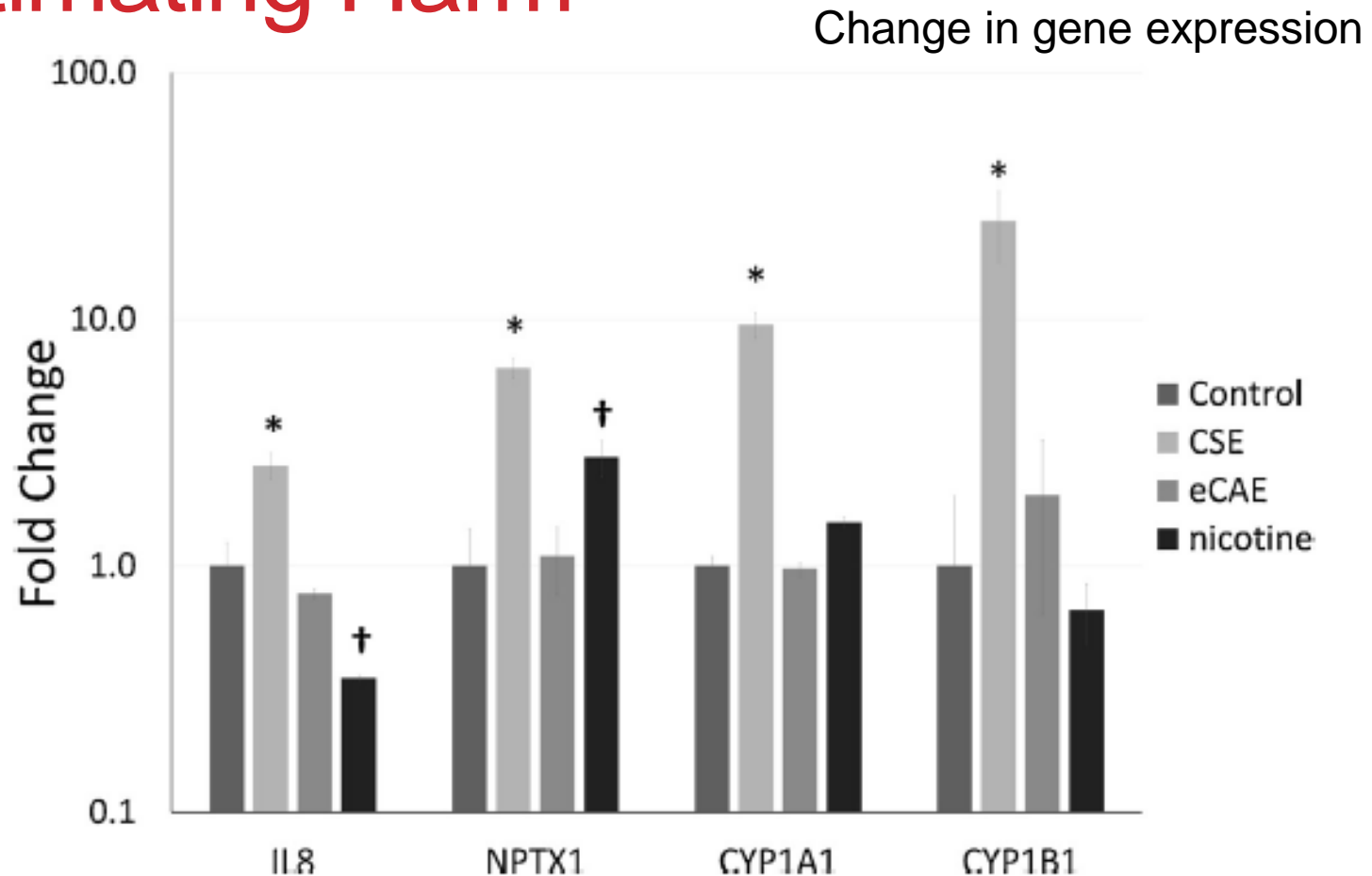
Estimating Harm

Change in mRNA expression



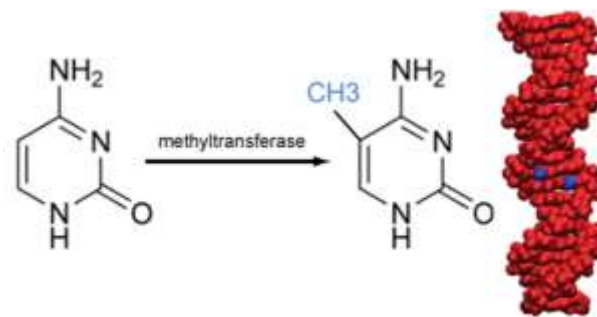
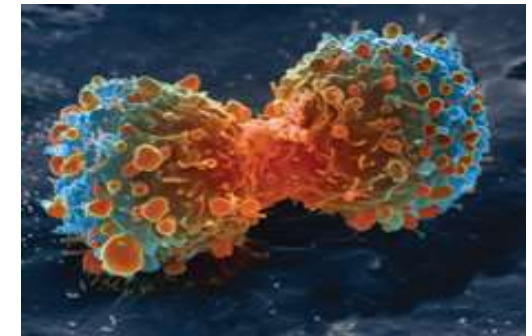
Teasdale et al. (2016). Drug Alcohol Depend.

Estimating Harm

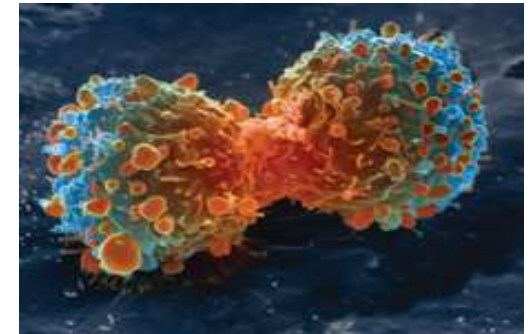


Teasdale et al. (2016). Drug Alcohol Depend.

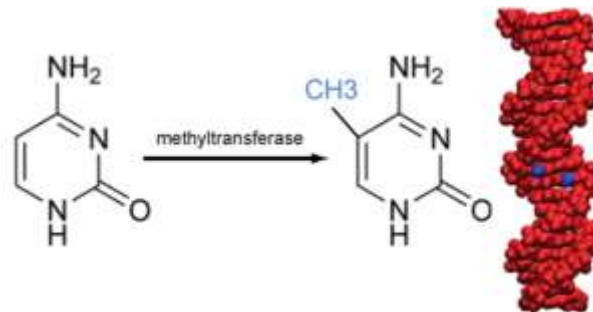
Estimating Harm



Estimating Harm



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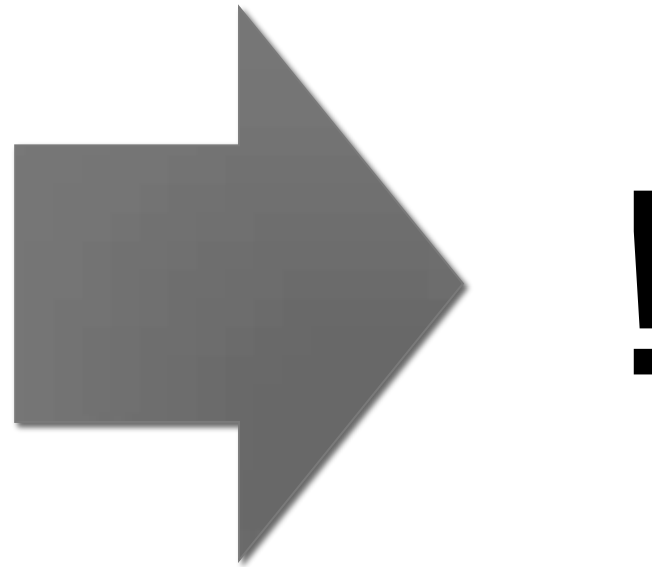
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Estimating Harm

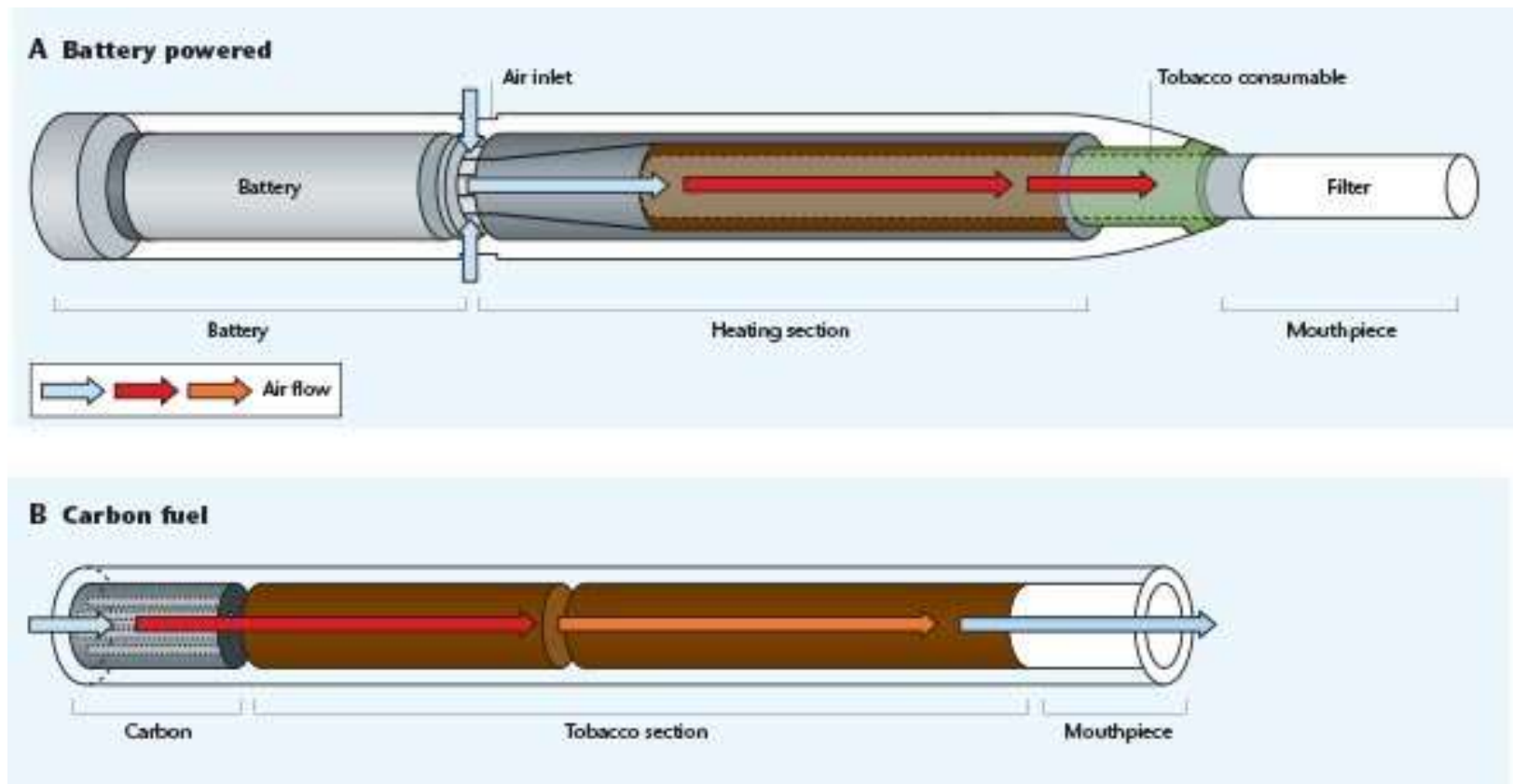
- Flavours
- Inhalation Topography
- Nicotine concentration
- Battery strength
- Device

Estimating Harm

- Flavours
- Inhalation Topography
- Nicotine concentration
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- Device



Emerging Products



Conclusions

- Stepped approach to estimating harm:
 - Toxicant levels
 - Biological impact in model systems
 - Biological impact in humans
- Several challenges:
 - Large analytical space
 - Rapidly changing landscape
 - Emerging products (e.g. heat-not-burn)

Acknowledgements

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<http://www.bristol.ac.uk/expsych/research/brain/targ/>



UKCTAS

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