Harm Reduction with E-cigarettes

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Conflict of Interests:

- I have written commissioned expert opinions for Pharmaceutical and Electronic Cigarette companies.
- I am financially and ideally independent from my clients and express my personal views based on the scientific literature.
- The expenses for my travel to Brussels are covered by Dustin Dahlmann (BfTG), who asked me to participate at this meeting.

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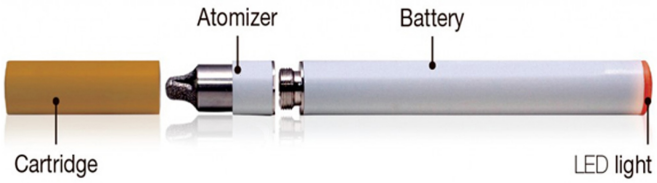
Except nicotine delivery, vaporizers have nothing in common with combustible cigarettes

Cigalikes



Rebuidable atomizers

Suggested entry-level devices

coil (metal wire)

+ cotton

+ liquid

+ heat

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Tobacco Smoke

nicotine (~10 mg/cigarette, ~1 mg in the smoke)
>5.000 compounds
>60 established cancerogens
nitrogen oxides (NO, NO_2, N_2O_4)
carbon monoxide (CO)

solid particles (tar) ->harmful lung deposits

Documented Consequences:

cancer, COPD, emphysema, cardiovascular disease (atherosklerosis, CAD, myocardial infarction, stroke, impaired circulation), and many others.

→ worldwide 6,000.000 deaths/year according to WHO

Aerosol from Vaporizers

nicotine (max. 2 %, equiv. to 20 mg/ml)
propylene glycol (1,2-propane-diol)
glycerol
food flavors
trace levels of aldehydes (upon heating)

liquid droplets -> dissolved and absorbed

Documented Consequences:

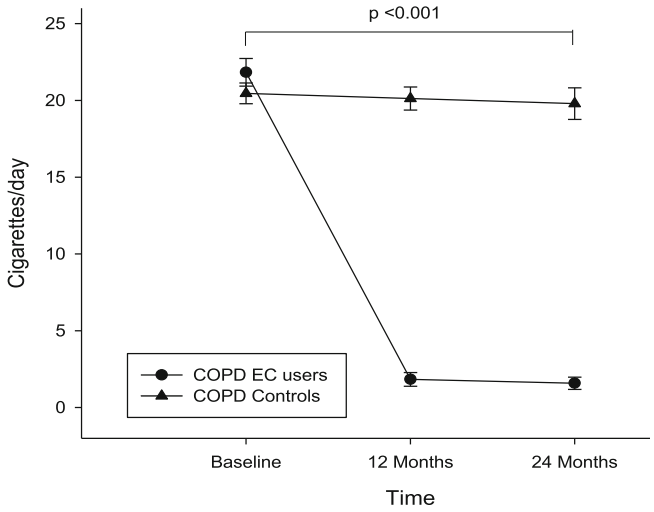
irritation of airways (desired throat-hit?), occasionally allergies to flavors or PG

→ no documented damage to health (>100 million person years)

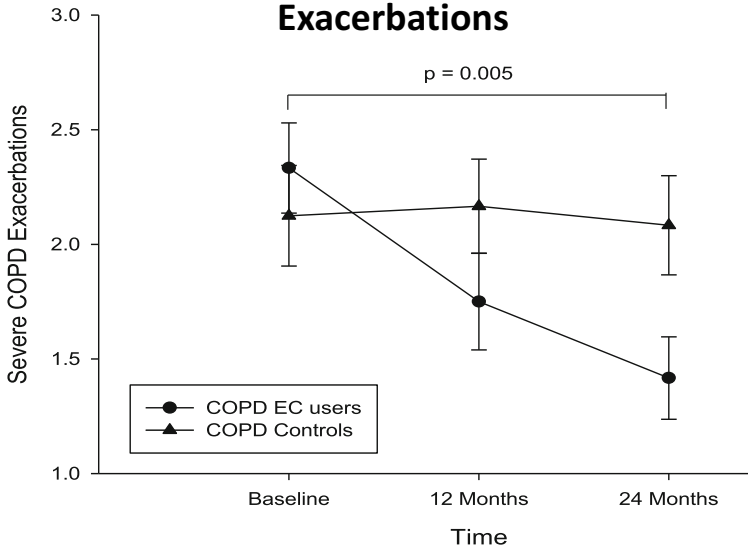
→ documented health improvement (lung, cardiovascular, fitness)

Harm Reduction in COPD Smokers Switching to E-Cigs

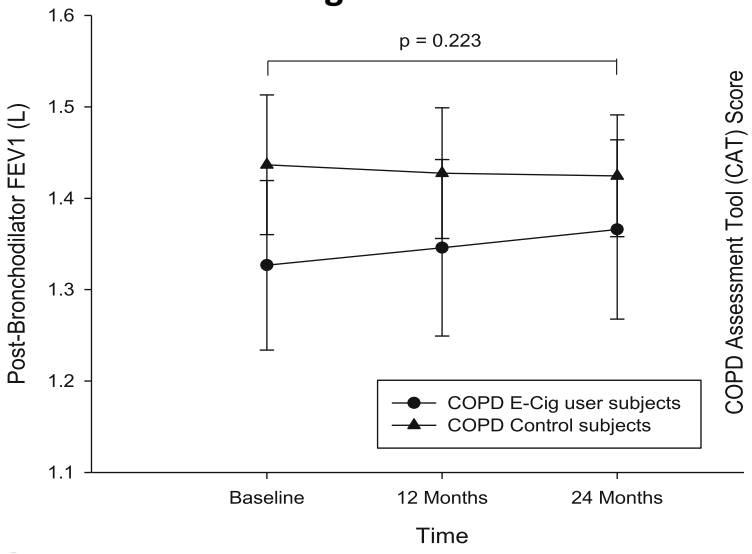
Cigarette consumption



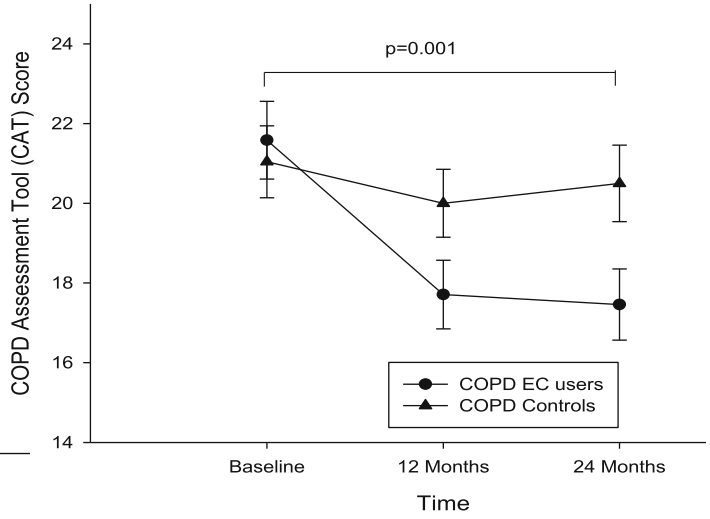
Exacerbations



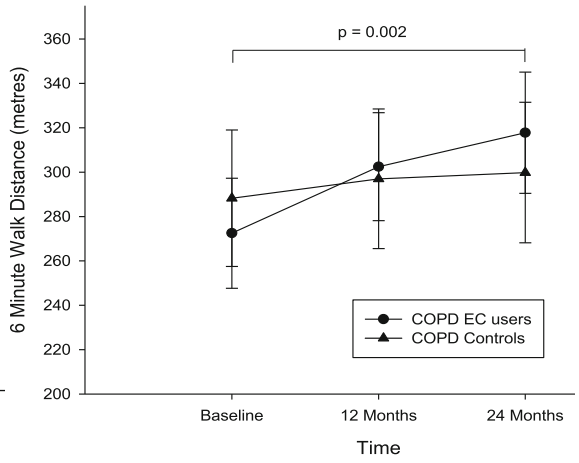
Lung function



CAT Score (QoL)



Physical Performance



Polosa et al., *Respir. Res.* **17**, 166, 2016

High Res Graphs kindly provided by Riccardo Polosa

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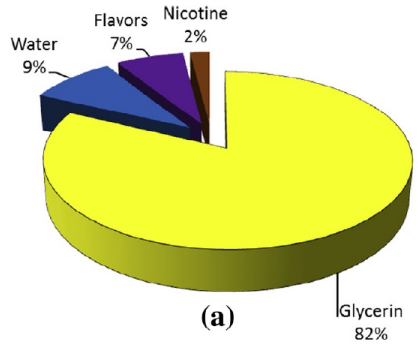
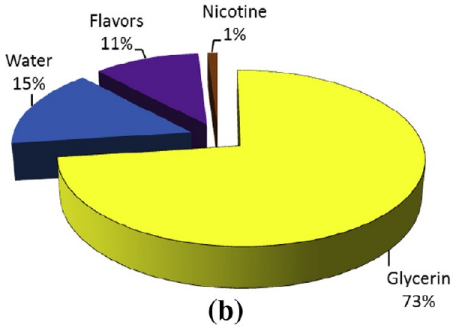
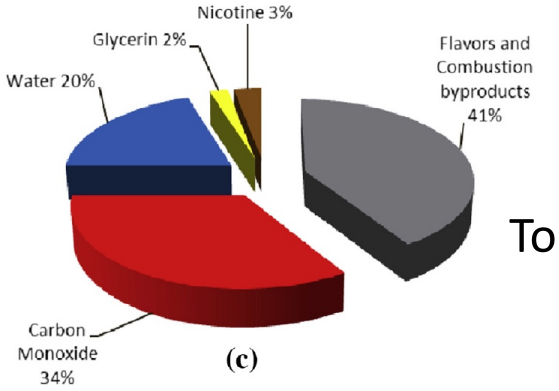


E-liquid

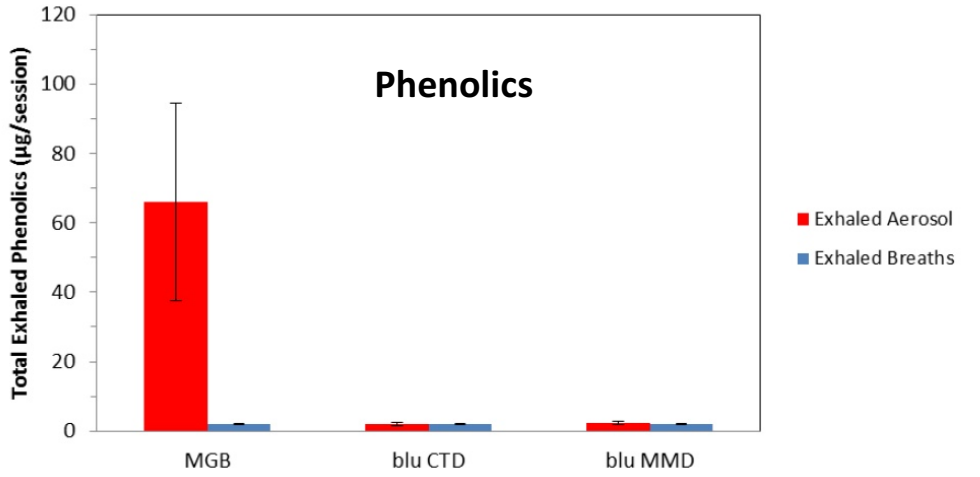


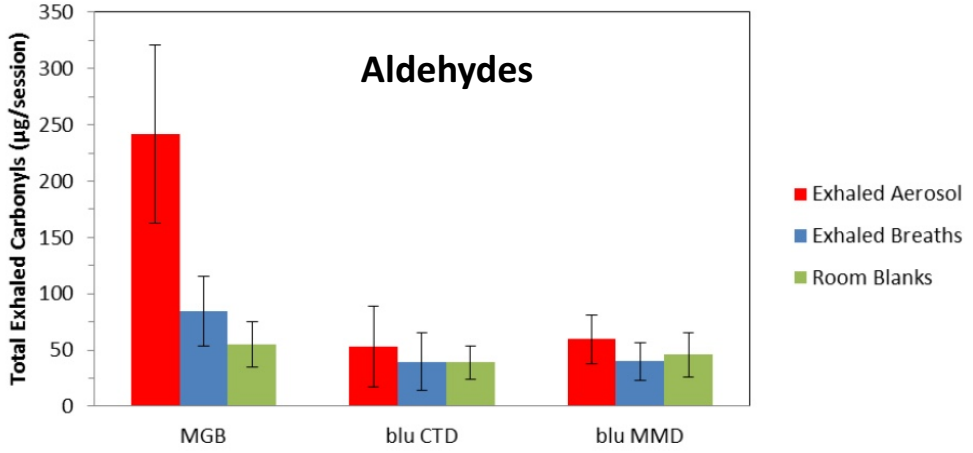
E-cig emission



Tobacco smoke

Figure 4. Total exhaled phenolics for exhaled aerosol and breaths for Marlboro Gold Box (MGB), blu Classic Tobacco Disposable (blu CTD) and blu Magnificent Menthol Disposable (blu MMD).





Tayyarah & Long, *Regul. Toxicol. Pharmacol.* **70**, 704-10, 2014

Long, G.A., *Int. J. Environ. Res. Public Health* **11**, 11177-91, 2014

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Arterial and venous carbon monoxide: 2 weeks after switching

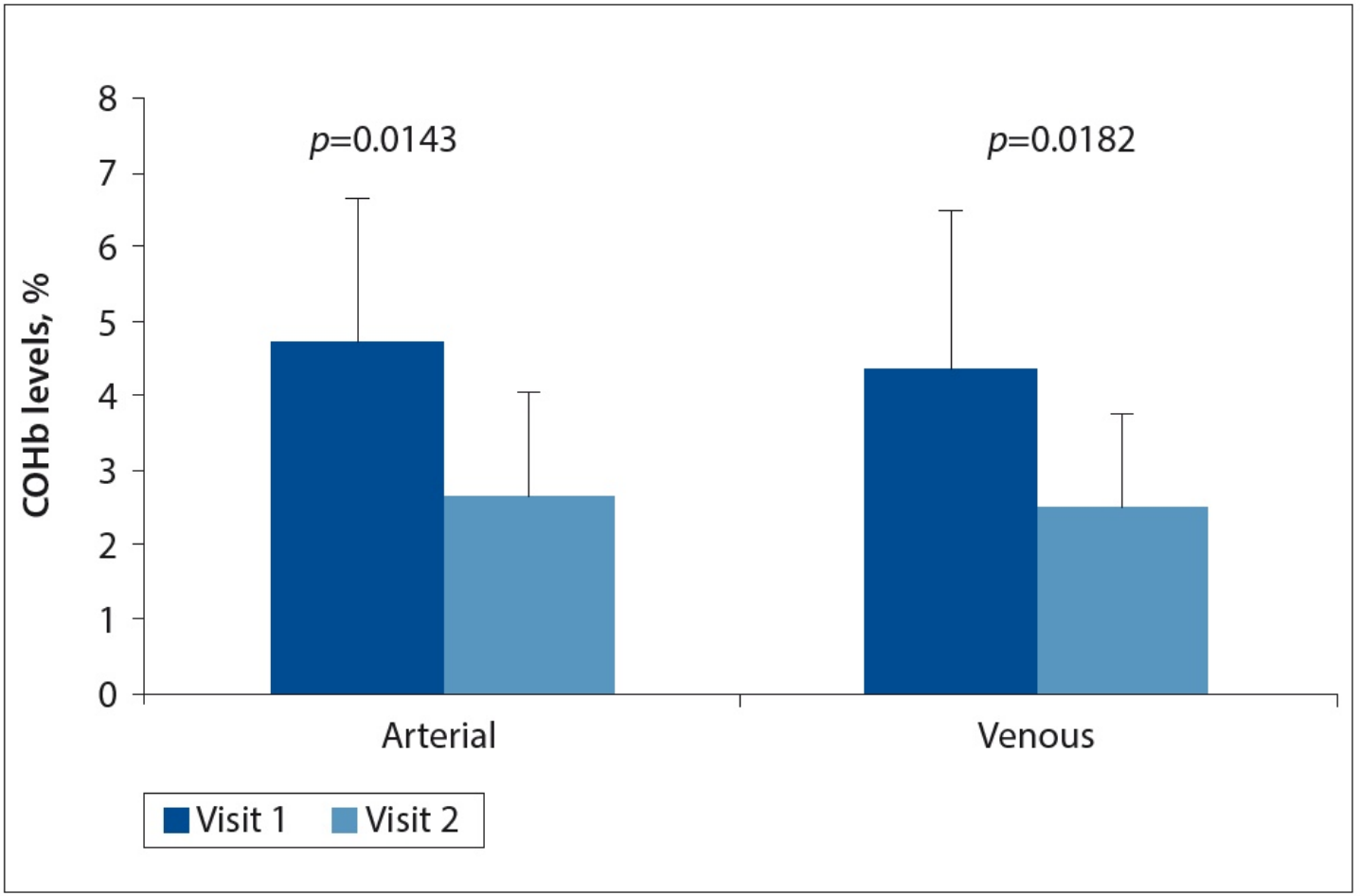

Fig. 1. Arterial and venous COHb levels (mean ±SD) at baseline (visit 1) and after 14 days of smoking Twisp e-cigarettes (n=13).

van Staden et al., *S. Afr. Med. J.* **11**, 865-8, 2013

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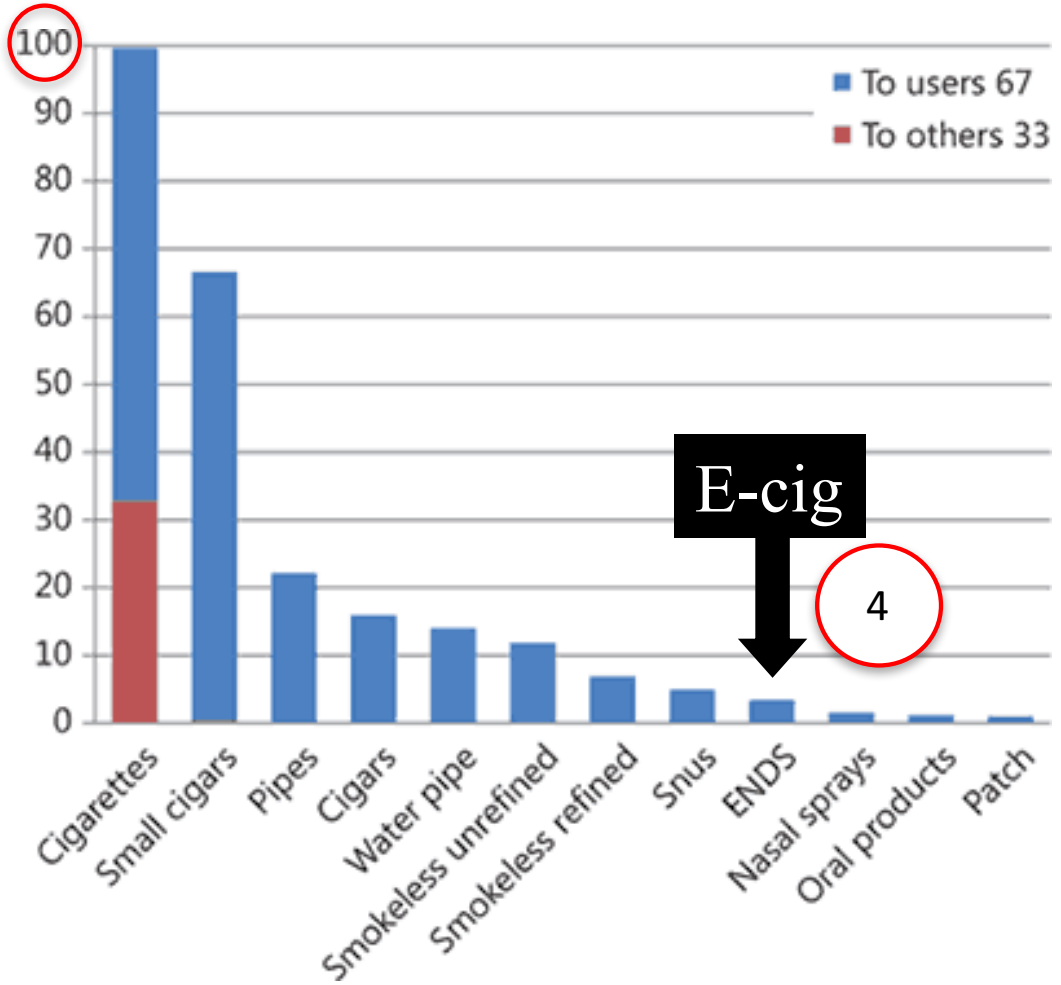
Nicotine containing products: Risk estimates

David J. Nutt, DM, FRCP, FRCPSYCH, FSB, FMEDSCI
Director of Neuropsychopharmacology
Division of Brain Sciences
Imperial College, London (UK)

co-authors:
L.D. Phillips, D. Balfour, H.V. Curran, M. Dockrell, J. Foulds, K. Fagerstrøm, K. Letlape, A. Milton, R. Polosa, J. Ramsey, & D. Sweanor



Nutt et al., Estimating the harms of nicotine-containing products using the MCDA approach.
Eur. Addict. Res. **20**, 218-225 (2014)

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GOV.UK

Public Health England

- the current best estimate is that e-cigarettes are at least 95% less harmful than smoking;
- there is no evidence so far that e-cigarettes are acting as a route into smoking for children or non-smokers;
- e-cigarettes have significant potential to help reduce tobacco use and the serious harm it causes to smokers, those around them and wider society.

Advice from PHE on the use of e-cigs in public places and workplaces:

- Maintain and support compliance with smokefree requirements by emphasising a clear distinction between smoking and vaping.
  Smoking is defined clinically and in law, and e-cigarette use does not meet the definition in either context.

Source: https://www.gov.uk/government/news/e-cigarettes-around-95-less-harmful-than-tobacco-estimates-landmark-review

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TC Online First, published on October 2, 2017 as 10.1136/tobaccocontrol-2017-053759

Research paper

OPEN ACCESS

Potential deaths averted in USA by replacing cigarettes with e-cigarettes

David T Levy,[1] Ron Borland,[2] Eric N Lindblom,[3] Maciej L Goniewicz,[4] Rafael Meza,[5] Theodore R Holford,[6] Zhe Yuan,[7] Yuying Luo,[7] Richard J O'Connor,[4] Raymond Niaura,[8] David B Abrams[1,8]

Our projections show that a strategy of replacing cigarette smoking with vaping would yield substantial life year gains, even under pessimistic assumptions regarding cessation, initiation and relative harm.

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Tobacco harm reduction instead of abstinence only ("quit or die") policy

- massively reduced risk for smokers (overwhelming evidence and general agreement);
- success of harm reduction policy in the past (needle exchange, opiate replacement, condom programs);
- nicotine replacement therapy is largely ineffective (~95 % failure, hardly better than placebo);
- ~6 out of 9 millions (67 %) regular vapers in the EU had stopped smoking in 2014 (Eurobarometer);
- Longterm health risks cannot be excluded with certainty. However, this applies to any new poduct, and there is no plausible reason for concern (except the psychological association of vaping with smoking).
- Restrictive legal regulation of vaping is associated with reduced rates of sustained abstincence.
  (OR = 1.95; Yong et al., Nicotine Tob. Res. 2017).
- Warnings from (potential) minimal risks of vaping without communication of the benefits results in fatal misjudgement of the public.

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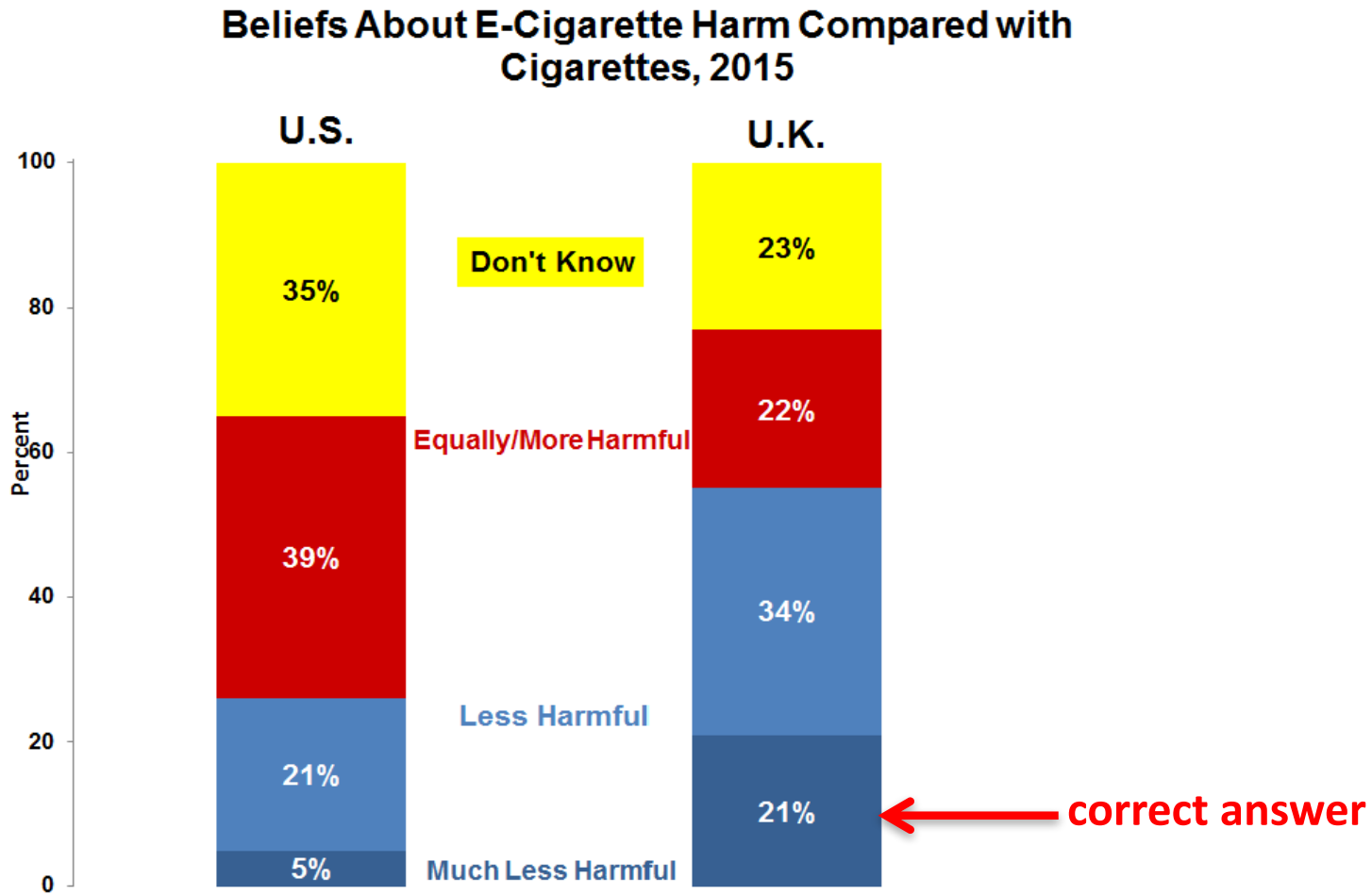
95 % (US) and 79 % (UK) of the public are not aware of the undisputed fact that vaping is much less harmful than smoking.



https://rodutobaccotruth.blogspot.co.at/2016/07/uk-e-cigarette-perceptions-more.html)

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Overly restrictive regulations of vaping in the TPD2

Limited volume of liquid containers (10 ml)

- Commercially available e-liquids (max. 20 mg/ml) don't pose any health risk if unintentionally swallowed or spilled over the skin. To overcome very slow permeation of nicotine through skin, medicinal patches contain complex formulations that enhance the delivery and the resorption of nicotine.
- Upon intentional absuse, e.g. drinking of e-liquid, immediate vomitting reduces the amount of bioavailable nicotine. The lethal dose is ~1 g, but suicide attempts by swallowing up to 4 g of pure nicotine failed due to vomitting.
- Average consumption: 5 ml of liquid per day -> ~180 bottles/year
  180 x 10 million vapers = 1.800 millions (1.8 billions) of discarded plastic bottles/year in the EU.

Regulation of hardware

- Constant levels of nicotine delivery: not achievable by standard devices and unnecessary;
  As in smoking, the desired nicotine delivery is adjusted by users *via* puff frequency, duration and strenght.
- Child- and tamper-proof, protection against breakage or leakage:
  Based on overestimation of nicotine toxicity; might result in (unintended?) bans of refillable tank systems used by most experienced longterm vapers.
- These provisions favor closed cartridge systems marketed by the tobacco industry for maximal earnings.

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Suggestions for a revised legislation of vaping in the EU

- Don't regulate products which don't contain tobacco in a tobacco product directive.
- Abandon the restriction of container size to 10 ml. Warnings to keep liquids out of the reach of children should be obligatory to protect toddlers.
- Don't regulate hardware (atomizers or batteries) beyond the existing directives for electronic devices.
- Prohibit the sale of disposable "cigalikes" for the sake of environmental protection and to impede vaping by minors.
- Allow public advertisements to emphasize the health benefits for smokers. Unlike tobacco cigarettes, vaping is not a thread to public health but an opportunity to prevent tobacco-associated disease.
- Prevent divergent regulations in EU member states. The TPD2 was passed to harmonize the market, but in fact every state has its own particular rules (flavors, online sale, approval procedures, tax etc.).

- **Don't oversleep or delay the "Kodak Moment" of nicotine consumption.**

Michael Russell (1976)
"People smoke for the nicotine but die from the tar."

Note: This file contains additional slides not shown due to time constraints.
Please, contact me per e-mail (mayer@uni-graz.at) if you wish to become an e-cig expert.

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Additional information

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Vaping – a gateway into or out of smoking?

never-smokers

X >99 % of vapers are (ex-)smokers

vaping

"associated with" falsely interpreted as "leads to" (causality)

smoking

Interpretation of association as causality leads to the preposterous conclusion that vaping leads to criminal behavior.

drinking liquor

use of illicit drugs

crime

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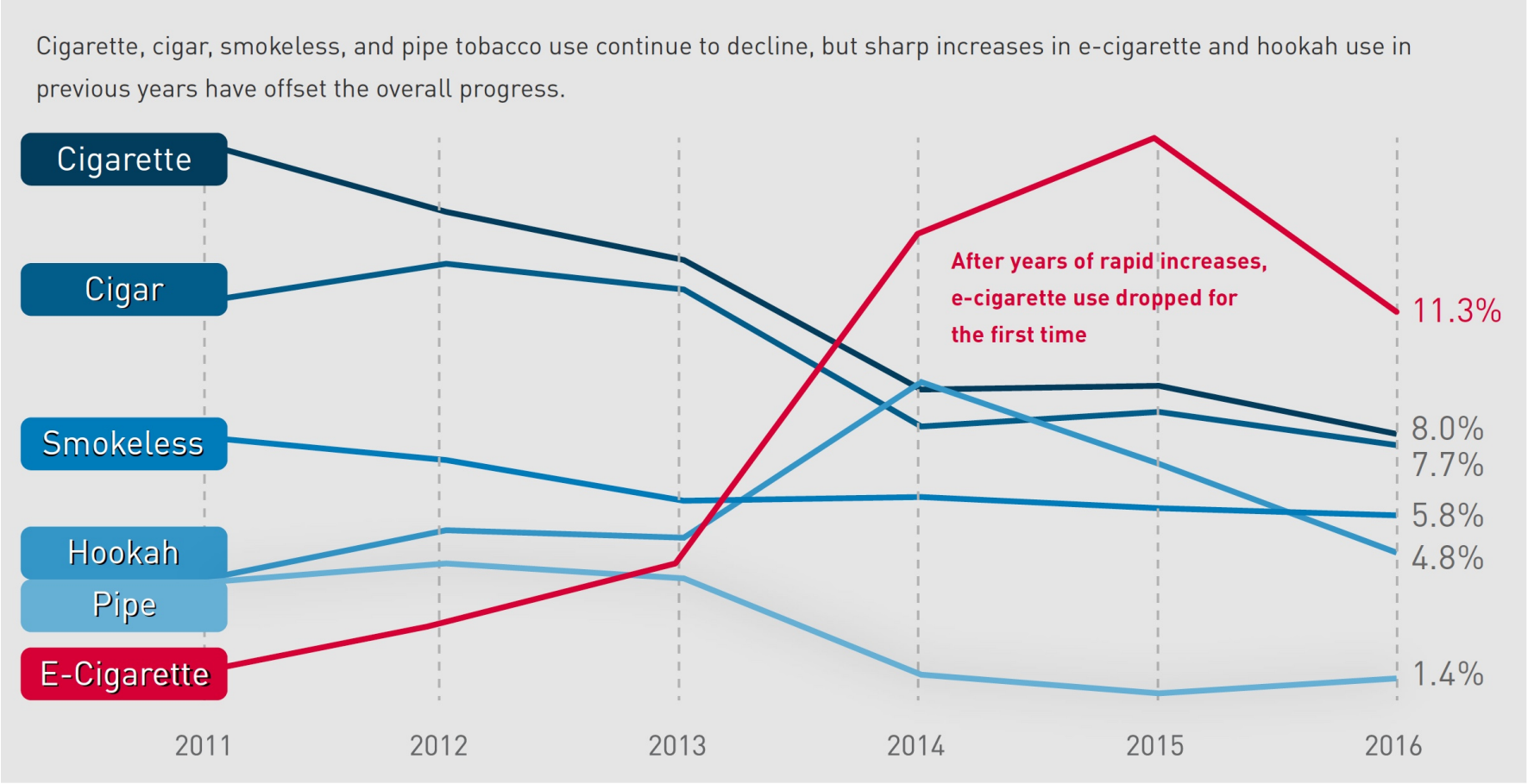
Youth Tobacco Use in the U.S.

Key Findings From the 2016 National Youth Tobacco Survey

https://www.fda.gov/downloads/TobaccoProducts/PublicHealthEducation/ProtectingKidsfromTobacco/UCM569880.pdf



Data from: Jamal et al. Tobacco use among middle and high school students — United States, 2011–2016. *MMWR Morb Mortal Wkly Rep.* 2017;66:597-603.

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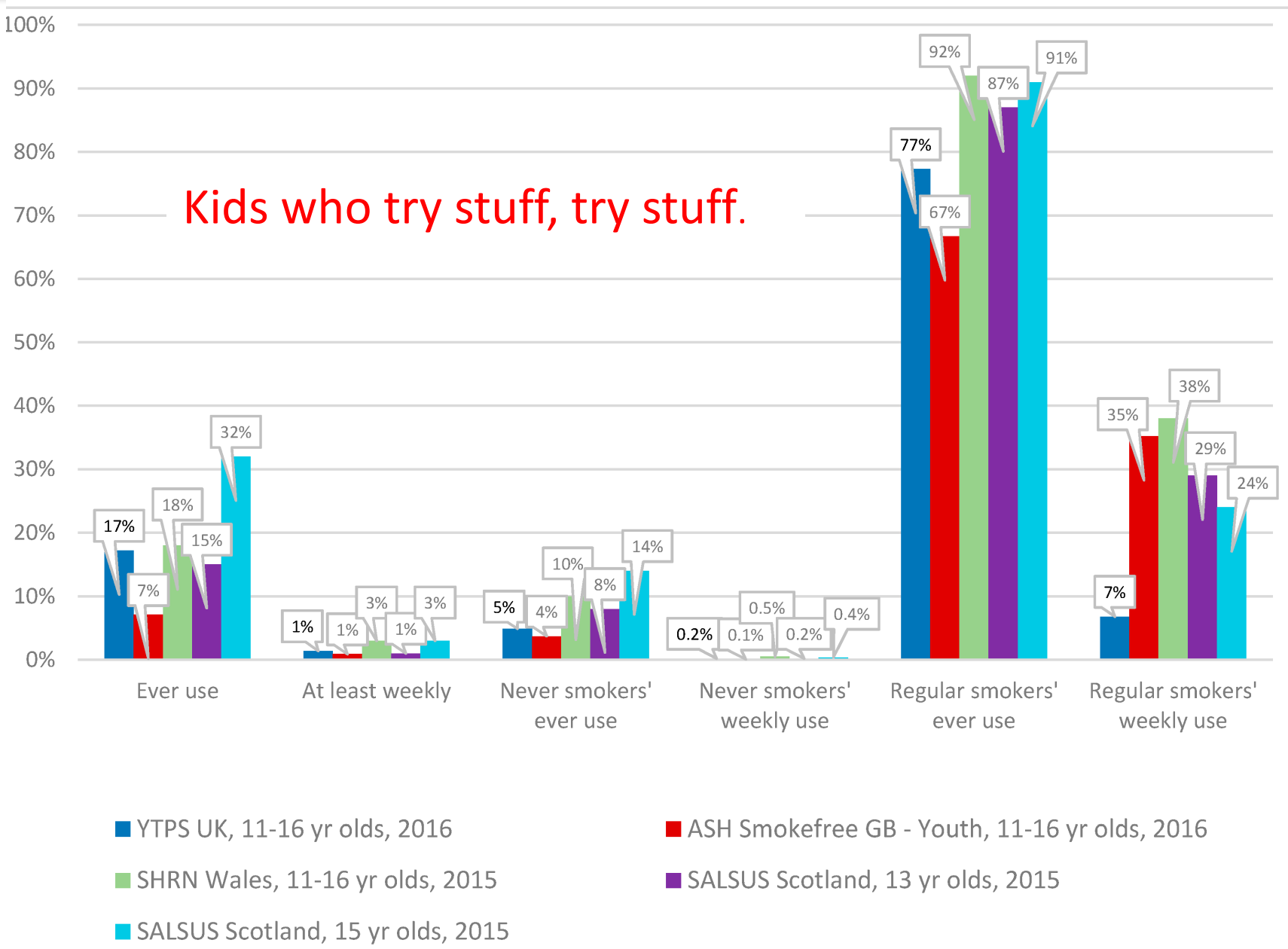

Bauld et al., *Int. J. Environ. Res. Public Helath* **14**, 973, 2017

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Use of e-cigs by minors

- Protection of youth (or adult non-smokers) is an acclaimed argument of the abstinence only fraction in tobacco control for overly restrictive regulation of products with documented health benefits for smokers.

- A virtually time-constant fraction of minors (15-20 %) exhibit risk-seeking behavior and try illegal stuff.
- Regular use of e-cigs by never-smoking minors is negligible (<0.5 %).
- More than 90 % of kids experimenting with e-cigs are using disposable "cigalikes" filled with nicotine-free liquid.
- Flavors are essential for satisfaction of adult vapers and not marketed to attract children.
- Kids purchase cheap disposable "cigalikes" in supermarkets or tobacco shops rather than the costly devices sold in vapeshops.
- Vapeshops haven't sold e-cigs to minors long before laws for youth protection had been passed.

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Emission of particulate matter, aldehydes and other toxic compounds

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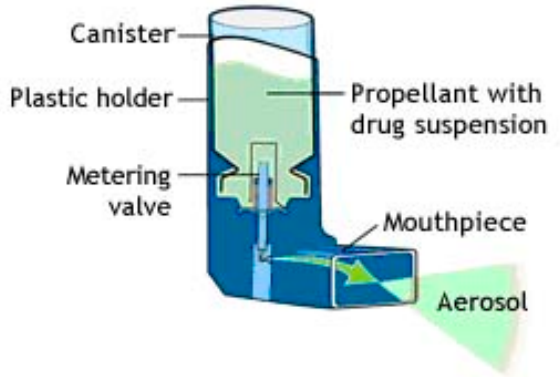
Particulate matter (PM) in aerosols – smoke *vs.* mist

- Smoke
  solid particles (tar, black carbon) formed by incomplete combustion of fossil fuels and burning plant material

- Mist (fog, vapor)
  liquid droplets formed by E-cigs and medicinal metered-dose inhalers

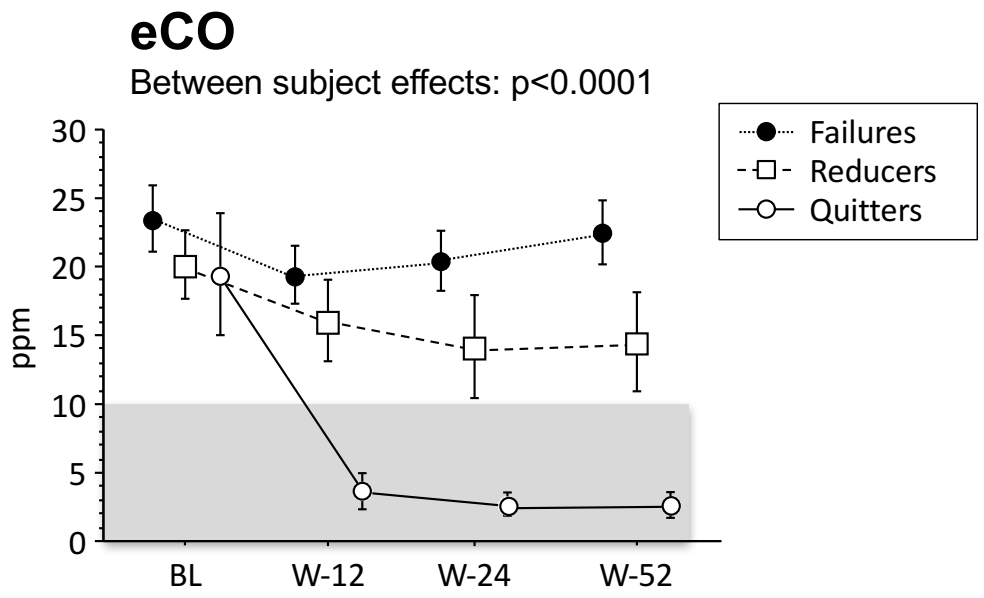


Effect of abstinence/reduction on eCO in smokers switching to ECs

by courtesy of Riccardo Polosa

CHANGES IN BREATHOMICS:
1-YR RANDOMIZED SMOKING CESSATION TRIAL OF ECs

D. Campagna, F. Cibella, P. Caponnetto, et al. Eur J Clin Invest 2016



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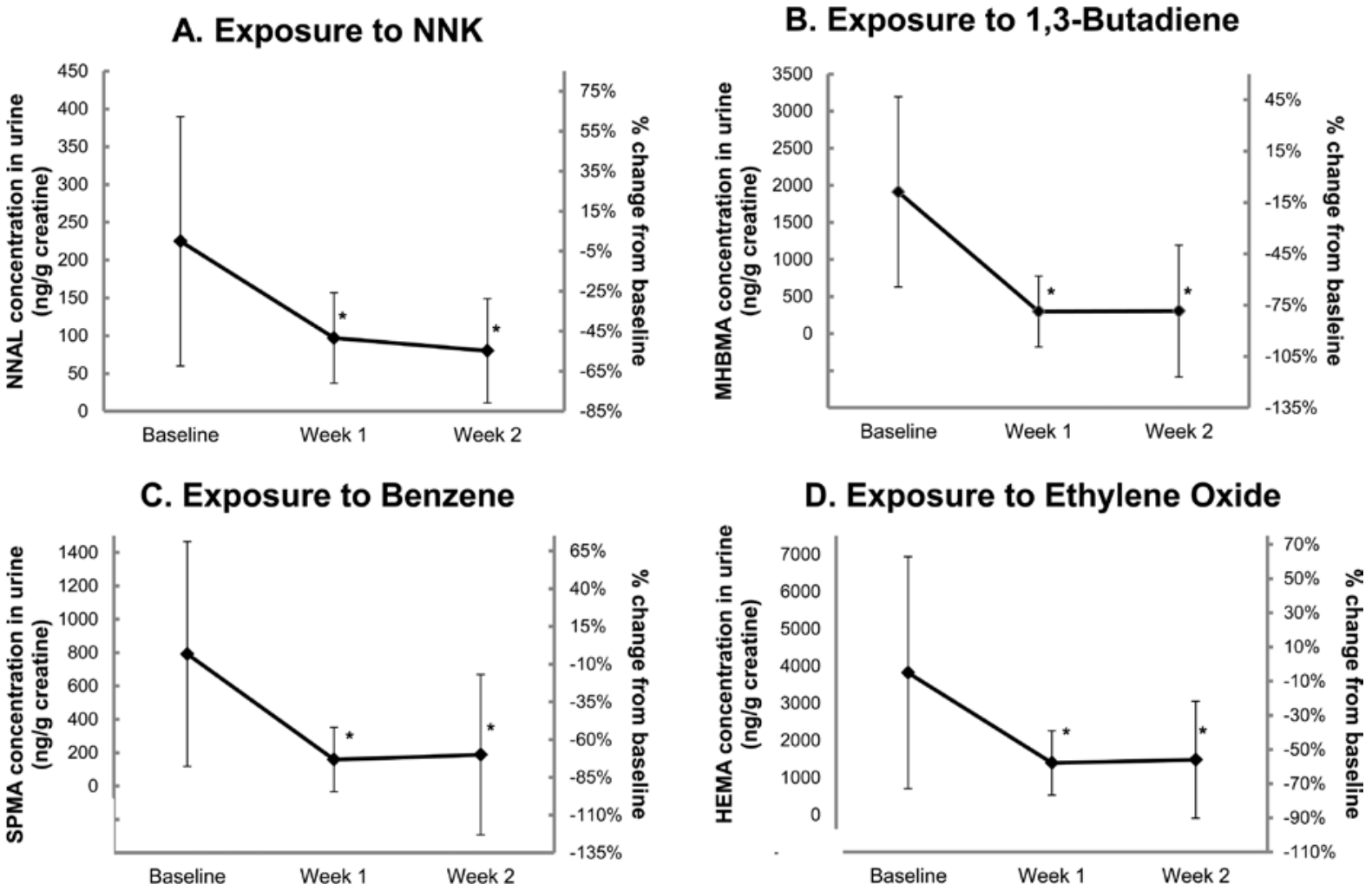
Reduced exposure to toxicants in e-cig users



Goniewicz et al., Nicotine *Tob. Res.* **19**, 160-7, 2017

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Comparison of sample toxicants emitted by tobacco cigarettes and e-cigarettes

Toxic compound	**Tobacco cigarette** (µg in mainstream smoke)	**E-cigarette** (µg per 15 puffs*)	**Average ratio** (conventional vs electronic cigarette)
Formaldehyde	1.6–52	0.20–5.61	9
Acetaldehyde	52–140	0.11–1.36	450
Acrolein	2.4–62	0.07–4.19	15
Toluene	8.3–70	0.02–0.63	120
NNN**	0.005–0.19	0.00008–0.00043	380
NNK**	0.012–0.11	0.00011–0.00283	40

* The authors assumed smokers of e-cigarettes would take an average of 15 puffs per vaping session, corresponding to smoking one tobacco cigarette.
** Tobacco-specific nitrosamine, a carcinogenic compound that originates in the curing and processing of tobacco.

adapted from Goniewicz et al., *Tob. Control* **23**, 133-9, 2014

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Aldehydes: Tobacco cigarette (MGB) vs. e-cigs

MGB			Blu CTD			Blu MMD		
Subject	Acetaldehyde	Hydroquinone	Subject	Acetaldehyde	Hydroquinone	Subject	Acetaldehyde	Hydroquinone
	227.6	70.6	11	<LOQ	<LOD	21	16.7	<LOD
1	186.0	60.0		<LOQ	<LOD		35.3	<LOD
	221.0	69.1		<LOQ	<LOD		38.9	<LOD
	134.7	41.3	12	<LOQ	<LOD	22	<LOQ	<LOD
2	129.8	33.2		<LOQ	<LOD		<LOQ	<LOD
	107.7	31.9		<LOQ	<LOD		<LOQ	<LOD
	131.2	32.2	13	<LOQ	<LOD	23	<LOQ	<LOD
3	169.0	47.4		86.4	<LOD		<LOQ	<LOD
	128.1	52.5		44.2	<LOD		<LOQ	<LOD
	115.6	48.5	14	<LOQ	<LOD	24	5.4	<LOD
4	119.3	47.3		<LOQ	<LOD		7.2	<LOD
	124.1	42.5		<LOQ	<LOD		9.9	<LOD
	195.4	18.4	15	<LOQ	<LOD	25	<LOQ	<LOD
5	122.0	13.3		<LOQ	<LOD		<LOQ	<LOD
	196.3	20.0		<LOQ	<LOD		<LOQ	<LOD
	208.0	99.5	16	<LOQ	<LOD	26	<LOQ	<LOD
6	116.9	103.5		<LOQ	<LOD		<LOQ	<LOD
	116.0	83.9		<LOQ	<LOD		<LOQ	<LOD
	<LOQ	22.8	17	<LOQ	<LOD	27	<LOQ	<LOD
7	88.1	8.79		<LOQ	<LOD		<LOQ	<LOD
	48.1	25.9		<LOQ	<LOD		6.2	<LOD
	380.2	29.1	18	<LOD	<LOD	28	<LOQ	<LOD
8	193.7	37.7		24.2	<LOD		<LOQ	<LOD
	189.7	30.9		<LOQ	<LOD		7.1	<LOD
	285.2	73.0	19	<LOQ	<LOD	29	6.5	<LOD
9	126.6	26.8		<LOQ	<LOD		8.9	<LOD
	104.6	81.6		<LOQ	<LOD		7.6	<LOD
	217.6	43.0	20	6.9	<LOD	30	<LOQ	<LOD
10	162.7	46.2		<LOQ	<LOD		<LOQ	<LOD
	114.1	64.0		<LOQ	<LOQ		5.4	<LOD
Avg *	156.7	46.8		<9.73 *	<0.421 *		<8.29 *	<0.367 *
SD	68.8	24.7		16.5	0.3		8.2	0.0

Long, G.A., *Int. J. Environ. Res. Public Health.* **11**, 11177-91, 2014

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High levels of aldehydes are generated under "dry puff" conditions

Table 1 Aldehyde levels in e-cigarette aerosol under normal and 'dry puff' conditions. Levels approached or exceeded those in tobacco cigarette smoke only under dry puff conditions, which are detected and avoided by the consumers.

	Formaldehyde (µg/10 puffs) n = 3	*Acetaldehyde (µg/10 puffs) n = 3*	*Acetone (µg/10 puffs) n = 3*	*Acrolein (µg/10 puffs) n = 3*
6.5 watts				
Atomizer 1	6.5 (1.7)	ND	ND	ND
Atomizer 2	3.7 (1.6)	0.8 (0.4)	ND	0.2 (0.1)
P-value[a]	NS	NS	NS	NS
7.5 watts				
Atomizer 1	6.1 (1.3)	ND	ND	ND
Atomizer 2	ND	0.8 (0.5)	ND	1.3 (0.8)
P-value[a]	0.001	NS	NS	0.045
9 watts				
Atomizer 1	9.5 (2.3)	3.5 (0.9)	ND	0.8 (0.6)
Atomizer 2[b]	119.2 (15.9)	58.9 (12.8)	4.6 (1.0)	48.4 (10.0)
P-value[a]	< 0.001	0.002	0.002	0.001
10 watts				
Atomizer 1	11.3 (2.6)	4.5 (1.2)	ND	1.0 (0.6)
Atomizer 2[b]	344.6 (56.0)	206.3 (33.3)	22.5 (7.1)	210.4 (48.8)
P-value[a]	0.001	< 0.001	0.006	0.002
	Formaldehyde (µg/cigarette) n = 50	*Acetaldehyde (µg/ cigarette) n = 50*	*Acetone (µg/ cigarette) n = 50*	*Acrolein (µg/ cigarette) n = 50*
Tobacco cigarette[c]	74.0 (23.7)	1240.3 (147.7)	641.9 (71.2)	120.4 (14.7)
P-value (9 W)[d]	< 0.001	< 0.001	< 0.001	< 0.001
P-value (10 W)[e]	< 0.001	< 0.001	< 0.001	< 0.001

[a]Repeated-measures analysis of variance (ANOVA). [b]Dry puff conditions, as detected by seven electronic cigarette users. [c]Data from Counts *et al.* (Health Canada Intense puffing regime) [10]. [d]One-way ANOVA, comparing data tobacco cigarettes with values from 9-W power setup. [e]One-way ANOVA, comparing data tobacco cigarettes with values from 9-W power setup. ND = not determined; NS = not significant.

Farsalinos et al., *Addiction* **110**, 1352-6, 2015

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Using e-cigs under "dry puff" conditions equals eating burned toast

Formaldehyde Facts
From the CDC and WHO

It is everywhere, produced naturally by plants, animals and humans

Sources: antiseptics, perma press fabrics, cosmetics, shampoo, shaving cream, mouthwashes medicines, vitamins, cooking, smoking

Occurs naturally in fruits-vegetables (3 - 6 mg/kg)

Airborne Formaldehyde[1]

Average daily exposure (air):	**0.5 - 1.1 mg**
E-Cigarette Use:	**Same as background[2]**
Smoker (20 cigarettes):	**1 - 2 mg**

[1] WHO Air Quality Guidelines Chapter 5.8, 2013

[2] Indoor Air 23: 25-31, 2013

by courtesy of Brad Rodu

Formaldehyde Facts
The Link To Cancer is Grossly Exaggerated

Claim that formaldehyde causes nasopharyngeal cancer based on National Cancer Institute study of 10 industry sites:

Excess cancers at only 1 site, where workers exposed to other risk factors (sulfuric acid mists, mineral acid, metal dusts). Other 9 sites had lower NPC numbers[1]

Comprehensive Meta-Analyses of All Studies[2,3]

Case-Control Studies	**RR= 1.2 (1.0 – 1.5)**
Cohort Studies	**RR= 0.7 (0.4 – 1.3)**

[1]Marsh et al. Regulatory Toxicology and Pharmacology 42: 275, 2005 and 48: 308, 2007
[2]Bosetti et al. Annals of Oncology 19: 29, 2007
[3]Bachand et al. Critical Reviews in Toxicology, 40: 85, 2010

by courtesy of Brad Rodu

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Passive vaping: Unrestricted use of e-cigarettes in a small room

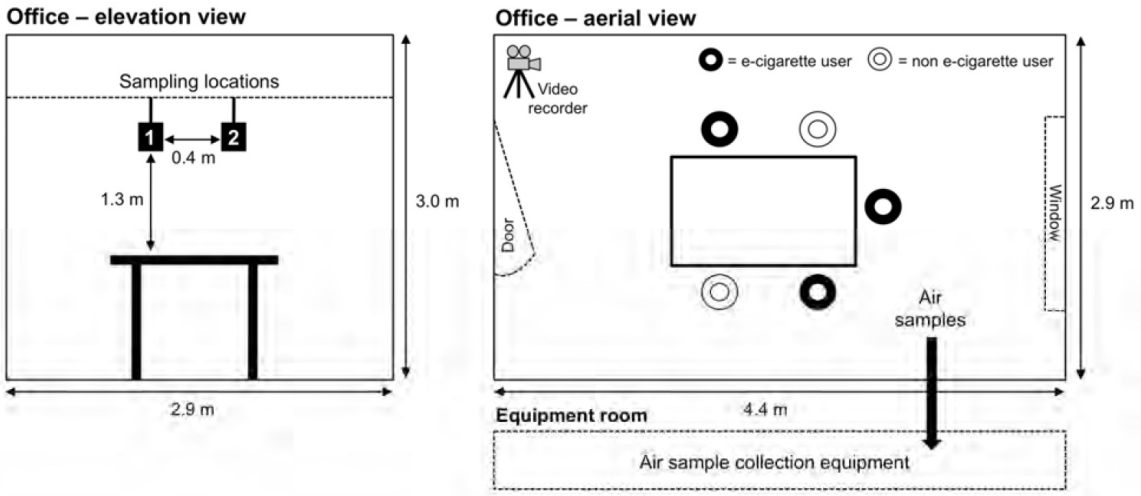
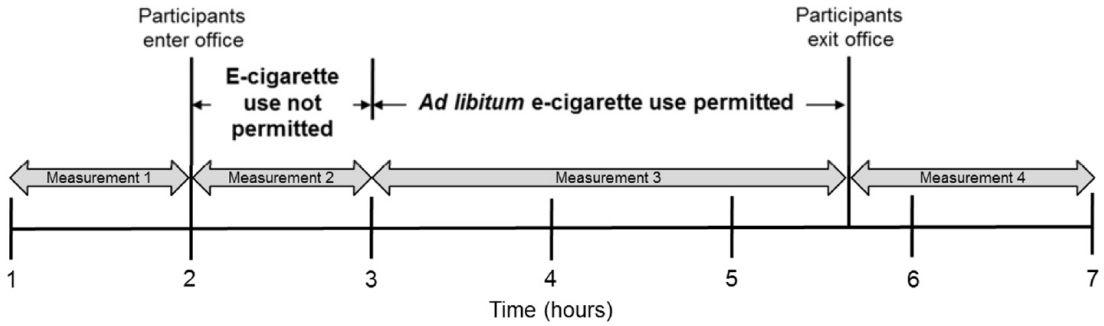


Figure 1. The layout of the meeting room used in this study (not drawn to scale). Sampling locations and positions of the e-cigarette users and non-users during the meeting are highlighted.



O'Connell et al., *Int. J. Environ. Res. Public Health.* **12**, 4889-907, 2015

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Volatile organic compounds

Table 1. Average indoor air concentrations of VOCs (including nicotine, propylene glycol and glycerol (principle components of the e-liquid)) and low molecular weight carbonyls (µg/m³) measured before, during and after use of e-cigarettes from two independent sampling sites.

Chemical Compound	Background (before Participants Enter Room)	Room Occupied (No Vaping)	Room Occupied (Vaping Permitted)	Room Unoccupied (after Participants Leave Room)	Air Quality Guidelines or UK Workplace Exposure Limit as Published (WEL; 8 h Average) (mg/m³)	Air Quality Guidelines or UK Workplace Exposure Limit * (WEL; 8 h Average) (µg/m³)
	Measurement 1 (µg/m³)	Measurement 2 (µg/m³)	Measurement 3 (µg/m³)	Measurement 4 (µg/m³)		
Propylene glycol	<0.5	<0.5	203.6	10.2	UK WEL: 474	474,000
Glycerol	<150	<225	<250	<200	UK WEL: 10	10,000
Nicotine	<7.0	<7.0	<7.0	<7.0	UK WEL: 0.5	500
Isoprene	<0.5	6.2	9.5	<0.5	Not established	Not established
Acetone	1.3	9.2	10.7	1.2	UK WEL: 1210	1,210,000
Propan-2-ol	55.3	13.6	8.0	29.2	UK WEL: 999	999,000
2,2,4-Trimethyl-1,3-pentanediol diisobutyrate	<0.5	<0.5	1.5	2.2	Not established	Not established
Di-isobutyl phthalate	3.5	4.4	2.3	2.8	UK WEL: 5	5000
Formaldehyde	32.0	31.0	37.6	21.0	WHO: 0.1	100
Acetaldehyde	9.0	6.5	12.4	6.0	EU Indoor Air Quality: 0.2	200
Acrolein	<2.0	<2.0	<2.0	<2.0	UK WEL: 0.23	230
Total VOC	65.0	237.0	379.8	129.0	UK Building Regulations: 0.3 (8 h average)	300

* converted to µg/m³ to facilitate comparison with analytical findings in this study.

O'Connell et al., *Int. J. Environ. Res. Public Health.* **12**, 4889-907, 2015c

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Polycyclic aromatic hydrocarbons

Table 2. Average indoor air concentrations of US EPA "priority list" of 16 PAHs (µg/m^3) measured before, during and after use of e-cigarettes from two independent sampling sites.

Chemical Compound	Background (before Participants Enter Room)	Room Occupied (No Vaping)	Room Occupied (Vaping Permitted)	Room Unoccupied (after Participants Leave Room)
	Measurement 1 (µg/m^3)	Measurement 2 (µg/m^3)	Measurement 3 (µg/m^3)	Measurement 4 (µg/m^3)
Acenaphthene	<1.25	<1.25	<1.25	<1.25
Acenaphthylene	<1.25	<1.25	<1.25	<1.25
Anthracene	<1.25	<1.25	<1.25	<1.25
Benz[a]anthracene	<1.25	<1.25	<1.25	<1.25
Benzo[b]fluoranthene	<1.25	<1.25	<1.25	<1.25
Benzo[k]fluoranthene	<1.25	<1.25	<1.25	<1.25
Benzo[ghi]perylene	<1.25	<1.25	<1.25	<1.25
Benzo[a]pyrene	<1.25	<1.25	<1.25	<1.25
Chrysene	<1.25	<1.25	<1.25	<1.25
Dibenz[ah]anthracene	<1.25	<1.25	<1.25	<1.25
Fluoranthene	<1.25	<1.25	<1.25	<1.25
Fluorene	<1.25	<1.25	<1.25	<1.25
Indeno[1,2,3-cd]pyrene	<1.25	<1.25	<1.25	<1.25
Naphthalene	<1.25	<1.25	<1.25	<1.25
Phenanthrene	<1.25	<1.25	<1.25	<1.25
Pyrene	<1.25	<1.25	<1.25	<1.25

O'Connell et al., *Int. J. Environ. Res. Public Health.* **12**, 4889-907, 2015

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Trace metals

Table 3. Average indoor air concentrations of US "EPA Method 29" metals (plus aluminium and phosphorous) (µg/m³) measured before, during and after use of e-cigarettes from two independent sampling sites.

Chemical Compound	Background (before Participants Enter Room)	Room Occupied (No Vaping)	Room occupied (Vaping Permitted)	Room unoccupied (after Participants Leave Room)	UK Workplace Exposure Limit as Published (WEL; 8 h Average) (mg/m³)	UK Workplace Exposure Limit * (WEL; 8 h Average) (µg/m³)
	Measurement 1 (µg/m³)	Measurement 2 (µg/m³)	Measurement 3 (µg/m³)	Measurement 4 (µg/m³)		
Aluminium	<2.0	<2.0	<2.0	<2.0	10	10,000
Antimony	<1.0	<1.0	<1.0	<1.0	0.5	500
Arsenic	<1.0	<1.0	<1.0	<1.0	0.1	100
Barium	<1.0	<1.0	<1.0	<1.0	0.5	500
Beryllium	<2.0	<2.0	<2.0	<2.0	0.002	2.0
Cadmium	<1.0	<1.0	<1.0	<1.0	0.025	25
Chromium	<1.0	<1.0	<1.0	<1.0	0.5	500
Cobalt	<1.0	<1.0	<1.0	<1.0	0.1	100
Copper	<1.0	<1.0	<1.0	<1.0	1	1000
Lead	<1.0	<1.0	<1.0	<1.0	Not established	Not established
Manganese	<1.0	<1.0	<1.0	<1.0	0.5	500
Mercury	<1.0	<1.0	<1.0	<1.0	0.02	20
Nickel	<1.0	<1.0	<1.0	<1.0	0.1	100
Phosphorus	<10.0	<10.0	<10.0	<10.0	Not established	Not established
Selenium	<1.0	<1.0	<1.0	<1.0	0.1	100
Silver	<2.0	<2.0	<2.0	<2.0	0.1	100
Thallium	<2.0	<2.0	<2.0	<2.0	0.1	100
Zinc	<1.0	<1.0	<1.0	<1.0	Not established	Not established

* converted to µg/m³ to facilitate comparison with analytical findings in this study.

O'Connell et al., *Int. J. Environ. Res. Public Health.* **12**, 4889-907, 2015

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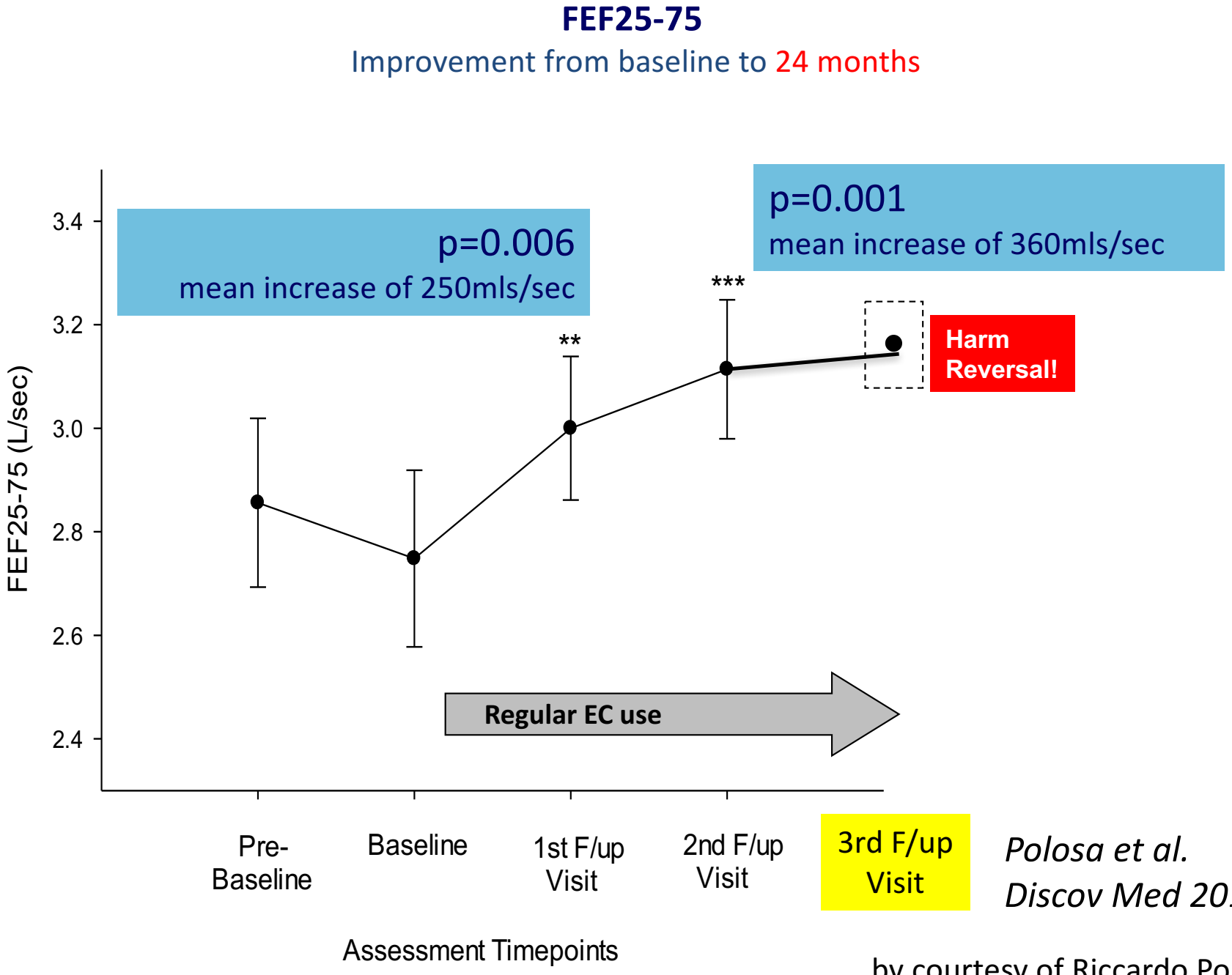
Benefits on lung function

Mild to moderate asthmatics (according to GINA criteria)



Polosa et al. Discov Med 2016

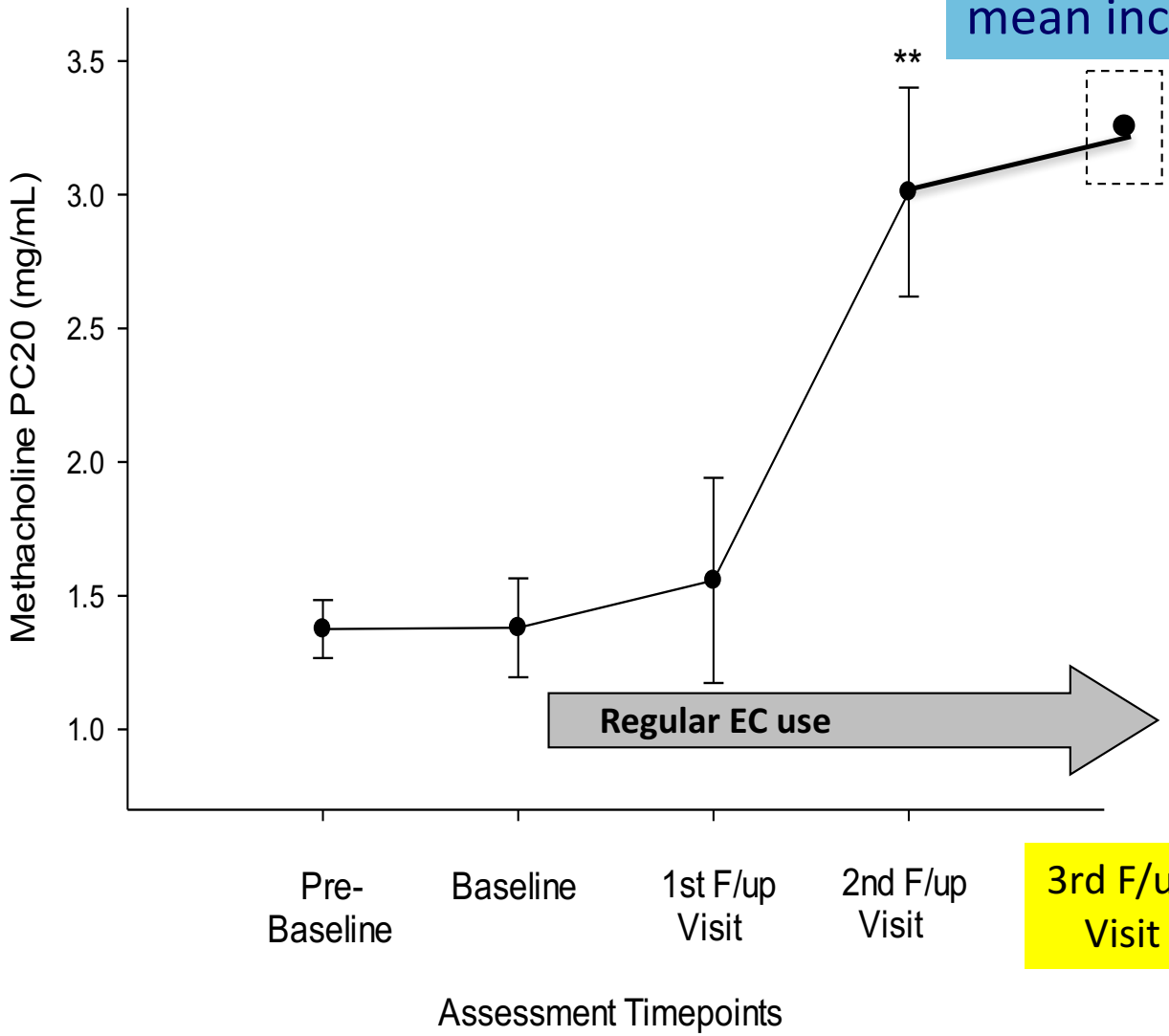
by courtesy of Riccardo Polosa

Mild to moderate asthmatics (according to GINA criteria)

Methacholine PC20

Improvement from baseline to 24 months

p=0.003
mean increase of 1.2 DD



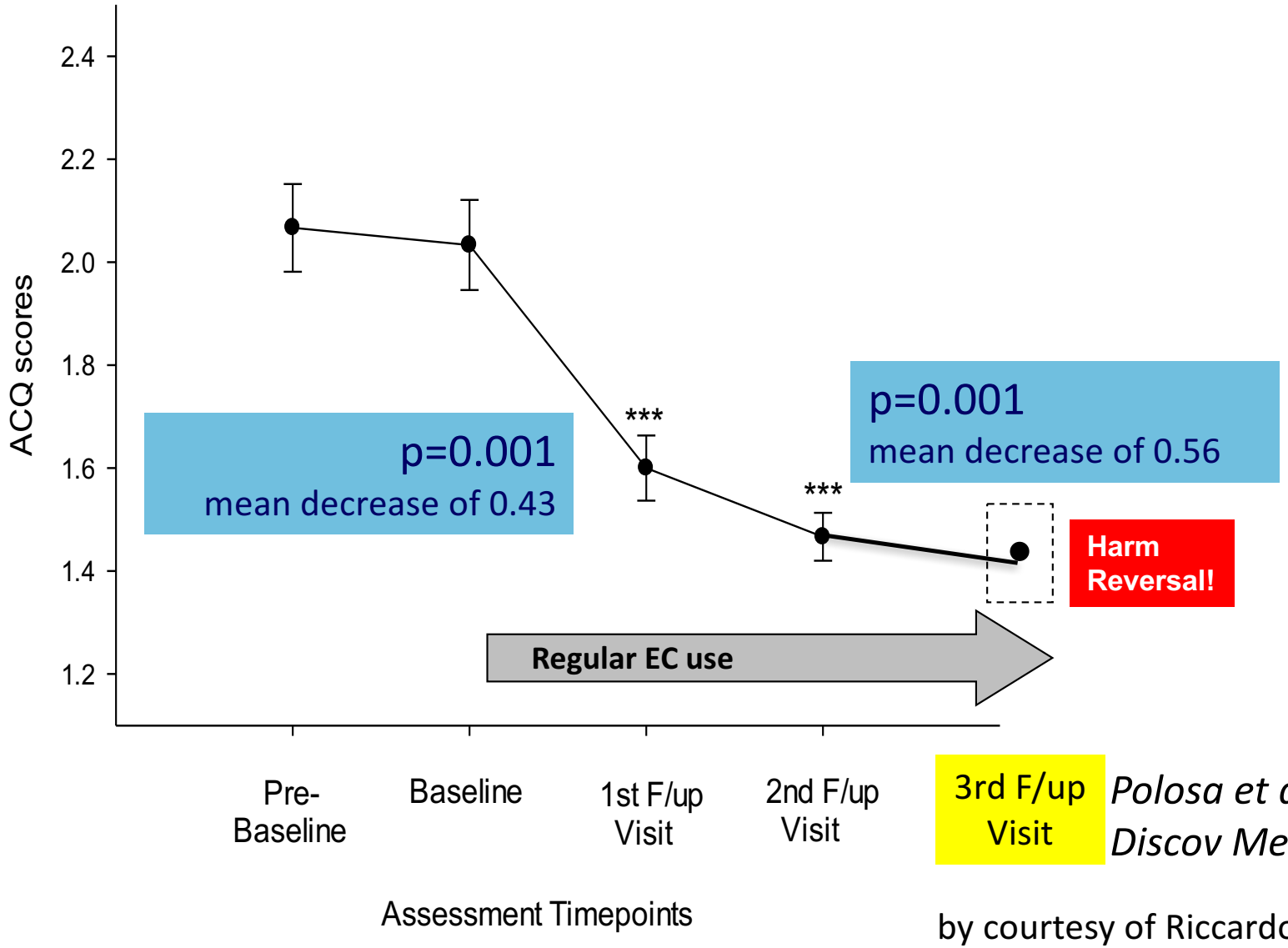
Polosa et al. Discov Med 2016

by courtesy of Riccardo Polosa

Mild to moderate asthmatics (according to GINA criteria)

Juniper's ACQ

Improvement from baseline to 24 months



Polosa et al. Discov Med 2016

by courtesy of Riccardo Polosa

Vaping and asthma exacerbations

Parameter	Baseline N=18	1st follow-up visit (6 months) N=18		2nd follow-up visit (12 months) N=18		3nd follow-up visit w/o relapsers (24 months) N=16	
			p value to Baseline		*p value to Baseline*		*p value to Baseline*
Cigarettes/day	21.9 (±4.5)	5.0 (±2.6)	*<0.001*	3.9 (±1.0)	*<0.001*	3.5 (±1.22)	*<0.001*
Exacerbations	1.17 (±0.9)	0.87 (±0.7)	*0.296*	0.78 (±0.7)	*0.153*	0.81 (±0.66)	*0.190*

Frequent exacerbators (≥ 2 exacerbations; n=6) halved their exacerbations at both follow-up visits

Exacerbation rate increased from 0 at 12 months to 2 at 24 months in the two patients relapsing to tobacco smoking

by courtesy of Riccardo Polosa

RESPIRATORY SYMPTOMS IN E-CIG USERS

K. Farsalinos et al. Int. J. Environ. Res. Public Health 2014

Side effects/accidents	Total (n = 19,353)	Current smokers (n = 3682)	Former smokers (n = 15,671)	Statistic	*p* value
		Dual users	Single users		
Asthma (N = 1173)					
Worse	14 (1.1)	5 (2.2)	9 (0.8)		
Stable	303 (23.2)	78 (34.4)	225 (20.8)	$\chi^2 = 27.3$	<0.001
Improved	856 (65.4)	116 (51.1)	742 (68.6)		
COPD (N = 1062)					
Worse	10 (0.8)	4 (1.7)	6 (0.6)		
Stable	151 (12.7)	39 (17.0)	112 (11.7)	$\chi^2 = 9.5$	0.009
Improved	901 (75.7)	158 (68.7)	743 (77.4)		

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Miler et al., J Addict Res Ther 2016, 7:4
DOI: 10.4172/2155-6105.1000290

Research Article Open Access

Changes in the Frequency of Airway Infections in Smokers Who Switched To Vaping: Results of an Online Survey

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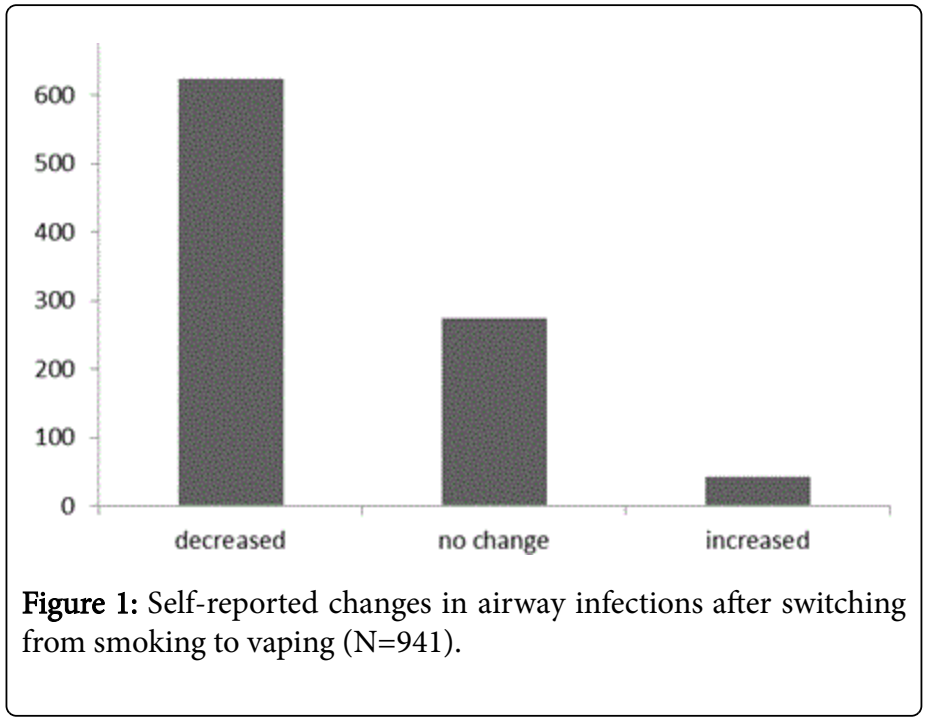

Figure 1: Self-reported changes in airway infections after switching from smoking to vaping (N=941).

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Harmful and beneficial effects of nicotine

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Potential harmful effects of nicotine

- Nicotine increases sympathetic tone, resulting in acute and transient increases in blood pressure, arterial stiffness and heart rate. These effects are harmless in healthy individuals but may be harmful in severe cardiovascular disease (chronic heart failure, coronary artery disease, survived myocardial dysfunction).
- Nicotine stimulates angiogenesis (formation of new blood vessels). While this effect is beneficial in wound healing, it may support tumor growth in cancer and interfere with the efficacy of chemotherapy.
- Nicotine may impair embryonic development, but nicotine replacement therapy had no effect on birth outcome in a large clinical study (observations of children 2 years after delivery).
  The SNAP trial: a randomised placebo-controlled trial of nicotine replacement therapy in pregnancy--clinical effectiveness and safety until 2 years after delivery, with economic evaluation. *Health Technol. Assess*. **18**, 1-128, 2014.
- Various effects in cells and laboratory animals with uncertain clinical relevance.
- Oral or intravenous application of high amounts of nicotine as a bolus (>100 mg) results in vomitting, diarrhea, headache, and dizziness. In the absence of vomitting, the lethal dose is around 1,000 mg (not 60 mg as disseminated until 2014).
  Mayer, B.: How much nicotine kills a human? Tracing back the generally accepted lethal dose to dubious self-experiments in the nineteenth century. *Arch. Toxicol.* **88**, 5-7 (2014)

The Facts
Poison ”Reports” in Children Under 6 years in 2015

All Exposures		547,286	
Cosmetics and personal care products		141,139	26%
Household cleaners		114,031	21
Foreign bodies		66,589	12
Pesticides + plants		61,247	11
Arts, crafts, office supplies + deodorizers		36,876	7
Tobacco products		12,280	2.2
Cigarettes	6,556		1.2
E-cigarettes	2,567		0.5
Alcohols		9,805	1.8

American Association of Poison Control Centers, 2015:
https://aapcc.s3.amazonaws.com/pdfs/annual_reports/2015_AAPCC_NPDS_Annual_Report_33rd_PDF.pdf

by courtesy of Brad Rodu

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Potential beneficial effects of nicotine and propylene glycol

- Nicotine improves cognition and mood, particularly in the elderly, in depression, and individuals with cognitive impairment (including schizophrenic patients).
  (for recent reviews see: Gandelman et al., Neurosci. Biobehav. Rev. 2017; Majdi et al., Rev. Neurosci. 2017; Campos et al., Curr. Drug Abuse Rev. 2016; Featherstone & Siegel, Int. Rev. Neurobiol. 2015)
- Nicotine protects against M. Parkinson.
  (for recent reviews see: Ma et al., Transl. Neurodegener. 2017; Jurado-Coronel, Curr. Pharm. Des. 2016; Barreto et al., Front Aging Neurosci. 2015)
- Nicotine protects against M. Alzheimer.
  (for recent reviews see: Echeverria et al. Prog. Neurobiol. 2016; Lombardo & Maskos, Neuropharmacology, 2015)
- Nicotine protects against ulverative colitis.
  (for recent reviews see: Aliment Pharmacol. Ther. 2012; Lakhan & Kirchgessner, J. Transl. Med. 2011; Bastida et al., World J. Gastroenterol. 2011)
- Nicotine exerts central and peripheral anti-inflammatory effects.
  (for recent publications see: Bagdas et al., Curr. Neuropharmacol. 2017; Revathikumar et al., J. Neuroinflammation 2016; Bao et al., Pacenta 2016)
- Propylene glycol may exhibit antibacterial/antiviral activity.
  (Robertson et al., J. Exp. Med. 1942; Robertson et al., J.Exp. Med. 1943; Jennings & Bigg, Res. Program, 1946; Gwatkin, R. Can. J. Comp. Med. Vet. Sci. 1947; Miler et al., J. Addict. Res. Ther. 2016; Miler & Hajek, Med. Hypoth. 2017)

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Cigarette vs. nicotine dependence

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Revision of the term "nicotine dependence" by Karl Fagerstrøm

Commentary

Determinants of Tobacco Use and Renaming the FTND to the Fagerström Test for Cigarette Dependence

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Received April 6, 2011; accepted May 26, 2011

Nicotine Tob. Res. **14**, 1382-90, 2012

Determinants of Cigarette Dependence

- Pharmacological (nicotine plus others, in particular monoamine oxidase inhibitors)
- Throat hit mediated by activation of nicotinergic receptors on sensory fibers in the airways
- Habit and Conditioning (smoking-associated behavior)

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Evidence against the concept of nicotine addiction (according to Fagerstrøm)

- Animals do not self-administer nicotine as readily as they do “hard drugs” like amphetamine, cocaine, and heroin.
- Nicotine is also a relatively weak reinforcer in human laboratory studies.
- Abstinent smokers seem to prefer a much reduced nicotine content cigarette over nicotine-containing products like gum, and the reduced nicotine cigarette reduces craving. The so-called "scratch" in the throat [throat hit] may be of importance for these effects.
- Although nicotine replacement treatment is an effective aid for quitting smoking, its efficacy is moderate even if doses that replace most or all nicotine from the cigarettes are used.
- There is no evidence for the abuse of pure nicotine.

For details and references see:
Fagerstrøm, K.: Determinants of tobacco use and renaming the FTND to the Fagerstrøm test for cigarette dependence. *Nicotine Tob. Res.* **14**, 1382-90, 2012

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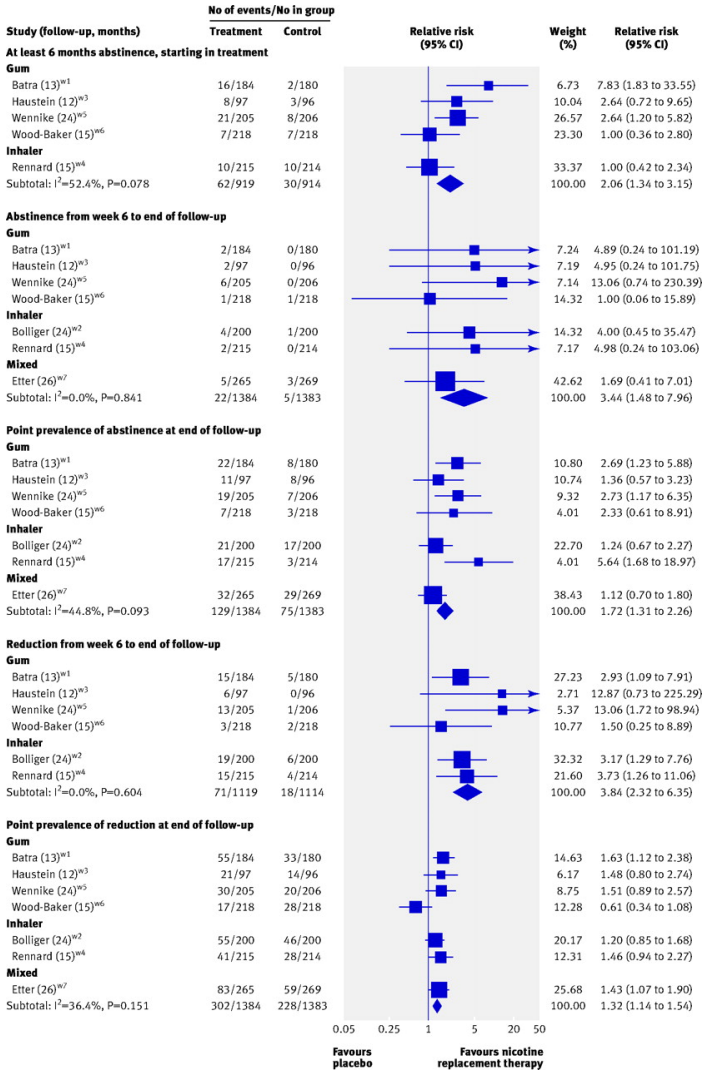
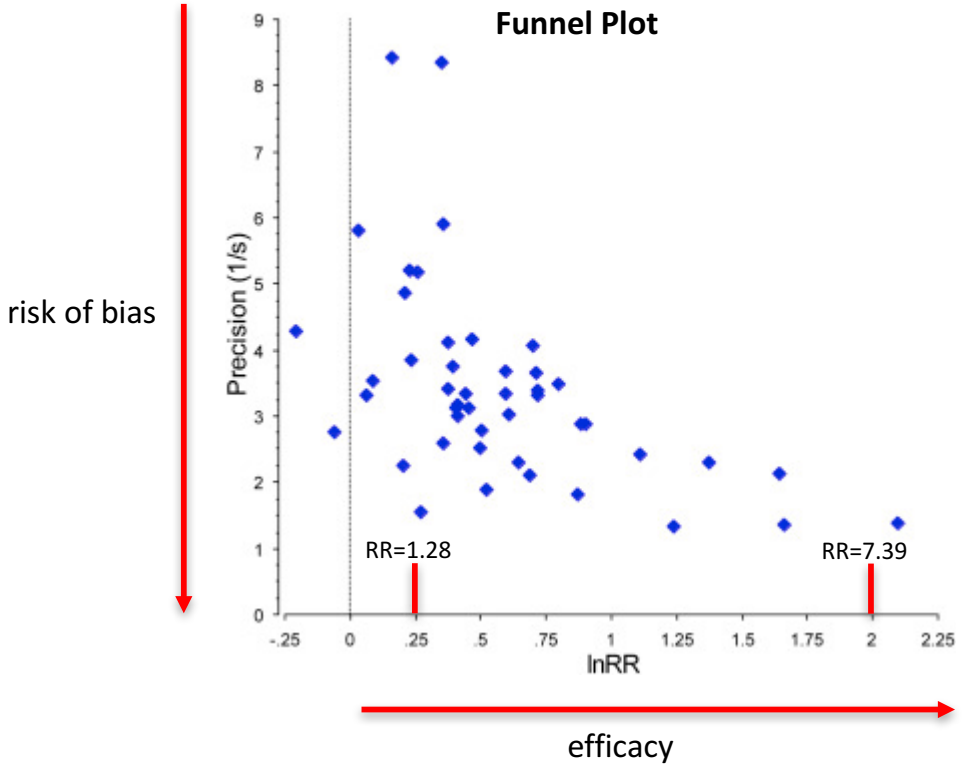
Smoking Cessation: Lack of efficacy of pharmaceutical nicotine replacement therapy (NRT)



Effectiveness and safety of nicotine replacement therapy assisted reduction to stop smoking: systematic review and meta-analysis.
Moore et al. *Brit. Med. J.* **338**, b1024 (2009)

- Abstinence rates continuously decrease with time.
- A large metaanalysis published 2009 showed quit rates of 6.75 % vs. 3.28 % (placebo) after 6 months (93.25 % failure).
- This small effect dissolves when meta-regression accommodates multiple sources of bias (selection, performance, detection, attrition).



Stanley & Massey, *J. Clin. Epidemiol.* **79**, 41-45 (2016)

Clinical Trials Are Wrong For Measuring Consumer Behaviors

- Clinical Trials are great when doctors want the best treatment for a disease
- Clinical Trials are awful when we want to know consumers' preferences
- Smokers are not sick, and they don't want to be "treated."
- Smokers want truthful information so they can make educated choices, maximizing their health and welfare

by courtesy of Brad Rodu