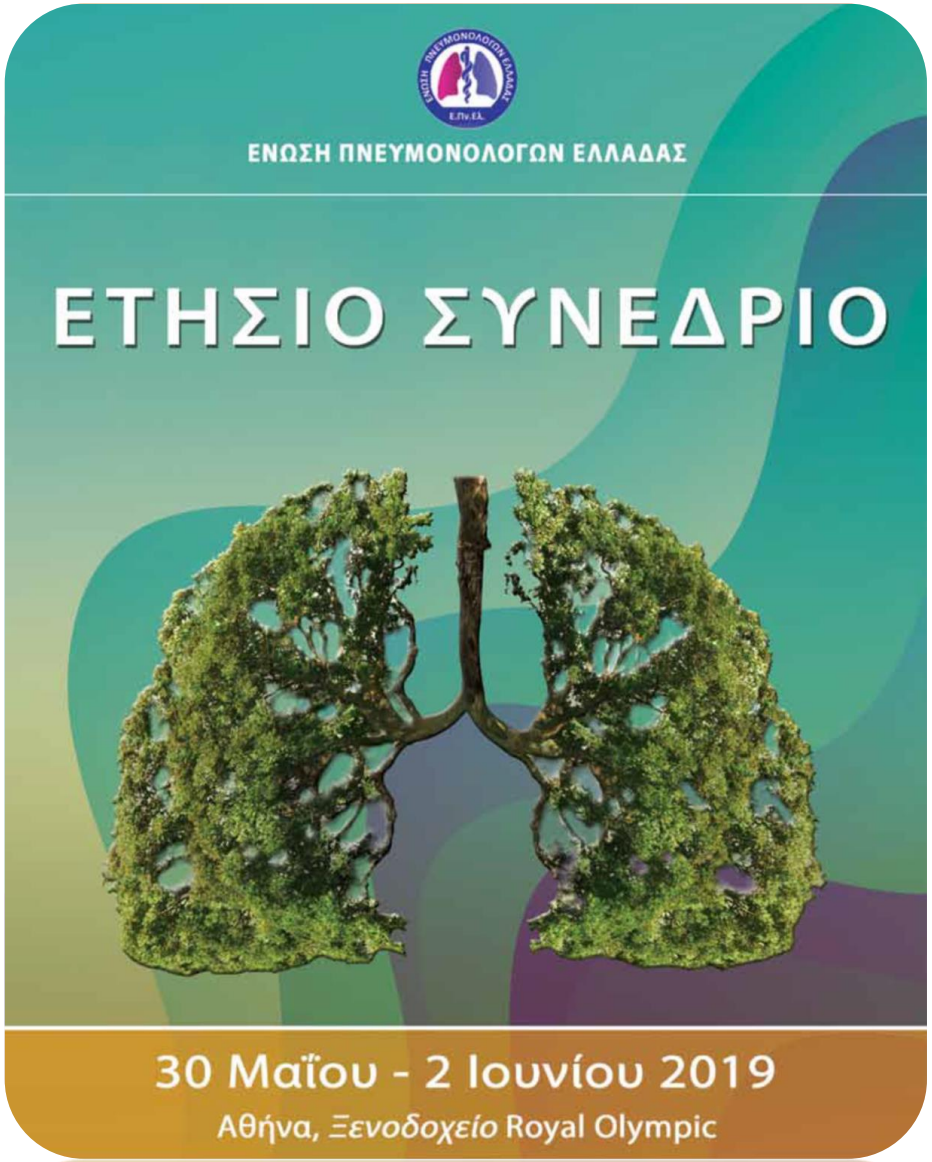


Νέα καπνικά προϊόντα

- Νομοθεσία και στάση επιστημονικής κοινότητας

Γλυνός Κωνσταντίνος
Πνευμονολόγος-Εντατικολόγος
Ιατρικός Σύμβουλος GSK

Προσωπική Δήλωση Σύγκρουσης Συμφερόντων

Εργάζομαι ως ιατρικός σύμβουλος στην εταιρεία GlaxoSmithKline

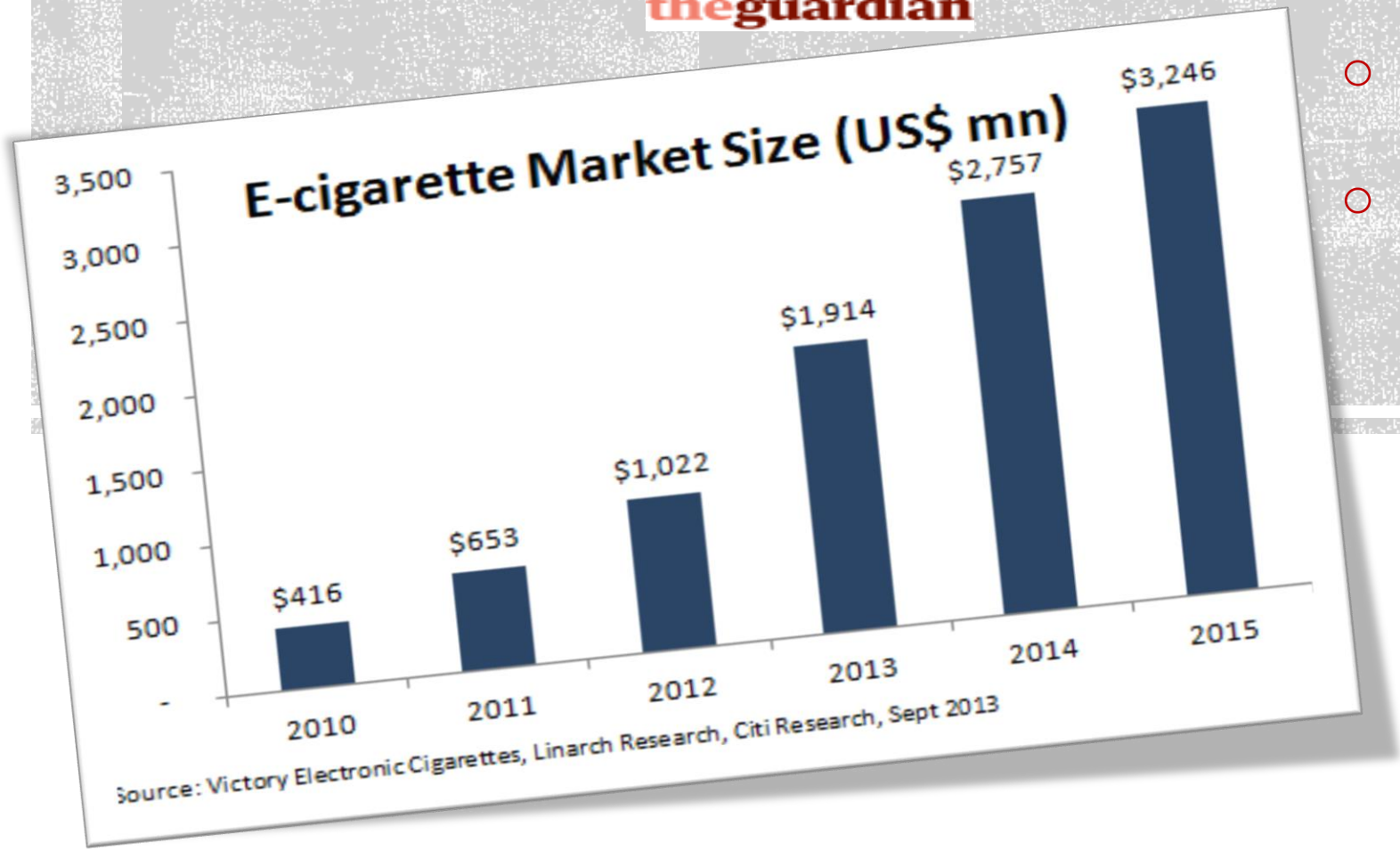
Γλυνός Κωνσταντίνος
Πνευμονολόγος-Εντατικολόγος
Ιατρικός Σύμβουλος GSK

IS THIS THE *END* OF CIGARETTE SMOKING ?

THE ENDS *ELECTRONIC NICOTINE DELIVERY SYSTEMS*

Boom in e-cigarette sales

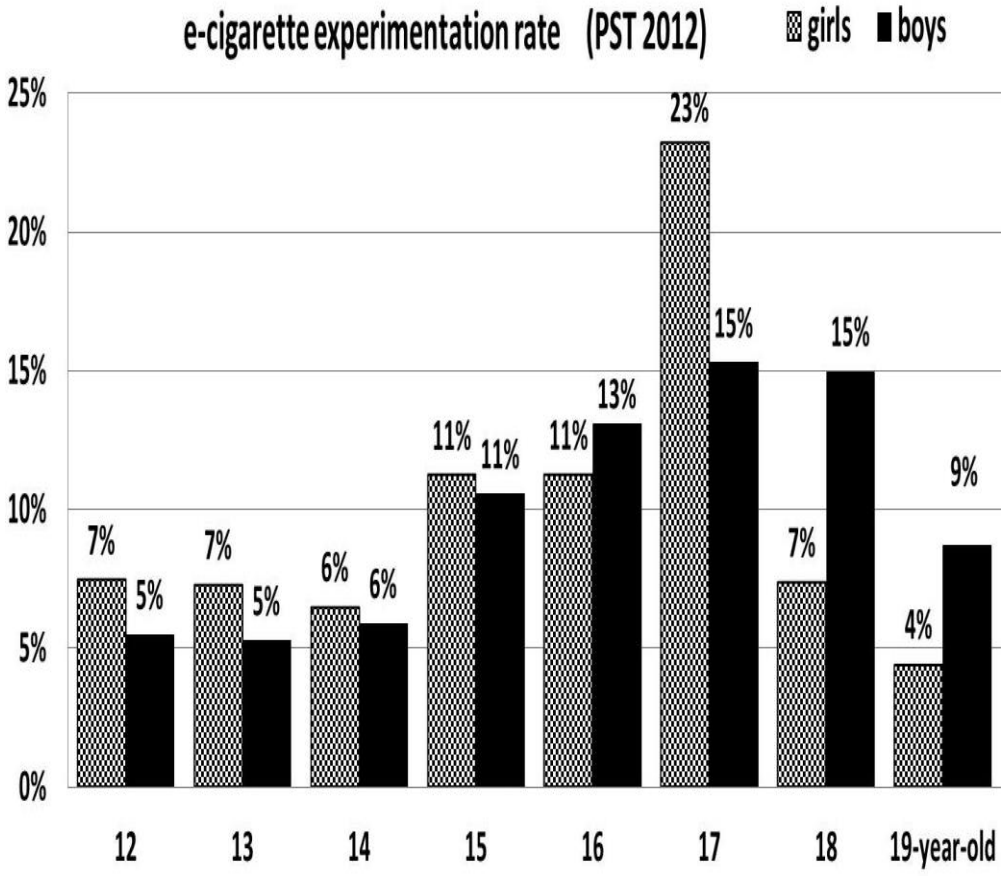
theguardian



- 7,764 unique flavors
- 466 brands

the ENDS

…and the beginners



Dautzenberg B et al. ***Open Journal of Respiratory Diseases 2013***

USA

1.78 million students had tried ENDS by the end of 2012

United Kingdom

10% of smokers used ENDS

The number of ENDS users rose to around 1.3 million in 2013

France

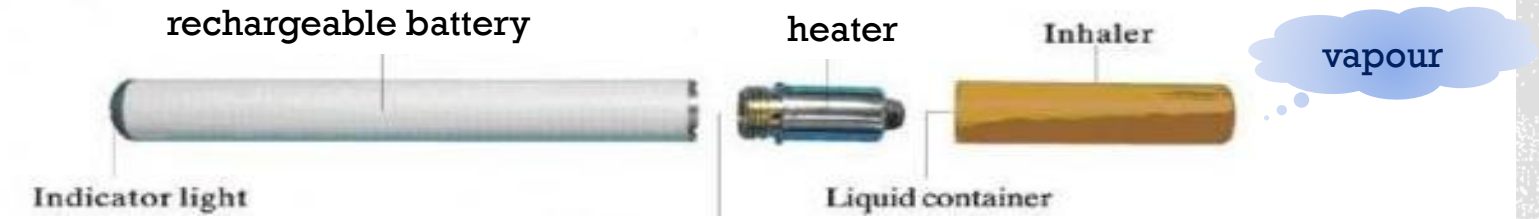
For teenager's, ENDS have become not a product to aid quit tobacco but a product for experimentation and initiation of cigarette use

Adkison SE et al Am J Preventive Med 2013
US Centers for Disease Control and Prevention. Morbidity and Mortality Weeky Report -September 6 2013
Grana R et al Circulation 2014

the ENDS & the IQOS

Type of studies	Research subject
Chemical studies	Evaluation of ENDS liquids /aerosols
Toxicological studies	Evaluation the ENDS effect on cell or animals
Clinical studies	Studies on humans

Grana R et al Circulation 2014



THE LITTLE WE KNOW...

THE ENDS *ELECTRONIC NICOTINE DELIVERY SYSTEMS*

Type of studies	Research subject
Chemical studies	Evaluation of ENDS liquids /aerosols
Toxicological studies	Evaluation the ENDS effect on cell or animals
Clinical studies	Studies on humans

The Little We Know…

- ✓ Small amounts of heavy metals and at least 20 known carcinogens [1]
- ✓ glycerol forms acrolein, which causes respiratory tract irritation [2]

- ✓ Cyto-toxicity in embryonic cells [2,] oxidative stress [2,3]
- ✓ lung tissue destruction and airway hyperreactivity in mice
- ✓ Memory impairment [7]
- ✓ cardiovascular toxicity [7]

3

- ✓ increased dynamic airway resistance [4]
- ✓ inhibition of pulmonary anti-viral/microbial defense mechanisms [5]
- ✓ Bronchitis, cough, and emphysema [7]
- ✓ COPD-emphysema pathogenesis [6]
- ✓ contact dermatitis and burns [7]

1. Grana R et al Circulation 2014 , 2. Bahl et al *Reprod Toxicol. 2012, 3.* US Environmental Protection Agency. Acrolein. http://www.epa.gov 2013, 4. Vardavas CI et al Chest. 2012, 5 .Sussan TE et al PLoS 2015, 6. Kaisar et al **Toxicology. 2016,7. Qasim et al J Am Heart Assoc. 2017**

the ENDS

Chemical studies

Table 1. Levels of Toxicants in E-Cigarette Aerosol Compared With Nicotine Inhaler and Cigarette Smoke

Toxicant	Range In Content In Aerosol From 12 E-Cigarette Samples per 15 Puffs*	Range In Content In Conventional Cigarette Micrograms In Mainstream Smoke From 1 Cigarette	Content In Nicotine Inhaler Mist per 15 Puffs*
Formaldehyde, μg	0.2–5.61	1.6–52	0.2
Acetaldehyde, μg	0.11–1.36	52–140	0.11
Acrolein, μg	0.07–4.19	2.4–62	ND
o-Methylbenzaldehyde, μg	0.13–0.71	…	0.07
Toluene, μg	ND–0.63	8.3–70	ND
p,m-xylene, μg	ND–0.2	…	ND
NNN, ng	ND–0.00043	0.0005–0.19	ND
NNK, ng	ND–0.00283	0.012–0.11	ND
Cadmium, ng	ND–0.022	…	0.003
Nickel, ng	0.011–0.029	…	0.019
Lead, ng	0.003–0.057	…	0.004

✓**The levels of toxicants in the aerosol were lower than in cigarette smoke but higher than with a nicotine inhaler**

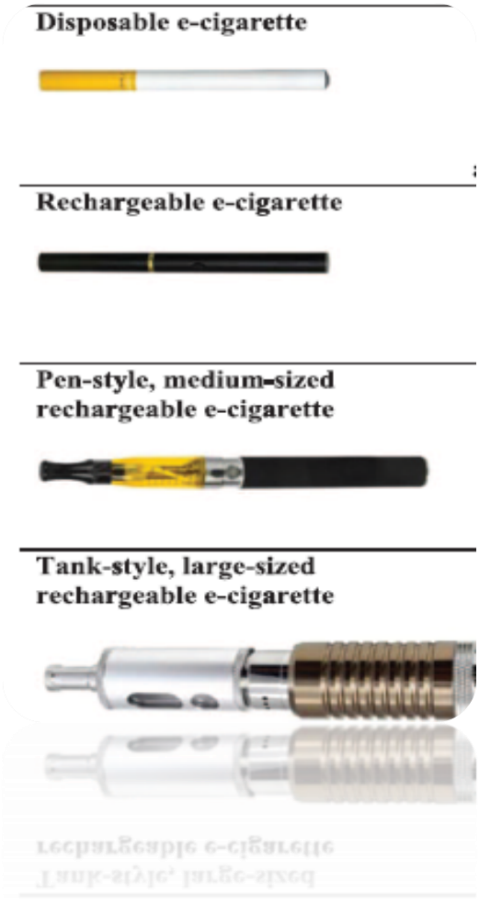
Grana R et al Circulation 2014
Goniewicz ML, et al *Tob Control. 2014*

the ENDS

Chemical studies

✓A puff of ENDS = 20% of the **nicotine** contained in a puff of a conventional cigarette.

✓**Propylene glycol** is authorised as an additive in foods and medications



But …

➢American Chemistry Council warns against inhalation exposure to propylene glycol mists.

➢When heated and vaporized :

X **propylene glycol** forms propylene oxide – carcinogen (class 2B)

X **glycerol** forms acrolein, which causes upper respiratory tract irritation

Grana R et al Circulation 2014
US Environmental Protection Agency. Acrolein. http://www.epa.gov 2013
Laino T et al *J Phys Chem A. 2012*
Henderson TR *Solar Energy. 1981*

the ENDS

Chemical studies

Secondhand Exposure- indoor Pollution

Bystanders may be exposed to nicotine and other toxins (at levels much lower than cigarettes) through passive exposure to the e-cigarette aerosol.

✓ **Flouris** et al : Serum cotinine in nonsmokers sitting in the chamber was similar for cigarette smoke and e-cigarette aerosol exposure

X **Schober** et al : Elevated nicotine, 1,2-propanediol, glycerin, aluminum, and 7 polycyclic aromatic hydrocarbons classified as probable carcinogens

Flouris AD, *Inhal Toxicol. 2013*
Schober W *Int J Hyg Environ Health 2013*

the ENDS

Chemical studies

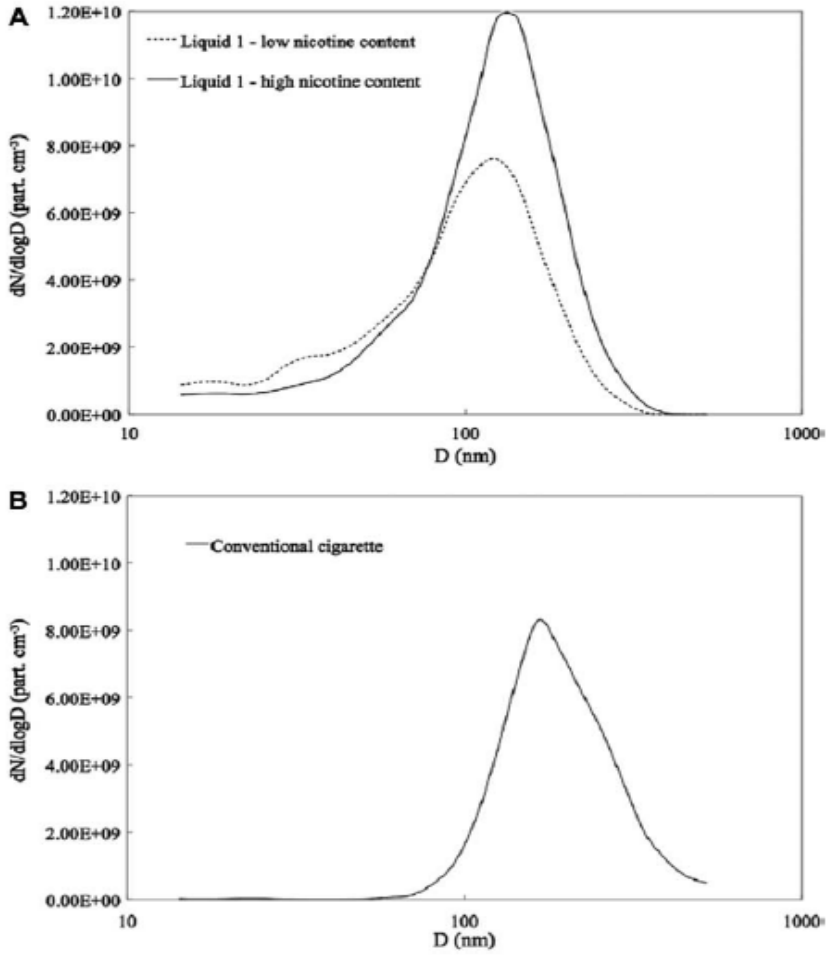
Size does matter?

X Higher e-liquid nicotine content was associated with higher particle numbers in the resulting aerosol of the ENDS[1]

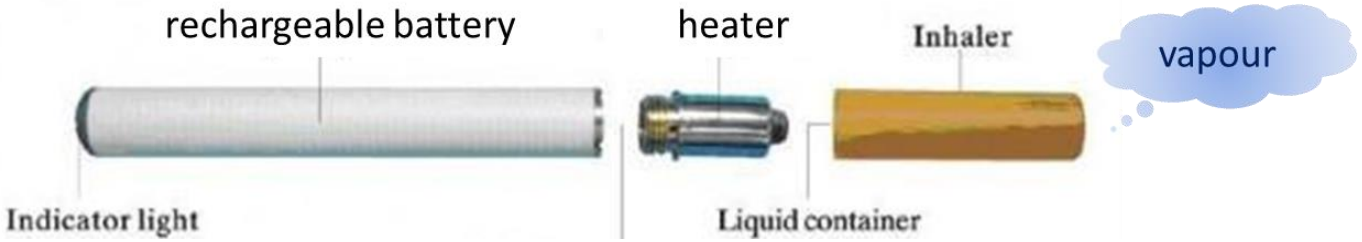
X The particle size distribution and number of particles delivered by the ENDS are similar to those of conventional cigarettes [1]

X Particle concentrations of the aerosol emitted from the electronic cigarette are 300-3000 times higher than that of the ambient air [2]

Ultrafine particles



1. Fuoco FC et al Environ Pollut. 2014; 2. Zervas E et al Inhal Toxicol 2018



THE ENDS

ELECTRONIC NICOTINE DELIVERY SYSTEMS

Type of studies	Research subject
Chemical studies	Evaluation of ENDS liquids /aerosols
Toxicological studies	Evaluation the ENDS effect on animals
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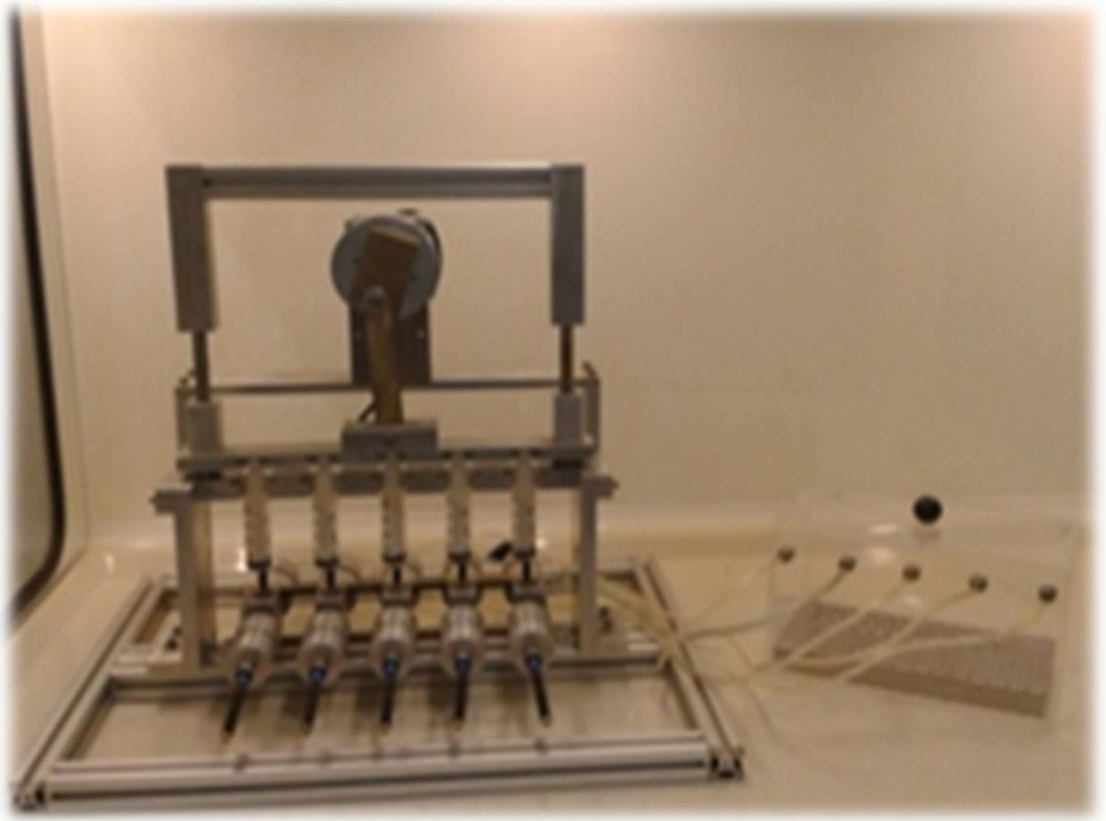


the ENDS

Toxicological studies

In vitro

✓ ENDS vapour extracts showed significantly higher **cell viability** compared to CS extract.[1]

X ENDS cyto-toxicity tested in vitro with embryonic cells correlated with the flavour fluids[2]

X ENDS induce DNA strand breaks and cell death independently of nicotine in cell lines[3]

X Electronic cigarette liquid increases inflammation and virus infection in primary human airway epithelial cells [4]

In vivo

X e-cigarette exposure induces **pathological responses** that result in lung tissue destruction and airway hyperreactivity in mice [3,6]

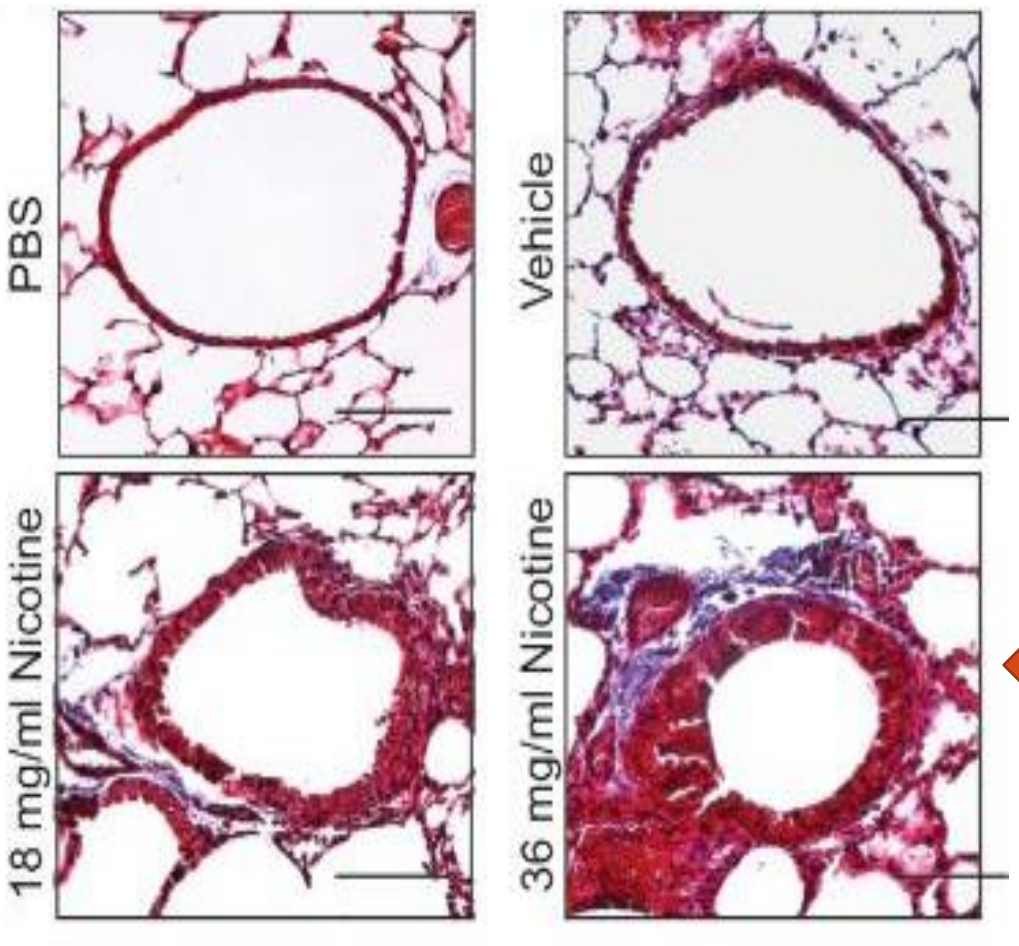
X E-Cigarettes increases **acute lung inflammation** in exposed mice [5]

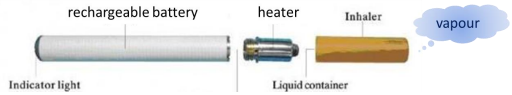
X electronic cigarettes and e-juices with flavorings induce toxicity, oxidative stress, and inflammatory response in lung epithelial cells and in mouse lung [7]

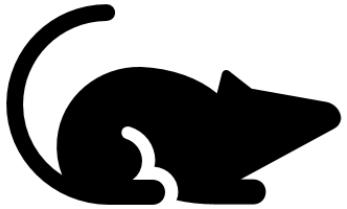
1. Farsalinos K.E. et al Int. J. Environ. Res. Public Health 2013, 2. Bahl et al Reprod Toxicol. 2012; 3. Foronjy R et al ERS abstract 2014; 4. Wu Q, et al PLoS One. 2014 5. Vicky Yu, Oral oncology 2016; 6. Garcia-Arcos I, Foronjy R. Thorax 2016; Lerner CA et al PLoS One 2015

the ENDS

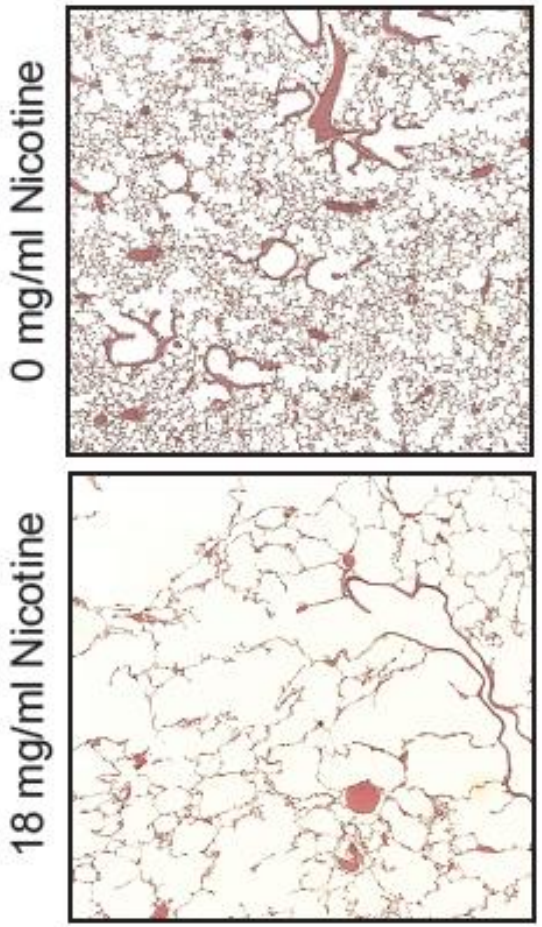
Toxicological studies-In vivo







fibrosis



emphysema

Garcia-Arcos I, Foronjy R. Thorax 2016

THE E-CIGARETTE MODEL

Am J Physiol Lung Cell Mol Physiol 315: L662–L672, 2018.
First published August 9, 2018; doi:10.1152/ajplung.00389.2017.

RESEARCH ARTICLE | *Electronic Cigarettes: Not All Good News?*

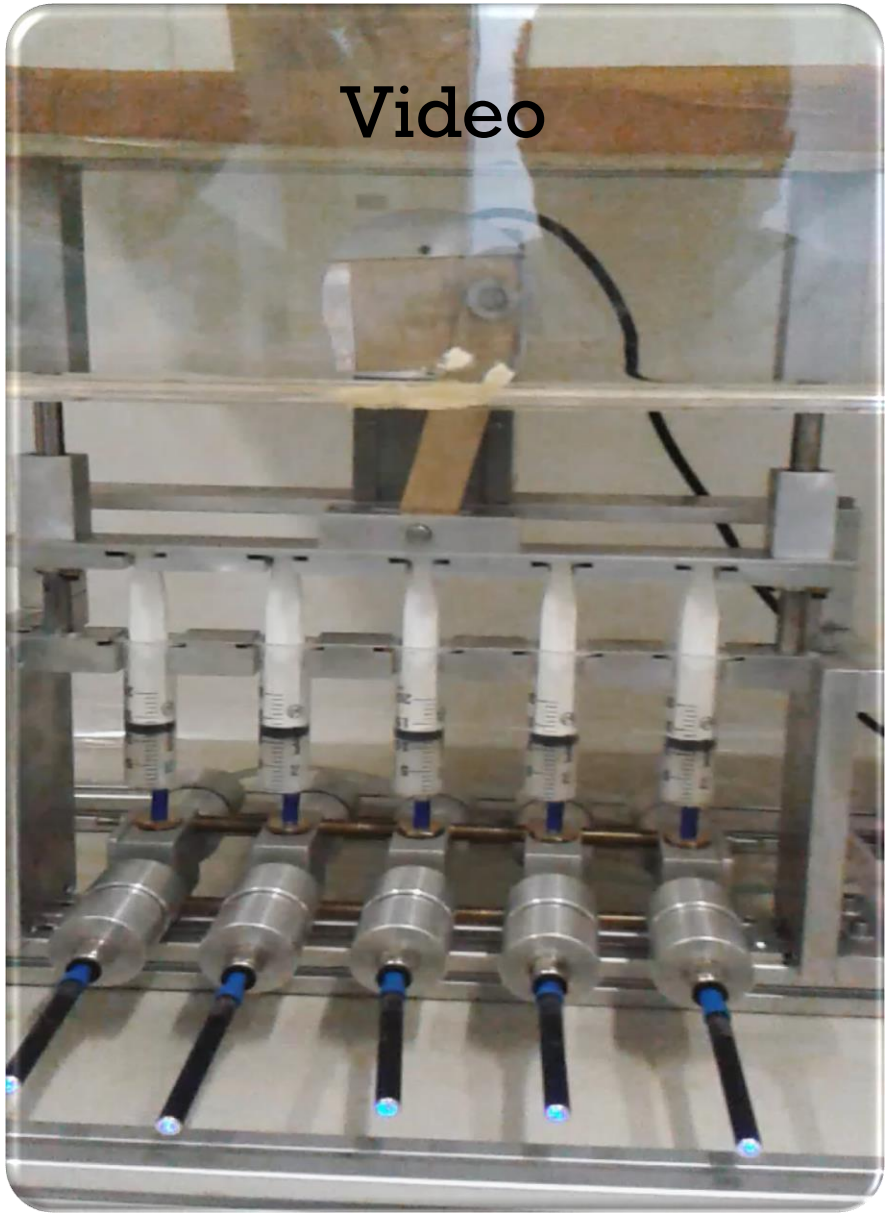
Comparison of the effects of e-cigarette vapor with cigarette smoke on lung function and inflammation in mice

Constantinos Glynos,[1] Sofia-Iris Bibli,[2,3] Paraskevi Katsaounou,[1] Athanasia Pavlidou,[1,2] Christina Magkou,[4] Vassiliki Karavana,[1] Stavros Topouzis,[5] Ioannis Kalomenidis,[1] Spyros Zakynthinos,[1] and Andreas Papapetropoulos[1,2]

[1]George P. Livanos and Marianthi Simou Laboratories, Evangelismos Hospital, 1st Department of Pulmonary and Critical Care, National, Kapodistrian University of Athens Medical School, Greece; [2]Laboratory of Pharmacology, Faculty of Pharmacy, National and Kapodistrian University of Athens, Athens, Greece; [3]Institute for Vascular Signaling, Centre for Molecular Medicine, Goethe University, Frankfurt am Main, Germany; [4]Department of Histopathology, Evangelismos Hospital, Athens, Greece; and [5]Laboratory of Molecular Pharmacology, Department of Pharmacy, University of Patras, Patras, Greece

Submitted 29 August 2017; accepted in final form 7 August 2018

AMERICAN JOURNAL of PHYSIOLOGY
Lung Cellular and Molecular Physiology



Glynos C et al Am J Physiol Lung Cell Mol Physiol 315: L662–L672, 2018

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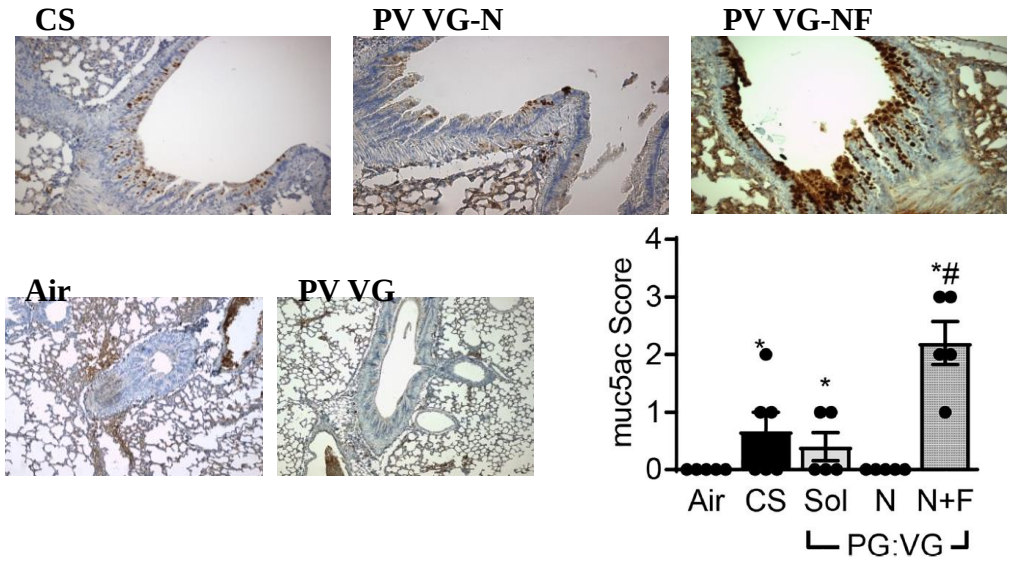
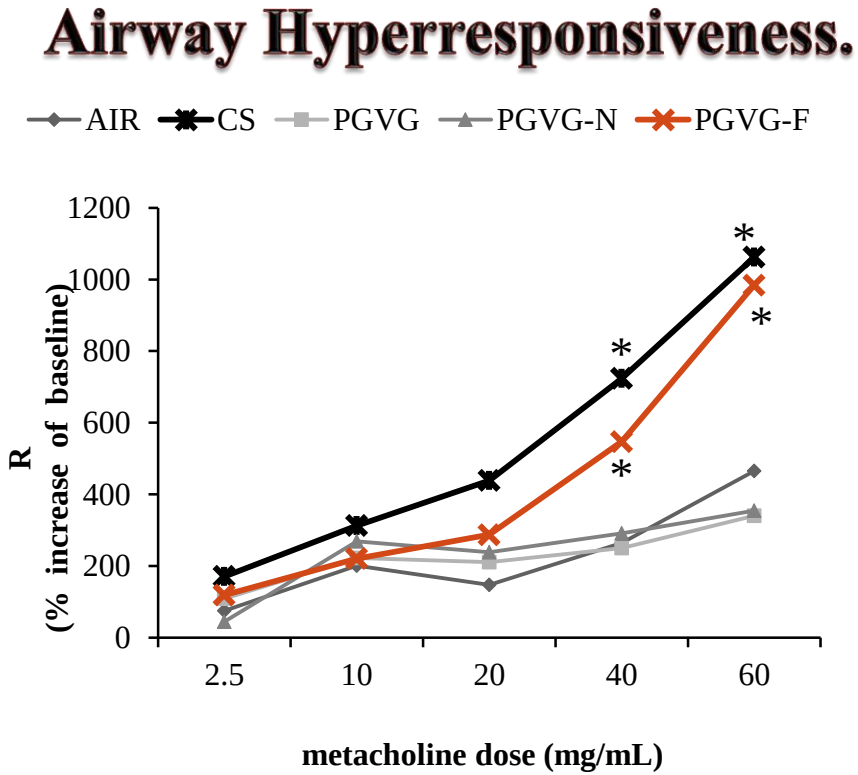


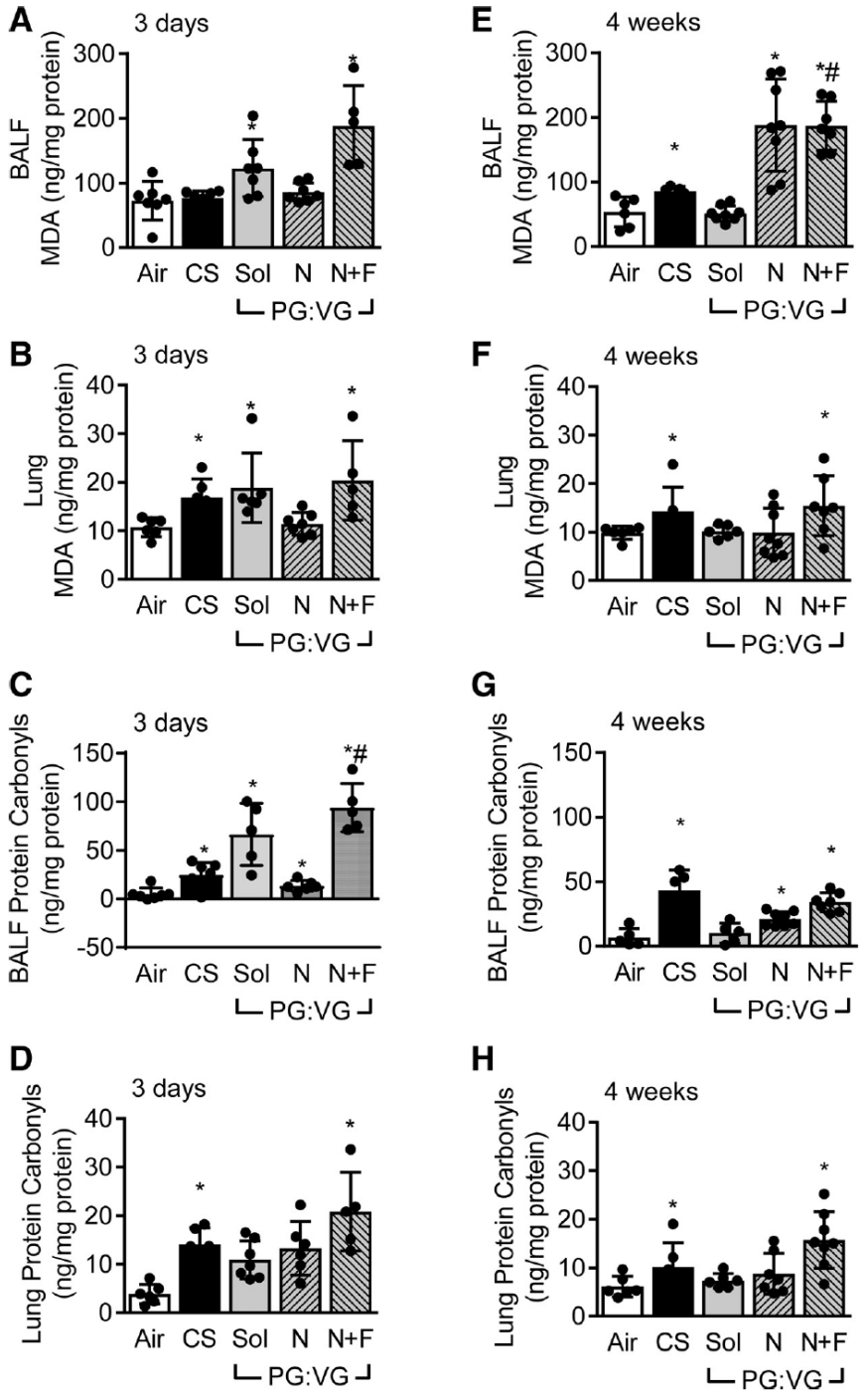


CS and PGVG-F groups exhibited a pronounced Muc-5ac production in the airways of mice and increase of the airway resistance in response to methacholine upon 3-days exposure compared to air-exposed mice

Glynos C et al *Am J Physiol Lung Cell Mol Physiol* 315: L662–L672

3 days or 4 weeks ?

ENDs induce oxidative stress compared to air-exposed mice



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3 days or 4 weeks ?

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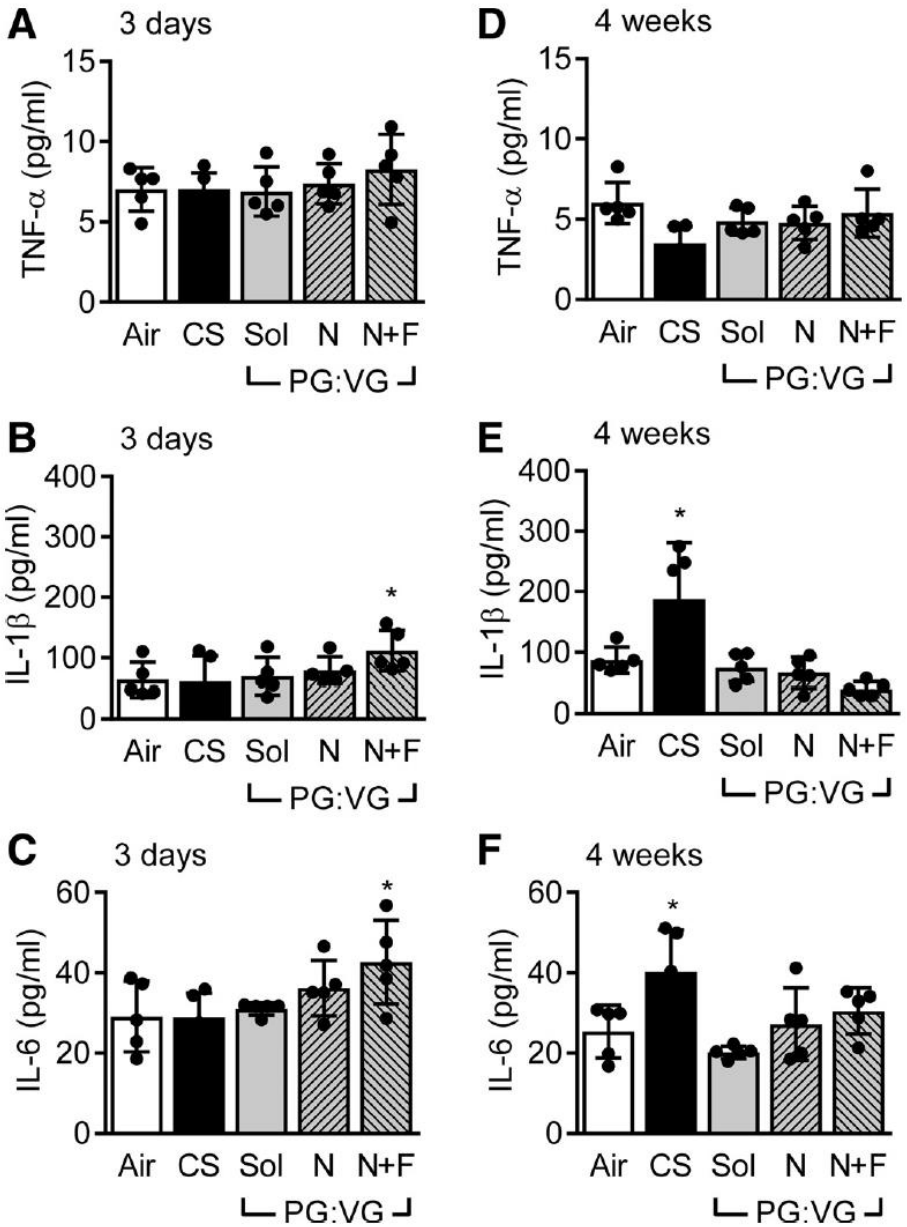
ENDs increases IL-1β and IL-6 compared to air-exposed mice



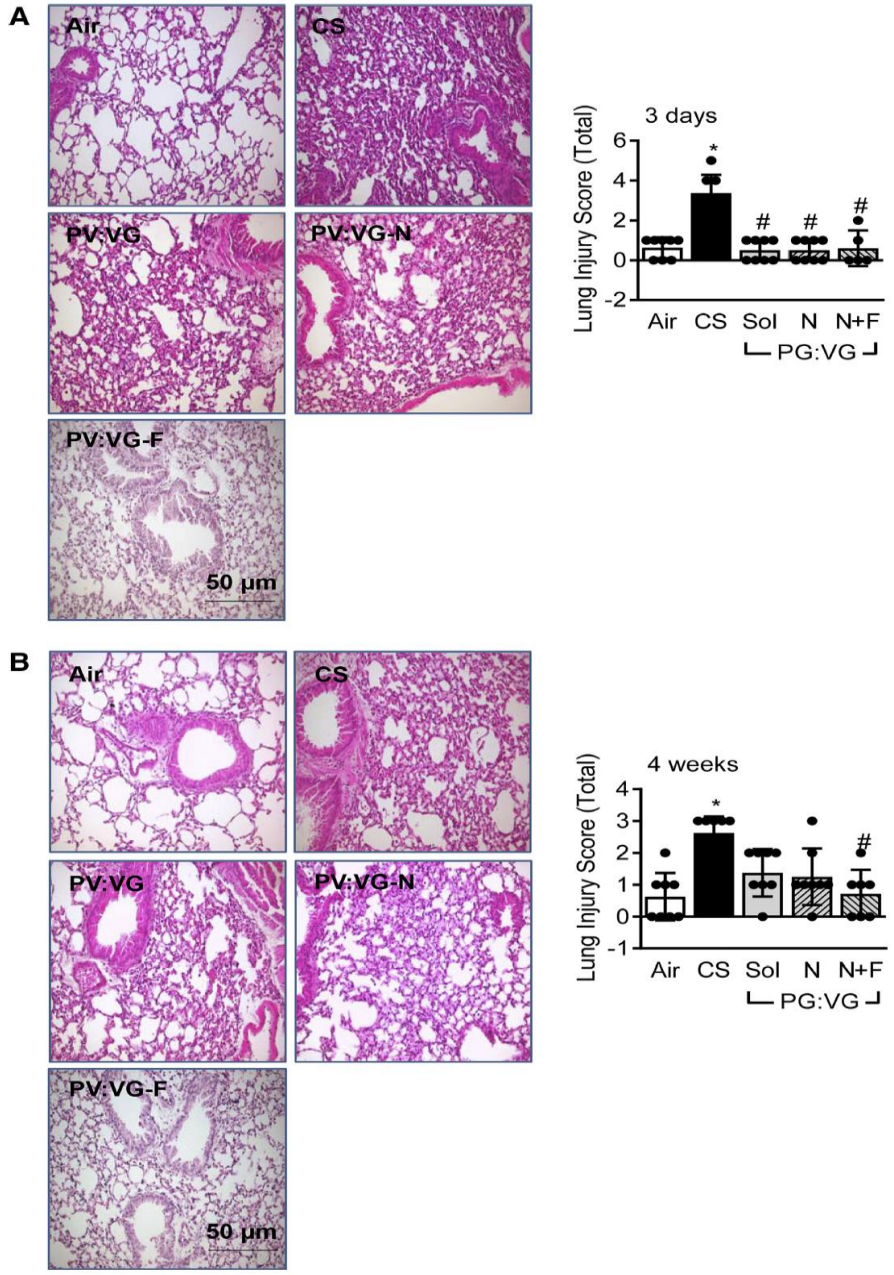
Glynos C et al *Am J Physiol Lung Cell Mol Physiol* 315: L662–L672

3 days or 4 weeks ?

ENDs induce oxidative stress compared to air-exposed mice

ENDs increases IL-1β and IL-6 compared to air-exposed mice

Lung histological changes are evident after smoking but not after vaping



Glynos C et al *Am J Physiol Lung Cell Mol Physiol* 315: L662–L672

THE ENDS

ELECTRONIC NICOTINE DELIVERY SYSTEMS

Type of studies	Research subject
Chemical studies	Evaluation of ENDS liquids /aerosols
Toxicological studies	Evaluation the ENDS effect on animals
Clinical studies	Studies on humans

The biological role of the ENDS

Clinical studies

X **Vardavas 2012**[1]: A pilot study of healthy smokers' pulmonary function upon acute ENDS exposure -5 min :

- no effect on spirometry

X increased dynamic airway resistance (18%)

X decreased FeNO (16%)

✓ **Flouris AD 2013**[2]:

✓Short-term effects of the ENDS on pulmonary function: no significant effect.

✓Only smoking induces an acute adverse effect on respiratory function

✓ **Polosa R 2014** [3] : A small retrospective study to report for the first time the effects of e-cigs in asthmatic smokers who quit or reduced their tobacco

✓ **significant improvements in spirometry data, asthma control & AHR**

1. Vardavas CI et al Chest. 2012; 2. Flouris AD et al, Inhal Toxicol. 2013; 3. Polosa R et al Int J Environ Res Public Health. 2014

The biological role of the ENDS

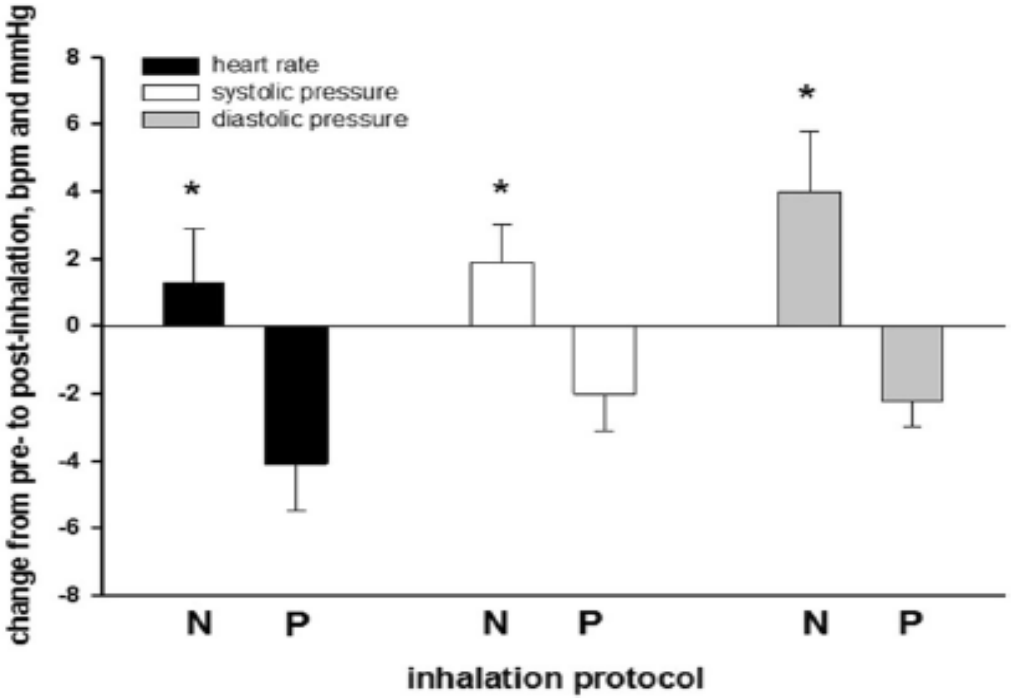
Clinical Case Reports

Respiratory system

- ✓ Case report of electronic cigarettes possibly associated with eosinophilic pneumonitis in a previously healthy active-duty sailor.
  Thota D, Latham E. J Emerg Med. 2014

- ✓ A case report of subacute bronchial toxicity induced by an electronic cigarette.
  Hureaux J, Drouet M, Urban Thorax. 2014

Cardiovascular system



Acute inhalation of vaporized nicotine increases arterial pressure in young non-smokers: a pilot study.
Cooke WH et al. Clin Auton Res. 2015

The biological role of the ENDS

Clinical Study in Greece

Acute effects of short term use of e-cigarette on airway physiology

		Nicotine=11mg				Nicotine=0mg
		COPD smokers (n=16)	Asthma smokers (n=11)	Smokers (n=28)	Non smokers (n=9)	Non smokers (n=12)
DN_2/L, %pred	Pre	299±182	141±52	98±35	92±39	88±25
	Post	316±185	172±65*	106±29	97±38	99±22
Raw, kPa $L^{-1}sec^{-1}$	Pre	0.43±0.18	0.38±0.13	0.29±0.12	0.25±0.07	0.24±0.04
	Post	0.47±0.17	**0.40±0.11***	**0.31±0.13***	**0.29±0.06***	**0.32±0.08****
SGaw, sec^{-1} kPa^{-1}	Pre	0.54±0.19	0.84±0.31	1.16±0.47	1.31±0.22	1.20±0.27
	Post	0.52±0.19	0.80±0.33	1.03±0.40*	1.11±0.18*	0.95±0.18*

A Palamidas, St Tsikrika, Katsaounou P, S Vakali, S Genimmata, G Kaltsakas, Ch Gratziou, NG Koulouris. Tob. Prev. Cessation 2017

the ENDS

Electronic Nicotine Delivery Systems

Forum of International Respiratory Societies 2014

The health risks of the ENDS, have not been adequately studied.

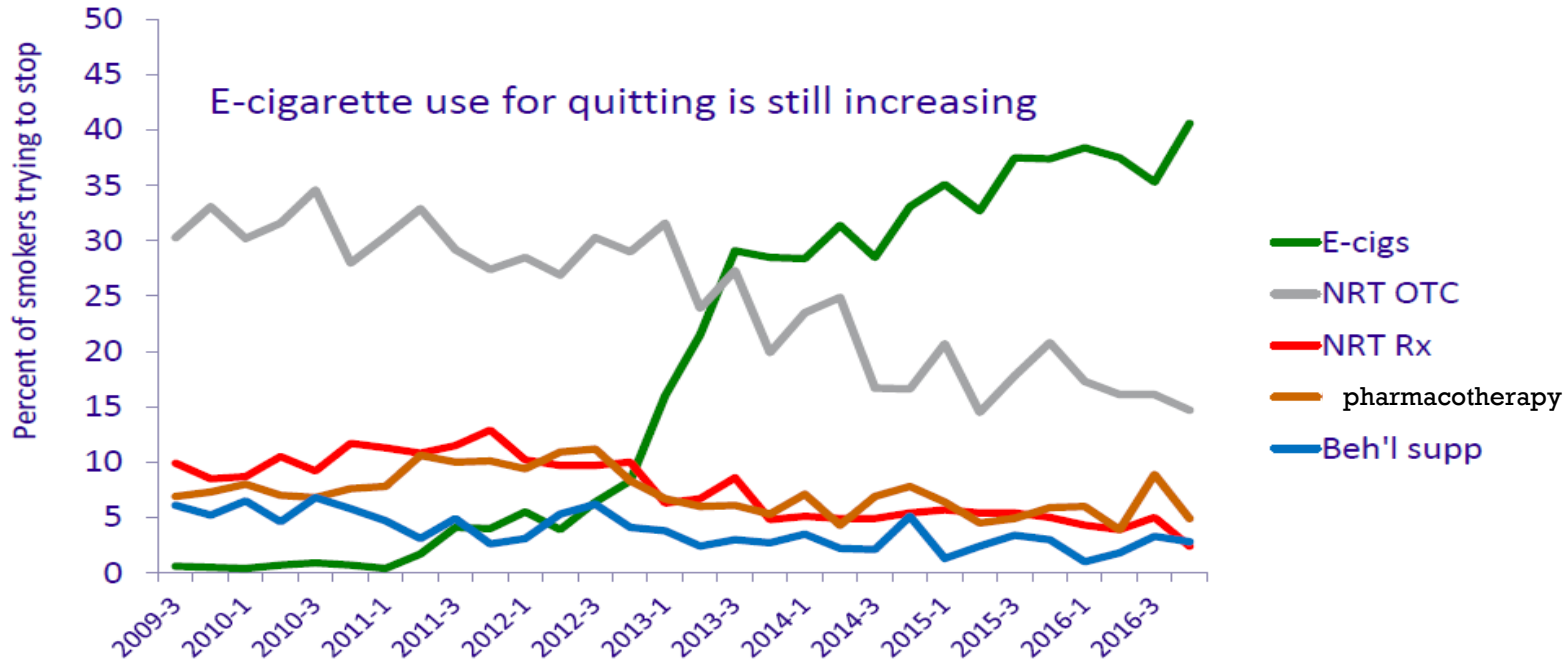
Because nicotine is highly addictive, affects many bodily cells and functions, and is known to have many adverse effects, it is prudent to restrict usage of he ENDS at least until their safety can be established.

Electronic Cigarettes: A position statement of the Forum of International Respiratory Societies AJRCCM 2014

ENDS as a *smoking cessation tool?*

Changes in smoking cessation assistance in the European Union between 2012 and 2017: pharmacotherapy versus counselling versus e-cigarettes.

Use of e-cigarettes for smoking cessation assistance increased (3.7% to 9.7%)%), while use of pharmacotherapy (14.6% to 11.1%)%) and smoking cessation services (7.5% to 5.0%)%) declined

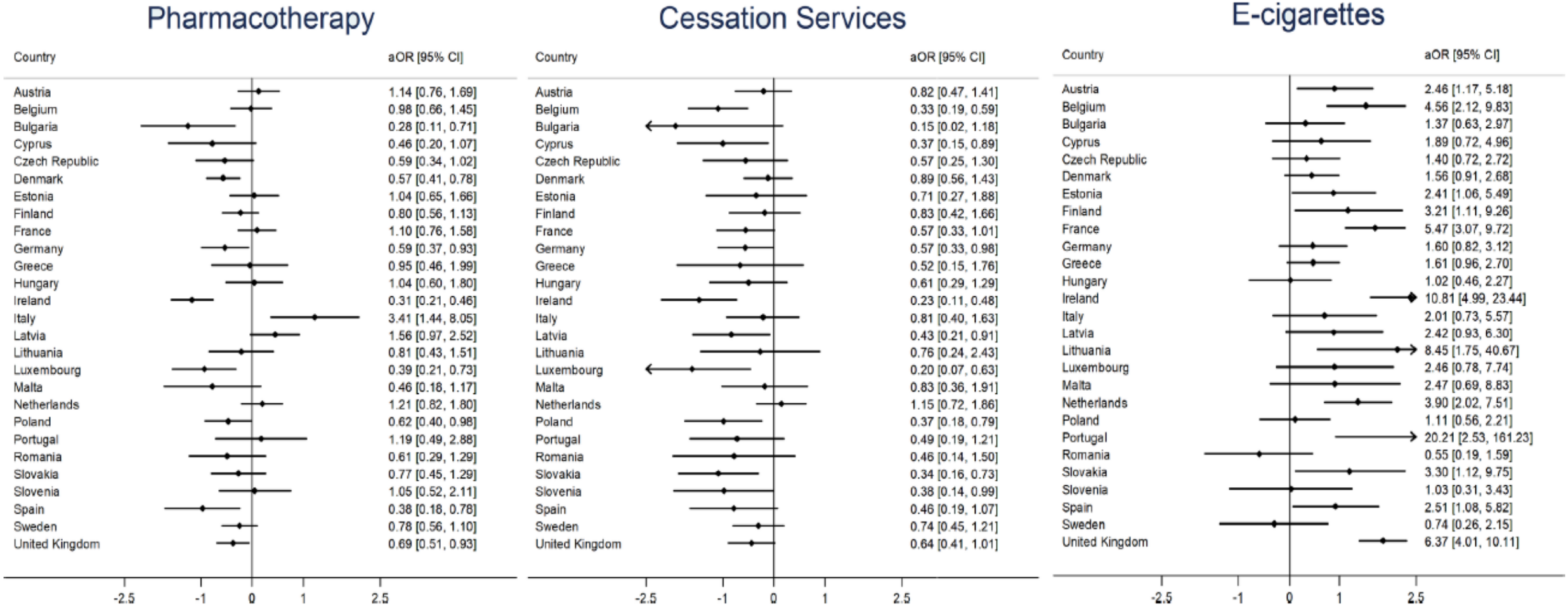


Source:
N=12244 adults who smoke and tried to stop or who stopped in the past year; method is coded as any (not exclusive) use

Filippidis FT Tob Control. 2019

ENDS as a *smoking cessation tool?*

Research paper



ENDS as a *smoking cessation tool?*

Not statistical significance between NRTs & e-cigarette

BUT …

- ✓ e-cigarette was compared to the less effective first line smoking cessation drug (NRTs).
- ✓ All e-cigarette had lower smoking cessation rates (4%-9%-13%) than placebo(9%-15,6%) in smoking cessation

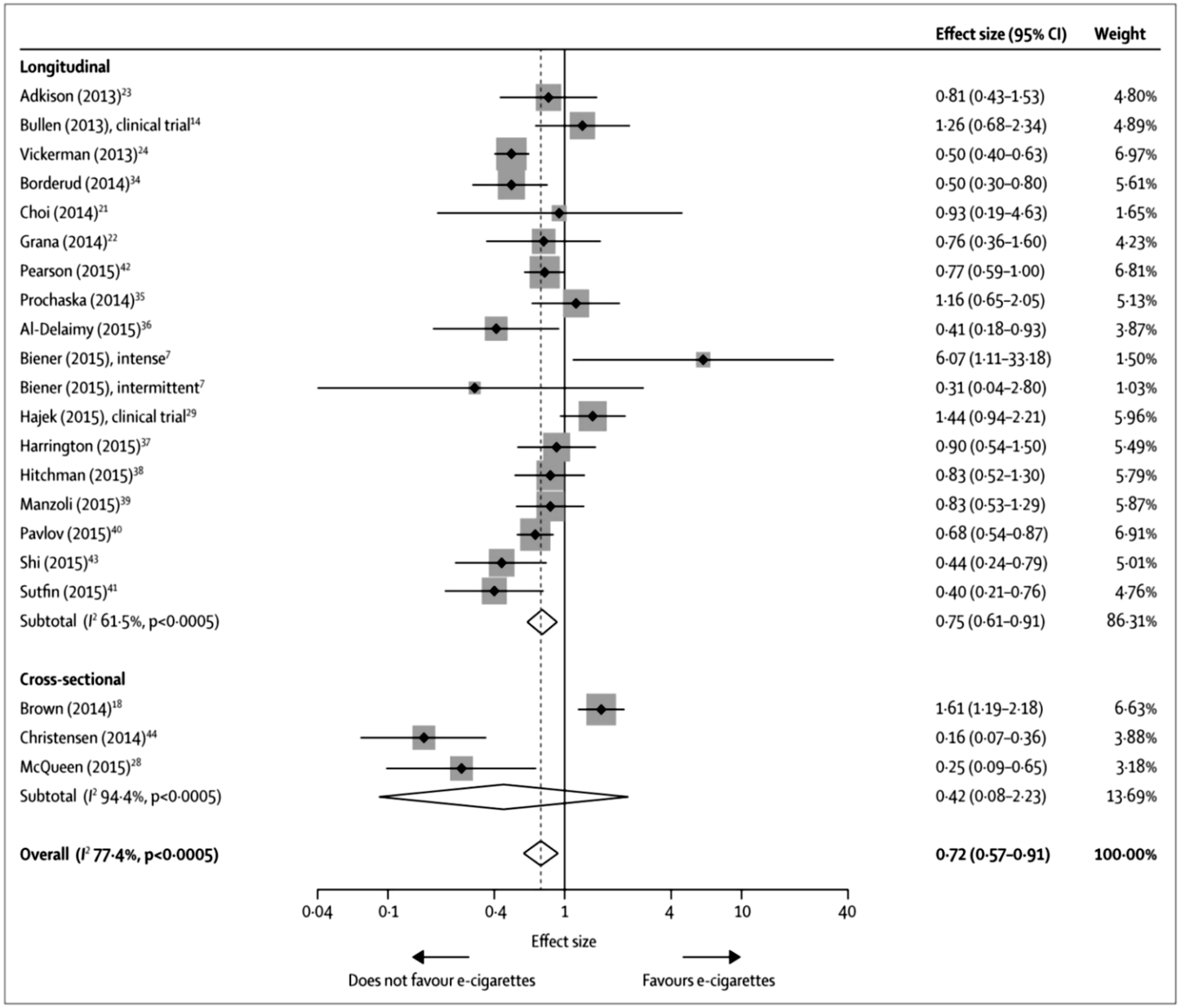
ASCEND trial

- Bullen C, Howe C, Laugesen M, McRobbie H, Parag V, Williman J, Walker N.
- Electronic cigarettes for smoking cessation: a randomised controlled trial.
- Lancet. 2013

- O'Brien B, Knight-West O, Walker N, Parag V, Bullen C.
- E-cigarettes versus NRT for smoking reduction or cessation in people with mental illness: secondary analysis of data from the ASCEND trial.
- Tob Induc Dis. 2015

ECLAT trial

- Caponnetto P1, Campagna D, Cibella F, Morjaria JB, Caruso M, Russo C, Polosa R.
- EffiCiency and Safety of an eLectronic cigAreTte (ECLAT) as tobacco cigarettes substitute: a prospective 12-month randomized control design study.
- PLoS One. 2013 Jun 24;8(6): e66317.



Odds of quitting smoking, stratified by longitudinal versus cross-sectional studies

ENDS as a *smoking cessation tool?*

E-cigarettes and smoking cessation in real-world and clinical settings: a systematic review and meta-analysis

- ✓ Odds of quitting cigarettes were **28%** **lower in those who used e-cigarettes** compared with those who did not use e-cigarettes
  (odds ratio [OR] 0·72, 95% CI 0·57-0·91)

- ✓ e-cigarette use is **associated with reduced smoking cessation** in the real world

Kalkhoran S, Glantz SA.et al. Lancet Respir Med 2016.

"While vaping may not be 100% safe, most of the chemicals causing smoking related disease are absent and the chemicals that are present pose limited danger.

Public Health England

Protecting and improving the nation's health

E-cigarettes: an evidence update

A report commissioned by Public Health England

Electronic cigarettes as a harm reduction strategy?

Who can we measure harm reduction?

- Smoking causes 2x more deaths than HIV, AIDS, alcohol abuse, motor crashes, drug use and suicide combined
- On average smokers die 10 years earlier than non-smokers

✓ The **European Commission**

EUROPEAN COMMISSION

The use of refillable electronic e-cigarettes, and the potential exposure to e-liquids containing nicotine in high concentrations, may pose risks to public health

EUR-Lex. Report 2017

PubMed.gov
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10 years
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Humans
Other Animals

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Filters: Manage Filters

Sort by:
Best match | Most recent

Best matches for iqos:

IQOS labelling will mislead consumers.
McKelvey K et al. Tob Control. (2018)

IQOS: examination of Philip Morris International's claim of reduced exposure.
St Helen G et al. Tob Control. (2018)

Revolution or redux? Assessing IQOS through a precursor product.
Elias J et al. Tob Control. (2018)

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1. Point-of-sale marketing of heated tobacco products in Israel: cause for concern.
Halpern-Felsher B.
Isr J Health Policy Res. 2019 May 27;8(1):47. doi: 10.1186/s13584-019-0316-6.
PMID: 31133053 **Free Article**
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Tobacco-specific nitrosamines (TSNA) in heated tobacco product **IQOS**. [Tob Control. 2018]

Vascular endothelial function is impaired by aerosol from a single **IQOS** H[[Tob Control. 2018]

Awareness, experience and prevalence of heated tobacco product, **IQOS** [Tob Control. 2018]

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Database: Select

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Any data for IQOS?

Type of studies	Research subject
Chemical studies	Evaluation of IQOS aerosols
Toxicological studies	Evaluation the IQOS effect on cell or animals
Clinical studies	Studies on humans

Less than Little We Know… for IQOS

- ✓ iQOS: evidence of pyrolysis and release of a toxicant from plastic[1]

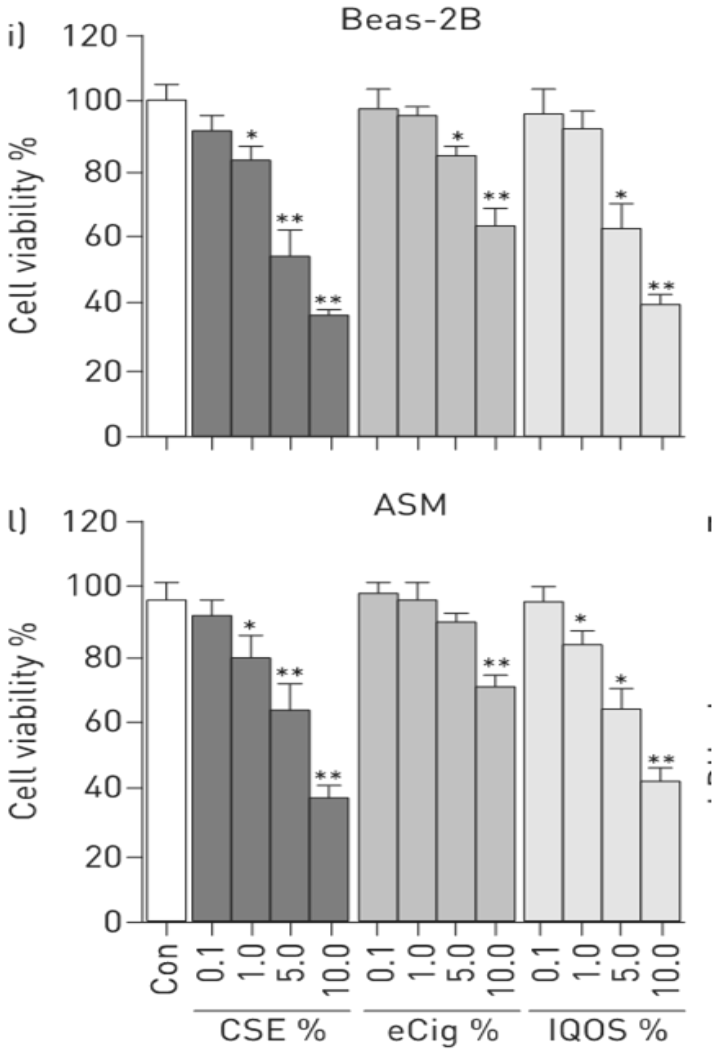
- ✓ Induces cellular toxicity with increasing concentration [2,]
- ✓ contributes to altered mitochondrial function [2]
- ✓ Vascular endothelial function is impaired [3]
- ✓ Passive exposure to pollutants from CS and ENDS, IQOS in passenger cars [4]

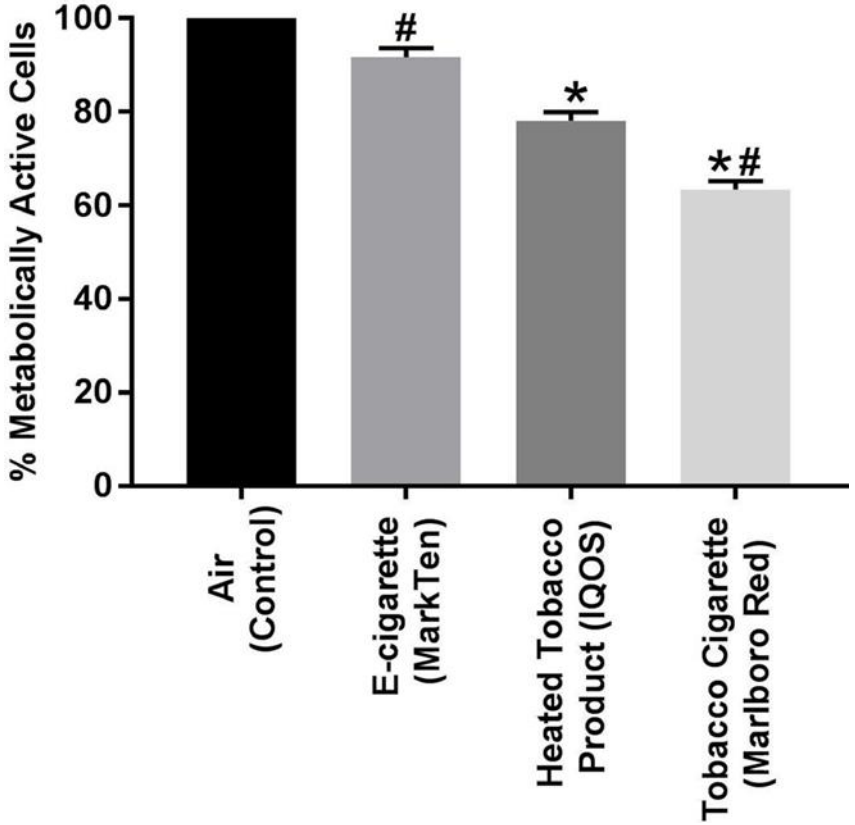
- ✓ Short-term use has a minimal impact on eCO, is equally effective in reducing cigarette craving and withdrawal symptoms as an e-cigarette, and is slightly preferred [5]
- ✓ A 5-year single-center cohort observational study to assess differences in lung function between users of the iQOS and CS [6]

1. Davis B et al Tob Control. 2018; 2. Sohal SS et al ERJ open 2019; 3. Nabavizadeh P et al Tob Control. 2018; 4. Schober W et al Int J Hyg Environ Health. 2019; 4. Adriaens K et al. Int J Environ Res Public Health. 2018; 5. Salman R et al Nicotine Tob Res. 2018; 6. Sharman A et al JMIR Res Protoc. 2018

Toxicological studies

IQOS: Induces cellular toxicity with increasing concentration





Sohal SS et al ERJ open 2019

Leigh NJ et al Tob Control 2018;

Any data for IQOS?

Are HTPs safer than conventional tobacco?

- ✓ Currently, there is no evidence to demonstrate that HTPs are less harmful than conventional tobacco products.
- ✓ Some tobacco industry-funded studies have claimed that there are significant reductions in the formation of and exposure to harmful and potentially harmful constituents relative to standard cigarettes.
- ✓ However, there is currently no evidence to suggest that reduced exposure to these chemicals translates to reduced risk in humans.
- ✓ Therefore, additional independent studies will be required to substantiate claims of reduced risk/harm.

http://www.who.int/tobacco/publications/prod_regulation/heated-tobacco-products/en/
http://www.who.int/tobacco/publications/prod_regulation/heat-not-burn-products-information-sheet/en/

European Respiratory Society

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Healthy Lungs For Life

ERS Position Paper on Tobacco Harm Reduction

A statement by the ERS Tobacco Control Committee

The ERS Tobacco Control Committee (TCC) published the position paper on tobacco harm reduction in May 2019.

The ERS TCC believe that current strategies which support the use of alternative nicotine delivery products for smoking cessation are not effective as they are based upon incorrect assumptions and undocumented claims about the safety and effectiveness of alternative nicotine delivery products for smoking cessation.

Therefore, the statement brings together scientifically-backed arguments for why a tobacco harm reduction strategy should not be used as a population-based strategy in tobacco control, including that harm reduction arguments are:

- Based on incorrect claims that smokers cannot or will not quit smoking
- Reliant upon undocumented assumptions that alternative nicotine delivery products are highly effective as a smoking cessation aid
- Built on incorrect assumptions that smokers will replace conventional cigarettes with alternative nicotine delivery products
- Ignorant to the lack of evidence to show that alternative nicotine delivery products are safe for human health

The ERS Tobacco Control Committee (TCC) published the position paper on tobacco harm reduction in May 2019.

- ✓ Οποιαδήποτε μορφή END/iQOS δεν πρέπει να διαφημίζεται ως ασφαλές προϊόν και αποτελεσματικό για τη διακοπή του καπνίσματος.
- ✓ **Δε θα πρέπει να το χρησιμοποιούν ανήλικοι.**
- ✓ Απαιτούνται περισσότερα δεδομένα επιστημονικών μελετών για να αποσαφηνιστεί η ασφάλεια και αποτελεσματικότητα της χρήσης ENDs / iQOS
- ✓ Διαθέτουμε αποτελεσματικότατα και ασφαλή φάρμακα και τεχνικές διακοπής του καπνίσματος.

ERS EUROPEAN RESPIRATORY SOCIETY

Human lungs are made to breath clean air

Ευχαριστώ