

THE *E*-CIGARETTE SUMMIT

Science, Regulation & Public Health

The Royal Society • London • November 15th, 2018



Unanswered questions in tobacco harm reduction research

Konstantinos Farsalinos, MD, MPH
Researcher
Onassis Cardiac Surgery Center, Greece
University of Patras, Greece
National School of Public Health, Greece

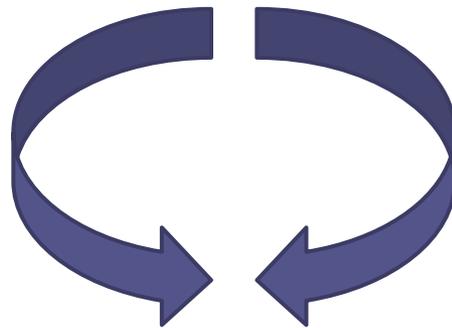


ΠΑΝΕΠΙΣΤΗΜΙΟ
ΠΑΤΡΩΝ
UNIVERSITY OF PATRAS



Science is about never knowing everything

- Problems that need to be addressed
- Questions that need to be answered
- Answers create new questions
- New problems found → new efforts to solve them



Prejudice in tobacco harm reduction research

- Scientists more willing to look for problems rather than benefits
 - A lot of research about e-cigarettes being gateway TO smoking
 - Little research about e-cigarettes being gateway FROM smoking
- Funding focused mostly on searching for problems
 - Further motivation for scientists to look for problems
- Abstinence-only approach, denial for harm reduction potential
 - This approach has still not solved the smoking problem globally
 - Harm reduction as a strategy has been accepted in other areas
- Predisposition
 - It looks like smoking, it is used like smoking, so it must be bad
 - Associations assumed to have causal link

Example of predisposition

- E-cigarettes and myocardial infarction

Table 2. Univariate and Multivariable Associations Between E-cigarette Use and Myocardial Infarction of NHIS 2014 and 2016 Combined

Characteristics	Unadjusted model		Adjusted model	
	OR (95% CI)	p-value	OR (95% CI)	p-value
E-cigarette use				
Never	ref		ref	
Former	0.79 (0.67, 0.94)	0.009	1.06 (0.86, 1.30)	0.608
Some days	1.06 (0.79, 1.44)	0.665	1.16 (0.83, 1.62)	0.392
Daily	1.69 (1.19, 2.39)	0.003	1.79 (1.20, 2.66)	0.004

Conclusion (authors): “Daily e- cigarette use, adjusted for smoking conventional cigarettes as well as other risk factors, is associated with increased risk of myocardial infarction.”

Increased risk clearly implies a **causal link** and temporal definition of events (e-cigarette use preceding infarction, which CANNOT be determined from this cross sectional study)

Inconsistent association

National Health Interview Survey (NHIS) 2016 and 2017

E-cigarette use and Coronary Heart Disease

Variable	OR	95% CI	P value
E-cigarette use			
Never (referent)			
Daily	1.52	0.91-2.53	0.109
Some days	1.19	0.73-1.92	0.481
Former	1.10	0.89-1.36	0.392
Smoking			
Daily	1.67	1.41-1.98	< 0.001
Some days	1.70	1.28-2.25	< 0.001
Former	1.50	1.35-1.67	< 0.001

Association vs. causal inference

National Health Interview Survey (NHIS) 2016 and 2017

Taking prescribed anti-cholesterol medication and Coronary Heart Disease

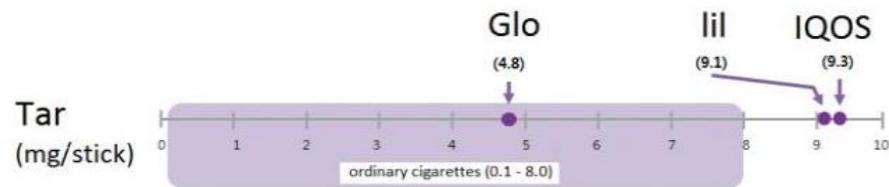
Variable	OR	95% CI	P value
Taking medication			
No (referent)			
Yes	2.05	1.65-2.55	< 0.001
Having high cholesterol			
No (referent)			
Yes	1.42	1.15-1.75	0.001

Conclusion (!!!!): “Ever being prescribed anti-cholesterol medication, adjusted for having hypercholesterolemia as well as other risk factors, is associated with increased risk of coronary heart disease.”

OBVIOUSLY NOT

Example of predisposition

- Korea Ministry of Food and Drug Safety



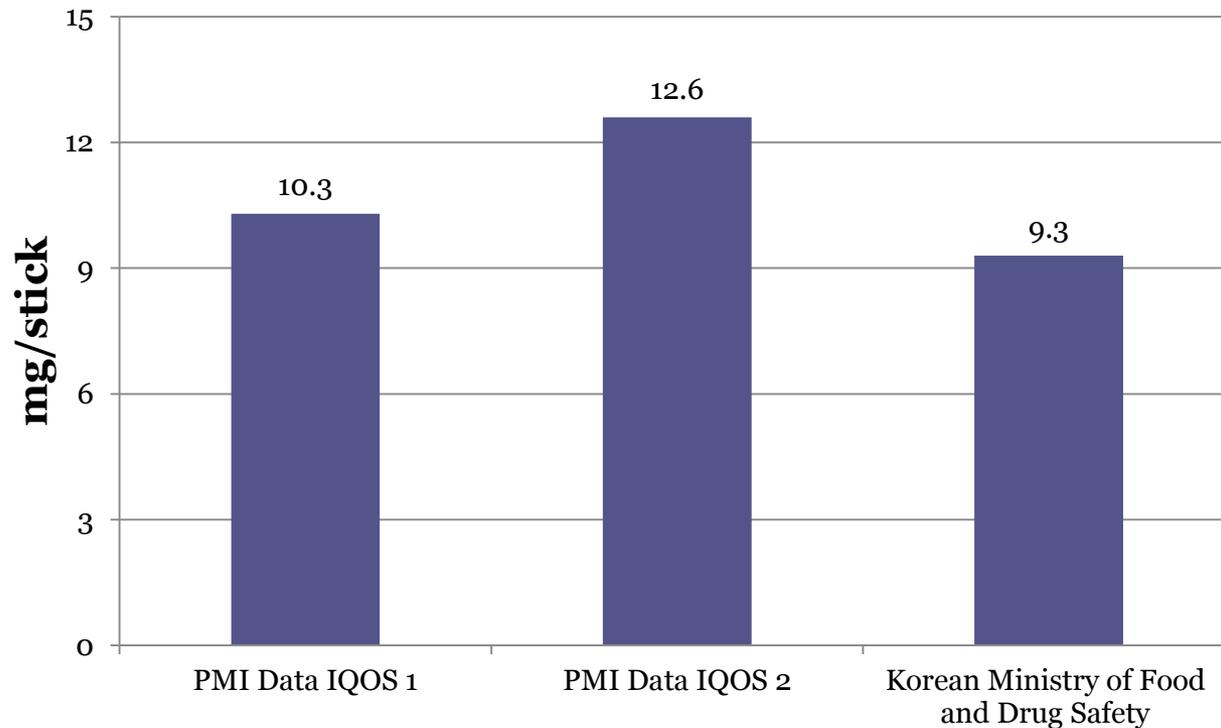
Source: Ministry of Food and Drug Safety

“The tar content of two heat-not-burn cigarettes was higher than ordinary tobacco, which indicates they could have other harmful substances not found in the latter,” it said.

“The Ministry of Food and Drug Safety Thursday dispelled the misconception of heat-not-burn cigarettes being healthier than ordinary cigarettes” (source: Korea Biomedical Review)

Example of predisposition

“The Ministry of Food and Drug Safety Thursday dispelled the misconception of heat-not-burn cigarettes being healthier than ordinary cigarettes” (source: Korea Biomedical Review)



(Schaller et al., Regul Toxicol Pharmacol 2016)

The end justifies the means?

- We don't want people to become dependent on nicotine
 - So, let's create a message that helps our goal
- “No tobacco products are safe”
 - No information on degree of risks
 - “... *the right to health information is independently related to the need to promote health literacy. This right should be respected whether or not harm reduction policies are judged advisable*” (Kozlowski & Edwards, Tob Control 2005)
 - Criticism that people think e-cigarettes are less harmful than smoking because this predicts future use
 - But this is true. Is it ethical to create misperceptions?
- WHO Ottawa Charter, 1986
 - Empowerment in public health
 - Ensure people's access to information on public health issues
 - Ensure people's access to tools (*products*) that help them promote their health

Precautionary approach

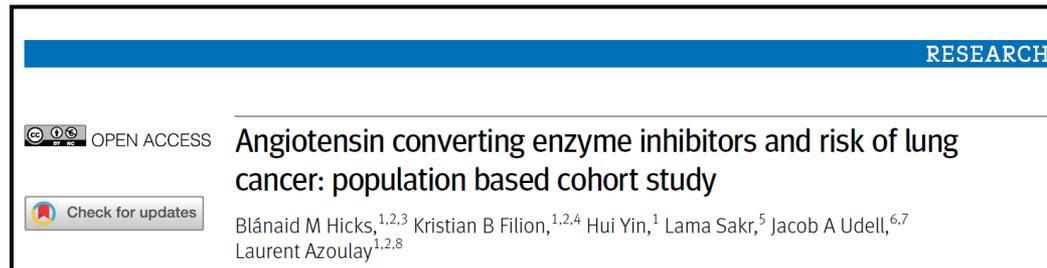
- Past history of tobacco cigarettes is used to assume the effects of harm reduction products
 - Bans, severe restrictions, classify e-cigarette use as smoking, etc.
- Justified or an abuse of precaution?
 - *“... precautionary approach, which in many cases could be described as misleading, originating from ideological opposition”*
 - *“the application of this principle justifies taking precautionary measures before “full scientific certainty” has been achieved, but there must be at least some evidence of risk or harm.” (Farsalinos & Le Houezec, Risk Manag Healthc Policy 2015)*
 - *The debate is about net harm or benefit, not about the absence of any harm*
- Avoiding theoretical harms can cause harm to other population groups
 - Protecting kids vs. harming smokers

Do we know everything in THR science?

- Obviously not
- Products are new - We need decades to fully quantify the epidemiological effects of THR products
 - The same quote can be used for every new medication or any other new consumer product
 - There has never been any product which has been marketed after decades of epidemiological research (because this is impossible to happen)
- How can we deal with this?

Maybe follow other examples?

ACE-inhibitors: discovered in 1975, launched in 1981 (captopril)



RESEARCH

OPEN ACCESS

Check for updates

Angiotensin converting enzyme inhibitors and risk of lung cancer: population based cohort study

Blánaid M Hicks,^{1,2,3} Kristian B Filion,^{1,2,4} Hui Yin,¹ Lama Sakr,⁵ Jacob A Udell,^{6,7} Laurent Azoulay^{1,2,8}

2018: 10-30% higher risk of lung cancer compared to ARBs

BMJ 2018;363:k4337 doi: 10.1136/bmj.k4337 (Published 24 October 2018)

Page 1 of 2



EDITORIALS

Angiotensin converting enzyme inhibitors and lung cancer

Any extra risk must be balanced against the mortality benefits of ACEI use

Deirdre Cronin-Fenton *associate professor*

Editorial: “Nonetheless, in an individual patient, concerns about the long term risk of lung cancer should be balanced against gains in life expectancy associated with use of ACEIs”

Prioritize research

- Seeking best possible information as soon as possible
- Long term epidemiological studies on young, healthy smokers
 - Time +++++
 - Cost +++++
- Short term follow-up in specific subpopulations
 - Examining subjects with established smoking-related disease
 - Secondary prevention
 - Look beyond disease outcomes (biomarkers of exposure/effect)
- Observational studies
 - Not the best quality evidence, but feasible and realistic

Prioritize research

- Seeking best possible information as soon as possible
- Clarify the chemistry profile of products
 - Rapid
 - Cheap (compared to clinical studies)
- Toxicological modeling
 - Set standardized conditions and exposure levels that could have clinical context
 - Compare with smoking
- Innovation – understand the product dynamics
 - Improve the safety/risk profile of products
 - Enhance the effectiveness in substituting smoking
 - Change our conventional attitude towards research (RCTs, one product for all)

Outcome

- Population effects
 - Identify who is using THR products
 - Examine why they use THR products
 - Measure the impact of THR products on the smoking habit
 - Understand population perceptions and misperceptions
 - Address healthcare professionals misperceptions
- Finding the right balance
 - Measure intended (beneficial) and unintended (adverse) effects
 - Identify where the balance lies (benefit / risk ratio)
- Decisions based on the knowns
 - Not based on what we don't know and what may theoretically happen, but on what we know and measure
 - Of course maintain a cautious approach and be ready to adjust recommendations

Decisions based on knowns

- Decisions based on the knowns
 - Of course, maintain a cautious approach
 - Focus on current knowledge, keep in mind the uncertainty in making decisions
 - Flexible framework to adjust to new evidence
- Truthful, evidence based information to everyone
 - Informed decisions require proper information
 - Proper information = current knowledge

THANK YOU

