Cochrane Tobacco Advisory Group :
https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD010216.pub8/full

Potential biases in the review process

We consider the review process we used to be robust. For outcome assessment, we followed the standard methods used for Cochrane Tobacco Addiction Review Group cessation reviews. Our search strategy included the Cochrane Tobacco Addiction Group Specialized Register, and we were able to capture a number of ongoing studies. ***However, there may be unpublished data that our searches did not uncover****. We also considered participants lost to follow-up as continuing to smoke, which is standard practice in this field. There are concerns that frequently updating meta-analyses can lead to issues with multiple testing; we followed Cochrane guidance in conducting this living systematic review and hence do not adjust for multiple testing (Brooker 2019).*

Four of our review authors are authors of the included studies*. These authors were not involved in the decisions about inclusion of their studies, or in risk of bias assessment for these studies; this approach is standard across all Cochrane reviews (regardless of subject area) and has been approved by the Cochrane editorial office as sufficient to avoid bias.*

Our review includes studies funded by the tobacco/vaping industry ***- Cochrane guidelines (not tobacco addiction-specific) mandate that studies be included regardless of funder, in order that the reviews remain transparent and rigorous****. As noted throughout the results section, we removed studies with tobacco or vaping industry funding in sensitivity analyses; our conclusions were unchanged when we did this. This means that studies funded by tobacco or vaping industries do not influence our conclusions. We do not receive any funding from tobacco or vaping industries, and maintain a firm stance of independence.*

Comment:
We were advised they update their 'review' monthly – a colleague had this info from a Canadian colleague who had examined the report closely. ***But they certainly include both unpublished and industry funded research (tobacco) and these contribute to their conclusions****. If you look at the most recent update and* ***CSUR research is cited****, that was the piece referred to which was given as a poster presentation at an SRNT conference two and a half years previously. Colleagues also noted that the report heavily referenced publications where members of the group overseeing it were co-authors.*

Meanwhile:

https://www.sciencemediacentre.org/expert-reaction-to-unpublished-conference-abstract-on-vaping-smoking-and-exercise/

September 8, 2024

expert reaction to unpublished conference abstract on vaping, smoking and exercise

An unpublished conference abstract presented at the *European Respiratory Society Congress 2024* looks at the association between exercise performance and vaping/smoking.

Rachel Richardson, Manager at the Methods Support Unit at Cochrane, said:

"There are several reasons to be cautious about the findings of this study and the way in which the press release has been phrased. I list below some of the key limitations.

"**Firstly, this is unpublished research**, and so independent scientists have not yet scrutinised the methods and the results. Peer review is a crucial part of the scientific process and it is a major concern that these findings are being widely disseminated without this scrutiny.

"Secondly, the fact that the study authors seem to have found an association between performance in exercise testing and vaping in young people cannot be interpreted to mean that vaping causes a reduced capacity for exercise. There could be many other reasons for this finding, for example, people who vape may exercise less regularly than people who do not. The authors do note in their presentation that all groups were 'physically active', but there could still be major differences in the amount of exercise undertaken. It is also important to note that this is a very small sample, and may not be representative of all young people who do and do not vape.

"Thirdly, the results presented in the press release are not up to date. The authors now have more data from an additional 15 participants and this will be presented at the conference."

Prof Kevin McConway, Emeritus Professor of Applied Statistics at The Open University, said:

"It's always frustrating to try to judge the quality of a research study, being presented at a conference, on the basis of so little information. We have a fairly brief press release, a very brief summary (abstract) of the work. In this case I've also seen the slides that are due to be shown at the presentation, which do add a little more (the slides are also based on data from an extra five participants per group). But the study has not yet been through a full peer review, and important details about what was actually done (or not done) are just not available, not yet anyway.

"The quote in the press release from Dr Filippos Filippidis of Imperial College, who was not involved in the research, begins with the important point that it's hard, in a study like this, to know what is actually causing the differences between the groups of young people in response to testing during exercise. There are good reasons for that doubt.

"This is an observational study. The researchers made, it appears, a lot of careful physiological measurements on the study participants. (I can't comment on whether these measurements are appropriate because I'm not an exercise physiologist.) But the researchers did not allocate young people to be cigarette smokers or vapers or non-smokers. The participants were put into these groups on the basis of the choices on

using cigarettes or vapes that they had made themselves. The researchers then observed various physiological characteristics.

“The three groups (tobacco smokers, vapers, non-smokers) would have differed in many ways apart from whether they smoked, vaped or did neither. The information we have on the study (mostly from the slides) does give some details, for example of the participants’ ages, heights and weights, and of measures of lung and circulatory system function while resting. But apart from that, we have rather few details on how the groups compared. So it remains possible that the observed differences in response to exercise are actually caused, not by whether they smoke or vape, but by some other difference, perhaps in lifestyle.

“It could even be that cause and effect goes in a different direction altogether. Maybe some people chose not to use tobacco or vapes because they were more involved in sport and exercise, and it’s this previous involvement in sport that is the cause of their better physiological response to exercise, rather than the fact that they chose not to smoke or vape.

“Or it could indeed be that the differences in response to exercise are in fact caused by the smoking or vaping. The issue is that we just can’t tell, at any rate on the basis of the information available.

“I think it’s also going beyond the data that we’ve seen to conclude that the effects of tobacco smoking and vaping are very similar in their effects, as Dr Faisal says in his quote in the press release (‘*In this regard, our research indicated that vaping is no better than smoking*.’) At one level they perhaps are similar, but no information has been provided on how much and how often the smokers and vapers actually smoked or vaped. If, on average, the tobacco smokers smoked rather rarely, but the vapers made very heavy use of possibly illegal vapes, then it makes no real sense to try to draw conclusions on how the effects of tobacco and vapes compare, I’d say. Again, we need more information to be clear about what’s going on.”

Declared interests

Rachel Richardson: I have no interests to declare.

Prof Kevin McConway: “I am a Trustee of the SMC and a member of its Advisory Committee. My quote above is in my capacity as an independent professional statistician.”

Centre for Substance Use Research (CSUR)

- Centre for Substance Use Research (CSUR), Tobacco Tactics, updated 06 September 2024, accessed 10 September 2024.

The *Centre for Substance Use Research* (CSUR) is based in Glasgow, Scotland and conducts consultancy and research for tobacco and e-cigarette companies. It has also received funding from the Foundation for a Smoke-Free World.

Background

Neil McKeganey founded the *Centre for Drug Misuse Research* at the University of Glasgow in 1994 to carry out research on Scotland's drug problem. Its projects were funded by UK research councils and the UK government, among others. In 2011, the Centre became entirely independent of the University[1] and was renamed the *Centre for Substance Use Research* (CSUR) in November 2015.[2]

In 2016, the University confirmed it was not in any way affiliated with the CSUR and McKeganey no longer held any position there, honorary or otherwise.[3]

On its website the CSUR describes itself as "a specialist research agency assisting companies with the behavioural research required to obtain a marketing authorization through the Pre-Market Tobacco Product Application (PMTA) Process."[4]

As of 2024, it stated:

Centre for Substance Use Research Ltd is a "multidisciplinary research agency providing behavioural science support to companies submitting applications for PMTA, MRTP and TPD approval."[4]

PMTA, Pre-Market Tobacco Applications, and MRTP, Modified Risk Tobacco Product applications, are specific to the US,[5] and the TPD, Tobacco Products Directive, to the European Union.

Staff

The website states that "The team within CSUR comprises post-doctoral researchers in behavioural science, experts in marketing, cyber security, and media."[6]

Neil McKeganey and Marina Barnard are Directors of CSUR (also referred to as CSURES as of February 2021).[4]

Christopher Russell, previously Deputy Director of CSUR,[7] was listed as a Special Advisor of CSUR in 2023.[8] He has been a director of Russell Burnett Research and Consultancy Ltd since 2019,[9] which has "received funding from e-cigarette/tobacco product manufacturers" to conduct research relating to nicotine and tobacco products.[10]

McKeganey and Russell have been listed as speakers at tobacco industry events including the Global Tobacco and Nicotine Forum (GTNF)[11][12][13] and the Tobacco Science Research Conference.[14]

Russell was also listed as a speaker at the 'New Approaches' conference in 2023 and 2024. New Approaches is held annually at the Harvard Club of New York City, in the same week as the United Nations General Assembly.[15][16]

For a list of staff see the CSUR website.

Relationship with the Tobacco Industry

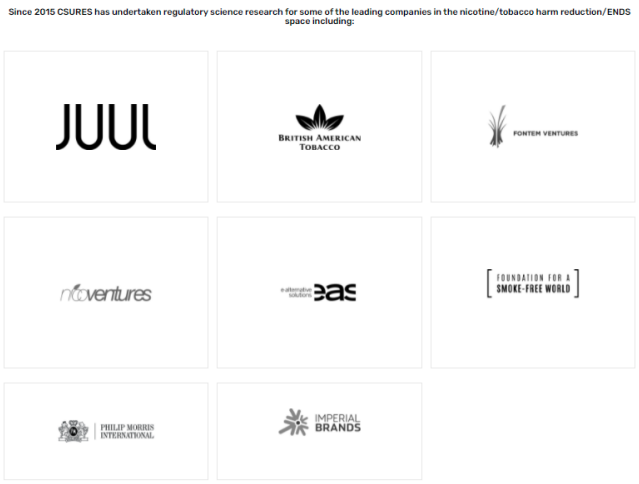

Image 1: CSUR funding (Source: CSUR website, accessed June 2021)

CSUR has undertaken work for tobacco companies including Philip Morris International (PMI), British American Tobacco (BAT), Nicoventures, a subsidiary of BAT, Imperial Brands and Fontem Ventures, a subsidiary of Imperial (see Image 1).

CSUR also works with JUUL Labs, in which Altria has a share, and has received funding from the Foundation for a Smoke-Free World (see below for details).[17] CSUR has published multiple academic papers which declare support from either tobacco companies or tobacco company subsidiaries.[18][19]

Opposed Plain Packaging in the UK

In 2014, McKeganey helped BAT oppose the introduction of Plain Packaging in the UK. McKeganey prepared a 82 page report for BAT which was included in BAT's submission to the UK's second public consultation on plain packaging in 2014.[2021] In the report, McKeganey supports BAT's view that there is no evidence to suggest that plain packaging will reduce smoking prevalence, and that packaging is not "a factor that influences people's decisions to start, stop, or re-start smoking".[2021]

In May 2016, dismissing the legal challenges to the UK's plain packaging legislation brought by the big four tobacco companies, the High Court of Justice's ruling criticised McKeganey's findings and the methodology they were based on:[21]

"What I find unacceptable is the preparation of a report which by its total refusal to engage with any of this contramaterial simply conveys the impression that it does not exist and that the best way to refute it is to ignore it. Yet, at the same time and inconsistently, Professor McKeganey accepts that the principles of transparency and openness are "foundational tablets of the scientific enterprise". Had Professor McKeganey confronted head-on the contrary evidence, including that from the tobacco companies, then it is hard to see how he could have advanced the opinions that he did; at the very least he would have been compelled to provide a proper rationale for why his opinion could be sustained in the light of this inconsistent evidence."

Work with JUUL Labs

More recently, McKeganey and CSUR have been working for e-cigarette company JUUL Labs. Altria has held a 35% share in JUUL since December 2018. A number of outputs written with CSUR are published on the JUUL Labs website.[22] Others are listed on the CSUR website.[18] Some have been co-authored by PinneyAssociates, which also works with JUUL Labs and tobacco companies.[22]

In March 2019, JUUL Labs promoted a study by CSUR (funded by JUUL) which found that the JUUL e-cigarettes "dramatically" cut adult smokers' cigarettes consumption.[23] This paper was published in the *Journal of Pulmonary and Respiratory Medicine*, which has been described as a "predatory journal".[2425]

In 2021, CSUR contributed a paper to a special issue of the *American Journal of Health Behavior*, sponsored by JUUL Labs.[2627] The paper was co-authored with JUUL Labs and PinneyAssociates. There was criticism of the journal, which defended the publication of the special issue.[28]

Received Funding from the Foundation for A Smoke-Free World

The Foundation for A Smoke-Free World (FSFW), which is wholly funded by Philip Morris International, awarded two grants to CSUR in May 2018 totalling US$189,004. One grant for US$96,063 was provided to "develop a centre of excellence in behaviour research related to smoking cessation", another for US$92,941 was provided for research on the "determinants and impact of switching to reduced risk products".[29]

In 2022 CSUR received another grant from FSFW of US$154,564 to "Develop a protocol for an intervention trial to assess the long-term health effects of switching from combustibles to tobacco harm reduction products among Type 2 diabetic smokers in Bangladesh".[30]

Advocacy and research organisation PROGGA, expressed concerns around the study, stating "The timing of this campaign is particularly concerning, as the Ministry of Health and Family Welfare is currently working on amending the tobacco control law, which could potentially ban e-cigarettes and vaping altogether".[31]

Participated in roundtable with MSPs

On 12 February 2021, Holyrood Magazine hosted a video conference roundtable about the role e-cigarettes could play in meeting Scotland's target of a tobacco free generation by 2034. The meeting was attended by MSPs Donald Cameron (Conservatives), Emma Harper (SNP), Richard Lyle (SNP) and Brian Whittle (Conservatives).[32]

CSUR co-director Neil McKeganey was also present, stating that despite substantial progress in reducing smoking in Scotland, "we are still not seeing the smoking end game" and that "there is an obligation on us to consider what role e-cigarettes can play in further reducing smoking prevalence".[33] Other speakers included representatives from the Scottish Grocers' Federation and We Vape.[33]

"Flagship" Studies

Annual Study on E-cigarette Use

CSUR's website stated that in 2021 it would be conducting the first of an annual study of "Real-World ENDS Use", stating that:

"What has been missing in this [ENDS, or e-cigarette research] are studies assessing the relative impact of different brands and types of ENDS devices. In 2021 CSURES [sic] will undertake research assessing 9 of the top ENDS devices on sale in the U.K. comparing the relative rates with which these devices are enabling adult smokers in the US and U.K. to quit and reduce their cigarette consumption".[34]

Tobacco Products Prevalence Study

In 2021, CSUR launched a study on prevalence and patterns of use of different e-cigarette brands and products in the US.[35] Its website stated that the study aimed "to estimate the prevalence and patterns of use of 20 ENDS brands and over 200 ENDS devices sold in the United States. This research is designed to provide ENDS manufacturers with population-level use data on their products for submission to FDA in seeking PMTA approval."[35]

In 2023, the study was expanded to include heated tobacco products and nicotine pouches.[36] Brands monitored in the study include those owned by JTI, Altria, BAT and Imperial Brands.

Paper on single-use e-cigarettes

CSUR received funding from BIDI (Kaival Brands), towards the publication of a paper on the prevalence of the use of single use, or 'disposable' e-cigarettes in the US.[37] The paper was cited by Bidi Vapour in a press release published in July 2023, which stated that its 'disposable' products were "not implicated in the recent growth in the use of disposable e-cigarettes by U.S. youth".[38] PMI began marketing Kaival's single use e-cigarette, outside of the US, in July 2022, as *VEEBA,* later renamed *VEEV NOW*.[39]

- For details see E-cigarettes: Tobacco Company Interests in Single Use Products

TobaccoTactics Resources

- JUUL Labs
- Foundation for a Smoke-Free World
- Foundation for a Smoke-Free World Centres of Excellence
- PinneyAssociates

Relevant Links

- CSUR website

References

1. ↑Centre for Drug Misuse Research, Letter Re: Impact of Suboxone and Methadone on the Recovery from Opiate Dependency, 3 February 2012, Document released by Scotland A research Ethics Committee following Freedom of Information request from Action for Smoking and Health (ASH) May 2016
2. ↑Companies House, Centre for Substance Use Research, Name Change registered 24 November 2015
3. ↑University of Glasgow response to Freedom of Information request from ASH, 23 June 2016
4. ↑[abc]CSUR, Homepage, no date, accessed August 2024
5. ↑US Food and Drug Administration, website, accessed June 2021

6. ↑
7. ↑CSUR, About Us, website, undated, archived February 2021, accessed October 2023
8. ↑CSUR, About Us, website, undated, archived June 2023, accessed October 2023
9. ↑RUSSELL BURNETT RESEARCH & CONSULTANCY LTD, Companies House, website, undated, accessed October 2023
10. ↑K. Farsalinos, C. Russell, R. Polosa, G. Lagoumintzis, A. Barbouni, Patterns of flavored e-cigarette use among adults vapers in the United States: an online cross-sectional survey of 69,233 participants (Preprint), 10 March 2023, doi: 10.21203/rs.3.rs-2658498/v1
11. ↑GTNF, Seoul 2023 Speakers, website, undated, accessed October 2023
12. ↑Global Tobacco and Nicotine Forum 2018, Look Who's Talking, archived August 2018, accessed May 2021
13. ↑Global Tobacco & Nicotine Forum, 2019 Speakers and Panelists, 2019, accessed September 2019
14. ↑74th Tobacco Science Research Conference: Program Booklet and Abstracts, August 29-31 2021, accessed October 2023
15. ↑New Approaches Conference, Speakers 2023, website, undated, accessed October 2023
16. ↑New Approaches Conference, 23 September 2024, Harvard Club of New York City, website, undated, accessed September 2024
17. ↑CSUR, Funding, accessed June 2021
18. ↑[ab]CSUR, Publications, website, undated, accessed October 2023
19. ↑N. McKeganey, S. Notley, J. Coyle, G. Barnard, Why Do Some Adults Who are Smoking Perceive E-cigarettes to be More Harmful than Combustible Cigarettes? (Preprint), 23 August 2023, doi: 10.21203/rs.3.rs-3273011/v1
20. ↑[ab]British American Tobacco, Consultation on the introduction of regulations for the standardised packaging of tobacco products. Response of British American Tobacco UK Limited, BAT website, 7 August 2014, accessed May 2019
21. ↑[abc]British American Tobacco, Philip Morris, Japan Tobacco International and Imperial Tobacco against Secretary of State for Health, Royal Courts of Justice, 19 May 2016, accessed July 2016
22. ↑[ab]JUUL Labs, Publication Library, Search results for "Centre for Substance Use Research", JUUL Labs Science website, accessed June 2021
23. ↑JUUL Labs, Peer-Reviewed Study: Adult Smokers Using Juul Dramatically Cut Quantity of Cigarettes Smoked, JUUL Labs website, 1 March 2019, archived September 2020, accessed June 2021
24. ↑A. Ault, E-Cig Giant Juul Touts Positive Study in a Questionable Journal, *Medscape*, 20 March 2019, accessed March 2019
25. ↑A. Severin, N. Low, Readers beware! Predatory journals are infiltrating citation databases, Editorial, *Int J Public Health,* July 2019, 64, 1123–1124, doi:10.1007/s00038-019-01284-3
26. ↑*American Journal of Health Behavior,* JUUL Special Issue*,* Volume 45, Number 3, May 2021

27. ↑S. Shiffman, M.A. Sembower, E.M. Augustson, et al, The Adult JUUL Switching and Smoking Trajectories (ADJUSST) Study: Methods and Analysis of Loss-to-Follow-Up, *American Journal of Health Behavior*, Volume 45, Number 3, May 2021, doi:10.5993/AJHB.45.3.3
28. ↑I. Torjesen, Academic journal is criticised for publishing special issue funded by tobacco industry, *BMJ,* 14 May 2021; 373:n1247 doi: 10.1136/bmj.n1247
29. ↑Foundation for a Smoke-Free World, Form 990-PF, 2018 Tax Return, 13 May 2019, accessed May 2019
30. ↑Foundation for a Smoke-Free World, Form 990-PF, 2022 Tax Return, 15 May 2023, accessed May 2023
31. ↑Progga expresses concern over e-cigarette research in Bangladesh, *New Age*, 24 May 2023, accessed October 2023
32. ↑Scottish Parliament, Register entry search returns, undated, accessed July 2024
33. ↑[ab]J. Thomson, Associate feature: Changing direction: vaping's role in achieving Scotland's 2034 smoke-free target, *Holyrood*, 6 April 2021, accessed July 2024
34. ↑CSUR, Areas of research expertise: Flagship Study: Comparative Assessment Of Real-World ENDS Use (CARE Study), website, accessed June 2021
35. ↑[ab]CSUR, Areas of Research Expertise: Flagship Study: ENDS Prevalence, website, undated, archived September 2021, accessed October 2023
36. ↑CSUR, Tobacco Products Prevalence Study, website, undated, accessed October 2023
37. ↑N. McKeganey, A. Patton, V. Marza, G. Barnard, When it comes to assessing the impact of e-cigarettes, estimates of device prevalence matter: the BIDI Stick disposable device, *Harm Reduction Journal*, 5 July 2023, 20(85), doi: 10.1186/s12954-023-00820-y
38. ↑Bidi Vapor, Not All Flavored Disposable Vape Tied to Youth Use, Study Finds, press release, 19 July 2023, accessed October 2023
39. ↑Kaival Brands, Kaival Brands Reaches Agreement with Philip Morris International for International Electronic Nicotine Delivery System Product Distribution, 13 June 2022, accessed October 2023

from The New Venture Fund, Smokefree South West, and the Economic and Social Research Council (ESRC) Knowledge Exchange Opportunities scheme. These funders have had no input into the research reported on this website or its conclusions. They are not responsible for its content or publication, nor do they necessarily endorse it. Published by the University of Bath. Read the General Disclaimer.

blogs.bmj.com /bmjebmspotlight/2018/09/16/cochrane-a-sinking-ship/

Cochrane – A sinking ship?

BMJ 17/09/2018

By Maryanne Demasi, PhD

A scandal has erupted within the Cochrane Collaboration, the world's most prestigious scientific organisation devoted to independent reviews of health care interventions. One of its highest profile board members has been sacked, resulting in four other board members staging a mass exodus.

They are protesting, what they describe as, the organisation's shift towards a commercial business model approach, away from its true roots of independent, scientific analysis and open public debate.

There are concerns that Cochrane has become preoccupied with "brand promotion" and "commercial interests", placing less importance on transparency and delivering "trusted evidence".

It began as a simmering personality clash, between the CEO and a board member, but now has boiled over into a spectacular war of words, where the underlying issues of Cochrane have bubbled to the surface, with many insiders predicting the beginning of the end of Cochrane.

The dispute

A meeting of the Trustees of Cochrane was convened in an effort to resolve an ongoing dispute between the CEO of Cochrane Collaboration, Mark Wilson and one of the founding fathers of the Cochrane Collaboration in 1993, Director of the Nordic Cochrane Centre, Peter C. Gøtzsche.

It began with, what might be perceived as, fairly trivial issues. Wilson accused Gøtzsche of using Cochrane's letterhead on a complaint to the European Medicines Agency about its evaluation of possible harms of HPV vaccines and testifying in a court case without overtly declaring his expert testimony was expressing 'personal' not 'Cochrane' views.

Wilson alleged that it constituted a breach in the 'Spokesperson Policy', a claim denied by Gøtzsche. The dispute intensified after several people complained to the Board about Gøtzsche's 'take no prisoners' approach to critiques of industry-funded science.

Gøtzsche is well-known for his blunt criticisms over the harms of breast cancer screening programs, the overuse of psychiatric drugs, and has referred to the drug

industry as ‘organised crime’. But his most recent article, with co-authors Lars Jørgensen and Tom Jefferson, was a stinging critique of the quality and methodology of Cochrane’s HPV vaccines review. [1]

Immediate backlash ensued and the Cochrane leadership, accused Gøtzsche’s team of causing reputational damage to the organisation, fuelling anti-vaxxers and risking “the lives of millions of women world-wide by affecting vaccine uptake rates”, according to a complaint by the editor of the Cochrane group that published the HPV review.

Gøtzsche stood by his group’s paper, sparking an urgent, internal review at Cochrane. On 3 Sept 2018, Cochrane’s Editor in Chief, David Tovey, and his Deputy, Karla Soares-Weiser, issued a statement claiming that the criticisms of the HPV vaccine review had been ‘substantially overstated’ and ‘inaccurate and sensationalized.’

“People all over the world have interpreted the Cochrane editors’ criticism of us as being the ‘final word’” said Gøtzsche in frustration. “The editors did not even address our most important concern that the harms of the HPV vaccine had been greatly under-reported and that much of the clinical data is not included in the review”.

Legal Review

The Board of Trustees agreed to engage the services of an external law firm to independently assess the dispute between Gøtzsche and Wilson. In July 2018, Gøtzsche was presented with 400 pages of documents, containing allegations that he had breached Cochrane policies and damaged its reputation.

Gøtzsche retaliated by submitting a 66-page dossier outlining, in painstaking detail, allegations that Wilson’s leadership team was ‘destroying’ Cochrane by treating it like it was a “brand or product”, accusing Wilson of “serious abuse and mismanagement of Cochrane”, “tampering with meeting minutes” and “management by fear”.

The lawyers poured over the mountain of documents and were expected to deliver a verdict in time for the 13 Sept Governing Board meeting. Twelve hours before the meeting started, the Counsel’s report was delivered to the Board with a caveat that inadequate time was granted for a thorough review of all the issues.

Nonetheless, the report found that none of the serious allegations against the Cochrane executive could be substantiated, nor did it find that Gøtzsche had breached the Spokesperson Policy or had acted inappropriately in his role as Trustee.

The Board Meeting

Co-chair, Marguerite Koster, allowed Gøtzsche ‘five minutes’ to state his case. Witnesses in the room say Gøtzsche was constantly interrupted before being asked to leave the room while the other Board members discussed the situation. Gøtzsche was given no further opportunity that day to defend himself.

After more than 6 hours of deliberation, the remaining 12 Board members voted on whether Gøtzsche could remain as their 13th Governing Board member and continue to practice under the Cochrane license.

Five voted to remain, six voted to remove and one abstained. In the end, a 'minority' vote [6 out of 13] saw Gøtzsche vacated from his position and lose his Cochrane membership. After 25 years of service to Cochrane and author of 17 Cochrane reviews, Gøtzsche would officially learn of his fate by an email.

"No clear reasoned justification has been given for my expulsion aside from accusing me of causing 'disrepute' for the organization", claims Gøtzsche. "This is the first time in 25 years that a member has been excluded from membership of Cochrane".

Several board members were shocked over the treatment of Gøtzsche.

"The legal assessment essentially exonerated Peter of breaching the Spokesperson Policy so his enemies spent the day inventing new excuses to get rid of him", said one member. "To expel Peter is totally disproportionate," said another of Gøtzsche's supporters. "It was like looking for any behavioural pretext to fire him."

The following day, 14 Sept 2018, four members resigned from the Governing Board in solidarity for Gøtzsche and because they felt something drastic had to happen in order to save the organisation.

See here: Why we resigned

"What should happen now, is that entire Board should resign and start again", said one member after their resignation.

On 15 Sept 2018, a statement to Cochrane Directors, from the co-chairs of the Governing Board, mentioned that four members resigned and that changes to the board were afoot, but did not mention Gøtzsche's expulsion from the Board.

"I don't understand why they are sticking they're head in the sand", said one board member. "They should do something now to address everyone's concerns".

Cochrane's sinking ship

The events that have unfolded in the last few days have consequences for Cochrane far beyond dealing with the public embarrassment of losing more than a third of its Governing Board.

Much of Gøtzsche's scientific work at the Nordic Cochrane Centre, has focused on exposing the flaws in clinical trials and the undue influence of the drug industry on medical research.

In addition, there are the issues raised in a recent editorial, co-authored by Dr Tom Jefferson from Centre for Evidence-Based Medicine, Oxford. It explains the problems behind the reliance of data from published journal articles, many of which are likely to contain 'unfathomable bias'.

"We know that the biomedical journals publish articles which are neutral at best, but are mostly positive and tend to emphasize benefits and downplay or even ignore harms," says Jefferson.

"What you end up within the medical journals is a shoe-horn version or a summarized version and you don't know what criteria go into choosing which bits goes into the print version. So that introduces unfathomable bias".

Jefferson's answer to whether we should ignore evidence from journal articles was 'probably' unless urgent steps aren't taken to address the issue of reporting bias: cherry picking and spin of research findings

This presents Cochrane with an enormous problem. The lifeblood of the organisation is in carrying out systematic reviews. The basic evidence, upon which these reviews are founded, is largely at risk of bias, especially for interventions where there is a huge market.

"The contention that Cochrane has been publishing reviews that are mainly beneficial to the sponsors of these interventions is probably a fact," says Jefferson. "If your review is made up of studies which are biased and in some cases are ghost written or the studies are cherry picked and you don't take that into account in your review, then its garbage in and garbage out – its just that the 'garbage out' is systematically synthesised with a nice little Cochrane logo on it".

As for the data behind the HPV vaccines, it's a question of whether anyone has seen the full data set. "The answer is no-one outside the vaccine manufacturers. Not the drug regulators and certainly not, independent scientists" says Jefferson. "So if you were to ask me what I think of HPV vaccines, I would say 'I don't know' because I haven't seen the full data set".

Furthermore, Gøtzsche says that Cochrane's policy regarding the conflicts of interest of the authors of reviews is inadequate. "I proposed a year ago that there should be no authors of Cochrane reviews that have financial conflicts of interests with companies related to the products considered in the reviews," says Gøtzsche "But Cochrane did nothing about it".

Currently, Cochrane allows up to half of the authors on a review to have conflicts of interest, a policy that is widely criticized by insiders, and largely unknown to the public.

So why hasn't Cochrane done anything about it?

“Cochrane has become too sensitive to criticism of the pharmaceutical industry”, says one board member. Insiders say a ‘possible concern’ might be that Cochrane fears that Gøtzsche’s criticism of the HPV vaccines review would negatively impact its sponsorship from the Bill & Melinda Gates Foundation.

Scientific censorship

Cochrane has been accused of ‘scientific censorship’ and is now in ‘damage control’ to contain the PR nightmare.

Publicly, Cochrane has always maintained it encourages debate about scientific issues, including controversial ones. “Cochrane values constructive criticism of its work and publicly recognises this through the Bill Silverman Prize … with a view to helping to improve its work, and thus achieve its aim of helping people make well-informed decisions about health care”, states Cochrane.

However, the reality is very different. “They don’t believe in democratic plural science”, said one outgoing board member. “Good governance of science always requires open debates. The prestige of a scientific institution has to do with its ability to manage critical debates, not censor them”.

“Science needs to be challenged, it should not be politically correct, it is not consensus seeking,” says Gøtzsche. “You cannot call a public challenge to science ‘controversial’, it’s a pejorative term. It’s simply what our job as scientists requires of us”.

The future of Cochrane

Cochrane is in a moral crisis and many say it has lost a democratic leadership. “On dozens of issues, the Board can only vote yes or no with very little opportunity to amend or modify the executive team´s proposals,” says Gøtzsche.

The entire US Cochrane Centre has already closed down in the spring of 2018, in frustration over management and other centre directors are also contemplating leaving Cochrane. Whereas those who’ve been critical of Cochrane’s direction, have simply withdrawn, Gøtzsche spoke out publicly and has borne the consequences.

“A recovery from this dire situation would call for the dissolution of the present board, new elections and a broad-based participatory debate about the future strategy and governance of the organization”, says Gøtzsche. The Annual General Meeting on Monday (17th Sept) might shed light on Cochrane’s future.

DISCLOSURE: *Maryanne Demasi is a science reporter and* a researcher working with Prof Peter C. Gøtzsche, the Nordic Cochrane Centre, and was present in Edinburgh at the time of the meeting, but not present in the discussion room

Cochrane Collaborative concludes that e-cigs as medicines help a few people shop smoking (again); still ignoring differences between medicines and consumer products as well as dual use

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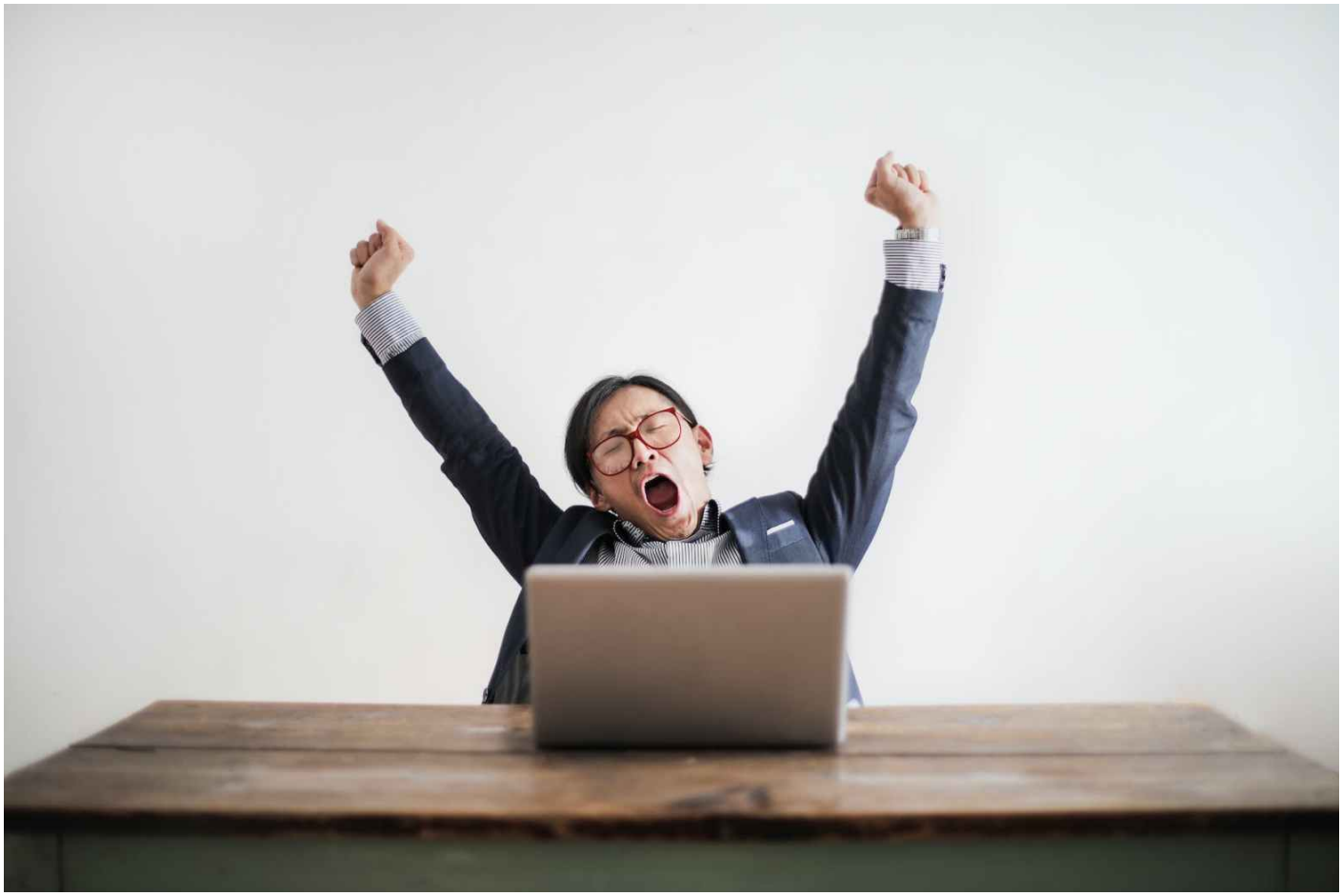

On January 8, 2024, the Cochrane Collaborative published yet another meta-analysis of randomized controlled trials concluding that e-cigarettes help a few people stop smoking. While industry and other pro-e-cigarette interests will make a big deal of this, the fact is ***that there is nothing new here***.

Here is their primary conclusion:

> There is high certainty that nicotine EC increases quit rates compared to nicotine replacement therapy (NRT) (RR 1.59, 95% CI 1.29 to 1.93; I^2 = 0%; 7 studies, 2544 participants). In absolute terms, this might translate to an additional four quitters per 100 (95% CI 2 to 6 more).

Compare this to what they reported way back in November 2022:

> There was high certainty that quit rates were higher in people randomized to nicotine EC than in those randomized to nicotine replacement therapy (NRT) (RR 1.63, 95% CI 1.30 to 2.04; I^2 = 10%; 6 studies, 2378 participants). In absolute terms, this might translate to an additional four quitters per 100 (95% CI 2 to 6).

Just for kicks, here is what we concluded in our meta-analysis, published in 2021:

> The RCTs that compared quitting among smokers who were provided e-cigarettes to smokers with conventional therapy found e-cigarette use was associated with more quitting (relative risk = 1.555; 95% CI = 1.173, 2.061).

These risk estimates are all essentially the same.

Cochrane continues to ignore two critical points:

1. The real world evidence does not show short-term (less than a year or so) associations between smokers using e-cigarettes as consumer products with having stopped smoking and the long-term real world evidence shows ***less stopping cigarettes***.
2. Dual use is an important complication of giving people e-cigarettes; Cochrane does not consider dual use an adverse effect despite the fact that dual use is more dangerous than smoking alone.

And, of course, only 4 smokers per 100 given e-cigs actually stopped smoking, a tiny effect. More important, one high quality RCT that looked found that more smokers given e-cigs become dual users than stop smoking cigarettes, so giving smokers e-cigarettes likely ***increases harm***.

Those facts likely won't stop e-cig promoters from touting this "new" Cochrane review. In response, people should cite the recent WHO Call to Action on Electronic Cigarettes that clearly ***makes the distinction between e-cigarettes as consumer products and medicines, highlighting the lack of evidence that e-cigarettes, as consumer products have not been shown to help smokers "switch completely":***

> Cessation strategies should be based on the best available evidence of efficacy, synergistic with other tobacco control measures and subject to monitoring and evaluation. ***Based on the current evidence, it is not recommended that governments permit sale of e-cigarettes as consumer products in pursuit of a cessation objective. Any government pursuing a smoking cessation strategy utilizing e-cigarettes should control the conditions under which the products are accessed to ensure appropriate clinical conditions and regulate the products as medicines (including requiring marketing authorization as medicines).*** The decision to pursue a smoking cessation objective, even in such a controlled form, should be made only after considering national circumstances, along with the risk of uptake and after exhausting other proven cessation strategies. [emphasis added]

As I noted above, no doubt e-cig advocates will try an make a big deal about this "new" ***meta-analysis. The reality is nothing has changed on this point in years.***

This may well be the last Cochrane report on e-cigs and smoking, since it Cochrane UK is closing down in March 2024 because it lost its funding. If these repetitive reports are typical of its work, I'm not surprised about the funding.

COCHRANE CLOSED - MARCH 2024

Cochrane

UK

Cochrane UK in Oxford to close at the end of March 2024

We are sorry to announce that Cochrane UK, based in Oxford, will close at the end of March 2024 with the end of National Institute for Health and Care Research (NIHR) **funding.**

Since Cochrane UK was established - as the first Cochrane centre - it has delivered a varied programme of work. For example, providing training, events (including four Colloquia, the inaugural one in Oxford, then Dublin and Edinburgh, with a fourth planned in London in September 2023) and resources for Cochrane contributors and others; supporting the dissemination of Cochrane evidence; and monitoring the impact of Cochrane Reviews.

In the early years, Cochrane UK conducted a programme of methods research and helped establish the Cochrane Central Register of Studies. Cochrane UK also founded Students 4 Best Evidence, a global network for students interested in evidence-based health care and carries out outreach work teaching school children, and others, about evidence-based decision-making.

The Cochrane UK team will continue to deliver on our current work programme until the end of the contract.

Important note: Cochrane UK is a regional centre within Cochrane, supporting Cochrane activities in the UK. The funding of Cochrane is not affected by this news - Cochrane will continue to produce Cochrane Reviews.

Read a statement on Cochrane.org

Any questions? Please get in touch: general@cochrane.nhs.uk

Cochrane

Trusted evidence.

Informed decisions.

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A fond farewell to our closing review groups

Today marks the closure of the UK-based Cochrane Review Groups whose funding from the National Institute for Health and Care Research (NIHR) has come to an end.

Over Cochrane's 30-year history, thanks to the work of Cochrane Review Groups, over 16,000 new and updated Cochrane Reviews have been published covering a wide range of disciplines. These have led to countless policy changes, saving and improving many lives across the world.

Cochrane CEO Catherine Spencer and Editor in Chief Karla Soares-Weiser have thanked members of groups that are closing for their contributions:

"We want to express our heartfelt gratitude for your outstanding contributions to Cochrane and evidence-based healthcare, and the countless lives you have positively impacted through your dedication and hard work. The exceptional reviews produced by Cochrane Review Groups have been a cornerstone of our organization's reputation for producing high-quality evidence, and your passion and commitment have been instrumental in achieving that."

The review group model served Cochrane well over three decades, but in that time the world has changed along with funding pressures and priorities. To ensure that Cochrane can continue to produce trusted evidence for decades to come, a change programme is underway to transition to a new model for producing evidence syntheses. Over the coming years Cochrane will continue to support funded review groups to produce evidence syntheses, while running pilot projects to test different approaches.

"We are grateful to the NIHR for providing stable funding for Cochrane's UK-based review groups, which helped Cochrane to become the well-respected organisation it is today," says Karla. "We are now in a strong position to move forward and build on this excellent foundation, for which we owe immense gratitude to our Cochrane Review Groups across the world. Some UK based groups have secured alternative sources of funding to develop and write evidence syntheses, while others are seeking funds to enable them to do so. For others, we share and recognise the sadness that will be felt at their closure but we salute the contribution made by this community of people.

“Isaac Newton wrote ‘if I have seen further it is by standing on the shoulders of giants’, in reference to the scientific and philosophical ideas that preceded and enabled his theories. At Cochrane, every review we publish, every guideline we influence and every life we improve is only possible thanks to decades of work from review groups. To everyone who has worked in a Cochrane Review Group, I would like to say: you are all giants.”

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The updated Cochrane review of e-cigarettes — and what it should mean for Canada

Admin ⋮

Last week, the UK based health charity, Cochrane, released its sixth report on the evidence on the use of e-cigarettes for smoking cessation. This post reflects on how this and other Cochrane conclusions could serve Canadian efforts to reduce smoking at the population and individual levels.

In brief:

1) Cochrane establishes that in clinical trials, E-cigarettes fail 10 times more often than they succeed (roughly the same as NRT). Other reviews have shown that in real life they are even less successful.

2) The products used in the studies reviewed by Cochrane are different than those on the market in Canada. The U.S. Surgeon General recommends that because of the wide variation in products and usage it is not prudent to draw generalized conclusions about their efficacy as stop-smoking medications.

3) Cochrane reviews show that other stop-smoking medications do better in clinical trials. (The ones that, unlike e-cigarettes, have been assessed and authorized on the basis of their safety, efficacy and quality.)

4) Any advice to a smoker to use e-cigarettes to quit smoking (or to reduce the harms from continued nicotine use) should be tailored to individual circumstances and be individually delivered in a therapeutic context. Population-level encouragements for smokers to use e-cigarettes are imprudent. To date these have back-fired in Canada, resulting in more new nicotine addicts than former smokers.

Next verse, much the same as the first…

The Cochrane review on e-cigarettes that was published last week has the same central messages as the versions published in September 2021, the one published in April 2021, and the one published in October 2020. A major difference with earlier versions is the number of studies they accepted for their analysis: three that compared NRT to e-cigarettes were included in 2020, four in 2021 and six this year.

This study was released with considerable fanfare and extensive public relations efforts. Cochrane publishes several reports on tobacco issues (described at the end of this post) – few seem to get the same PR effort.

The press releases that accompanied the release of this update were clearly designed to encourage e-cigarette use by smokers. The lead author's statement linked to the release of the report, suggests that e-cigarettes are highly effective at helping smokers quit: *"For the first time, this has given us high-certainty evidence that e-cigarettes are even more effective at helping people to quit smoking than traditional nicotine replacement therapies, like patches or gums."*

Another coordinated press release was sent by well known e-cigarette enthusiasts. Professor John Britton presented e-cigarettes as a panacea for smoking cessation: *"All smokers should therefore try vaping as a means to end their dependency on smoking tobacco."* (The release made no mention that Dr. Britton has been engaged by Canadian commercial vaping interests to oppose flavour restrictions in New Brunswick.)

There are many reasons to disagree with these views.

Cochrane has confirmed that in clinical trials e-cigarettes are NOT very effective at helping smokers quit.

The reviewers memorably present their conclusions in a plain language summary: "*For every 100 people using nicotine e-cigarettes to stop smoking, 9 to 14 might successfully stop, compared with only 6 of 100 people using nicotine-replacement therapy, 7 of 100 using e-cigarettes without nicotine, or 4 of 100 people having no support or behavioural support only."*

Rather than confirm the superiority of e-cigarettes, these numbers confirm the inadequacy of both vaping products and NRT – even under the best of supervised therapeutic circumstances.

The Cochrane report on e-cigarettes concluded in effect that **90 of 100 smokers who use e-cigarettes to quit smoking will be smoking again within 6 months**, compared with 94 failures for every 100 who use NRT.

The relative risk for success between E-cigarettes and NRT is 1.63 (10 vs 6 successes per 100 tries). The relative risk for failure between NRT and E-cigarettes is 1.04 (94 vs 90 failures per 100 tries)

(Simon Chapman provides a good discussion of the high rate of failure in his blog "Would you take a drug that failed with 90% of users? New Cochrane data on vaping "success".)

Cochrane has confirmed that in clinical trials other stop-smoking medications available in Canada do better than e-cigarettes.

Other Cochrane reviews have assessed the effectiveness of pharmacotherapies for smoking cessation. These include the stop-smoking medications that have been approved by Health Canada following a review of their safety, efficacy and quality. (The safety, efficacy and quality of e-cigarettes is not examined by Health Canada before they are permitted for sale).

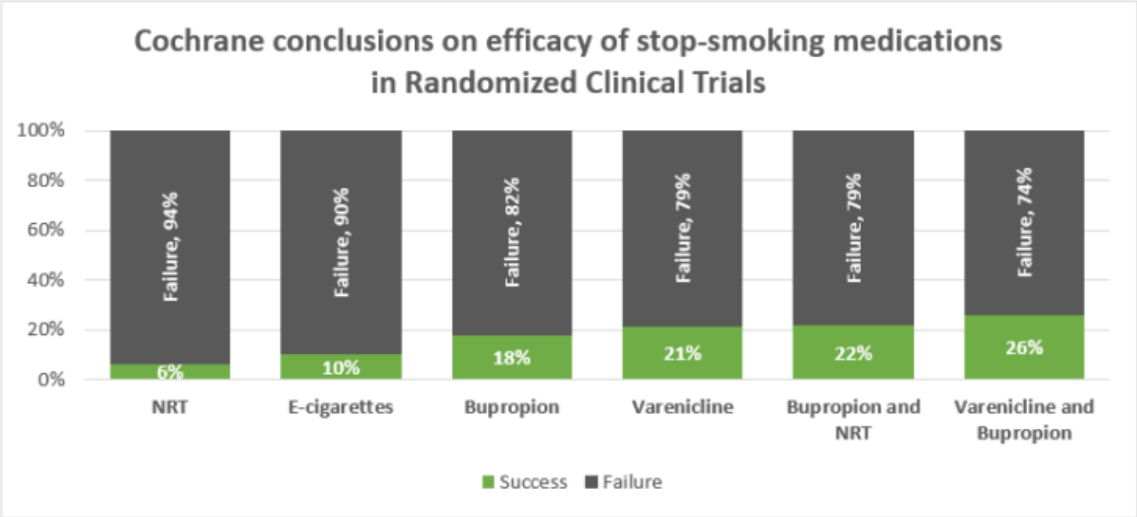
Among these medications are prescription medications Varenicline and Bupropion. These drugs do not replace nicotine from tobacco, but instead help the smoker end nicotine addiction by altering the brain's response to it. Varenicline reduces nicotine withdrawal symptoms and diminishes the rewarding effects of cigarettes. Through a different mechanism, Bupropion also decreases nicotine withdrawal symptoms and may diminish the rewarding effects of cigarettes. Other over-the-counter stop-smoking medications authorized for sale include the natural health product Cytisine and the prescription anti-depressant Nortriptyline.

A 2020 review by Cochrane looked at the effectiveness of some pharmacotherapies, using similar analytic methods to those used in the review on e-cigarettes. This review concluded that for every 100

people who tried to quit smoking:

- 17 to 20 were successful at quitting for at least 6 months if they used Bupropion alone (80 to 83 failed).
- 17 to 28 were successful if they used Bupropion and NRT (72 to 83 failed).
- 21 were successful if they used Varenicline alone (79 failed).
- 20 to 33 were successful if they used Varenicline and Bupropion (67 to 80 failed).

Cochrane's conclusions on efficacy of stop-smoking medications are displayed below:



Source:
Cochrane Library, Electronic cigarettes for smoking cessation (Review), 2022
Cochrane Library, Antidepressants for smoking cessation. 2020

Randomized Clinical Trials are designed for therapeutic medication and are not the right yardstick to assess consumer product use.

In developing its assessment of the effectiveness of e-cigarettes as cessation devices, the Cochrane reviewers considered only clinical trials that used randomized control trials (RCT). This may be the gold standard for assessing medications before granting licensing approval, but it does not reflect the reality of most smokers' quit attempts.

In RCT's, smokers are engaged and participating in a therapeutic cessation attempt, often using a specified e-cigarette product. In the real world, most try to quit without any external structure or support and use a variety of products.

Stan Glantz provides a good discussion of why Randomized Control Trials are not the best method for assessing stop-smoking products that are not sold as medicines.

This Cochrane review is out of step with other scientific assessments of the usefulness of e-cigarettes as quitting aids.

The Cochrane reviewers are only one of several research groups conducting systematic reviews of e-cigarettes efficacy for smoking cessation. Even among reviews that, like Cochrane, considered only

Randomized Control Trials, other scientists have concluded that even on the narrow question of whether e-cigarettes are superior to NRTs, the evidence is not there.

Reviewers of RCT's on e-cigarettes who came to different conclusions include:

- An Australian review of RCT's found limited evidence that in the clinical setting freebase nicotine e-cigarettes are efficacious as an aid to smoking, and that they double the likelihood of relapse to resuming smoking, strong evidence that e-cigarettes increase combustible smoking uptake in non-smokers and insufficient evidence that nicotine e-cigarettes are efficacious outside the clinical setting. (Banks et al, 2022)
- An Irish review of RCT's found "no clear evidence of a difference of effect" between e-cigarettes and NRT. (Quigley et al. 2021
- A review for the US Preventive Services Task Force found "inconsistent" results in RCT's and did not conclude that e-cigarettes were effective as a therapeutic product for smoking cessation. (Patnode et al, 2021)
- The U.S. Surgeon General found that there was too much variation in the products sold and the way they were used to make generalizations about whether or not they were effective for smoking cessation. (U.S. Surgeon General, 2020).

Reviewers who considered both RCTs and longitudinal or observational studies have found no benefit to quitting with e-cigarettes. These include:

- A Swedish review of RCT's and longitudinal studies that found no net benefit to the use of e-cigarettes for quitting smoking was found. (Hedman et al, 2021)
- A study following American smokers over time found no evidence that higher nicotine e-cigarettes (or lower nicotine cigarettes) improved successful quitting or prevented relapse (Chen et al, 2022)
- A US study looking at RCT's and observational studies which found that although e-cigarettes were effective when used as therapeutic interventions in clinical settings, this was not the case when they were sold as consumer products in the general population. (Wang et al, 2021).
- Another study using the same longitudinal study found that dual users were less likely to quit. (Osibogun et al, 2022)

Relevant also is a study conducted by Environics for Health Canada, which followed vapers over a two-year period finding no net reduction in smoking (Environics POR 113-20)

Outside of the United Kingdom, very few medical bodies recommend e-cigarettes for smoking cessation. Those which advise doctors to refrain from recommending e-cigarettes to smokers include the College of Family Physicians of Canada and U.S. Preventive Services Task Force. This summer, leading Canadian smoking cessation specialists Peter Selby and Laurie Zawertailo published a Clinical Practice review on Tobacco Addiction in the New England Journal of Medicine, concluding that even though they believed nicotine e-cigarettes may be more effective than nicotine-replacement therapy *"We would recommend against the use of e-cigarettes for smoking cessation given insufficient evidence to support their use."*

The role of e-cigarettes in smoking cessation is currently under review by the Canadian Task Force on Preventive Health Care.

This Cochrane review did not address the non-clinical (public health) consequences of e-cigarette use

There are a number of aspects of e-cigarette use that were not included in the Cochrane assessment, and many harms which were not included in their definition of “adverse consequences”. These include:

1) the increased health risks incurred by smokers who try e-cigarettes, but continue to smoke (dual users), thereby inhaling the different harmful chemicals in each type of product.

2) the increased health risks incurred by smokers who successfully quit with e-cigarettes, but who continue to use them. (The Hajek RCT found that those who successfully quit using NRT are half as likely to continue using nicotine as those who used e-cigarettes).

3) the initiation into nicotine use by young people who are influenced by messaging that encourages e-cigarette use.

4) the role of the tobacco industry in designing and supplying both cigarettes and e-cigarettes, and the commercial pressure that encourages them to market these in ways which maintain sales.

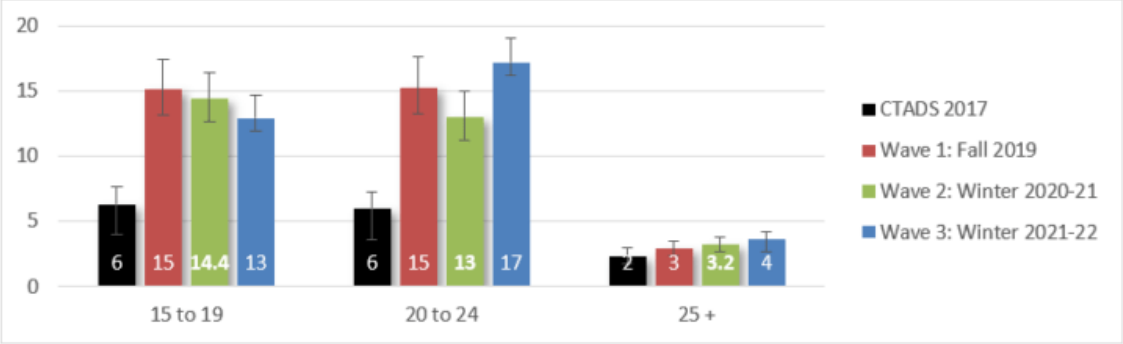
In the full (pay-walled) version of their report, the reviewers acknowledge this limitation of their study: *“Reviews of ECs for policymaking are often broader in scope than our review, which focuses exclusively on their role in supporting smoking cessation in people who smoke. Outside of smoking cessation, there remain unanswered questions about the impact of EC availability and use on young people; we will be evaluating this in a separate review.”*

There is no evidence that encouraging smokers to use e-cigarettes has benefitted health in Canada.

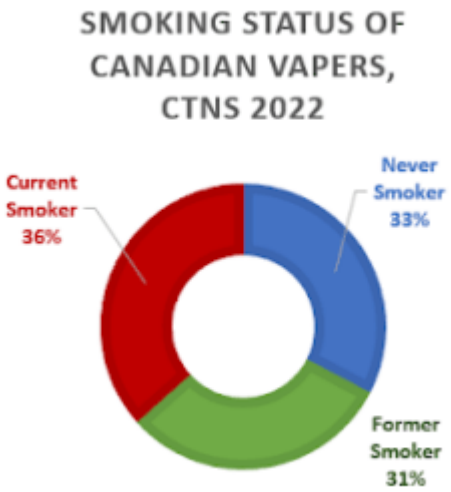
The federal policy decision in 2016 to liberalize the sale of vaping products as consumer goods remains controversial. Four years have passed since this policy became law with the 2018 Tobacco and Vaping Products Act)

The impact of this policy change is reflected in federal surveys, which show that the uptake of these products was largely among young people, and not among adult smokers.

FIGURE 1B: PREVALENCE OF PAST-MONTH VAPING BY AGE GROUP CTNS 2019 TO 2022



Although smoking rates continue to decline, Federal surveys show that this is chiefly due to the growing population of never smokers, and that the quitting rates in Canada have not increased since e-cigarettes were legalized.



Currently in Canada, two-thirds of e-cigarette users either continue to smoke cigarettes (36%) or have never smoked (33%).

More about the Cochrane reviews of tobacco interventions

Over the past 30 years, Cochrane (formerly the Cochrane Collaboration) has served health scientists by gathering, screening, reviewing and reporting on research on a wide range of health issues. The work of these scientists is guided by a conflict of interest policy which precludes reviewers from being employed in a commercial organization with an interest in the intervention, or having a direct commercial interest, such as owning a patent. Funding for the reviews can come from a variety of sources — this recent review on e-cigarettes was funded by Cancer Research UK.

Within Cochrane, the Tobacco Addiction Group (CTAG) is responsible for assessing tobacco-related science. This specialty group currently offers more than 80 reviews on tobacco-related topics ranging (alphabetically) from acupuncture to workplace interventions.

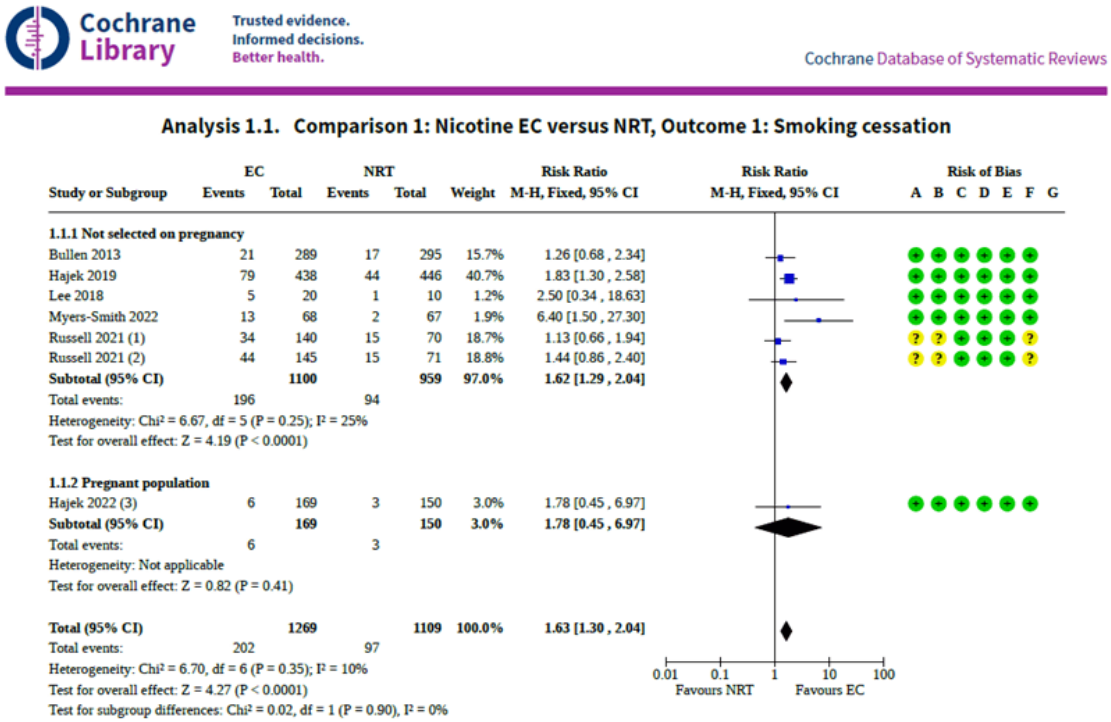
Some of these CTAG reports review the evidence on clinical topics (i.e. medicines, behavioural counselling, or alternative approaches like hypnosis and acupuncture). Others cover programmatic interventions (such as competitions, incentives, self-help materials and exercise programs). Public policy issues are also reviewed (like advertising, smoke-free spaces, or sales to minors laws.) Despite the preference for Randomized Control Trials (RCT), reviews sometimes include other study designs, like comparing population-level behaviours over time. In 2021, Cochrane updated its special collection on Stopping Tobacco Use.

(The Tobacco Addiction Group reports it is being disbanded effective March 2023 and says it is “no longer accepting any new submissions or proposals for reviews.”)

More about the Sixth Cochrane review of e-cigarettes

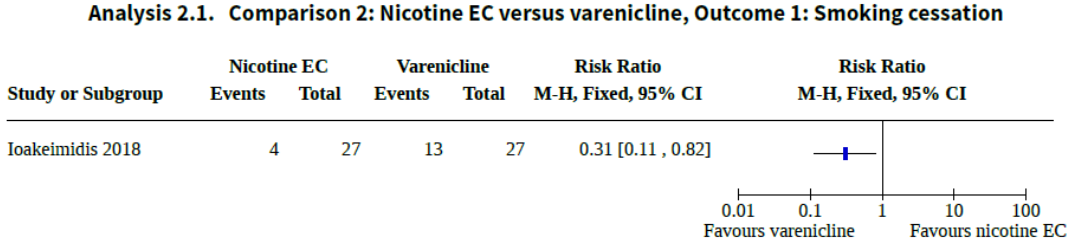
The estimate of the comparative benefits of e-cigarettes were based exclusively on clinical experiments that that made head-on-head comparisons of e-cigarettes and NRT by randomly assigning would-be quitters to trying e-cigarettes or using NRT. (Random Clinical Trials).

This group accepted only 6 RCT's for their study — two of which had been written by members of the Cochrane review team. This is shown in the detailed results of their review (available only behind a paywall), which list the studies and the amount of weight each carried in arriving at the final estimate. Two fifths (41%) was based on a 2019 study by Peter Hajek and 16% on a 2013 study by Chris Bullen. (Drs. Peter Hajek and Chris Bullen and co-author Dr. Hayden McRobbie were among the 12-member Cochrane review team).



The Hajek study has been discussed here before, with attention to the 'small-print' findings that did not make their way to the core publication — namely that in this study NRT performed twice as well as E-cigs at achieving nicotine abstinence and preventing dual-use. Those assigned to use NRT group had more than double the success in ending nicotine use (7% vs. 3.2%). Those assigned to use e-cigarettes had a much higher risk of becoming dual users (25.1% vs. 15.2%). This Cochrane update similarly left the issues of dual use and nicotine abstinence unaddressed.

The 'free' version of the Cochrane review on e-cigarettes released last week mentions that a comparison was made with Varenicline (a stop smoking medication available on prescription), but fails to mention that in this comparison, e-cigarettes did poorly. The full report presents the results of one head-to-head comparison between varenicline and e-cigarettes. (Ioakeimidis, 2018). This small study found those who used e-cigarettes were one-third as likely to quit as those who used varenicline.



Cochrane review update leaves big questions unanswered regarding vaping: implications for medical practitioners

To the Editor:

We read with great interest the recent correspondence by Pisinger and Vestbo [1], published in the *European Respiratory Journal*, which summarises the findings of a Cochrane review on electronic cigarettes for smoking cessation [2]. We strongly agree with Pisinger and Vestbo [1] that the authors have not presented a balanced scientific view and have overlooked the dangers of early, such as e-cigarette or vaping associated lung injury (EVALI), and long-term electronic cigarette use. This is an important public health issue, and we would like to further enhance this discussion.

This latest Cochrane review [2], with some authors having expressed past pro-vaping views, is an update to a review completed in 2014 [3], which we believe should be viewed with caution. The most notable aspect they overlook is that electronic cigarette studies do not provide acceptable figures for successful smoking cessation. One randomised controlled trial featured shows poor cessation rates and an alarming 80% of users trialling electronic cigarettes that continued vaping following the trial [4]. The other major result ignored was that 96.3% of subjects remained dependent on nicotine following the trial of electronic cigarettes [4]. The Cochrane update in 2020 continues to recommend electronic cigarettes as both a stand-alone and adjunctive cessation tool, whilst failing to acknowledge emerging studies which detail toxicity and pathology linked to electronic cigarette use.

In Australia, the Therapeutic Goods Administration (TGA) decided that as of 1 October, 2021, the importing of nicotine by consumers will require a prescription from a medical practitioner. In Australia, the TGA is tasked with the role of testing and approving new medications. It is therefore of interest that no liquid nicotine products are TGA approved, although it is the TGA that has confirmed that nicotine-containing electronic cigarettes can from October 2021 only be accessed by doctor's prescription. It is with great astonishment that products linked to the tobacco industry with undetermined chemical content and safety, can then be legally obtained through general medical practitioners, known as GPs in Australia. Worldwide, no vaping product has been put forward as a "medicine" and their efficacy and safety as cessation tool has yet to be properly assessed. Many Australian GPs are of course wary and concerned about prescribing electronic cigarettes as a smoking cessation aid, according to the public statements made by Australian Medical Association. However, GPs can refuse to prescribe electronic cigarettes whilst still providing other cessation tools and advice. We strongly believe that hesitance is warranted in relation to these new rules and that GPs should continue to offer alternative and safer cessation advice. In conjunction with this decision, the Australian government is providing AUD 1 million in funding towards a smoking cessation education campaign. Between now and 1 October we anticipate a slew of ripostes from pro-vaping groups and big tobacco in rebuttal to the decision. The updated Cochrane review from Hartmann-Boyce *et al.* [2] appears to maintain emphasis in the opposite direction, in relation to education surrounding the danger of electronic cigarette devices. TGA delegates note in their decisions that current available evidence does not support that electronic cigarettes are a safer alternative to smoking cessation aids currently available. They are also in agreeance that there is currently insufficient evidence to conclude whether electronic cigarettes can benefit smokers in quitting. The largest and most dangerous unknown with electronic cigarettes is the potential early and long-term harmful effects. Long-term effects could include damaging effects on cellular metabolism and DNA damage [5].

Cite this article as: McAlinden KD, Barnsley K, Weber HC, *et al.* Cochrane review update leaves big questions unanswered regarding vaping: implications for medical practitioners. *Eur Respir J* 2021; 57: 2100022 [https://doi.org/10.1183/13993003.00022-2021].

FIGURE 1 Electronic cigarette aerosol constituents and their pulmonary pathological implications.

Numerous researchers agree that the development of electronic cigarette-related illness will outweigh any short-term benefits, but the evidence for short-term benefit is lacking. The naivety and innocence of young vapers experimenting with a combination of inhalants could result in the development of ongoing respiratory distress and long-term management of damaged lungs. For those suffering from strong nicotine cravings, the most vulnerable may be persuaded to switch to vaping based on flawed evidence. Worse, some will continue "dual use" of both combustible tobacco products and electronic cigarettes,

resulting in adverse health outcomes. It is suggested that many people who use electronic cigarettes are not trying to quit; they simply want to vape and/or smoke. Electronic cigarettes are nothing more than an addictive recreational drug and can be overlooked as a magic remedy for nicotine addiction.

We have shown high concentrations of nicotine to be cytotoxic and therefore the blending of nicotine into e-liquids for the consumer is hazardous [5, 6]. We have also maintained our opinion that vaping with nicotine is an avoidable risk factor in the coronavirus disease 2019 (COVID-19) pandemic [7]. In a recently published study, we confirmed that electronic cigarette condensates increases the expression of SARS-CoV-2 (COVID-19) receptor angiotensin-converting enzyme-2 (ACE2) in primary human small airway epithelial cells and bronchial epithelial BEAS-2B cells [8]. Concentrations of nicotine and the production of other volatiles in electronic cigarette aerosols could lead to an epidemic similar to the EVALI outbreak in the USA [9]. Counterfeit electronic cigarette cartridges (containing THC and vitamin E acetate), particularly localised to, but not limited to, the USA, were deemed to be the source of EVALI admissions. Further electronic cigarette vapour constituents and their pathological implications in the lung are shown in figure 1. Of utmost importance, we amongst an array of other scientists have repeatedly shown electronic nicotine delivery devices to be toxic and in no regard a "safer" option to smoking tobacco [6]. We believe, however, that the remarkable modifiable nature of electronic cigarettes should be of the greatest concern in their apparent promotion by psychologists, parliamentarians and pro-vapers. Any combination of fluid can be placed into these devices which in themselves can be modified to aerosolise the liquid at various high wattages. Just as there is no regulation of the content and engineering of cigarettes in Australia, which have evaded any scrutiny for over a hundred years, nor is it apparent that there is any likelihood on the horizon of regulation of electronic cigarette content or engineering, due to the avoidance of scrutiny by manufacturers and their powerful lobbying endeavours. Tobacco manufacturers can lawfully insert anything they choose, however toxic, in their products and the same applies to electronic cigarette manufacturers. It was reported in the recent Australian Financial Review (20–21 February, 2021) that the tobacco industry contract-funded peak retailer organisations to promote electronic cigarettes, and successfully lobbied for a Senate enquiry. TGA director Prof. John Skerrit told the enquiry "I believe that smoking is more harmful than vaping but that does not make vaping harmless – in the same way that being hit by a car on the freeway is less harmful than being hit by a truck but it is not desirable."

With the responsibility of prescribing electronic cigarettes with nicotine to new and old vapers in Australia, GPs are also given the task of deeming (in practice, guessing) what concentration is "safe". Nicotine concentration has been shown to vary significantly in previously available e-liquids, and high nicotine concentrations have been shown to be cytotoxic [10]. Liquid nicotine can be lethal if swallowed by children, and one Australian coroner has reported this fact. Will Australian GPs be thoroughly educated in what could be a "safe" mixture for electronic cigarette consumers? Great responsibility will now lie with GPs and their professional associations.

We strongly believe that both tobacco smoke and electronic cigarette condensates in the lungs are neither healthy, nor safe. Coupled with the probability of long-term adverse health effects, this should be sufficient to convert the opinion of fence-sitters, parliamentarian, and pro-vapers with a conscience. Great caution should also be taken by policymakers when promoting such products. We do not believe that substantial evidence exists for electronic cigarettes to be used as a tool for smoking cessation. In our opinion, the risks of electronic cigarettes are far too great for them to be deemed safe to be prescribed by medical professionals.

Kielan Darcy McAlinden[1,5], Kathryn Barnsley[2,5], Heinrich C. Weber[1,3], Greg Haug[1,4], Collin Chia[1,4], Mathew Suji Eapen[1] and Sukhwinder Singh Sohal[1]

[1]Respiratory Translational Research Group, Dept of Laboratory Medicine, School of Health Sciences, College of Health and Medicine, University of Tasmania, Launceston, Australia. [2]School of Medicine, University of Tasmania, Hobart, Australia. [3]Dept of Paediatrics and Respiratory Medicine, Tasmanian Health Service – North West, Burnie, Australia. [4]Dept of Respiratory Medicine, Launceston General Hospital, Launceston, Australia. [5]Equal contributors.

Correspondence: Sukhwinder Singh Sohal, Respiratory Translational Research Group, Dept of Laboratory Medicine, School of Health Sciences, College of Health and Medicine, University of Tasmania, Locked Bag – 1322, Newnham Drive, Launceston, Tasmania 7248, Australia. E-mail: sssohal@utas.edu.au

Received: 6 Jan 2021 | Accepted: 13 March 2021

Conflict of interest: K.D. McAlinden has nothing to disclose. K. Barnsley has nothing to disclose. H.C. Weber has nothing to disclose. G. Haug has nothing to disclose. C. Chia has nothing to disclose. M.S. Eapen has nothing to disclose. S.S. Sohal reports personal fees for lectures from Chiesi, outside the submitted work.

Support statement: This work was supported by the Clifford Craig Foundation and Launceston General Hospital. Funding information for this article has been deposited with the Crossref Funder Registry.

References

1 Pisinger C, Vestbo J. A new Cochrane review on electronic cigarettes for smoking cessation: should we change our practice? *Eur Respir J* 2020; 56: 2004083.
2 Hartmann-Boyce J, McRobbie H, Lindson N, *et al.* Electronic cigarettes for smoking cessation. *Cochrane Database Syst Rev* 2020; 10: CD010216.
3 McRobbie H, Bullen C, Hartmann-Boyce J, *et al.* Electronic cigarettes for smoking cessation and reduction. *Cochrane Database Syst Rev* 2014; 12: CD010216.
4 Hajek P, Phillips-Waller A, Przulj D, *et al.* A randomized trial of e-cigarettes *versus* nicotine-replacement therapy. *N Engl J Med* 2019; 380: 629–637.
5 Sohal SS, Eapen MS, Naidu VGM, *et al.* IQOS exposure impairs human airway cell homeostasis: direct comparison with traditional cigarette and e-cigarette. *ERJ Open Res* 2019; 5: 00159-2018.
6 McAlinden KD, Eapen MS, Lu W, *et al.* The rise of electronic nicotine delivery systems and the emergence of electronic-cigarette-driven disease. *Am J Physiol Lung Cell Mol Physiol* 2020; 319: L585–L595.
7 McAlinden KD, Eapen MS, Lu W, *et al.* COVID-19 and vaping: risk for increased susceptibility to SARS-CoV-2 infection? *Eur Respir J* 2020; 56: 2001645.
8 McAlinden KD, Lu W, Ferdowsi PV, *et al.* Electronic cigarette aerosol is cytotoxic and increases ACE2 expression on human airway epithelial cells: implications for SARS-CoV-2 (COVID-19). *J Clin Med* 2021; 10: 1028.
9 Harris D, Lanspa M, Anderson B, *et al.* Prevalence of diagnoses and comorbid conditions in patients with e-cigarette, or vaping, associated lung injury (EVALI). *Eur Respir J* 2020; 56: Suppl. 64, 1999.
10 Omaiye EE, McWhirter KJ, Luo W, *et al.* High-nicotine electronic cigarette products: toxicity of JUUL fluids and aerosols correlates strongly with nicotine and some flavor chemical concentrations. *Chem Res Toxicol* 2019; 32: 1058–1069.