Transcript

Let’s talk e-cigarettes

Podcast 42, May 2025, Dr Steven Cook

Speaker 1: Musical intro & outro

Speaker 2: Nicola Lindson, NL

Speaker 3: Jamie Hartmann-Boyce, JHB

Speaker 4: Steven Cook

Musical intro

If asking your mate down the pub about vaping is what they probably say, no one agrees if it's safer or not, so you might as well smoke anyway. Now what your mate needs is a Cochrane review. All the facts have been checked at least twice. They find there's a lot that the experts agree on might give you different advice.

Speaker 2 NL

Hi, my name is Nicola and I'm a researcher based at the University of Oxford in the UK.

Speaker 3 JHB

And I'm Jamie and I'm a researcher based at the University of Massachusetts Amherst in the United States.

Speaker 2

We are both members of the Cochrane Tobacco Addiction Group. Welcome to this edition of let's talk e-cigarettes. This podcast is a companion to a research project being carried out at the University of Oxford where every month we research the e-cigarette research literature to find new studies. We then use these studies to update our Cochrane systematic reviews of e-cigarettes for smoking cessation and interventions for quitting vaping. This type of review is called a living systematic review and in each episode we start by going through the studies we found that month and then go into more detail about a particular study or topic related to e-cigarettes.

Speaker 2, JHB

Hi, everyone. This month we ran our searches. On May 1st we found one new ongoing study on the use of e-cigarettes for quitting smoking. And one paper linked to a study we already included in that review. We also found one new study of an intervention for vaping cessation and four new ongoing studies of interventions for quitting vaping. We'll tell you about those in a nutshell.

Speaker 3, NL

So our ongoing study looking at e-cigarettes for smoking cessation is reported in a trial registry and is called STEPS, which stands for the substance use trial of e-cigarettes or pharmacotherapy for smoking. It is being run out of the Medical University of South Carolina in the US and funded by the National Institute on Drug Abuse. It aims to look at whether nicotine vapes can help people who smoke and are in treatment for substance abuse disorder to stop smoking in comparison to combination NRT in the form of patches and lozenges. They aim to include 240 participants and to complete the study by the end of 2028. One new included study for the interventions for quitting vaping review is the study led by Professor Evans and published in the Journal JAMA in April comparing varenicline to placebo, we covered that study in our deep dive last month. So For more information on that, please listen to our April episode. Our first ongoing study on quitting vaping is looking at the development and evaluation of a culturally grounded intervention for rural Hawaiian youth. The study will compare a classroom based, culturally grounded intervention with no intervention. It's described as a prevention intervention, but we, including at this stage in case they also aim to help youth or ready vaping to quit. And if they present those results in a way we can use them. So this study is being carried out at the university, Hawaii and it is funded by the NIH. They plan to recruit 500 participants and to complete the study by mid 2027. The second ongoing study on quitting vaping is investigating a digital intervention, including text messages, photo messages and short form videos for smoking cessation among young adults in Korea. When this study defines smoking, they're including nicotine, vaping, which is why we are including this study here. However, when the study is complete we will need to see whether they split their results in a way that we can use in our study. The study is being conducted by researchers at the Ewha Women's University. They plan to recruit 60 participants, and it's not clear who the study is funded by as the information is coming from a trials registry with very limited information.

Speaker 2

Thanks, Nicola. The third new ongoing study of an intervention for quitting vaping is also available only via trial registry records. So we don't have that much information on it, but we know it aims to test a vaping cessation app in young people. It's due to complete in 2027 and this is a big trial. They're aiming to recruit over 1300 young adults aged 18 to 30 who vape. Participants are going to be randomized to one of two groups testing two different versions of this app for vaping cessation. This study is being led out of the University of Washington in the US and it's funded by the National Institute on Drug Abuse also in the US. The fourth new ongoing study looking at quitting vaping is led by Belinda Borrelli at Boston University in the US it actually is a published protocol in the journal JMIR Research Protocol so we have a bit more information on it. It's funded by the American Heart Association, and it's finished now, but results are not yet available. So for us it's still classed as an ongoing study until we're able to see those results. In this study, they randomized 119 high school students to a virtual reality intervention or to a control condition, including assessment only. In this study, they were looking both at vaping prevention and at vaping cessation, and as a result, the virtual reality program targeted things that have been associated with vaping like mood and stress in young people. As well as vaping prevention and cessation skills. So that's it for our quick summaries of this month's new and ongoing studies. It's been an active month. It's great to see more research getting underway and we look forward to seeing those results when they're available.

So for this month's deep dive. I had the pleasure of speaking with Steve Cook from the University of Michigan in the US. So, Steve is not an author of one of the studies we include in our review, but I invited him this month because we both attended and presented at the US E-Cigarette Summit in Washington, DC this May. Steve speaks really eloquently and cares passionately about what some might consider a slightly technical topic. Definitely a vital one: how best to establish the risks of vaping from available observational data sets. Just as a note, before we get started with this interview for reference, Steve has recently published a paper alongside someone who's been affiliated with JUUL and we do discuss this paper in this interview alongside other things. Steve himself is not affiliated with the tobacco or vaping industries. To start with, can you tell us about your background and what got you into e-cigarette research?

Speaker 4

Sure. My name is Steve Cook. I am a assistant research scientist in the School of Public Health, Department of Epidemiology at the University of Michigan. I joined the department in 2020 one week before the pandemic started,

Speaker 2

That's the time to start a new job.

Speaker 4

So it's a good introduction. I didn't meet people in person for, you know, sometimes up to a couple of years. But I started right before the pandemic. I came to Michigan as a postdoctoral research fellow working with Nancy Fleischer. When I joined the department, I had very little background in epidemiology, and I had no background in e-cigarette research.

Speaker 2

Wild.

Speaker 4

My pre-existing background and knowledge was in criminology and quantitative methods. I took a lot of social science classes. I talked for quite a long time and through the process of teaching and learning I developed the skill set and the kind of longitudinal quantitative methods and kind of research methods that are now apply to the world of e-cigarettes. But I didn't do that really on purpose. The reason that I applied for a job with Nancy was because I had two little kids and I really wanted to see them grow up. I wanted to be closer to home. I had a lecture ship job at Cardiff University in the UK, which I really, really loved. But it was a trade-off between family and personal life, and I decided that it was best to come home to take the post doc, have a bit of a career change and then that transition I thought it was gonna be temporary, so I didn't see myself as a tobacco researcher or e cigarette researcher. But the first paper that I led at the University of Michigan was on the prospective association between menthol cigarettes and smoking cessation, and during that research we found that menthol cigarette smokers were less likely to quit smoking, which I think was fairly widely known. But we also included e- cigarettes as kind of a covariate in the analysis.

Speaker 3

Obscure science term definition. Covariates are extra factors or variables that may influence the outcome in a study. Researchers include them in the analysis to better understand or adjust for their effects.

Speaker 4

And we found out that e-cigarette was associated with an increase in cessation generally that the effect was stronger among menthal smokers but non-menthal smoke.

Speaker

Hmm.

Speaker 4

Leading to the implication that maybe a menthol ban may actually help people quit smoking if they transition to e-cigarettes. So, I didn't know anything about the literature at that time. I read about the harm reduction approach and that's where I started to think about e-cigarettes harm reducing from there and I started to do some health effects research. Nancy Fleischer and Jenna Hirsch Tech got a rapid response project funded to look at the health effects. And because I did a longitudinal study with similar methods they asked me to be part of it. So that's how I got introduced to kind of the health effects literature indirectly through Nancy and that grant.

Speaker 2

I love the way that these things develop. I think we're very lucky in tobacco and e-cigarette research that you've found your way to us in a relatively circuitous way. So we've just seen each other in DC, where you were presenting at the E-cigarette summit. And I'm also aware of a new recent perspective piece you co-authored in I-Science. And I wondered if you could kind of briefly set the scene for why this work on observational studies of exposure to to tobacco and nicotine products matters.

Speaker 4

So, I didn't know Gal as well. He's the first author of the manuscript. From my perspective, the need for this type of best practice framework became obvious when I started to read the literature and then to try to replicate some of the findings. So when I started the health effects research, I had very little background again and kind of integrate research. And I replicated a couple of studies using data from the Population Assessment of Tobacco Health Study.

Speaker 3

So this study is also known as PATH, and it is a US survey of tobacco use that is regularly repeated.

Speaker 4

Not because I I didn't believe them or because I was trying to discredit what they were doing. I did it because I was trying to see how people did research and because it was a different field. I became the student and I just tried to replicate and within about an hour of my replication, I'm like this doesn't really pass like the smell test. There's something going on. I thought that this specific studies I was trying to replicate where I determined that I thought they were spurious and then I dug a little bit deeper into the PATH data and realized that there were quite a number of variables that I could use to look at, you know, some of the issues around cigarette smoking, confounding and temporality kind of reverse causation stuff.

Speaker 3

Confounders are hidden variables that can confuse the results of a study. They affect both the thing being studied and the outcome, making it hard to tell what's really causing what temporality in this context is the idea that A cause must happen before its effect. For example, a risk factor must come before a disease to be considered a possible cause. And reverse causation is when it looks like a causes B, but really B is causing a. This can happen if the timing of events is misunderstood or mismeasured.

Speaker 4

And I started to go down that avenue but like I'm a conflict avoider by personality and I really didn't want to start my career in tobacco research by, like, writing sassy commentaries and other people's research.

Speaker 2

I get it.

Speaker 4

I think it's counterproductive, but I also don't think that it advances the science and I don't want my reputation to be kind of the person criticizing research.

Speaker 2

Yeah.

Speaker 4

I took the job and chose kind of epidemiological science as a discipline because I want to produce knowledge. It's not to criticize other people's knowledge.

Speaker 2

Absolutely. Yeah.

Speaker 4

So I didn't know what to do with it and we had this kind of back and forth. I met Gal. We started by talking specifically about problems with some of the existing literature areas. We think that were a problem in terms of like the science. Again, we didn't want to write a negative piece. So we wrote this best practices piece as a way to talk about how can we do this, the science, more carefully to ensure that we minimize the risks associated with spurious association.

Speaker 2

Yeah.

Speaker 4

And maximize the predictive accuracy of what we're doing. So, the back story of the paper was it started as kind of a criticism of the literature, but it kind of evolved and changed into more of a best practices framework. And the idea that we need to stop future research from replicating and reproducing the same problems that we're seeing in a lot of the studies.

Speaker 2

Yeah. Nice. Absolutely. And so one of the real challenges when it comes to e-cigarettes, I think it's fair to say is all of the conflicting information and uncertainty out there around long-term health effects, right? We have randomized trials of e-cigarettes and people who smoke, but those don't follow-up people for very long until you know the last five years or so. We had very few people who vaped who didn't have any history of smoking, which also made it more difficult to look at. And yet, of course, people want to know what are the long-term health harms of e-cigarettes in a way that's beyond just like the toxins, but actually was going to happen to them in terms of diseases. So, what do you think if someone was going out to do this research or reading a paper that was reporting this sort of research, what are your kind of red flags or green flags? What are things you'd look for or be alarmed by.

Speaker 4

Right. Great question. And I do think of things in terms of like red flags. I think that the main red flags are cross-sectional data. So asking people at one point in time.

You know, do you use these cigarettes and then have you ever in your life had a health outcome specifically, you know, like a myocardial infarction or a stroke, or COPD, or chronic long term health outcome, we can't really separate the cause and effect. It becomes really hard in the e-cigarte literature because a lot of people who use who smoke cigarettes use e- cigarettes after they already have the symptoms or in some cases, after they've even had the health effect.

Speaker 2

Exactly.

Speaker 4

And the inability to disentangle the timing of that is a real problem, and so I think that some of the studies that are published are actually finding a switching effect, that it's not a health effect. It's like there's a group of people who use these cigarettes after they get sick. That's what I mean when I referred to reverse causation earlier.

Speaker 2

Yeah.

Speaker 4

So that's like red flag #1. Red Flag number 2 is about cigarette smoking histories.

Speaker 2

Mm-hmm.

Speaker 4

The best studies and the e-cigarette literature that don't use PATH typically look at cigarette smoking status. So, like current / former / never cigarette smoker, they adjust for it and if that's the data you have, that's all you can do. That's better than not adjusting for it, but it doesn't really deal with the underlying confounding.

Speaker 2

Yeah.

Speaker 4

So, in other words, it's like how much you smoke cigarettes for and how long you've smoked cigarettes for really matter and the people who use e-cigarettes. And this is true not just of like the first and second wave of PATH. I think it continues to be true, but the people who use e-cigarettes tend to have the longest cigarette smoking histories.

Speaker

Hmm.

Speaker 4

And because they smoke more cigarettes for longer periods of time, adjusting for status doesn't adjust for differences in cigarette-years.

Speaker 3

Cigarette pack years are a way to measure how much a person has smoked over time.

Speaker 4

And so it's like a confounding effect that they can't really deal with or adjust for. So that's really hard. Yeah. I think that at minimum, we should be adjusting for cigarette smoking histories and other tobacco products and other combustible products. So I think with, like, younger populations, we need to adjust for cannabis use and vaping cannabis.

Speaker 2

Yeah. Totally.

Speaker 4

Because that's an important confounder, and without these adjustments, we can't really look at the independent effect of e-cigarette exposure on the outcomes and we don't have the luxury of having randomized clinical trials, right? We have messy data and what we're trying to do is adjust for potential confounders and if those confounders aren't adjusted for, it increases their chance of like a Type 1 error or saying somebody has the health outcome when they don't, which is why I think some of the results are spurious.

Speaker 2

Yeah.

Speaker 4

So that's the second big red flag and the third one, which is also related and I think it's important is the idea of pre-existing conditions. The idea that you actually have high or elevated respiratory symptoms at baseline when you start using  e-cigarettes. And again, it makes it hard to kind of compare apples to apples. It's like, what's the counterfactual? What would happen if that person kept smoking? You know, I think that our framework and what we've tried to like push forward is not just like, how can we look at the harmful health effects, but you can take the same research question and flip it upside down and also look at what are the protective factors, you know, what's the harm reducing effect of changing to e-cigarettes if you're a lifelong cigarette smoker, does it delay kind of the onset of some of these chronic diseases but trying to make sure that people are being thoughtful about how they set these things up and the other red flag which shouldn't be a red flag, but it is. It is kind of the idea of like biological plausibility, like there should be a mechanism that underlies the study that you're doing. So the idea that you know, using these cigarettes once or twice in your life might increase the risk of something like. COPD which is like a chronic and long term health outcome. I think is a problem, so the studies that don't have that are problematic. I think at best and I was really, really shocked entering the space to find out how many of these studies were getting published.

Speaker 2

Ohh so many like an explosion of literature in this space, yeah.

Speaker 4

It's an explosion and it's exhausting to try to keep up with the literature. And when you see those main concerns, then you're like, it's hard to take the results seriously. Really.

Speaker 2

Absolutely.

Speaker 4

Especially when the caveats and the limitations section don't talk about these, the magnitude and scope of the limitations. So yeah, So what are you left with kind of like one further step is it's not just the studies that have been published. Now  I'm starting to see stuff on cancer and mortality in e-cigarettes and they're taking cross-sectional studies and linking it with other data sets and reproducing the same problems.

Speaker 2

Yeah.

Speaker 4

That make it hard to us for us to identify the independent effect of e-cigarrete use.

Speaker 2

Absolutely. And you know, I've also seen examples where, to be fair to the authors of the papers, sometimes they're very clear that they're not looking at, you know, they haven't used methods to infer causality. They're talking about associations. And then you see a press release or press coverage of it that is totally written in causal language. So the way these are interpreted is a challenge.

Speaker 4

And that's the thing. It's how people read them. Not everybody has training and causality versus association, and it makes it tricky. I actually think this is maybe like a little bit of a side note, but I actually think that we should try to approximate causation with epidemiological research.

Speaker 2

Exactly.

Speaker 4

Realizing that we can never achieve it, but we're trying to answer a question. So what we are trying to do is say do these cigarettes increase the risk of a specific health outcome? And I don't think the best studies in the field, including the stuff that we've managed to publish answers the question, but it does provide a framework of how we can limit concerns and, over time, get a better estimate of what the health effects are.

Speaker 2

Yeah.

Speaker 4

Knowing that there's error and it's not perfect, but the ability to do careful science, we live in a world where people are trying to publish papers to add to their CV. Nul findings don't get published the same way that positive significant associations get published, so the literature reflects that. I can only imagine how hard it is for someone who's grappling with trying to quit cigarette smoking, who then looks at the literature and they get conflicting information. And not all these studies are created equal. When they get summed together in meta-analysis, it makes it seem like we have a consensus in the literature. When that's not really the case.

Speaker 2

Thank you so much. Alright, so I've gotta wrap this up, but what would you? Will you leave us with some thoughts or one thought about what you'd most like to see done next in this research space. If you had like a magic wand or tons of research funding that you could just throw at someone, what would it be?

Speaker 4

Right. That's like asking my 5 year old what she wants for Christmas. It's like a dangerous thing to ask. I can say like a couple of general things and maybe one specific.

Speaker 2

OK. Yeah.

Speaker 4

Like next step for like research that I'm thinking about in terms of general research, I think we need more prospective data.

Speaker 3

Prospective longitudinal data is information collected by following the same people overtime, starting in the present and moving into the future. This helps track how things change and may help uncover causes.

Speaker 4

Need longitudinal data. I think that we need better prospective longitudinal data. We shouldn't use cross-sectional studies. We need detailed cigarette smoking histories for surveys that ask about cross-sectional outcomes if they have one follow up question that asks how many years ago has it been since you had the diagnosis? That would go a long way in helping with temporality and the same with the e-cigarette exposures. So I think that those things could help us do better research.

Speaker 2

Yeah.

Speaker 4

I think that we should probably stop publishing as many cross-sectional studies that are out there and focus on the prospective literature and try to get access to resources. And I think in terms of like something practically that can and should be done is I think we need to think more carefully about how we measure e-cigarette exposure e-cigarettes have been around for roughly 15 years right now in the in the marketplace, in the epidemiological literature. Anyway, we can actually start to approximate a dose effect. So the duration of cigarette use I think is going to be an important determinant of some of these downstream chronic health effects. And I think that the ability to measure that is something that we should start taking. Seriously.

Speaker 2

Absolutely awesome. Well, that is it for me. Do you have anything else you'd like to add?

Speaker 4

No, I think that's great.

Speaker 2

That was perfect. Thank you so much, Steve.

Speaker 3

It was really great to hear, to hear more about that kind of methodological side of things Jamie and I think Steve did a great job of talking about this kind of more technical topic. So and apologies to the listener that there are some more kind of technical terms in there and we've tried to kind of explain those, but I think Steve did do a great job of, you know, explaining something which just is you just can't help talking about it in a slightly technical way. And I think it's also really important because obviously it's not just relevant to e-cigarette research, this is relevant to lots of of different research and thinking about how we interpret data. But you know, it's been really critical in e-cigarette research because obviously there are studies that have found kind of differing things using differing methods and we have to kind of look into these things that that Steve spoke about in order to kind of make sense of it, and I think, you know, none of these concepts are new. It's things that we should bear in mind when we're using these methodologies, but it's just people being responsible about communicating the the kind of limitations of the research and that I think as you mentioned in the interview, part of the issue can be the way the press reports it cannot really take that into account. And if people aren't aware of or of read the papers themselves, who may mention the limitations. That's when things can quite easily be misinterpreted.

Speaker 2

Absolutely. And you know, when Steve gave this talk in DC one of his motivations for doing it was to say please, can we not repeat these mistakes when it comes to oral nicotine pouches or other products further down the line? You know what Steve is talking about are the principles of good epidemiological research and holding people to account and making sure that studies which are looking at the effects of newer nicotine products are doing it in a responsible way is really important, but one of the things that also struck me in hearing from him was just the innate limitations in some of the data sets that are collected and simultaneously, how absolutely vital those good, thorough data sets are. Where we have prospective data and we have a sense of the timings of events and data collection, and long may those sets continue to be available because I don't know what we do without them.

Speaker 3

Yeah, I absolutely agree.

Speaker 2

Right. Alright, well, just leave it down to Nicola and I and we'll sort everything out.

Speaker 3

If only it was that easy.

Speaker 2

All right. Well, thank you all so much for listening. Thanks so much for Steve to come on and talk about these topics with us and tune in next month for another episode of Let's Talk E-cigarettes.

Please subscribe on iTunes or Spotify and stay tuned for our next episode.

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Musical outro

Vaping is safer than smoking may help you quit in the end. But remember to mention the findings we have can't tell us what will happen long term, even though we know vaping is safer than smoking, we may still find cause for concern, if you're thinking about switching to vaping do it. That's what the experts agree. Smoking so bad for you they all concur that vaping beats burning there's much to learn of effect long term yet to be seen.