Transcript September 2022 podcast Let's talk e-cigarettes

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> Music Intro.
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> If asking your mate down the pub about vaping. Here's what they probably say. No one agrees if it's safer on 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 and might give you different advice.

NL: Hi, I'm Nicola Lindson

JHB: and I'm Jamie Hartman-Boyce.

NL: We're both researchers based at the University of Oxford, where we work with 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 search the e-cigarette research literature to find new studies. We then use these studies to update our Cochrane systematic review of e-cigarettes for smoking cessation. This is called a living systematic review. In each episode, we start by going through the studies we have found that month and then go into more detail about a particular study or topic related to e-cigarettes.

JHB: So we took a little break over the summer. It's great to be back, and that means in this podcast, we are covering what we found over the last three months, July, August and September of 2022. It's been a busy summer. We found six new included studies, two new ongoing studies, and 13 records linked to previously identified studies. We'll tell you a little bit more about those six new studies in a nutshell.

NL: So the first study I'm gonna tell you about is one by Edmiston and colleagues that looked at 450 people who smoked, who were either asked to continue smoking as normal, switch to tobacco flavour cartridge, e-cigarettes, or menthol flavour cartridge, e-cigarettes. The headline finding from them is that biomarkers of harm were reduced in those people who used e-cigarettes compared to continuing to smoke as usual. However of note, this study was carried out by Altria Client Services LLC, who manufacture cigarettes.

The second study I'm going to tell you about was led by Kylie Morphett at the University of Queensland, Australia, and was a randomized trial of 1,712 participants that compared short-term use of NRT, long-term use of NRT or long-term use of NRT and or a first generation e-cigarette for quitting smoking. No significant difference in quit rates was detected between groups of participants. This study was funded by the National Health and Medical Research Council of Australia.

Now the third study and the last study I'm going to talk to you about today is an abstract reported at the annual conference of the Society for Research on Nicotine and Tobacco this year, so 2022, and it was also led by Kylie Morphett at the University of Queensland. The study had a randomized crossover design and recruited people, diagnosed with or receiving treatment for HIV or Hepatitis C or receiving opioid substitution therapy. One of the groups received nicotine replacement therapy and referral to a quit line, whereas the second group also received electronic cigarettes on top of

that standard treatment. Participants in the first arm were then also offered e-cigarettes after six months if there were still smoking. So these researchers found that offering e-cigarettes to the population studied who traditionally have low quit rates, appeared to produce higher quit rates than only offering the standard treat. This study was funded by the Australian Government.

JHB: Thanks, Nicola. And so there's three more studies to cover in this nutshell. Two of them are conducted by colleagues at the University of Salford, which is in the northwest of England. And both of these were single arm studies, essentially testing out interventions in a particularly socially deprived area.

So in the first one of these, led by Dr. Margaret Coffey 1,022 people who smoked were encouraged to switch to e-cigarettes. This was a preliminary study. They call it a pilot study, and they don't present long term data, but they found that 62% of participants had managed to quit smoking at four weeks. The study was supported by Salford City Council. It was actually published back in 2020 in perspectives of public health, but it was only just now picked up by our searches.

In a more recent single arm study. Also led by the University of Salford. A team led by Dr. Allen Price evaluated a pharmacy supported e-cigarette smoking cessation intervention in 871 adults who smoked. They looked at both kind of the hard outcomes as well as people's experiences of the intervention and service users and pharmacists spoke positively about it. Their findings were promising at four weeks. They showed quite a few people quitting smoking, but very few people were followed up at 12 months meaning the longer term results are unclear. That project was funded by Trafford Metropolitan Borough Council, and it was published in July of this year in BMC Public. The final study is from Harry Tattan-Birch and colleagues at University College London. It was published in Nicotine and Tobacco Research this June, and supported by Pfizer, Cancer Research UK and the UK Prevention Research Partnership Consortium, I had the pleasure of speaking to Harry about the study in this month's deep dive.

So, Harry, if you could start by just telling us a little bit about yourself and what brought you into doing e-cigarette research. .

HTB: Yeah, so I'm a PhD student at UCL, University College London, in epidemiology, focusing mainly on the effects of e-cigarettes and other nicotine products like heated tobacco and nicotine pouches on smoking prevalence. But my background's actually a bit strange in that my undergraduate degree was in physics and business. My master's was in psychology. And now I've sort of shifted into epidemiology.

JHB: Ah. What made you make the shift? Was it that you specifically wanted to work in tobacco or did you, were you like, I wanna do epidemiology, and then tobacco came along with that?

HTB: Well, initially I was more bored with planets and more interested in people, so that's why I moved to, to the psychology sort of side. And then, yeah, I took a research assistant role at UCL focusing on this trial that we'll discuss today actually. And yeah, I just found the e-cigarette area to be really interesting as a researcher because you can come at it from so many different angles and it requires knowledge and thinking about so many different domains.

JHB: Yeah, it's not straightforward. It's good to have an interdisciplinary background for that reason. I think I also, my undergraduate was in English literature. My master's was in the history of medicine, and then somehow I ended up getting a DPhil in primary care health sciences. So, there you go.

HTB: That's just the way it goes.

JHB: Exactly. I think it's a strength in many ways. Yeah. Uh, or at least I'd like to tell myself that. So the reason why we invited you on the podcast this month is because of your recent study of e-cigarettes as an adjunct to varenicline though we'll ask you a few other things too, but if we start off just talking about that study and how you decided to do it, or how the team decided to do it, and how it fits into the other work that your team has going on.

HTB: Yeah. Yeah. So I should say this was jointly led by myself with Loren Kock and Lion Shahab. So it, it wasn't just me, it was leading it. And a massive thanks to everyone at the NHS stopped smoking services where they actually did most of the work for the trial. So the aim of the trial was really to figure out whether adding e-cigarettes to treatment at stop smoking services with Champix or varenicline, which is a pill that essentially helps people quit smoking by blocking the nicotine receptors in the brain. Whether adding e-cigarettes to that treatment would help more people quit smoking than just using the champix, the varenicline pills alone. That that was the, the idea. Uh, and there were some, some hiccups, as I'm sure get into later.

JHB: Fantastic. So it was a randomized controlled trial, is that right? And it set out to look at differences in smoking cessation rates as well as safety.

HTB: Yeah, exactly.

JHB: Yeah. So tell us what happened with this trial. Trials don't always go as we. Hope they will.

HTB: So well. The trial was, as I said, at, NHS, stopped smoking services. The participants in the trial were basically people who came into the service asking to try and quit smoking and who were eligible to use varenicline, and they basically had a 50 50 chance of getting an e-cigarette with their varenicline. So there's two groups. One who gets the varenicilne and an e-cigarette, and one who just gets the varenicline. And then we followed them up for a few weeks to see how many, we still not smoking cigarettes in each of the two groups, we aimed to get 1,200 participants. But we ended up getting 92.

JHB: What happened? And, and the reason for.

HTB: Well first COVID happened, uh, which meant it made it a pain to try to give people the e-cigarettes for one. And also the way that we verified whether someone had quit smoking is using carbon monoxide monitors where people breathe into a monitor and it basically tells you the amount of carbon monoxide in their breath. The problem is we couldn't get them to do that if they weren't coming to the sessions, but we figured out a way to basically make it all remote as everything's sort of been going. COVID, but just as we figured that out, varenicline was pulled from the market, um, because it contained carcinogens above a certain limit, which was very annoying cause that basically meant we couldn't continue with the trial. But nonetheless, I, I do think we get some useful, albeit noisy, data from the 92 participants that did take part in the trial.

JHB: So what information do we have from those 92 Harry?

HTB: So the, the main findings were quite uncertain, but around half of the people in the e-cigarette group had quit at the 12 week follow up point compared to about a third in the control group. So it was about 50% higher rates of quitting in those given the e-cigarette. But because there's so few participants using some statistics jargon, the confidence interval span from anything from a 10% less success in quitting in the e-cigarette, people using e-cigarette, to 160% higher. So, there was really a big range of things that we couldn't rule out, but this is really where I guess Cochrane reviews and meta-analysis comes in because all these little pieces of data when they might not be definitive on their own, but they're useful in a meta-analysis.

JHB: And as long as more people do studies of varenicline and e-cigarettes as an adjunct too, which is contingent on Varenicline becoming easily available again. Yes. Yeah. And did you learn anything about safety? Was there any evidence that combining varenicline with e-cigarettes was either making people feel worse or leading to any unwanted outcomes?

HTB: So there wasn't really any strong evidence for any difference in adverse events or side effects between the people using e-cigarettes and not. But then again, we only had 92 participants. So if there were any moderate or small sized effects, we're not gonna pick them up. We're only gonna be able to see massive differences between the groups.

JHB: What might we've expected to see based on, I don't know, maybe I'm wrong here, but I would think maybe the most similar studies to this prior to the advent of e-cigarettes would be ones that might test NRT as an adjunct to varenicline. Did those show any promise or do we think there's something about e-cigarettes that might be different.

HTB: Some of the studies found similar differences as we found in our study, but also others didn't seem to show as large an effect. I feel like with NRT, this is off the top of my head, but I think there might have been more success with faster acting NRT product. So, stuff that similar to an e-cigarette, the nicotine is absorbed and into the body very quickly, unlike a patch where it takes a long time before the person actually gets the effect of the nicotine.

JHB: Can you just explain to lay listeners, right? If we think about varenicline's role as essentially trying to block the rewards that we get from nicotine, is it then weird to give people a nicotine containing product and expect that that would help.

HTB: Yeah. Well, absolutely. That's the first thing that everyone says because yeah, it does seem counterintuitive. But there's a couple of reasons why it might still be useful to give people an e-cigarette, even though the varenicline is blocking the rewards somewhat. First is that it doesn't fully block all the nicotine receptors. So there is still some effect and reward that people feel when they're using nicotine, while using varenicline, but just much less than if they weren't using it. Another thing is that there's the behavioural and habit side of using or smoking that e-cigarettes replicate. But you don't get when you're just taking a pill twice a day. So it helps to replace that. And then finally, when someone has used Champix for a while, they, they don't continue using it forever. They'll only use it for a certain amount of time. And at least speaking with some of the participants in the trial, they find it useful to have the e-cigarette as for backup, when they would be in situations when they would be at risk of smoking. So they might be out at the pub and they know that if someone offers 'em a cigarette, they might not be able to refuse. They have an e-cigarette hand or something.

JHB: And did you get any other insights, I suppose, from participants taking part in this trial? Or was there anything that they said or otherwise in terms of the study results that your team found surprising?

HTB: I guess not, not necessarily surprising, but some people felt that the vape was harsh in when they inhaled it, which I would now expect based on the sort of the vape that we gave them. We didn't use nicotine salts e-liquid, which is vapers will probably know it's easier to inhale high nicotine concentrations. With that sort of e-liquid, then with a normal one. So that was something that we found.

JHB: Thanks. And I suppose kind of maybe a difficult question to answer as we don't really know what the state is with varenicline or drugs in the same class in the UK, but does your team have any

research planned on the back of this? If varenicline came back on the market, would another big trial be on its way? Or are you kind of switching tact a bit?

HTB: It would be interesting to look at this more, to get some more data to make sure it's less noisy. And, and even if varenicline doesn't come back on the scene, there's other drugs that do essentially the same thing in the brain, like cytisine.

And if e-cigarettes could be combined with these, then that's another treatment option. And yeah, I think, I think it is important because there's potential for this to be one of the best if or the best treatment for smoking cessation because we, we know that e-cigarettes are more effective than some other treatments, and that varenicline is probably more effective than most the, the medical treatments. So yeah, combining them together could be, quite valuable. Yeah.

JHB: Holds a lot of promise, I think. So kind of switching topics now, though, we are an e-cigarette podcast because obviously I know about your Cochrane review and other work on heated tobacco products. I just wanted to pick your brain a little bit on those because I think our listeners might be interested in that topic as well. So I was wondering, first of all, if you could just tell us a little bit for those of us unfamiliar with them about what we mean when we talk about heated tobacco products and how they are similar or dissimilar to regular cigarettes or e-cigarettes.

HTB: So, as I'm sure most listeners know, an e-cigarette works by heating up a liquid that contains nicotine usually, but it doesn't actually heat up any tobacco leaf or roundup tobacco it's just that nicotine extract from the tobacco. Whereas a heated tobacco product works by directly sort of heating a, a lump of tobacco, but the aim is to heat it up to just enough high enough temperature to the nicotine vapour, but not so hot that it causes the tobacco to burn. And I guess the most popular heat tobacco product's called ICOS, IQOS, which people might have seen around, and it sort of resembles a vape with a cigarette sticking out the end of it. And that's because it works by heating these small special cigarette sticks, that one sticks into the end of the device and they, they're not especially popular in Europe or America, but they have become quite popular in some parts of Eastern Europe and also in Japan.

JHB: And so far from your research on heated tobacco products, what would you say kind of the main message are, do we know much? What do we know? What don't we know?

HTB: So while there's three different things that we looked at in the review of heat tobacco. The first is whether they help people to stop smoking conventional cigarette.

The second is, how safe are they relative to either using nothing or cigarettes?

And then finally, what sort of effect has the introduction of heated tobacco had at the population level? Has it reduced the amount of people are smoking?

And for the first question, well, there were no studies looking at whether heated tobacco helps people to quit smoking conventional cigarettes. So in that regard, it's much less data than with e-cigarettes.

For the, the safety data, there was no long term cohort studies looking at whether people who use heated tobacco are more likely to get certain diseases or die than people who don't. But that's kind of what you'd expect for such a new product and are similar really with e-cigarettes.

But what we do have is quite a lot of data looking at the biomarkers, basically the levels of toxins in people's blood or urine, who use these products or who switch from smoking to using heated tobacco. And what that data shows is on pretty much every toxin you measure when people switch

to heated tobacco, it reduces substantially compared with people who continue to smoke. And that's again, similar to e-cigarettes. But what was found is that for certain toxins, they might be slightly higher in people who switch to heated tobacco compared with those who just use nothing at all, like completely stop using nicotine.

JHB: Yeah, it's about the spectrum of risk, isn't it, and where things sit on there. Yeah. And did you find anything about your third outcome, which was population level?

HTB: So there was some evidence at the population level. Obviously with population level data it's always a bit more uncertain cause you don't have the sort of control that you have in an experiment where you can randomize people to get different treatments.

But basically what the data seemed to show is that in Japan, after the introduction of ICOS, which is popular heated tobacco product, the rate of decline in cigarette sales seemed to accelerate. It seemed to drive down cigarette sales when heated tobacco was introduced. Which seems to suggest that there was some substitution between people moving from cigarettes to heated tobacco, but it doesn't necessarily mean that people could completely stop smoking. It could just be that people reduced the number of cigarettes they were smoking and then replaced it with some ICOS.

JHB: Yeah, that makes sense. And what do you think, I mean, it's such a new area that obviously loads more research needs to be done, but what do you think are kind of the most important areas for more research in this area?

HTB: Well, I think like a e-cigarettes, I'd like to see more and more cohort data being collected and looking at the long term health effect where people have taken care to distinguish correlation from causation. Because you see a lot of the studies that have come out have been pretty bad at, but they basically can't tell you anything about the differences, the effects of using different products on health because they just haven't really taken care to distinguish those things. And also looking at the population level, whether there's been changes in smoking prevalence ie, the percentage of people who are smoking, not just cigarette sales.

JHB: Yeah, that makes a lot of sense. Thank you. That is really interesting. Do you have anything else you wanna add?

HTB: No, I think that's everything.

JHB: Brilliant. All right. Thank you so much, Harry. Thank you.

NL: So it's really great to hear from Harry there, and he kind of talks about an issue that's been quite close to my own heart around the unavailability of varenicline, as you know, Jamie, I was also hoping to carry out a trial using varenicline. So it was a bit of a headache when. Um, became unavailable, but also it does have really important implications for people who are trying to stop smoking. As Harry mentioned, the reason it was taken off the market is because through testing it was found that it has slightly higher levels of a carcinogen called nitrosamine than would usually be allowed to appear in a food or medicinal product. Actually, nitrosomines appear in most of the food. Drinks that we consume, but it's just, it has to be below a certain level in order for it to be

JHB: marketed. The irony is, as far as I understand, that they're, they're in a much higher level in cigarettes. Yes. Which makes this whole situation even more of a shame.

NL: Yeah. And so it was pulled off the market and so hasn't been available worldwide for some time. As we understand it, there are some generic forms of varenicline, so usually varenicline is manufactured by Pfizer, but some other companies are now starting to remanufacture it and make it

available again. However, unfortunately in the UK where we are based, it's still not available for people to get through the NHS, which is how they would usually get it through a prescription from their healthcare professional.

So that's a real shame. And the reason why that's a real shame is because varenicline, in terms of the kind of main smoking cessation medications available, NRT, Bupropion, and varenicline, that has been found to be the most effective and helpful to, for helping people to quit smoking. So, and it's also seen as an essential medicine by the WHO, which means that it should be available for people to use to help them to quit smoking. So it not being available is a real blow. But Jamie, I was just thinking about how this really feeds into the electronic cigarette research and makes it all more important at the moment when we don't have varenicline as an option. Obviously e-cigarettes then are a really important option for people to have to help them to quit smoking.

JHB: Absolutely. Nicola, I think we need as many options available to people as we can to help people quit smoking and the loss of varenicline, if only temporary, has been a real blow and it's a good thing at least we have nicotine, e-cigarettes and nicotine replacement therapies and more traditional forms, which can also increase chances of quitting. But we kinda look forward to seeing how this situation develops over the next few months.

NL: Yeah, and fingers crossed that medicine will become available to people again soon.

JHB: All right. Well, that is it from us this month. Thank you so much for listening. We hope you all had great summers. Thank you for Harry coming on this month to talk to us about his study and his work on heated tobacco products, and we'll talk to you next month.

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

Musical extract: 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 of switching to vaping do it, that's what the experts agree, smoking's so bad for you they all concur that vaping beats burning there's much to learn of effects long term yet to be seen.

JHB: thank you to Jonathan Livingston Banks for running searches to Ailsa Butler for producing this podcast. And to all of you for tuning in music is written with Johnny Berliner and I, and performed by. Our living systematic review is supported by funding from Cancer Research UK, the Cochrane Tobacco Addiction Group also receives core infrastructure funding from the National Institutes for Health Research.

The views expressed in this podcast are those of Nicola and I, and do not represent those of the funder.