

Transcript March 2022 podcast Let's talk e-cigarettes

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Music Intro.

If asking your mate down the pub about vaping. Here's 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 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 this month we carried out our searches on the 1st of March, we found one record, which was a protocol for an ongoing study that we had picked up in previous searches. And that you can hear more about in our January podcast, where I interviewed Dr. Sharon Cox. So in this month's deep dive. We're doing something a bit different.

We're talking to let's talk e-cigarettes' very own Ailsa Butler, who as well as being the wonderful producer of this podcast, is a researcher in our team. Earlier this year, we were successful in securing some funding from the University of Oxford's public policy challenge fund, where we worked with some policy partners, including action on smoking and health here in England, and also in England, the Office for Health Improvement and Disparities and proposed three projects, which kind of just take a bit of a deeper dive as it were into the studies that are already in our existing Cochrane review of e-cigarettes for smoking cessation.

What we wanted to do is look at three angles that are really policy relevant at the moment. The first of those is the longer-term use of e-cigarettes in people who are given them to quit smoking. And that is what Ailsa is going to be talking to us about today. The second, just to give you teasers for what you might be getting in the April and May versions of this podcast are on various different biomarkers of harm, and also on different flavours and whether or not those might play a role in helping people to quit smoking. But with out further ado, I'll hand over to Alyssa to talk to us about this unpublished research, which is currently undergoing peer review, but what she has presented at the society for research on nicotine and tobacco's annual meeting. Welcome Ailsa.

ARB: Thank you very much. Nice to be here. Yes. I've been editing the podcast series and it's really good to be here to talk to you today about our recent research. As Jamie said, we look back at the 61

studies included in our review and eligible studies from our recent searches to see whether people given an e-cigarette as a stop smoking intervention, carry on to use e-cigarettes longer-term.

There were 19 studies involving nearly 8,000 people that reported information on e-cigarette use at longer than six months. 14 of these were randomized controlled trials, and most studies took place in the UK, in the U S, for five of the studies we contacted the authors directly for this infant. So of these 19 studies, 16 were eligible to be pooled and it was shown that 54% of people continue to use e-cigarettes at six months or longer. And this didn't vary by device type or by time, the three studies that were not included in the pooled analysis, because bod has been used nicotine patches or their own devices, also all have more than 50% use of e-cigarettes at 16.

JHB: Great. Thanks Ailsa. So I think the first thing to pick up on that is we have over 60 studies in our review.

And any of those studies that gave participants nicotine e-cigarettes, as it were, we're eligible for inclusion here, but only 16 of those reported on how many people were still using nicotine e-cigarettes at six months or longer. This is something that we wanted to look at because we just received lots of emails and queries from policymakers charities, et cetera, from lots of different countries saying, but do you collect data on this? Because I think there are concerns that yes e-cigarettes might help people quit smoking, but what are the implications if people are then using those e-cigarettes long-term. And that's why we wanted to look into this. And as Ailsa said, in those 16 studies, we found that of those people given nicotine, e-cigarettes essentially a study start 50% or more on average, we're still using an e-cigarette at six months or longer.

ARB: Yes, that's right. Jamie. Then when we looked at all the studies that had information on this, there was heterogeneity some studies reported high levels of continued e-cigarette use while other studies reported lower use of e-cigarettes.

JHB: So for example, when we say there was a lot of heterogeneity here, the prevalence of e-cigarette use of six months or longer ranged from 17% in Lee 2018 to 92% of participants still using e-cigarettes in Bell 2017. And we don't know. All of the things that are driving that difference, both of these were small studies, which means you're kind of more likely to have findings due to chance. But Lee, the one with that really low rate compared to the others was in 30% suspense, 18 of them were followed up in the e-cigarette arm they're using cig-a-likes and those were veterans awaiting surgery. Whereas in Bell, we had people using refillable e-cigarettes and this was in a group of 30 people who were HIV positive, so potential differences there in terms of the study population, but also in terms of the devices they are given and perhaps their interests in use of these devices.

But also we also did a further analysis didn't we, cause we wondered if this would be different in those people who had successfully transitioned off of combustible cigarettes entirely. So those people were essentially the intervention of e-cigarette worked in the sense that they were no longer smoking when they were followed up.

ARB: Yes. We looked at people who had stopped smoking in the e-cigarette arms, bear in mind that most people not successful in quitting. There were nine studies that had information on e-cigarette use in successful. Of the people who successfully quit using an e-cigarette. The pool data showed that 70% of people were still using e-cigarettes at six months or longer. We broke this down by device type. We found that a higher proportion of successful quitters were using the newer devices for refillables this was 81%. And for pods, it was 70%. And for the older cig-a-likes, this was lower at 40. Only one study contributed to the pod group. What would also be interesting to find out is whether e-cigarettes promotes the success of not going back to combustible cigarettes. So, the

relapse rate, we want to look at, whether e-cigarettes play a role in preventing relapse to combustible cigarettes.

JHB: Absolutely. And I think one of the things we tried to do when we were writing up this paper and thinking about this analysis is really present, continued use of e-cigarettes as essentially value neutral.

We were interested in how many people were still using them. And I think different people might interpret that information differently. So some might interpret that information with a degree of alarm, because we know though considerably safer than cigarettes. E-cigarettes are not risk-free and there might be concerns around longer-term use of them.

But we also know that it could be that the fact that people are continuing to use nicotine e-cigarettes is helping them stay quit in the longer term. And I think for me, the first study that really highlighted this as something we should be thinking about was the study by Peter Hajek who's an author of ours. It was a large randomized controlled trial published in the New England Journal of Medicine. And it showed that the people given a nicotine e-cigarette are more likely to successfully quit smoking than people using nicotine replacement therapy. But one of the comments I'm one of the things people kept on picking up was that yes, but of the people who successfully quit smoking in each arm, way more people were still using nicotine e-cigarettes than were using nicotine replacement therapy.

And Ailsa it's also interesting you said that thing about possibly device type having an influence. What we found was it certainly wasn't a one size fits all answer. There was a lot of variation in the study.

ARB: That's right. So as well as looking at people who are given e-cigarettes and pooling data across those studies, in terms of how many people were using these at six months or longer, we were also interested in looking at how longer-term e-cigarette use compared to other stop smoking aids participants were given most notably nicotine replacement.

There were five studies, which compared nicotine e-cigarettes with nicotine replacement therapy or NRT, and also reported on the number of people still using their study products at six months or longer. The findings from these five studies showed differing results. There was high heterogeneity or differences between the studies and we didn't pool the results.

In three studies Bullen in 2013, Hajek 2019, and Myers Smith, 2021 more people were using nicotine e-cigarettes than NRT at 6 months. As Jamie just mentioned in hijack 2019 more people were using nicotine e-cigarettes than NRT at 12 months. And that was something that was picked up a lot in the media. When the study came out in 2019. Dr Myers Smith and colleagues similarly found in their 2021 study, there were more people using e-cigarettes than NRT at six months. Dr Myers Smith has recently spoken about their study on this podcast series. One of the first randomized control trials we had in this review Bullen 2013 also found that at six months more people were using e-cigarettes than NRT, even though this was a study of cig-a-likes.

However, by contrast Russell 2021, a study of pod devices found no difference in the proportion of participants still using study product at longest follow-up and one smaller study Lee 2018 of cig-a-likes with 30 participants should a higher proportion of participants still using NRT. So a lot more work to be done, to understand whether the continued use of e-cigarettes is one of the things that makes them more effective for helping people quit smoking compared to, for example, NRT or other more traditional stop smoking treatments.

JHB: One of the particular things I think that we didn't look at, but it would be great to look at is that we've noticed a lot of e-cigarettes that he's now when they describe the intervention they're using and the behavioral support given to people, essentially, they describe it as, okay people were given an e-cigarette, told that that was a tool to help them transition off smoking. Once that they had quit smoking completely, when they felt that they weren't no longer risk of relapse of returning to smoking, then to try and transition off the nicotine e-cigarettes. But how do people know that? How does someone who has smoked and managed to switch to e-cigarettes. Do they wake up one day and think of absolutely sure. I'm not gonna go back to smoking. So I'm going to give up on my nicotine e-cigarette as well. How do people transition off of nicotine? E-cigarettes are their withdrawal symptoms, et cetera. So I think that's an area where I'm anticipating we're going to be seeing more research in the future.

ARB: Yes. Jamie, as you say, certainly be important to look at this question of the timing of transitioning off e-cigarettes and also in terms of future research would be good to have term studies to provide this information because we need to be able to look further into the future than the normal six months, I know that it's difficult to receive funding for long-term studies, but it might even be possible to write a section into grant applications in order to be able to come back to the study one year on two years on so that this really important long-term data is gathered.

JHB: Absolutely. And I think it, there's obviously a resource angle here when it comes to longer follow-up of studies. But I think even that most basic information, like let's say, just sending a survey to your participants and saying, are you smoking. Are you vaping and doing that for a couple of years after study, I make that sound easy. It's definitely not easy, but if more studies did that, we'd be really happy. And it would be, we'd be able to say more because really the vast majority of these studies, when we say six months or longer, the follow-up time for we are talking about the six months and we don't know how use kind of changes over time.

And also one of the things that we don't know from these studies is whether people are using the same nicotine e-cigarettes or the same e-liquid that they're given it study start six months later. Or if they're experimenting, if they're trying different products, because most of these studies are only providing e-cigarettes for a limited amount of time.

And what are people doing then after the fact, are they going out, how are they finding different devices to use? How are they making those decisions? And I think that would be really interesting to know more about.

ARB: Yes, that's a really important point about e-cigarette devices or, or strengths or flavors.

JHB: So Ailsa, when we think about the studies that we're going to see in the future, what do you want to see them do?

What would help inform this analysis better?

ARB: We'd like to see future studies reporting cigarette use. I'll make a mention here of King's college's e-cigarette registry. This is a nationwide registry of participants in e-cigarette trials to evaluate long-term health outcomes associated with their use. And this is funded by Cancer Research UK.

We'd like to see the use of individual patient data to test the relationship of longer-term use of e-cigarettes with smoking cessation and relapse. It'll be of interest to look at this by e-cigarette device type and then of use. And by social characteristics. It will be informative to compare relapse rates in successful combustible cigarette quitters who do and do not use e-cigarettes.

We'd also like to encourage research into the harms caused by e-cigarettes. It is really important to have accurate information on this. As we have seen in our study that people may continue to use e-cigarettes longer term.

And so Ailsa, could you just tell us what the conclusions are from this review.

ARB: Sure, in the studies included in this review, we found that just over half of people, given nicotine electronic cigarettes, that study start, we're still using e-cigarettes at six months or more.

And 70% of successful quitters were found to still be using e-cigarettes at six months or more. We recommend that future studies collect and report data on continued e-cigarette use for more than six months as it is really important to assess whether the use of e-cigarettes is transitional or persistent.

JHB: So, thank you, Ailsa, for anyone who wants to learn more about that research, we're hoping that it will be available in a published article at some point it will let you know when it is. Finally. I think Ailsa would just be nice for people to get to know a little bit more about you. So what's your background? What did you do before you came to work with me and Nicola on e-cigarettes and how have you found working in the e-cigarettes field.

ARB: Thanks Jamie.

Well, I've always worked in health and science. I've worked in both policy and research in HIV. I've also worked in infectious diseases and vaccination policies for children. And my PhD was concerned with this work. More recently and very interestingly, my works turned to non-communicable health topics linked to for example, overweight and now smoking.

As you know, the health-related burden is very high and there's no easy solution such as a vaccine. For a number of years, I worked in parliament for the All-Party Parliamentary Group on HIV and AIDS before treatment was available. At that time, the emphasis was on education and behaviour change, for example, condom use. A very important part of this was harm reduction for example, the importance of needle exchange schemes to reduce transmission, not just of HIV, but for example, hepatitis B, among people using intravenous drugs.

The role of needle exchange schemes in terms of protecting people remains important today. I see this harm reduction theme with e-cigarettes. I'm interested in the potentially very important harm reduction role that e-cigarettes can play for people who currently smoke combustible cigarettes. I'm really interested in behaviour change and addiction, and working on this project is very much involved in both of these areas. I'm really pleased to be working on this fast, moving review with you, Jamie and Nicola, with the e-cigarette team in Oxford and our wider author team across the world. I'm very pleased to be working on a Cochrane review. I very much value this approach of bringing together the best available evidence.

So that policy is based on the most up-to-date evidence. Smoking is the leading cause of preventable illness across the world. And many people still relapsed to smoking. We need to find out what role e-cigarettes can play in this.

JHB: So is there anything that has surprised you about working one-cigarettes .

ARB: Well, just the breadth of interest in different areas.

For example, the health implications wrote of flavours, youth uptake, longer-term use role in quitting smoking potential role in preventing uptake of combustible cigarettes, and that e-cigarettes

may become a prescribed stop smoking treatment in the UK. I've been interested by the different approaches to e-cigarette policy around the world, for example in the UK e-cigarettes are looked on more as a stop smoking tool and there's regulation against advertising and nicotine levels, in the U S some restricted advertising is allowed, but they worry about youth. The approach in Australia is for e-cigarettes to only be available as a quitting tool on prescription.

I'm also interested that there's a lot of misinformation circulating about e-cigarettes for example, in the media, another reason to bring together and assess the best available evidence.

NL: So, Ailsa what we usually ask our guests on let's talk e-cigarettes is what are their kind of hopes and dreams for the future of the field, I suppose and if in an ideal world, if you could carry out any study what would that be?

ARB: I spend a lot of time looking at all the data and it'd be great to see longer-term studies for all of our outcomes, including the health related outcomes, trajectories of cessation, and longer-term use of e-cigarettes also to see studies that had a straightforward randomized control design rather than crossover design, as this makes comparison much more tricky. Information on the safety of e-cigarettes will be important in terms of the health implications of longer-term e-cigarettes.

Having said that our data indicate that e-cigarettes are less harmful than combustible cigarettes. So transitioning to e-cigarettes from combustible cigarettes, even if e-cigarette use is longer term should be of health benefit to the individual. And as I mentioned earlier, I'm interested in youth use and am watching that space.

JHB: So thank you, Ailsa.

NL: It's been really great working on this kind of slightly separate project. Hasn't it? Jamie, and kind of using the information that we already have in the e-cigarette review to look at something slightly different. And I suppose what I found really interesting about the fact that a lot of people were using e-cigarettes long-term links into a kind of age, old problem with treatment for stopping smoking.

So what we have seen a lot with traditional stop smoking medications, and one of the things that we really think affects how successful they are and helping people quit is that a lot of people aren't very good at adhering to that treatment, or basically using it, how they've been asked to do by a doctor.

For example, people don't necessarily, for example, use their nicotine patches every day, or if they've been given nicotine gum, they probably don't use it as much as they perhaps should do. And maybe one of the things that is driving the success of e-cigarettes is that people are more inclined to use it and more inclined to use it as much as they should to kind of abate their cigarette cravings. And maybe that's why then people are going on to use it in the long-term, just because it is something that they potentially enjoy using that they get something out of. Whereas they haven't had that with those traditional smoking therapies.

JHB: I think it's a really good point because, I mean, I think it's a problem with all sorts of medications, right.

And I suppose it's possibly a double-edged sword of e-cigarettes, right? If, if this is a mechanism by which they're more successful than traditional medicines, and it's because essentially they're more enjoyable to use, right? There are fewer barriers to their use that obviously that is great for people who smoke and are trying to quit and transitioned to e-cigarettes.

However, we haven't seen young people in great quantities going out and using nicotine patches or taking various kinds of prescription drugs that might help them quit smoking. Because recreationally,

quite frankly, those aren't that fun. And so we have now a product, which is maybe more enjoyable from a user perspective.

And I think that's where there's a lot of opportunity, but we also have to be sure that we're making kind of nuanced policy decisions to make sure that the benefits of these products are there for the people who stand most to benefit. But also that we're not kind of introducing them to a younger generation who might've never started smoking or using nicotine e-cigarettes had they not been as nice to use, essentially.

NL: Yeah. And I think following on from that, interestingly, we've been seeing, obviously in the searches, we do the literature that there are more and more studies coming out now looking at the success of interventions to help people stop vaping and something that'd be really interesting to see as how easy people do find it to stop vaping, because it could be that obviously people move on to vaping and that they find that as addictive as they find cigarettes, but it could be that people's addiction to e-cigarettes is nowhere near what it is to cigarettes.

And I guess we'll kind of get an indication of that in these studies that are looking at helping people to quit vaping. You know, either people will actually find it very easy and there might be light touch interventions that mean, you know, everyone can, can quit an e-cigarette or it could be that we find it's as difficult as cigarettes, or it could just be somewhere in the middle, but I guess that will be a really interesting next thing to find out

JHB: It'll be fascinating. And I think it'll be something where there's a lot of variation, not only for individuals. So we know some people find it much harder to quit smoking than others.

And that's due to various factors. Genetics being a major one, but it's also one of the really difficult things about e-cigarettes is I remember kind of early, under immediate interviews and people saying, are they as addictive as smoking. And basically even with the best research in the world, not being able to answer that question in any clear way, we didn't have the best research in the world at that time but even if we had all of our ideal studies, the reality is that even though we know nicotine, isn't the harmful ingredient in cigarettes, it is what's kind of driving and fueling that addiction. And one of the things about e-cigarettes is that they have such markedly different between device kind of nicotine profiles, not just in terms of the amount of nicotine that might be in the e-liquid, but actually possibly more importantly, the way that that nicotine is then kind of processed by your body. The various ways your brain responds to it. And so there'll always be differences and essentially the different nicotine profiles of these devices, which probably will feed into how addictive they are. And though it was thought kind of when cig-a-likes first came out and the first-generation devices, the kind of wisdom that was maybe not tested, but was often spoken about was they probably won't be as addictive because essentially they're just nowhere near as good at delivering nicotine as traditional cigarettes are, but now we're in this phase where essentially technology is evolving with one of the main purposes, really, to be getting better and better at delivering nicotine. So it'll be interesting to do that comparison and kind of addiction levels within different groups of the population between cigarettes and e-cigarettes, but also within nicotine e-cigarettes looking at the ways in which all of these different factors might influence how addicted someone is and how difficult it might be to transition off vaping. If they come to a point where they wish to do so.

NL: So lots of work still to be done.

JHB: Thank goodness. Cause we certainly like e-cigarette research, right? Well, that's it from us this month. Thank you so much for listening. Thanks to Ailsa, for producing this podcast as always, and

also for coming on as our guest speaker. And we hope to be able to talk to you again over the next couple of months, about some of the other projects that we're doing in this area.

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.