

## Transcript June 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: This month, we ran our searches on the 1st of June and found two papers linked to an already included study and three new included studies. We'll tell you a bit more about two of those new included studies in a nutshell.

The first study led by Dr. Katrina Vickerman and Optum Health was funded by the national Institute of drug abuse in the US and published in the journal, Nicotine and Tobacco Research. The study enrolled 96 dual users of cigarettes, and e-cigarettes who called a state quit line. They were randomized to receive either enhanced e-cigarette coaching or treatment as usual from the quit line. In the enhanced e-cigarette coaching arm, coaches discussed e-cigarettes as a quitting tool, similar to the way they might discuss nicotine replacement therapy. This was a feasibility study, potentially paving the way for a larger trial and as such, it only followed up participants at three months, the authors concluded that the intervention led to high levels of satisfaction and engagement from users, and that cessation rates were promising and more evaluation in a full trial. So watch this space.

NL: The second new study is reported in a conference abstract presented at the American Geriatric Society annual conference in 2022. It was a student presentation by Bonafont Reyes from the University of Puerto Rico and focuses on understanding the racial and ethnic differences in switching from combustible cigarettes to e-cigarettes in people with COPD. 48 participants were randomized to receive either nicotine replacement therapy or e-cigarettes and everyone received counselling. Smoking behaviour was only reported up to 12 weeks. And so this data isn't eligible for our review.

However, the researchers also looked at the effects of using the treatments on C O P D symptoms, which is relevant to us.

They report that there was a trend towards decreased breathlessness and C O P D symptoms in people randomized to the e-cigarette arm in comparison to those in the nicotine replacement therapy arm. The study appears to be supported through funding from the New York University.

JHB: And our third study presented the results from Hajek at al's trial of e-cigarettes compared to nicotine replacement therapy for smoking cessation and pregnancy. For our regular listeners this might sound familiar to you. We spoke to Professor Tim Coleman about this study back in May, 2021, when results weren't yet in. This month, the study's long awaited results have been published in the journal Nature Medicine. I interviewed Dr. Francesca Pesola about the results in this month's deep dive.

So to start off with, can you tell us a bit about yourself and what brought you to studying e-cigarettes?

FP: Sure. Uh, so my name is Francesca Pelosa and I'm a statistician working with Peter Hajek at the Wolfson Institute of Population Health Queen Mary University of London. I started working in the field of electronic cigarettes nearly five years ago, I would say. At the time I was working in cancer prevention research. So we were looking at electronic cigarette and making cessation as a kind of way to help smokers reduce the risk by quitting. And at the time we were collaborating already with Peter Hajek and then I just moved across to his unit.

I was the trial statistician for the tech trial that was published in 2019. And that trial found that electronic cigarettes were twice as effective as NRT, nicotine replacement therapy, in helping people quit smoking through the stop smoking services. And that was quite an exciting result and it was quite exciting to be part of that project.

JHB: Awesome. Yeah. So what was your role in the recent study comparing e-cigarettes to nicotine patches for smoking cessation and pregnancy?

FP: So again, I, I was the trial statistician for the trial. I was mostly involved in developing the statistical analysis plan and carrying out the analysis. And then I was involved in drafting up the manuscript and interpreting the results for the manuscript that was published in Nature Medicine last May.

JHB: Great. We were super excited to see that. We've already had professor Tim Coleman on a few months ago telling us about the study, but if you would just kind of remind us in your mind what the critical things we should know about the study were in terms of how it was designed and what it set out to look at that would be great.

FP: Sure. So the study was a randomised control trial. It was funded by the National Institute of Health Research. The main idea behind that the study is the fact that smoking during pregnancy can have a negative outcomes on the baby. So it mostly related to miscarriage and stillbirths, but figures from the UK, showing that even though smoking during pregnancy have been decreasing, the rates

have been decreasing over the, over the years still 10% of women are found to still be smoking at end of pregnancy. So there's obviously a need to identify some smoking cessation aids to help these women quit, at least during the pregnancy, I suppose, if not beyond ideally. So the, there are, there are a couple of trials I've been looking at nicotine replacement therapy and they have found that these products are quite effective in helping women stopping and they're safe. But this trial was the very first one that was really looking at the effectiveness and the safety of electronic cigarettes in pregnant women. The nicotine patches were our comparator because obviously they're quite a well-established product and they have been found to be useful and safe in pregnancy. They were quite a good comparator to have as a baseline.

JHB: Brilliant. And what were its main findings?

FP: Main findings were that electronic cigarettes are just as safe if not potentially safer than NRT. So we found that the incidence rate of most of the adverse birth outcomes were similar across the two study arms. But what we found was that the proportion of babies that were born with low birth weight, which we define as less than 2.5 kilos, was higher in the NRT arm. Which again we thought was an interesting finding. So that's from the safety aspect of the question. And then from the smoking cessation and the effectiveness of electronic cigarettes overall in the main analysis, we found that the rates were very similar between the two study arms, slightly higher in the electronics arm, but not significantly so, but what we had considered on setting up the study and luckily the analysis plan, was that what we had found previously is that very often you find participants in these kind of smoking cessation trials might start using the non-allocated product. So that they might be using patches in the NRT arm, and then they might also be vaping so they might be using an electronic cigarette. So if they then quit, then you're not quite sure if it's because they're using the patch or they're also helped by the electronic cigarette.

JHB: Absolutely.

FP: So mindful of this, we pre-specify the sensitivity analysis where we are going to exclude the abstainers that were using the non-allocated product and we found this to actually be happening more often in the NRT arm than the electronic cigarette arm, which again is something that we had seen before. And once we ran the sensitivity analysis, which we do find that the quit rates are higher in the electronic cigarette arm than the NRT arm, this is very interesting because you know, you, you kind of have to think about these potential switching of products that, that happens in these kind of trials. And I think it happens in real in the real world as well that people start sampling different products, of course, to help themselves stop smoking.

JHB: Yeah, and I imagine there's an added incentive to do so if you're pregnant as well, and kind of very aware that within the trial period, you want to try everything you can to quit smoking. So that makes total sense to me.

Were there any particular challenges in undertaking this study?

FP: From my perspective, um, one of the challenges that we found was that the primary outcome sustained validated abstinence. So there had to be abstinence since the start of the trial to the end of pregnancy and it had to be validated. Saliva samples were used to validate the self-report of having quit. But what happened was that, uh, so, so the samples to collect the saliva will be sent to the participants and they were then given instructions on how to take the sample and how to post it

back. So they had an already stamped envelope to post them back. But what we found was that the return rates were quite low. So we had just over 50% of the samples that we posted out were actually returned, which I suppose happens quite often, not just in studies, but in general, you get envelopes and then you forget to post them back within the timeframe. But that meant that of the women that were reporting to be abstinent we couldn't validate all of them. And then obviously we have to classify them as non-abstainers, who are still smoking at the end of pregnancy. So that was one of the difficulties. So it was also good to have a secondary outcome. Report abstinence, because then again, we could see a difference between the two arms with more women quitting in the electronic cigarette than the NRT arm.

JHB: It's really interesting. I can see that it would always be a challenge to get those envelopes back, but having small children myself, I can imagine particularly immediately having given birth that might not be top of my. Priority list so, yeah. Yeah. It doesn't totally surprise me.

FP: Absolutely.

JHB: and was there anything that surprised you or the team in terms of your study results?

FP: So, one of the thing that surprised us was, as I mentioned, the fact that we found higher incidence rate of babies with low birth weight in the NRT arm compared to the electronics cigarette arm. And we are kind of speculating at the moment that potentially the women in the electronic cigarette arm stopped smoking, but they were still using electronic cigarettes you know, we find that they're using electronic cigarettes even at near the end of pregnancy time. Mm. So they're sustaining the nicotine level through vaping potentially while we are expecting the women in the NRT arm are probably sustaining the nicotine level by still smoking. Yeah. So if, if we assume that they might have similar level of nicotine intake by the end of the study, then it is possible that it's not nicotine, which is often considered responsible for restrictive, foetal growth, but it's most likely there is some of the other chemicals in tobacco that the NRT are mostly still in-taking that might be responsible for that.

JHB: Yeah.

FP: But obviously the data are not conclusive and we are running some secondary analysis on the data from the trial, and we hope that we'll be able to shed a bit more light on this, hopefully not too long. It's sitting on my desk.

JHB: We look forward to seeing it when it's out. And do you think this study is likely to change practice? You know, it's the first big one of e-cigarettes in pregnant women. Do you expect that it'll have an impact in terms of what advice people who are pregnant might be given?

FP: We hope that it will have some impact on real life practice. And definitely having shown that they're just as safe as NRT and effective in helping women quit smoking. We hoping that within the stop smoking services that currently offering electronic cigarette to the general public, that there will feel more comfortable and reassured that it's okay to also offer them to pregnant women.

JHB: Yeah. Okay. And what advice do you think should be given to pregnant women who smoke about vaping? If any, based on this study?

FP: I think the key message is that women were still smoking during pregnancy or smoking women who were pregnant were struggling to quit cold turkey or struggling to quit using other products should really consider using electronic cigarettes because they could really help in reducing the risk of smoking to the babies.

JHB: And what research do you think should be done following your study? What do you think if there could be one next big study and funding, wasn't an issue? What do you think that study should be?

FP: My answer kind of goes back to one of your earlier. Of like the impact it can have. And I think this is a really large study and it addressed the two main questions of safety and, um, effectiveness of electronic cigarettes. But I think it would be good to have some replication of the findings. And if the study were to be replicated, I think it would be good to use some of the newer vaping devices that might be even more effective at delivering nicotine so that maybe the effect would be even greater and more women will be able to successfully quit.

And then I guess the other question is in the study, the two arms received behavioural support. So again is one of those questions, how effective would they be without the behavioural support? I think that would be the next question, because that would open up the scope a lot more, because women might be able to just source the electronic cigarette and still get help in, in the quitting process.

JHB: Absolutely. Excellent. Well, that is it for me. Is there anything else that you would've wanted to cover that we didn't cover, any key message you'd like to leave our listeners with?

FP: I guess the message is if, you know, if you're a smoker and you're finding it difficult to quit smoking, even if you're pregnant, you should really consider trying electronic cigarette to help you in this process.

Thanks a lot for having me on the podcast and presenting this results.

JHB: Great. Thank you so much for coming.

NL: It's really great to see the results of that study out. And I really enjoyed listening to that conversation between you and Francesca, Jamie. I think the first thing is that what this, you know, women smoking in pregnancy really shows it's just how addictive smoking actually is because women who are pregnant and concerned about the health of their children also find it very difficult to quit. It's not just a foregone conclusion that they're immediately going to be able to quit. And I think that just speaks to the strength of that addiction and how we really need to do things to help everybody, to quit smoking.

JHB: Absolutely. I think it talks to the fact that for a lot of people being motivated to quit smoking simply isn't enough. They need other support to help them quit.

NL: Yeah, definitely. Um, and the other thing that I thought was super interesting about this study, particularly as somebody who's been involved in running trials before myself, is that fact that some of the women used e-cigarettes in the NRT arm, despite not being advised to, and that obviously many of the women didn't return their saliva samples for completely understandable reasons. They're both really interesting examples of how trials don't always go the way we expect them to. And I think what was really good here was that the team managed to predict that these things might happen through obviously having a long history and running these kind of trials and they were able to then find ways to allow for that in their analysis and the results that were found in the original analysis were different to what they found in those adjusted analysis. So if they hadn't allowed for those adjustments, then the results of the trial could have potentially been misleading and would've amounted to different conclusions and different ways to use those results in practice.

JHB: Absolutely. I think that's one of the ways in which it was nice to be talking to the trial statistician which we haven't done before, but to hear about how they thought through the analyses they were gonna do and how they conducted them.

NL: Yeah. I thought that was a really interesting insight, which we, as you say, we haven't had before. Another thing that I think is potentially a really important thing going forward for future research, I suppose, is that finding that Francesca said they had women who were randomized to use e-cigarettes had fewer babies with low birth weight. And that seems to be a really important finding. That's not necessarily come out before. And I think it'd be really interesting to see future research that investigates, what are those specific causes of low birth weight in women that smoke? Because that, again, can inform treatment. And I think, again, thinking ahead to future research, these safety findings are been potentially quite reassuring and it means that now there are these devices that deliver nicotine more effectively. I think probably ethics committees and clinicians will be less worried about running trials using those devices because they'll have seen that actually, the safety findings from this study were very encouraging and that there's potentially not too much to worry about in terms of giving pregnant women, these newer devices.

JHB: Absolutely. I'd love to see more studies in this area. I think we really need them and hopefully this will kind of pave the way for more of them to come out.

Well, I think that's it from us this month and that's actually it from us for the rest of the summer. We are. Taking a break in July and August and we'll return with an update on e-cigarette evidence in September this year. I hope you all enjoy your summers or winters if you're in a different hemisphere from us. Thanks so much for listening and as always, thanks so much to Dr. Pesola and all of the other people we've had on to talk to us about e-cigarette.

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.