# **Transcript**

Let's talk e-cigarettes Podcast 45, Ryan Courtney

Speaker 1: Musical intro and outro

Speaker 2: Nicola Lindson

Speaker 3: Jamie Hartmann-Boyce

Speaker 4: Ryan Courtney

## Speaker 1

If asking your mate down the pub about vaping, here's what they'd 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.

#### Speaker 2

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

# Speaker 3

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 3

Hi everyone and welcome to this month's episode of Let's Talk e-cigarettes. In this month we are covering searches done in both August and September as Nicola and I took some time off in August. I hope all you did too and had great holidays. We're back and happy to say the e-cigarette research field remains very active. So, in the searches from the last two months, we found two new ongoing studies of interventions for quitting vaping and four new studies for our review of e-cigarettes for quitting smoking. I'm going to have Nicola start us off with those two new ongoing studies on quitting vaping.

#### Speaker 2

Thanks, Jamie. So, the two ongoing studies were both identified through trial registries. The first is titled A Trial of Varenicline for E-cigarette Cessation. It will include an estimated 326 participants reporting daily use of nicotine containing e-cigarettes and

will compare varenicline to placebo. The researchers plan to measure quitting ecigarettes at six months and it's being carried out by researchers at Yale University and the Medical University of South Carolina and is funded by the National Cancer Institute. The second ongoing study is titled Promoting Healthier Lifestyles and Preventing Chronic Diseases in Underserved Urban Communities Across Europe and is being carried out at the University of Valencia. It will recruit an estimated 900 people. It won't specifically recruit people who are vaping and will test a multi-component environmental intervention, but vaping will be measured at both baseline and follow-up. The study appears to be funded by the EU funding programme Horizon Europe.

## Speaker 3

Thanks so much, Nicola. So, moving on to our studies in which people who smoke are given an e-cigarette to help them quit. The first one is by Professor Patricia Cioe and colleagues at Brown University in the US. This one is funded by the National Institutes of Health and the National Institute of Drug Abuse. In this study, 35 people who smoked and lived with HIV were randomized to either a standardized research e-cigarette or a usual brand cigarette, where they were just supposed to keep on smoking as usual. Participants were followed up for six weeks, and the focus was on inflammatory biomarkers. People in the e-cigarette condition significantly reduced their cigarettes per day compared to the control condition. So, in the e-cigarette condition, they reduced by about 40% versus about 17% in the control condition. But they didn't find any statistically significant difference in biomarkers between the two groups. Only one person completely transitioned away from smoking. Dual use was by far the most common outcome for participants who were provided with the e-cigarette. The authors conclude that more research is needed to enhance the efficacy of e-cigarette interventions in people living with HIV.

## Speaker 2

The second new included study was led by Professor Billy Bonevski at Flinders University in Australia, who appeared on the February 2022 episode of this podcast. It's published in the Lancet Public Health Journal. The study recruited 363 people who were tobacco smokers who had been discharged from inpatient alcohol or drug withdrawal units where smoking was not allowed. They were randomly split into a group that received a 12-week supply of either nicotine e-cigarettes or combination nicotine replacement therapy, meaning patches and another form such as gum. They found similar quit rates between the groups at nine months follow-up and similar numbers of people reporting serious health issues. None of these reported health issues were deemed to be related to the treatment. The study was funded by the National Health and Medical Research Council of Australia. The lead author of the third new included study was Lynne Dawkins, formerly of London South Bank University in the UK. This study also recruited a specific population, in this case people experiencing homelessness. 477 people from 32 homeless centres were randomly assigned to either get a refillable e-cigarette with four weeks supply of e-liquid or minimal support including signposting to stop smoking services. Quit rates were low in both arms, but slightly higher in the e-cigarette group. The study was funded by the UK's National Institute for Health and Care Research.

## Speaker 3

Thanks so much, Nicola. So, for the 4th new study this month, you'll be hearing about it in our deep dive. This month, I had the pleasure of interviewing Professor Ryan Courtney from the University of New South Wales in Australia about their new trial published in the Annals of Internal Medicine, which tested vaporized nicotine products for smoking cessation among people experiencing social disadvantage. This study was funded by the Australian National Health and Medical Research Council, and I'll let Ryan tell you more about it.

So, to get started, can you first tell us about your background and what got you into e-cigarette research?

## Speaker 4

Sure, yeah. So, background was actually in undergrad in psychology, so I went through that with honours for a few years. And then, funny enough, finished that and then wasn't really all too sure what I wanted to do. I was quite young at that point, about 22, and I probably didn't have that much lived experience in terms of life, so I didn't think the clinical setting was quite my thing at that time point. And applied as a research assistant, funny enough, and yeah, it worked in a health behaviour research unit at the University of Newcastle for about three to six months and then really started to enjoy it, working different health risk behaviours in the unit at the time and then gravitated towards actually working in bowel cancer screening and really where it started I guess was in the prevention space in that time point, trying to look at risk appropriate screening for bowel cancer screening and medical advice seeking. So, it was a bit of a different trajectory, but it was a really good opportunity to start to work on a randomised control trial, which was really exciting, and working with that design was really something that I finally got passionate about. Yeah, worked through that and then finished my PhD and then started a post-doctoral fellowship at the University of New South Wales. And at that time point, yeah, there was a bit of work going on in smoking cessation among socially disadvantaged smokers. And pretty much ever since then, I never let go and kept going with it. Yeah, it's been a journey, but a few RCTs along the way, some ups and downs, obviously, sometimes seeing a new effect, sometimes not. But yeah, it's been a blast.

#### Speaker 3

That's so cool. And so, tell us a little bit about your new trial. What did you set out to look at? In what populations? Were there any challenges getting it off the ground?

#### Speaker 4

Yeah, in terms of challenges, yeah, there was quite a few. COVID was one, obviously.

#### Speaker 3

Yeah.

## Speaker 4

In Australia in particular, we've been a country where there's been lots of regulatory changes in terms of access to vaping, how they're marketed and supplied. So, with that, we'd obviously commenced the trial but halfway through the trial we had to relabel

products and make changes. So it wasn't, yeah it's just part and parcel of being compliant obviously with regulatory standards which we had to do. But really I think in terms of this new trial, what was new about it, you know when we first started obviously this trial probably when it was funded about five or six years ago, at that time point there was probably only a few RCTs that had demonstrated at a high quality level that vaping was more effective than NRT. And the world did sort of move on. I know that RCTs take a long time, Jamie, and this one's no different.

## Speaker 3

Yeah.

## Speaker 4

But the world probably had moved on during the trial, where we started to see, particularly in the living review for Cochrane, that there was more studies popping up, particularly in general populations, that vaping was superior to nicotine replacement therapy. But I guess in that Cochrane review, there's lots of different priority groups. But in particular, we looked at low socioeconomic status and smokers that have received a government pension allowance. So, I think the novelty in this trial was actually demonstrating that the effect we find in the general population can also be held within a very disadvantaged population group as well. So in this study... participants had to have government pension or allowance to be eligible for the study. So we use that as what we call a proxy marker of disadvantage.

#### Speaker 2

Obscure science definition.

A proxy marker is a standing measurement that researchers use when the thing they really want to measure is too difficult, expensive or time consuming to track directly.

#### Speaker 4

And we obviously found a three times higher quit rate, 29% versus close to 10% in the NRT group. So yeah, I think to the novelty in this trial as well, we use nicotine salts, which was pretty new even when it was published not so long ago.

#### Speaker 2

Nicotine salts are a form of nicotine e-liquid used in vapes that are made by combining with an acid so that they are less harsh to inhale.

#### Speaker 4

But even when we started it in its infancy, it was one of the first trials that actually did recruit people with nicotine salts in a large trial and evaluate it and with flavours as well and probably optimal nicotine delivery as well. We had 4% or 40 milligrams per ml.and nicotine salt group. And we also had a tank device that had 18 milligrams per ml as well. So, there's probably a few factors of why I think it actually did go so well. But I mean, a lot of thought had to go into design and with multiple flavours, multiple devices. But in the end, I think that's what led to such a high quit rate as well, which was good.

#### Speaker 3

Really impressive quit rate. And you can't always assume, as you know, that these interventions that might work in the general population and work as well in subpopulation. So I think it's wonderful to have this study out here. Yeah, congratulations.

Speaker 4

Oh, thank you. Yeah.

Speaker 3

Did anything you find surprise you?

#### Speaker 4

Well, when we started, as I said earlier, there was only a few studies. So... When you look at the sample size calculation we originally had,

#### Speaker 2

Sample size calculation is the process of figuring out how many people need to be included in the study to get results that are trustworthy and not just due to chance.

#### Speaker 4

We erred on obviously a lower conservative quit rate. And I think if I remember back to the sample size calculation, I think originally we thought about 14% might quit in the vaping group. But at the same time, a lot of that data had come from freebase e-liquids using one flavour. So, there's some limitations that go into that import. And then for the first time, we were starting to use a different device that really the world didn't know all that much about at the time. From a pharma kinetics So far we knew that it looks good with nicotine delivery. I think it was maybe Peter Hajek's group in the UK did one of the first good studies comparing, it was Juul, I think, and it's delivery mechanism. I think it was an Addiction paper. So we knew a little bit about the promise in terms of treatment delivery, which, you know, and everyone sort of, I think, sparked up a bit in terms of like, we've always had treatments that just quite, we weren't quite there optimally at delivering withdrawal relief and cravings relief as well. So, it was looking promising, but then again, we still didn't have that time point, long-term quit rate data. So, I think the fact that the quit rate was as high as it was in the vaping group was quite phenomenal, but I think also the fact that we paired it with brief advice. So during the trial, there was two check-in calls, but those calls only went for about five to 10 minutes, and there was only really one point in those calls where we were sort of talking about, you know, what's your quit status, whether or not they were quit at that point or not, and some very brief advice that we'd standardise and give. But alongside that, the package was just, I think it was five weeks, but I think it was very brief text message support as well. So, to get 29% quit, six month continuous abstinence with, you know, I think we were paying 3.6 cents for a text and there wasn't that many texts over that period. So that was phenomenal. I think you take the good with not sure how people view this, whether or not it's bad, but people have different views on maintenance use and, you know, whether or not have we gone far enough just to move someone from a smoker to a vaper. But we did notice that there was still a high maintenance use, continued use amongst those that quit. So, 58%, I think that surprised me. I knew it was a good vehicle of nicotine delivery. So they definitely work really well and people, but then again,

whether or not at what time point then the shift should be made actually to switch away from vaping as well. I think there is still some risks associated with ongoing vaping, albeit a lot less than the comparative which would be smoking. I think, yeah, the world needs to shift away from just thinking about, you know, I think the question of whether or not vaping works for smoking cessation is now done. I think it's like, how do we use this and harness it more? Yeah. And allow, and probably greater access and availability, in a sense, and trying to support smokers to use these products to quit would be a good outcome, yeah.

## Speaker 3

Yeah, yeah, absolutely. So that really nicely leads us to our next question. What do you think should be done next following these findings, either in terms of research or practice or communications or all three?

# Speaker 4

Yeah, I think every country's grappling with the regulatory control around vaping. Obviously, being from Australia, which is very far removed to the northern hemisphere, but we have a medical model here where access has to go via prescription and pharmacy, which could work really well because we know that doctors are really important in terms of providing support for any type of smoking cessation. And we know that pharmacists as well are another vehicle to drive that. And when you pair that with treatment and behavioural support wrapped around it, you'll get a really good outcome. But unfortunately in Australia, we don't have enough doctors prescribing it and not enough pharmacies either. Like there's I think close to 6,000 pharmacies in I think only about 1/3 stock any vapes.

Speaker 3 Oh wow.

## Speaker 4

It hasn't really, in terms of being a vehicle or a mechanism, uptake hasn't happened. But whereas, there's different models as well overseas with recreational models as well. So, I think in Australia we're really grappling, I think, with trying to make sure that... vaping is used as a vehicle to support smokers to quit. And I think, yeah, as I said earlier, I don't think we need any more studies to look at whether or not vaping is superior to nicotine replacement therapy in particular, albeit we don't know direct comparators. We've got another clinical trial we only just started last week, actually, comparing vaping to varenicline. So, I think that's another direct comparator that the world doesn't know about yet, actually, how it compares directly. I think longer term as well, the flavours argument as well. How many flavours do we need and does it matter whether or not you use tobacco or do we need the extra flavours? From what I've read in terms of systematic reviews, I think that's inconclusive at the moment just because there's not enough studies to evaluate that. I think as always, like dose, we're not really sure what the optimal dose is, but obviously in our trial we used a higher dose compared to most trials that use sort of 12, 18 milligrams per ml. So that's probably an important thing, but then does that drive high maintenance use at the end, or if they'd used a lower percentage product, would they have just changed the way they vaped

anyway and we were in the same outcome? So, to figure that out, you'd have to sort of switch around the different doses, different flavours. But I think that in terms of the longer term trajectory, I guess that we know now that vaping is such a good smoking cessation aid. For some people that do quit smoking, a significant portion will need support to stop vaping, I think, in the longer term and may want to stop vaping. So I think we need to adapt to that and then move towards what are effective interventions to support their longer-term dual switching away from, obviously they've moved away from smoking, but then also vaping. But I think dual use as well, I think, you know, in our studies still there was a significant amount of dual use at follow-up as well. And, in particular, I think that's a new area that needs to be tackled as well, I think in terms of the evolution of what vaping has become and how we support people that may be both smoking and vaping at the same time when we do clinical interactions in particular. Yeah.

## Speaker 3

Yeah, awesome. I hope all those things get done. I totally agree. Well, thank you so much. This is great. And I like I'm very hopeful that your trial, you know, I think it is quite unique in a number of ways. And one of those is that it is a big, very definitive trial conducted in Australia. And so I hope it also maybe helps potentially make clinicians and pharmacists feel more comfortable about the evidence in your particular context. So fingers crossed.

Speaker 4 Yeah, I think.

Speaker 3 Yeah.

Speaker 4

So yeah.

Speaker 3

Congratulations and thank you again.

## Speaker 4

All right well thank you so much I appreciate your time yeah yeah very very good I think in particular the equity angle here I mean yeah we knew a lot about vaping in a general population but it's nice to see that what we've found in general population also stands for a very high need and priority group.

Speaker 3 Absolutely.

Speaker 4

So yeah look forward to the next trial as well and hopefully speak to you again soon Jamie.

Speaker 3 Yeah me too. All right.

Speaker 4 All right.

#### Speaker 2

As you know, Jamie, I think it's really important to look at this population as we know that people in this group are less able to quit. But in this trial, obviously, six month quit rates were really high compared to what we'd usually expect to see, which is great. I think it's also worth noting that the number of people reporting serious health effects was really similar across the vaping and nicotine replacement therapy groups as well. So that's also something else that's encouraging. We're always looking for more safety data, as that's something that people still feel quite uncertain about. Yeah. The other thing that I think we could take from this study is the fact that they were using one of the more new devices, e-cigarette devices, as Ryan mentioned, because as we think that the developments in e-cigarettes have led to better delivery of nicotine, which then better mimics cigarettes, so is more likely to help people to switch. We know that one of the limitations of our review when we were nearer to the start of it was that a lot of the studies looked at the older devices and we weren't sure whether they were going to be working in the same way as the devices currently on the market. So, it's really great that now we have more studies looking at these newer models that are already included in the review, but we're getting more and more that can be included in future updates to give us more confidence in our findings.

#### Speaker 3

That's absolutely right, Nicola. I mean, I think this is a great trial. It got a lot of attention when it came out. It's just really promising in terms of looking at these interventions and accessing this group and supporting them with quitting smoking, which is something I know Ryan's really passionate about.

#### Speaker 2

Yeah, it's a really interesting study.

#### Speaker 3

Great. Well, that's it from us this month. Thank you all so much for listening. Thank you for Ryan for coming on to the interview. We look forward to looking at the new ecigarette research and telling you more about it next month.

Please subscribe on iTunes or Spotify, and stay tuned for our next episode. Thank you to Jonathan Livingston Banks for running searches, to Ailsa Butler for producing this podcast, and of course to all of you for tuning in. The music is written by Jonny Berliner and I and performed by Jonny. Our living systematic reviews are supported by funding from Cancer Research UK. The views expressed in this podcast are those of Nicola and I and do not represent those of the funders.

# Speaker 1

Switching to 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'll 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 bees burning But there's much to learn of effects long term yet to be seen