

Transcript

Let's talk e-cigarettes

Podcast 29, February 2024, Reto Auer

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Speaker 3: Jamie Hartmann-Boyce, JHB

Speaker 4: Reto Auer, RA

Musical intro

If asking your mate down the pub about vaping is what they probably say, no one agrees if it's safer or not, so you might as well smoke anyway. Now what your mate needs is a Cochrane review. All the facts have been checked at least twice. They find there's a lot that the experts agree on 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 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've found that month and then go into more detail about a particular study or topic related to E cigarettes.

Speaker 3

This month we ran our searches on the 1st of February 2024, we found one new included study, 3 references linked to previously included studies in our review and three new ongoing studies. So a busy month and first Nicola's going to tell you about that one new study in a nutshell.

Speaker

Yeah.

Speaker 2

Thanks, Jamie. The only new study found in our searches this month was published by Doctor Linn, based at Peking University and their colleagues. It was published in the JAMA Internal Medicine Journal, and it's a trial based across 7 sites in China of 1068 participants. So the participants who took part in the study, needed to be smoking at least 10 cigarettes per day and be motivated to quit smoking. They were then randomised to a nicotine cartridge-based e-cigarette, or the stop smoking medication vareniline or nicotine chewing gum. So three groups and all of the treatments were provided for 12 weeks alongside an intervention to join a self-help Internet forum. So basically just very minimal behavioural support was given. After six months, participants in the e-cigarrete arm have similar rates of quitting to those in the varenicline arm, and both the E-cigarrete arm and the varenicline arm had higher rates of quitting than the nicotine gum arm, so that's really reflecting other research that we're kind of seeing in this area. This study was funded by the Scientific Research Project Fund of China, Japan, Friendship hospital.

Speaker 3

Thanks Nicola. Now moving on to those 3 ongoing studies, also in a nutshell. The first of them is a randomized controlled trial that's planned to be conducted in the UK in adults who are receiving treatment for mental illness who also smoke. Participants are going to be randomly allocated to one of two groups. The first group will receive an e-cigarette and an E liquid used for four weeks. In addition to the usual care they're receiving. In the second group, participants will receive their care as usual, so that will be the control group, but at the end of the six month follow up, they'll also receive an e-cigarette and some E liquid. This trial is being run out of the University of York and University College London and is funded by Yorkshire Cancer Research, and they're planning to complete the study in April of 2025. The second new ongoing study is a randomized controlled trial in South Africa, which is going to be conducted among people who smoke and are living with HIV or AIDS. It's sponsored by NYU Langone Health and they plan to recruit 90 participants and randomize them to one of three arms. The 1st is going to be referral to a telephone quit line. The second is going to be a nicotine replacement arm, and the third is going to be an E cigarettes arm and they anticipate that they'll complete that this summer. The third ongoing study is a randomized controlled trial plan in people who smoke living in Pakistan. This is a pretty big study. The authors plan to randomize 600 participants in total to three different groups. The first of those being nicotine E cigarettes. The second of those being nicotine pouches, and the third being usual care, so the control arm. This study is funded by the foundation for a Smoke free World, which has been associated with the tobacco industry.

In this month's deep dive. I had the pleasure of interviewing Professor Reto Auer from the University of Bern in Switzerland on his new study published in the New England Journal of Medicine in February called Electronic nicotine delivery systems for smoking cessation. And funded by the Swiss National Science Foundation, this is a really big trial and we've been really excited to see its results for a while. They randomized over 1000 participants. And I'll hand over to Rito to tell you what they found.

Speaker 4

So thank you so much for this interview. I'm a primary care doc working 30% in Switzerland and I'm also a researcher at BIHAM. So a couple of years ago, and I think it happened to many clinicians that around the world, we were faced with questions from our patients. You know, is it safe? Is it effective to quit smoking, so we set up this study to answer these questions.

Speaker 3

And can you tell us more about your new study? What did you set out to look at? Why were you making the choices you were in terms of what you were comparing?

Speaker 4

We did something pragmatic meaning in clinics in Switzerland if I would set up the best smoking cessation advice I could give to smokers willing to quit. Then they will typically receive counselling based on cognitive behavior therapy, but also motivational interviewing which is really strong in Switzerland and also shared decision making saying there's no best option to quit smoking. The best option is the one they choose so we also use decision aids to help people take the choice if they want to use nicotine replacement therapy, smoking cessation drug therapy or nothing or something else, and then to have them go to the pharmacy and buy it, because that's what happens in Switzerland. They're not reimbursed by health insurance in Switzerland. Some insurance reimburse them, but most don't. That smoking cessation drugs are reimbursed but the others, the others are not. And then, as we know, we need to follow participant up for two months. So we did that per phone at 1, 2, 4, 8 weeks. Everybody got this intervention because that would be what we would do best in our context in Switzerland. And the research question was, well, what happens if we add now E-cigarette. And we worked with vapers that were telling us, hey, you know, the choice of aromas and the the fact that it can change the concentration over time is really important. The device chosen a simple device for beginners.

And for the e-liquids give a range of choice of e-liquids. So a couple of decisions we took is that we gave them for free and why did we that because we want to make sure they use our product

because we also had a whole process where we selected the e-liquid in a producer that was fulfilling very strict criteria for quality. We tested the device with the e-liquid in the lab. We did a PKPD study and then we did the randomized trial. Because we really want to know. You know what happens when we have a device we can kind of know exactly what's in it. Knowing what it does in selected participants and then test it in the randomized trial, as you would expect for pharmaceutical products basically. But as you know, the Pharmaceutical industry is not investing in E cigarettes and so since we are most physician and healthcare professionals, that was our main concern is to know what we give participant and then see the effect in participants. And so that's the reason why there might be good criticism that offering the device is not the same that recommending it. So really people should be aware of this limitation in extrapolation of their results in their clinical setting. So everybody got this counseling, everybody could use nicotine replacement therapy and the intervention group received these E cigarettes and again the other choice was people don't ask if they can buy a cigarette. So why? Why would we recommend strictly how should they do it with e-cigarettes and they were able to choose a range of e-liquid. We had 24 different liquids and aromas, and it was a nightmare to coordinate all this. You can imagine in five centuries to have all this with shipping and all this. So it was really complex.

Speaker 3

Oh wow.

Speaker

Yeah.

Speaker 3

Ohh my gosh.

Speaker 4

And then and then they could choose on a table. I think in the supplement people can see the image, how that worked. And so the first time they could pick the one they liked most, they received 10. Bottles and then they could order as as many as they wanted for as as often they want it, and they chose what they were using. Also, if they were using them less than they would receive less concentrated, they could mix it. There was another paper where we described a little bit that is in the pipeline exactly how that happened. So it's really saying, what do people do when we don't really counsel them? The only thing we did is those who were smoking a lot in the intervention group we also recommended nuclear replacement therapy to add because we know it's hard to fulfill the detail. It's. The freebase nicotine. Now I always mix up these terms. It's not nicotine salts, you know. Because when we launched the study, these were just beginning and also we want to see if people can stop also with these ones.

Speaker 3

Yeah, that makes a lot of sense. And did you encounter any challenges and kind of setting up the study or conducting it, I mean it's a huge undertaking what you're describing there.

Speaker 4

I mean challenge is part of running trials. So the first thing was when we planned the whole study, it was still not allowed to use nicotine in Switzerland. So they were the vapes, but it was banned to have nicotine in the vape. So initially our whole protocol was to ship them from France to the directly at all. Then suddenly there was a decision in in Switzerland that came from the administrated law and judgement that allowed suddenly nicotine. So that simplified.

Speaker 3

Wow. Oh my goodness.

Speaker 4

Our processes so we could have them shipped to. The clinic and then give it to the participant and then send it directly proposed. Then there was in the middle of the EVALI epidemic, yes. You know where we were really looking into it and then that were a lot of discussion to kind of understand what was going on.

Speaker 3

Yeah. Yeah.

Speaker 4

And a lot of pressure, a lot of questions, and very soon we knew it was not because of the E cigarettes, but it was more. Because of the vitamin E acetates.

Speaker 3

That's right, yeah.

Speaker 4

And so we set up then a data safety monitoring board and had all the group of experts helping us take a decision if we should stop or continue. So we continued the trial. And then came covid. And so we're really lucky that we were living in Switzerland for that side. Of course, there are some sad things that we didn't have so much closed. So that's a political decision. Switzerland took that we were still able to mostly run the trial. But of course, for validation of the outcome.

Speaker

Oh.

Speaker 4

There were some issue to have people go back to clinics so for sometime the validation of the outcome was more difficult than we did that perform. But we still. I think we're still OK with the follow up rates and and so as always, so many challenges, but that's the beauty of running randomized trials. If you don't like that, then don't do randomized trials.

Speaker

Yeah.

Speaker 3

Don't do it. No, I am very impressed by all of the obstacles that were overcome. And one of the things that I was really excited about with your study is that most of the especially big studies in our review are based in the US and the UK. And it is so nice to have a study based somewhere else in Switzerland. And you've touched upon a few things about Switzerland that might be relevant in terms of the context, one of which being it sounds like the price of nicotine replacement therapy to the person who might buy it, the other being that when it first started, nicotine wasn't allowed in E cigarettes. Is there anything else about the Swiss context we should be aware of when we think about the results from your study?

Speaker 4

Well, Switzerland is specific, so I think for the interpretation of the results, we have a high smoking rate in Switzerland and the possibility to get dedicated smoking cessation counseling especially for underserved population is not that good. So you can have a free call or you can go online.

Speaker

Mm-hmm.

Speaker 4

But as soon as you want to see a primary care physician or a counselor, then it's it can be covered by the health insurance, but we have very high deductible. So many don't go to the physician or to a healthcare professional to get smoking cessation counseling. That might be different and why I'm saying this is that, you notice, the control group we have very high smoke cessation rates and that's similar to other studies. There was another study conducting 217 that also had 25% smoke inhalation rate in the control group and that's different than running a trial in the UK.

Speaker

Oh.

Speaker 3

It is, yeah.

Speaker 4

You know when you see the trial by Hayek et al in New England 219 they had lower rates of smoking cessation and I don't think we of course we could interpret this, that we were phenomenal in our

counseling. But I think there's also another thing. It's another pair of shoes of having people stop smoking in Switzerland than in the UK because the case mix is different.

Speaker 3

Yeah.

Speaker 4

Most maybe already stopped, right? And so that's one of the things that is important in the Swiss context. The other is also that we are testing field for the tobacco industry. We have the three major tobacco industries sadly being located at the headquarters Switzerland that influences a lot how these are regulated. The implementation of policies. I don't think it does make a big difference for our study, but that's still, yeah. And the last point is about the nicotine replacement therapy. So you will certainly ask what surprised me? What surprised me is, you know, little physical therapy is relatively expensive.

Speaker

Yeah.

Speaker 4

In Switzerland and Germany, Germany, it's also and it's a scandal. Right. It's a true scandal.

Speaker 3

How expensive is it?

Speaker 4

You know it's 10 times more than in France.

Speaker 3

Oh my gosh.

Speaker 4

So a pack of cigarette is between 7:00 and 10:00 Swiss francs, which is similar to the euro and the dollar. I don't know exchange it, but one patch in Switzerland would be 7 francs. So about \$7.00. And it's. I think it's on a dollar in France. And and it's a scandal.

Speaker 3

Ohh my gosh.

Speaker 4

And we don't speak a lot about this and I think my motivation also for e-cigarettes, it's probably the first progressive measure we have for smokers in Switzerland. It's extremely expensive to quit with nicotine replacement therapy. But what surprised me was despite these concerns, first the control group received a 50 francs voucher kind of go and buy nicotine replacement therapy and they could buy anything with it. But we still had at one week and that's in the supplement 64% who said that they were using nicotine replacement therapy. So you would say, oh, but nobody buys this. And the truth is, many do.

Speaker 3

Yeah, yeah.

Speaker 4

And that the control group wasn't that much of a bad treatment. I mean, at one week we have about 70% who are either using it in replacement therapy and other smoke cessation drugs. So I think that was really what surprised me when I saw the results that I was always a bit you know, wary maybe the control group wasn't that well treated, but at the same time I think might be that it was a fair comparison, but the readers should decide on that.

Speaker 3

Yeah, that makes sense. So what were your main findings?

Speaker 4

So the main findings, so we report on the six month visit and our main outcome was the smoking cessation rate. And as you know in the literature, the continued smoking abstinence, that means since target quit date until six months, no cigarette validated by anabasine and if anabasine not available by carbon monoxide. It's important is that the relative risk is a 1.77, so so more people quit

smoking. And then we have other measure of this. The seven day point prevalence or sustained abstinence and all the outcomes basically on the efficacy outcomes show that providing E cigarettes for free for six months compared to the standard of care within counseling works better than just standard of care counseling. The other, the other finding and I think you also worked on this. It's of course is cigarettes do give this nicotine hit, which is what smokers crave, and so we're really happy that we're able to publish Table 3 even if it's secondary outcome and it wasn't defined in the statistical analysis plan. But I think we noticed this over time. How important that question is.

Speaker

Oh.

Speaker 4

Is when you look at how many really quit smoking in the last seven days, we have 38% control group and 59% in the intervention group. That's a 20% more smoking rate right so that's good. At the same time, if you look exposure to nicotine, be it from tobacco, e-cigarettes or nicotine replacement therapy, then those who were abstinent of nicotine at six months were 33% versus 20%. So that's 10%, that's 13% less. And what it means is some people probably couldn't quit without e-cigarette. But you have another group who might have well be tobacco and nicotine upstairs without e-cigarette. And there's no effective drug without second adverse events. You know, it's not the adverse event but, but of course and and I'm in Switzerland and we decided 20 years ago and it was a vote from the population that people who use heroin should be allowed to use the heroin they need and when we prescribe heroin, we don't prescribe heroin so that they quit heroin. We do that so that they don't die from the consequence of using it. And for me, it's kind of a similar approach to saying, look, we prescribe this. It's not that you quit nicotine, it's that you stop smoking. But at the same time now what needs to be done is that some predictors of who is quitting with smoking but at the same time, who might not need it and and you know how our colleagues some say ohh it's not smoking cessation because they're still using nicotine and other say yes it's stopped smoking because what's important for me is nicotine and I don't care what they think.

Speaker 3

Hmm. Yeah. Yeah.

Speaker 4

What I care about is that we inform participants about this in smokers, that it's a good device to quit smoking, but not necessarily to quit nicotine.

Speaker

Mm-hmm.

Speaker 4

And to end on my comparison with heroin. And I know people might hate this first 80% of people use heroin without problems, right. And that's a taboo of there are people the majority uses heroin now and then. And it's not everybody. The only thing is there's no advertisement on Instagram for heroin right. And so that's the big issue with these cigarettes.

Speaker 3

Absolutely. Absolutely. How was your study received? You know, I saw a great editorial about it. I've seen a lot about it in the news. Have you been surprised by any of the feedback or the coverage that you've gotten on it?

Speaker 4

We were really honored to be considered in in New England first for as a researcher, that's wonderful to have this level of editorial work to improve the work and to have such a broad audience reading your work. So, this is a huge, and having an editorial too from Professor Rigotti that we value a lot is a boom. And we were expecting that we will make nobody happy. And that's actually what happened. So, you know how tense this field is. We're not paid by the tobacco industry or the vaping industry. We're trying to answer questions of our of our patients. And there are good sides to e-cigarettes and there are bad sides to e-cigarettes. And our work is now to we try to do that as neutrally as possible, and I hope we wrote it also as neutral as possible so that other

groups now internationally will take a decision. And there are extremes in this. And I think from both extremes, I'm always surprised how people just see just one side. Oh, it's wonderful it helps quitting and the other say, oh, but it's not there's so limitations. And it's not true. And but that's fine. That's part of the debate. And if you make everybody happy then probably you're wrong.

Speaker 3

Yeah, I think, at least that's what I tell myself as well, be reassuring. All right, so following your study, what do you think should happen next in terms of research, in terms of policy and practice what would you like to see in the next few years?

Speaker 4

Well so this is work we hope we can contribute to this large body of evidence that has been summarized in the outstanding Cochrane review. I mean, we're part of it, we're happy we can contribute to these large endeavor and no study can give you all the results. You absolutely need to see that in the whole so. Personally, we are working on a range of sub-analysis of the trial, but as you know it's an ongoing trial at 12, 24 and now 60 month and I think that will be the first time that we can continue to follow participant because that's a really important question how people change.

Speaker 3

Ohh, fantastic. That's amazing.

Speaker 4

And the other is just on the study results that clinicians, stakeholders, general population looks at the results and see if they need to change the the guidelines or consider this. So one of the work and I think that's also Nancy Ricotti who was pointing to that is less about the if than the how. Because there are huge challenges in e-cigarettes you know which one? What are the safety standards? How can we do that on the relative part for the physician, you contribute something that is not a medical device. For me as a primary care doc, I don't see a big problem with that because that's what I do. Every day but but for all this might be a more bigger issue. So I think there's there's a lot to be done and the other is we doing also some qualitative work. And I think in the UK you did that, there was a lot of qualitative work just to have the voice of the smokers come out. You know what do patients want and how do they live it and both have people for which it didn't work and.

Speaker 3

Absolutely.

Speaker 4

Others it worked. But these stories are important. That's the stories that drive me.

Speaker 3

Yeah, that's wonderful. Thank you so much for coming on. I really appreciate it.

Speaker 4

Thank you for your excellent question and for this opportunity.

Speaker 3

My pleasure.

Speaker 2

Well, it's really great to hear about that study, Jamie, because as we know, a lot of the studies in e-cigarettes are being carried out in the US and the UK. So it's nice to hear a study coming out of a different place and thinking about how kind of treatment is delivered and how trials are carried out might differ there and the impact that that could have. Although obviously we're kind of seeing that this study had very similar effects to other studies that are included in our review. So that's always really encouraging and this trial is likely to have a really high impact.

Speaker 3

That's right, Nicola. And it's, I think, like our most international month ever on this podcast, because only one of the studies we talked about is in the UK we have the one in China, you mentioned an ongoing one in South Africa and ongoing one in Pakistan. And then professor Auer's study in Switzerland. So, it's great to see the research expanding geographically.

Speaker 2

Yeah, really great.

Speaker 3

Well, thank you so much everyone for listening. Stay tuned next month for our March episode of Let's Talk E Cigarettes.

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

Musical outro

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

Speaker 3

Thank you to Jonathan Livingstone-Banks for running searches to Ailsa Butler for producing this podcast and to all of you for tuning. In music is written with Jonny Berliner and I and performed by Johnny. Our living systematic review is 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.