

Opinion

E-cigarettes and pregnancy. Is a closer look appropriate?

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Cigarette smoking is perhaps the single most important avoidable causes of adverse pregnancy outcomes^{1,2} and is a particularly important problem for women at social disadvantage, such as Indigenous Australians.³ Fortunately, pregnancy motivates many women to stop smoking^{4,5} with about 40% of smokers quitting in the first trimester.^{6,7} However, women who quit in early pregnancy are likely to be those with the best prognosis, leaving the more 'dedicated' smokers as the subjects of quit programs.

Quit programs are generally ineffective for women who continue to smoke past the first trimester⁸ with the worst results for women at greatest risk: those who are heavy smokers; have partners who also smoke; and have limited access to antenatal care.⁹ Trials of nicotine replacement therapy (NRT) in pregnancy have also been disappointing¹⁰ as the majority of pregnant women who commence NRT therapy in clinical trials stop using it before completion of the trial.¹¹ 'Vaping' – the use of e-cigarettes – is now an important trend,¹² and a recent trial found that e-cigarettes are at least as effective as other forms of NRT in smokers, but seem to have higher rates of compliance presumably due to their similarity to the act of smoking.¹³ In the light of these findings, is it time to look more closely at vaping in pregnancy?

Smoking in pregnancy

Estimates from Australia suggest that about one woman in seven smokes during pregnancy.¹⁴ This rate is similar to overseas experience, and while the prevalence of smoking varies between countries, there is, unfortunately, no evidence that smoking rates in young women are decreasing globally.¹ Because most studies rely on self-reporting and

are likely to underestimate the number of pregnant smokers, real levels of smoking in pregnancy may actually be higher.¹⁵ The imperative for smoking cessation is compounded by the effect that exposure to 'second-hand smoke' may have on other children in a family by contributing to otitis media and chronic middle-ear effusion, childhood asthma, and lower respiratory tract illnesses.^{16–19} Cigarette smoking is associated with a host of dose-dependent adverse outcomes in pregnancy, including growth restriction and preterm birth, as well as stillbirth, abruption, gestational hypertension, chorioamnionitis, birth defects and neurodevelopmental conditions in children.²

Quit programs and nicotine replacement therapy in pregnancy

It is difficult to stop smoking, and the majority of smokers who attempt to quit, whether on their own or with assistance such as counselling, supported behavioural therapies, or NRT will not be successful.²⁰ Unfortunately, the heavier the smoker the less likely any intervention will work.²¹ In general, psychosocial support for pregnant smokers needs to be comprehensive and intensive to have any effect, and the evidence for this is from a relatively small number of trials.²²

Clinical trials of NRT for smoking cessation in pregnancy have had disappointing results because trial participants do not continue with the treatment and relapse to smoking.²⁰ Yet secondary analyses of such trials show that those pregnant women who actually use the NRT reduce their cigarette use.¹¹ This is good news for that small group as systematic review suggests that those smokers who switch to NRT in pregnancy have decreased risks of preterm birth and low birthweight compared to those who continue to smoke.²³ Data about neonatal outcomes following NRT in pregnancy are a little more difficult to interpret, as many studies have not adjusted for confounding factors associated with malformations.²³

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Received 16 December 2014; accepted 1 January 2015.

E-cigarettes and 'vaping'

E-cigarettes, sometimes referred to as 'electronic nicotine delivery systems' (ENDS), have become popular over the last decade. The e-cigarette delivers nicotine and flavourings in a steam vapour that is inhaled by the user: inhaling from an e-cigarette is colloquially referred to as vaping. Designed to replicate smoking behaviour, e-cigarettes are battery-powered devices consisting of cartridge that is filled with liquid nicotine, a heating element, and some supplemental electronics.²⁴ E-cigarettes differ from other forms of NRT because they **simulate the hand-mouth repetitive motions of cigarette smoking and provide the visual cue of steam vapour that is similar to smoke.**

E-cigarette cartridges typically contain nicotine, glycerine, propylene glycol and tobacco flavouring.²⁵ The greatest volume of cartridge solution is usually propylene glycol.²⁶ In some cases, other contaminants such as diethylene glycol (a recognised carcinogen) have been identified in a small number e-cigarette cartridges,²⁷ but these contaminants probably arise from use of impure propylene glycol.²⁸ In contrast, smoke from tobacco cigarettes contains many hundreds of potentially carcinogenic chemicals, including volatile organic compounds (VOCs), polycyclic aromatic hydrocarbons (PAHs) and tobacco-specific N-nitrosamines (TSNAs).²⁹ On balance, studies of the vapour from e-cigarettes are reassuring when compared with traditional cigarettes.²⁴ The amount of total TSNAs isolated from an e-cigarette is approximately the same as that in other nicotine products.^{26,28} A review of the relevant literature found that **e-cigarettes have either low or undetectable levels of particulate matter, trace metals, VOCs, PAHs and TSNAs when compared to cigarette smoke.**²⁴

E-cigarettes appear to have a nicotine pharmacokinetic profile roughly equivalent to nicotine inhalers.³⁰ Although early versions of e-cigarettes were found to deliver nicotine unpredictably, **more recent studies reported that refill solutions were labelled accurately and contained consistent nicotine concentrations.**³¹ The amount of nicotine delivered to the circulation is less than occurs with smoking a conventional cigarette.³² Serum concentrations typically peak at 1.3 ng/mL after vaping an e-cigarette for about 20 minutes, compared to 2.1 ng/mL 30 minutes after using a nicotine inhaler, and up to 13.4 ng/mL after 15 minutes of smoking a tobacco cigarette.³⁰

In summary, e-cigarettes appear to be a safer alternative to conventional smoking,^{32,33} and they deliver a similar quantity of nicotine and have comparable toxicity to nicotine patches.³⁴ **While there appears to be a small potential for harm from nicotine exposure in pregnancy, the potential is considerably less than continued smoking.**³⁵⁻³⁷ For all of these reasons, Professor of Physiology at Lincoln Memorial University Dominic Palazollo has concluded that:

'Compared to the harmful effects of smoking, these studies suggest that vaping could be used as a possible

harm reduction tool. There is evidence supporting e-cigarettes as an aide for smoking cessation, at least as successful as currently-available FDA-approved NRTs'.²⁴

In Australia and New Zealand, e-cigarettes are **regulated as pharmaceuticals if they are promoted for human therapeutic use – that is, smoking cessation. Nicotine itself, when used for nontherapeutic purposes, is captured under Schedule 7 of the SUSMP as a 'dangerous poison' and state- and territory-based legislation require a permit to possess, purchase or otherwise deal with it.** Some states and territories also have tobacco control legislation that prohibits the sale of products that 'resemble tobacco products', and increasingly e-cigarettes that resemble pens or lip gloss are being marketed to avoid being captured by tobacco control regulations.

E-cigarettes in pregnancy

Pregnancy is a special situation where there is a limited window to reduce the risk of harm to the fetus, and **it may be that e-cigarettes have a role where other interventions have been unsuccessful.** The available data suggest that e-cigarettes have **a risk profile very similar to that of currently available forms of NRT,** but that trial participants are more likely to use them because of the similarities to conventional smoking. The best evidence we have is that NRT is safer than continued smoking, certainly for women who smoke more than five cigarettes a day in pregnancy.³⁷

A number of health bodies, such as the British Medical Association (BMA), stand against the free availability of e-cigarettes, and the Australian Medical Association (AMA) has expressed concerns that e-cigarettes might be an 'entry into smoking, not necessarily ... an exit from smoking'.³⁸ Arguments put forward are that e-cigarette usage might increase rates of cigarette smoking by attracting new recruits and reducing the success of quit attempts, a situation referred to as 'renormalising smoking'.³⁹ Other objections have even been based on the fact that explosions of the heating mechanisms in e-cigarettes have been reported and that fire might be a theoretical risk. However, **in Australia alone, an average of 14 people die from fires associated with smoking every year,** and smoking is associated with more than 4500 fires each year, including perhaps 7% of all bushfires.⁴⁰

Finding better ways of helping pregnant smokers to quit is obviously a public health priority.⁴¹ At the moment, searches of the major Australian and international clinical trial registries reveal **no trials of e-cigarettes in pregnancy;** indeed, pregnancy is usually high on the list of exclusion criteria for such clinical trials. In the light of new information from clinical trials, is there a case to reconsider evaluating e-cigarettes for women who continue to smoke in pregnancy?

Ethics committees are likely to be hesitant to approve trials of e-cigarettes in pregnancy, but an important first

step might well be observational studies. There are few published clinical trials of e-cigarettes at present, and at this time, e-cigarettes **do not appear to have gained licensing approval as a therapeutic good**, a situation that might present a barrier to trials. However, in the light of this gathering information, perhaps it is time to take look to e-cigarettes in clinical trials during pregnancy. Should they prove to be an acceptable and safe harm-reducing alternative to tobacco cigarette smoking for the duration of pregnancy, the benefits to babies and the health system will be worth it.

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