To burn or not to burn: similar effects of different types of prenatal tobacco exposure on infant lung function

Brian G. Oliver [1,2] and Paul S. Foster[2]

[1]School of Life Sciences, University of Technology Sydney, Ultimo, NSW, Australia. [2]The Woolcock Institute of Medical Research and Faculty of Medicine, Health and Human Sciences, Macquarie University, Sydney, NSW, Australia.

Corresponding author: Brian G. Oliver (Brian.oliver@uts.edu.au)

Shareable abstract (@ERSpublications)
The first study to describe the harmful effects of snus on the unborn infant provides evidence to help clinicians and mothers collectively to make an informed choice about quitting the use of snus before planning pregnancies https://bit.ly/3vJnBxW

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The smoke from tobacco has been inhaled by humans for thousands of years but it was the rise in the popularity of tobacco smoking in Europe *circa* the 1600s, which prompted King James I of England to declare that cigarette smoking is "harmefull to the braine, dangerous to the lungs". These and other warnings about the adverse health effects of cigarette smoking were largely ignored by the medical community until the 1950s. The history of the eventual acceptance by the wider medical community is eloquently described by Wynder [1], who provided the "definitive proof" of the association between cigarette smoking and lung cancer.

Whilst it is obvious these days that cigarette smoking is detrimental to human health, other cigarette alternatives such as snuff (inhaled powered tobacco), snus (powered tobacco that is placed in the mouth), chewing tobacco, electronic cigarettes and smokeless (heat-not-burn) tobacco devices are still viewed as not being dangerous or as less harmful than cigarette smoking. This idea of a safer version of cigarette smoking held by the general public and some of the scientific and medical community is partially driven by profit margins, resulting in industry-led "scientific reviews", for example [2], and tobacco industry-sponsored clinicians and scientists. Direct marketing campaigns have also been undertaken – for example, following petition by a tobacco company, the USA Food and Drug Administration, in 2019, allowed a one company to advertise their snus products as follows: "Using General Snus instead of cigarettes puts you at a lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis" [3]. We only have to look at the rules surrounding which journals will accept publications that are funded, or have authors who have had funding from, the tobacco industry to see the divide in the community. Furthermore, many influential medical journals have no rules in place.

As a community of respiratory clinicians and scientists, we must ask ourselves why young people are still becoming addicted to tobacco products. Have we failed in our public health campaigns? Are governments not providing adequate funding for scientific studies? Is Big Tobacco winning? In a nonsmoker, any form of tobacco use can only be seen as a life-limiting pursuit. However, globally, young people are using cigarette alternatives with an alarming increase in frequency, with numbers of users doubling or tripling in the last 5 years. The introduction of e-cigarettes and debate around their place in society has, in some ways, become a smoke screen obfuscating the adverse health effects associated with the use of other cigarette alternatives. In this issue of *ERJ Open Research*, Bains *et al.* [4] investigate whether the use of a type of smokeless tobacco, snus, during pregnancy effects infant lung function. Whilst snus and other smokeless tobacco products (excluding e-cigarettes) have a relatively low global usage rates, in Norway and Sweden, 20.1% and 25% of younger males and 6% and 7% of younger females, respectively, are users [5]. Similar observations have been made with e-cigarettes globally [6], where usage in women has doubled in recent years.

BAINS *et al.* [4] carried out their clinical trial in Norway and Sweden, where a subset of non-selected mothers from the prospective general population-based birth cohort Preventing Atopic Dermatitis and Allergies in Children were enrolled prospectively, with lung function data collected from 1163 infants. Around 10% of mothers used nicotine products, with 60% of these using snus exclusively. They found that infant lung function was reduced by the maternal use of nicotine containing products, with similar effects when comparing maternal cigarette smoking or snus usage. The study was carried out at a time before e-cigarettes were introduced in these countries.

This study is important for several reasons.

1) It is the first study to show that snus usage in pregnancy impairs infant lung function.
2) By gestational week 6, 86% of mothers reported quitting nicotine products, this means that the effects on infant lung function occurred in an ∼2-mm fetus at a developmental stage when the lungs are just beginning to form. It would be difficult to estimate the health effects with reference to the half-life of every toxin from cigarettes/e-cigarettes but we do know that within 1 week of quitting, nicotine levels are essentially zero; therefore, it is likely that the adverse health effects are not driven by persistent nicotine and perhaps other tobacco-derived toxin exposures.
3) Whilst this study included only "largely healthy" infants and there was similar birth weight in the nicotine and non-nicotine groups, it would be reasonable to assume that infant gestational weight in this study would not be affected by the use of tobacco products (in the first trimester). Smoking in the third trimester is typically associated with reduced birth weight. This is a subtle but very important scientific point, as being born with a low birth weight is associated with subsequent lung health abnormalities.
4) The similar effects of snus and tobacco smoking on infant lung function illustrate that smokeless tobacco is not a safer alternative to cigarette smoking, and that combustion products are not driving these effects. Whilst it is tempting to extend this observation to other tobacco alternatives, studies of a similar design are needed to draw such conclusions.
5) The influence of tobacco products early in pregnancy on lung function raises interesting questions for epidemiological studies. This study used questionnaires administered during pregnancy to assess exposure to tobacco products, thus avoiding recall bias. Outside of the context of a clinical trial, and especially with unplanned pregnancies, a woman might not be aware that they are pregnant and therefore may continue to use tobacco products until pregnancy is confirmed. In this context, a woman might perceive that they have abstained from tobacco use during pregnancy, and thus clinical histories and epidemiological studies might miss important information.

The study does have some limitations. Any study that relies upon surveys and not upon biomarkers will have an element of misreporting; for example, smokers typically under-report usage. Infant lung function is difficult to measure, and the relationship between infant lung function and the development of asthma and/or COPD is not perfectly linear, and often our assumptions are based on studies of prematurely born cohorts (see the reviews by SANCHEZ-SOLIS [7] and SIMPSON *et al.* [8]). However, this study does provide the ideal cohort for future longitudinal studies, providing that environmental tobacco smoke and other environmental toxicants can be assessed throughout life. Whilst not stipulated in the study, the ethnicity of participants in this study is likely to be relatively homogeneous as both counties have ∼20% of people born in another country. There may be differences with other European populations and people from different regions of the world. Furthermore, there are known transgenerational effects of cigarette smoking on the development of asthma [9] and other chronic diseases. Given the use of snus in these countries has occurred for ∼200 years, it may be possible that transgenerational effects are contributing to the outcomes of this study.

Importantly, this is the first study to describe the harmful effects of snus on the unborn infant, providing evidence to help clinicians and mothers collectively to make an informed choice about quitting the use of snus before planning pregnancies.

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