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Negating intergenerational nicotine addiction among Indigenous Australians

On average, Indigenous Australians live eight years less than non-Indigenous Australians, according to the most recent report by the Australian Bureau of Statistics [1]. Also, Indigenous Australian children are more than twice as likely to die during childhood compared to their non-Indigenous counterparts [2]. A large proportion of this disparity is due to the high rates of tobacco cigarette smoking among Indigenous Australians [3]. Smoking during pregnancy harms not only the mother but also the unborn foetus, causing a spectrum of complications, leading to poor health and reduced life expectancy. Therefore, smoking cessation is essential but is often difficult to accomplish, but could be achieved with the help of e-cigarettes [4]. From our research, we showed that replacing tobacco cigarettes with e-cigarettes during pregnancy was not as detrimental to the offspring compared to continuous tobacco cigarette smoking during pregnancy. Therefore, pregnant Indigenous Australians who are unable to quit smoking using other means could turn to e-cigarettes. This could potentially close the mortality gap between Indigenous and non-Indigenous Australians.

Indigenous Australians have a lower life expectancy and higher child mortality compared to non-Indigenous Australians. Approximately 23% of this health burden gap is accounted for by higher rates of tobacco cigarette smoking among Indigenous Australians [3]. Indigenous Australians aged 15 and over were almost three times as likely to be daily smokers compared to their non-Indigenous counterparts (39% vs 14%). Among pregnant women, this disparity was even higher, where Indigenous Australians were almost four times more likely to smoke compared to non-Indigenous Australians (44% vs 12%) [5].

As a result of this high smoking rate, lung cancer is the most common and fatal cancer among Indigenous Australians, who are 70% more likely to die from lung cancer compared to non-Indigenous Australians [6]. Also, smoking during pregnancy leads to a range of gestational complications, such as low birth weight, preterm birth, and SIDS. Furthermore, *in-utero* exposure to tobacco cigarette smoke impacts every organ system, leading to a range of complications in later life [4]. For example, prenatal tobacco smoke exposure is linked to increased nicotine addiction during adolescence [7], fuelling a vicious cycle of intergenerational tobacco smoking if not adequately controlled. Therefore, it is clear that pregnant Indigenous Australians must either stop smoking or find an alternative nicotine source to increase their life expectancy and reduce their child mortality. However, smoking cessation can be challenging to achieve, even when the harms are well known and advertised. One potential solution which was investigated in our research was the use of e-cigarettes as a harm minimisation strategy.

E-cigarettes are hand-held, electronic devices which heat an e-liquid (usually consisting of nicotine and flavouring compounds suspended in propylene glycol and/or glycerine) to produce an aerosol, which can then be inhaled by the user [8]. Compared to tobacco cigarettes, e-cigarettes produce fewer toxic chemicals and in lower amounts [9], making them a potentially safer nicotine source. However, the impacts of switching from tobacco cigarettes to e-cigarettes during pregnancy (e-cigarette replacement) had not been previously investigated. Furthermore, due to the recent emergence of e-cigarettes, their intergenerational impacts have not been studied in humans.

Therefore, we aimed to understand the impacts of e-cigarette replacement and to determine if it was more or less harmful to the offspring compared to continuous tobacco smoke exposure. Female mice were either exposed to tobacco cigarette smoke from pre-gestation to lactation or tobacco cigarette smoke during pre-gestation and then e-cigarette vapour (tobacco flavour, same nicotine exposure) during gestation and lactation. The phenotype of the adult male offspring (13 weeks old) was investigated, and the organs were collected to examine markers of tissue damage. We found that intrauterine tobacco smoke exposure resulted in damage to the kidneys, associated with an increase

in oxidative stress, inflammation, and fibrosis. This damage was significant enough to impair renal function, which could be life-threatening due to the crucial role of the kidneys in removing waste from the blood. On the other hand, e-cigarette replacement was less damaging to the kidneys, and there was no reduction in kidney function in the offspring [10]. Also, e-cigarette replacement was less harmful to the brains of the offspring [11], potentially reducing the likelihood of intergenerational nicotine addiction and succumbing to future tobacco smoking. Thus, we confirmed that maternal smoking during pregnancy is detrimental to the offspring. Furthermore, we also concluded that e-cigarette replacement was less damaging to the offspring compared to maternal cigarette smoke exposure.

However, e-cigarette vaping is not harmless, and certain e-liquids could be extremely harmful, highlighted by the recent cases of vaping associated deaths within the USA [12]. Also, steps must be taken to ensure e-cigarettes are only used as a smoking cessation aid or harm minimisation strategy, and not as a recreational habit. They should also be used alongside current smoking cessation protocols and could be especially helpful among pregnant women who are unable to quit smoking using other means.

The high smoking rate among Indigenous Australians is a significant crisis that must be dealt with promptly. We have shown that replacing tobacco cigarettes with e-cigarettes during pregnancy was less detrimental to the offspring when compared with continuous tobacco cigarette smoking during pregnancy. However, caution must still be taken since e-cigarettes are not harmless and could potentially produce other problems. Thus, e-cigarettes could be used as an alternative nicotine replacement therapy or a harm minimisation tool among pregnant Indigenous Australians who are unable to quit smoking using other means. This could potentially bridge the gap in life expectancy and child mortality between Indigenous and non-Indigenous Australians.

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