Editorial Commentary

Is e-cigarette use associated with future cigarette use among youth and vice versa?

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Over the last decade, traditional tobacco has been regulated. Unfortunately, the e-cigarette has been becoming a new challenge to global health. Since the invention of the smoke-free vapor by Hon Lik in the early 2000s (1), e-cigarette use has spread quickly around the world. It is estimated that Americans spent 4 billion dollars on an e-cigarette in 2018 and e-cigarette would outsell traditional tobacco in 5 or 10 years (2). While firstly designed to help quit smoking and reduce harm to smokers, growing evidence shows that e-cigarette is not helpful with smoking quit and are proven potentially detrimental (3-5). However, despite unproven effectiveness in quitting smoking and potential harm, the e-cigarette has spread rapidly among non-smokers including adolescents. It is reported that, in the United States, 20.8% of high school students used an e-cigarette in 2018, outweighing 8.1% of having used traditional cigarettes (6). Such a pandemic has a series of problems. Nicotine can harm the brain development of adolescents and other harmful substances in the e-cigarette are reported to cause severe consequences including lung injury (7,8). Studies on the relationship between e-cigarette use and traditional cigarette use among youth are controversial. Park *et al.* (4) and Temple *et al.* (9) found that cigarette use among youths is with higher intention to use traditional cigarettes and higher prevalence of substance use, while many other studies proved no apparent association. What is more, most of the research has discovered that the relationship between e-cigarette use and cigarettes is unidirectional, which limits the trajectory understanding of the association between e-cigarette and cigarettes.

In 2018, Bold and colleagues carried out a cross-lagged and reciprocal study and found that e-cigarette use among youth was associated with subsequent cigarette use while cigarette use was not associated with subsequent e-cigarette use across three waves (2013, 2014 and 2015) in 3 public schools in Connecticut (10). Besides, they also found an increase in both e-cigarette and cigarette use as time increases across the above three waves. Due to ethical problems, trajectories of e-cigarette and cigarette use cannot be conducted using a randomized controlled trial. Thus, Bold et al. conducted this study by using an observational cohort design. Odds ratio (OR) and corresponding confidential interval (CI) were the primary indicators used to adjust all mentioned longitudinal associations. It is shown that past-month e-cigarette use had much higher probability to cigarette use (over seven times from wave 1 to wave 2: OR =7.08, 95% CI: 2.34–21.42; near four times from wave 2 to wave 3: OR =3.87, 95% CI: 1.86–8.06), while cigarette use during last 30 days did not predict future e-cigarette use (from wave 1 to wave 2: OR =2.02, 95% CI: 0.67–6.08; from wave 2 to wave 3: OR =1.90, 95% CI: 0.77–4.71).

There are some strengths and limitations of the study. First, authors have taken ways to control selection bias, information bias, attribution bias and confounders (repeated surveys across three schools selecting a diverse demographic, anonymous method and unique 5-factor identification codes, matching strategy and comparable

match rates with other studies, adjusting five co-variables and matching strategy). Second, controlling for the autoregressive effect was another proper consideration to find the stability and directionality of associations across three waves. Third, the criteria used in the study design were good evidence-based. For example, SES was assessed by using the Family Affluence Scale, repeated surveys were carried out to ascertain diverse geography which was based on government's data, and match rates were compared to those data from authoritative journals. However, despite the above strengths, there are still some limitations we need to concern. First, the authors said that "parents were contacted in advance of the study and could indicate if they did not want their child to participate." We know the characteristics of those parents who agreed their child's participation would be different from those who refused. Authors could reduce such selection bias by analyzing how many parents have refused, why they refused, and comparing whether there are any differences between parents who agreed and who disagreed to participate. Second, although authors have considered a recall bias problem by choosing binary results as the primary outcome, there is still a potential recall bias problem. The bias is because students were asked about their past-month yes or no using of e-cigarette and cigarette. Accurate memory of 30 days ago is doubted.

More importantly, the real-world situation is much more complicated. Several pieces of literature have found that family history of e-cigarette, friends smoking, mental health, media and advertising exposure, environmental access, and stress are all associated with e-cigarette and cigarette use (11-14). Regarding e-cigarette use and afterward cigarette use, many other articles focusing on youth from other countries/areas have found comparable results (15,16). However, of cigarette use and afterward, e-cigarette use among youth, another bidirectional and cross-lagged design found a different result (16).

To summarize, though there are still some potential biases, confounders, and other issues, both internal validity and external validity of point "e-cigarette use is associated with future cigarette use" seems plausible. However, we are not confident with the external validity of the point "cigarette use is not associated with future e-cigarette use." Whether the association between e-cigarette use and future cigarette use is causal is still an open question. At last, we need more reciprocal studies with a larger sample, more diverse ethnics, age-stratified and longer follow-up time to answer this question.

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Ethical Statement: The author is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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