whether cognitive impairment was reversed. The advantage of both these approaches would be to minimize reverse causality and known and unknown confounding. In our opinion, this is the best way to clarify the causal nature of the association between impaired lung function and dementia and, if this is the case, potentially shed light on the underlying mechanism.

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**FINANCIAL/NONFINANCIAL DISCLOSURES:** See earlier cited article for author conflicts of interest.

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**DOI:** https://doi.org/10.1016/j.chest.2020.04.037

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# Vaping Nicotine Is Far Less Harmful Than Smoking Tobacco

**To the Editor:**

In a previous issue of *CHEST* (May 2020), Bozier et al[1] reviewed the recent research on the potential health effects of e-cigarettes. We would like to comment on several of the claims made in the article.

The most relevant question for smokers is whether vaping nicotine is less harmful than smoking the cigarettes it is designed to replace. The evidence suggests it is far less harmful. The National Academies of Sciences, Engineering, and Medicine report[2] found substantial evidence that "exposure to potentially toxic substances from e-cigarettes is significantly lower compared with combustible tobacco cigarettes" and "reduced short-term adverse health outcomes in several organ systems."[2]

The authors quite rightly conclude that "e-cigarette use is not risk-free for non-smokers." However, international studies of adults and youth show that current use of e-cigarettes by never smokers is rare, and regular use is very rare, usually $<0.5\%$.

Most of the research on the harms of e-cigarettes is from in vitro and animal studies. How these findings translate to health effects in humans is uncertain, when many human studies show substantial health improvements in smokers who switch to vaping.

The recent outbreak of lung injuries in the United States electronic-cigarette, or vaping, product use-associated lung injury (EVALI)[3] was not due to nicotine vaping. Most, if not all, cases were the result of vaping black-market tetrahydrocannabinol contaminated with vitamin E acetate.[4] No cases have been associated with commercial nicotine vaping.

The authors claim that we cannot exclude the possibility that "e-cigarettes pose a similar, lesser, or greater cancer risk than cigarette smoking" because of the presence of carcinogens and potential adverse effects in two studies. Given the greatly reduced number of carcinogens and their lower concentration in e-cigarette vapor, it is very likely that the cancer risk from vaping is only a tiny fraction of the risk from smoking.[4]

Finally, the authors appear to misunderstand the role of tobacco harm reduction in questioning the value of vaping as a quitting aid when many ex-smokers continue to vape after quitting. Replacing a high-risk behavior with a far less harmful one is a well-accepted public health strategy, for example, methadone maintenance for heroin addiction.

Evidence from randomized controlled trials, population studies, and better-quality observational studies shows that e-cigarettes are effective quitting aids.[5] The authors are correct that short-term nicotine replacement therapy is less harmful than vaping, but it is also far less effective for quitting, and very few smokers use it.

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**FINANCIAL/NONFINANCIAL DISCLOSURES:** The authors have reported to *CHEST* the following: C. P. M. has received funding from Pfizer Australia, Johnson & Johnson Pacific and Perrigo Australia for teaching, consulting, and conference expenses. C. P. M. has never received any funding or payments from e-cigarette or tobacco companies; serves as a Board member of the Australian Tobacco Harm Reduction Association (ATHRA), a health promotion charity. ATHRA has received donations in the past from Australian vape shops. This formally ceased in March 2019. None declared (M. H.).

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**DOI:** https://doi.org/10.1016/j.chest.2020.02.077

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# Response

**To the Editor:**

We thank Drs Mendelsohn and Hall for their response to our systematic review of current literature surrounding the (potential) health effects of e-cigarettes.[1] We acknowledge their commitment to improving health outcomes for tobacco cigarette smokers and welcome their opinion in the current debate. While supporting our conclusion that "smokers who switch to e-cigarettes may experience harm reduction," they disagree with our cautious approach by not endorsing e-cigarettes as a harm reduction strategy.

Harm reduction is founded on the understanding that complete abstinence is an unrealistic goal. This is likely untrue for most smokers, with recent data from the National Health Interview Survey and Cancer Control Supplement reporting that 80% of older adults who had ever smoked had successfully quit.[2] Nonetheless, if we consider those tobacco smokers who are unable to successfully quit despite the use of tobacco cessation counseling and pharmacotherapy, one must assess the harm reduction efficacy of e-cigarettes. In arguing that "e-cigarettes are effective quitting aids," Drs Mendelsohn and Hall draw on two randomized controlled trials of e-cigarettes as a smoking cessation tool. Hajek et al[3] reported one-year smoking abstinence rates of 18% in those using e-cigarettes vs 9.9% in the nicotine replacement therapy (NRT) group. Recently, Walker et al[4] reported 6-month smoking abstinence rates of 7% with e-cigarettes plus nicotine patches vs 2% with nicotine patches alone. Thus, e-cigarettes may be more effective at promoting smoking abstinence than NRT, but the effect is rather modest. When also considering that e-cigarette use may increase the risk of smoking relapse[5] and promote smoking initiation,[5] we are left questioning the public health benefit of e-cigarettes. We acknowledge that from an individual perspective, e-cigarettes may be an appropriate harm reduction strategy. However, this would require identification of the subset of smokers in whom e-cigarettes are efficacious for smoking cessation. At present, such a phenotype is unknown.

Drs Mendelsohn and Hall acknowledge that e-cigarettes are not without risk. It is therefore important to ask whether long-term e-cigarette use sufficiently lowers risk to translate to improvements in long-term health outcomes. The evidence of little harm reduction after reduction of tobacco smoking without complete abstinence[6,7] makes this question particularly pertinent. The limited evidence in humans reveals short-term improvements in respiratory health for tobacco smokers who transition to e-cigarettes.[8] However, emerging preclinical evidence suggests that long-term use may increase the risk for lung cancer and pre-cancerous bladder lesions.[9] However, whether the toxicant burden associated with lifetime e-cigarette use, on top of previous tobacco smoking history, does or does not contribute to life-time risk of respiratory disease, cardiovascular disease, cancer, and mortality is unknown.

The goal of our review was to systematically summarize the recent literature, regardless of the findings, on the possible health effects of e-cigarette use. We hope that in doing so it has provided much-needed clarity as to the current evidence and will be an impetus for future research and regulation.

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**FINANCIAL/NONFINANCIAL DISCLOSURES:** See earlier cited article for author conflicts of interest.

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**DOI:** https://doi.org/10.1016/j.chest.2020.04.018

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