The Health Effects of Electronic Cigarettes

TO THE EDITOR: The statement by Dinakar and O'Connor (Oct. 6 issue)[1] that the use of electronic cigarettes (e-cigarettes) is increasing among minors and young adults is inaccurate, since this trend has recently reversed.[2,3] Miscoding "use" for "experimentation" abnormally inflates these statistics; many of these young people were experimenting and certainly were not using e-cigarettes regularly. Notably, experimentation with e-cigarettes is now associated with an accelerated rate of decline in smoking among youths.[2-4]

Although the findings of trials on the efficacy of e-cigarettes as smoking-cessation tools are inconclusive, "vaping" (e-cigarette use) is having huge effects in the general population, and many smokers are quitting.[5] In the United Kingdom, approximately 850,000 cigarette smokers switched exclusively to vaping, and another 650,000 who smoked and vaped have now stopped both.

With regard to the health effects of aerosol emissions from e-cigarettes, projecting results from cell lines or studies in animals to humans is highly speculative. These studies are not replicating normal conditions of use and lack standardized protocols for e-vapor production and exposure. Likewise, transient effects of vaping on health measurements in studies in humans are clinically irrelevant and without prognostic value. By emphasizing the limited risks of e-cigarette use, the authors do not acknowledge its public health potential.

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THE AUTHORS REPLY: The trend in cigarette smoking among minors in the United States does indeed show a heartening decline, with the rate of current use of cigarettes decreasing significantly from 28% in 1991 to 11% in 2015.[1] This decrease in the use of combustible tobacco has been accompanied by the increasing use of e-cigarettes by minors between 2011 and 2015, with smaller and nonsignificant changes between 2014 and 2015.[1,2] In 2015, the use of e-cigarettes among teens was reported to be higher than the use of traditional tobacco cigarettes or any other tobacco product.[1,2]

We agree that an inherent challenge in the interpretation of such survey data is the potential misclassification of infrequent experimentation as regular use. We disagree with the interpretation that experimentation with e-cigarettes "is now associated with an accelerated rate of decline in smoking among youths." A recent longitudinal study involving a school-based cohort revealed that youths who had ever used e-cigarettes at baseline "were more likely to report initiation of combustible tobacco use over the next year" than were nonusers of e-cigarettes.[3]

Our review of in vitro studies, studies in animals, and studies of short-term physiological effects of e-cigarette use in human research volunteers was intended to give readers a balanced overview of the limited existing literature on the biologic effects of e-cigarettes. We think that our article provides a balanced review of the potential benefits and risks of the use of e-cigarettes as a smoking-cessation or smoking-reduction aid.

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Since publication of their article, the authors report no further potential conflict of interest.

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More on Treatment Outcomes in Multidrug-Resistant Tuberculosis

TO THE EDITOR: Zignol et al. (Sept. 15 issue)[1] suggest that within 10 years, molecular technologies will replace conventional phenotypic testing in surveys of drug resistance and surveillance of tuberculosis. To avoid the overestimation of drug resistance, wider implementation of testing for minimal inhibitory concentration (MIC) must occur first, for four main reasons. First, most commercial molecular assays do not provide information on the type of mutation. Second, different mutation types may be associated with different phenotypic MICs and different clinically relevant levels of resistance, which may lead to unnecessary discontinuation of a drug or incorrectly identifying a patient as having multidrug resistance (e.g., in the case of low-level resistance to isoniazid).[2] Third, different mutation types may suggest different levels of phenotypic cross-resistance or susceptibility.[2] Fourth, the level of phenotypic resistance for the same mutation may vary in different geographic areas.[3] Farhat et al. found that even the least complex molecular assay for antimicrobial susceptibility testing would require the detection of 238 mutations in 18 loci, and the meaning of these mutations may not be clear from a clinical point of view in the absence of MIC results.[4]

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No potential conflict of interest relevant to this letter was reported.

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TO THE EDITOR: The simplified definitions of treatment outcomes proposed for multidrug-resistant (MDR) tuberculosis (i.e., bacillary resistance to at least isoniazid and rifampin) by Günther and colleagues (Sept. 15 issue)[1] prompted us to apply the simplified definitions to previously published data from our clinical trial,[2] TMC207-C208, in which bedaquiline or placebo was added to a preferred background regimen for the first 24 weeks of treatment in 160 patients with newly diagnosed, smear-positive, MDR tuberculosis. Patients were followed for an additional 96 weeks, during which they completed the background regimen. On the basis of current outcome definitions from the World Health Organization (WHO), MDR tuberculosis cure rates at 120 weeks were 58% with bedaquiline and 32% with placebo ($P=0.003$).[2] After applying the simplified definitions to our final data set, cure was achieved in 48% of patients with bedaquiline and in 20% with placebo ($P<0.001$) (Table 1). Rather than limiting follow-up to 1 year after treatment completion, which is fairly routine, our protocol required follow-up for 120 weeks from baseline, which is not a rou-

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