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Clearing Some of the Haze around E-cigarette or Vaping Product Use-Associated Lung Injury (EVALI)

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E-cigarette or vaping product use-associated lung injury (EVALI) is a severe pulmonary illness associated with the use of e-cigarettes or vaping products that was officially identified and named in 2019. From 2019–2020, The U.S. Centers for Disease Control and Prevention (CDC) reported 2,807 patients hospitalized with EVALI in the United States, and 68 died from their illness (1). Despite the thousands of individuals affected and the severity of the illness, follow-up with these individuals was relatively sparse, and we know little about the long-term consequences of EVALI. Only one retrospective study of similar size has been reported thus far on the 1-year outcomes of EVALI (2). In this issue of *AnnalsATS*, Blagev and colleagues (pp. 1892–1899) report the first prospective cohort study examining 1-year outcomes in patients with EVALI, which includes quantitative survey analysis of respiratory symptomology and mental health questionnaires (3). With such limited data reported thus far, the study by Blagev and colleagues is essential for our understanding of the long-term outcomes of EVALI.

It is especially important that we continue to elucidate the long-term consequences of EVALI as cases are still being reported and the numbers of those affected are still growing (2). Although EVALI has been primarily associated with individuals who vaped tetrahydrocannabinol-containing e-cigarettes that included the additive vitamin E acetate (VEA) (1), approximately 20% of patients reported using only nicotine e-cigarettes (4). Further, there have been sporadic cases of respiratory disease associated with e-cigarette use for years prior to the naming of EVALI and inclusion of VEA in e-cigarettes (5, 6). These cases highlight that EVALI remains an ongoing risk to e-cigarette users in the population and is a potential source for long-term illness.

In this study, Blagev and colleagues sought to determine the long-term respiratory, cognitive, mood disorder, and vaping behavior outcomes in patients suffering from an initial episode of EVALI. This study has many strengths, including patients who were prospectively enrolled from two health systems (University of Utah

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and Intermountain Health) and outcomes that were recorded at 1 year post-EVALI using several methods. Patients were screened for cognitive function, depression, anxiety, post-traumatic stress disorder (PTSD), and vaping behaviors using validated tools. Also, patient respiratory disability, pulmonary function, and prior coronavirus disease 2019 (COVID-19) infection were recorded. The authors used multivariable regression to identify risk factors for post-EVALI vaping behaviors. Further, they assessed if the most severe cases of EVALI (e.g., admitted to the intensive care unit) were associated with cognitive, respiratory, or mood symptoms at 1 year.

The 1-year follow-up window used by Blagev and colleagues goes substantially beyond the CDC recommended 48-hour follow up after initial presentation, which was due to roughly 25% of EVALI patients being rehospitalized in that same 48 hour window (7). This longer assessment window allows for the field to better understand continued e-cigarette use patterns, which appears to be a risk factor for readmission and may play a role in persistent physiological effects (7). The prospective design may allow for consensus building in the high variability in long-term EVALI outcomes reported in the literature (2, 3, 8–10).

In this issue, Blagev and colleagues describe the largest EVALI follow-up cohort study conducted thus far, with 73 patients who had a follow-up at 12 months. Similar to prior cohorts of EVALI patients, most patients were male, young (mean age 31), White, and did not require intensive care unit (ICU) admission (59%). Patients who presented as an outpatient and were not admitted were included in this cohort. At 12-months follow-up, 39% of patients had cognitive impairment, 59% reported anxiety and/or depression, and 62% had PTSD related to their EVALI episode. Nearly half of patients had persistent respiratory symptoms on follow-up, though the majority of these patients had normal pulmonary function testing. Despite all of these patients suffering

a severe, acute health event related to their vaping, only 38% of participants had reported quitting all vaping and smoking behaviors at 1 year. Interestingly, younger age was associated with reduced vaping behavior post-EVALI. ICU admission was not found to be associated with cognitive impairment, mood symptoms, or respiratory symptoms on follow-up.

The prospective assessment of mental health in EVALI patients conducted by Blagev and colleagues is useful. Generally, e-cigarette use has been associated with mental health problems, particularly in youth and young adults. For example, a systematic review of 40 studies found associations of e-cigarette use with a variety of disorders including anxiety, depression, suicidality, PTSD, and attention-deficit/hyperactivity disorder and conduct disorder (11). More recently, a retrospective study examined rates of mental health conditions in EVALI patients and found that 64% of 140 patients were diagnosed with a mental health condition (12). This prospective assessment of mental health in EVALI patients further strengthens the associative link and raises the mental health consequences of e-cigarette use as a key public health issue.

Despite these key findings, there are some limitations to this study. While 73 patients represent the largest cohort of EVALI follow-up so far, this only represents 37% of the total patients diagnosed with EVALI in these health systems (197). There could be unintended biases around the subset of patients who participated in the follow-up study versus the general EVALI population at large. Recall bias could explain the greater frequency of reported persistent respiratory symptoms in the current study compared with findings from Triantafyllou and colleagues in 2021 that examined all EVALI diagnoses in a retrospective manner with electronic medical records (2). Both studies showed that pulmonary function testing appeared to normalize in the long term. There was no control group for comparison, nor baseline data for the

participants in this study. As the authors suggest, this limits the ability to conclude a clear causal link between the high prevalence of cognitive and pulmonary limitations with the EVALI diagnosis versus an association.

Overall, the study published by Blagev and colleagues helps to “clear some of the haze” around EVALI, particularly regarding the long-term implications of EVALI. This study represents a substantial contribution to the field, with a more detailed validation of the work by Triantafyllou and colleagues in 2021, showing that while a significant number of patients continue to have respiratory symptoms, it appears that pulmonary function testing does improve over time (2). Blagev and colleagues highlight the concerning fact that many of the patients suffering EVALI are dependent on some constituent in vaping products, as most patients in both studies continued to vape following EVALI. This represents a critical feature of these patients, as there are clear reports of recurrent EVALI with continued vaping behavior (13). Further, Blagev and colleagues found significant cognitive and mood disorders present for these patients 1 year after EVALI diagnosis, many directly related to the EVALI episode (62% with PTSD). Screening for mental health disorders and ensuring access to mental health resources is likely an important component of follow-up care for patients with EVALI. Despite the limited data on nicotine or cannabis cessation approaches in adolescents and younger adults (14, 15), outpatient management to follow and address long-term needs regarding pulmonary symptomatology, mental health, and chemical dependence appears to be critical for EVALI patients. The work of Blagev and colleagues is a critical addition to the current understanding of the long-term health effects of EVALI. Due to the increasing prevalence of vaping, more studies on this topic are urgently needed. ■

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