

Vaping and Mental Health Conditions in Children: An Umbrella Review

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ABSTRACT: The e-cigarette (EC) epidemic began in the United States (US) in 2007; since 2014 EC is the most commonly used form of tobacco. However, the mental health implications of vaping are grossly unknown. The aim of this umbrella review is to provide a state-of-the-art summary of existing research concerning vaping and mental health conditions in children. Following the PRISMA Statement 2020 guidelines, a systematic search was conducted across PubMed, Cochrane Library, and Google Scholar up to April 15th, 2022 to locate relevant studies. The Joana Briggs Institute (JBI) methodology for umbrella reviews and quality appraisal tool was utilized. Six studies, pooling a total of 846,510 adolescents aged 21 years or below, were included by collating 85 primary clinical studies. Of these, 58.8% of the primary clinical studies originated in the US, with 4.7% from Canada, South Korea, and the United Kingdom each; 3.5% each from England and Taiwan; 2.4% each from Australia, France, Hawaii, Mexico, and Russia; and 1.2% each from Denmark, Greece, Hong Kong, Iceland, New Zealand, Poland, and Switzerland. Overall, significant associations were found between mental health outcomes, including depression and suicidality, among current EC users and those who had ever used EC. Compared to adolescents who had never used EC, both depression and anxiety were reportedly higher among EC users. Impulsive behaviors, reported as impulsivity, were also found to be correlated with the adoption of EC use. However, there is a lack of evidence regarding the impact of EC use on mental health outcomes in children. This umbrella review highlights the urgent need to further explore the effects of current EC use from a psychiatric and public health perspective.

KEYWORDS: Vaping, e-cigarette, mental health, children, adolescents, depression, suicidality, anxiety, impulsivity

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Introduction

The E-cigarette (EC) epidemic among youth began with the distribution of ECs in the United States in 2007. Since 2014, these products have become the most commonly used tobacco form.¹ While a shift from a combustible cigarette (CC) use to EC use has been an area of key progress, the tobacco sphere continues to penetrate society. EC is designed to deliver flavors, nicotine, and other chemicals delivered via inhaled aerosol.¹ Products range from e-cigarettes, vaping pens, tank systems, e-hookahs, and electronic nicotine delivery systems (ENDS); they may appear as regular cigarettes, pipes or cigars, USBs, and pens.² Most of the EC in use have a heating system, batteries, and a liquid-holding tank.² The use of EC is referred to as vaping and these systems can be utilized to deliver marijuana, other drugs.² “Puff Bar (26.1%), Vuse (10.8%), SMOK (9.6%), JUUL (5.7%), and Suorin (2.3%)” were the most commonly used EC brands among current high school students, as reported by the CDC and FDA.³ The nation’s youth e-cigarette epidemic is largely attributed to flavored tobacco products including menthol and other flavors. In the US, 27.5% of high school students use EC⁴; the 3 largest market users originate from the US, the United Kingdom, and Japan. The global EC market was valued at \$20.4 billion, in 2021—this is expected to grow to \$30 billion by 2027.⁵ Alarming, EC use among the youth rose by 1800%

between the years 2011 and 2019.⁴ Three in 4 users aged between 15 and 21 years are unaware that EC contains nicotine.⁴

The mental health implications of vaping in children are largely unknown, although data may associate the changes with those seen with tobacco cigarettes. Mental health concerns among children related to vaping, other than addiction have been largely neglected.⁶ While smoking CC has been an established risk factor for adverse mental health, the reasons for the underemphasis of EC as a potential determinant of mental health are unknown.⁷ Smokers may also view EC products as a modality to improve dysphoric symptoms, without recognizing that smoking cessation may lead to the improvement of said symptoms.⁶ The aim of this umbrella review is to provide an updated summary of the existing research syntheses related to vaping and mental health conditions in children, focusing on the mental health consequences of vaping in this group.

Methods

Search strategy

This umbrella review was conducted adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines and the Joana Briggs Institute (JBI) methodology for umbrella reviews.^{8,9} We searched PubMed, Cochrane library, and Google Scholar to locate the studies.



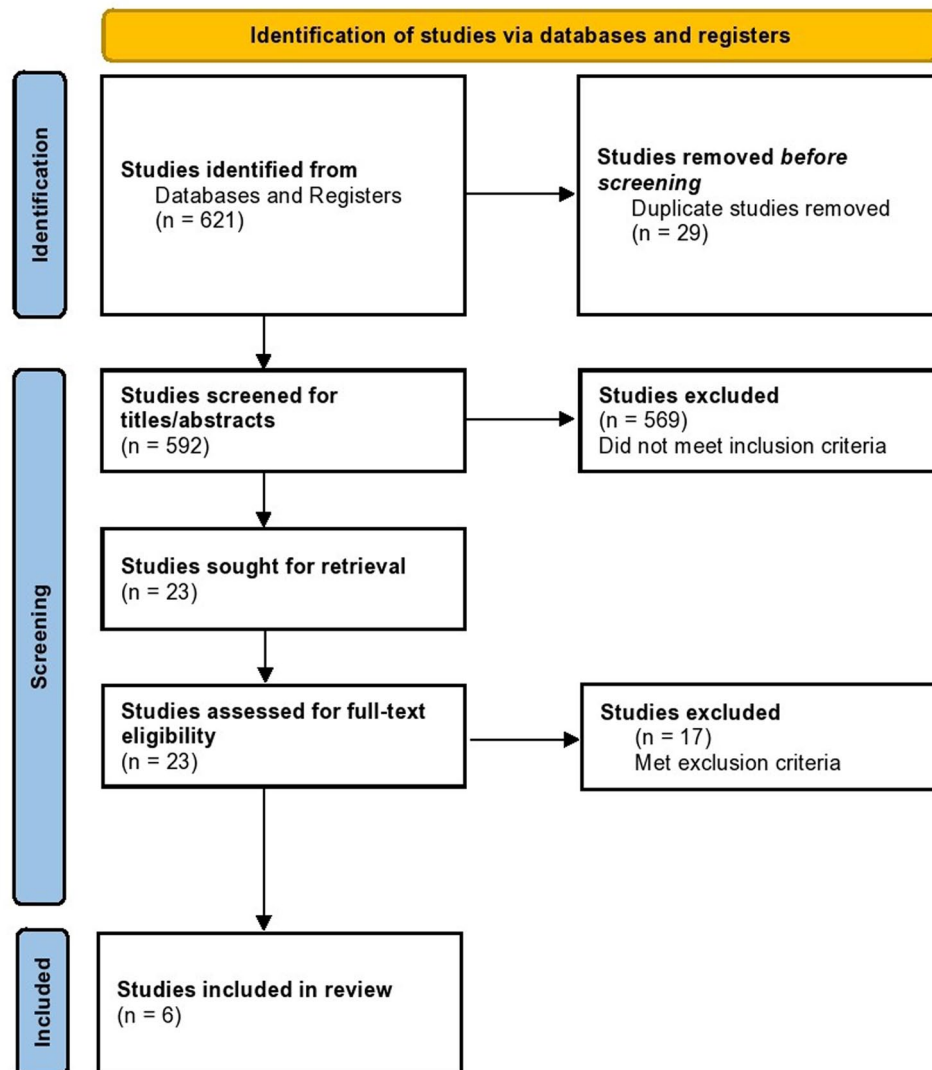


Figure 1. PRISMA flowchart depicting the study selection process.

The search terms are enlisted in Supplemental Materials. All databases and additional sources were searched from inception until April 15, 2022. All citations were stored in EndNote X9 (Clarivate Analytics).

The PRISMA flowchart is depicted in Figure 1. A total of 621 studies were identified through the databases and other sources searching. Twenty-nine duplicates were removed before screening; 592 studies were screened for titles/abstracts. Of these, 23 were assessed for full-text screening. Post-full-text screening, 6 reviews were included in this umbrella review. The excluded studies ($n = 17$) are enlisted in Table 1 with reasons.

Inclusion and exclusion criteria

This umbrella review included a systematic review and meta-analytical studies. These studies included national sample studies, cohorts, case series, and case reports as well. Children/adolescents aged 21 years or less that were exposed to electronic cigarettes/vaping were included. Mental health consequences

were enlisted wherever available. No date restrictions were applied; however, non-English articles were excluded. In addition, studies that did not analyze the <21 years age group were excluded even if they reported on EC and mental health outcomes. A manual search of the bibliography of all screened studies was conducted.

Data extraction and synthesis

Two reviewers (AMK and ZS) identified the articles for inclusion by screening titles and abstracts, followed by a full-text review. Any discrepancies were resolved by active discussion between the 2 reviewers or with a third person (SA) to reach a consensus. The data extraction tool was adapted from the JBI data extraction tool used for research syntheses. The 2 authors extracted data into the following domains: the PICO framework, year of publication, type of review, number of primary clinical studies included, sample size, locations, and key findings of EC and mental health outcomes. The findings based on

Table 1. Full-text studies excluded in this umbrella review.

AUTHORS	STUDIES/REPORTS INCLUDED	SCREENING RESULT	REASON FOR EXCLUSION	DOI
Lim (2022) ¹⁰	17	Excluded	Reports of epidemiological studies that share the global prevalence of cannabis vaping, not related to mental health outcomes	https://doi.org/10.1001/jamapediatrics.2021.4102
Notley (2021) ¹¹	60	Excluded	Focused on interest and enjoyment in flavors, with no mental health indicators/sequelae	https://doi.org/10.1111/add.15723
Bozier (2020) ¹²	225	Excluded	Focus on cardiopulmonary, general health, and oral manifestations	https://doi.org/10.1016/j.chest.2019.12.042
Selph (2020) ¹³	30	Excluded	Focus on quitting interventions	https://doi.org/10.1001/jama.2020.3332
Gonsalves (2020) ¹⁴	23	Excluded	Focus on pulmonary outcomes only	https://doi.org/10.1016/j.jpeds.2020.09.040
Pericot-Valverde (2018) ¹⁵	66	Excluded	No demaracation of adult populations and pediatric populations aged 18-21 years	https://doi.org/10.1016%2Fj.addbeh.2018.04.024
Glasser (2017) ¹⁶	686	Excluded	Focus on ENDS and general outcomes	https://doi.org/10.1016%2Fj.amepre.2016.10.036
Garcia (2020) ¹⁷	19	Excluded	Focus on autonomic cardiovascular effects	https://doi.org/10.1007%2Fs10286-020-00683-4
O'Brien (2021) ¹⁸	21	Excluded	Focus on causal and temporal relationships between e-cigarette and tobacco use	https://doi.org/10.1186/s12889-021-10935-1
Gentry (2019) ¹⁹	9	Excluded	Focus on the adult population	https://doi.org/10.1093%2Fntnr%2Fntnr054
Lee (2020) ²⁰	35	Excluded	Focus on marketing, product and design	https://doi.org/10.1001%2Fjamapediatrics.2020.0259
Smith (2021) ²¹	15	Excluded	Focus on social aspects and norms	https://doi.org/10.1016/j.drugpo.2021.103227
Kinouani (2019) ²²	6	Excluded	Focus on motivations	https://doi.org/10.1080/08889707.2019.1671937
Tzortzi (2020) ²³	133	Excluded	Reports of suicidal ideation in adults >21 years	https://doi.org/10.3390/ijerph17072248
Fluharty (2017) ²⁴	148	Excluded	Lack of <21 years findings	https://doi.org/10.1093/ntr/ntw140
Gogliettino (2016) ²⁵	5	Excluded	Lack of focus on mental health outcomes, but addresses white matter development that is linked to symptoms of depression. Age group until 28 years.	https://doi.org/10.1016%2Fj.drugalcdep.2016.02.015
Underner (2021) ²⁶	NA	Excluded	Non-English language text	https://doi.org/10.1016/j.encep.2020.11.008

the included reviews were further segregated (study-level) by providing a synthesis of the primary clinical studies among included reviews. The findings were reported on prevalence rates (proportion, percentage, OR/aOR, or other measures), and in most cases, 95% confidence intervals (CI) were reported.

Methodological quality

The JBI critical appraisal tool was used to assess the quality of included reviews. The JBI critical appraisal checklist for systematic reviews and research synthesis checklist was used. Two reviewers (AMK and ZS) evaluated all 6 of the included reviews. A consensus was reached for the final quality ratings. The articles were grouped under the following: low (0-4), medium (5-7), and high-quality (8-10) studies.

Additionally, studies that were eligible for inclusion underwent quality appraisal using the AMSTAR-2 checklist. While there are many variants to appraise systematic reviews/meta-analyses, the AMSTAR-2 checklist is the most commonly used one to assess the methodological quality of systematic reviews, with and without a meta-analysis of randomized and non-randomized studies.²⁷ This checklist comprises 16 questions and consists of 7 domains that can determine the validity of included reviews and conclusions. The critical domains include the presence of an a-priori review protocol, adequate literature search, and exclusion criteria justification of individual studies. assessment of the risk of bias, the appropriateness of statistical methods, sources of publication bias if a meta-analysis is conducted and considerations of potential biases during result interpretation.

This umbrella review was registered with PROSPERO: CRD42022312130. No funding was obtained for this study.

Results

Characteristics of the included reviews

Summary findings of included reviews are enlisted in Table 2. The study populations had diverse characteristics. The sample size of the included studies was 846 510. While studies also focused on young adults, we only included data from adolescents aged 21 years and below. Racial and ethnic minorities were represented across the studies. The participants were recruited from many resources including national sample data, in-schools, and longitudinal and cross-sectional surveys. The included reviews (n = 6) originated from both high-income and low and middle-income countries.²⁸⁻³³ The number of primary studies in the included reviews under the umbrella framework was 85. The primary studies across all reviews originated from the US (n = 50, 58.8%), Canada/South Korea/UK each (n = 4, 4.7%), England/Taiwan each (n = 3, 3.5%), Australia/France/Hawaii/Mexico/Russia each (n = 2, 2.4%), Denmark/Greece/Hong Kong/Iceland/New Zealand/Poland/Switzerland each (n = 1, 1.2%). All 6 reviews were published between 2016 and 2021. Two of the 6 studies were scored as high-quality reviews.

Whereas, the other 4 reviews were classified as medium-quality reviews (Table 2).

Umbrella review findings

Becker et al²⁸ included 221 691 adolescents aged 12 to 18. Of those, 28 239 (12.7%) used EC. Among the sample that used EC, 16 333 (57.8%) were lifetime and ever EC users. A 1522 (5.4%) were current users (used in the previous month to the previous year). On noting EC and CC (lifetime) use, 6170 (21.8%) adolescents were documented, whereas 1236 (4.4%) used EC and CC in the previous month to the previous year. Finally, EC and cannabis/marijuana/other illicit drugs were abused by 2978 (10.5%) adolescents.

Chan et al²⁹ included 11 primary clinical studies of non-smokers aged <18 years at baseline. Meta-analytical findings suggested that longitudinal associations between initiating vaping and smoking were found (OR = 2.93, 95% CI = 3.63-12.31). Of the 11 studies that Chan et al pooled, 7 of them (N = 24 971) examined associations between lifetime vaping at enrollment and smoking initiation during the follow-up period. Key findings comprised of the following. Chan et al reported that EC use led to 6 times higher odds of commencing CC use as compared to never EC users. Further, low-age (12-15 years) youths had higher risks of CC initiation and use. Young never smokers (11- to 18-year-olds) were more likely to try CC if they tried EC in the past. Chen and colleagues also found a prospective association between every use of EC and smoking initiation among Asian populations. Ever-use of EC was robustly associated with CC initiation but with a modest increase in CC use. The review also ascertained that the youth population (aged 11-18 years) in Great Britain had the association of ever-EC use to CC initiation. Adolescents who use EC are more likely to begin smoking cigarettes. Chen's examination of past-month smoking and vaping initiation pooled in 17 564 children.²⁹ On this front, regional sample findings determined EC use associations with CC smoking behaviors, including both initiation and follow-up. US statewide sample estimates determined that EC use was ascertained as an independent risk factor for future smoking among non-smokers/past smokers' youth. Lifetime vaping was also associated with past 6-month vaping and smoking initiation. Whereas ever EC users at baseline were more likely to initiate combustible tobacco use in the next year.

Rothrock et al³⁰ included a total of 28 primary clinical studies with 458 357 adolescents aged 10 to 19 years. of these participants, 146 059 were binge drinkers and 373 150 individuals had drunkenness.³⁰ In their analysis, Rothrock et al³⁰ pooled 373 150 adolescents. They determined that EC users had higher risks for any alcohol use as compared to non-EC users (OR = 6.62, 95% CI = 5.67-7.72). Furthermore, EC users had higher risks for drunkenness/binge drinking as compared to non-EC users (OR = 6.73, 95% CI = 4.5-10.07).³⁰

In their review, Soneji et al³² included 4 primary clinical studies with adolescents aged 14-20 years pooling in 10 705 adolescents. Based on findings from prospective longitudinal panel data in a national sample study, Soneji found that the youth recent vapers and non-CC smokers had nearly 5 times the risk of reporting cigarette smoking at follow-up (RR=4.78); recent vapers were twice likely to report smoking (RR=2.15); vaping did not predict smoking cessation.³⁴ The authors also reported that the adjusted prevalence of current EC or CC use in 2014 was 13.7%, which is higher than the 9% prevalence determined in 2004 before EC was introduced. Never smokers and those who used EC were more likely to smoke CC (OR=2.87, 95% CI=2.03-4.05); moreover, the uptake of CC among EC never and recent EC users was predicted by rebelliousness and perception of EC being healthier alternatives. Past-6-month use of any combustible tobacco was more frequent in baseline EC users (30.7%) as compared to never users (8.1%); on adjusting for interpersonal and environmental risk factors for smoking, the likelihood of CC use was computed (OR=2.73, 95% CI=2-3.73). Overall, Soneji and colleagues found that EC ever users as compared to non-users were more likely to initiate CC users over the next year.

Hua and Talbot³³ reported a total of 6 cases of children with vaping-related effects. Among these cases, there are many causes of vaping-related effects including suicide attempts, and mechanical injuries related to ADHD.³³ General EC findings were related to opioid addiction and the abuse of other drugs that led to suicide attempts and poisonings caused by intentional abuse/misuse of EC.³³

Chadi et al³¹ reported a total of 14 primary studies assessing the associations between marijuana and ENDS use in 130 780 children with a median/mean age of fewer than 18 years. In summary, the authors assessed marijuana use among those aged 18 or below, which was higher (aOR=4.29, 95% CI=3.14-5.87) as compared to those older than age 18 (aOR=2.3, 95% CI=1.4-3.79). EC users were more likely to be older, Caucasian, male, and with poorer academic scores as compared to non-EC users. Generally, EC users were also more likely to report smoking CC, drinking, seeking sensation, and abusing drugs. Moreover, increased EC use was linked to higher odds of current marijuana use (aOR=1.7, 95% CI=1.3-2) and heavy marijuana use (aOR=1.6, 95% CI=1.2-2.2). The authors also found that user groups including EC and alcohol/other drug use had similar behavioral health behaviors and physical health. Of note, EC-only users had lesser mental health symptoms and less alcohol/other drug use as compared to CC-only and EC/CC users. Dual (CC and EC) users were more likely to use cannabis as compared to EC-only users with increased frequency of use (1-2 times a week: aOR=2.04, 95% CI=1.26-3.31; 3-6 times a week: aOR=4.8, 95% CI=2.72-8.46, daily: aOR=10.67, 95% CI=5.56-20.49). EC users were more likely than CC users to report blunt (aOR=1.81, 95% CI=1.21-2.71) and hookah use (aOR=3.12, 95% CI=1.9-5.13), however, no differences were reported in smokeless tobacco, cigar,

or marijuana use. EC experimentation was higher among those who smoked 10 or more CC (OR=5.67, 95% CI=3.11-10.34) and among ever-CC users (OR=4.46, 95% CI=2.81-7.09). With increased student age, the likelihood to consume EC reduced, whereas students with more spending money were more likely to use EC. The most frequent reasons for trying EC a curiosity (64.5%) and being recommended to try (24.2%); current CC smokers tried EC to quit CC smoking (16.6%), whereas other users tried EC for harm reduction (27.8%).³¹

Mental Health Findings

Depression

Based on our umbrella synthesis, 2 of the 6 studies reported depression findings associated with vaping. Becker et al²⁸ and Chadi et al³¹ included a total of 10 primary studies in their review. Becker et al's key findings were overall significant with depressive symptoms, with similar reporting seen by Chadi et al.³¹

Becker et al found that EC-only users compared to no use were associated with depressive symptoms (aOR=1.37, 95% CI=1.19-1.57). However, there were also findings of no significance for medium/high depressive symptoms in children who exclusively used EC use. When correlating baseline depressive symptoms with odds of commencing EC use, there was an associative link reported (aOR=1.015, 95% CI=1.003-1.023); moreover, sustained EC use compared to no use led to increases in depressive symptoms over time ($b=1.272$); sustained EC users also had a significant association between past 30-day EC use and depressive symptoms ($b=1.611$). Chadi et al³¹ found that never vs. ever-tobacco users "Center for Epidemiologic Studies Depression Scale (CES-D)" values were 13.31 (10.99) versus 16.88 (12.45) in mean (SD) respectively; this means that ever-tobacco users had higher levels of depression as measured ($P<.001$). CES-D values were lower in EC users as compared to CC users though; EC=2.85 (1.4) and CC-only=3.19 (1.54). Among EC users, Chadi et al found inconclusive findings for outcomes of stress-coping including decision-making coping (OR=0.99, 95% CI=0.9-1.09), anger coping (OR=0.96, 95% CI=0.9-1.03), and social-support coping (OR=0.94, 95% CI=0.9-0.99); the multivariate model examined associations between these variables and lifetime EC use among schoolers, which did not have any relevant shifts.

On the whole, Becker et al reported largely significant findings of EC users with higher measures of depression, sadness, and hopelessness compared to non-users, however, the levels were lower than CC/dual users. Additionally, depressive symptoms (aOR=1.21) were associated with the past 30-day use of vaporized cannabis. When comparing both reviews reporting depressive findings, there was only one case where no significant links were found between EC use and medium/high depression. Whereas, all other counts were suggestive of a cause-and-effect, and correlative shift in mental health outcomes.

Suicidality

Suicidality was reported in 2 of the 6 included reviews by Becker et al and Hua. In total, the 2 reviews pooled 4 primary studies and 1 case report. While Becker et al reported an associative relationship between suicidality with EC use, Hua and Talbot³³ reported a case of accidental ingestion of EC refill liquid by a 13-year-old male, unrelated to psychiatric overlays.

Becker et al's review, pooled in 105 815 adolescents, where past-12-month EC-only use was associated with suicidal ideation (aOR=1.23), cumulative higher rates of suicidal planning ($\chi^2=17$, $P<.001$), and suicide attempts ($\chi^2=9.64$, $P=.002$). However, Becker et al also reviewed studies where suicidal ideation had insignificant links with EC use in the past 12 months. On logistic regression analysis, suicidal ideation (aOR=1.58, 95% CI=1.31-1.89), suicidal plans (aOR=2.44, 95% CI=1.94-3.08), suicide attempts (aOR=2.44, 95% CI=1.85-2.44), and serious suicide attempts (aOR=3.09, 95% CI=1.51-6.32) were observed at higher likelihoods compared to non-EC users, which is a key finding. EC past-30-day use was, however, associated with suicide ideation (aOR=2.49, 95% CI=1.82-3.42), suicide planning (aOR=4.63, 95% CI=3.22-6.67), and suicide attempts (aOR=6.17, 95% CI=6.17, 95% CI=4.13-9.24). Odds ratios for suicide plans were higher in females, which is a singular finding reported by Becker et al. The suicide attempt reported by Hua and Talbot³³ by a 13-year-old male was unlinked with the psychiatric manifestation of EC use. However, the ease of availability and the low dose required for toxicity was the key cause of nicotine poisoning in the child.

Impulsivity

Impulsivity was reported by Becker et al, Chadi et al, and Hua et al; 3 of the 6 reviews addressed the manifestation of vaping use. Becker et al²⁸ reviewed outcomes of 10 697 adolescents where behavioral impulsivity was associated with earlier age of EC onset, which also predicted frequency of EC use ($B=-0.25$, $P=.02$); EC-only (OR=1.26, 95% CI=1.18-1.35) users and EC/CC (OR range=1.45-1.77) users had higher levels of impulsivity as compared to never users. In simpler terms, impulsivity was increased in EC users compared to never users. Another key finding reported by Becker was that impulsivity was associated with past-30-day vaporized cannabis use (aOR=1.37). In the review by Hua and Talbot,³³ there was no psychiatric linkage to impulsivity; 1 case of mechanical injuries in an 18-year-old male with ADHD was reported; the injury occurred due to a spontaneous explosion of an EC battery. Now, Chadi et al³¹ included 2668 participants in their review; based on the TCI impulsivity scale, never versus ever tobacco users reported as mean (SD) were 2.34 (1.49) and 2.8 (1.37) ($P=.004$) respectively. Our key learnings from both Becker and Chadi's reviews are that TCI and regression findings suggest that impulsivity is higher for EC-only and EC/CC users as compared to never users.

Anxiety disorder

Anxiety disorder was only reported in 2 of the 6 reviews included in this umbrella review. Becker et al and Chadi et al³¹ pooled a total of 3 primary clinical studies. Anxiety was a common denominator among both reviews.

For instance, Becker et al analyzed 4075 participants. They found that 19.9% of adolescents using nicotine EC had anxiety and were doing illicit substance vaping (aOR=1.96, 95% CI=1.18-3.14). Contrary to popular belief, Becker et al additionally found that CC users compared to EC users had lower levels of anxiety sensitivity. Chadi et al³¹ synthesized 2488 participants where anxiety symptoms were reported in non-users (2.83 (1.47)), EC-only users (2.74 (1.38)), and CC-only users (3.16 (1.69)); the highest ratio was present in CC-only users, followed by non-users, and thereby EC-users. To sum up, Chadi et al reported higher anxiety symptoms in CC users compared to EC users, and data was uncertain on non-users compared to EC users' anxiety symptoms.

Critical appraisal includes studies. In accordance with the AMSTAR-2 Checklist findings, we assessed findings across 16 domains (Table 3). When assessing if the included reviews included PICO in the research question, 3 reviews [Becker et al²⁸, Rothrock et al,³⁰ and Chadi et al³¹] included them, whereas Chan et al²⁹ and Soneji et al³² partially did; Hua and Talbot³³ did not include a PICO framework with the research question. On assessing whether methods were established prior to conducting the reviews, Becker et al,²⁸ Chan et al,²⁹ and Rothrock et al³⁰ fully established them, Chadi et al³¹ and Soneji et al³² established them partially and Hua and Talbot³³ not at all. The study design selection and literature search strategy were fully established and reported in all reviews excluding Hua's and Talbot³³ where it was partially stated.

The study selection and data extraction were performed in duplicates in all reviews fully excluding Chan's et al²⁹ and Hua's and Talbot³³ reviews where no pairing was established. Only Becker et al²⁸ and Rothrock et al³⁰ partially justified the list of studies they excluded whereas all other reviews did not justify exclusion. All reviews included in this umbrella review describe the primary studies they included in adequate detail. On assessing whether a satisfactory technique was applied to assess for risk of bias, all reviews fully satisfied the criteria excluding Soneji et al³² and Hua and Talbot³³ who did not assess for biases. All included reviews reported sources of funding and conflicts of interest (Table 3).

On assessing whether the included reviews used appropriate statistical combinations for the meta-analysis, Becker et al²⁸ and Hua and Talbot³³ did not, while Chan et al²⁹, Rothrock et al,³⁰ Chadi et al,³¹ and Soneji et al³² used appropriate methods for statistical testing. Considering the potential impact of risk of bias in individual studies and accounting for bias when interpreting results, Chan et al,²⁹ Rothrock et al,³⁰ and Chadi et al³¹ fully accounted for them, whereas Becker et al,²⁸

Table 3. Quality appraisal of the included reviews using the AMSTAR-2 tool.

AUTHORS	RESEARCH QUESTION INCLUDED PICO	REVIEW METHODS ESTABLISHED PRIOR TO REVIEW	EXPLANATION OF STUDY DESIGN SELECTION	COMPREHENSIVE LITERATURE SEARCH STRATEGY	STUDY SELECTION PERFORMED IN DUPLICATE	DATA EXTRACTION PERFORMED IN DUPLICATE	LIST OF EXCLUDED STUDIES WITH JUSTIFICATION	DESCRIBE STUDIES IN ADEQUATE DETAIL	SATISFACTORY TECHNIQUE FOR ASSESSING ROB	REPORT SOURCES OF FUNDING
Becker et al ¹¹	Green	Green	Green	Green	Green	Green	Yellow	Green	Green	Green
Chan et al ¹²	Yellow	Green	Green	Green	Red	Red	Red	Green	Green	Green
Rothrock et al ¹³	Green	Green	Green	Green	Green	Green	Yellow	Green	Green	Green
Chadi et al ¹⁴	Green	Yellow	Yellow	Green	Green	Green	Red	Green	Green	Green
Soneji et al ¹⁵	Yellow	Yellow	Green	Green	Green	Green	Red	Green	Red	Red
Hua and Talbot ¹⁶	Red	Red	Yellow	Yellow	Red	Red	Red	Green	Green	Green

Abbreviation: PICO, population or participants, and conditions of interest; Interventions or exposures; Comparisons or control groups; Outcomes of interest. Green=yes; red=no; and orange=partial yes.

Table 3. Quality appraisal of the included reviews using the AMSTAR-2 tool (continued).

AUTHORS	USE APPROPRIATE METHODS FOR STATISTICAL COMBINATION OF RESULTS (FOR META-ANALYSIS)	ASSESS POTENTIAL IMPACT OF ROB IN INDIVIDUAL STUDIES ON THE RESULTS (FOR META-ANALYSIS)	ACCOUNT FOR ROB IN INDIVIDUAL STUDIES WHEN INTERPRETING RESULTS	EXPLANATION FOR AND DISCUSSION OF HETEROGENEITY IN RESULTS	INVESTIGATE PUBLICATION BIAS AND DISCUSS IMPACT (FOR QUANTITATIVE SYNTHESIS)	REPORTED CONFLICT OF INTEREST
Becker et al ¹¹	Red	Red	Red	Yellow	Red	Green
Chan et al ¹²	Green	Green	Green	Yellow	Green	Green
Rothrock et al ¹³	Green	Green	Green	Yellow	Green	Green
Chadi et al ¹⁴	Green	Green	Green	Green	Red	Green
Soneji et al ¹⁵	Green	Green	Red	Red	Yellow	Green
Hua and Talbot ¹⁶	Red	Red	Red	Red	Red	Green

Abbreviation: RoB, risk of bias. Green=yes; red=no; and orange=partial yes.

Soneji et al,³² and Hua and Talbot³³ did not at all. When we appraised the reviews for explanation and discussion of the heterogeneity of results, only Chadi et al³¹ fully accounted for them, whereas Becker et al,²⁸ Chan et al,²⁹ and Rothrock et al³⁰ partially did so, and Soneji et al³² and Hua and Talbot³³ did not at all. Finally, on appraising if the sources of publication bias and discussions of impact were made, only Chan et al²⁹ and Rothrock et al³⁰ fully accounted for them, whereas Becker et al,²⁸ Chadi et al,³¹ and Hua and Talbot³³ did not account for publication bias; Soneji et al³² reported and discussed biases partially (Table 3).

Discussion

In this umbrella review, the primary studies originated largely from the US (58.8%), followed by Canada, South Korea, and the United Kingdom (4.7% each).^{28–33} The 6 reviews were published between 2016 and 2021. The key mental health findings of our umbrella review included (i) depression, (ii) suicidality, (iii) impulsivity, and (iv) anxiety disorder. A cross-sectional analysis of a representative sample in the US found that former and current electronic cigarette (EC) users were more likely to have a history of depression compared to non-users. The study also found that sustained EC use and frequency of use were associated with an increase in depression symptoms over a 12-month period.³⁵ Similarly, in our umbrella review, depression outcomes were associated with mental health outcomes including depression by Becker et al²⁸ and Chadi et al³¹ where outcomes of 119 747 children were pooled in. Our study found that depressive symptoms on a whole had higher associations with EC-only, EC/CC use as compared to no use; these trends were noticed with lifetime EC-only use and with the past 30 days of use. Our findings are also supported by current literature where links are proposed between mental health and nicotine—which is known to increase depressive feelings. Cullen et al reported study findings of nearly 30 000 EC users, frequent vaping leads to an estimated 2.4 higher likelihood of being diagnosed with depression.³⁶

A review of 7 studies assessed the impact of vaping and electronic cigarette (EC) use on mental health.³⁷ The review found that suicide attempts were significantly more common among EC users compared to non-users.³⁷ Data from a survey of Korean middle and high school students also found that students who had used ECs in the past 30 days had higher rates of suicidal ideation, suicide planning, and attempts compared to non-EC users.³⁸ Previous studies have linked nicotine addiction from combustible cigarettes with an increased risk of suicidality.^{39,40} Our review found that suicidality was more common in electronic cigarette (EC) users, with higher rates of suicidal ideation, suicide plans, and suicide attempts observed in individuals with past-12-month EC use (Becker et al²⁸). In 1 case, suicide planning was found to be higher among females, however, the findings were not conclusive and further research is needed to fully understand the relationship between EC use and suicidality in female. Electronic cigarette (EC) use has

been linked to a range of mental health issues in adolescents, including impulsivity, anxiety, and suicidality. A cross-sectional survey of 927 EC users found that impaired self-regulation and behavioral impulsivity predicted trying ECs at a younger age, and that early-age consumption was associated with a higher risk of frequent EC use.⁴¹ This review also found that earlier age of EC onset and ever-use of combustible cigarettes was associated with high impulsivity. A review of 13 366 participants found that earlier age of EC onset and ever-use of combustible cigarettes was associated with high impulsivity as measured by the Temperament and Character Inventory (TCI) impulsivity scale and analytical models (odds ratios >1). It is important to further study the longitudinal relationship between EC use and impulsivity in order to fully understand the impact of EC use on impulsivity in adolescents.

Data from a national survey of children and youth aged 3 to 17 years in the US found that 7.1% of EC users were diagnosed with anxiety. EC use has also been found to be more common among individuals with substance use disorders and psychiatric disorders.^{42,43} In our review, anxiety disorder was reported by Becker et al and Chadi et al,³¹ pooling in 6563 participants. Anxiety was associated with illicit substance vaping (OR = 1.96) and lowered anxiety sensitivity among CC compared to EC users.

The authors of the study by Bhavne and Chadi⁴⁴ discuss the risks of electronic cigarettes (EC) and vaping use among youth globally, with a focus on the situation in India. They mention that even though vaping is banned in India, it still poses a significant threat to youth in the country. Due to the increasing usage of EC, healthcare workers are often times required to treat vaping-associated lung injuries. EC and vaping use among youth is a significant public health concern, and it is important for countries like India to consolidate public health measures to prevent mental and physical damage incurred by vaping.

Duan et al⁴⁵ examined the relationship between electronic cigarette (EC) use and cannabis use over a 4-year period and assessed for any mental health impacts of EC use. The authors found that at baseline, both cannabis and EC use were significantly associated with each other. When considering the initiation of cannabis use over the course of the study, they found that individuals with internalizing mental health problems (OR = 2.51) were more likely to initiate cannabis use. This study is particularly important because both cannabis use and EC use have been linked to severe internalizing mental health problems. The authors of this study recommend that efforts should be made to curb the use of electronic cigarettes (ECs) due to the longitudinal association between EC use and cannabis initiation. To address this issue, specific interventions should be implemented nationally to target youth who have been exposed to ECs.⁴⁵

E-cigarette vaping-associated lung injury (EVALI) is a serious concern among young adolescents in the US, with cases approaching epidemic levels. The use of nicotine and tetrahydrocannabinol in e-cigarettes has been linked to

long-term health implications, including mental health problems, morbidity, and even mortality. Reddy et al⁴⁶ studied e-cigarette vaping-associated lung injury (EVALI) in pediatric intensive care units. Among young adolescents, EVALI has been largely reported in the US, nearing epidemic levels.⁴⁶ In their retrospective case series, the authors reported nicotine EC and tetrahydrocannabinol use among 6 patients aged 17 years.⁴⁶ While none of the pediatric patients died, there were many concerns raised for the long-term implications e-cigarettes have on the young; including but not limited to mental health well-being, morbidity—specifically lung health, and mortality.⁴⁶

A study by Jacobs et al⁴⁷ examined the motivations behind vaping and its impact on behavior by examining the sensitivities of the behavioral activation system (BAS) and behavioral inhibition system (BIS) in relation to cannabis and vaping. The study found that among 2467 students in the 11th grade in California, those who used nicotine were more likely to have fun-seeking scores ($P < .05$) and lower BIS scores compared to non-users ($P < .05$). On the other hand, those with higher BIS scores were less likely to consume cannabis (OR = 0.91).⁴⁷ While the authors specifically targeted outcomes of behaviors, we believe that different forms of motivation must be studied.⁴⁷ These will help in designing public programs that can target different adolescent groups to reduce trends of cannabis and nicotine vaping.⁴⁷

Rahmandar et al⁴⁸ write that over 1.7 million high school students use EC, but they find that a large proportion of them include Caucasians who self-identify as transgender and gay, lesbian, and youth with disabilities. While the authors' focus is on the racial and ethnic targets, we find that key regulations and recommendations targeted at the pre-specified groups may help in curbing the EC epidemic and improve community-level mental health outcomes.⁴⁸

Our umbrella review has certain limitations. First, we included only those studies that self-identified as systematic/meta-analysis studies in the title, abstract, keyword, or methods. Nonetheless, we carried out a thorough search of the reference lists of included studies to ensure that no omissions were made. Second, the effect sizes across the included reviews were insufficient in quantitative terms, where included reviews only included case presentations. Third, while the 6 reviews included in this umbrella review were published after 2016, the primary clinical studies were dating back to the earlier-usage of EC. Finally, it is important to consider that the primary original studies included in this umbrella review may have overlapped, therefore overrepresenting the findings of given studies.

Conclusion

This umbrella review included data from 846,510 children aged 21 years or younger, representing a diverse range of ethnicities and geographical backgrounds. So far, there has been no umbrella review addressing the relationship between vaping and mental health outcomes in children. To date, there has

been no umbrella review addressing the mental health outcomes of children who use electronic cigarettes (ECs). While mounting evidence links EC use to mental health outcomes, it is crucial to address these potential consequences in children. Future reviews should examine the duration of EC exposure and evaluate the impacts on depression, suicidality, anxiety, and impulsivity to establish concrete associations. This, in turn, will enable more effective mental health and policy-based interventions to be designed to safeguard public health.

Author contribution

The authors confirm contribution to the paper as follows: study conception and design: AMK and ZS; data collection: ZS; analysis and interpretation of results: AMK, SA and ZS. draft manuscript preparation: AMK, SA, ZS and PF. All authors reviewed the results and approved the final version of the manuscript.

Supplemental Material

Supplemental material for this article is available online.

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