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Vaping and harm in young people: umbrella review

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ABSTRACT

Objective To appraise and synthesise the evidence on short and longer term harms of vaping in young people.

Data sources KSR Evidence (systematic reviews); Medline, Embase, and PsycInfo (umbrella reviews); and reference screening.

Study selection Systematic and umbrella reviews evaluating any potential harms from e-cigarettes in young people.

Data synthesis Searches identified 56 reviews for inclusion from 384 unique articles. A consistent significant association between vaping and smoking initiation was found, supporting a causal relationship, with pooled ORs of 1.50–26.01 (21 systematic reviews), most of which suggested that young people using e-cigarettes are about three times more likely than those not using them to initiate smoking. Five systematic reviews demonstrated a substantial association between e-cigarettes and substance use, with pooled ORs of 2.72–6.04 for marijuana, 4.50–6.67 for alcohol and 4.51–6.73 for binge drinking. Asthma was the most common respiratory outcome, with consistent associations (ORs: 1.20–1.36 for diagnosis and 1.44 for exacerbation). Three systematic reviews found associations between vaping and suicidal outcomes, and six included investigation of injuries, predominantly documenting explosion incidents. Significant associations between vaping and other harmful outcomes included pneumonia, bronchitis, lower total sperm counts, dizziness, headaches, migraines and oral health harms, but this evidence was largely derived from limited surveys or case series/reports.

Conclusions This study found that there were consistent associations between vaping and subsequent smoking, marijuana use, alcohol use, asthma, cough, injuries and mental health outcomes. The findings support the implementation of policy measures to restrict sales and marketing of e-cigarettes to young people.

Trial registration number PROSPERO CRD42024569728.

INTRODUCTION

Youth vaping has increased markedly in recent years. The US Centers for Disease Control and Prevention estimated in 2024 that 5.9% of American middle and high schoolers were currently using e-cigarettes,[1] and the WHO describes the rise in children vaping around the world as "alarming".[2] Across WHO Europe region countries, e-cigarette use among those aged 15–16 years has been shown to range from 5.5% to 41%.[3] For adults, e-cigarettes have been adopted and advocated as a smoking cessation tool by public health bodies in the UK and some other countries.[2 4] However, the WHO is concerned about vapes being "aggressively marketed" to young people and has called on governments around the world to strengthen their vaping policies.[2 5]

The harm or safety of vaping products is thus a timely question for tobacco control internationally, and evidence synthesis is one lever to improve the evidence base underpinning policy in this area. There is ongoing concern about the harms of vaping in young people, especially whether e-cigarettes increase the risk of smoking initiation, a key area where a contemporary synthesis of evidence would be valuable. Although four umbrella reviews exist, these do not focus on young people alone or do so only for a narrow set of outcomes (such as smoking initiation).[6–9] No umbrella review to date has specifically focused on young people and considered a full range of potential physical and mental health impacts in this age group. We therefore conducted an umbrella review to identify systematic reviews on the acute and longer-term harms of vaping in young people.

METHODS

This overview of reviews is reported in line with PRIOR (preferred reporting items for overviews of reviews: online supplemental file 2)[10] and followed a prespecified protocol (PROSPERO CRD42024569728). The inclusion criteria were broad to provide an overall understanding of the health implications of vaping among young people (table 1).

Search methods

KSR Evidence database was searched on 4 July 2024, with update searches on 21 November 2024. KSR Evidence aims to include all systematic reviews, meta-analyses and health technology assessment reports published in the past decade and includes sensitive searches of several databases (including Medline, Embase, CINAHL, PsycInfo and the Cochrane Database of Systematic Reviews).[11] We also checked the references of included systematic reviews for related systematic reviews.

We included umbrella reviews to identify further systematic reviews; findings from these umbrella reviews are reported separately to avoid duplication. As KSR Evidence does not include umbrella reviews, we conducted a separate search on 21 November 2024 on Medline, Embase and PsycInfo for these, limited to a publication date of 2015 onwards, reflecting the major shift in types of e-cigarette devices being used by young people at this time (specifically the dominance of rechargeable tank/reservoir models after this point, followed by the surge in disposable vapes),[12] to avoid including reviews focused solely on 'cigalikes' or other

Table 1 Inclusion and exclusion criteria for reviews on the harms of vaping in young people

	Inclusion criteria	Exclusion criteria
Population	Children, young adults, adolescents and youths (<25 years), including reviews with wider age ranges if separate analysis of young people was provided, and reviews of subgroups, such as disease or condition specific groups (eg, pregnant women) if <25 years	Adults aged >24 years. Animals or in vitro studies
Exposure	Use of e-cigarettes/vaping (legal or illegal), electronic nicotine delivery systems and electronic non-nicotine delivery systems	Marijuana vaping, aromatherapy vaping, traditional cigarettes and cigars, secondhand vaping and nicotine patches
Comparator(s)	None or any with no specific criteria. Comparators can be defined by the criteria of the reviews themselves (often young people who have never used e-cigarettes, or those who are not currently using them)	No exclusions
Outcome	Physical and mental health harms (respiratory outcomes including e-cigarette or vaping use associated lung injury, uptake of conventional cigarette smoking or uptake of substance use, cardiovascular outcomes, gastrointestinal outcomes, mental health outcomes including depression or anxiety, and any other negative outcome)	Cigarette quitting, positive benefits (such as reduced stress), pregnancy harms to fetus, accidental overdose or poisoning
Setting	All countries/settings	None
Study design	Systematic review, umbrella review	Scoping review, non-systematic literature review, commentary, editorial or letter, primary study (randomised controlled trial or observational study)
Restrictions	After 2014. English language (or translation available). All types of publication.	Before 2015. Non-English language paper where no translation was available

obsolete devices. Search results were deduplicated in EndNote (Clarivate).[13] Title and abstract screening were undertaken independently by two reviewers in Covidence (Covidence AS)[14] with disagreements resolved by discussion or with a third reviewer. Full text screening was also undertaken in Covidence by two reviewers, with disagreements resolved in the same way.

Data extraction

Data were extracted on study characteristics, methods and results of the included systematic reviews and umbrella reviews in Covidence (see online supplemental files). In some reviews, there was a wider age range than our inclusion criteria; in such instances, only the results relating to young people were extracted. One reviewer carried out data extraction which was checked by a second reviewer.

Methodological quality

The quality of the included systematic reviews was assessed by one reviewer using AMSTAR 2[15] and then checked by a second reviewer. Study overlap was assessed by calculating corrected covered areas (CCA; 0–5%=slight; 6–10%=moderate; 11–15%=high; >15%=very high overlap; CCA=N-r/(rc)-r, where N is the number of times publications appeared in reviews, r is the number of rows and c is the number of columns; see online supplemental file).[16] Forest plots were created using odds ratios (ORs) from meta-analyses reported in those reviews that included a meta-analysis.

Patient and public involvement

The Youth Advisory Panel of the UK Association for Young People's Health (AYPH) provided input on emerging results, implications and dissemination via a presentation to an online meeting of the panel by one research team member, and a discussion co-facilitated by an AYPH Youth Engagement and Partnership Project Manager.

RESULTS

The database searches identified 425 records (381 after duplicates removed) and an additional three records were found from reference list checking (figure 1). After screening 384 unique records, 195 full text papers were examined, and 56 reviews were included. The main reason for exclusion at full text review stage was a lack of analysis of data relating to young people (see online supplemental file). The included systematic reviews were published between 2016 and 2024, with 84% (47/56) published from 2020 onwards. Results are presented according to health outcome (table 2).

E-cigarette use and smoking initiation and relapse

Twenty-one systematic reviews[9 17–37] and four umbrella reviews[6–9] (one study[9] described itself as an umbrella review and systematic

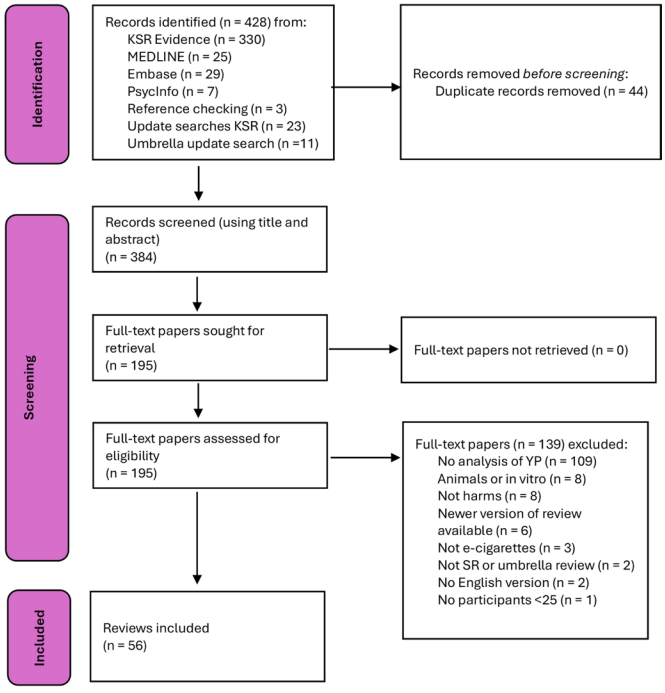

Figure 1 Flow diagram for included systematic reviews and umbrella reviews. SR, systematic review; YP, young people.

Table 2 Study characteristics

	No	%
Review types		
Umbrella reviews	4	7.1
Systematic reviews	52	92.9
Harm outcomes*		
Smoking initiation	24	42.9
Substance use	6	10.7
Asthma	8	14.3
Respiratory (excluding asthma)	10	17.9
Injuries	7	12.5
Mental health	9	16.1
Cardiovascular	3	5.4
Oral health	5	8.9
Fertility	2	3.6
Other (COVID, headache/migraine, vascular damage, renal)	4	7.1
Quality assessment		
High	1	1.8
Moderate	2	3.6
Low	14	25.0
Critically low	39	69.6

*Percentages sum to >100 because some reviews reported on multiple harms.

review) assessed the evidence that e-cigarette use increases the risk of conventional cigarette use (online supplemental file 1). Fourteen countries were represented in the included primary studies: USA, Canada, Mexico, UK, Germany, Netherlands, Taiwan, Finland, Romania, Switzerland, Belgium, South Korea, Thailand and Lebanon. Where the total number of participants included was reported, this ranged from 2084 to 779 937.

Smoking Initiation

Four umbrella reviews included systematic reviews assessing the association of e-cigarettes and conventional cigarettes.[6–9] None was limited to young people. While our umbrella review identified 21 systematic reviews for inclusion, the four previous umbrella reviews included eight,[7] three,[9] two[8] and one review,[6] respectively. The included systematic reviews[9 17 18 20 26 27 29 34 38] within these umbrella reviews were all captured and included in our review, except Zhong *et al*,[38] which only measured intentions to smoke, not actual smoking behaviours. All umbrella reviews found evidence that young people who use e-cigarettes are more likely than young people who do not to initiate cigarette smoking.

All 21 systematic reviews demonstrated an association between e-cigarette use and subsequent initiation of smoking independent of whether they assessed ever or current e-cigarette use with ever or current smoking. The reviews included 323 primary studies (90 unique), mostly longitudinal cohorts with follow-up durations of 4 months to 2 years; 46% (41/90) of the primary studies were included in multiple reviews ranging from 2 to 16 reviews (online supplemental table). The degree of overlap was high (CCA=13%).[39]

ORs ranged from 1.50–26.01, with most reporting that young people using e-cigarettes are about three times more likely than those not using them to initiate smoking. Within individual reviews, there was heterogeneity in the magnitude of ORs of primary studies, but the consistent, statistically significant associations between e-cigarettes and smoking initiation are clear from the adjusted ORs presented in the 12 systematic reviews with pooled meta-analysis (online supplemental file 1 and figure 2). ORs were significant whether using adjusted or unadjusted values (factors adjusted for were mostly sex, age and socioeconomic status, with some results adjusted for other variables, such as psychosocial/behavioural risk factors and family/peer smoking). While all review authors concluded that the use of e-cigarettes was associated with an increased risk in smoking initiation, some questioned whether this was a causal effect.

Flavoured e-liquid and smoking initiation

Previous research has found that flavoured e-cigarettes are more popular among younger people,[40] but only one systematic review studied associations between the use of e-liquid flavours and continued vaping and tobacco smoking uptake or cessation.[25] The study found no evidence that flavoured e-liquid use versus unflavoured use was specifically associated with tobacco

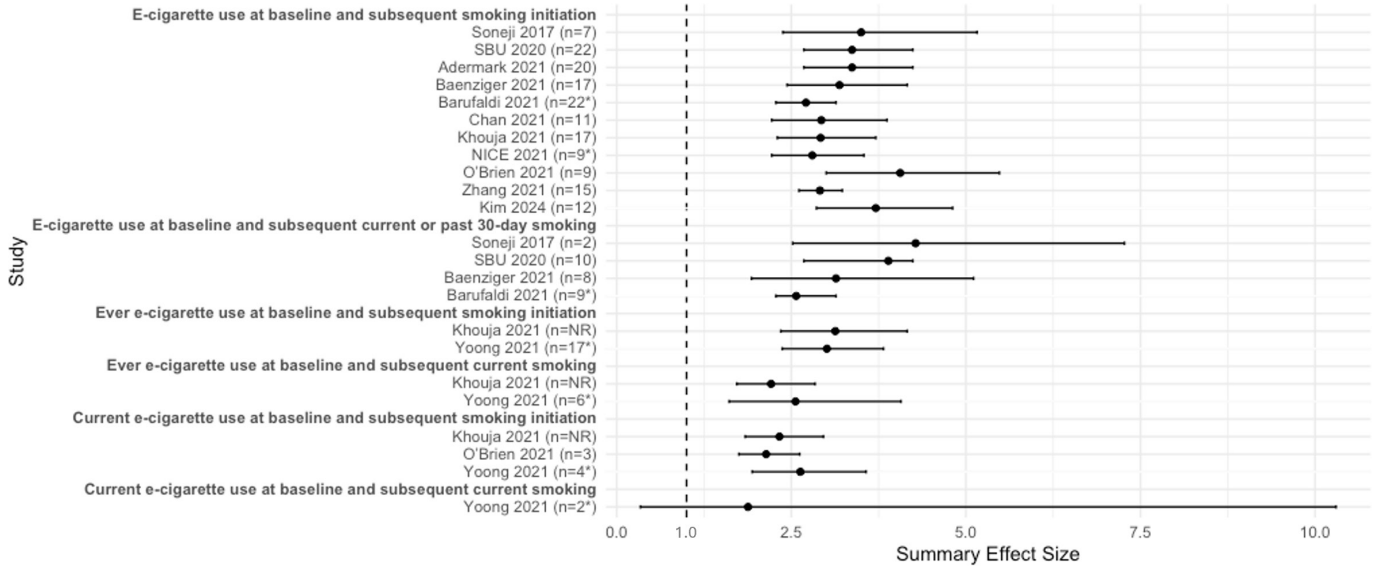

Figure 2 Forest plot for e-cigarette use and smoking initiation in previous meta-analyses.*denotes risk ratios, otherwise odds ratios. n = number of studies pooled within each review. NR = not reported.

smoking uptake,[25] but with only three included studies, the authors recommended more research.

Smoking relapse

One systematic review studied relapse (the probability of transitioning from former to current cigarette smoking) and included young people, but only one longitudinal study (with a Markov model) specifically included young people.[21] This primary study found that the probability of relapse was higher among young people using e-cigarettes in the past 30 days than those who had never used them. An umbrella review[9] also focused on relapse, but included only adults.

Quality assessment

The quality of the included reviews ranged from high (one systematic review)[22] or moderate (one systematic review[41] and one umbrella review)[8] to low (eight reviews) or critically low (13 reviews) (online supplemental table). The results were highly consistent, irrespective of quality assessment. Some reviews had fewer included studies, perhaps due to the date the searches were conducted or narrower inclusion criteria, such as limited populations studied (eg, Asian Americans[37] or Asian and Pacific Islanders),[36] a tight scope on flavoured vs unflavoured e-cigarettes,[25] or a sole focus on smoking relapse.[21] However, many other reasons for the exclusion of primary studies were largely unexplained.

E-cigarette use and subsequent substance use

One umbrella review[7] assessed associations between e-cigarette use and substance use. The review concluded that moderate evidence exists for associations between e-cigarette use and alcohol (OR 3.72, 95% CI 2.03 to 6.83) and marijuana use (OR 2.89, 95% CI 1.61 to 5.19). We included an additional systematic review[42] to those included in the umbrella review[7] and excluded one systematic review[43] in the umbrella review[7] because it only assessed how commonly e-cigarette technology was used as an illicit drug delivery system.

Five systematic reviews comprising 91 primary studies (61 unique) assessed the association between e-cigarette use and substance use; again, bidirectional relationships cannot be fully parsed, but these were mainly longitudinal studies with 1–7 year follow-up and cross-sectional surveys. Thirty-four per cent (21/61) of primary studies were included in multiple reviews (online supplemental table). The degree of overlap was high (CCA=12%). Country settings for primary studies were the US, UK, Australia, Sweden, Hong Kong, Poland, Russia, Iceland, Canada, Switzerland, China, Greece, France, Mexico, South Korea, Iceland, Taiwan and Germany. The total number of participants, where reported, ranged from 7551 to 373 150.

Marijuana use

Four systematic reviews demonstrated significantly greater odds of past or current e-cigarette use and subsequent marijuana use in adolescents and young adults, with adjusted OR 2.72, 95% CI 2.06 to 3.61[44], adjusted OR 3.47, 95% CI 2.63 to 4.59[45], OR 6.04, 95% CI 3.80 to 9.60[46] and OR 5.15, 95% CI 2.94 to 9.00,[42] respectively (figure 3). This association was reported to be greater in younger populations in two reviews.[45 46]

Alcohol use

Three systematic reviews identified significantly greater odds of alcohol use for young people using e-cigarettes compared with those never using them: OR 4.50, 95% CI 3.31 to 6.13[46], OR 6.62, 95% CI 5.67 to 7.72[47] and OR 6.67, 95% CI 2.85 to 15.59[42] (online supplemental table). This relationship was also apparent with binge drinking: OR 4.51, 95% CI 3.13 to 6.51[46] and OR 6.73, 95% CI 4.50 to 10.07[47] (figure 3). As with cannabis use, the relationship between e-cigarette use and alcohol use was significantly greater in adolescent samples than adult samples (log OR 0.96 (OR 2.61), z=4.21, p<0.001).[46]

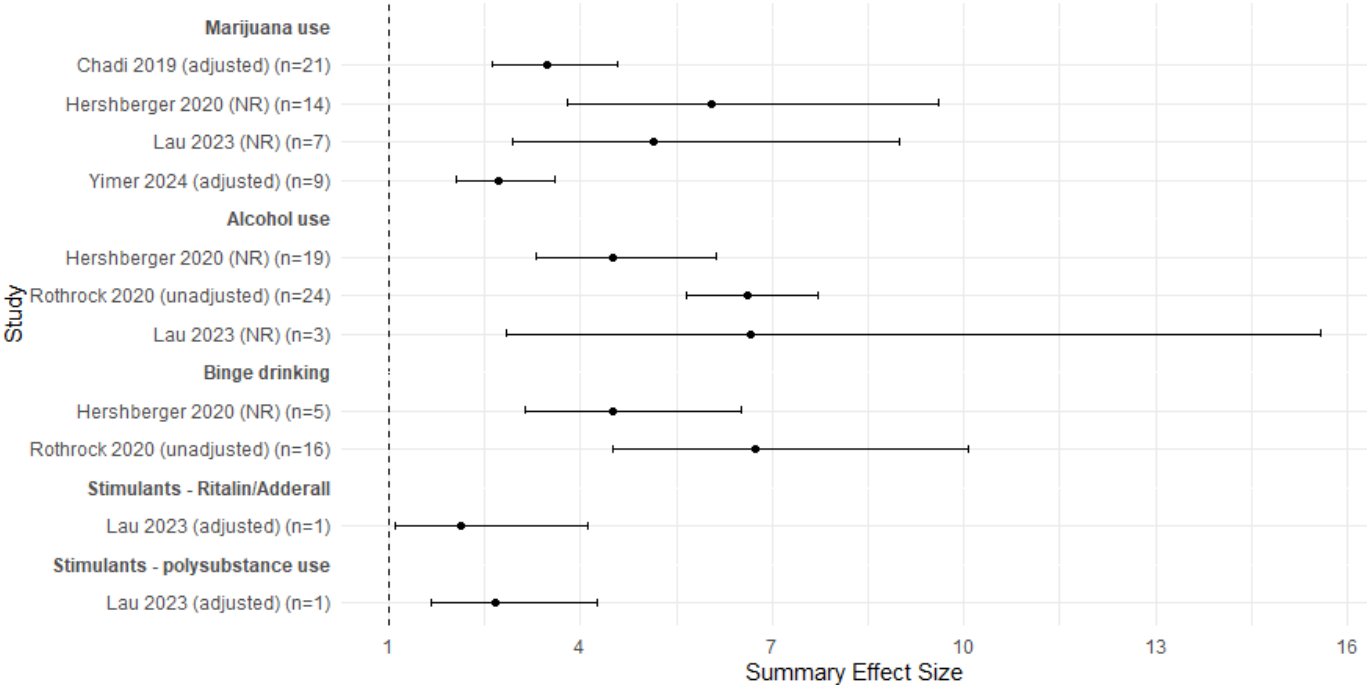

Figure 3 Forest plot for all drug initiation use and abuse, and e-cigarette use versus never use. NR = adjusted or unadjusted status of effect size was not reported.

Stimulant use

One systematic review showed increased odds of non-prescribed Ritalin/Adderall use (OR 2.13, 95% CI 1.10 to 4.11) from one longitudinal cohort, but not for painkillers, sedatives or tranquillisers in young people using e-cigarettes compared with those never using them.[42]

Quality assessment

All included reviews on substance use were rated as critically low quality due to significant methodological limitations. Issues included: lack of a priori methods, not listing excluded studies and inadequate reporting on risk of bias impacts. The searches in Lau *et al*[42] were deemed problematic, which may help explain the small number of included studies in this, the most recent review identified.

Respiratory outcomes

One umbrella review[7] reported on the impacts on respiratory outcomes (online supplemental table). This review was not limited to young people and included fewer systematic reviews related to young people than our umbrella review: two on asthma,[48 49] two on e-cigarette or vaping product use associated lung injury (EVALI)[50 51] and one on acute eosinophilic pneumonia.[52] This umbrella review's pooled RR was 1.13 (95% CI 1.09 to 1.18), with the authors concluding that high level evidence exists that electronic nicotine delivery system use can exacerbate asthma.

Fifteen systematic reviews[34 48–60] reported on the impacts on respiratory outcomes (online supplemental table). Primary studies were conducted in the US, South Korea, Canada and Kuwait. The total number of included participants, where reported, ranged from 162 182 to 483 948.

Asthma

Within the seven systematic reviews with asthma as an outcome, 47 primary studies were included, of which 20 were unique. Most studies were cross-sectional and the degree of overlap was very high (CCA=23%).

In all meta-analyses conducted within the reviews, statistically significant increases in asthma diagnosis or exacerbation were observed with e-cigarette use (whether measured as any use, ever use or current use) (figure 4). Overall, the reviews concluded that there was an increased risk of young people who vape developing asthma or asthma exacerbation, with pooled adjusted ORs of 1.20–1.36 for diagnosis and 1.44 for exacerbation.

Respiratory outcomes (excluding asthma)

One systematic review of the effect of e-cigarette use on coughing included six cross-sectional surveys, and one retrospective medical chart review from the US, Canada, Switzerland and Hong Kong, which found that adolescent use of e-cigarettes was associated with increased coughing, and young people who vape are more likely to report coughing compared with those who do not vape.[53] There was no pooled meta-analysis, but higher ORs were reported for young people with more frequent use (adjusted OR range 1.30–2.13). Four of these cross-sectional surveys were reported in another review.[60] There was no pooled meta-analysis, but the authors concluded that there was an association between e-cigarette use and effects on respiratory systems.

Three reviews[48 50 51] reported on case series of EVALI of upwards of 53 cases, showing that these cases had occurred in patients as young as 13 years,[51] with a wide range of outcomes,

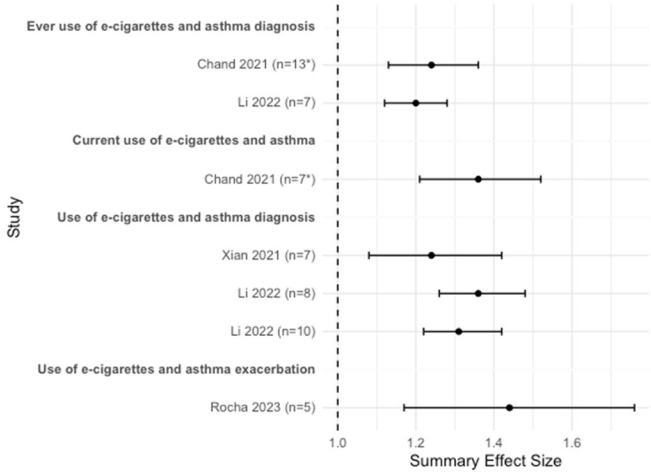

Figure 4 Forest plot for meta-analyses of e-cigarette use and asthma diagnosis or exacerbation versus never use. Ever use, current use and use reflect terminology used in original reviews. *Chand *et al*: ever use of e-cigarettes and asthma diagnosis - includes two studies on adults (18+); current use of e-cigarettes and asthma - includes one study on adults (18+).

and that e-cigarette use was "involved in damage related to the development of pulmonary disease", with e-liquids containing tetrahydrocannabinol (THC) a feature in 80% of cases.[50]

Other systematic reviews reported cross-sectional data on increased wheezing,[60] dyspnoea[60] and bronchitis,[58 60] and potential increases in allergic rhinitis.[60] Four reviews[34 48 52 59] highlighted respiratory problems (pneumonia, bronchitis and pneumothorax) using case reports.

Quality assessment

All respiratory outcome reviews were rated as critically low quality, except two on asthma which were rated as low quality.[54 57] The lack of an adequate search strategy in the reviews may help explain the low number of included studies, while lack of overlap was partly explained by different exposure or outcome measures.

Burns and other injuries

One umbrella review[6] examined risk of injuries resulting from using e-cigarettes and reported on five US case reports in young people (four explosions and one inadvertent aspiration). Another umbrella review[7] included three systematic reviews[48 61 62] that we included but reported no young person-specific results or conclusions.

Six systematic reviews[48 59 62–65] including 34 individual studies examined the risk of injuries resulting from using e-cigarettes in young people. Primary studies were conducted in the US, UK, France, Canada, Germany and Malaysia. The degree of overlap was very high (CCA=24%).

The six reviews predominantly included case reports and case series, as well as three surveillance system based studies. The reviews reported incidents of explosions among young people, resulting in projectile and burn injuries. Body parts affected were the mouth/face and hands, when e-cigarettes exploded mid-use, as well as lower limbs, when e-cigarettes exploded in pockets. Other less frequent injuries involved inadvertent aspiration of e-cigarette parts (outcomes reported alongside these injuries related to accidental or intentional poisoning were excluded

given our review's focus on e-cigarette devices used as intended by manufacturers).

Quality assessment

Five of the included systematic reviews were rated as critically low quality, while the remaining systematic review and the one umbrella review were rated as low quality. The most common weaknesses were not using a PECO framework, not addressing heterogeneity (perhaps reflecting the lack of statistical analyses due to case report data) and not providing lists of excluded studies.

Mental health

Two umbrella reviews[7 8] included one of the systematic reviews that we included (Becker *et al*[66] in both cases), with one[8] combining these findings with that of an individual study.[45] A further umbrella review[6] included a study (Marsden *et al*) found in our other systematic reviews, but reported no young person specific or mental health related results.[6]

Seven systematic reviews[57 58 66–70] included 63 individual studies (of which 54 were unique) examining associations between vaping and mental health. Studies were predominantly cross-sectional surveys, which complicates assessments of directionality/causality, and longitudinal studies. There was little overlap between these reviews (CCA=4%). Primary studies were conducted in the US, South Korea, UK and Taiwan.

Depression and suicidal outcomes

One umbrella review found,[7] as per the Becker *et al* review that it was based on,[66] that e-cigarette use was associated with greater depression and suicidality (as well as attention deficit/hyperactivity disorder, eating disorders and stress) among adolescents. The other umbrella review[8] was similarly focused predominantly on Becker *et al*, concluding that e-cigarette-only use compared with no use was associated with depressive symptoms (adjusted OR 1.37, 95% CI 1.19 to 1.57) and that past 30-day e-cigarette use was associated with suicide ideation (adjusted OR 2.49, 95% CI 1.82 to 3.42), suicide planning (adjusted OR 4.63, 95% CI 3.22 to 6.67) and suicide attempts (adjusted OR 6.17, 95% CI 4.13 to 9.24), with ORs for suicide plans greater in female adolescents.

The only systematic review to incorporate a meta-analysis[67] found a pooled OR for children and adolescents who vape of 1.46 (95% CI 1.33 to 1.59) for suicide ideation, 2.23 (95% CI 1.74 to 2.71) for suicide planning and 2.46 (95% CI 1.94 to 2.98) for suicide attempts. One further review found that e-cigarette use was associated with depression and suicidality in adolescents,[58] while another[68] found conflicting results in relation to depression associations in this age group from its included studies.

Other mental health related outcomes

Other systematic reviews synthesised evidence on adolescent weight concerns[69] - finding that higher concerns were associated with higher frequency of e-cigarette use - or sleep complaints.[57 70] The latter two reviews found respectively that adolescents who vaped had shorter total sleep time on weekends and that those who used both e-cigarettes and conventional cigarettes reported insufficient sleep significantly more often than those who used conventional cigarettes only.

Given the heterogeneity in outcomes involved, a meta-analysis was not possible; the absence of meta-analyses in all but one systematic review also precluded a forest plot for this outcome.

Quality assessment

One included umbrella review was rated as moderate quality, while the other was critically low. Of the seven systematic reviews, two were rated as low quality while the others were critically low. Common weaknesses were not addressing heterogeneity, not reporting included studies' funding sources and not justifying study design.

Cardiovascular disorders

Three systematic reviews included studies examining associations between use of e-cigarettes and cardiovascular outcomes in youth.[48 59 65] One umbrella review[7] included a section on cardiovascular disease, but its included systematic reviews were all excluded from ours because none undertook young person specific analyses, while its own cardiovascular section similarly included no young person specific results.

The three systematic reviews only incorporated two individual studies reporting cardiovascular outcomes in young people: a case report from Turkey[71] and a cross-sectional study of 270 Russian students.[72] The cross-sectional study found that an arterial stiffness marker was significantly higher in young people who vaped than those who did not. The case report dated from 2014 and involved acute myocardial ischaemia in a 24-year-old man with an absence of other risk factors; the report concluded that nicotine in the e-liquid may have been the cause.

Quality assessment

Of the three included systematic reviews, one was rated low quality and the other two were critically low. As elsewhere, common issues were not listing excluded studies and not adequately considering heterogeneity.

Oral health

Livingston *et al*[58] and Bozier *et al*[34] both included a cross-sectional study[73] of 65 528 students in South Korea on oral health that indicated that e-cigarette use was associated with significantly increased odds of gingival pain and/or bleeding, tongue and/or inside cheek pain and cracked or broken teeth. The review by Livingston *et al* also reported on the PATH longitudinal study[74] which indicated that, among 13 650 participants aged 12–17 years in the US, e-cigarette use alone was not significantly more likely than non-use to be associated with self-reported diagnosed dental problems. These reviews did not report comprehensive search strategies.

Guo *et al*[75] included six cross-sectional studies and one case-control study with 6827 young participants and found an association with e-cigarette use and dry mouth (xerostomia), with a higher prevalence in those aged <25 years than those aged >25 years (30%, 95% CI 28 to 32 vs 20%, 95% CI 18 to 23). One of these cross-sectional surveys[76] (975 US adolescents aged 13–17 years) was also reported by Kurdys-Bykowska *et al*[60] alongside one of 3488 children (aged 6–12 years) in Zurich,[77] which also reported higher rates of dry mouth. Another review reported a higher risk of throat dryness in young people who vaped (from one cross-sectional survey[78] of 520 paediatricians collecting information on children and adolescents in Canada).[61]

Other harm outcomes

Two systematic reviews[65 79] included the same cross-sectional study[80] of 1221 Danish young men that found that those who used e-cigarettes daily had significantly lower total sperm counts than those who did not use e-cigarettes. This study was rated a low risk of bias by the review authors.[65]

One review reporting the results of a cross-sectional survey of 975 US adolescents[76] indicated that dizziness or lightheadedness and headaches or migraines were more likely to be reported among those using e-cigarettes compared with those not using them (43.8% vs 14.6%, p=0.002).[60]

Valadez-Cuen *et al*[81] concluded that people using e-cigarettes were at a higher risk of contracting COVID-19, but only one cross-sectional online survey of 4351 participants was restricted to young people aged 13–24 years.[82] This review was rated as critically low quality and did not report a comprehensive search strategy.

There was limited evidence for other harms. One systematic review[79] reported on a cross-sectional study[83] which concluded that, among 441 adolescents and young adults with paediatric onset chronic kidney disease (CKD), occasional e-cigarette use was not associated with disease progression, proteinuria or elevated blood pressure. In the same review, another cross-sectional study[72] found e-cigarette use was related to higher albuminuria values (an early marker of CKD) after measuring urine albumin levels in 270 young volunteers. One systematic review[84] assessed the implications of vaping on surgical wound healing; one of the case reports[85] included was of a patient aged <25 years with acute e-cigarette consumption affecting flap tissue oximetry due to acute vasoconstriction.

DISCUSSION

The systematic reviews included in this umbrella review, which have primarily examined longitudinal, individual level studies, consistently indicated a significant association between e-cigarette use and later cigarette smoking in young people. These repeated strong associations in prospective cohort studies are consistent with a causal relationship between vaping and subsequent smoking. Inferring causality remains challenging,[26] and authors' conclusions within the reviews vary as to whether the relationship between e-cigarettes and smoking is causal,[20 27] reflecting the contested/uncertain nature of this interpretation elsewhere and plausible competing explanations for these associations. Nonetheless, given the consistent associations we observed with increased smoking and multiple possible harms to health and wellbeing in this age group, which are consistent with possible causal effects, the evidence supports policy measures to protect young people who do not smoke from the potential risks associated with vaping. These are therefore proposed on a precautionary basis in light of definitive evidence of causality not yet being established.

Multiple theories attempt to explain the relationship between e-cigarette use and smoking: the gateway effect[86] (vaping may increase subsequent smoking risk), the diversion effect[87] (vaping may reduce smoking by creating an alternative) and the common liability hypothesis[88] (no causal relationship). The consistency in the evidence we present is striking; e-cigarette use raises the likelihood of future cigarette smoking among youth and young adults. It may also increase smoking frequency and intensity (ie, the gateway effect). While population data show opposing trends, with smoking rates generally falling as vaping rises, theoretically supporting a diversion effect,[23 88 89] smoking trends measured in population studies are also influenced by other factors, such as public smoking bans, taxation and restrictions on purchasing and packaging. Our findings also provide evidence against the diversion effect because, under this hypothesis, people vaping would be less likely to smoke than those not vaping.

We also found associations between e-cigarette use and subsequent substance use. Certain behaviours, such as e-cigarette, alcohol and marijuana use, often cluster, potentially fulfilling similar social and psychological roles.[24 90 91] Many of the included studies within the reviews used adjusted ORs where available, which sometimes extended beyond assessing sex, gender and socioeconomic status variables. Many studies also used longitudinal designs with long follow-up periods, suggesting a gateway theory as opposed to a reverse gateway theory. This is supported by one of the systematic reviews[43] included in Asfar *et al*[7] which indicated that vape equipment can be used as a drug delivery system for illicit drugs and found that, of 861 respondents, 39.5% of people using electronic nicotine delivery systems had used them to vape recreational drugs, with marijuana being the most common (18.0%).

Our findings furthermore suggest that there is a link between current and ever use of e-cigarettes and an asthma diagnosis or exacerbation of existing asthma. In studies investigating e-cigarettes in real world settings, it is difficult to eliminate confounding due to the complex nature of these settings and the limitations of observational studies. However, the consistency in the findings indicates at least an association between e-cigarettes and increased asthma risk.

Acute exposure to e-cigarette vapour can cause coughing, bronchospasm and inflammatory responses in airways.[92 93] However, evidence for other respiratory harms associated with e-cigarette use in young people is lacking. While the evidence we present suggests that coughing may be associated with e-cigarette use,[53] more research is required for pneumonia,[52] bronchitis[58] and allergic rhinitis. Case reports and case series were identified for EVALI within the reviews. Most of these cases have been connected with the use of e-liquids containing THC and vitamin E acetate. However, many more case reports have been reported to regulatory agencies in the US and elsewhere, not all implicating THC.[94–96]

Our review also found repeated significant associations between e-cigarette use and mental health outcomes. The two umbrella reviews to date have largely been based on a single systematic review (Becker *et al*),[66] and those authors rate their evidence for links with depression as weak to moderate and for links with suicide as weak, citing the frequency of cross-sectional designs and possible confounding. Given the severity of these outcomes, urgent longitudinal research is merited. Other areas for further research include oral health, fertility, headaches or migraines, and dizziness or lightheadedness, while the limited number of reviews incorporating cardiovascular outcomes likely reflects our focus on youth populations where cardiovascular events are rarer than in adults.

A serious common harm of e-cigarettes is addiction. However, addiction as an outcome was noticeably absent from included reviews. This may be because it is an established property of nicotine and thus deemed self-evident. However, nicotine is one of the most addictive substances known, and there is clear evidence that young people are experiencing addiction to it as a direct consequence of use of e-cigarettes, including having difficulty in quitting.[97–99] Being caught in the addiction cycle of withdrawal, craving and satiation can significantly impact daily functioning[100] and children's behaviour in schools, as well as increasing social exclusion and stigma.[101 102] These areas of concern remain important avenues for future research.

Another striking gap in the evidence we collected, given the considerable interest in the role of nicotine on neurodevelopment,[103 104] is the potential influence of e-cigarettes on adolescent brain development. Only one umbrella review considered this in relation to young people (Banks *et al*)[6] but found no evidence concerning e-cigarettes and brain development (or neurological

outcomes generally). Systematic reviews assessing tobacco use and neurocognitive impairment[105 106] indicate that findings from research on young people may differ from adults. A previous non-systematic review synthesised the evidence on e-cigarettes and brain development, suggesting harmful effects,[107] and a scoping review found that e-cigarette use among young people is associated with poor academic achievement, with a lack of evidence on the causal direction.[108]

Use of both e-cigarettes and cigarettes together is also increasingly prevalent and was not the focus of this umbrella review. However, this dual use delivers a wider range of toxins than solely smoking or vaping; evidence from a systematic review indicates that risks of harm may be higher than using either product alone.[109]

Most of the systematic reviews we included were rated as low or critically low quality using AMSTAR 2 (multiple analyses have found that AMSTAR 2 rates most reviews as critically low).[110–112] As with all quality assessments, it was challenging to distinguish the quality of systematic review reporting from the quality of the review's conduct.[111] An issue for most reviews was the lack of an excluded studies list (with reasons for exclusion). This is a critical item in AMSTAR 2 and therefore resulted in downgrading of many of the reviews.

Strengths and weaknesses

While we were able to identify other umbrella reviews on the topic of harmful effects of e-cigarettes, none focused on a full range of potential harms in adolescents or young people. Indeed, our umbrella review is, to our knowledge, the most comprehensive synthesis of systematic reviews that has taken place to date on the wider risks of vaping in young people.

Another strength of our research is that, once early findings began to emerge, we discussed them with young people directly at a youth public health forum. Participants advised on how their age group might view our results, citing frustration at instances elsewhere when vaping is portrayed as much safer than smoking, and how we could best disseminate results effectively.

As with all umbrella reviews, we were dependent on the quality of the included systematic reviews, and our results lack some of the granular detail that can be ascertained in a single systematic review. Much of the evidence available for outcomes other than smoking uptake is cross-sectional; there was a paucity of population based (ecological) analyses which could have helped assess if changes in vaping prevalence and smoking prevalence were associated at the population level. Furthermore, although we restricted our searches to 2015 onwards (see methods), there were some limited data within the included reviews that predated 2015. We have, however, provided a comprehensive high-level overview of the research on harmful impacts of e-cigarettes in young people and, by measuring the overlap in included studies, have been able to provide an overview for the risk of inflating research results when primary studies' findings are shared multiple times.

Future evidence

There were 12 systematic reviews registered on PROSPERO between 2020 and 2024 categorised as ongoing and aiming to evaluate the harms of e-cigarettes in young people (although many reviews registered on PROSPERO might never be completed or published). Three focus on respiratory outcomes[113–115] and one on asthma.[116] One review is examining smoking initiation[117] but, given our consistent findings on this harm, it is unlikely to change the conclusions of our review. Two focus on substance use,[118 119] one on dental caries,[120] one on depression[121] and one on physical activity.[122] Two reviews are investigating general harms.[123 124]

Policy implications

Our findings support the implementation of policy measures to restrict sales and marketing of e-cigarettes to young people, and restrictions on advertising design features that are designed for, or likely to appeal to, young people. Such efforts may form part of a wider set of measures to restrict harms, including raising the public's and young people's awareness of these harms, and counter-marketing to raise public and policy awareness of the marketing and strategies that e-cigarette companies have targeted at children and young people. Little research focuses on evidence regarding access to e-cigarettes. In an evidence gap map,[125] seven studies were identified on taxation and other price policies, and two on clean indoor air policies.

CONCLUSIONS

Systematic reviews showed consistent evidence that higher risks of smoking initiation, substance use (marijuana, alcohol and stimulants), asthma, coughing, injuries and adverse mental health outcomes are associated with e-cigarette use in young people. Other harms such as pneumonia, bronchitis, headaches, migraines, dizziness/lightheadedness, low sperm count and oral health harms are possibly associated with e-cigarette use in young people but require further research.

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