

Are electronic cigarettes an effective aid to smoking cessation or reduction among vulnerable groups? A systematic review of quantitative and qualitative evidence
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ABSTRACT

Introduction: Smoking prevalence remains high in some vulnerable groups, including those who misuse substances, have a mental illness, are homeless or are involved with the criminal justice system. E-cigarette use is increasing and may support smoking cessation/reduction.

Methods: Systematic review of quantitative and qualitative data on the effectiveness of e-cigarettes for smoking cessation/reduction among vulnerable groups. Databases searched were MEDLINE, EMBASE, PsychINFO, CINAHL, ASSIA, ProQuest Dissertations and Theses and Open Grey. Narrative synthesis of quantitative data and thematic synthesis of qualitative data.

Results: 2628 records and 46 full texts were screened; 9 studies were identified for inclusion. Due to low quality of evidence, it is uncertain whether e-cigarettes are effective for smoking cessation in vulnerable populations. A moderate quality study suggested e-cigarettes were as effective as nicotine replacement therapy. Four studies suggested significant smoking reduction, however three were uncontrolled and had sample sizes below 30. A prospective cohort study found no differences between e-cigarette users and non-users. No significant adverse events and minimal side effects were identified. Qualitative thematic synthesis revealed barriers and facilitators associated with each component of the COM-B (capability, opportunity, motivation, behaviour) model, including practical barriers; perceptions of effectiveness for cessation/reduction; design features contributing to automatic and reflective motivation; smoking bans facilitating practical opportunity; and social connectedness increasing social opportunity.

Conclusion: Further research is needed to identify the most appropriate device types for practicality and safety, level of support required in e-cigarette interventions, and to compare e-cigarettes with current best practice smoking cessation support among vulnerable groups.

IMPLICATIONS

Smoking prevalence among people with mental illness, substance misuse, homelessness or criminal justice system involvement remains high. E-cigarettes could support cessation. This systematic review found limited quantitative evidence

assessing effectiveness. No serious adverse events were identified. Qualitative thematic synthesis revealed barriers and facilitators mapping to each component of the COM-B (capability, opportunity, motivation, behaviour) model, including practical barriers; perceived effectiveness; design features contributing to automatic and reflective motivation; smoking bans facilitating practical opportunity; and social connectedness increasing social opportunity. Further research should consider appropriate devices for practicality and safety, concurrent support, and comparison with best practice smoking cessation support.

INTRODUCTION

Smoking prevalence remains high among some vulnerable groups, including those who misuse substances, have a mental illness, are homeless or are involved with the criminal justice system (CJS) (1). Prevalence is estimated at 88% among substance misusers (2), 77% among people who are homeless (3), 74% in prisons (4), 33% among people with mental illness (5), and 75% in serious mental illness (SMI) (6).

Attributable morbidity and mortality is considerable. Mortality among substance misusers who concurrently smoked was four times higher than non-smokers (7) and tobacco-related causes were the leading cause of death among people receiving inpatient substance misuse treatment (8). People with SMI or homelessness have significantly reduced life expectancy, to which high smoking prevalence contributes considerably (9-12). Wilcox estimates more prisoners in the United States of America (USA) die from second hand smoke than are legally executed (13).

Key barriers to smoking cessation among vulnerable groups remain. Among those with mental illness and/or substance misuse, perceptions that smoking is beneficial for managing symptoms, part of daily routine, culture and identity, and provides social connectedness are key barriers (14, 15).

Electronic cigarette (e-cigarette) use has grown rapidly, and may support smoking cessation, but there is little evidence on long term effects. A Cochrane review identified two RCTs suggesting e-cigarettes are more effective for long term smoking

cessation compared with placebo e-cigarettes and one RCT found no significant differences between e-cigarettes and nicotine patch (16). However, overall evidence was considered of 'low' or 'very low' quality due to low event rates and wide confidence intervals. No serious adverse events were identified but long term safety data was lacking. Qualitative research in the general population suggests e-cigarettes are able to attain to all the aspects of smoking considered important, being pleasurable, replacing habitual aspects and providing social connectedness (17).

Estimated e-cigarette use prevalence among tobacco smokers in the United Kingdom (UK) is 21.9%, and 36.5% report 'ever use' (18). In the USA 15.9% report current use and 47.6% ever use (19). USA estimates suggest current use among smokers in community mental health treatment is 22% (20) and ever use among acute psychiatric admissions 11% and increasing (21). Ever and current use among substance misusers are 73% and 33.8% respectively (22). Past month e-cigarette use was estimated as 12-51% among homeless tobacco smokers (23-25). No CJS data was available. Reasons for e-cigarette use include smoking cessation/reduction, (22-28) curiosity/experimentation, (22, 24, 28) use where smoking is banned, (23, 24, 26-28) lower cost (24-26) and harm reduction (24-27).

E-cigarettes are regulated differently from smoking cessation therapies in many countries, and consequently funded differently, e.g. in the UK, unlike nicotine replacement therapy (NRT), bupropion and varenicline, e-cigarettes are not available on prescription and users must buy them. For vulnerable groups with potentially limited income, including the homeless, those in inpatient services and prison populations, cost may be a barrier. In view of the difference in funding mechanisms between e-cigarettes and other methods of smoking cessation support in many countries, health economics outcomes, such as economic impact of the adoption of e-cigarettes among vulnerable groups compared with other options for smoking cessation/reduction, are of interest.

In settings where smoking is banned e-cigarettes are often included without consideration of potential benefits. 'Smoke-free' homeless shelters, psychiatric hospitals and prisons are common and increasing. The UK National Institute for Health and Care Excellence (NICE) currently do not recommend e-cigarettes (29),

whilst a Public Health England (PHE) evidence update suggests smokers who have struggled to quit, or do not wish to, should be encouraged to switch to e-cigarettes as they are around 95% safer, but highlight that continued vigilance and further research is needed (30). To date, there has been no systematic review of the effectiveness of e-cigarettes for vulnerable groups.

This report aims to (i) systematically review evidence for the effectiveness of e-cigarettes for smoking cessation and reduction among these vulnerable groups; and (ii) identify barriers and facilitators to e-cigarette use.

The protocol was registered on PROSPERO (31). Review questions were:

- Are e-cigarettes effective and cost-effective for smoking cessation or reduction for vulnerable groups?
- Are any adverse events associated with e-cigarette use in vulnerable groups?
- What are the barriers and facilitators to e-cigarette use for vulnerable groups?

METHODS

A systematic review of quantitative and qualitative literature on the effectiveness of e-cigarettes for smoking cessation and reduction among vulnerable groups, and barriers and facilitators to e-cigarette use, was conducted.

Inclusion criteria

Study design

A range of designs were included as scoping searches suggested limited available controlled evidence. The following study designs were eligible:

- For assessing effectiveness: randomised controlled trials (RCTs), cluster randomised controlled trials (cRCTs), quasi-RCTs, controlled before and after

studies (CBA), interrupted time series (ITS), cohort studies, case-control studies and uncontrolled before and after studies (uBA).

- For assessing quantitative data on barriers and facilitators to e-cigarette use: longitudinal, cross-sectional or cohort surveys.
- For assessing qualitative data on barriers and facilitators to e-cigarette use: qualitative studies with any recognised method of data collection (e.g. interviews, focus groups) and analysis from any discipline or theoretical tradition (e.g. grounded theory, thematic analysis).

Participants

Participants and carers' of any age in any country/setting in at least one of the following vulnerable groups:

- *Mental illness*: Anyone diagnosed with a condition in the International Classification of Diseases and Related Health Problems 10 (ICD-10) classification of Mental and Behavioural Disorders (32) or the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (33) and/or who was an inpatient or outpatient in a mental health treatment/rehabilitation centre. Those with transient psychiatric symptoms (e.g. self-reported depressive symptoms but no diagnosis/treatment for depressive disorder) were excluded as they were felt to face different challenges for smoking cessation e.g. time spent in a treatment facility and medication interactions.
- *Substance misuse*: People in treatment/recovery for any form of substance misuse including illegal and prescribed drugs, legal highs and alcohol. 'In treatment' included inpatient and outpatient substance misuse treatment. Participants were considered in 'recovery' if they met the UK Drugs Policy Definition of 'voluntarily sustained control over substance use which maximises health and wellbeing and participation in the rights, roles and responsibilities of society' (34). Medication assisted recovery, such as methadone programmes, were included, as well as abstinence-based programmes. Focus was on treatment/recovery rather than casual substance

misuse, as they were thought to face different challenges for smoking cessation e.g. time spent in a treatment facility.

- *Homeless*: Individuals meeting national criteria for homelessness in the country/countries where the study was conducted or those accessing services for the homeless (35). In the UK, legally a person is homeless if they have no accommodation they are entitled to occupy, or the accommodation they are entitled to occupy is in such poor condition they cannot be reasonably expected to occupy it (36).
- *Criminal justice system (CJS)*: Those detained at any stage, including police custody, people on remand/convicted and detained in any prison type/category and those on probation.

These four vulnerable groups, and not others, were chosen because they have particularly high smoking prevalence, suggesting smoking has not been de-normalised among these groups, and because there is some overlap between the groups, for example prevalence of mental illness and/or substance misuse is high among the homeless (37) and people involved with the CJS (38).

Interventions

Studies investigating e-cigarettes, defined as 'electronic devices that heat a liquid into an aerosol for inhalation. The liquid usually comprises propylene glycol and glycerol, with or without nicotine and flavours, and stored in disposable or refillable cartridges or a reservoir' (16). Disposable, non-rechargeable e-cigarettes, rechargeable e-cigarettes with replaceable pre-filled cartridges, and rechargeable e-cigarettes with a refillable tank reservoir into which 'e-liquid' is added were included (39). 'Heat not burn' products, in which heated tobacco is vaporised, were excluded (40).

Comparison group

- E-cigarette versus another type of nicotine or non-nicotine e-cigarette;

- E-cigarette versus smoking cessation intervention (e.g. NRT, behavioural intervention);
- E-cigarette versus no or delayed intervention.

Uncontrolled before and after studies were included if baseline measurements were reported. Weaknesses of such designs are considered in quality assessment below.

Outcome measures

Studies reporting on any of the primary or secondary outcomes were included.

Primary outcomes

- Smoking cessation at longest follow-up, by any measure, self-report and preferably expired-air carbon monoxide (eCO) verified and in accordance with the Russell Standards (41).
- Serious or non-serious adverse events. Adverse event was defined as 'any undesirable experience' associated with use (42). It was considered serious if it led to death, threatened life, hospitalisation (initial or prolonged), permanent damage/disability, congenital anomaly, required intervention to prevent permanent impairment/damage, or other important medical events which may jeopardise the patient and/or require medical/surgical intervention. Of particular interest were interactions with prescribed psychiatric medications, fires caused by e-cigarette chargers or self-harm associated with e-liquid.
- Perceived barriers and facilitators to e-cigarette use.

Secondary outcomes

- Smoking reduction, assessed by self-report and preferably confirmed biochemically, at longest follow up;
- Retention in a smoking cessation, substance misuse, mental health or other treatment programme.

- Health economics outcomes.

Database searches

Following searches from similar systematic reviews (15, 16, 35) a strategy was developed in MEDLINE using MeSH and free text terms (Box 1), tested against a sample of relevant papers and adapted for other databases.

Searches were from 2004, when modern e-cigarettes became available (16) to March 2017. Reference lists of included studies and systematic reviews were screened. Searches were not restricted by language but studies without a full text available in English would have been excluded, although none relevant were identified. Articles not referring to any included vulnerable group(s) or to e-cigarettes by any recognisable name, in the title/abstract, were excluded.

Data extraction

Search results were merged using Endnote and de-duplicated. Titles and abstracts were screened according to pre-specified inclusion/exclusion criteria by one author (SG) with 10% double screened by a second (CN). There were two discrepancies, which were resolved by discussion. Potentially included full text articles were retrieved and reviewed and 10% double screened, with no discrepancies. Data were extracted using a standardised data extraction sheet by SG and a sample (four studies) double checked by CN, with no discrepancies. Double screening and data extraction of only a sample was necessary due to resource limitations, and has been done in similar reviews (15, 43, 44).

Quality assessment

RCTs/cRCTs would have been appraised using the Cochrane risk of bias tool (45), although none were identified. Other quantitative studies were assessed using the Effective Public Health Practice Project (EPHPP) criteria (46), and qualitative studies using the Critical Appraisal Skills Programme (CASP) checklist (47), by SG, and a sample (four studies) double checked by CN with no discrepancies. Results were used to inform narrative synthesis (48).

Data synthesis

Due to heterogeneity of design, participants, interventions and outcomes suggested by scoping searches, narrative synthesis of quantitative data was planned from the protocol stage, based on guidance by Popay et al. (48-50). A thematic analysis of reported qualitative data was conducted (51, 52). Data were entered into Excel to assist with coding. 'First-level' codes aimed to summarise the meaning of the text or capture authors' original language. Coding was identified as original data or author interpretation. Synthesis involved organisation of first level codes into second level descriptive themes, summarising first level codes whilst remaining close to the included studies. Third level analytical themes were then developed. This stage involved 'going beyond' or 'interpreting' the first and second level codes to capture the line of argument (53) and generate new findings from pooled data.

To explore relationships in the data, themes emerging from qualitative data were mapped onto the COM-B model, a 'behaviour system' within which capability, motivation and opportunity interact to generate behaviour, which also influences each of these components (54). Capability includes both practical and psychological components, motivation includes automatic and reflective processes, and opportunity includes physical aspects, such as physical accessibility, and social aspects, such as community or family support. The model has been applied to tobacco control (54) and general population e-cigarette use (55) but not as part of a systematic review on e-cigarette use among vulnerable groups. Application of the COM-B model was considered appropriate for this systematic review because relating data to the conditions which this established theory assumes must be met for behaviour to change, which are likely different for vulnerable groups compared

with the general population, may provide insights into how to facilitate switching from combustible tobacco to e-cigarettes.

RESULTS

The PRISMA Flow Diagram (56) reports records identified, duplicates, records screened and included/excluded, full text articles assessed and studies included in narrative synthesis (Figure 1).

Study characteristics

Searches revealed 9 studies meeting the inclusion criteria. Five quantitative studies were included (total participants n=1089). Of the included quantitative interventional studies (total participants n=133), there was one secondary analysis (57) of an RCT (58), and three uncontrolled before and after studies (6, 59-61) (one study was reported in both a conference abstract (61) and a full article (59)). One cohort observational study was included (n=956) (21). Four qualitative studies were included (62-65); three involving focus groups (n=128) (63-65) and one qualitative analysis of online postings (62). Five studies were performed in the USA (6, 21, 60, 63, 64) and one in each of Australia (65), Italy (59, 61), New Zealand (57) and international posters online (62).

Participants

Six studies included participants with mental illness (6, 21, 57, 59, 61, 62, 65), two homelessness (63, 64), and one substance misusers (60). No studies involving the CJS were identified. Attrition was minimal.

Mental illness populations were heterogeneous and included people reporting being prescribed one or more psychiatric medications (57), SMI diagnosis (6), schizophrenia (59, 61) and acute psychiatric admissions (21). Self-report psychiatric medication use is likely less accurate for case ascertainment than ICD-10/DSM-IV criteria. Qualitative studies included community mental health clients (65) and posters discussing e-cigarettes in the context of mental illness online (62).

Two qualitative and no quantitative studies involving homeless populations were identified. One recruited from homeless shelters (63). The second included homeless parents living in family shelters (64).

Only one quantitative study (60) and no qualitative studies focussed on substance misusers. The study involved people on methadone and may not be representative of users of other substances. Number of participants included in each study are reported in Table 1. Participant characteristics of quantitative and qualitative studies are detailed in Supplementary Tables 1 and 2 respectively.

Interventions and comparisons

Four intervention studies were identified (6, 57, 59, 60). The main intervention focus was free provision of e-cigarettes, suggesting researchers may have considered cost a barrier. Only one study included behavioural support (low intensity voluntary telephone counselling) (57). One study offered e-cigarette use instructions plus telephone technical and medical assistance (59). The remaining studies provided only instructions for use (6, 60). No explicit theoretical basis for interventions were described. One study emphasised collecting 'real-life' data hence no encouragement or motivational support was provided (59). All suggested e-cigarettes may be considered a harm reduction strategy (6, 57, 59, 60). See Supplementary Table 3 for further intervention details.

Outcomes

Five studies addressed smoking cessation (6, 21, 57, 59, 60), four adverse events (6, 57, 59, 60), five smoking reduction (6, 21, 57, 59, 60) and four reported qualitative data on barriers and facilitators to e-cigarette use (62-65).

Quality assessment

Four of the included quantitative studies were rated globally as weak (6, 21, 59, 60) using the EPHPP criteria (46), and one was rated moderate (57). Included qualitative studies were of moderate quality, with global scores calculated based on the CASP checklist ranging from 6-8 out of ten. Further details on the scores for each criteria are available in Supplementary Tables 4 and 5.

Primary outcomes

Smoking cessation

Four interventional studies assessed smoking cessation outcomes among those receiving an e-cigarette intervention (6, 57, 59, 60). Smoking cessation varied from 0.0% (60) - 14.3% (59) (details of how each study defined smoking cessation are provided in Table 1). Three studies included people with mental illness (6, 57, 59) and one, people on methadone (60). Three studies were rated as weak on quality appraisal and included fewer than 30 participants, making statistical analyses potentially unreliable (6, 59, 60). The fourth was rated moderate and was the only study with a control group (57). There were no significant differences between nicotine e-cigarette, non-nicotine e-cigarette and NRT, however this secondary analysis of an RCT had limited power. None of the included studies met all parts of the Russell Standards. Two studies partially met them. O'Brien et al. assessed

biochemically verified continuous abstinence at 6 months (57) and Caponetto et al. assessed 52-week complete self-reported and CO verified abstinence (not even a puff) for 30 days before assessment (59).

One observational study involving people with mental illness found no significant difference between e-cigarette users and non-users (21) (Table 1). Participants were part of an RCT comparing brief, extended and usual smoking cessation treatment, so may not be representative of wider mental illness populations.

Adverse events

No serious adverse events were reported (6, 57, 59, 60). Some side effects were reported, commonly cough, headache and throat irritation. O'Brien et al. compared adverse events/month among e-cigarette users with and without mental illness and found no significant difference (0.05 events/month in both groups ($p=0.592$, IRR 0.89, 95% CI 0.59-1.35)) (57). Adverse event counts were similar between nicotine e-cigarette, placebo e-cigarette and NRT but small numbers prohibited significance testing. Caponetto et al. reported side effects experienced among people with mental illness resolved over time (59), but no data beyond 52 weeks were available. For further detail see Supplementary Table 6.

Barriers and facilitators

Four moderate quality qualitative studies reporting data relating to these outcomes (62-65) were thematically synthesised and mapped to the COM-B model (Figure 2). How qualitative data link to each aspect of the framework is discussed below, with barriers and then facilitators presented, with illustrative quotes. Supplementary Table 7 details which themes arose from which studies.

Physical capability

Physically accessing, safely operating and maintaining supplies to use an e-cigarette was a barrier (62, 65):

“I think you would have to be organised and organise your finances and make sure that when it does run out you’ve got something to fill it up with, because that would be the time when you go, “Oh bugger I’ve run out of this” and you would go and buy a packet of cigarettes or whatever.” (65)

Concerns were raised about safely refilling, charging, and cleaning. Potential danger of ‘e-liquid’ for those at risk of self-harm was concerning (62, 63, 65):

“I think what the OP [original poster] means is that nicotine on its own is more poisonous than cyanide and arsenic. 60 mg will kill a light smoker, and I believe 45 mg is enough to kill many people who don’t smoke. Giving nicotine juice to someone with major depressive disorder may not be the best idea in the world.” (62)

Assistance from family/carers and design (e.g. closed cartridges) were suggested solutions (62):

“My mother has schizophrenia . . . She has a terrible smokers cough and I think if I could get her to swap to e-cigarettes it would make a hell of a difference . . . Trouble is it needs to be dead simple. Even the recharging could cause problems and the refilling almost certainly would have to be done periodically by members of the family . . . Good charge and easy to charge. Maybe affordable enough to have a few so she can wait for a family member to refill or very easy to refill.” (62)

Psychological capability

E-cigarettes were considered less harmful than cigarettes and were an alternative source of nicotine for cessation (62-65) and reduction (62, 63, 65):

“I quit through vaping, not just a little tiny one but it’s good to invest on something expensive. Although you’re trading one addiction for another, it’s

the lesser of the two evils. I was a pack a day smoker and I quit within two weeks.” (62)

“yeah an e-cigarette really helped me to quit smoking. Like even when I was pregnant and trying to quit smoking I used a patch, like the doctors prescribed me a patch to quit smoking and that didn't even work as well as the e-cigarette did.” (63)

Physical opportunity

Some spent more money personalising e-cigarette/vaping equipment than they previously did on cigarettes, whilst others found them cheaper (62, 65). Balancing personalisation with affordability was considered necessary:

“Let's not talk about money. I've fallen deep into the rabbit hole. Turn away and save yourselves, but it's too late for me. Cigarette money is now going on vape gear. Anyway . . . ” (62)

“The mods and juices are so cheap that it is like it is non-existent to my budget. I don't have to skip on dates like when I was taking concerta.” (62)

E-cigarette use where smoking is banned was a facilitator (62, 63):

“I'm a frequent flier at “Happy Camp.” That's how my family and I jokingly refer to the mental health floor at the hospital. Regular as clockwork, I think life is out of control every five years or so. The last time, 2009, we were still allowed to go outside (up on the roof LOL) twice a day to smoke. I'm guessing that won't be the case next year when I'm ready for an emotional oil change. I've definitely got to get to vaping full time by then. I don't know that they will allow vaping, but I figure it is a much better bet than smoking.” (62)

Social opportunity

Reversal of the de-normalisation of smoking was feared (63):

“I remember when...a couple of years back they used to have this commercial for Newports and it'd be like a dude...a DJ...a black dude. You know and I even had something to say about like when they started the Blu [e-

cigarette]...I was like oh my god, they're allowing smoking on TV because you don't really see that too often. I don't remember seeing a commercial promoting smoking, so it was like advertising directed to me, but the whole Newport thing, that was a whole culture, you know like this is what you do, you're cool, you're high, you're drinking and by the way, have a Newport.” (63)

Family/friends, healthcare professionals and online posters facilitated e-cigarette initiation and provided moral and practical support. E-cigarettes were socially acceptable and provided a community of ‘vapers’ with opportunities for interaction and connectedness (62):

“Have a renewed sense of self-worth and no longer feel like a second class citizen because I have a nicotine addiction that makes me a social pariah because of the smell and stigma attached to analogue cigarettes. Thank you so much to the/r/electronic_cigarette community for acting as a catalyst to such a positive change in my life!!!” (62)

Automatic motivation

Physical side effects (e.g. sore throat) were a barrier (62, 65):

“I found a problem with them and I tried them for a while and I get a bit of asthma and I found with the vapour it would make my lungs rattle a bit, so I would worry that long term you might get pleurisy or something from taking in the moisture, a bit of fluid on the lungs.” (65)

Visible vapour provided an experience similar to smoking which NRT cannot offer. Views on device appearance and flavour were mixed (62, 63, 65):

“It doesn't look like a cigarette should, would not make me want to smoke it.” (65)

[Referring to inhaler, in contrast to EC] “No good [. . .] because the vapour you see the smoke coming out and you're drawing on something, the vapour is going to work.” (65)

Reflective motivation

Concerns about continued or worsening habit/addiction were barriers (62, 63, 65):

“I went through it faster than I probably would have a pack of cigarettes and then also my brother enlightened me, he was like e-cigarettes they say they're supposed to be better for you because it's vapor this and that, but really it's not because it gives you the opportunity to smoke cigarettes in places where you can't smoke. So you're smoking that and you're in an environment where it's not smoking, but the e-cigarette is allowed, but technically yeah you're not harming anybody else, but you're still smoking...you're still harming yourself, so you're smoking more than you normally would smoke.” (63)

E-cigarettes were perceived to have both beneficial and negative effects on psychiatric symptoms and medication side effects (62, 65):

“I have PTSD, anxiety symptoms from that, and TBI-related memory issues and micro seizures. For me, vaping is pretty much the same as smoking, in terms of how it helps me calm down and handle stress.” (62)

“Vaping doesn't really do it for me. That's due to there being chemicals in burnt tobacco that function very similar to antidepressants (which is one of the big things that makes tobacco addicting). Vaping doesn't have those, and thus only has the effects of nicotine, which aren't as strong.” (62)

E-cigarettes were more desirable than NRT (62-65):

“Of the cessation tools discussed, participants were much more interested in e-cigarettes or replacing smoking with an alternative habit than they were in using either patches or medication..” (64) [Author interpretation]

Ability to take charge of nicotine addiction was empowering (62), facilitated by ability to choose and personalise the device (62, 65):

“Now this kit was pretty good, I barely felt the nicotine, but I started to feel confident, and felt a lot of my anxiety drift away. I've been starting to regain control of my life; hell I'm even posting on reddit. Vaping not only saved my life, but freed me from a cage.”(62)

“The thing is they’re not trying to look like a cigarette. They are clearly something different. You can personalise them and they come in different colours. You can get some that are a bit quirky. They treat you like an adult with something you might want.” (65)

Some considered e-cigarettes an alternative habit to smoking. It was a hobby associated with a community of ‘vapers’, both valued distractions from other life challenges (e.g. mental illness) (62, 65):

“Vaping works for my anxiety because I’m a fidgeter and a comfort eater. I need something to do with my hands, and often that something is to put things in my mouth. Vaping satisfies both of those comfort mechanisms. I can get the same effect with a Rubik’s Cube and a lollipop, except I’m diabetic so the lollipop is a terrible idea.” (62)

“OK, here’s from someone who also suffers social anxiety, vaping has helped in more ways than quitting smoking. It’s a conversation starter. People will approach you. People will want to know what you’re doing. At first it’s overwhelming but over time it’s helped build my confidence in extreme ways.” (62)

Secondary outcomes

Smoking reduction

Five studies reported on smoking reduction (6, 21, 57, 59, 60). A moderate quality study of people on medication for mental illness suggested a reduction of 9.9 cigarettes/day among 16mg nicotine e-cigarette users compared with 5.7 among patch users (Table 2) (57). This difference was statistically significant and, if sustained, may lead to clinically significant differences, but the study lasted only 26 weeks and included only 86 participants. There was some evidence from three weak quality uncontrolled before and after studies of statistically significant smoking reduction from baseline to follow up for participants with mental illness (6, 59) and

substance misuse (60). Reduction was confirmed with eCO among those with mental illness. However, as there was no control group, it is unclear if these reductions would have occurred without e-cigarettes. An observational study found no significant reduction in smoking among e-cigarette users (21).

Other treatment and health economics outcomes

No studies reported on treatment retention or health economics.

DISCUSSION

The primary objective of this systematic review was to assess effectiveness of e-cigarettes for smoking cessation among vulnerable groups. Due to low quality of available evidence, whether e-cigarettes are effective remains uncertain. There was some evidence from a moderate quality study that e-cigarettes were as effective as NRT for smoking cessation. There was some evidence from four studies of statistically and clinically significant smoking reduction, however, three were uncontrolled and had sample sizes less than 30. There were no differences between e-cigarette users and non-users in a prospective cohort study, although there were limitations in case ascertainment (participants asked about “all forms of tobacco use”) and as participants were recruited from an RCT of smoking cessation interventions, those who had already stopped/reduced smoking using e-cigarettes may not have participated (16).

Villanti et al. propose methodological criteria for determining whether a study provides sufficient information to establish whether e-cigarettes facilitate smoking

cessation/reduction: 1) examines outcome of interest; 2) assesses e-cigarette use for cessation as exposure of interest; 3) employs appropriate control/comparison; 4) ensures measurement of exposure preceded outcome; 5) evaluates dose and exposure duration; and 6) evaluates type and quality of device (66). All the included quantitative studies assessed cigarette abstinence. Only two studies assessed e-cigarette use for cessation as the exposure of interest (57, 60). Only one study included an appropriate control group (57). The four interventional studies ensured exposure preceded outcome (6, 57, 59, 60). None evaluated dose, exposure duration or device quality. None of the included studies met all parts of the Russell Standards. Two studies partially met them. O'Brien et al. assessed biochemically verified continuous abstinence at 6 months (57) and Caponetto et al. assessed 52-week complete self-reported and CO verified abstinence (not even a puff) for 30 days before assessment (59).

Qualitative thematic synthesis revealed barriers and facilitators mapping to each component of the COM-B model, and suggests e-cigarettes have the potential to be able to attain to key aspects of smoking addiction, being pleasurable, replacing habitual aspects, providing an alternative identity as a 'vaper' and facilitating social connectedness through a vaping community. It also suggests vulnerable groups may require additional support to enable e-cigarette use, in terms of choosing a device, using it safely, access to e-cigarettes and accessing the social connectedness 'vaping' can provide.

No serious adverse events were reported. Qualitative studies highlighted concerns about e-liquid access for those at risk of self-harm, which case reports show has been used in intentional overdose (67). Future studies should consider how design adaptations could improve safety.

Included interventions provided minimal support alongside e-cigarettes. This is similar to studies of e-cigarette interventions among the general population (16), but in contrast to combined behavioural support and NRT offered by English stop smoking services (68). Triangulation with qualitative data highlights importance of e-cigarettes as an empowering way of providing control over nicotine addiction. Further

research is needed to establish whether e-cigarettes are effective alone or with support.

Strengths and limitations of the evidence base

Three of the five included quantitative studies had sample sizes of less than 30. Some studies included only self-report smoking reduction, risking recall bias. Neither the uncontrolled before and after studies nor the cohort study adjusted for confounders. Failure to adjust for confounders, including level of nicotine dependence, in cohort studies of NRT led to underestimation of effectiveness (16, 69).

Overall quantitative evidence was weak. Qualitative evidence was moderate. Much available qualitative data was from a single study analysing online posts about e-cigarettes for those with mental illness. Those who are motivated to post online are more likely to have strong views, reducing transferability. However, such methods obtained rich data from participants using a self-initiated innovative nicotine delivery device.

Heterogeneity of included studies in terms of participants, interventions, comparisons and outcomes reduced comparability and prohibited meta-analysis. All included studies were from high income countries, thus generalisability to other settings is limited, and publication bias is a possibility.

No data were found on the CJS. E-cigarettes are a consumer product that entered and have proliferated in the market largely outside the health arena, in contrast to medicinally licensed products (e.g. NRT) (17). This may be why little data is available for the CJS, where access to such consumer products is restricted. As more prisons become smoke-free, with some recognising the potential role of e-cigarettes in supporting smoking abstinence, this evidence gap may begin to be filled.

No data were available on health economics outcomes. Further research is needed into how e-cigarettes, if effective for smoking cessation/reduction, could best be funded for vulnerable groups.

None of the included studies discussed 'vaping' other substances (e.g. cannabis), which may be of concern (30), particularly among substance misusers.

Strengths and limitations of this review

Strengths include the comprehensive search strategy, triangulation of quantitative and qualitative data, application of behaviour change theory and focus on underserved populations.

The scope of this review specified four vulnerable groups (people with mental illness, substance misuse, homelessness or CJS involvement), but other groups may also be considered vulnerable, including young people, pregnant women, lower socioeconomic groups and indigenous populations (35), and the effect of e-cigarettes on these groups should be considered in future studies.

That it was only feasible to independently double screen 10% of citations is a limitation. Richness of qualitative synthesis was restricted by the limitations of available data. Triangulation of qualitative and quantitative data and application of the qualitative data to a recognised theory of behaviour change has attempted to make the most of extremely limited available data.

Implications

This review highlights the need for further research into the role of e-cigarettes for vulnerable groups and the challenge of making recommendations for public health policy.

The available evidence assessing effectiveness of e-cigarettes for smoking cessation for vulnerable groups was limited. No serious adverse events were identified, and side effects were minimal. In view of the harm caused by tobacco, recommendations from PHE that e-cigarettes be considered for those who have

been unable to stop smoking (30) appears appropriate for vulnerable groups as well as the general population.

Qualitative data highlighted concerns about e-cigarettes reversing de-normalisation of smoking (63). However, tobacco is arguably yet to be de-normalised among these groups (35). Consideration of the differences in harm between e-cigarettes and tobacco is needed before including the former in smoking bans. PHE report negligible levels of nicotine in ambient air and no health risks for bystanders have been identified (30). The South London and Maudsley NHS Foundation Trust, an English mental health trust, implemented a 'smoke-free' policy including guidance supporting e-cigarette use in bedrooms and grounds for patients who have tried other cessation methods (70).

No cost-effectiveness studies were identified. Unlike NRT, e-cigarettes are unlicensed and not available on prescription, thus users pay for them (30). 'Starter kits' including battery, charger and replaceable nicotine cartridges cost £17-90 (71).

Future directions

Pilot studies comparing different intervention designs for usability and safety for vulnerable groups would be beneficial. Adequately powered RCTs comparing e-cigarettes with best practice smoking cessation support are needed. Comparison of e-cigarette interventions with and without associated support would help to identify how they may be used effectively. Qualitative process evaluations alongside trials could elucidate method of action and acceptability. Cost-effectiveness studies are required. No studies were found involving the CJS. With moves towards banning smoking in UK prisons (72) and elsewhere (73) such research is needed. Future studies should also consider the role e-cigarettes could play in smoking relapse prevention for vulnerable groups.

CONCLUSION

Due to the low quality of available evidence it is uncertain whether e-cigarettes are effective for smoking cessation for vulnerable groups. However, included studies identified no serious adverse events and qualitative studies suggested e-cigarettes could attain to key aspects of smoking addiction, including habit and social connectedness. In view of the harm tobacco causes, PHE recommendations that e-cigarettes be considered for those unable to stop smoking appear appropriate for vulnerable groups as well as the general population. Further research is needed to identify the most appropriate type of device, level of support required and to compare e-cigarettes with best practice smoking cessation support among vulnerable groups.

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Box 1. Search strategy as used in MEDLINE

Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

- 1 e-cig\$.mp
- 2 electr\$ cigar\$.mp
- 3 electronic nicotine.mp
- 4 (vape or vaper or vapers or vaping).ti,ab.
- 5 1 OR 2 OR 3 OR 4
- 6 Exp Mental Health Services/
- 7 Exp Mental disorders/
- 8 Mentally ill persons/
- 9 Mental health/
- 10 (mental health OR suicide OR depression OR anxiety OR emotional distress OR psychological distress OR schizophrenia OR bipolar OR manic depression).ti,ab.
- 11 6 OR 7 OR 8 OR 9 OR 10
- 12 Substance-Related Disorders/
- 13 exp Alcohol-Related Disorders/
- 14 Amphetamine-Related Disorders/
- 15 Cocaine-Related Disorders/
- 16 Inhalant Abuse/
- 17 Marijuana Abuse/
- 18 exp Opioid-Related Disorders/
- 19 Phencyclidine Abuse/
- 20 Substance Abuse, Intravenous/
- 21 exp Alcohol Drinking/
- 22 Marijuana Smoking/
- 23 Methadone/
- 24 exp Substance Abuse Treatment Centers/
- 25 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 or 24
- 26 exp Homeless Persons/
- 27 exp Housing/
- 28 Homeless*.ti,ab.
- 29 26 OR 27 OR 28
- 30 Prisons/
- 31 Prisoners/
- 32 (Prison* OR crime* OR criminal* OR detain* OR detention).ti,ab.
- 33 (correctional facility OR correction centre OR correctional health service* OR jail).ti,ab.
- 34 Juvenile delinquency/
- 35 (juvenile delinquency OR juvenile behavior).ti,ab.
- 36 30 OR 31 OR 32 OR 33 OR 34 OR 35
- 37 Vulnerable populations/
- 38 11 OR 25 OR 29 OR 36 OR 37
- 39 5 AND 38
- 40 limit 39 to humans
- 41 limit 40 to yr="2004 –Current"

Table 1. Summary of quantitative findings for smoking cessation

RCT SECONDARY ANALYSIS									
Study ID	Outcome	Total participants	Method of outcome assessment	Time of follow up	Intervention group 1 n/N (%)	Intervention group 2 n/N (%)	Control group n/N (%)	Significance test	Quality of evidence (EPHPP)
O'Brien 2015	Biochemically verified continuous Abstinence	86	Continuous smoking abstinence six months after quit day, verified by an exhaled breath carbon monoxide measurement of <10 ppm using a Bedfont Micro Smokerlyzer.	26 weeks	2/39 (5.1%)	0/12 (0.0%)	5/35 (14.3%)	0.245 (patch vs. 16 mg e-cig) - (16 mg vs. 0 mg e-cig) 0.115 (patch vs. combined e-cig)	Moderate
UNCONTROLLED BEFORE AND AFTER STUDIES									
Study ID	Outcome	Total participants (retained at last follow up)	Method of outcome assessment	Time of follow up	Intervention group 1 n/N (%)	Intervention group 2 n/N (%)	Control group n/N (%)	Significance test	Quality of evidence (EPHPP)
Stein 2016	Biochemically confirmed smoking cessation	12	Carbon monoxide-confirmed abstinence (expired breath scores <8 parts per million) in persons who self-reported abstinence in the 7 days immediately prior to assessment	Week 7 Week 9	1/12 (8.3%) 0/12 (0.0%)				Weak
Caponnetto 2013	Self-report and biochemically verified abstinence from tobacco	14 (12)	Complete self-reported abstinence from tobacco smoking (not even a puff) for the 30 day period prior to assessment plus eCO concentration ≤10 ppm	52 weeks	2/14 (14.3%)				Weak

smoking							
Pratt 2016	Smoking abstinence.	21	Self-reported smoking abstinence in the week prior to assessment	4 weeks	2/21 (9.5%)		Weak
			CO levels \leq 4 ppm	4 weeks	2/21 (9.5%)		
			Both of the above criteria met	4 weeks	1/21 (4.8%)		

OBSERVATIONAL STUDIES

Study ID	Outcome	Total participants (retained at last follow up)	Method of outcome assessment	Time of follow up	E-cigarette users (%)	Non-e-cigarette users (%)	Significance test	Quality of evidence (EPHPP)
Prochaska 2014	Tobacco abstinence	956	Unclear	18 months	21%	19%	$\chi^2=0.12, p=.726$	Weak

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Table 2. Summary of quantitative findings for smoking reduction

SMOKING REDUCTION – DATA FROM SECONDARY ANALYSIS OF AN RCT								
Study ID	Outcome	Total participants	Time of follow up	Intervention group 1 (SD)	Intervention group 2 (SD)	Control group (SD)	Significance test	Quality of evidence
O'Brien 2015	Mean reduction in cigarettes smoked per day (among those who did not quit) from baseline to follow up	86	26 weeks	9.9 (7)	4.7 (3.5)	5.7 (6.3)	0.035 (patch vs. 16 mg e-cig) 0.068 (16 mg vs. 0 mg e-cig) 0.083 (patch vs. combined e-cig)	Moderate
	Percentage reduction in cigarettes smoked per day (among those who did not quit)	86	26 weeks	49% (30%)	31% (30%)	29% (30%)	0.025 (patch vs. 16 mg e-cig) 0.153 (16 mg vs. 0 mg e-cig) 0.049 (patch vs. combined e-cig)	Moderate
SMOKING REDUCTION IN UNCONTROLLED BEFORE AND AFTER STUDIES								
Outcome	Study ID	Total participants	Mean (SD) at baseline	Time of follow up	Mean (SD) at follow up	Mean reduction	Significance test	Quality of evidence
Cigarettes per day	Stein 2016	12	17.8 (5.3)	Week 3	5.4*	-12.4 (95% CI -15.0 to -9.9)	P<0.001	Weak
				Week 5	3.0*	-14.8 (95% CI -17.4 to -12.2)		
				Week 7	3.9*	-13.9 (95% CI -16.6 to -11.2)		
				Week 9	7.0*	-10.8 (95% CI -13.4 to -8.2)	P<0.001	
	Caponnetto 2013	14	19†	52 weeks	13†	-6*	NR	Weak
	Pratt 2016‡	21	27	4 weeks	10	-17	NR	Weak

eCO	Caponnetto 2013	14	25†	52 weeks	15†	-10*	NR	Weak
	Pratt 2016	21	27.37ppm (16.9)	4 weeks	15.21ppm (9.2)	-12.16*	P=0.004	Weak
Cigarettes per week	Pratt 2016	21	191.9 (159.3)	4 weeks	66.7 (76.3)	-125.2*	P=0.005	Weak

OBSERVATIONAL PROSPECTIVE COHORT STUDY

Study ID	Outcome	Method of outcome assessment	Time of follow up	E-cigarette users mean reduction	Non-e-cigarette users mean reduction	Significance test	Quality of evidence
Prochaska 2014	Smoking reduction	Self-report reduction in cigarettes per day	18 months	-7.1 (SD 12.5)	-6.6 (SD 11.0)	F(1,703)=.12, p=.730	Weak
		Self-report cigarettes per day	18 months	10 (8.9)	10.1 (9.0)	F(1,710)=.01, p=50.915).	
		≥50% reduction	18 months	51%	51%	X2=.001, p=.978.	

*Calculated for the purposes of this review

† Data extracted from a graph

‡ Self-reported weekly tobacco use divided by 7 to provide comparable measure

Figure 1. Study flow diagram for systematic review of the effectiveness of e-cigarettes for vulnerable groups (56)

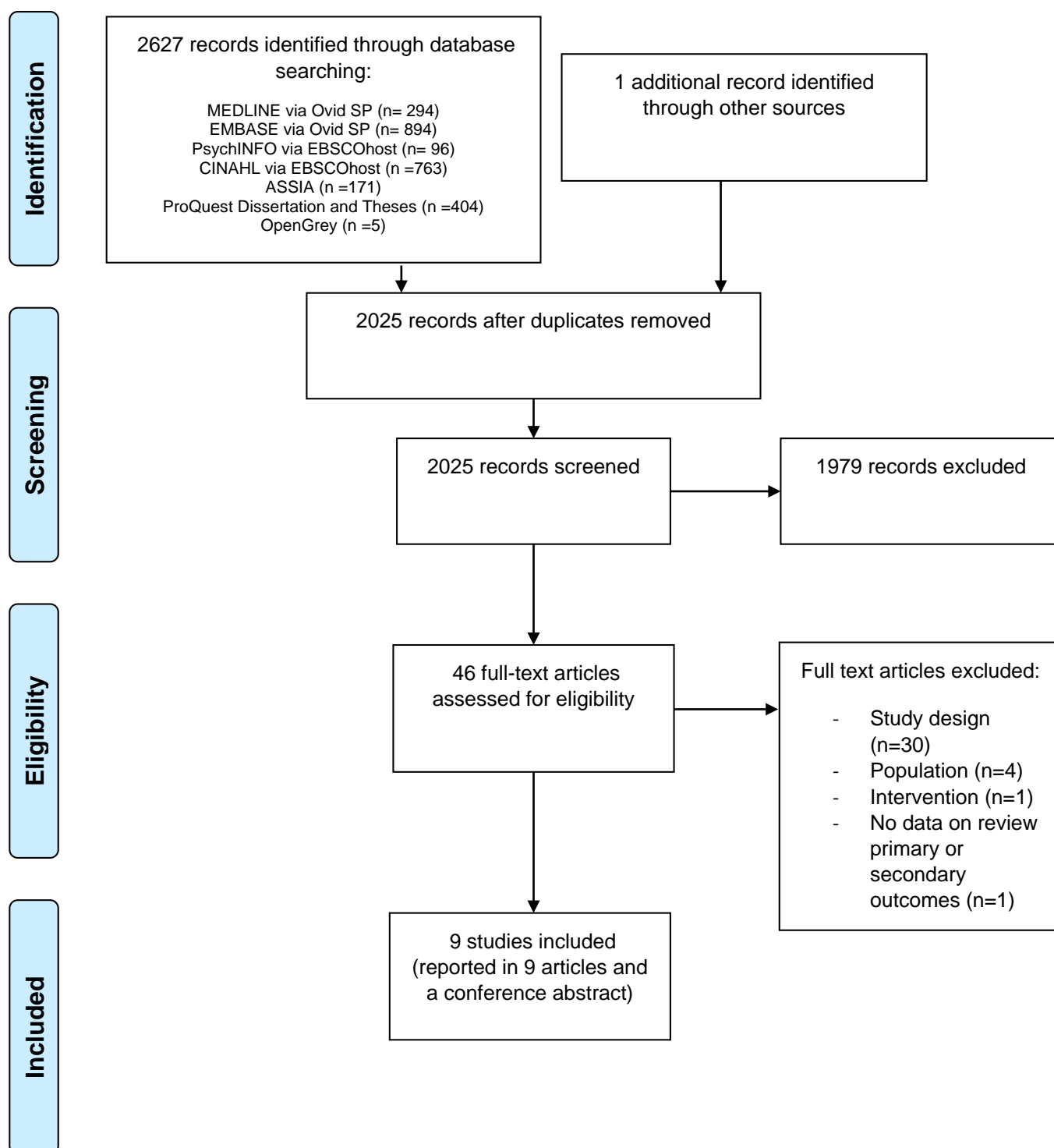


Figure 2. Analytical themes mapped to the COM-B model of behaviour change (note some themes are mapped to more than one component)

Physical capability	Psychological capability	Physical opportunity	Social opportunity	Automatic motivation	Reflective motivation
A) Design	D) Motivation for harm reduction	F) Combustible cigarette bans	H) Social connectedness and support	J) Design	L) Continued or worsening addiction/habit
B) Practical barriers	E) Motivation for smoking cessation	G) Cost	I) Reversing de-normalisation of tobacco use	K) Physical side effects	M) Design
C) Safety					N) Effect on psychiatric symptoms and medication side effects
					O) Empowerment
					P) Hobby/habit/distraction
					Q) Preferred to NRT/pharmacotherapy
					R) Social connectedness and support

■ Barriers
 ■ Facilitators
 ■ Act as both barriers and facilitators