National Institute for Health and Care Excellence

Draft for Consultation

Tobacco: preventing uptake, promoting quitting and treating dependence: update

[F] and [G] Evidence reviews for e-cigarettes and young people

NICE guideline <number>

Evidence reviews underpinning recommendations 1.6.3 to 1.6.4 and research recommendations in the NICE guideline

June 2021

Draft for Consultation

These evidence reviews were developed by PH-IGD

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ISBN:

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Future cigarette use among children, young people and young adults who do not smoke and use e-cigarettes

Review question

In children, young people and young adults who do not smoke[a], is e-cigarette use associated with future smoking status?

Introduction

There have been questions about the use of e-cigarettes in people who don't smoke, and about whether they increase likelihood of smoking in the future.

In England, experimentation with e-cigarettes among young people has increased in recent years. Data from the ASH Smoke-free Great Britain – Youth Survey in 2018, reported by PHE (Vaping in England: an evidence update February 2019) found that 11.7% of 11-18 year olds had tried e-cigarettes once or twice, 1.8% used them monthly and a further 1.7% used them weekly (this figure was age dependent: 0.4% of 11 year olds and 2.6% of 18 year olds used e-cigarettes weekly).

The majority of those who had never smoked had also never used an e-cigarette (93.9%). The remainder had either used e-cigarettes or chose not to disclose their use. In addition, of those who had tried an e-cigarette, 30% had never tried a conventional cigarette, demonstrating that e-cigarettes are not only used by young people who smoke. It is important to understand whether use of e-cigarettes ("vaping") by those who don't smoke is associated with future smoking. This review aims to determine the likelihood of taking up smoking in children, young people and young adults who use e-cigarettes.

PICO table

Table 1: PICO inclusion criteria

Population	Included: Children, young people and young adults who have not smoked in the past and do not at baseline smoke habitually or experimentally. Excluded: Children, young people and young adults who used to, or at baseline, smoke habitually or experimentally. People aged 25 or over.
Prognostic factor	Use of e-cigarettes.
Outcomes	Critical outcomes: Smoking status at longest available follow-up. Measured as: • Smoking habitually or experimentally (relative risk or hazard ratio) Where biochemically validated measures are available, these will be preferred to self-reported measures.

[a] Throughout, smoking refers to the use of all smoked tobacco products. 'Smoking' or 'smoking habitually' refers, unless specifically stated otherwise, to people who smoke weekly or more often. Smoking experimentally is defined as smoking less than weekly.

	Important outcomes Intention to smoke

Methods and process

This evidence review was developed using the methods and processes described in Developing NICE guidelines: the manual (2018). Further methods are detailed in the methods chapter for this guideline. Methods specific to this review are described in 'Synthesis and appraisal of public health studies', and in the review protocol in appendix A.

Declarations of interest were recorded according to NICE's 2018 conflicts of interest policy.

See Methods document for details of rationale for GRADE judgements.

Identification of public health evidence

Included studies

The reviews presented here are new reviews for this guideline. A joint search was used to identify relevant studies for the two reviews in this document, the review on barriers and facilitators to e-cigarette use for cessation and harm reduction, and the review on long-term health effects of e-cigarette use. A systematic search was undertaken in January 2019 for studies published since 1998 and in the English language. It was decided to search for studies in the past 20 years (from when protocols were written). This limit is applied because before this point it is judged that the context – specifically the acceptability and prevalence of smoking – is too different to be relevant and applicable to the guideline. Searches for literature on e-cigarettes will also be limited due to the novelty of the technology.

Website searches were conducted in line with the protocol. Further details on the search strategy are available in Appendix B.

After removal of duplicates 5280 unique database results were identified. 76 papers from this search and one paper published after the searches with potential to answer the review questions were ordered for full-text review. Of these, 22 papers (19 studies) met the inclusion criteria for this review. 18 of the 19 studies have a cohort design, and 1 is an interrupted time series study.

The website searches identified a further 67 results that were screened separately. No includes from website searches were identified.

Rerun searches were carried out in November 2019. 1,560 articles were identified. Twenty-three were requested for full-paper assessment. None met the inclusion criteria for this review.

Rerun searches were carried out in July 2020. 1,382 articles were identified. Four studies were requested for full-paper assessment, none of these met the inclusion criteria for this review.

Excluded studies

See Appendix K for a full list of excluded studies and the reasons for exclusion.

1 Synthesis and appraisal of public health studies included in the evidence review

2 Table 2: Summary of studies included in the evidence review

Study	Setting	Population	Factor(s)	Outcome(s)	Definition of smoking
Aleyan 2018 and Hammond 2017 Cohort (prospective)	Canada High school students (13-16)	Students at the schools 9,501 participants	Past 30 day use of e-cigarette	• Smoking initiation (2 years follow-up) • Daily smoking for 7 days (1 year follow-up)	Smoking 'even 1 or 2 puffs'
Barrington-Trimis 2016 Barrington-Trimis 2018 Cohort (prospective)	USA Grade 11-12 students (16-18)	Students at the schools 298 participants	Ever use of e-cigarettes	• Smoking initiation (16 months follow-up)	Smoking 'even 1 or 2 puffs'
Best 2018 Cohort (prospective)	Scotland, UK Year 1-6 students (11-18)	Students at the schools 2,125 participants	Ever use of e-cigarettes	• Trying a cigarette (1 year follow-up)	Smoking 'even 1 or 2 puffs'
Bold 2018 Barrington-Trimis 2018 Cohort (prospective)	USA High school students (mean age 15)	Students at the schools 795 participants	Past 30 day use of e-cigarettes	• Past 30-day smoking (6 months and 18 months)	Smoking 'even 1 or 2 puffs'
Conner 2018 Cohort (prospective)	England, UK School students (mean age 13)	Students at the schools 1,726 participants	Ever use of e-cigarettes	• Ever cigarette use (1 year follow-up)	Ever use
East 2018 Cohort (retrospective)	Great Britain (11-18)	Online survey of young people 923 participants	Ever use of e-cigarettes	• Ever cigarette use (4 months follow-up)	Smoking 'even a puff'.
Hallingberg 2019* Interrupted time series analysis	England, Scotland and Wales National surveys of young people (11-16)	Young people 248,324 participants	Exposure to e-cigarettes in an unregulated environment (from 2010 until 2015).	• Ever smoking (17-year time trend) • Regular smoking (once weekly or more) (17-year time trend)	Responding to a list of statements and not answering 'I have never smoked'.

Study	Setting	Population	Factor(s)	Outcome(s)	Definition of smoking
Leventhal 2015 Barrington-Trimis 2018 Cohort (prospective)	USA Public high schools students (14-15)	Students at the schools 2,530 participants	Lifetime e-cigarette use at baseline	• Past 6-month combustible tobacco use (6-12 month follow-up)	Smoking 'even a few puffs'.
Loukas 2018 Cohort (prospective)	USA College students (18-29)	Students at the colleges 2,558 participants	Ever use of e-cigarettes	• Ever cigarette use (6-18 month follow-up)	Answering lifetime cigarette use
Lozano 2017 Cohort (prospective)	Mexico Public middle school students (12-15)	Students at the schools 6,574 participants	Trial of e-cigarettes	• Trial of conventional cigarettes (20 month follow-up)	Smoking 'even 1 or 2 puffs'.
Miech 2017 Cohort (prospective)	USA Grade 12 students (17-18)	Students at the schools 347 participants	Past 30-day use of e-cigarettes	• Smoking initiation (13 month follow-up)	Smoking 'once or twice'.
Morgenstern 2018 Cohort (prospective) investigated as part of a cluster RCT	Germany School students (14-18)	Students at the schools 2,186 participants	Ever use of e-cigarettes	• Ever smoking cigarettes (6 month follow-up)	Answering smoking a few puffs or more.
Primack 2015 Cohort (prospective)	USA national sample (mean age 19.5)	Adolescents and young adults 694 participants	Ever use of e-cigarettes	• Smoking initiation (1-year follow-up) • Susceptibility to smoking (1-year follow-up)	Smoking 'at least 1 puff'
Primack 2018 Cohort (prospective)	USA national sample (18-30)	Young adults 915 participants	Ever use of e-cigarettes	• Smoking initiation (18 month follow-up)	Smoking 'at least 1 puff'
Spindle 2017 Cohort (prospective)	USA, University students (mean age 18.5)	Students at the university 3,757 participants	• Ever use of e-cigarettes • Past 30-day e-cigarette use	• Ever cigarette use (1-year follow-up) • Current cigarette use (past 30-day use) (1-year follow-up)	Smoking cigarettes on even 1 occasion.
Treur 2018	Netherlands	Students at the schools	• Ever use of e-cigarettes	• Ever cigarette use	Smoking more than twice

Study	Setting	Population	Factor(s)	Outcome(s)	Definition of smoking
Cohort (prospective)	Secondary school students (11-17)	2,100 participants	with nicotine • Ever use of e-cigarettes without nicotine	(6 month follow-up) •	
Unger 2016 Cohort (prospective)	USA High school students (mean age 22.7)	Hispanic young adults who were recruited as school students. 1,332 participants	Past 30-day e-cigarette use	• Past 30-day cigarette smoking (1-year follow-up)	Unclear
Watkins 2018 Cohort (prospective)	USA (12-17)	Young people 10,384 participants	Ever only use of e-cigarette	• Ever cigarette use (1-year follow-up) • Past 30-day cigarette use	Smoking 'even 1 or 2 puffs'
Wills 2016 Wills 2017 Cohort (prospective)	USA High school students (14-17)	Students at the schools 1,136 participants	Ever use of e-cigarette	• Smoking initiation (1-year follow-up)	Any smoking at follow up.

See appendix D for full evidence tables.

*This study was included in this review despite including people who smoke because the average prevalence across the time investigated showed people who had ever or regularly smoked to be a minority. For the same reason, it is not included in the evidence for the review on children, young people and young adults who do smoke.

Evidence appraisal

- This review addresses an association question. Cohort and time series evidence was therefore assessed using the QUIPS tool, according to the NICE Manual.
- All GRADE ratings start at 'high', and are downgraded as appropriate. See appendix F for full GRADE tables.
- Assessments for Risk of Bias in GRADE were drawn from the RoB tool assessment, and a particular emphasis on adjusting for confounders identified as important by the committee (levels of peer smoking, levels of family smoking).
- Event and participant numbers were not provided by some studies. Event and participant numbers presented in GRADE tables are the sum of those studies which presented these numbers. Footnotes indicate where some studies in the table did not provide numbers.
- See Appendix F for full GRADE tables.

Data synthesis

19 studies were identified for inclusion in this review. Where studies reported results at various follow-up points, all were data extracted. The outcome with longest follow-up from baseline was used in meta-analysis. Risk ratio was chosen to present the results.

Where studies reported association of baseline e-cigarette use with smoking at follow-up by baseline smoking susceptibility, results for all groups were extracted. Separate meta-analyses were conducted for those susceptible, those not susceptible and groups where susceptibility was not reported (the latter either explicitly combined all susceptibilities, or didn't report any information on susceptibility in which case it is likely that all susceptibilities were combined). This is a deviation from protocol, which did not specify that data would be presented according to baseline susceptibility. Although the committee did not consider that these groups needed to be treated differently, this method of presentation was retained to avoid needing to use raw data rather than effect estimates adjusted for confounders as reported in the studies. There was also a clear and consistent effect in all groups.

Where results were presented as effect estimates by percentile, results closest to the interquartile range were selected to be representative of the odds for presence vs absence of that characteristic. For example, where results are presented for various percentiles of the propensity-to-smoke distribution, those closest to the 25th percentile (for absence of propensity to smoke) and 75th percentile (for presence of propensity to smoke) were used in meta-analysis.

Meta-analysis

Meta-analysis was conducted on the following outcomes:

- Ever smoking: 18 studies measured smoking initiation between baseline and follow-up among baseline non-smokers. Most studies measured this as any smoking, even a puff. Several studies measured smoking in the past 30 days or the past 6 months at follow-up data collection. These were considered to come under the definition of 'experimental smoking' (smoking less than once a week, as per the protocol) and so were combined in meta-analysis (see Figures 1-16 and GRADE profiles 1-3).
- Habitual smoking: one study measured habitual smoking and defined this as smoking for seven consecutive days between baseline and follow-up. This is not the same as habitual smoking as defined by this guideline (weekly smoking) (see GRADE profile 4).
- Intention to smoke: one study measured susceptibility to smoking at follow-up, which was judged to be similar enough to *intention to smoke* to be presented in this review (see GRADE profile 5)
- Change in the rate of decline in smoking after introduction of e-cigarettes: one ITS study investigated whether the increased popularity of e-cigarettes around 2010 had changed the rate of decline in smoking among young people. Outcomes included change in the rate of decline in ever smoking and change in the rate of decline in regular smoking. Both outcomes were also explored in subgroups by sex and age (see Figures 17-20 and GRADE profile 6).

As per the pre-specified approach to heterogeneity, where meta-analyses had an I^2 of ≥50%, a random effects model was used.

An MID was not identified from literature for this review. The committee agreed that any taking up of smoking is important and set the MID at the line of no effect.

Subgroups

For the purposes of combining for meta-analysis, past-30 day e-cigarette use at baseline was combined with ever-use of e-cigarettes at baseline. Where studies reported results by both factors, both were extracted into evidence tables, but the 'ever use' factor was used in the meta-analysis. A subgroup analysis was conducted to investigate the effect of these differing categories on the outcome. Subgroup analyses were also conducted to determine whether there were significant differences according to age. This was only possible for the outcome of ever smoking. Where one or more of the subgroups had significant heterogeneity (≥50%), a random effects model was used.

There were no significant differences in ever smoking among those who had used e-cigarettes in the past 30 days at baseline compared with those who had ever used e-cigarettes at baseline (susceptibility not reported: P = 0.25; susceptible: P = 0.72; non-susceptible: P = 0.75). All groups had relative risks above 1. (Figures 4-6.)

There were no significant differences in ever smoking among young people compared with young adults (susceptibility not reported: P = 0.59; non-susceptible: P = 0.55). All groups had relative risks above 1. (Figures 7-8.)

Sensitivity analysis

Sensitivity analysis was conducted to determine whether there were significant differences according to risk of bias in the study, or presence vs absence of adjustments for peer and family smoking, identified by the committee as particularly important potential confounders. These judgements informed the GRADE domain for risk of bias. This was only possible for the outcome of ever smoking.

Among those where susceptibility was not reported, the risk of ever smoking was significantly higher in the studies with acceptable risk of bias (3.06 95% CI 2.39, 3.91) compared with those at high risk of bias (2.26 95% CI 1.64, 3.21) (P = 0.14). This indicates that bias is not inflating the outcome. (Figure 10.)

However, among those not susceptible to smoking, there were no significant differences in ever smoking in studies with acceptable compared with high risk of bias (P= 0.99), and among those susceptible to smoking, risk of ever smoking was significantly higher in studies with high risk of bias (1.72 95% CI 1.54, 1.93) compared with those at acceptable risk of bias (1.36 95% CI 1.27, 1.46) (P = 0.0005). In all risk of bias subgroups for all susceptibilities, effects were significant and meaningful in the same direction (increased risk in the exposed group). (Figures 11-12.)

There were no significant differences in ever smoking between studies that had made adjustments for family and peer smoking compared with those who had made other or no adjustments (susceptibility not reported: P = 0.66; susceptible: P = 0.89; non-susceptible: P = 0.75). All groups had relative risks above 1. (Figures 13-15.)

Funnel plot

As there were more than ten studies contributing to the outcome on ever smoking for groups where susceptibility was not reported, publication bias was assessed using a funnel plot as described in the methods chapter (see Figure 21). The standard errors were mostly similar for the included studies, and so were clustered. There is little suggestion of publication bias, and therefore the outcome was not downgraded for this domain.

Economic evidence

No economic evidence was considered for this review question, as per the protocol.

Resource impact

No additional resource expected for this review.

Summary of the evidence

This table is a very high-level overview of the results presented in the GRADE tables. These results should not be considered apart from the GRADE tables, which contain more information about confidence in the evidence and limitations (Appendix F).

Table 3: Evidence summary

Outcome	Summary	Confidence	GRADE profile
Ever smoking (among different baseline susceptibilities to smoking)	Exposure to e-cigarettes was significantly associated with an increase in ever smoking. This effect was found among groups where susceptibility was not reported, those who were susceptible at baseline, and those who were not susceptible at baseline. Effects were not significantly different by age or level of e-cigarette use at baseline.	Susceptibility not reported: Moderate Susceptible: Low Non-susceptible: Moderate	1
Ever smoking (by nicotine content of e-cigarettes at baseline)	Exposure to e-cigarettes was significantly associated with an increase in ever smoking among those who used nicotine e-cigarettes and those who used e-cigarettes without nicotine. Subgroups were significantly different: those using e-cigarettes with nicotine had higher risk of ever smoking than those without nicotine.	With nicotine: Low (1 study) Without nicotine: Low (1 study)	2
Ever smoking (among those with no peer smoking at baseline)	Exposure to e-cigarettes was significantly associated with an increase in ever smoking among those who had no peer smoking at baseline.	Moderate (1 study)	3
Habitual smoking	Exposure to e-cigarettes was significantly associated with an increase in habitual smoking.	Moderate (1 study)	4
Intention to smoke among those not susceptible to smoking	Exposure to e-cigarettes was significantly associated with an increase in intention to smoke.	Low (1 study)	5
Change in the rate of decline in ever smoking after increased popularity of e-cigarettes	An effect was not detected of an increased exposure of the population to e-cigarettes on rate of decline in ever smoking.	Low (1 study)	6
Change in the rate of decline in regular smoking after increased popularity of e-cigarettes	An effect was not detected of an increased exposure of the population to e-cigarettes on rate of decline in ever smoking.	Low (1 study)	6

Future cigarette use among children, young people and young adults who use e-cigarettes and cigarettes

Review question

In children, young people and young adults who smoke[b], is e-cigarette use associated with future smoking status?

Introduction

Regular (at least weekly) use of e-cigarettes among young people (11-16) is below 3% (Evidence review of e-cigarettes and heated tobacco products 2018 Public Health England). It is not known whether e-cigarette use among young people who smoke (dual use) is associated with future smoking status. There are also questions about whether increased rates of e-cigarette use ("vaping") are associated with reduced rates of cigarette smoking among those who aren't actively trying to quit smoking.

This review aims to determine the likelihood of stopping smoking in children, young people and young adults who smoke and also use e-cigarettes recreationally (not specifically for cessation).

PICO table

Table 4: PICO inclusion criteria

Population	Included: Children, young people and young adults[c] who smoke. Excluded: Children, young people and young adults who smoke and are actively trying to stop. People aged 25 or over. Children, young people and young adults who do not smoke habitually. People who smoke but have never used e-cigarettes. •
Prognostic factor	Recreational use of e-cigarettes (experimental or habitual).
Outcomes	Critical outcomes: • Smoking status at longest available follow-up. Measured as: • Smoking habitually or stopping smoking (relative risk or hazard ratio)

[b] Throughout, smoking refers to the use of all smoked tobacco products. 'Smoking' or 'smoking habitually' refers, unless specifically stated otherwise, to people who smoke weekly or more often. Smoking experimentally is defined as smoking less than weekly.

[c] For the purposes of this guidance, children are aged 5-11, young people are 12-17 and young adults are 18-24 inclusive.

- Where biochemically validated measures are available, these will be preferred to self-reported measures.
- Important outcomes
- Intention to smoke
- Attitudes towards smoking
- Health-related quality of life (using validated patient-report measures, for example EQ-5D).

Methods and process

Much of this review (for example, the methods) is similar to the review for children, young people and young adults who use e-cigarettes and don't smoke. Where this is the case, "see the above review" will be stated. Where something is relevant for both reviews in this document (e-cigarette use and future smoking among both baseline smokers and baseline non-smokers), "both reviews" will be stated.

See 'methods and process' under the above review.

Identification of public health evidence

Included studies

See 'Included studies' under the above review.

Two studies were included in this review. One cohort study from the original searches met the inclusion criteria for this review (Unger 2016). This study is also included in the above review. Rerun searches were carried out in November 2019. 1,560 articles were identified. Twenty-three were requested for full-paper assessment. Of these, one was included (Stanton 2019).

Excluded studies

See 'Excluded studies' under the above review .

Table 5: Summary of studies included in the evidence review

Study	Setting	Population	Factor(s)	Outcome(s)	Definition of smoking
Unger 2016 Cohort (prospective)	USA Ex-high school students (mean age 22.7)	Hispanic young adults who were recruited as school students and had smoked in the last 30 days at baseline. 1,332 participants	Past 30-day e-cigarette use	• Past 30-day cigarette smoking	• Unclear

Study	Setting	Population	Factor(s)	Outcome(s)	Definition of smoking
Stanton 2019 Cohort (prospective)	USA Grade 11-12 students (16-18)	Students at the schools 1,497 participants	Ever use of e-cigarettes	• Change in number of days smoked cigarettes (of past 30)	• Ever use is 'even 1 or 2 puffs'

See appendix D for full evidence tables.

Synthesis and appraisal of public health studies included in the evidence review

Evidence appraisal

- This review addresses a prognostic question. Evidence from cohort studies and time series studies was therefore assessed using the QUIPS risk of bias tool, according to the NICE manual.
- All GRADE ratings start at 'high' and are downgraded as appropriate.

Economic evidence

No economic evidence was considered for this review question, as per the protocol.

Resource impact

Please see this section under the above review.

Summary of the evidence

This table is a very high-level overview of the results presented in the GRADE tables. These results should not be considered apart from the GRADE tables, which contain more information about confidence in the evidence and limitations (Appendix F).

Table 6: Evidence summary

Outcome	Summary	Confidence	GRADE profile
Past-month continued cigarette smoking	An effect was not detected for exposure to e-cigarettes on past-month continued smoking.	Very Low (1 study)	7
Change in number of days smoked cigarettes (of past 30)	An effect was not detected of exposure to e-cigarettes on number of days people smoked cigarettes.	Very Low (1 study)	8

The committee's discussion of the evidence (both reviews)

Interpreting the evidence

The outcomes that matter most

Outcomes about smoking status mattered most to the committee. Of these, outcomes indicating sustained smoking status were better indicators of future health effects than outcomes about smoking which was not habitual or long term. Intention to smoke was an

important outcome, but as it measures intentions rather than actual behaviour it was a secondary outcome.

The committee did not consider outcomes according to baseline susceptibility to be particularly useful in making recommendations because they were interested in the population as a whole. Susceptibly was also defined differently across studies.

Confidence in the evidence

Children, young people and young adults who don't smoke

The committee agreed that the risk of bias of the included studies was mixed, ranging from 'acceptable' to 'high'. The main concerns about potential bias came from confounding. The studies adjusted for a range of confounders in logistic regression models, but the committee discussed that even in a study adjusting for many reasonable confounders, residual confounding may remain. This may be due to the mis-match between the factor itself (for example, the strength of an individual's self-efficacy) and the way the factor is expressed when it is adjusted for; in this review factors are measured through survey items. The studies did not all adjust for the main factors the committee considered to predict smoking: peer smoking and family smoking. These factors might be unevenly present in the exposed (to e-cigarettes) and unexposed groups. Of the 18 included cohort studies, eight studies adjusted for peer smoking and seven for family smoking.

The committee also noted that sensitivity analysis by risk of bias (high vs acceptable, Figure 10-12) and by confounders (adjusting for peer and family vs other adjustments, Figure 13-15) did not result in effect estimates which were markedly different from each other. This increases confidence that studies at high risk of bias are not substantially different from studies at acceptable risk of bias.

There was significant statistical heterogeneity among the study results, but the committee agreed that combining them in a meta-analysis was appropriate and important for summarising and discussing the data. They agreed that the effect was consistently in the direction of increased risk among exposed groups, with only a small minority of effect estimates having confidence intervals which included the line of no effect, which was also the minimal important difference.

Heterogeneity was explored by conducting subgroup analysis by age (young person vs young adult, Figures 7-9) and type of baseline e-cigarette use (past 30-day use vs ever use, Figures 4-6). Generally, heterogeneity was unchanged by this analysis, with the exception that removing studies reporting ever e-cigarette use reduced heterogeneity to 0 (among studies where baseline susceptibility was not reported, Figure 4). The committee did not consider that this explained wider heterogeneity as the effect was not present for groups who were or were not susceptible at baseline.

The committee did not downgrade for indirectness for studies conducted within the OECD but outside of the UK. They did discuss that rules around advertising of e-cigarettes or tobacco products may be very different in some contexts, for example the USA, compared with the UK and that this might affect the results. The three UK-based studies (Best 2018; Conner 2017; East 2018) showed an association between current e-cigarette use and future ever smoking h which was like that found in the larger group. This indicates that the effect is consistent across a variety of regulatory contexts. The committee did agree to downgrade the ITS study (GRADE profile 6), which reported outcomes at the population level and did not provide information about individual risks, for indirectness. This evidence was therefore of low confidence.

The meta-analysis results from cohort studies about the association between e-cigarette use and future smoking among those who didn't smoke at baseline agreed to be precise (Figures 1-16). All the effects were therefore meaningful according to the MID.

The committee discussed that the low confidence evidence about ever smoking by type of baseline e-cigarette use (Figure 16) they discussed these in the context of the biopsychosocial model of smoking, that there may be both a biological pathway (through nicotine) and a behavioural and psychological pathway (through habit-forming). The committee noted that only one study contributed to this result and the committee chose not to differentiate between types of e-cigarettes in recommendations.

One study showed that exposure to e-cigarettes was associated with increased habitual smoking, defined as smoking every day for seven consecutive days at any point during follow-up. The committee discussed that this is more likely to indicate a sustained habit, but they were unsure whether this level of smoking was sufficient to indicate a sustained addiction.

Children, young people and young adults who smoke

The committee agreed that the imprecision of the association between e-cigarette use and future smoking among those who did smoke at baseline (GRADE profile 7) meant that no conclusions could be drawn on the association at this point, particularly as only one study contributed to the outcome. Likewise, there was no significant difference in the number of past 30 days people had smoked between those using and not using e-cigarettes at baseline, leading the committee to conclude that there was no clear evidence about the impact of e-cigarette use on future smoking habits among those who smoke. The committee chose not to make recommendations based on this evidence.

Benefits and harms

The committee discussed the fact that any health impacts of using e-cigarettes compared with not using them, among non-smokers, was not the focus of this review, but will be considered in another review in this guideline update.

Only a very small proportion of children, young people and young adults who have never smoked use e-cigarettes, and therefore might be exposed to increased risk of trying smoking in the future. The size of that risk is unclear. The committee discussed that it is possible that people moving from e-cigarettes to smoking might have been at higher risk for smoking for other reasons (for example, peer or family smoking). In these cases, it is even possible that e-cigarette use delayed the onset of smoking use (although as there is no evidence for this).Because there was no health benefit to never-smokers using e-cigarettes and because the harm of smoking is so great, the committee agreed there was justification to strongly discourage use of e-cigarettes in these groups.

Evidence indicates that e-cigarettes are likely to be effective for cessation (see evidence review [K]). The committee agreed that children, young people and young adults should not be told that e-cigarettes are to be avoided by all people at all times. They agreed that the emphasis should be placed on discouraging use among never smokers specifically.

Cost effectiveness and resource use

The committee did not expect that the new recommendations would incur significant additional resource, but instead they recommend that information about e-cigarettes should appear in campaigns and in school curricula which are already occurring for the purpose of preventing the uptake of smoking. The committee emphasised the importance of continued education about the harms of tobacco, which should not be displaced by education about e-cigarettes. Care should be taken about how to integrate these two issues while not conflating them.

Other factors the committee took into account

This review aims to consider whether an association is present. The committee discussed the difficulties with this and the types of evidence available, noting that it is difficult to decide whether there is a causal link between e-cigarette use and future smoking status.

The cohort studies showed evidence of an association between e-cigarette use and ever smoking. The ITS study showed that although there was a slight slowing in the decline in regular smoking (of 3%) among 13- and 15-year olds during a period of 'unregulated growth of e-cigarettes' (after 2010 until 2015) compared with before (1998-2010), this change was not significant. In addition, there was no change in the decline in ever smoking. They acknowledged that the proportion of children, young people and young adults who have never smoked and who use e-cigarettes is small enough that changes within this group may not be evident when looking at population-level data. Because of this, they made a research recommendation that levels of e-cigarette and tobacco use in this population be monitored further.

The committee also took into account that none of the studies measured smoking status as an established habit. With the exception of one study reporting habitual smoking, all cohort studies considered 'ever smoking', 'past 30-day smoking' or 'past 6-month smoking'. The committee agreed that the reported outcomes could not be extrapolated to conclude that e-cigarettes are associated with established smoking without further research.

The committee agreed that there was no health benefit to children, young people or young adults who don't smoke using e-cigarettes, and they decided to recommend that this behaviour is discouraged.

Recommendations supported by this evidence review

This evidence review supports recommendations 1.6.3 & 1.6.4 and the research recommendation on e-cigarettes and established future smoking.

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Appendices

Appendix A – Review protocols

Review protocol 1: Future cigarette use among children, young people and young adults who use e-cigarettes

ID	Field (based on PRISMA-P	Content
I	Review question	In children, young people and young adults who do not smoke[4], is e-cigarette use associated with future smoking status?
II	Type of review question	Prognostic review
III	Objective of the review	Regular (at least weekly) use of e-cigarettes among young people (11-16) is below 3% (Evidence review of e-cigarettes and heated tobacco products 2018 Public Health England), and use among young people who have never smoked is even lower. However, it is important to understand whether use of e-cigarettes ("vaping") among this young people who have never smoked is associated with future smoking. This review aims to determine the likelihood of taking up smoking in children, young people and young adults who use e-cigarettes.

[4] Throughout, smoking refers to the use of all smoked tobacco products. 'Smoking' or 'smoking habitually' refers, unless specifically stated otherwise, to people who smoke weekly or more often. Smoking experimentally is defined as smoking less than weekly.

IV	Eligibility criteria – population/disease/condition/issue/domain	Included: Children, young people and young adults who have not in the past and do not at baseline smoke habitually or experimentally. Excluded: Children, young people and young adults who used to, or at baseline, smoke experimentally or habitually. People aged 25 or over. Setting All settings in OECD countries only
V	Eligibility criteria – predictive factors	Use of e-cigarettes.
VII	Outcomes and prioritisation	Quantitative outcomes Critical outcomes: • Smoking status at longest available follow-up. Measured as: o Smoking habitually or experimentally (relative risk or hazard ratio)

		Where biochemically validated measures are available, these will be preferred to self-reported measures. Important outcomes • Intention to smoke
VIII	Eligibility criteria – study design	Included study designs: • Systematic reviews of included study designs • Prospective cohort studies • Retrospective cohort studies • Interrupted time series Excluded study designs • RCTs (including cluster RCTs) • Case control studies • Qualitative studies • Cross-sectional surveys • Cost-utility (cost per QALY)

		• Cost benefit (i.e. net benefit) • Cost-effectiveness (Cost per unit of effect) • Cost minimization • Cost-consequence
IX	Other inclusion exclusion criteria	Studies This is a new review question for this update. Systematic reviews Relevant systematic reviews (SRs) identified from database searches will be citation searched. Highly relevant systematic reviews may be included as a primary source of data. These SRs will be assessed against the inclusion criteria for this protocol, and their quality will be assessed using the ROBIS tool. Where the SR is highly relevant and of high quality, details or data from the systematic review may be used. In addition to any SRs meeting the above criteria, other primary studies will be included if they were published after the publication date of the SR and meet the protocol inclusion criteria. Exclusions • Only studies published in 1998 onwards will be included. • Only papers published in the English language will be included. • Only full published studies (not protocols or summaries even where they include some data) will be included.

X	Proposed sensitivity/sub-group analysis, or meta-regression	The following factors will be of interest in any meta-regression or subgroup analyses:
		• Type of e-cigarette use at baseline
		  ○ Habitual versus experimental e-cigarette use and association with future smoking status
		  ○ Nicotine versus non-nicotine containing e-cigarette use and association with future smoking status
		  ○ First vs second vs third generation e-cig use at baseline
		• Age at baseline
		  ○ Children vs young people vs young adults
		• Socioeconomic deprivation
		  ○ Reported as low socioeconomic status vs other
		• Levels of family / peer smoking
		  ○ Family / peer smoking present vs absent

XI	Selection process – duplicate screening/selection/analysis	The review will use the priority screening function within the EPPI-reviewer systematic reviewing software. Double screening will be carried out for 10% of titles and abstracts by a second reviewer. Disagreements will be resolved by discussion. Inter-rater reliability will be assessed and reported. If below 90%, a second round of 10% double screening will be considered. The study inclusion and exclusion lists will be checked with members of the PHAC to ensure no studies are excluded inappropriately.
XII	Data management (software)	EPPI Reviewer will be used: • to store lists of citations • to sift studies based on title and abstract

		• to record decisions about full text papers • to order freely available papers via retrieval function • to request papers via NICE guideline Information Services • to store extracted data Cochrane Review Manager 5 will be used to perform meta-analyses. Any meta-regression analyses will be undertaken using the R software package.
XIII	Information sources – databases and dates	The same search will be used to identify evidence for RQ4.1, RQ6.2, RQ6.3 and RQ 6.4 as the search terms overlap. The results will be updated as appropriate before each review commences. The following methods will be used to identify the evidence: • the databases listed below will be searched with an appropriate strategy. • the websites listed below will be searched or browsed with an appropriate strategy. • selected studies that are potentially relevant to the current review will be identified from the bibliography of any systematic reviews identified during the search process that are not being included in their own right. • forward citation searching will be done using selected studies prioritised from any scoping searches or relevant systematic reviews identified in the search process. Database strategies The principal search strategy is listed in Appendix A. The search strategy will take this broad approach:

		(E-cigarettes OR Vaping) AND Limits Feedback on the principal database strategy will be sought from PHAC members. The principal search strategy will be developed in MEDLINE (Ovid interface) and then adapted, as appropriate, for use in the other sources listed, taking into account their size, search functionality and subject coverage. The databases will be: • Applied Social Science Index and Abstracts (ASSIA) via ProQuest • Cochrane Central Register of Controlled Trials (CENTRAL) via Wiley • Cochrane Database of Systematic Reviews (CDSR) via Wiley • Embase via Ovid • Health Management Information Consortium (HMIC) via Ovid • MEDLINE via Ovid • MEDLINE-in-Process (including Epub Ahead-of-Print) via Ovid • PsycINFO via Ovid • Social Policy and Practice (SPP) via Ovid Database search limits Database functionality will be used, where available, to exclude: • non-English language papers • animal studies • editorials, letters and commentaries

		• conference abstracts and posters • registry entries for ongoing or unpublished clinical trials • duplicates. Sources will not be limited by date. The database search strategies will not use any search filters for specific study types. Citation searching Forwards citation searching will be conducted using Web of Science (WOS) Core Collection. Only those references which NICE can access through its WOS subscription will be added to the search results. Only papers published in the English language will be included in the search results. Duplicates will be removed in WOS before downloading. Websites The following websites will be searched with an appropriate strategy: • Health Services/Technology Assessment Texts (HSTAT) https://www.ncbi.nlm.nih.gov/books/NBK16710 • NICE Evidence Search https://www.evidence.nhs.uk • Tobacco Control Database for the WHO European Region http://data.euro.who.int/tobacco The websites of relevant organisations, including the ones below, will be browsed: • Action on Smoking and Health (ASH) http://ash.org.uk/home

		• Local Government Association https://www.local.gov.uk • National Centre for Smoking Cessation and Training http://www.ncsct.co.uk • NHS Digital https://digital.nhs.uk • Northern Ireland Assembly http://www.niassembly.gov.uk/ • Public Health England https://www.gov.uk/government/organisations/public-health-england • Royal College of Paediatrics and Child Health https://www.rcpch.ac.uk/ • Royal College of Physicians https://www.rcplondon.ac.uk • Scottish Government https://www.gov.scot • Smokefree NHS https://www.nhs.uk/smokefree • Smoking Toolkit Study http://www.smokinginengland.info • Treat Tobacco http://www.treatobacco.net/en/index.php • UK Centre for Tobacco and Alcohol Studies http://ukctas.net/index.html • University of Bath Tobacco Control Research Group https://researchportal.bath.ac.uk/en/organisations/uk-centre-for-tobacco-control-studies • University of Stirling Centre for Tobacco Control Research https://www.stir.ac.uk/about/faculties-and-services/health-sciences-sport/research/research-groups/centre-for-tobacco-control-research/publications • Welsh Government https://gov.wales/?lang=en The website results will be reviewed on screen and documents in English and that are potentially relevant to review question 4.1 or 6.3 will be listed with their title and abstract (if available) in a Word document. The initial screening decision will be made using this Word file. Any items selected for review at full text will be added to EPPI-Reviewer.

		Quality assurance The guidance Information Services team at NICE will quality assure the principal search strategy and peer review the strategies for the other databases. Any revisions or additional steps will be agreed by the review team before being implemented. Any deviations and a rationale for them will be recorded alongside the search strategies. Search results The database search results will be downloaded to EndNote before duplicates are removed using automated and manual processes. The de-duplicated file will be exported in RIS format for loading into EPPI-Reviewer for data screening.
XIV	Identify if an update	This question is a new question for the Tobacco update.
XV	Author contacts	Please see the guideline development page.
XVI	Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual
XVII	Search strategy – for one database	See appendix B.
XVIII	Data collection process – forms/duplicate	A standardised evidence table format will be used, and published as appendix D (effectiveness evidence tables) or H (economic evidence tables).

XIX	Data items – define all variables to be collected	For details please see evidence tables in appendix D (effectiveness evidence tables) or H (economic evidence tables).
XX	Methods for assessing bias at outcome/study level	The QUIPS checklist will be used to critically appraise individual studies. For details please see Developing NICE guidelines: the manual The risk of bias across all available evidence will be evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/
XXI	Criteria for quantitative synthesis (where suitable)	For details please see section 6.4 of Developing NICE guidelines: the manual Non-randomised studies are at risk of confounding. These studies should adjust for confounders which are decided by the committee to have important potential to affect the result, or the allocation into intervention or control groups. These factors are: - Peer or family smoking - Baseline smoking status (where sample includes people who smoke) - Socioeconomic status Where adjusted results are provided, these will be used in analysis. Where no adjustment has taken place, this will be considered when assessing risk of bias.

XXII	Methods for analysis – combining studies and exploring (in)consistency	Heterogeneity Data from different studies will be pooled in a meta-analysis where they are investigating the same outcome and where the resulting meta-analysis may be useful for decision-making. It is anticipated that studies included in the review will be heterogeneous with respect to participants, interventions, comparators, setting and study design. Where significant between study heterogeneity in methodology, population, intervention or comparator is identified by the reviewer in advance of data analysis, random effects models will be used. If methodological heterogeneity is not identified in advance but the I2 value is ≥50%, random effects models will also be used. If the I^2 value is above 50%, heterogeneity will be judged to be serious and so will be downgraded by one level in GRADE. If the I^2 value is above 75%, heterogeneity will be judged to be very serious and will be downgraded by two levels in GRADE. If the studies are found to be too heterogeneous to be pooled statistically, a narrative synthesis will be conducted. Imprecision No minimally important difference (MID) thresholds relevant to this guideline were identified from the COMET database or other published source. MIDs were agreed by committee. Uncertainty is introduced where confidence intervals cross the MID threshold. If the confidence interval crosses one lower MID threshold, this indicates 'serious' risk of imprecision. Crossing both MID thresholds indicates 'very serious' risk of

		imprecision in the effect estimate. Where the MID is 'any significant change' there is effectively only one threshold (the line of no effect), and so only one opportunity for downgrading. In this instance, outcomes will be downgraded again if they are based on small samples (<300 people). MIDs for outcomes will be included in the methods section of the individual reviews.
XXIII	Meta-bias assessment – publication bias, selective reporting bias	For details please see Appendix H of Developing NICE guidelines: the manual.
XXIV	Assessment of confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual.
XXV	Rationale/context – Current management	For details please see the introduction to the evidence review.
XXVI	Describe contributions of authors and guarantor	A multidisciplinary committee will develop the guideline. The committee will be convened by Public Health Internal Guidelines Development (PH-IGD) team and chaired by Sharon Hopkins in line with section 3 of Developing NICE guidelines: the manual. Staff from Public Health Internal Guidelines Development team will undertake systematic literature searches, appraise the evidence, conduct meta-analysis where appropriate and draft the guideline in collaboration with the committee. Cost-effectiveness analysis will be conducted by YHEC where appropriate. For details please see Developing NICE guidelines: the manual.

XXVII	Sources of funding/support	PH-IGD is funded and hosted by NICE
XXVIII	Name of sponsor	PH-IGD is funded and hosted by NICE
XXIX	Roles of sponsor	NICE funds PH-IGD to develop guidelines for those working in the NHS, public health and social care in England.
XXX	PROSPERO registration number	NA

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1 Review protocol 2: Future cigarette use among children, young people and young adults who use e-cigarettes and cigarettes

ID	Field (based on PRISMA-P)	Content
I	Review question	In children, young people and young adults who smoke[5], is e-cigarette use associated with future smoking status?
II	Type of review question	Prognostic review
III	Objective of the review	Regular (at least weekly) use of e-cigarettes among young people (11-16) is below 3% (Evidence review of e-cigarettes and heated tobacco products 2018 Public Health England). It is not known whether e-cigarette use among young people who smoke (dual use) is associated with future smoking status. There are also questions about whether increased rates of e-cigarette use ("vaping") is associated with reduced rates of cigarette smoking among those who aren't actively trying to quit smoking. This review aims to determine the likelihood of stopping smoking in children, young people and young adults who smoke and also use e-cigarettes.
IV	Eligibility criteria – population/disease/condition/issue/domain	Included: Children, young people and young adults[6] who smoke. Excluded:

[5] Throughout, smoking refers to the use of all smoked tobacco products. 'Smoking' or 'smoking habitually' refers, unless specifically stated otherwise, to people who smoke weekly or more often. Smoking experimentally is defined as smoking less than weekly.

[6] For the purposes of this guidance, children are aged 5-11, young people are 12-17 and young adults are 18-24 inclusive.

		Children, young people and young adults who smoke and are actively trying to stop. People aged 25 or over. Children, young people and young adults who do not smoke habitually. People who smoke but have never used e-cigarettes. Setting As in RQ4.1.
V	Predictive factors	Recreational use of e-cigarettes (experimental or habitual). Excluded: Use of e-cigarettes specifically for cessation.
VII	Outcomes and prioritisation	Quantitative outcomes Critical outcomes: Smoking status at longest available follow-up. Measured as: • Smoking habitually or stopping smoking (relative risk or hazard ratio)

		Where biochemically validated measures are available, these will be preferred to self-reported measures. Important outcomes • Intention to smoke • Attitudes towards smoking • Health-related quality of life (using validated patient-report measures, for example EQ-5D).
VIII	Eligibility criteria – study design	Included study designs: • Systematic reviews of included study designs • Prospective cohort studies • Retrospective cohort studies • Interrupted time series Excluded study designs • RCTs (including cluster RCTs) • Cross-sectional surveys

		• Case control studies • Epidemiological studies • Qualitative studies • Cost-utility (cost per QALY) • Cost benefit (i.e. net benefit) • Cost-effectiveness (Cost per unit of effect) • Cost minimization • Cost-consequence
IX	Other inclusion exclusion criteria	Studies This is a new review question for this update. Systematic reviews Relevant systematic reviews (SRs) identified from database searches will be citation searched. Highly relevant systematic reviews may be included as a primary source of data. These SRs will be assessed against the inclusion criteria for this protocol, and their quality will be assessed using the ROBIS tool. Where the SR is highly relevant and of high quality, details or data from the systematic review may be used. In addition to any SRs meeting the above criteria, other primary studies will be included if they were published after the publication date of the SR and meet the protocol inclusion criteria.

		Full economic analyses and costing studies identified from searches will be included. Costing data will not be used for the purpose of the effectiveness review. Health economics reviews and modelling will be conducted by the York Health Economics Consortium (YHEC). Exclusions • Only studies published in 1998 onwards will be included. • Only papers published in the English language will be included. • Only full published studies (not protocols or summaries even where they include some data) will be included.

X	Proposed sensitivity/sub-group analysis, or meta-regression	The following factors will be of interest in any meta-regression or subgroup analyses:
		• Type of e-cigarette use at baseline
		  ○ Habitual versus experimental e-cigarette use and association with future smoking status
		  ○ Nicotine versus non-nicotine containing e-cigarette use and association with future smoking status
		  ○ First vs second vs third generation e-cig use at baseline
		• Age at baseline
		  ○ Children vs young people vs young adults
		• Socioeconomic deprivation
		  ○ Reported as low socioeconomic status vs other
		• Levels of family / peer smoking
		
		Family / peer smoking present vs absent

XI	Selection process – duplicate screening/selection/analysis	The review will use the priority screening function within the EPPI-reviewer systematic reviewing software. Double screening will be carried out for 10% of titles and abstracts by a second reviewer. Disagreements will be resolved by discussion. Inter-rater reliability will be assessed and reported. If below 90%, a second round of 10% double screening will be considered. The study inclusion and exclusion lists will be checked with members of the PHAC to ensure no studies are excluded inappropriately.
XII	Data management (software)	EPPI Reviewer will be used: • to store lists of citations • to sift studies based on title and abstract • to record decisions about full text papers • to order freely available papers via retrieval function • to request papers via NICE guideline Information Services • to store extracted data Cochrane Review Manager 5 will be used to perform meta-analyses. Any meta-regression analyses will be undertaken using the R software package.
XIII	Information sources – databases and dates	The same search will be used to identify evidence for RQ4.1, RQ6.2, RQ6.3 and RQ 6.4 as the search terms overlap. The results will be updated as appropriate before each review commences. The following methods will be used to identify the evidence: • the databases listed below will be searched with an appropriate strategy.

		• the websites listed below will be searched or browsed with an appropriate strategy. • selected studies that are potentially relevant to the current review will be identified from the bibliography of any systematic reviews identified during the search process that are not being included in their own right. • forward citation searching will be done using selected studies prioritised from any scoping searches or relevant systematic reviews identified in the search process. Database strategies The principal search strategy is listed in Appendix A. The search strategy will take this broad approach: (E-cigarettes OR Vaping) AND Limits Feedback on the principal database strategy will be sought from PHAC members. The principal search strategy will be developed in MEDLINE (Ovid interface) and then adapted, as appropriate, for use in the other sources listed, taking into account their size, search functionality and subject coverage. The databases will be: • Applied Social Science Index and Abstracts (ASSIA) via ProQuest • Cochrane Central Register of Controlled Trials (CENTRAL) via Wiley • Cochrane Database of Systematic Reviews (CDSR) via Wiley • Embase via Ovid • Health Management Information Consortium (HMIC) via Ovid

		• MEDLINE via Ovid • MEDLINE-in-Process (including Epub Ahead-of-Print) via Ovid • PsycINFO via Ovid • Social Policy and Practice (SPP) via Ovid Database search limits Database functionality will be used, where available, to exclude: • non-English language papers • animal studies • editorials, letters and commentaries • conference abstracts and posters • registry entries for ongoing or unpublished clinical trials • duplicates. Sources will not be limited by date. The database search strategies will not use any search filters for specific study types. Citation searching Forwards citation searching will be conducted using Web of Science (WOS) Core Collection. Only those references which NICE can access through its WOS subscription will be added to the search results. Only papers published in the English language will be included in the search results. Duplicates will be removed in WOS before downloading.

		Websites The following websites will be searched with an appropriate strategy: • Health Services/Technology Assessment Texts (HSTAT) https://www.ncbi.nlm.nih.gov/books/NBK16710 • NICE Evidence Search https://www.evidence.nhs.uk • Tobacco Control Database for the WHO European Region http://data.euro.who.int/tobacco The websites of relevant organisations, including the ones below, will be browsed: • Action on Smoking and Health (ASH) http://ash.org.uk/home • Local Government Association https://www.local.gov.uk • National Centre for Smoking Cessation and Training http://www.ncsct.co.uk • Northern Ireland Assembly http://www.niassembly.gov.uk/ • NHS Digital https://digital.nhs.uk • Public Health England https://www.gov.uk/government/organisations/public-health-england • Royal College of Paediatrics and Child Health https://www.rcpch.ac.uk/ • Royal College of Physicians https://www.rcplondon.ac.uk • Scottish Government https://www.gov.scot • Smokefree NHS https://www.nhs.uk/smokefree • Smoking Toolkit Study http://www.smokinginengland.info • Treat Tobacco http://www.treatobacco.net/en/index.php • UK Centre for Tobacco and Alcohol Studies http://ukctas.net/index.html

		• University of Bath Tobacco Control Research Group https://researchportal.bath.ac.uk/en/organisations/uk-centre-for-tobacco-control-studies • University of Stirling Centre for Tobacco Control Research https://www.stir.ac.uk/about/faculties-and-services/health-sciences-sport/research/research-groups/centre-for-tobacco-control-research/publications • Welsh Government https://gov.wales/?lang=en The website results will be reviewed on screen and documents in English and that are potentially relevant to review question 4.1 or 6.3 will be listed with their title and abstract (if available) in a Word document. The initial screening decision will be made using this Word file. Any items selected for review at full text will be added to EPPI-Reviewer. Quality assurance The guidance Information Services team at NICE will quality assure the principal search strategy and peer review the strategies for the other databases. Any revisions or additional steps will be agreed by the review team before being implemented. Any deviations and a rationale for them will be recorded alongside the search strategies. Search results

		The database search results will be downloaded to EndNote before duplicates are removed using automated and manual processes. The de-duplicated file will be exported in RIS format for loading into EPPI-Reviewer for data screening.
XIV	Identify if an update	This question is a new question for the Tobacco update.
XV	Author contacts	Please see the guideline development page.
XVI	Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual
XVII	Search strategy – for one database	See appendix B.
XVIII	Data collection process – forms/duplicate	A standardised evidence table format will be used, and published as appendix D (effectiveness evidence tables) or H (economic evidence tables).
XIX	Data items – define all variables to be collected	For details please see evidence tables in appendix D (effectiveness evidence tables) or H (economic evidence tables).
XX	Methods for assessing bias at outcome/study level	The QUIPS checklist will be used to critically appraise individual studies. For details please see Developing NICE guidelines: the manual The risk of bias across all available evidence will be evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/

XXI	Criteria for quantitative synthesis (where suitable)	For details please see section 6.4 of Developing NICE guidelines: the manual Non-randomised studies are at risk of confounding. These studies should adjust for confounders which are decided by the committee to have important potential to affect the result, or the allocation into intervention or control groups. These factors are: - Peer or family smoking - Baseline smoking status (where sample includes people who smoke) - Socioeconomic status Where adjusted results are provided, these will be used in analysis. Where no adjustment has taken place, this will be considered when assessing risk of bias.
XXII	Methods for analysis – combining studies and exploring (in)consistency	Heterogeneity Data from different studies will be pooled in a meta-analysis where they are investigating the same outcome and where the resulting meta-analysis may be useful for decision-making. It is anticipated that studies included in the review will be heterogeneous with respect to participants, interventions, comparators, setting and study design. Where significant between study heterogeneity in methodology, population, intervention or comparator is identified by the reviewer in advance of data analysis, random effects models will be used. If methodological heterogeneity is not identified in advance but the I2 value is ≥50%, random effects models will also be used.

		If the I^2 value is above 50%, heterogeneity will be judged to be serious and so will be downgraded by one level in GRADE. If the I^2 value is above 75%, heterogeneity will be judged to be very serious and will be downgraded by two levels in GRADE. If the studies are found to be too heterogeneous to be pooled statistically, a narrative synthesis will be conducted. Imprecision No minimally important difference (MID) thresholds relevant to this guideline were identified from the COMET database or other published source. MIDs were agreed by committee. Uncertainty is introduced where confidence intervals cross the MID threshold. If the confidence interval crosses one lower MID threshold, this indicates 'serious' risk of imprecision. Crossing both MID thresholds indicates 'very serious' risk of imprecision in the effect estimate. Where the MID is 'any significant change' there is effectively only one threshold (the line of no effect), and so only one opportunity for downgrading. In this instance, outcomes will be downgraded again if they are based on small samples (<300 people). MIDs for outcomes will be included in the methods section of the individual reviews.
XXIII	Meta-bias assessment – publication bias, selective reporting bias	For details please see Appendix H of Developing NICE guidelines: the manual.

XXIV	Assessment of confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual.
XXV	Rationale/context – Current management	For details please see the introduction to the evidence review.
XXVI	Describe contributions of authors and guarantor	A multidisciplinary committee will develop the guideline. The committee will be convened by Public Health Internal Guidelines Development (PH-IGD) team and chaired by Sharon Hopkins in line with section 3 of Developing NICE guidelines: the manual. Staff from Public Health Internal Guidelines Development team will undertake systematic literature searches, appraise the evidence, conduct meta-analysis where appropriate and draft the guideline in collaboration with the committee. Cost-effectiveness analysis will be conducted by YHEC where appropriate. For details please see Developing NICE guidelines: the manual.
XXVII	Sources of funding/support	PH-IGD is funded and hosted by NICE
XXVIII	Name of sponsor	PH-IGD is funded and hosted by NICE
XXIX	Roles of sponsor	NICE funds PH-IGD to develop guidelines for those working in the NHS, public health and social care in England.
XXX	PROSPERO registration number	NA

1

Appendix B – Literature search strategies

Search approach

A joint search was done for both reviews because there was overlap in the search terms. The strategy comprehensively covered e-cigarettes and vaping, without including any search terms for the population or outcomes.

The MEDLINE strategy below was run after QA, peer review and consultation with the committee. The strategy was adapted as appropriate to the other databases listed in the protocol (see the sources tables below). The searches were done on 7 January 2019.

Additional search results were identified from the scoping searches for this topic. These were used for forwards citation searching and reference harvesting using Web of Science.

Further searches were undertaken for grey literature using the websites listed in the protocol. These results were screened separately in Word.

Full details of all the search strategies are available in a separate document from the NICE guidance Information Services team.

Sources searched to identify the evidence

Database name	Date searched	Database Platform	Database segment or version	No. of records
Applied Social Science Index and Abstracts (ASSIA)	07/01/2019	ProQuest	1987 - current	673
Cochrane Central Register of Controlled Trials (CENTRAL)	07/01/2019	Wiley	Cochrane Central Register of Controlled Trials Issue 1 of 12, January 2019	413
Cochrane Database of Systematic Reviews (CDSR)	07/01/2019	Wiley	Cochrane Database of Systematic Reviews Issue 1 of 12, January 2019	16
Embase	07/01/2019	Ovid	Embase 1974 to 2019 January 04	2493
Educational Resources Information Center (ERIC)	07/01/2019	ProQuest	1966 - current	69
Health Management Information Consortium (HMIC)	07/01/2019	Ovid	HMIC Health Management Information Consortium 1979 to September 2018	117
MEDLINE	07/01/2019	Ovid	Ovid MEDLINE(R) 1946 to January 04, 2019	2530
MEDLINE-in-Process (including	07/01/2019	Ovid	Ovid MEDLINE(R) Epub Ahead of Print January 04, 2019, Ovid MEDLINE(R) In-	1278

Epub Ahead-of-Print)			Process & Other Non-Indexed Citations January 04, 2019	
PsycINFO	07/01/2019	Ovid	PsycINFO 1806 to December Week 5 2018	1387
Social Policy and Practice (SPP)	07/01/2019	Ovid	Social Policy and Practice 201810	5
Scoping searches	07/01/2019	-	-	7
Web of Science	07/01/2019	Clarivate	Web of Science Core Collection (1990-present)	546

Database strategy – main search as run in MEDLINE and adapted for other sources

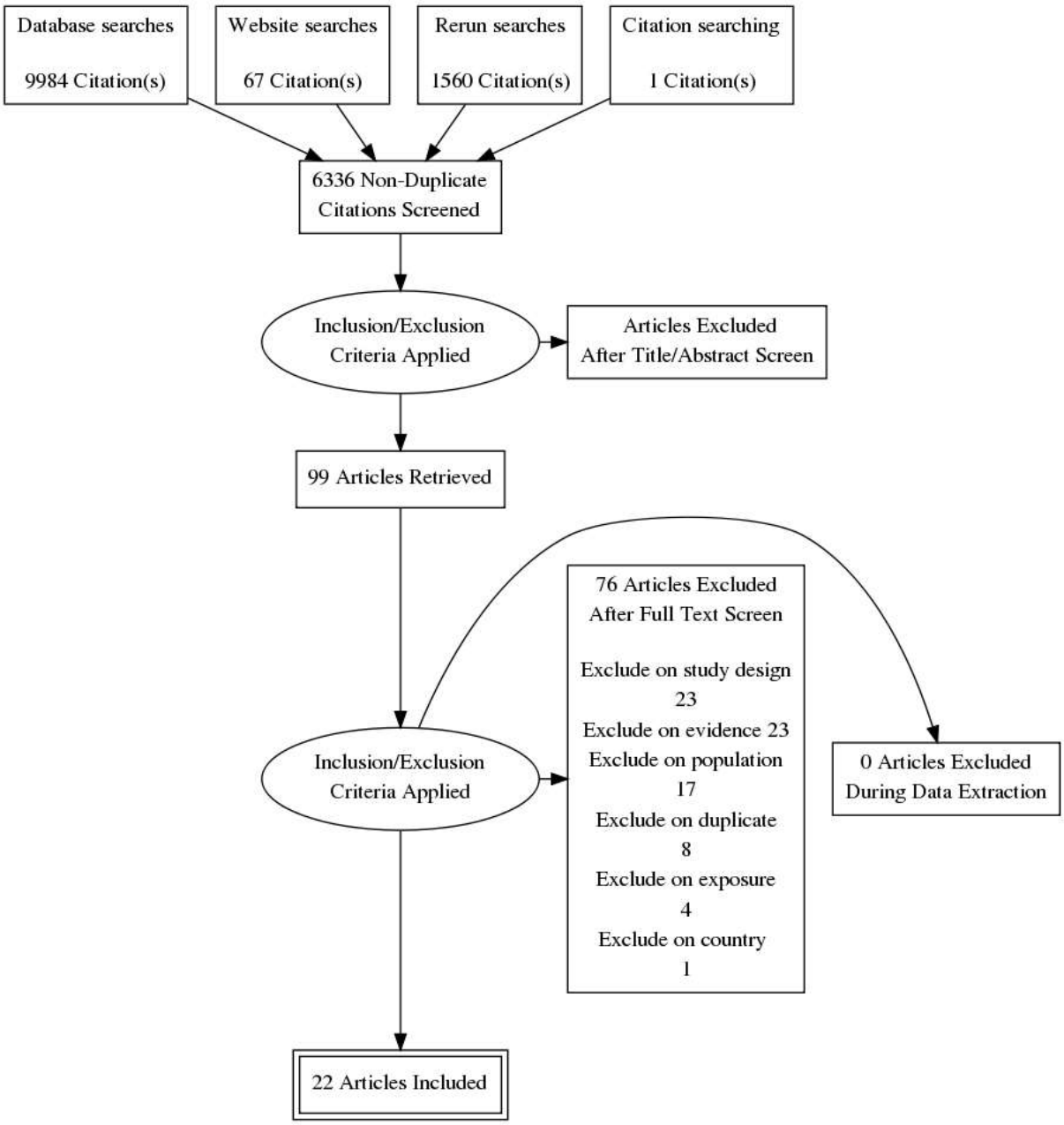
Database(s): Ovid MEDLINE(R) 1946 to January 04, 2019

#	Searches	Results
1	Electronic Nicotine Delivery Systems/	2118
2	Vaping/	221
3	(ecig* or e-cig* or e-voke* or juul* or vape* or vaping* or ENNDS).ti,ab.	2000
4	(electronic* adj3 (tobacco* or nicotin* or cigar* or cigs or vapor* or vapour*)).ti,ab.	1596
5	((tobacco* or nicotin* or cigar* or cigs) adj3 (vapor* or vapour* or device* or inhalator* or inhaler*)).ti,ab.	613
6	((tobacco* or nicotin* or cigar* or cigs) adj3 (dual* or multiple* or multi) adj3 ("use" or uses or user* or usage* or using*)).ti,ab.	287
7	(nicotin* and (ENDS or ANDS)).ti,ab.	221
8	(nicotin* adj3 deliver* system*).ti,ab.	251
9	(polytobacco* or poly tobacco* or poly-tobacco* or multitobacco* or multi tobacco* or multi-tobacco*).ti,ab.	68
10	or/1-9	3464
11	Animals/ not (Animals/ and Humans/)	4499580
12	10 not 11	3292
13	limit 12 to (letter or historical article or comment or editorial or news or case reports)	635
14	12 not 13	2657
15	limit 14 to english language	2530

Key to search operators

/	Medical Subject Heading (MeSH) term
.ti	Searches the title field
.ab	Searches the abstract field
*	Truncation symbol (searches all word endings after the stem)
adj*n*	Adjacency operator to retrieve records containing the terms within a specified number (*n*) of words of each other

Appendix C – Public health evidence study selection



Review among children, young people and young adults who don't smoke: 22 articles

Review among children, young people and young adults who do smoke: 2 articles

Appendix D – Public health evidence tables

Future cigarette use among children, young people and young adults who use e-cigarettes and don't smoke

Aleyan 2018

Bibliographic reference/s	**Aleyan Sarah, Cole Adam, Qian Wei, and Leatherdale Scott T (2018) Risky business: a longitudinal study examining cigarette smoking initiation among susceptible and non-susceptible e-cigarette users in Canada. BMJ open 8(5), e021080** **Hammond David, Reid Jessica L, Cole Adam G, and Leatherdale Scott T (2017) Electronic cigarette use and smoking initiation among youth: a longitudinal cohort study. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne 189(43), E1328-E1336**
Study name	Aleyan 2018
Registration	Not reported
Study type	Cohort (unclear whether prospective or retrospective)
Study dates	2013-2016 (2 year follow-up) [1-year follow-up for Hammond paper]
Objective	To determine whether baseline use of e-cigarettes among never-smoking youth predicted cigarette smoking initiation over a 2-year period
Country/ Setting	Canada, Ontario and Alberta. 89 high schools
Cohort source	COMPASS
Number entering into study (invited)	45,298 participants (89 secondary schools) at baseline. Sample is 9,688 who had not smoked at baseline.
Number of participants evaluated	9,501 (6,689 not susceptible to smoking, 2,812 susceptible) Power not reported.
Prognostic factor	Current (past-30 day) e-cigarette users. Assessed by asking 'In the last 30 days, did you use any of the following? (Mark all that apply)'. Students could choose one or more tobacco/nicotine products, including e-cigarettes ('electronic cigarettes that look like cigarettes/cigars, but produce vapour instead of smoke'). Respondents who reported having used e-cigarettes in the past 30 days were categorised as current e-cigarette users, while all others were categorised as non-current users. E-cigarettes may or may not contain nicotine. Type of e-cigarette device not investigated.
Baseline study sample characteristics	Characteristics of current and non-current e-cigarette users among students who reported never smoking cigarettes at baseline.

	Exposed (n = 206)	Unexposed (n = 9295)	Significant difference (P value)
Grade 9 (age 13-14)	51.5	54.8	No (0.6117)

<table>
<tr><td>Bibliographic reference/s</td><td>Aleyan Sarah, Cole Adam, Qian Wei, and Leatherdale Scott T (2018) Risky business: a longitudinal study examining cigarette smoking initiation among susceptible and non-susceptible e-cigarette users in Canada. BMJ open 8(5), e021080

Hammond David, Reid Jessica L, Cole Adam G, and Leatherdale Scott T (2017) Electronic cigarette use and smoking initiation among youth: a longitudinal cohort study. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne 189(43), E1328-E1336</td></tr>
<tr><td>Study name</td><td>Aleyan 2018</td></tr>
<tr><td></td><td>
<table>
<tr><td>Grade 10 (age 14-15)
Grade 11 (age 15-16)
(%)</td><td>45.6
2.9</td><td>42.2
2.9</td><td></td></tr>
<tr><td>Female (%)</td><td>37.9</td><td>52.6</td><td>Yes (<0.0001)</td></tr>
<tr><td>Ethnicity</td><td>65% white, 4.9% Black, remainder is other / mixed; Asian, Off-Reserve Aboriginal; Hispanic / Latin American.</td><td>70.9% white, 2.6% Black, remainder is other / mixed; Asian, Off-Reserve Aboriginal; Hispanic / Latin American.</td><td>Yes (0.0015)</td></tr>
<tr><td>Has friends who smoke cigarettes (%)</td><td>36.4</td><td>18.3</td><td>Yes (<0.0001)</td></tr>
<tr><td>Susceptible to future smoking (% yes)</td><td>64.6</td><td>28.8</td><td>Yes (<0.0001)</td></tr>
</table>
Study uses non-probability sampling and so is not representative.</td></tr>
<tr><td>Attrition</td><td>Sample is those who completed baseline and follow-up studies, information on attrition not given.</td></tr>
<tr><td>Inclusion and exclusion criteria</td><td>• Inclusion: Grade 9-12 students who reported never having tried smoking, even a puff or two.
• No exclusion criteria reported</td></tr>
<tr><td>Data collection</td><td>COMPASS student questionnaire used to collect student health behaviours as per cohort processes.

<u>Susceptibility to smoking (both):</u> Students were asked: ‘Do you think in the future you might try smoking cigarettes?’, ‘If one of your best friends were to offer you a cigarette, would you smoke it?’ and ‘At any time during the next year, do you think you will smoke a cigarette?’ Consistent with Pierce’s validated construct, individuals who responded ‘definitely not’ to all three questions were categorised as non-susceptible to future smoking (i.e., low risk). Individuals who responded positively to at least one item were categorised as susceptible to future smoking (i.e., high risk).</td></tr>
<tr><td>Outcome measure</td><td><u>Smoking initiation (Aleyan):</u> assessed by asking students: ‘Have you ever tried smoking a cigarette, even a puff or two?’ Individuals who responded ‘yes’ were classified as ever-smokers.</td></tr>
</table>

<table>
<tr><td>Bibliographic reference/s</td><td>Aleyan Sarah, Cole Adam, Qian Wei, and Leatherdale Scott T (2018) Risky business: a longitudinal study examining cigarette smoking initiation among susceptible and non-susceptible e-cigarette users in Canada. BMJ open 8(5), e021080

Hammond David, Reid Jessica L, Cole Adam G, and Leatherdale Scott T (2017) Electronic cigarette use and smoking initiation among youth: a longitudinal cohort study. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne 189(43), E1328-E1336</td></tr>
<tr><td>Study name</td><td>Aleyan 2018</td></tr>
<tr><td></td><td><u>Daily smoking initiation (Hammond):</u> ever having smoked daily for 7 consecutive days (no at baseline and yes at follow-up)</td></tr>
<tr><td>Follow up</td><td>Smoking initiation: 2 years
Daily smoking: 1 year</td></tr>
<tr><td>Critical outcomes measures and effect size. (time points)</td><td>Smoking initiation (trying smoking, even a puff)
Baseline past-30 day e-cigarette users vs non-users (non-susceptible never smokers only) 2-year follow-up
<table>
<tr><td></td><td>Exposed n = 73</td><td>Unexposed n = 6,616</td><td>aOR* (95% CI)</td><td>aRR** calculated by analyst</td></tr>
<tr><td>Number who had tried smoking at follow-up (%)</td><td>33 (45.2)</td><td>893 (13.5)</td><td>5.28 (3.32, 8.43)</td><td>3.35 (2.53, 4.21)</td></tr>
</table>
*Reported by study. Confidence intervals calculated by review team.
**Calculated by review team. The unexposed group prevalence used to calculate the aRR was 0.135.

Baseline past-30 day e-cigarette users vs non-users (susceptible never smokers only) 2-year follow-up
<table>
<tr><td></td><td>Exposed n = 133</td><td>Unexposed n = 2679</td><td>aOR* (95% CI)</td><td>aRR** calculated by analyst</td></tr>
<tr><td>Number who had tried smoking at follow-up (%)</td><td>83 (62.4)</td><td>964 (36.1)</td><td>2.78 (2.07, 3.73)</td><td>1.69 (1.49, 1.88)</td></tr>
</table>
*Reported by study. Confidence intervals calculated by review team.
**Calculated by review team. The unexposed group prevalence used to calculate the aRR was 0.361

Results also reported for susceptibility to smoking at follow-up but not extracted as not listed in protocol.

Daily smoking (smoking daily for 7 days)
Baseline past-30 day e-cigarette users vs non-users 1-year follow-up
<table>
<tr><td></td><td>Exposed n = 780</td><td>Unexposed n = 17911</td><td>aOR* (95% CI)</td><td>aRR** calculated by analyst</td></tr>
</table></td></tr>
</table>

Bibliographic reference/s	**Aleyan Sarah, Cole Adam, Qian Wei, and Leatherdale Scott T (2018) Risky business: a longitudinal study examining cigarette smoking initiation among susceptible and non-susceptible e-cigarette users in Canada. BMJ open 8(5), e021080** **Hammond David, Reid Jessica L, Cole Adam G, and Leatherdale Scott T (2017) Electronic cigarette use and smoking initiation among youth: a longitudinal cohort study. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne 189(43), E1328-E1336**
Study name	Aleyan 2018

Number who had smoked daily for 7 days at follow-up (%)	136 (17.4)	551 (3.1)	1.79 (1.41, 2.28)	1.74 (1.39, 2.19)

*Reported by study. Before adjustments, the results were OR 6.97 (5.65, 8.60) – adjustments made a large difference.

**Calculated by review team. The unexposed group prevalence used to calculate the aRR was 0.135.

The following is not reported:

- Outcome by habitual vs experimental e-cig use at baseline
- Outcome by nicotine vs non-nicotine e-cigs
- Outcome by e-cig type
- Outcome by age category
- Outcome by socioeconomic deprivation
- Outcome by family / peer smoking presence vs absence.

Important outcomes measures and effect size. (time points)	Not reported.
Statistical Analysis	Statistical methods: Generalised estimating equation (GEE) models fit to adjust for clustering within schools. Logistic regression model assessed relationship between baseline e-cig use and smoking susceptibility at follow-up, stratifying by smoking susceptibility at baseline. A multinomial logistic regression model assessed whether e-cig use among non-susceptible youth at baseline predicted susceptibility to future smoking / smoking initiation. A binary logistic regression model did the same for susceptible youth at baseline. Confounders: Analyses adjusted for gender, grade, self-reported ethnicity, self-reported spending money and the number of friends who smoke cigarettes at baseline. Aleyan: Those with missing data were excluded. Hammond: missing data was assessed on a case by case basis.
Risk of bias (ROB)	Smoking initiation

Outcome	Risk of bias	Comments

Bibliographic reference/s	**Aleyan Sarah, Cole Adam, Qian Wei, and Leatherdale Scott T (2018) Risky business: a longitudinal study examining cigarette smoking initiation among susceptible and non-susceptible e-cigarette users in Canada. BMJ open 8(5), e021080** **Hammond David, Reid Jessica L, Cole Adam G, and Leatherdale Scott T (2017) Electronic cigarette use and smoking initiation among youth: a longitudinal cohort study. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne 189(43), E1328-E1336**		
Study name	Aleyan 2018		
QUIPS tool	Study participation	High	Characteristics described. Sample will be younger than overall population due to requirement to have linked data excluding the oldest children at baseline. Little description of methods in paper. Baseline sample described, but population not described -authors state not representative because of non-probability sampling.
	Study attrition	Moderate	Sample is those who completed baseline and follow-up studies, information on attrition not given. Response rate for cohort as a whole at follow-up is 79.9% - sample is a small proportion of this.
	Prognostic factor management	Moderate	PF well defined and measured consistently for exposed and unexposed. Subjective measure so possible that students were not truthful.
	Outcome measurement	Moderate	Outcome well defined and measured consistently for exposed and unexposed. Subjective measure so possible that students were not truthful. Unlikely to be differential based on PF
	Study confounding	Moderate	Confounders are present in baseline data and are significant between exposed and unexposed. Controlled for in the analysis.
	Statistical analysis and reporting	Low	Analysis controls for clustering. No apparent selective reporting of results.
	Overall Risk of Bias	High risk of bias	
	Daily smoking (smoking daily for 7 days): As for previous outcome.		

Bibliographic reference/s	**Aleyan Sarah, Cole Adam, Qian Wei, and Leatherdale Scott T (2018) Risky business: a longitudinal study examining cigarette smoking initiation among susceptible and non-susceptible e-cigarette users in Canada. BMJ open 8(5), e021080** **Hammond David, Reid Jessica L, Cole Adam G, and Leatherdale Scott T (2017) Electronic cigarette use and smoking initiation among youth: a longitudinal cohort study. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne 189(43), E1328-E1336**
Study name	Aleyan 2018
Source of funding	COMPASS funded by Canadian Institutes of Health Research (CIHR) Institute of Nutrition, Metabolism and Diabetes and CIHR Institute of Population and Public Health. In addition, Hammond: Ontario Ministry of Health and Long-Term Care Health Systems Research Fund, CIHR.
Comments	No interests declared. Authors note that non-nicotine-containing e-cigarettes account for a greater proportion of the e-cigarette market in Canada than in many other countries. Authors conclude that young who use e-cigs at baseline are more likely to report having smoked or having smoked daily for 7 days at follow-up, after adjustments. Unclear whether effects are causal. But youth who try e-cigarettes may be different from those who do not.
Additional references	Hammond David, Reid Jessica L, Cole Adam G, and Leatherdale Scott T (2017) Electronic cigarette use and smoking initiation among youth: a longitudinal cohort study. CMAJ : Canadian Medical Association journal 189(43), E1328-E1336 The above publication is the 1-year results for which the current paper presents 2-year results.

Barrington-Trimis 2016

Bibliographic reference/s	Barrington-Trimis Jessica L, Urman Robert, Berhane Kiros, Unger Jennifer B, Cruz Tess Boley, Pentz Mary Ann, Samet Jonathan M, Leventhal Adam M, and McConnell Rob (2016) E-Cigarettes and Future Cigarette Use. Pediatrics 138(1),
Study name	Barrington-Trimis 2016
Registration	NA
Study type	Cohort (prospective)
Study dates	2014 to 2015 – follow-up 1 year
Objective	To assess whether e-cigarette use increases likelihood of initiation of cigarettes once they may legally be bought (age 18).
Country/ Setting	Southern California (11th and 12th grade students in schools)
Cohort source	Southern California Children's Health Study (CHS)

<table>
<tr><td>Bibliographic reference/s</td><td>Barrington-Trimis Jessica L, Urman Robert, Berhane Kiros, Unger Jennifer B, Cruz Tess Boley, Pentz Mary Ann, Samet Jonathan M, Leventhal Adam M, and McConnell Rob (2016) E-Cigarettes and Future Cigarette Use. Pediatrics 138(1),</td></tr>
<tr><td>Study name</td><td>Barrington-Trimis 2016</td></tr>
<tr><td>Number entering into study (invited)</td><td>426 people contacted (all 213 never-smoking e-cigarette users, and a randomly selected frequency matched sample of never-smoking, never e-cigarette users)</td></tr>
<tr><td>Number of participants evaluated</td><td>298 (152 unexposed, 146 exposed)
No power information reported</td></tr>
<tr><td>Prognostic factor</td><td><u>Ever use of e-cigarettes:</u> assessed by response to survey question about number of days e-cigarettes were used in the past 30 days. “Never tried” (not even one or two puffs) was classified as a never-user.

Type of e-cigarette or nicotine content data not collected by survey.</td></tr>
<tr><td>Baseline study sample characteristics</td><td>Characteristics
<table>
<tr><td></td><td>Exposed (n = 146)</td><td>Unexposed (n = 152)</td><td>Significant difference</td></tr>
<tr><td>Grade 11 (age 16-17)
Grade 12 (age 17-18)
(%)</td><td>55.5
44.5</td><td>52
48</td><td>No</td></tr>
<tr><td>Female (%)</td><td>41.8</td><td>41.5</td><td>No</td></tr>
<tr><td>Ethnicity</td><td>49% Hispanic white, 41% non-Hispanic white, 10% other</td><td>49% Hispanic white, 43% non-Hispanic white, 8% other</td><td>No</td></tr>
<tr><td>Susceptibility to smoking (yes, %)*</td><td>33.6</td><td>18.4</td><td>Yes</td></tr>
<tr><td>Others at home use cigarettes (yes, %)</td><td>19.9</td><td>16.5</td><td>No</td></tr>
<tr><td>Friends use cigarettes (yes, %)</td><td>22.6</td><td>10.5</td><td>Yes</td></tr>
<tr><td>Friends are friendly to cigarette use (yes, %)</td><td>32.9</td><td>19.1</td><td>Yes</td></tr>
<tr><td>Parental education ≤12th grade (%)</td><td>28.8</td><td>30.0</td><td>No</td></tr>
</table>
*Susceptibility to cigarette use: Adolescents were classified as having no susceptibility if they responded “definitely not” to questions about intention to initiate use of cigarettes in the future.

Self-administered questionnaires completed by parents of participants were used to determine gender, ethnicity, parental education.
Significant differences between those using e-cigs and not using e-cigs in susceptibility to smoking, and friends’ use of / friendliness towards cigarette use.
Representativeness of sample not reported – unexposed group was matched to exposed group.</td></tr>
<tr><td>Attrition</td><td>5/303 participants who completed baseline assessment did not complete follow-up assessment (1.7%) due to not reporting data on cigarette use. Participants with follow-up data were more likely to have a parent with at least a college</td></tr>
</table>

<table>
<tr><td>Bibliographic reference/s</td><td>Barrington-Trimis Jessica L, Urman Robert, Berhane Kiros, Unger Jennifer B, Cruz Tess Boley, Pentz Mary Ann, Samet Jonathan M, Leventhal Adam M, and McConnell Rob (2016) E-Cigarettes and Future Cigarette Use. Pediatrics 138(1),</td></tr>
<tr><td>Study name</td><td>Barrington-Trimis 2016</td></tr>
<tr><td></td><td>education, but authors test for this and state there is no interaction with the outcome. No other notable differences.</td></tr>
<tr><td>Inclusion and exclusion criteria</td><td>Students who had never smoked.
Exclusion criteria not reported.</td></tr>
<tr><td>Data collection</td><td>Baseline data collection took place in classrooms with study staff supervision. Follow-up data collection was online.

All participants were 18 years of age or older at follow-up. Participants turning 18 were sent a link to the follow-up online survey by e-mail (using e-mail address provided at the 11th- and 12th-grade data collection); additional attempts to contact participants were made by text message and telephone calls. Those not responding or who had not provided other contact information were sent letters soliciting participation to the last known residential address or were contacted through parents or other contacts previously provided by participants.

Susceptibility: Participants were asked the following questions, with 4 response options (definitely not, probably not, probably yes, definitely yes): (1) At any time in the next year, do you think you will use these products? (2) Do you think in the future you will experiment with these products? (3) If one of your best friends were to offer you these products would you use them? “Definitely not” to all was non-susceptible.</td></tr>
<tr><td>Outcome measure</td><td>Smoking initiation: assessed by asking students (who had never smoked at baseline): ‘Have you ever tried smoking a cigarette, even a puff or two?’ Individuals who responded ‘yes’ were classified as ever-smokers.
Measured by self-reported survey</td></tr>
<tr><td>Follow up</td><td>Due to length of data collection periods, time between baseline and follow-up could have been between 8 and 26 months. Authors state average is 16 months.</td></tr>
<tr><td>Critical outcomes measures and effect size. (time points)</td><td>Smoking initiation (trying smoking, even a puff)
Baseline ever e-cigarette users vs non-users among non-smokers (16 month follow-up)
<table>
<tr><td></td><td>Exposed n = 146</td><td>Unexposed n = 152</td><td>aOR* (95% CI)</td><td>aRR**</td></tr>
<tr><td>Number who had tried smoking at follow-up (%)</td><td>59 (40.4)</td><td>16 (10.5)</td><td>5.48 (2.69, 11.2)</td><td>3.73 (2.28, 5.41)</td></tr>
</table>
*Reported by study. Adjusted for use of any combustible tobacco product at initial evaluation (cigarettes, cigars, hookah, pipes), gender, ethnicity, grade and highest parental education.
**Calculated by review team. The unexposed group prevalence used to calculate the aRR was 0.105.

Baseline ever e-cigarette users vs non-users (non-susceptible never smokers only) 16 month follow-up</td></tr>
</table>

<table>
<tr><td>Bibliographic reference/s</td><td>Barrington-Trimis Jessica L, Urman Robert, Berhane Kiros, Unger Jennifer B, Cruz Tess Boley, Pentz Mary Ann, Samet Jonathan M, Leventhal Adam M, and McConnell Rob (2016) E-Cigarettes and Future Cigarette Use. Pediatrics 138(1),</td></tr>
<tr><td>Study name</td><td>Barrington-Trimis 2016</td></tr>
<tr><td></td><td>
<table>
<tr><td></td><td>Exposed n = 94
Number (%)</td><td>Unexposed n = 122
Number (%)</td><td>aOR* (95% CI)</td><td>aRR** calculated by analyst</td></tr>
<tr><td>Number who had tried smoking at follow-up (%)</td><td>34 (36.2)</td><td>7 (5.7)</td><td>9.69 (4.02, 23.4)</td><td>6.73 (3.49, 10.96)</td></tr>
</table>
*Reported by study. Adjusted for gender, ethnicity, grade and highest parental education.
**Calculated by review team. The unexposed group prevalence used to calculate the aRR was 0.0507.

Baseline ever e-cigarette users vs non-users (susceptible never smokers only) 16 month follow-up
<table>
<tr><td></td><td>Exposed n = 51
Number (%)</td><td>Unexposed n = 28
Number (%)</td><td>aOR* (95% CI)</td><td>aRR** calculated by analyst</td></tr>
<tr><td>Number who had tried smoking at follow-up</td><td>24 (47.1)</td><td>9 (32.1)</td><td>2.12 (0.79, 5.74)</td><td>1.56 (0.85, 2.28)</td></tr>
</table>
*Reported by study. Adjusted for gender, ethnicity, grade and highest parental education.
**Calculated by review team. The unexposed group prevalence used to calculate the aRR was 0.321.
The following is not reported:

Outcome by habitual vs experimental e-cig use at baseline
Outcome by nicotine vs non-nicotine e-cigs
Outcome by e-cig type
Outcome by age category
Outcome by socioeconomic deprivation
Outcome by family / peer smoking presence vs absence.

</td></tr>
<tr><td>Important outcomes measures and effect size. (time points)</td><td>No important outcomes reported.</td></tr>
<tr><td>Statistical Analysis</td><td>Logistic regression was used to evaluate association between e-cig use at baseline and cigarette use at follow-up. All models were adjusted for gender, ethnicity, grade and highest parental education, factors that have been associated both with e-cigarette use and cigarette use in previous studies.
Confounding: Potential confounding by history of combustible tobacco use other than cigarettes at initial evaluation, social environment characteristics, age at initial evaluation, age at follow-up, and time from initial evaluation to follow-up (in months) was evaluated on the basis of a change in effect estimate of >10% with</td></tr>
</table>

<table>
<tr><td>Bibliographic reference/s</td><td colspan="3">Barrington-Trimis Jessica L, Urman Robert, Berhane Kiros, Unger Jennifer B, Cruz Tess Boley, Pentz Mary Ann, Samet Jonathan M, Leventhal Adam M, and McConnell Rob (2016) E-Cigarettes and Future Cigarette Use. Pediatrics 138(1),</td></tr>
<tr><td>Study name</td><td colspan="3">Barrington-Trimis 2016</td></tr>
<tr><td></td><td colspan="3">inclusion of any of these variables. A missing indicator category was included where appropriate.

In sensitivity analyses, models evaluating the risk of initiation of cigarettes were restricted to nonusers of any combustible tobacco product at initial evaluation (cigarettes, cigars, hookah, pipes).

Clustering: no analysis to conduct for clustering.</td></tr>
<tr><td>Risk of bias (ROB)
QUIPS tool</td><td colspan="3">Smoking initiation (between baseline e-cig users vs non-users)</td></tr>
<tr><td></td><td>Outcome</td><td>Judgement</td><td>Comments</td></tr>
<tr><td></td><td>Study participation</td><td>High</td><td>Baseline sample clearly described, but similarity to source population and not described. CHS cohort is a pre-existing cohort and recruitment not described. Representativeness not described.</td></tr>
<tr><td></td><td>Study attrition</td><td>Low</td><td>Attrition very low (1.7% overall) and similar between groups. Drop-outs evaluated and not dissimilar from completing sample in meaningful way. Reasons for drop outs described.</td></tr>
<tr><td></td><td>Prognostic factor management</td><td>Moderate</td><td>Fairly well defined PF. Self-reported. Measured consistently across groups. Good proportion of data on PF.</td></tr>
<tr><td></td><td>Outcome measurement</td><td>Moderate</td><td>Outcome well defined and measured consistently for exposed and unexposed. Subjective measure so possible that students were not truthful. Unlikely to be differential based on PF</td></tr>
<tr><td></td><td>Study confounding</td><td>Moderate</td><td>Important confounders (peer and family smoking, susceptibility) measured and are different at baseline. Results presented by susceptibility. Peer and family smoking not controlled for, but authors state results did not differ appreciably.</td></tr>
<tr><td></td><td>Statistical analysis and reporting</td><td>Low</td><td>Analysis did not control for clustering. No apparent selective reporting of results.</td></tr>
<tr><td></td><td>Overall Risk of Bias</td><td colspan="2">Acceptable risk of bias</td></tr>
</table>

Bibliographic reference/s	Barrington-Trimis Jessica L, Urman Robert, Berhane Kiros, Unger Jennifer B, Cruz Tess Boley, Pentz Mary Ann, Samet Jonathan M, Leventhal Adam M, and McConnell Rob (2016) E-Cigarettes and Future Cigarette Use. Pediatrics 138(1),
Study name	Barrington-Trimis 2016
	Other outcome details: smoking by susceptible and non-susceptible groups: as for previous outcome.
Source of funding	National Cancer Institute at the National Institutes of Health and the Food and Drug Administration Center for Tobacco Products.
Comments	- Authors state that the association of e-cigarettes with initiation of cigarette use was much stronger among those classified as not susceptible to becoming smokers, and that these findings suggest that e-cigarette use may promote smoking during the transition to adulthood, even in those considered to be at lower risk because of personal or environmental factors. - The authors state that the above partly addresses the argument that e-cig use among never smoking adolescents may be a marker for those who would have begun to smoke anyway.
Additional references	Barrington-Trimis Jessica L, Kong Grace, Leventhal Adam M, Liu Feifei, Mayer Margaret, Cruz Tess Boley, Krishnan-Sarin Suchitra, and McConnell Rob (2018) E-cigarette Use and Subsequent Smoking Frequency Among Adolescents. Pediatrics 142(6), The above paper is superseded by the current paper, in which the authors have included a larger sample from the same cohort.

Best 2018

Bibliographic reference/s	**Best Catherine, Haseen Farhana, Currie Dorothy, Ozakinci Gozde, MacKintosh Anne Marie, Stead Martine, Eadie Douglas, MacGregor Andy, Pearce Jamie, Amos Amanda, Frank John, and Haw Sally (2017) Relationship between trying an electronic cigarette and subsequent cigarette experimentation in Scottish adolescents: a cohort study. Tobacco control ,**
Study name	Best 2018
Registration	Not reported
Study type	Cohort (prospective)
Study dates	2015-2016
Objective	To determine whether young never smokers in Scotland who have tried an e-cigarette are more likely than those who have not, to try a cigarette during the following year.
Country/ Setting	Scotland, UK
Cohort source	Determining the Impact of Smoking Point-of-Sale Legislation Among Youth (DISPLAY) study. From 4 schools in Scotland.
Number entering into study (invited)	3807
Number of participants evaluated	2125 Power not reported.

<table>
<tr><td>Bibliographic reference/s</td><td>Best Catherine, Haseen Farhana, Currie Dorothy, Ozakinci Gozde, MacKintosh Anne Marie, Stead Martine, Eadie Douglas, MacGregor Andy, Pearce Jamie, Amos Amanda, Frank John, and Haw Sally (2017) Relationship between trying an electronic cigarette and subsequent cigarette experimentation in Scottish adolescents: a cohort study. Tobacco control ,</td></tr>
<tr><td>Study name</td><td>Best 2018</td></tr>
<tr><td>Prognostic factor</td><td>Ever e-cigarette use: Assessed by asking whether participants had heard of e-cigarettes (Y/N). If Y, Which ONE of the following is closest to describing your experience of e-cigarettes/ vapourisers /shisha pens?" with response options of 'I have never used them', 'I have tried them once or twice', 'I use them sometimes (more than once a month)' or 'I use them often (more than once a week)'. Young people who responded that they had never heard of e-cigarettes were coded as having 'never used them'.</td></tr>
<tr><td>Baseline study sample characteristics</td><td>Characteristics of those never-smokers completing baseline assessment (also includes people who did not complete follow-up and so are not part of the analysed sample – no other information reported by authors)
<table>
<tr><th>Characteristic</th><th>Sample (n = 3001)*</th></tr>
<tr><td>Age
Year 1 (mean 12.5 years) (%)
Year 2 (mean 13.5 years) (%)
Year 3 (mean 14.5 years) (%)
Year 4 (mean 15.5 years) (%)
Year 5 (mean 16.5 years) (%)
Year 6 (mean 17.5 years) (%)</td><td>
682 (22.7)
716 (23.9)
557 (18.6)
514 (17.1)
334 (11.1)
198 (6.6)</td></tr>
<tr><td>Female (%)</td><td>1477 (49.4)</td></tr>
<tr><td>Ethnicity (non-white, %)</td><td>226 (7.6)</td></tr>
<tr><td>Susceptibility to smoking (Yes, %)</td><td>771 (26.3)</td></tr>
<tr><td>Family smoking (a family member smokes, %)</td><td>980 (32.8%)</td></tr>
<tr><td>Peer smoking (any friends smoke, %)</td><td>613 (23.7)</td></tr>
<tr><td>SES** Low (%)
Medium (%)
High (%)</td><td>965 (32.2)
1008 (33.6)
1028 (34.3)</td></tr>
<tr><td>From school with high deprivation (%)</td><td>1405 (46.9)</td></tr>
</table>
*some missing data for each characteristic
** As determined by the Family Affluence Scale and divided into tertiles.
No formal tests for representativeness but authors check against national survey for 2013 and state that there was not any significant deviation.</td></tr>
<tr><td>Attrition</td><td>29.6% (1127/3807) dropped out between baseline and follow-up.
Authors report that there was no difference in baseline e-cigarette status between those who were and were not lost to follow up – similar proportion attrition between groups.</td></tr>
<tr><td>Inclusion and exclusion criteria</td><td>Students at cohort schools aged 11-18 who have never smoked at baseline.
Exclusion criteria not reported.</td></tr>
<tr><td>Data collection</td><td>Data collected through a survey. Survey administered by class teachers under exam conditions and took roughly 40 minutes to complete. Absent pupils were given 2 weeks to complete the survey. Parents were given opportunity to opt out. Pupils provided active consent by completing the survey.</td></tr>
</table>

<table>
<tr><td>Bibliographic reference/s</td><td>Best Catherine, Haseen Farhana, Currie Dorothy, Ozakinci Gozde, MacKintosh Anne Marie, Stead Martine, Eadie Douglas, MacGregor Andy, Pearce Jamie, Amos Amanda, Frank John, and Haw Sally (2017) Relationship between trying an electronic cigarette and subsequent cigarette experimentation in Scottish adolescents: a cohort study. Tobacco control ,</td></tr>
<tr><td>Study name</td><td>Best 2018</td></tr>
<tr><td></td><td>No information on blinding
Susceptibility to smoking was assessed through two questions “If one of your friends offered you a cigarette or hand-rolled cigarettes (roll-ups), would you smoke it?” and “Do you think you will smoke a cigarette or hand-rolled cigarettes (roll-ups) at any time during the next year?”. The response option for these questions was ‘definitely yes’, ‘probably yes’, ‘probably not’ and ‘definitely not’. If respondents answered anything other than ‘definitely not’ to either of these questions then they were coded as being susceptible to smoking.</td></tr>
<tr><td>Outcome measure</td><td>Trying a cigarette: Respondents were asked “Have you ever smoked cigarettes or hand-rolled cigarettes (roll-ups), even if it is just one or two puffs?” to which they could respond ‘yes’ or ‘no’. Young people who responded ‘yes’ at follow-up were treated as having tried a cigarette.</td></tr>
<tr><td>Follow up</td><td>1 year</td></tr>
<tr><td>Critical outcomes measures and effect size. (time points)</td><td>Trying a cigarette
Baseline ever e-cigarette users vs non-users (among baseline non-smokers) 1-year follow-up
<table>
<tr><td></td><td>Exposed n = 183</td><td>Unexposed n = 1942</td><td>aRR* (95% CI)</td></tr>
<tr><td>Number who had tried smoking at follow-up (%)</td><td>74 (40.4)</td><td>249 (12.8)</td><td>4.22 (2.83, 6.36)</td></tr>
</table>
*Reported by study. Adjusted for age, sex, school, ethnicity, family affluence (FAS), smoking within the family, smoking by friends, susceptibility to smoking.

Results by age (entire age range is within category of “young people” which is the category to be used for subgroup analysis).
Authors split the group by age (under 14s vs 14 and over) to see whether results are different by age. Authors don’t state which of the models has supplied these results, so unclear what has been controlled for. No event numbers supplied.
<table>
<tr><td>Under 14s</td><td>OR (95% CI)
(920 children)</td><td>aRR (95% CI)</td></tr>
<tr><td>Use of cigarettes at follow-up among baseline e-cig users vs non-users</td><td>3.46 (1.80, 6.68)</td><td>Can’t calculate as no unexposed group prevalence</td></tr>
</table>
<table>
<tr><td>14 and over</td><td>OR (95% CI)
(882 children)</td><td>aRR (95% CI)</td></tr>
<tr><td>Use of cigarettes at follow-up among baseline e-cig users vs non-users</td><td>2.32 (1.40, 3.87)</td><td>Can’t calculate as no unexposed group prevalence</td></tr>
</table>
The following is not reported:</td></tr>
</table>

<table>
<tr><td>Bibliographic reference/s</td><td colspan="3">Best Catherine, Haseen Farhana, Currie Dorothy, Ozakinci Gozde, MacKintosh Anne Marie, Stead Martine, Eadie Douglas, MacGregor Andy, Pearce Jamie, Amos Amanda, Frank John, and Haw Sally (2017) Relationship between trying an electronic cigarette and subsequent cigarette experimentation in Scottish adolescents: a cohort study. Tobacco control ,</td></tr>
<tr><td>Study name</td><td colspan="3">Best 2018</td></tr>
<tr><td></td><td colspan="3">• Outcome by habitual vs experimental e-cig use at baseline
• Outcome by nicotine vs non-nicotine e-cigs
• Outcome by e-cig type
• Outcome by age category (child vs young person vs young adult)
• Outcome by socioeconomic deprivation
• Outcome by family / peer smoking presence vs absence.</td></tr>
<tr><td>Important outcomes measures and effect size. (time points)</td><td colspan="3">No important outcomes reported</td></tr>
<tr><td>Statistical Analysis</td><td colspan="3">Multivariate logistic regression. Three models used: the model reported here is the one which controlled for the most factors: age, sex, ethnicity, family affluence, smoking within the family, smoking by friends, susceptibility to smoking.
An indicator for school was included to make explicit the effect of school as school-level smoking norms are an important influence on smoking behaviour. This is interpreted as adjusting for clustering.
Effect of missing data tested using multiple imputation by chained equations.</td></tr>
<tr><td rowspan="4">Risk of bias (ROB) QUIPS tool</td><td colspan="3">Trying an e-cigarette</td></tr>
<tr><td>Outcome</td><td>Judgement</td><td>Comments</td></tr>
<tr><td>Study participation</td><td>Moderate</td><td>Characteristics of population not described. Sample key characteristics described and attempts by author to check representativeness.</td></tr>
<tr><td>Study attrition</td><td>Moderate</td><td>Attrition differentially affected males, young people from lower socioeconomic groups and those with more smokers in their social circle. Authors state that this likely means they underestimate the proportions of young people who initiate smoking during the follow up year. However, there is no difference in baseline e-cigarette status between those who were and were not lost to follow up. Therefore number of smoking initiators is probably underestimated in both groups.

Response rate sufficient. Drop outs described.</td></tr>
<tr><td>Prognostic factor management</td><td>Moderate</td><td>PF well defined and measured consistently for exposed and unexposed.</td></tr>
</table>

Bibliographic reference/s	**Best Catherine, Haseen Farhana, Currie Dorothy, Ozakinci Gozde, MacKintosh Anne Marie, Stead Martine, Eadie Douglas, MacGregor Andy, Pearce Jamie, Amos Amanda, Frank John, and Haw Sally (2017) Relationship between trying an electronic cigarette and subsequent cigarette experimentation in Scottish adolescents: a cohort study. Tobacco control ,**		
Study name	Best 2018		
			Subjective measure so possible that students were not truthful.
	Outcome measurement	Moderate	Outcome well defined and measured consistently for exposed and unexposed. Subjective measure so possible that students were not truthful. Unlikely to be differential based on PF
	Study confounding	Moderate	Important confounders generally controlled for, but might not cover unknown confounders.
	Statistical analysis and reporting	Low bias	Analysis controls for clustering. No apparent selective reporting of results.
	Overall Risk of Bias	Acceptable risk of bias	
	Other outcome details: smoking initiation by age: won't be used in meta-analysis as is excess information (splits in greater detail than will be useful for recommendations). High risk of bias due to lack of clarity on confounders adjusted for or modelling used, and no event data.		
Source of funding	UK National Institute for Health Research (NIHR)		
Comments	- Particular relevance due to setting - Authors acknowledge that outcome looks only at whether participants have tried smoking, and not whether they have become regular smokers. However, they state that trying smoking is correlated with becoming a smoker. - At the time of research, there were no age restrictions on buying e-cigarettes, which there now are (age 18). Uncertain what impact this would have on outcome.		
Additional references	Supplementary file online.		

Bold 2018

Bibliographic reference/s	**Bold Krysten W, Kong Grace, Camenga Deepa R, Simon Patricia, Cavallo Dana A, Morean Meghan E, and Krishnan-Sarin Suchitra (2018) Trajectories of E-Cigarette and Conventional Cigarette Use Among Youth. Pediatrics 141(1),**
Study name	Bold 2018
Registration	Not reported
Study type	Cohort (prospective)
Study dates	2013-2015
Objective	To determine whether e-cigarette use among young people leads to cigarette use, or whether cigarette use leads to e-cigarette use.

<table>
<tr><td>Bibliographic reference/s</td><td>Bold Krysten W, Kong Grace, Camenga Deepa R, Simon Patricia, Cavallo Dana A, Morean Meghan E, and Krishnan-Sarin Suchitra (2018) Trajectories of E-Cigarette and Conventional Cigarette Use Among Youth. Pediatrics 141(1),</td></tr>
<tr><td>Study name</td><td>Bold 2018</td></tr>
<tr><td>Country/ Setting</td><td>USA, Connecticut.
3 high schools</td></tr>
<tr><td>Cohort source</td><td>No reported name</td></tr>
<tr><td>Number entering into study (invited)</td><td>1408 invited</td></tr>
<tr><td>Number of participants evaluated</td><td>808 participants evaluated (completed wave 1, 2 and 3): 39 of these had some cigarette use at baseline (4.8%).
For model which adjusts for covariates, data only available for 795 participants.
Power not reported.</td></tr>
<tr><td>Prognostic factor</td><td>E-cigarette use in past 30 days: Assessed by asking whether participants had tried an e-cigarette (Y/N). If Y, they were asked how many days out of the past 30 they used e-cigarettes. Any number of days in past month constituted use.</td></tr>
<tr><td>Baseline study sample characteristics</td><td>Characteristics at baseline among smokers and non-smokers
<table>
<tr><td></td><td>Sample (n = 808)</td></tr>
<tr><td>Mean age years (SD)</td><td>15.0 (0.9)</td></tr>
<tr><td>Female (%)</td><td>53</td></tr>
<tr><td>Past month e-cig use (%)(EXPOSED GROUP)</td><td>72 (8.9)</td></tr>
<tr><td>Ethnicity</td><td>87.6% white, 5.7% Asian, 5.1% Hispanic, 2.6% Black or African American, 3% other</td></tr>
<tr><td>Susceptibility to smoking</td><td>Not reported</td></tr>
<tr><td>Family smoking</td><td>Not reported</td></tr>
<tr><td>Peer smoking</td><td>Not reported</td></tr>
<tr><td>SES* (SD)</td><td>5.92 (1.38)</td></tr>
</table>
*Measured with the Family Affluence Scale, range 0 (low) to 8 (high)

• Study does not split participants into two groups (those that used e-cigs at baseline and those who didn't).
• Schools selected to provide a variation on demographic characteristics. May not be generalisable beyond the sample.</td></tr>
<tr><td>Attrition</td><td>1408 students completed baseline data collection and 808 formed the longitudinal sample completing baseline, follow up 1 and follow up 2. 42.6% did not complete all three data points.
Authors state that the sample for analysis did not differ significantly from those who did not complete in terms of sociodemographic characteristics or substance use. Match rates (across time points) were comparable across schools and grades.</td></tr>
<tr><td>Inclusion and exclusion criteria</td><td>All children attending one of the three schools.
No exclusion criteria reported</td></tr>
<tr><td>Data collection</td><td>Data collected through a survey. Surveys distributed during homeroom (form time) lessons. Parents were given opportunity to opt out. Pupils informed that</td></tr>
</table>

<table>
<tr><td>Bibliographic reference/s</td><td>Bold Krysten W, Kong Grace, Camenga Deepa R, Simon Patricia, Cavallo Dana A, Morean Meghan E, and Krishnan-Sarin Suchitra (2018) Trajectories of E-Cigarette and Conventional Cigarette Use Among Youth. Pediatrics 141(1),</td></tr>
<tr><td>Study name</td><td>Bold 2018</td></tr>
<tr><td></td><td>participant was voluntary. Surveys were anonymous with unique codes to link across waves.
Student data provided:
SES: Family Affluence Scale: assessed the following: (1) whether an adolescent's family owns a car, van, or truck (no = 0, yes = 1); (2) whether an adolescent has his or her own bedroom (no = 0, yes = 1); (3) the number of laptops and/or computers an adolescent's
family owns (none = 0, 1 = 1, 2 = 2, >2 = 3); and (4) whether an adolescent's family had vacationed in the past 12 months (not at all = 0, once = 1, twice = 2, more than twice = 3). Responses were added to create a total SES score.
Ever use of other tobacco products: at baseline, participants were asked whether they had ever used other tobacco products (cigars, hookah, blunts, smokeless tobacco) (Y/N).</td></tr>
<tr><td>Outcome measure</td><td>Trying a cigarette: Respondents were asked "Have you ever tried a cigarettes, even just one or two puffs?" to which they could respond 'yes' or 'no'. If Y, they were asked how many days out of the past 30 they had smoked a cigarette. Any number of days in past month constituted use.</td></tr>
<tr><td>Follow up</td><td>Follow-up 1: 6 months
Follow up 2: 18 months (1 year after follow-up 1)</td></tr>
<tr><td>Critical outcomes measures and effect size. (time points)</td><td>Past 30-day smoking
Assessment of a pathway between past-month e-cigarette use and future cigarette use (baseline to follow-up)
<table>
<tr><td></td><td>aOR* (95% CI)</td><td>aRR** calculated by analyst</td></tr>
<tr><td>Number who had tried smoking at follow-up (%)</td><td>7.08 (2.34, 21.42)</td><td>5.33 (2.18, 10.19)</td></tr>
</table>
*Reported by study. Adjusted for sex, ethnicity, SES, use of other tobacco products.
**Prevalence of unexposed group not reported by study. Prevalence used to calculate aRR is 0.054 (prevalence of whole group at follow-up 1)
This is the result used in meta-analysis.

Assessment of a pathway between past-month e-cigarette use and future cigarette use (follow-up1 to follow-up 2)
<table>
<tr><td></td><td>aOR* (95% CI)</td><td>aRR** calculated by analyst</td></tr>
<tr><td>Number who had tried smoking at follow-up (%)</td><td>3.87 (1.86, 8.06)</td><td>3.11 (1.73, 5.04)</td></tr>
</table>
*Reported by study. Adjusted for sex, ethnicity, SES, use of other tobacco products.
**Prevalence of unexposed group not reported by study. Prevalence used to calculate aRR is 0.085 (prevalence of whole group at follow-up 1)

The following is not reported:
• Outcome by habitual vs experimental e-cig use at baseline</td></tr>
</table>

<table>
<tr><td>Bibliographic reference/s</td><td colspan="3">Bold Krysten W, Kong Grace, Camenga Deepa R, Simon Patricia, Cavallo Dana A, Morean Meghan E, and Krishnan-Sarin Suchitra (2018) Trajectories of E-Cigarette and Conventional Cigarette Use Among Youth. Pediatrics 141(1),</td></tr>
<tr><td>Study name</td><td colspan="3">Bold 2018</td></tr>
<tr><td></td><td colspan="3">• Outcome by nicotine vs non-nicotine e-cigs
• Outcome by e-cig type
• Outcome by age category
• Outcome by socioeconomic deprivation
• Outcome by family / peer smoking presence vs absence.</td></tr>
<tr><td>Important outcomes measures and effect size. (time points)</td><td colspan="3">No important outcomes reported</td></tr>
<tr><td>Statistical Analysis</td><td colspan="3">Missing data: data was missing for 6.5% of cases and was handled by using maximum likelihood estimation with robust standard errors.
Clustering: school was included as a covariate across all waves to account for potential school cohort effects – this is interpreted as adjusting for clustering.
Statistical Analysis: Reciprocal predictive pathways between e-cigarette and cigarette use at each wave (baseline, follow up 1 and follow up 2) to use of the other product at the next wave (e.g. e-cig use at baseline predicting cigarette use at follow-up 1)
Confounders: Results are adjusted for “all covariates” (reported by authors). Named covariates are sex, ethnicity, SES, use of other tobacco products.</td></tr>
<tr><td>Risk of bias (ROB)
QUIPS tool</td><td colspan="3">Past 30-day smoking</td></tr>
<tr><td></td><td>Outcome</td><td>Judgement</td><td>Comments</td></tr>
<tr><td></td><td>Study participation</td><td>High</td><td>Schools selected to provide a variation on demographic characteristics. May not be generalisable beyond the sample. Sampling described – purposive. Inclusion and exclusion criteria not explicit. Baseline sample not described for all relevant characteristics.</td></tr>
<tr><td></td><td>Study attrition</td><td>Moderate</td><td>42.6% did not complete all three data points. Authors state that the sample for analysis did not differ significantly from those who did not complete in terms of sociodemographic characteristics or substance use. Match rates (across time points) were comparable across schools and grades. Reasons for loss to follow up not provided, and drop outs not described.</td></tr>
<tr><td></td><td>Prognostic factor management</td><td>Moderate</td><td>PF well defined and measured consistently for exposed and unexposed. Subjective measure so possible that students were not truthful. However, PF group not separated out and events not reported by e-cig baseline status.</td></tr>
</table>

Bibliographic reference/s	**Bold Krysten W, Kong Grace, Camenga Deepa R, Simon Patricia, Cavallo Dana A, Morean Meghan E, and Krishnan-Sarin Suchitra (2018) Trajectories of E-Cigarette and Conventional Cigarette Use Among Youth. Pediatrics 141(1),**		
Study name	Bold 2018		
	Outcome measurement	Moderate	Outcome well defined and measured consistently for exposed and unexposed. Subjective measure so possible that students were not truthful.
	Study confounding	High	Unclear what confounders are measured and controlled for as list not provided by authors who report that "all" confounders considered.
	Statistical analysis and reporting	Moderate	Analysis controls for clustering. No apparent selective reporting of results but results not reported per baseline group.
	Overall Risk of Bias	High risk of bias	
	Other outcome details: None		
Source of funding	National Institute on Drug Abuse and the Food and Drug Administration Center for Tobacco Products		
Comments	- Study is indirect because PF group not separated out and events not reported by e-cig baseline status. - Event data not provided, so results could not be converted to risk ratio. - Authors report that rates of e-cig and cigarette use increase in general over time in the sample as a whole. - Authors state that study is observational so causal relationship can't be ascertained. - Authors report that the direction of effect is not seen in reverse: i.e. use of cigarettes does not predict future use of e-cigarettes. Not in scope for this review.		
Additional references	Barrington-Trimis Jessica L, Kong Grace, Leventhal Adam M, Liu Feifei, Mayer Margaret, Cruz Tess Boley, Krishnan-Sarin Suchitra, and McConnell Rob (2018) E-cigarette Use and Subsequent Smoking Frequency Among Adolescents. Pediatrics 142(6), The above paper reports on the current study and was used for reference only.		

Conner 2018

Bibliographic reference/s	**Conner Mark, Grogan Sarah, Simms-Ellis Ruth, Flett Keira, Sykes-Muskett Bianca, Cowap Lisa, Lawton Rebecca, Armitage Christopher J, Meads David, Torgerson Carole, West Robert, and Siddiqi Kamran (2017) Do electronic cigarettes increase cigarette smoking in UK adolescents? Evidence from a 12-month prospective study. Tobacco control ,**
Study name	Conner 2018
Registration	Not reported
Study type	Cohort (prospective)
Study dates	2014-2015

<table>
<tr><td>Bibliographic reference/s</td><td>Conner Mark, Grogan Sarah, Simms-Ellis Ruth, Flett Keira, Sykes-Muskett Bianca, Cowap Lisa, Lawton Rebecca, Armitage Christopher J, Meads David, Torgerson Carole, West Robert, and Siddiqi Kamran (2017) Do electronic cigarettes increase cigarette smoking in UK adolescents? Evidence from a 12-month prospective study. Tobacco control ,</td></tr>
<tr><td>Study name</td><td>Conner 2018</td></tr>
<tr><td>Objective</td><td>To assess the relationships between e-cigarette use and subsequent cigarette use in a sample of UK adolescents.</td></tr>
<tr><td>Country/ Setting</td><td>England, Leeds / Staffordshire</td></tr>
<tr><td>Cohort source</td><td>No specific cohort name.
Cohort is from 20 control schools from a cluster randomised controlled trial looking at a school-based smoking initiation intervention. Because of average age, and that authors report data is from one school year, likely to be UK year 9.</td></tr>
<tr><td>Number entering into study (invited)</td><td>2836</td></tr>
<tr><td>Number of participants evaluated</td><td>Longitudinal analysis: 1726 (matched across baseline and follow-up).
Power not reported</td></tr>
<tr><td>Prognostic factor</td><td><u>Ever use of e-cigarettes:</u> assessed by response to survey question about whether participants had heard of e-cigarettes (Y / N / don’t know). And which of the following was closest to describing their experience of e-cigarettes or vapourisers: I have never used them; I have tried them once or twice; I use them sometimes (more than once a month but less than once a week); I use them often (more than once a week)). Dichotomised into never vs ever use of e-cigarettes.

Type of e-cigarette or nicotine content data not collected by survey.</td></tr>
<tr><td>Baseline study sample characteristics</td><td>Characteristics of participants who have never smoked at baseline
<table>
<tr><td>Characteristic</td><td>Sample* (n = 1726)</td></tr>
<tr><td>Mean age years (SD)</td><td>13.18 (0.39)</td></tr>
<tr><td>Female (%)</td><td>898 (52.0)</td></tr>
<tr><td>Ethnicity</td><td>Not reported</td></tr>
<tr><td>Ever use of e-cigarettes (%) (EXPOSED GROUP)</td><td>343 (19.9)</td></tr>
<tr><td>Susceptibility to smoking</td><td>Not reported</td></tr>
<tr><td>Family smoking (anyone in family smokes) (%)</td><td>1060 (61.4)</td></tr>
<tr><td>Peer smoking (any friends smoke) (%)</td><td>676 (38.5)</td></tr>
<tr><td>SES**(mean, SD)</td><td>13.82 (6.55)</td></tr>
</table>
*Baseline characteristics combined for both those who had and those who hadn’t used e-cigarettes at baseline (the exposed and unexposed groups)
**measured as percentage of students receiving free school meals (reported as mean and SD based on school-level data)
Authors don’t report whether the sample is representative of the population.</td></tr>
<tr><td>Attrition</td><td>470/2196 (21.4%) baseline non-smokers did not complete both baseline and follow-up data collection.</td></tr>
</table>

Bibliographic reference/s	**Conner Mark, Grogan Sarah, Simms-Ellis Ruth, Flett Keira, Sykes-Muskett Bianca, Cowap Lisa, Lawton Rebecca, Armitage Christopher J, Meads David, Torgerson Carole, West Robert, and Siddiqi Kamran (2017) Do electronic cigarettes increase cigarette smoking in UK adolescents? Evidence from a 12-month prospective study. Tobacco control ,**
Study name	Conner 2018
	Authors consider whether there are significant differences between baseline characteristics in completers vs non-completers. Differences are that males and participants with three or more family members who smoke and those with weaker intentions not to smoke are more likely to drop out. No difference for friends smoking, ever use of e-cigarettes, lower levels of family smoking, free school meals and measures for attitudes, norms, self-efficacy related to cigarettes. This may reduce frequency of smoking at follow-up, but as proportions dropping out were similar in those who used and did not use e-cigs at baseline, it may reduce for similar amount across groups.
Inclusion and exclusion criteria	Inclusion criteria is control group for the cluster RCT reported elsewhere. Exclusion criteria not reported.
Data collection	Data collected as part of a 4-year cluster RCT. Head teachers consented to school participation. Parents could opt out. Adolescents consented by completing the questionnaire. Blinding not reported. Additional student data provided: Participants were also asked about intention to smoke (‘I plan not to smoke’, ‘I don’t want to smoke’ and ‘I will try not to smoke’; strongly disagree to strongly agree;) attitude towards smoking (7 statements For me, smoking would be… good–bad; beneficial–harmful; pleasant– unpleasant; enjoyable–unenjoyable; wise–foolish; fun–not fun; healthy–unhealthy’) norms about smoking (5 statements (‘Most of my friends think…’; ‘My best male friend thinks…’; ‘My best female friend thinks…’; ‘My family think…’; ‘People who are important to me think…’; I should smoke–I should not smoke) Perceived behavioural control (3 statements I am confident I could resist smoking’, strongly disagree to strongly agree; ‘For me to not smoke would be…’, difficult–easy; ‘How much control do you feel you have over not smoking?’ no control–complete control) Self-efficacy (six statements (‘I can say no to smoking, even at school’; ‘I can say no to smoking even when I am offered a cigarette’; ‘I can say no to smoking, even if my friends want me to smoke’; ‘I can say no to smoking, even if I was the only one in the group not smoking’; ‘I can say no to smoking, even if I feel a bit left out of the group’; ‘I can say no to smoking, even if I feel like smoking’; strongly disagree-strongly agree).
Outcome measure	Ever cigarette use: assessed by response to survey question asking participants to select one of the following: ‘I have never smoked; I have only tried smoking once; I used to smoke sometimes, but I never smoke cigarettes now; I sometimes smoke cigarettes now, but I don’t smoke as many as one a week; I usually smoke between one and six cigarettes a week; and I usually smoke more than six cigarettes a week’. Dichotomised into smoked vs never smoked.

<table>
<tr><td>Bibliographic reference/s</td><td>Conner Mark, Grogan Sarah, Simms-Ellis Ruth, Flett Keira, Sykes-Muskett Bianca, Cowap Lisa, Lawton Rebecca, Armitage Christopher J, Meads David, Torgerson Carole, West Robert, and Siddiqi Kamran (2017) Do electronic cigarettes increase cigarette smoking in UK adolescents? Evidence from a 12-month prospective study. Tobacco control ,</td></tr>
<tr><td>Study name</td><td>Conner 2018</td></tr>
<tr><td></td><td>Measured by self-reported survey and validated against a measure of breath carbon monoxide (CO) levels (using Micro+ Smokerlyzer CO Monitor; Bedfont Scientific Limited, Kent, England, UK). Valid and reliable for judging regular smoking, but not occasional smoking.</td></tr>
<tr><td>Follow up</td><td>1 year between baseline and follow-up</td></tr>
<tr><td>Critical outcomes measures and effect size. (time points)</td><td>Ever smoking
Baseline ever e-cigarette users vs non-users 1-year follow-up among baseline non-smokers
<table>
<tr><td></td><td>Exposed n = 343</td><td>Unexposed n = 1383</td><td>aOR* (95% CI)</td><td>aRR** calculated by analyst</td></tr>
<tr><td>Number of young people who had tried smoking at follow-up (%)</td><td>118 (34.4)</td><td>134 (9.7)</td><td>4.06 (2.94, 5.60)</td><td>3.13 (2.47, 3.87)</td></tr>
</table>
*Reported by study. Adjusted for percentage of children at a school eligible for free school meals; sex; family smoking; friends' smoking; intentions to smoke; attitudes towards smoking; norms around smoking; perceive behavioural control; self-efficacy.
**Calculated by review team. The unexposed group prevalence used to calculate the aRR was 0.097.

The study also reports the relationship between e-cigarette use and future smoking with covariate interactions:
<table>
<tr><td>Among baseline never smokers</td><td>Odds of ever smoking at 1-year follow-up</td><td>Risk of ever smoking at 1-year follow-up*</td></tr>
<tr><td>Never used e-cigarettes and Friend smokers = none</td><td>1.00 (reference)</td><td>NA</td></tr>
<tr><td>Ever used e-cigarettes and friend smokers = none</td><td>7.74 (4.68—12.79)</td><td>4.68 (3.45, 5.97)</td></tr>
<tr><td>Never used e-cigarettes and Friend smokers = a few</td><td>2.57 (1.72 to 3.84)</td><td>2.23 (1.61, 5.97)</td></tr>
<tr><td>Ever used e-cigarettes and friend smokers = a few</td><td>7.84 (5.08–12.09)</td><td>4.71 (3.64, 5.82)</td></tr>
<tr><td>Never used e-cigarettes and friend smokers = most</td><td>6.32 (2.68 to 14.91)</td><td>4.17 (2.30, 6.35)</td></tr>
<tr><td>Ever used e-cigarettes and friend smokers = most</td><td>8.75 (3.68–20.83)</td><td>5.00 (2.92, 7.12)</td></tr>
</table></td></tr>
</table>

Bibliographic reference/s	**Conner Mark, Grogan Sarah, Simms-Ellis Ruth, Flett Keira, Sykes-Muskett Bianca, Cowap Lisa, Lawton Rebecca, Armitage Christopher J, Meads David, Torgerson Carole, West Robert, and Siddiqi Kamran (2017) Do electronic cigarettes increase cigarette smoking in UK adolescents? Evidence from a 12-month prospective study. Tobacco control ,**		
Study name	Conner 2018		
	Authors point out that among people who had no friends that smoke, compared with people who had not used e-cigs at baseline, those who used e-cigs had greater odds of trying smoking by follow up (7.74 (4.68—12.79)). * Calculated by review team. The unexposed group prevalence not reported for specific groups, so overall unexposed prevalence used to calculate the aRR (0.097)		
Important outcomes measures and effect size. (time points)	No important outcomes reported.		
Statistical Analysis	Analysis: Several models were used. The one extracted was Model 2, which controlled for the clustering of adolescents within schools (assumed to control for clustering), and baseline covariates (percentage of children at a school eligible for free school meals; sex; family smoking; friends' smoking; intentions to smoke; attitudes towards smoking; norms around smoking; perceive behavioural control; self-efficacy). Missing data: Tested for differences on each baseline measure between adolescents who had complete vs missing values. Authors report repeating regressions with imputation to assess impact of baseline missing values.		
Risk of bias (ROB) QUIPS tool	Ever smoking		
	Outcome	**Judgement**	**Comments**
	Study participation	High	Characteristics of population not described. Most key characteristics described but representativeness not discussed
	Study attrition	Moderate	Response rate is adequate (>80%). Completers and non-completers are somewhat different, but attrition is not differential by exposure. Characteristics controlled for in analysis.
	Prognostic factor management	Moderate	PF well defined and measured consistently for exposed and unexposed. Subjective measure so possible that students were not truthful.
	Outcome measurement	Low	Outcome well defined and measured consistently for exposed and unexposed. Subjective measure so possible that students were not truthful. Unlikely to be differential based on PF. Attempt to validate using

Bibliographic reference/s	**Conner Mark, Grogan Sarah, Simms-Ellis Ruth, Flett Keira, Sykes-Muskett Bianca, Cowap Lisa, Lawton Rebecca, Armitage Christopher J, Meads David, Torgerson Carole, West Robert, and Siddiqi Kamran (2017) Do electronic cigarettes increase cigarette smoking in UK adolescents? Evidence from a 12-month prospective study. Tobacco control ,**		
Study name	Conner 2018		
			CO monitoring, although this will only detect recent / frequent smoking which is rare in this population.
	Study confounding	Low	Susceptibility to smoking not measured but a variety of other factors in its place (see 'data collection'). Validity tested and acceptable. Measured consistently and controlled for in the analysis.
	Statistical analysis and reporting	Low	Analysis controls for clustering. No apparent selective reporting of results.
	Overall Risk of Bias	Acceptable	
	Other outcome details: none		
Source of funding	UK National Institute for Health Research		
Comments	- Authors point out that the outcome measured is any smoking, which does not indicate regular smoking. - Authors do not report detailed CO monitoring results, but state that baseline CO levels among never smokers were low, and were significantly higher at follow-up among those classified as initiating compared with not initiating. - Authors state that e-cigarette use was a bigger risk factor in groups considered least at risk (i.e. no friends who smoke at baseline).		
Additional references	None		

East 2018

Bibliographic reference/s	**East Katherine, Hitchman Sara C, Bakolis Ioannis, Williams Sarah, Cheeseman Hazel, Arnott Deborah, and McNeill Ann (2018) The Association Between Smoking and Electronic Cigarette Use in a Cohort of Young People. The Journal of adolescent health : official publication of the Society for Adolescent Medicine 62(5), 539-547**
Study name	East 2018
Registration	Not reported
Study type	Cohort (retrospective)
Study dates	2016
Objective	To explore the association between ever e-cigarette use and smoking initiation among baseline never smokers (and between ever smoking and e-cigarette initiation but this is outside of scope.

<table>
<tr><td>Bibliographic reference/s</td><td>East Katherine, Hitchman Sara C, Bakolis Ioannis, Williams Sarah, Cheeseman Hazel, Arnott Deborah, and McNeill Ann (2018) The Association Between Smoking and Electronic Cigarette Use in a Cohort of Young People. The Journal of adolescent health : official publication of the Society for Adolescent Medicine 62(5), 539-547</td></tr>
<tr><td>Study name</td><td>East 2018</td></tr>
<tr><td>Country/ Setting</td><td>Great Britain</td></tr>
<tr><td>Cohort source</td><td>Cohort from the 2016 Action on Smoking and Health Great Britain Youth survey.
Ipsos MORI online panels were used to recruit respondents – non-probability quota sampling. Quotas set in respect of age, gender and government office region to ensure representativeness.</td></tr>
<tr><td>Number entering into study (invited)</td><td>2916 completing baseline survey</td></tr>
<tr><td>Number of participants evaluated</td><td>After excluding partial responses and those who smoked at baseline, final study sample was 923.
Power not reported</td></tr>
<tr><td>Prognostic factor</td><td><u>Ever use of e-cigarettes:</u> respondents classified as never users of e-cigarettes (never used, not even a puff) or ever users of e-cigarettes. Those who had been never users at baseline but users at follow-up were classed as initiators.

Type of e-cigarette or nicotine content data not collected by survey.</td></tr>
<tr><td>Baseline study sample characteristics</td><td>Characteristics of entire sample at baseline, which also includes those who smoked at baseline.
<table>
<tr><td>Characteristic</td><td>Sample (n = 1152)</td></tr>
<tr><td>Number in each age group
11-13 (%)
14-15 (%)
16--18 (%)</td><td>
438 (38.02)
338 (29.32)
376 (32.64)</td></tr>
<tr><td>Female (%)</td><td>620 (53.82)</td></tr>
<tr><td>Ethnicity</td><td>Not reported</td></tr>
<tr><td>Susceptible to smoking (%)</td><td>146 (12.67)</td></tr>
<tr><td>At least one parent smokes (%)</td><td>343 (29.77)</td></tr>
<tr><td>At least one sibling smokes (%)</td><td>54 (4.69)</td></tr>
<tr><td>Some friends smoke (%)</td><td>727 (63.11)</td></tr>
</table>
*Baseline characteristics combined for both those who had and those who hadn’t used e-cigarettes at baseline (the exposed and unexposed groups)
Original sample representative.</td></tr>
<tr><td>Attrition</td><td>1447 of baseline survey completers did not complete follow-up (50.3%)
Those lost to follow-up differed on most covariates (ever smoking, ever using e-cigs, age 16-18, school performance, alcohol use, susceptibility to using e-cigs, having friends who smoke, having friends who use e-cigs, having siblings who use e-cigs). Those lost to follow up were more likely to have ever smoked or used a cigarette.</td></tr>
</table>

<table>
<tr><td>Bibliographic reference/s</td><td>East Katherine, Hitchman Sara C, Bakolis Ioannis, Williams Sarah, Cheeseman Hazel, Arnott Deborah, and McNeill Ann (2018) The Association Between Smoking and Electronic Cigarette Use in a Cohort of Young People. The Journal of adolescent health : official publication of the Society for Adolescent Medicine 62(5), 539-547</td></tr>
<tr><td>Study name</td><td>East 2018</td></tr>
<tr><td>Inclusion and exclusion criteria</td><td>11-18 years of age.
No exclusion criteria reported.</td></tr>
<tr><td>Data collection</td><td>Respondents invited by email to participants in an online survey about smoking. Up to 8 email reminders sent to maximise follow-up rates. Participants entered into a prize draw as incentive (no further details given). Participants drawn from Ipsos MORI’s online panels – made up of volunteers from the general public and validated by Ipsos MORI. Informed consent provided by parents of those 11-15, or by individuals themselves if aged 16-18.

Data collected for the following measures:
Range of demographic data
Smoking susceptibility (binary, Pierce susceptibility score); smoking among friends, parents, siblings (also repeated for e-cig use among these groups); opinion of whether public approved of smoking or e-cig use (binary).
Blinding not reported.</td></tr>
<tr><td>Outcome measure</td><td><u>Ever use of cigarettes:</u> respondents classified as never users of cigarettes (never smoked, not even a puff) or ever users of cigarettes. Those who had been never users at baseline but users at follow-up were classed as initiators.</td></tr>
<tr><td>Follow up</td><td>4-6 months between baseline (April 2016) and follow up (August – October 2016)
Summarised using lower bound as no summary provided by authors.</td></tr>
<tr><td>Critical outcomes measures and effect size. (time points)</td><td>Smoking initiation
Baseline ever e-cigarette users vs non-users 4 month follow-up among baseline non-smokers
<table>
<tr><td></td><td>Exposed n = 21</td><td>Unexposed n = 902</td><td>aOR* (95% CI)</td><td>aRR** calculated by analyst</td></tr>
<tr><td>Number who had tried smoking at follow-up (%)***</td><td>11 (52.6)</td><td>74 (8.2%)</td><td>10.57 (3.33, 33.50)</td><td>5.92 (2.80, 9.14)</td></tr>
</table>
*Reported by study. Adjusted for XX.
**Calculated by review team. The unexposed group prevalence used to calculate the aRR was 0.082.
***absolute numbers calculated by review team from percentages

The following is not reported:
• Outcome by habitual vs experimental e-cig use at baseline
• Outcome by nicotine vs non-nicotine e-cigs
• Outcome by e-cig type
• Outcome by age category</td></tr>
</table>

Bibliographic reference/s	**East Katherine, Hitchman Sara C, Bakolis Ioannis, Williams Sarah, Cheeseman Hazel, Arnott Deborah, and McNeill Ann (2018) The Association Between Smoking and Electronic Cigarette Use in a Cohort of Young People. The Journal of adolescent health : official publication of the Society for Adolescent Medicine 62(5), 539-547**
Study name	East 2018
	• Outcome by socioeconomic deprivation • Outcome by family / peer smoking presence vs absence.
Important outcomes measures and effect size. (time points)	None reported
Statistical Analysis	Adjusted logistic regression. Weighted data was used – weighting conducted according to age, gender and government office region, and adjusted for attrition on age, gender, GOR ever smoking and ever cigarette use. Adjusted for all variables (age, gender, school performance, problem behaviour, monthly alcohol use, smoking susceptibility, friends smoking, family smoking, views about public approval of smoking and e-cigarettes). Authors report that missing data were excluded listwise from all analyses. Not surveyed by cluster so no adjustments for clustering required.
Risk of bias (ROB) QUIPS tool	Smoking Initiation

Outcome	Judgement	Comments
Study participation	Low	Sample should be representative of source population based on reported survey methods. Sampling frame described. Recruitment online. Inclusion and exclusion criteria somewhat explained.
Study attrition	Moderate	Attrition is high (50%). Respondents lost to follow-up differed substantially from those retained. Information collected from drop outs and analysis controlled.
Prognostic factor management	Moderate	PF well defined and measured consistently for exposed and unexposed. Subjective measure so possible that students were not truthful.
Outcome measurement	Moderate	Outcome well defined and measured consistently for exposed and unexposed. Subjective measure so possible that students were not truthful.

Bibliographic reference/s	**East Katherine, Hitchman Sara C, Bakolis Ioannis, Williams Sarah, Cheeseman Hazel, Arnott Deborah, and McNeill Ann (2018) The Association Between Smoking and Electronic Cigarette Use in a Cohort of Young People. The Journal of adolescent health : official publication of the Society for Adolescent Medicine 62(5), 539-547**		
Study name	East 2018		
			Unlikely to be differential based on PF.
	Study confounding	Moderate	Ethnicity not measured. Differences between exposed and unexposed groups not displayed. Potential that unknown confounders persist.
	Statistical analysis and reporting	Low	No apparent selective reporting of results.
	Overall Risk of Bias	Acceptable	
	Other outcome details: none		
Source of funding	Cancer Research UK UK Public Health Research Consortium		
Comments	- Authors also conduct a causal mediation analysis to estimate a pathway between e-cigarette and cigarette use. This analysis also showed a direct causal effect on smoking of ever e-cigarette use, but no effect of baseline ever e-cig use on smoking initiation mediated by e-cig escalation. - The analysis excluded respondents who responded “prefer not to say” or “don’t know” to the questions about smoking / e-cig use at baseline / follow up (n = 65).		
Additional references	None		

Hallingberg 2019

Bibliographic reference/s	**Hallingberg B,Maynard OM, Bauld L, et al. Tob Control Epub ahead of print: 5 April 2019. doi:10.1136/ tobaccocontrol-2018-054584**
Study name	Hallingberg 2019
Registration	Research registry number: researchregistry4336
Study type	Interrupted time series analysis
Study dates	1998-2015
Objective	To examine whether during a period of limited e-cigarette regulation (prior to the Tobacco Product Directive (TPD) introduction in May 2016) and rapid growth in their use, smoking began to become renormalised among young people.
Country/ Setting	England, Scotland and Wales National surveys
Cohort source	Various surveys: • Smoking Drinking and Drug Use Among Young People in England Survey (SDDU) (annual) • Scottish Adolescent Lifestyle and Substance Use Survey (SALSUS) (biennial)

<table>
<tr><td>Bibliographic reference/s</td><td>Hallingberg B,Maynard OM, Bauld L, et al. Tob Control Epub ahead of print: 5 April 2019. doi:10.1136/ tobaccocontrol-2018-054584</td></tr>
<tr><td>Study name</td><td>Hallingberg 2019</td></tr>
<tr><td></td><td>• Health Behaviour in School-aged Children (HBSC) survey (Wales, from 1998 to 2013 every 2 to 4 years) and the School Health Research Network (SHRN) survey (2015).
• The HBSC survey takes place every 2 to 4 years, with the SHRN survey developed from the 2013 survey and an SHRN survey conducted in 2015 (as of 2017, HBSC is integrated into SHRN survey

All surveys are nationally representative samples of secondary school students. SDDU and HBSC/SHRN is 11-16 year olds; SALSUS is 13 and 15 year olds.</td></tr>
<tr><td>Number entering into study (invited)</td><td>Numbers invited to surveys unknown</td></tr>
<tr><td>Number of participants evaluated</td><td>248,324 young people in the sample</td></tr>
<tr><td>Prognostic factor</td><td>Exposure to e-cigarettes in an unregulated environment (until 2015).
2010 selected as the year e-cigarettes became suddenly popular.</td></tr>
<tr><td>Baseline study sample characteristics</td><td>Characteristics of entire sample<table><tr><td>Characteristics</td><td>Sample (n = 248,324)</td></tr><tr><td>Mean age years (SD)</td><td>Range 11-16</td></tr><tr><td>Female (%)</td><td>Approx 49.8%</td></tr><tr><td>Ethnicity</td><td>Not reported</td></tr><tr><td>Susceptibility to smoking</td><td>Not reported</td></tr><tr><td>Family smoking</td><td>Not reported</td></tr><tr><td>Peer smoking</td><td>Not reported</td></tr></table></td></tr>
<tr><td>Attrition</td><td>Not applicable as data is not panel data.</td></tr>
<tr><td>Inclusion and exclusion criteria</td><td>Inclusion: All participants of the included surveys</td></tr>
<tr><td>Data collection</td><td>SHRN: Survey was online, closed-response, self-complete survey available in English and Welsh. Schools managed implementation using IT facilities. Schools advised to oversee survey-taking.
HBSC: Within each participating school, one mixed ability class (approximately 25 students) from each school year 7–11 was randomly selected by the school to participate. SDDU: Trained fieldworkers attended data collection at schools. Teachers present.
Randomly selected pupils within a school selected. Self-completion paper questionnaire completed with supervision by a NatCen interviewer, in exam conditions
SALSUS: self-completion survey administered by teachers in mixed ability classes under exam conditions. Transitions being made to online.
Variation in survey methods over time.</td></tr>
</table>

<table>
<tr><td>Bibliographic reference/s</td><td>Hallingberg B,Maynard OM, Bauld L, et al. Tob Control Epub ahead of print: 5 April 2019. doi:10.1136/ tobaccocontrol-2018-054584</td></tr>
<tr><td>Study name</td><td>Hallingberg 2019</td></tr>
<tr><td></td><td>Sociodemographic information: sex and school year groups / age collected for participants. SES reported using free school meals (SDDU, SALSUS) or using the Family Affluence Scale (FAS, HBSC, SHRN). Dichotomised.</td></tr>
<tr><td>Outcome measure</td><td>Self-reported ever smoking:
Participants were asked to identify themselves from a list of statements (‘I have never smoked’ coded as never smokers and compared with all other responses) (SDDU, SALSUS).
Participants asked at what age they had smoked a cigarette (more than just a puff). Participants responding never were compared with all others (HBSC/SHRN)
Regular smoking:
Participants reporting smoking between 1 and 6 cigarettes per week, or more (SDDU, SALSUS)
Participants reporting that they smoke at least once a week or more frequently (HBSC/SHRN)</td></tr>
<tr><td>Follow up</td><td>17 year time trend analysis (1998, 2015)</td></tr>
<tr><td>Critical outcomes measures and effect size. (time points)</td><td>Change in rate of decline in ever smoking post-2010

The change in the overall rate of decline for ever smoking was not significant.
i.e. decline in rates of ever smoking did not slow down or speed up significantly more after e-cigs became more prevalent.
<table>
<tr><td></td><td>Group</td><td>aOR (95% CI)</td><td>aRR calculated by analyst</td></tr>
<tr><td rowspan="5">Change of rate of decline in ever smoking post-2010</td><td>Overall</td><td>1.01 (0.99 to 1.03)</td><td>1.00 (0.99, 1.02)</td></tr>
<tr><td>Female subgroup</td><td>1.05 (1.01, 1.08) the decline slowed</td><td>1.03 (1.01, 1.05) the decline slowed</td></tr>
<tr><td>Male subgroup</td><td>0.98 (0.95, 1.01)</td><td>0.99 (0.96, 1.01)</td></tr>
<tr><td>13 year olds</td><td>1.07 (1.03, 1.10) the decline slowed</td><td>1.04 (1.02, 1.07) the decline slowed</td></tr>
<tr><td>15 year olds</td><td>0.96 (0.94, 0.99) the decline increased</td><td>0.97 (0.96, 1.07)</td></tr>
</table>
Authors note that the slowing decline was limited to groups for whom rates had declined rapidly before 2010, indicating a floor effect?

Change in decline in regular smoking post-2010
The change in the rate of decline for regular smoking was not significant.
i.e. decline in rates of regular smoking did not slow down or speed up significantly more after e-cigs became more prevalent.</td></tr>
</table>

<table>
<tr><td>Bibliographic reference/s</td><td colspan="4">Hallingberg B,Maynard OM, Bauld L, et al. Tob Control Epub ahead of print: 5 April 2019. doi:10.1136/ tobaccocontrol-2018-054584</td></tr>
<tr><td>Study name</td><td colspan="4">Hallingberg 2019</td></tr>
<tr><td></td><td colspan="4">
<table>
<tr><td></td><td>Group</td><td>aOR (95% CI)</td><td>aRR calculated by analyst</td></tr>
<tr><td rowspan="5">Change of rate of decline in regular smoking post-2010</td><td>Overall</td><td>1.04 (1.00, 1.08)</td><td>1.03 (1.00, 1.07)</td></tr>
<tr><td>Female subgroup</td><td>1.07 (1.02, 1.12) the decline slowed</td><td>1.06 (1.02, 1.11) the decline slowed</td></tr>
<tr><td>Male subgroup</td><td>1.01 (0.96, 1.06)</td><td>1.01 (0.96, 1.05)</td></tr>
<tr><td>13 year olds</td><td>1.14 (1.06, 1.23) the decline slowed</td><td>1.13 (1.05, 1.21) the decline slowed</td></tr>
<tr><td>15 year olds</td><td>1.01 (0.97, 1.06)</td><td>1.01 (0.97, 1.05)</td></tr>
</table>

To convert to risk ratio, a prevalence was required. The study reports that prevalence of ever smokers was 60% in 1998 and 19% in 2015, and that regular smoking was at 19% in 1998 and 5% in 2015. Under the assumption that the decline was proportionate each year, prevalence in 2010 calculated as 31% (0.31) for ever smoking and 9% (0.09) for regular smoking
</td></tr>
<tr><td>Important outcomes measures and effect size. (time points)</td><td colspan="4">Contextual information:
From 1998 to 2015, among children aged 13 and 15, the percentage of ever smokers decreased from 60% (n=3 792) to 19% (n=6 852) while regular smokers decreased from 19% (n=1 209) to 5% (n=1 618; note 2015 did not include data from England)</td></tr>
<tr><td>Statistical Analysis</td><td colspan="4">Segmented time series regression analyses.
1998: starting time point when youth smoking peaked prior to a decline.
2010: treated as a timepoint for the naturally occurring intervention of e-cigarettes, at which point authors state that surveys identify emergence of e-cigarette use from 2011.
Pre-intervention is 1998-2010, post intervention is 2011-2015.
Year group and sex included as covariates.
Quadratic term added to model to allow for structural departures from linearity.
Extent of non-response low (<2%), so authors conducted analysis on complete-case basis.</td></tr>
<tr><td>Risk of bias (ROB)
QUIPS tool</td><td colspan="4">Change in rate of decline in ever smoking post-2010
<table>
<tr><th>Outcome</th><th>Judgement</th><th>Comments</th></tr>
<tr><td>Study participation</td><td>Moderate</td><td>Sample described as representative. Sampling frame somewhat described (two-stage cluster sampling). Sample not described.</td></tr>
<tr><td>Study attrition</td><td>NA</td><td>Attrition not relevant for study design.</td></tr>
<tr><td>Prognostic factor management</td><td>Moderate</td><td>‘Intervention’ makes assumptions about a point-in-time change when change is likely to be more gradual – but well reasoned.</td></tr>
</table>
</td></tr>
</table>

Bibliographic reference/s	**Hallingberg B,Maynard OM, Bauld L, et al. Tob Control Epub ahead of print: 5 April 2019. doi:10.1136/ tobaccocontrol-2018-054584**		
Study name	Hallingberg 2019		
	Outcome measurement	Moderate	Outcome measured differently across surveys but fairly well matched measures.
	Study confounding	Moderate	Adjusted for sex and year group but not other potential confounders.
	Statistical analysis and reporting	Low	Model well reported and conducted.
	Overall Risk of Bias	Acceptable	
	Other outcome details: Change in rate of decline in regular smoking post-2010: As above		
Source of funding	National Institute for Health Research Centre for the Development and Evaluation of Complex Interventions for Public Health Improvement (DECIPHer) British Heart Foundation, Cancer Research UK, Economic and Social Research Council, Medical Research Council, Welsh Government, Wellcome Trust (under UK Clinical Research Collaboration)		
Comments	- Authors note some slowing in the decline of alcohol and tobacco use which they say may suggest a change in trend was not unique to tobacco use. - Authors point out that survey methods are heterogeneous. - Adjusting for clustering may have led to a change in trends by widening confidence intervals. - Perceived acceptability of smoking behaviour declined faster after 2010		
Additional references	None		

Leventhal 2015

Bibliographic reference/s	**Leventhal Adam M, Strong David R, Kirkpatrick Matthew G, et al (2015) Association of electronic cigarette use with initiation of combustible tobacco product smoking in early adolescence. JAMA: Journal of the American Medical Association 314(7), 700-707**
Study name	Leventhal 2015
Registration	Not reported
Study type	Cohort (prospective)
Study dates	2013 - 2014
Objective	To evaluate whether e-cigarette use among 14-year-olds who have never tried combustible tobacco is associated with risk of initiating use of combustible tobacco products (Leventhal 2015)
Country/ Setting	USA, Los Angeles (California) 10 public high schools
Cohort source	No specific cohort name.

<table>
<tr><td>Bibliographic reference/s</td><td>Leventhal Adam M, Strong David R, Kirkpatrick Matthew G, et al (2015) Association of electronic cigarette use with initiation of combustible tobacco product smoking in early adolescence. JAMA: Journal of the American Medical Association 314(7), 700-707</td></tr>
<tr><td>Study name</td><td>Leventhal 2015</td></tr>
<tr><td></td><td>Cohort is from 10 public high schools in Los Angeles. Following one year group (grade 9, 14-15 years old) from Spring 2013 to Autumn 2015 with 5 6-monthly surveys.</td></tr>
<tr><td>Number entering into study (invited)</td><td>4100 students were eligible
3396 students were enrolled after consent / assent non-providers removed.</td></tr>
<tr><td>Number of participants evaluated</td><td>2530
Power not reported</td></tr>
<tr><td>Prognostic factor</td><td>Lifetime e-cigarette use at baseline (question based on Youth Behaviour Risk Surveillance (YBRS) and Monitoring the Future (MTF) Surveys. Measured by self-report survey.</td></tr>
<tr><td>Baseline study sample characteristics</td><td>[baseline never-smokers]
<table>
<tr><td></td><td>Exposed (n = 222)</td><td>Unexposed (n = 2308)</td><td>Significant difference</td></tr>
<tr><td>Mean age years (95% CI)</td><td>14.10 (14.05,14.15)</td><td>14.05 (14.04, 14.07)</td><td>Yes</td></tr>
<tr><td>Female (%)</td><td>91 (41.4)</td><td>1252 (54.3)</td><td>Yes</td></tr>
<tr><td>Ethnicity</td><td>47.2T Hispanic, 18.7% Asian, 9.8% White, 7% Native Hawaiian / Pacific Islander.</td><td>43.9% Hispanic, 19% Asian, 16.9% White, 4.7% Black / African American</td><td>Yes</td></tr>
<tr><td>Highest parental education (High school graduate or higher n, %)</td><td>169 (76.1)</td><td>1788 (77.4)</td><td>Yes (in spread overall)</td></tr>
<tr><td>Susceptibility to smoking* (M, 95% CI)</td><td>1.22 (1.16, 1.27)</td><td>1.10 (1.09, 1.11)</td><td>Yes</td></tr>
<tr><td>Family smoking (n, %)</td><td>150 (70.8)</td><td>1337 (60.3)</td><td>Yes</td></tr>
<tr><td>Peer smoking** (M, 95% CI)</td><td>0.46 (0.32, 0.59)</td><td>0.20 (0.17, 0.23)</td><td>Yes</td></tr>
</table>
*range 1-4, higher is more susceptible
** range 1-5, higher is more peer smoking
Not reported to be representative – purposive sampling.</td></tr>
<tr><td>Attrition</td><td>28/2558 provided no follow up data at either follow-up time point. Attrition 1.1%.
Authors report those without follow-up data did not differ in baseline e-cig use or sociodemographic characteristics (except age, drop outs were older).</td></tr>
<tr><td>Inclusion and exclusion criteria</td><td>Inclusion criteria: Ninth-grade students who provided active verbal or written assent (and consent provided by parents).English-speaking. Not in special education.
No further exclusion criteria reported.</td></tr>
<tr><td>Data collection</td><td>40 schools approached because of diverse demographic characteristics. 10 schools agreed to participate.</td></tr>
</table>

Bibliographic reference/s	**Leventhal Adam M, Strong David R, Kirkpatrick Matthew G, et al (2015) Association of electronic cigarette use with initiation of combustible tobacco product smoking in early adolescence. JAMA: Journal of the American Medical Association 314(7), 700-707**
Study name	Leventhal 2015
	Data collected through self-report surveys during in-classroom data collection every 6 months. Data collected on prognostic factor, outcome, and covariates. Covariates as follows: Sociodemographic factors: age, gender, ethnicity, and highest parental education were assessed using self-report responses to investigator-defined forced choice items. Family and peer factors: family living situation, measured with the item, "Who do you live with most of the time?" (both biological parents vs. other). Family history of smoking was measured using the question, "Does anyone in your immediate family (brothers/sisters/parents/grandparents) have a history of smoking cigarettes?" (yes/no). Peer smoking was assessed by responses to the item, "In the last 30 days, how many of your five closest friends have smoked cigarettes?" (range: 0–5). Factors potentially associated with trying smoking: depressive symptoms were measured using the 20-item Center for Epidemiologic Studies Depression Scale (CESD) composite sum past week frequency rating (e.g., 0=Rarely or none of the time [0–1 days] to 3=Most or all of the time [5–7 days]). Impulsivity was measured with the 5-item Temperament and Character Inventory Impulsivity subscale sum score, which assesses tendency towards acting on instinct without conscious deliberation. Ever use of non-nicotine/tobacco substances was measured using MTF/YRBS items assessing ever use of alcohol and 13 separate illicit and prescription substances of abuse (use of ≥1 vs. 0 substances). Delinquent behaviour was measured with a mean of frequency ratings for engaging in 11 different behaviours (e.g., stealing, lying to parents; 1=Never to 6=Ten or more times) in the past 6 months. Susceptibility to smoking was measured by a three-item index, averaging responses to "Would you try smoking a cigarette if one of your best friends offered it to you?," "Do you think you would smoke in the next 6 months?," and "Are you curious about smoking?" (1=Definitely Not, 2=Probably Not, 3=Probably Yes, 4=Definitely Yes). Smoking outcome expectancies were assessed using the average of the two responses for "I think I might enjoy…smoking" and (reversed) "I think I might feel bad…from smoking" (1=Strongly Disagree, 2=Disagree, 3=Agree, 4=Strongly Agree).
Outcome measure	Past 6-month combustible tobacco use, even a few puffs (question based on Youth Behaviour Risk Surveillance (YBRS) and Monitoring the Future (MTF) Surveys. Measured by self-report survey (combined result for cigarettes, cigars and waterpipe (shisha)). Separate results also reported
Follow up	6 and 12-month follow up data collected, results presented as averaged across the two follow-ups (estimate for time of data collection not significant, no change in prevalence of tobacco use across follow-u measures).
Critical outcomes measures and	Past 6-month use of combustible tobacco Baseline ever e-cigarette users vs non-users among baseline non-smokers, average of 6- and 12-month follow-up

<table>
<tr><td>Bibliographic reference/s</td><td>Leventhal Adam M, Strong David R, Kirkpatrick Matthew G, et al (2015) Association of electronic cigarette use with initiation of combustible tobacco product smoking in early adolescence. JAMA: Journal of the American Medical Association 314(7), 700-707</td></tr>
<tr><td>Study name</td><td>Leventhal 2015</td></tr>
<tr><td>effect size. (time points)</td><td>
<table>
<tr><td></td><td>Exposed n = 222</td><td>Unexposed n = 2308</td><td>aOR** (95% CI)</td><td>aRR*** calculated by analyst</td></tr>
<tr><td>Number who had tried combustible tobacco at follow-up (%)*</td><td>6 month: 67 (30.7)

12 month: 54 (25.2)</td><td>6 month:182 (8.1)

12 month: 210 (9.3)</td><td>2.73 (2.00, 3.73)</td><td>2.31 (1.81, 2.90)</td></tr>
</table>
*N are slightly different for each time period
**Reported by study. Adjusted for all covariates (see ‘data collection’).
***Calculated by review team. The unexposed group prevalence used to calculate the aRR was 0.104, average of prevalence at 6 and 12 months.
The following is not reported:

Outcome by habitual vs experimental e-cig use at baseline
Outcome by nicotine vs non-nicotine e-cigs
Outcome by e-cig type
Outcome by age category
Outcome by socioeconomic deprivation
Outcome by family / peer smoking presence vs absence.

</td></tr>
<tr><td>Important outcomes measures and effect size. (time points)</td><td>No important outcomes reported.</td></tr>
<tr><td>Statistical Analysis</td><td>Repeated measures generalised linear mixed models (GLMMs) (an extension of logistic regression) was used. All models included baseline e-cig ever-use, school, and time as fixed effects. Reported results are adjusted for all covariates (see ‘data collection’).
Missing data on covariates were accounted for using multiple imputation approach (Markov chain Monte Carlo method).
Clusters were not adjusted for in the analysis.</td></tr>
<tr><td>Risk of bias (ROB) QUIPS tool</td><td>Past 6-month use of combustible tobacco
<table>
<tr><th>Outcome</th><th>Judgement</th><th>Comments</th></tr>
<tr><td>Study participation</td><td>Moderate</td><td>Population characteristics not described. Sample not chosen to be representative, but to be diverse. Baseline sample well described.</td></tr>
<tr><td>Study attrition</td><td>Low</td><td>Very low attrition (<2%). Drop-outs mostly similar.</td></tr>
<tr><td>Prognostic factor management</td><td>Moderate</td><td>PF well defined and measured consistently for exposed and</td></tr>
</table>
</td></tr>
</table>

Bibliographic reference/s	**Leventhal Adam M, Strong David R, Kirkpatrick Matthew G, et al (2015) Association of electronic cigarette use with initiation of combustible tobacco product smoking in early adolescence. JAMA: Journal of the American Medical Association 314(7), 700-707**		
Study name	Leventhal 2015		
			unexposed. Subjective measure so possible that students were not truthful.
	Outcome measurement	Moderate	Outcome well defined and measured consistently for exposed and unexposed. Subjective measure so possible that students were not truthful.
	Study confounding	Moderate	Wide range of possible confounders measured and adjusted for. Authors report that they have adequate psychometric properties.
	Statistical analysis and reporting	Low	No apparent selective reporting of results but results not reported per baseline group.
	Overall Risk of Bias	Acceptable risk of bias	
	Other outcome details: None		
Source of funding	National Institutes of Health.		
Comments	- Authors point out common risk factors for both e-cig and combustible tobacco. E-cig use before tobacco could be due, authors report, to perceived lower harm of e-cigs, availability of flavours etc. Shared risk factors controlled for as far as possible. - Covariates of advertising exposure, sensation seeking and academic performance not explored. - Limitation is that e-cig is any use, with product type not explored.		
Additional references	Barrington-Trimis Jessica L, Kong Grace, Leventhal Adam M, Liu Feifei, Mayer Margaret, Cruz Tess Boley, Krishnan-Sarin Suchitra, and McConnell Rob (2018) E-cigarette Use and Subsequent Smoking Frequency Among Adolescents. Pediatrics 142(6), The above paper reports on the current study and was used for reference only.		

Loukas 2018

Bibliographic reference/s	**Loukas Alexandra, Marti C Nathan, Cooper Maria, Pasch Keryn E, and Perry Cheryl L (2018) Exclusive e-cigarette use predicts cigarette initiation among college students. Addictive behaviors 76, 343-347**
Study name	Loukas 2018
Registration	Not reported
Study type	Cohort (prospective)
Study dates	2014-2016

<table>
<tr><td>Bibliographic reference/s</td><td>Loukas Alexandra, Marti C Nathan, Cooper Maria, Pasch Keryn E, and Perry Cheryl L (2018) Exclusive e-cigarette use predicts cigarette initiation among college students. Addictive behaviors 76, 343-347</td></tr>
<tr><td>Study name</td><td>Loukas 2018</td></tr>
<tr><td>Objective</td><td>To determine whether use of e-cigarettes are associated with future cigarette initiation, and whether this is dependent on baseline non-cigarette tobacco product use.</td></tr>
<tr><td>Country/ Setting</td><td>USA, Texas.
Austin, Dallas, Houston and San Antonio.</td></tr>
<tr><td>Cohort source</td><td>Those taking part on the Marketing and Promotions across Colleges in Texas project (Project M-PACT).
Cohort was made up of students enrolled at one of 24 colleges.</td></tr>
<tr><td>Number entering into study (invited)</td><td>13714 were eligible</td></tr>
<tr><td>Number of participants evaluated</td><td>2558</td></tr>
<tr><td>Prognostic factor</td><td><u>Ever use of e-cigarettes:</u> assessed at baseline with an item adapted from the PATH study, “Have you ever used an ENDS product, (i.e. e-cigarette, vape pen, or e-hookah) as intended (i.e. with nicotine cartridges and/or e-liquid/e-juice), even one or two puffs?” Respondents were considered ever e-cigarette users if they responded “yes” to this question.
Nicotine content and generation of devices not reported.</td></tr>
<tr><td>Baseline study sample characteristics</td><td>Characteristics at baseline
<table>
<tr><td>Characteristics</td><td>Sample* (n = 2558)</td></tr>
<tr><td>Mean age years (SD)</td><td>19.71 (1.61)</td></tr>
<tr><td>Female (%)</td><td>67.7</td></tr>
<tr><td>Ethnicity</td><td>31.8% White, 27.4% Hispanic, 23.4% Asian, 9.8% African American, 7.5% other</td></tr>
<tr><td>Susceptibility to smoking (yes %)</td><td>6.3</td></tr>
<tr><td>Family smoking (yes %)</td><td>52.5</td></tr>
<tr><td>Peer smoking (yes %)</td><td>52.7</td></tr>
<tr><td>Ever e-cigarette use (EXPOSED GROUP) (%)</td><td>22.2</td></tr>
</table>
*characteristics are for those who used and did not use e-cigarettes at baseline combined.
Representativeness not reported</td></tr>
<tr><td>Attrition</td><td>216/2774 (0.94%) completed baseline surveys and did not complete any of the three follow-up surveys. Excluded from analysis

Attrition rates of these 2,558 students were 9.8% at wave 2 (n=2,307 completed), 10.9% at wave 3 (n=2,279 completed), and 8.2% at wave 4 (n=2349 completed).</td></tr>
<tr><td>Inclusion and exclusion criteria</td><td>Participants were included if they were between 18-29 years old (only 18-25 used in analysis due to high proportion of 26-29y/o who had tried smoking) and were attending college or a vocational / technical programme.</td></tr>
<tr><td>Data collection</td><td>Informed consent was sought. Those who provided it completed an online survey to provide information on the predictive factor, outcome, and covariates:</td></tr>
</table>

<table>
<tr><td>Bibliographic reference/s</td><td>Loukas Alexandra, Marti C Nathan, Cooper Maria, Pasch Keryn E, and Perry Cheryl L (2018) Exclusive e-cigarette use predicts cigarette initiation among college students. Addictive behaviors 76, 343-347</td></tr>
<tr><td>Study name</td><td>Loukas 2018</td></tr>
<tr><td></td><td>Socio-demographics: sex, race/ethnicity, age in years, and type of college attended (two-year/four-year).
Cigarette Use Susceptibility: Two items were used to assess the intrapersonal factor of cigarette susceptibility at baseline. Never cigarette users were classified as susceptible to cigarette use if they responded anything other than “definitely not” to the item, “If one of your friends were to offer you these products, would you smoke/use it?” or to the item, “Do you think you will use any of the following in the next 12 months?”
Interpersonal Factors: Family-of-origin tobacco use: asked about smoking in immediate family when the participant were growing up. Any family members with smoking meant family smoking was present. Peer cigarette use was assessed with one item, “How many of your close friends smoke/use cigarettes.” Any friends smoking meant peer smoking was present.
Ever Other Tobacco Use: Baseline ever use of other combustible tobacco products (large cigars/cigarillos/little cigars, hookah) or smokeless tobacco were assessed with items adapted from the Youth Tobacco Survey and the Population Assessment of Tobacco and Health (PATH) Survey (National Institutes of Health, 2015). Ever use, even one or two puffs.
Blinding not reported.</td></tr>
<tr><td>Outcome measure</td><td>Ever Cigarette Use: At follow-up, participants were asked: “How many cigarettes have you smoked in your entire life?” If students indicated cigarette use, they were coded as initiators.</td></tr>
<tr><td>Follow up</td><td>6-18 months (the three follow-up points appear to be merged to provide results)</td></tr>
<tr><td>Critical outcomes measures and effect size. (time points)</td><td>Ever cigarette use
Baseline ever e-cigarette users vs never users (among never cigarette smokers at baseline) 6-18 month follow-up
<table>
<tr><td></td><td>Exposed n = 567*</td><td>Unexposed n = 2000*</td><td>aOR** (95% CI)</td><td>aRR*** *calculated by analyst</td></tr>
<tr><td>Number who initiate cigarette use (%)</td><td>114 (20.1)</td><td>168 (8.4)</td><td>1.36 (1.01, 1.83)</td><td>1.32 (1.01, 1.71)</td></tr>
</table>
*Calculated by review team from percentages
**Reported by study. Adjusted for all covariates listed under ‘data collection’.
***Calculated by review team. The unexposed group prevalence used to calculate the aRR was 0.084.

The following is not reported:
• Outcome by habitual vs experimental e-cig use at baseline
• Outcome by nicotine vs non-nicotine e-cigs
• Outcome by e-cig type
• Outcome by age category
• Outcome by socioeconomic deprivation
• Outcome by family / peer smoking presence vs absence.</td></tr>
</table>

<table>
<tr><td>Bibliographic reference/s</td><td colspan="3">Loukas Alexandra, Marti C Nathan, Cooper Maria, Pasch Keryn E, and Perry Cheryl L (2018) Exclusive e-cigarette use predicts cigarette initiation among college students. Addictive behaviors 76, 343-347</td></tr>
<tr><td>Study name</td><td colspan="3">Loukas 2018</td></tr>
<tr><td>Important outcomes measures and effect size. (time points)</td><td colspan="3">No important outcomes reported</td></tr>
<tr><td>Statistical Analysis</td><td colspan="3">Multivariable, multilevel discreate-time hazard models were fit to evaluate whether ENDS use predicted cigarette initiation over the 1.5 year period. Respondents were nested within the college they attended.

For the outcome among baseline non-cigarette users, baseline variables were entered simultaneously to determine if e-cigarette use uniquely predicted subsequent cigarette initiation over and above the sociodemographic, other tobacco use, intrapersonal and interpersonal variables.</td></tr>
<tr><td>Risk of bias (ROB)
QUIPS tool</td><td colspan="3">Outcome name</td></tr>
<tr><td></td><td>Outcome</td><td>Judgement</td><td>Comments</td></tr>
<tr><td></td><td>Study participation</td><td>High</td><td>Study does not report generalisability to population or population characteristics.</td></tr>
<tr><td></td><td>Study attrition</td><td>High</td><td>No information on drop outs or difference from completers. Reasons for loss to follow up not described.</td></tr>
<tr><td></td><td>Prognostic factor management</td><td>Moderate</td><td>PF well defined, measured consistently across sample. Self-reported.</td></tr>
<tr><td></td><td>Outcome measurement</td><td>Moderate</td><td>Outcome measure well defined, measured consistently across sample. Self-reported.</td></tr>
<tr><td></td><td>Study confounding</td><td>Moderate</td><td>Confounders identified and taken into account in the analysis. Measured consistently across sample.</td></tr>
<tr><td></td><td>Statistical analysis and reporting</td><td>Moderate</td><td>Data not comprehensively reported.</td></tr>
<tr><td></td><td>Overall Risk of Bias</td><td colspan="2">High risk of bias</td></tr>
<tr><td></td><td colspan="3">Other outcome details: None</td></tr>
<tr><td>Source of funding</td><td colspan="3">National Cancer Institute and the Food and Drug Administration (FDA) Center for Tobacco Products.</td></tr>
<tr><td>Comments</td><td colspan="3">- Authors state that results show that e-cig use at baseline is more strongly associated with cigarette smoking initiation among those who have never used any form of tobacco at baseline, than among those who have. Among those who have used another form of tobacco, e-cigarettes was not associated with future cigarette smoking initiation.
- Authors remind that this study is in relation to initiation / onset, not established smoking.</td></tr>
</table>

Bibliographic reference/s	**Loukas Alexandra, Marti C Nathan, Cooper Maria, Pasch Keryn E, and Perry Cheryl L (2018) Exclusive e-cigarette use predicts cigarette initiation among college students. Addictive behaviors 76, 343-347**
Study name	Loukas 2018
Additional references	None

Lozano 2017

Bibliographic reference/s	**Lozano Paula, Barrientos-Gutierrez Inti, Arillo-Santillan Edna, Morello Paola, Mejia Raul, Sargent James D, and Thrasher James F (2017) A longitudinal study of electronic cigarette use and onset of conventional cigarette smoking and marijuana use among Mexican adolescents. Drug and alcohol dependence 180, 427-430**
Study name	Lozano 2017
Registration	Not reported
Study type	Cohort (prospective)
Study dates	2015-2016
Objective	To evaluate whether e-cigarette trial among Mexican youth who had not previously smoked cigarettes increased the likelihood of trial and use of conventional cigarettes at 20-month follow-up
Country/ Setting	Mexico (Mexico City, Guadalajara Monterrey)
Cohort source	No specific cohort name. 60 public middle schools (for children aged 12-15) from the three largest cities in Mexico. They were selected using a stratified, multi=stage random sampling scheme.
Number entering into study (invited)	Around 12,422 participants were invited to take part (calculated from attrition rates provided). Approximately 10,435 completed baseline assessment.
Number of participants evaluated	6574 students were followed up, and of these 4695 had not tried cigarettes, cocaine or marijuana at baseline and had no missing data. Power not reported
Prognostic factor	Trial of e-cigarettes: measured by asking participants via a survey: “Have you ever tried e-cigarettes?” (Y/N). Nicotine content and type of e-cigarette not reported.
Baseline study sample characteristics	Characteristics of baseline never-smokers

Characteristic	Sample* (n = 4695)
Age (%)	
11 to 12	33
13 or more	67
Female (%)	52
Ethnicity	Not reported
Parental education (%)	
Primary	16
Secondary	38
High school	19

Bibliographic reference/s	**Lozano Paula, Barrientos-Gutierrez Inti, Arillo-Santillan Edna, Morello Paola, Mejia Raul, Sargent James D, and Thrasher James F (2017) A longitudinal study of electronic cigarette use and onset of conventional cigarette smoking and marijuana use among Mexican adolescents. Drug and alcohol dependence 180, 427-430**
Study name	Lozano 2017
	<table><tr><td>University Unknown</td><td>19 8</td></tr><tr><td>Sensation seeking** mean (SD)</td><td>2.67 (1.02)</td></tr><tr><td>Susceptibility to smoking</td><td>Not reported</td></tr><tr><td>Parent smoking (%)</td><td>36</td></tr><tr><td>Sibling smoking (%)</td><td>10</td></tr><tr><td>Peer smoking (%)</td><td>23</td></tr><tr><td>Online ‘tobacco product’ advertising (%) Never Sometimes Always</td><td> 53 40 7</td></tr><tr><td>E-cigarette trial (EXPOSED GROUP) (%)</td><td>5</td></tr></table>*Sample combined for baseline ever and never e-cigarette users. **range 1-4, higher scores represent greater sensation seeking. Authors report that the sample of public schools were representative of public schools but were only from three major cities.
Attrition	37% attrition in the whole sample (3861/10435 dropped out, calculated by review team from percentages), attrition in the baseline non-smoking sub-sample not reported. Authors report statistically significant differences between some potentially confounding variables among completers and those lost to follow-up. A sensitivity analysis reported to have shown similar results to the main analysis.
Inclusion and exclusion criteria	Participants who attended middle schools in the named cities and had never tried conventional cigarettes, cocaine or marijuana, and who provided active consent. Exclusion criteria not reported.
Data collection	Parents were given opt-out consent opportunity. Participants were required to provide active consent. Self-administered questionnaires were completed under the supervision of trained research staff unaffiliated with the schools. **Sociodemographic characteristics**: age, sex and parental education, which was defined as the highest level reported for either parent (i.e., primary, secondary, high school, university, unknown) . **Social network smoking behaviour**: parent smoker (either vs. none), sibling smoker (any vs. none), smoking among close friends (any vs. none). **Personal risk factors**: included a four-item scale of sensation seeking (i.e., “I like to do frightening things”; alpha= .80), previously validated for Mexican youth; trial of alcohol; binge drinking (more than 3 alcoholic beverages in the last 30 days); trial of drugs (ever use of marijuana, cocaine). **Internet tobacco product advertising:** was queried with a general question that could capture either e-cigarette or conventional cigarette advertising (“When you are on the internet, how often do you see tobacco advertising?”). This was included because the internet is likely the primary mode to encounter e-cigarette information and marketing in countries where e-cigarettes are banned.

<table>
<tr><td>Bibliographic reference/s</td><td>Lozano Paula, Barrientos-Gutierrez Inti, Arillo-Santillan Edna, Morello Paola, Mejia Raul, Sargent James D, and Thrasher James F (2017) A longitudinal study of electronic cigarette use and onset of conventional cigarette smoking and marijuana use among Mexican adolescents. Drug and alcohol dependence 180, 427-430</td></tr>
<tr><td>Study name</td><td>Lozano 2017</td></tr>
<tr><td></td><td>Blinding not reported.</td></tr>
<tr><td>Outcome measure</td><td>Trial of Conventional Cigarettes: Participants were asked: “Have you ever tried or experimented with cigarette smoking, even one or two puffs?” (yes/no).
Conventional Cigarette Use: To measure current smoking, students were asked: “During the past 30 days, on how many days did you smoke cigarettes?”, with current smokers defined as those who reported smoking at least once.</td></tr>
<tr><td>Follow up</td><td>20 months</td></tr>
<tr><td>Critical outcomes measures and effect size. (time points)</td><td>Trial of cigarettes
Baseline ever e-cigarette users vs never users (among never cigarette smokers at baseline) 20 month follow-up
<table>
<tr><td></td><td>Exposed n = 235</td><td>Unexposed n = 4460</td><td>aRR*</td></tr>
<tr><td>Number who tried smoking (%)</td><td>101 (43)</td><td>1070 (24)</td><td>1.41 (1.18, 1.70)</td></tr>
</table>
*Reported by study. Adjusted for sex, age, parent SES, sensation seeking, friends that smoke, parents that smoke, siblings that smoke, tried alcohol, binge drinking and internet tobacco product advertising.

The following is not reported:
Outcome by habitual vs experimental e-cig use at baseline
Outcome by nicotine vs non-nicotine e-cigs
Outcome by e-cig type
Outcome by age category
Outcome by socioeconomic deprivation
Outcome by family / peer smoking presence vs absence.</td></tr>
<tr><td>Important outcomes measures and effect size. (time points)</td><td>No important outcomes reported</td></tr>
<tr><td>Statistical Analysis</td><td>Generalised estimating equations (GEE) were used to account for clustering.
Trial and current use of conventional cigarettes was regressed on e-cigarette trial at baseline.
Models were adjusted for: sex, age, parent SES, sensation seeking, friends that smoke, parents that smoke, siblings that smoke, tried alcohol, binge drinking and internet tobacco product advertising.
Missing data was removed, no further information provided on how missing data was dealt with.</td></tr>
<tr><td>Risk of bias (ROB)
QUIPS tool</td><td>Outcome name
<table>
<tr><th>Outcome</th><th>Judgement</th><th>Comments</th></tr>
</table></td></tr>
</table>

Bibliographic reference/s	**Lozano Paula, Barrientos-Gutierrez Inti, Arillo-Santillan Edna, Morello Paola, Mejia Raul, Sargent James D, and Thrasher James F (2017) A longitudinal study of electronic cigarette use and onset of conventional cigarette smoking and marijuana use among Mexican adolescents. Drug and alcohol dependence 180, 427-430**		
Study name	Lozano 2017		
	Study participation	Low	Authors state that the sample is representative of middle schools in the three cities in Mexico. Data presented for sample but not population. Inclusion and exclusion criteria given.
	Study attrition	Moderate	Fairly high attrition between baseline and follow-up (37%) although authors state that sensitivity analysis using propensity score analysis shows similar direction and magnitude of effect. Drop outs not described.
	Prognostic factor management	Moderate	PF well defined, measured consistently across sample. Self-reported.
	Outcome measurement	Moderate	Outcome measure well defined, measured consistently across sample. Self-reported.
	Study confounding	Moderate	Key confounders are identified and measured. Measured consistently for all participants. Accounted for in analysis. Susceptibility to smoking not included, but advertising exposure included.
	Statistical analysis and reporting	High	Results for the second outcome measure (use of cigarettes in past 30 days) not reported.
	Overall Risk of Bias	High risk of bias	
	Other outcome details: None		
Source of funding	Fogarty International Center and the National Cancer Institute of the United States' National Institute of Health		
Comments	- Authors also measured past 30 day cigarette use (see 'data collection') but did not present results for this outcome. - One of the few studies which takes into account a measure of exposure to cigarettes and e-cigarettes (through advertising measure) and controls for it.		
Additional references	None		

Miech 2017

Bibliographic reference/s	**Miech Richard, Patrick Megan E, O'Malley Patrick M, and Johnston Lloyd D (2017) E-cigarette use as a predictor of cigarette smoking: results from a 1-year follow-up of a national sample of 12th grade students. Tobacco control 26(e2), e106-e111**
Study name	Miech 2017
Registration	Not reported
Study type	Cohort (prospective)
Study dates	2014-2015
Objective	To prospectively examine e-cigarette use as a predictor of future cigarette smoking among youth without any previous cigarette smoking experience
Country/ Setting	USA, nationwide survey
Cohort source	Monitoring the Future (MTF) study Classroom questionnaires used since 1975 to survey nationally representative samples of US 12-th graders (age 17-18) across 48 states. Target sample is all schools with 25 or more students enrolled in 12th grade.
Number entering into study (invited)	122 schools surveyed in 2014 (105 public, 17 private). 13015 participants at baseline (82% response rate. Random 2/3 received questions on e-cigarette use. Of this sample, a random 1,643 were selected for this study. 822 individuals.
Number of participants evaluated	347 participants completed follow-up surveys for evaluation Power not reported.
Prognostic factor	Recent vaping: Participants were asked "during the last 30 days, on how many days (if any) have you used electronic cigarettes (e-cigarettes)?" Those who answered 1 or more were classified as recent vapers. Nicotine content or generation of e-cigarettes not reported.
Baseline study sample characteristics	Characteristics among baseline sample (includes both those who have and have not ever smoked) Characteristics / Sample (n = 347) Mean age years (mode) / 19 Female (%, SE) / 56.26 (2.80) Ethnicity (%) / Non-white 38.89 (2.77) Susceptibility to smoking* / Not reported Sees great risk in smoking* (%, SE) / 80.88 (2.28) Family smoking / Not reported Peer smoking / Not reported Recently vaped (during past 30 days) (%, SE) / 15.60 (1.97) Recently smoked (during past 30 days) (%, SE) / 10.13 (1.68) *Perceived risk in smoking is considered by the authors to be a measure of susceptibility to smoking.
Attrition	58% attrition. 475/822 did not complete the follow-up survey. Drop outs not discussed.

<table>
<tr><td>Bibliographic reference/s</td><td>Miech Richard, Patrick Megan E, O'Malley Patrick M, and Johnston Lloyd D (2017) E-cigarette use as a predictor of cigarette smoking: results from a 1-year follow-up of a national sample of 12th grade students. Tobacco control 26(e2), e106-e111</td></tr>
<tr><td>Study name</td><td>Miech 2017</td></tr>
<tr><td>Inclusion and exclusion criteria</td><td>Not reported</td></tr>
<tr><td>Data collection</td><td>Not reported by authors, but Monitoring the Future website states that participants are given flyers explaining the study, and letters are sent to parents (opt-out approach). Local Institute for Social Research representatives conduct and monitor the questionnaire following standardised procedures. Questionnaires are classroom based. Follow-up questionnaires are mailed with a small monetary gift.
Blinding not reported.</td></tr>
<tr><td>Outcome measure</td><td>Smoking initiation: participants were asked “what best describes your cigarette smoking in the last 12 months?”. Participants that answered “smoked once of twice” or more were considered initiators.</td></tr>
<tr><td>Follow up</td><td>13 months (average over participants)</td></tr>
<tr><td>Critical outcomes measures and effect size. (time points)</td><td>Smoking initiation
Baseline recent (past 30-day) e-cigarette users vs non recent-users (baseline never-cigarette users) 13 month follow-up
<table>
<tr><td></td><td>Exposed n = 54*</td><td>Unexposed n = 293*</td><td>aRR** (95% CI)</td></tr>
<tr><td>Number who smoke n (%)</td><td>17* (31)</td><td>21* (7)</td><td>4.78 (1.91, 11.96)</td></tr>
</table>
*Calculated by review team from percentages
**Reported by study. Adjusted for sex, ethnicity, binge drinking in the past 2 weeks, marijuana use in the past 30 days.

The following is not reported:
Outcome by habitual vs experimental e-cig use at baseline
Outcome by nicotine vs non-nicotine e-cigs
Outcome by e-cig type
Outcome by age category
Outcome by socioeconomic deprivation
Outcome by family / peer smoking presence vs absence</td></tr>
<tr><td>Important outcomes measures and effect size. (time points)</td><td>No important outcomes reported</td></tr>
<tr><td>Statistical Analysis</td><td>Missing data: analysis used multiple imputation with 20 imputed data sets. Missing data was uncommon, so imputation had little effect on study results.
Multivariable models controlled sex, ethnicity, binge drinking in the past 2 weeks, marijuana use in the past 30 days.
Cluster not adjusted for.</td></tr>
<tr><td></td><td>Smoking initiation</td></tr>
</table>

Bibliographic reference/s	**Miech Richard, Patrick Megan E, O'Malley Patrick M, and Johnston Lloyd D (2017) E-cigarette use as a predictor of cigarette smoking: results from a 1-year follow-up of a national sample of 12th grade students. Tobacco control 26(e2), e106-e111**		
Study name	Miech 2017		
Risk of bias (ROB) QUIPS tool	**Outcome**	**Judgement**	**Comments**
	Study participation	Moderate	Authors report that non-response did not lead to a substantial upward or downward bias of the study's prevalence estimates for smoking and vaping in comparison to other nationally representative, school-based surveys. Other characteristics not considered. Sampling frame somewhat described. Baseline sample somewhat described.
	Study attrition	High	High attrition (>50%). Limited investigation of drop outs.
	Prognostic factor management	Moderate	PF moderately well defined. Measured consistently for exposed and unexposed. Subjective measure so possible that students were not truthful.
	Outcome measurement	Moderate	Outcome moderately well defined. Measured consistently for exposed and unexposed. Subjective measure so possible that students were not truthful.
	Study confounding	High	Difference in confounders between unexposed and exposed groups not reported. Stratification reportedly carried out and showed proportionate amounts of various confounders in each group but detailed reporting not conducted.
	Statistical analysis and reporting	Moderate	No apparent selective reporting of results but reporting is not comprehensive.
	Overall Risk of Bias	High	
	Other outcome details: None		
Source of funding	National Institute on Drug Abuse (part of National Institutes of Health)		
Comments	Authors state that their data do not contain specific questions related to tobacco use such as smoking susceptibility, smoking expectations, rebelliousness, affiliation with smokers in the community, and perception of friends' attitudes toward smoking. Such questions would allow more comprehensive, statistical control of the predisposition of youth to smoke cigarettes.		

Bibliographic reference/s	**Miech Richard, Patrick Megan E, O'Malley Patrick M, and Johnston Lloyd D (2017) E-cigarette use as a predictor of cigarette smoking: results from a 1-year follow-up of a national sample of 12th grade students. Tobacco control 26(e2), e106-e111**
Study name	Miech 2017
Additional references	None

Morgenstern 2018

Bibliographic reference/s	**Morgenstern Matthis, Nies Alina, Goecke Michaela, and Hanewinkel Reiner (2018) E-Cigarettes and the Use of Conventional Cigarettes. Deutsches Arzteblatt international 115(14), 243-248**
Study name	Morgenstern 2018
Registration	This study was registered with the German Registry of Clinical Studies (DRKS-ID: DRKS00009424).
Study type	Cohort (prospective) investigated as part of a cluster RCT
Study dates	2015-2016
Objective	To determine whether use of e-cigarettes by young people at baseline can motivate to start smoking conventional cigarettes
Country/ Setting	Germany, Lower Saxony and Schleswig-Holstein (North West) 196 classes from 61 schools.
Cohort source	Not a named cohort Cohort from a cluster RCT across schools in two districts in Germany, participants can be aged 14-18.
Number entering into study (invited)	4163 students were surveyed at baseline, and of these 2358 had never tried cigarettes at baseline.
Number of participants evaluated	Of the 2358, 2186 were able to be followed up and analysed. Power not reported.
Prognostic factor	Ever e-cigarette use: Participants were asked whether they had ever used e-cigarettes (Y/N) Nicotine content and generation of e-cigarette not reported
Baseline study sample characteristics	Characteristics among baseline sample (includes those who have and haven't used e-cigarettes)

Characteristic*	Sample (n = 2186)
Mean age years (SD)	15.49 (0.65)
Female (%)	53.6
Ethnicity (% with no migration background)**	76.3
Parents qualifications (completing secondary education) (%)	48.8
SES*** (mean, SD)	5.99 (1.52)
Susceptibility to smoking	Not reported
Family smoking	Not reported
Peer smoking	Not reported
Sensation seeking (mean, SD)	-0.2 (1)

<table>
<tr><td>Bibliographic reference/s</td><td>Morgenstern Matthis, Nies Alina, Goecke Michaela, and Hanewinkel Reiner (2018) E-Cigarettes and the Use of Conventional Cigarettes. Deutsches Arzteblatt international 115(14), 243-248</td></tr>
<tr><td>Study name</td><td>Morgenstern 2018</td></tr>
<tr><td></td><td><table><tr><td>Ever used e-cigarettes (EXPOSED GROUP) (n, %)</td><td>313 (14.3)</td></tr></table>*impulsivity, anxiety sensitivity, hopelessness, extraversion, agreeableness, conscientiousness, neuroticism, openness, alcohol use, binge drinking, cannabis ues and other illegal drug use also measured
** Approximated by country of birth, language spoken at home and religion
*** range 1-10, higher score is higher status (assumed)

Representativeness of sample not reported</td></tr>
<tr><td>Attrition</td><td>172/2358 were lost to follow up (7.3%).
Those lost to follow up were different from completers in their: migration background, sensation seeking, impulsivity, hopelessness, extraversion, e-cigarette use, cannabis use, other illegal drug use at baseline.</td></tr>
<tr><td>Inclusion and exclusion criteria</td><td>Students in 10th grade in one of the identified schools who had never tried conventional cigarettes. Exclusion criteria not described.</td></tr>
<tr><td>Data collection</td><td>Survey method (online, in class etc.) not reported.
The following sociodemographic characteristics were collected: age, sex, type of school attended, the German federal state, and participation in the alcohol prevention program “Keep a Clear Head”, as well as country of birth (mother, father, self), the language predominately spoken at home, and religion. As an indicator of socio - economic status, information about the parents’ school-leaving qualification was obtained. This was complemented by data on self-rated socioeconomic status which were collected using a 10-step scale. Respondents were asked to position themselves in comparison to people living in Germany (1 = ”people with the least money, lowest education, worst jobs or jobless“, 10 = ”people with the most money, highest education, best jobs“).
Five personality traits (extraversion, conscientiousness, agreeableness, neuroticism, and openness) were measured, using 10 items.
The Substance Use Risk Profile Scale (SURPS) was used, covering 4 distinct personality constructs (hopelessness, anxiety sensitivity, sensation seeking, impulsivity).</td></tr>
<tr><td>Outcome measure</td><td>Ever smoking cigarettes: Participants were asked “How many cigarettes have you smoked in your life so far?”. Those responding anything other than “none” (other options are only a few puffs, 1-19, 20-100, more than 100) assumed by review team to have been defined as ever smoking.
Blinding not reported</td></tr>
<tr><td>Follow up</td><td>6 months</td></tr>
<tr><td>Critical outcomes measures and effect size. (time points)</td><td>Ever cigarette use
Baseline ever e-cigarette users vs never-users (baseline never-cigarette users) 6 month follow-up<table><tr><td></td><td>Exposed n = 313</td><td>Unexposed n = 1873</td><td>aRR* (95% CI)</td></tr></table></td></tr>
</table>

Bibliographic reference/s	**Morgenstern Matthis, Nies Alina, Goecke Michaela, and Hanewinkel Reiner (2018) E-Cigarettes and the Use of Conventional Cigarettes. Deutsches Arzteblatt international 115(14), 243-248**
Study name	Morgenstern 2018

Number who have tried smoking smoke (%)	68*** (21.6)	185** (9.9)	2.18 (1.68, 2.83)

*Reported by study. Adjusted for sociodemographic, personality traits, substance use.

**Calculated by review team. The unexposed group prevalence used to calculate the aRR was sociodemographic, personality traits, substance use.

*** Calculated by review team.

The following is not reported:

- Outcome by habitual vs experimental e-cig use at baseline
- Outcome by nicotine vs non-nicotine e-cigs
- Outcome by e-cig type
- Outcome by age category
- Outcome by socioeconomic deprivation
- Outcome by family / peer smoking presence vs absence.

Important outcomes measures and effect size. (time points)	No important outcomes reported
Statistical Analysis	Multiple regression model (Poissons regressions with robust error variances) which included all variables (sociodemographic, personality traits, substance use) was used to determine the main effect. Clustering was adjusted for using random axis intercepts for the class and school level. Authors report that random effects were not significant, so they were eliminated.
Risk of bias (ROB) QUIPS tool	Ever cigarette use

Outcome	Judgement	Comments
Study participation	High	Source population not described, and representativeness of sample not explored. Sample key characteristics described (but not according to exposure). Authors report an 84.5% response rate at baseline.
Study attrition	Low	Attrition is low (7.3%). Those lost to follow up described in relation to the sample completing the study. Differences are significant but are controlled for in the analysis. Drop outs had less often used e-cigarettes which could affect precision.

Bibliographic reference/s	**Morgenstern Matthis, Nies Alina, Goecke Michaela, and Hanewinkel Reiner (2018) E-Cigarettes and the Use of Conventional Cigarettes. Deutsches Arzteblatt international 115(14), 243-248**		
Study name	Morgenstern 2018		
	Prognostic factor management	Moderate	PF well defined. Measured consistently for exposed and unexposed. Subjective measure so possible that students were not truthful.
	Outcome measurement	Moderate	Outcome well defined. Measured consistently for exposed and unexposed. Subjective measure so possible that students were not truthful.
	Study confounding	High	Some key confounders not measured: but not family and peer levels of smoking. Other confounders well measured and controlled for in the analysis. Differences in confounder measures between exposed and unexposed groups not reported.
	Statistical analysis and reporting	Low	No selective reporting of results apparent.
	Overall Risk of Bias	High risk of bias	
	Other outcome details: None		
Source of funding	Federal Center for health Education on behalf of the Federal Ministry for Health		
Comments	- Authors do not account for levels of smoking in family or friends, which could confound the results. - Ever smoking may not be a close indicator for future regular smoking. - Authors report that nicotine-containing liquids are used by about one third of the e-cigarette consuming adolescents in Germany (based on national surveys) but nicotine in this study is not reported.		
Additional references	None		

Primack 2015

Bibliographic reference/s	**Primack Brian A, Soneji Samir, Stoolmiller Michael, Fine Michael J, and Sargent James D (2015) Progression to Traditional Cigarette Smoking After Electronic Cigarette Use Among US Adolescents and Young Adults. JAMA pediatrics 169(11), 1018-23**
Study name	Primack 2015
Registration	Not reported
Study type	Cohort (prospective)
Study dates	2012-2104

<table>
<tr><td>Bibliographic reference/s</td><td>Primack Brian A, Soneji Samir, Stoolmiller Michael, Fine Michael J, and Sargent James D (2015) Progression to Traditional Cigarette Smoking After Electronic Cigarette Use Among US Adolescents and Young Adults. JAMA pediatrics 169(11), 1018-23</td></tr>
<tr><td>Study name</td><td>Primack 2015</td></tr>
<tr><td>Objective</td><td>To determine whether baseline use of e-cigarettes among non-smoking and non-susceptible adolescents and young adults is associated with subsequent progression along an established trajectory to traditional smoking.</td></tr>
<tr><td>Country/ Setting</td><td>USA (national sample)</td></tr>
<tr><td>Cohort source</td><td>Dartmouth Media, Advertising and Health Study</td></tr>
<tr><td>Number entering into study (invited)</td><td>728 participants completed baseline survey</td></tr>
<tr><td>Number of participants evaluated</td><td>After imputing missing data and fixing recanting, sample was 694.
Authors state that power was limited.</td></tr>
<tr><td>Prognostic factor</td><td>Ever use of e-cigarettes: participants were asked whether they had ever used an e-cigarettes and those who had were counted as ever-users.
Nicotine content and generation of e-cigarettes not reported.</td></tr>
<tr><td>Baseline study sample characteristics</td><td>Characteristics of sample at baseline.
<table>
<tr><td></td><td>Exposed (n = 16)</td><td>Unexposed (n = 678)</td><td>Significant difference</td></tr>
<tr><td>Mean age years (SD)</td><td>19.5 (2.0)</td><td>20.0 (2.4)</td><td>No</td></tr>
<tr><td>Female (%)</td><td>5 (31.3)</td><td>369 (54.4)</td><td>No</td></tr>
<tr><td>Ethnicity</td><td>Non-Hispanic white 75%, non-Hispanic black 6.3%, Hispanic 6.3%, other 12.5%.</td><td>Non-Hispanic white 76.5%, non-Hispanic black 6.8%, Hispanic 7.7%, other 9.0%.</td><td>No</td></tr>
<tr><td>Susceptibility to smoking</td><td colspan="3">All participants non-susceptible</td></tr>
<tr><td>Family smoking (parents)*</td><td>0.44 (0.81)</td><td>0.44 (0.74)</td><td>No</td></tr>
<tr><td>Peer smoking**</td><td>0.94 (0.85)</td><td>0.74 (0.66)</td><td>No</td></tr>
<tr><td>Maternal education level***, mean (SD)</td><td>7.5 (1.8)</td><td>6.8 (2.5)</td><td>No</td></tr>
<tr><td>Sensation seeking tendency, mean (SD)</td><td>2.6 (0.5)</td><td>2.1 (0.5)</td><td>Yes</td></tr>
</table>
*range 0-3, 0 never smoker, 1 former smoker, 2 nondaily smoker, 3 daily smoker.
**range 0-3, higher number is greater proportion of friends who smoke
***range 1-10, higher is more advanced.
Authors state that baseline sample is not nationally representative but that rates of tobacco use in sample were similar to national estimates.</td></tr>
<tr><td>Attrition</td><td>30.4% (221/728 baseline completers did not complete follow-up survey).
Loss to follow-up was associated with being male, being older, and parental smoking.</td></tr>
<tr><td>Inclusion and exclusion criteria</td><td>Participants had to be never smokers who were not susceptible to smoking at baseline. Judged by responding definitely no when asked if they would try a cigarette if offered by a friend, and when asked if they think they will try a</td></tr>
</table>

<table>
<tr><td>Bibliographic reference/s</td><td>Primack Brian A, Soneji Samir, Stoolmiller Michael, Fine Michael J, and Sargent James D (2015) Progression to Traditional Cigarette Smoking After Electronic Cigarette Use Among US Adolescents and Young Adults. JAMA pediatrics 169(11), 1018-23</td></tr>
<tr><td>Study name</td><td>Primack 2015</td></tr>
<tr><td></td><td>cigarette in the next year (other options: probably no, probably yes, definitely yes).
Exclusion criteria not reported.</td></tr>
<tr><td>Data collection</td><td>Participants over 18 provided verbal consent, those under 18 provided parental verbal informed consent. Survey is internet-based and described as a visual survey.
Data collected for predictive factor, outcomes and covariates as follows:
Demographic factors: sex, age, ethnicity, maternal education level (range 0 [did not complete eighth grade] to 10 [completed a graduate or professional degree]).
Other measures:
Sensation-seeking tendency: based on 6 items, such as “I like to do dangerous things”
Parental smoking was assessed as never (0), former (1), occasional (2), and daily (3), and scores for mothers and fathers were averaged.
Peer smoking: Participants were asked how many of the respondents' close friends smoked cigarettes, with response choices of none (0), few (1), more than a few (2), or most (3).
Blinding not reported.</td></tr>
<tr><td>Outcome measure</td><td>Initiating smoking: participants who have smoked at least one puff of a cigarette in their lifetime.
Susceptibility to smoking: Participants who become susceptible to smoking at follow-up [extracted as similar to ‘intention to smoke’ which is an important outcome]. Susceptibility to future smoking was assessed with 2 items: “If one of your friends offered you a cigarette, would you try it?” and “Do you think you will smoke a cigarette sometime in the next year?” Responses included “definitely yes,” “probably yes,” “probably no,” and “definitely no.” Those who responded “definitely no” to both measures are considered non-susceptible never smokers.</td></tr>
<tr><td>Follow up</td><td>12 months</td></tr>
<tr><td>Critical outcomes measures and effect size. (time points)</td><td>Smoking initiation
Baseline ever e-cigarette users vs never e-cigarette users (baseline non-susceptible never smokers only) 1-year follow-up
<table>
<tr><td></td><td>Exposed n = 16</td><td>Unexposed n = 678</td><td>aOR* (95% CI)</td><td>aRR** calculated by analyst</td></tr>
<tr><td>Number who have initiated smoking (%)</td><td>6 (37.5)</td><td>65 (9.6)</td><td>8.3 (1.2, 58.6)</td><td>4.88 (1.18, 8.97)</td></tr>
</table>
*Reported by study. Adjusted for age, sex, ethnicity maternal educational level, sensation-seeking tendency, parental smoking, peer smoking.
**Calculated by review team. The unexposed group prevalence used to calculate the aRR was 0.096.</td></tr>
<tr><td>Important outcomes measures and effect size. (time points)</td><td>Susceptibility to smoking
Baseline ever e-cigarette users vs never e-cigarette users (baseline non-susceptible never smokers only) 1-year follow-up</td></tr>
</table>

<table>
<tr><td>Bibliographic reference/s</td><td>Primack Brian A, Soneji Samir, Stoolmiller Michael, Fine Michael J, and Sargent James D (2015) Progression to Traditional Cigarette Smoking After Electronic Cigarette Use Among US Adolescents and Young Adults. JAMA pediatrics 169(11), 1018-23</td></tr>
<tr><td>Study name</td><td>Primack 2015</td></tr>
<tr><td></td><td>
<table>
<tr><td></td><td>Exposed n = 16</td><td>Unexposed n = 678</td><td>aOR* (95% CI)</td><td>aRR** calculated by analyst</td></tr>
<tr><td>Number who are susceptible to smoking (%)</td><td>5 (31.3)</td><td>63 (9.3)</td><td>8.5 (1.3, 57.2)</td><td>5.01 (1.26, 9.19)</td></tr>
</table>
*Reported by study. Adjusted for age, sex, ethnicity maternal educational level, sensation-seeking tendency, parental smoking, peer smoking.
**Calculated by review team. The unexposed group prevalence used to calculate the aRR was 0.093.

The following is not reported:
Outcome by habitual vs experimental e-cig use at baseline
Outcome by nicotine vs non-nicotine e-cigs
Outcome by e-cig type
Outcome by age category
Outcome by socioeconomic deprivation
Outcome by family / peer smoking presence vs absence.</td></tr>
<tr><td>Statistical Analysis</td><td>Statistical Analysis: Multinomial logistic regression model was used. Adjusted for age, sex, ethnicity, maternal educational level, sensation-seeking tendency, parental smoking, peer smoking.
Missing data: results from 32 imputed data sets using a chained equation approach were combined. Imputation model carried out to 25 iterations. Contradictory reports (i.e. current smoker at baseline and never smoker at follow-up) addressed by assuming reports were accurate until a participant contradicted themselves.</td></tr>
<tr><td>Risk of bias (ROB)
QUIPS tool</td><td>Smoking initiation
<table>
<tr><th>Outcome</th><th>Judgement</th><th>Comments</th></tr>
<tr><td>Study participation</td><td>High</td><td>Authors state that baseline sample is not nationally representative. Source population not described. Sample described.</td></tr>
<tr><td>Study attrition</td><td>Moderate</td><td>Attrition is moderately high (30%) and authors report that those lost to follow-up were systematically different from those continuing. Data imputation attempted to minimise this.</td></tr>
<tr><td>Prognostic factor management</td><td>Moderate</td><td>Fairly well defined PF. Self-reported. Measured consistently across groups. Good proportion of data on PF.</td></tr>
<tr><td>Outcome measurement</td><td>Moderate</td><td>Outcome well defined and measured consistently for</td></tr>
</table></td></tr>
</table>

Bibliographic reference/s	**Primack Brian A, Soneji Samir, Stoolmiller Michael, Fine Michael J, and Sargent James D (2015) Progression to Traditional Cigarette Smoking After Electronic Cigarette Use Among US Adolescents and Young Adults. JAMA pediatrics 169(11), 1018-23**		
Study name	Primack 2015		
			exposed and unexposed. Subjective measure so possible that students were not truthful.
	Study confounding	Moderate	Collects data for and adjusts for many of the important confounders identified. Measurements consistent across exposed and unexposed.
	Statistical analysis and reporting	Low	No apparent selective reporting of results.
	Overall Risk of Bias	High risk of bias	
	Other outcome details: Susceptibility to smoking: as above		
Source of funding	National Cancer Institute and National Center for Advancing Translational Sciences		
Comments	- Participants received $25 for completion of the survey at each wave. - Sample is only those who are not susceptible to smoking (using study measure). - Authors explain that although the risk of smoking is elevated, the size of the population (young people using e-cigarettes) may be relatively small (2.3% of the overall sample in this study). - Authors state that at the time of the study there were no regulations on age limits of sale of e-cigarettes, restrictions on marketing etc. - Study did not include outcomes of established smoking		
Additional references	None		

Primack 2018

Bibliographic reference/s	**Primack Brian A, Shensa Ariel, Sidani Jaime E, Hoffman Beth L, Soneji Samir, Sargent James D, Hoffman Robert M, Fine Michael J (2018) Initiation of traditional cigarette smoking after electronic cigarette use among tobacco-naïve US young adults. The American Journal of Medicine 131, 443.e1-443.e9**
Study name	Primack 2018
Registration	Not reported
Study type	Cohort (prospective)
Study dates	2013-2014
Objective	To determine the association between baseline e-cigarette use and initiation of cigarette smoking among a nationally representative population of young adults who never smoked cigarettes.
Country/ Setting	USA (Nationally representative sample)
Cohort source	Growth from Knowledge market research institute

<table>
<tr><td>Bibliographic reference/s</td><td>Primack Brian A, Shensa Ariel, Sidani Jaime E, Hoffman Beth L, Soneji Samir, Sargent James D, Hoffman Robert M, Fine Michael J (2018) Initiation of traditional cigarette smoking after electronic cigarette use among tobacco-naïve US young adults. The American Journal of Medicine 131, 443.e1-443.e9</td></tr>
<tr><td>Study name</td><td>Primack 2018</td></tr>
<tr><td>Number entering into study (invited)</td><td>1,506 participants represented the baseline sample</td></tr>
<tr><td>Number of participants evaluated</td><td>915 participants completed follow-up and included in analysis.
Authors state that power was limited due to a small number of e-cigarette smokers at baseline.</td></tr>
<tr><td>Prognostic factor</td><td>Ever use of an e-cigarette: participants were asked whether they had ever used an e-cigarettes and those who responded yes were counted as ever-users.
Nicotine content and generation of e-cigarettes not reported.</td></tr>
<tr><td>Baseline study sample characteristics</td><td>Characteristics of sample at baseline (unweighted)
<table>
<tr><td></td><td>Exposed (n = 16)</td><td>Unexposed (n = 899)</td><td>Significant difference</td></tr>
<tr><td>Age years (%)</td><td>18-20 =31.3
21-23 = 31.3
24-26 = 25.0
27-30 = 12.5</td><td>18-20 = 21.6
21-23 = 32.7
24-26 = 24.1
27-30 = 21.6</td><td>No</td></tr>
<tr><td>Female (%)</td><td>56.3</td><td>61.7</td><td>No</td></tr>
<tr><td>Ethnicity*</td><td>White, non-Hispanic 31.3%, Black, non-Hispanic 18.8%, Hispanic 18.8%, Other 31.3%.</td><td>White, non-Hispanic 31.3%, Black, non-Hispanic 18.8%, Hispanic 18.8%, Other 31.3%.</td><td>Yes (0.01)</td></tr>
<tr><td>Relationship status</td><td>Single 37.5%,
In a committed relationship 62.5%.</td><td>Single 51.6%,
In a committed relationship 48.4%.</td><td>No</td></tr>
<tr><td>Living situation</td><td>With parent/guardian 31.3%, with significant other 31.3%, other 37.5%</td><td>With parent/guardian 36.9%, with significant other 27.9%, other 35.2%</td><td>No</td></tr>
<tr><td>Yearly household income</td><td>Low (<$30,000) 25.0%, medium ($30,000-$74,999) 50.0%, high (≥$75,000) 25.0%.</td><td>Low (<$30,000) 25.0%, medium ($30,000-$74,999) 37.9%, high (≥$75,000) 37.0%.</td><td>No</td></tr>
<tr><td>Education level</td><td>High school or less 50.0%, some college 31.3%, bachelor’s degree or higher 18.8%.</td><td>High school or less 27.6%, some college 39.7%, bachelor’s degree or higher 32.7%.</td><td>No</td></tr>
</table></td></tr>
</table>

Bibliographic reference/s	**Primack Brian A, Shensa Ariel, Sidani Jaime E, Hoffman Beth L, Soneji Samir, Sargent James D, Hoffman Robert M, Fine Michael J (2018) Initiation of traditional cigarette smoking after electronic cigarette use among tobacco-naïve US young adults. The American Journal of Medicine 131, 443.e1-443.e9**
Study name	Primack 2018
	<table><tr><td>Self-esteem**</td><td>Low 18.8%, high 81.3%</td><td>Low 29.2%, high 70.8%</td><td>No</td></tr><tr><td>Sensation seeking</td><td>Low 18.8%, medium 31.3%, high 50.0%</td><td>Low 33.6%, medium 33.6%, high 32.7%</td><td>No</td></tr><tr><td>Rebelliousness</td><td>Low 25.0%, medium 25.0%, high 50.0%.</td><td>Low 32.0%, medium 38.6%, high 29.3%.</td><td>No</td></tr></table> *Race/ethnicity was self-reported ** Item states “I have high self-esteem”, to which participants could respond with increasing levels of agreement. Authors state that the sample was nationally representative.
Attrition	60.8% of study sample completing the study (591/1,506 did not complete the follow-up survey) Authors state this was unlikely to change results due to no demographic differences between those retained and those not retained.
Inclusion and exclusion criteria	• Participants had to be never smokers of cigarettes at baseline aged 18 to 30 years. Judged by responding no to asking participants about ever use of cigarettes. • Exclusion criteria not reported.
Data collection	Initiation of cigarette smoking at baseline and follow-up, e-cigarette use at baseline were obtained from online survey. Growth from Knowledge provided self-reported information on age, sex, race, ethnicity and education level. Self-esteem information was collected using a validated 1-item scale and sensation seeking tendency based on the validated Likert-type 4 items scale such as “I like to do dangerous things”. Rebelliousness was assessed using a 3-item validated Likert-type subscale which included “I tend to go against the rules”. Source of household income is not clearly reported whether obtained from survey or Growth from Knowledge. Information on blinding not reported.
Outcome measure	Initiation of cigarette smoking: participants progressing from never smoker at baseline to having had at least 1 puff of cigarette by follow-up.
Follow up	18 months
Critical outcomes measures and effect size. (time points)	Cigarette smoking initiation Baseline ever e-cigarette users vs never e-cigarette users at 18-month follow-up based on weighted results. Authors stated that unweighted and weighted results were similar in terms of significance and odds ratios, therefore only weighted results were presented given their greater external generalisability.

<table>
<tr><td>Bibliographic reference/s</td><td>Primack Brian A, Shensa Ariel, Sidani Jaime E, Hoffman Beth L, Soneji Samir, Sargent James D, Hoffman Robert M, Fine Michael J (2018) Initiation of traditional cigarette smoking after electronic cigarette use among tobacco-naïve US young adults. The American Journal of Medicine 131, 443.e1-443.e9</td></tr>
<tr><td>Study name</td><td>Primack 2018</td></tr>
<tr><td></td><td>
<table>
<tr><td></td><td>Exposed n = 16</td><td>Unexposed n = 899</td><td>aOR* (95% CI)</td><td>aRR** calculated by analyst</td></tr>
<tr><td>Number who have initiated smoking (%)</td><td>6 (37.5)</td><td>81 (9.0)</td><td>6.82 (1.65 – 28.25)</td><td>4.28 (1.55 – 7.47)</td></tr>
</table>
*Reported by study. Adjusted for age, sex, race/ethnicity, relationship status, living situation, yearly household income, education level, self-esteem, sensation seeking, rebelliousness and incorporating survey weights (to adjust for non-response, non-coverage, under-sampling or over-sampling). Survey weighting was applied to adjust for nonresponse, as well as noncoverage, undersampling, or oversampling resulting from the sample design.
**Calculated by review team. The unexposed group prevalence used to calculate the aRR was 0.102

The following is not reported:
Outcome by habitual vs experimental e-cig use at baseline
Outcome by nicotine vs non-nicotine e-cigs
Outcome by e-cig type
Outcome by age category
Outcome by socioeconomic deprivation
Outcome by family / peer smoking presence vs absence.</td></tr>
<tr><td>Important outcomes measures and effect size. (time points)</td><td>No important outcomes reported</td></tr>
<tr><td>Statistical Analysis</td><td>Statistical analysis: Multivariable logistic regression analysis was used. Adjusted for age, sex, race/ethnicity, relationship status, living situation, yearly household income, education level, self-esteem, sensation seeking, rebelliousness and survey weights (to adjust for non-response, non-coverage, under-sampling or over-sampling)

3 sets of sensitivity analyses (all continuous covariates, all analyses without survey weights, all analyses including covariates that demonstrated bivariable associations of $p < 0.15$). All sensitivity analyses showed consistent results with primary analyses.</td></tr>
<tr><td>Risk of bias (ROB)
QUIPS tool</td><td>Initiation of cigarette smoking
<table>
<tr><th>Outcome</th><th>Judgement</th><th>Comments</th></tr>
<tr><td>Study participation</td><td>Low</td><td>Authors state that the baseline sample is nationally representative of the population</td></tr>
</table>
</td></tr>
</table>

Bibliographic reference/s	**Primack Brian A, Shensa Ariel, Sidani Jaime E, Hoffman Beth L, Soneji Samir, Sargent James D, Hoffman Robert M, Fine Michael J (2018) Initiation of traditional cigarette smoking after electronic cigarette use among tobacco-naïve US young adults. The American Journal of Medicine 131, 443.e1-443.e9**		
Study name	Primack 2018		
			but source is not described. Sample and place of recruitment described. Exclusion criteria not reported.
	Study attrition	Moderate	Attrition is high (39.2%) despite authors note that this was unlikely to change results substantially because there were no demographic differences between those retained and those not retained. Drop outs are not described, and no attempt to deal with missing data.
	Prognostic factor (PF) management	Moderate	Fairly well defined PF. Self-reported. Measured consistently across groups. Good proportion of data on PF.
	Outcome measurement	Moderate	Outcome well defined and measured consistently for exposed and unexposed. Subjective measure so possible that participants were not truthful.
	Study confounding	Moderate	Collects data for and adjusts for many of the important confounders identified.
	Statistical analysis and reporting	Low	No apparent selective reporting of results.
	Overall Risk of Bias	Acceptable risk of bias	
	Other outcome details None		
Source of funding	National Cancer Institute		
Comments	Participant age included young adults aged 18-30 years of age, median age was 23 years (interquartile range of 20-26). Incentive of $20 cash-equivalent for participants who completed both baseline and follow-up surveys. Authors note limited statistical power of study was low due to small number of e-cigarette smokers at baseline, however the study found significant results. The authors note that the small number of e-cigarette smokers may be due to baseline data being collected in 2013, with e-cigarette use increasing substantially since then.		
Additional references	None		

Spindle 2017

Bibliographic reference/s	**Spindle Tory R, Hiler Marzena M, Cooke Megan E, Eissenberg Thomas, Kendler Kenneth S, and Dick Danielle M (2017) Electronic cigarette use and uptake of cigarette smoking: A longitudinal examination of U.S. college students. Addictive behaviors 67, 66-72**
Study name	Spindle 2017
Registration	Not reported
Study type	Cohort (prospective)
Study dates	2014-2015
Objective	To examine the extent to which e-cigarette use among never cigarette smokers at baseline was predictive of cigarette smoking at follow-up. Study also considers whether factors predictive of the onset of cigarette smoking also predicted onset of e-cigarette use [out of scope].
Country/ Setting	USA, Virginia. University setting
Cohort source	Spit for Science (S4S) cohort Cohort study of all students at Virginia Commonwealth University (VCU), from 2011.
Number entering into study (invited)	Unclear how many students attend VCU and were invited to complete the survey. 5779 students completed the baseline survey in 2014.
Number of participants evaluated	4748 students completed the follow-up survey, of these 3757 had also completed the baseline survey and form the analytical sample. Power not reported.
Prognostic factor	Ever e-cigarette use: participants were asked how many e-cigarettes they had used in their lifetime. Participants were considered to have ever used e-cigarettes if they had used these products on even one occasion. Current e-cigarette use: Participants were asked how many days during the last 30 they had used e-cigarettes. Participants were considered current users if they had used these products at least once in the past 30 days. Nicotine content and generation of e-cigarette not reported.
Baseline study sample characteristics	Characteristics of exposed and unexposed groups combined at baseline

Characteristics	Sample
Mean age years (SD)	18.5 (0.43)
Female (%)	62
Ethnicity	47% White, 19% Black, 17% Asian, 6% Hispanic, 7% Mixed race, 4% other.
Susceptibility to smoking	Not reported
Family smoking	Not reported
Peer smoking (measured as peer deviance*)	Data collected by study but not reported
Marijuana use, anxiety, depression, stressful life events, impulsivity (lack of perseverance, lack of premeditation, negative urgency, positive urgency, sensation seeking)	Data collected by study but not reported

*assessed with 6 survey items about the student's friends' use of substances (see 'data collection')

Bibliographic reference/s	**Spindle Tory R, Hiler Marzena M, Cooke Megan E, Eissenberg Thomas, Kendler Kenneth S, and Dick Danielle M (2017) Electronic cigarette use and uptake of cigarette smoking: A longitudinal examination of U.S. college students. Addictive behaviors 67, 66-72**
Study name	Spindle 2017
	Authors report that the sample was representative of the students attending VCU in terms of gender and ethnic makeup (other factors not reported).
Attrition	991/4748 (20.9%) baseline participants did not complete follow-up Those lost to follow-up were more likely to have greater levels of peer deviance (see 'data collection'). Other covariates did not differ.
Inclusion and exclusion criteria	• Students who reported never smoking at baseline and attended VCU. • Exclusion criteria not reported.
Data collection	Survey filled out online after providing informed consent online. Participants then invited to complete a follow-up survey. Data was collected on prognostic factor, outcome, and various covariates as follows: Demographic factors, ever marijuana use (not current use), ever and current use of smokeless tobacco, little cigars / cigarillos, hookah (measured in the same way as the outcome measure). Other factors measured which authors report have previously been associated with cigarette smoking: • Anxiety and depression were each measured using subsets of four items from the Symptom Checklist (SCL)-90 that measures symptoms of anxiety (i.e., "feeling fearful," "suddenly scared for no reason," "nervousness or shakiness inside," "spells of terror or panic") or depression (i.e., "feeling blue," "worrying too much about things," "feeling hopeless about the future," "feeling no interest in things") within the last 30 days on a five-point Likert scale. • Peer deviance was measured by six items addressing how many of the student's friends (from "none" to "all") had smoked cigarettes, drank alcohol, gotten drunk, had problems with alcohol, been in trouble with the law, and smoked marijuana. • Stressful life events were measured by 12 items addressing whether the student had experienced a potentially stressful life event in the past 12 months (e.g., "separation from loved one or close friend," "serious illness or injury," experiencing physical or sexual assault"). Each endorsement of a stressful life event was summed to create an overall score. • The impulsivity subscales including: lack of perseverance, lack of premeditation, negative urgency, positive urgency, and sensation seeking were assessed using three items from the UPPS-P Impulsive Behavior Scale. Each of these items was measured on a four point Likert scale. Example items from these subscales include: lack of perseverance ("I finish what I start"), lack of premeditation ("I usually think carefully before doing anything"), negative urgency ("when I am upset, I often act without thinking"), positive urgency ("I tend to act without thinking when I am really excited"), and sensation seeking ("I quite enjoy taking risks").
Outcome measure	Ever cigarette use: participants were asked how many cigarettes they had smoked in their lifetime. Participants were considered to have ever used cigarettes if they had used these products on even one occasion. Current cigarette use: Participants were asked how many days during the last 30 they had smoked cigarettes. Participants were considered current users if they had used these products at least once in the past 30 days.

<table>
<tr><td>Bibliographic reference/s</td><td>Spindle Tory R, Hiler Marzena M, Cooke Megan E, Eissenberg Thomas, Kendler Kenneth S, and Dick Danielle M (2017) Electronic cigarette use and uptake of cigarette smoking: A longitudinal examination of U.S. college students. Addictive behaviors 67, 66-72</td></tr>
<tr><td>Study name</td><td>Spindle 2017</td></tr>
<tr><td>Follow up</td><td>12 months</td></tr>
<tr><td>Critical outcomes measures and effect size. (time points)</td><td>
Ever cigarette use
Ever e-cigarette users vs never e-cigarette users at 12 month follow-up
<table>
<tr><td></td><td>Exposed n = 153</td><td>Unexposed n = 2163</td><td>aOR* (95% CI)</td><td>aRR** calculated by analyst</td></tr>
<tr><td>Number who have tried smoking (%)</td><td>45 (29.4)</td><td>230 (10.6</td><td>3.37 (1.91, 5.94)</td><td>2.69 (1.74, 3.90)</td></tr>
</table>
** Calculated by review team. The unexposed group prevalence used to calculate the aRR was 0.106.
This is the outcome used in meta-analysis (the remaining three outcomes use “past 30 days” measures which are not preferred to “ever” measures).

Current e-cigarette users vs non-current e-cigarette users at 12 month follow-up
<table>
<tr><td></td><td>Exposed n = not reported</td><td>Unexposed n = not reported</td><td>aOR* (95% CI)</td><td>aRR** calculated by analyst</td></tr>
<tr><td>Number who have tried smoking (%)</td><td>not reported</td><td>not reported, assumed 10.6%*</td><td>3.41 (1.57, 7.41)</td><td>2.71 (1.48, 4.41)</td></tr>
</table>
**Calculated by review team. No unexposed prevalence reported, so unexposed prevalence for ever e-cigarette use used (0.106): this is likely to be conservative as it represents the highest possible prevalence of current use.

Current cigarette use
Ever e-cigarette users vs never e-cigarette users at 12 month follow-up
<table>
<tr><td></td><td>Exposed n = 153</td><td>Unexposed n = 2163</td><td>aOR* (95% CI)</td><td>aRR** calculated by analyst</td></tr>
<tr><td>Number who currently smoke (%)</td><td>11 (7.2)</td><td>27 (1.2)</td><td>3.30 (1.20, 9.05)</td><td>3.22 (1.20, 8.36)</td></tr>
</table>
**Calculated by review team. The unexposed group prevalence used to calculate the aRR was 0.0102.

Current e-cigarette users vs non-current e-cigarette users at 12 month follow-up
<table>
<tr><td></td><td>Exposed n = not reported</td><td>Unexposed n = not reported</td><td>aOR* (95% CI)</td><td>aRR** calculated by analyst</td></tr>
<tr><td>Number who currently smoke (%)</td><td>not reported</td><td>not reported, assumed 1.2%*</td><td>1.15 (0.15, 9.06)</td><td>1.14 (0.15, 8.37)</td></tr>
</table>
</td></tr>
</table>

Bibliographic reference/s	**Spindle Tory R, Hiler Marzena M, Cooke Megan E, Eissenberg Thomas, Kendler Kenneth S, and Dick Danielle M (2017) Electronic cigarette use and uptake of cigarette smoking: A longitudinal examination of U.S. college students. Addictive behaviors 67, 66-72**
Study name	Spindle 2017
	**Calculated by review team. No unexposed prevalence reported, so unexposed prevalence for ever e-cigarette use used (0.0102): this is likely to be conservative as it represents the highest possible prevalence of current use. *aOR reported by study. Adjusted for gender, age, ethnicity, anxiety, depression, stressful life events, peer deviance, impulsivity (lack of perseverance, lack of premeditation, negative urgency, positive urgency, sensation seeking), ever use of other tobacco products.
Important outcomes measures and effect size. (time points)	No important outcomes reported
Statistical Analysis	Multivariate logistic regressions were conducted. Responses to prognostic factor and outcome were dichotomised. Results were adjusted for gender, age, ethnicity, anxiety, depression, stressful life events, peer deviance, impulsivity (lack of perseverance, lack of premeditation, negative urgency, positive urgency, sensation seeking), ever use of other tobacco products. Participants recanting were judged to be a small percentage (around 3%) and was not adjusted for. Missing data approaches not reported.
Risk of bias (ROB) QUIPS tool	Ever cigarette use (among ever e-cigarette users)

Outcome	Judgement	Comments
Study participation	Low	Study authors report that sample is similar to population (VCU students) and that rates of other substance use is comparable to national surveys. Population data (gender, ethnicity) described.
Study attrition	High	Attrition is moderately high (20.9%). Some demographic differences between those lost to follow up and those continuing. Reasons for loss to follow-up not reported.
Prognostic factor management	Moderate	Fairly well defined PF. Self-reported. Measured consistently across groups. Good proportion of data on PF.
Outcome measurement	Moderate	Fairly well defined outcome. Self-reported. Measured consistently across groups. Good proportion of data on outcome.

Bibliographic reference/s	**Spindle Tory R, Hiler Marzena M, Cooke Megan E, Eissenberg Thomas, Kendler Kenneth S, and Dick Danielle M (2017) Electronic cigarette use and uptake of cigarette smoking: A longitudinal examination of U.S. college students. Addictive behaviors 67, 66-72**		
Study name	Spindle 2017		
	Study confounding	High	Family smoking and smoking susceptibility not measured. Other confounders measured consistently and adjusted for in analysis.
	Statistical analysis and reporting	Moderate	Some outcome data is sparse although no major outcomes not reported.
	Overall Risk of Bias	High risk of bias	
	Other outcome details: **Ever cigarette use (among current e-cigarette users):** High (statistical analysis and reporting domain 'moderate') Current cigarette use (among ever e-cigarette users): as for main outcome **Current cigarette use (among current e-cigarette users):** High (statistical analysis and reporting domain 'moderate')		
Source of funding	Virginia Commonwealth University, National Institute on Alcohol Abuse and Alcoholism, National Center for Research Resources, National Institutes of Health Roadmap for Medical Research supported Spit for Science. National Institute on Drug Abuse of the National Institutes of Health also supported this publication.		
Comments	• Authors state that as the data is from a single university, results may not be generalisable outside of this setting. • Authors point out that this study did not include all covariates associated with smoking (e.g. harm perceptions, exposure to advertising) • Study did not include information about nicotine content or e-cigarette models		
Additional references	None		

Treur 2018

Bibliographic reference/s	**Treur Jorien L, Rozema Andrea D, Mathijssen Jolanda J. P, van Oers , Hans , and Vink Jacqueline M (2018) E-cigarette and waterpipe use in two adolescent cohorts: cross-sectional and longitudinal associations with conventional cigarette smoking. European journal of epidemiology 33(3), 323-334**
Study name	Treur 2018
Registration	Not reported
Study type	Cohort (prospective)
Study dates	2014-2015
Objective	To determine whether the use of alternative tobacco products (e-cigarettes with nicotine, e-cigarettes without nicotine, waterpipe) are associated with conventional smoking in adolescents.
Country/ Setting	Netherlands School setting

Bibliographic reference/s	**Treur Jorien L, Rozema Andrea D, Mathijssen Jolanda J. P, van Oers , Hans , and Vink Jacqueline M (2018) E-cigarette and waterpipe use in two adolescent cohorts: cross-sectional and longitudinal associations with conventional cigarette smoking. European journal of epidemiology 33(3), 323-334**
Study name	Treur 2018
Cohort source	Unnamed cohort. Cohort consisted of individuals enrolled in a study that investigated the impact of school smoking policy on changes in adolescents' smoking behaviour. 19 secondary schools randomly selected from across the Netherlands were included. Students aged 11-17.
Number entering into study (invited)	6819 adolescents in the cohort, unclear how many participants completed baseline, and how many completed follow-up data collection.
Number of participants evaluated	2100 participants provided data at both baseline and follow-up. Power information not reported.
Prognostic factor	Ever-use of e-cigarettes with nicotine: Participants were asked how old they were when they first used e-cigarettes with nicotine. Those answering "I never used this substance" were classed as never users. Ever-use of e-cigarettes without nicotine: Participants were asked how old they were when they first used e-cigarettes without nicotine. Those answering "I never used this substance" were classed as never users. Generation of e-cigarette not reported. Data on waterpipe also collected, but this is not a prognostic factor in this review.
Baseline study sample characteristics	Characteristics of sample not reported. Authors report that this cohort is representative, but this might refer to the cross-sectional sample which is significantly larger than the longitudinal sample.
Attrition	Attrition unclear as authors do not report number of participants completing baseline survey. 6819 participants completed either the baseline or follow-up survey, and only 2100 participants completed both, so attrition is likely to be high. Those lost to follow-up not investigated
Inclusion and exclusion criteria	• Participants who reported that they had never smoked cigarettes or only tried them once or twice were classified as never smokers and were included. • Exclusion criteria not reported.
Data collection	Survey. Participants provided informed consent and parents were informed as opportunity to opt out. Data was collected on the prognostic factor and outcome measure, and covariates as follows: Demographic factors: sex, age, ethnicity, educational attainment (0 = low, 1 = average, 2 = middle and 3 = high) Propensity to smoke: this is a composite score based on three risk factors: - Personality: assessed with the validated 'Substance Use Risk Profile Scale' (SURPS). The SURPS provides sum scores for anxiety sensitivity, hopelessness, sensation seeking and impulsivity. - Susceptibility to peer pressure, measured by asking adolescents 'Imagine that you are with a group of friends who all smoke. They offer you a cigarette,

<table>
<tr><td>Bibliographic reference/s</td><td>Treur Jorien L, Rozema Andrea D, Mathijssen Jolanda J. P, van Oers , Hans , and Vink Jacqueline M (2018) E-cigarette and waterpipe use in two adolescent cohorts: cross-sectional and longitudinal associations with conventional cigarette smoking. European journal of epidemiology 33(3), 323-334</td></tr>
<tr><td>Study name</td><td>Treur 2018</td></tr>
<tr><td></td><td>would you take the cigarette and smoke with them?', with answer categories ranging from 1 'Definitely not' to 7 'Definitely yes'.
- Intention to smoke, measured by asking adolescents 'Are you planning to smoke in the coming 6 months?', with answer categories ranging from 1 'Definitely not' to 7 'Definitely yes'.
Blinding not reported</td></tr>
<tr><td>Outcome measure</td><td>Smoking status: Participants were asked how old they were when they first used cigarettes. Participants were also asked whether they had ever smoked, even just one cigarette or a few puffs. Those answering that they had never smoked cigarettes or only tried them once or twice were classified as a never smoker. Those who smoked once in a while or daily were classed as current smokers. Those who smoked but quit were classified as former smokers.</td></tr>
<tr><td>Follow up</td><td>6 months</td></tr>
<tr><td>Critical outcomes measures and effect size. (time points)</td><td>Ever use of cigarettes
Baseline users of e-cigarettes with nicotine vs never-users (baseline never cigarette users only)
<table>
<tr><td></td><td>Exposed n = not reported</td><td>Unexposed n = not reported</td><td>aOR* (95% CI)</td><td>aRR** calculated by analyst</td></tr>
<tr><td>Number initiating smoking (%)</td><td>not reported</td><td>not reported</td><td>11.90 (3.36, 41.22)</td><td>4.77 (2.54, 6.33)</td></tr>
</table>
*Reported by study. Adjusted for age, sex, educational attainment, smoking propensity, intervention status.
**Prevalence used to calculate the aRR was the study-reported prevalence of use of e-cigarettes with nicotine across the whole group (0.137).

Baseline users of e-cigarettes without nicotine vs never-users (baseline never cigarette users only)
<table>
<tr><td></td><td>Exposed n = not reported</td><td>Unexposed n = not reported</td><td>aOR* (95% CI)</td><td>aRR** calculated by analyst</td></tr>
<tr><td>Number initiating smoking (%)</td><td>not reported</td><td>not reported</td><td>5.36 (2.73, 10.52)</td><td>2.35 (1.81, 2.77)</td></tr>
</table>
*Reported by study. Adjusted for age, sex, educational attainment, smoking propensity, intervention status.
** Prevalence used to calculate the aRR was the study-reported prevalence of use of e-cigarettes with nicotine across the whole group (0.294).

Ever use of cigarettes among sample with a below median propensity of conventional smoking at baseline</td></tr>
</table>

Bibliographic reference/s	**Treur Jorien L, Rozema Andrea D, Mathijssen Jolanda J. P, van Oers , Hans , and Vink Jacqueline M (2018) E-cigarette and waterpipe use in two adolescent cohorts: cross-sectional and longitudinal associations with conventional cigarette smoking. European journal of epidemiology 33(3), 323-334**
Study name	Treur 2018

	Exposed n = not reported	Unexposed n = not reported	aOR* (95% CI)	aRR** calculated by analyst
E-cigarettes with nicotine users initiating smoking (%)	not reported	not reported	7.80 (1.90, 32.04)	4.04 (1.69, 6.10)
E-cigarettes without nicotine users initiating smoking (%)	not reported	not reported	6.07 (2.18, 16.90)	2.44 (1.62, 2.98)

Ever use of cigarettes among sample with above median propensity of conventional smoking at baseline

	Exposed n = not reported	Unexposed n = not reported	aOR* (95% CI)	aRR** calculated by analyst
E-cigarettes with nicotine users initiating smoking (%)	not reported	not reported	2.89 (1.47, 5.68)	2.30 (1.38, 3.46)
E-cigarettes without nicotine users initiating smoking (%)	not reported	not reported	3.30 (2.33, 4.67)	1.97 (1.68, 2.25)

Prevalence used to calculate the aRR for e-cigarettes with nicotine was 0.294; without nicotine was 0.137 (see above tables).

For the purpose of meta-analysis, the results from e-cigarettes with nicotine are carried forward (both cannot be used together due to double counting).

The following is not reported:

- Outcome by habitual vs experimental e-cig use at baseline
- Outcome by nicotine vs non-nicotine e-cigs
- Outcome by e-cig type
- Outcome by age category
- Outcome by socioeconomic deprivation
- Outcome by family / peer smoking presence vs absence.

Important outcomes measures and effect size. (time points)	No important outcomes reported

<table>
<tr><td>Bibliographic reference/s</td><td colspan="3">Treur Jorien L, Rozema Andrea D, Mathijssen Jolanda J. P, van Oers , Hans , and Vink Jacqueline M (2018) E-cigarette and waterpipe use in two adolescent cohorts: cross-sectional and longitudinal associations with conventional cigarette smoking. European journal of epidemiology 33(3), 323-334</td></tr>
<tr><td>Study name</td><td colspan="3">Treur 2018</td></tr>
<tr><td>Statistical Analysis</td><td colspan="3">Generalized estimation equation (GEE) used to correct for clustering within schools, and to analyse whether use of e-cigs was associated with conventional cigarette use at follow-up.
Adjusted for age, sex, educational attainment, smoking propensity, intervention status (no school policy intervention and school policy intervention)
Correction for multiple testing applied.</td></tr>
<tr><td rowspan="10">Risk of bias (ROB)
QUIPS tool</td><td colspan="3">Ever use of cigarettes among baseline users of e-cigarettes with nicotine vs never users</td></tr>
<tr><td>Outcome</td><td>Judgement</td><td>Comments</td></tr>
<tr><td>Study participation</td><td>Moderate</td><td>Source population unclear and not described. Schools randomly selected. Sample described as representative, but unclear whether this applies to longitudinal.</td></tr>
<tr><td>Study attrition</td><td>High</td><td>Attrition unclear but likely to be high. Those lost to follow-up not described.</td></tr>
<tr><td>Prognostic factor management</td><td>Moderate</td><td>PF well defined, measured consistently, good proportion of data. Self-reported.</td></tr>
<tr><td>Outcome measurement</td><td>Moderate</td><td>Outcome well defined, measured consistently, good proportion of data. Self-reported.</td></tr>
<tr><td>Study confounding</td><td>High</td><td>Some key confounders not considered (peer smoking, family smoking). Other confounders considered, measured consistently, adjusted for in analysis.</td></tr>
<tr><td>Statistical analysis and reporting</td><td>Moderate</td><td>Main results presented but not comprehensively described (modelling etc)</td></tr>
<tr><td>Overall Risk of Bias</td><td colspan="2">High risk of bias</td></tr>
<tr><td colspan="3">Other outcome details:
Ever use of cigarettes among baseline users of e-cigarettes without nicotine vs never users: as above
Ever use of cigarettes among sample with a below median propensity of conventional smoking at baseline: as above
Ever use of cigarettes among sample with above median propensity of conventional smoking at baseline: as above</td></tr>
<tr><td>Source of funding</td><td colspan="3">European Research Council, Netherlands Organization for Health Research and Development, National Institute for Public Health and the Environment.</td></tr>
</table>

Bibliographic reference/s	**Treur Jorien L, Rozema Andrea D, Mathijssen Jolanda J. P, van Oers , Hans , and Vink Jacqueline M (2018) E-cigarette and waterpipe use in two adolescent cohorts: cross-sectional and longitudinal associations with conventional cigarette smoking. European journal of epidemiology 33(3), 323-334**
Study name	Treur 2018
Comments	- Study looks at two cohorts, however only one cohort provides data on the same participants at baseline and follow-up (the second cohort is repeat cross-sectional and so data is not extracted on it). - Study sample was from a study with school smoking policy interventions. Analyses were controlled for intervention status. - Peer smoking and family smoking is not investigated as a covariate in this study.
Additional references	None

Unger 2016

Bibliographic reference/s	**Unger Jennifer B, Soto Daniel W, Leventhal Adam (2001) E-cigarette use and subsequent cigarette and marijuana use among Hispanic young adults. Drug and Alcohol dependence 163, 261-264**
Study name	Unger 2016
Registration	Not reported
Study type	Cohort (prospective)
Study dates	2014 -2015
Objective	To assess whether e-cigarettes change the likelihood of non-smokers subsequently transitioning to cigarette use.
Country/ Setting	USA
Cohort source	Project RED study
Number entering into study (invited)	Participants included 1,445 Hispanic young adults who originally participated as Grade 9 students in 2005 (followed up annually until 2015).
Number of participants evaluated	1,332 participants completed both 2014 and 2015 surveys. Authors do not report information on power but acknowledge that the analyses were based on a small number of participants.
Prognostic factor	Past-month e-cigarette use in 2014: participants were asked whether they had used an e-cigarette in the past month and responding either yes or no. No information on nicotine content or generation of e-cigarette.
Baseline study sample characteristics	Baseline sample included all Hispanic participants, with a mean age of 22.7 years (SD 0.39 years) and 59% were female. Limited generalisability as participants were originally recruited as students from high schools in Los Angeles, USA.
Attrition	92% of participants completed both surveys, loss to follow up: 8%. Participants who dropped out were not investigated.

<table>
<tr><td>Bibliographic reference/s</td><td>Unger Jennifer B, Soto Daniel W, Leventhal Adam (2001) E-cigarette use and subsequent cigarette and marijuana use among Hispanic young adults. Drug and Alcohol dependence 163, 261-264</td></tr>
<tr><td>Study name</td><td>Unger 2016</td></tr>
<tr><td>Inclusion and exclusion criteria</td><td>• Participants were categorised into 2 groups as either past-month cigarette smokers or past-month non-smokers based on cigarette use in 2014. Past-month non-smokers are of relevance to this review.
• Exclusion criteria not reported.</td></tr>
<tr><td>Data collection</td><td>Participants use of combustible cigarettes, e-cigarettes, age, sex, past-month use of alcohol and other tobacco products (hookah, cigars, little cigars and smokeless tobacco) collected by online surveys in 2014 and 2015. Participants were contacted by email, text message, phone call and/or social media to complete online survey.
Information on blinding not reported.</td></tr>
<tr><td>Outcome measure</td><td><u>Past- month cigarette smoker in 2015:</u> participants were asked on their use of combustible cigarettes and classified according to their use in the last month. Response options were yes or no.</td></tr>
<tr><td>Follow up</td><td>1 year</td></tr>
<tr><td>Critical outcomes measures and effect size. (time points)</td><td>Past-month cigarette smoker in 2015
Baseline past-month e-cigarette user vs non e-cigarette user at 1 year follow-up
<table>
<tr><td></td><td>Exposed n = 42</td><td>Unexposed n = 1,014</td><td>aOR* (95% CI)</td><td>aRR** calculated by analyst</td></tr>
<tr><td>Number who become past-month cigarette smokers in 2015 (%)</td><td>11 (26)</td><td>71 (7)</td><td>3.32 (1.55 – 7.10).</td><td>2.86 (1.49 – 4.98)</td></tr>
</table>
*Reported by study. Adjusted for age, sex, past-month use in 2014: alcohol, cigar, little cigar, hookah and smokeless tobacco. The authors report this as past-month e-cigarette/marijuana use in 2014.
**Calculated by review team. The unexposed group prevalence used to calculate the aRR was 0.07.
The following is not reported:
• Outcome by nicotine vs non-nicotine e-cigs
• Outcome by e-cig type
• Outcome by age category
• Outcome by socioeconomic deprivation
• Outcome by family / peer smoking presence vs absence.</td></tr>
<tr><td>Important outcomes measures and effect size. (time points)</td><td>No important outcomes reported.</td></tr>
<tr><td>Statistical Analysis</td><td><u>Statistical analysis:</u> Sample was stratified into 2 groups: past-month cigarette smokers and past-month cigarette non-smokers. Within each group logistic regression analysis was conducted to determine the likelihood of being a past-</td></tr>
</table>

Bibliographic reference/s	**Unger Jennifer B, Soto Daniel W, Leventhal Adam (2001) E-cigarette use and subsequent cigarette and marijuana use among Hispanic young adults. Drug and Alcohol dependence 163, 261-264**		
Study name	Unger 2016		
	month cigarette smoker in 2015. Analysis adjusted for age, sex, past-month use in 2014 of alcohol, cigar, little cigar, hookah and smokeless tobacco. Authors do not report any methods used to account for missing data.		
Risk of bias (ROB) QUIPS tool	Past-month cigarette smoker in 2015		
	Outcome	**Judgement**	**Comments**
	Study participation	High	The source and baseline sample population are not clearly described. Authors state that as participants were recruited from high schools, this limits the generalisability of the results.
	Study attrition	Moderate	Attrition is low at 8%, however no reason for loss to follow up are provided. Differences between drop outs and completers are not mentioned, and authors do not report any methods to account for missing data.
	Prognostic factor management	High	Prognostic factor is not well defined and is self-reported. Prognostic factor is measured consistently across groups, however in the results past-month e-cigarette use is grouped in combination with marijuana use.
	Outcome measurement	Moderate	Outcome is not clearly defined.
	Study confounding	Moderate	Collects data for and adjusts for many of the important confounders identified. Data was not collected for impulsivity, rebelliousness or sensation seeking.
	Statistical analysis and reporting	Moderate	Data mostly presented, although some is unclear. Analysis did not control for clustering.
	Overall Risk of Bias	High risk of bias	
	Other outcome details: No other outcome reported.		
Source of funding	National Institutes of Health		
Comments	Authors report that findings should be interpreted cautiously as they are based on a small number of participants who initiated cigarette smoking over a 1- year period.		

Bibliographic reference/s	**Unger Jennifer B, Soto Daniel W, Leventhal Adam (2001) E-cigarette use and subsequent cigarette and marijuana use among Hispanic young adults. Drug and Alcohol dependence 163, 261-264**
Study name	Unger 2016
	Authors note that frequency/amount of cigarette and e-cigarette use within the past month were not assessed, therefore it is not clear whether the findings reflect experimental use or habitual use. -The survey did not include questions to assess impulsivity, rebelliousness or sensation seeking.
Additional references	None

Watkins 2018

Bibliographic reference/s	**Watkins Shannon L, Glantz Stanton A, Chaffee Benjamin W (2018) Association of noncigarette tobacco product use with future cigarette smoking among youth in the population assessment of tobacco and health (PATH) study, 2013-2015. JAMA paediatrics 172(2),181-187.**
Study name	Watkins 2018
Registration	Not reported
Study type	Cohort (prospective)
Study dates	Wave 1: September 2013- December 2014 Wave 2: October 2014 – October 2015
Objective	To estimate the longitudinal association between non-cigarette tobacco use and subsequent cigarette smoking initiation amongst US youth.
Country/ Setting	USA
Cohort source	Population assessment of tobacco and health (PATH) study
Number entering into study (invited)	11,996 participants completed wave 1 and wave 2 survey.
Number of participants evaluated	10,384 participants were included in the complete analysis: 10,384 for wave 1 and 10,380 for wave 2. Authors state that power was limited based on the number of past 30-day users of some tobacco products.
Prognostic factor	Ever only use of e-cigarette: participants were asked if they had ever tried a single product (including e-cigarette, hookah, non-cigarette combustible tobacco, or smokeless tobacco) and no other tobacco product. Study notes these single products including e-cigarette as non-cigarette tobacco product. Ever only use of e-cigarette is of relevance to this review.
Baseline study sample characteristics	Characteristics of sample not reported specifically for participants who had only ever used e-cigarettes, however authors note that the sample is nationally representative and reflected the non-institutionalised youth population at baseline. Participants who completed waves 1 and 2 were aged between 12-17 years with a mean age of 14.3 years, 49.1% were female and 52.5% were of white ethnicity.
Attrition	Loss to follow up was 12.1% between waves 1 and 2.

<table>
<tr><td>Bibliographic reference/s</td><td>Watkins Shannon L, Glantz Stanton A, Chaffee Benjamin W (2018) Association of noncigarette tobacco product use with future cigarette smoking among youth in the population assessment of tobacco and health (PATH) study, 2013-2015. JAMA paediatrics 172(2),181-187.</td></tr>
<tr><td>Study name</td><td>Watkins 2018</td></tr>
<tr><td>Inclusion and exclusion criteria</td><td>Participants had never tried a cigarette at baseline. Exclusion criteria not reported.</td></tr>
<tr><td>Data collection</td><td>The PATH study featured a 4-stage, stratified probability sample design at baseline that oversampled adult tobacco users, young adults (18-24 years) and black adults. The PATH youth sample included participants whose parents were sampled for the PATH adult survey, with 2 youths selected per household.
Data was collected by survey at both baseline and follow-up using in-person computer-assisted interviews at home.</td></tr>
<tr><td>Outcome measure</td><td>New cigarette initiation between waves 1 and 2 assessed by:
Ever use of cigarette: participants responded to the question have you ever smoked a cigarette, even 1 or 2 puffs (response options yes or no).
Cigarette past 30-day use: participants responded to the question have you smoked a cigarette at least 1 day in the past 30 days (response options yes or no).</td></tr>
<tr><td>Follow up</td><td>1 year</td></tr>
<tr><td>Critical outcomes measures and effect size. (time points)</td><td>Cigarette ever use at follow-up
Baseline ever e-cigarette users vs never users of any other tobacco product or e-cigarette at 1 year follow-up

<table>
<tr><td></td><td>Exposed n = 255</td><td>Unexposed n = 9,058</td><td>aOR* (95% CI)</td><td>aRR** calculated by analyst</td></tr>
<tr><td>Number who initiate cigarette smoking (%)</td><td>39 (15.3)</td><td>317 (3.5)</td><td>2.99 (1.98 - 4.53)</td><td>2.80 (1.91 – 3.33)</td></tr>
</table>
*Reported by study. Adjusted for sex, age, race/ethnicity, parental educational level, urban residence, sensation seeking, alcohol ever use, living with tobacco user, notice of cigarette warning labels, tobacco advertising receptivity and summer season.
**Calculated by review team. The unexposed group prevalence used to calculate the aRR was 0.0349.

Cigarette past 30-day use
Baseline ever e-cigarette users vs never users of any other tobacco product or e-cigarette at 1 year follow-up

<table>
<tr><td></td><td>Exposed n = 255</td><td>Unexposed n = 9,058</td><td>aOR* (95% CI)</td><td>aRR** calculated by analyst</td></tr>
<tr><td>Number who initiate cigarette smoking (%)</td><td>14 (5.4)</td><td>145 (1.6)</td><td>2.12 (1.11 - 4.03)</td><td>2.08 (1.11 – 3.84)</td></tr>
</table>
*Reported by study. Adjusted for sex, age, race/ethnicity, parental educational level, urban residence, sensation seeking, alcohol ever use, living with tobacco</td></tr>
</table>

<table>
<tr><td>Bibliographic reference/s</td><td colspan="3">Watkins Shannon L, Glantz Stanton A, Chaffee Benjamin W (2018) Association of noncigarette tobacco product use with future cigarette smoking among youth in the population assessment of tobacco and health (PATH) study, 2013-2015. JAMA paediatrics 172(2),181-187.</td></tr>
<tr><td>Study name</td><td colspan="3">Watkins 2018</td></tr>
<tr><td></td><td colspan="3">user, notice of cigarette warning labels, tobacco advertising receptivity and summer season.
**Calculated by review team. The unexposed group prevalence used to calculate the aRR was 0.016.

The following is not reported:
Outcome by nicotine vs non-nicotine e-cigs
Outcome by e-cig type
Outcome by age category
Outcome by socioeconomic deprivation
Outcome by family / peer smoking presence vs absence.</td></tr>
<tr><td>Important outcomes measures and effect size. (time points)</td><td colspan="3">No important outcomes reported.</td></tr>
<tr><td>Statistical Analysis</td><td colspan="3">Statistical analysis: weighted logistic regression models to obtain unadjusted and adjusted relative odds of wave 2 cigarette smoking initiation across groups of wave 1 noncigarette tobacco use. Adjusted for sex, age, race/ethnicity, parental educational level, urban residence, sensation seeking and seasonal variation in tobacco use. Models also used sample weights accounting for non-response.
Missing data: Multiple imputation by chained equations (30 imputations) to account for missing data in independent variables.</td></tr>
<tr><td>Risk of bias (ROB)
QUIPS tool</td><td colspan="3">Cigarette ever use at follow-up

<table><tr><th>Outcome</th><th>Judgement</th><th>Comments</th></tr><tr><td>Study participation</td><td>Moderate</td><td>Sample reportedly representative of the population. However, no sample or population characteristics described for e-cigarette single product users.</td></tr><tr><td>Study attrition</td><td>Moderate</td><td>Attrition is reasonable at 12.1% between waves 1 and 2, however reasons for loss to follow up and drop outs are not described. Authors do not report whether there were important differences between drop outs and participants that completed follow-up. However, data imputation was completed to account for missing data.</td></tr><tr><td>Prognostic factor management</td><td>Moderate</td><td>Prognostic factor fairly well defined. Self-reported. Measured consistently between both groups.</td></tr></table></td></tr>
</table>

Bibliographic reference/s	**Watkins Shannon L, Glantz Stanton A, Chaffee Benjamin W (2018) Association of noncigarette tobacco product use with future cigarette smoking among youth in the population assessment of tobacco and health (PATH) study, 2013-2015. JAMA paediatrics 172(2),181-187.**		
Study name	Watkins 2018		
	Outcome measurement	Moderate	Outcome fairly well defined and measured consistently for exposed and unexposed. Subjective measure so possible that participants were not truthful.
	Study confounding	Moderate	Collects data for and adjusts for many of the important confounders identified.
	Statistical analysis and reporting	Moderate	No apparent selective reporting of results.
	Overall Risk of Bias	Acceptable risk of bias.	
	Other outcome details: Cigarette past 30-day use (as above)		
Source of funding	US National Cancer Institute, Food and Drug Administration Centre for Tobacco Products, National Institute on Drug Abuse and US National Centre for Advancing Translational Sciences.		
Comments	-Participants were given $25 upon completion of questionnaire at each wave. -Parental consent was requested for participating youths. -Authors report that in-home computer-assisted interviews used in PATH may have resulted in different prevalence estimates compared with in-school surveys, with an unknown effect on associations between noncigarette tobacco use and initiation of cigarette smoking. -Authors report that not accounting for poly-tobacco use will overestimate the magnitude of the effects of e-cigarettes alone.		
Additional references	None		

Wills 2016 and Wills 2017*

Bibliographic reference/s	**Wills Thomas A, Sargent James D, Gibbons Frederick X, Pagano Ian, and Schweitzer Rebecca (2016) E-cigarette use is differentially related to smoking onset among lower risk adolescents. Tobacco control 26(5), 534-539** **Wills Thomas A, Knight Rebecca, Sargent James D, Gibbons Frederick X, Pagano Ian, and Williams Rebecca J (2017) Longitudinal study of e-cigarette use and onset of cigarette smoking among high school students in Hawaii. Tobacco control 26(1), 34-39**
Study name	Wills 2016 and Wills 2017
Registration	Not reported
Study type	Cohort (prospective)
Study dates	2013-2014
Objective	2016: To test whether the effect of e-cigarette use for smoking onset differs for youth who have lower vs higher propensity to smoke.

<table>
<tr><td>Bibliographic reference/s</td><td>Wills Thomas A, Sargent James D, Gibbons Frederick X, Pagano Ian, and Schweitzer Rebecca (2016) E-cigarette use is differentially related to smoking onset among lower risk adolescents. Tobacco control 26(5), 534-539

Wills Thomas A, Knight Rebecca, Sargent James D, Gibbons Frederick X, Pagano Ian, and Williams Rebecca J (2017) Longitudinal study of e-cigarette use and onset of cigarette smoking among high school students in Hawaii. Tobacco control 26(1), 34-39</td></tr>
<tr><td>Study name</td><td>Wills 2016 and Wills 2017</td></tr>
<tr><td></td><td>(Results measure the interaction between baseline e-cigarette use and baseline propensity to smoke on smoking initiation at follow-up).

2017: To examine how e-cigarette use among adolescents is related to subsequent smoking behaviour.</td></tr>
<tr><td>Country/ Setting</td><td>USA, Hawaii
High school setting</td></tr>
<tr><td>Cohort source</td><td>Unnamed cohort.
Cohort is students from six high schools (four public and two private) in Hawaii, between 9th grade (14-15 years) and 11th grade (16-17 years).</td></tr>
<tr><td>Number entering into study (invited)</td><td>3340 participants invited into study (review team calculated from percentages).
2338 completed baseline data collection.</td></tr>
<tr><td>Number of participants evaluated</td><td>2016: 1136 participants completed both baseline and follow-up data collection.
Power information not reported
2017: unclear</td></tr>
<tr><td>Prognostic factor</td><td>Ever e-cigarette use: Participants were asked “which of the following is most true for you about smoking electronic cigarettes (e-cigarette, Volcanos)?”. Responses were from “I have never smoked an e-cigarette in my life” to “I usually smoke e-cigarettes every day”. Assumed, but not reported, that selecting never were classed as ‘never users’ and any other response as ‘ever users’.
Type of e-cigarette and generation not reported.</td></tr>
<tr><td>Baseline study sample characteristics</td><td>2016: Characteristics of longitudinal sample at baseline (including both baseline smokers and non-smokers) (2017 does not report baseline characteristics)
<table>
<tr><td>Characteristics</td><td>Sample (n = 1136)</td></tr>
<tr><td>Mean age years (SD)</td><td>14.8 (0.7)</td></tr>
<tr><td>Female (%)</td><td>57</td></tr>
<tr><td>Ethnicity</td><td>34% Asian-American, 17% Caucasian, 25% Filipino-American, 17% Native Hawaiian or other Pacific Islander, 7% other.</td></tr>
<tr><td>Family structure</td><td>15% single parent, 9% stepparent family, 66% two biological parents, 10% extended family.</td></tr>
<tr><td>Father’s education (finished high school or more, %)</td><td>96</td></tr>
<tr><td>Susceptibility to smoking*</td><td>Not reported</td></tr>
<tr><td>Family smoking</td><td>Not reported</td></tr>
<tr><td>Peer smoking</td><td>Not reported</td></tr>
<tr><td>Rebelliousness** (mean, SD)</td><td>6.48 (3.05)</td></tr>
</table></td></tr>
</table>

Bibliographic reference/s	**Wills Thomas A, Sargent James D, Gibbons Frederick X, Pagano Ian, and Schweitzer Rebecca (2016) E-cigarette use is differentially related to smoking onset among lower risk adolescents. Tobacco control 26(5), 534-539** **Wills Thomas A, Knight Rebecca, Sargent James D, Gibbons Frederick X, Pagano Ian, and Williams Rebecca J (2017) Longitudinal study of e-cigarette use and onset of cigarette smoking among high school students in Hawaii. Tobacco control 26(1), 34-39**
Study name	Wills 2016 and Wills 2017
	Parental support** (mean, SD): 25.98 (6.91) Willingness to smoke** (mean, SD): 3.28 (0.86) *Partly covered under by propensity to smoke measure **Combined to make composite measure for propensity to smoke. Higher scores indicate a higher level of the indicated variable. Rebelliousness: range 4-20 Parental support: range 7-35 Willingness to smoke: range 3-15 Representative of schools in Hawaii
Attrition	2016: 1202/2338 (51.4%) baseline participants did not complete follow-up. Both: Attrition effects tested for and some evidence of differential attrition (higher among those with higher rebelliousness / lower parental support). Small differences observed. 71% of missing cases at both data collection points were due to parents not returning consent form.
Inclusion and exclusion criteria	All 9th and 10th grade students with adequate English language ability. Baseline never-smokers only included in the analysis. Exclusion criteria not reported.
Data collection	Signed parental consent and student assent were required at each assessment. Survey administered in paper format, taking 40 minutes to complete. Trained research staff in school classrooms administered the survey. Numerical codes preserved anonymity and linked participants across data collection points. Other information collected from participants included the following: 2016 and 2017: Demographic: sex, age, family structure, parental education, ethnicity. 2016 and 2017: • Rebelliousness: Participants were asked to indicate how much they identified with 5 statements, on a 5-point Likert scale (‘not at all true for me’ to ‘very true for me’). E.g. I like to break the rules. • Parental support: Participants were asked to indicate how much they identified with 7 statements, on a 5-point Likert scale (‘not at all true for me’ to ‘very true for me’). E.g. when I feel bad about something, my parent will listen. • Willingness to smoke: Participants were asked how likely they would be to take each of three actions (take one puff, smoke a whole cigarette, take some cigarettes to try later) in response to being with a group of friends where cigarettes were available if they wanted. Likeliness to take each action assessed on a 4-point scale (from ‘not at all willing’ to ‘very willing’).

<table>
<tr><td>Bibliographic reference/s</td><td>Wills Thomas A, Sargent James D, Gibbons Frederick X, Pagano Ian, and Schweitzer Rebecca (2016) E-cigarette use is differentially related to smoking onset among lower risk adolescents. Tobacco control 26(5), 534-539

Wills Thomas A, Knight Rebecca, Sargent James D, Gibbons Frederick X, Pagano Ian, and Williams Rebecca J (2017) Longitudinal study of e-cigarette use and onset of cigarette smoking among high school students in Hawaii. Tobacco control 26(1), 34-39</td></tr>
<tr><td>Study name</td><td>Wills 2016 and Wills 2017</td></tr>
<tr><td></td><td>2016: responses about rebelliousness, parental support and willingness to smoke were combined into a composite measure for propensity to smoke.
2017:
Parental monitoring: Participants were asked to indicate how much they agreed with the statement ‘my parent knows where I am after school’ on a 5-point scale (assumed Likert).
Sensation seeking: Participants were asked to indicate how much they agreed with the statement ‘I like to do dangerous things for fun’ on a 5-point scale (assumed Likert).
Blinding not reported.</td></tr>
<tr><td>Outcome measure</td><td><u>Cigarette smoking initiation</u>: Participants were asked “which of the following is most true for you about smoking cigarettes?”. Responses were from “I have never smoked a cigarette in my life” to “I usually smoke cigarettes every day”. Baseline never smokers reporting any smoking at follow up were considered to have initiated smoking</td></tr>
<tr><td>Follow up</td><td>1 year</td></tr>
<tr><td>Critical outcomes measures and effect size. (time points)</td><td>2016: Smoking initiation (interaction between e-cigarette use and propensity to smoke at baseline)
Baseline ever e-cigarette users vs never-users 1-year follow-up (among baseline never-smokers)
<table>
<tr><th></th><th>Propensity percentile</th><th>Exposed n = 168*</th><th>Unexposed n = 872*</th><th>aOR** (95% CI)</th><th>aRR*** calculated by analyst</th></tr>
<tr><td rowspan="5">Number who initiate smoking (%)</td><td>10th</td><td>Not reported</td><td>Not reported</td><td>2.23 (1.57, 3.17)</td><td>1.97 (1.48, 2.58)</td></tr>
<tr><td>25th</td><td>Not reported</td><td>Not reported</td><td>2.18 (1.56, 3.06)</td><td>1.94 (1.47, 2.51)</td></tr>
<tr><td>50th</td><td>Not reported</td><td>Not reported</td><td>1.76 (1.47, 2.10)</td><td>1.63 (1.40, 1.88)</td></tr>
<tr><td>75th</td><td>Not reported</td><td>Not reported</td><td>1.42 (1.31, 1.54)</td><td>1.36 (1.27, 1.46)</td></tr>
<tr><td>90th</td><td>Not reported</td><td>Not reported</td><td>1.32 (1.19, 1.47)</td><td>1.28 (1.17, 1.40)</td></tr>
</table>
*Calculated by review team from percentages</td></tr>
</table>

<table>
<tr><td>Bibliographic reference/s</td><td>Wills Thomas A, Sargent James D, Gibbons Frederick X, Pagano Ian, and Schweitzer Rebecca (2016) E-cigarette use is differentially related to smoking onset among lower risk adolescents. Tobacco control 26(5), 534-539

Wills Thomas A, Knight Rebecca, Sargent James D, Gibbons Frederick X, Pagano Ian, and Williams Rebecca J (2017) Longitudinal study of e-cigarette use and onset of cigarette smoking among high school students in Hawaii. Tobacco control 26(1), 34-39</td></tr>
<tr><td>Study name</td><td>Wills 2016 and Wills 2017</td></tr>
<tr><td></td><td>**Reported by study. Adjusted for gender, ethnicity, father’s education.
***Calculated by review team. The unexposed group prevalence used to calculate the aRR was 0.106, calculated from unexposed prevalence at follow-up (92/872 initiated smoking).

For the purposes of meta-analysis, the 25th percentile result is categorised as “non-susceptible” and the 75th percentile result is categorised as “susceptible”.

2017: Smoking initiation
Baseline ever e-cigarette users vs never-users 1-year follow-up (among baseline never-smokers)
<table>
<tr><td></td><td>Exposed n = 215*</td><td>Unexposed n = 926*</td><td>aOR** (95% CI)</td><td>aRR*** calculated by analyst</td></tr>
<tr><td>Number who initiate smoking (%)</td><td>42 (19.5)*</td><td>50 (5.4)*</td><td>1.67 (1.17, 2.39)</td><td>1.61 (1.16, 2.22)</td></tr>
</table>
*Calculated by review team from percentages
**Reported by study. Adjusted for age, gender, ethnicity, parental education, parental support, rebelliousness.
***Calculated by review team. The unexposed group prevalence used to calculate the aRR was 0.054.

2017: smoking initiation (by frequency of e-cig use at baseline)
Baseline e-cigarette users vs never-users 1-year follow-up (among baseline never-smokers)
<table>
<tr><td>Number who initiate smoking (%)</td><td>Exposed n = *</td><td>Unexposed n = *</td><td>aOR** (95% CI)</td><td>aRR*** calculated by analyst</td></tr>
<tr><td>Experimental (yearly / monthly) vs never e-cig use</td><td>*</td><td>*</td><td>4.17 (2.03, 8.57)</td><td>3.56 (1.92, 6.08)</td></tr>
<tr><td>Regular (weekly / daily) vs never e-cig use</td><td>*</td><td>*</td><td>4.09 (2.43, 6.88)</td><td>3.51 (2.56, 5.22)</td></tr>
</table>
*Not reported in the paper and not calculable
**Reported by study. Adjusted for age, gender, ethnicity, ‘parenting and personality variables’ (assume to be all for 2017 in ‘data collection’).</td></tr>
</table>

Bibliographic reference/s	**Wills Thomas A, Sargent James D, Gibbons Frederick X, Pagano Ian, and Schweitzer Rebecca (2016) E-cigarette use is differentially related to smoking onset among lower risk adolescents. Tobacco control 26(5), 534-539** **Wills Thomas A, Knight Rebecca, Sargent James D, Gibbons Frederick X, Pagano Ian, and Williams Rebecca J (2017) Longitudinal study of e-cigarette use and onset of cigarette smoking among high school students in Hawaii. Tobacco control 26(1), 34-39**
Study name	Wills 2016 and Wills 2017
	***Calculated by review team. The unexposed group prevalence used to calculate the aRR was 0.054, as per the overall prevalence above (prevalence for these outcomes not reported by the study)
Important outcomes measures and effect size. (time points)	No important outcomes reported
Statistical Analysis	2016: Multilevel logistic regression analysis was used to assess the interaction between e-cigarette use and smoking propensity for predicting smoking onset. The model was adjusted for clustering within schools Complete-case model was used (complete outcome data at baseline and follow-up). Baseline missing values were computed using multiple imputations with 20 imputations based on the Markov Chain Monte Carlo method. Results were adjusted for gender, ethnicity, father's education. 2017: Multilevel logistic regression analysis was used to assess the interaction between e-cigarette use smoking onset. Model adjusted for covariates. The model was adjusted for clustering within schools. A full-information analysis was used to include those who did not have complete data at baseline and follow-up. Based on multiple imputation, employing Markov Chain Monte Carlo Method.
Risk of bias (ROB) QUIPS tool	2016: Smoking initiation (interaction between e-cigarette use and propensity to smoke at baseline)

Outcome	Judgement	Comments
Study participation	Low	Sample described as representative of Hawaiian high schools. Sampling frame described. Inclusion criteria given. Participation at baseline was 70%. Baseline sample characteristics described.
Study attrition	Moderate	Attrition is high (>50%). Some analysis of differences between lost to follow-up and completers. Some differences exist which may differentially affect exposed and unexposed groups.

Bibliographic reference/s	**Wills Thomas A, Sargent James D, Gibbons Frederick X, Pagano Ian, and Schweitzer Rebecca (2016) E-cigarette use is differentially related to smoking onset among lower risk adolescents. Tobacco control 26(5), 534-539** **Wills Thomas A, Knight Rebecca, Sargent James D, Gibbons Frederick X, Pagano Ian, and Williams Rebecca J (2017) Longitudinal study of e-cigarette use and onset of cigarette smoking among high school students in Hawaii. Tobacco control 26(1), 34-39**		
Study name	Wills 2016 and Wills 2017		
	Prognostic factor management	Moderate	PF moderately well defined: how it is dichotomised is not explicit. Measured consistently. Self-reported.
	Outcome measurement	Moderate	Outcome well defined. Measured consistently. Self-reported.
	Study confounding	Moderate	Peer and family smoking not measured or adjusted for. Other confounders (sociodemographic) adjusted for, and propensity to smoke is part of the analysis.
	Statistical analysis and reporting	Low	No apparent selective reporting, model well described.
	Overall Risk of Bias	Acceptable risk of bias	
	Other outcome details: 2017: Smoking initiation. Study participation: Moderate (characteristics not described). Study attrition: Low (full-information analysis used) Overall: Acceptable risk of bias 2017: Smoking initiation (by frequency of e-cig use at baseline) Overall: As for smoking initiation		
Source of funding	National cancer Institute		
Comments	• Overall results for exposed vs unexposed not presented. • Results suggest that although smoking initiation is higher among those who use e-cigs at baseline, and among those with a higher propensity to smoke, the effect of having used e-cigs at baseline for smoking onset was greater among participants with lower propensity to smoke. • Authors point out that the measure of e-cig use did not capture types of product or context of use. At the time of the study, most models were cig-a-likes.		
Additional references	None		

*Two publications reporting on the same data from the same cohort. Publication year is used to indicate where data is from. Where no publication year is present in a field, data is consistent across the two publications.

Future cigarette use among children, young people and young adults who use e-cigarettes and smoke

Unger 2016

Bibliographic reference/s	**Unger Jennifer B, Soto Daniel W, Leventhal Adam (2001) E-cigarette use and subsequent cigarette and marijuana use among Hispanic young adults. Drug and Alcohol dependence 163, 261-264**
Study name	Unger 2016
Registration	Not reported
Study type	Cohort (prospective)
Study dates	2014 -2015
Objective	To assess whether e-cigarettes change the likelihood of young adults who smoke continuing to smoke at follow-up.
Country/ Setting	USA, Los Angeles
Cohort source	Project RED study Participants originally recruited in 9th grade (14 years old) in 2015, and subsequently followed up annually.
Number entering into study (invited)	Participants included 1,445 Hispanic young adults who originally participated in the high school survey in 2005 (annually until 2015).
Number of participants evaluated	1,332 participants completed both 2014 and 2015 surveys. Authors do not report information on power but acknowledge that the analyses were based on a small number of participants.
Prognostic factor	Past-month e-cigarette use: participants were asked whether they had used an e-cigarette in the past month and responding either yes or no. No information on nicotine content or generation of e-cigarette. Unclear whether e-cigarettes were being used recreationally (of interest) or for cessation (not of interest).
Baseline study sample characteristics	Characteristics of those who completed baseline and follow-up surveys

	Sample (n = 1332)
Age (mean, SD)	22.7 (0.39)
Female (%)	59
Ethnicity	Hispanic
Susceptibility to smoking (yes, %)*	Not reported
Family smoking	Not reported
Peer smoking	Not reported

	Limited generalisability as participants were originally recruited as students from high schools in Los.
Attrition	92% of participants completed both surveys, loss to follow up: 8%. Participants who dropped out were not investigated.

<table>
<tr><td>Bibliographic reference/s</td><td>Unger Jennifer B, Soto Daniel W, Leventhal Adam (2001) E-cigarette use and subsequent cigarette and marijuana use among Hispanic young adults. Drug and Alcohol dependence 163, 261-264</td></tr>
<tr><td>Study name</td><td>Unger 2016</td></tr>
<tr><td>Inclusion and exclusion criteria</td><td>• Participants were categorised into 2 groups as either past-month cigarette smokers or past-month non-smokers based on cigarette use in 2014. Past-month smokers are of relevance to this review.
• Exclusion criteria not reported.</td></tr>
<tr><td>Data collection</td><td>Participants; use of combustible cigarettes, e-cigarettes, age, sex, past-month use of alcohol and other tobacco products (hookah, cigars, little cigars and smokeless tobacco) collected by online surveys in 2014 and 2015. Participants were contacted by email, text message, phone call and/or social media to complete online survey.
Information on blinding not reported.</td></tr>
<tr><td>Outcome measure</td><td><u>Past-month cigarette smoking in 2015:</u> participants were asked about their use of combustible cigarettes and classified according to their use in the last month. Response options were yes or no.</td></tr>
<tr><td>Follow up</td><td>1 year</td></tr>
<tr><td>Critical outcomes measures and effect size. (time points)</td><td>Past-month continued cigarette smoking
Baseline past-month e-cigarette user vs non e-cigarette user (among past month cigarette users)
<table>
<tr><td></td><td>Exposed n = 76</td><td>Unexposed n = 200</td><td>aOR* (95% CI)</td><td>aRR** calculated by analyst</td></tr>
<tr><td>Number who had smoked in the past month in 2015 (%)</td><td>48 (63)</td><td>116 (58)</td><td>1.31 (0.73, 2.36)</td><td>1.11 (0.87, 1.32)</td></tr>
</table>
*Reported by study. Adjusted for age, sex, past-month use in 2014: alcohol, cigar, little cigar, hookah and smokeless tobacco. The authors report this as past-month e-cigarette/marijuana use in 2014.
**Calculated by review team. The unexposed group prevalence used to calculate the aRR was 0.58.

The following is not reported:
• Outcome by nicotine vs non-nicotine e-cigs
• Outcome by e-cig type
• Outcome by age category
• Outcome by socioeconomic deprivation
• Outcome by family / peer smoking presence vs absence.</td></tr>
<tr><td>Important outcomes measures and effect size. (time points)</td><td>No important outcomes reported.</td></tr>
<tr><td>Statistical Analysis</td><td><u>Statistical analysis:</u> Sample was stratified into 2 groups: past-month cigarette smokers and past-month cigarette non-smokers. Within each group logistic regression analysis was conducted to determine the likelihood of being a past-</td></tr>
</table>

Bibliographic reference/s	**Unger Jennifer B, Soto Daniel W, Leventhal Adam (2001) E-cigarette use and subsequent cigarette and marijuana use among Hispanic young adults. Drug and Alcohol dependence 163, 261-264**		
Study name	Unger 2016		
	month cigarette smoker in 2015. Analysis adjusted for age, sex, past-month use in 2014 of alcohol, cigar, little cigar, hookah and smokeless tobacco. Authors do not report any methods used to account for missing data.		
Risk of bias (ROB) QUIPS tool	Past-month continued cigarette smoking in 2015		
	Outcome	**Judgement**	**Comments**
	Study participation	High	The source and baseline sample population are not clearly described. Authors state that as participants were recruited from high schools, this limits the generalisability of the results.
	Study attrition	Moderate	Attrition is low at 8%, however no reason for loss to follow up are provided. Differences between drop outs and completers are not mentioned, and authors do not report any methods to account for missing data.
	Prognostic factor management	High	Prognostic factor is not well defined and is self-reported. Prognostic factor is measured consistently across groups however is reported in combination with marijuana use in the results.
	Outcome measurement	Moderate	Outcome is not clearly defined
	Study confounding	Moderate	Various relevant potential confounders are considered and adjusted for, but peer smoking and family smoking not considered.
	Statistical analysis and reporting	Moderate	Data mostly presented, although some is unclear.
	Overall Risk of Bias	High risk of bias	
	Other outcome details: None		
Source of funding	National Institutes of Health		
Comments	- Authors note that frequency/amount of cigarette and e-cigarette use within the past month were not assessed, therefore it is not clear whether the findings reflect experimental use or habitual use. -The survey did not include questions to assess impulsivity, rebelliousness or sensation seeking.		

Bibliographic reference/s	**Unger Jennifer B, Soto Daniel W, Leventhal Adam (2001) E-cigarette use and subsequent cigarette and marijuana use among Hispanic young adults. Drug and Alcohol dependence 163, 261-264**
Study name	Unger 2016
	- Because it is unclear whether e-cigarettes were being used recreationally (of interest) or for cessation (not of interest), results should be interpreted with caution. If cessation is the aim of use, then the study is testing their effectiveness for cessation. The review is instead meant to track whether recreational use replaces smoking over time.
Additional references	None

Stanton 2019

Bibliographic reference/s	**Stanton Cassandra A, Bansal-Travers Maansi, Johnson Amanda L, et al. (2019) Longitudinal e-Cigarette and Cigarette Use Among US Youth in the PATH Study (2013-2015). Journal of the National Cancer Institute 111(10), 1088-1096**
Study name	Stanton 2019
Registration	Not reported
Study type	Cohort (prospective)
Study dates	Wave 1: September 2013- December 2014 Wave 2: October 2014 – October 2015
Objective	To describe weighted longitudinal bidirectional transitions in ENDS and cigarette use and to determine if ever- compared to never-ENDS use at baseline is associated with changes in cigarette smoking at follow-up.
Country/ Setting	USA
Cohort source	Population assessment of tobacco and health (PATH) study
Number entering into study (invited)	11,996 participants completed wave 1 and wave 2 survey.
Number of participants evaluated	1,497 participants evaluated. Power not reported
Prognostic factor	Ever use of e-cigarette: participants were asked if they had ever tried e-cigarettes (at baseline) or e-products (including e-cigarettes, e-cigars, e-pipes, and e-hookah) at follow-up. Baseline ever users were compared to baseline never users. No information on nicotine content or generation of e-cigarette. Unclear whether e-cigarettes were being used recreationally (of interest) or for cessation (not of interest).
Baseline study sample characteristics	Characteristics of sample not reported specifically for participants who had smoked at baseline.
Attrition	18.6% of baseline ever-smokers did not provide data towards the outcome reported for this review.

<table>
<tr><td>Bibliographic reference/s</td><td>Stanton Cassandra A, Bansal-Travers Maansi, Johnson Amanda L, et al. (2019) Longitudinal e-Cigarette and Cigarette Use Among US Youth in the PATH Study (2013-2015). Journal of the National Cancer Institute 111(10), 1088-1096</td></tr>
<tr><td>Study name</td><td>Stanton 2019</td></tr>
<tr><td>Inclusion and exclusion criteria</td><td>Inclusion and exclusion criteria not reported – analyses all participants who completed baseline and follow-up of the PATH cohort survey.</td></tr>
<tr><td>Data collection</td><td>The PATH youth sample included participants whose parents were sampled for the PATH adult survey, with 2 youths selected per household.
Data was collected by survey at both baseline and follow-up using in-person computer-assisted interviews at home in Spanish or English.</td></tr>
<tr><td>Outcome measure</td><td>Change in number of days smoked cigarettes: Change in the number of days smoked cigarettes in the past-30-days from W1 to W2. Self-report.</td></tr>
<tr><td>Follow up</td><td>1 year</td></tr>
<tr><td>Critical outcomes measures and effect size. (time points)</td><td>Change in number of days smoked cigarettes
Baseline ever e-cigarette users vs never users, among baseline ever-smokers (1 year)

<table>
<tr><td></td><td>Exposed n = 712</td><td>Unexposed n = 785</td><td>mean difference *</td></tr>
<tr><td>Change in number of days smoked in past 30 (mean, 95% CI)</td><td>1.44 (0.93, 1.95)</td><td>2.08 (1.40, 2.76)</td><td>-0.64 (-1.49, 0.21)</td></tr>
</table>
**Calculated by review team.</td></tr>
<tr><td>Important outcomes measures and effect size. (time points)</td><td>No important outcomes reported.</td></tr>
<tr><td>Statistical Analysis</td><td><u>Statistical analysis:</u> Propensity score matching used to estimate likelihoods and to draw matched analytic samples. Regression used to estimate effect of baseline ENDS use on follow-up cigarette smoking in matched samples. (goal of PSM is to balance covariate distributions in exposed and unexposed groups to minimise confounding.</td></tr>
<tr><td>Risk of bias (ROB)
QUIPS tool</td><td>Number of days smoking in past 30
<table>
<tr><th>Outcome</th><th>Judgement</th><th>Comments</th></tr>
<tr><td>Study participation</td><td>Moderate</td><td>Sample reportedly not representative of population due to (non-weighted) PSM method used. But sample from well-known cohort study with rigorous sampling methods.</td></tr>
<tr><td>Study attrition</td><td>Moderate</td><td>Attrition is reasonable at 18.6% between waves 1 and 2. Unclear whether even between exposed</td></tr>
</table></td></tr>
</table>

Bibliographic reference/s	**Stanton Cassandra A, Bansal-Travers Maansi, Johnson Amanda L, et al. (2019) Longitudinal e-Cigarette and Cigarette Use Among US Youth in the PATH Study (2013-2015). Journal of the National Cancer Institute 111(10), 1088-1096**		
Study name	Stanton 2019		
			and unexposed and reasons for loss to follow up and dropouts are not described.
	Prognostic factor management	Moderate	Prognostic factor fairly well defined. Self-reported. Measured consistently between both groups.
	Outcome measurement	Moderate	Outcome fairly well defined and measured consistently for exposed and unexposed. Subjective measure so possible that participants were not truthful.
	Study confounding	Moderate	PSM used to reduce confounding. Outcome not adjusted specifically.
	Statistical analysis and reporting	Low risk	No apparent selective reporting of results.
	Overall Risk of Bias	Acceptable risk of bias.	
	Other outcome details: None		
Source of funding	National Institute on Drug Abuse, National Institutes of health, center for Tobacco Products, food and Drug Administration, Department of health and Human Services.		
Comments	This study reports on the same waves of the PATH cohort study – and therefore the same participants - as Watkins 2018 in the review (in this document) about people who don't smoke at baseline. Some information about the cohort in this table is derived from Watkins 2018, where it is clear that the details will be the same for this paper. -Participants were given $25 upon completion of questionnaire at each wave. -Parental consent was requested for participating youths. -Authors report that in-home computer-assisted interviews used in PATH may have resulted in different prevalence estimates compared with in-school surveys, with an unknown effect on associations between noncigarette tobacco use and initiation of cigarette smoking.		
Additional references	None		

Appendix E – Forest plots

Future cigarette use among children, young people and young adults who use e-cigarettes and don't smoke

Exposed vs unexposed to e-cigarettes at baseline

Overall results for ever smoking

Figure 1: Ever smoking (among groups where susceptibility was not reported)

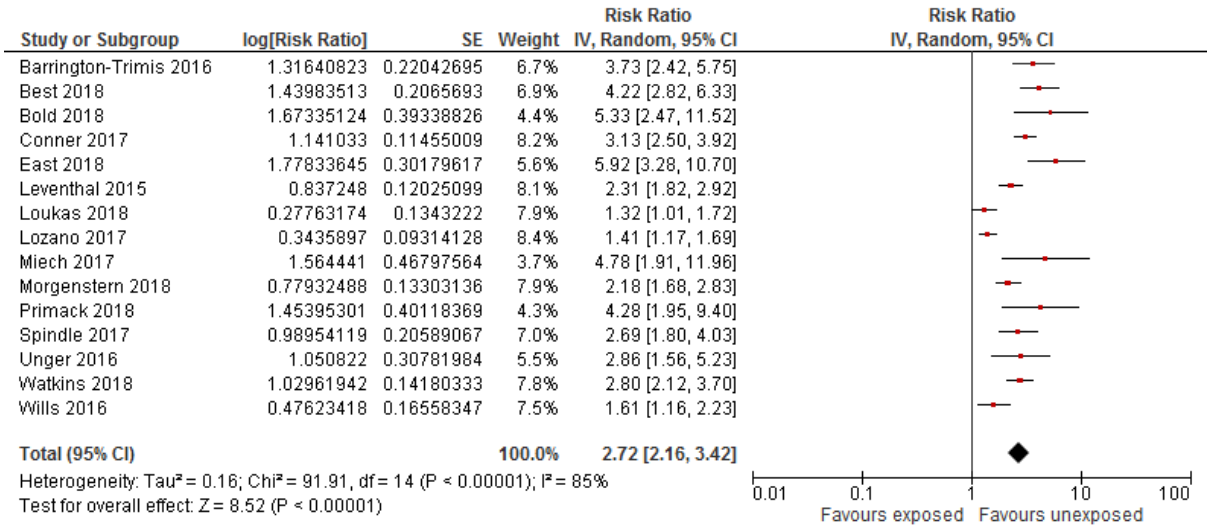
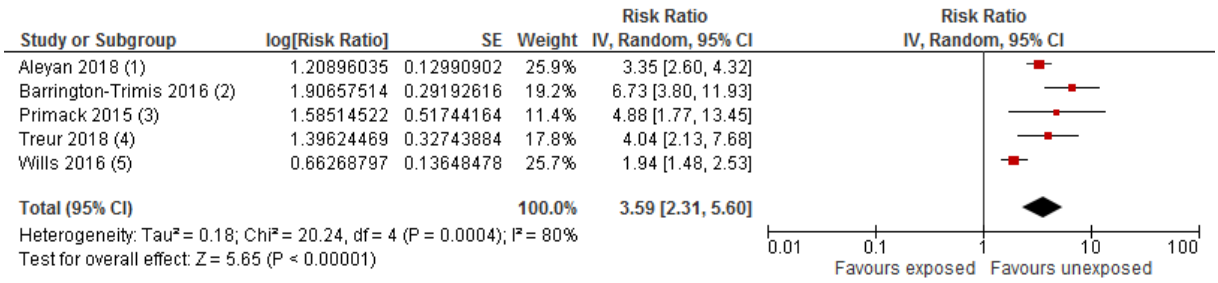
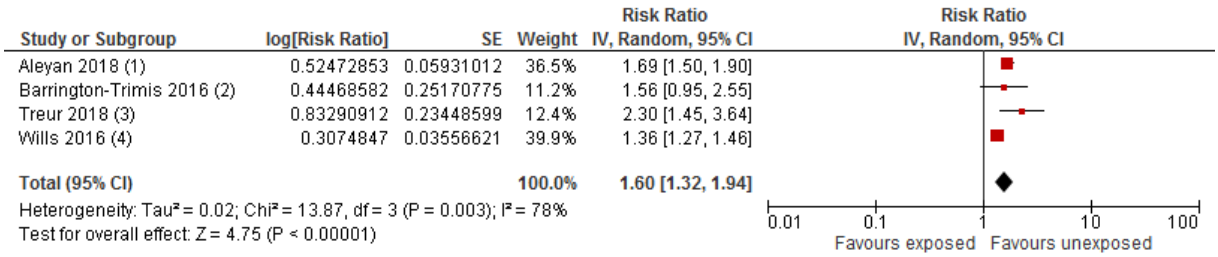


Figure 2: Ever smoking among baseline non-susceptible



Footnotes
(1) 2 questions; definitely not to both
(2) 3 questions; definitely not to both
(3) 2 questions; definitely not to both
(4) Propensity to smoke (composite measure of personality [SURPS], susceptibility [1 item] and intention to smoke). Below median propensity....
(5) Propensity to smoke (composite measure of rebelliousness, parental support and willingness to smoke). 25th percentile.

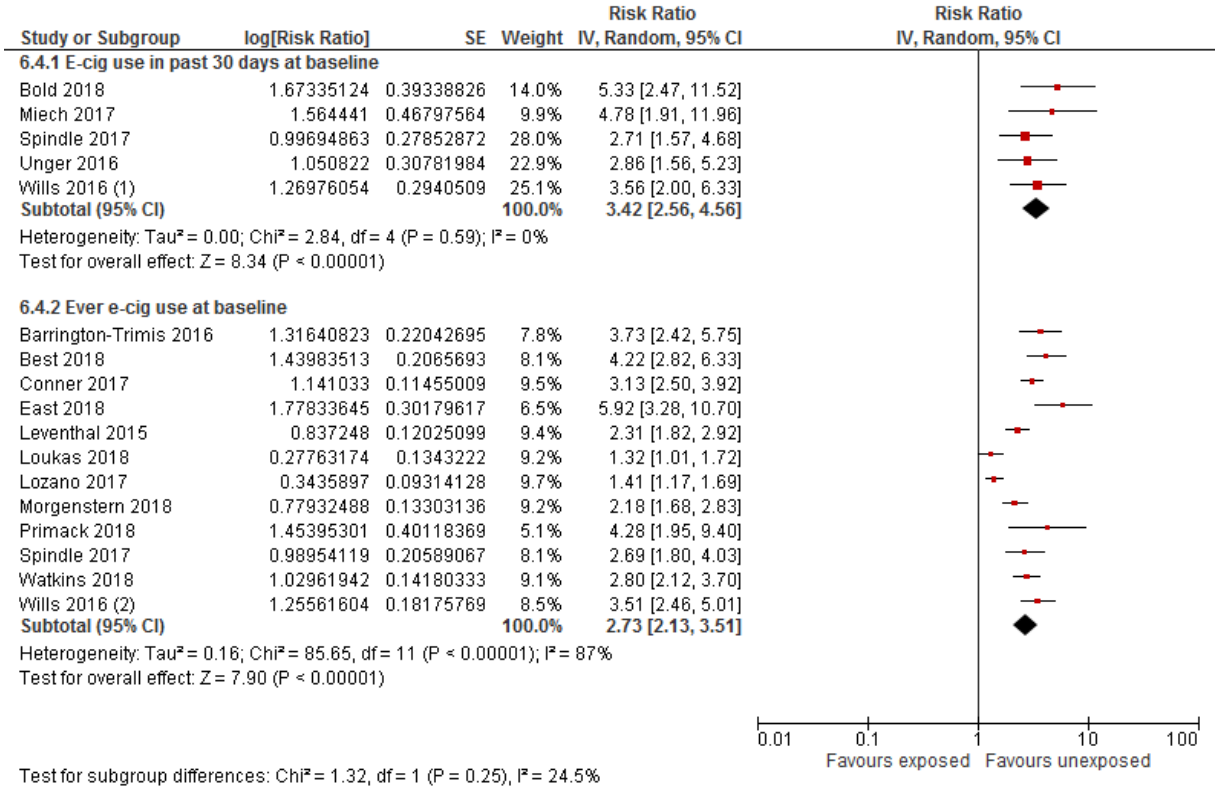
Figure 3: Ever smoking among baseline susceptible



Footnotes
(1) 2 questions; other than definitely not to both
(2) 3 questions; other than definitely not to both
(3) Propensity to smoke (composite measure of personality [SURPS], susceptibility [1 item] and intention to smoke). Above median propensity....
(4) Propensity to smoke (composite measure of rebelliousness, parental support and willingness to smoke). 75th percentile.

Ever smoking – subgroup by type of e-cigarette exposure

Figure 4: Ever smoking among groups where susceptibility was not reported



Test for subgroup differences: Chi² = 1.32, df = 1 (P = 0.25), I² = 24.5%

Footnotes
(1) Defined by study as regular use (weekly / daily)
(2) Defined by study as experimental use (yearly / monthly)

Figure 5: Ever smoking among baseline non-susceptible

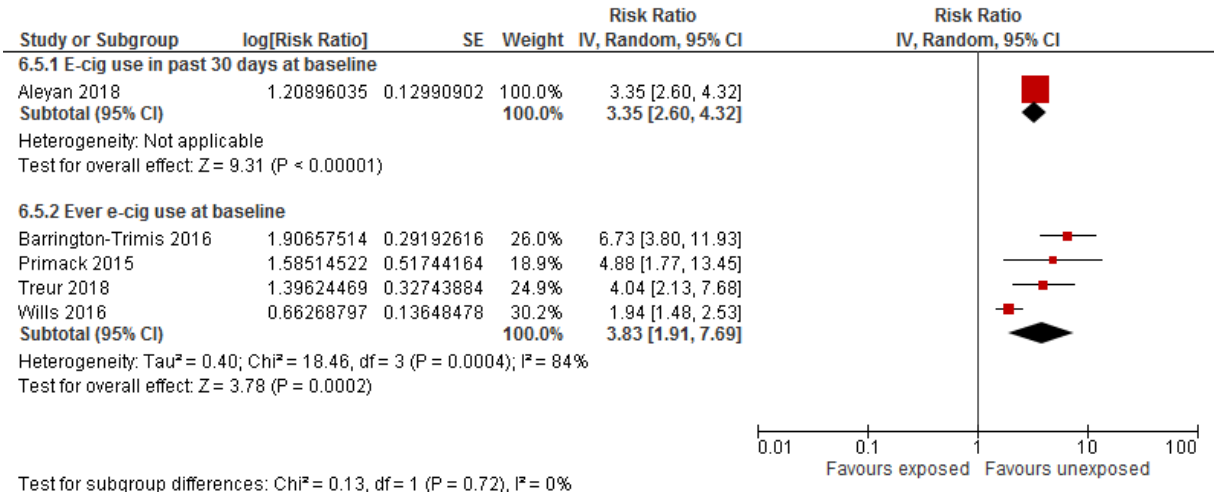
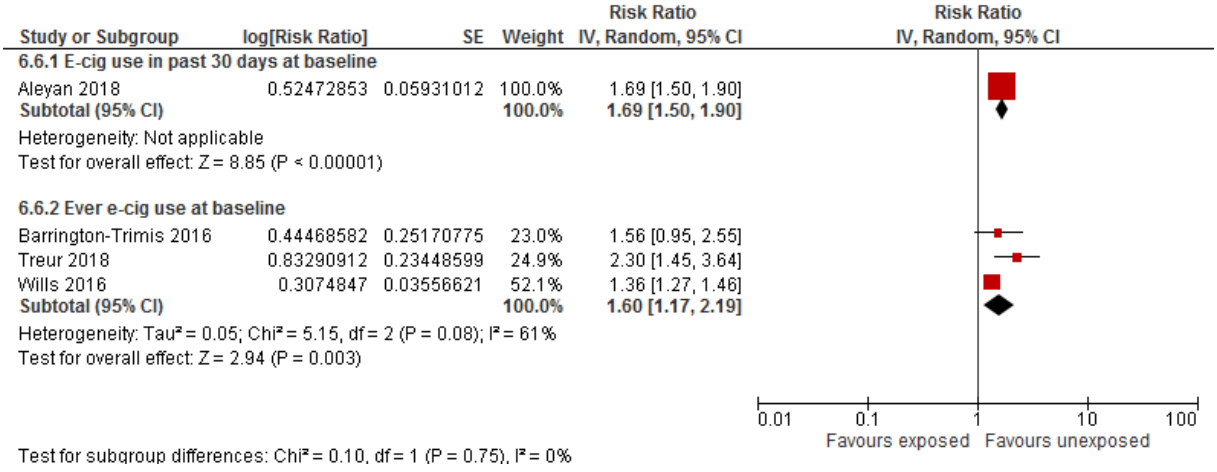


Figure 6: Ever smoking among baseline susceptible



Ever smoking – subgroup by age of sample

Figure 7: Ever smoking

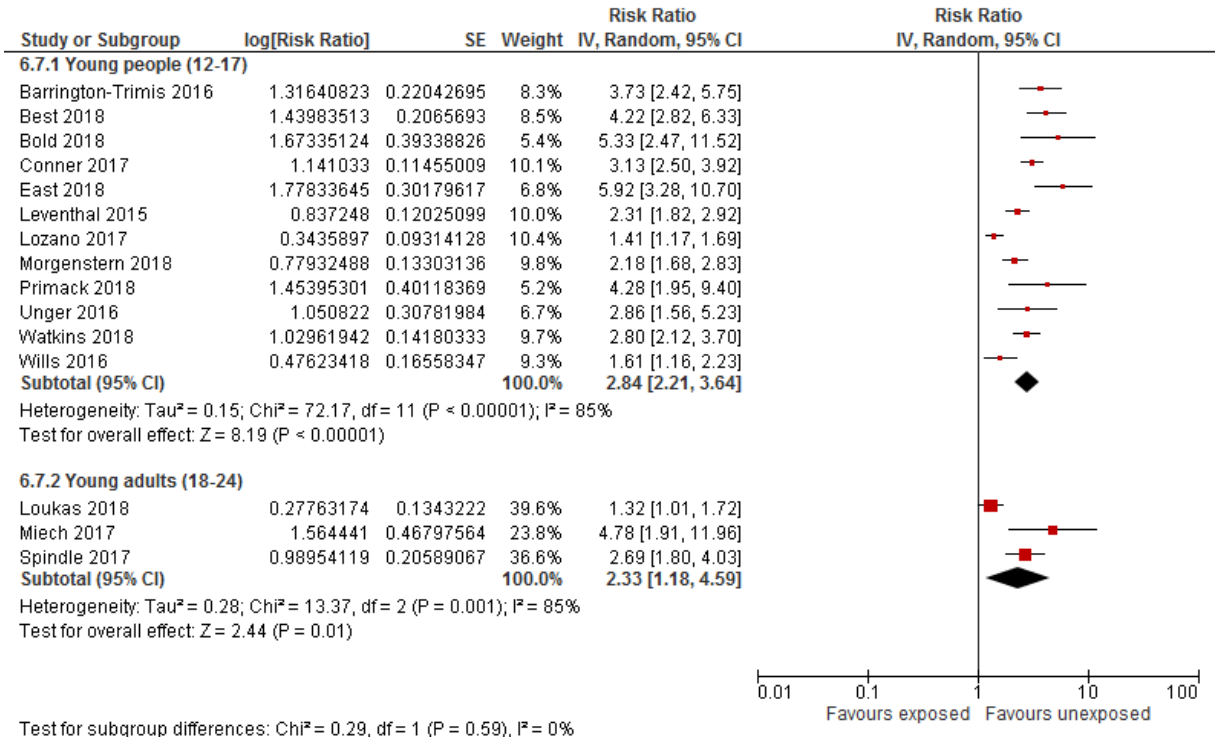


Figure 8: Ever smoking among baseline non-susceptible

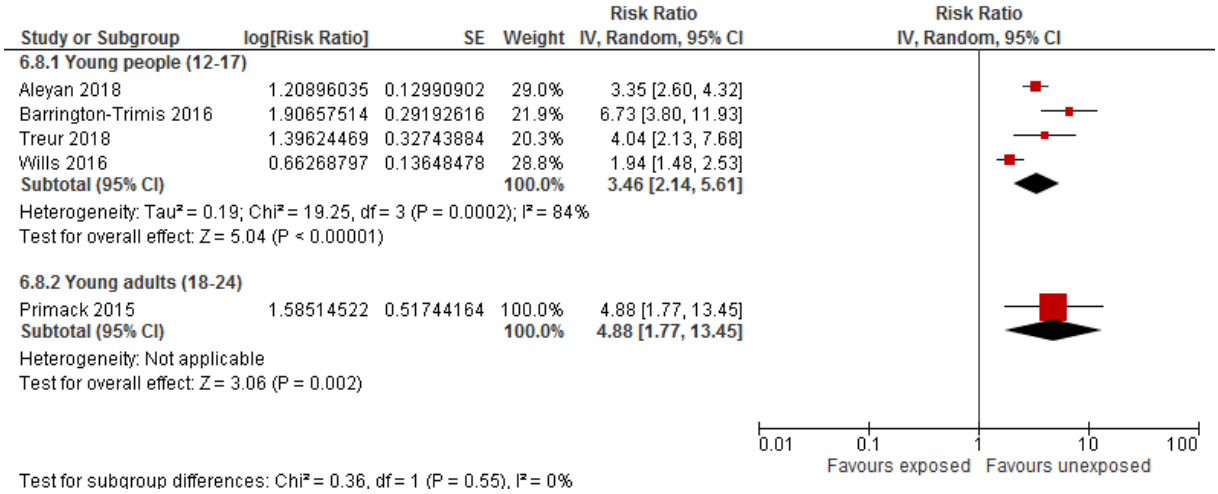


Figure 9: Ever smoking among baseline susceptible

Subgroup not possible, all studies report on young people only

Ever smoking – sensitivity analysis by risk of bias

Figure 10: Ever smoking

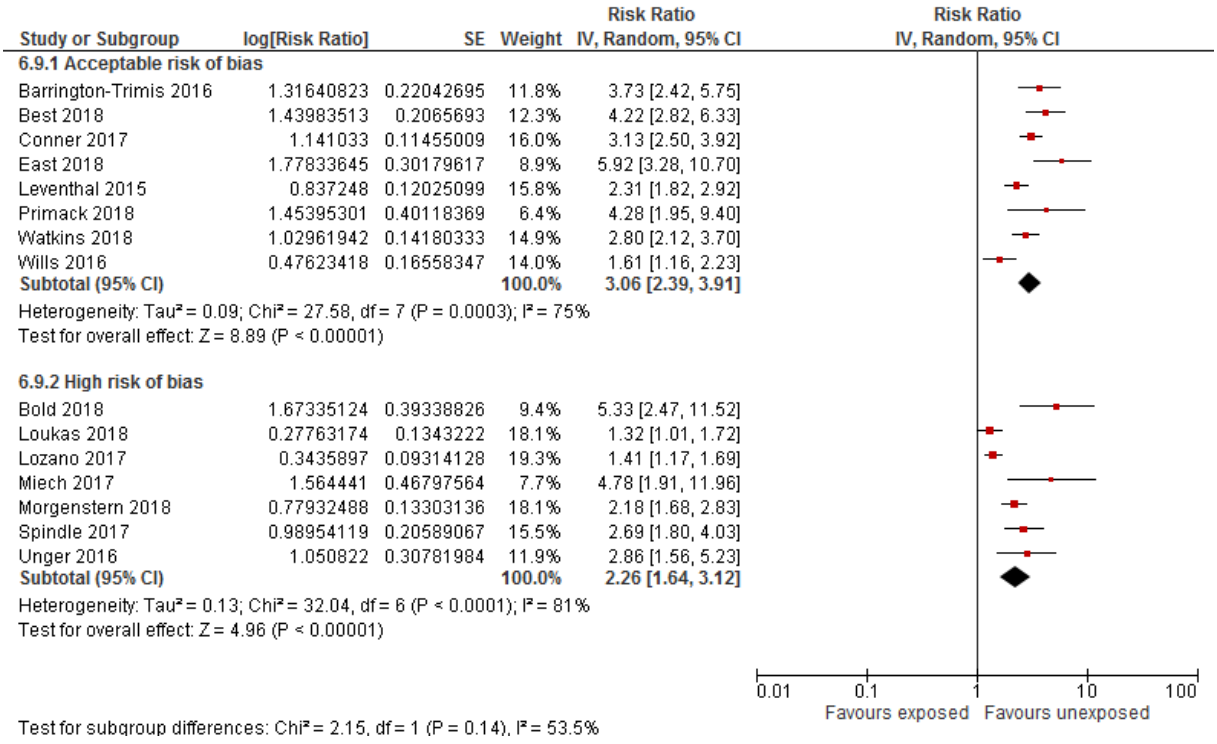


Figure 11: Ever smoking among baseline non-susceptible

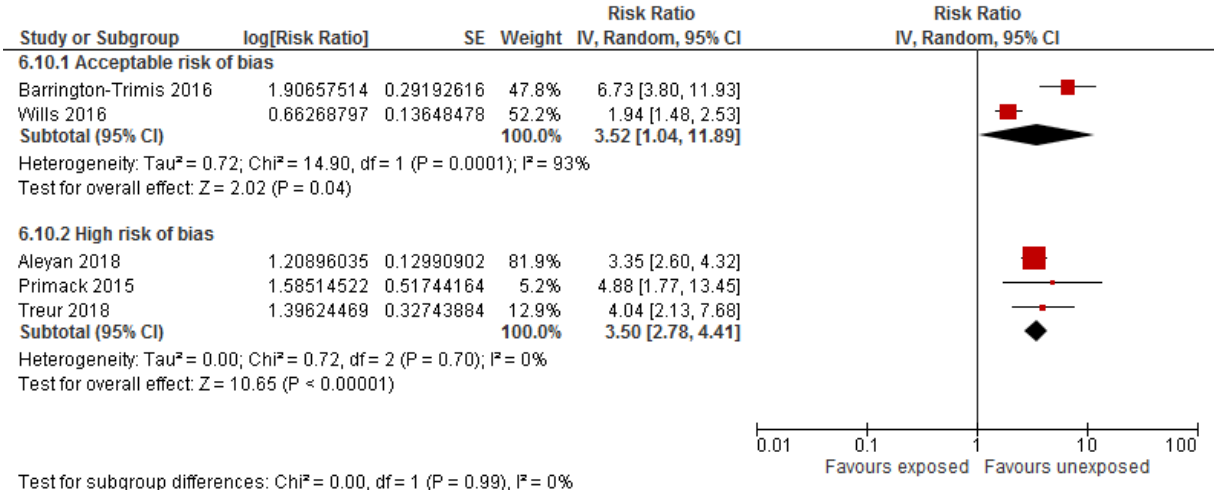
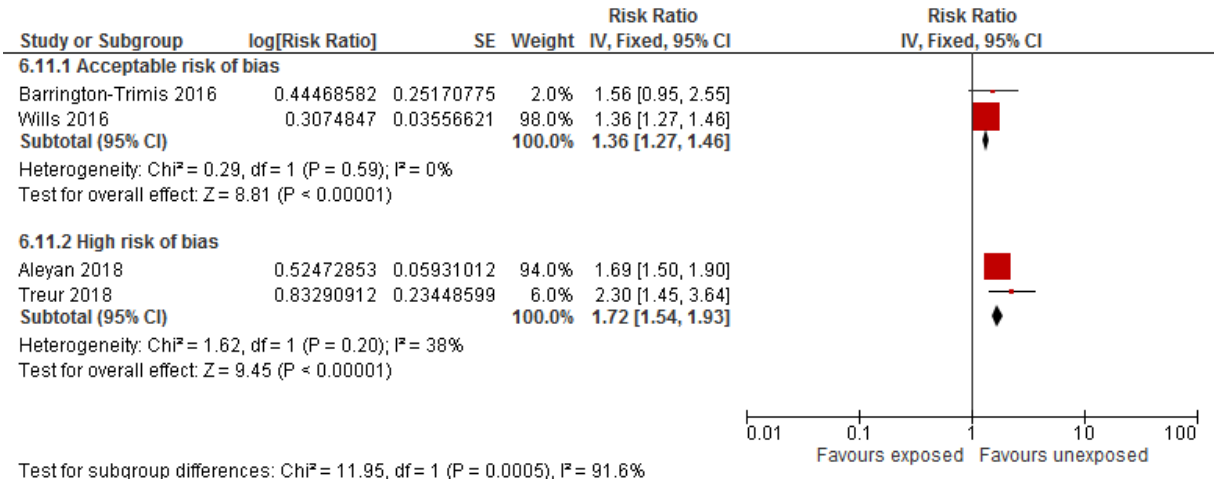


Figure 12: Ever smoking among baseline susceptible



Ever smoking – sensitivity analysis by adjustments for confounders

Figure 13: Ever smoking

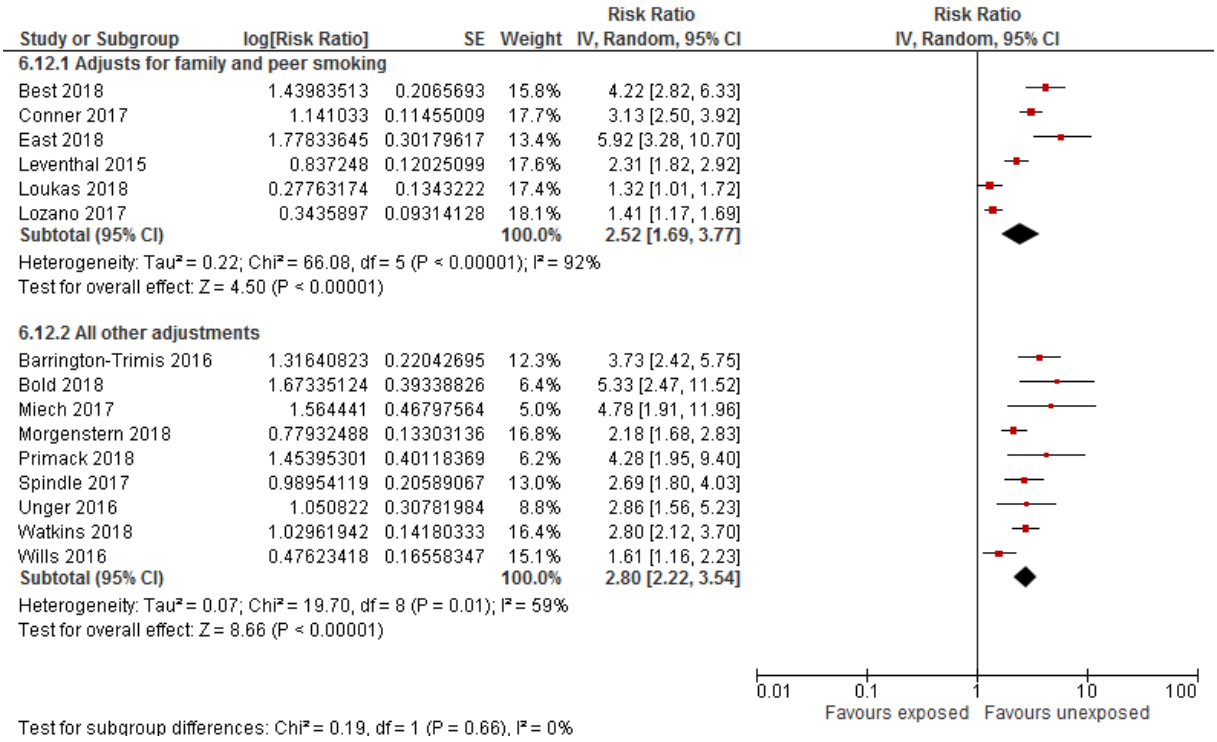


Figure 14: Ever smoking among baseline non-susceptible

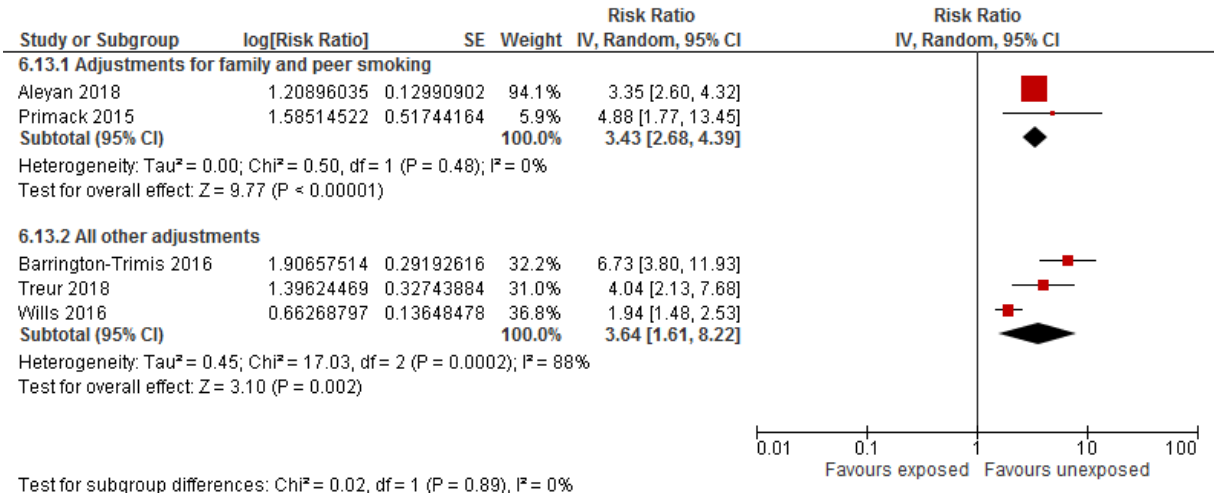
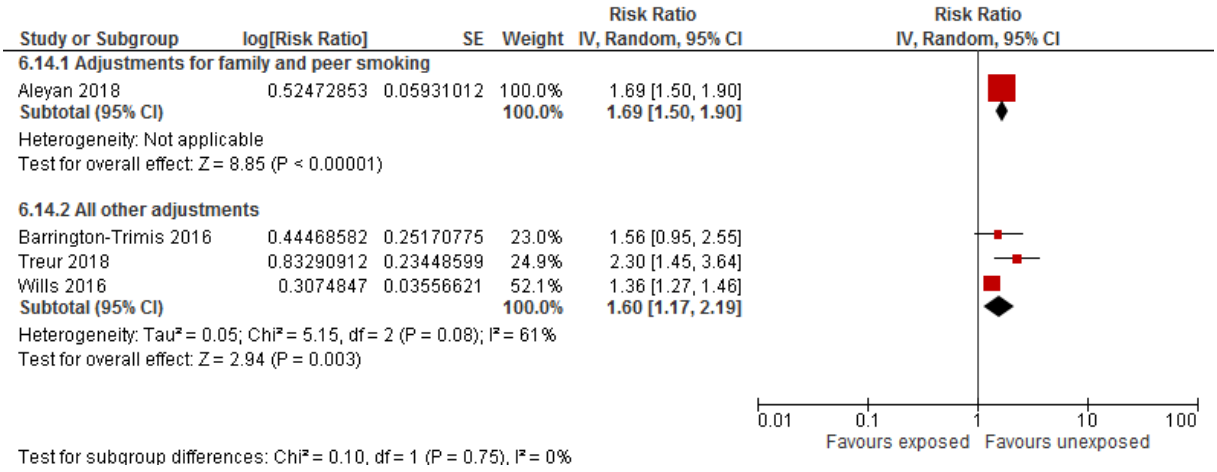
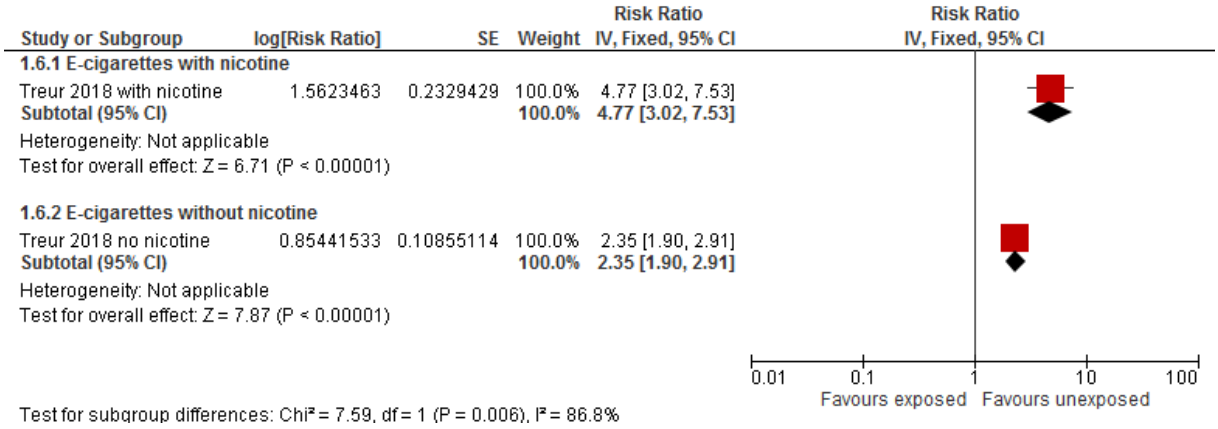


Figure 15: Ever smoking among baseline susceptible



Ever smoking according to other factors

Figure 16: Ever smoking by type of baseline e-cigarette use (nicotine vs non-nicotine)



Change in the rate of decline in smoking since introduction of e-cigarettes

Figure 17: Ever smoking: change in the rate of decline (subgroup by sex)

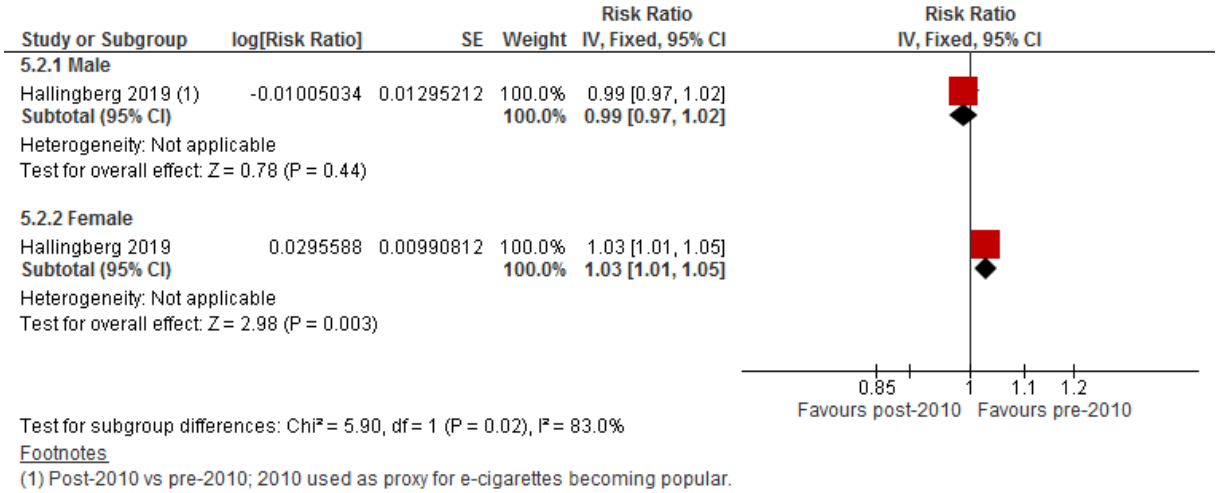


Figure 18: Ever smoking: change in the rate of decline (subgroup by age)

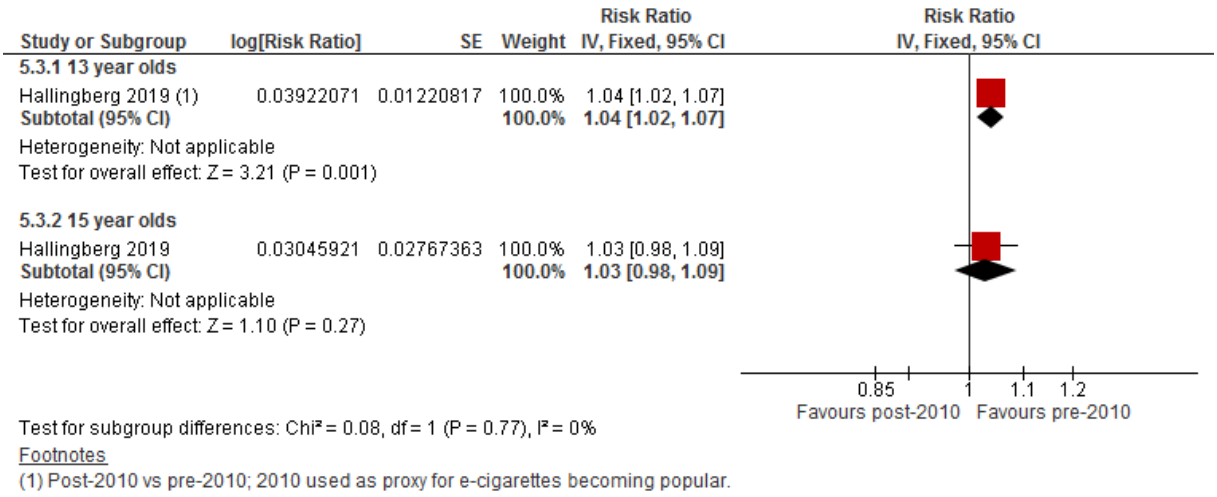


Figure 19: Regular smoking: change in the rate of decline (subgroup by sex)

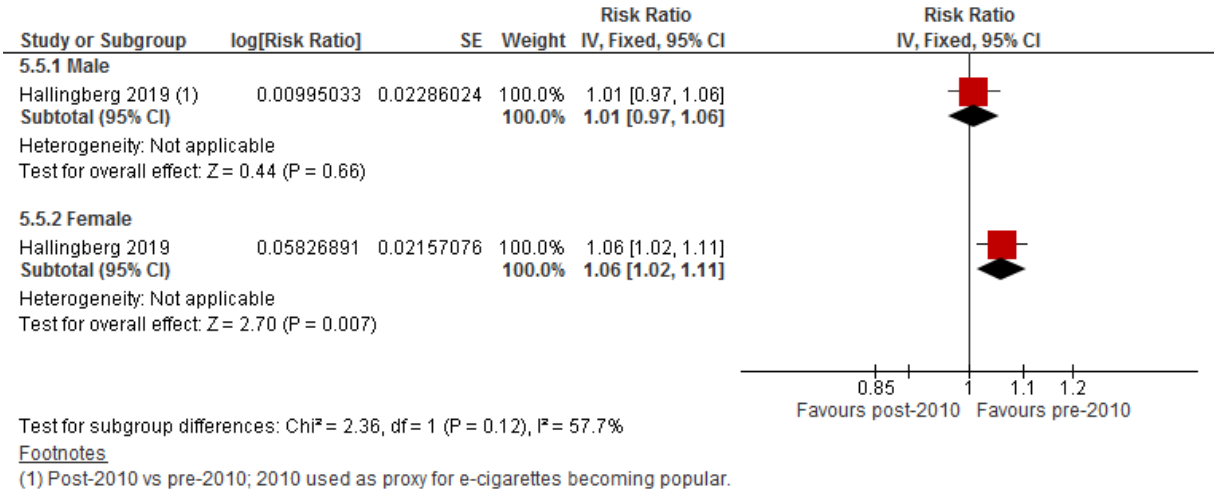


Figure 20: Regular smoking: change in the rate of decline (subgroup by age)

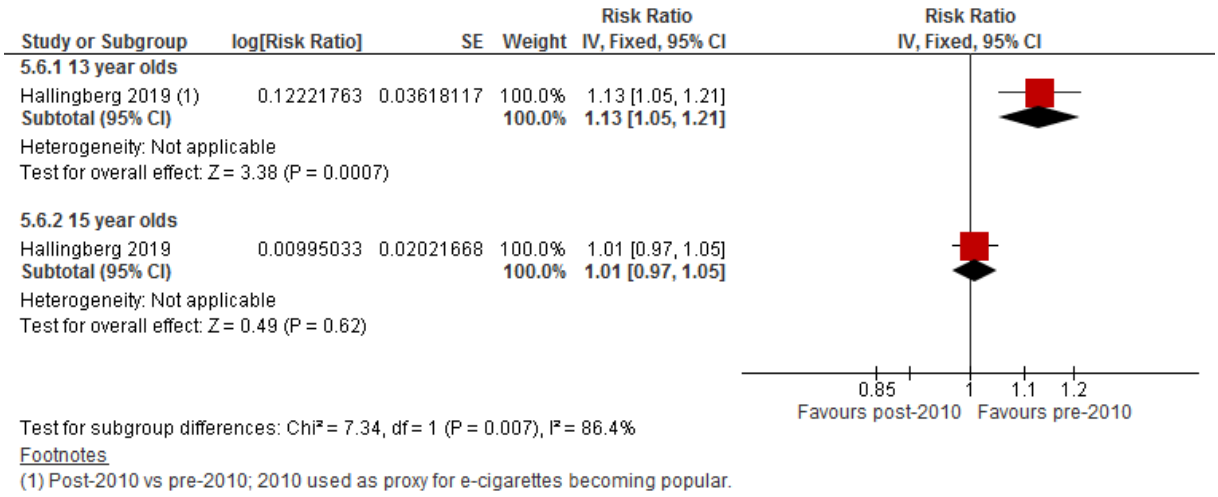
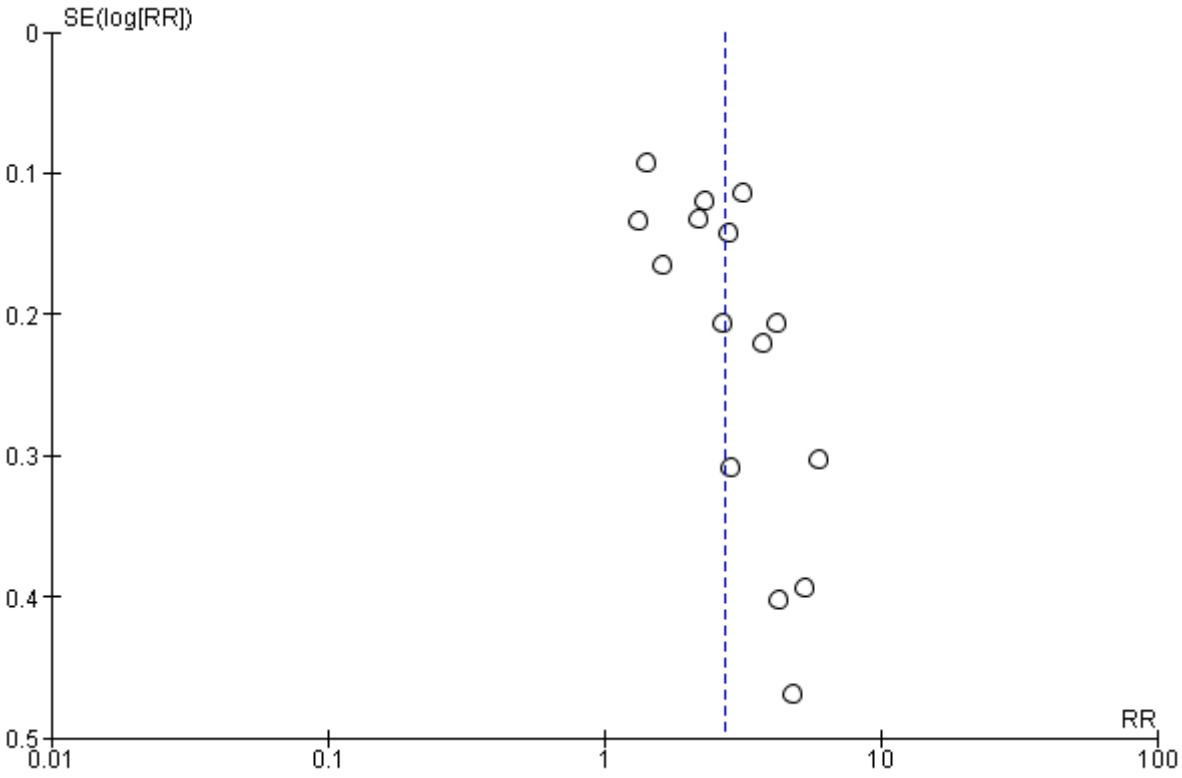


Figure 21: Funnel plot for ever smoking (linked to Figure 1)



Future cigarette use among children, young people and young adults who use e-cigarettes and smoke

Exposed vs unexposed to e-cigarettes at baseline

No meta-analysis was conducted as only one study in this review.

Appendix F – GRADE tables

Future cigarette use among children, young people and young adults who use e-cigarettes and don't smoke

Profile 1: Ever smoking (among different baseline susceptibilities)

Quality assessment							No of patients		Effect		Confidence
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Exposed to e-cig	Unexposed to e-cig	Relative (95% CI)	Absolute	
Ever smoking: among those where susceptibility was not reported (follow-up 4-20 months; assessed with: Self-report survey)											
15 a-o	Cohort	no serious[1]	serious[2]	no serious indirectness	no serious imprecision	none	757/3099 (24.4%)[3]	2013/36741 (5.5%)	RR 2.72 (2.16 to 3.42)	95 more per 1000 (from 61 more to 139 more)	⊕⊕⊕O MODERATE
Ever smoking: among those non-susceptible to smoking at baseline (follow-up 6-24 months; assessed with: Self-report survey)											
5 a, o, p, q, r,	Cohort	no serious[4]	serious[2]	no serious indirectness	no serious imprecision	none	71/183 (38.8%)[5]	965/7416 (13%)	RR 3.59 (2.31 to 5.60)	325 more per 1000 (from 167 more to 570 more)	⊕⊕⊕O MODERATE
Ever smoking: among those susceptible to smoking at baseline (follow-up 6-24 months; assessed with: Self-report survey)											
4 a, o, p, q	Cohort	no serious[4]	very serious[2]	no serious indirectness	no serious imprecision	none	72/184 (39.1%)[3]	1681/2707 (62.1%)	RR 1.60 (1.32 to 1.94)	373 more per 1000 (from 193 more to 584 more)	⊕⊕OO LOW

[1] The difference between ever smoking according to risk of bias was significant. However, high risk of bias studies had a smaller effect than studies with acceptable risk of bias, and both groups of studies had significant and meaningful effects in the same direction. Therefore studies were not downgraded for risk of bias.
[2] I2 higher than 75% but studies with smallest and largest effect sizes show same direction of effect, are all significant, and are all meaningful.
[3] Two studies did not report absolute figures. One study values not included as they are weighted for population.
[4] The difference between ever smoking according to risk of bias was not significant. Therefore studies were not downgraded for risk of bias.
[5] Two studies did not provide absolute figures, and these were not calculable.
[6] I2 higher than 75%

Profile 2: Ever smoking by nicotine-content of e-cigarette at baseline

Quality assessment							No of patients		Effect		Confidence
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Exposed to e-cig	Unexposed to e-cig	Relative (95% CI)	Absolute	
Ever smoking by e-cigarette type - E-cigarettes with nicotine (follow-up 6 months; assessed with: Self-report paper survey)											
1 q	Cohort	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-[2]	-[2]	RR 4.77 (3.02 to 7.53)	-[2]	⊕⊕OO LOW
Ever smoking by e-cigarette type - E-cigarettes without nicotine (follow-up 6 months; assessed with: Self-report paper survey)											
1 q	Cohort	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-[2]	-[2]	RR 2.35 (1.90, 2.91)	-[2]	⊕⊕OO LOW

[1] Potential selection bias in longitudinal sample. Attrition unclear but likely high. Family or peer smoking not adjusted for. Statistical analysis not clearly reported.
[2] Study did not report event data.

Profile 3: Ever smoking (among those with no peer smoking at baseline)

Quality assessment							No of patients		Effect		Confidence
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Exposed to e-cig	Unexposed to e-cig	Relative (95% CI)	Absolute	
Ever smoking among those with no friends who are smokers (follow-up 6 months; assessed with: Self-report)											
1 d	Cohort	Serious risk of bias[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-[2]	-[2]	RR 4.68 [3.56, 6.16]	-[2]	⊕⊕⊕O MODERATE

[1] Adjusts for key confounders, attrition bias not significant, some risk of selection bias.

[2] Study did not report event data.

Profile 4: Habitual smoking

Quality assessment							No of patients		Effect		Confidence
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Exposed to e-cig	Unexposed to e-cig	Relative (95% CI)	Absolute	
Habitual smoking (follow-up 12 months; assessed with: Self-report paper survey (daily smoking for past 7 days))											
1 p	Cohort	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	136/780 (17.4%)	551/17911 (3.1%)	RR 1.74 (1.39 to 2.18)	23 more per 1000 (from 12 more to 36 more)	⊕⊕⊕O MODERATE

[1] Potential selection bias as sample-population comparison not reported. Potential attrition bias. Family smoking not adjusted for.

Profile 5: Intention to smoke

Quality assessment							No of patients		Effect		Confidence
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Exposed to e-cig	Unexposed to e-cig	Relative (95% CI)	Absolute	
Intention to smoke among non-susceptible non-smokers (follow-up 12 months; assessed with: Self-report internet survey (susceptibility measure))											
1 r	Cohort	Serious[1]	no serious inconsistency	Serious[2]	no serious imprecision	none	5/16 (31.3%)	63/678 (9.3%)	RR 5.01 (1.86 to 13.53)	373 more per 1000 (from 80 more to 1000 more)	⊕⊕OO LOW

[1] Potential selection bias as sample-population comparison not reported. Moderate attrition (30%), so potential attrition bias. Family and peer smoking adjusted for.

[2] Named outcome of interest is intention to smoke. This study measures susceptibility to smoking. Partial indirectness.

Profile 6: Change in the rate of decline in smoking (post-2010 vs pre-2010; 2010 used as proxy for e-cigarettes becoming popular)

Quality assessment							No of patients		Effect		Confidence
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Smoking over time - time trend	Control	Relative risk (95% CI)	Absolute	
Change in rate of decline in ever smoking (follow-up 17 years; assessed with: National data (self-report survey))											
1 s	ITS	no serious risk of bias	no serious inconsistency	serious[1]	serious[2]	none	248,324 respondents in total		1.00 (0.99, 1.02)	-[3]	⊕⊕OO LOW
Change in rate of decline in regular smoking (follow-up 17 years; assessed with: National data (self-report survey))											
1 s	ITS	no serious risk of bias	no serious inconsistency	serious[1]	serious[2]	none	248,324 respondents in total		1.03 (1.00, 1.07)	-[3]	⊕⊕OO LOW

[1] Study provides time trend data, not panel data. Cannot determine within-person changes.
[2] Confidence intervals overlap the line of no effect (MID).
[3] Study did not report event data.

a) Barrington-Trimis 2016
b) Best 2018
c) Bold 2018
d) Conner 2017
e) East 2018
f) Leventhal 2015
g) Loukas 2018
h) Lozano 2017
i) Miech 2017
j) Morgenstern 2018

k) Primack 2018
l) Spindle 2017
m) Unger 2016
n) Watkins 2018
o) Wills 2016
p) Aleyan 2018
q) Treur 2018
r) Primack 2015
s) Hallingberg 2019

Future cigarette use among children, young people and young adults who use e-cigarettes and smoke

Profile 7: Past-month continued cigarette smoking

Quality assessment							No of patients		Effect		Confidence
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Exposed to e-cigs	Unexposed to e-cigs	Relative (95% CI)	Absolute	
Past-month continued cigarette smoking (follow-up 12 months; assessed with: Self-report survey)											
1 a	Cohort	serious[1]	NA	serious[2]	very serious[3]	none	48/76 (63.2%)	116/200 (58%)	RR 1.11 (0.90 to 1.37)	64 more per 1000 (from 145 fewer to 371 more)	⊕OOO VERY LOW

[1] Concerns about selection bias and generalisability of results, prognostic factor and outcome are not clearly defined. Outcome was not adjusted for peer or family smoking.
[2] Unclear from study whether e-cigarettes were being used for cessation purposes or recreationally

[3] Confidence interval for effect estimate includes the line of no effect (MID). Sample includes less than 300 participants across both exposed and unexposed groups.

a Unger 2016

Profile 8: Change in number of days smoked cigarettes

Quality assessment							No of patients		Effect		Confidence
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Exposed to e-cigs*	Unexposed to e-cigs*	Relative (95% CI)	Absolute*	
Change in number of days out of past 30 smoked cigarettes (follow-up 12 months; assessed with: Self-report survey)											
1 a	Cohort	serious[1]	NA	serious[2]	serious[3]	none	712 1.44 (0.93, 1.95)	785 2.08 (1.40, 2.76)	-	-0.64 (-1.49, 0.21)	⊕OOO VERY LOW

* Mean difference in days, 95% confidence interval

[1] Concerns about representativeness of the result; reasons for and spread of attrition.
[2] Unclear from study whether e-cigarettes were being used for cessation purposes or recreationally
[3] Confidence interval for effect estimate includes the line of no effect (MID).

a) Stanton 2019

Appendix G – Economic evidence study selection

No economic evidence was considered for this review question, as per the protocol.

Appendix H – Economic evidence tables

No economic evidence was considered for this review question, as per the protocol.

Appendix I – Health economic evidence profiles

No economic evidence was considered for this review question, as per the protocol.

Appendix J – Health economic analysis

No economic evidence was considered for this review question, as per the protocol.

Appendix K – Excluded studies

Public health studies for both reviews

Study Citation	Reason for excluding
Alawsi F, Nour R, and Prabhu S (2015) Are e-cigarettes a gateway to smoking or a pathway to quitting?. British dental journal 219(3), 111-5	Exclude on study design – systematic review, citations checked
Anonymous (2015) Do young e-cigarette users become smokers?. Archives of Disease in Childhood ,	Exclude on evidence – no data presented
Auf Rehab, Trepka Mary Jo, Selim Mazen, Ben Taleb, Ziyad , De La Rosa , Mario , Bastida Elena, and Cano Miguel Angel (2018) E-cigarette use is associated with other tobacco use among US adolescents. International journal of public health ,	Exclude on study design – cross-sectional
Berg Carla J, Barr Dana Boyd, Stratton Erin, Escoffery Cam, and Kegler Michelle (2014) Attitudes toward E-Cigarettes, Reasons for Initiating E-Cigarette Use, and Changes in Smoking Behavior after Initiation: A Pilot Longitudinal Study of Regular Cigarette Smokers. Open journal of preventive medicine 4(10), 789-800	Exclude on target group – sample average age is 36
Berg Carla J, Haardorfer Regine, Payne Jackelyn B, Getachew Betelihem, Vu Milkie, Guttentag Alexandra, and Kirchner Thomas R (2018) Ecological momentary assessment of various tobacco product use among young adults. Addictive behaviors 92, 38-46	Exclude on study design – ecological momentary assessment
Berry Kaitlyn M, Reynolds Lindsay M, Collins Jason M, Siegel Michael B, Fetterman Jessica L, Hamburg Naomi M, Bhatnagar Aruni, Benjamin Emelia J, and Stokes Andrew (2019) E-cigarette initiation and associated changes in smoking cessation and reduction: the Population Assessment of Tobacco and Health Study, 2013-2015. Tobacco control 28(1), 42-49	Exclude on target group – 25+ only
Binns Colin, Lee Mi Kyung, and Low Wah Yun (2018) Children and E-Cigarettes: A New Threat to Health. Asia-Pacific journal of public health 30(4), 315-320	Exclude on study design – non-systematic review of literature
Bold Krysten W, Kong Grace, Cavallo Dana A, Camenga Deepa R, and Krishnan-Sarin Suchitra (2016) Reasons for Trying E-cigarettes and Risk of Continued Use. Pediatrics 138(3),	Exclude on evidence – reasons for using e-cigarettes only
Brikmanis Kristin, Petersen Angela, and Doran Neal (2017) E-cigarette use, perceptions, and cigarette smoking intentions in a community sample of young adult nondaily cigarette smokers. Psychology of addictive behaviors : journal of the Society of Psychologists in Addictive Behaviors 31(3), 336-342	Exclude on evidence
Bunnell Rebecca E, Agaku Israel T, Arrazola Rene A, Apelberg Benjamin J, Caraballo Ralph S, Corey Catherine G, Coleman Blair N, Dube Shanta R, and King Brian A (2015) Intentions to smoke cigarettes among never-smoking US middle and high school electronic cigarette users: National Youth Tobacco Survey, 2011-2013. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco 17(2), 228-35	Exclude on study design – cross-sectional
Camenga D (2016) E-cigarette use associated with tobacco smoking. Journal of Pediatrics 178, 303-306	Exclude on study design – summary of included paper

Cardenas Victor M, Evans Victoria L, Balamurugan Appathurai, Faramawi Mohammed F, Delongchamp Robert R, and Wheeler J Gary (2016) Use of electronic nicotine delivery systems and recent initiation of smoking among US youth. International journal of public health 61(2), 237-41	Exclude on study design - cross-sectional
Chaffee Benjamin W, and Cheng Jing (2018) Tobacco product initiation is correlated with cross-product changes in tobacco harm perception and susceptibility: Longitudinal analysis of the Population Assessment of Tobacco and Health youth cohort. Preventive medicine 114, 72-78	Exclude on target group – non-users of e-cigarettes
Chaffee Benjamin W, Watkins Shannon Lea, and Glantz Stanton A (2018) Electronic Cigarette Use and Progression From Experimentation to Established Smoking. Pediatrics 141(4),	Exclude on target group – people who had tried smoking
Chatterjee Kshitij, Alzghoul Bashar, Innabi Ayoub, and Meena Nikhil (2016) Is vaping a gateway to smoking: a review of the longitudinal studies. International journal of adolescent medicine and health 30(3),	Exclude on study design – systematic review, citations checked
Chen J C (2018) Flavored E-cigarette Use and Cigarette Smoking Reduction and CessationA Large National Study among Young Adult Smokers. Substance Use & Misuse 53(12), 2017-2031	Exclude on target group – only smokers at baseline
Coleman Blair N (2016) The association between electronic cigarette use and cigarette smoking behavior among young adults in the United States. Dissertation Abstracts International: Section B: The Sciences and Engineering 76(11-B(E)), No-Specified	Exclude on study design - cross-sectional
Czoli Christine D, Hammond David, Reid Jessica L, Cole Adam G, and Leatherdale Scott T (2015) Use of Conventional and Alternative Tobacco and Nicotine Products Among a Sample of Canadian Youth. The Journal of adolescent health : official publication of the Society for Adolescent Medicine 57(1), 123-5	Exclude on study design - cross-sectional
Delnevo Cristine D, Villanti Andrea C, Wackowski Olivia A, Gundersen Daniel A, and Giovenco Daniel P (2016) The influence of menthol, e-cigarettes and other tobacco products on young adults' self-reported changes in past year smoking. Tobacco control 25(5), 571-4	Exclude on target group - cross-sectional
Dunbar Michael S, Davis Jordan P, Rodriguez Anthony, Tucker Joan S, Seelam Rachana, and D'Amico Elizabeth J (2018) Disentangling Within- and Between-Person Effects of Shared Risk Factors on E-cigarette and Cigarette Use Trajectories From Late Adolescence to Young Adulthood. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco ,	Exclude on evidence – associations between alcohol / marijuana / mental health and cigarette / e-cigarette use
Durmowicz Elizabeth L (2014) The impact of electronic cigarettes on the paediatric population. Tobacco control 23 Suppl 2, ii41-6	Exclude on evidence – review with non-relevant information
Dutra Lauren M, and Glantz Stanton A (2017) E-cigarettes and National Adolescent Cigarette Use: 2004-2014. Pediatrics 139(2),	Exclude on evidence – modelling only
Eastwood B, Dockrell M J, Arnott D, Britton J, Cheeseman H, Jarvis M J, and McNeill A (2015) Electronic cigarette use in young people in Great Britain 2013-2014. Public health 129(9), 1150-6	Exclude on study design - repeat cross-sectional
Gmel Gerhard, Baggio Stephanie, Mohler-Kuo Meichun, Daeppen Jean-Bernard, and Studer Joseph (2016) E-cigarette use in young Swiss men: is vaping an effective way of reducing or quitting smoking?. Swiss medical weekly 146, w14271	Exclude on evidence – does not measure e-cig use at baseline

Goettsch Claudia, Goettsch Winfried, Brux Melanie, Haschke Claudia, Brunssen Coy, Muller Gregor, Bornstein Stefan R, Duerrschmidt Nicole, Wagner Andreas H, and Morawietz Henning (2011) Arterial flow reduces oxidative stress via an antioxidant response element and Oct-1 binding site within the NADPH oxidase 4 promoter in endothelial cells. Basic research in cardiology 106(4), 551-61	Duplicate / wrong review
Goldenson Nicholas I, Leventhal Adam M, Stone Matthew D, McConnell Rob S, and Barrington-Trimis Jessica L (2017) Associations of Electronic Cigarette Nicotine Concentration With Subsequent Cigarette Smoking and Vaping Levels in Adolescents. JAMA pediatrics 171(12), 1192-1199	Exclude on target group – does not separate exposed and unexposed
Gray N (2016) Why we should remain sceptical about e-cigarettes. Pharmaceutical Journal 296(7890), 355-356	Exclude on study design – no data presented
Hair Elizabeth C, Romberg Alexa R, Niaura Raymond, Abrams David B, Bennett Morgane A, Xiao Haijun, Rath Jessica M, Pitzer Lindsay, and Vallone Donna (2018) Longitudinal Tobacco Use Transitions Among Adolescents and Young Adults: 2014-2016. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco ,	Exclude on evidence – transition probabilities by age only
Hampson Sarah E, Andrews Judy A, Severson Herbert H, and Barckley Maureen (2015) Prospective Predictors of Novel Tobacco and Nicotine Product Use in Emerging Adulthood. The Journal of adolescent health : official publication of the Society for Adolescent Medicine 57(2), 186-91	Exclude on intervention – does not separate e-cig use from other substances
Hanewinkel Reiner, and Isensee Barbara (2015) Risk factors for e-cigarette, conventional cigarette, and dual use in German adolescents: a cohort study. Preventive medicine 74, 59-62	Exclude on target group – does not separate exposed and unexposed groups
Huang Li-Ling, Kowitt Sarah D, Sutfin Erin L, Patel Tanha, Ranney Leah M, and Goldstein Adam O (2016) Electronic Cigarette Use Among High School Students and Its Association With Cigarette Use And Smoking Cessation, North Carolina Youth Tobacco Surveys, 2011 and 2013. Preventing chronic disease 13, E103	Exclude on study design - cross-sectional
Huh Jimi, and Leventhal Adam M (2016) Progression of Poly-tobacco Product Use Patterns in Adolescents. American journal of preventive medicine 51(4), 513-7	Exclude on target group – does not consider e-cig use on its own, pairs with tobacco use
Jamal Ahmed, Gentzke Andrea, Hu S Sean, Cullen Karen A, Apelberg Benjamin J, Homa David M, and King Brian A (2017) Tobacco Use Among Middle and High School Students - United States, 2011-2016. MMWR. Morbidity and mortality weekly report 66(23), 597-603	Exclude on study design - cross-sectional
Kasza Karin A, Borek Nicolette, Conway Kevin P, Goniewicz Maciej L, Stanton Cassandra A, Sharma Eva, Fong Geoffrey T, Abrams David B, Coleman Blair, Schneller Liane M, Lambert Elizabeth Y, Pearson Jennifer L, Bansal-Travers Maansi, Murphy Iilun, Cheng Yu-Ching, Donaldson Elisabeth A, Feirman Shari P, Gravely Shannon, Elton-Marshall Tara, Trinidad Dennis R, Gundersen Daniel A, Niaura Raymond S, Cummings K Michael, Compton Wilson M, and Hyland Andrew J (2018) Transitions in Tobacco Product Use by U.S. Adults between 2013-2014 and 2014-2015: Findings from the PATH Study Wave 1 and Wave 2. International journal of environmental research and public health 15(11),	Exclude on evidence – data not extractable

Kinnunen Jaana M, Ollila Hanna, Lindfors Pirjo L, and Rimpela Arja H (2016) Changes in Electronic Cigarette Use from 2013 to 2015 and Reasons for Use among Finnish Adolescents. International journal of environmental research and public health 13(11),	Exclude on study design - cross-sectional
Lechner William V, Janssen Tim, Kahler Christopher W, Audrain-McGovern Janet, and Leventhal Adam M (2017) Bi-directional associations of electronic and combustible cigarette use onset patterns with depressive symptoms in adolescents. Preventive medicine 96, 73-78	Exclude on target group – sample does not smoke or use e-cigarettes at baseline
Levy David T, Warner Kenneth E, Cummings K Michael, Hammond David, Kuo Charlene, Fong Geoffrey T, Thrasher James F, Goniewicz Maciej Lukasz, and Borland Ron (2018) Examining the relationship of vaping to smoking initiation among US youth and young adults: a reality check. Tobacco control ,	Exclude on evidence – data not usable
Lippert Adam M (2017) Temporal Changes in the Correlates of U.S. Adolescent Electronic Cigarette Use and Utilization in Tobacco Cessation, 2011 to 2013. Health education & behavior : the official publication of the Society for Public Health Education 44(2), 254-261	Exclude on study design – not cohort or time series
Loukas Alexandra, Batanova Milena, Fernandez Alejandra, and Agarwal Deepti (2015) Changes in use of cigarettes and non-cigarette alternative products among college students. Addictive behaviors 49, 46-51	Exclude on evidence – does not separate exposed and unexposed groups
Merianos Ashley L, Mancuso Tierney F, Gordon Judith S, Wood Kelsi J, Cimperman Katherine A, and Mahabee-Gittens E Melinda (2018) Dual- and Polytobacco/Nicotine Product Use Trends in a National Sample of High School Students. American journal of health promotion : AJHP 32(5), 1280-1290	Exclude on study design -
Morgenstern M, Nies A, Goecke M, and Hanewinkel R (2018) E-cigarettes and the use of conventional cigarettes - A cohort study in 10th grade students in Germany. Deutsches Arzteblatt International 115(14), 243-248	Duplicate / wrong review - duplicate
Penzes Melinda, Foley Kristie L, Nadasan Valentin, Paulik Edit, Abram Zoltan, and Urban Robert (2018) Bidirectional associations of e-cigarette, conventional cigarette and waterpipe experimentation among adolescents: A cross-lagged model. Addictive behaviors 80, 59-64	Exclude on target group – sample characteristics unclear on prognostic factor
Porter Lauren, Duke Jennifer, Hennon Meredith, Dekevich David, Crankshaw Erik, Homsi Ghada, and Farrelly Matthew (2015) Electronic Cigarette and Traditional Cigarette Use among Middle and High School Students in Florida, 2011-2014. PloS one 10(5), e0124385	Exclude on study design - cross-sectional
Ramo Danielle E, Young-Wolff Kelly C, and Prochaska Judith J (2015) Prevalence and correlates of electronic-cigarette use in young adults: findings from three studies over five years. Addictive behaviors 41, 142-7	Exclude on study design - cross-sectional
Schneider Sven, and Diehl Katharina (2016) Vaping as a Catalyst for Smoking? An Initial Model on the Initiation of Electronic Cigarette Use and the Transition to Tobacco Smoking Among Adolescents. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco 18(5), 647-53	Exclude on evidence – modelling only

Selya Arielle S, Dierker Lisa, Rose Jennifer S, Hedeker Donald, and Mermelstein Robin J (2018) The Role of Nicotine Dependence in E-Cigarettes' Potential for Smoking Reduction. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco 20(10), 1272-1277	Exclude on evidence – sample is actively trying to quit
Selya Arielle S, Rose Jennifer S, Dierker Lisa, Hedeker Donald, and Mermelstein Robin J (2018) Evaluating the mutual pathways among electronic cigarette use, conventional smoking and nicotine dependence. Addiction (Abingdon, and England) 113(2), 325-333	Exclude on evidence
Silveira Marushka L, Conway Kevin P, Green Victoria R, Kasza Karin A, Sargent James D, Borek Nicolette, Stanton Cassandra A, Cohn Amy, Hilmi Nahla, Cummings K Michael, Niaura Raymond S, Lambert Elizabeth Y, Brunette Mary F, Zandberg Izabella, Tanski Susanne E, Reissig Chad J, Callahan-Lyon Priscilla, Slavit Wendy I, Hyland Andrew J, and Compton Wilson M (2018) Longitudinal associations between youth tobacco and substance use in waves 1 and 2 of the Population Assessment of Tobacco and Health (PATH) Study. Drug and alcohol dependence 191, 25-36	Exclude on evidence – combines e-cigarette and cigarette use into one state
Snow Erika, Johnson Tye, Ossip Deborah J, Williams Geoffrey C, Ververs Duncan, Rahman Irfan, and McIntosh Scott (2018) Does E-cigarette Use at Baseline Influence Smoking Cessation Rates among 2-Year College Students?. Journal of smoking cessation 13(2), 110-120	Exclude on target group - sample is actively trying to quit
Soneji Samir, Barrington-Trimis Jessica L, Wills Thomas A, Leventhal Adam M, Unger Jennifer B, Gibson Laura A, Yang JaeWon, Primack Brian A, Andrews Judy A, Miech Richard A, Spindle Tory R, Dick Danielle M, Eissenberg Thomas, Hornik Robert C, Dang Rui, and Sargent James D (2017) Association Between Initial Use of e-Cigarettes and Subsequent Cigarette Smoking Among Adolescents and Young Adults: A Systematic Review and Meta-analysis. JAMA pediatrics 171(8), 788-797	Exclude on study design – systematic review, citations checked
Sutfin Erin L, Reboussin Beth A, Debinski Beata, Wagoner Kimberly G, Spangler John, and Wolfson Mark (2015) The Impact of Trying Electronic Cigarettes on Cigarette Smoking by College Students: A Prospective Analysis. American journal of public health 105(8), e83-9	Exclude on evidence – looks at whether cigarette use leads to future e-cig use
Westling Erika, Rusby Julie C, Crowley Ryann, and Light John M (2017) Electronic Cigarette Use by Youth: Prevalence, Correlates, and Use Trajectories From Middle to High School. The Journal of adolescent health : official publication of the Society for Adolescent Medicine 60(6), 660-666	Exclude on evidence – descriptive only
White Joanna, Li Judy, Newcombe Rhiannon, and Walton Darren (2015) Tripling use of electronic cigarettes among New Zealand adolescents between 2012 and 2014. The Journal of adolescent health : official publication of the Society for Adolescent Medicine 56(5), 522-8	Exclude on study design – cross sectional
Wills Thomas A, Gibbons Frederick X, Sargent James D, and Schweitzer Rebecca J (2016) How is the effect of adolescent e-cigarette use on smoking onset mediated: A longitudinal analysis. Psychology of addictive behaviors : journal of the Society of Psychologists in Addictive Behaviors 30(8), 876-886	Exclude on evidence – evaluating model fit only
Zhong Jieming, Cao Shuangshuang, Gong Weiwei, Fei Fangrong, and Wang Meng (2016) Electronic Cigarettes Use and Intention to Cigarette Smoking among Never-Smoking Adolescents and Young	Exclude on study design – systematic review, citations checked

Adults: A Meta-Analysis. International journal of environmental research and public health 13(5),	

Public health rerun search

Study Citation	Reason for excluding
Aleyan Sarah, Gohari Mahmood R, Cole Adam G, and Leatherdale Scott T (2019) Exploring the Bi-Directional Association between Tobacco and E-Cigarette Use among Youth in Canada. International journal of environmental research and public health 16(21),	Exclude on evidence: Does not report tobacco smokers and non-tobacco smokers separately in analysis.
Barrington-Trimis Jessica L, Kong Grace, Leventhal Adam M, Liu Feifei, Mayer Margaret, Cruz Tess Boley, Krishnan-Sarin Suchitra, and McConnell Rob (2018) E-cigarette Use and Subsequent Smoking Frequency Among Adolescents. Pediatrics 142(6),	Exclude as duplicate: identified at original search
Barrington-Trimis Jessica L, Liu Fei, Unger Jennifer B, Alonzo Todd, Cruz Tess Boley, Urman Robert, Pentz Mary Ann, Berhane Kiros, and McConnell Rob (2019) Evaluating the predictive value of measures of susceptibility to tobacco and alternative tobacco products. Addictive behaviors 96, 50-55	Exclude on population: users of e-cigarettes not separated out.
Berry Kaitlyn M, Fetterman Jessica L, Benjamin Emelia J, Bhatnagar Aruni, Barrington-Trimis Jessica L, Leventhal Adam M, and Stokes Andrew (2019) Association of Electronic Cigarette Use With Subsequent Initiation of Tobacco Cigarettes in US Youths. JAMA network open 2(2), e187794	Exclude as duplicate: identified at original search
Chaffee Benjamin W, Watkins Shannon Lea, and Glantz Stanton A (2018) Electronic Cigarette Use and Progression From Experimentation to Established Smoking. Pediatrics 141(4),	Exclude on population : includes ex-smokers
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Economic studies

No economic evidence was considered for this review question, as per the protocol.

Appendix L – Research recommendations

Research recommendation 9

Is e-cigarette use in children, young people and young adults who do not smoke associated with future established smoking?

Why this is important

More evidence is needed about whether e-cigarette use is linked with habitual smoking (rather than experimental smoking) in the future, the factors that determine this link, and the levels of e-cigarette use in people under 25.

Rationale for research recommendation

Importance to 'patients' or the population	A very small proportion of children, young people and young adults who have never smoked use e-cigarettes, and therefore might be exposed to increased risk of trying smoking in the future.
Relevance to NICE guidance	It is important to determine the extent of this risk in order to ascertain if interventions need to be developed to address this risk.
Relevance to the NHS	Because the harm of smoking is so great, it is important to determine if there is an association between children and young people who have never smoked but use e-cigarettes and future established smoking status.
National priorities	The Tobacco Control Plan (Department of Health 2017) set out a national ambition to reduce the prevalence of 15 year olds who regularly smoke from 8% to 3% or less by the end of 2022.
Current evidence base	The proportion of children, young people and young adults who have never smoked and who use e-cigarettes is small enough that changes within this group may not be evident when looking at population-level data. None of the studies measured smoking status as an established habit. With the exception of one study reporting habitual smoking, all cohort studies considered 'ever smoking', 'past 30-day

	smoking' or 'past 6-month smoking'. The committee agreed that the reported outcomes could not be extrapolated to conclude that e-cigarettes are associated with established smoking without further research.
Equality considerations	The committee discussed that it is possible that people moving from e-cigarettes to smoking might have been at higher risk of smoking for other reasons (for example, peer or family smoking). In 2016, 25% secondary school pupils reported having 'ever used' e-cigarettes compared to 19% who reported that they had tried smoking 'at least once'. Pupils were more likely to smoke if they lived in households with other smokers (NHS Digital – Statistics on Smoking England 2019).

Modified PICO table

Population	Children and young people below the age of 25 who do not smoke but use e-cigarettes.
Association factor	Use of e-cigarettes
Outcome	Association between use of e-cigarettes and future established smoking status.