Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Stanton A. Glantz, Nhung Nguyen, and Andre Luiz Oliveira da Silva. Population-Based Disease Odds for E-Cigarettes and Dual Use versus Cigarettes. NEJM Evid. DOI: 10.1056/EVIDoa2300229.

Population-based disease odds for e-cigarettes and dual use vs. cigarettes
SUPPLEMENTAL MATERIALS

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SUPPLEMENTARY METHODS

Search strategy

Searches designed to capture a wide range of disease outcomes in population samples were conducted for peer-reviewed papers published January 1, 2005 through October 1, 2023.

PubMed:
(e-cigarette* OR ENDS OR “electronic nicotine delivery systems” OR "Electronic Nicotine Delivery Systems"[Mesh] OR vaping OR “Vaping”[Mesh]) AND (heart OR "Heart Diseases"[Mesh] OR cardiac OR cardiovascular OR stroke OR "Stroke"[Mesh] OR infarct* OR vascular OR "Vascular Diseases"[Mesh] OR lung OR "Lung Diseases"[Mesh] OR pulmonary OR asthma OR “Asthma”[Mesh] OR COPD OR “chronic obstructive pulmonary disease*” OR bronchitis OR cancer OR “Neoplasms”[Mesh] OR pregnancy OR "Pregnancy"[Mesh] OR pregnant OR dental OR oral OR periodont* OR "Periodontal Diseases"[Mesh] OR caries OR "Dental Caries"[Mesh] OR cavities OR "oral microbiome" OR tooth OR "Tooth Diseases"[Mesh] OR teeth OR "dry mouth" OR "Mouth Diseases"[Mesh] OR “Metabolic dysfunction”[Mesh]) AND (odds OR "Odds Ratio"[Mesh] OR “hazard ratio” OR "relative risk" OR "Risk"[Mesh] OR "Risk Factors"[Mesh] OR epidemiolog* OR "Epidemiology"[Mesh] OR “epidemiology"[Subheading]) NOT (“smoking cessation” OR "Smoking Cessation"[Mesh] OR EVALI OR addiction OR initiation OR gateway OR perception OR "Perception"[Mesh] OR attitude OR "Attitude"[Mesh] OR awareness OR "Awareness"[Mesh] OR telomere OR "Telomere"[Mesh])

Web of Science:
(e-cigarette* OR “electronic nicotine delivery systems” OR vaping) AND (heart OR cardiac OR cardiovascular OR stroke OR infarct* OR vascular OR lung OR pulmonary OR asthma OR COPD OR “chronic obstructive pulmonary disease*” OR bronchitis OR cancer OR neoplasm* OR pregnancy OR pregnant OR dental OR oral OR periodont* OR caries OR cavities OR "oral microbiome" OR tooth OR teeth OR "dry mouth" OR “metabolic dysfunction”) AND (odds OR “hazard ratio” OR "relative risk" OR risk OR "risk factors" OR epidemiolog*) NOT (“smoking cessation” OR EVALI OR addiction OR initiation OR gateway OR perception OR attitude OR awareness OR telomere)

Embase (limit to articles/articles in press):
('electronic cigarette'/exp OR 'electronic cigarette' OR 'vaping'/exp OR 'vaping') AND ('heart'/exp OR 'heart' OR 'heart disease'/exp OR 'heart disease' OR 'cardiac'/exp OR 'cardiac' OR 'cardiovascular disease'/exp OR 'cardiovascular disease' OR 'cerebrovascular accident'/exp OR 'cerebrovascular accident' OR 'infarction'/exp OR 'infarction' OR vascular OR 'vascular disease'/exp OR 'vascular disease' OR 'lung'/exp OR 'lung' OR 'lung disease'/exp OR 'lung disease' OR pulmonary OR 'asthma'/exp OR 'asthma' OR 'chronic obstructive lung disease'/exp OR 'chronic obstructive lung disease' OR 'bronchitis'/exp OR 'bronchitis' OR 'malignant neoplasm'/exp OR 'malignant neoplasm' OR 'pregnancy'/exp OR 'pregnancy' OR pregnant OR 'dental'/exp OR 'dental' OR oral OR 'periodontal disease'/exp OR 'periodontal disease' OR periodont* OR 'dental caries'/exp OR 'dental caries' OR cavities OR 'oral microbiome'/exp OR 'oral microbiome' OR 'tooth'/exp OR 'tooth' OR 'tooth disease'/exp OR 'tooth disease' OR 'xerostomia'/exp OR 'xerostomia' OR 'mouth disease'/exp OR 'mouth disease' OR ‘metabolic dysfunction’) AND ('odds ratio'/exp OR 'odds ratio' OR odds OR 'hazard ratio'/exp OR 'hazard ratio' OR 'risk factor'/exp OR 'risk factor' OR 'risk'/exp OR 'risk' OR 'epidemiology'/exp OR 'epidemiology' OR epidemiolog*) NOT ('smoking cessation'/exp OR 'smoking cessation' OR evali OR 'addiction'/exp OR 'addiction' OR 'initiation'/exp OR initiation OR 'gateway'/exp OR gateway OR 'perception'/exp OR perception OR 'attitude'/exp OR attitude OR 'awareness'/exp OR awareness OR 'telomere'/exp OR telomere) AND [2005-2022]/py

PsycINFO (limit to peer review):
(e-cigarette* OR “electronic nicotine delivery systems” OR vaping) AND (heart OR cardiac OR cardiovascular OR stroke OR infarct* OR vascular OR lung OR pulmonary OR asthma OR COPD OR “chronic obstructive

pulmonary disease*" OR bronchitis OR cancer OR neoplasm* OR pregnancy OR pregnant OR dental OR oral OR periodont* OR caries OR cavities OR "oral microbiome" OR tooth OR teeth OR "dry mouth" OR 'metabolic dysfunction') AND (odds OR "hazard ratio" OR "relative risk" OR risk OR "risk factors" OR epidemiolog*) NOT ("smoking cessation" OR EVALI OR addiction OR initiation OR gateway OR perception OR attitude OR awareness OR telomere)

We also included studies identified in public comments submitted to FDA on August 1, 2022 on proposed flavored tobacco product standards[1,2] in the screening set and studies cited in reviews identified in the searches above.

"Initiation," "gateway" and "addiction" were included as exclusion criteria because we wanted to capture studies on the association of disease with e-cigarette use among users, not factors that predicted e-cigarette initiation. Preliminary searches without these exclusion terms captured a large number of irrelevant studies.

"Telomere" is included as an exclusion term because "ENDS" captured many irrelevant papers on telomere ends. EVALI (e-cigarette and vaping associated lung injury) was excluded because it is acute syndrome primarily associated with cannabis vaping.

Metabolic dysfunction was not explicitly included in the original search done on September 12, 2022. It was added after metabolic dysfunction emerged from the original search. To check if the search strategy missed papers any relevant papers, we conducted additional searches for papers published January 1, 2005 through September 12, 2022, with "metabolic syndrome" ("metabolic syndrome[Mesh]" in PubMed) in place of the list of diseases in the searches above. Doing so did not identify any additional papers for inclusion.

Searches were updated from September 13, 2022 through October 1, 2023, including metabolic syndrome, using the searches listed above.

There was no limitation on language. None of the few non-English language papers identified in the searches were included in the final set of studies. Google Translate was used to translate abstracts for papers that did not include English language abstracts.

Qualifications of searchers

Dr. Glantz, a retired Professor of Medicine, has published several meta-analyses, including two on e-cigarettes and smoking cessation,[3,4] and reviewed meta-analyses for major journals as well as two textbooks on biostatistics. He served as an associate editor of Journal of American College of Cardiology for 10 years, where he was responsible for statistical review of papers. Dr. Nguyen, an epidemiologist, and Assistant Professor of Medicine, has published papers on epidemiology of tobacco use, including on e-cigarette use and dual tobacco use. Dr. Oliveira da Silva is a postdoctoral fellow and realized this work on his sabbatical leave from the Brazilian Health Regulatory Agency (ANVISA) where he is responsible for scientific, enforcement and registration issues related to regulation of tobacco products. (The statements and opinions expressed in the article are those of the authors and are based on current scientific evidence. They do not represent any institutional guideline and/or opinion of ANVISA, the Ministry of Health and/or the Brazilian Government.) Peggy Tahir, a Research & Copyright Librarian advised on structuring the literature searches. She has been providing research support for systematic reviews at UCSF since 2015 and, as of May 2023, was coauthor on 26 peer-reviewed systematic or scoping reviews and has provided many additional systematic review consultations, including mentoring students on how to conduct systematic reviews.

Inclusion and exclusion criteria

Inclusion criteria were: Population-based epidemiological studies of disease in current e-cigarette and dual users that permit comparison to cigarette smokers or nonusers among people using e-cigarettes as consumer products. Associations could be reported as OR, relative risks, hazard ratios, incident rate ratios, or prevalence ratios, taking into account cigarette and dual use (either in multivariate models or through stratification) if present. There were no age or language restrictions.

Exclusion criteria were: Studies that included smokers as well as e-cigarette users but did not account for dual use, studies that did not report adjusted ORs (or equivalent) that we need to do the analysis, non-peer reviewed studies, conference abstracts, prevalence and use pattern studies, cessation studies, initiation studies, determinants of e-cigarette use, addiction studies, mental health studies, mediation studies, studies where the independent variable was ever (as opposed to current) e-cigarette use, biomarker studies, studies of only e-cigarette users, EVALI, clinical trials or studies of disease in clinical settings, experimental studies and other studies used to elucidate pathophysiological mechanisms, reviews, meta-analyses and commentaries.

While included in the original PROSPERO protocol, studies of only ever e-cigarette and cigarette smokers were excluded from the final analysis based on feedback from peer reviewers.

Data extraction

Title and abstract screening, full text review, and data extraction were done independently by two reviewers using Covidence with differences resolved by consensus.

When studies included multiple measures of the same outcome (e.g., myocardial infarction and stroke or composite cardiovascular outcomes), we selected the one with the most similar to the other papers in that outcome category. Studies that reported more than one outcome (e.g., asthma and COPD) were categorized into both outcomes.

When studies reported results based on both ever and current use of e-cigarettes or cigarettes, we used the current use values. If a study reported frequency of use (e.g., non-daily and daily use), we used the highest level of exposure (e.g., daily use) reported for both e-cigarettes and cigarettes.

When studies presented models with different numbers of potential confounders, we selected the most highly adjusted model.

When studies reported both never e-cigarette users and non-current users as the reference group, we selected never users.

When studies presented results using both multivariate (including e-cigarette use and cigarette use as separate independent variables, with dual use indicated by both variables set to “yes”) and stratified approaches (in which respondents were categorized as sole e-cigarette, sole cigarette, dual users and nonusers), we recorded results of both approaches and selected the ORs with the smallest magnitude (so that any biases are toward lowering the estimated effects). A few studies reported relative risk, hazard ratio, or incident rate ratio; these measures were treated as approximations of ORs.

The following characteristics of studies were recorded:

- design: longitudinal or cross-sectional
- modeling: multivariate or stratified, as defined above
- reference group: never or non-current use of each tobacco product

- outcome: current (past 12 month) or ever disease presence
- age group: adult (minimum age ≥ 18) or youth (minimum age < 18) samples
- sample size
- most recent year of data collection
- covariates (potential confounders)

When necessary to clarify methodology or reported results we emailed corresponding authors.

Calculation of $OR_{ecig\ vs\ cig}$ and $OR_{dual\ vs\ cig}$

E-cigarette vs cigarette OR

We compared odds of the health outcomes associated with e-cigarette use with those of cigarette use using

$$OR_{ecig\ vs\ cig} = \frac{OR_{ecig}}{OR_{cig}}$$

where the reference conditions for OR_{ecig} and OR_{cig} are people who do not use the product. When not directly reported, we calculated $OR_{ecig\ vs\ cig}$ by dividing reported OR_{ecig} by OR_{cig}. To calculate the 95% confidence interval for this odds ratio, we first took the logarithm of both sides of this equation:

$$\ln OR_{ecig\ vs\ cig} = lnOR_{ecig} - lnOR_{cig}$$

We computed the standard errors associated with each of these ORs from the associated 95% confidence intervals:

$$s = \frac{\ln OR_{upper} - lnOR_{lower}}{2 \times 1.960}$$

To get the standard error for $\ln OR_{ecig\ vs\ cig}$ we used the formula for the variance of a difference of two independent variables:

$$s_{ecig\ vs\ cig} = \sqrt{s_{ecig}^2 + s_{cig}^2}$$

Dual use vs cigarette only OR

Because the odds associated with e-cigarette use and cigarette use compared to no product use are independent in the multivariate logistic regressions, the e-cigarette OR is the marginal OR of e-cigarette use over no product use, controlling for cigarette smoking. Therefore, it is also an estimate of the OR of dual use (e-cigarettes plus cigarettes) compared to smoking alone, because

$$OR_{ecig} = \frac{OR_{ecig} \times OR_{cig}}{OR_{cig}} = \frac{OR_{dual}}{OR_{cig}} = OR_{dual\ vs\ cig}$$

If $OR_{dual\ vs\ cig}$ was reported directly (in stratified models), we used that estimate. When it was not reported, we computed

$$OR_{dual\ vs\ cig} = \frac{OR_{dual}}{OR_{cig}}$$

as described above.

In studies that reported both multivariate and stratified results, we used the results with the smallest OR in the meta-analysis so that any biases are toward estimating smaller effects.

Sensitivity analysis of assumption that OR_{ecig} and OR_{cig} are independent

OR_{ecig} and OR_{cig} are not independent because both use the same group of nonusers of either e-cigarettes and cigarettes as the same reference group. When the two variables are correlated,

$$s_{ecig-cig} = \sqrt{s_{ecig}^2 + s_{cig}^2 - 2rs_{ecig}s_{cig}}$$

where r is the correlation of the estimates of the two ORs. The correlation, r, is not reported in the papers, so we conducted a sensitivity analysis assuming the actual standard error of the difference was ¼ of the value computed assuming that the results estimates are independent, which corresponds to r around 0.9.

Adjustment for multiple studies using the same dataset

Forty-nine of the 124 (40%) of the ORs used in the meta-analysis came from studies in which different investigators published different papers using the same dataset (e.g., BRFSS) from the same year (e.g., 2017) to study the same outcome (e.g., asthma) (Table S4). Such multiple studies are not identical replicates due to differences in details of study design (including differences in covariates, analytical approach, or handling of missing data), as evidenced by different sample sizes and effect size estimates. Because these studies are not identical, we did not drop any of them from the meta-analysis. Nevertheless, when multiple studies are based on the same underlying dataset, the results are likely to be correlated to an unknown extent. Following advice for handling duplicate studies in meta-reviews[5-7] and accounting for multiple comparisons analysis in an earlier meta-analysis,[4] we inflated the standard errors (and, so, confidence intervals) for ORs using Bonferroni corrections to reduce the contribution of the individual studies to the pooled estimates in the meta-analyses. Specifically, we inflated (multiplied) the standard errors (resulting is corresponding increases in the width of the confidence intervals) by the ratio of Bonferroni-adjusted z values divided by $z_{0.05}$. For example, if there were 2 studies using the same dataset, the inflator (multiplier) is

$$\frac{z_{.05/2}}{z_{.05}} = \frac{z_{.025}}{z_{.05}} = \frac{2.393980}{1.959964} = 1.221441$$

Thus, the inflator (multiplier) is 1 if there is a single study using a dataset, 1.143594 if there are 2 studies using the same dataset, 1.221441 if there are 3 studies, 1.274363 if there are 4 studies, 1.314223 if there are 5 studies, and 1.346074 if there are 6 studies.

Studies that analyzed youth and adult subsamples separately in the same dataset were not considered overlapping. Several longitudinal studies reported results from PATH for different years and across different waves. We applied the procedure described above to these studies based on the latest year of data collection. We did not attempt to adjust for the fact that some of the respondents carry over between PATH waves for papers that used different time periods because attrition and recruitment of new respondents in the PATH cohort means that the specific sample is not constant over time.

Monte Carlo estimates of odds ratio for the combined effects of sole e-cigarette and dual use

Many e-cigarette users are dual users, including 39.1% (95% CI 36.8%-41.4%) of US e-cigarette users in 2018-2019[8] and 66.7% (62.7%-70.9%) of Swedish e-cigarette users in 2016,[9] making it important to consider dual use when assessing the overall population risks of e-cigarette use, including both sole and dual users.

Let *d* equal fraction of e-cigarette users who are dual users. The overall odds of the disease compared to cigarette use combining sole e-cigarette use and dual use is

$$OR_{all\ vs\ cig} = d\ OR_{dual\ vs\ cig} - (1-d)\ OR_{ecig\ vs\ cig}$$

We estimated the distribution of $OR_{all\ vs\ cig}$ by doing 10,000 random draws of d from a normal distribution and $OR_{dual\ vs\ cig}$ and $OR_{ecig\ vs\ cig}$ from log normal distributions using the observed means and 95% confidence intervals (converted to standard errors) of the observed levels of dual use. d was drawn from a normal distribution because the values were all far from 0 and 1.

SUPPLEMENTARY RESULTS

Risk of bias assessment

The ROBINS-E protocol includes detailed questions about each study whose answers are combined using an algorithm to obtain the risk of bias scores. Following this protocol, all studies scored a having low risk of bias (Table S3), generally because they were well-established population samples designed to assess overall determinants of health.

Among prespecified potential confounders, all controlled for age and sex and most controlled for race/ethnicity (87/107=81%), education and/or socioeconomic status (94/107=88%), BMI (78/107=73%), comorbid conditions (84/107=79%), non-cigarette tobacco use (50/107=47%). Thirty percent (32/107) controlled for former smoking, either by stratifying on smoking status (current, former, never; 15/32=47%), as a categorical variable in a multivariate analysis (13/32=41%), by controlling for smoking duration (years or pack-years; 3/32=9%) or both as a categorical variable and as smoking duration (1/32=3%). Nine papers[10-18] reporting OR of having an asthma attack controlled for previous diagnosis of asthma, which may have over-corrected the estimates of the association between product use and having had an asthma attack, biasing the results toward the null.

They used well-established and validated self-report questions to assess exposure (e-cigarette and cigarette use) and outcomes. Self-reported diagnosis of cardiovascular disease[19,20] and COPD[21,22] has been validated against medical records. Population prevalence estimates in PATH are similar to results in NHANES for cardiovascular[23] and oral diseases.[24]

No respondents were excluded based on reported exposure (e-cigarette or cigarette use), either at baseline or, for the longitudinal studies, during follow-up. Except for PATH, which oversampled tobacco users, respondents were recruited independent of e-cigarette or cigarette use (and before it was measured) generally based on national probability samples. Studies using PATH used provided weights to adjust for oversampling tobacco users. Most studies had low levels of missing data and there was no evidence of bias presented regarding patterns of missing data. Most studies used listwise deletion; 11 used multiple imputation.[17,25-34]

There was no evidence of selective reporting of results.

Sensitivity analyses

95% confidence intervals and associated p values in the sensitivity analyses were not adjusted for multiple comparisons. Doing so would have made confidence intervals wider and p values larger (i.e., less likely to be <0.05), so using uncorrected intervals and p values biases the analysis toward concluding sensitivity. As discussed below, even using unadjusted p values very few of the results suggested sensitivities.

Study design characteristics (Table S6) were unlikely to affect results. Only 4 of the unadjusted p values were less than 0.05, and the pattern of small uncorrected p values was not consistent across the study characteristics. The ORs for dual use vs. cigarettes and e-cigarettes vs. no product use fell by 3-4% per year (p=0.009), but not for other ORs. Whether the risks associated with e-cigarettes has changed over time warrants further research as new data accumulates.

Limiting the data only to studies that reported odds ratios changed a few numbers, but not the whether the 95% confidence intervals for pooled results included 1.00 or the directionality of the associations (compare Table S7 with Table 1).

About half (20/42) the studies of asthma and one-third of the oral disease (3/10) studies were of youth. There was no significant difference in odds ratios between youth and adults for asthma (unadjusted $p \geq 0.376$ for all outcomes) or oral disease studies (unadjusted $p \geq 0.108$ for all outcomes; Table S8). Studies for other outcomes only included adults.

There were not significant differences between the different detailed outcomes for cardiovascular disease, stroke, metabolic dysfunction, or oral disease for e-cigarette vs. cigarette use and dual use vs. cigarettes (unadjusted $p \geq 0.166$; Table S9). There was significant heterogeneity for asthma for e-cigarettes vs. cigarettes and for COPD for dual use vs cigarettes and dual use vs no product use for COPD diagnosis vs respiratory symptoms, but none of these heterogeneities led to a change in qualitative conclusions (footnotes in Table S9). The results were insensitive to deleting individual studies (Figures S5 and S6) suggest that this heterogeneity did not materially affect the conclusions.

Dropping individual studies did not materially affect the estimates of the pooled effects from the meta-analyses for e-cigarettes and dual use compared to cigarettes (Figures S5 and S6). There were only two cases, both oral disease studies of e-cigarettes compared to cigarettes,[33,35] where the significance of the confidence intervals of the pooled estimates moved above or below 1.00. This may be due to the fact that the confidence interval for all the oral disease studies was close to 1.00.

Assuming independent estimates of OR_{ecig} and OR_{cig} when computing $OR_{ecig\ vs\ cig}$ did not materially affect the conclusions of the meta-analysis of $OR_{ecig\ vs\ cig}$ (Table S10). In addition, 13 studies provided both direct estimates of $OR_{dual\ vs\ cig}$ as well as information that allowed computing it from OR_{dual} and OR_{cig}. Twelve of the 13 estimates were within 1% of each other[13,14,29,34,36-42] and the computed value for the other one was within the 95% confidence interval for the direct estimate.[43]

Possible confounding by former smoking

Including former smoking in the analysis was not associated with the estimated ORs for any outcome (Table S6). In addition, 10 ORs for e-cigarettes vs. non-use were reported among former smokers (stroke,[37] asthma,[44-46] COPD,[44,47-49] and difficulty concentrating[50]; Table S3). There was no differences in OR_{ecig} between the ORs determined from the entire sample and the ORs determined from former smokers and the values in the same studies based on the entire sample (p=0.274 by paired t-test).

Studies of never smokers definitively exclude the possibility that OR_{ecig} is confounded by current or former smoking. Most (8/14) studies of asthma[10-12,44-46,51-58] and COPD[11,40,44,47,49,53,57,59] (6/8) found significantly elevated ORs associated with e-cigarette use among never smokers. Indeed, the pooled OR for asthma (OR=1.49; 95% CI 1.30-1.77) and COPD: (2.29; 1.52-3.46) were higher than the estimates based on the entire sample, which included current and former smokers (asthma: 1.24; 1.19-1.30; COPD: 1.46; 1.31-1.61; Table 1). A single study of metabolic dysfunction[60] reported a significant increase in OR of disease associated with e-cigarette use in never smokers, but single studies of cardiovascular[61] or oral disease[62] did not. In addition, two papers published after October 1, 2023 – one of asthma in youth[63] and one of myocardial infarction in adults[64] – reported significant associations between e-cigarette use and disease in never smokers.

CONFLICT OF INTEREST DISLOSURES

Dr Glantz reported receiving personal fees from the World Health Organization outside the submitted work. Dr. Oliveira da Silva realized this work on his sabbatical leave from the Brazilian Health Regulatory Agency (ANVISA). Dr. Nguyen has no disclosures to report. The statements and opinions expressed in the article are those of the authors and are based on current scientific evidence. They do not represent any institutional guideline and/or opinion of ANVISA, the Ministry of Health and/or the Brazilian Government.

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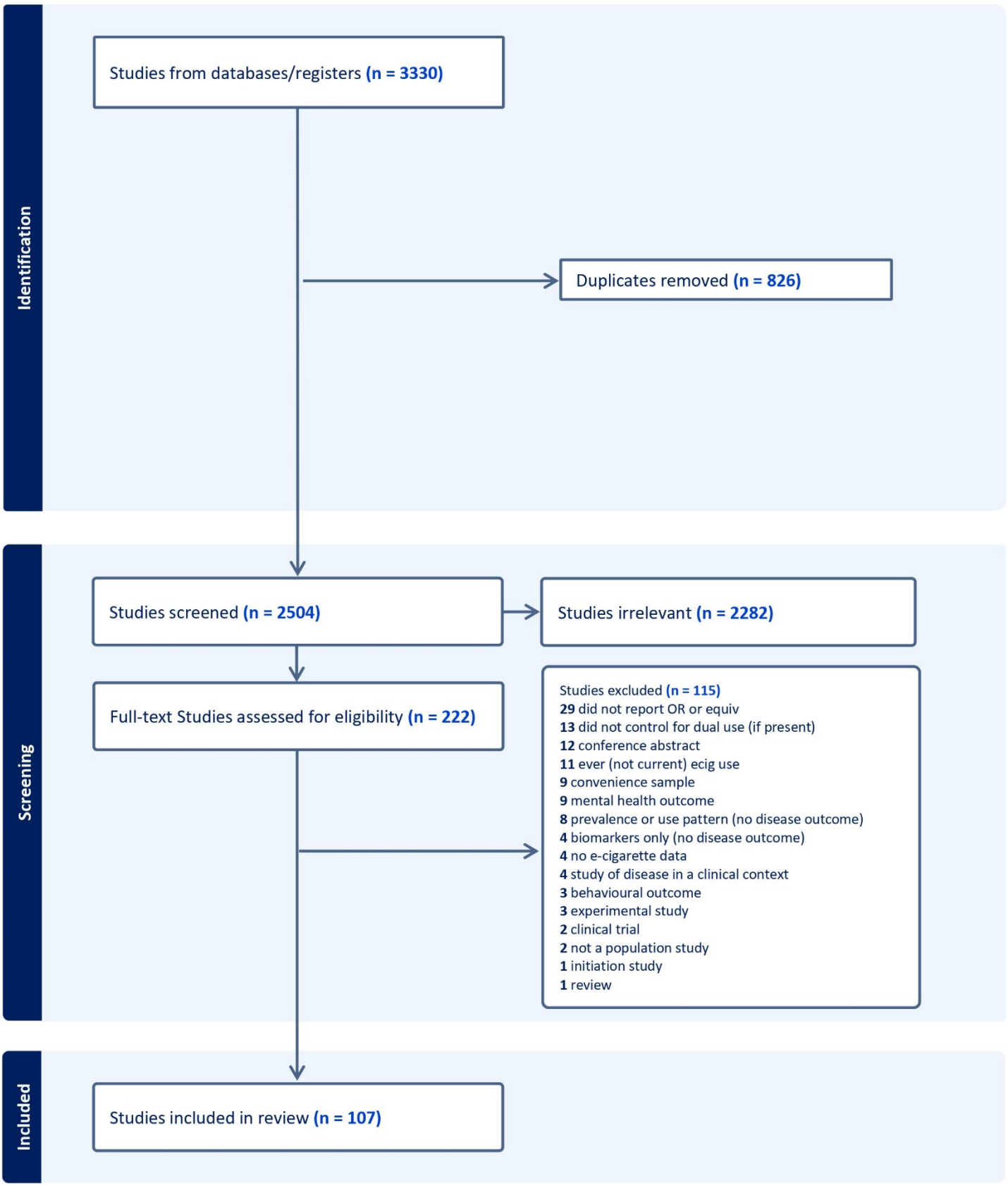


Figure S1. PRISMA diagram. Papers that "did not report OR or equiv" either did not report ORs (or other risk estimates) or did not report estimates that could be used in this analysis.

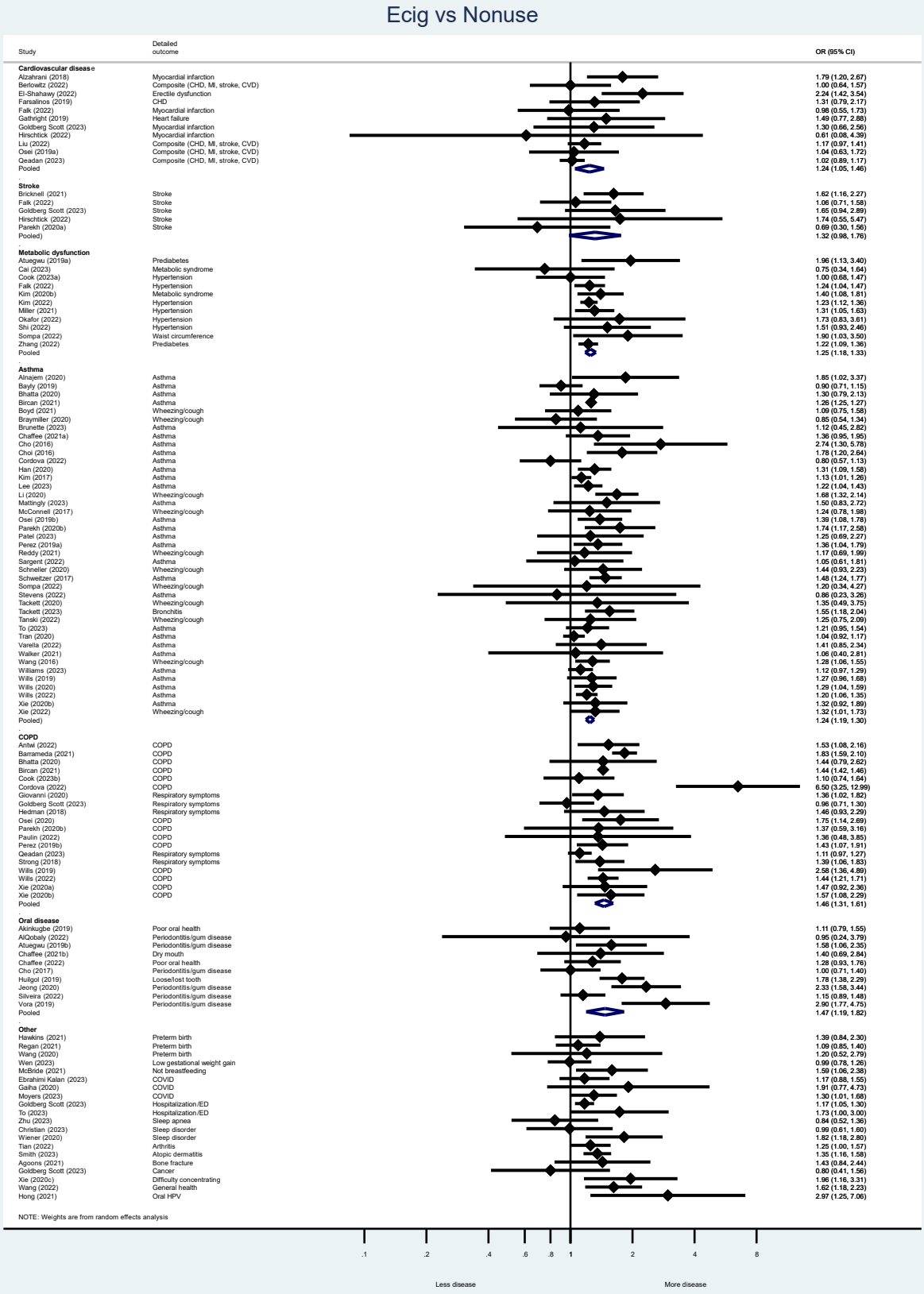


Figure S2. E-cigarette use is significantly associated with increased odds of disease compared to no product use for all outcomes (OR=1.31-1.54). Diamonds show point estimates and 95% confidence intervals for pooled ORs from random effects meta-analysis. Confidence intervals include Bonferroni adjustments. Results for "other" studies were not pooled.

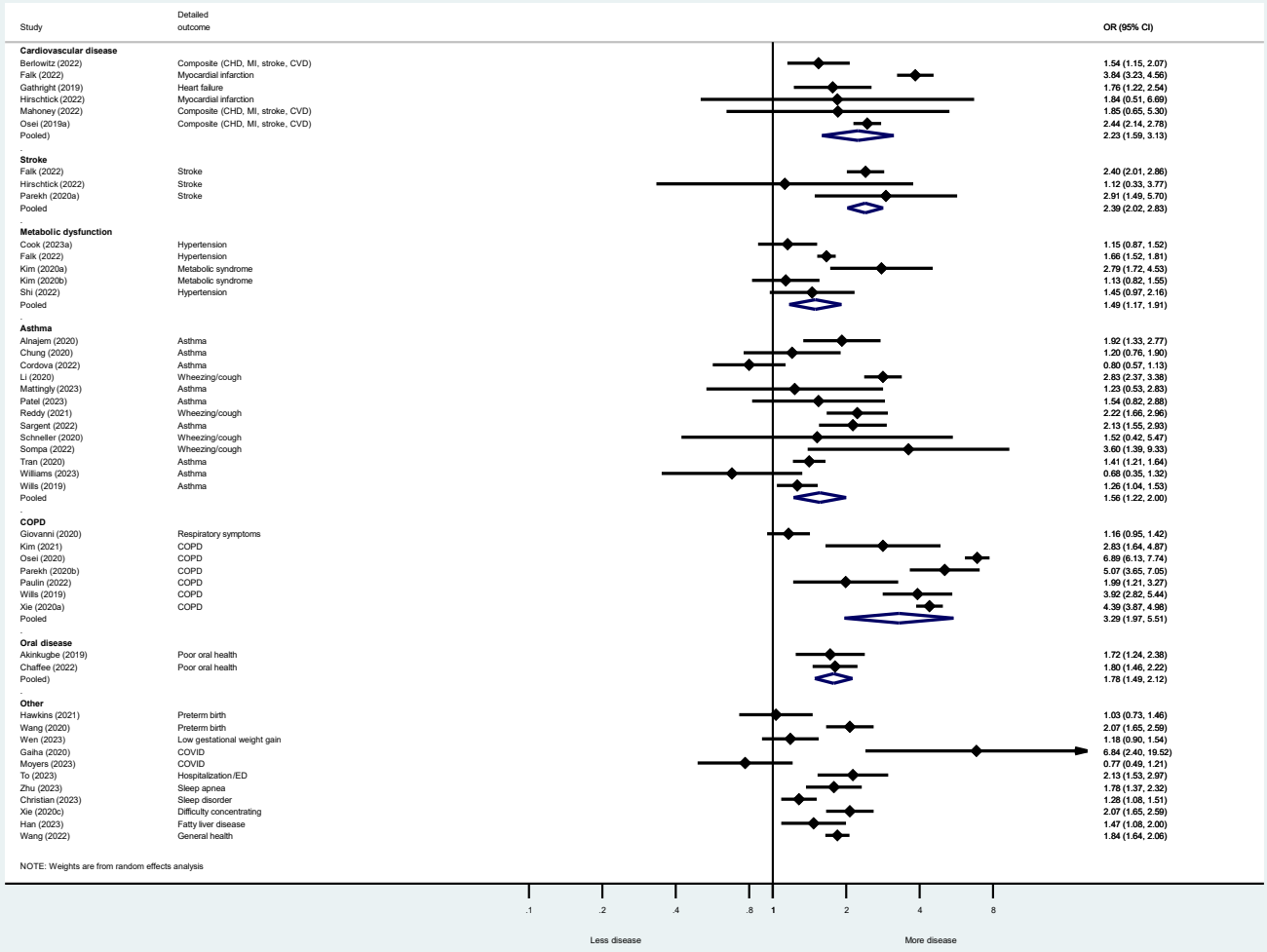


Figure S3. Dual use vs. no product use. Diamonds show point estimates and 95% confidence intervals for pooled ORs from random effects meta-analysis. Confidence intervals include Bonferroni adjustments. Results for “other” studies were not pooled.

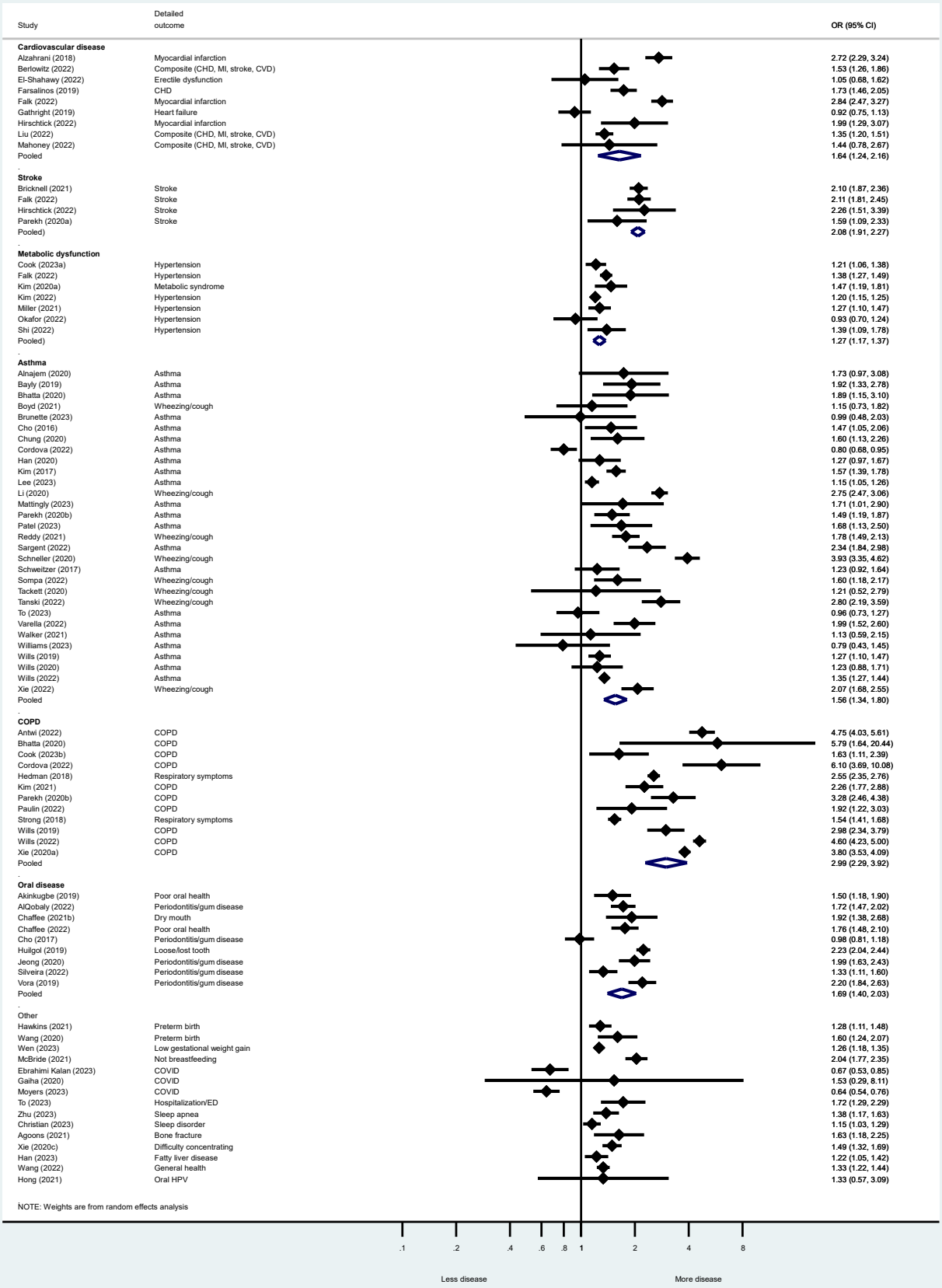
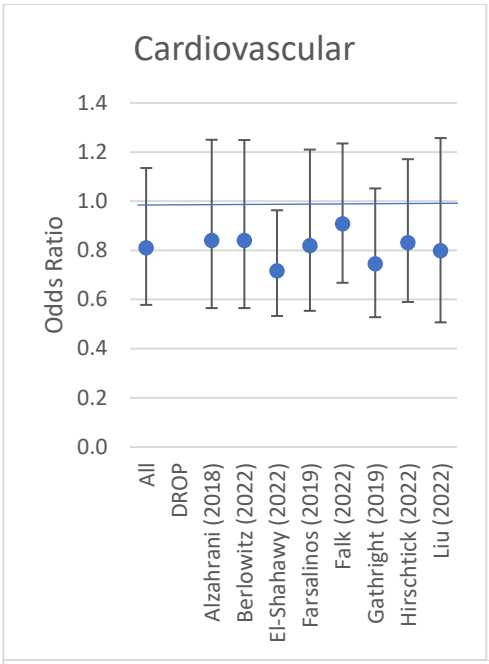
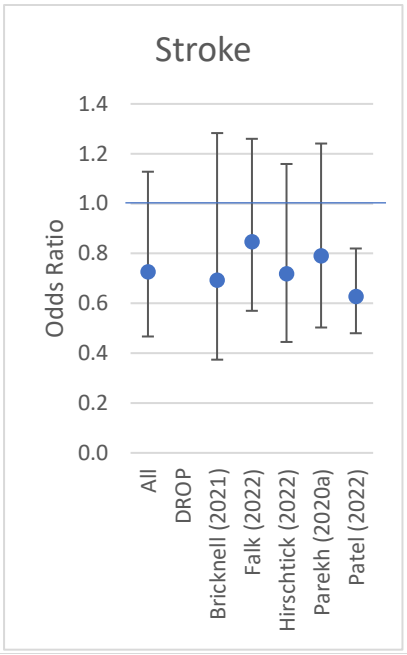
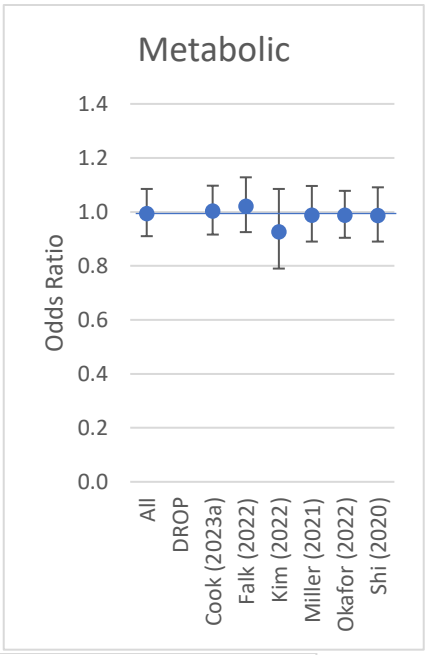
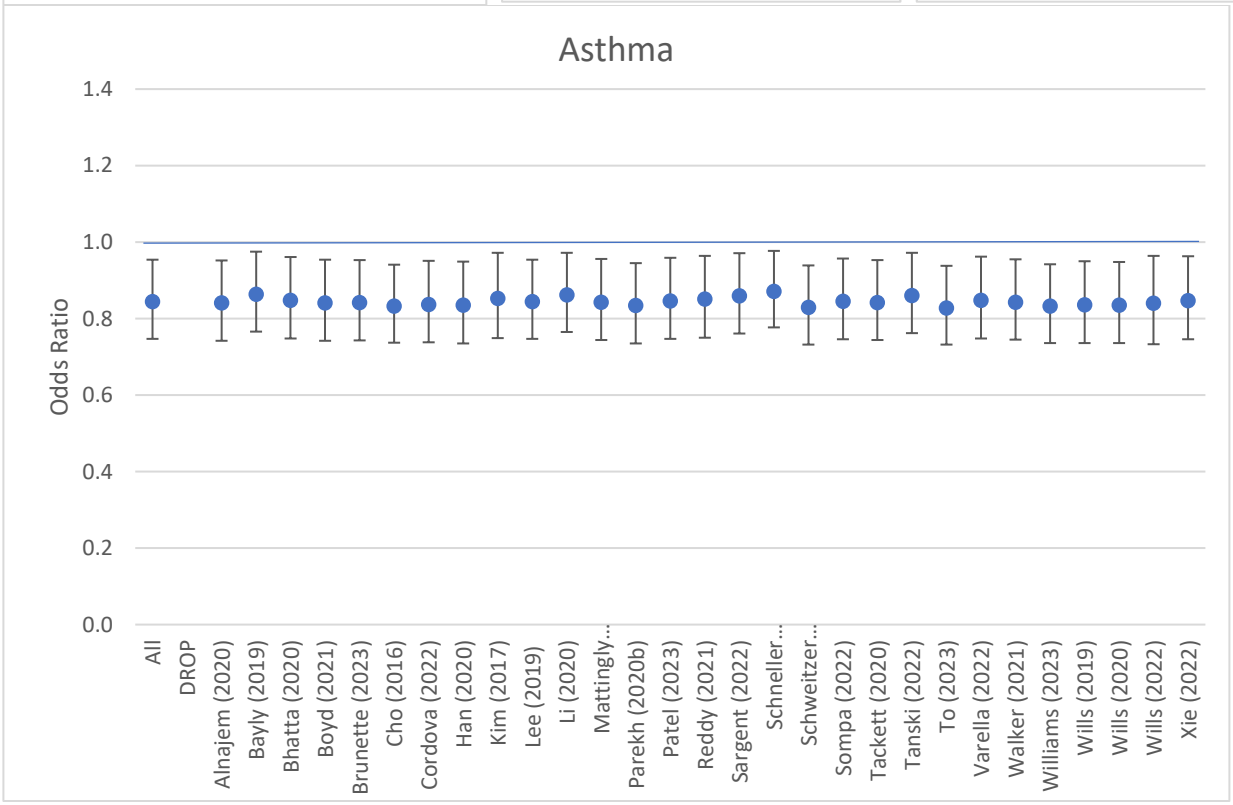


Figure S4. Cigarettes use vs. no product use. Diamonds show point estimates and 95% confidence intervals for pooled ORs from random effects meta-analysis. Confidence intervals include Bonferroni adjustments. Results for "other" studies were not pooled.


Cardiovascular
Odds Ratio
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
All
DROP
Alzahrani (2018)
Berlowitz (2022)
El-Shahawy (2022)
Farsalinos (2019)
Falk (2022)
Gathright (2019)
Hirschtick (2022)
Liu (2022)


Stroke
Odds Ratio
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
All
DROP
Bricknell (2021)
Falk (2022)
Hirschtick (2022)
Parekh (2020a)
Patel (2022)


Metabolic
Odds Ratio
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
All
DROP
Cook (2023a)
Falk (2022)
Kim (2022)
Miller (2021)
Okafor (2022)
Shi (2020)


Asthma
Odds Ratio
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
All
DROP
Alnajem (2020)
Bayly (2019)
Bhatta (2020)
Boyd (2021)
Brunette (2023)
Cho (2016)
Cordova (2022)
Han (2020)
Kim (2017)
Lee (2019)
Li (2020)
Mattingly...
Parekh (2020b)
Patel (2023)
Reddy (2021)
Sargent (2022)
Schneller...
Schweitzer...
Sompa (2022)
Tackett (2020)
Tanski (2022)
To (2023)
Varella (2022)
Walker (2021)
Williams (2023)
Wills (2019)
Wills (2020)
Wills (2022)
Xie (2022)

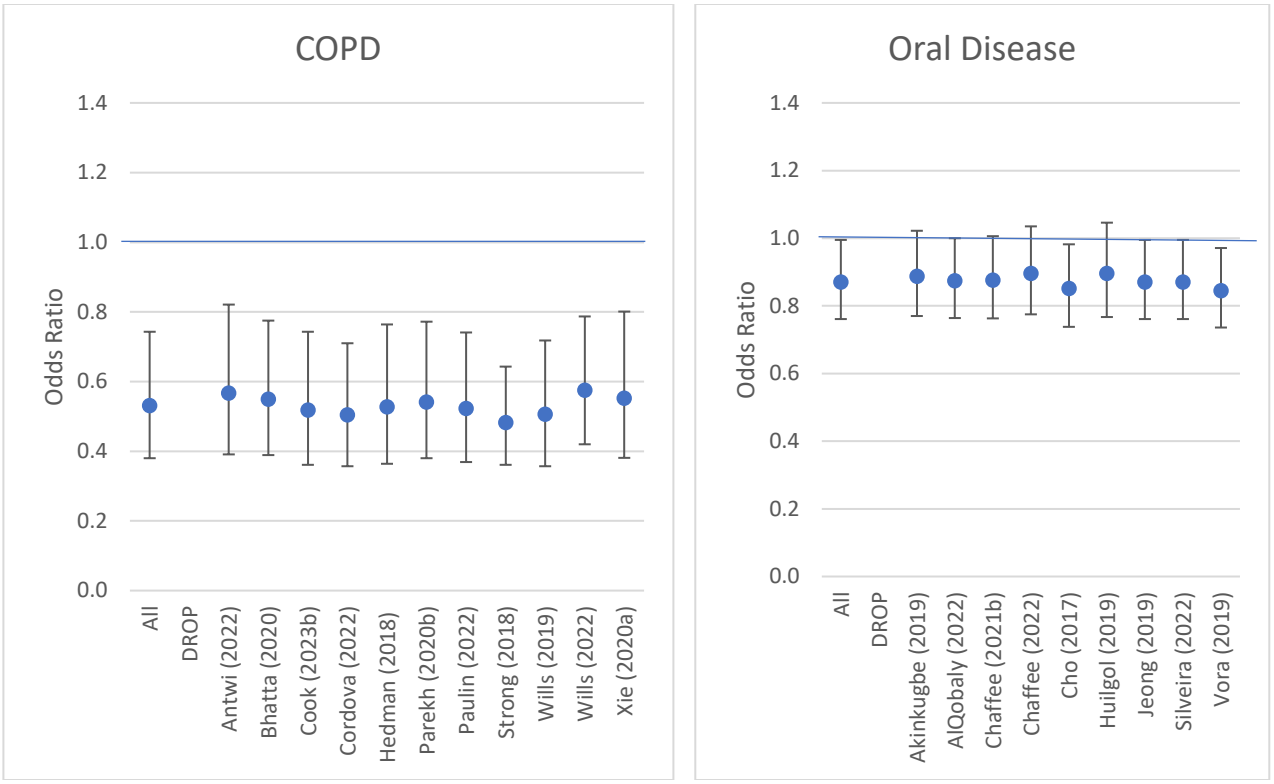
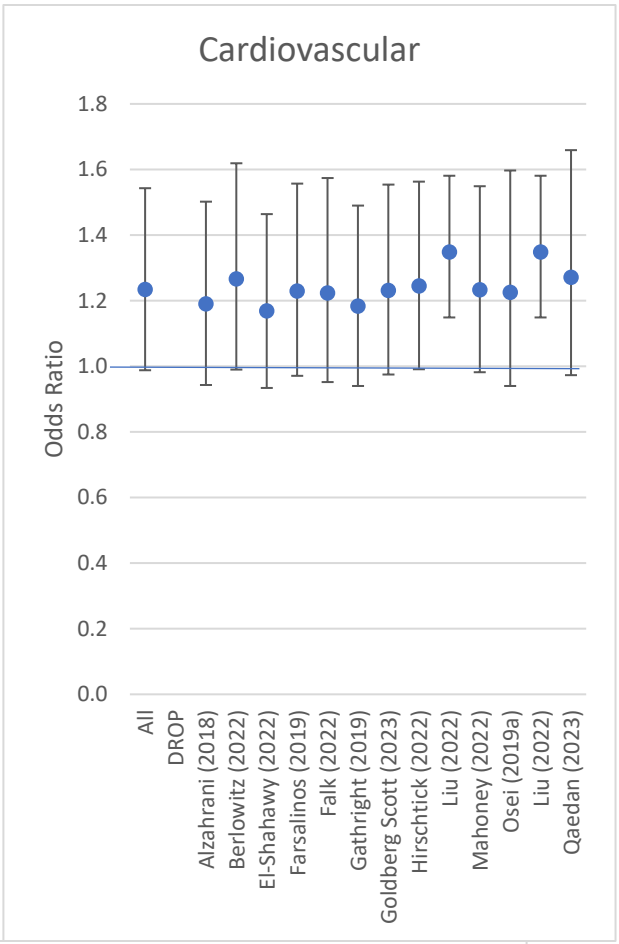
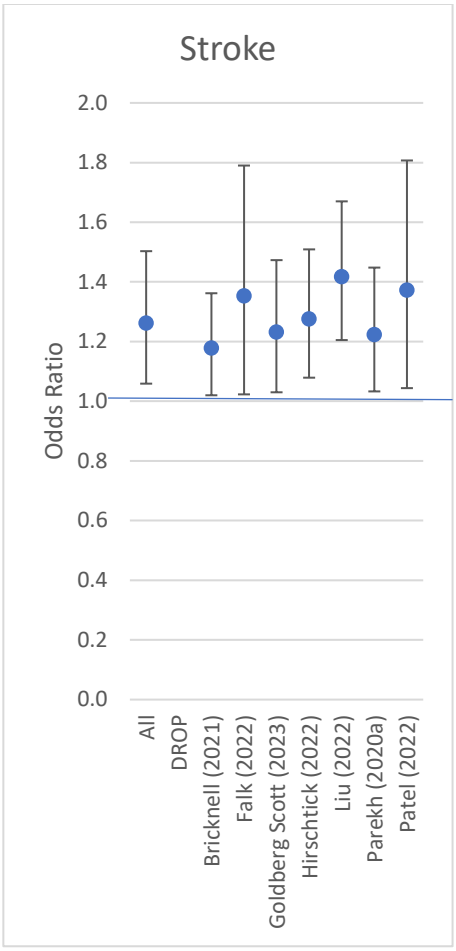
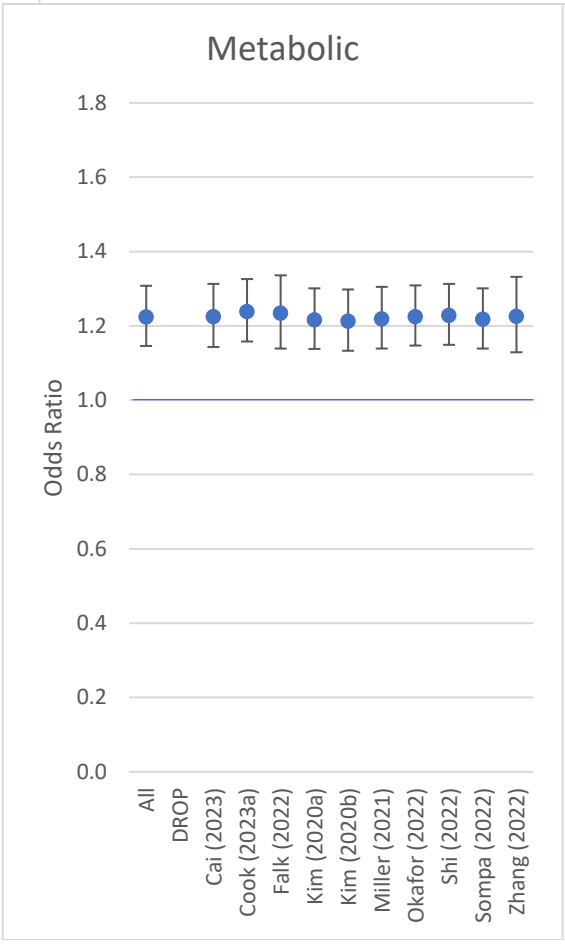
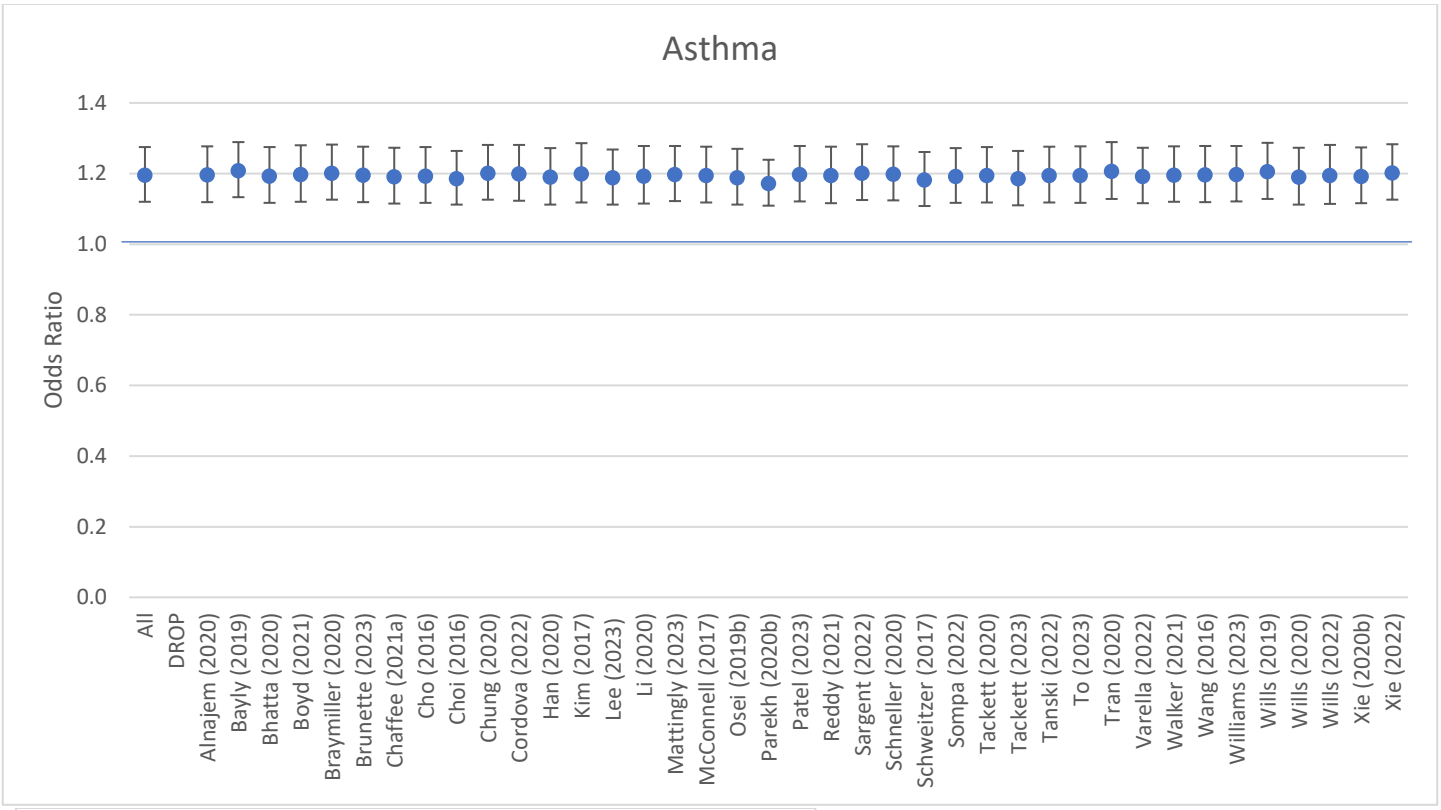


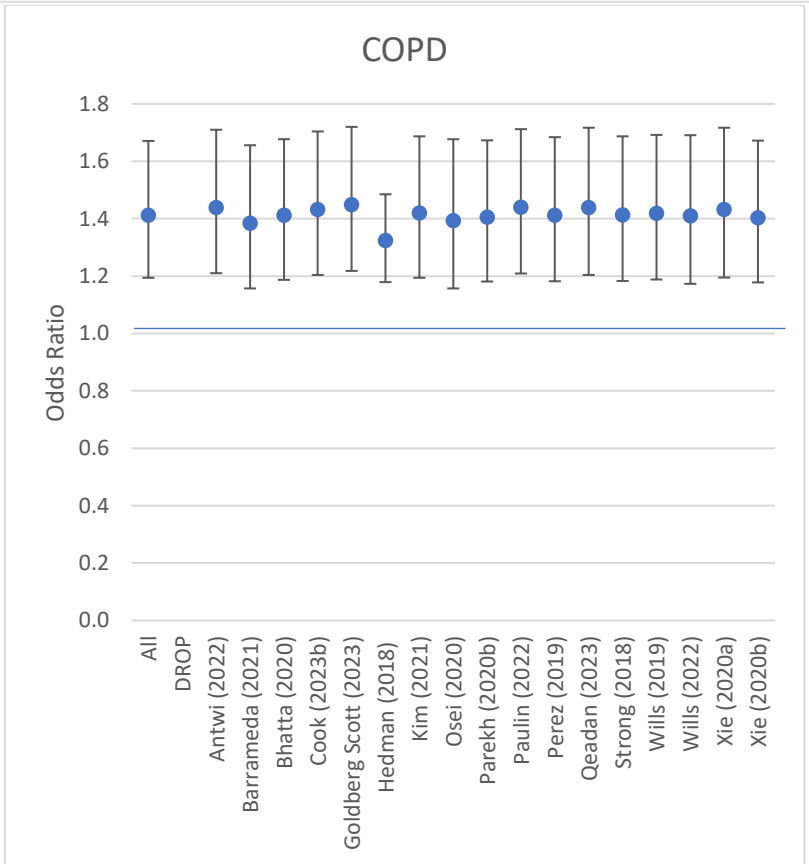
Figure S5. Dropping each study in turn and re-running the meta-analyses for the odds ratio of e-cigarette use to cigarette smoking has little effect on the pooled OR estimates.


Cardiovascular
Odds Ratio
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
All
DROP
Alzahrani (2018)
Berlowitz (2022)
El-Shahawy (2022)
Farsalinos (2019)
Falk (2022)
Gathright (2019)
Goldberg Scott (2023)
Hirschtick (2022)
Liu (2022)
Mahoney (2022)
Osei (2019a)
Liu (2022)
Qaedan (2023)


Stroke
Odds Ratio
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
All
DROP
Bricknell (2021)
Falk (2022)
Goldberg Scott (2023)
Hirschtick (2022)
Liu (2022)
Parekh (2020a)
Patel (2022)


Metabolic
Odds Ratio
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
All
DROP
Cai (2023)
Cook (2023a)
Falk (2022)
Kim (2020a)
Kim (2020b)
Miller (2021)
Okafor (2022)
Shi (2022)
Sompa (2022)
Zhang (2022)





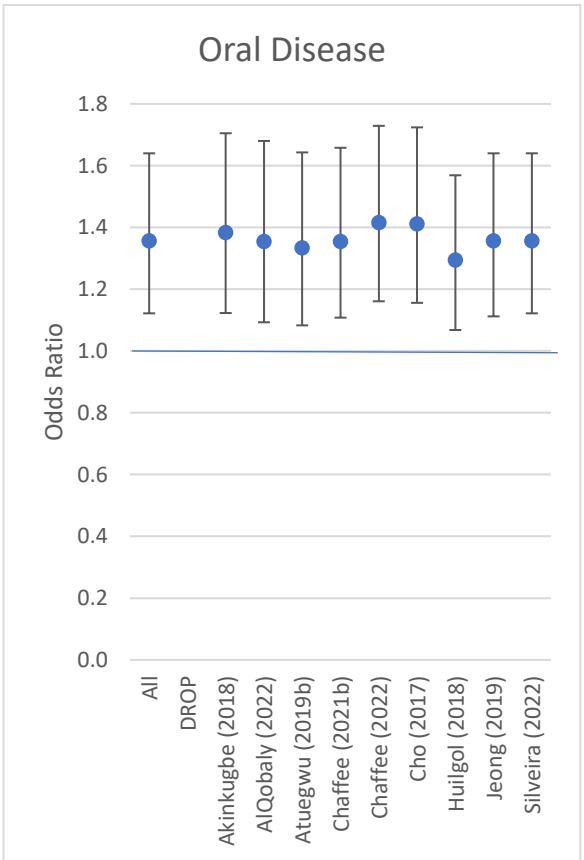


Figure S6. Dropping each study in turn and re-running the meta-analyses for the odds ratio of dual use to cigarette smoking has little effect on the pooled ORs estimates.

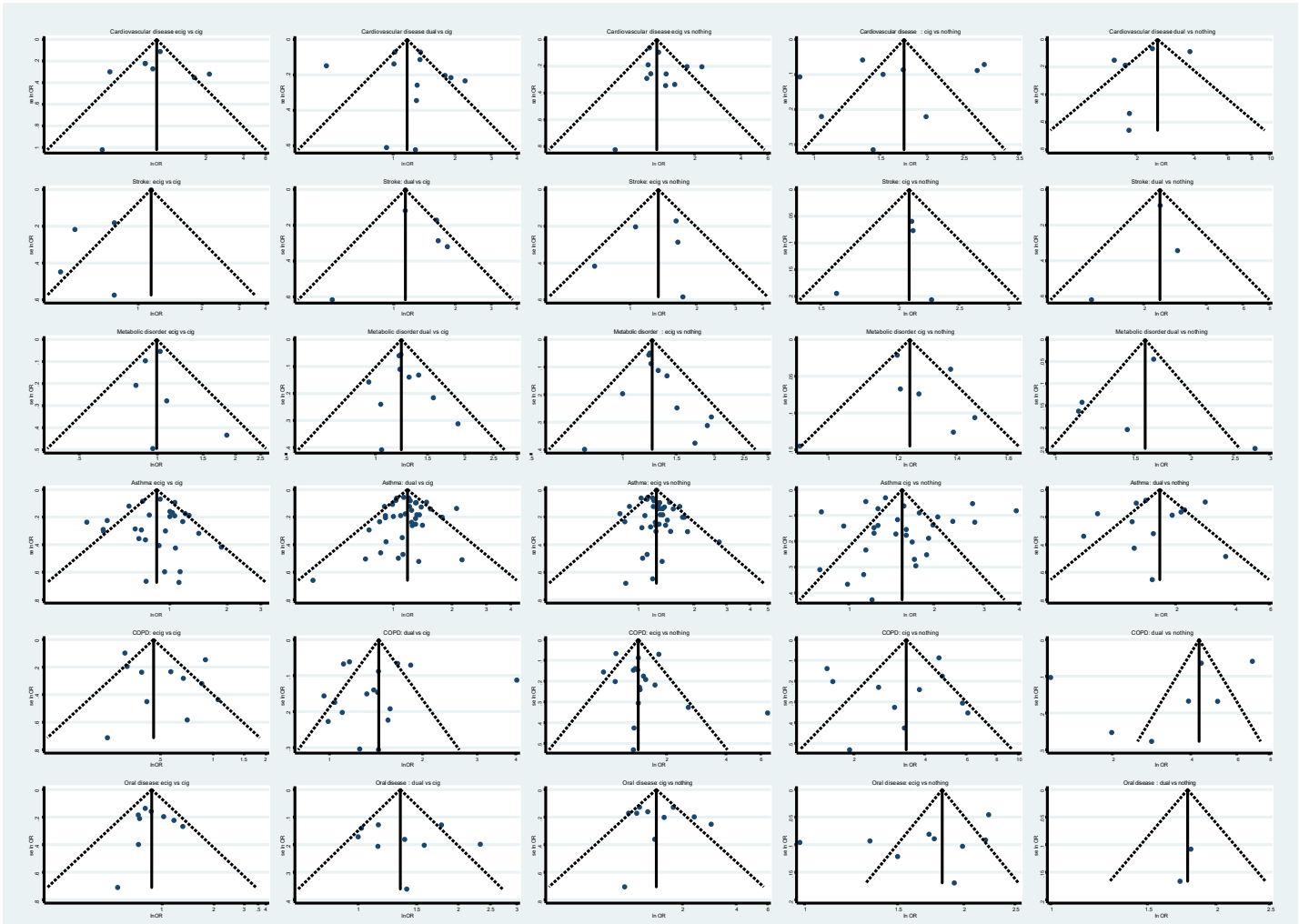


Figure S7. Funnel plots generally do not indicate publication bias, which is consistent with the results from Begg and Egger tests (Table S11). The funnel plot and Egger test suggested possible publication bias for dual use vs. cigarettes for cardiovascular disease. Funnel plots (but not Begg or Egger tests) suggested possible publication bias for cigarettes vs. nothing for cardiovascular disease and cigarettes vs nothing and dual use vs. nothing for asthma. Diagonal lines are pseudo 95% confidence limits for summary treatment effect in the absence of publication bias or other sources of heterogeneity. Trim and fill analysis did not suggest that accounting for possible publication bias affected the conclusions (Table S12).

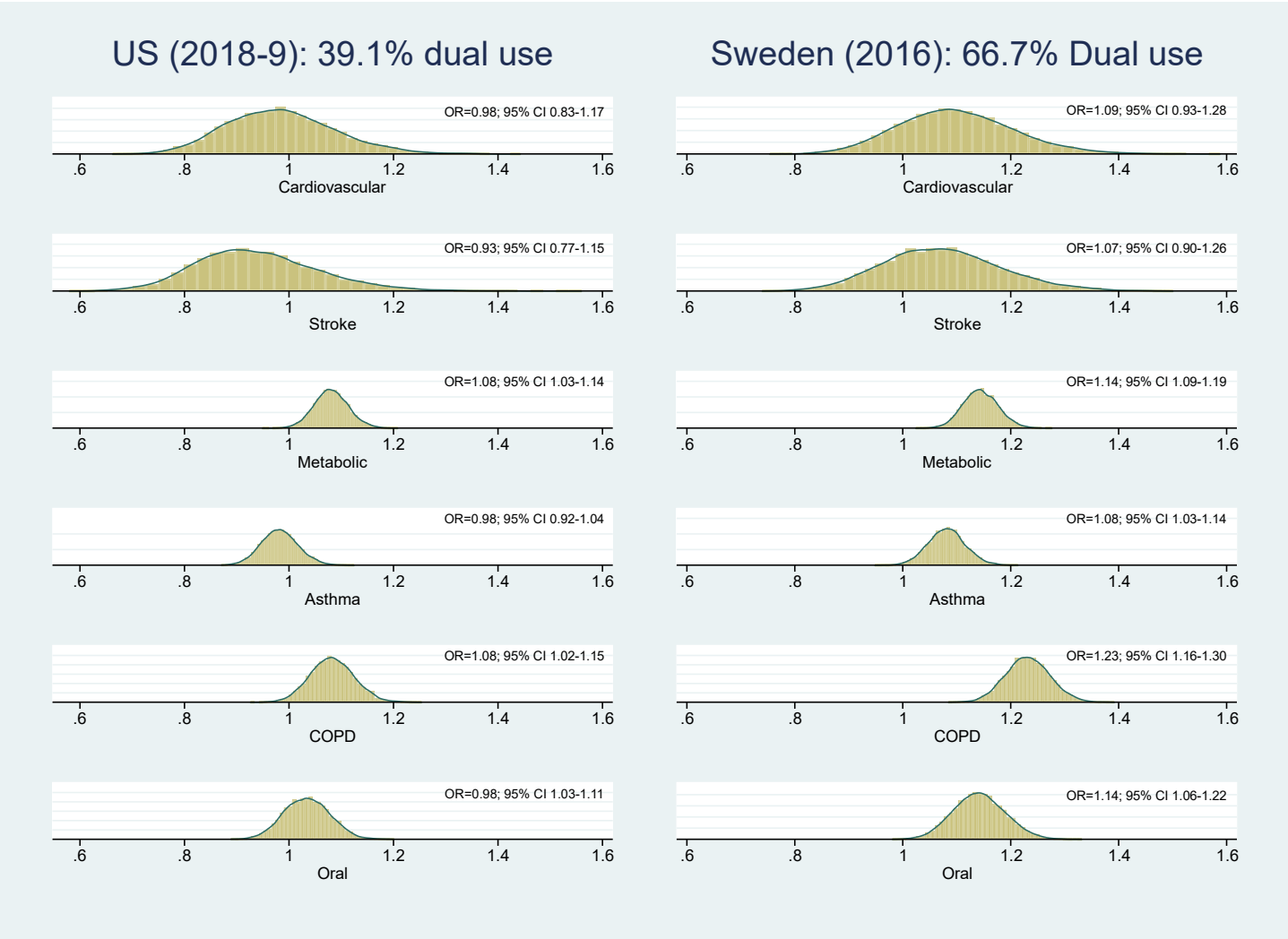


Figure S8. The overall OR of sole e-cigarette and dual use compared to cigarettes alone is higher than for sole use. Combined. The results are sensitive to the level of dual use. With 39.1% dual use, the probabilities of OR>1 are 0.90 for cardiovascular disease, >0.99 for metabolic dysfunction. 0.44 for asthma, 0.12 for COPD and 0.87 for oral disease. These results are sensitive to the level of dual use. For 66.7% dual use, these probabilities increase to >0.99 for cardiovascular disease, metabolic dysfunction, asthma and oral disease and 0.97 for COPD.

Table S1. Studies	
Agoons (2021)	Agoons DD, Agoons BB, Emmanuel KE, Matawalle FA, Cunningham JM. Association between electronic cigarette use and fragility fractures among US adults, American Journal of Medicine Open, Volumes 1–6, 2021, 100002, ISSN 2667-0364, https://doi.org/10.1016/j.ajmo.2021.100002.
Akinkugbe (2019)	Akinkugbe AA. Cigarettes, E-cigarettes, and Adolescents' Oral Health: Findings from the Population Assessment of Tobacco and Health (PATH) Study. JDR Clin Trans Res. 2019 Jul;4(3):276-283. doi: 10.1177/2380084418806870. Epub 2018 Oct 15. PMID: 30931714.
Alnajem (2020)	Alnajem A, Redha A, Alroumi D, Alshammasi A, Ali M, Alhussaini M, Almutairi W, Esmaeil A, Ziyab AH. Use of electronic cigarettes and secondhand exposure to their aerosols are associated with asthma symptoms among adolescents: a cross-sectional study. Respir Res. 2020 Nov 16;21(1):300. doi: 10.1186/s12931-020-01569-9. PMID: 33198741; PMCID: PMC7670675.
AlQobaly (2022)	AlQobaly L, Abed H, Alsahafi Y, Sabbah W, Hakeem FF. Does smoking explain the association between use of e-cigarettes and self-reported periodontal disease? J Dent. 2022 Jul;122:104164. doi: 10.1016/j.jdent.2022.104164. Epub 2022 May 14. PMID: 35580834.
Alzahrani (2018)	Alzahrani T, Pena I, Temesgen N, Glantz SA. Association Between Electronic Cigarette Use and Myocardial Infarction. Am J Prev Med. 2018 Oct;55(4):455-461. doi: 10.1016/j.amepre.2018.05.004. Epub 2018 Aug 22. Erratum in: Am J Prev Med. 2019 Oct;57(4):579-584. PMID: 30166079; PMCID: PMC6208321
Antwi (2022)	Antwi GO, Rhodes DL. Association between E-cigarette use and chronic obstructive pulmonary disease in non-asthmatic adults in the USA. J Public Health (Oxf). 2022 Mar 7;44(1):158-164. doi: 10.1093/pubmed/fdaa229. PMID: 33348361.
Atuegwu (2019a)	E-cigarette use is associated with a self-reported diagnosis of prediabetes iAtuegwu NC, Perez MF, Oncken C, Mead EL, Maheshwari N, Mortensen EM. E-cigarette use is associated with a self-reported diagnosis of prediabetes in never cigarette smokers: Results from the behavioral risk factor surveillance system survey. Drug Alcohol Depend. 2019 Dec 1;205:107692. doi: 10.1016/j.drugalcdep.2019.107692. Epub 2019 Oct 28. PMID: 31707269; PMCID: PMC6893144.
Atuegwu (2019b)	Atuegwu NC, Perez MF, Oncken C, Thacker S, Mead EL, Mortensen EM. Association between Regular Electronic Nicotine Product Use and Self-reported Periodontal Disease Status: Population Assessment of Tobacco and Health Survey. Int J Environ Res Public Health. 2019 Apr 9;16(7):1263. doi: 10.3390/ijerph16071263. PMID: 30970567; PMCID: PMC6479961.
Barrameda (2021)	Barrameda R, Nguyen T, Wong V, Castro G, Rodriguez de la Vega P, Lozano J, Zevallos J. Use of E-Cigarettes and Self-Reported Lung Disease Among US Adults. Public Health Rep. 2020 Nov/Dec;135(6):785-795. doi: 10.1177/0033354920951140. Epub 2020 Sep 24. PMID: 32972319; PMCID: PMC7649986.
Bayly (2019)	Bayly JE, Bernat D, Porter L, Choi K. Secondhand Exposure to Aerosols From Electronic Nicotine Delivery Systems and Asthma Exacerbations Among Youth With Asthma. Chest. 2019 Jan;155(1):88-93. doi: 10.1016/j.chest.2018.10.005. Epub 2018 Oct 22. PMID: 30359612; PMCID: PMC6688978.
Berlowitz (2022)	Berlowitz JB, Xie W, Harlow AF, Hamburg NM, Blaha MJ, Bhatnagar A, Benjamin EJ, Stokes AC. E-cigarette Use and Risk of Cardiovascular Disease: A Longitudinal Analysis of the PATH Study, 2013-2019. Circulation. 2022 May 6. doi: 10.1161/CIRCULATIONAHA.121.057369. Epub ahead of print. PMID: 35514292.
Bhatta (2020)	Bhatta DN, Glantz SA. Association of E-Cigarette Use With Respiratory Disease Among Adults: A Longitudinal Analysis. Am J Prev Med. 2020 Feb;58(2):182-190. doi: 10.1016/j.amepre.2019.07.028. Epub 2019 Dec 16. PMID: 31859175; PMCID: PMC6981012.
Bircan (2021)	Bircan E, Bezirhan U, Porter A, Fagan P, Orloff MS. Electronic cigarette use and its association with asthma, chronic obstructive pulmonary disease (COPD) and asthma-COPD overlap syndrome among never cigarette smokers. Tob Induc Dis. 2021 Oct 21;19:75. doi: 10.18332/tid/142579. Erratum in: Tob Induc Dis. 2021 Oct 21;19:74. PMID: 34720794; PMCID: PMC8530195.
Boyd (2021)	Boyd CJ, McCabe SE, Evans-Polce RJ, Veliz PT. Cannabis, Vaping, and Respiratory Symptoms in a Probability Sample of U.S. Youth. J Adolesc Health. 2021 Jul;69(1):149-152. doi: 10.1016/j.jadohealth.2021.01.019. Epub 2021 Mar 3. PMID: 33676824; PMCID: PMC8238794.

Table S1. Studies	
Braymiller (2020)	Braymiller JL, Barrington-Trimis JL, Leventhal AM, Islam T, Kechter A, Krueger EA, Cho J, Lanza I, Unger JB, McConnell R. Assessment of Nicotine and Cannabis Vaping and Respiratory Symptoms in Young Adults. JAMA Netw Open. 2020 Dec 1;3(12):e2030189. doi: 10.1001/jamanetworkopen.2020.30189. PMID: 33351085; PMCID: PMC7756238.
Brunette (2023)	Brunette MF, Halenar MJ, Edwards KC, Taylor KA, Emond JA, Tanski SE, Woloshin S, Paulin LM, Hyland A, Lauten K, Mahoney M, Blanco C, Borek N, DaSilva LC, Gardner LD, Kimmel HL, Sargent JD. Association between tobacco product use and asthma among US adults from the Population Assessment of Tobacco and Health (PATH) Study waves 2-4. BMJ Open Respir Res. 2023 Feb;10(1):e001187. doi: 10.1136/bmjresp-2021-001187. PMID: 36750276; PMCID: PMC9906250.
Bricknell (2021)	Bricknell RAT, Ducaud C, Figueroa A, Schwarzman LS, Rodriguez P, Castro G, Zevallos JC, Barengo NC. An association between electronic nicotine delivery systems use and a history of stroke using the 2016 behavioral risk factor surveillance system. Medicine (Baltimore). 2021 Sep 10;100(36):e27180. doi: 10.1097/MD.0000000000027180. PMID: 34516517; PMCID: PMC8428735.
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Table S1. Studies	
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Xie (2020a)	Xie Z, Ossip DJ, Rahman I, Li D. Use of Electronic Cigarettes and Self-Reported Chronic Obstructive Pulmonary Disease Diagnosis in Adults. Nicotine Tob Res. 2020 Jun 12;22(7):1155-1161. doi: 10.1093/ntr/ntz234. PMID: 31830263; PMCID: PMC7291797.
Xie (2020b)	Xie W, Kathuria H, Galiatsatos P, Blaha MJ, Hamburg NM, Robertson RM, Bhatnagar A, Benjamin EJ, Stokes AC. Association of Electronic Cigarette Use With Incident Respiratory Conditions Among US Adults From 2013 to 2018. JAMA Netw Open. 2020 Nov 2;3(11):e2020816. doi: 10.1001/jamanetworkopen.2020.20816. PMID: 33180127; PMCID: PMC7662143.
Xie (2020c)	Xie Z, Ossip DJ, Rahman I, O'Connor RJ, Li D. Electronic cigarette use and subjective cognitive complaints in adults. PLoS One. 2020 Nov 2;15(11):e0241599. doi: 10.1371/journal.pone.0241599. PMID: 33137145; PMCID: PMC7605645.
Xie (2022)	Xie W, Tackett AP, Berlowitz JB, Harlow AF, Kathuria H, Galiatsatos P, Fetterman JL, Cho J, Blaha MJ, Hamburg NM, Robertson RM, DeFilippis AP, Hall ME, Bhatnagar A, Benjamin EJ, Stokes AC. Association of Electronic Cigarette Use with Respiratory Symptom Development among U.S. Young Adults. Am J Respir Crit Care Med. 2022 Jun 1;205(11):1320-1329. doi: 10.1164/rccm.202107-1718OC. PMID: 35089853.
Zhang (2022)	Zhang Z, Jiao Z, Blaha MJ, Osei A, Sidhaye V, Ramanathan M Jr, Biswal S. The Association Between E-Cigarette Use and Prediabetes: Results From the Behavioral Risk Factor Surveillance System, 2016-2018. Am J Prev Med. 2022 Jun;62(6):872-877. doi: 10.1016/j.amepre.2021.12.009. Epub 2022 Mar 3. PMID: 35597566.
Zhu (2023)	Zhu H, Wu M. A cross-sectional study on the relationship between electronic cigarette and combustible cigarette use with obstructive sleep apnea among U.S. adults: result from NHANES 2015-2018. Arch Public Health. 2023 Apr 13;81(1):54. doi: 10.1186/s13690-023-01083-6. PMID: 37055806; PMCID: PMC10099817.

Table S2. Characteristics and results from included studies (values used in meta-analysis appear in ***bold italics***; all are OR unless otherwise noted)																
Study	**Outcome**	**Sample**	**Sample size**	**Adult or Youth***	**Years data collected**	**Diagnosis: Current † or Ever**	**Cross-sectional or Longitudinal**	**Reference use: Never or Non-Current**	**No. studies of dataset**	**Model: Multivariate, Stratified, or Both**	**E-cigarette risk (95%CI)**	**Cigarette risk (95%CI)**	**Dual Use risk**	**Sole e-cigarette or e-cigarette risk**	**Where to find reported results**	**Notes**
Cardiovascular disease																
Alzahrani (2018)	Myocardial infarction	NHIS	69046	A	2014, 2016	E	C	N	1	M	***Daily e-cigarette use vs. never ecig use =1.79 (1.20-2.66)***Some day vs. never =1.16 (0.83 - 1.62)¶Former vs. never=1.06 (0.86 - 1.30)	***Daily smokers vs. never smokers = 2.72 (2.29-3.24)*** current vs. never= 2.64 (2.24 - 3.12) Some day smokers vs. Never smokers= 2.36 (1.80 - 3.09) Former smokers vs. Never smokers =1.70 (1.51 - 1.91)			Table 2	
Berlowitz (2022)	Incident CVD (people with no CVD history)	PATH	24027	A	2013-2019	C	L	NC	3	S	***sole ENDS vs. nonusers = 1.00 (0.69 - 1.45)***	***sole cig vs. nonusers = 1.53 (1.30 - 1.79)***	***DU vs. nonuse=1.54 (1.21 - 1.96)*** ***DU vs. sole cig=1.01 (0.81 - 1.26)***	***sole ENDS vs. sole Cig = 0.66 (0.46 - 0.94)***	Table (no number)	Hazard ratio
El-Shahawy (2022)	Erectile dysfunction (age 20-65; no CVD)	PATH	13711	A	2016-2018	C	C	N	2	M	***Daily vs. never = 2.24 (1.50 - 3.34)*** Some day vs. never=1.43 (0.88 - 2.31) Former vs never: 1.12 (0.87 - 1.45)	***Current vs. never=1.05 (0.72 - 1.53)*** Former vs. never= 0.84 (0.60 - 1.19)	***DU vs. never users of both ENDS and cig= 1.68 (1.05 - 2.69)*** among people without CVD diagnosis	Current ENDS users who were former smokers vs. Never users of both=1.85 (1.06 - 3.24) among people without CVD diagnosis	Tables 2-4	We used age-restricted CVD-free sample (i.e., aged <65 years with no reported CVD; n=11,207). There were many sensitivity analyses.
Falk (2022)	coronary artery disease, myocardial infarction	NHIS	84,553	0	2014, 2016, 2017, 2018	1	0	1	1	2	Coronary artery disease: 0.86 (0.52-1.41) ***Myocardial infarction: 0.98 (0.56-1.75)***	Coronary artery disease: 1.86 (1.61-2.15) ***Myocardial infarction: 2.84 (2.44-3.29)***	Coronary artery disease: 2.21 (1.82-2.14) ***Myocardial infarction: 3.84 (3.23-4.56)***		Table 1	MI selected at random from two outcomes.

Table S2. Characteristics and results from included studies (values used in meta-analysis appear in *bold italics*; all are OR unless otherwise noted)

Study	Outcome	Sample	Sample size	Adult or Youth*	Years data collected	Diagnosis: Current † or Ever	Cross-sectional or Longitudinal	Reference use: Never or Non-Current	No. studies of dataset	Model: Multivariate, Stratified, or Both	E-cigarette risk (95%CI)	Cigarette risk (95%CI)	Dual Use risk	Sole e-cigarette or e-cigarette risk	Where to find reported results	Notes
Farsalinos (2019)	Coronary Heart Disease	PATH	59770	A	2016-2017	E	C	N	1	M	For CHD: ***Daily use vs. never = 1.31 (0.79 - 2.17)*** Some days vs. never = 1.13 (0.70 - 1.83) Former vs. never= 1.03 (0.83-1.28) For MI: *Daily use vs. never =1.35 (0.80-2.27)* Some days vs. never = 1.22 (0.78 - 1.91) Former vs. never=0.96 (0.77 - 1.20)	For CHD: **Daily use vs. never =1.73 (1.46 - 2.05)** Some days vs. never = 1.75 (1.32 - 2.32) Former<=6 years vs. never= 1.96 (1.58 - 2.44) Former > 6 year vs. never = 1.43 (1.28 - 1.60) For MI: *Daily use vs. never =3.13 (2.63 - 3.73)* some days vs. never = 2.47 (1.79 - 3.40) Former<=6 years vs. never= 2.82 (2.22 - 3.57) Former > 6 year vs. never = 1.51 (1.32 - 1.74)			Tables 2-3	
Gathright (2019)	Heart failure	PATH	32320	A	2013-2014	E	C	NC	1	S	***Current (y vs. n)= 1.49 (0.77-2.88)***	***current (y vs. n) = 0.92 (0.75 – 1.14)***	***Current (y vs. n)= 1.76 (1.22 – 2.54)***		text	Conducted three separate logistic regressions through which cigarette use, e-cigarette use, and dual use were the outcomes. HF was the independent variable in each

Table S2. Characteristics and results from included studies (values used in meta-analysis appear in *bold italics*; all are OR unless otherwise noted)

Study	Outcome	Sample	Sample size	Adult or Youth*	Years data collected	Diagnosis: Current † or Ever	Cross-sectional or Longitudinal	Reference use: Never or Non-Current	No. studies of dataset	Model: Multivariate, Stratified, or Both	E-cigarette risk (95%CI)	Cigarette risk (95%CI)	Dual Use risk	Sole e-cigarette or e-cigarette risk	Where to find reported results	Notes
Goldberg Scott (2023)	myocardial infarction	Kaiser Permanente Research Bank	96,148	0	2015-2019	0	1	1	1	1	Longitudinal [cross-sectional in brackets]: ***Myocardial infarction: 1.30 (0.66-2.55)*** [1.22; 0.90-1.66] Additional cross-sectional: Hypertension (diagnosis + medication): 0.99 (0.87-1.14) Hypertension (diagnosis + no medication): 1.09 (0.84-1.42) Non-stroke cerebrovascular disease: 1.55 (1.21-1.99)				Table 3 (longitudinal) and Table 2 (cross-sectional)	Hazard ratios (HR) for longitudinal results OR for cross-sectional results Longitudinal results used in meta-analysis. Cross sectional results (based on larger sample sizes) also reported (Table 2). People with history of heart attack, stroke or cancer prior to survey excluded.
Hirschtick (2022)	Incident first MI (age 40+)	PATH	11031	A	2013-2019	C	L	NC	3	S	***combined: 1.22 (0.48-5.49)*** MI: exclusive ecig vs. non-current use: 0.61 (0.12-3.04) ***exclusive ENDS vs. exclusive cig = 0.3 (0.06-1.59)*** stroke: exclusive ecig vs. non-current use: 1.74 (0.55-5.49) ***exclusive ENDS vs. exclusive cig = 0.77 (0.25-2.38)***	***combined: 2.10 (1.61-2.74)*** MI: exclusive cig vs. non-current use: 1.99 (1.40-2.84) stroke: 2.26 (1.51-3.39)	***combined: 1.49 (0.67-3.31)*** *MI:* *dual vs. non-current use: 1.84 (0.64-5.30)* ***dual vs. exclusive cig = 0.93 (0.35-2.48)*** *stroke:* *dual vs. non-current use: 1.12 (0.33-3.79)* ***dual vs. exclusive cig = 0.50 (0.15-1.60)***		Table 4 and text	Hazard ratio Excluded people who had MI or stroke at baseline computed time varying HR (not OR) MI selected at random
Liu (2022)	Composite	BRFSS	253561	A	2020	E	C	N	1	B	***Current ecig vs never user:*** ***Multivariable: 1.17 (0.97-1.412)*** ***Stratified: 1.25 (0.80-1.95)***	***Current cig smoker vs never smoker:*** ***Multivariable: 1.45 (1.33-1.58)*** ***Stratified: 1.35 (1.20-1.51)***	***Current dual user vs never user of either product:*** ***Stratified: 1.79 (1.37-2.34)***	***Current user vs never user of either product:*** ***Stratified:*** ***ecig: 1.25 (0.80-1.95)*** cig: 1.35 (1.20-1.51)	Table 2 and Figure 2A	Multivariable estimates also include sleep duration as covariate. Also present data on former users and age-stratified results.

Table S2. Characteristics and results from included studies (values used in meta-analysis appear in ***bold italics***; all are OR unless otherwise noted)																
Study	**Outcome**	**Sample**	**Sample size**	**Adult or Youth***	**Years data collected**	**Diagnosis: Current † or Ever**	**Cross-sectional or Longitudinal**	**Reference use: Never or Non-Current**	**No. studies of dataset**	**Model: Multivariate, Stratified, or Both**	**E-cigarette risk (95%CI)**	**Cigarette risk (95%CI)**	**Dual Use risk**	**Sole e-cigarette or e-cigarette risk**	**Where to find reported results**	**Notes**
Mahoney (2022)	incident CVD (age 40+; no CVD history)	PATH	7820	A	2013-2019	C	L	NC	3	S	NA (due to very small sample size)		***DU vs. never users= 1.85 (0.78 - 4.37)***	***sole combustible tob vs. never users=1.44 (0.87 - 2.39)*** tob quitters vs. never users= 1.18 (0.33 - 4.26)	Table 2	ORs for exclusive combustible tobacco included cigarettes, cigars, hookah.
Osei (2019a)	Composite of coronary heart disease, myocardial infarction, or stroke	BRFSS	449092	A	2016-2017	E	C	N	1	S	Among never smokers: ***current vs. never = 1.04 (0.63 - 1.72)*** Daily vs. never= 1.35 (0.74 - 2.46***)*** occasional use vs. never = 0.95 (0.50 - 1.82) Among current smokers: ***current vs. never= 1.36 (1.18 - 1.56)*** Daily vs. never=1.59 (1.20 - 2.08) Occasional use vs. never = 1.30 (1.12 - 1.52)		***DU vs. current smoker with never use of ENDS=1.36 (1.18 - 1.56)*** ***DU vs. never use of both = 2.44 (2.14 - 2.78)*** DU with daily use of ENDS vs. current smokers with never use of ENDS= 1.59 (1.20 - 2.08)		Table 2 and text	
Qeadan (2023)	aggregate measure cardiovascular disease	PATH	18,893	0	2014-2018	0	1	0	2	1	***Adverse cardiovascular conditions: 1.02 (0.90-1.15)***				Table 3	Adverse cardiovascular condition: high blood pressure, high cholesterol, stroke, heart attack (i.e., myocardial infarction) and/or need for bypass surgery, congestive heart failure, or other heart condition "Dual use" in the paper is dual use of e-cigs and illicit drug (not nicotine cigarette), so was not extracted
Stroke																

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Study	Outcome	Sample	Sample size	Adult or Youth*	Years data collected	Diagnosis: Current † or Ever	Cross-sectional or Longitudinal	Reference use: Never or Non-Current	No. studies of dataset	Model: Multivariate, Stratified, or Both	E-cigarette risk (95%CI)	Cigarette risk (95%CI)	Dual Use risk	Sole e-cigarette or e-cigarette risk	Where to find reported results	Notes
Bricknell (2021)	Stroke	BRFSS	465,594	0	2016	1	0	1	1	1	***Every day vs never=1.62 (1.18-2.31)*** Some days vs never = 1.28 (1.02-1.61) Former vs never = 1.09 (0.98-1.23)	***Every day vs never = 2.1 (1.9-2.4)*** Some day vs never = 1.8 (1.6-2.1) Former vs never = 1.3 (1.2-1.4)			Tables 2-3	
Falk (2022)	stroke	NHIS	84,553	0	2014, 2016, 2017, 2018	1	0	1	1	2	***Stroke: 1.06 (0.59-1.91)***	***Stroke: 2.11 (1.82-2.46)***	***Stroke: 2.40 (2.01-2.86)***		Table 1	.
Goldberg Scott (2023)	stroke	Kaiser Permanente Research Bank	96,148	0	2015-2019	0	1	1	1	1	Longitudinal [cross-sectional in brackets]: ***Stroke: 1.65 (0.94-2.89)*** [1.16; 0.77-1.66] Additional cross-sectional: Non-stroke cerebrovascular disease: 1.55 (1.21-1.99)				Table 3 (longitudinal) and Table 2 (cross-sectional)	Hazard ratios (HR) for longitudinal results OR for cross-sectional results Longitudinal results used in meta-analysis. Cross sectional results (based on larger sample sizes) also reported (Table 2). People with history of heart attack, stroke or cancer prior to survey excluded.
Hirschtick (2022)	Incident first stroke (age 40+)	PATH	11031	0	2013-2019	0	1	0	1	2	***exclusive ecig vs. non-current use: 1.74 (0.55-5.49)*** ***exclusive ENDS vs. exclusive cig = 0.77 (0.25-2.38)***	***exclusive cig vs. non-current use: 2.26 (1.51-3.39)***	***dual vs. non-current use: 1.12 (0.33-3.79)*** ***dual vs. exclusive cig = 0.50 (0.15-1.60)***		Table 4 and text	Excluded people who had MI or stroke at baseline computed time varying HR (not OR)
Parekh (2020a)	Stroke (age 18-44)	BRFSS	161529	0	2016-2017	1	0	1	2	2	Stratified ***current sole ecig use vs never use both: 0.69 (0.34–1.42)*** ***Among former smokers: 2.54 (1.16-5.56)***	Stratified ***Current sole cig vs never use both: 1.59 (1.14-2.22)***	Stratified ***Dual use vs never use both: 2.91 (1.62-5.25)*** ***Dual use vs smokers: 1.83 (1.06-3.17)***	Stratified ***Sole ecig users vs never use both: 0.69 (0.34-1.42)*** ***Sole e-cig users vs sole cig users: 0.43 (0.20-0.93)***	Text and Figure 1	Results are based on full multivariant model (model 3)

Table S2. Characteristics and results from included studies (values used in meta-analysis appear in ***bold italics***; all are OR unless otherwise noted)																
Study	**Outcome**	**Sample**	**Sample size**	**Adult or Youth***	**Years data collected**	**Diagnosis: Current † or Ever**	**Cross-sectional or Longitudinal**	**Reference use: Never or Non-Current**	**No. studies of dataset**	**Model: Multivariate, Stratified, or Both**	**E-cigarette risk (95%CI)**	**Cigarette risk (95%CI)**	**Dual Use risk**	**Sole e-cigarette or e-cigarette risk**	**Where to find reported results**	**Notes**
Patel (2022)	Stroke	NHANES	79825	0	2015-2018	1	0	0	1	2	***Current e-cig vs cig: 1.15 (1.15-1.16)*** Current ecig vs non-current ecig: 1.60 (1.60-1.61)		***Dual vs cig: 1.14 (1.14-1.15)***		Table 3	
Metabolic dysfunction																
Atuegwu (2019a)	Prediabetes	BRFSS	71,541	A	2017	E	C	N	1	S	Among never smokers: ***Current vs never: 1.96(1.13 - 3.40)***				Table 2	Participants who were current or former smokers of conventional cigarettes or who had a history of diabetes, gestational prediabetes or gestational diabetes excluded. Including history of prediabetes as independent variable may over-specify model and bias results toward the null.

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Study	Outcome	Sample	Sample size	Adult or Youth*	Years data collected	Diagnosis: Current † or Ever	Cross-sectional or Longitudinal	Reference use: Never or Non-Current	No. studies of dataset	Model: Multivariate, Stratified, or Both	E-cigarette risk (95%CI)	Cigarette risk (95%CI)	Dual Use risk	Sole e-cigarette or e-cigarette risk	Where to find reported results	Notes
Cai (2023)	metabolic syndrome	NHANES	5121	0	2015-2018	0	0	1	2	3	***Multivariate: 1.30 (1.13-1.50)*** ***Stratified: 0.75 (0.38-.49)***		Stratified: ***Dual vs never users: 1.35 (1.15-1.58)*** [Table 6] ***Dual vs cigs: 1.21 (1.00-1.46)*** [Table 6] Current ecig among current cig: 1.53 (1.22-1.91) [Table 4]	Sole e-cig (Stratified): 0.75 (0.38-1.49)	(Tables 3 [multivariate], 4 [stratified] and 6 [dual use])	Report Prevalence Ratios (PR) using Poisson regression. MetS was defined when any of following conditions were present: (1) abdominal obesity, (2) elevated triglycerides, (3) elevated fasting glucose ,(4) reduced high-density lipoprotein (HDL) cholesterol, (5) elevated blood pressure. Also present results for former e-cig users and former smokers.
Cook (2023a)	Incident hypertension	PATH	17,539	A	2013-2019	C	L	N	1	S	***current e-cig vs never: 1.00 (0.68 - 1.47)***	***current cig vs. never:. 121 (1.06 - 1.38)***	***current dual vs never use of either product: 1.15 (0 .87 - 1.52)***		Table 4	HR, with exposures lagged one wave respondents had no self-reported heart condition (congestive heart failure, heart attack, or stroke) at baseline Due to skip pattern in Waves 4 and 5, classified respondents who did not report seeing a doctor during the past year as not having hypertension
Falk (2022)	hypertension, diabetes mellitus	NHIS	84,553	0	2014, 2016, 2017, 2018	1	0	1	1	2	***Hypertension: 1.24 (1.05-1.48)*** Diabetes: 1.11 (0.97-1.26)	***Hypertension: 1.38 (1.28-1.50)*** Diabetes: 1.14 (1.02-1.27)	***Hypertension: 1.66 (1.52-1.81)*** Diabetes: 1.22 (1.11-1.34)		Table 1	Hypertension selected at random from two outcomes.

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Study	Outcome	Sample	Sample size	Adult or Youth*	Years data collected	Diagnosis: Current † or Ever	Cross-sectional or Longitudinal	Reference use: Never or Non-Current	No. studies of dataset	Model: Multivariate, Stratified, or Both	E-cigarette risk (95%CI)	Cigarette risk (95%CI)	Dual Use risk	Sole e-cigarette or e-cigarette risk	Where to find reported results	Notes
Kim (2020a)	Metabolic syndrome (Korea)	KNHANES	7505	A	2013-2017	C	C	N	1	S			***DU vs. never smokers without past-month use of ENDS= 2.79 (1.72 - 4.53)*** ***DU vs. cigarette-only smokers = 1.57 (1.03 - 2.40)***	***sole cig vs. never smokers without past-month use of ENDS = 1.47 (1.20 - 1.82)***	Table 4	Other outcomes included waist circumference (WC); blood pressure; high-density lipoprotein; Elevated fasting glucose; Elevated triglycerides.
Kim (2020b)	Metabolic syndrome	KNHANES	14,738	A	2013-2015	C	C	N	1	M	***current e-cig vs never: 1.40 (1.08 - 1.81)***		***Dual current vs never: 1.13 (0.82 - 1.55)***		Tables 4 (Model 4; multivariate) and Table 5 (among current active smokers; to get direct estimate of dual use)	Also report ever user results and details for MetS components: abdominal obesity, high triglyceride, high fasting glucose, low HDL, high blood pressure
Kim (2022)	Hypertension	Korea Community Health Survey	275,762	A	2019	C	C	N	1	S	***Current e-cig user vs never user:*** ***All: 1.23 (1.03 - 1.48)*** Male: 1.22 (1.02 - 1.48) Female: 1.41 (0.74 - 2.70)	***Current smoker vs never smoker:*** ***All: 1.20 (1.15 - 1.25)*** Male: 1.16 (1.11 - 1.22) Female: 1.35 (1.24 - 1.48)	***Current dual user vs never user:*** ***All: 1.25 (1.13 - 1.40)*** Male: 1.24 (1.11 - 1.39) Female: 1.44 (0.96 - 2.16)	***Sole ecig vs nothing:*** ***All 1.23 (1.03 - 1.48)*** Male: 1.22 (1.02 - 1.48) Female: 1,41 (0.74 - 2.70)	Tables 2 and 3	Separate male and femal estimates combined with fixed effects meta-analysis/ Direct measurement of blood pressure. Also report results stratifying smoking by pack-years and age of initiation.

Table S2. Characteristics and results from included studies (values used in meta-analysis appear in ***bold italics***; all are OR unless otherwise noted)															
Study	**Outcome**	**Sample**	**Sample size**	**Adult or Youth***	**Years data collected**	**Diagnosis: Current † or Ever**	**Cross-sectional or Longitudinal**	**Reference use: Never or Non-Current**	**No. studies of dataset**	**Model: Multivariate, Stratified, or Both**	**E-cigarette risk (95%CI)**	**Cigarette risk (95%CI)**	**Dual Use risk**	**Sole e-cigarette or e-cigarette risk**	**Where to find reported results**	**Notes**
Miller (2021)	Hypertension (age 18-55)	PATH	19147	A	2015-2016	C	C	N	1	B	***Current ecig vs not current: 1.31 (1.05-1.63)***	***Current cig vs not current: 1.27 (1.10-1.47)*** **Versus never smokers** Former smoker 1.28 (1.05 - 1.57) Exclusive smoker 1.36 (1.15 - 1.62) **Versus former smoker** Exclusive smoker: 1.06 (0.87 - 1.30)	***Dual use vs never smoker 1.77 (1.32 - 2.39)*** ***DU vs. sole cig= 1.30 (0.99 - 1.71)***	**Versus never smokers** ***Exclusive vaper (never smoker) : 1.32 (0.50-3.53)*** Exclusive vaper (former smoker): 1.42 (0.98 - 2.06) **Versus former smokers** Exclusive vaper (never smoker): 1.03 (0.38 - 2.83) Exclusive vaper (former smoker): 1.11 (0.74 - 1.66) **Versus exclusive smokers** ***Exclusive vaper (never smoker): 0.96 (0.37 - 2.57)*** Exclusive vaper (former smoker): 1.30 (0.99 - 1.71)	Table 2 and Figure 2	

Table S2. Characteristics and results from included studies (values used in meta-analysis appear in *bold italics*; all are OR unless otherwise noted)

Study	Outcome	Sample	Sample size	Adult or Youth*	Years data collected	Diagnosis: Current † or Ever	Cross-sectional or Longitudinal	Reference use: Never or Non-Current	No. studies of dataset	Model: Multivariate, Stratified, or Both	E-cigarette risk (95%CI)	Cigarette risk (95%CI)	Dual Use risk	Sole e-cigarette or e-cigarette risk	Where to find reported results	Notes
Okafor (2022)	Hypertension	NHANES	7940	A	2015-2018	C	C	N	2	S	***High blood pressure: 1.73 (0.91-3.30)*** HDL-C: 1.33 (0.79 - 2.26) LDL: 0.52 (0.22 - 1.22) Triglycerides: 1.03 (0.40 - 2.64) Fasting blood glucose: 1.41 (0.56 - 3.51)	***High blood pressure: 0.93 (0.73 - 1.20)*** HDL-C: 1.89 (1.56 - 2.29) LDL: 1.16 (0.84 - 1.58) Triglycerides: 1.58 (1.04 - 2.38) Fasting blood glucose: 0.88 (0.63 - 1.22)	***High blood pressure: 0.98 (0.51-1.89)*** HDL-C: 1.73 (1.06 - 2.82) LDL: 1.16 (0.84 - 1.58) Triglycerides: 1.54 (0.67 - 3.55) Fasting blood glucose: 0.99 (0.61 - 1.59)	E-cig vs smoking: ***High blood pressure: 1.85 (0.88-3.89)*** HDL-C: 0.70 (0.43 - 1.15) LDL: 0.45 (0.52 - 1.98) Triglycerides: 0.65 (0.23 - 1.81) Fasting blood glucose: 1.59 (0.62 - 4.09) Dual use vs smoking: ***High blood pressure: 1.05 (0.52-2.11)*** HDL-C: 0.91 (0.54 - 1.53) LDL: 1.02 (0.52 - 1.98) ¶Triglycerides: 0.97 (0.39 - 2.43) Fasting blood glucose: 1.11 (0.63 - 1.98)	Table 2 (adjusted model, including former smokers)	Excluded people with history of cardiovascular disease, stroke or diabetes
Shi (2022)	Hypertension	PATH	16,434	A	2013-2018	C	L	NC	1	S	***Both: 1.51 (0.93 - 2.46)*** Male: 1.17 (0.56 - 2.46) Female: 1.84 (0.96 - 3.52)	***Both: 1.39 (1.08 - 1.77)*** Male: 1.10 (0.77 - 1.58) Female: 1.69 (1.21 - 2.36)	***Both: 1.45 (0.97 - 2.16)*** Male: 1.18 (0.65 - 2.14) Female: 1.71 (1.00 - 2.93)		Table 2, consistent users	Hazard ratio Incident hypertension Cox model lagged one year Male and female results pooled with fixed effects meta-analysis

Table S2. Characteristics and results from included studies (values used in meta-analysis appear in *bold italics*; all are OR unless otherwise noted)

Study	Outcome	Sample	Sample size	Adult or Youth*	Years data collected	Diagnosis: Current † or Ever	Cross-sectional or Longitudinal	Reference use: Never or Non-Current	No. studies of dataset	Model: Multivariate, Stratified, or Both	E-cigarette risk (95%CI)	Cigarette risk (95%CI)	Dual Use risk	Sole e-cigarette or e-cigarette risk	Where to find reported results	Notes
Sompa (2022)	Waist circumference (age around 24; Sweden)	Swedish BAMPSE	2265	A	2018-2020	C	C	NC	1	M	Current ecig use vs non-current use controlling for smoking: ***Waist circumference (≥80 cm for women and ≥93 cm for men): 1.9 (1.0 - 3.4)*** BMI (≥25 kg/m^2): 1.8 (1.0 - 3.2) Body fat (≥33% for women and ≥20% for men): 2.6 (1.4 - 4.6)				Table 6	Also considered snus and other tobacco products. Those results and dual use with those products not included.
Zhang (2022)	Prediabetes	BRFSS	600,046	A	2016-2018	E	C	N	1	B	***Multivariate, including cig use as a covariate: Current e-cig: 1.22 (1.10 - 1.37)*** ***Stratified: current ecig among never smokers: 1.54 (1.17 - 2.04)***		***Stratified: current dual: 1.14 (0.97 - 1.34)***		Tables 3 and 4	
Asthma																
Alnajem (2020)	Asthma (age 16-19; Kuwait)	school-based cross-sectional study in Kuwait	1565	Y	2019	C	C	N	1	S	***Current ecig vs never ecig & never smoker: 1.85 (1.03 – 3.41)*** ***Current ecig in former smokers: 1.71 (1.05– 2.78)***	***Current smoker vs never ecig & never smoker: 1.73 (1.01 – 3.21)***	***Current dual use vs never ecig never smoker: 1.92 (1.33 – 2.76)***		Table 2	Prevalence ratio The paper also contains on current wheeze and current uncontrolled asthma symptoms. There are also other combinations of current and former ecig and cig use Also shows significant asthma risk associated with secondhand aerosol (1.56 (1.13–2.16))

Table S2. Characteristics and results from included studies (values used in meta-analysis appear in *bold italics*; all are OR unless otherwise noted)

Study	Outcome	Sample	Sample size	Adult or Youth*	Years data collected	Diagnosis: Current † or Ever	Cross-sectional or Longitudinal	Reference use: Never or Non-Current	No. studies of dataset	Model: Multivariate, Stratified, or Both	E-cigarette risk (95%CI)	Cigarette risk (95%CI)	Dual Use risk	Sole e-cigarette or e-cigarette risk	Where to find reported results	Notes
Bayly (2019)	Asthma (Age 11-17)	Florida Youth Tobacco survey	11830	Y	2016	C	C	NC	1	M	risk for asthma attack: ***current vs. never= 0.90 (0.71 - 1.15)*** former vs. never=1.01 (0.81 - 1.25) secondhand ENDS aerosol exposure (y/n)= 1.27 (1.11 - 1.47)	Risk for asthma attack: ***current vs. never=1.92 (1.28-2.68)*** former vs. never=1.23 (0.99 - 1.52) secondhand exposure=1.19 (1.05 - 1.35)			Table 2	
Bhatta (2020)	Incident asthma (age 18-65)	PATH	20531	A	2013-2016	C	L	NC	3	M	***Wave 3: current vs. never = 1.30 (0.87 - 1.95)*** Wave 2: current vs. never = 1.56 (1.10 - 2.22) former vs. never = 1.23 (0.90 - 1.69)	***Wave 3: current vs. never = 1.89 (1.26 - 2.83)*** Wave 2: current vs. never =1.57 (1.02 - 2.42) former vs. never =0.87(0.53 - 1.42)			Appendix Table 6	
Bircan (2021)	Asthma	BRFSS	8736	A	2016-2018	E	C	N	2	S	Current vs never ecigs (among never smokers) ***asthma (OR=1.26, 95% CI: 1.25 - 1.27)*** ACOS (OR=2.27; 95% CI: 2.23 - 2.31)				Figure 3	All are never smokers
Boyd (2021)	Wheezing	PATH	14,798	A	2016-2018	C	C	NC	6	M	***Wheezing or whistling in chest: 1.09 (0.830 - 1.44)*** Sleep disturbed by wheezing: 1.33 (0.752 - 2.36) Speech limited because of wheezing: 1.24 (0.686 - 2.25) Wheezy during or after exercise: 1.07 (0.802 - 1.44) Dry cough at night: 1.09 (0.885 - 1.36)	***Wheezing or whistling in chest: 1.15 (0.82 - 1.62)*** Sleep disturbed by wheezing: 0.739 (0.405 - 1.34) Speech limited because of wheezing: 0.820 (0.433 - 1.55) Wheezy during or after exercise: 1.09 (0.773 - 1.54) Dry cough at night: 1.27 (0.947 - 1.71)			Table 2, fully adjusted models	Including history of asthma as independent variable may over-corrected the model and so underestimated risks of ecigs and cigs

Table S2. Characteristics and results from included studies (values used in meta-analysis appear in *bold italics*; all are OR unless otherwise noted)

Study	Outcome	Sample	Sample size	Adult or Youth*	Years data collected	Diagnosis: Current † or Ever	Cross-sectional or Longitudinal	Reference use: Never or Non-Current	No. studies of dataset	Model: Multivariate, Stratified, or Both	E-cigarette risk (95%CI)	Cigarette risk (95%CI)	Dual Use risk	Sole e-cigarette or e-cigarette risk	Where to find reported results	Notes
Braymiller (2020)	wheezing	Southern California Happiness and Health Study	2396	A	2018-2019	C	C	N	1	M	Used ecigs >= 3 of past 30 days vs never: ***Wheeze: 0.85 (0.54 - 1.35)*** Shortness of breath: 0.96 (0.64 - 1.42) Bronchitis symptoms: 0.96 (0.63 - 1.46)				Table 3, full adjustment	Results controlled for cigarette smoking but smoking results not presented. Also reports 1-2 d in past 30 days; past 6 mo but not past 30 days, lifetime but not in past 6 mo.
Brunette (2023)	Incident asthma in people without COPD	PATH	10,267	A	2014-2017	C	L	N	2	M	***Current e-cig vs. non-current=1.12 (0.50 - 2.51)***	***Current cigarette vs. non-current=0.99 (0.53 - 1.86)***			Table 3	Adjusted risk ratio Use longitudinal results rather than cross-sectional results at baseline. Also present regression analysis for Asthma Control Test (ACT). Did complete case analysis, with multiple imputation as a sensitivity analysis. MI results were similar to complete case analysis."

Table S2. Characteristics and results from included studies (values used in meta-analysis appear in *bold italics*; all are OR unless otherwise noted)

Study	Outcome	Sample	Sample size	Adult or Youth*	Years data collected	Diagnosis: Current † or Ever	Cross-sectional or Longitudinal	Reference use: Never or Non-Current	No. studies of dataset	Model: Multivariate, Stratified, or Both	E-cigarette risk (95%CI)	Cigarette risk (95%CI)	Dual Use risk	Sole e-cigarette or e-cigarette risk	Where to find reported results	Notes
Chaffee (2021a)	Adverse respiratory symptoms: bronchitis, asthma , and shortness of breath (age 13-21)	Pooled data from 4 ongoing studies	10483	Y	2018-2020	C	C	NC	1	M	**Risk for Asthma** ***6-30 days vs. never= 1.36 (0.95-1.95)*** 1-5 days vs. never = 1.27 (0.91 - 1.77) ever vs. never = 0.99 (0.85 - 1.15) **Risk for Bronchitis** 6-30 days vs. never= 1.56 (1.37 - 1.77) 1-5 days vs. never = 1.11 (0.94 - 1.31) ever vs. never = 1.07 (0.93 – 1.22) **Risk for Shortness of Breath:** 6-30 days vs. never = 1.68 (1.35 - 2.08) 1-5 days vs. never = 1.27 (0,95 - 1.17) ever vs. never = 1.08 (0.93 - 1.26)				Figure 1	
Cho (2016)	Asthma (10th-12th graders; Korea)	KYRBS	35904	Y	2014	C	C	N	1	B	***current vs. never = 2.77 (1.31 - 5.85)*** former vs. never = 0.96 (0.42 - 2.19)	Multivariate: ***current vs. never = 2.77 (1.31 - 5.85)*** former vs. never = 0.96 (0.42 - 2.19) Stratified: ***Current ecig vs never ecig among never smokers 2.74 (1.30 - 5.78)***	***DU vs. sole smokers = 1.30 (0.86 - 1.96)***		Table 5-6	
Choi (2016)	Asthma (9th-12th graders)	Pooled data from 4 ongoing studies	36085	Y	2012	C	C	NC	1	M	**Risk for asthma attack:** ***current (y/n)= 1.78 (1.20 - 2.64)***				Figure 1	

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Study	Outcome	Sample	Sample size	Adult or Youth*	Years data collected	Diagnosis: Current † or Ever	Cross-sectional or Longitudinal	Reference use: Never or Non-Current	No. studies of dataset	Model: Multivariate, Stratified, or Both	E-cigarette risk (95%CI)	Cigarette risk (95%CI)	Dual Use risk	Sole e-cigarette or e-cigarette risk	Where to find reported results	Notes
Chung (2020)	Asthma (age 13-18, Korea)	KYRBS	60040	Y	2018	C	C	NC	1	S	**Asthma** na Allergic Rhinitis Current ecig never cig vs nothing: 1.0 (0.4 - 2.2)	**Asthma** ***Current cig vs never cig never ecig: 1.6 (1.1 - 2.2)*** Allergic rhinitis Current cig vs never cig never ecig: 1.3 (1.1 - 1.6)	**Asthma** ***Current dual vs never ecig never cig: 1.2 (0.80 - 2.0)*** Allergic rhinitis Current dual use vs never cig never ecig: 1.6 (1.2 - 2.2)		Table 4 (asthma) and Table 3 (allergic rhinitis) Model 2 results Data for never HTP users	Report all combinations of current and former use. Also report HTP results
Cordova (2022)	Asthma	PATH	26072	A	2013-2018	C	L	N	6	S	***Current ENDS vs never: Asthma: 0.8 (0.6 - 1.0)*** Bronchitis: 0.8 (0.5 - 1.6)	***Current cig vs never: Asthma: 0.8 (0.7 - 0.9)*** Bronchitis: (1.7 (1.3 - 2.2)	***Current ENDS plus cig vs never: Asthma: 0.8 (0.6 - 1.0)*** Bronchitis: 2.3 (1.6 - 3.5)	***Current ENDS only vs never use among never smokers: Asthma: 0.8 (0.6 - 1.0)*** Bronchitis: 0.8 (0.5 - 1.6)	Table 2	Used extremely conservative Bonferroni correction when interpreting results (Required p<.0017=.05/30 to call something significant; 30 = 6 models x 5 parameters). Polyproduct users considered a separate group.
Han (2020)	Asthma (9th-12th graders)	YRBSS	21532	Y	2015, 2017	C	C	N	2	M	**In model including ecigs, cigs, marijuana *≥10 days/mo cigs vs none:1.31 (1.11 - 1.54)*** <10 days/mo vs none: 1.13 (0.97 - 1.31) **In model just including ecigs** ≥10 days/mo cigs vs none:1.25 (1.09 - 1.45) <10 days/mo vs none: 1..25 (1.09 - 1.45)	**In model including ecigs, cigs, marijuana *≥10 days/mo cigs vs none:1.27 (1.00 - 1.61)*** <10 days/mo vs none: 1.03 (0.85 - 1.25) **In model just including cigs** ≥10 days/mo cigs vs none:1.65 (1.31 - 2.08) <10 days/mo vs none: 1..24 (1.05 - 1.47)			Table 1 (Model 4)	Multivariate model (Model 4) include ecigs and cigs in the same model (as well as marijuana) so e-cig OR is also OR for dual use vs cigs.

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Study	Outcome	Sample	Sample size	Adult or Youth*	Years data collected	Diagnosis: Current † or Ever	Cross-sectional or Longitudinal	Reference use: Never or Non-Current	No. studies of dataset	Model: Multivariate, Stratified, or Both	E-cigarette risk (95%CI)	Cigarette risk (95%CI)	Dual Use risk	Sole e-cigarette or e-cigarette risk	Where to find reported results	Notes
Kim (2017)	Asthma (age 12-18)	KYBWS	216056	Y	2011-2013	C	C	NC	1	M	***current (yes vs. no)= 1.13 (1.01 - 1.26)***	***≥20 days/month = 1.57 (1.38 – 1.77)*** 6–19 day/month = 1.32 (1.08 – 1.61) 1–5 days/month = 1.39 (1.20 – 1.62)			Table 3 (Model 3)	
Lee (2023)	Asthma	NHIS	218911	A	2016-2019	C	C	NC	1	B	***Current e-cig vs. non-current:*** ***Asthma attack: 1.22 (1.04 - 1.43)*** ER visit due to asthma: 1.14 (0.85 - 1.54)	***Current cig smokers vs. never smoker:*** ***Asthma attack: 1.15 (1.05 - 1.26)*** ER visit due to asthma: 1.13 (0.96 - 1.34)	***Ecig risk among current smokers:*** ***Asthma attack: 1.11 (0.89 - 1.39)*** ER visit for asthma: 1.24 (0.85 - 1.80)	***Ecig risk among never smokers:*** ***Asthma attack: 1.96 (1.34 - 2.87)*** ER visit for asthma: 1.73 (0.83 - 3.63)	Tables 2, 4 and 5	Also report risks for former smokers. Including history of COPD might bias results toward null.
Li (2020)	Wheezing	PATH	28171	A	2014-2015	C	C	NC	1	S	***current vapers vs nonusers: 1.68 (1.32 – 2.14)*** ***Current vapers vs. current smokers: 0.61 (0.48 – 0.77)*** Current vapers who were ex-Smokers vs. Ex-smokers: 1.54 (1.20 - 1.98)	***current smokers vs nonusers: 2.75 (2.47 - 3.06)*** current smokers vs never smokers: 3.33 (2.87 - 3.85) Ex-smokers vs. Never-Smokers: 1.43 (1.26 - 1.63)	***dual users vs nonusers: 2.83 (2.37 - 3.38)*** ***dual users vs current smokers: 1.03 (0.88 – 1.20)***	***Current vapers who never smoked vs. Never-Smokers: 1.49 (0.84 - 2.67)***	Table 2 and Table 3	The nonusers group was defined as adult respondents who has both “no” values in the current established cigarette smoker variable and the current established e-cigarette user variable.
Mattingly (2023)	Incident asthma	PATH	9141	Y	2013-2019	C	L	N	3	S	***Current vs never: 1.50 (0.92 - 2.44)***	***Current vs never: 1.71 (1.11 - 2.64)***	***Current vs never: 1.23 (0.62 - 2.43)***		Table 3	HR lagged one wave Excluded youth with asthma at baseline Due to sample size limitations, collapsed dual cigarette and ENDS and dual ENDS and OC categories to represent dual combustibles and ENDS use Dividing dual use into so many categories may have diluted e-cigarette effect

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Study	Outcome	Sample	Sample size	Adult or Youth*	Years data collected	Diagnosis: Current † or Ever	Cross-sectional or Longitudinal	Reference use: Never or Non-Current	No. studies of dataset	Model: Multivariate, Stratified, or Both	E-cigarette risk (95%CI)	Cigarette risk (95%CI)	Dual Use risk	Sole e-cigarette or e-cigarette risk	Where to find reported results	Notes
McConnell (2017)	Wheezing (high school students)	Southern California Children's Health Study	2086	Y	2014	C	C	N	1	B	***Risk for wheeze: current vs. never= 1.24 (0.78 - 1.98***) Risk for bronchitis: current vs. never= 1.41 (0.92 - 2.17) former vs. never = 1.71 (1.20 - 2.43) 1-2 days vs. never = 1.37 (0.79 - 2.37) >= 3 days vs. never= 1.64 (0.88 - 3.05)			wheeze: ***among never smokers:*** ***current vs. never ENDS=1.52 (0.89 - 2.61)*** Bronchitis: among never smokers: current vs. never ENDS=1.52 (0.89 - 2.61) former vs. never ENDS= 1.70 (1.11 - 2.59)	Wheeze: Figure 4 and text Bronchitis: Figure 1-3 Table E1	
Osei (2019b)	Asthma	BRFSS	402822	A	2016, 2017	C	C	N	5	M	***current vs. never = 1.39 (1.15 - 1.68) among never-smokers***				text	
Parekh (2020b)	Asthma (women age 18–44)	BRFSS	131965	A	2016-2017	C	C	N	5	S	***Current e-cigarette users with history of combustible cigarette smoking vs never users of anything: 1.33 (0.95 – 1.86)*** ***Current e-cigarette users without history of combustible cigarette smoking vs never users of anything = 1.74 (1.29 – 2.35)***	***Current combustible cigarette smokers without history of e-cigarette use vs never users of anything: 1.49 (1.25 – 1.77)***	***Current dual users (e-cigarette + combustible cigarette) vs never users of anything: 2.11 (1.72 – 2.59)***	***Current e-cigarette users without history of combustible cigarette smoking vs never users of anything: 1.74 (1.29 – 2.35)*** Former e-cigarette users without history of combustible cigarette smoking vs never users of anything: 1.14 (0.98 – 1.32)	Table 4	
Patel (2023)	incident asthma	PATH	9141	1.0	2013-2019	0	1	0	3	2	1.25 (0.77-2.04)	1.68 (1.21-2.32)	1.54 (0.92-2.57)		Table 4	Report Hazard Ratio (HR)

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Study	Outcome	Sample	Sample size	Adult or Youth*	Years data collected	Diagnosis: Current † or Ever	Cross-sectional or Longitudinal	Reference use: Never or Non-Current	No. studies of dataset	Model: Multivariate, Stratified, or Both	E-cigarette risk (95%CI)	Cigarette risk (95%CI)	Dual Use risk	Sole e-cigarette or e-cigarette risk	Where to find reported results	Notes
Perez (2019a)	Asthma	BRFSS	373,860	A	2016-2017	E	C	N	5	S	Among never smokers: ***Current ecig user: 1.36 (1.11 - 1.68)*** Daily e-cig vs never: 1.81 (1.23 - 2.66) Someday e-cig vs never: 1.26 (0.99 - 1.60) Former ecig vs never: 1.11 (1.00 - 1.23)				Text and Table 2	Never smokers
Reddy (2021)	Wheezing or cough (age 12+)	PATH	20882	Y	2015-2018	C	L	NC	6	S	Daily vs. someday= 0.88 (0.52 – 1.50) ***sole ENDS vs. noncurrent use= 1.17 (0.79 - 1.74)***	***sole smokers vs. noncurrent use=1.78 (1.56 - 2.03)*** Daily vs. someday=1.81 (1.46 – 2.26)	***DU vs. none current use= 2..22 (1.79 - 2.75)*** ***DU vs. sole cig= 1.24 (1.00 - 1.55).*** DU vs. sole ENDS= 1.90 (1.23 - 2.93)	***sole ENDS vs. noncurrent use= 1.17 (0.79 - 1.74)***	Table 2	
Sargent (2022)	Asthma (adults without COPD)	PATH	19295	A	2014-2016	C	C	N	3	S	**Cross-sectional association (Tab 2):** ***Sole ENDS vs. never=1.05 (0.67 - 1.63);*** ORs were attenuated by adjustment for cigarette pack-years from unadjusted OR=1.53 (0.98 - 2.40) to adjusted OR=1.05 (0.67 - 1.63); There was also an increase in respiratory symptoms with higher intensity of e-cigarette use, but the trend did not reach statistical significance (p = 0.12) Longitudinal association (Tab 3): Sole ENDS vs. never= 1.58 (0.84 - 2.96)	**Cross-sectional association (Tab 2):** ***Sole cig vs. never=2.34 (1.92 - 2.85)*** There was a significant linear increase in % with functionally-important respiratory symptoms (at a cutoff of ≥3) with higher intensity of smoking. Each additional 5 pack-years: aOR= 1.13 (1.09 - 1.16) Longitudinal association (Tab 3): Sole cig vs. never= 2.80 (2.08 - 3.76)	**Cross-sectional association (Tab 2):** ***DU vs. never= 2.13 (1.64, 2.77)*** post hoc testing indicated that risk ratios for dual use of cigarettes+e-cigarettes were never different compared to exclusive cigarette use Longitudinal association (Tab 3): Dual use vs. never= 2.64 (1.88 - 3.70)	***Sole cig vs. never=2.34 (1.92 - 2.85)***	Table 2	Relative risk There were many types of analyses for other outcomes in Tab 3-4. This study contrasts with increased risk of dual use in the analyses of PATH data reported by Reddy et al.

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Study	Outcome	Sample	Sample size	Adult or Youth*	Years data collected	Diagnosis: Current † or Ever	Cross-sectional or Longitudinal	Reference use: Never or Non-Current	No. studies of dataset	Model: Multivariate, Stratified, or Both	E-cigarette risk (95%CI)	Cigarette risk (95%CI)	Dual Use risk	Sole e-cigarette or e-cigarette risk	Where to find reported results	Notes
Schneller (2020)	Wheezing	PATH	28,082	A	2015-2016	C	C	NC	3	S	***Wheezing: 1.44 (1.01 - 2.06)*** Speech limited by wheezing: 1.44 (0.73 - 2.83) Wheezy during exercise: 1.04 (0.73 - 1.48)	***Wheezing: 3.93 (3.45 - 4.49)*** Speech limited by wheezing: 2.17 (1.08 - 2.80) Wheezy during exercise: 1.04 2.80 (2.37 - 3.32)	***Wheezing: 1.52 (0.53-4.32)*** Speech limited by wheezing: 0.63 (0.04 - 10.31) Wheezy during exercise: 2.32 (0.53 - 10.04)		Figure 1 and Table 1	Fact that asthma is a covariate may over-correct model and bias results toward null. Also reported sleep disturbed by wheezing, but divided based on how many nights per week.
Schweitzer (2017)	Asthma (9th-12th graders)	Hawaii YRBSS	6089	Y	2015	C	C	NC	1	M	Risk for current asthma (vs. never have asthma) ***current (y/n) =1.48 (1.24 - 1.78)*** ever (y/n)= 1.22 (1.01 - 1.47)	Risk for current asthma (vs. never have asthma) ***current (y/n) =1.23 (0.92 - 1.64)*** ever (y/n)= 1.25 (1.05 - 1.54)			Table 3	
Sompa (2022)	Wheezing (age 22-25; Sweden)	Swedish BAMPSE	2270	A	2018-2020	C	C	NC	1	S	***Sole e-cig current use vs. non-current users of ecig-cig-snus= 1.2 (0.3 - 3.8)***	***Current sole smoking vs. non-current users of ecig-cig-snus= 1.6 (1.2 - 2.2)***	***Dual use ecigs+cigs vs. non-current users of ecig-cig-snus: 3.6 (1.4 - 9.4)***		Table 4	Also considered snus and other tobacco products. Those results and dual use with those products is not included.
Stevens (2022)	Functionally important respiratory symptoms	PATH	3899	Y	2016-2018	C	L	N	6	S	***Current e-cig use among never combustible tobacco users: 0.86 (0.32 - 2.32)***			***Sole e-cig use among never combustible tobacco users: 0.86 (0.32-2.32)***	Table 2	Require presence of two symptoms for "yes". Also report results among ever combustible tobacco product users.
Tackett (2020)	Wheezing (age 12-17; no asthma at baseline)	PATH	7049	Y	2015-2018	C	L	NC	6	M	Ecig use within past __ vs no ecig use in the past year or never use: ***Past 30 d 1.35 (0.63 - 2.88)*** Past 7 d 0.74 (0.28 - 1.97) Pat year 1.37 (0.91 - 2.05)	***Combustible tobacco use in past 30 days vs not: 1.21 (0.65 - 2.25***) combustible tob included cigarettes, traditional cigars, cigarillos, filtered cigars, pipes, hookahs, bidis, and kreteks			Table 2	Use of e-cigarettes was assessed at wave 3. Categories are mutually exclusive.

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Study	Outcome	Sample	Sample size	Adult or Youth*	Years data collected	Diagnosis: Current † or Ever	Cross-sectional or Longitudinal	Reference use: Never or Non-Current	No. studies of dataset	Model: Multivariate, Stratified, or Both	E-cigarette risk (95%CI)	Cigarette risk (95%CI)	Dual Use risk	Sole e-cigarette or e-cigarette risk	Where to find reported results	Notes
Tackett (2023)	wheeze, bronchitic symptoms, shortness of breath	Southern California Children's Health Study	2094	1	2014-2018	0	0	0	1	1	Concurrent wave e-cig use (lag 0): Wheeze: 1.41 (0.99-2.01) ***Bronchitic symptoms: 1.55 (1.18-2.05)*** Shortness of breath: 1.48 (1.01-2.18) Prior wave e-cig use (lag 1): Wheeze: 1.77 (1.14-2.74) Bronchitic symptoms: 1.23 (0.86-1.74) Shortness of breath: 1.41 (0.96-2.09)			E-cig use with no past 30 day cig or cannabis use (lag 0): Wheeze: 2.92 (0.85-10.10) ***Bronchitic symptoms: 1.86 (0.83-4.19)*** Shortness of breath: 1.53 (0.65-3.63)	Table 3 (Model 2, lag 0) and 4 (No past 30 day cig or cannabis use, lag 0)	Used lag 0 results because immediate irritating effects of e-cigs probably important; some may have stopped or started between waves, which would create misclassification errors. Selected bronchitis at random from among three possibilities. Authors conducted several sensitivity analyses
Tanski (2022)	Wheezing or cough (age 12-24)	PATH	21054	Y	2016-2017	C	C	N	2	M	***Current noncombustible use only vs never use of anything: 0.87 (0.67 - 1.13)*** ***Daily use vs. never use=1.25 (0.80 - 1.96)***	***Current combustible use only vs never use of anything: 1.52 (1.29 - 1.80)*** ***Daily use vs. never use=2.80 (2.25 - 3.47)***			Table 2 Model 1 Table 2 Model 2	Treated diagnosis with asthma as a covariate, which may have over-corrected results
To (2023)	Asthma	CCHS	2700	A	2015-2018	C	C	NC	1	M	***Current e-cig vs non-current: 1.21 (0.95 - 1.54)***	***Current cigarette vs. non-current: 0.96 (0.73 - 1.27)***			Table 3	Analyses included 2,700 matched CCHS participants, 505 (2.4% of 20,725 participants) EC users propensity score matched to 2,195 nonusers. Also looked at interactions with sex and several other variables

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Study	Outcome	Sample	Sample size	Adult or Youth*	Years data collected	Diagnosis: Current † or Ever	Cross-sectional or Longitudinal	Reference use: Never or Non-Current	No. studies of dataset	Model: Multivariate, Stratified, or Both	E-cigarette risk (95%CI)	Cigarette risk (95%CI)	Dual Use risk	Sole e-cigarette or e-cigarette risk	Where to find reported results	Notes
Tran (2020)	Asthma	BRFSS	186,036	A	2016-2018	C	C	NC	2	M	***Every day e-cig: 1.04 (0.93 - 1.15***) Someday e-cig: 1.18 (1.10 - 1.27)		***Every day e-cig/ Smokes every day 1.41 (1.23 - 1.61)*** Some days e-cig/ Smokes every day 2.01(1.86 - 2.16) Every day e-cig/ Smokes some days 3.64(3.17 - 4.17) Some days e-cig/ Smokes some days 2.73 (2.52 - 2.97) Every day e-cig/ Former smoker 7.20 (6.42 - 8.06) Some days e-cig// Former smoker 1.17 (1.07 - 1.27)		Table 3	
Varella (2022)	Asthma	BRFSS	18079	A	2017	C	C	N	5	M	***Current e-cig user vs never user: Daily: 1.41 (0.96 - 2.08)*** Some days: 1.49 (1.06 - 2.11)	***Current smoker vs never smoker: 1.99 (1.62 - 2.44)***			Table 2	Include asthma and COPD history likely biases result toward null. Also data on former ecig users and former smokers
Walker (2021)	Asthma	BRFSS	2387	A	2016-2017	C	C	NC	5	M	***Current ecig vs noncurrent: 1.06 (0.50 - 2.21)***	***Current smoker vs not: 1.13 (0.69 - 1.84)***			Table 2	Kentucky BRFSS
Wang (2016)	Cough or phlegm (adolescents in Hong Kong)	Chinese adolescents in Hong Kong	45128	Y	2012-2013	C	C	NC	1	B	**Multivariate** ***current (y/n) = 1.28 (1.06 - 1.56)*** **Stratified** among ever smoker: 1.39 (1.14 - 1.70) ***among former smoker: 1.40 (1.02 - 1.91)*** among experimental smoker: 1.09 (0.66 - 1.80)		**Stratified** ***DU vs. sole smoker = 1.15 (0.81-1.62)***	**Stratified** ***sole ENDS vs. never tob user = 2.06 (1.24 - 3.42)***	Table (no number) aOR for ENDS reported by smoking status	

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Study	Outcome	Sample	Sample size	Adult or Youth*	Years data collected	Diagnosis: Current † or Ever	Cross-sectional or Longitudinal	Reference use: Never or Non-Current	No. studies of dataset	Model: Multivariate, Stratified, or Both	E-cigarette risk (95%CI)	Cigarette risk (95%CI)	Dual Use risk	Sole e-cigarette or e-cigarette risk	Where to find reported results	Notes
Williams (2023)	asthma	California Student Tobacco Survey	113,922	1	2019-2020	0	0	0	1	2	***1.12 (0.97-1.28)***	***0.79 (0.43-1.45)***	***0.68 (0.35-1.32)***	***E-cig: 1.12 (0.97-1.28)*** Cig: 0.79 (0.43-1.45)	Table 3	Multinomial regression including all combinations of e-cigarette, cigarette and cannabis use. Only odds of recent asthma associated with e-cigarette only, cigarette only and dual (e-cigarette+cigarette) extracted
Wills (2019)	Asthma	Hawaii BRFSS	8087	A	2016	C	C	NC	2	S	***current (y/n)= 1.27 (0.96 – 1.67) among total sample*** current (y/n)=1.33 (1.00 - 1.77) among nonsmokers current (y/n)= 0.92 (0.73 – 1.15) among smokers	***current (y/n) = 1.27 (1.10 – 1.47) among overall sample*** ***current cig vs. current ENDS=1.00 (0.74 - 1.35)***	***DU vs. neither = 1.26 (1.04 – 1.53)*** ***DU vs. sole cig = 0.99 (0.80 – 1.22)*** DU vs. sole ENDs =1.00 (0.73 – 1.35)		Table 2	
Wills (2020)	Asthma (9th-12th graders)	YRBSS	14765	Y	2017	E	C	NC	2	B	***current ENDS (y/n, Tab 3)= 1.30 (1.10 - 1.53)*** ***sole ENDS vs. neither (Tab 4)=1.29 (1.07 - 1.55***) ever (y/n)=1.16 (1.01 - 1.33)	***current Cig (y/n)= 1.24 (1.03 - 1.51)*** ***Sole cig vs. neither=1.23 (0.92 - 1.64)*** ever (y/n)= 1.01 (0.81 - 1.25)	***Current vs. neither= 1.62 (1.32 - 1.99)*** ever vs. neither = 1.13 (0.97 - 1.31) ***DU vs. sole Cig=1.32 (0.95 - 1.84)***	***sole ENDS. vs. sole Cig=1.06 (0.76 - 1.46)***	Tables 3-4 and text	
Wills (2022)	Asthma	BRFSS	116,585	A	2020	C	C	N	1	M	***Current daily e-cig vs never ecig or cig (Tab 3): 1.20 (1.06 - 1.35)***	***Current daily cig vs never ecig or cig (Tab 3): 1.35 (1.27 - 1.44)***		***Current daily ecig vs nothing among nonsmokers: 1.48 (1.14 - 1.90)***	Tables 3 and 5A	Table 5B uses ever smoking, not current smoking, so could not be used to get dual use risk.
Xie (2020b)	Incident asthma (no respiratory conditions at baseline)	PATH	21618	A	2013-2018	C	L	N	6	M	***current vs. never: IRR= 1.32 (1.01 - 1.72) for asthma*** ever vs. never=1.24 (1.01 - 1.53) former vs. never= 1.19 (0.95 - 1.50)				Table 2 (Model d; fully adjusted model)	There were other analyses restricted among health participants in Tab 3-4

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Study	Outcome	Sample	Sample size	Adult or Youth*	Years data collected	Diagnosis: Current † or Ever	Cross-sectional or Longitudinal	Reference use: Never or Non-Current	No. studies of dataset	Model: Multivariate, Stratified, or Both	E-cigarette risk (95%CI)	Cigarette risk (95%CI)	Dual Use risk	Sole e-cigarette or e-cigarette risk	Where to find reported results	Notes
Xie (2022)	wheezing or cough (age 18-24; no respiratory disease at baseline)	PATH	6378	A	2014-2019	C	L	NC	3	B	Among the total sample: ***current vs. never=1.32 (1.06 – 1.65)*** former vs. never=1.20 (1.04 – 1.39) Among never smokers: ***current vs. never= 1.86 (1.35 – 2.58)*** former vs. never= 1.22 (1.00 – 1.49)	***sole cig vs. none=2.07 (1.75 – 2.46)***	***DU vs. none current use of both= 1.88 (1.41 – 2.51)*** ***DU vs. sole cig= 0.91 (0.67 – 1.23)***	***sole ENDS vs. none= 1.62 (1.23 – 2.12)*** ***sole cig vs. none=2.07 (1.75 – 2.46)*** ***sole ENDS vs. sole cig= 0.78 (0.58 – 1.05)***	Tables 2-3 Figure 2A	
COPD/respiratory																
Antwi (2022)	COPD (no asthma history)	BRFSS	177209	A	2018	E	C	N	2	B	**Multivariate Model** ecig use controlling for cig use vs never ENDS use: ***Daily user 1.53 (1.11 – 2.03)*** Some days 1.43 (1.13 – 1.80) Former user 1.46 (1.28 – 1.67) ***Among former smokers: 1.90 (1.25-2.88)***	**Multivariate model** ***Current smokers vs never controlling for ecig use: 4.75 (4.11 - 5.49)***	**Stratified** ***Daily ecig vs never among current smokers: 0.99 (0.67 – 1.46)*** Some day ecig vs never among current smokers: 1,22 (0.92 – 1.61)	**Stratified** Among never smokers: ***Daily ecig use vs never: 3.17 (1.04 – 9.63)*** Some days vs never 1.61 (0.87 – 3.09) Former vs never: 1.55 (1.01 – 2.38)	Tables 2 and 3	
Barrameda (2021)	COPD, emphysema, or chronic bronchitis	BRFSS	459098	A	2016	E	C	N	1	B	**Single multivariable model including ecigs and cigs** ***Every day vs never: 1.83 (1.59 - 2.10)*** Some-day vs never: 2.33 (2.07 - 2.62) Former vs never: 1.92 (1.82 - 2.03) **Among former smokers** Every day vs never: 1.46 (1.23-1.88) Some-day vs never: 2.05 (1.42 - 2.94) Former vs never: 2.05 (1.78 - 2.37)		**Among current smokers** ***Every day ecig vs never: 1.47 (1.13-1.92)*** Some-day vs never: 1.82 (1.56 - 2.14) Former vs never: 1.65 (1.48 - 1.84)	**Among never smokers** ***Every day vs never: 4.36 (1.76 - 10.77)*** Some-day vs never: 1.27 (0.77 - 2.08) Former vs never: 1.58 (1.24 - 2.02)	Tab 3	Table 2 presents multivariate model including ecigs and cigs in the same model, so ecig effect is also marginal effect of ecigs over cigs, i.e., dual use. In addition, Table 3 includes results stratified by cig use so ecig risks among cig smokers is also a direct estimate of dual use risk

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Study	Outcome	Sample	Sample size	Adult or Youth*	Years data collected	Diagnosis: Current † or Ever	Cross-sectional or Longitudinal	Reference use: Never or Non-Current	No. studies of dataset	Model: Multivariate, Stratified, or Both	E-cigarette risk (95%CI)	Cigarette risk (95%CI)	Dual Use risk	Sole e-cigarette or e-cigarette risk	Where to find reported results	Notes
Bhatta (2020)	Incident COPD	PATH	23760	A	2013-2016	C	L	NC	1	M	***Risk at Wave 2 current vs, never = 1.44 (0.79 - 2.62)*** former vs. never = 1.82 (1.23 - 2.69) Risk at Wave 3 current vs, never = 1.41 (0.86 - 2.33)	***Risk at Wave 2 current vs. never=5.79 (1.64 - 20.44)*** former vs. never=1.47 (0.42 - 5.20) Risk at Wave 3 current vs. never=14.59 (5.34 - 39.90)			Appendix Table 6	
Bircan (2021)	COPD	BRFSS	8736	A	2016-2018	E	C	N	2	S	Current vs never ecigs (among never smokers) ***COPD (OR=1.44; 95% CI: 1.42 - 1.46)*** ACOS (OR=2.27; 95% CI: 2.23 - 2.31)				Figure 3	All are never smokers
Cook (2023b)	Incident COPD	PATH	9861	A	2013-2019	C	L	N	S	M	***Current vs. never e-cig: 1.1 (0.78 - 1.56)***	***Current vs. never smoking: 1.63 (1.16 - 2.27)*** Former smoking vs. never smoking: 0.85 (0.59 - 1.23)			Table 3	Hazard ratio Independent variable is ENDS use, not specifically e-cigarettes. People with existing COPD at baseline excluded
Cordova (2022)	Incident COPD	PATH	26072	A	2013-2018	C	L	N	2	S	***Current ENDS vs never: COPD: 6.5 (3.7 - 11.5)***	***Current cig vs never: COPD: 6.1 (4.0 - 9.1)***	***Current ENDS plus cig vs never: COPD: 5.4 (3.4 - 8.7)***	***Current ENDS only vs never use among never smokers: COPD: 6.5 (3.7 - 11.5)***	Table 2	Used extremely conservative Bonferroni correction when interpreting results (Required p<.0017=.05/30 to call something significant; 30 = 6 models x 5 parameters). Polyproduct users considered a separate group

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Study	Outcome	Sample	Sample size	Adult or Youth*	Years data collected	Diagnosis: Current † or Ever	Cross-sectional or Longitudinal	Reference use: Never or Non-Current	No. studies of dataset	Model: Multivariate, Stratified, or Both	E-cigarette risk (95%CI)	Cigarette risk (95%CI)	Dual Use risk	Sole e-cigarette or e-cigarette risk	Where to find reported results	Notes
Giovanni (2020)	Chronic respiratory symptoms: daily cough, sputum production, or breathlessness	BRFSS	87,067	A	2017	C	C	NC	4	S	Prevalence ratio ***Age 18-35: 1.36 (1.08 - 1.70)*** Age 36-54: 1.16 (0.67 - 2.01) Age >=55: 1.00 (0.69 - 1.46) ***Among former smokers: 0.89 (0.57-1.40)***		***Age 18-35: 1.16 (0.99 - 1.36***) Age 36-54: 1.03 (0.91 - 1.17) Age >=55: 0.98 (0.89 - 1.09)		Table 2	Prevalence ratio Including cardiac and respiratory disease as covariates may over-corrected results Also reported results for remote and recent former smokers.
Goldberg Scott (2023)	influenza, pneumonia	Kaiser Permanente Research Bank	96,148	0	2015-2019	0	1	1	1	1	Longitudinal: ***Influenza: 0.96 (0.71-1.31)*** Pneumonia: 1.02 (0.74-1.40) Additional cross-sectional: COPD: 2.16 (1.77-2.63) Asthma: 0.94 (0.78-1.14)				Table 3 (longitudinal) and Table 2 (cross-sectional)	Hazard ratios (HR) for longitudinal results OR for cross-sectional results Longitudinal results used in meta-analysis. Cross sectional results (based on larger sample sizes) also reported (Table 2). People with history of heart attack, stroke or cancer prior to survey excluded.
Hedman (2018)	Cough, sputum production, chronic productive cough, wheeze (Sweden)	Obstructive Lung Disease in Northern Sweden study and West Sweden Asthma Study	30272	A	2016	C	C	N	1	S	***sole ENDS vs. none=1.46 (0.93 - 2.29)*** ENS with former smoking vs. none= 1.47 (0.91 - 2.37)	***sole smokers vs. none= 2.55 (2.36 - 2.77)*** Former smoker without ENDS vs. non= 1.27 (1.19 - 1.36)	***DU vs. none= 4.03 (3.23 - 5.02)***		Table 3 and Supplement doc	
Kim (2021)	Spirometry-defined COPD (age 40+; Korea)	KNHANES	12919	A	2013-2018	C	C	N	1	S		***Current sole smokers vs never users of both: 2.26 (1.77 – 2.88)*** Former smokers vs never smokers: 1.67 (1.31 – 2.12)	***Dual users vs never users of both: 2.83 (1.64 – 4.86)***		Table 3	

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Osei (2020)	COPD, bronchitis, or emphysema	BRFSS	705159	A	2016-2017	E	C	N	4	S	***Among never smokers: current vs. never=1.75 (1.25 - 2.45)*** daily vs. never=2.64 (1.43 - 4.89) occasionally vs. never=1.51 (1.03 - 2.23) Among former smokers: ***current vs. never= 2.13 (1.82 - 2.50)*** daily vs. never=2.05 (1.72 - 2.44) occasionally vs. never= 2.30 (1.71 - 3.08)		***DU vs. never tob=6.89 (6.29 - 7.55)*** ***DU vs. sole cig= 1.66 (1.50 - 1.84)*** DU with daily vaping vs. sole cig= 1.64 (1.34 - 2.00) DU with occasional vaping vs. sole cig = 1.67 (1.50 - 1.86)		Table 2 and main text	
Parekh (2020b)	COPD (woman age 18-44)	BRFSS	131965	A	2016-2017	E	C	N	4	S	***Current e-cigarette users without history of combustible cigarette smoking vs never users of anything: 1.37 (0.71 – 2.63)*** ***Former smokers: 2.65 (1.53-4.58)*** Current e-cigarette users with history of combustible cigarette smoking vs never users of anything: 2.65 (1.53 – 4.58) Former e-cigarette users without history of combustible cigarette smoking vs never users of anything: 1.67 (1.21 – 2.30)	***Current combustible cigarette smokers without history of e-cigarette use vs never users of anything: 3.28 (2.62 – 4.12)***	***Current dual users (e-cigarette + combustible cigarette) vs never users of anything: 5.07 (3.91 – 6.56***)		Table 4	

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Paulin (2022)	Incident COPD	PATH	13752	A	2013-2019	E	L	N	1	S	***Current ecig use vs nothing:*** ***Never tobacco use as reference:*** ***Longitudinal: 1.36 (0.55 - 3.39)*** Cross-sectional at Wave 1: 2.22 (1.44 - 3.42) ***Exclusive cigarette as reference group:*** ***Longitudinal: 0.71 (0.26 - 1.92)*** Cross-sectional at Wave 1: 0.74 (0.46 - 1.19)	***Current cig use vs. nothing: Never tobacco use as reference:*** ***Longitudinal: 1.92 (1.29 - 2.86)*** Cross-sectional at Wave 1: 3.00 (2.37 - 3.80)	***Current dual use vs nothing:*** ***Never tobacco use as reference:*** ***Longitudinal: 13.10 (2.39 - 4.02)*** Cross-sectional at Wave 1: 1.99 (1.29 - 3.07) ***Exclusive cigarette as reference group:*** ***Longitudinal: 1.03 (0.86 - 1.24)*** Cross-sectional at Wave 1: 1.04 (0.77 - 3.40)		Tables 3 and 4	Relative risk Longitudinal analysis presented incident COPD at Waves 2-5 among people who did not report COPD at Wave 1. Multivariable model also included other combusted and noncombusted tobacco products and former users
Perez (2019b)	COPD, bronchitis, or emphysema	PATH	3642	A	2013-2014	E	C	NC	1	M	***current (y/n)= 1.43 (1.12 – 1.85) in the propensity-matched sample (controlling for pack-years of smoking)*** current (y/n)=1.47 (1.21 – 1.79) for total sample Daily vs. never=1.59 (1.06 – 2.37), someday vs. never=1.97 (1.55 – 2.49) Former vs. never= 1.73 (1.46 – 2.06)			***current ecig (y/n) =2.94 (1.73 – 4.99) for nonsmokers***	Table 2 and Main text section 3.2	
Qeadan (2023)	aggregate measure of respiratory disease	PATH	18,893	0	2014-2018	0	1	0	3	1	***Adverse respiratory condition: 1.11 (0.99-1.23)***				Table 3	Adverse respiratory condition: asthma, COPD, chronic bronchitis, emphysema, or other lung or respiratory condition "Dual use" in the paper is dual use of e-cigs and illicit drug (not nicotine cigarette), so was not extracted

Table S2. Characteristics and results from included studies (values used in meta-analysis appear in *bold italics*; all are OR unless otherwise noted)

Study	Outcome	Sample	Sample size	Adult or Youth*	Years data collected	Diagnosis: Current † or Ever	Cross-sectional or Longitudinal	Reference use: Never or Non-Current	No. studies of dataset	Model: Multivariate, Stratified, or Both	E-cigarette risk (95%CI)	Cigarette risk (95%CI)	Dual Use risk	Sole e-cigarette or e-cigarette risk	Where to find reported results	Notes
Strong (2018)	COPD, bronchitis, emphysema, asthma	PATH	32320	A	2013-2014	E	C	NC	2	M	***Sole ENDS vs. non-current users= 1.39 (1.09 – 1.76)***	***Cig only vs. non-current users= 1.54 (1.43 – 1.66)***	***DU vs. non-current users= 2.07 (1.71 – 2.51)***		Main text section 3.5	
Wills (2019)	COPD	Hawaii BRFSS	8087	A	2016	E	C	NC	1	S	risk for COPD: current ***(y/n) = 2.58 (1.36 – 4.89) for the total sample*** ever (y/n)=1.29 (0.94 − 1.77) for smokers	***current (y/n)= 2.98 (2.34 − 3.78) for the total sample***	***DU vs. neither = 3.92 (2.82 – 5.44)*** ***DU vs. Cig= 1.32 (0.98 – 1.77)*** DU vs. ENDS= 1.52 (0.81 – 2.87)	***Sole cig vs. none=2.98 (2.34 – 3.78)*** current ***ecig vs current cig: 0.86 (0.46 - 1.61)*** [current Cig vs. current ENDS = 1.16 (0.62 – 2.17)]	Table 3	
Wills (2022)	COPD	BRFSS	117,063	A	2020	E	C	N	1	M	***Current daily e-cig vs never ecig or cig (Tab 3): 1.44 (1.21 - 1.71)***	***Current daily cig vs never ecig or cig (Tab 3): 4.60 (4.23 – 5.00)***		***Current daily ecig vs nothing among nonsmokers: 1.16 (0.57 - 2.36)***	Tables 3 and 5A	Table 5B uses ever smoking, not current smoking, so could not be used to get dual use risk. Wills is running the dual use numbers for me and will send.
Xie (2020a)	COPD	BRFSS	887182	A	2016, 2017	E	C	N	4	S	***Current ecig who never smoked vs never users of both: 1.47 (1.01 - 2.12)*** ***Current ecig who never smoked vs current cig: 0.39 (0.27 - 0.56)*** ***Current ecig vs never among ex-smokers: 3.24 (2.78 - 3.78)*** Current ecig vs cig among ex-smokers: 0.85 (0.73 - 0.99)	***Current smokers vs never users: 3.80 (3.58 - 4.02)***	***Dual users vs never users of both: 4.39 (3.98 - 4.85)*** ***Dual users vs current smokers: 1.16 (1.05 - 1.27)***		Table 1	Also contains results stratified by age

Table S2. Characteristics and results from included studies (values used in meta-analysis appear in ***bold italics***; all are OR unless otherwise noted)																
Study	**Outcome**	**Sample**	**Sample size**	**Adult or Youth***	**Years data collected**	**Diagnosis: Current † or Ever**	**Cross-sectional or Longitudinal**	**Reference use: Never or Non-Current**	**No. studies of dataset**	**Model: Multivariate, Stratified, or Both**	**E-cigarette risk (95%CI)**	**Cigarette risk (95%CI)**	**Dual Use risk**	**Sole e-cigarette or e-cigarette risk**	**Where to find reported results**	**Notes**
Xie (2020b)	incident COPD (no respiratory disease at baseline)	PATH	21618	A	2013-2018	C	L	N	3	M	For COPD: ***current vs. never = 1.57 (1.15-2.13)*** ever vs. never= 1.62 (1.28 - 2.04) former vs. never= 1.66 (1.29 - 2.12) Any respiratory condition for the total sample: current vs. never =1.31 (1.08 - 1.59) ever vs. never= 1.28 (1.10 - 1.48) former vs. never=1.28 (1.09 - 1.51)			Any respiratory condition among nonsmokers: current ENDS vs. never = 1.35 (0.87 - 2.09) ever ENDS vs. never= 1.37 (1.05 - 1.79) former ENDS vs. never= 1.38 (1.03 - 1.84)	Table 2	Incident rate ratio

Oral disease																
Akinkugbe (2019)	dental health issues, such as cavities, gum disease or dental stains (age 12-17)	PATH	13650	Y	2013-2014	C	C	NC	1	S	**Past year dental problems:** ***Current ecig only vs non-current: 1.11 (0.79 - 1.55)*** Ever ecig only vs never: 1.12 (0.90 - 1.38) **Ever dental problems:** Current ecig only vs non-current: 1.27 (0.95 - 1.70) Ever ecig vs never: 1.28 (1.07 - 1.54)	**Past year dental problems:** ***Current cig only vs non-current: 1.50 (1.18-1.90)*** Ever cig only vs never: 1.34 (1.13 - 1.58) **Ever dental problems:** Current cig only vs non-current: 1.47 (1.17 - 1.83) Ever cig vs never: 1.29 (1.10 - 1.51)	**Past year dental problems:** ***Current dual vs non-current:: 1.72 (1.24 - 2.38)*** Ever dual vs never:1.43 (1.22 - 1.67) **Ever dental problems:** Current dual vs non-current: 1.59 (1.20 - 2.09) Ever dual vs never: 1.45 (1.24 - 1.68)		Tables 4 and 5	
AlQobaly (2022)	Periodontal disease	NHANES	8129	A	2015-6 & 2017-8	E	C	N	1	B	**Periodontal disease Multivariate** ***Current vs never: 1.38 (0.97 - 1.97)*** Ever vs never: 1.43 (1.18 - 1.73) ***Among former smokers: 1.72 (0.76-3.87)*** **Bone loss Multivariate** Current v never: 1.80 (1.30 - 2.49) Ever v never: 0.92 (0.65 - 1.29)	**Periodontal disease Multivariate** ***Current vs never: 1.72 (1.47 - 2.02)*** Ever vs. never: 1.43 (1.13 - 1.82) **Bone loss Multivariate** Current v never: 2.75 (2.17 - 3.48) Ever v never: 1.90 (0.51 - 2.39)	**Stratified (among current smokers)** **Periodontal disease** ***Current ecig (dual) vs never (sole smoking): 1.65 (1.03 - 2.64)*** **Bone loss** Current ecig (dual) vs. never (sole smoking): 2.41 (1.58 - 3.70) Ever vs never (sole smoking): 1.13 (0.68 - 1.89)	**Periodontal disease** **Stratified (Among never smokers)** ***Current vs never: 0.95 (0.24 - 3.82)*** Ever vs never: 0.94 (0.48 - 1.42) **Bone loss** **Stratified (Among never smokers)** Current vs never: 0.13 (0.01 - 1.30) Ever vs never: 0.80 (0.27 - 2.35)	Tables 2 and 3 (Model 2) and 4 (stratified)	Model 2 contains ecig and smoking (as well as passive smoking) in same model so also is marginal risk of dual use compared to smokers More combinations in paper
Atuegwu (2019b)	Incident periodontal disease (no history of gum disease at baseline)	PATH	18289	A	2013-2016	C	L	N	1	M	Ecig use at all three times vs no ecig use controlling for cig and other tobacco use: ***Any periodontal disease (either of previous two): 1.58 (1.06 - 2.34)*** New gum disease: 1.76 (1.12 - 2.76) Bone loss around teeth: 1.67 (1.06 - 2.63)				Table 2	

Chaffee (2021b)	Xerostomia (high school students)	public high school students in rural Northern California	976	Y	2020-2021	C	C	NC	1	M	**Dry mouth** ***Current e-cig use (6-30 days in past 30) vs nonuse: 1.40 (0.69 - 2.84)*** Current ecig use (1-5 days in past 30) vs nonuse: 1.22 (0.84 - 1.78) **Xerostomia** Current e-cig use (6-30 days in past 30) vs nonuse: 0.96 (0.90 - 1.01) Current ecig use (1-5 days in past 30) vs nonuse: 1.05 (0.99 - 1.11)	**Dry mouth** ***Current use (cig, cigar, hookah): vs nonuse: 1.92 (1.38 - 2.68)*** **Xerostomia** Current combustible tob use vs nonuse: 1.13 (0.99 - 1.29)			Table 4	Current combustible tob products included cigarettes, cigars, and/or hookah
Chaffee (2022)	Poor or fair oral health	PATH	24,984	A	2016-2018	C	C	N	1	S	***e-cig only vs never tobacco:*** ***Last 12 months: 1.28 (0.93 - 1.75)***	***Cig only vs never tobacco: 1.76 (1.48 - 2.10)***	***Dual vs never tobacco: 1.80 (1.46 - 2.23)***		Table 5	Many other outcomes reported; selected self-rated oral health because it was most global.
Cho (2017)	Gingival pain and/or bleeding, tongue and/or inside-cheek pain, cracked or broken tooth (age xx, Korea)	KYRBWS	33309	Y	2016	C	C	N	1	M	***gingival pain and/or bleeding*** ***Daily ecig vs never:1.00 (0.72 - 1.41)*** 1-29 days vs never: 0.88 (0.74 - 1.05) **cracked or broken tooth** daily ecig vs never: 1.65 (1.19 - 2.27) nondaily vs never: 1.26 (1.06 - 1.51) **tongue and/or inside-cheek pain**, Daily ecig vs never: 1.54 (1.05 - 2.26) Nondaily vs never: 1.08 (0.88 - 1.33)	***gingival pain and/or bleeding*** ***Daily cig vs never:0.98 (0.81-1.18)*** 1-29 days vs never: 1.14 (0.95 - 1.35) **cracked or broken tooth** daily cig vs never: 1.33 (1.08 - 1.63) nondaily vs never: 1.13 (0.93 - 1.38) **tongue and/or inside-cheek pain**, Daily cig vs never: 0.80 (0.62 - 1.02) Nondaily vs never: 1.02 (0.82 - 1.28)			Table 4 (ORs for cigarettes) Tables 5, 6 and 7 (Model 3)	Also data on former ecig users and ecig with/without nicotine (Table 8), not tabulated
Huilgol (2019)	Poor oral health: at least one permanent tooth removed due to non-traumatic cause	BRFSS	456343	A	2016	E	C	NC	1	M	***Daily ecig vs nonusers: 1.78 (1.39 – 2.30)*** Nondaily vs nonuser: 1.08 (0.87 – 1.32)	***Current smoking (y/n): 2.231 (2.041 - 2.438)***			Table 2	Smoking risk in Fig 2, but to small to read OR. Emailed author to get exact numbers.
Jeong (2020)	Periodontal disease (Korea)	KNHANES	13551	A	2013-2015	C	C	N	1	M	E-cigarette vs no tobacco: [both]***2.33 (1.58 - 3.44)**** [male] 2.34 (1.52 – 3.59) [female] 2.27 (0.89 – 5.80)	Cigarette vs no tobacco: [both] ***1.99 (1.69 - 2.53)**** [male] 2.17 (1.76 – 2.68) [female] 1.73 (1.32 – 2.27)			Table 2	Separate male & female results pooled using a fixed effect meta-analysis

Silveira (2022)	Gum disease	PATH	18925	A	2013-2019	C	L	N	1	M	***Current ecig vs. non-current:*** ***gum disease: 1.15 (0.89 - 1.47)*** precancerous oral lesions: 0.56 (0.26 - 1.20) bone loss around teeth: 0.95 (0.69 - 1.31) bleeding after brushing or flossing: 1.27 (1.04 - 1.54) loose teeth: 1.01 (0.75 - 1.35) one or more teeth removed: 1.03 (0.80 - 1.33)	***Current cig smoker vs non-current:*** ***gum disease: 1.33 (1.11 - 1.60)*** precancerous lesions: 1.47 (0.87 - 2.48) bone loss around teeth: 0.99 (0.77 - 1.27) bleeding after brushing or flossing: 0.94 (0.81 - 1.10) loose teeth: 1.35 (1.05 - 1.75) one or more teeth removed: 1.43 (1.18 - 1.74)			Tables 3 and 4	Hazard ratio Sample included people without oral disease at Wave 1 or 3. Including cigarette pack years as independent variable might dilute estimated cigarette effect.
Vora (2019)	Gum disease	PATH	32300	A	2013-2014	E	C	N	2	S	**Gum disease diagnosis** ***current ecig only vs never tobacco: 2.9 (1.9 - 4.5)*** **Gum disease treatment** current ecig only vs never tobacco: 2.3 (1.3 - 4.1) **Pre-cancerous lesion diagnosis:** current ecig only vs never tobacco: 2.4 (0.5 - 12.4)	**Gum disease diagnosis** ***current cig only vs never tobacco: 2.2 (1.9 - 2.6)*** **Gum disease treatment** current cig only vs never tobacco: 1.5 (1.3 - 1.7) **Pre-cancerous lesion diagnosis:** current cig only vs never tobacco: 2.0 (0.9 - 4.1)	**Gum disease diagnosis** ***current multiple prod vs never tobacco: 2.8 (2.4 - 3.4)*** **Gum disease treatment** current multiple prod vs never tobacco: 1.6 (1.4 - 1.9) **Pre-cancerous lesion diagnosis:** current multiple prod vs never tobacco: 3.6 (1.7 - 7.7)		Table 4	Other forms of tobacco use also in multivariate model as well as former users. Don't present products used by multiple product users.

Other																
Hawkins (2021)	Preterm birth	PRAMS	57,046	A	2016-2017	C	C	NC	1	S	***preterm birth: 1.39 (0.84 - 2.30)*** small for gestational age: 0.78 (0.48 - 1.27)	***preterm birth: 1.28 (1.10 - 1.47)*** small for gestational age: 2.30 (2.01 - 2.63)	***preterm birth: 1.03 (0.73-1.46)*** small for gestational age: 1.93 (1.31 - 2.83)		Table 3	Based on ecig use in last 3 months of pregnancy Preterm birth outcome selected at random for all three studies that measured it

Regan (2021)	Preterm birth	PRAMS	79,176	A	2016-2018	C	C	NC	1	B	Prevalence ratios PRE-TERM BIRTH (N=11,576): Overall (controlling for smoking in multivariate model): ***E-cig during pregnancy vs not: 1.09 (0.85 - 1.40)*** E-cig use before pregnancy vs not: 0.97 (0.81 - 1.17) Stratified; smoked during pregnancy: E-cig use before pregnancy vs not: 1.10 (0.79 - 1.54) Stratified; did not smoke during pregnancy: ***E-cig during pregnancy vs not: 1.69 (1.20 - 2.39)*** E-cig use before pregnancy vs not: 0.89 (0.72 - 1.10) SGA (N=11,288): Overall (controlling for smoking in multivariate model): E-cig during pregnancy vs not: 1.22 (0.95 - 1.56) E-cig use before pregnancy vs not: 0.97 (0.81 - 1.16) Stratified; did not smoke during pregnancy: E-cig during pregnancy vs not: 1.10 (0.65 - 1.86) E-cig use before pregnancy vs not: 1.08 (0.86 - 1.36) Stratified; smoked during pregnancy: E-cig use before pregnancy vs not: 0.82 (0.63 - 1.08) LBW (N=13,959): Overall (controlling for smoking in multivariate model): E-cig during pregnancy vs not: 1.33 (1.06 - 1.66) E-cig use before			PRETERM BIRTH: ***Dual use during pregnancy vs cigs: 0.82 (0.59-1.14)*** SGA: Dual use during pregnancy vs cigs: 1.15 (0.89-1.48) LBW: Dual use during pregnancy vs cigs: 1.05 (0.80-1.38)	Table 2	Prevalence ratio "e-cigarette use relative to pregnancy was classified into the following categories: e-cigarette use in the 3 months before pregnancy but not during the last 3 months of pregnancy, e-cigarette use during the last 3 months of pregnancy (these respondents could have also used e-cigarettes before pregnancy), and nonuse defined as no e-cigarette use in the 3 months before pregnancy or during the last 3 months of pregnancy." "We assessed for possible interaction between combustible cigarette smoking during pregnancy and e-cigarette use during pregnancy by including combustible cigarette smoking as an interaction term in the models and performed additional analyses stratified by combustible cigarette smoking during pregnancy."

											pregnancy vs not: 1.08 (0.92 - 1.26) Stratified; smoked during pregnancy: E-cig use before pregnancy vs not: 1.07 (0.81 - 1.41) Stratified; did not smoke during pregnancy: E-cig during pregnancy vs not: 1.88 (1.38 - 2.57) E-cig use before pregnancy vs not: 1.06 (0.89 - 1.28)					
Wang (2020)	Preterm birth	PRAMS	31,973	A	2016	C	C	NC	1	S	Based on last 3 months of pregnancy: ***Preterm birth: 1.2 (0.5 - 2.7)*** SGA: 2.4 (1.0 - 5.7)	***Preterm birth: 1.6 (1.2 - 2.0)*** SGA: 2.4 (1.8 - 2.9)	***Preterm birth: 1.3 (0.8 - 2.3)*** SGA: 2.3 (1.3 - 4.1)		Table 4	Preterm birth outcome selected at random for all three studies that measured it
Wen (2023)	Low gestational weight	PRAMS	176,882	A	2016-2020	C	C	NC	1	S	***Current vs non-current e-cig: 0.99 (0.78 - 1.27)***	***Current cig vs non-current: 1.26 (1.18 - 1.35)***	***Current dual vs current nonuse: 1.18 (0.96 - 1.64)***	***Cig vs e-cig: 1.27 (0.99-1.64) so ecig vs cig: 0.79 (0.61 - 1.01) Dual users vs cigarettes: 0.93 (0.75 - 1.15)***	Table 4	Exposure based on e-cigarette and cigarette use during last three months of pregnancy The classification of a stratified analysis is based on the structure of Table 4.
McBride (2021)	Did not breastfeed for at least 3 months	PRAMS	42,827	A	2016-2018	C	C	NC	1	M	**Prenatal e-cig use vs not: 1.59 (1.12 - 2.50)**	**Prenatal cig use vs not: 2.04 (1.79 - 2.38)**			Table 3	E-cig use in last 3 months or pregnancy. Reported ORs for breastfeeding: inverted ORs to obtain ORs for not breastfeeding (undesirable outcome)
Ebrahimi Kalan (2023)	COVID-19 infection	NHIS	29,482	0	2021	1	0	1	2	2	1.17 (0.92-1.50)	0.67 (0.54-0.82)	2 or more tobacco products: 0.85 (0.63-1.15) [not necessarily e-cigarettes]		Table 3	Disease coded as current because NHIS conducted in 2021 and the COVID-19 epidemic started in the US in 2020.

Gaiha (2020)	COVID diagnosis (age 13-24)	online national survey of adolescents and young adults	4351	Y	2020	C	C	N	1	S	***current ecigs only vs no cigs no ecigs: 1.91 (0.77 - 4.73)***	***current cigs vs no cigs no ecigs: 1.53 (0.29 - 8.14)***	***dual use vs never ecigs never cigs: 6.84 (2.40 - 19.55)***		Table 2	
Moyers (2023)	COVID-19 infection	NHIS	28344	0	2021	0	0	0	2	2	***1.30 (1.04-1.63)***	***0.64 (0.55-0.74)***	***0.77 (0.52-1.14)***		Table 2	Disease coded as current because NHIS conducted in 2021 and the COVID-19 epidemic started in the US in 2020.
Goldberg Scott (2023)	ER visit, hospitalization, death	Kaiser Permanente Research Bank	96,148	0	2015-2019	0	1	1	1	1	Longitudinal ***ER visit: 1.17 (1.05-1.30)*** Hospitalization: 1.18 (0.98-1.43) Death: 1.84 (1.02-3.32)				Table 3 (longitudinal) and Table 2 (cross-sectional)	Hazard ratios (HR) People with history of heart attack, stroke or cancer prior to survey excluded. Used ER visits because largest number of events in "Other" group
To (2023)	health services use (hospitalization or ER visit)	CCHS	2700	1	2015-2018	0	0	0	1	2	***HSU: 1.73 (1.00-3.00)***	***HSU: 1.72 (1.29 - 2.29)***	***HSU: 2.13 (1.53 - 2.98)***	HSU: ***e-cig: 1.73 (1.00-3.00)*** cig: 1.72 (1.29 - 2.29)	Table 3	Propensity score matching with 5 controls per case Canadian Community Health Survey linked to Discharge Abstract Database National Ambulatory Care Reporting System Also reported all-cause health services utilization (HSU: hospitalization or ER visit) accounting for gender and e-cig x cig interactions as well as main effects.
Zhu (2023)	Obstructive sleep apnea	NHANES	11,248	A	2015-2018	C	C	NC	1	S	***Current vs. non-current: 0.84 (0.52 - 1.37)***	***Current vs non-current:1.38 (1.17 - 1.63)***	***Current vs non-current: 1.78 (1.37 - 2.32)***		Table 4	

Christian (2023)	sleep duration	Kentucky BRFSS	18,907	0	2016-2017	0	0	0	1	2	***Current ecig, never smoked: 0.99 (0.61-1.60)***	***Current smoker, never ecig: 1.15 (1.02-1.28)***	***Current e-cig, current smoker 1.28 (1.08-1.51)***	***Current ecig, never smoked: 0.99 (0.61-1.60)*** Current smoker, never ecig: 1.15 (1.02-1.28)	Table 2	Sleep <7 hours coded as "short" Prevalence odds ratios (POR) using Poisson regression
Wiener (2020)	Sleep disorder	NHANES	2889	A	2015-2016	C	C	N	1	M	***Current vs never: 1.82 (1.18 - 2.79)***				Table 2 model 2	
Tian (2022)	Arthritis	BRFSS	924,882	A	2016-2018	E	C	N	1	S	***Sole current e-cig vs never among never smokers: 1.25 (1.00 - 1.57)***			***Current dual use vs current smoker: 1.55 (1.42 - 1.69)***	Table 4	
Smith (2023)	atopic dermatitis	NHIS	28,563	0	2021	1	0	0	1	1	***1.35 (1.16-1.58)***			***Among never smokers: 1.61 (1.28-2.02)***	Table 2	
Agoons (2021)	Fragility bone fractures	NHANES	5569	A	2017-2018	E	C	N	1	B	***Current vs never ecig users: 1.43 (0.84 - 2.45)*** Ever vs never ecig users: 1.46 (1.12 - 1.89) Former ecig vs never users: 1.46 (1.10 - 1.94)	***Current smoker vs never smoker never ecig user 1.63 (1.18 - 2.25)***	***Dual use vs never smoker never ecig user: 2.41 (1.28 - 4.55)***		Tables 2 and 3	Prevalence ratio
Goldberg Scott (2023)	Cancer	Kaiser Permanente Research Bank	96,148	0	2015-2019	0	1	1	1	1	Longitudinal [cross-sectional in brackets]: ***Any cancer: 0.80 (0.41-1.55)*** [0.84; 0.67-1.06] Lung cancer: 1.00 (0.14-7.42) [2.64; 1.42-4.92]				Table 3 (longitudinal) and Table 2 (cross-sectional)	Hazard ratios (HR) for longitudinal results OR for cross-sectional results Longitudinal results used in meta-analysis. Cross sectional results (based on larger sample sizes) also reported (Table 2). People with history of heart attack, stroke or cancer prior to survey excluded. Used any cancer because lung cancer based on a single incident case.
Xie (2020c)	Difficulty concentrating	BRFSS	886,603	A	2016-2017	C	C	NC	1	S	***Current ecig who never smoked: 1.96 (1.16 - 3.30)*** Current ecig among former smokers: 1.94 (1.40 - 2.71)	***Current smokers who never used ecigs: 1.49 (1.32 - 1.69)***	***Current ecig who also currently smoke: 2.07 (1.66 - 2.60)***		Table 2	

Han (2023)	Non-alcoholic fatty liver disease	Korea NHANES	7096	A	2016-2020	C	C	N	1	S		***Current vs never smoker: HSI: 1.22 (1.05 - 1.42)*** NRS: 2.13 (1.87 - 2.42) KNS: 1.33 (1.14 - 1.55)	***Current dual user vs never user of either product: HSI: 1.47 (1.08 - 1.99)*** NRS: 2.21 (1.70 - 2.86) KNS: 1.35 (1.01 - 1.81).		Table 2	NAFLD defined by Hepatic Steatosis Index (HSI), NAFLD Ridge Score (NRS), and KNHANES NAFLD score (KNS) Excluded people with underlying chronic liver disease Former smokers without history of e-cigarette use excluded to account for the confounding effects of smoking cessation Excluded e-cigarette only users due to small sample size Age differences may explain why dual users, with a greater proportion of young people, appear to have fewer pack-years than cigarette only smokers HSI randomly selected for quantitative meta-analysis
Wang (2022)	Ordered logistic regression on health status (1= excellent, 5=poor)	NHIS and MEPS	109133	A	2015-2018	C	C	NC	1	S			***Current dual use vs never tobacco use: 1.84 (1.64 - 2.06)*** ***Current dual use vs current smoking: 1.39 (1.22 - 1.57)***	***exclusive ecig vs. never tob user = 1.62 (1.18 - 2.23)*** ***current sole cig vs never tobacco use: 1.33 (1.22 - 1.44)*** ***exclusive ecig vs smoker: 1.22 (0.88 - 1.69)***	Communication with author	Except for exclusive ecig vs never to user, results obtained from communication with Yingning Wang The paper as published included former smokers/OTP users in dual use group, so was not comparable to other papers. Dr. Wang ran the results using more standard definitions

Nguyen (2023)	impaired vision	Investigator survey using Qualtrics	4351	1	2020	0	0	0	1	2	1.14 (0.80-1.61) [inverted from 0.88 (0.62-1.25)]	2.08 (1.23-3.45) [inverted from 0.48 (0.29-0.81)]	1.39 (0.86-2.220 [inverted from 0.72 (0.45-1.16)]		Table 4 (Past 30 day use)	According to email from authors, AOR <1 indicates worse outcomes: 1. I am completely blind, 2, Very poor, 3. Poor, 4. Fair, 5. Good, 6. Excellent. Answers dichotomized as 1 = Excellent to Fair; and 0 = Poor to Completely Blind. So we inverted reported AORs so that AOR>1 indicates worse outcomes
Hong (2021)	Oral human papillomavirus -16 infection	NHANES	9266	A	2013-2016	C	C	NC	1	M	***Oral HPV-16: 2.97 (1.25 - 7.06)*** Any oral HPV: 1.05 (0.69 - 1.58)	***Oral HPV-16: 1.33 (0.57 - 3.08)*** Any oral HPV: 1.80 (1.05 - 3.09)			Table 1	"Interaction terms between current smoking and e-cigarette use were not significant, suggesting that the main effect of e-cigarette use on HPV-16 did not differ by concurrent cigarette smoking."

Bold italicized values used in meta-analysis; other results presented for information
*Adults defined as minimum age 18+; Youth defined as minimum age <18
†Current diagnosis usually past 12 months

Table S3. Potential confounders and risk of bias

Study	Potential confounders								Risk of bias* (ROBINS-E)						
	Age	Sex	Race/ ethnicity	Education, socioeconomic status	BMI	other tobacco product use	comorbid conditions	Former smoking†	Confounding	Exposure measurement	Participant selection	Missing data	Outcome measurement	Selection of reported result	Overall
Agoons (2021)	age	Sex	race/ethnicity	education	BMI, physical activity		steroid use, family history of osteoporosis		L	L	L	L	L	L	L
Akinkugbe (2019)	age	sex	race/ethnicity	parental education			diabetes		L	L	L	L	L	L	L
Alnajem (2020)	age	sex				exposure to secondhand smoke and aerosols		S	L	L	L	L	L	L	L
AlQobaly (2022)	age	sex	race/ethnicity	education			diabetes and dental visit	S	L	L	L	L	L	L	L
Alzahrani (2018)	age	sex	race/ethnicity		BMI		hypertension, diabetes mellitus, hypercholesterolemia	C	L	L	L	L	L	L	L
Antwi (2022)	age	sex	race/ethnicity	education, marital status, past month leisure time	BMI, physical activity			S	L	L	L	L	L	L	L
Atuegwu (2019a)	age	sex	race/ethnicity	education, marital status	BMI, exercise	smokeless	diet, alcohol use, asthma, heart disease, hypercholesterolemia, hypertension, tested blood sugar in past 3 years, depression, history of prediabetes		L	L	L	L	L	L	L
Atuegwu (2019b)	age	sex	race/ethnicity	income, education		other tobacco product, secondhand smoke exposure	prescription drug abuse, stomach, duodenal or peptic ulcer, marijuana use, alcohol use, illicit drug abuse		L	L	L	L	L	L	L

Table S3. Potential confounders and risk of bias

Study	Potential confounders								Risk of bias* (ROBINS-E)						
	Age	Sex	Race/ ethnicity	Education, socioeconomic status	BMI	other tobacco product use	comorbid conditions	Former smoking†	Confounding	Exposure measurement	Participant selection	Missing data	Outcome measurement	Selection of reported result	Overall
Barrameda (2021)	age	sex	race/ethnicity	education, annual household income, health insurance, personal physician, metropolitan status, marital status	BMI, exercise	tobacco chewing	alcohol use	C	L	L	L	L	L	L	L
Bayly (2019)	age	sex	race/ethnicity	metropolitan status, housing type		Cigar, hookah, secondhand smoke, secondhand aerosol			L	L	L	L	L	L	L
Berlowitz (2022)	age	sex	race/ethnicity	education	BMI	cigars, cigarillos, pipes, snus, other smokeless tobacco	hypertension, hypercholesterolemia, diabetes, close relative with MI or heart surgery, marijuana use		L	L	L	L	L	L	L
Bhatta (2020)	age	sex	race/ethnicity	poverty level	BMI		hypertension, hypercholesterolemia, diabetes	C	L	L	L	L	L	L	L
Bircan (2021)	age	sex	race/ethnicity	education, marital status, income level, employment status, health insurance coverage, not being able to afford a doctor	BMI, physical activity				L	L	L	L	L	L	L

Table S3. Potential confounders and risk of bias

Study	Potential confounders								Risk of bias* (ROBINS-E)						
	Age	Sex	Race/ ethnicity	Education, socioeconomic status	BMI	other tobacco product use	comorbid conditions	Former smoking†	Confounding	Exposure measurement	Participant selection	Missing data	Outcome measurement	Selection of reported result	Overall
Boyd (2021)	age	sex	race/ethnicity	household income, region			cannabis use, asthma		L	L	L	L	L	L	L
Braymiller (2020)	age	sex	race/ethnicity	overall personal financial situation	BMI		cannabis use		L	L	L	L	L	L	L
Bricknell (2021)	age	sex	race/ethnicity	poverty level	BMI		coronary artery disease, chronic kidney disease, diabetes mellitus	C	L	L	L	L	L	L	L
Brunette (2023)	age	sex	race/ethnicity	education, urbanicity	BMI	cigarette pack years, secondhand smoke exposure, marijuana		C	L	L	L	L	L	L	L
Cai (2023)	age	gender	race/ethnicity	income	BMI	chewing tobacco, snuff, snus			L	L	L	L	L	L	L
Chaffee (2021a)	age	sex	race/ethnicity	personal income	BMI		hypertension, hypercholesterolemia, diabetes, cannabis use		L	L	L	L	L	L	L
Chaffee (2021b)	age	sex	race/ethnicity		physical activity	cigars, hookah, snuff, chewing tobacco, snus, nicotine ¶pouches, nicotine tablets/lozenge	asthma, alcohol use, cannabis use		L	L	L	L	L	L	L
Chaffee (2022)	age	sex	race/ethnicity	educational attainment, income	BMI	cigars, smokeless tobacco, hookah, pipe, secondhand smoke	diabetes, alcohol use, marijuana use		L	L	L	L	L	L	L

Table S3. Potential confounders and risk of bias

Study	Potential confounders								Risk of bias* (ROBINS-E)						
	Age	Sex	Race/ ethnicity	Education, socioeconomic status	BMI	other tobacco product use	comorbid conditions	Former smoking†	Confounding	Exposure measurement	Participant selection	Missing data	Outcome measurement	Selection of reported result	Overall
Cho (2016)	age	sex	race/ethnicity	high school grade, city size, student's economic status, residential type, multi-cultural family status, academic performance	BMI	secondhand smoke exposure, attempt to quit smoking	stress, atopic dermatitis history, allergic rhinitis history, asthma history		L	L	L	L	L	L	L
Cho (2017)	age	sex		school grade, economic status, city size	obesity, vigorous sports activity	attempt to quit smoking, secondhand smoking at home	carbonated drink, overweight status, stress, alcohol use		L	L	L	L	L	L	L
Choi (2016)	age	sex	race/ethnicity	metropolitan status, housing type		exposure to secondhand smoke, positive social norm towards smoking			L	L	L	L	L	L	L
Christian (2023)	age	sex	race/ethnicity	education, income, employment status	BMI		alcohol, number of chronic diseases (coronary heart disease, stroke, current asthma, and chronic obstructive pulmonary disease summed and classified to reflect the number of chronic diseases: none, 1, or ≥ 2)		L	L	L	L	L	L	L
Chung (2020)	age	sex		socioeconomic status, residential area	BMI, regular exercise, sedentary time	exposure to secondhand smoke			L	L	L	L	L	L	L

Table S3. Potential confounders and risk of bias

Study	Potential confounders								Risk of bias* (ROBINS-E)						
	Age	Sex	Race/ ethnicity	Education, socioeconomic status	BMI	other tobacco product use	comorbid conditions	Former smoking†	Confounding	Exposure measurement	Participant selection	Missing data	Outcome measurement	Selection of reported result	Overall
Cook (2023a)	age	sex	race/ethnicity	education, uninsured	BMI	other combustible tobacco use, cigarette pack years	asthma at baseline		L	L	L	L	L	L	L
Cook (2023b)	age	sex	race/ethnicity	household income	BMI	former smoking, cigarette pack-years	family history of heart attack/bypass surgery, diabetes and binge drinking		L	L	L	L	L	L	L
Cordova (2022)	age	sex	race/ethnicity	education, income, marital status		noncombustible tobacco product use, former users of any product	internalizing behavior, externalizing behavior, respiratory disorders (asthma adjusts for COPD and bronchitis), substance use, alcohol,		L	L	L	L	L	L	L
Ebrahimi Kalan (2023)	age	sex, sexual orientation	race/ethnicity	education, poverty level, employed		cigars, pipe/waterpipe, smokeless	social distancing at work, psychological distress, having >=1 health condition, region		L	L	L	L	L	L	L
El-Shahawy (2022)	age	sexual orientation	race/ethnicity	educational attainment, income, region	BMI, physical activity	other tobacco product use	diabetes, hypertension, hypercholesterolemia, mental health status		L	L	L	L	L	L	L
Falk (2022)	age	sex			BMI										
Farsalinos (2019)	age	sex	race		BMI		hypertension, hypercholesterolemia, diabetes		L	L	L	L	L	L	L
Gaiha (2020)	age	gender	race/ethnicity	region, mother's education	BMI		complying with county shelter-in-place orders and state percentage of COVID-19 positive cases		L	L	L	L	L	L	L
Gathright (2019)	age	sex	race/ethnicity	education, income					L	L	L	L	L	L	L
Giovanni (2020)	age	sex			BMI		cardiac or respiratory disease, marijuana use	S	L	L	L	L	L	L	L

Table S3. Potential confounders and risk of bias

Study	Potential confounders								Risk of bias* (ROBINS-E)						
	Age	Sex	Race/ ethnicity	Education, socioeconomic status	BMI	other tobacco product use	comorbid conditions	Former smoking†	Confounding	Exposure measurement	Participant selection	Missing data	Outcome measurement	Selection of reported result	Overall
Goldberg Scott (2023)	age	sex, sexual orientation	race/ethnicity	education	BMI		history of COPD, hyperlipidemia, hypertension, marijuana, alcohol, physical activity, KP region		L	L	L	L	L	L	L
Han (2020)	age	sex	race/ethnicity		BMI		dental visit in the previous year, marijuana use		L	L	L	L	L	L	L
Han (2023)	age	Only men		income, education level, occupation	BMI		alcohol, physical activity		L	L	L	L	L	L	L
Hawkins (2021)	age	only women	race/ethnicity	education, household income, insurance, WIC, marital status			first prenatal care visit, language preference, plurality, parity, age at delivery, method of payment for delivery		L	L	L	L	L	L	L
Hedman (2018)	age	sex		education					L	L	L	L	L	L	L
Hirschtick (2022)	age	sex	race/ethnicity	education			baseline clinical risk factors, including family history of premature heart disease (MI at age <50), hypertension, diabetes	C	L	L	L	L	L	L	L
Hong (2021)	age	sex		income, marital status			Self-reported sexual behaviors, HPV vaccination, other substance use		L	L	L	L	L	L	L
Huilgol (2019)	age (grade)	sex	race/ethnicity	education, income, region		smokeless tobacco	alcohol use, soda intake, dental visit history, physical health status, depression, diabetes mellitus		L	L	L	L	L	L	L
Jeong (2020)	age	sex		household income, marital status, occupation, region			alcohol use, number of walking days in a week, self-reported health status, stress level, dental related variables, such as self-reported oral health status, dental caries, toothache within the past year, the experience of dental damage		L	L	L	L	L	L	L

Table S3. Potential confounders and risk of bias

Study	Potential confounders								Risk of bias* (ROBINS-E)						
	Age	Sex	Race/ ethnicity	Education, socioeconomic status	BMI	other tobacco product use	comorbid conditions	Former smoking†	Confounding	Exposure measurement	Participant selection	Missing data	Outcome measurement	Selection of reported result	Overall
Kim (2017)	age	sex		residential area, family economic status	obesity, physical activity				L	L	L	L	L	L	L
Kim (2020a)	age	only males		education, household income, residence location, occupational status, marital status	BMI		perceived high stress, depressive mood, suicidal thoughts, self-rated health status, alcohol use, comorbidities, and family history of disease		L	L	L	L	L	L	L
Kim (2020b)	age	sex		education, income	BMI, physical activity		alcohol use		L	L	L	L	L	L	L
Kim (2021)	age	sex		residence, education, income	BMI		High risk drinking		L	L	L	L	L	L	L
Kim (2022)	age	sex		marital status, region, household income, education, occupational category	BMI, physical activity	alcohol use			L	L	L	L	L	L	L
Lee (2023)	age	sex	race/ethnicity	education, employed, marital status, region, insurance	BMI		taking hypertension medications, taking low-dose aspirin, diabetes, COPD, BMI, have a doctor	C	L	L	L	L	L	L	L
Li (2020)	age	sex	race/ethnicity	income	BMI	secondhand smoke exposure	self-reported asthma, physical health, mental health	S	L	L	L	L	L	L	L

Table S3. Potential confounders and risk of bias

Study	Potential confounders								Risk of bias* (ROBINS-E)						
	Age	Sex	Race/ ethnicity	Education, socioeconomic status	BMI	other tobacco product use	comorbid conditions	Former smoking†	Confounding	Exposure measurement	Participant selection	Missing data	Outcome measurement	Selection of reported result	Overall
Lui (2022)	age	sex	race	education	BMI, physical activity	chewing tobacco	diabetes, depression, COPD, sleep duration	S	L	L	L	L	L	L	L
Mahoney (2022)	age	sex			BMI	cigars, cigarillos, filtered cigars, pipe tobacco, hookah, smokeless tobacco, snus pouches, dissolvable tobacco	hypertension, hypercholesterolemia, diabetes, family history of premature heart disease		L	L	L	L	L	L	L
Mattingly (2023)	age	sex	race/ethnicity	parental education, urbanicity	BMI	secondhand smoke exposure, household use of combustible tobacco products (cigars, cigarillos, filtered cigars, hookah, pipe tobacco), exclusive OC use, dual cigarettes and OC use, polytobacco use			L	L	L	L	L	L	L

Table S3. Potential confounders and risk of bias

Study	Potential confounders								Risk of bias* (ROBINS-E)						
	Age	**Sex**	**Race/ ethnicity**	**Education, socioeconomic status**	**BMI**	**other tobacco product use**	**comorbid conditions**	**Former smoking†**	**Confounding**	**Exposure measurement**	**Participant selection**	**Missing data**	**Outcome measurement**	**Selection of reported result**	**Overall**
McBride (2021)	age	only women	race/ethnicity	education, marital status	BMI		parity, gestational weight gain, mode of delivery, preterm or term birth, infant sex, insurance during pregnancy, WIC during pregnancy, quality of prenatal care, gestational age of the infant at birth, infant's sex		L	L	L	L	L	L	L
McConnell (2017)	11th & 12th grade students	sex	ethnicity	parental education, community, acculturation based on language of questionnaire, housing conditions, ownership of a dog or cat		secondhand smoke exposure at home			L	L	L	L	L	L	L
Miller (2021)	age	sex	race/ethnicity	education, household income, insurance status, marital status	BMI, physical activity		heavy alcohol use, hypercholesterolemia, diabetes mellitus	S	L	L	L	L	L	L	L
Moyers (2023)	age	sex	race/ethnicity	education, urbanicity, region	obesity		diabetes, COPD, coronary heart disease or heart attack, obesity		L	L	L	L	L	L	L
Nguyen (2023)	age	gender	race/ethnicity			contact lens use, cannabis use	blunts, cigars/cigarillos		L	L	L	L	L	L	L
Okafor (2022)	age	sex	race/ethnicity	income, educational attainment	BMI, physical activity	other tobacco product use	alcohol use		L	L	L	L	L	L	L
Osei (2019a)	age	sex	race/ethnicity	educational status, income	BMI, physical activity		diabetes, heavy alcohol drinking, hypertension, hypercholesterolemia		L	L	L	L	L	L	L

Table S3. Potential confounders and risk of bias

Study	Potential confounders								Risk of bias* (ROBINS-E)						
	Age	Sex	Race/ ethnicity	Education, socioeconomic status	BMI	other tobacco product use	comorbid conditions	Former smoking†	Confounding	Exposure measurement	Participant selection	Missing data	Outcome measurement	Selection of reported result	Overall
Osei (2019b)	age	sex	race/ethnicity	income, education	BMI				L	L	L	L	L	L	L
Osei (2020)	age	sex	race/ethnicity	income, education			Chronic bronchitis, emphysema, or chronic obstructive pulmonary disease	S	L	L	L	L	L	L	L
Parekh (2020a)	age	sex	race/ethnicity	education, income, marital status, health insurance, region	BMI, physical activity		alcohol use, diabetes, and hypertension, cholesterol	S	L	L	L	L	L	L	L
Parekh (2020b)	age	Only women	race/ethnicity	marital status, income, education, health insurance	BMI		binge drinking	S	L	L	L	L	L	L	L
Patel (2022)	age	sex	race/ethnicity	income	BMI		diabetes, cholesterol, hypertension, depression, cancer, substance abuse (marijuana, cocaine, heroin, methamphetamine, illegal injectable drug), alcohol use, and preventive aspirin use		L	L	L	L	L	L	L
Patel (2023)	age	sex	race/ethnicity	parental education, urbanicity	BMI	secondhand smoke, household combustible tobacco use			L	L	L	L	L	L	L
Paulin (2022)	age	sex	race/ethnicity	education, urbanicity		cigarette pack years, secondhand smoke	marijuana use, COPD comorbidity index, asthma diagnosis	D	L	L	L	L	L	L	L
Perez (2019a)	age	sex	race/ethnicity	education, income, marital status	BMI	smokeless tobacco	history of diabetes, heart attack, angina, coronary artery disease, stroke	S	L	L	L	L	L	L	L

Table S3. Potential confounders and risk of bias

Study	Potential confounders								Risk of bias* (ROBINS-E)						
	Age	Sex	Race/ ethnicity	Education, socioeconomic status	BMI	other tobacco product use	comorbid conditions	Former smoking†	Confounding	Exposure measurement	Participant selection	Missing data	Outcome measurement	Selection of reported result	Overall
Perez (2019b)	age	sex	race/ethnicity	poverty level, census region, education	BMI	traditional or filtered cigars, cigarillos, pipe, hookah, oral tobacco, and cigars with marijuana (blunts)	asthma, hypertension, hypercholesterolemia, congestive heart failure, stroke, heart attack, and diabetes, history of exposure to heroin	S	L	L	L	L	L	L	L
Qeadan (2023)	age	gender	race/ethnicity	education, income, marital status, employment, region, health insurance	BMI	smoking duration	alcohol, diabetes		L	L	L	L	L	L	L
Reddy (2021)	age	sex	race/ethnicity				Self-reported history of asthma, COPD, chronic bronchitis, or emphysema		L	L	L	L	L	L	L
Regan (2021)	age	only women	race/ethnicity	education, income, health insurance, marital status, maternal residence	BMI		WIC, service during pregnancy, parity, obstetric risk factors		L	L	L	L	L	L	L
Sargent (2022)	age	sex	race/ethnicity	income, urbanicity	BMI (overweight)	cigars (traditional cigars, cigarillos, and filtered cigars), pipe tobacco, hookah, snus pouches, other smokeless tobacco, secondhand smoke	asthma, congestive heart failure, heart attack, diabetes, cancer, use of antihypertensives known to cause coughing or wheezing (beta blockers, angiotensin receptor blockers, and ace inhibitors), marijuana use		L	L	L	L	L	L	L
Schneller (2020)	age	sex	race/ethnicity	health insurance	BMI	secondhand smoke exposure,	asthma		L	L	L	L	L	L	L

Table S3. Potential confounders and risk of bias

Study	Potential confounders								Risk of bias* (ROBINS-E)						
	Age	Sex	Race/ ethnicity	Education, socioeconomic status	BMI	other tobacco product use	comorbid conditions	Former smoking†	Confounding	Exposure measurement	Participant selection	Missing data	Outcome measurement	Selection of reported result	Overall
						Rules about smoking a combustible product inside your home, rules about using ENDS inside your home									
Schweitzer (2017)	age	sex	race/ethnicity	education	BMI (overweight)		marijuana use		L	L	L	L	L	L	L
Shi (2022)	age	sex	race/ethnicity	education	BMI, physical activity	traditional cigar, hookah, cigarillo, filtered cigar, cigar, blunt, snus, pipe, smokeless tobacco, or dissolvable tobacco	disease-related covariates (CVD, hypercholesterolemia, and diabetes mellitus), family history of hypertension, heavy alcohol use		L	L	L	L	L	L	L
Silveira (2022)	age	sex	race/ethnicity	education, income		cigarette pack years, cigar, pipe, hookah, smokeless tobacco, snus	diabetes, heavy alcohol use, marijuana, flossing		L	L	L	L	L	L	L
Smith (2023)	age	sex	race	education	BMI		diabetes, asthma		L	L	L	L	L	L	L

Table S3. Potential confounders and risk of bias

Study	Potential confounders								Risk of bias* (ROBINS-E)						
	Age	Sex	Race/ ethnicity	Education, socioeconomic status	BMI	other tobacco product use	comorbid conditions	Former smoking†	Confounding	Exposure measurement	Participant selection	Missing data	Outcome measurement	Selection of reported result	Overall
Sompa (2022)	All respondents around 24y	sex		educational level, occupational status, parental socioeconomic status	BMI, WC, body fat percentage	waterpipe use, snus, second-hand tobacco exposure, parental smoking habit			L	L	L	L	L	L	L
Stevens (2022)	age	sex	race/ethnicity	income	BMI	secondhand smoke exposure,	chronic disease (high blood pressure, high cholesterol, diabetes		L	L	L	L	L	L	L
Strong (2018)	age	sex	race/ethnicity			cigars, cigarillos, and filtered cigars, pipes, hookah, smokeless tobacco	marijuana use		L	L	L	L	L	L	L
Tackett (2020)	age	sex	race/ethnicity	income		traditional cigars, cigarillos, filtered cigars, pipes, hookahs, bidis, kreteks, secondhand smoke			L	L	L	L	L	L	L
Tackett (2023)	age	sex	race	parental education		cannabis, survey wave	secondhand smoke from ecigs, cigs, cannabis		L	L	L	L	L	L	L
Tanski (2022)	age	sex	race/ethnicity		obesity (based on BMI)	secondhand smoke exposure, marijuana use,	asthma status		L	L	L	L	L	L	L
Tian (2022)	age	sex	race/ethnicity	education, income	BMI				L	L	L	L	L	L	L
To (2023)	age‡	sex		education, income, urbanicity	BMI		mental health, life stress	C	L	L	L	L	L	L	L

Table S3. Potential confounders and risk of bias

Study	Potential confounders								Risk of bias* (ROBINS-E)						
	Age	Sex	Race/ ethnicity	Education, socioeconomic status	BMI	other tobacco product use	comorbid conditions	Former smoking†	Confounding	Exposure measurement	Participant selection	Missing data	Outcome measurement	Selection of reported result	Overall
Tran (2020)	age	sex	race/ethnicity	education, income, marital status, health-care coverage				C	L	L	L	L	L	L	L
Varella (2022)	age	sex	race/ethnicity	education, employment status, income, marital status, insurance status,		exercise in past 30 days	asthma history, COPD history	C	L	L	L	L	L	L	L
Vora (2019)	age	sex	race/ethnicity	education, income, employment, medical insurance			diabetes, visit to dentist in last 12 months	C D	L	L	L	L	L	L	L
Walker (2021)	age	sex	race	education, employment, marital status, income	obesity, BMI				L	L	L	L	L	L	L
Wang (2016)	age	sex		family affluence		secondhand smoke exposure		S	L	L	L	L	L	L	L
Wang (2020)	age	All women	race/ethnicity	education, marital status	BMI		previous preterm history, plurality, Kotelchuck index of prenatal care, drinking alcohol before pregnancy, gestational weight gain		L	L	L	L	L	L	L
Wang (2022)	age	sex	race/ethnicity	education, income level, marital status, region of residence, health insurance coverage	BMI	cigars, pipes, smokeless tobacco	alcohol consumption		L	L	L	L	L	L	L
Wen (2023)	age	Only women	race/ethnicity	education, insurance, marital status	BMI prepregnancy		pre-pregnancy diabetes, hypertension		L	L	L	L	L	L	L

Table S3. Potential confounders and risk of bias

Study	Potential confounders								Risk of bias* (ROBINS-E)						
	Age	Sex	Race/ ethnicity	Education, socioeconomic status	BMI	other tobacco product use	comorbid conditions	Former smoking†	Confounding	Exposure measurement	Participant selection	Missing data	Outcome measurement	Selection of reported result	Overall
Wiener (2020)	age	sex	race/ethnicity	education, health insurance, federal poverty level	BMI		chronic disease, alcohol use		L	L	L	L	L	L	L
Williams (2023)	age	sex	race/ethnicity	parental education		cannabis	Household use of e-cigs, cigs, or cannabis		L	L	L	L	L	L	L
Wills (2019)	age	sex	race/ethnicity	education, financial stress	BMI	secondhand smoke exposure		D	L	L	L	L	L	L	L
Wills (2020)	age	sex	race/ethnicity		BMI (overweight status, obesity status)		marijuana use		L	L	L	L	L	L	L
Wills (2022)	age	sex	race/ethnicity	education	BMI		marijuana use	C	L	L	L	L	L	L	L
Wen (2023)	age	All women	race/ethnicity	education, insurance, marital status	BMI pre-pregnancy		pre-pregnancy diabetes, hypertension		L	L	L	L	L	L	L
Xie (2020a)	age	sex	race/ethnicity	marital status, education, income, employment status	BMI		general health	S	L	L	L	L	L	L	L
Xie (2020b)	age	sex	race/ethnicity	education, region	BMI	other combustible products	use of illicit substances (i.e., heroin, inhalants, or hallucinogens), hypertension, cholesterol, heart failure, stroke, diabetes	D	L	L	L	L	L	L	L
Xie (2020c)	age	sex		employment, education, income	BMI, physical activity		general health, mental health, alcohol, cannabis use	S	L	L	L	L	L	L	L
Xie (2022)	age	sex	race		BMI	cigar, cigarillo, filtered cigar, pipe, hookah, smokeless, snus exposure, secondhand smoke	marijuana use, other recreational drug use	C	L	L	L	L	L	L	L

Table S3. Potential confounders and risk of bias

Study	Potential confounders								Risk of bias* (ROBINS-E)						
	Age	Sex	Race/ ethnicity	Education, socioeconomic status	BMI	other tobacco product use	comorbid conditions	Former smoking†	Confounding	Exposure measurement	Participant selection	Missing data	Outcome measurement	Selection of reported result	Overall
Zhang (2022)	age	sex	race/ethnicity	education	BMI, physical activity	smokeless tobacco	history of heart disease, cancer, depressive disorder, COPD, asthma, test for blood sugar in past 3 years	C	L	L	L	L	L	L	L
Zhu (2023)	age	all male		marital status	BMI		drinking		L	L	L	L	L	L	L

* L=low, M=moderate, H=high. Domain 4: Risk of bias due to post-exposure interventions excluded because no studies had post-exposure interventions.
† C = control for former smoking as covariate; S = stratify on former smoking; D = duration of smoking (years or pack years) as covariate
‡ Age included in propensity matching but not multivariable regressions

Table S4. Studies that used the same dataset to study the same outcome in the same year*							
Year	**BFRSS**	**NHANES**	**NHIS**	**PATH**	**PRAMS**	**YRBSS**	**Other†**
2012							***Asthma (youth)*** Choi (2016)
2013							***Asthma (youth)*** Kim (2017) Wang (2016)
2014				***Cardiovascular*** Gathright (2019) ***COPD*** Perez (2019b) Strong (2018) ***Oral disease*** Vora (2019) ***Oral disease (youth)*** Akinkugbe (2019)			***Asthma (youth)*** Cho (2016) McConnell (2017)
2015				***Asthma*** Li (2020)			***Metabolic*** Kim (2020b) ***Oral disease*** Jeong (2020)
2016	***Stroke*** Bricknell (2021) ***Asthma*** Wills (2019) ***COPD*** Barrameda (2021) ***Oral disease*** Huilgol (2019)	***Other*** Hong (2021) Wiener (2020)	***Cardiovascular*** Alzahrani (2018)	***Metabolic*** Miller (2021) ***Asthma*** Bhatta (2020) Sargent (2022) Schneller (2020) ***COPD*** Bhatta (2020) ***Oral disease*** Atuegwu (2019b)	***Other*** Wang (2020)		***Cardiovascular*** Alzahrani (2018) ***Asthma*** Wills (2019) ***Asthma (youth)*** Bayly (2019) ***COPD*** Hedman (2018) ***Oral disease (youth)*** Cho (2017)
2017	***Cardiovascular*** Osei (2019a) ***Stroke*** Parekh (2020a) ***Metabolic*** Atuegwu (2019a) ***Asthma*** Osei (2019b) Parekh (2020b) Perez (2019a) Varella (2022) Walker (2021) ***COPD*** Giovanni (2020) Osei (2020) Parekh (2020b) Xie (2020a) ***Other*** Christian (2023) Xie (2020c)			***Cardiovascular*** Farsalinos (2019) ***Asthma (youth)*** Tanski (2022) ***Asthma*** Brunette (2023)	***Other*** Hawkins (2021)	***Asthma (youth)*** Han (2020)‡ Wills (2020)‡	***Metabolic*** Kim (2020a) ***Asthma (youth)*** Schweitzer (2017)

Table S4. Studies that used the same dataset to study the same outcome in the same year*							
Year	**BFRSS**	**NHANES**	**NHIS**	**PATH**	**PRAMS**	**YRBSS**	**Other†**
2018	***Metabolic*** Zhang (2022) ***Asthma*** Bircan (2021) Tran (2020) ***COPD*** Antwi (2022) Bircan (2021) ***Other*** Tian (2022)	***Cardiovascular*** Patel (2022) ***Metabolic*** Cai (2023) Okafor (2022) ***Oral disease*** AlQobaly (2022) ***Other*** Agoons (2021) Zhu (2023)	***Cardiovascular*** Falk (2022) ***Stroke*** Falk (2022) ***Metabolic*** Falk (2022) ***Other*** Wang (2022)	***Cardiovascular*** El-Shahawy (2022) Qeadan (2023) ***Metabolic*** Shi (2022) ***Asthma*** Boyd (2021) Cordova (2022) Xie (2020b) ***Asthma (youth)*** Reddy (2021) Stevens (2022) Tackett (2020) ***COPD*** Cordova (2022) Qeadan (2023) Xie (2020b) ***Oral disease*** Chaffee (2022)	***Other*** McBride (2021) Regan (2021)		***Asthma*** To (2023) ***Asthma (youth)*** Chung (2020) Tackett (2023) ***COPD*** Kim (2021) ***Other*** Wang (2022) To (2023) Zhu (2023)
2019			***Asthma*** Lee (2023)	***Cardiovascular*** Berlowitz (2022) Hirschtick (2022) Mahoney (2022) ***Stroke*** Hirschtick (2022) ***Metabolic*** Cook (2023a) ***Asthma*** Xie (2022) ***Asthma (youth)*** Patel (2023) ***COPD*** Paulin (2022) Cook (2023b) ***Oral disease*** Silveira (2022)			***Cardiovascular*** Goldberg Scott (2023) ***Stroke*** Goldberg Scott (2023) ***Metabolic*** Kim (2022) ***Asthma*** Braymiller (2020) ***Asthma (youth)*** Alnajem (2020) ***COPD*** Goldberg Scott (2023) ***Other*** Goldberg Scott (2023) §
2020	***Cardiovascular*** Liu (2022) ***Asthma*** Wills (2022) ***COPD*** Wills (2022)				***Other*** Wen (2023)		***Metabolic*** Sompa (2022) ***Asthma*** Sompa (2022) ***Asthma (youth)*** Chaffee (2021a) Wiliams (2023) ***Other*** Gaiha (2020) Han (2023) Nguyen (2023)

Table S4. Studies that used the same dataset to study the same outcome in the same year*							
Year	**BFRSS**	**NHANES**	**NHIS**	**PATH**	**PRAMS**	**YRBSS**	**Other†**
2021			***Other*** Smith (2023) ***Other: COVID*** Ebrahmi Kalan (2023) Moyers (2023)				***Oral disease (youth)*** Chaffee (2021b)
Total studies	26	8	9	39	5	2	35
Studies sharing datasets	14	2	2	27	0	2	0

*Based on last year of data collection. For "Other" outcomes, see Table S2.
†Studies in which no two studies used the same dataset for the same outcome and year. Datasets are: Canadian Community Health Survey, Florida Youth Tobacco Survey, Hawaii BRFSS, Hawaii YRBSS, Hong Kong Youth Survey, Kaiser Permanente Research Bank, KNHANES, KYRBS, KYRBWS, Korea Community Health Survey, Obstructive Lung Disease in Northern Sweden, Southern California Children's' Health Study, Southern California Happiness and Health Study, investigator-initiated surveys.
‡Both used YRBSS is 2017.
§ Contributed two "Other" outcomes: health services utilization and cancer.

Table S5. Study Characteristics (number of ORs/total)								
	Cardiovascular	**Stroke**	**Metabolic dysfunction**	**Asthma**	**COPD**	**Oral disease**	**Other**	**All studies**
Study design								
Cross-sectional[a]	7/12 (58%)	4/6 (67%)	10/12 (83%)	32/42 (76%)	13/20 (65%)	8/10 (80%)	20/22 (91%)	94/124 (76%)
Reference condition: Never use[b]	5/12 (42%)	2/6 (33%)	2/12 (17%)	23/42 (55%)	6/20 (30%)	3/10 (30%)	14/22 (64%)	55/124 (44%)
Disease measure: Current[c]	6/12 (50%)	2/6 (33%)	9/12 (75%)	39/42 (93%)	9/20 (45%)	7/10 (70%)	18/22 (82%)	90/124 (73%)
Source of OR estimates: Multivariable modeling[d]								
Ecig vs Cig	4/8 (50%)	1/5 (20%)	0/6 (0%)	14/29 (48%)	5/11 (45%)	5/9 (56%)	3/14 (21%)	32/82 (39%)
Dual vs Cig	5/12 (42%)	2/6 (33%)	3/10 (30%)	24/39 (62%)	9/17 (53%)	7/9 (78%)	8/20 (40%)	58/113 (51%)
Ecig vs none	5/11 (56%)	2/5 (40%)	4/11 (36%)	24/41 (59%)	10/19 (53%)	6/10 (60%)	8/20 (40%)	60/117 (51%)
Dual vs none	0/6 (0%)	0/3 (0%)	1/5 (20%)	1/13 (8%)	0/7 (0%)	0/2 (0%)	0/11 (0%)	2/47 (4%)
Cig vs none	3/9 (33%)	1/4 (25%)	1/7 (14%)	15/30 (50%)	5/12 (42%)	6/9 (67%)	2/15 (13%)	33/86 (38%)
Control for former smoking	3/12 (25%)	3/6 (50%)	2/12 (17%)	15/42 (36%)	12/20 (60%)	2/10 (20%)	2/22 (9%)	39/124 (31%) [e]
Sample: Adult[e]	12/12 (100%)	6/6 (100%)	10/10 (100%)	22/42 (52%)	20/20 (100%)	7/10 (70%)	19/22 (86%)	98/134 (79%)

[a] Remaining ORs longitudinal
[b] Remaining ORs non-current e-cigarette use
[c] Remaining ORs ever disease
[d] Remaining ORs stratified modeling
[e] Of the 39 ORs that controlled for former smoking, 17 (44%) did so my including smoking status (current, former, never) in a multivariate model, 16 (41%) stratified on smoking status, 5 (13%) included smoking duration (years or pack years) in a multivariate model, and 1 (3%) included both smoking status and duration in a multivariate model.
[f] Remaining studies youth

Table S6. Unadjusted p values from sensitivity analysis of odds ratios to study characteristics* controlling for outcome†

Odds ratio	Longitudinal vs cross-section	Reference (never vs non-current use)	Diagnosis (current vs ever)	Multivariate vs stratified estimate	Former smoking (vs not considering)	Year
E-cigarette vs cigarette‡	0.814	0.930	0.797	0.918	0.652	0.953
Dual use vs cigarette	0.028§	0.056	0.543	0.004¶	0.469	0.009º
E-cigarette vs no product use	0.233	0.311	0.585	0.574	0.071	0.009#
Dual use vs no product use	0.186	0.187	0.956	^	0.262	0.234
Cigarette vs no product use	0.941	0.987	0.970	0.502	0.969	0.218

* P values for coefficients in a metaregression of the natural logarithm of the odds ratios against study design characteristics (longitudinal vs. cross-sectional; whether the reference condition was never use or non-current use, whether product use was current or ever, whether the diagnosis was current or ever, and whether the estimate was based on multivariate or stratified estimates, whether the analysis accounted for former smoking (coded as 0/1 dummy variables), and last year of data collection (continuous, centered on 2017) controlling for the outcome (6 effects coded dummy variables; "Other" is coded as -1 for the 6 dummy variables).

† Outcome effects coded dummy variables for outcome (not shown)

‡ An additional model found that whether the OR was computed or from direct observation did not significantly affect the results (p=0.914).

§ $OR_{\text{longitudinal vs cross-sectional}} = 0.85$; 95% CI 0.73-0.98.

¶ $OR_{\text{multivariate vs stratified}} = 0.94$; 95% CI 0.90-0.98.

º $OR_{\text{per year}} = 0.96$; 95% CI 0.93-0.99

$OR_{\text{per year}} = 0.97$; 95% CI 0.95-0.99

^ Dropped from model due to collinearity.

Table S7. Pooled adjusted* odds ratios of disease (95% CI) based only on studies that reported odds ratios						
	Cardiovascular	**Stroke**	**Metabolic dysfunction**	**Asthma**	**COPD/respiratory**	**Oral disease**
Comparison to cigarette use						
E-cigarettes vs cigarettes	0.87 (0.58-1.31)	0.72 (0.45-1.159)	1.00 (0.88-1.12)	0.88 (0.77-1.00)	0.51 (0.35-0.74)	0.87 (0.75-1.00)
Dual use vs. cigarettes	1.28 (1.05-1.48)	1.25 (1.05-1.48)	1.25 (1.16-1.34)	1.21 (1.12-1.29)	1.50 (1.24-1.83)	1.39 (1.12-1.73)
Comparison to no use						
E-cigarette vs. non use	1.28 (1.06-1.55)	1.17 (0.77-1.80)	1.26 (1.18-1.34)	1.24 (1.18-1.31)	1.53 (1.36-1.72)	1.53 (1.21-1.94)
Dual use vs. non use	2.53 (1.76-3.47)	2.43 (2.05-2.88)	1.66 (1.16-2.40)	1.48 (1.07-2.05)	4.65 (3.48-6.21)	1.78 (1.49-2.12)
Cigarette vs. non use	1.61 (1.15-2.26)	2.07 (1.89-2.27)	1.27 (1.14-1.40)	1.49 (1.27-1.76)	3.30 (2.46-4.42)	1.74 (1.44-2.12)
* Adjusted for covariates listed in Table S3						

Table S8. Unadjusted p values from sensitivity analysis of odds ratios comparing adults and youth					
	Ecig vs Cig	**Dual vs Cig**	**Ecig vs Nonuse**	**Dual vs Nonuse**	**Cig vs Nonuse**
Asthma	0.739	0.376	0.574	0.617	0.915
Oral disease	0.924	0.264	0.108	NA	0.128
NA: Not available due to small sample size.					

Table S9. Unadjusted p values for heterogeneity within disease outcomes*						
	Cardiovascular	**Stroke**	**Metabolic dysfunction**	**Asthma**	**COPD**	**Oral disease**
E-cigarette vs cigarette	0.166	1.000	NA	0.005†	0.200	0.341
Dual use vs cigarette	0.276	1.000	0.395	0.172	0.025¶	0.537
E-cigarette vs no product use	0.104	1.000	0.636	0.321	0.037#	0.797
Dual use vs no product use	NA	1.000	NA	0.010‡	0.036º	NA
Cigarette vs no product use	0.003¥	1.000	0.313	0.002§	0.124	0.720

* P values for coefficients in a metaregression of the natural logarithm of the odds ratios against specific outcomes
P=1.000 for stroke because there is no heterogeneity; all outcomes are stroke
NA = Not available due to sample size

† For asthma: $OR_{ecig\ vs\ cig}$ = 0.93; 95% CI 0.82-1.05
For wheezing: $OR_{ecig\ vs\ cig}$ = 0.62; 95% CI 0.50-0.77

‡ For asthma: $OR_{dual\ vs\ no\ use}$ = 1.33; 95% CI 1.08-1.63
For wheezing: OR_{dual} = 2.64; 95% CI 2.26-3.08

§ For asthma: OR_{cig} = 1.38; 95% CI 1.24-1.54
For wheezing: OR_{cig} = 2.14; 95% CI 1.66-2.75

¶ For COPD: $OR_{dual\ vs\ cig}$ = 1.38; 95% CI 1.22-1.57
For respiratory symptoms: $OR_{dual\ vs\ cig}$ = 1.57; 95% CI 0.82-3.00

For COPD: $OR_{dual\ vs\ cig}$ = 1.59; 95% CI 1.40-1.80
For respiratory symptoms: $OR_{dual\ vs\ cig}$ = 1.20; 95% CI 1.04-1.37

º For COPD: OR_{dual} = 4.11; 95% CI 3.03-5.58
For respiratory symptoms: OR_{dual} = 1.16; 95% CI 0.95-1.42

¥ For myocardial infarction: OR_{cig} = 2.72; 95% CI 2.41-3.07
For composite: OR_{cig} = 1.40; 95% CI 1.27-1.54
For erectile dysfunction: OR_{cig} = 1.05; 95% CI 0.68-1.62
For coronary heart disease: OR_{cig} = 1.73; 95% CI 1.46-2.05
For heart failure: OR_{cig} = 0.92; 95% CI 0.75-1.13

Table S10. Sensitivity analysis of meta-analyses of e-cigarettes vs cigarettes assuming ORs for e-cigarettes and cigarettes are independent, OR (95%CI)		
	Main model	**Assuming SEs cut by factor of 4**
Cardiovascular disease	0.81 (0.58-1.14)	0.77 (0.56-1.06)
Stroke	0.73 (0.47-1.13)	0.69 (0.46-1.03)
Metabolic dysfunction	0.99 (0.91-1.09)	1.04 (0.92-1.16)
Asthma/bronchitis	0.84 (0.75-0.95)	0.85 (0.76-0.95)
COPD/respiratory	0.53 (0.38-0.74)	0.53 (0.39-0.73)
Oral disease	0.87 (0.76-1.00)	0.87 (0.76-1.00)

Table S11. Unadjusted p values for Begg and Egger tests* for publication bias						
Odds ratio	**Cardiovascular**	**Stroke**	**Metabolic Dysfunction**	**Asthma**	**COPD/respiratory**	**Oral disease**
E-cigarette vs cigarette	0.711/0.869	0.999/0.040†	0.707/0.849	0.866/0.899	0.876/0.288	0.466/0.868
Dual use vs cigarette	0.837/0.693	0.707/0.321	0.858/0.595	0.397/0.987	0.902/0.872	0.602/0.701
E-cigarette vs nonuse	0.999/0.262	0.462/0.679	0.350/0.225	0.694/0.966	0.484/0.710	0.371/0.674
Dual use vs nonuse	0.707/0.464	0.999/0.719	0.462/0.637	0.951/0.646	0.368/0.340	0.999/NA
Cigarette vs non-use	0.754/0.723	0.999/0.530	0.999/0.601	0.830/0.736	0.945/0.999	0.466/0.151
* Display: (p value for Begg)/(p value for Egger) †This one statistically significant result may be a statistical artifact of doing 60 tests. NA Not available; inadequate data to compute						

Table S12. Trim and fill analysis of publication bias (random effects model)						
	Original estimate			After fill and trim		
	OR	95% CI	No. studies	OR	95% CI	No. studies
E-cigarette vs cigarette						
Cardiovascular	0.81	(0.58-1.14)	8	0.81	(0.58-1.14)	8
Stroke	0.73	(0.47-1.13)	5	0.73	(0.47-1.13)	5
Metabolic	0.99	(0.91-1.09)	6	0.99	(0.91-1.09)	6
Asthma	0.84	(0.75-0.95)	29	0.77	(0.68-0.87)	34
COPD	0.53	(0.38-0.74)	11	0.35	(0.18-0.51)	17
Oral disease	0.87	(0.76-1.00)	9	0.87	(0.76-1.00)	9
Dual use vs cigarette						
Cardiovascular	1.23	(1.05-1.46)	12	1.00	(0.81-1.25)	16
Stroke	1.26	(1.06-1.50)	6	1.23	(1.04-1.45)	7
Metabolic	1.22	(1.15-1.31)	10	1.22	(1.15-1.31)	10
Asthma	1.20	(1.12-1.28)	39	1.20	(1.12-1.28)	39
COPD	1.41	(1.12-1.64)	17	1.41	(1.19-1.67)	17
Oral disease	1.27	(1.15-1.39)	9	1.36	(1.12-1.64)	9
E-cigarette vs nonuse						
Cardiovascular	1.24	(1.05-1.46)	11	1.24	(1.05-1.46)	11
Stroke	1.32	(0.99-1.76)	5	1.32	(0.99-1.76)	5
Metabolic	1.25	(1.18-1.33)	11	1.25	(1.15-1.34)	13
Asthma	1.24	(1.19-1.40)	41	1.21	(1.15-1.27)	47
COPD	1.46	(1.31-1.61)	19	1.46	(1.31-1.61)	19
Oral disease	1.27	(1.19-1.82)	10	1.47	(1.19-1.82)	10
Dual use vs nonuse						
Cardiovascular	2.23	(1.59-3.14)	6	2.23	(1.59-3.14)	6
Stroke	2.39	(2.02-2.83)	3	2.39	(2.02-2.83)	3
Metabolic	1.49	(1.17-1.91)	5	1.49	(1.17-1.91)	5
Asthma	1.56	(1.22-2.00)	13	1.60	(1.21-2.00)	13
COPD	3.29	(1.97-5.51)	7	3.29	(1.97-5.51)	7
Oral disease	1.78	(1.49-2.12)	2	1.78	(1.45-2.12)	2
Cigarette vs nonuse						
Cardiovascular	1.64	(1.24-2.16)	9	1.63	(1.24-2.15)	8
Stroke	2.08	(1.91-2.27)	4	2.05	(1.60-2.63)	5
Metabolic	1.27	(1.17-1.91)	7	1.24	(1.14-1.35)	6
Asthma	1.56	(1.34-1.80)	30	1.53	(1.32-1.75)	29
COPD	2.99	(2.29-3.92)	12	3.10	(2.21-4.36)	11
Oral disease	1.69	(1.40-2.03)	9	1.41	(1.12-1.78)	12

Table S13. Summary of qualitative findings in "other" studies*					
	E vs C (Fig 1)	**D vs C (Fig 2)**	**E vs nothing (Fig S1)**	**D vs nothing (Fig S2)**	**C vs nothing (Fig S3)**
Preterm birth (Hawkins 2021; Regan 2021; Wang 2020)	0	0	0	0, +	+
Low gestational weight (Wen 2023)	0	0	0	0	+
Not breastfeeding McBride 2021)	0	+	+		+
COVID (Ebrahimi Kalan 2023; Gaiha 2020; Moyers 2023)	0, 0, +	0, 0	0, 0, 0	+, 0	–, 0, –
Hospitalization/Emergency Dept. (Goldberg Scott, 2023; To 2023)	0	+, 0	0	+	0
Sleep apnea (Zhu 2023)	0	0	0	+	+
Sleep disorder (Christian 2023; Wiener 2020)	0	+, 0	0, +	+	+
Arthritis (Tian 2022)		+	+		
Atopic dermatitis (Smith 2023)			+		
Bone fracture (Agoons 2021)	0	0	0		+
Cancer (Goldberg Scott 2023)		+	0		
Difficulty concentrating (Xie 2020c)	0	+	+	+	+
Nonalcoholic fatty liver disease (Han 2023)		+		+	+
General health (Wang 2022)	0	+	+	+	+
Impaired vision (Nguyen 2023)					
Oral HPV (Hong 2021)	0	+	+		0
* + = OR 95% confidence interval above 1.0; 0 = OR 95% CI includes 1.0. – = OR 95% CI below 1.0. E = e-cigarette, C = cigarette, D = dual use					

Table S14. Explanation for GRADE level of confidence ratings for e-cigarette vs. cigarette and dual use vs cigarette OR	
Criteria	**Rating and justification**
1. Risk of bias	
Bias occurs when the results of a study do not represent the truth because of inherent limitations in design or conduct of a study. In practice, it is difficult to know to what degree potential biases influence the results and therefore certainty is lower in the estimated effect if the studies informing the estimated effect could be biased. GRADE is used to rate the body of evidence at the *outcome level* rather than the study level. Authors must, therefore, make a judgement about whether the risk of bias in the individual studies is sufficiently large that their confidence in the estimated treatment effect is lower.	All studies included in this meta-analysis had low risk of bias (Table S3), yielding high confidence according to the ROBINS-E standard for observational studies.
2. Imprecision	
The GRADE approach to rating imprecision focuses on the 95% confidence interval around the best estimate of the *absolute effect*† Certainty is lower if the clinical decision is likely to be different if the true effect was at the upper versus the lower end of the confidence interval. Authors may also choose to rate down for imprecision if the effect estimate comes from only one or two small studies or if there were few events.	Except for oral disease where the upper 95% CI was just below 1.0 (p=0.042), conclusions about comparisons of e-cigarette to cigarette had high confidence because the 95% CIs either broadly spanned 1.0 (with correspondingly large p values: 0.221 for cardiovascular. 0.154 for stroke, and 0.886 for metabolic dysfunction; Table 1) or clearly excluded 1.0 (with correspondingly small p values: 0.007 for asthma and <0.001 for COPD). Because one of the estimates of the upper 95% confidence interval fall below 1.0 when dropping individual studies for cardiovascular disease and four for oral disease do (Figure S6), the confidence for imprecision is moderate for cardiovascular and oral disease for the e-cigarette to cigarette comparison. All comparisons of dual use to cigarette odds had a p value near 0.05 for cardiovascular disease (p=0.064), so we score imprecision as moderate for this outcome. All the other assessments have high confidence because the 95% CI's broadly exclude 1.0 (p≤0.009 in those cases).
3. Inconsistency	
Certainty in a body of evidence is highest when there are several studies that show consistent effects. When considering whether or not certainty should be rated down for inconsistency, authors should inspect the similarity of point estimates and the overlap of their confidence intervals, as well as statistical criteria for heterogeneity (e.g., the I^2 and chi-squared test).‡	The studies were broadly consistent regarding to exposure and outcome measures, using similar measures of exposure (e-cigarette and cigarette use in the past 30 days) and disease presence (mostly self-report of diagnosis using similar validated questions). In the sensitivity analysis for the effects of study characteristics (Table S6), there were several significant p values for dual use vs. cigarettes, so inconsistency is rated moderate for all outcomes. There were not significant differences between the different detailed outcomes for cardiovascular disease, stroke, metabolic dysfunction, or oral disease for e-cigarette vs. cigarette use and dual use vs. cigarettes (p≥0.166; Table S9). There was significant heterogeneity for asthma for e-cigarettes vs. cigarettes and for COPD for dual use vs cigarettes and dual use vs no product use for COPD diagnosis vs respiratory symptoms, but none of these heterogeneities led to a change in qualitative conclusions (footnotes in Table S9). The results were insensitive to deleting individual studies (Figures S5 and S6) suggest that this heterogeneity did not materially affect the conclusions. Cardiovascular disease, stroke, metabolic dysfunction, and oral disease were rated high confidence and asthma for e-cigarette vs. cigarette and COPD for dual vs. cigarette moderate because the heterogeneity p values were significant.
4. Indirectness	

Table S14. Explanation for GRADE level of confidence ratings for e-cigarette vs. cigarette and dual use vs cigarette OR

Criteria	Rating and justification
Evidence is most certain when studies directly compare the interventions of interest in the population of interest, and report the outcome(s) critical for decision making. Certainty can be rated down if the patients studied are different from those for whom the recommendation applies. Indirectness can also occur when the interventions studied are different than the real outcomes (for example, a study of a new surgical procedure in a highly specialised centre only indirectly applies to centres with less experience). Indirectness also occurs when the outcome studied is a surrogate for a different outcome – typically one that is more important to patients.	Certainty was high because the samples were generally from large probability samples of the entire population, include the variety of e-cigarette use as consumer products in the general population. Outcomes and exposures were measured reasonably consistently across studies.
5. Publication bias	
Publication bias is perhaps the most vexing of the GRADE domains, because it requires making inferences about missing evidence. Several statistical and visual methods are helpful in detecting publication bias, despite having serious limitations. Publication bias is more common with observational data and when most of the published studies are funded by industry.	Certainty that publication bias does not account for results was high. While there were a few isolated indications of significant publication bias, they never appeared consistently across the four measures we used (funnel plots, Begg and Eger tests, and trim and fill analysis).
Overall certainty	
An overall GRADE quality rating can be applied to a body of evidence across outcomes, usually by taking the lowest quality of evidence from all of the outcomes that are critical to decision making. **Certainty** / **What it means** Very low – The true effect is probably markedly different from the estimated effect Low – The true effect might be markedly different from the estimated effect Moderate – The true effect is probably close to the estimated effect High – T true effect is similar to the estimated effect	We scored overall confidence using the lowest score for each situation, resulting in moderate confidence for most conclusions and high confidence for some (Table S15)

* Entries in this column are abridged direct quotes from *BMJ's* summary of the GRADE criteria.[6] Because we are assessing associations in populations, studies are not downgraded for being observational (as opposed to randomized controlled trials).
† None of the studies reported absolute effects. All assessments are based on reported OR (or other measures of association with disease diagnosis).
‡ I^2 is not a reliable measure of heterogeneity because of large sample sizes; see text for explanation.

Table S15. GRADE Level of Confidence Ratings*						
	Cardiovascular	**Stroke**	**Metabolic dysfunction**	**Asthma**	**COPD**	**Oral disease**
E-cigarette vs cigarette						
Risk of bias	High	High	High	High	High	High
Imprecision	Moderate	High	Moderate	High	High	Moderate
Inconsistency	High	High	High	Moderate	High	High
Indirectness	High	High	High	High	High	High
Publication bias	High	High	High	High	High	High
Overall	Moderate	High	Moderate	Moderate	High	Moderate
Dual vs cigarette						
Risk of bias	Moderate	High	High	High	High	High
Imprecision	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate
Inconsistency	High	High	High	High	Moderate	High
Indirectness	High	High	High	High	High	High
Publication bias	High	High	High	High	High	High
Overall	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate
E-cigarette vs nothing						
Risk of bias	High	High	High	High	High	High
Imprecision	Moderate	Moderate	Moderate	High	High	High
Inconsistency	High	High	High	High	Moderate	High
Indirectness	High	High	High	High	High	High
Publication bias	High	High	High	High	High	High
Overall	Moderate	Moderate	Moderate	High	Moderate	High
Dual vs nothing						
Risk of bias	High	High	High	High	High	High
Imprecision	High	High	High	High	High	High
Inconsistency	High	High	High	Moderate	Moderate	Moderate
Indirectness	High	High	High	High	Moderate	High
Publication bias	High	High	High	High	High	High
Overall	High	High	High	Moderate	Moderate	Moderate
Cigarette vs nothing						
Risk of bias	High	High	High	High	High	High
Imprecision	High	High	High	High	High	High
Inconsistency	High	High	High	Moderate	High	High
Indirectness	High	High	High	High	High	High
Publication bias	High	High	High	High	High	High
Overall	High	High	High	Moderate	High	High
* See Table S14 for the logic for the e-cigarette vs. cigarette and dual use vs. cigarette comparisons. The logic for the other comparisons to no use follow similar logic.						

STATA DO FILES

```
*IMPORT DATA AND DO PRELIMINARY CALCULATIONS
local condensed_excel "Condensed-1Oct2023E.xlsx"
import excel `condensed_excel', sheet("Data") cellrange(A1:AW125) firstrow
label var study "Study"
label define outcome 10 "Cardiovascular disease" 20 "Asthma" 30 "COPD" 40 "Oral disease" 50 "Metabolic
dysfunction" ///
        60 "Stroke" 100 "Other",replace
label values outcome outcome
* create effects coded summmy variables for outcome
tabulate outcome, generate(outcome_)
replace outcome_1=-1 if outcome_7==1
replace outcome_2=-1 if outcome_7==1
replace outcome_3=-1 if outcome_7==1
replace outcome_4=-1 if outcome_7==1
replace outcome_5=-1 if outcome_7==1
replace outcome_6=-1 if outcome_7==1
drop outcome_7
label var outcome2 "Detailed outcome"
label define outcome2 11 "Composite (CHD, MI, stroke, CVD)" 12 "Myocardial infarction" 13 "Stroke" 14  "Erectile
dysfunction" ///
        15 "Heart failure" 16 "Hypertension" 17 "CHD" ///
        21 "Asthma" 22 "Wheezing/cough" 23 "Bronchitis" ///
        31 "COPD" 32 "Respiratory symptoms" ///
        41 "Poor oral health" 42 "Periodontitis/gum disease" 43 "Dry mouth" 44 "Loose/lost tooth" ///
        51 "Metabolic syndrome" 52 "Hypertension" 53 "Prediabetes" 54 "Waist circumference" ///
        61 "Stroke"  ///
        101 "Bone fracture" 102 "Cancer" 103 "Skin cancer" 104 "COVID" 105 "Obesity" 106 "General health" 107
"Depression" ///
        108 "Arthritis" 109 "Oral HPV" 110 "Sleep disorder" 111 "Difficulty concentrating" 112 "Preterm birth"
///
        113 "Not breastfeeding" 114 "Low gestational weight gain" 115 "Fatty liver disease" 116
"Hospitalization/ED" 117 "Sleep apnea" ///
        118 "Impaired visiion" 119 "Atopic dermatitis", replace
label values outcome2 outcome2
label var samplesize "Sample size of study"
label var adult "Adult or Youth sample"
label define adult 0 "Adult (min age 18+)" 1 "Youth (min age <18)"
label values adult adult

label var year "Last year data collected"
gen year_c=year-2017
label var year_c "Last year data collected (centered on 2016.5)"
label var diagnosis "When diagnosed"
label define diagnosis 0 "Current (usually last 12 mo)" 1 "Ever"
label values diagnosis diagnosis
label var longitudinal "Longitudinal or cross-section"
label define longitudinal 1 "Longitudinal" 0 "Cross-sectional"
label values longitudinal longitudinal
label var reference "Reference condition"
label define reference 0 "Never use" 1 "Non-current use"
label values reference reference
label var n_shared "Number of studies sharing same dataset"
label var model "Statistical model"
label define model 1 "Multivariate" 2 "Stratified" 3 "Both"
label values model model

*SE inflators for cases where several studies used same dataset for same outcome
*in same year using Bonferroi correction.  (Numbers are ratios of Bonferroni-
*adjusted z values divided by 1.959964.
matrix SEinflator = (1, 1.143594, 1.221441, 1.274363, 1.314223, 1.346074)

label var EM "Ecig risk (multivariate)"
gen EM_ln=ln(EM)
gen EMlo_ln=ln(EMlo)
gen EMhi_ln=ln(EMhi)
gen EMse=(EMhi_ln-EMlo_ln)/(2*1.96)

label var ES "Ecig risk (stratified)"
gen ES_ln=ln(ES)
gen ESlo_ln=ln(ESlo)
gen EShi_ln=ln(EShi)
gen ESse=(EShi_ln-ESlo_ln)/(2*1.96)

label var CM "Cig risk (multivariate)"
gen CM_ln=ln(CM)
gen CMlo_ln=ln(CMlo)
```

```
gen CMhi_ln=ln(CMhi)
gen CMse=(CMhi_ln-CMlo_ln)/(2*1.96)

label var CS "Cig risk (stratified)"
gen CS_ln=ln(CS)
gen CSlo_ln=ln(CSlo)
gen CShi_ln=ln(CShi)
gen CSse=(CShi_ln-CSlo_ln)/(2*1.96)

label var DNM "Dual vs nothing (multivariate)"
gen DNM_ln=ln(DNM)
gen DNMlo_ln=ln(DNMlo)
gen DNMhi_ln=ln(DNMhi)
gen DNMse=(DNMhi_ln-DNMlo_ln)/(2*1.96)

label var DNS "Dual vs nothing (stratified)"
gen DNS_ln=ln(DNS)
gen DNSlo_ln=ln(DNSlo)
gen DNShi_ln=ln(DNShi)
gen DNSse=(DNShi_ln-DNSlo_ln)/(2*1.96)

label var DSM "Dual vs smoking (multivariate)"
gen DSM_ln=ln(DSM)
gen DSMlo_ln=ln(DSMlo)
gen DSMhi_ln=ln(DSMhi)
gen DSMse=(DSMhi_ln-DSMlo_ln)/(2*1.96)

label var DSS "Dual vs smoking (stratified)"
gen DSS_ln=ln(DSS)
gen DSSlo_ln=ln(DSSlo)
gen DSShi_ln=ln(DSShi)
gen DSSse=(DSShi_ln-DSSlo_ln)/(2*1.96)

label var ECM "Ecig vs cig (multivariate)"
gen ECM_ln=ln(ECM)
gen ECMlo_ln=ln(ECMlo)
gen ECMhi_ln=ln(ECMhi)
gen ECMse=(ECMhi_ln-ECMlo_ln)/(2*1.96)

label var ECS "Ecig vs cig (stratified)"
gen ECS_ln=ln(ECS)
gen ECSlo_ln=ln(ECSlo)
gen ECShi_ln=ln(ECShi)
gen ECSse=(ECShi_ln-ECSlo_ln)/(2*1.96)

label var EN "Ecig vs nothing among never smokers (stratified)"
gen EN_ln=ln(EN)
gen ENlo_ln=ln(ENlo)
gen ENhi_ln=ln(ENhi)
gen ENse=(ENhi_ln-ENlo_ln)/(2*1.96)

label var EN "Ecig vs nothing among former smokers (stratified)"
gen EF_ln=ln(EF)
gen EFlo_ln=ln(EFlo)
gen EFhi_ln=ln(EFhi)
gen EFse=(EFhi_ln-EFlo_ln)/(2*1.96)

/*Merge the multivariate and stratified results, selecting the smaller OR for the cases where both are available
These are the cases where there are both as of 1 Oct 2023:

. list study EM ES E if model==3
     +---------------------------------------+
     |            study     EM     ES      E |
     |---------------------------------------|
  9. |       Liu (2022)   1.17   1.25   1.17 |
 20. |       Cai (2023)    1.3    .75    .75 |
 26. |    Miller (2021)   1.31   1.32   1.31 |
 30. |     Zhang (2022)   1.22   1.54   1.22 |
 39. |       Cho (2016)   2.77   2.74   2.74 |
     |---------------------------------------|
 45. |       Lee (2023)   1.22   1.96   1.22 |
 48. | McConnell (2017)   1.24      .   1.24 |
 66. |      Wang (2016)   1.28   2.06   1.28 |
 69. |     Wills (2020)    1.3   1.29   1.29 |
 72. |       Xie (2022)   1.32   1.62   1.32 |
     |---------------------------------------|
 73. |     Antwi (2022)   1.53   3.17   1.53 |
 74. | Barrameda (2021)   1.83   4.36   1.83 |
 94. |  AlQobaly (2022)   1.38    .95    .95 |
```

```
104. |     Regan (2021)   1.09   1.69   1.09 |
118. |    Agoons (2021)   1.43      .   1.43 |
     +---------------------------------------+
*/
gen E=.
gen Elo=.
gen Ehi=.
label var E "Ecig risk"
gen whichE=.
label var whichE "Source of E pooled value"
label values whichE model
replace E=EM if model==1 | (model==3 & EM<ES)
replace Elo=EMlo if model==1 | (model==3 & EM<ES)  //EM<ES also handles ES missing
replace Ehi=EMhi if model==1 | (model==3 & EM<ES)
replace whichE=1 if model==1 | (model==3 & EM<ES)
replace E=ES if model==2 | (model==3 & ES<EM)
replace Elo=ESlo if model==2 | (model==3 & ES<EM)
replace Ehi=EShi if model==2 | (model==3 & ES<EM)
replace whichE=2 if model==2 | (model==3 & ES<EM)
replace whichE=. if E==.
gen E_ln=ln(E)
gen Elo_ln=ln(Elo)
gen Ehi_ln=ln(Ehi)
gen Ese=(Ehi_ln-Elo_ln)/(2*1.96)

*Inflate SE and CI to account for shared studies
gen EseI=Ese*SEinflator[1,n_shared]
gen Elo_lnI=E_ln-1.96*EseI
gen Ehi_lnI=E_ln+1.96*EseI

/* Here are studies where model=3 (both) for cig risks as of 1 Oct 2023:

. list study CM CS C if model==3
     +---------------------------------------+
     |            study     CM     CS      C |
     |---------------------------------------|
  9. |       Liu (2022)   1.45   1.35   1.35 |
 20. |       Cai (2023)      .      .      . |
 26. |    Miller (2021)   1.27      .   1.27 |
 30. |     Zhang (2022)      .      .      . |
 39. |       Cho (2016)   1.47      .   1.47 |
     |---------------------------------------|
 45. |       Lee (2023)   1.15      .   1.15 |
 48. | McConnell (2017)      .      .      . |
 66. |      Wang (2016)      .      .      . |
 69. |     Wills (2020)   1.24   1.23   1.23 |
 72. |       Xie (2022)      .   2.07   2.07 |
     |---------------------------------------|
 73. |     Antwi (2022)   4.75      .   4.75 |
 74. | Barrameda (2021)      .      .      . |
 94. |  AlQobaly (2022)   1.72      .   1.72 |
104. |     Regan (2021)      .      .      . |
118. |    Agoons (2021)      .   1.63   1.63 |
     +---------------------------------------+
*/

gen C=.
gen Clo=.
gen Chi=.
label var C "Cig risk"
gen whichC=.
label var whichC "Source of C pooled value"
label values whichC model
replace C=CM if model==1 | (model==3 & CM<CS)  //CM<CS handles CS missing
replace Clo=CMlo if model==1 | (model==3 & CM<CS)
replace Chi=CMhi if model==1 | (model==3 & CM<CS)
replace whichC=1 if model==1 | (model==3 & CM<CS)
replace C=CS if model==2 | (model==3 & CS<CM)
replace Clo=CSlo if model==2 | (model==3 & CS<CM)
replace Chi=CShi if model==2 | (model==3 & CS<CM)
replace whichC=2 if model==2 | (model==3 & CS<CM)
replace whichC=. if C==.
gen C_ln=ln(C)
gen Clo_ln=ln(Clo)
gen Chi_ln=ln(Chi)
gen Cse=(Chi_ln-Clo_ln)/(2*1.96)

*Inflate SE and CI to account for shared studies
gen CseI=Cse*SEinflator[1,n_shared]
```

```
gen Clo_lnI=C_ln-1.96*CseI
gen Chi_lnI=C_ln+1.96*CseI

*Compute OR for ecig vs cig comparison
*Multivariate
gen ECCMse_diff=sqrt(EMse^2+CMse^2)
gen ECCM_ln=EM_ln-CM_ln
gen ECCM=exp(ECCM_ln)
label var ECCM "Ecig v cig (computed, multivariate)"
gen ECCMlo_ln=ECCM_ln-1.96*ECCMse_diff
gen ECCMhi_ln=ECCM_ln+1.96*ECCMse_diff
gen ECCMlo=exp(ECCMlo_ln)
gen ECCMhi=exp(ECCMhi_ln)
*Stratified
gen ECCSse_diff=sqrt(ESse^2+CSse^2)
gen ECCS_ln=ES_ln-CS_ln
gen ECCS=exp(ECCS_ln)
label var ECCS "Ecig v cig (computed,  stratified)"
gen ECCSlo_ln=ECCS_ln-1.96*ECCSse_diff
gen ECCShi_ln=ECCM_ln+1.96*ECCSse_diff
gen ECCSlo=exp(ECCSlo_ln)
gen ECCShi=exp(ECCShi_ln)

* Compute EC from E and C
gen ECse=sqrt(Ese^2+Cse^2)
gen EC_ln=E_ln-C_ln
gen EC=exp(EC_ln)
label var EC "Ecig v cig"
gen EClo_ln=EC_ln-1.96*ECse
gen EChi_ln=EC_ln+1.96*ECse
gen EClo=exp(EClo_ln)
gen EChi=exp(EChi_ln)

/* When EC is computed both the E and C numbers come from the same kind of study
(multivariate or stratified) so we can use that to define whichEC*/
gen whichEC=.
label var whichEC "Source of EC estimate"
label values whichEC model
replace whichEC=whichE if EC<.   //In these cases whichE=whichC

/* These are comparisons of the computed ECs (EC) vs directly measured ECs (ECS) as of 1 Oct 2023:

. list study ECS EC if ECS<.
     +---------------------------------+
     |              study    ECS     EC |
     |---------------------------------|
  2. |  Berlowitz (2022)    .66    .66 |
  8. | Hirschtick (2022)     .3     .3 |
 16. | Hirschtick (2022)    .77    .77 |
 17. |    Parekh (2020a)    .43    .43 |
 18. |      Patel (2022)   1.15   1.15 |
     |---------------------------------|
 26. |     Miller (2021)    .96    .96 |
 27. |     Okafor (2022)   1.85   1.85 |
 46. |         Li (2020)    .61    .61 |
 69. |      Wills (2020)   1.06   1.06 |
 72. |        Xie (2022)    .78    .78 |
     |---------------------------------|
 85. |     Paulin (2022)    .71    .71 |
 89. |      Wills (2019)    .86    .86 |
 91. |       Xie (2020a)    .39    .39 |
106. |        Wen (2023)    .79    .79 |
122. |       Wang (2022)   1.22   1.22 |
     +---------------------------------+

Note that the computed values are very close to the directly observed values when we have both.
*/

*But, if there is a directly reported value of EC use that instead of the computed values.
*This will let us pick up a couple more values
gen directEC=.
replace directEC=0 if whichEC < .
replace directEC=1 if ECS < .
label var directEC "EC source"
label define directEC 0 "Computed" 1 "Direct estimate", replace
label values directEC directEC
replace whichEC=2 if directEC==1
replace EC=ECS if directEC==1
replace EClo=ECSlo if directEC==1
```

```
replace EChi=ECShi if directEC==1
replace EC_ln=ln(EC) if directEC==1
replace EClo_ln=ln(EClo) if directEC==1
replace EChi_ln=ln(EChi) if directEC==1
replace ECse=(EChi_ln-EClo_ln)/(2*1.96)
*/

/* There are no studies (as of 1 Oct 2023) that have dual vs nothing numbers for both multivariate
and stratified models, so merging the data doesn't have to account for model=3 (both)

. list study DNM DNS
     +-----------------------------------+
     |                study    DNM     DN |
     |-----------------------------------|
  1. |      Alzahrani (2018)      .      . |
  2. |      Berlowitz (2022)      .   1.54 |
  3. |     El-Shahawy (2022)      .      . |
  4. |     Farsalinos (2019)      .      . |
  5. |           Falk (2022)      .   3.84 |
     |-----------------------------------|
  6. |      Gathright (2019)      .   1.76 |
  7. | Goldberg Scott (2023)      .      . |
  8. |     Hirschtick (2022)      .   1.84 |
  9. |            Liu (2022)      .      . |
 10. |        Mahoney (2022)      .   1.85 |
     |-----------------------------------|
 11. |          Osei (2019a)      .   2.44 |
 12. |         Qeadan (2023)      .      . |
 13. |      Bricknell (2021)      .      . |
 14. |           Falk (2022)      .    2.4 |
 15. | Goldberg Scott (2023)      .      . |
     |-----------------------------------|
 16. |     Hirschtick (2022)      .   1.12 |
 17. |        Parekh (2020a)      .   2.91 |
 18. |          Patel (2022)      .      . |
 19. |       Atuegwu (2019a)      .      . |
 20. |            Cai (2023)      .      . |
     |-----------------------------------|
 21. |          Cook (2023a)      .   1.15 |
 22. |           Falk (2022)      .   1.66 |
 23. |           Kim (2020a)      .   2.79 |
 24. |           Kim (2020b)   1.13   1.13 |
 25. |            Kim (2022)      .      . |
     |-----------------------------------|
 26. |         Miller (2021)      .      . |
 27. |         Okafor (2022)      .      . |
 28. |            Shi (2022)      .   1.45 |
 29. |          Sompa (2022)      .      . |
 30. |          Zhang (2022)      .      . |
     |-----------------------------------|
 31. |        Alnajem (2020)      .   1.92 |
 32. |          Bayly (2019)      .      . |
 33. |         Bhatta (2020)      .      . |
 34. |         Bircan (2021)      .      . |
 35. |           Boyd (2021)      .      . |
     |-----------------------------------|
 36. |     Braymiller (2020)      .      . |
 37. |       Brunette (2023)      .      . |
 38. |       Chaffee (2021a)      .      . |
 39. |            Cho (2016)      .      . |
 40. |           Choi (2016)      .      . |
     |-----------------------------------|
 41. |          Chung (2020)      .    1.2 |
 42. |        Cordova (2022)      .     .8 |
 43. |            Han (2020)      .      . |
 44. |            Kim (2017)      .      . |
 45. |            Lee (2023)      .      . |
     |-----------------------------------|
 46. |             Li (2020)      .   2.83 |
 47. |      Mattingly (2023)      .   1.23 |
 48. |      McConnell (2017)      .      . |
 49. |          Osei (2019b)      .      . |
 50. |        Parekh (2020b)      .      . |
     |-----------------------------------|
 51. |          Patel (2023)      .   1.54 |
 52. |         Perez (2019a)      .      . |
 53. |          Reddy (2021)      .   2.22 |
 54. |        Sargent (2022)      .   2.13 |
 55. |      Schneller (2020)      .   1.52 |
```

56.	Schweitzer (2017)	.	.
57.	Sompa (2022)	.	3.6
58.	Stevens (2022)	.	.
59.	Tackett (2020)	.	.
60.	Tackett (2023)	.	.
61.	Tanski (2022)	.	.
62.	To (2023)	.	.
63.	Tran (2020)	1.41	1.41
64.	Varella (2022)	.	.
65.	Walker (2021)	.	.
66.	Wang (2016)	.	.
67.	Williams (2023)	.	.68
68.	Wills (2019)	.	1.26
69.	Wills (2020)	.	.
70.	Wills (2022)	.	.
71.	Xie (2020b)	.	.
72.	Xie (2022)	.	.
73.	Antwi (2022)	.	.
74.	Barrameda (2021)	.	.
75.	Bhatta (2020)	.	.
76.	Bircan (2021)	.	.
77.	Cook (2023b)	.	.
78.	Cordova (2022)	.	.
79.	Giovanni (2020)	.	1.16
80.	Goldberg Scott (2023)	.	.
81.	Hedman (2018)	.	.
82.	Kim (2021)	.	2.83
83.	Osei (2020)	.	6.89
84.	Parekh (2020b)	.	5.07
85.	Paulin (2022)	.	1.99
86.	Perez (2019b)	.	.
87.	Qeadan (2023)	.	.
88.	Strong (2018)	.	.
89.	Wills (2019)	.	3.92
90.	Wills (2022)	.	.
91.	Xie (2020a)	.	4.39
92.	Xie (2020b)	.	.
93.	Akinkugbe (2019)	.	1.72
94.	AlQobaly (2022)	.	.
95.	Atuegwu (2019b)	.	.
96.	Chaffee (2021b)	.	.
97.	Chaffee (2022)	.	1.8
98.	Cho (2017)	.	.
99.	Huilgol (2019)	.	.
100.	Jeong (2020)	.	.
101.	Silveira (2022)	.	.
102.	Vora (2019)	.	.
103.	Hawkins (2021)	.	1.03
104.	Regan (2021)	.	.
105.	Wang (2020)	.	2.07
106.	Wen (2023)	.	1.18
107.	McBride (2021)	.	.
108.	Ebrahimi Kalan (2023)	.	.
109.	Gaiha (2020)	.	6.84
110.	Moyers (2023)	.	.77
111.	Goldberg Scott (2023)	.	.
112.	To (2023)	.	2.13
113.	Zhu (2023)	.	1.78
114.	Christian (2023)	.	1.28
115.	Wiener (2020)	.	.
116.	Tian (2022)	.	.
117.	Smith (2023)	.	.
118.	Agoons (2021)	.	.
119.	Goldberg Scott (2023)	.	.
120.	Xie (2020c)	.	2.07

```
121. |            Han (2023)      .   1.47 |
122. |           Wang (2022)      .   1.84 |
123. |         Nguyen (2023)      .      . |
124. |           Hong (2021)      .      . |
     +--------------------------------------+
*/

*Inflate SE and CI to account for shared studies
gen ECseI=ECse*SEinflator[1,n_shared]
gen EClo_lnI=EC_ln-1.96*ECseI
gen EChi_lnI=EC_ln+1.96*ECseI

gen DN=.
gen DNlo=.
gen DNhi=.
label var DN "Dual vs. nothing"
gen whichDN=.
label var whichDN "Source of DN pooled value"
label values whichDN model
replace DN=DNM if model==1
replace DNlo=DNMlo if model==1
replace DNhi=DNMhi if model==1
replace whichDN=1 if model==1
replace DN=DNS if model==2
replace DNlo=DNSlo if model==2
replace DNhi=DNShi if model==2
replace whichDN=2 if model==2
replace whichDN=. if DN==.
gen DN_ln=ln(DN)
gen DNlo_ln=ln(DNlo)
gen DNhi_ln=ln(DNhi)
gen DNse=(DNhi_ln-DNlo_ln)/(2*1.96)

*Inflate SE and CI to account for shared studies
gen DNseI=DNse*SEinflator[1,n_shared]
gen DNlo_lnI=DN_ln-1.96*DNseI
gen DNhi_lnI=DN_ln+1.96*DNseI

/* Dual vs cig comparison

In the multivariate models that include only ecigs and cigs, the ecig vs nothing
risk is also the dual vs cigs risk because ecigs and cigs have independent effects.
Specifially, the ecig risk is also the marginal risk above smoking.

As a result, we have three different estimates of the dual vs cig comparison:

1. Estimate using the ecig vs nothing risk as an estimate of dual use vs cig risk (EM)
2. Direct estimates from multivariate models (DSM)
3. Direct estimates from stratified models (DSS)
4. Calculate estimate from stratified dual vs nothing (DNS) and cig vs nothing (CNS)
   [added to accomodate Chaffee (2022)](DSSSC)

Because there are a few studies in which we have multiple estimates, we will pick the
estimate with the smallest point estimates.
*/

* Compute DCCS from DSS and CS (for case 4)
gen DCCSse=sqrt(DNSse^2+CSse^2)
gen DCCS_ln=DNS_ln-CS_ln
gen DCCS=exp(DCCS_ln)
label var DCCS "Dual v cig stratified (computed)"
gen DCCSlo_ln=DCCS_ln-1.96*DCCSse
gen DCCShi_ln=DCCS_ln+1.96*DCCSse
gen DCCSlo=exp(DCCSlo_ln)
gen DCCShi=exp(DCCShi_ln)

gen DC=.
gen DClo=.
gen DChi=.
label var DC "Dual vs cig risk"
gen whichDC=.
label var whichDC "Source of DC pooled value"
label define whichDC 1 "Marginal multivariate marginal ecig risk" 2 "Direct multivariate" 3 "Direct Stratified"
4 "Computed stratified"
label values whichDC whichDC
*Find the smallest point estimate of the risk
gen DCmin=.
replace whichDC=1 if EM<.
replace DCmin=EM if EM<.
```

```
replace whichDC=2 if DSM<DCmin & DSM<.
replace DCmin=DSM if DSM<DCmin & DSM<.
replace whichDC=3 if DSS<DCmin & DSS<.
replace DCmin=DSS if DSS<DCmin & DSS<.
replace whichDC=4 if DCCS<DCmin & DCCS<. & DSS==.   //don't use computed value if directly reported value
replace DCmin=DCCS if DCCS<DCmin & DCCS<. & DSS==.

*Now store the selected values
replace DC=EM if whichDC==1
replace DClo=EMlo if whichDC==1
replace DChi=EMhi if whichDC==1
replace DC=DSM if whichDC==2
replace DClo=DSMlo if whichDC==2
replace DChi=DSMhi if whichDC==2
replace DC=DSS if whichDC==3
replace DClo=DSSlo if whichDC==3
replace DChi=DSShi if whichDC==3
replace DC=DCCS if whichDC==4
replace DClo=DCCSlo if whichDC==4
replace DChi=DCCShi if whichDC==4
gen DC_ln=ln(DC)
gen DClo_ln=ln(DClo)
gen DChi_ln=ln(DChi)
gen DCse=(DChi_ln-DClo_ln)/(2*1.96)
```

/* Here are the values as of 1 Oct 2023 (including code for case 4):

. list study EM DSM DNS CS DSS DCCS DC whichDC

	study	EM	DSM	DNS	CS	DSS	DCCS	DC	whichDC
1.	Alzahrani (2018)	1.79	.	.	.	.	.	1.79	Marginal multivariate marginal ecig risk
2.	Berlowitz (2022)	.	.	1.54	1.53	1.01	1.006536	1.01	Direct Stratified
3.	El-Shahawy (2022)	2.24	.	1.68	.	.	.	2.24	Marginal multivariate marginal ecig risk
4.	Farsalinos (2019)	1.31	.	.	.	.	.	1.31	Marginal multivariate marginal ecig risk
5.	Falk (2022)	.	.	3.84	2.84	.	1.352113	1.352113	Computed stratified
6.	Gathright (2019)	.	.	1.76	.92	.	1.913043	1.913043	Computed stratified
7.	Goldberg Scott (2023)	1.3	.	.	.	.	.	1.3	Marginal multivariate marginal ecig risk
8.	Hirschtick (2022)	.	.	1.84	1.99	.93	.9246231	.93	Direct Stratified
9.	Liu (2022)	1.17	.	.64	1.35	.	.4740741	.4740741	Computed stratified
10.	Mahoney (2022)	.	.	1.85	1.44	.	1.284722	1.284722	Computed stratified
11.	Osei (2019a)	.	.	2.44	.	1.36	.	1.36	Direct Stratified
12.	Qeadan (2023)	1.02	.	.	.	.	.	1.02	Marginal multivariate marginal ecig risk
13.	Bricknell (2021)	1.62	.	.	.	.	.	1.62	Marginal multivariate marginal ecig risk
14.	Falk (2022)	.	.	2.4	2.11	.	1.137441	1.137441	Computed stratified
15.	Goldberg Scott (2023)	1.65	.	.	.	.	.	1.65	Marginal multivariate marginal ecig risk
16.	Hirschtick (2022)	.	.	1.12	2.26	.5	.4955752	.5	Direct Stratified
17.	Parekh (2020a)	.	.	2.91	1.59	1.83	1.830189	1.83	Direct Stratified
18.	Patel (2022)	.	.	.	.	1.14	.	1.14	Direct Stratified
19.	Atuegwu (2019a)	.	.	.	.	.	.	.	.
20.	Cai (2023)	1.3	.	1.35	.	1.21	.	1.21	Direct Stratified
21.	Cook (2023a)	.	.	1.15	1.21	.	.9504132	.9504132	Computed stratified
22.	Falk (2022)	.	.	1.66	1.38	.	1.202899	1.202899	Computed stratified
23.	Kim (2020a)	.	.	2.79	1.47	1.57	1.897959	1.57	Direct Stratified
24.	Kim (2020b)	1.4	.	.	.	.	.	1.4	Marginal multivariate marginal ecig risk
25.	Kim (2022)	.	.	.	1.2	.	.	.	.
26.	Miller (2021)	1.31	.	1.77	.	1.3	.	1.3	Direct Stratified
27.	Okafor (2022)	.	.	.	.93	1.05	.	1.05	Direct Stratified
28.	Shi (2022)	.	.	1.45	1.39	.	1.043165	1.043165	Computed stratified
29.	Sompa (2022)	1.9	.	.	.	.	.	1.9	Marginal multivariate marginal ecig risk
30.	Zhang (2022)	1.22	.	1.14	.	.	.	1.22	Marginal multivariate marginal ecig risk
31.	Alnajem (2020)	.	.	1.92	1.73	.	1.109827	1.109827	Computed stratified
32.	Bayly (2019)	.9	.	.	.	.	.	.9	Marginal multivariate marginal ecig risk
33.	Bhatta (2020)	1.3	.	.	.	.	.	1.3	Marginal multivariate marginal ecig risk
34.	Bircan (2021)	.	.	.	.	.	.	.	.
35.	Boyd (2021)	1.09	.	.	.	.	.	1.09	Marginal multivariate marginal ecig risk
36.	Braymiller (2020)	.85	.	.	.	.	.	.85	Marginal multivariate marginal ecig risk
37.	Brunette (2023)	1.12	.	.	.	.	.	1.12	Marginal multivariate marginal ecig risk
38.	Chaffee (2021a)	1.36	.	.	.	.	.	1.36	Marginal multivariate marginal ecig risk
39.	Cho (2016)	2.77	.	.	.	1.3	.	1.3	Direct Stratified
40.	Choi (2016)	1.78	.	.	.	.	.	1.78	Marginal multivariate marginal ecig risk
41.	Chung (2020)	.	.	1.2	1.6	.	.75	.75	Computed stratified
42.	Cordova (2022)	.	.	.8	.8	.	1	1	Computed stratified
43.	Han (2020)	1.31	.	.	.	.	.	1.31	Marginal multivariate marginal ecig risk
44.	Kim (2017)	1.13	.	.	.	.	.	1.13	Marginal multivariate marginal ecig risk

45.	Lee (2023)	1.22	.	1.11	.	.	.	1.22	Marginal multivariate marginal ecig risk
46.	Li (2020)	.	.	2.83	2.75	1.03	1.029091	1.03	Direct Stratified
47.	Mattingly (2023)	.	.	1.23	1.71	.	.7192982	.7192982	Computed stratified
48.	McConnell (2017)	1.24	.	.	.	.	.	1.24	Marginal multivariate marginal ecig risk
49.	Osei (2019b)	1.39	.	.	.	.	.	1.39	Marginal multivariate marginal ecig risk
50.	Parekh (2020b)	.	2.11	.	1.49	.	.	2.11	Direct multivariate
51.	Patel (2023)	.	.	1.54	1.68	.	.9166666	.9166666	Computed stratified
52.	Perez (2019a)	.	.	.	.	.	.	.	.
53.	Reddy (2021)	.	.	2.22	1.78	1.24	1.247191	1.24	Direct Stratified
54.	Sargent (2022)	.	.	2.13	2.34	.	.9102564	.9102564	Computed stratified
55.	Schneller (2020)	.	.	1.52	3.93	.	.3867684	.3867684	Computed stratified
56.	Schweitzer (2017)	1.48	.	.	.	.	.	1.48	Marginal multivariate marginal ecig risk
57.	Sompa (2022)	.	.	3.6	1.6	.	2.25	2.25	Computed stratified
58.	Stevens (2022)	.	.	.	.	.	.	.	.
59.	Tackett (2020)	1.35	.	.	.	.	.	1.35	Marginal multivariate marginal ecig risk
60.	Tackett (2023)	1.55	.	.	.	.	.	1.55	Marginal multivariate marginal ecig risk
61.	Tanski (2022)	1.25	.	.	.	.	.	1.25	Marginal multivariate marginal ecig risk
62.	To (2023)	1.21	.	.	.	.	.	1.21	Marginal multivariate marginal ecig risk
63.	Tran (2020)	1.04	.	.	.	.	.	1.04	Marginal multivariate marginal ecig risk
64.	Varella (2022)	1.41	.	.	.	.	.	1.41	Marginal multivariate marginal ecig risk
65.	Walker (2021)	1.06	.	.	.	.	.	1.06	Marginal multivariate marginal ecig risk
66.	Wang (2016)	1.28	.	.	.	1.15	.	1.15	Direct Stratified
67.	Williams (2023)	.	.	.68	.79	.	.8607595	.8607595	Computed stratified
68.	Wills (2019)	.	.	1.26	1.27	.99	.992126	.99	Direct Stratified
69.	Wills (2020)	1.3	.	1.62	1.23	1.32	1.317073	1.3	Marginal multivariate marginal ecig risk
70.	Wills (2022)	1.2	.	.	.	.	.	1.2	Marginal multivariate marginal ecig risk
71.	Xie (2020b)	1.32	.	.	.	.	.	1.32	Marginal multivariate marginal ecig risk
72.	Xie (2022)	1.32	.	1.88	2.07	.91	.9082125	.91	Direct Stratified
73.	Antwi (2022)	1.53	.	.	.	.99	.	.99	Direct Stratified
74.	Barrameda (2021)	1.83	.	1.47	.	.	.	1.83	Marginal multivariate marginal ecig risk
75.	Bhatta (2020)	1.44	.	.	.	.	.	1.44	Marginal multivariate marginal ecig risk
76.	Bircan (2021)	.	.	.	.	.	.	.	.
77.	Cook (2023b)	1.1	.	.	.	.	.	1.1	Marginal multivariate marginal ecig risk
78.	Cordova (2022)	.	.	.	6.1	.	.	.	.
79.	Giovanni (2020)	.	.	1.16	.	.	.	.	.
80.	Goldberg Scott (2023)	.96	.	.	.	.	.	.96	Marginal multivariate marginal ecig risk
81.	Hedman (2018)	.	.	.	2.55	4.03	.	4.03	Direct Stratified
82.	Kim (2021)	.	.	2.83	2.26	.	1.252212	1.252212	Computed stratified
83.	Osei (2020)	.	.	6.89	.	1.66	.	1.66	Direct Stratified
84.	Parekh (2020b)	.	.	5.07	3.28	.	1.545732	1.545732	Computed stratified
85.	Paulin (2022)	.	.	1.99	1.92	1.04	1.036458	1.04	Direct Stratified
86.	Perez (2019b)	1.43	.	.	.	.	.	1.43	Marginal multivariate marginal ecig risk
87.	Qeadan (2023)	1.11	.	.	.	.	.	1.11	Marginal multivariate marginal ecig risk
88.	Strong (2018)	1.39	2.07	.	.	.	.	1.39	Marginal multivariate marginal ecig risk
89.	Wills (2019)	.	.	3.92	2.98	1.32	1.315436	1.32	Direct Stratified
90.	Wills (2022)	1.44	.	.	.	.	.	1.44	Marginal multivariate marginal ecig risk
91.	Xie (2020a)	.	.	4.39	3.8	1.16	1.155263	1.16	Direct Stratified
92.	Xie (2020b)	1.57	.	.	.	.	.	1.57	Marginal multivariate marginal ecig risk
93.	Akinkugbe (2019)	.	.	1.72	1.5	.	1.146667	1.146667	Computed stratified

```
 94. |       AlQobaly (2022)   1.38      .      .      .   1.65          .       1.38   Marginal multivariate marginal ecig risk |
 95. |       Atuegwu (2019b)   1.58      .      .      .      .          .       1.58   Marginal multivariate marginal ecig risk |
     |-----------------------------------------------------------------------------------------------------------------------------|
 96. |       Chaffee (2021b)    1.4      .      .      .      .          .        1.4   Marginal multivariate marginal ecig risk |
 97. |        Chaffee (2022)      .      .    1.8   1.76      .   1.022727   1.022727                         Computed stratified |
 98. |            Cho (2017)      1      .      .      .      .          .          1   Marginal multivariate marginal ecig risk |
 99. |        Huilgol (2019)   1.78      .      .      .      .          .       1.78   Marginal multivariate marginal ecig risk |
100. |          Jeong (2020)   2.33      .      .      .      .          .       2.33   Marginal multivariate marginal ecig risk |
     |-----------------------------------------------------------------------------------------------------------------------------|
101. |       Silveira (2022)   1.15      .      .      .      .          .       1.15   Marginal multivariate marginal ecig risk |
102. |           Vora (2019)      .      .      .    2.2      .          .          .                                          . |
103. |        Hawkins (2021)      .      .   1.03   1.28      .   .8046875   .8046875                         Computed stratified |
104. |          Regan (2021)   1.09      .    .82      .      .          .       1.09   Marginal multivariate marginal ecig risk |
105. |          Wang (2020)      .      .   2.07    1.6      .    1.29375    1.29375                         Computed stratified |
     |-----------------------------------------------------------------------------------------------------------------------------|
106. |            Wen (2023)      .      .   1.18   1.26    .93   .9365079        .93                           Direct Stratified |
107. |        McBride (2021)   1.59      .      .      .      .          .       1.59   Marginal multivariate marginal ecig risk |
108. | Ebrahimi Kalan (2023)      .      .      .    .67      .          .          .                                          . |
109. |          Gaiha (2020)      .      .   6.84   1.53      .   4.470589   4.470589                         Computed stratified |
110. |         Moyers (2023)      .      .    .77    .64      .   1.203125   1.203125                         Computed stratified |
     |-----------------------------------------------------------------------------------------------------------------------------|
111. | Goldberg Scott (2023)   1.17      .      .      .      .          .       1.17   Marginal multivariate marginal ecig risk |
112. |             To (2023)      .      .   2.13   1.72      .   1.238372   1.238372                         Computed stratified |
113. |            Zhu (2023)      .      .   1.78   1.38      .   1.289855   1.289855                         Computed stratified |
114. |      Christian (2023)      .      .   1.28   1.15      .   1.113043   1.113043                         Computed stratified |
115. |         Wiener (2020)   1.82      .      .      .      .          .       1.82   Marginal multivariate marginal ecig risk |
     |-----------------------------------------------------------------------------------------------------------------------------|
116. |           Tian (2022)      .      .      .      .   1.55          .       1.55                           Direct Stratified |
117. |          Smith (2023)   1.35      .      .      .      .          .       1.35   Marginal multivariate marginal ecig risk |
118. |         Agoons (2021)   1.43      .   2.41   1.63      .   1.478528       1.43   Marginal multivariate marginal ecig risk |
119. | Goldberg Scott (2023)     .8      .      .      .      .          .         .8   Marginal multivariate marginal ecig risk |
120. |           Xie (2020c)      .      .   2.07   1.49      .   1.389262   1.389262                         Computed stratified |
     |-----------------------------------------------------------------------------------------------------------------------------|
121. |            Han (2023)      .      .   1.47   1.22      .   1.204918   1.204918                         Computed stratified |
122. |           Wang (2022)      .      .   1.84   1.33   1.39   1.383459       1.39                           Direct Stratified |
123. |         Nguyen (2023)      .      .      .      .      .          .          .                                          . |
124. |           Hong (2021)   2.97      .      .      .      .          .       2.97   Marginal multivariate marginal ecig risk |
     +-----------------------------------------------------------------------------------------------------------------------------+
*/

*Make condensed version of whichDC that is just multivariate or stratified
gen whichDC_ms=whichDC
replace whichDC_ms=1 if (whichDC==1 | whichDC==2)
replace whichDC_ms=2 if (whichDC==3 | whichDC==4)
label values whichDC_ms model

*Inflate SE and CI to account for shared studies
gen DCseI=DCse*SEinflator[1,n_shared]
gen DClo_lnI=DC_ln-1.96*DCseI
gen DChi_lnI=DC_ln+1.96*DCseI

save metaanalysis.dta, replace

*now merge with study characteristics
clear
local condensed_excel "Condensed-1Oct2023D.xlsx"
import excel `condensed_excel', sheet("Citations") cellrange(A1:AD108) firstrow
drop B
drop Age-comorbidconditions
```

```
rename Y BMI
rename AA comorbid
label var former_smoking "Controlled for former smoking"
* Key for former_smoking strong values: C: Former smoking is covariate; S: Stratified on when smoked; P: Pack
years covariate; CP: Covariate and pack years
save "studycharacteristics.dta", replace
clear
*Now merge with info from data tab in master spreadsheet
use metaanalysis.dta
*The merge sorts results by study; we want them sorted by outcome
*This is to put the outcomes in the right order for meta-analysis output
gen sequence=_n
merge m:1 study using "studycharacteristics.dta"
sort sequence
drop sequence

*Create variable to indicate if former smoking considered in paper
gen former=0
label var former "Controlled for former smoking"
label define yesno 1 "Yes" 0 "No"
label values former yesno
replace former=1 if former_smoking !=""

save "metaanalysis+chars.dta", replace


*META-ANALYSES
*SE inflators for cases where several studies used same dataset for same outcome
*in same year using Bonferroi correction.  (Numbers are ratios of Bonferroni-
*adjusted z values divided by 1.959964.
matrix SEinflator = (1, 1.143594, 1.221441, 1.274363, 1.314223, 1.346074)

*meta-analyses (using inflated SEs)
metan EC_ln EClo_lnI EChi_lnI, random eform lcols(study outcome2) effect(OR) xlabel(.1,.2,.4,.6,.8,1,2,4,8) ///
       favours ("Cigarettes riskier" # "E-cigarettes riskier") aspect(1.30) texts(160) ///
       title("Ecig vs Cig", size(vsmall)) nooverall ///
       nobox saving(ECfancyI, replace) nowt by(outcome)
graph export ECfancyI.svg, as(svg) replace

metan DC_ln DClo_lnI DChi_lnI, random eform lcols(study outcome2) effect(OR) xlabel(.1,.2,.4,.8,1,2,4,6) ///
       favours ("Cigarettes riskier" # "Dual use riskier") aspect(1.30) texts(220)  title("Dual vs Cig", ///
       size(vsmall)) nooverall       nobox saving(DCfancyI, replace) nowt by(outcome)
graph export DCfancyI.svg, as(svg) replace

metan E_ln Elo_lnI Ehi_lnI, random eform lcols(study outcome2) effect(OR) xlabel(.1,.2,.4,.6,.8,1,2,4,8) ///
       favours ("Less disease" # "More disease") aspect(1.30) texts(220)  title("Ecig vs Nonuse", ///
       size(vsmall)) nooverall nobox saving(EfancyI, replace) nowt by(outcome)
graph export EfancyI.svg, as(svg) replace

metan C_ln Clo_lnI Chi_lnI, random eform lcols(study outcome2) effect(OR) xlabel(.1,.2,.4,.6,.8,1,2,4,8) ///
       favours ("Less disease" # "More disease") aspect(1.30) texts(160)  title("Cig vs Nonuse", ///
       size(vsmall)) nooverall nobox saving(CfancyI, replace) nowt by(outcome)
graph export CfancyI.svg, as(svg) replace

metan DN_ln DNlo_lnI DNhi_lnI, random eform lcols(study outcome2) effect(OR) xlabel(.1,.2, .4,.8,1,2,4,8) ///
       favours ("Less disease" # "More disease") aspect(0.7) texts(120)  title("Dual use vs Nonuse",
size(vsmall)) nooverall ///
       nobox saving(DNfancyI, replace) nowt by(outcome)
graph export DNfancyI.svg, as(svg) replace

* do analysis of asthma stratified by age
metareg EC_ln adult if outcome==20, eform wsse(ECseI)
metareg DC_ln adult if outcome==20, eform wsse(DCseI)
metareg E_ln adult if outcome==20, eform wsse(EseI)
metareg C_ln adult if outcome==20, eform wsse(CseI)
metareg DN_ln adult if outcome==20, eform wsse(DNseI)
metan EC_ln EClo_lnI EChi_lnI if outcome==20, random eform lcols (study) nograph by(adult)
metan DC_ln DClo_lnI DChi_lnI if outcome==20, random eform nograph lcols (study) by(adult)
metan E_ln Elo_lnI Ehi_lnI if outcome==20, random eform nograph lcols (study)by(adult)
metan C_ln Clo_lnI Chi_lnI if outcome==20, random eform nograph lcols (study) by(adult)
metan DN_ln DNlo_lnI DNhi_lnI if outcome==20, random eform lcols(study) by (outcome2) nograph

*Meta-analyses of cardiovascular outcomes stratifying on second level outcomes
metan EC_ln EClo_lnI EChi_lnI if outcome==10, random eform lcols(study) by (outcome2) nograph
metan DC_ln DClo_lnI DChi_lnI if outcome==10, random eform lcols(study) by (outcome2) nograph
metan E_ln Elo_lnI Ehi_lnI if outcome==10, random eform lcols(study) by (outcome2) nograph
metan C_ln Clo_lnI Chi_lnI if outcome==10, random eform lcols(study) by (outcome2) nograph
metan DN_ln DNlo_lnI DNhi_lnI if outcome==10, random eform lcols(study) by (outcome2) nograph
```

```
*Meta-analyses of asthma stratifying on astha vs wheeze
metan EC_ln EClo_lnI EChi_lnI if outcome==20, random eform lcols(study) by (outcome2) nograph
metan DC_ln DClo_lnI DChi_lnI if outcome==20, random eform lcols(study) by (outcome2) nograph
metan E_ln Elo_lnI Ehi_lnI if outcome==20, random eform lcols(study) by (outcome2) nograph
metan C_ln Clo_lnI Chi_lnI if outcome==20, random eform lcols(study) by (outcome2) nograph
metan DN_ln DNlo_lnI DNhi_lnI if outcome==20, random eform lcols(study) by (outcome2) nograph

*Meta-analyses on COPD stratifying on COPD vs respiratory conditions
metan EC_ln EClo_lnI EChi_lnI if outcome==30, random eform lcols(study) by (outcome2) nograph
metan DC_ln DClo_lnI DChi_lnI if outcome==30, random eform lcols(study) by (outcome2) nograph
metan E_ln Elo_lnI Ehi_lnI if outcome==30, random eform lcols(study) by (outcome2) nograph
metan C_ln Clo_lnI Chi_lnI if outcome==30, random eform lcols(study) by (outcome2) nograph
metan DN_ln DNlo_lnI DNhi_lnI if outcome==30, random eform lcols(study) by (outcome2) nograph

* check for age effect in oral diseases
metareg EC_ln adult if outcome==40, eform wsse(ECseI)
metareg DC_ln adult if outcome==40, eform wsse(DCseI)
metareg E_ln adult if outcome==40, eform wsse(EseI)
metareg C_ln adult if outcome==40, eform wsse(CseI)
*metareg DN_ln adult if outcome==40, eform wsse(DNseI) -- not enough cases
metan EC_ln EClo_lnI EChi_lnI if outcome==40, random eform lcols (study) nograph by(adult)
metan DC_ln DClo_lnI DChi_lnI if outcome==40, random eform nograph lcols (study) by(adult)
metan E_ln Elo_lnI Ehi_lnI if outcome==40, random eform nograph lcols (study)by(adult)
metan C_ln Clo_lnI Chi_lnI if outcome==40, random eform nograph lcols (study) by(adult)
metan DN_ln DNlo_lnI DNhi_lnI if outcome==40, random eform lcols(study) by (outcome2) nograph

* sensitivity analyses
metareg EC_ln longitudinal reference diagnosis whichEC former year_c outcome_1-outcome_6, eform wsse(ECseI)
metareg EC_ln longitudinal reference diagnosis whichEC directEC former year_c outcome_1-outcome_6, eform
wsse(ECseI)
metareg DC_ln longitudinal reference diagnosis whichDC former year_c  outcome_1-outcome_6, eform wsse(DCseI)
metareg E_ln  longitudinal reference diagnosis whichE  former year_c  outcome_1-outcome_6, eform wsse(EseI)
metareg C_ln  longitudinal reference diagnosis whichC  former year_c outcome_1-outcome_6, eform wsse(CseI)
metareg DN_ln longitudinal reference diagnosis whichC  former year_c outcome_1-outcome_6, eform wsse(DNseI)

*sensitivity analysis to see if cutting SE by factor of 4 for EC affects conclusion
gen ECse4I=ECseI/4
gen EClo_ln4I=EC_ln-1.96*ECse4I
gen EChi_ln4I=EC_ln+1.96*ECse4I
* set CIs
metan EC_ln EClo_ln4I EChi_ln4I, eform random nograph effect(OR) lcols(study) nooverall by(outcome)
drop ECse4I EClo_ln4I EChi_ln4I

*Heterogenuity analysis
quietly tabulate outcome2 if outcome==10, generate(cvd_)
quietly tabulate outcome2 if outcome==60, generate(stroke_)
quietly tabulate outcome2 if outcome==50, generate(meta_)
quietly tabulate outcome2 if outcome==20, generate(asthma_)
quietly tabulate outcome2 if outcome==30, generate(copd_)
quietly tabulate outcome2 if outcome==40, generate(oral_)

metareg EC_ln cvd_1-cvd_5 if outcome==10, wsse(ECseI) eform
*metareg EC_ln stroke_1 if outcome==60, wsse(ECseI) eform  all stroke studies have stroke as outcome
metareg EC_ln meta_1-meta_4 if outcome==50, wsse(ECseI) eform
metareg EC_ln asthma_1-asthma_3 if outcome==20, wsse(ECseI) eform
metareg EC_ln copd_1-copd_2 if outcome==30, wsse(ECseI) eform
metareg EC_ln oral_1-oral_4 if outcome==40, wsse(ECseI) eform

metareg DC_ln cvd_1-cvd_5 if outcome==10, wsse(DCseI) eform
metareg DC_ln meta_1-meta_4 if outcome==50, wsse(DCseI) eform
metareg DC_ln asthma_1-asthma_3 if outcome==20, wsse(DCseI) eform
metareg DC_ln copd_1-copd_2 if outcome==30, wsse(DCseI) eform
metareg DC_ln oral_1-oral_4 if outcome==40, wsse(DCseI) eform

metareg E_ln cvd_1-cvd_5 if outcome==10, wsse(EseI) eform
metareg E_ln meta_1-meta_4 if outcome==50, wsse(EseI) eform
metareg E_ln asthma_1-asthma_3 if outcome==20, wsse(EseI) eform
metareg E_ln copd_1-copd_2 if outcome==30, wsse(EseI) eform
metareg E_ln oral_1-oral_4 if outcome==40, wsse(EseI) eform

*metareg DN_ln cvd_1-cvd_5 if outcome==10, wsse(DNseI) eform  skip because insufficient observations
*metareg DN_ln meta_1-meta_4 if outcome==50, wsse(DNseI) eform skip because insufficient observations
metareg DN_ln asthma_1-asthma_3 if outcome==20, wsse(DNseI) eform
metareg DN_ln copd_1-copd_2 if outcome==30, wsse(DNseI) eform
* metareg DN_ln oral_1-oral_4 if outcome==40, wsse(DNseI) eform skip because insufficient observations

metareg C_ln cvd_1-cvd_5 if outcome==10, wsse(CseI) eform
metareg C_ln meta_1-meta_4 if outcome==50, wsse(CseI) eform
metareg C_ln asthma_1-asthma_2 if outcome==20, wsse(CseI) eform
```

```
metareg C_ln copd_1-copd_2 if outcome==30, wsse(CseI) eform
metareg C_ln oral_1-oral_4 if outcome==40, wsse(CseI) eform

drop cvd_* stroke_* meta_* asthma_* copd_* oral_*

*tablulate some descriptive statistics about study characteristics
tab outcome year, row
tab outcome adult, row
tab outcome longitudinal, row
tab outcome diagnosis, row
tab outcome reference, row
tab outcome model, row
tab outcome whichEC, row
tab outcome whichDC, row
tab outcome whichDC_ms, row
tab outcome whichE, row
tab outcome whichC, row
tab outcome whichDN, row

tab outcome former, row
tab former_smoking
tab former_smoking, m

*Do meta-analyses limiting studies to ones that estimated ORs (as opposed to other risk measures)
metan EC_ln EClo_lnI EChi_lnI if risk=="OR", random eform lcols(study outcome2) nograph by(outcome)
metan DC_ln DClo_lnI DChi_lnI if risk=="OR", random eform lcols(study outcome2) nograph by(outcome)
metan E_ln Elo_lnI Ehi_lnI if risk=="OR", random eform lcols(study outcome2) nograph by(outcome)
metan C_ln Clo_lnI Chi_lnI if risk=="OR", random eform lcols(study outcome2) nograph by(outcome)
metan DN_ln DNlo_lnI DNhi_lnI if risk=="OR", random eform lcols(study outcome2) nograph by(outcome)

* List and meta-analyze studies that present ecig risks among never smokers
list study outcome EN ENlo ENhi if EN<.
gen ENseI=ENse*SEinflator[1,n_shared]
gen ENlo_lnI=EN_ln-1.96*ENseI
gen ENhi_lnI=EN_ln+1.96*ENseI
metan EN_ln ENlo_lnI ENhi_lnI, nograph random eform lcols(study) effect (OR)  by (outcome)
drop ENseI ENlo_lnI ENhi_lnI

* Compare computed and directly estimated EC values, which can be done for some of the stratified studies
list study outcome model ECS  ECCS EC if ECS<. & ECCS<.
list study outcome DSS DCCS if DSS<. & DCCS<.

* Tabulate outcomes by age of sample
tab adult outcome, col
metareg EC adult outcome_1-outcome_6, wsse (ECseI)
metareg DC adult outcome_1-outcome_6, wsse (DCseI)

*Tabulate outcomes by when diagnosed
tab diagnosis outcome, col
metareg EC diagnosis outcome_1-outcome_6, wsse (ECseI)
metareg DC diagnosis outcome_1-outcome_6, wsse (DCseI)

* Compare E with E among people who never smoked
gen Ediff=EN-E
replace Ediff=0 if abs(Ediff)<.005
list outcome study E EN Ediff if EN<.
drop Ediff

* List studies where there is directly observed ORdualvscig amd computed ORdual vs cig
list study DSS DCCS if DSS<. & DCCS<.

* Data sources
tab sample2, sort

* Number of significant and non-significant ORs for E (ecig vs nothing)
gen sig=.
replace sig=0 if E<.
replace sig=1 if (Elo < 1 & Ehi < 1) | (Elo > 1 & Ehi > 1)
label var sig "Significant OR for ecig vs nothing"
label values sig yesno
tab sig outcome, col chi
drop sig

*Compare E based on whole sample with EF (based on former smokers only)
*Just use point estimates (which understates variability so biases the results
*toward finding a significant difference.
gen EEF_diff=E-EF
gen EEF_ratio=E/EF
list study E EF EEF_diff EEF_ratio if EF<.
```

```
ttest EEF_diff==0
ttest EEF_ratio=1
drop EEF_diff EEF_ratio


**MONTE CARLO ESTIMATE OF COMBINED EFFECTS OF SOLE AND DUAL E-CIGARETTE USE
log using "MonteCarlo_US.log", replace
clear

*10,000 replications
set obs 10000
set seed 5653

*Draw random fraction of dual use based on 2019 US observed 39.1% (95% CI 36.8%-41.4%) dual use

gen dualr=rnormal(.391,0.01173)

*CVD
gen cvECr=exp(rnormal(-0.210721031,0.172386591)) // rnormal(EC_ln, ECseI)  OR 0.81 (0.58-1.14)
gen cvDCr=exp(rnormal(0.207014169, 0.112712437))   // rnormal(DC_ln, DCseI)  OR 1.23(0.99-1.54)
gen Cardiovascular= (1-dualr)*cvECr + dualr*cvDCr
hist Cardiovascular, saving(Cardiovascular,replace) xscale(range(.7 1.3)) yscale(off)  kdensity ///
       text (3.7 1.45 "OR=0.98; 95% CI 0.83-1.17", size(small))
graph export Cardiovascular.svg, as(svg) replace
summarize Cardiovascular, detail
* Find where overall OR crosses 1.0
sort Cardiovascular
cumul Cardiovascular, gen(CVcum)
replace CVcum=1-CVcum
list Cardiovascular CVcum if Cardiovascular>0.9995 & Cardiovascular<1.0005

*Stroke
gen sECr=exp(rnormal(-0.314710745, 0.22378577)) // rnormal(EC_ln, ECseI)  OR 0.73 (0.47-1.13)
gen sDCr=exp(rnormal(0.207014169, 0.112712437))   // rnormal(DC_ln, DCseI)  OR 1.23 (0.99-1.54)
gen Stroke= (1-dualr)*sECr + dualr*sDCr
hist Stroke, saving(Stroke,replace) xscale(range(.7 1.3)) yscale(off)  kdensity ///
       text (3.7 1.45 "OR=0.93; 95% CI 0.77-1.15", size(small))
graph export Stroke.svg, as(svg) replace
summarize Stroke, detail
* Find where overall OR crosses 1.0
sort Stroke
cumul Stroke, gen(Scum)
replace Scum=1-Scum
list Stroke Scum if Stroke>0.9995 & Stroke<1.0005

*Metabolic
gen mECr=exp(rnormal(-0.010050336, 0.046042953)) // OR 0.99 (0.91-1.09)
gen mDCr=exp(rnormal(0.198850859, 0.033230917)) // OR 1.22(1.15-1.31)
gen Metabolic= (1-dualr)*mECr + dualr*mDCr
hist Metabolic, saving(Metabolic,replace) xscale(range(.7 1.3))  yscale(off)  kdensity ///
       text (15 1.45 "OR=1.08; 95% CI 1.03-1.14", size(small))
graph export Metabolic.svg, as(svg) replace
summarize Metabolic, detail
sort Metabolic
cumul Metabolic, gen(Mcum)
*compute upper tail
replace Mcum=1-Mcum
list Metabolic Mcum if Metabolic>0.9995 & Metabolic<1.0005

*Asthma
gen aECr=exp(rnormal(-0.174353387, 0.06030326))  // OR 0.84 (0.75-0.95)
gen aDCr=exp(rnormal(0.182321557, 0.034064131))   // OR 1.20 (1.12-1.28)
gen Asthma= (1-dualr)*aECr + dualr*aDCr
hist Asthma, saving(Asthma,replace) xscale(range(.7 1.3)) yscale(off)  kdensity ///
       text (15 1.45 "OR=0.98; 95% CI 0.92-1.04", size(small))
graph export Asthma.svg, as(svg) replace
summarize Asthma, detail
sort Asthma
cumul Asthma, gen(Acum)
replace Acum=1-Acum
list Asthma Acum if Asthma>0.9995 & Asthma<1.0005

*COPD
gen coECr=exp(rnormal(-0.139262067, 0.070009399)) // OR 1.41 (1.12-1.27)
gen coDCr=exp(rnormal(0.343589704, 0.03206332)) // OR 1.48 (1.25-1.76)
gen COPD= (1-dualr)*coECr + dualr*coDCr
hist COPD, saving(COPD,replace) xscale(range(.7 1.3)) yscale(off)  kdensity ///
       text (10 1.45 "OR=1.08; 95% CI 1.02-1.15", size(small))
graph export COPD.svg, as(svg) replace
```

```
summarize COPD, detail
sort COPD
cumul COPD, gen(COcum)
replace COcum=1-COcum
list COPD COcum if COPD>0.9995 & COPD<1.0005

*oral
gen oECr=exp(rnormal(-0.12783,0.066674685)) // OR 0.87 (0.76-1.00)
gen oDCr=exp(rnormal(0.2390169, 0.048352501))     // OR 1.27 (1.15-1.39)
gen Oral= (1-dualr)*oECr + dualr*oDCr
hist Oral, saving(Oral,replace) xscale(range(.7 1.3)) yscale(off)  kdensity ///
       text (10 1.45 "OR=0.98; 95% CI 1.03-1.11", size(small))
graph export Oral.svg, as(svg) replace
summarize Oral, detail
sort Oral
cumul Oral, gen(Ocum)
replace Ocum=1-Ocum
list Oral Ocum if Oral>0.9995 & Oral<1.0005

graph combine "Cardiovascular" "Stroke" "Metabolic" "Asthma" "COPD" "Oral", rows(6) saving(All_histograms,
replace) xcommon ysize(11) xsize(8) title("US (2018-9): 39.1% dual use")
graph export All_histograms.svg, as(svg) replace
log close
```