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Population-Based Disease Odds for E-Cigarettes and Dual Use versus Cigarettes

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Abstract

BACKGROUND—E-cigarettes are promoted as less harmful than cigarettes. There has not been a direct comparison of health effects of e-cigarettes or dual use (concurrently using e-cigarettes and cigarettes) with those of cigarettes in the general population.

METHODS—Studies in PubMed, EMBASE, Web of Science, and PsychINFO published through October 1, 2023, were pooled in a random-effects meta-analysis if five or more studies were identified with a disease outcome. We assessed risk of bias with Risk Of Bias In Non-randomized Studies of Exposure and certainty with Grading of Recommendations, Assessment, Development, and Evaluations. Outcomes with fewer studies were summarized but not pooled.

RESULTS—We identified 124 odds ratios (94 cross-sectional and 30 longitudinal) from 107 studies. Pooled odds ratios for current e-cigarette versus cigarette use were not different for cardiovascular disease (odds ratio, 0.81; 95% confidence interval, 0.58 to 1.14), stroke (0.73; 0.47 to 1.13), or metabolic dysfunction (0.99; 0.91 to 1.09) but were lower for asthma (0.84; 0.74 to 0.95), chronic obstructive pulmonary disease (0.53; 0.38 to 0.74), and oral disease (0.87; 0.76 to 1.00). Pooled odds ratios for dual use versus cigarettes were increased for all outcomes (range, 1.20 to 1.41). Pooled odds ratios for e-cigarettes and dual use compared with nonuse of either product were increased (e-cigarette range, 1.24 to 1.47; dual use, 1.49 to 3.29). All studies included were assessed as having a low risk of bias. Results were generally not sensitive to study characteristics. Limited studies of other outcomes suggest that e-cigarette use is associated with additional diseases.

CONCLUSIONS—There is a need to reassess the assumption that e-cigarette use provides substantial harm reduction across all cigarette-caused diseases, particularly accounting for dual use.

Introduction

The 2018 National Academies of Science, Engineering and Medicine report *Public Health Consequences of E-Cigarettes* concluded that “whether e-cigarettes have an overall positive

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Disclosures

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or negative impact on public health is currently unknown."[1] Public Health England's 2015 report concluded that e-cigarettes are 95% safer than cigarettes based on the fact that e-cigarettes do not produce combustion products.[2] An umbrella review using a literature search through July 2020 found the evidence for most disease outcomes "insufficient."[3] As of October 2023, however, many epidemiological studies had reported the odds of human disease associated with e-cigarettes as actually used in the general population. Meta-analyses found increased odds of asthma[4–6] and chronic obstructive pulmonary disease[5] (COPD) associated with e-cigarette use independent of cigarette use. There have not been meta-analyses of other disease outcomes, although three meta-analyses found that e-cigarettes adversely affected cardiovascular function[7–9] and one found negative effects on dental implants.[10] One qualitative summary of six studies concluded that switching completely from cigarettes to e-cigarettes was associated with lower odds of respiratory disease and no change in cardiovascular disease.[11] Another study concluded that dual (concurrent) use of e-cigarettes and cigarettes was associated with odds of disease that were the same as or higher than those found with exclusive smoking.[12]

Some regulatory bodies continue to assume that e-cigarettes are substantially less toxic than cigarettes. In its 2022 proposed rule ending menthol as a characterizing flavor in cigarettes,[13] following Levy et al.[14] the U.S. Food and Drug Administration (FDA) assumed that e-cigarettes are 15% as toxic as cigarettes and dual use had risks similar to those of smoking. No specific evidence is cited to support these assumptions. FDA's marketing granted orders for RJ Reynolds' Vuse Solo[15,16] and other e-cigarettes[17,18] assuming that e-cigarettes are substantially less harmful than cigarettes based on the fact that many biomarkers of exposure or potential harm are lower in e-cigarette users than in users of cigarettes and are similar to those in smokers who are dual users.[19]

A 2021 review and modeling analysis of biomarker data estimated that e-cigarettes were one-third as harmful as cigarettes.[20] Another review of biomarkers in clinical trials of e-cigarettes for smoking cessation in high-income countries concluded that switching from cigarettes to e-cigarettes or dual use reduced some biomarkers of potential harm.[21] The number of biomarkers in these analyses was small compared with the number of toxicants in cigarettes and e-cigarettes. E-cigarettes and conventional cigarettes are different products. Research has focused on known cigarette-related toxicants (largely combustion products that are not present or present at much lower levels in e-cigarettes) even though e-cigarettes also deliver thousands of chemicals and have a toxicant profile different from that of cigarettes.[22] In addition, the dose–response relationships between exposure and risk may not be linear, which means that a reduction in measures of exposure may not translate into proportionate reductions in harm. Consistent with a nonlinear dose–response, a meta-analysis of the effects of reducing cigarette consumption found no all-cause mortality benefit.[23] Another study found that smoking one cigarette a day generates about 53% of the risk of coronary heart disease for men and 38% for women and 64% of the risk of stroke for men and 36% for women compared with smoking 20 cigarettes a day.[24]

Since e-cigarettes are often presented as a less harmful alternative to cigarettes,[2,13–18] the comparison of most interest for potential harm reduction for smokers is comparison of e-cigarettes to cigarettes. In addition, many adult e-cigarette users continue to smoke

cigarettes (dual use); 39.1% of U.S. e-cigarette users in 2018 to 2019,[25] 66.7% in Sweden in 2016,[26] and 85.3% in Korea in 2013 to 2017[27] were dual users, making it important to compare the odds of disease associated with dual use to those found with exclusive cigarette use. In addition, the high prevalence of e-cigarette use among youth who have never smoked cigarettes[28,29] makes it important to quantify the risks of e-cigarette use compared with nonuse.

This study provides a systematic review and meta-analysis of the associations between current e-cigarette use and dual use and disease outcomes in the general population compared with cigarette use and compared with not using either product.

Methods

This research was conducted following the Meta-analysis Of Observational Studies in Epidemiology reporting guidelines and registered with PROSPERO (CRD42022357914).

DATA

Study Identification—We searched PubMed, EMBASE, Web of Science, and PsychINFO for articles published from January 1, 2005 (before e-cigarettes entered the U.S. market), through October 1, 2023, for population epidemiological studies that reported the association between e-cigarette use as consumer products in the general population and diseases with no geographic or language restrictions. See Supplementary Methods in the Supplementary Appendix for specific searches, inclusion and exclusion criteria, and the data extraction protocol provided with the full text of this article at evidence.nejm.org. Diseases with at least five articles were used for quantitative meta-analysis; other outcomes were qualitatively summarized.

Exposure Definitions—Current e-cigarette users self-reported using e-cigarettes some days or every day or 1day or more during the past 30days.

Current smokers self-reported having smoked 100 cigarettes in their lifetime and smoking some days or every day or 1 day or more during the past 30 days.

Current dual users were current users of both e-cigarettes and cigarettes.

Disease Outcomes—Disease outcomes were self-reported diagnoses, using questions such as “Has a doctor, nurse, or other health professional told you that you had ___?” or identified through direct clinical observation such as NHANES (National Health and Nutrition Evaluation Survey).[30] Disease was categorized as “current” (diagnosis within the last 12 months or less) or “ever.”

ASSESSMENT OF RISK OF BIAS AND CERTAINTY OF CONCLUSIONS

Two reviewers used the Risk Of Bias In Non-randomized Studies of Exposure (ROBINS-E) to assess risk of bias in individual studies[31] and Grading of Recommendations, Assessment, Development, and Evaluations[32] (GRADE) to assess confidence in conclusions. Differences were resolved by consensus.

ANALYSIS

We computed pooled odds ratios of each disease outcome for e-cigarettes and dual use compared with cigarettes as well as nonuse (never or noncurrent use). When articles reported relative risk, prevalence ratio, hazard ratio, or incident rate ratio, we used it as an estimate of odds ratio.[33] When an article did not report odds ratios of e-cigarette use versus cigarette use ($OR_{ecig\ versus\ cig}$) and odds ratios of dual use versus cigarette use ($OR_{dual\ versus\ cig}$), we calculated these odds ratios as detailed in Supplementary Methods.

Primary Analysis—The odds ratios and 95% confidence intervals (CIs) were pooled using random effects meta-analyses with Stata 15.1 *metan*. The CIs have not been adjusted for multiple comparisons. When more than one article used the same data set, we inflated the standard errors for the individual estimates using a Bonferroni correction to account for the likelihood that odds ratio estimates were correlated (details in Supplementary Methods).

Because some e-cigarette users continue to smoke, we estimated the overall odds of disease associated with e-cigarette use accounting for dual use compared with the cigarettes alone using a Monte Carlo analysis (see Supplementary Methods).

Sensitivity Analyses—We conducted sensitivity analyses to examine whether study characteristics (e.g., design, samples, control for former smoking, and last year of data collection) affected the results[34,35] with meta-regression using Stata *metareg* of the natural logarithm of the odds ratios against study characteristics, controlling for the outcome. We tested whether treating all measures of associations (e.g., relative risk and hazard ratio) as approximations of odds ratios affected the results by repeating the meta-analyses among only studies that reported odds ratios.

Heterogeneity—The sample sizes in the individual studies were large, so I^2 and the chi-squared test are not good measures of heterogeneity.[34] Heterogeneity across studies for particular disease outcomes was assessed in two ways: using meta-regression with effects-coded differences in detailed outcomes within disease categories and examining whether holding one study out substantially changed the meta-analyses of the remaining studies and assessment of forest plots.[35]

Publication Bias—Publication bias was assessed using funnel plots and Begg, Egger, and trim-and-fill tests with Stata's *metafunnel*, *metabias*, and *metatrim*.

ETHICS

Ethical approval was not required for this review of published studies. S.A.G. designed the study, did the analysis, and wrote the first draft. All authors participated in data gathering and revising the manuscript and take responsibility for the integrity of the data and the accuracy of the data analysis.

Results

STUDY SELECTION

We identified 107 studies[26,27,36–140] (Tables S1–S3 in the Supplementary Appendix; PRISMA flowchart: Fig. S1). Over three-fourths (84/107) were published from 2020 to 2023. Most were based on large U.S. nationally representative surveys (PATH[141] [Population Assessment of Tobacco and Health], 39; BFRSS[142] [Behavioral Risk Factor Surveillance System], 28; NHANES[30], 8; PRAMS[143] [Pregnancy Risk Assessment Monitoring System], 5; NHIS[144] [National Health Interview Survey], 9; YRBSS[145] [Youth Risk Behavior Surveillance System], 3). The rest were from other U.S. surveys (15) or national surveys out-side the United States (Korea, 10; Sweden, 2; China, 1; Kuwait, 1). The sample sizes were large, ranging from 976 to 924,882 (median, 21,618; interquartile range, 9204 to 85,810). Most (88/107 [82%]) reported odds ratios. Four[102,103,108,119] (4%) reported relative risks, nine[46,62,63,72,76,88,101,109,112] (8%) reported hazard ratios, five[36,38,53,71,107] (4%) reported prevalence ratios, and one[135] (1%) reported incidence rate ratios.

There were at least 5 studies of the following disease outcomes: 12 of cardiovascular disease (coronary heart disease, erectile dysfunction, or myocardial infarction), 6 of stroke, 12 of metabolic dysfunction (metabolic syndrome and its components: obesity, hypertension, high blood sugar [prediabetes], high serum triglycerides, and low serum high-density lipoprotein), 42 of asthma, 20 of COPD, and 10 of oral disease (poor oral health, gum disease [gingivitis, periodontitis], tooth cracking or loss, and xerostomia). We found 22 studies of other conditions that were summarized without pooling odds ratios: preterm birth,[75,107,127] low gestational weight gain,[129] not breastfeeding,[89] coronavirus disease 2019 infection,[65,69,92] hospitalization or emergency department visit,[72,121] sleep apnea,[140] sleep disorders,[60,130] arthritis,[120] atopic dermatitis,[113] bone fracture,[36] cancer,[72] difficulty concentrating,[137] general health,[128] fatty liver disease,[74] impaired vision,[93] and oral human papillomavirus.[77] These studies reported a total of 124 risk estimates, all of which are considered approximations of odds ratios. Fifty of the 124 odds ratios (40%) were from studies that shared one or more data sets (Table S4).

Table S5 summarizes study characteristics for each outcome. Most odds ratios were from cross-sectional (94/124 [76%]) versus longitudinal designs, noncurrent e-cigarette (versus never) use as the reference condition (69/124 [56%]), and current (versus ever) presence of disease (90/124 [73%]). Nearly half of the odds ratios (60/124 [48%]) were from stratified models, 40% (49/124) were from multivariate models, and 12% (15/124) were from both. About half the e-cigarette versus cigarette (50/82 [61%]) and dual use versus cigarette odds ratios (55/113 = 49%) were based on stratified estimates. One third of odds ratios (39/124 [31%]) controlled for former smoking, either by including it as a covariate (17/39 [44%]), by stratifying on smoking status (16/38 [41%]), by including smoking duration as a covariate (5/39 [13%]), or by including both smoking status and duration as covariates (1/39 [3%]). All odds ratios for cardiovascular, stroke, metabolic dysfunction, and COPD studies, 52% of asthma odds ratios, and 70% of the oral disease odds ratios were estimated using adult samples.

RISK OF BIAS ASSESSMENT

As detailed in the Supplemental Results, all studies scored as having a low risk of bias (Table S3), generally because they used well-established population-based samples designed to assess overall determinants of health.

META-ANALYSIS FINDINGS

Comparisons to Cigarette Use—Comparing e-cigarette with cigarette use, the confidence intervals for the pooled odds ratios for cardiovascular disease (coronary heart disease, erectile dysfunction, and myocardial infarction; odds ratio, 0.81; 95% CI, 0.58 to 1.14), stroke (0.73; 0.47 to 1.13), and metabolic dysfunction (0.99; 0.91 to 1.09) included 1 (Fig. 1 and Table 1). The odds ratios for asthma (0.84; 0.75 to 0.95), COPD (0.53; 0.38 to 0.74), and oral disease (0.87; 0.76 to 1.00) were below 1.

Dual use was associated with higher point estimates for odds of disease compared with cigarettes for all outcomes, ranging from 1.20 to 1.41 (Fig. 2 and Table 1).

Comparisons to No Use—E-cigarette use compared with nonuse of e-cigarettes was associated with higher point estimates for disease for all outcomes, ranging from 1.24 to 1.47 (Fig. S2 and Table 1).

Dual use compared with nonuse of e-cigarettes or cigarettes was associated with increased odds of disease, ranging from 1.49 to 3.29 (Fig. S3 and Table 1).

Cigarette use compared with nonuse of cigarettes was also associated with increased odds of disease, ranging from 1.27 to 2.99 (Fig. S4 and Table 1).

SENSITIVITY ANALYSES AND POSSIBLE CONFOUNDING BY FORMER SMOKING

As detailed in Supplemental Results, study design characteristics, including whether the analysis controlled for former smoking (yes versus no) (Table S6), limiting the analysis to directly reported odds ratios (Table S7), youth versus adult samples (Table S8), variability in detailed outcomes within diseases categories (Table S9), variability between individual studies (Figs. S5 and S6), and the assumption that OR_{ecig} and OR_{cig} are independent (Table S10) were unlikely to have affected the main findings. Studies of never smokers also yielded increased odds ratios for e-cigarettes.

PUBLICATION BIAS

Taken together, funnel plots (Fig. S7), Begg and Egger tests (Table S11), and trim-and-fill tests (Table S12) did not exhibit evidence of publication bias.

OVERALL ODDS RATIOS COMBINING EXCLUSIVE E-CIGARETTE USE AND DUAL USE

Accounting for the fact that some e-cigarette users use only e-cigarettes and some are dual users increases the overall odds ratio of disease associated with all e-cigarette use in the population because dual use is associated with an odds ratio greater than 1 for all outcomes (Fig. S8). Based on 39.1% U.S. dual use in 2019,[25] the probabilities of odds ratios greater than 1 are 0.42 for cardiovascular disease, 0.28 for stroke, greater than 0.99 for metabolic

dysfunction, 0.30 for asthma, 0.98 for COPD, and 0.77 for oral disease. These results are sensitive to prevalence of dual use. In Sweden in 2016, when dual use was 66.7%,[26] these probabilities increased to 0.82 for cardiovascular disease, 0.74 for stroke, and more than 0.99 for metabolic dysfunction, asthma, COPD, and oral disease.

QUALITATIVE SUMMARY OF OTHER OUTCOMES

Among the 22 studies of other conditions (Table S13, Figs. 1 and 2, and Figs. S1–S3) where there were not enough studies to do a formal meta-analysis, individual studies of not breastfeeding, difficulty concentrating, and general health showed that $OR_{ecig\ versus\ cig}$ was not different from 1 in all but one study. OR_{dual} versus cig and OR_{ecig} were greater than 1 in about half the studies. These findings should be interpreted cautiously, because they are based on only one to three studies for each outcome.

GRADE EVALUATION

We have moderate confidence in the conclusions that e-cigarettes and cigarettes have comparable odds of disease for all outcomes, except COPD, for which we have high confidence (Tables S14 and S15). We have moderate confidence for the conclusion that dual use is associated with higher odds of disease than cigarettes for all outcomes (Tables S14 and S15). Confidence for comparisons of e-cigarettes, cigarettes, and dual use versus no product use was moderate to high, depending on the specific outcome.

Discussion

Observational evidence from 124 odds ratios of disease in 107 population-based epidemiological studies of real-world use of e-cigarettes revealed that the odds of disease associated with e-cigarette use were not different from those associated with cigarette smoking for cardiovascular diseases, stroke, and metabolic dysfunction but were lower for asthma, COPD, and oral disease (Table 1 and Fig. 1). Although lower than for cigarettes, the reduced odds ratios associated with e-cigarette use compared with cigarettes for asthma (odds ratio, 0.84), COPD (odds ratio, 0.53), and oral disease (odds ratio, 0.87) are 3 to 10 times the 15% risk that the FDA[13] or the 5% risk that Public Health England[2] have quoted. The odds of disease associated with dual use were higher than for smoking for all outcomes (odds ratio, 1.20 to 1.41; Table 1 and Fig. 2).

OR_{ecig} values for asthma and COPD are similar to those in earlier meta-analyses based on fewer studies[4–6] and consistent with qualitative summaries[11] that concluded that switching from cigarettes to e-cigarettes was associated with lower risk of respiratory disease but not cardiovascular diseases and that dual use was associated with higher risks than smoking.[12] Although COPD takes many years to develop fully, changes begin to appear within a few years.[90,146] The lower COPD OR_{ecig} for e-cigarette use may reflect the fact that e-cigarette users are, on average, younger than cigarette smokers[146] and not enough time may have passed for the e-cigarette risks to be fully manifest.

The odds ratios identified in the epidemiological studies are higher than those predicted by biomarker studies.[20] This direct evidence of disease diverges from conclusions based solely on biomarkers of exposure to tobacco products,[19–21,147] which calls into question the FDA's

policy of authorizing tobacco companies to make modified risk claims about products based solely on the fact that some biomarkers of exposure associated with e-cigarettes are lower than those associated with cigarettes.[148] Our results are consistent with pathophysiological evidence that shows a wide range of adverse cardiovascular,[9,149–159] pulmonary,[5,151,152,159–161] and oral health effects[10,162] associated with e-cigarette use.

E-cigarettes expose users to a different toxic chemical mix than cigarettes,[22] including compounds formed during heating and aerosolization that are not present in the e-liquid itself.[163–165] Although there is some overlap, dual use of e-cigarettes and cigarettes together delivers a wider range of toxins than either does alone. These facts, combined with the observation that daily cigarette consumption among exclusive smokers and dual users was not different,[166–168] may explain the higher odds ratios observed among dual users compared with cigarette smoking alone. It is important to account for dual use when assessing population health impacts of e-cigarette use, because the increased odds ratios associated with dual use compared with just smoking applies among smokers who use e-cigarettes who do not "switch completely," raising the overall population impact associated with e-cigarette use (Fig. S8). Continued dual use should be listed as an adverse event in randomized controlled trials of e-cigarettes for smoking cessation, because it is a much more likely outcome than "complete switching."[169]

E-cigarette findings are unlikely to be the results of confounding with current or former smoking because all the studies either controlled for smoking in the statistical model or stratified on smoking, with e-cigarette users among never smokers analyzed separately from current and, often, former smokers. Results from studies of former smokers were not different from the overall analysis of all studies, and most studies of never smokers (where there are no former smokers) found increases in the odds of disease in e-cigarette users compared with nonusers.

LIMITATIONS

E-cigarette devices and liquids differ in emissions and have changed over time. Common measures of e-cigarette use in most population studies did not capture data on specific devices or e-liquids, and thus, we could not assess these details.

Dual use includes a wide range of behaviors, with some individuals being predominantly smokers and others mostly using e-cigarettes. Another limitation is that few of the studies controlled for duration and frequency/intensity of e-cigarette and cigarette use, so we could not examine dose–response relations.

Most (76%) of the studies were cross-sectional (Table S5), which does not allow for establishing causality. For our primary comparisons of e-cigarettes versus cigarettes as well as the secondary comparisons of e-cigarettes versus nonuse and cigarettes and nonuse, there was no difference between the results of longitudinal and cross-sectional studies (Table S6). More longitudinal studies that last long enough to allow full manifestation of disease are needed to confirm the relationships reported in this meta-analysis.

Most of the disease outcomes were based on self-reported diagnoses. However, self-reported diagnosis of cardiovascular disease[170,171] and COPD[172,173] was validated against medical records. Population prevalence estimates in PATH are similar to results in NHANES for cardiovascular[174] and oral diseases.[56]

E-cigarettes have been on the market for less than 20 years, which may not be long enough to observe the full manifestation of the disease impact. Even so, the available data revealed association with several diseases. To the extent that the likelihood that disease will be manifest increases with time, our estimates may underestimate the long-term associations of e-cigarette use with diseases.

CONCLUSIONS

Direct epidemiological evidence based on actual use of e-cigarettes in the general population suggests that, at least for cardiovascular disease, stroke, and metabolic dysfunction, the odds of disease between current e-cigarette and cigarette use were similar. For asthma, COPD, and oral disease, although lower than with cigarettes, the odds of disease were still substantial.

Current dual use was associated with 20 to 40% higher odds of disease than smoking, suggesting increased overall population risks for e-cigarettes even for respiratory disease. The available data are also inconsistent with the FDA's assumption, made in its authorizations to sell Vuse Solo,[16] NJOY,[18] and Logic[17] e-cigarettes, and the IQOS heated tobacco product,[175] that dual use is less harmful or, at most, no more harmful than smoking.[15,176] The dual-use findings are particularly important because dual use is a common behavior among adults who use e-cigarettes[25–27,169,177] that can overcome any population benefit for those who "switch completely" even for respiratory and oral diseases.

The findings of increased odds of several diseases for e-cigarettes compared with nonuse illustrates the substantial risks for people, particularly youth and young adults, who initiate nicotine use with e-cigarettes and former smokers who restart nicotine use with e-cigarettes. Even without considering the millions of youth who initiate nicotine use with e-cigarettes,[28] these results suggest a need for a careful reassessment of the assumption that e-cigarettes are a substantially less harmful alternative to cigarettes, particularly given the fact that, as consumer products, e-cigarettes are not associated with increased smoking cessation[178,179] and, over the long run, are associated with less cessation and increased odds of becoming a dual user.[180,181]

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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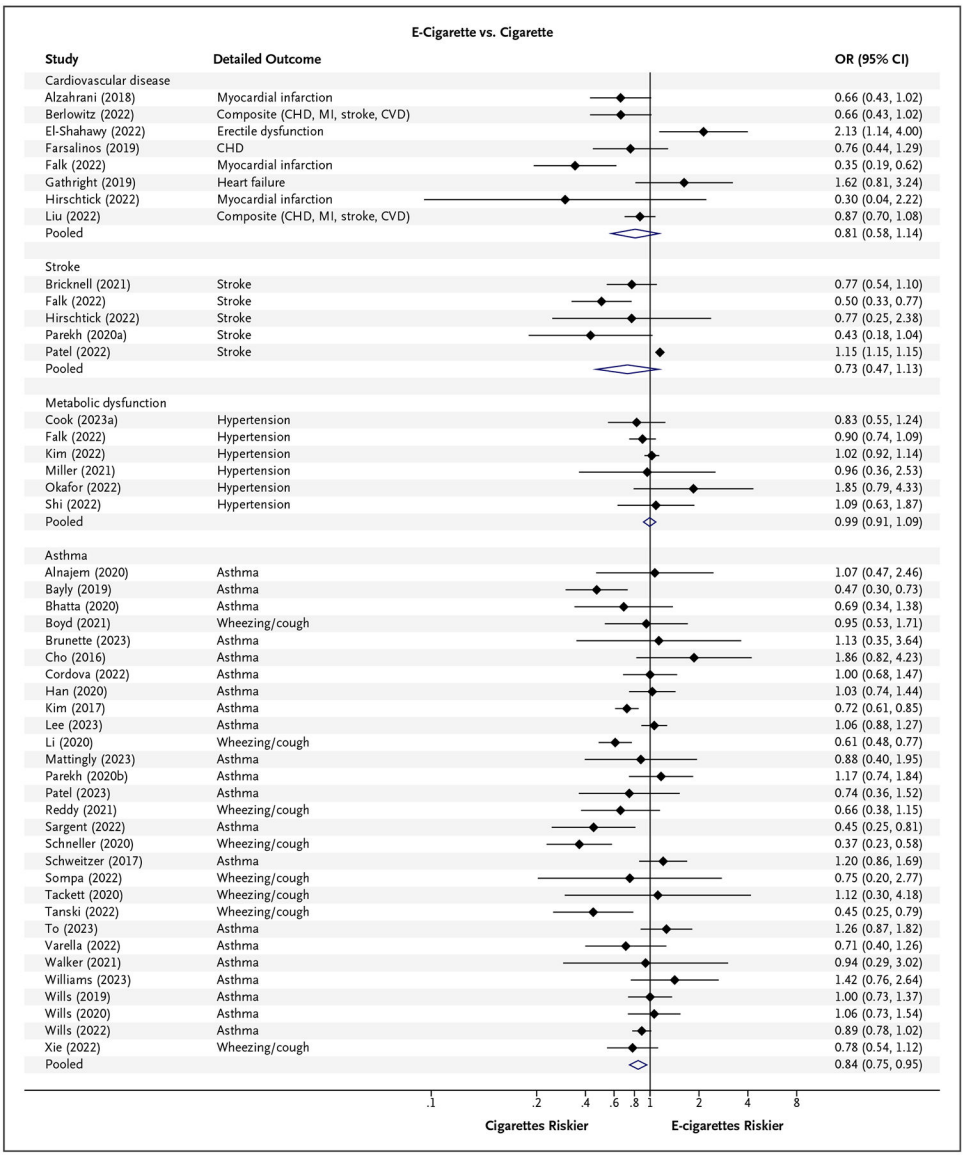


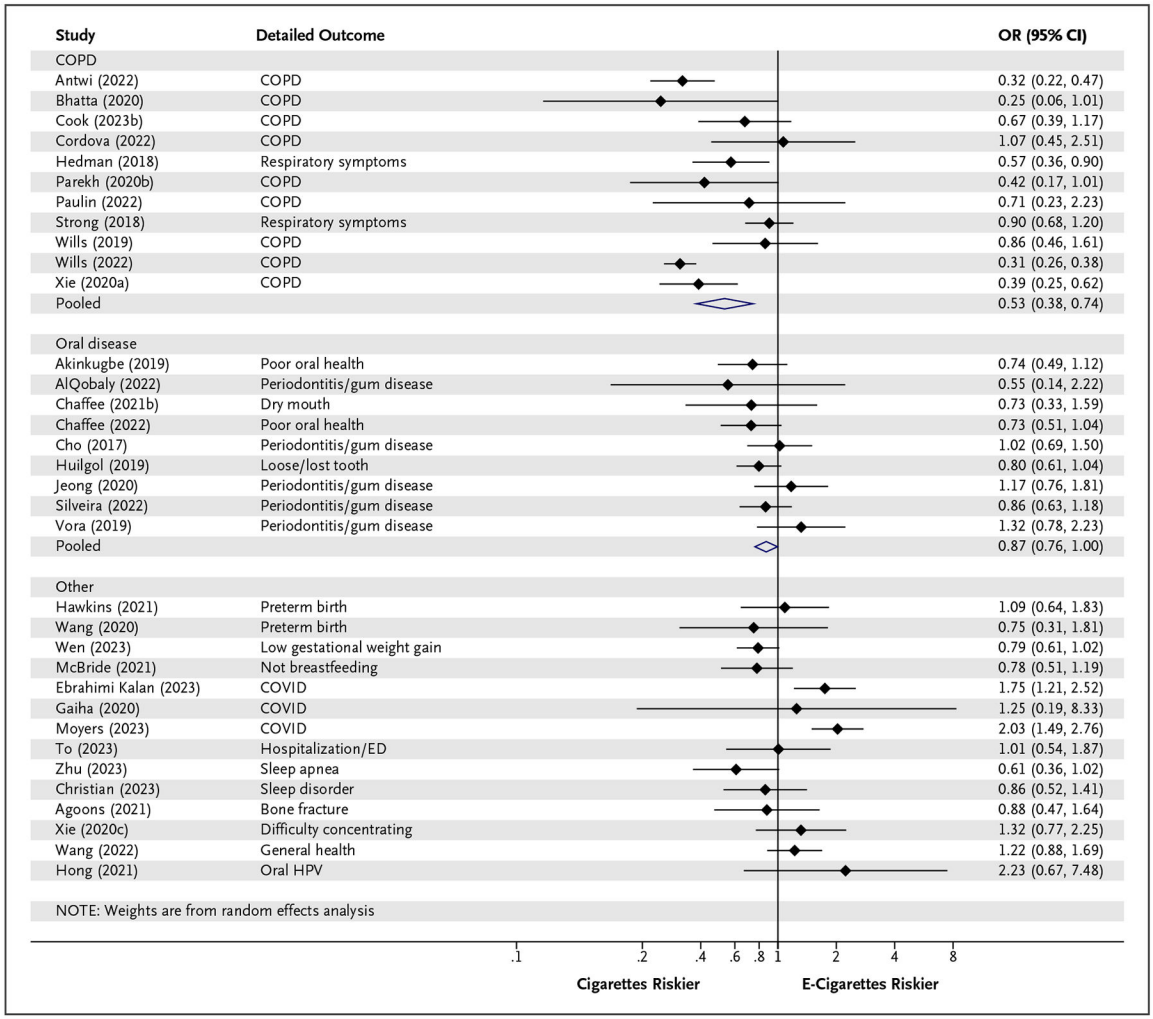
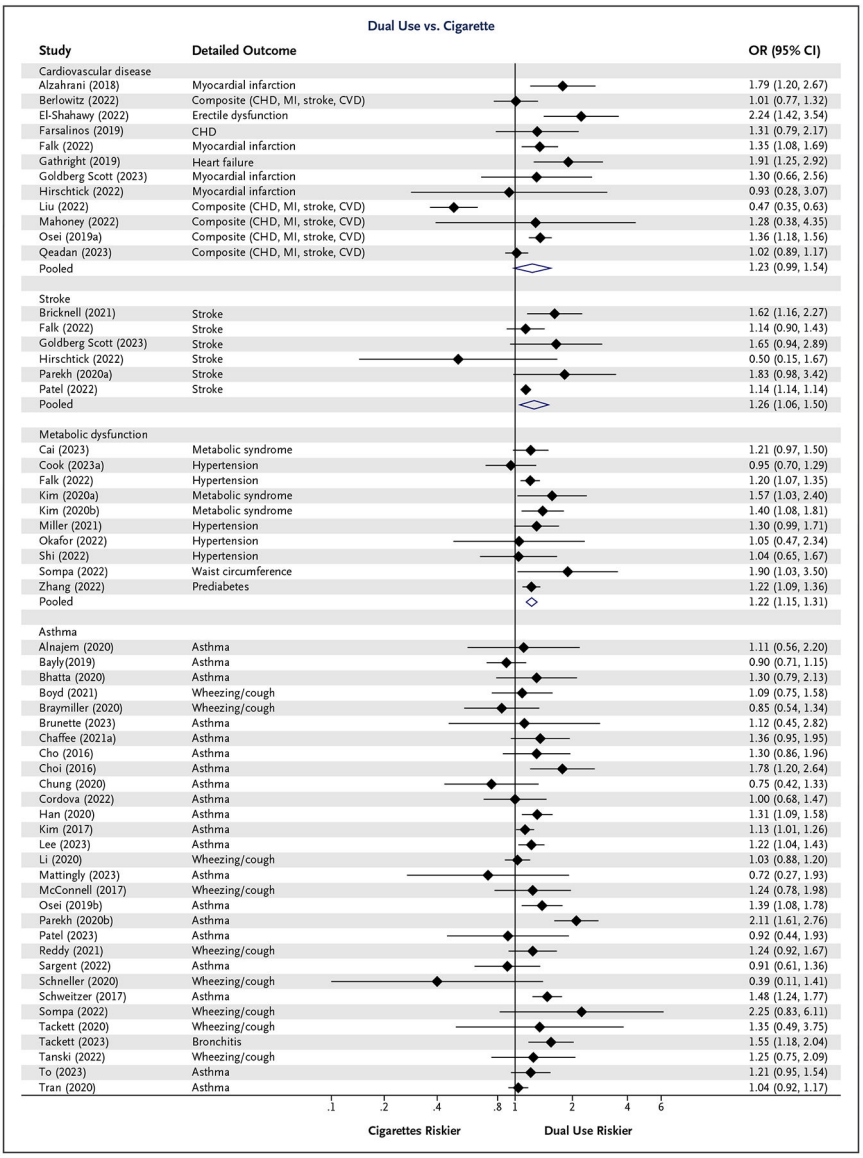


Figure 1.

Comparative Disease Odds Ratios for E-Cigarette Use and Cigarette Smoking.

E-cigarette use and cigarette smoking have similar odds of disease for cardiovascular disease, stroke, and metabolic dysfunction and lower odds for asthma (odds ratio, 0.84), COPD (odds ratio, 0.53), and oral disease (odds ratio, 0.87). Confidence intervals include Bonferroni adjustments. Diamonds show point estimates and 95% confidence intervals for pooled odds ratios from random effects meta-analysis. Results for “other” studies were not pooled. CHD denotes coronary heart disease; CI, confidence interval; COPD, chronic obstructive pulmonary disease; COVID, coronavirus disease 2019; CVD, cardiovascular disease; ED, emergency department; HPV, human papillomavirus; MI, myocardial infarction; and OR, odds ratio.



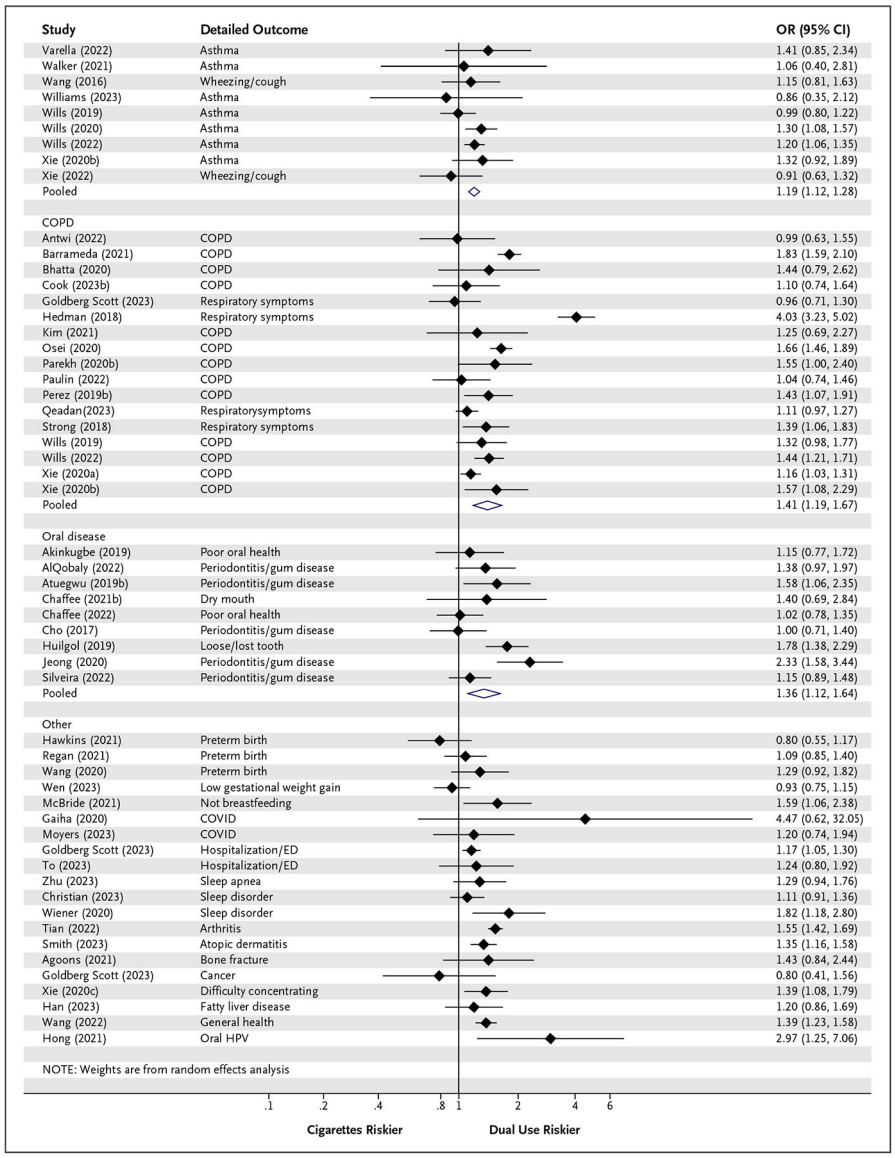


Figure 2.

Comparative Disease Odds Ratios for Cigarette Smoking and Dual Use.

Point estimates for odds ratios of disease of all outcomes are above 1 in dual users compared to cigarette smokers (odds ratio, 1.12 to 1.41). Confidence intervals include Bonferroni adjustments. Diamonds show point estimates and 95% confidence intervals for pooled odds ratios from random effects meta-analysis. Results for “other” studies were not pooled. CHD denotes coronary heart disease; CI, confidence interval; COPD, chronic obstructive pulmonary disease; COVID, coronavirus disease 2019; CVD, cardiovascular disease; ED, emergency department; HPV, human papillomavirus; MI, myocardial infarction; and OR, odds ratio.

Table 1.

Pooled Adjusted* Odds Ratios of Each Disease Outcome (95% Confidence Intervals) from the Meta-analyses.

Comparisons	Cardiovascular	Stroke	Metabolic Dysfunction	Asthma	COPD	Oral Disease
Comparison to cigarette use						
E-cigarettes vs. cigarettes	0.81 (0.58–1.14)	0.73 (0.47–1.13)	0.99 (0.91–1.09)	0.84 (0.75–0.95)	0.53 (0.38–0.74)	0.87 (0.76–1.00)
Dual use vs. cigarettes	1.23 (0.99–1.54)	1.26 (1.06–1.50)	1.22 (1.15–1.31)	1.20 (1.12–1.28)	1.41 (1.12–1.64)	1.27 (1.15–1.39)
Comparison to no use						
E-cigarette vs. nonuse	1.24 (1.05–1.46)	1.32 (0.99–1.76)	1.25 (1.18–1.33)	1.24 (1.19–1.30)	1.46 (1.31–1.61)	1.47 (1.19–1.82)
Dual use vs. nonuse	2.23 (1.59–3.14)	2.39 (2.02–2.83)	1.49 (1.17–1.91)	1.56 (1.22–2.00)	3.29 (1.97–5.51)	1.78 (1.49–2.12)
Cigarette vs. nonuse	1.64 (1.24–2.16)	2.08 (1.91–2.27)	1.27 (1.17–1.37)	1.56 (1.34–1.80)	2.99 (2.29–3.92)	1.69 (1.40–2.03)

*Adjusted for covariates listed in Table S3. COPD denotes chronic obstructive pulmonary disease.

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