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Topical Review

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Comparison of e-Cigarette and Cigarette Use and Dual Use Associations With Disease: Updated Systematic Review and Meta-Analysis

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Abstract

Objective: Electronic cigarettes (e-cigarettes) are often presented as a less harmful alternative to combustible cigarettes (hereinafter, cigarettes). This study updates an earlier meta-analysis of 107 population studies of e-cigarette disease risks.

Methods: We pooled data from studies in PubMed, EMBASE, Web of Science, and PsychINFO from January 1, 2005, through January 1, 2025, in a random-effects meta-analysis if we identified ≥5 studies for a disease outcome.

Results: We identified 142 odds ratios (ORs) (107 [75%] from cross-sectional studies and 35 [25%] from longitudinal studies) from 124 articles, including 18 new articles. Comparing e-cigarette use with cigarette use, the ORs (95% CIs) for metabolic dysfunction (1.00 [0.91-1.09]) and oral disease (0.89 [0.78-1.02]) were not different from 1.0. The ORs (95% CIs) for cardiovascular disease (0.76 [0.58-0.99]), stroke (0.62 [0.47-0.82]), asthma (0.84 [0.74-0.95]), chronic obstructive pulmonary disease (0.55 [0.40-0.76]), and fetal growth (0.64 [0.44-0.92]) were ≤1.0. Pooled ORs for dual use versus cigarette use were increased for all outcomes (range, 1.22-1.42) except fetal growth (0.99). Pooled ORs for e-cigarette use, compared with nonuse of e-cigarettes, were increased for all outcomes (e-cigarette range, 1.24-1.53) except fetal growth (1.20). Dual use was associated with increased ORs for all outcomes (1.49-3.17). Studies had a low risk of bias. Results were generally not sensitive to study characteristics. Confidence in conclusions was mostly moderate to high except for stroke, where confidence was low for some outcomes, and fetal growth, for which confidence was very low for all outcomes.

Conclusion: The growing literature increases confidence that e-cigarette use is associated with disease outcomes indistinguishable from or approaching cigarette use, with dual use associated with higher ORs. E-cigarettes should not be promoted as a safer alternative to cigarettes.

Keywords

cardiovascular disease, metabolic syndrome, oral health, respiratory disease, tobacco, systematic review

Electronic cigarettes (e-cigarettes) are often presented as a less harmful alternative to combustible cigarettes (hereinafter, cigarettes).[1-14] For example, in 2024, the UK Royal College of Physicians concluded, "Using e-cigarettes for harm reduction to reduce morbidity and mortality from combustible tobacco is based on clear evidence that e-cigarettes cause less harm to health than combustible tobacco."[1] This conclusion is based on the fact that, compared with cigarette users, e-cigarette users experience lower levels of biomarkers of exposure to some toxicants in cigarette smoke or lower levels of some biomarkers of potential harm such as oxidative stress, inflammation, heart rate, blood pressure, or lung function.[1] It is important to move beyond these indirect measures of harm and compare the actual disease risks of e-cigarettes with the actual disease risks of cigarettes. It is also important to compare the risks of dual use (concurrent use of cigarettes and e-cigarettes) with the risks of smoking alone because dual use is common. In the United States, 39.1% of e-cigarette users in 2018-2019 were dual users[15]; in Sweden, 66.7% in 2016[16]; in Europe, 52.6% in 2017-2018[17]; and in Korea, 85.3% in 2013-2017.[18]

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A 2024 systematic review and meta-analysis of 107 population studies of the association between e-cigarette use and disease outcomes published through October 1, 2023, found that (1) for some outcomes, e-cigarette disease risks were similar to cigarette disease risks, and for other outcomes, risks were lower but still substantial[19]; (2) dual use was associated with higher risks of disease outcomes than cigarette use alone; and (3) e-cigarette use was associated with increased disease risk compared with not using e-cigarettes. The objective of our study was to update the 2024 analysis. This growing literature supports the hypothesis that e-cigarette use is associated with disease approaching or indistinguishable from smoking for several diseases, with dual use associated with higher disease risk than just smoking.

Methods

This study used the same search, selection, and analytical methods detailed in the earlier systematic review and meta-analysis[19] following Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) reporting guidelines and registered with PROSPERO (CRD42022357914) as a living review.

We searched PubMed, EMBASE, Web of Science, and PsychINFO for articles published from January 1, 2005 (before e-cigarettes entered the US market), through January 1, 2025, reporting the association between disease and the use of e-cigarettes as consumer products in the general population. We had no age or language restrictions, and we did not screen for potential conflicts of interest with e-cigarette or tobacco companies or related advocacy organizations. Details on searches, inclusion and exclusion criteria, the data extraction protocol, exposure definitions, disease assessment, and risk of bias assessment are described in the Supplement. If we identified ≥5 studies for a disease outcome, we included them in a quantitative meta-analysis; we qualitatively summarized other outcomes.

Primary outcomes were odds of disease associated with current use of e-cigarettes and dual use compared with cigarette use; secondary outcomes were comparisons with no product use (no e-cigarette use or cigarette use). When articles reported relative risk (RR), prevalence ratio (PR), hazard ratio (HR), or incidence rate ratio (IRR), we considered it an estimate of the corresponding odds ratio[20] (OR). We refer to all these measures collectively as risk estimates. When an article did not report the ORs for e-cigarette use versus cigarette use or the ORs for dual use versus cigarette use, we calculated these ORs (Supplement).

The ORs were pooled by using random-effects meta-analyses, accounting for the fact that sometimes >1 article used the same dataset. We also conducted sensitivity, heterogeneity, and publication bias analyses and assessed certainty of conclusions (Supplement).

Because some e-cigarette users continue to use cigarettes, we computed the overall OR associated with all use of e-cigarettes as the weighted average of the OR associated with sole e-cigarette use and dual use where the weighting factor was the probability of dual use. To account for uncertainty in the level of dual use and the ORs, we used the Monte Carlo analysis (Supplement).

We used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) to score the overall certainty of the risk conclusions based on our analysis (Supplement).

Ethical Considerations

As of September 3, 2022, when the protocol was registered with PROSPERO, the institution was the University of California, San Francisco. We did not submit a protocol to the university's Human Research Protection Program because the program's guidelines indicate that systematic reviews and meta-analyses of published studies do not involve human participants and, therefore, do not require institutional review board review.

Results

We included 124 articles in our analysis[16,18,21-142] (eFigure 1 and eTables 1-4 in the Supplement). Of these, 18 were new articles, published from October 2, 2023, through January 1, 2025.[23,27,31,36,40,55,57,60,73,78,81,83,89,91,103,116,130,140] (One article included in the earlier meta-analysis[19] was retracted[143] and is not included in this updated analysis). Of these 124 articles, 81% (n=100) were published during 2020 up until January 1, 2025. Most (81%; n=100) reported ORs; 4 (3%) reported RRs,[100,101,107,119] 10 (8%) reported HRs,[34,52,53,65,69,85,99,103,108,111] 7 (6%) reported PRs,[21,24,43,55,64,81,106] and 3 (2%) reported IRRs.[23,91,136]

These studies reported a total of 142 risk estimates. Most were based on large US nationally representative surveys: the Population Assessment of Tobacco and Health (PATH)[144] (n=46), the Behavioral Risk Factor Surveillance System (BRFSS)[145] (n=30), the National Health Interview Survey (NHIS)[146] (n=11), the National Health and Nutrition Examination Survey (NHANES)[147] (n=9), the Pregnancy Risk Assessment Monitoring System (PRAMS)[148] (n=6), and the Youth Risk Behavior Surveillance System (YRBSS)[149] (n=3). The rest were from other US surveys (n=16) or national surveys outside the United States: Korea (n=11), Sweden (n=2), Canada (n=1), China (n=1), France (n=1), Kuwait (n=1), and international (United States, Canada, and England) (n=1). The sample sizes were large, ranging from 976 to 924 882 (median [IQR]: 20 707 [8736-84 553]). Fifty-seven of the 142 ORs (40%) were from studies that shared datasets (eTable 5 in the Supplement).

We found ≥5 risk estimates for cardiovascular disease (CVD) (n=15; coronary heart disease, erectile dysfunction, myocardial infarction, or composite outcome), stroke (n=5), metabolic dysfunction (n=14; metabolic syndrome and its components: obesity, hypertension, high blood glucose [prediabetes], high serum triglycerides, low serum high-density

lipoprotein), asthma (n = 49), chronic obstructive pulmonary disease (COPD) (n = 21), oral disease (n = 12; poor oral health, gum disease [gingivitis, periodontitis], tooth cracking or loss, xerostomia), and fetal growth (n = 6; small for gestational age, low gestational weight gain, low birth weight). We found 20 studies of other conditions that were summarized without pooling ORs: COVID-19 infection,[56,62,90] hospitalization or emergency department visit,[65,121] sleep apnea,[142] sleep disorders,[50,131] arthritis,[120] atopic dermatitis,[112] not breastfeeding,[86] bone fracture,[21] cancer,[65] difficulty concentrating,[138] general health,[128] fatty liver disease,[67] impaired vision,[92] and oral human papillomavirus (HPV).[70]

Most ORs were from cross-sectional studies (75%; 107 of 142) rather than longitudinal studies (25%; 35 of 142); 42% (n = 59) used never (vs noncurrent) e-cigarette use as the reference condition; and 74% (n = 105) used current (vs ever) presence of disease as the reference condition (eTable 6 in the Supplement). Approximately half of the ORs for e-cigarette use versus cigarette use (62%; 56 of 90) and dual use versus cigarette use (48%; 60 of 125) were based on stratified estimates. About one-third of ORs (32%; 45 of 142) controlled for former smoking by including it as a covariate (47%; 21 of 45), by stratifying on smoking status (40%; 18 of 45), by including smoking duration as a covariate (11%; 5 of 45), or by including both smoking status and duration as covariates (2%; 1 of 45). All ORs for studies on CVD, stroke, metabolic dysfunction, and COPD; 49% of ORs for studies on asthma; 75% of ORs for studies on oral disease; and 83% of ORs for studies on fetal growth were estimated by using adult samples.

For the same reasons detailed in the earlier meta-analysis,[19] all studies in this current analysis had a low risk of bias (eTable 3 in the Supplement).

Comparing e-cigarette use with cigarette use alone, the pooled ORs of metabolic dysfunction (1.00; 95% CI, 0.91-1.09) and oral disease (0.89; 95% CI, 0.78-1.02) were not different from 1.0 (Figure 1; Table). The ORs for CVD (0.76; 95% CI, 0.58-0.99), stroke (0.62; 95% CI, 0.47-0.82), asthma (0.84; 95% CI, 0.74-0.95), COPD (0.55; 95% CI, 0.40-0.76), and fetal growth (0.64; 95% CI, 0.44-0.92) were <1.0. Including the new studies led to 2 changes since the earlier meta-analysis[19]; the risks of CVD and stroke are now lower than the risks of cigarette use. There were not enough studies to include fetal disease in the earlier meta-analysis.[19]

Dual use, compared with cigarette use, was significantly associated with higher odds of CVD (OR = 1.29; 95% CI, 1.07-1.53), stroke (OR = 1.39; 95% CI, 1.05-1.82), metabolic dysfunction (OR = 1.24; 95% CI, 1.16-1.32), asthma (OR = 1.22; 95% CI, 1.14-1.30), COPD (OR = 1.41; 95% CI, 1.19-1.66), and oral disease (OR = 1.42; 95% CI, 1.17-1.72), consistent with the earlier meta-analysis[19] (Figure 2; Table). New data for fetal growth (OR = 0.99; 95% CI, 0.84-1.17) showed that dual use was indistinguishable from cigarette use.

E-cigarette use, compared with nonuse of e-cigarettes, was associated with CVD (OR = 1.24; 95% CI, 1.06-1.45), metabolic dysfunction (OR = 1.26; 95% CI, 1.19-1.34), asthma (OR = 1.27; 95% CI, 1.21-1.32), COPD (OR = 1.45; 95% CI, 1.32-1.60), and oral disease (OR = 1.53; 95% CI, 1.24-1.88), but not stroke (OR = 1.29; 95% CI, 0.95-1.75) or fetal growth (OR = 1.20; 95% CI, 0.92-1.55) (eFigure 2 in the Supplement; Table).

Dual use, compared with nonuse of e-cigarettes or cigarettes, was associated with increased odds of disease for all outcomes, ranging from 1.49 (metabolic dysfunction) to 3.17 (COPD) (eFigure 3 in the Supplement; Table), as in the earlier analysis.[19]

Cigarette use, compared with nonuse of cigarettes, was also associated with increased odds of disease for all outcomes, ranging from 1.27 (metabolic dysfunction) to 2.90 (COPD) (eFigure 4 in the Supplement; Table), as before.[19]

Sensitivity analyses revealed that study design characteristics (eTable 7 in the Supplement) were unlikely to affect results. Only 3 of the unadjusted P values were $\leq .05$, and the pattern of small, uncorrected P values was not consistent across study characteristics. The single consistent change from the earlier meta-analysis[19] was that the overall risks did not change significantly over time (eTable 7 in the Supplement vs Table S6 in the earlier article[19]).

Additional sensitivity analyses and an assessment of publication bias are described in the Supplement. In particular, including former smoking as a possible confounder in the analysis was not associated with the estimated ORs for any outcome (eTable 7 in the Supplement). In addition, studies of never smokers that definitively exclude the possibility that the OR for e-cigarette use versus nonuse (OR_{ecig}) is confounded by current or former smoking report associations between e-cigarette use and disease (Supplement).

The 20 studies of other conditions (eTable 14 in the Supplement; Figures 1 and 2, eFigures 2-4 in the Supplement) where we did not have enough studies to conduct a meta-analysis covered the following outcomes: COVID-19, hospitalization or emergency department visit, sleep apnea, sleep disorder, bone fracture, not breastfeeding, difficulty concentrating, general health, oral HPV, and smell or taste disorder. The results of these 20 studies showed that the ORs for using e-cigarettes, compared with using cigarettes, were not different from 1.0 in all but 2 studies[56,90] of COVID-19. The OR for dual use (compared with cigarette use) and the OR for e-cigarette use (compared with nonuse) were ≥ 1.0 in more than half of these studies. The ORs for e-cigarette use (compared with nonuse) were >1.0 for individual studies of sleep disorders, arthritis, atopic dermatitis, difficulty concentrating, nonalcoholic fatty liver disease, general health, oral HPV, and smell or taste disorder. These findings should be interpreted cautiously because they were based on only 1 to 3 studies for each outcome.

The application of GRADE criteria indicated low confidence in the conclusion that e-cigarette use is associated with lower or indistinguishable odds of CVD; moderate or high confidence in the conclusion that the odds of disease are indistinguishable for metabolic dysfunction and oral disease; moderate confidence in the conclusions for stroke, asthma, COPD, and oral disease; and very low confidence in the

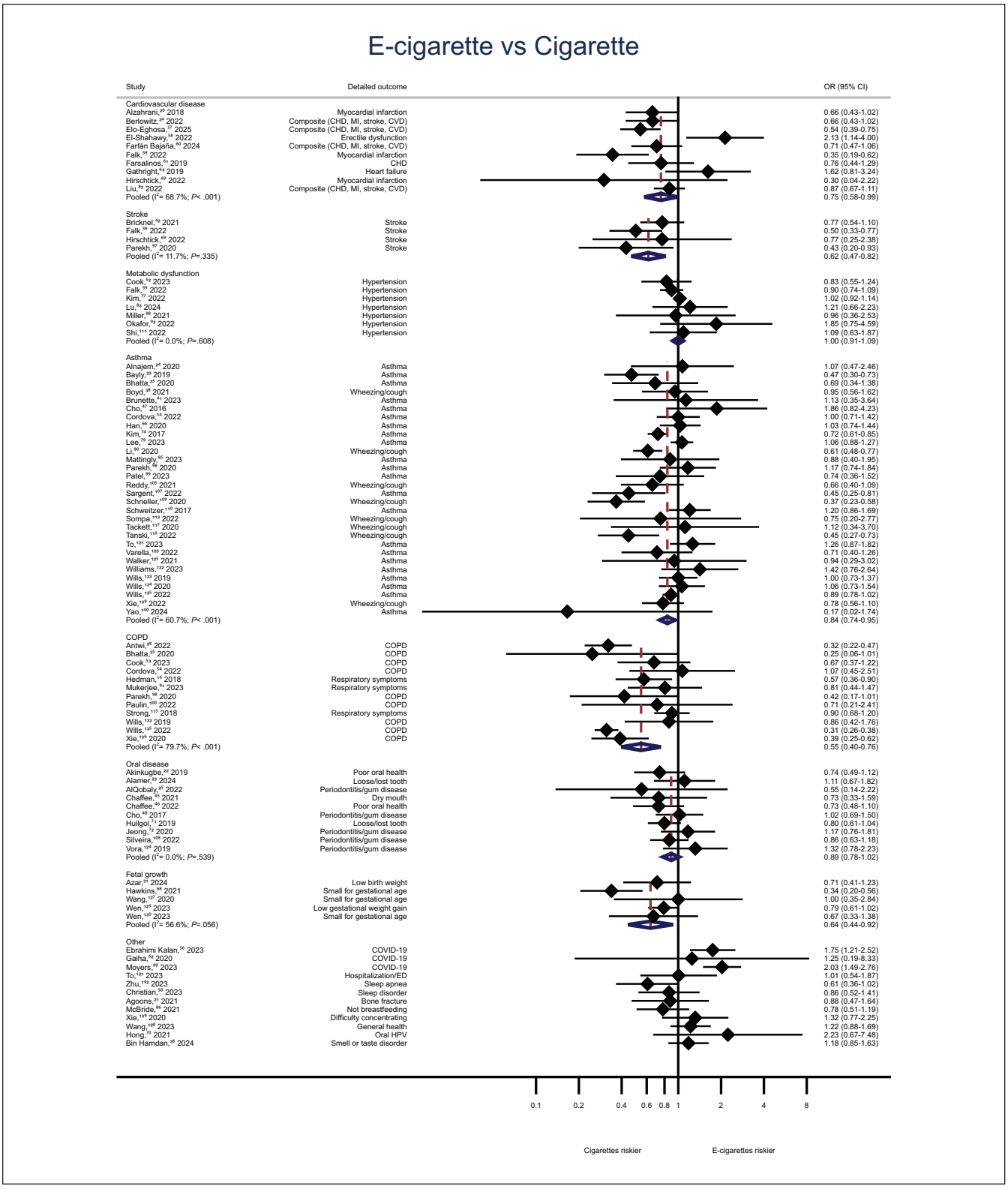

Figure 1. Point estimates and 95% CIs for pooled ORs from a random-effects meta-analysis comparing e-cigarette use with combustible cigarette use. E-cigarette use has similar ORs of disease as cigarette smoking for metabolic dysfunction and oral disease and lower ORs for CVD, stroke, asthma, COPD, and fetal growth. 95% CIs include Bonferroni adjustments. Results for "other" studies were not pooled. Dashed lines indicate pooled estimates. Abbreviations: CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; e-cigarette, electronic cigarette; ED, emergency department; HPV, human papillomavirus; MI, myocardial infarction; OR, odds ratio.

Table. Pooled adjusted[a] odds ratios (95% CI) for selected disease outcomes from a meta-analysis of population studies of the disease risks of electronic cigarette use, cigarette use, dual use, and nonuse, 2005-2025[b]

Comparison	CVD	Stroke	Metabolic dysfunction	Asthma	COPD	Oral disease	Fetal growth
Comparison with cigarette use							
E-cigarette use versus cigarette use	0.76 (0.58-0.99)	0.62 (0.47-0.82)	1.00 (0.91-1.09)	0.84 (0.74-0.95)	0.55 (0.40-0.76)	0.89 (0.78-1.02)	0.64 (0.44-0.92)
Dual use versus cigarette use	1.29 (1.07-1.53)	1.39 (1.05-1.82)	1.24 (1.16-1.32)	1.22 (1.14-1.30)	1.41 (1.19-1.66)	1.42 (1.17-1.72)	0.99 (0.84-1.17)
Comparison with nonuse							
E-cigarette use versus nonuse of e-cigarettes	1.24 (1.06-1.45)	1.29 (0.95-1.75)	1.26 (1.19-1.34)	1.27 (1.21-1.32)	1.45 (1.32-1.60)	1.53 (1.24-1.88)	1.20 (0.92-1.55)
Dual use versus nonuse of e-cigarettes or cigarettes	2.23 (1.59-3.14)	2.40 (2.03-2.84)	1.49 (1.17-1.91)	1.56 (1.24-1.96)	3.17 (1.95-5.14)	1.77 (1.46-2.15)	1.64 (1.17-2.31)
Cigarette use versus nonuse of cigarettes	1.64 (1.33-2.02)	2.07 (1.90-2.26)	1.27 (1.18-1.37)	1.56 (1.35-1.81)	2.90 (2.32-3.76)	1.71 (1.44-2.05)	1.99 (1.39-2.86)

Abbreviations: COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; e-cigarette, electronic cigarette.

[a] Adjusted for covariates listed in eTable 3 in the Supplement.

[b] Data were pooled data from studies published from January 1, 2005, through January 1, 2025, in a random-effects meta-analysis if ≥5 studies were identified for a disease outcome. There were no age or language restrictions.

conclusions for fetal growth (eTables 15 and 16 in the Supplement). We have moderate confidence in the conclusion that dual use, compared with cigarette use, was associated with higher odds of disease for all outcomes except stroke and fetal growth, where confidence was low and very low, respectively (eTables 15 and 16 in the Supplement). Confidence in the comparisons of e-cigarette use and dual use versus no product use was moderate to high, except for stroke, where it was low, and fetal growth, where it was very low. Confidence in the comparisons of cigarette use and dual use versus no product use was moderate to high, except for stroke, where it was low, and fetal growth, where it was very low.

Accounting for the fact that some e-cigarette users use only e-cigarettes and some are dual users increases the overall OR of disease associated with all e-cigarette use in the population because dual use is associated with ORs >1.0 for all outcomes (eFigure 5 in the Supplement). Based on the estimate that 39.1% of e-cigarette users in the United States were dual users in 2019,[15] the probabilities of an OR being >1.0 were 0.36 for CVD, 0.22 for stroke, >0.99 for metabolic dysfunction, 0.38 for asthma, 0.08 for COPD, 0.94 for oral disease, and 0.01 for fetal growth. These results are sensitive to the prevalence of dual use. In Sweden in 2016, when dual use was 66.7%,[16] these probabilities increased to 0.92 for CVD, 0.86 for stroke, >0.99 for metabolic dysfunction and asthma, 0.98 for COPD, >0.99 for oral disease, and 0.05 for fetal growth. The low levels for fetal growth were based on OR estimates with very low confidence.

Discussion

Observational evidence from 142 ORs of disease in 124 population-based epidemiological studies of actual (real-world) use of e-cigarettes revealed that the odds of disease associated with e-cigarette use were not detectably different from the odds associated with cigarette use for metabolic dysfunction and oral disease, but were lower for CVD, stroke, asthma, COPD, and fetal growth (Table; Figure 1). The ORs associated with e-cigarette use, compared with cigarette use, for CVD (OR=0.76), stroke (OR = 0.62), asthma (OR=0.84), COPD (OR=0.55), oral disease (OR=0.89), and fetal growth (OR=0.62), while lower than for cigarette use, were 3 to 10 times the 15% risk that the US Food and Drug Administration (FDA)[6] or the 5% risk that Public Health England[8] has quoted. The odds of disease associated with dual use were higher than for cigarette use for all outcomes, with ORs ranging from 1.22 to 1.42 (Table and Figure 2), except fetal growth (OR=0.99). These results give high confidence that the widely prevalent argument that e-cigarettes are 95% safer than cigarettes[8,10] is incorrect and should no longer be claimed or used.

While the overall conclusions of this updated analysis are broadly similar to the earlier meta-analysis based on studies published through October 1, 2023,[19] we observed 5 differences in the detailed results of the updated, larger dataset. First, the risks of CVD and stroke associated with e-cigarette use, compared with cigarette use, are now detectably lower. Second, the risk of oral disease associated with e-cigarette use, which was previously lower than the risk associated with cigarette use, is now indistinguishable. Third, we added fetal growth to the quantitative meta-analysis because 6 (≥5) studies were available. (As noted previously, however, we have very low confidence in conclusions about the fetal studies because of the way e-cigarette use was measured.) Fourth, we identified several additional disease outcomes. Fifth, the association between disease risk and e-cigarette use, which previously varied over time, is now stable (eTable 7 in the Supplement [$P \geq .16$] vs Table S6 in the earlier article[19]), suggesting that changes in e-cigarette devices over time have not had major effects on disease risk.

The finding that dual use is associated with higher risks than cigarette use has important implications for whether

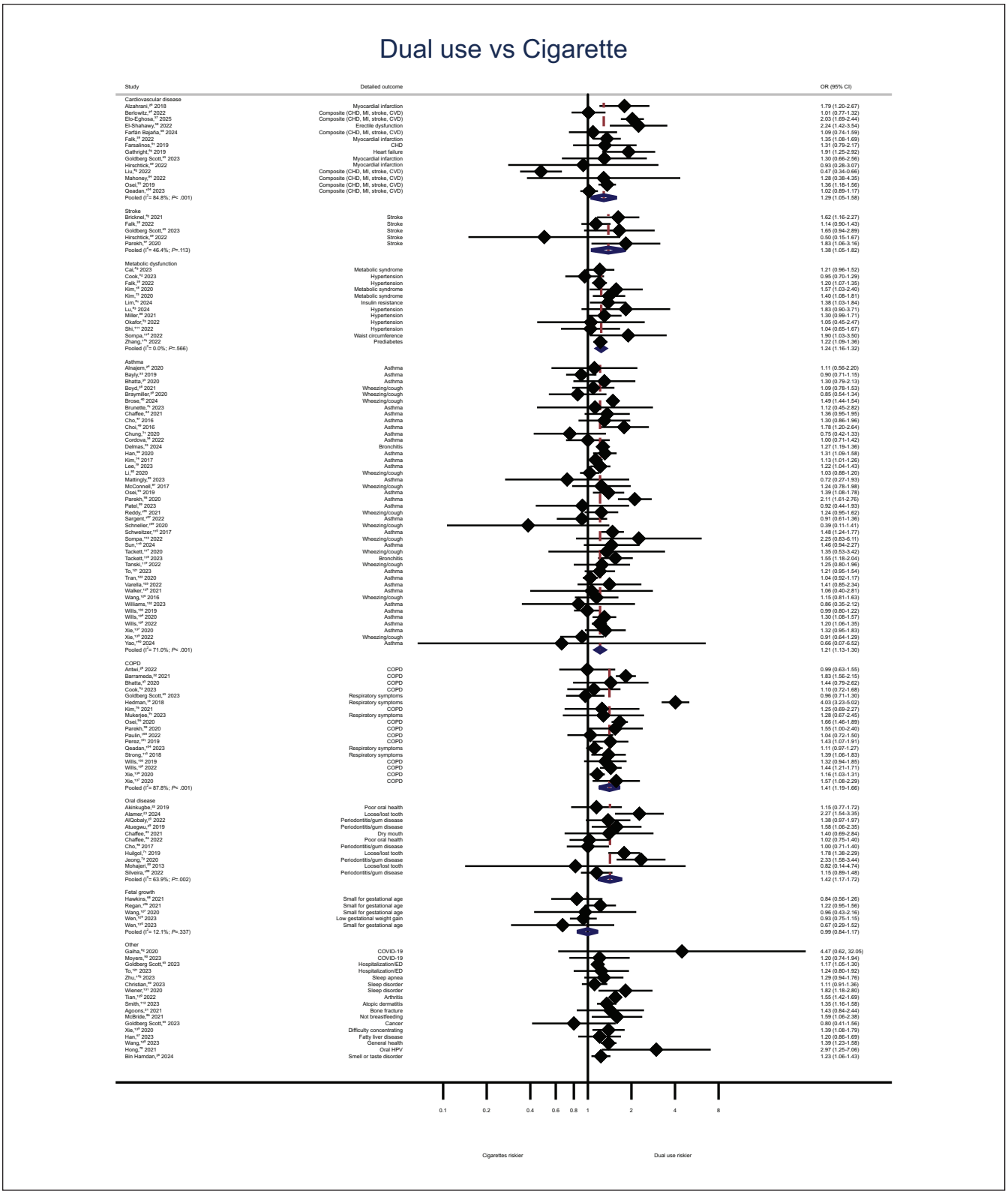

Figure 2. Point estimates and 95% CIs for pooled ORs from a random-effects meta-analysis comparing dual use (concurrently using e-cigarettes and combustible cigarettes) with cigarette use. ORs of disease of all outcomes are >1.0 among dual users than among cigarette smokers except for fetal growth. 95% CIs include Bonferroni adjustments. Results for "other" studies were not pooled. Dashed lines indicate pooled estimates. Abbreviations: CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; ED, emergency department; HPV, human papillomavirus; MI, myocardial infarction; OR, odds ratio.

using e-cigarettes is actually a harm reduction strategy. In a naturalistic randomized controlled trial in which smokers were provided free e-cigarettes, 2.7 smokers became dual users for every smoker who stopped using cigarettes,[150,151] and in a large population study of people trying to quit smoking, 3.9 smokers became dual users for every smoker who stopped using cigarettes.[152] While, on average, the population study found that dual users consumed fewer cigarettes than sole smokers and had more smoke-free days,[153] these individuals are captured in our definition of dual use, which includes anyone who smoked cigarettes or used e-cigarettes in the past 30 days, so the conclusion that accounting for dual use increases harm still applies. A meta-analysis of the effects of cigarette reduction did not find any significant difference in all-cause mortality, all-cancer risks, or smoking-related/tobacco-related cancer risk, and it found mixed results on CVD (coronary heart disease and stroke combined).[154] Future studies need to report dual use as well as changes in cigarette use and consider dual use an adverse outcome.

The ORs of e-cigarette use for asthma and COPD are similar to the ORs in earlier meta-analyses that were based on fewer studies[155-158] and consistent with qualitative summaries[159] that concluded that switching from cigarettes to e-cigarettes was associated with a lower risk of respiratory disease but not CVD and that dual use was associated with higher risks than smoking cigarettes only.[160] Our meta-analysis of 6 studies of the association between e-cigarette use and fetal growth found a lower risk for e-cigarette use than for cigarette use, but with very low confidence. Another meta-analysis[161] of 23 studies that was based on a more extensive search for pregnancy-related topics than ours and that used different ways of assessing exposure and pooling outcomes found that prenatal e-cigarette use was associated with adverse maternal (OR = 1.53; 95% CI, 1.27-1.85) and neonatal (OR = 1.53; 95% CI, 1.34-1.76) outcomes. These differences further reduce confidence in conclusions on the fetal growth studies included in our analysis.

Our systematic review included only 1 article that reported cancer results,[65] which is not enough to produce a quantitative estimate for risks of e-cigarette or dual use or comparisons with cigarette use. However, some evidence from studies that did not meet our inclusion criteria indicates that e-cigarettes increase cancer risk. A large case-control study[162] found that daily dual users had nearly 40 times the odds (OR = 38.7; 95% CI, 31.5-47.6) of developing lung cancer as people who did not smoke or use e-cigarettes, which is 4 times the risk for smoking only cigarettes (OR = 9.6; 95% CI, 8.7-10.6). An abstract describing a large cohort study from Korea[163] that controlled for level of smoking found elevated lung cancer risk among former smokers who continued to use e-cigarettes. E-cigarette users and cigarette smokers experience similar levels of DNA damage,[164] more than twice the amount found in people who do not use either product. At least 543 cancer-related genes are adversely affected in people who use e-cigarettes, and 44% of cancer-related genes are adversely affected by cigarettes.[164] Breathing e-cigarette aerosol causes lung cancer and bladder hyperplasia[165] and promotes breast cancer progression and lung metastasis in mice.[166] Several biological pathways have been identified through which e-cigarette exposure changes the tumor microenvironment in a way that promotes metastasis of tumors once they are established.[167,168] These studies suggest the need to look beyond e-cigarettes as carcinogens (cancer initiators) to include tumor promotion, which also points to the importance of dual use. In 2025, the Clinical Oncology Society of Australia concluded, "E-cigarettes are likely to cause lung cancer and oral cancer."[169] Cancer accounts for about one-third of smoking-caused deaths in the United States.[170]

Because our current study used the same protocol as the earlier meta-analysis,[19] the same limitations discussed there and in correspondence about the article[171] apply here.

Public Health Implications

The accumulating epidemiological evidence based on actual use of e-cigarettes in the general population continues to indicate that, at least for some diseases, there are no detectable differences in the odds of disease between current e-cigarette use and current cigarette use; for other diseases, the risks of e-cigarette use, while lower than the risks of cigarette use, are still much higher than what has been suggested by some public health authorities that promote e-cigarettes as a harm reduction strategy.[1-6,8] These results also suggest that tobacco company advertisements promoting e-cigarettes to reach a future without cigarettes[9-14] would likely be a future with levels of disease and death not so different from today.

The new results reported here illustrate how quickly evidence on e-cigarettes and disease is accumulating and the need to make decisions based on up-to-date data. For example, while a review using a literature search through July 2020 found evidence for most disease outcomes "insufficient,"[172] a substantial evidence base now exists on the association between e-cigarette use and disease. Indeed, 81% of the studies (101 of 124) included in our current analysis were published during or after 2020 (Figure 3).

The finding that, except for fetal growth (where we have very low confidence in the results), dual use has higher risks of disease than cigarette use alone is important because dual use is common in the population[15-18] and a more likely outcome than "switching completely" among people[150,151] using e-cigarettes to quit smoking.[150-152] Accounting for dual use means that even for diseases where sole e-cigarette use poses lower risks than cigarette use, the overall effect of e-cigarette use on disease burden will be higher (eFigure 8 in the Supplement). Future population studies and randomized controlled trials should report results for dual use. Regulatory decisions about whether e-cigarettes are "appropriate for the protection of public health," the legal standard[173] the FDA is required to use, need to account for dual use. Randomized controlled trials of e-cigarettes for smoking cessation should treat

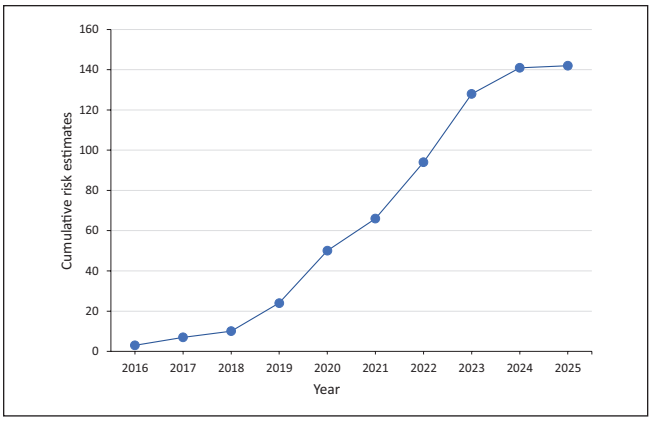

Figure 3. The number of risk estimates for the association between electronic cigarettes (e-cigarettes) and disease. The number of available risk estimates has rapidly increased in recent years, highlighting the importance of making clinical and policy decisions based on current data. The leveling off in 2025 likely reflects the fact that the search for studies ended on January 1, 2025.

dual use as an adverse outcome because it poses a higher risk than cigarette use, which may lead to the conclusion that e-cigarettes as a clinical cigarette cessation intervention increase rather than reduce harm. In addition, as consumer products, e-cigarettes are not associated with increased smoking cessation,[174,175] and in the long run, they are associated with decreases in cessation and increases in the odds of becoming a dual user.[176,177]

The findings of increased odds of several diseases for e-cigarette use compared with nonuse of e-cigarettes illustrate the substantial risks for people, particularly children, adolescents, and young adults, who initiate nicotine use with e-cigarettes and former smokers who restart nicotine use with e-cigarettes.

As of January 2025, e-cigarettes had been on the market for less than 20 years, so the risks reported here may underestimate actual long-term risks. For example, e-cigarette users are, on average, younger than cigarette smokers[177] and not enough time may have passed for the e-cigarette–related COPD risks to fully manifest.[87,178,179]

As discussed in detail in the earlier meta-analysis based on fewer studies,[19] the disease risks identified in the epidemiological studies are higher than predicted by biomarkers of exposure to tobacco products.[180-183] Now is the time to move beyond indirect measures of health impact (biomarkers) to actual disease when making clinical and policy decisions about e-cigarettes.

E-cigarette use is associated with disease outcomes indistinguishable from or approaching the disease outcomes associated with cigarette use for major smoking-caused diseases. Health care providers and public health authorities should stop promoting e-cigarettes as a meaningfully safer alternative to cigarette smoking. Dual use, which is common among adult e-cigarette users, is associated with a higher risk of disease than cigarette use alone.

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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, or the Brazilian government.

Supplemental Material

Supplemental material for this article is available online. The authors have provided these supplemental materials to give readers additional information about their work. These materials have not been edited or formatted by *Public Health Reports*'s scientific editors and, thus, may not conform to the guidelines of the *AMA Manual of Style*, 11th Edition.

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