# Supplementary Online Content

Soneji S, Barrington-Trimis JL, Wills TA, et al. Association between initial use of e-cigarettes and subsequent cigarette smoking among adolescents and young adults: a systematic review and meta-analysis. *JAMA Pediatr*. Published online June 26, 2017. doi:10.1001/jamapediatrics.2017.1488

**eTable 1.** Summary of Search Results

| Database | Platform | Years covered | Dates Conducted | # Results |
|---|---|---|---|---|
| Medline | Pubmed | 1946-current | July 28, 2016<br>December 15, 2016<br>February 13, 2017 | 2471 |
| Embase | Embase.com | 1974-current | July 28, 2016<br>December 13, 2016<br>February 7, 2017 | 3156 |
| Web of Science | WOS | 1900-current | July 28, 2016<br>December 15, 2016<br>February 13, 2017 | 2055 |
| Cochrane Library | Wiley | Issue #, date<br>DSR - Iss7, July 2016<br>Dare-Iss2, April 2015<br>Trials-Iss6, June 2016<br>methods-Iss3, July 2012<br>tech-Iss2, April 2016 | July 28, 2016<br>December 15, 2016<br>February 17, 2017 | 240 |
| Society for Research on Nicotine & Tobacco | — | 2016 | September 1, 2016 | 803 |
| Society for Behavioral Medicine | — | 2016 | September 1, 2016 | 34 |
| NIH Tobacco Regulatory Science Conference | — | 2016 | September 1, 2016 | 167 |
| | | | Total | 8926 |
| | | | Total with Duplicates Removed | 6959 |

**eTable 2.** Pubmed Run (Conducted on July 28, 2016)

| Search | Query | Items Found |
|---|---|---|
| #3 | Search (#1 AND #2) | 2,044 |
| #2 | Search Tobacco Use[mesh] OR Tobacco[mesh] OR Tobacco use disorder[mesh] OR Tobacco Products[mesh] OR Cigarette*[tiab] OR Tobacco[tiab] OR Smoking[tiab] OR smoker*[tiab] OR cigar*[tiab] | 292,817 |
| #1 | Search Electronic Cigarettes[mesh] OR (Nebulizers and Vaporizers[mesh] AND (tobacco[mesh] OR tobacco[tiab] OR nicotine[mesh] OR nicotine[tiab])) OR (Drug Delivery Systems[mesh] AND (tobacco[mesh] OR tobacco[tiab] OR nicotine[mesh] OR nicotine[tiab])) OR Electronic Cigarette*[tiab] OR E-Cig*[tiab] OR electronic nicotine delivery system*[tiab] OR vape*[tiab] OR vaping[tiab] | 2,231 |

**Table 3.** Cochrane Library (Wiley) Run (Conducted on July 28,2016)

| ID | Search | Hits |
|---|---|---|
| #1 | Electronic Cigarette* or E-Cig* or electronic nicotine delivery system* or vape* or vaping or nebulize*:ti,ab,kw (Word variations have been searched) | 3,344 |
| #2 | Cigarette* or Tobacco or Smoking or smoker* or cigar*:ti,ab,kw (Word variations have been searched) | 20,039 |
| #3 | #1 and #2 | 196 |

**eTable 4.** Keyword Search Terms for Society for Nicotine & Tobacco and Society for Behavioral Medicine Annual Meetings and NIH Tobacco Regulatory Science Conference

| Keywords |
|---|
| Electronic cigarette* |
| E-cig* |
| Electronic nicotine delivery system |
| Vape* |
| Vaping |
| Tobacco |
| Smoking |
| Cigarette |
| |

**eTable 5.** Psychosocial and Behavioral Characteristics Included in Studies

| Study | Covariate | Details |
|---|---|---|
| Leventhal et al. (2015) | Depressive Symptoms | 20-item Center for Epidemiologic Studies Depression Scale |
| | Impulsivity | 5-item Temperament and Character Inventory impulsivity subscale |
| | Delinquent Behavior | Sum of frequency ratings for engaging in 11 different behaviors (e.g., stealing, lying to parents) |
| | Substance Use | Ever use of alcohol and 13 separate illicit and prescription substances of abuse |
| | Family History of Smoking | "Does anyone in your immediate family (brothers, sisters, parents, or grandparents) have a history of smoking cigarettes?" |
| | Peer Smoking | "In the last 30 days, how many of your 5 closest friends have smoked cigarettes?" |
| | Smoking Susceptibility | "Would you try smoking a cigarette if one of your best friends offered it to you?"<br>"Do you think you would smoke in the next 6 months?"<br>"Are you curious about smoking?"<br>(definitely not, probably not, probably yes, definitely yes) |
| | Smoking Expectancies | Average of the 2 responses for "I think I might enjoy …smoking" and (reversed) "I think I might feel bad ... from smoking."(1 strongly disagree, 2 disagree, 3 agree, 4 strongly agree) |
| Primack et al. (2015) | Sensation Seeking | Composite measure of sensation-seeking tendency previously found to be related to cigarette smoking and other high-risk health behaviors based on 6 items, such as "I like to do dangerous things" |
| | Parental Smoking | Never (0), former (1), occasional (2), and daily (3), and scores for mothers and fathers were averaged |
| | Peer Smoking | # of respondents' close friends smoked cigarettes, with response choices of none (0), few (1), more than a few (2), or most (3) |
| Barrington-Trimis et al. (2016) | Cigarette Use in Home | "Does anyone who lives with you now use cigarettes?" |
| | Peer Smoking | "How many of your□4 closest friends use [cigarettes]?" (0–4 friends) |
| | Peer Acceptability of Smoking | "How would your best friends act toward you if you used cigarettes?" (very unfriendly, unfriendly, friendly, or very friendly) |
| Primack et al. (2016) | Self-Esteem | Single-Item Self-Esteem Scale |
| | Sensation Seeking | 4-item validated Likert-type scale that included items such as "I like to do dangerous things" |
| | Rebelliousness | Validated Likert-type subscale of Smith and Fogg that included items such as "I tend to go against the rules" |
| Unger et al. (2016) | Past Month Use of Alcohol | — |
| | Past Month Use of Other Tobacco Products | Hookah, cigars, little cigars, smokeless tobacco |
| Hornik | Sensation Seeking | 4-item validated Likert-type scale that included items such as "I like to do frightening things" |

| | | |
|---|---|---|
| et al. (2016) | Ever Cigarette Use | "Have you ever tried smoking cigarettes, even one or two puffs?" |
| | Cigarette Use in Home | "Does anyone who lives with you now smoke cigarettes?" |
| | Peer Smoking | "How many of your 4 closest friends smoke cigarettes?" (0-4 friends) |
| Spindle et al. (2016) | Depression | 4 items from the Symptom Checklist (SCL)-90. Items are measured on 5-point Likert scales and included "feeling blue," "worrying too much about things," "feeling hopeless about the future," "feeling no interest in things." |
| | Anxiety | 4 items from the SCL-90. Items are measured on 5-point Likert scales and included "feeling fearful," "suddenly scared for no reason," "nervousness or shakiness inside," "spells of terror or panic." |
| | Impulsivity | 5 subscales from the UPPS-P Impulsive Behavior Scale. Subscales each consisted of 3 items measured on 4-point Likert scales. Subscales included: lack of perseverance, lack of premeditation, negative urgency, positive urgency, and sensation seeking. |
| | Stressful Life Events | 12 items inquiring about potentially stressful life events in the past 12 months (e.g., "separation from loved one or close friend"). Stressful life events were summed to create an overall score. |
| | Peer Deviance | 6 items addressing how many of the student's friends (from "none" to "all") had smoked cigarettes, drank alcohol, gotten drunk, had problems with alcohol, been in trouble with the law, and smoked marijuana. Items were summed to create an overall peer deviance score. |
| | Other Tobacco Use | Ever use of "smokeless tobacco," "little cigars/cigarillos," and "hookah." |
| Miech et al. (2017) | Binge Drinking, Past 2 Weeks | "Think back over the last 2 weeks. How many times (if any) have you had 5 or more drinks in a row?" |
| | Marijuana Use, Past 30 Days | "On how many occasions (if any) have you used marijuana (weed, pot) or hashish (hash, hash oil) during the last 30 days?" |

**eTable 6.** Quality of Studies Assessment (Newcastle – Ottawa Scale)

| Category | Criteria | Leventhal et al. (2015) | Primack et al. (2015) | Wills et al. (2015) | Barrington-Trimis et al. (2015) | Unger et al. (2016) | Hornik & Gibson (2016) | Primack et al. (2016) | Spindle et al. (2016) | Miech et al. (2017) |
|---|---|---|---|---|---|---|---|---|---|---|
| Selection | Representativeness of the exposed cohort | b* | b* | b* | b* | b* | b* | b* | b* | b* |
| | Selection of the non-exposed cohort | a* | a* | a* | a* | a* | a* | a* | a* | a* |
| | Ascertainment of exposure | c | c | c | c | c | c | c | c | c |
| | Demonstration that outcome of interest was not present at start of study | a* | a* | a* | a* | a* | a* | a* | a* | a* |
| Compara-bility | Comparability of cohorts on the basis of the design or analysis | * | * | * | * | * | * | * | * | * |
| Outcome | Assessment of outcome | c | c | c | c | c | c | c | c | c |
| | Was follow-up long enough for outcomes to occur[1] | a* | a* | a* | a* | a* | a* | a* | a* | a* |
| | Adequacy of follow-up of cohorts[2] | b* | c | c | c | b* | d | c | b* | c |
| Total # of stars (*) | | 6 | 5 | 5 | 5 | 6 | 5 | 5 | 6 | 5 |

[1]6 months considered adequate follow up time

[2]Studies with <20% loss to follow-up received one star for adequacy of follow-up of cohorts

Note: Lev=Leventhal et al. (2015); Pri=Primack et al. (2015); Wil=Wills et al. (2016); Bar=Barrington-Trimis et al. (2016); Ung=Unger et al. (2016); Hor=Hornik et al. (2016); Spi=Spindle et al. (2016); Mie=Miech et al. (2017). Letters refer to the grade as denoted by the Newcastle – Ottawa Scale rubric (http://www.ohri.ca/programs/clinical_epidemiology/nosgen.pdf).

**eTable 7.** Risk of Bias (ROBINS-I)

| Study | Confounding | Selection | Measurement of Intervention | Missing Data | Measurement of Outcomes | Reported Result | Overall |
|---|---|---|---|---|---|---|---|
| Lev (2015) | Moderate | Low | Low | Low | Low | Moderate | Moderate |
| Pri (2015) | Moderate | Low | Low | Low | Low | Moderate | Moderate |
| Wil (2016) | Moderate | Low | Low | Low | Low | Moderate | Moderate |
| Bar (2016) | Moderate | Low | Low | Low | Low | Moderate | Moderate |
| Pri (2016) | Moderate | Low | Low | Low | Low | Moderate | Moderate |
| Ung (2016) | Moderate | Low | Low | Low | Low | Moderate | Moderate |
| Hor (2016) | Moderate | Low | Low | Low | Low | Moderate | Moderate |
| Spi (2016) | Moderate | Low | Low | Low | Low | Moderate | Moderate |
| Mie (2017) | Moderate | Low | Low | Low | Low | Moderate | Moderate |

Note: Moderate=the study is sound for a non-randomized study with regard to this domain but cannot be considered comparable to a well-performed randomized trial; Low=the study is comparable to a well-performed randomized trial with regard to this domain. Lev=Leventhal et al. (2015); Pri=Primack et al. (2015); Wil=Wills et al. (2016); Bar=Barrington-Trimis et al. (2016); Ung=Unger et al. (2016); Hor=Hornik et al. (2016); Spi=Spindle et al. (2016); Mie=Miech et al. (2017).

**eTable 8.** Pooled Adj. Odds Ratio Varying Prob. of Publishing Study with Largest Standard Error

| Probability of publishing study with largest standard error | OR [95% CI] | P-value for hypothesis of overall treatment effect | P-value for hypothesis that no selection remains unexplained |
|---|---|---|---|
| 1 | 3.46 (2.34-5.14) | <0.001 | 0.065 |
| 0.85 | 3.32 (2.24-4.93) | <0.001 | 0.090 |
| 0.73 | 3.16 (2.14-4.66) | <0.001 | 0.114 |
| 0.63 | 3.01 (2.05-4.40) | <0.001 | 0.142 |
| 0.55 | 2.86 (1.97-4.14) | <0.001 | 0.184 |
| 0.48 | 2.72 (1.89-3.90) | <0.001 | 0.246 |
| 0.42 | 2.59 (1.82-3.69) | <0.001 | 0.340 |

Note: Adj.=Adjusted; Prob.=Probability; OR=odds ratio; CI=confidence interval

**eTable 9.** Pooled Adj. Odds Ratio: Copas Selection Model and Random Effects Model

| Model | OR [95% CI] | P-value for hypothesis of overall treatment effect | P-value for hypothesis that no selection remains unexplained |
|---|---|---|---|
| Copas Selection | 3.16 (2.14-4.66) | < 0.0001 | 0.114 |
| Random Effects | 3.50 (2.38-5.16) | < 0.0001 | — |

Note: Adj.=Adjusted; OR=odds ratio; CI=confidence interval

**eTable 10.** Source of Data from Each Study in Systematic Review and Meta-Analysis

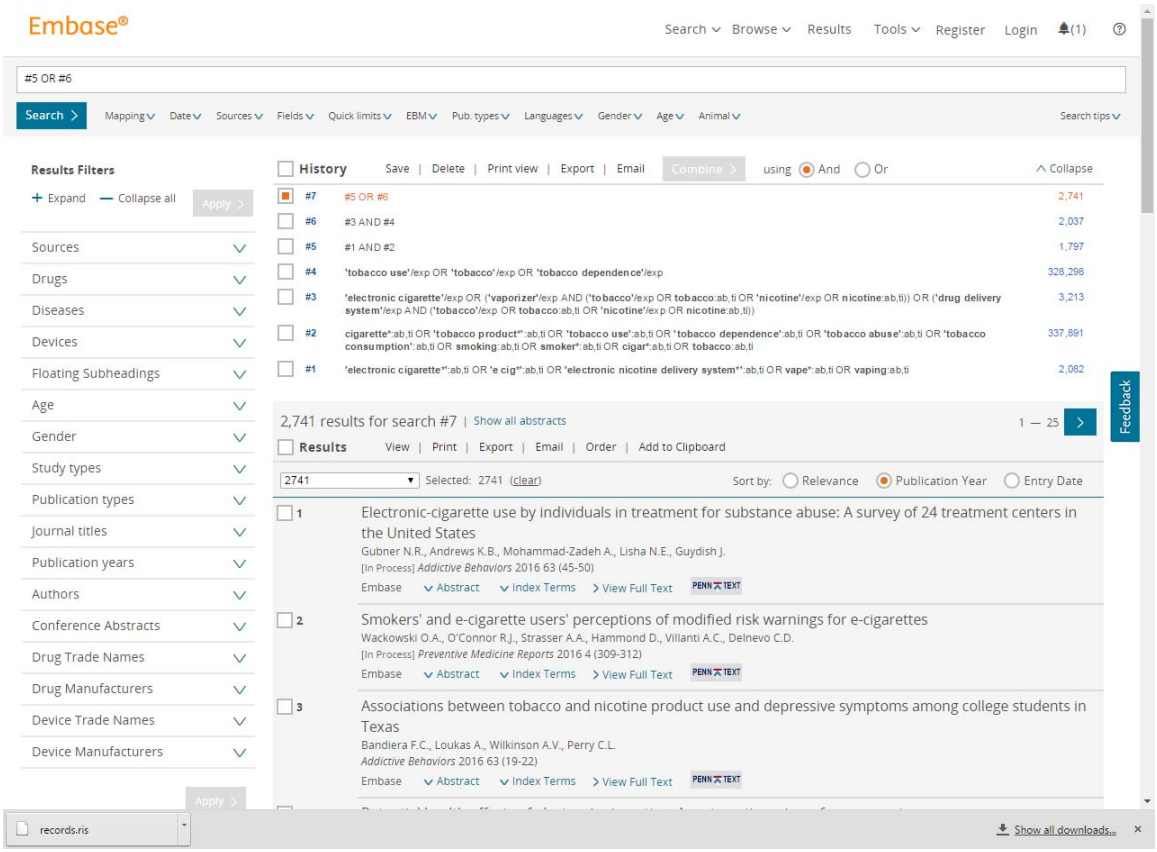
| Study[1] | Summary Information | Transition Probabilities | Unadjusted OR | Adjusted OR |
|---|---|---|---|---|
| Leventhal et al. (2015) | Age of Sample: Table 1<br>Study Period: Methods<br>Follow-Up Period: Methods<br>Loss to Follow-Up: Figure | Derived from 1-6 month and 7-12 month transition probabilities in Table 3 | Table 4 | Table 4 |
| Primack et al. (2015) | Age of Sample: Table 1<br>Study Period: Methods<br>Follow-Up Period: Methods<br>Loss to Follow-Up: Methods | Table 2 | Derived from counts in Table 2 | Table 3 |
| Wills et al. (2015) | Age of Sample: Methods<br>Study Period: Methods<br>Follow-Up Period: Methods<br>Loss to Follow-Up: Methods | Derived from counts in Table 2 | Derived from counts in Table 2 | Table 4 |
| Barrington-Trimis et al. (2016) | Age of Sample: Results<br>Study Period: Methods<br>Follow-Up Period: Methods<br>Loss to Follow-Up: Figure 1 | Table 2 | Derived from counts in Table 2 | Table 2 |
| Unger et al. (2016) | Age of Sample: Results<br>Study Period: Material and Methods<br>Follow-Up Period: Material and Methods<br>Loss to Follow-Up: Material and Methods | Figure 1 | Derived from counts and transition probabilities in Results | Table 1 |
| Hornik et al. (2016) | Age of Sample: Method<br>Study Period: Method<br>Follow-Up Period: Method<br>Loss to Follow-Up: Method | Additional analysis by authors | Additional analysis by authors | Additional analysis by authors |
| Primack et al. (2016) | Age of Sample: Methods<br>Study Period: Methods<br>Follow-Up Period: Methods<br>Loss to Follow-Up: Methods | Table 2 | Derived from counts in Results and transition probabilities in Table 2 | Table 3 |
| Spindle et al. (2017) | Age of Sample: Methods<br>Study Period: Methods | Derived from counts in Table 1 | Derived from counts in Table 1 | Table 3 |

| | | | | |
|---|---|---|---|---|
| | Follow-Up Period: Methods<br>Loss to Follow-Up: Methods | | | |
| Miech et al. (2017) | Age of Sample: Methods<br>Study Period: Methods<br>Follow-Up Period: Methods<br>Loss to Follow-Up: Methods | Table 2 | Derived from transition probabilities in Table 2 and counts in Appendix Table A1 | Table 2 |

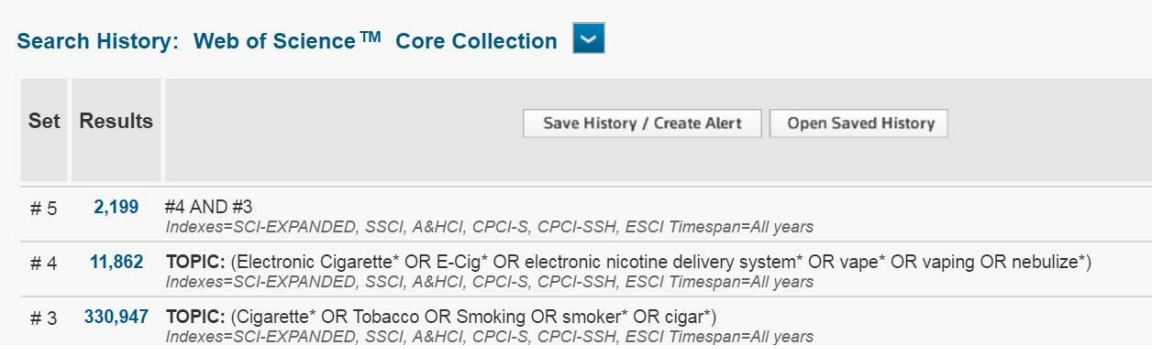
[1]Each study is hyperlinked to its unique journal or conference proceeding website

Note: OR=odds ratio.

**eFigure 1.** Embase Run (Conducted on July 28, 2016)



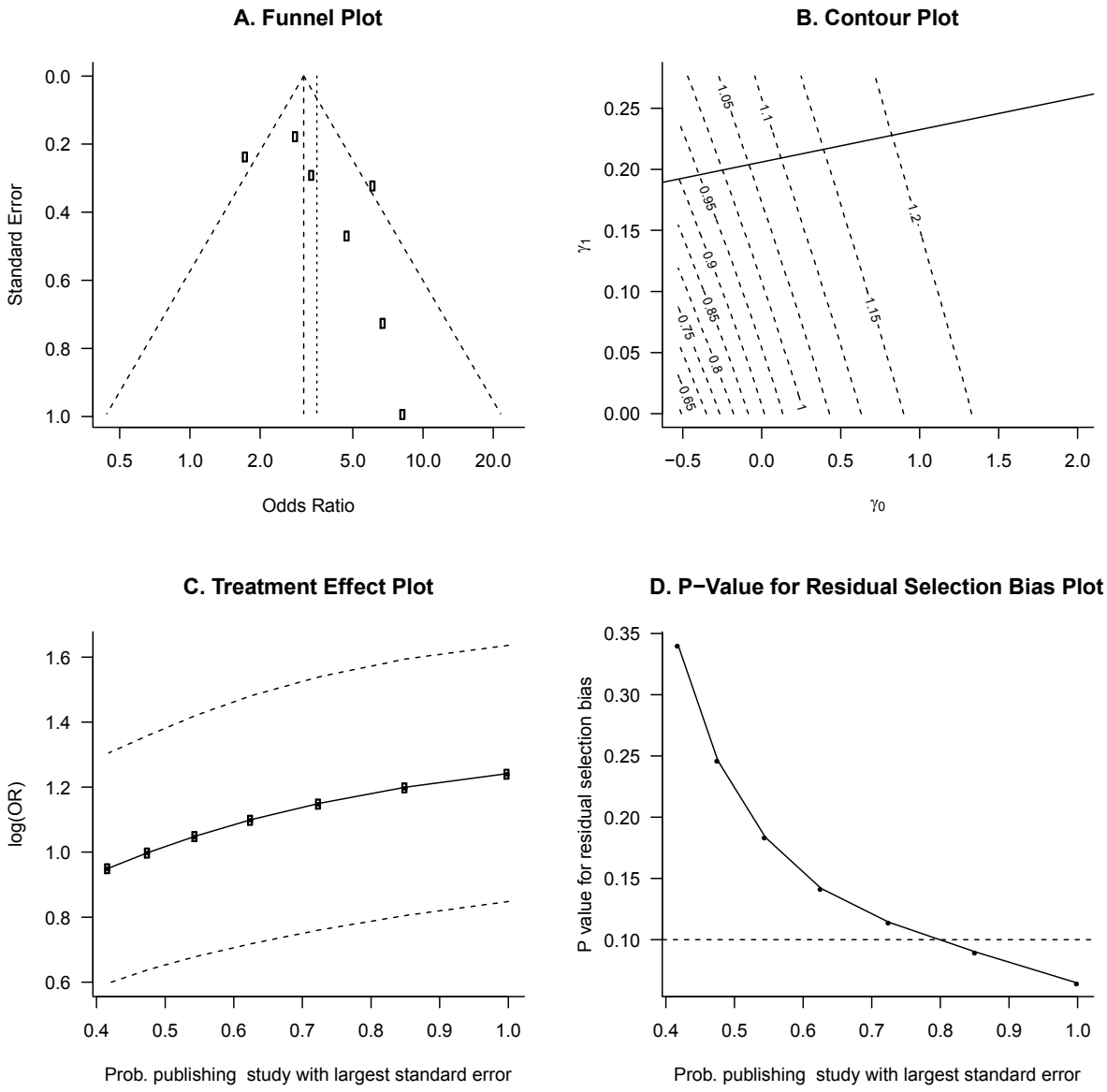
**eFigure 2.** Web of Science Run (Conducted on July 28, 2016)



Search History: Web of Science™ Core Collection

| Set | Results | Save History / Create Alert \| Open Saved History |
|---|---|---|
| # 5 | 2,199 | #4 AND #3<br>*Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years* |
| # 4 | 11,862 | **TOPIC:** (Electronic Cigarette* OR E-Cig* OR electronic nicotine delivery system* OR vape* OR vaping OR nebulize*)<br>*Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years* |
| # 3 | 330,947 | **TOPIC:** (Cigarette* OR Tobacco OR Smoking OR smoker* OR cigar*)<br>*Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years* |

**eFigure 3.** Copas Selection Modelling



**eAppendix.** Selection Bias: Copas Selection Modeling

Two of the seven studies on cigarette smoking initiation fell outside the 95% confidence intervals denoted by the diagonal dashed lines shown in the funnel plot (Figure A1, Panel A), which suggests possible heterogeneity and publication bias. We then assessed the sensitivity of the meta-analysis to selection mechanisms of varying strength.[1,2] Specifically, $\gamma_0$ is approximately equal to the probit of the probability that a study with a large standard error is published and $\gamma_1$ is approximately equal to the probit of the probability that a study with precision equal to the inverse of its standard error is published. The contour plot (Figure A1, Panel B) suggests that the logarithm of the estimated adjusted pooled odds ratio from the meta-analysis may be sensitive (i.e., varies between 0.7 and 1.25) to the range of $(\gamma_0, \gamma_1)$ values. We further explore this sensitivity in Figure A1, Panels C and D. As the probability of publishing the study with the largest standard error decreases from 100% to 40%, the estimated adjusted pooled odds ratio deceases from 3.57 ($e^{1.27}$) to 2.59 ($e^{0.95}$; Figure A1, Panel C). Notably, the confidence interval of the adjusted pooled odds ratio remains above 1 (i.e., confidence interval of log odds ratio remains above 0) across the range of probabilities of publishing the study with the largest standard error. For each of the selection probabilities shown in Figure A1, Panel C, the Copas selection model calculates a p-value for the test of any remaining selection bias. Selection mechanisms for which this p-value is not statistically significant (i.e., p-value ≥ 10%) correspond to more plausible estimates of the adjusted pooled odds ratio under the Copas selection model.[1] The model indicates statistically significant residual publication bias (i.e., p-value < 10%) until the probability of publishing the study with the largest standard error falls just below 65%. In other words, estimated adjusted pooled odds ratios corresponding to probabilities of publishing the study with the largest standard error below 60% are the most plausible under the model. Notably, all of these estimated adjusted pooled odds ratios are statistically significant (Table E1). Overall, adjusting for selection bias, the estimated adjusted pooled odds ratio equaled 3.16 (95% CI: 2.14-4.66) compared to 3.50 (95% CI: 2.38-5.16) under the baseline random effects model (Table E2).

## References


1. Carpenter JR, Schwarzer G, Rücker G, Künstler R. Empirical evaluation showed that the Copas selection model provided a useful summary in 80% of meta-analyses. *J Clin Epidemiol*. 2009;62(6):624-631.e4. doi:10.1016/j.jclinepi.2008.12.002.

2. Schwarzer G, Carpenter J, Rücker G. Empirical evaluation suggests Copas selection model preferable to trim-and-fill method for selection bias in meta-analysis. *J Clin Epidemiol*. 2010;63(3):282-288. doi:10.1016/j.jclinepi.2009.05.008.