Figure 1. Association of EC use with asthma in the human population

				Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
Bayly 2019	0.239	0.0711	7.8%	1.27 [1.10, 1.46]	-
Bhatta 2020	0.4447	0.18	3.2%	1.56 [1.10, 2.22]	
Cho 2016a (1)	1.008	0.3808	0.9%	2.74 [1.30, 5.78]	
Cho 2016b (2)	-0.0408	0.4208	0.8%	0.96 [0.42, 2.19]	
Choi 2016	0.7885	0.2069	2.6%	2.20 [1.47, 3.30]	
Chung - 2019a (3)	-0.5108	0.8998	0.2%	0.60 [0.10, 3.50]	· · · · · · · · · · · · · · · · · · ·
Chung 2019b (4)	0.793	0.2375	2.1%	2.21 [1.39, 3.52]	
Fedele 2016	0.2927	0.0808	7.2%	1.34 [1.14, 1.57]	
Han (F) 2020	0.2546	0.1671	3.6%	1.29 [0.93, 1.79]	+
Han (M) 2020	0.0488	0.1282	4.9%	1.05 [0.82, 1.35]	- -
Kim 2017	0.1222	0.0556	8.6%	1.13 [1.01, 1.26]	-
Larsen 2016	0.5766	0.2238	2.3%	1.78 [1.15, 2.76]	
Lee 2019	0.207	0.108	5.8%	1.23 [1.00, 1.52]	
McConnel 2017	0.5365	0.1793	3.2%	1.71 [1.20, 2.43]	│ — - —
Osei 2019	0.3293	0.0967	6.4%	1.39 [1.15, 1.68]	
Perez 2019a (5)	0.3075	0.1048	6.0%	1.36 [1.11, 1.67]	
Perez 2019b (6)	0.1044	0.0524	8.8%	1.11 [1.00, 1.23]	-
Schweitzer 2017	0.392	0.0826	7.1%	1.48 [1.26, 1.74]	
Wang 2016	0.7227	0.2586	1.9%	2.06 [1.24, 3.42]	
Wang 2018	0.3221	0.1212	5.2%	1.38 [1.09, 1.75]	→
Wills 2019	0.2852	0.1458	4.2%	1.33 [1.00, 1.77]	
Wills 2020	0.2624	0.0831	7.1%	1.30 [1.10, 1.53]	-
Total (95% CI)			100.0%	1.35 [1.25, 1.46]	•
Heterogeneity: Tau ² =	0.01; Chi ² = 46.60	. df = 21	(P = 0.00 ⁻	1); I² = 55%	
Test for overall effect:		0.1 0.2 0.5 1 2 5 10 Favors No Asthma Favors Asthma			

Footnotes

(1) Among current EC users

(2) Among former EC users

(3) Among current EC users

(4) Among former EC users

(5) Among current EC users(6) Among former EC users

Figure 2. Association of ENDS with alcohol use (ENDS nonuser vs ENDS users)

				Odds Ratio		Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI		IV, Random, 95% Cl
3artoli 2014	0.9123	0.4638	3.3%	2.49 [1.00, 6.18]		
Camenga 2014	2.8837	0.2837	3.6%	17.88 [10.25, 31.18]		
Chen 2018	2.8391	0.8518	2.5%	17.10 [3.22, 90.79]		
Dai 2018	0.6419	0.14	3.7%	1.90 [1.44, 2.50]		_
Demissi 2017	0.9632	0.0465	3.8%	2.62 [2.39, 2.87]		
Dunbar 2017	-0.4005	0.2436	3.6%	0.67 [0.42, 1.08]		
Enlow 2018	-0.1054	0.5791	3.0%	0.90 [0.29, 2.80]		
Geidne 2016	1.4816	0.572	3.1%	4.40 [1.43, 13.50]		
Giovachini 2017	1.206	0.3739	3.4%	3.34 [1.61, 6.95]		
Hughes 2015	-0.0943	0.2783	3.6%	0.91 [0.53, 1.57]		
laber 2018	1.4327	0.4438	3.3%	4.19 [1.76, 10.00]		
lensen 2018	2.2246	0.0269	3.8%	9.25 [8.77, 9.75]		
Jiang 2016	1.1506	0.2047	3.7%	3.16 [2.12, 4.72]		
Kaleta 2016	1.4586	0.1438	3.7%	4.30 [3.24, 5.70]		
<ong 2017<="" td=""><td>0.6881</td><td>0.3192</td><td>3.5%</td><td>1.99 [1.06, 3.72]</td><td></td><td></td></ong>	0.6881	0.3192	3.5%	1.99 [1.06, 3.72]		
_ee 2016	0.9821	0.4664	3.3%	2.67 [1.07, 6.66]		
_ee 2019	0.9594	0.1024	3.7%	2.61 [2.14, 3.19]		_
lanes 2019	0.0488	0.0096	3.8%	1.05 [1.03, 1.07]		•
Ailicic & Leatherdale 2017	0.8459	0.0618	3.8%	2.33 [2.06, 2.63]		
Dh (F) 2019	2.5096	0.2506	3.6%	12.30 [7.53, 20.10]		-
Dh (M) 2019	1.9169	0.1198	3.7%	6.80 [5.38, 8.60]		
Roberts 2018	0.3716	0.1841	3.7%	1.45 [1.01, 2.08]		
3addleson 2015	0.1398	0.3537	3.5%	1.15 [0.57, 2.30]		
Suris 2015	0.9632	0.3497	3.5%	2.62 [1.32, 5.20]		
Favolacci 2016	0.5766	0.6157	3.0%	1.78 [0.53, 5.95]		
Fhrasher 2015	0.2927	0.0905	3.7%	1.34 [1.12, 1.60]		_
Vestling 2017	2.8501	0.635	2.9%	17.29 [4.98, 60.02]		
Villiams & White 2018	-0.01	0.6033	3.0%	0.99 [0.30, 3.23]		
Wong 2018	2.1041	0.3249	3.5%	8.20 [4.34, 15.50]		
Fotal (95% CI)			100.0%	2.94 [1.87, 4.63]		
Heterogeneity: Tau ² = 1.41;	Chi ² = 6607.85 df =	28 (P < 1			<u> </u>	
est for overall effect: Z = 4.6					0.1	0.2 0.5 1 2 5

Figure 3. Association of ENDS with marijuana use (ENDS nonuser vs ENDS users)

				Odds Ratio		Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI		IV, Random, 95% Cl
Audrain-McGovern 2018	1.3002		4.5%	3.67 [2.51, 5.36]		
Azagba 2018	1.953	0.1799	4.6%	7.05 [4.96, 10.03]		
Bluestein 2017	0.6471	0.2665	4.1%	1.91 [1.13, 3.22]		· · · · · · · · · · · · · · · · · · ·
Camenga 2014	3.3721	0.5693	2.5%	29.14 [9.55, 88.94]		
Cohn 2015	1.1939	0.3636	3.6%	3.30 [1.62, 6.73]		
Conway 2018	2.2721	0.0788	4.9%	9.70 [8.31, 11.32]		-
Curran 2018	1.9315	0.1112	4.8%	6.90 [5.55, 8.58]		
Dai 2018	0.6419	0.1481	4.7%	1.90 [1.42, 2.54]		_
Dautzenberg 2015	0.6419	0.1849	4.5%	1.90 [1.32, 2.73]		
Demissi 2017	1.3083	0.079	4.9%	3.70 [3.17, 4.32]		
Dunbar 2017	1.9387	0.1324	4.8%	6.95 [5.36, 9.01]		
Fotiou 2015	0.7885	0.2412	4.3%	2.20 [1.37, 3.53]		
Jaber 2018	2.4484	0.2362	4.3%	11.57 [7.28, 18.38]		–
Kong 2017	-0.0202	0.6132	2.3%	0.98 [0.29, 3.26]		
Kristjansson 2017	1.3481	0.2117	4.4%	3.85 [2.54, 5.83]		
McCabe 2017	1.6034	0.0995	4.9%	4.97 [4.09, 6.04]		
Milicic & Leatherdale 2017	1.7138	0.0573	5.0%	5.55 [4.96, 6.21]		
Saddleson 2015	0.8629	0.172	4.6%	2.37 [1.69, 3.32]		
Sutfin 2013	-0.0619	0.1959	4.5%	0.94 [0.64, 1.38]		-
Tavolacci 2016	0.892	0.1855	4.5%	2.44 [1.70, 3.51]		
Unger 2016	0.678	0.3419	3.7%	1.97 [1.01, 3.85]		
Westling 2017	2.936	0.5713	2.5%	18.84 [6.15, 57.73]		
White 2015	0.8065	0.2174	4.4%	2.24 [1.46, 3.43]		│ ─ • ──
Williams & White 2018	1.5872	0.5327	2.7%	4.89 [1.72, 13.89]		
Total (95% CI)			100.0%	3.81 [2.97, 4.89]		•
Heterogeneity: $Tau^2 = 0.32^{\circ}$	Chi ² = 365.49, df = 3	23 (P < N	00001) 1		0.1	
Heterogeneity: Tau² = 0.32; Chi² = 365.49, df = 23 (P < 0.00001); l² = 94% Test for overall effect: Z = 10.52 (P < 0.00001)						0.2 0.5 1 2 5 1 avors ENDS Nonusers Favours ENDS Users

Figure 4.	Association of ENDS with smoking cessation (OR) – Meta-analysis from observational
studies.	

Al-Delaimy 2015 -0.8916 0.4179 1.5% 0 Amato 2017 -0.2107 0.2864 1.8% 0 Berry 2015 0.3784 0.2184 2.0% 1 Biener 2015a (1) 1.8034 0.8666 0.7% 6.0 Biener 2015b (2) -1.1712 1.1229 0.5% 0 Bowler 2017 -0.1508 0.1483 2.1% 0 Browe 2015 -0.3147 0.2032 2.0% 0 Browe 2014 0.6931 0.2357 0.4504 1.5% 0 Choiz 2014 -0.0726 0.819 0.8% 0 Christensen 2014 -1.8326 0.4137 1.5% 0 ElKhoury Lesueur 2018 -1.772 0.1315 2.2% 0 Giovenco & Delnevo 2018a (3) 1.1669 0.192 2.2% 0 Giovenco & Delnevo 2018a (3) 1.168 0.0845 2.3% 1 Giovenco & Delnevo 2018a (5) -0.4005 0.0843 2.2% 0 Giovenco & Delnevo 2018a (5) -0.4005 0.0845 2.3% 1 <	Indom, 95% Cl IV, Random, 95% Cl 11 [0.43, 1.53]
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Choi 2014 -0.0726 0.819 0.8% 0 Christensen 2014 -1.8326 0.4137 1.5% 0 Ekanem 2017 -0.6349 0.2101 2.0% 0 El-Khoury Lesueur 2018 -1.772 0.1315 2.2% 0 Farsalinos 2019 0.3436 0.1834 2.1% 1 Siovenco & Delnevo 2018a (3) 1.1569 0.0403 2.2% 0 Siovenco & Delnevo 2018b (4) -0.9676 0.1192 2.2% 0 Siovenco & Delnevo 2018b (4) -0.8675 0.5271 1.3% 0 Somajee 2019 0.5128 0.0495 2.3% 1 Strana 2014 -0.2744 0.3798 1.6% 0 Harrington 2015 -0.1663 0.2328 2.0% 0 Jackson 2020 0.1222 0.2651 1.9% 0 Johnson 2019a (6) 0.4947 0.1545 2.1% 1 Johnson 2019a (7) 0.6366 0.109 2.2% 1 Alkhoran 2019	33 [0.19, 4.63]
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Ekanem 2017 -0.6349 0.2101 2.0% 0 El-Khoury Lesueur 2018 -1.772 0.1315 2.2% 0 Farsalinos 2019 0.3365 0.1664 2.1% 1 Flacco 2019 0.3466 0.1834 2.1% 1 Giovenco & Delnevo 2018a (3) 1.1569 0.1093 2.2% 3 Giovenco & Delnevo 2018c (5) -0.4005 0.6433 2.2% 0 Gomajee 2019 0.5128 0.0495 2.3% 1 Grana 2014 -0.2744 0.3798 1.6% 0 Hajek 2015 -0.1054 0.2606 1.9% 0 Harington 2015 -0.1064 0.2328 2.0% 1 Jackson 2020 0.1222 0.2661 1.9% 1 Johnson 2019a (6) 0.4947 0.1545 2.1% 1 Johnson 2019a (6) 0.4947 0.1545 2.1% 1 Johnson 2019a (7) 0.6366 0.109 2.2% 1 Johnson 2019a (8)	33 [0.35, 0.80]
El-Khoury Lesueur 2018 -1.772 0.1315 2.2% 0 Farsalinos 2019 0.3365 0.1664 2.1% 1 Flacco 2019 0.3436 0.1834 2.2% 3 Giovenco & Delnevo 2018a (3) 1.1569 0.1093 2.2% 3 Giovenco & Delnevo 2018c (5) -0.4005 0.0643 2.2% 0 Gomajee 2019 0.5128 0.0495 2.3% 1 Grana 2014 -0.2744 0.3798 1.6% 0 Harington 2015 -0.1054 0.2606 1.9% 0 Hefner 2016 1.0438 0.671 1.0% 2.6 Hitchman 2015 -0.1643 0.228 2.0% 0 Jackson 2020 0.1222 0.2651 1.9% 0 Johnson 2019a (6) 0.4947 0.1545 2.1% 1 Johnson 2019a (8) -0.3011 0.1545 2.1% 1 Johnson 2019a (8) -0.3011 0.1545 2.1% 1 Kalkhoran 2020a (11)	7 [0.13], 0.22]
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Piper 2020 1.0986 0.6086 1.1% 3 Prochaska 2014 0.1484 0.2905 1.8% 1 Shi 2015 -0.821 0.2986 1.8% 0 Sutfin 2015 -0.9163 0.3275 1.7% 0 Sweet 2019 0.5933 0.3522 1.7% 1 /erplaetse 2019a (13) 0.4447 0.1366 2.1% 1 /erplaetse 2019b (14) -0.1863 0.12 2.2% 0	i8 [0.53, 0.87]
Prochaska 2014 0.1484 0.2905 1.8% 1 Shi 2015 -0.821 0.2986 1.8% 0 Sutfin 2015 -0.9163 0.3275 1.7% 0 Sweet 2019 0.5933 0.3522 1.7% 1 /erplaetse 2019a (13) 0.4447 0.1936 2.1% 1 /erplaetse 2019b (14) -0.1863 0.12 2.2% 0	
Shi 2015 -0.821 0.2986 1.8% 0 Sutfin 2015 -0.9163 0.3275 1.7% 0 Sweet 2019 0.5933 0.3522 1.7% 1 Verplaetse 2019a (13) 0.4447 0.1936 2.1% 1 /erplaetse 2019b (14) -0.1863 0.12 2.2% 0	7 [0.59, 1.00]
Sutfin 2015 -0.9163 0.3275 1.7% 0 Sweet 2019 0.5933 0.3522 1.7% 1 /erplaetse 2019a (13) 0.4447 0.1936 2.1% 1 /erplaetse 2019b (14) -0.1863 0.12 2.2% 0	77 [0.59, 1.00]
3weet 2019 0.5933 0.3522 1.7% 1 /erplaetse 2019a (13) 0.4447 0.1936 2.1% 1 /erplaetse 2019b (14) -0.1863 0.12 2.2% 0	77 (0.59, 1.00)
/erplaetse 2019a (13) 0.4447 0.1936 2.1% 1 /erplaetse 2019b (14) -0.1863 0.12 2.2% 0	77 (0.59, 1.00)
/erplaetse 2019b (14) -0.1863 0.12 2.2% 0	77 [0.59, 1.00]
	77 [0.59, 1.00]
//ckerman //113 -0.6931 0.1179 2.2% 0	77 (0.59, 1.00)
	77 [0.59, 1.00] 10 [0.91, 9.89] 6 [0.66, 2.05] 14 [0.25, 0.79] 10 [0.21, 0.76] 17 [0.91, 3.61] 16 [1.07, 2.28] 13 [0.66, 1.05]
	77 [0.59, 1.00] 10 [0.91, 9.89] 6 [0.66, 2.05] 14 [0.25, 0.79] 10 [0.21, 0.76] 17 [0.91, 3.61] 16 [1.07, 2.28] 13 [0.66, 1.05] 10 [0.40, 0.63]
-	77 [0.59, 1.00] 10 [0.91, 9.89] 6 [0.66, 2.05] 14 [0.25, 0.79] 10 [0.21, 0.76] 17 [0.91, 3.61] 18 [1.07, 2.28] 13 [0.66, 1.05] 10 [0.40, 0.63] 15 [0.11, 0.57]
	77 [0.59, 1.00] 00 [0.91, 9.89] 6 [0.66, 2.05] 14 [0.25, 0.79] 10 [0.21, 0.76] 11 [0.91, 3.61] 13 [0.66, 1.05] 13 [0.66, 1.05] 15 [0.11, 0.57] 6 [1.04, 1.29]
Zhuang 2016b (16) -0.1393 0.288 1.8% 0	77 [0.59, 1.00]
Fotal (95% CI) 100.0% 0.	77 [0.59, 1.00] 00 [0.91, 9.89] 6 [0.66, 2.05] 14 [0.25, 0.79] 10 [0.21, 0.76] 11 [0.91, 3.61] 13 [0.66, 1.05] 13 [0.66, 1.05] 15 [0.11, 0.57] 6 [1.04, 1.29]
Heterogeneity: Tau ² = 0.36; Chi ² = 801.39, df = 54 (P < 0.00001); l ² = 93%	77 [0.59, 1.00]
Fest for overall effect: Z = 1.28 (P = 0.20)	77 [0.59, 1.00]

(1) Intense users (2) Intermittent users

(3) Daily EC use (4) Less than daily EC use

(5) Prior but no current EC use

(6) NHIS data

(7) TUS-CPS daily cigarette smokers
(8) TUS-CPS less than daily cigarette smokers

(9) Any chronic medical condition

(10) No chronic medical condition

(11) Daily EC use

(11) Daily EC use
(12) Less than daily EC use
(13) Daily EC use
(14) Less than daily EC use
(15) EC use at both baseline and 2 year follow-up
(16) EC use at either baseline or 2 year follow-up, but not both

Figure 5.	Association	of ENDS with	combustible	cigarette sm	oking initiation

				Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
Auf 2018	1.3083	0.0999	5.7%	3.70 [3.04, 4.50]	
Barrington_Trimis 2016	1.6054	0.3757	3.0%	4.98 [2.38, 10.40]	→
Barrington_Trimis 2018	1.5195	0.1277	5.5%	4.57 [3.56, 5.87]	
Berry 2019	1.4085	0.163	5.1%	4.09 [2.97, 5.63]	_
Best 2017	0.8838	0.2026	4.7%	2.42 [1.63, 3.60]	
Chien 2019	0.7608	0.128	5.5%	2.14 [1.67, 2.75]	_
Conner 2017	1.4012	0.1641	5.1%	4.06 [2.94, 5.60]	
Conner 2019	1.0225	0.119	5.5%	2.78 [2.20, 3.51]	
East 2018	2.358	0.5885	1.8%	10.57 [3.34, 33.50]	│
Goldenson 2017	0.8154	0.2887	3.8%	2.26 [1.28, 3.98]	· · · · · · · · · · · · · · · · · · ·
Hammond 2017	0.7514	0.1158	5.6%	2.12 [1.69, 2.66]	
Leventhal 2015	0.5596	0.2361	4.4%	1.75 [1.10, 2.78]	
Loukas 2018	0.3075	0.1514	5.2%	1.36 [1.01, 1.83]	
Lozano 2017	0.47	0.1035	5.7%	1.60 [1.31, 1.96]	
McMillen 2019	1.8871	0.2964	3.7%	6.60 [3.69, 11.80]	
Miech 2017	1.884	1.1094	0.6%	6.58 [0.75, 57.88]	
Morgenstem 2018	0.9163	0.1775	5.0%	2.50 [1.77, 3.54]	_
Penzes 2018	1.2726	0.305	3.7%	3.57 [1.96, 6.49]	_
Primack 2015	2.1163	0.9972	0.8%	8.30 [1.18, 58.60]	
Primack 2018	1.9199	0.7246	1.3%	6.82 [1.65, 28.22]	→
Spindle 2017	1.2149	0.2892	3.8%	3.37 [1.91, 5.94]	
Treur 2018	2.4765	0.645	1.5%	11.90 [3.36, 42.13]	→
Unger 2016	1.2	0.3878	2.9%	3.32 [1.55, 7.10]	
Watkins 2018	0.9282	0.1743	5.0%	2.53 [1.80, 3.56]	
Wills 2017	1.0543	0.1757	5.0%	2.87 [2.03, 4.05]	
Total (95% CI)			100.0%	3.02 [2.52, 3.62]	•
Heterogeneity: Tau ² = 0.14	4; Chi² = 125.55. df:	= 24 (P <	0.00001); I ^z = 81%	
Test for overall effect: Z = '					0.1 0.2 0.5 1 2 5 10 Favors Non E-cigarettes Favors E-cigarettes