Supplemental table 3. Carbon monoxide data not contributing to meta-analyses[1]

Randomized trials, nicotine EC v comparator group

Study ID	Intervention/ comparator	Time point	Data	Between group difference[2] (↑ higher in EC/higher dose EC arm; ↔ equivocal; ↓ lower in EC/higher dose arm)
George 2019	Nicotine EC v non-nicotine EC v traditional cigarette	4 weeks	eCO measured but not reported in detail. Lowest tertile of CO at end of study was in those with "best compliance with EC and least dual use"	NE
Meier 2017	Nicotine EC v non-nicotine EC	1 week	Randomized crossover trial. eCO: Naturalistic (whilst smoking, no EC) mean 11.4 (SE 1.3), Nicotine EC 11.6 (SE 1.3), Non-nicotine EC 10.2 (SE 1.3)	↑
Tseng 2016	Nicotine EC v non-nicotine EC	1 and 3 weeks	No between-group difference in eCO was observed at any time point, no further data available	↔
Veldheer 2019	EC (nicotine, non-nicotine groups combined) v QuitSmart cigarette substitute	12 weeks	Change from baseline in eCO: QuitSmart -3.9 ppm (SD 10.4, n=72); EC arms -3.9 ppm (SD 12.5, n = 191)	↔
Walele 2018	Nicotine EC versus conventional cigarette	2 weeks	"At baseline, eCO was at 20.3 ppm (±8.4) in EVP subjects and at 21.3 ppm (±9.2) in CC subjects. In the EVP group, eCO levels dropped to 7.4 ppm at Week 1 and were between 7.6 and 9.0 ppm from Week 2 to EoS (eCO levels in non-smokers are typically ≤6 ppm (Bedfront, 2016)). In the CC group, eCO remained at levels close to baseline during the whole study (21.3–23.3 ppm)."	↓
Walker 2020	Nicotine EC + NRT v non-nicotine EC + NRT v NRT only	6 months	20% nicotine EC arm; 10% non-nicotine EC arm; 4% NRT only arm had eCO <8ppm at follow-up	↓

[1] eCO: exhaled carbon monoxide; NS: not specified

[2] NE: not estimable

Studies in which all groups received nicotine EC with no between-group difference in concentration

Study ID	Time point	Data	Direction over time[3] (↓ decline; ↔ equivocal; ↑ increase)
Caponetto 2013b	1 year	eCO reported graphically, "smoking reduction with "Categoria" e-Cigarette use was associated to a substantial decrease in the level of eCO". In figure, reductions from baseline in all groups, but particularly pronounced in people who quit smoking or reduced cigarette consumption by >50%	↓
Goniewicz 2017	2 weeks	Report significant decline in eCO from baseline ($p<0.05$) at 1 and 2 weeks.	↓
Hickling 2019	6 weeks[4]	Reduction from mean eCO (ppm) 25.67 (SD 17.16, n=45) at baseline to 22.09 (SD 15.93, n=45) at 6 weeks. At 24 weeks, no change (mean 26, SD 16.78, n = 31).	↓ 6 weeks ↔ 24 weeks
Ikonomidis 2018[5]	1 month	Reductions in eCO in people using EC + conventional cigarettes (baseline mean 15 ppm, SD 0.6, n=24; 1 month mean 12.5, SD 0.6, n = 24); people using EC only (baseline mean 13.9, SD 0.7, n=42; 1 month mean 4.2, SD 0.6, n=42); "noncompliant" group (baseline mean 18.5, SD 0.7, n = 4, 1 month mean 15.1, SD 0.6, n=4). (Slight increase in controls (given no intervention): baseline mean 15.3, SD 1, n=20; 1 month mean 16.4, SD 0.7, n = 20.)	↓
Martner 2019	4 weeks	Reported for individual participants (n=12), no averages given. "Following baseline, five participants showed immediate reductions in CO and high levels of EC use. Three showed more gradual reductions in CO and gradual increases in EC use. Two participants showed initial, but brief, reductions in CO and high levels of EC use, and two failed to appreciably reduce CO levels and showed relatively low EC use." (data for other participants lost or withdrawn)	NE
McRobbie 2015	4 weeks	Mean change from baseline in eCO (ppm): -12 (95% CI -16 to -8), n=33. Point estimate for reduction same in abstinent and smoking participants at 4 weeks.	↓
Pacifici 2015	1, 4, 8 months	At one month, EC users showed a significant decline in eCO; there was no significant change in non-EC users (people who had opted not to use the EC provided). At four and eight months, exhaled CO had declined in EC and non-EC users.	↓
Polosa 2011	2 years	Significant reduction in the average eCO across the whole cohort of 23.5 to 8 ppm at 24 months ($P = 0.011$)	↓

[3] NE: not estimable

[4] EC provided for 6 weeks; eCO measured at weeks 1-10 and 24

[5] Acute crossover trial followed by 'chronic phase' so treated as cohort for purposes of this review

Study ID	Time point	Data	Direction over time[3] (↓ decline; ↔ equivocal; ↑ increase)
Polosa 2014b	6 months	Measured eCO, report results graphically by group; at 24 weeks, CO appears to have significantly reduced amongst quitters and people reducing cigarette consumption by at least 50%, and appears to have remained stable in people who continued smoking at least half as many cigarettes as they had at baseline.	↓ quitters and people reducing cigarette consumption ↔ people who continued smoking at least half as many cigarettes as they had at baseline
Pratt 2016	4 weeks	Baseline mean eCO 27.27 ppm (n=19, no SD provided). At week 4, mean 15.21 (n=19)	↓
Pulvers 2018	4 weeks	Significant change in eCO (p <.001). Baseline mean 14.3 ppm, SD 12.7, n= 40. 4 weeks: mean 8.9, SD 8.35, n=40.	↓
Smith 2019	1 week	Study arms varied by PG/VG ratio. Reduced eCO in all groups. Combined mean: baseline 33.1 (SD 18.3), n =30; 1 week 26.5 (SD 16.1), n = 28)	↓
Strasser 2016	10 days	Randomized to 4 different brands of EC (similar nicotine content). eCO reductions in all arms. Blu: Baseline mean 19.2 (SD 9.8, n=6), day 10 mean 3.2 (2.2, n = 5)). Green smoke: Baseline 21.6 (8.8, n=6), day 10 mean 4.0 (3.4, n=5). V2: baseline mean 22.0 (8.1, n=6), day 10 mean 4.8 (3.5, n=5). White cloud: baseline mean 15.5 (3.5, n=6); day 10 mean 1.5 (0.7, n=2)	↓
Valentine 2018	8 weeks	Data provided in figures only, estimated baseline mean eCO (ppm) 9.3, SD 7.1, n=50. 8 weeks: 8.5, 95% CI 7.1 to 9.9, n = 31	↓
Van Staden 2013	2 weeks	Smokers who switched to EC had significant reduction in arterial (1.95%, 95% CI 0.47 to 3.44; P = 0.01) and venous (1.87%, 95% CI 0.38 to 3.36; P = 0.02) carboxyhaemoglobin levels.	↓
Walele 2018[6]	2 years	"The mean (±SD) eCO level in all subjects at Month 1 was 8.7 ppm (±6.5), and steadily decreased to reach 4.1 ppm (±3.1) at Month 24."	↓

[6] Short term RCT (see first table); all participants then given nicotine EC hence inclusion in this table, as well