

## Supplemental table 4. Heart rate data not contributing to meta-analyses

Randomized trials, nicotine EC v comparator group

Study ID	Intervention/ comparator	Time point	Data										Between group difference <sup>1</sup> (↑ higher in EC/higher dose EC arm; ↔ equivocal; ↓ lower in EC/higher dose arm)																																							
George 2019	Nicotine EC v non-nicotine EC	4 weeks	“No significant trend in difference among the three arms” Broke down results by smoking characteristics at baseline. Smoked ≤20 pack years (n=31): increased by 2.6 beats/min (95% CI: 0.3 to 5.0) for EC-nicotine; 5.2 beats/min (95% CI: 0.6 to 10.0) for nicotine-free. >20 pack-years (n = 82): decreased by 2.8 beats/min (95% CI: -5.2 to -0.4) for EC nicotine; decreased by 5.6 beats/min (95% CI: -10.4 to -0.8) for no-nicotine EC										↔																																							
Veldheer 2019	EC (nicotine, non- nicotine groups combined) v QuitSmart cigarette substitute	12 weeks	<table><tr><td rowspan="2">Group</td><td colspan="3">Baseline</td><td colspan="3">4 weeks</td><td colspan="3">12 weeks</td></tr><tr><td>Mean</td><td>SD</td><td>N</td><td>Mean (change)</td><td>SD</td><td>N</td><td>Mean (change)</td><td>SD</td><td>N</td></tr><tr><td>Sub</td><td>79.6</td><td>13.2</td><td>72</td><td>2.47</td><td>12.97</td><td>72</td><td>-1.89</td><td>12.29</td><td>72</td></tr><tr><td>EC</td><td>82.1</td><td>12.3</td><td>191</td><td>-1.73</td><td>11.32</td><td>191</td><td>-0.86</td><td>14.18</td><td>191</td></tr></table>	Group	Baseline			4 weeks			12 weeks			Mean	SD	N	Mean (change)	SD	N	Mean (change)	SD	N	Sub	79.6	13.2	72	2.47	12.97	72	-1.89	12.29	72	EC	82.1	12.3	191	-1.73	11.32	191	-0.86	14.18	191	↑									
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Walele 2018	Nicotine EC versus conventional cigarette	2 weeks	“no clinically significant changes”										NE																																							

<sup>1</sup> 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 <sup>2</sup> (↓ decline; ↔ equivocal; ↑ increase)
Hickling 2019	6 weeks <sup>3</sup>	Mean: baseline 80.65 bpm (SD 16.01); week 6 82 bpm, SD 15.76 (n=46)							↑
Ikonomidis 2018 <sup>4</sup>	1 month	Group	Baseline			1 Month			Mixed across groups
			Mean	SD	N	Mean	SD	N	
		E Cig+con-cig	70	9	24	72	8	24	
		E-cig only	73	8	42	70	7	42	
		Noncompliant	71	8	4	70	8	4	
		Controls	71	8	20	70	8	20	
Oncken 2015	2 weeks	“no significant changes”							↔
Van Staden 2013	2 weeks	“no significant changes”							↔
Walele 2018 <sup>5</sup>	2 years	Timepoint		Mean		SD		N	↓
		Baseline		72.3		10.8		206	
		Month 1		71.4		9.7		184	
		Month 6		71.6		9.9		141	
		Month 12		71.1		11.1		114	
		Month 18		69.1		10.9		104	
		Month 24		70.4		11.4		102	

<sup>2</sup> NE: not estimable

<sup>3</sup> EC provided for 6 weeks; HR measured at weeks 1-10 and 24

<sup>4</sup> Acute crossover trial followed by 'chronic phase' so treated as cohort for purposes of this review

<sup>5</sup> Short term RCT (see first table); all participants then given nicotine EC hence inclusion in this table, as well