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Carbon Monoxide Thresholds for Validating Self-Report as a Measure of Smoking Status in Clinical Trials

Supplement 1 Online Content

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eTable 1. Receiver Operator Characteristic (ROC) Curve Values by Treatment Group^{a,b,c}

ECO Value	Self-Reported Non-Smokers, ECO ≥ x ppm	Self-Reported Non-Smokers, ECO < x ppm	Self-Reported Smokers, ECO ≥ x ppm	Self-Reported Smokers ECO < x ppm	Sensitivity	Specificity	PPV	NPV	LR+	LR-	AUC
Active ^c											
12 ppm	6	66	127	104	55%	92%	95%	39%	6.6	0.49	0.73
11 ppm	6	66	141	90	61%	92%	96%	42%	7.3	0.43	0.76
10 ppm	6	66	154	77	67%	92%	96%	46%	8.0	0.36	0.79
9 ppm	7	65	162	69	70%	90%	96%	49%	7.2	0.33	0.80
8 ppm	7	65	170	61	74%	90%	96%	52%	7.6	0.29	0.82
7 ppm	11	61	179	52	77%	85%	94%	54%	5.1	0.27	0.81
6 ppm	13	59	184	47	80%	82%	93%	56%	4.4	0.25	0.81
5 ppm	16	56	188	43	81%	78%	92%	57%	3.7	0.24	0.80
4 ppm	21	51	195	36	84%	71%	90%	59%	2.9	0.22	0.78
3 ppm	23	49	201	30	87%	68%	90%	62%	2.7	0.19	0.78
2 ppm	27	45	204	27	88%	63%	88%	63%	2.4	0.19	0.75
Placebo ^c											
12 ppm	1	56	131	85	61%	98%	99%	40%	34.6	0.40	0.79
11 ppm	1	56	155	61	72%	98%	99%	48%	40.9	0.29	0.85
10 ppm	1	56	161	55	75%	98%	99%	50%	42.5	0.26	0.86
9 ppm	4	53	170	46	79%	93%	98%	54%	11.2	0.23	0.86
8 ppm	5	52	174	42	81%	91%	97%	55%	9.2	0.21	0.86
7 ppm	7	50	182	34	84%	88%	96%	60%	6.9	0.18	0.86
6 ppm	8	49	185	31	86%	86%	96%	61%	6.1	0.17	0.86
5 ppm	12	45	187	29	87%	79%	94%	61%	4.1	0.17	0.83
4 ppm	17	40	189	27	88%	70%	92%	60%	2.9	0.18	0.79
3 ppm	20	37	193	23	89%	65%	91%	62%	2.5	0.16	0.77
2 ppm	23	34	198	18	92%	60%	90%	65%	2.3	0.14	0.76
Control ^c											
12 ppm	2	26	108	54	67%	93%	98%	33%	9.3	0.36	0.80
11 ppm	2	26	124	38	77%	93%	98%	41%	10.7	0.25	0.85
10 ppm	3	25	128	34	79%	89%	98%	42%	7.4	0.24	0.84
9 ppm	3	25	131	31	81%	89%	98%	45%	7.5	0.21	0.85
8 ppm	3	25	134	28	83%	89%	98%	47%	7.7	0.19	0.86
7 ppm	3	25	138	24	85%	89%	98%	51%	8.0	0.17	0.87
6 ppm	4	24	140	22	86%	86%	97%	52%	6.0	0.16	0.86
5 ppm	6	22	144	18	89%	79%	96%	55%	4.1	0.14	0.84

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4 ppm	10	18	149	13	92%	64%	94%	58%	2.6	0.12	0.78
3 ppm	12	16	151	11	93%	57%	93%	59%	2.2	0.12	0.75
2 ppm	16	12	152	10	94%	43%	90%	55%	1.6	0.14	0.68

^a Abbreviations: EC = E-Cigarettes; Sens = Sensitivity; Spec = Specificity; PPV = Positive Predictive Value; NPV = Negative Predictive Value; LR+ = Positive Likelihood Ratio; LR- = Negative Likelihood Ratio; AUC = Area Under the Curve

^b Values for Sensitivity, Specificity, PPV, and NPV are all associated with 95% Confidence Intervals

^c Active = Participants in nicotine-EC arm; Placebo = Participants in non-nicotine-EC arm; Control = Participants who received counseling only

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eTable 2. Receiver Operator Characteristic (ROC) Curve Values by Household Smoking Status^{a,b,c}

ECO Value	Self-Reported Non-Smokers, ECO ≥ x ppm	Self-Reported Non-Smokers, ECO < x ppm	Self-Reported Smokers, ECO ≥ x ppm	Self-Reported Smokers, ECO < x ppm	Sensitivity	Specificity	PPV	NPV	LR+	LR-	AUC
Other Smoker^c											
12 ppm	2	34	116	77	60%	94%	98%	31%	10.8	0.42	0.77
11 ppm	2	34	137	56	71%	94%	99%	38%	12.8	0.31	0.83
10 ppm	3	33	146	47	76%	92%	98%	41%	9.1	0.27	0.84
9 ppm	4	32	154	39	80%	89%	97%	45%	7.2	0.23	0.84
8 ppm	4	32	159	34	82%	89%	98%	48%	7.4	0.20	0.86
7 ppm	7	29	161	32	83%	81%	96%	48%	4.3	0.21	0.82
6 ppm	7	29	165	28	85%	81%	96%	51%	4.4	0.18	0.83
5 ppm	11	25	166	27	86%	69%	94%	48%	2.8	0.20	0.77
4 ppm	13	23	175	18	91%	64%	93%	56%	2.5	0.15	0.77
3 ppm	15	21	180	13	93%	58%	92%	62%	2.2	0.12	0.76
2 ppm	16	20	182	11	94%	56%	92%	65%	2.1	0.10	0.75
No Other Smoker^c											
12 ppm	7	114	250	166	60%	94%	97%	41%	10.4	0.42	0.77
11 ppm	7	114	283	133	68%	94%	98%	46%	11.8	0.34	0.81
10 ppm	7	114	297	119	71%	94%	98%	49%	12.3	0.30	0.83
9 ppm	10	111	309	107	74%	92%	97%	51%	9.0	0.28	0.83
8 ppm	11	110	319	97	77%	91%	97%	53%	8.4	0.26	0.84
7 ppm	14	107	338	78	81%	88%	96%	58%	7.0	0.21	0.84
6 ppm	18	103	344	72	83%	85%	95%	59%	5.6	0.20	0.84
5 ppm	23	98	353	63	85%	81%	94%	61%	4.5	0.19	0.83
4 ppm	35	86	358	58	86%	71%	91%	60%	3.0	0.20	0.79
3 ppm	40	81	365	51	88%	67%	90%	61%	2.7	0.18	0.77
2 ppm	50	71	372	44	89%	59%	88%	62%	2.2	0.18	0.74

^a Abbreviations: EC = E-Cigarettes; Sens = Sensitivity; Spec = Specificity; PPV = Positive Predictive Value; NPV = Negative Predictive Value; LR+ = Positive Likelihood Ratio; LR- = Negative Likelihood Ratio; AUC = Area Under the Curve

^b Values for Sensitivity, Specificity, PPV, and NPV are all associated with 95% Confidence Intervals

^c Other Smoker = Participants had at least one other smoker in their primary household; No Other Smoker = Participants had no other smoker in their primary household

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eTable 3. Receiver Operator Characteristic (ROC) Curve Values Weighted by Visits per Participant^{a,b}

ECO Value	Self-Reported Non-Smokers, ECO ≥ x ppm	Self-Reported Non-Smokers, ECO < x ppm	Self-Reported Smokers, ECO ≥ x ppm	Self-Reported Smokers ECO < x ppm	Sensitivity	Specificity	PPV	NPV	LR+	LR-	AUC	κ (95% CI)
12 ppm	4.3											
		54.3	143.7	95.7	60%	93%	97%	36%	8.1	0.43	0.76	0.35 (0.30,0.40)
11 ppm	4.3											
		54.3	166	73.3	69%	93%	97%	43%	9.4	0.33	0.81	0.44 (0.39,0.50)
10 ppm	5.3											
		5.3	175.3	64	73%	91%	97%	45%	8.1	0.29	0.82	0.48 (0.43,0.54)
9 ppm	6.7											
		52	183.8	55.5	77%	89%	97%	48%	6.8	0.26	0.83	0.51 (0.45,0.57)
8 ppm	7.0											
		51.7	189.3	50	79%	88%	96%	51%	6.6	0.24	0.84	0.54 (0.48,0.60)
7 ppm	9.2											
		49.5	198.3	41	83%	84%	96%	55%	5.3	0.20	0.83	0.57 (0.50,0.63)
6 ppm	10.7											
		48	203	36.3	85%	82%	95%	57%	4.7	0.19	0.81	0.57 (0.51,0.64)
5 ppm	14.2											
		44.5	206.7	32.7	86%	76%	94%	58%	3.6	0.18	0.78	0.56 (0.49,0.63)
4 ppm	19.3											
		39.3	211.5	27.8	88%	67%	92%	59%	2.7	0.17	0.77	0.53 (0.46,0.61)
3 ppm	21.8											
		36.8	216.3	23	90%	63%	91%	62%	2.4	0.15	0.74	0.53 (0.46,0.61)
2 ppm	26.2											
		32.5	219.5	19.8	92%	55%	89%	62%	2.1	0.15	0.70	0.50 (0.43,0.58)

^a Abbreviations: EC = E-Cigarettes; Sens = Sensitivity; Spec = Specificity; PPV = Positive Predictive Value; NPV = Negative Predictive Value; LR+ = Positive Likelihood Ratio; LR- = Negative Likelihood Ratio; AUC = Area Under the Curve

^b Values for Sensitivity, Specificity, PPV, and NPV are all associated with 95% Confidence Intervals

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eTable 4. Comparison of AUC Between Treatment Groups^{a,*,}**

ECO Value	AUC (CI) Nicotine	AUC (CI) No Nicotine	AUC (CI) Counseling alone	Difference** AUC Nicotine / No Nicotine (CI, 95%)	Prob* Nicotine / No Nicotine	Difference** AUC Nicotine / Counseling alone (CI, 95%)	Prob* Nicotine / Counseling alone
12 ppm	0.73 (0.69; 0.78)	0.79 (0.76; 0.83)	0.80 (0.74; 0.86)	-0.06 (-0.117; 0.00008)	0.05	-0.064 (-0.133; 0.013)	0.114
11 ppm	0.76 (0.72; 0.81)	0.85 (0.82; 0.88)	0.85 (0.79; 0.91)	-0.086 (-0.142; -0.027)	0.002	-0.083 (-0.152; -0.007)	0.026
10 ppm	0.79 (0.75; 0.84)	0.86 (0.83; 0.90)	0.84 (0.78; 0.91)	-0.072 (-0.128; -0.016)	0.012	-0.05 (-0.124; 0.032)	0.234
9 ppm	0.80 (0.76; 0.85)	0.86 (0.82; 0.90)	0.85 (0.78; 0.92)	-0.056 (-0.114; 0.003)	0.062	-0.049 (-0.123; 0.03)	0.232
8 ppm	0.82 (0.77; 0.86)	0.86 (0.81; 0.90)	0.86 (0.79; 0.93)	-0.04 (-0.1; 0.019)	0.222	-0.042 (-0.115; 0.039)	0.316
7 ppm	0.81 (0.76; 0.86)	0.86 (0.81; 0.91)	0.87 (0.81; 0.94)	-0.049 (-0.121; 0.019)	0.158	-0.063 (-0.14; 0.02)	0.138
6 ppm	0.81 (0.76; 0.86)	0.86 (0.81; 0.91)	0.86 (0.79; 0.93)	-0.05 (-0.124; 0.02)	0.166	-0.054 (-0.135; 0.034)	0.238
5 ppm	0.80 (0.74; 0.85)	0.83 (0.77; 0.89)	0.84 (0.76; 0.92)	-0.031 (-0.109; 0.041)	0.46	-0.042 (-0.134; 0.057)	0.39
4 ppm	0.78 (0.72; 0.83)	0.79 (0.72; 0.85)	0.78 (0.69; 0.87)	-0.011 (-0.1; 0.077)	0.822	-0.006 (-0.114; 0.103)	0.954
3 ppm	0.78 (0.72; 0.83)	0.77 (0.71; 0.84)	0.75 (0.66; 0.85)	0.004 (-0.083; 0.093)	0.928	0.023 (-0.089; 0.134)	0.664
2 ppm	0.75 (0.69; 0.81)	0.76 (0.69; 0.82)	0.68 (0.59; 0.78)	-0.002 (-0.088; 0.089)	0.936	0.07 (-0.048; 0.179)	0.226

^a Abbreviations: CI = 95% Confidence Interval; AUC = Area Under the Curve; Prob = Probability; Nicotine = E-cigarette containing nicotine; No Nicotine = E-cigarette without nicotine; Counseling alone = No E-cigarette

*By bootstrap with 1,000 simulations

** By bootstrap with 1,000 simulations : Difference=mean of the 1,000 differences between AUC1-AUC2; Confidence interval calculated with 2.5 and 97.5 percentile of the 1,000 AUC differences.

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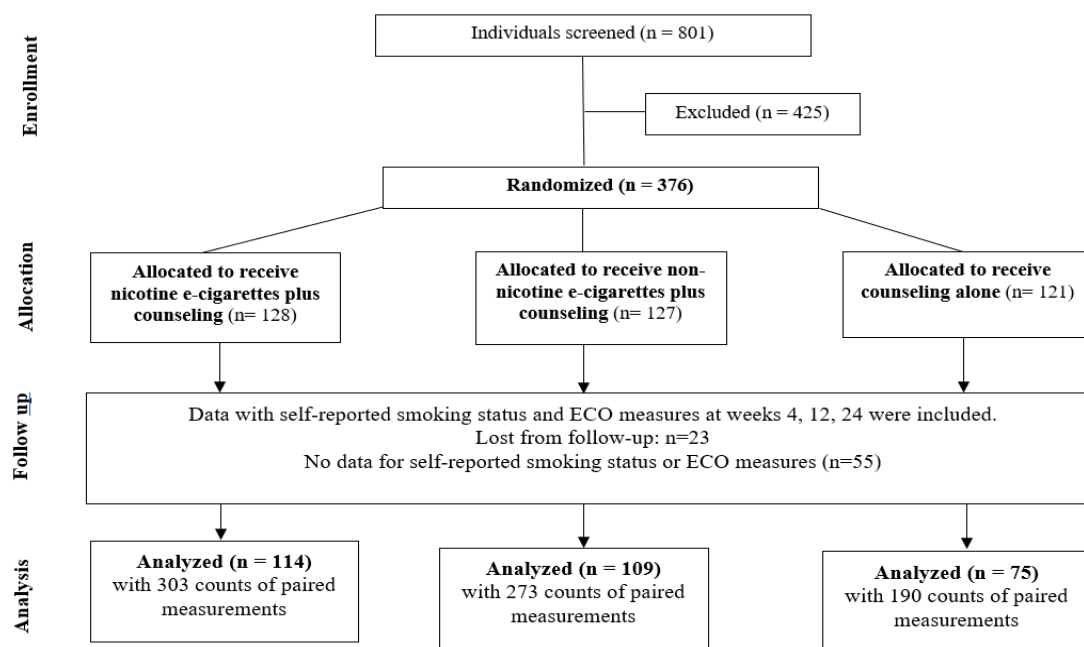
eTable 5. Comparison of AUC Between Household Smoking Habits^{a,*,}**

ECO Value	AUC (CI) Other Household Smoker	AUC (CI) No Household Smoker	Difference** AUC (CI, 95 %)	Prob*
12 ppm	0.77 (0.72; 0.82)	0.77 (0.74; 0.80)	0.002 (-0.056; 0.064)	0.94
11 ppm	0.83 (0.78; 0.88)	0.81 (0.78; 0.84)	0.017 (-0.042; 0.073)	0.574
10 ppm	0.84 (0.78; 0.89)	0.83 (0.8; 0.86)	0.01 (-0.053; 0.071)	0.734
9 ppm	0.84 (0.78; 0.90)	0.83 (0.8; 0.86)	0.015 (-0.058; 0.079)	0.66
8 ppm	0.86 (0.8; 0.91)	0.84 (0.81; 0.87)	0.02 (-0.052; 0.082)	0.556
7 ppm	0.82 (0.75; 0.89)	0.85 (0.81; 0.88)	-0.027 (-0.117; 0.053)	0.53
6 ppm	0.83 (0.76; 0.90)	0.84 (0.8; 0.88)	-0.007 (-0.097; 0.073)	0.864
5 ppm	0.78 (0.70; 0.86)	0.83 (0.79; 0.87)	-0.051 (-0.14; 0.042)	0.288
4 ppm	0.77 (0.69; 0.85)	0.79 (0.74; 0.83)	-0.012 (-0.105; 0.091)	0.758
3 ppm	0.76 (0.67; 0.84)	0.77 (0.73; 0.82)	-0.015 (-0.104; 0.086)	0.754
2 ppm	0.75 (0.67; 0.83)	0.74 (0.69; 0.79)	0.01 (-0.089; 0.111)	0.884

^a Abbreviations: CI = 95% Confidence Interval; AUC = Area Under the Curve; Prob = Probability
*By bootstrap with 1,000 simulations
** By bootstrap with 1,000 simulations : Difference=mean of the 1,000 differences between AUC1-AUC2; Confidence interval calculated with 2.5 and 97.5 percentile of the 1,000 AUC differences.

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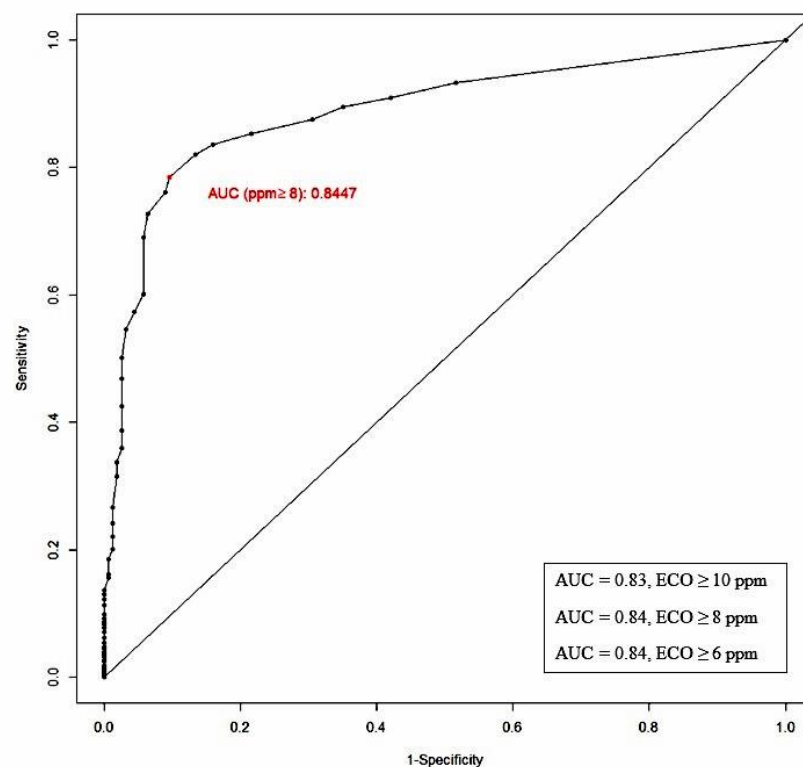
eFigure 1. Selection of E3 Trial Participants for Inclusion in Expired Carbon Monoxide Sub-study. Participants and data points included for analysis from the “Evaluating the Efficacy of E-Cigarette use for Smoking Cessation” (E3) Trial. Of the 376 participants who were randomized, only 298 participants provided at least one paired measurement of self-reported smoking status and corresponding expired carbon monoxide (ECO) level for inclusion in the analyses. The unit of analysis was participant visit, for which participants could contribute up to three measures. A total of 766 paired measures were used in the analyses.



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eFigure 2. Receiver Operator Characteristic (ROC) Curve for Expired Carbon Monoxide Versus Self-Reported Cigarette Use.

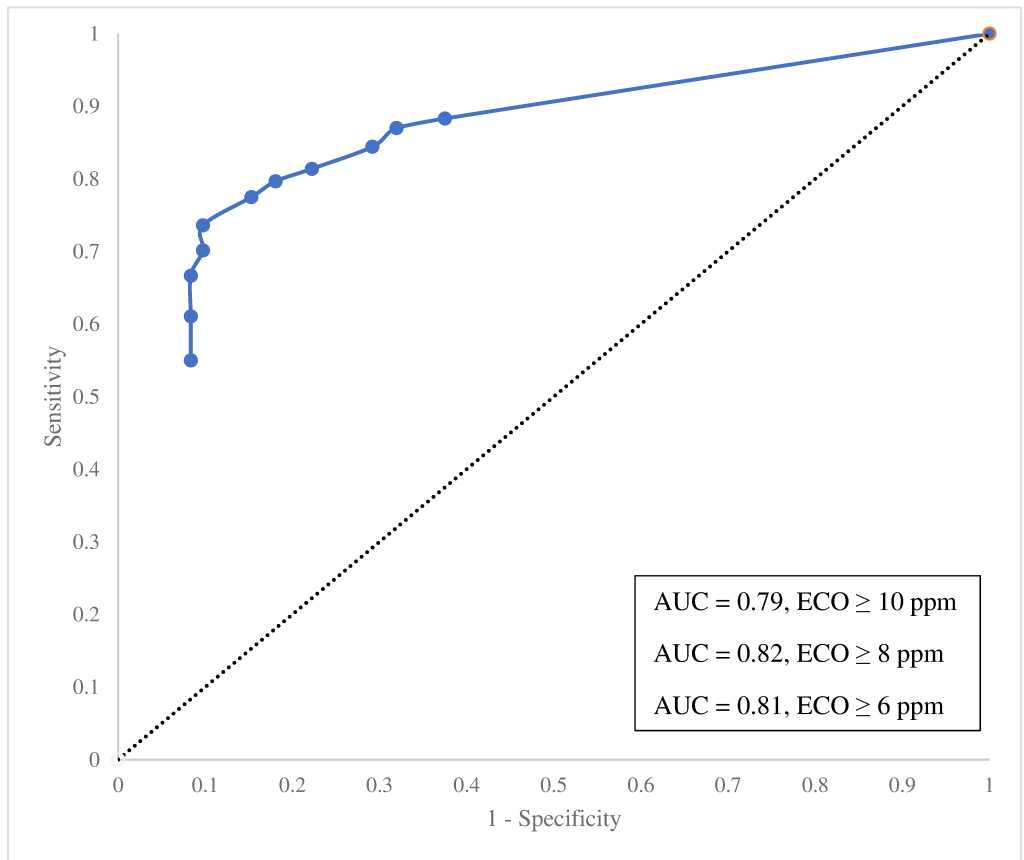
For the expired carbon monoxide (ECO) threshold ≥ 8 ppm and ≥ 6 ppm, the area-under-the-curve (AUC) calculated was 0.84, indicating that the ECO can discriminate between smokers and non-smokers at these levels. For ECO ≥ 10 ppm, AUC = 0.83.



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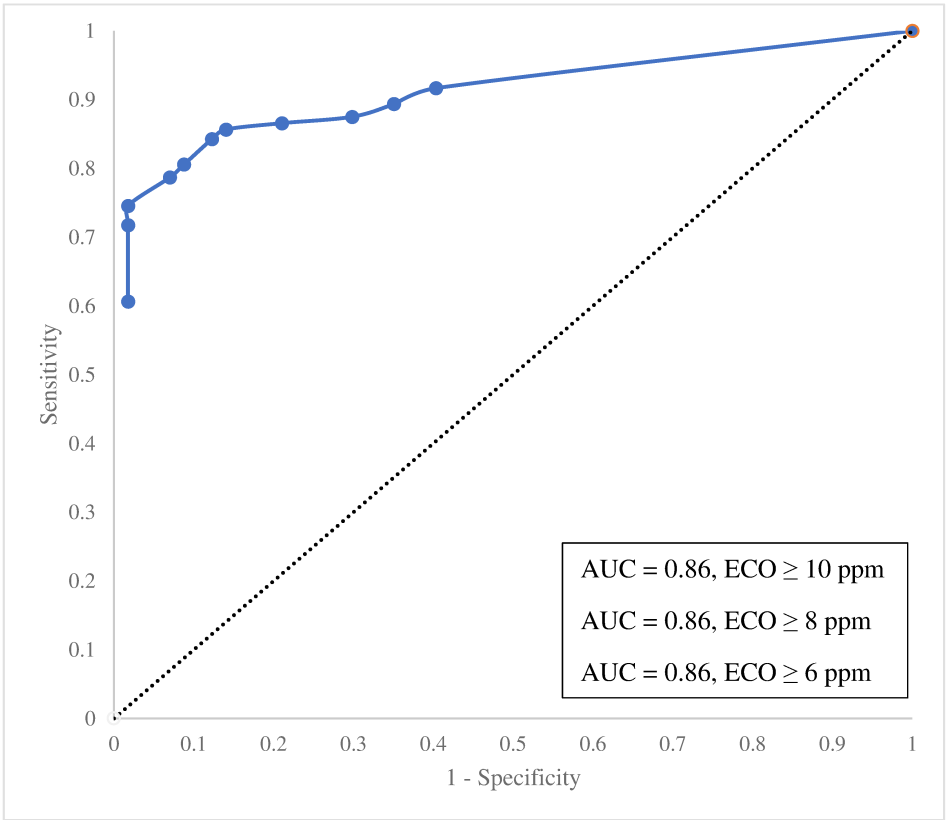
eFigure 3: Receiver Operator Characteristic (ROC) Curve for Expired Carbon Monoxide Concentration Against Self-Reported Cigarette Use by Treatment Group

eFigure 3a. Receiver Operator Characteristic (ROC) Curves for Nicotine E-Cigarette plus Counseling Group



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eFigure 3b. Receiver Operator Characteristic (ROC) Curves for Non-Nicotine E-Cigarette plus Counseling Group



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eFigure 3c. Receiver Operator Characteristic (ROC) Curves for Counseling Alone Group

