

Appendix A. Regression Result for the Association between Repeated Measures of Non-Combusted Product Use and Combusted Product Use

Variable	Level	Regression Coefficient Estimate	Standard Error	95% Confidence Interval		P-value
Intercept		0.36	1.59	-2.75	3.47	0.82
Amount of non-combusted product use per day		-0.42	0.12	-0.66	-0.18	<0.01
Condition (Reference: NNC)	VLNC1	-2.04	0.96	-3.91	-0.17	0.03
	VLNC2	-1.59	1.16	-3.86	0.68	0.17
Time window (Reference: Week 6 -Week 8)	Week 0 - week 1 (excluding the randomization day and week 1 visit day)	3.88	0.73	2.45	5.30	<0.0001
	Week 1 - week 2 (excluding the week 2 visit day)	2.80	0.62	1.59	4.01	<0.0001
	Week 2 - week 3 (excluding the week 3 visit day)	2.14	0.48	1.20	3.09	<0.0001
	Week 3 - week 4 (excluding the week 4 visit day)	0.93	0.43	0.08	1.78	0.03
	Week 4 - week 6 (excluding the week 6 visit day)	0.35	0.35	-0.35	1.04	0.32
Baseline amount of combusted product use per day		1.05	0.09	0.88	1.23	<0.0001

Marginal Generalized Estimating Equations (GEE) model for the repeated measures of amount of combusted product use during each visit, with the non-combusted product use as the independent variable, adjusting for week, experimental condition, and the baseline amount of combusted product use per day.

Appendix B. Regression Result for the Association between Repeated Measures of Non-Combusted Product Use and Number of 24-hour Abstinence Attempts

Variable	Level	Regression Coefficient Estimate	Standard Error	95% Confidence Interval		P-value
Intercept		-4.51	0.68	-5.84	- 3.17	<0.0001
Amount of non-combusted product use per day		0.08	0.02	0.04	0.13	<0.001
Condition (Reference: NNC)	VLNC1	2.09	0.81	0.50	3.68	0.01
	VLNC2	2.35	0.77	0.83	3.87	<0.01
Time window (Reference: Week 6 -Week 8)	Week 0 - week 1 (excluding the randomization day and week 1 visit day)	-2.52	0.66	-3.81	- 1.22	0.0001
	Week 1 - week 2 (excluding the week 2 visit day)	-1.41	0.46	-2.31	- 0.52	<0.01
	Week 2 - week 3 (excluding the week 3 visit day)	-1.04	0.31	-1.65	- 0.42	0.001
	Week 3 - week 4 (excluding the week 4 visit day)	-0.56	0.26	-1.08	- 0.05	0.03
	Week 4 - week 6 (excluding the week 6 visit day)	-0.37	0.18	-0.72	- 0.02	0.04

Marginal Generalized Estimating Equations (GEE) model for the repeated measures of 24-hour abstinence attempts, with the non-combusted product use as the independent variable, adjusting for week and experimental condition.

Appendix C. Regression Result for the Association between Repeated Measures of Non-Combusted Product Use and Carbon Monoxide (CO) Level

Variable	Level	Regression Coefficient Estimate	Standard Error	95% Confidence Interval		P-value
Intercept		1.38	1.69	-1.92	4.69	0.41
Amount of non-combusted product use per day		-0.14	0.11	-0.36	0.09	0.23
Condition (Reference: NNC)	VLNC1	-2.00	1.18	-4.33	0.32	0.09
	VLNC2	-3.48	1.09	-5.63	-1.34	<0.01
Time window (Reference: Week 6 -Week 8)	Week 0 - week 1 (excluding the randomization day and week 1 visit day)	2.37	1.12	0.17	4.57	0.03
	Week 1 - week 2 (excluding the week 2 visit day)	2.21	0.98	0.30	4.12	0.02
	Week 2 - week 3 (excluding the week 3 visit day)	0.68	0.93	-1.13	2.50	0.46
	Week 3 - week 4 (excluding the week 4 visit day)	0.87	0.97	-1.02	2.77	0.37
	Week 4 - week 6 (excluding the week 6 visit day)	0.41	0.81	-1.18	1.99	0.62
Baseline CO level		1.05	0.08	0.90	1.20	<.0001

Marginal Generalized Estimating Equations (GEE) model for the repeated measures of CO at each visit, with the non-combusted product use as the independent variable, adjusting for week, experimental condition, and the baseline CO level.

Appendix D. Regression Result for the Association between Repeated Measures of Non-Combusted Product Use and TNE Adjusted per Creatinine Level (Log-Transformed)

Variable	Level	Regression Coefficient Estimate	Standard Error	95% Confidence Interval		P-value
Intercept		0.32	0.94	-1.52	2.15	0.74
Amount of non-combusted product use per day		0.03	0.03	-0.02	0.09	0.23
Condition (Reference: NNC)	VLNC1	-0.85	0.20	-1.25	-0.45	<.0001
	VLNC2	-1.27	0.19	-1.64	-0.90	<.0001
Time window (Reference: Week 4 -Week 8)	Week 0 - week 4 (excluding the randomization day and week 4 visit day)	-0.16	0.09	-0.32	0.01	0.07
Baseline TNE level (Log-Transformed)		0.91	0.25	0.42	1.40	<0.001

Marginal Generalized Estimating Equations (GEE) model for the repeated measures of TNE level (log-transformed) at weeks 4 and 8, with the non-combusted product use as the independent variable, adjusting for week, experimental condition, and the baseline TNE level.

Appendix E. Regression Result for the Association between Repeated Measures of Non-Combusted Product Use and Total NNAL Adjusted per Creatinine Level (Log-Transformed)

Variable	Level	Regression Coefficient Estimate	Standard Error	95% Confidence Interval		P-value
Intercept		-0.07	0.12	-0.31	0.16	0.54
Amount of non-combusted product use per day		-0.07	0.02	-0.11	-0.03	<0.001
Condition (Reference: NNC)	VLNC1	-0.20	0.19	-0.58	0.18	0.31
	VLNC2	-0.61	0.16	-0.93	-0.29	<0.001
Time window (Reference: Week 4 -Week 8)	Week 0 - week 4 (excluding the randomization day and week 4 visit day)	0.06	0.07	-0.07	0.19	0.38
Baseline total NNAL level (Log-Transformed)		0.72	0.13	0.47	0.97	<.0001

Marginal Generalized Estimating Equations (GEE) model for the repeated measures of total NNAL per creatinine level (log-transformed) at weeks 4 and 8, with the non-combusted product use as the independent variable, adjusting for week, experimental condition, and the baseline total NNAL per creatinine level.

Appendix F. Alternative Tobacco Product Use, Amount of Cigarettes Smoked and Carbon Monoxide Levels at the Follow-up Visit (i.e., 12 Weeks Post Intervention) Compared to Baseline

	Follow-up N = 95	Baseline¹ N = 95	Change (follow-up minus Baseline)	Test	P- value
Alternative tobacco product use (N, %)	28 (29%)	23 (24%)	5%	McNemar	0.35
Cigarettes smoked per day (mean, SD)	12.14 (7.73)	15.02 (6.89)	-2.88 (6.75)	Paired t	<0.001
CO, ppm (mean, SD)	16.67 (9.13)	16.94 (7.32)	-0.26 (7.57)	Paired t	0.74
TNE, nmol/mg creatinine (geometric mean, 95% CI)	28.90 (21.21, 39.39)	33.47 (29.43, 38.08)	25% (75%) ²	Wilcoxon signed rank	0.02

¹Baseline data of the 95 subjects who had a corresponding follow-up measurement.

²Mean percent change (SD).