Supplementary Online Content

Koegelenberg CFN, Noor F, Bateman ED, et al. Efficacy of varenicline combined with nicotine replacement therapy vs varenicline alone for smoking cessation: a randomized clinical trial. *JAMA*. doi:10.1001/jama.2014.7195.

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods 1: Nicotine Use Inventory

Asked at the Baseline visit through to Visit 9 (Week 12):

- Has the participant smoked any cigarettes (even a puff) since the last study visit?
- Has the participant used any nicotine-containing products (e.g. nicotine gum, nicotine nasal spray, nicotine inhaler, nicotine lozenge, pipe, cigars, chew or snuff) since the last study visit or contact, other than that provided?
- Has the participant smoked any cigarettes (even a puff) in the last 7 days?
- Has the participant used any nicotine-containing products (e.g. nicotine patch, nicotine gum, nicotine nasal spray, nicotine inhaler, nicotine lozenge, pipe, cigars, chew, or snuff) in the last 7 days, other than that provided?

Asked at the Visit 10 (Week 13) through Visit 12 (Week 24):

- Has the participant smoked any cigarettes (even a puff) since the last visit or contact?
- Has the participant used any other tobacco products (e.g. pipe, cigars, chew or snuff) since the last visit or contact?
- Has the participant smoked any cigarettes (even a puff) in the last 7 days?
- Has the participant used any other tobacco products (e.g. pipe, cigars, chew or snuff) in the last 7 days?
- How many days have the participant smoked cigarettes since the last contact?

eMethods 2: The Wisconsin Scale for Withdrawal Symptoms

Please answer the following questions based on how you have felt or what you have noticed over the last 24 hours. Answer based on how you have felt in general during this time.

		Strongly Disagree	Disagree	Feel Neutral	Agree	Strongly Agree
1.	Food is not particularly appealing to me.	0	1	2	3	4
2.	I am getting restful sleep.	0	1	2	3	4
3.	I have been tense or anxious.	0	1	2	3	4
4.	My level of concentration is excellent.	0	1	2	3	4
5.	I awaken from sleep frequently during the night.	0	1	2	3	4
6.	I have felt impatient.	0	1	2	3	4
7.	I have felt upbeat and optimistic.	0	1	2	3	4
8.	I have found myself worrying about my problems.	0	1	2	3	4
9.	I have had frequent urges to smoke.	0	1	2	3	4
10.	I have felt calm lately.	0	1	2	3	4
11.	I have been bothered by the desire to smoke a cigarette.	0	1	2	3	4
12.	I have felt sad or depressed.	0	1	2	3	4
13.	I have been irritable, easily angered.	0	1	2	3	4
14.	I want to nibble on snacks or sweets.	0	1	2	3	4
15.	I have been bothered by negative moods such as anger, frustration, and irritability.	0	1	2	3	4
16.	I have been eating a lot.	0	1	2	3	4
17.	I am satisfied with my sleep.	0	1	2	3	4
18.	I have felt frustrated.	0	1	2	3	4
19.	I have felt hopeless or discouraged.	0	1	2	3	4
20.	I have thought about smoking a lot.	0	1	2	3	4
21.	I have felt hungry.	0	1	2	3	4
22.	I feel that I am getting enough sleep.	0	1	2	3	4
23.	It is hard to pay attention to things.	0	1	2	3	4
24.	I have felt happy and content.	0	1	2	3	4
25.	My sleep has been troubled.	0	1	2	3	4
26.	I have trouble getting cigarettes off my mind.	0	1	2	3	4
27.	It has been difficult to think clearly.	0	1	2	3	4
28.	I think about food a lot.	0	1	2	3	4

SCORING: The subscale to each item ranges from 0 (none) to 4 (severe) and is determined on how high they agreed on the scale. For the * items, the subscale is determined on how low they agreed. Each emotion is determined by the mean of each item that applies (e.g. the mean of #13, 15, and 18 determine the anger level).

Subscale	**Question Numbers (*these items are reverse scored)**
Anger	13, 15, 18
Anxiety	3, 6, 8, *10
Concentration	*4, 23, 27
Craving	9, 11, 20, 26
Hunger	*1, 14, 16, 21, 28
Sadness	*7, 12, 19, *24
Sleep	*2, 5, *17, *22, 25

The Wisconsin Scale for Withdrawal Symptoms was developed by the Center for Tobacco Research & Intervention of the University of Wisconsin for the use in research in tobacco dependence and the process of quitting. It can be accessed at http://www.ctri.wisc.edu/Researchers/researchers_measures&scales.htm.

eMethods 3: An additional post hoc logistic mixed hierarchical model analysis

The longitudinal dataset was further analyzed in Stata using a random intercept logistic mixed model (xtlogit) with maximum likelihood estimation to account for repeated measures within participants, with a fixed effect to account for clustering within study sites. The time periods used were 1 week, 2 weeks, 4 weeks, 8 weeks, 12 weeks, 16 weeks, and 6 months post TQD. An interaction term was generated for the effect of the interaction between time and treatment group. The main effects of time and treatment, and the intervention effect (measured by the interaction between time and treatment), as well as site, were specified as independent variables. Odds ratios and 95% CIs were reported.

eResults: The post-hoc logistic mixed hierarchical model analysis

The estimated odds of abstinence (over the time period 1 week post TQD to 6 months) in the placebo group was multiplied by 1.2 for every increase from one time point to the next, and the estimated odds of abstinence in the intervention group multiplied by 1.4 (1.20 x 1.18) from one time point to the next (eTable 1). The difference in rate of abstinence over time was significantly different in the two groups (*P* for interaction between time and group = 0.01). The bar graph (eFigure 1) shows that the abstinence rate in the placebo patch group improved initially, but levelled off around 8 weeks post TQD, while abstinence in the active patch group increased up to around 12 weeks post TQD.

eTable: Random intercept logistic mixed model

Effect	Odds ratio (95% CI)	*P* value
Time	1.20 (1.10-1.31)	<0.001
Treatment	0.95 (0.39-2.29)	0.90
Time x treatment	1.18 (1.04-1.34)	0.01
Site	0.91 (0.77-1.08)	0.27

eFigure: Bar graph comparing the abstinence over the time period 1 week post TQD to 6 months in the active and placebo NRT patch groups