Cardiovascular and neuropsychiatric risks of varenicline - Authors' reply

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1 Kotz D, Viechtbauer W, Simpson C, et al. Cardiovascular and neuropsychiatric risks of varenicline: a retrospective cohort study. *Lancet Respir Med* 2015; **3:** 761–68.

2 Singh S, Loke YK, Spangler JG, Furberg CD. Risk of serious adverse cardiovascular events associated with varenicline: a systematic review and meta-analysis. *CMAJ* 2011; **183:** 1359–66.

3 Stanbrook, Matthew (drstanbrook). So it may be that immediate quit period itself poses transient risks, rather than why you use to quit. Oct 30, 2015, 0050 h GMT. Tweet.

4 Kotz, Daniel (retweeted by rsjcguest). "In some instances, the HRs were not constant across the entire follow-up period (see paper), but always in the same direction. This is graphically displayed in the supplementary material." Nov 9, 2015. 1528 h GMT. Tweet.

5 Kotz, Daniel (retweeted by rsjcguest). "They should. We are currently looking at this in more detail as this question has been asked by others as well". Nov 9, 2015, 1524 h GMT. Tweet.

6 McEvoy JW, Blaha MJ, DeFilippis AP, et al. Cigarette smoking and cardiovascular events: role of inflammation and subclinical atherosclerosis from the MultiEthnic Study of Atherosclerosis. *Arterioscler Thromb Vasc Biol* 2015; **35:** 700–09.

Authors' reply

In their Correspondence on our retrospective cohort study into the cardiovascular and neuropsychiatric risks of varenicline for smoking cessation,[1] Lee Fidler and colleagues ask "whether propensity matching succeeded in balancing baseline covariates across groups". We have examined this important point further and take the opportunity to present additional data: the baseline characteristics of the two matched samples (nicotine replacement therapy *vs* bupropion and nicotine replacement therapy *vs* varenicline; table). Overall, trimming and matching of patients by propensity score succeeded in balancing potential confounders, although subtle differences remained. Notably, most present and previous diseases had a marginally higher prevalence rate at baseline (range 0·1–1·1%) in the bupropion and varenicline group than in their matched nicotine replacement therapy group. Consequently, users of bupropion and varenicline might have been at slightly higher risk of the neuropsychiatric and cardiovascular events of interest during follow-up in our propensity score analyses. However, if such differences had biased the findings from our analyses, the bias would not have been in favour of varenicline. Nevertheless, we found no evidence of an increased risk of any neuropsychiatric or cardiovascular event associated with varenicline compared with nicotine replacement therapy in the propensity score analyses.[1]

	NRT *vs* bupropion		NRT *vs* varenicline	
	NRT (N=6393)	Bupropion (N=6393)	NRT (N=50 163)	Varenicline (N=50 163)
Age (years)	37·7 (11·2)	37·2 (10·8)	37·8 (11·9)	37·6 (11·2)
Sex				
Women	3138 (49·1%)	3095 (48·4%)	24 720 (49·3%)	23 858 (47·6%)
Men	3255 (50·9%)	3298 (51·6%)	25 443 (50·7%)	26 305 (52·4%)
Socioeconomic status*	3·0 (1·3)	2·9 (1·3)	3·0 (1·3)	3·0 (1·3)
COPD	341 (5·3%)	355 (5·6%)	3286 (6·6%)	3554 (7·1%)
Diabetes	139 (2·2%)	162 (2·5%)	1946 (3·9%)	2114 (4·2%)
Peptic ulcer disease	82 (1·3%)	119 (1·9%)	968 (1·9%)	1105 (2·2%)
Renal disease	89 (1·4%)	146 (2·3%)	1006 (2·0%)	1178 (2·3%)
Rheumatological disease	82 (1·3%)	87 (1·4%)	777 (1·5%)	926 (1·8%)
Cancer	123 (1·9%)	127 (2·0%)	1074 (2·1%)	1220 (2·4%)
Alcohol misuse	277 (4·3%)	283 (4·4%)	2446 (4·9%)	2562 (5·1%)
Previous ischaemic heart disease	100 (1·6%)	100 (1·6%)	1161 (2·3%)	1267 (2·5%)
Previous cerebral infarction	47 (0·7%)	52 (0·8%)	444 (0·9%)	463 (0·9%)
Previous heart failure	6 (0·1%)	9 (0·1%)	72 (0·1%)	78 (0·2%)
Previous peripheral vascular disease	28 (0·4%)	30 (0·5%)	254 (0·5%)	319 (0·6%)
Previous arrhythmia	51 (0·8%)	69 (1·1%)	367 (0·7%)	470 (0·9%)
Previous depression	2114 (33·1%)	2137 (33·4%)	15 463 (30·8%)	15 340 (30·6%)
Previous self-harm	516 (8·1%)	586 (9·2%)	3997 (8·0%)	4254 (8·5%)

Data are n (%) or mean (SD). NRT=nicotine replacement therapy. COPD=chronic obstructive pulmonary disease. *Townsend index: 1 (lowest) to 5 (highest level of deprivation).

Table: **Patient characteristics at entry date to the cohort in the propensity score-matched samples**

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