

Appendix 4: Data on serious adverse cardiovascular events and mortality reported in RCTs of varenicline					
Study*	Treatment arms	No. of participants	No. of serious adverse cardiovascular events†	Nature of cardiovascular adverse events	No. of deaths from any cause
Double-blind RCTs					
A3051080, 2010 ¹⁶	Varenicline	394	1	Tachycardia/bradycardia	0
	Placebo	199	0	NA	0
A3051095, 2010 ¹⁷	Varenicline	493	1	Atrial flutter	0
	Placebo	166	0	NA	0
Fagerstrom et al, 2010 ¹⁸	Varenicline	214	0	NA	0
	Placebo	218	1	Cardiac failure	0
Gonzales et al, 2006 ¹⁹	Varenicline	352	2	Atrial fibrillation; stroke	0
	Bupropion	329	0	NA	0
	Placebo	344	2	Atrial fibrillation, acute myocardial infarction	1
Jorenby et al, 2006 ²⁰	Varenicline	344	1	Acute coronary syndrome	0
	Bupropion	342	1	Coronary artery occlusion	1
	Placebo	341	1	Ischemic heart disease	0
Nakamura et al, 2007 ²¹	Varenicline	465	1	Angina pectoris	1
	Placebo	154	0	NA	0
Niaura et al, 2008 ²²	Varenicline	160	2	Myocardial infarction; ventricular fibrillation	0
	Placebo	160	0	NA	0
Nides et al, 2006 ²³	Varenicline	383	1	Transient ischemic attack	0
	Bupropion	128	0	NA	0
	Placebo	127	0	NA	0
Oncken et al, 2006 ²⁴	Varenicline	518	2	Unstable angina; paroxysmal supraventricular tachycardia	0
	Placebo	129	0	NA	0
Rigotti et al, 2010 ^{9‡}	Varenicline	355	25	Prespecified adjudicated events	2
	Placebo	359	20	Prespecified adjudicated events	5
Tashkin et al, 2010 ²⁵	Varenicline	250	5	Nonfatal acute myocardial infarction; nonfatal angina pectoris; cerebrovascular accident; left ventricular dysfunction; sudden death	2
	Placebo	254	2	Ischemic stroke; Acute myocardial infarction	1
Tonstad et al, 2006 ²⁶	Varenicline	603	4	Suspected myocardial infarction; myocardial infarction; cerebral infarct and cerebral vein thrombosis; supraventricular tachycardia	2
	Placebo	607	0	NA	0
Tsai et al, 2007 ²⁷	Varenicline	126	1	Unstable angina and coronary occlusion	0
	Placebo	124	0	NA	0
Williams et al, 2007 ²⁸	Varenicline	251	6	Coronary artery disease; ventricular bigeminy and coronary angioplasty; stroke; cardiac catheterization; tachycardia, myocardial infarction	0
	Placebo	126	1	Worsening coronary artery disease	0
Open-label RCT					
Aubin et al, 2008 ²⁹	Varenicline	378	0	NA	0
	NRT	379	2	Myocardial infarction	0

Note: NA = not applicable, NRT = nicotine-replacement therapy.

*Citations of the studies are available in the reference list of the main article (www.cmaj.ca/lookup/doi/10.1503/cmaj.110218).

†Ischemic, arrhythmic, and congestive heart failure and cardiovascular death.

‡An additional 11 investigator-reported cardiovascular events (9 for varenicline v. 2 for placebo) were deemed to not meet criteria for adjudication.