

## Appendix 2: Multiple imputation and a complete case analysis

The factors used in the multiple imputation included outcome, age, gender, smoking status, BMI, hypertension, peripheral vascular disease, angina, chronic obstructive pulmonary disease (COPD), diabetes mellitus, chronic kidney disease, migraine, heart failure, oesophageal disease, potassium sparing diuretics, Angiotensin Converting Enzyme (ACE) inhibitors or Angiotensin Receptor Blockers (ARBs), other cardiovascular drugs, proton pump inhibitors, oral steroids, Anti-Inflammatory Non-Steroidal Drugs (NSAIDs) or COX-2 inhibitors and anti-psychotic medications.

A further analysis using only those patients without any missing data (n=68,224) showed that the adjusted HR was 1.20 (95%CI 1.12-1.27) which was similar to the main result. The baseline characteristics of patients in a complete case analysis are shown in table 1.

Table 1. Baseline characteristics

	<b>Cases N=34112</b>	<b>Controls N=34112</b>	<b>P value</b>
<b>Age (years, SD)</b>	67 (11.9)	67 (11.9)	-
<b>Gender (Male)</b>	15177 (44.5%)	15177 (44.5%)	-
<b>BMI (kg/m<sup>2</sup>)</b>			
<18.5	629 (1.8%)	597 (1.8%)	<0.01
18.5-24.9	11411 (33.5%)	11705 (34.3%)	
25-29.9	13595 (39.9%)	13745 (40.3%)	
≥30	8477 (24.8%)	8065 (23.6%)	
<b>Smoking status</b>			
None	7272 (21.3%)	5627 (16.5%)	<0.01
Current smoker	16117 (47.3%)	18534 (54.3%)	
Ex-smoker	10723 (31.4%)	9951 (29.2%)	
<b>Previous disease history</b>			
Angina	6985 (20.5%)	4328 (12.7%)	<0.01
HF	2168 (6.4%)	1506 (4.4%)	<0.01
PVD	1485 (4.4%)	865 (2.5%)	<0.01
Migraine	2211 (6.5%)	1887 (5.5%)	<0.01
Oesophageal disease	91 (0.27%)	62 (0.18%)	0.02
Diabetes	6275 (18.4%)	4687 (13.7%)	<0.01
CKD	3794 (11.1%)	3305 (9.7%)	<0.01
COPD	3788 (11.1%)	3194 (9.4%)	<0.01
<b>Previous medication history</b>			
CVD drugs	26289 (77.1%)	20998 (61.6%)	<0.01
ACE/ARB	14512 (42.5%)	11573 (33.9%)	<0.01
PPI	14964 (43.9%)	13546 (39.7%)	<0.01
Potassium	1576 (4.6%)	1168 (3.4%)	<0.01
Anti-psychotic	9785 (28.7%)	8743 (25.6%)	<0.01
HIV	3 (0.0%)	0 (0.0%)	--
Steroids	2814 (8.3%)	2404 (7.1%)	<0.01
NSAIDs	25549 (74.9%)	25988 (76.2%)	<0.01