

Supplementary Table 1. ICD-9 codes for outcome and covariates

Outcome	ICD-9 code
Gastric cancer	151, 151.0, 151.1, 151.2, 151.3, 151.4, 151.5, 151.6, 151.8, 151.9, 230.2
Covariates	
Personal history of smoking and smoking-induced disorders	491, 492, 496, V15.82
Alcohol induced disorders	291, 303, 305.0, 571.0, 571.1, 571.2, 571.3, 980.8, 980.9
Gastrointestinal diseases	
Gastric ulcer	531
Duodenal ulcer	532
Cardiovascular diseases and cardiovascular risk factors	
Atrial fibrillation	427.3
Congestive heart failure	402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 428
Hypertension	401-405
Ischemic heart disease	410-413, 414.0, 414.8, 414.9, 429.7
Stroke	430-432, 433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, 434.91, 436, 437.0, 437.1
Dyslipidemia	272.0-272.4
Obesity	278.0, 278.1
Hepatic and renal diseases	
Cirrhosis	571.2, 571.5, 571.6, 572.2-572.4, 573.5
Chronic renal failure	585

Supplementary Table 2. Description of various propensity score methods

PS analysis	Description
PS adjustment after trimming	Individuals in the non-overlapping parts of the PS distribution were excluded. The effect estimate was then derived by including the exposure of interest (metformin use) and the PS into the multivariable Cox regression model
PS matching without replacement	PS matching with 1:1 ratio without replacement matched each member of the non-exposure group to exposure group
PS weighting by IPTW with stabilisation	The PS was transformed and subsequently used as weights in the multivariable Cox proportional hazards model in predicting the outcome (i.e. weighted Cox regression using PS weights). The weight of each individual in the exposure group (metformin use) was $1/PS$ while that for the non-exposure group (non-metformin use) was $1/(1 - PS)$. To account for influence from individuals with extreme weights, 'stabilisation' was done by multiplying IPTW by a constant (i.e. the expected value of receiving the alternative treatment) so as to reduce the standard error of the effect estimate
PS, propensity score; IPTW, inverse probability treatment weighting	

Supplementary Table 3. Assessment of balance of covariates between the two groups before and after PS analysis

Characteristics	Before PS analysis			PS weighting by IPTW	PS matching
	Metformin users, No. (%) (n=5,368)	Non-metformin users, No. (%) (n=1,898)	Absolute standardised difference†	Absolute standardised difference†	Absolute standardised difference†
Median age at triple therapy, y (IQR)	63.8 (55.6 – 72.6)	69.7 (58.2 – 78.2)	0.37	0.02	0.13
Male sex	2716 (50.6)	1063 (56.0)	0.11	0.01	0.04
Median duration of follow-up, y (IQR)	7.5 (5.2 – 10.1)	5.8 (3.5 – 8.8)	n.a.	n.a.	n.a.
Time-weighted average HbA1c ≥ 7%	3437 (64.0)	754 (39.7)	0.51	0.04	0.10
Smoking	945 (17.6)	320 (16.9)	0.02	0.01	0.01
Alcohol	61 (1.1)	55 (2.9)	0.17	0.01	0.03
History of gastric ulcer	180 (3.4)	101 (5.3)	0.11	0.02	0.02
History of duodenal ulcer	198 (3.7)	97 (5.1)	0.08	0.01	0.03
Hypertension	3246 (60.5)	1257 (66.2)	0.12	0.01	0.02
Dyslipidemia	1483 (27.6)	499 (26.3)	0.03	0.04	0.01
Obesity	1097 (20.4)	191 (10.1)	0.26	0.01	0.09
Ischemic heart disease	1318 (24.6)	546 (28.8)	0.10	0.01	0.01
Atrial fibrillation	426 (7.9)	223 (11.7)	0.14	0.03	0.03
Congestive heart failure	579 (10.8)	422 (22.2)	0.37	0.01	0.01
Stroke	935 (17.4)	406 (21.4)	0.10	0.01	0.01
Chronic renal failure	346 (6.4)	424 (22.3)	0.65	0.01	0.20
Cirrhosis	148 (2.8)	126 (6.6)	0.24	0.01	0.02
Aspirin/ NSAIDs/COX-2 inhibitors*	2649 (49.3)	808 (42.6)	0.14	0.01	0.10
Statins*	3562 (66.4)	813 (42.8)	0.50	0.01	0.09
Proton pump inhibitors*	654 (12.2)	312 (16.4)	0.13	0.01	0.03
Insulin*	1575 (29.3)	500 (26.3)	0.07	0.02	0.03

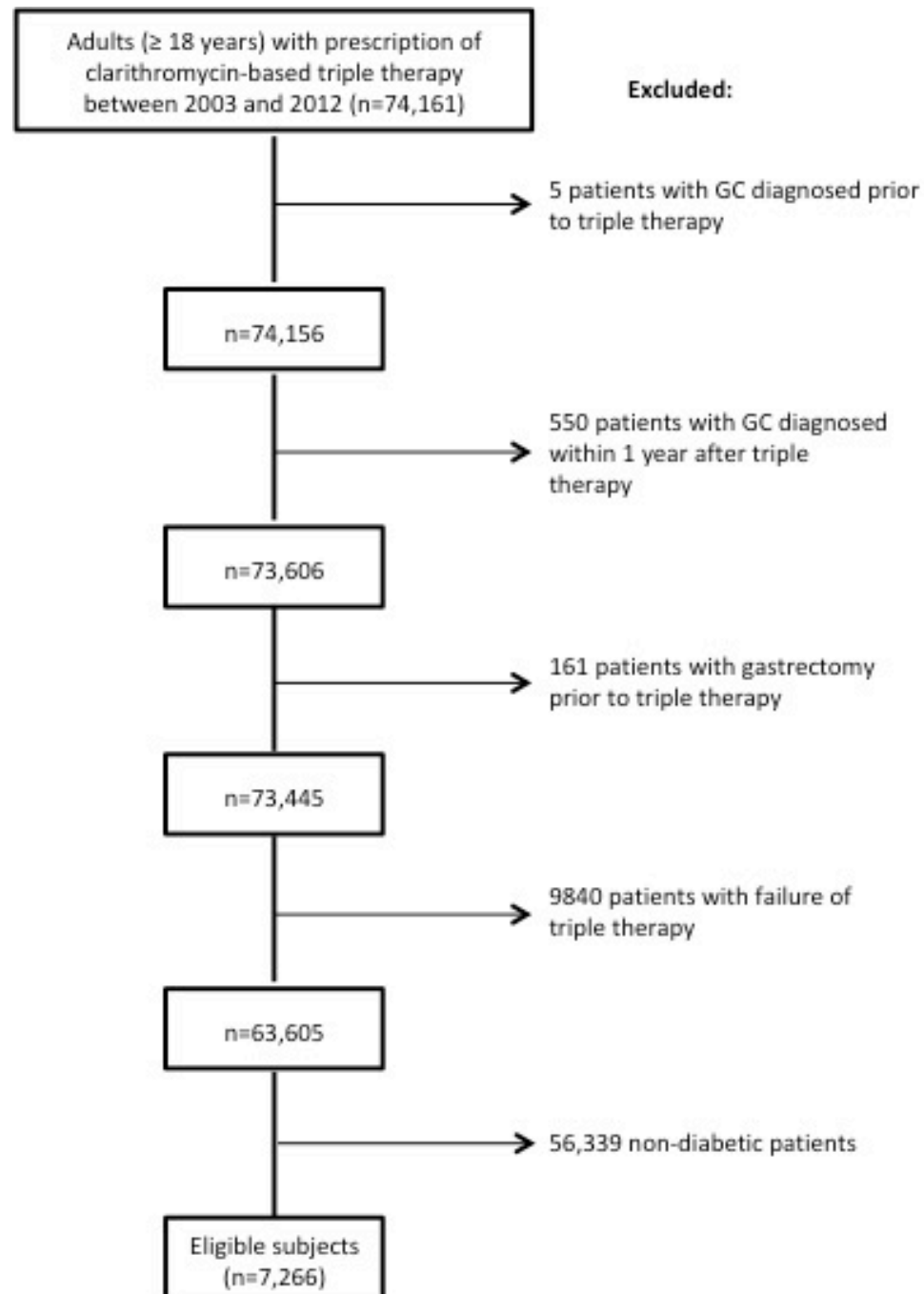
PS, propensity score; IPTW: inverse probability treatment weighting; n.a., not available; HbA1c, hemoglobin A1c;

NSAIDs, non-steroidal anti-inflammatory drugs; COX-2, cyclooxygenase-2

*Drug use was defined as use for more than 180 days

† Standardized difference is the difference in mean or proportion of covariates in the non-metformin vs metformin group divided by the pooled standard deviation. A standardised difference of below 0.2 indicates good balance.

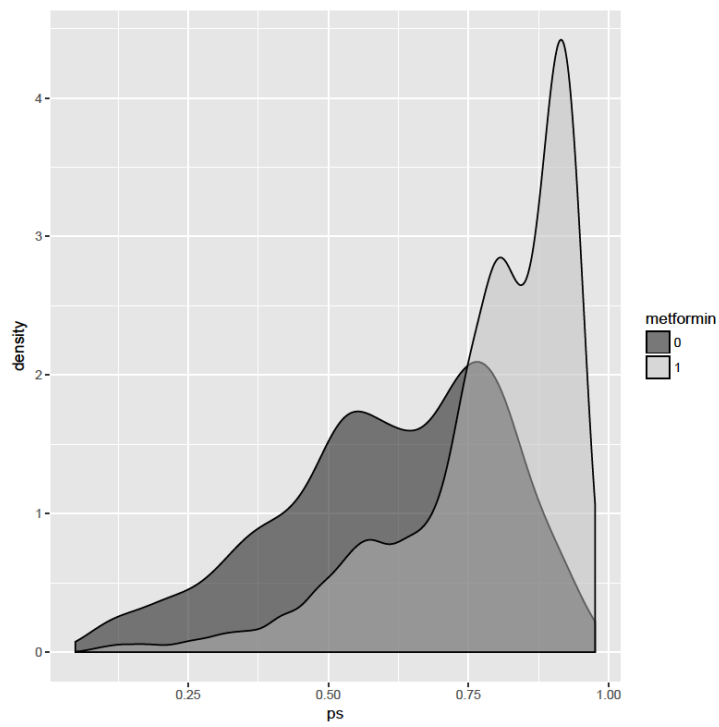
Supplementary Figure 1: Patient selection flow diagram



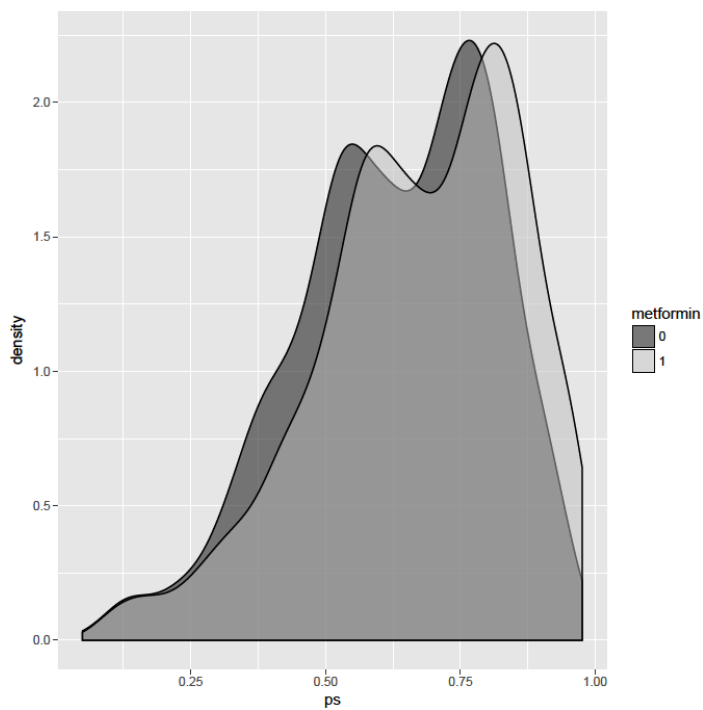
Abbreviations: GC, gastric cancer

Supplementary Figure 2. Propensity score distributions of metformin and non-metformin users

Before propensity score matching



After propensity score matching



Metformin: 0 = non-user; 1 = user

Supplementary Figure 3. Back to back histogram before and after propensity score matching

