

ONLINE SUPPLEMENT

Comprehensive comparative effectiveness and safety of first-line beta-blocker monotherapy in hypertensive patients: a large-scale multi-center observational study

Seng Chan You, MD, MS^{1,2}; Harlan M. Krumholz, MD, MS^{3,4}; Marc A. Suchard, MD, PhD^{5,6}; Martijn J. Schuemie, PhD^{5,7}; George Hripcsak, MD^{8,9}; RuiJun Chen, MD^{8,10}; Steven Shea, MD^{8,11}; Jon Duke, MD¹²; Nicole Pratt, PhD¹³; Christian G. Reich, MD, PhD¹⁴; David Madigan, PhD¹⁵; Patrick B. Ryan, PhD^{7,8}; Rae Woong Park, MD, PhD^{1,16,*}; Sungha Park, MD, PhD^{17,*}

*Co-corresponding authors

¹Department of Biomedical Informatics, Ajou University School of Medicine, Suwon, Korea

²Department of Preventive Medicine and Public Health, Yonsei University College of Medicine, Seoul, Korea

³Section of Cardiovascular Medicine, Department of Medicine, Yale University School of Medicine, New Haven, CT, USA

⁴Center for Outcomes Research and Evaluation, Yale-New Haven Hospital, New Haven, CT, USA

⁵Department of Biostatistics, Fielding School of Public Health, University of California, Los Angeles, CA, USA

⁶Department of Biomathematics, David Geffen School of Medicine at UCLA, University of California, Los Angeles, CA, USA

⁷Janssen Research and Development, Titusville, NJ, USA

⁸Department of Biomedical Informatics, Columbia University Irving Medical Center, New York, NY, USA

⁹Medical Informatics Services, New York-Presbyterian Hospital, New York, NY, USA

¹⁰Department of Medicine, Weill Cornell Medical College, New York, NY, USA

¹¹Department of Medicine, Vagelos College of Physicians & Surgeons, Columbia University, New York, NY, USA

¹²Georgia Tech Research Institute, Georgia Tech College of Computing, Atlanta, GA, USA

¹³Quality Use of Medicines and Pharmacy Research Centre, Clinical and Health Sciences, University of South Australia, Adelaide, SA, Australia

¹⁴Real World Solutions, IQVIA, Cambridge, MA, USA

¹⁵Department of Statistics, Columbia University, New York, NY, USA

¹⁶Department of Biomedical Sciences, Ajou University Graduate School of Medicine, Suwon, Korea

¹⁷Division of Cardiology, Severance Cardiovascular Hospital and Integrated Research Center for Cerebrovascular and Cardiovascular diseases, Yonsei University College of Medicine, Seoul, Korea

Address for co-correspondence:

Rae Woong Park, MD, PhD

Department of Biomedical Informatics, Ajou University School of Medicine, 164, World cup-ro, Yeongtong-gu, Suwon-si, Gyeonggi-do 16499, Republic of Korea

Tel: +82-31-219-4471, Fax: +82-219-4472

E-mail: veritas@ajou.ac.kr

Sungha Park, MD, PhD

Division of Cardiology, Severance Cardiovascular Hospital and Integrated Research Center for Cerebrovascular and Cardiovascular diseases, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Republic of Korea

Tel: +82-2-2228-8455, Fax: +82-2-393-2041

E-mail: shpark0530@yuhs.ac

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Methods. Data Source

Truven MarketScan Commercial Claims and Encounters (CCAE)

Truven Health MarketScan® Commercial Claims and Encounters Database (CCAE) represent data from individuals enrolled in United States employer-sponsored insurance health plans. The data includes adjudicated health insurance claims (e.g. inpatient, outpatient, and outpatient pharmacy) as well as enrollment data from large employers and health plans who provide private healthcare coverage to employees, their spouses, and dependents. Additionally, it captures laboratory tests for a subset of the covered lives. This administrative claims database includes a variety of fee-for-service, preferred provider organizations, and capitated health plans.

Optum ClinFormatics (Optum)

Optum Clinformatics Extended DataMart is an adjudicated US administrative health claims database for members of private health insurance, who are fully insured in commercial plans or in administrative services only (ASOs), Legacy Medicare Choice Lives (prior to January 2006), and Medicare Advantage (Medicare Advantage Prescription Drug coverage starting January 2006). The population is primarily representative of commercial claims patients (0-65 years old) with some Medicare (65+ years old) however ages are capped at 90 years. It includes data captured from administrative claims processed from inpatient and outpatient medical services and prescriptions as dispensed, as well as results for outpatient lab tests processed by large national lab vendors who participate in data exchange with Optum. This dataset also provides date of death (month and year only) for members with both medical and pharmacy coverage from the Social Security Death Master File (however after 2011 reporting frequency changed due to changes in reporting requirements) and location information for patients is at the US state level.

Optum® de-identified Electronic Health Record Dataset (PanTher)

Optum® de-identified Electronic Health Record Dataset represents Humedica's Electronic Health Record data a medical records database. The medical record data includes clinical information, inclusive of prescriptions as prescribed and administered, lab results, vital signs, body measurements, diagnoses, procedures, and information derived from clinical Notes using Natural Language Processing (NLP).

Table S1. Baseline characteristics between carvedilol and atenolol**Table S1 a. Baseline characteristics for carvedilol and atenolol new-users in the CCAE database before and after propensity score matching**

Characteristic	Before matching			After matching		
	Carvedilol, %	Atenolol, %	Std. diff	Carvedilol, %	Atenolol, %	Std. diff
Age group						
10-14	0.0	0.2	-0.05	0.0	0.1	-0.04
15-19	0.4	0.9	-0.07	0.4	0.5	-0.01
20-24	1.1	1.7	-0.05	1.2	1.3	-0.01
25-29	2.3	3.0	-0.04	2.6	2.6	0.00
30-34	4.1	5.3	-0.06	4.5	4.6	0.00
35-39	6.7	8.1	-0.06	7.5	7.2	0.01
40-44	9.6	11.7	-0.07	10.2	10.3	0.00
45-49	15.0	15.7	-0.02	15.5	15.3	0.01
50-54	18.1	18.0	0.00	18.0	17.8	0.00
55-59	20.3	17.9	0.06	19.4	19.6	0.00
60-64	20.5	15.9	0.12	18.9	19.0	0.00
65-69	2.0	1.5	0.03	1.8	1.8	0.00
70-74	0.0	0.0	-0.02	0.0	0.0	0.01
Gender: female	42.5	51.2	-0.18	45.3	45.2	0.00
Medical history: General						
Acute respiratory disease	28.1	24.6	0.08	27.3	27.6	-0.01
Attention deficit hyperactivity disorder	1.2	1.1	0.02	1.3	1.3	-0.01
Chronic liver disease	2.1	1.4	0.05	1.8	1.9	-0.01
Chronic obstructive lung disease	5.0	1.8	0.18	3.6	3.7	-0.01
Crohn's disease	0.5	0.3	0.03	0.5	0.4	0.02
Dementia	0.3	0.2	0.02	0.3	0.2	0.01
Depressive disorder	9.7	8.6	0.04	9.6	9.8	-0.01
Diabetes mellitus	16.2	6.2	0.32	12.9	13.5	-0.02
Gastroesophageal reflux disease	12.2	7.9	0.14	11.2	11.5	-0.01
Gastrointestinal hemorrhage	2.7	2.1	0.04	2.5	2.4	0.01
Human immunodeficiency virus infection	0.3	0.2	0.02	0.3	0.3	0.00
Hyperlipidemia	45.9	29.6	0.34	41.5	42.8	-0.03
Hypertensive disorder	100.0	100.0	0.00	100.0	100.0	0.00
Lesion of liver	0.9	0.3	0.07	0.6	0.6	0.01
Obesity	10.2	5.7	0.17	8.7	9.2	-0.02
Osteoarthritis	15.6	11.4	0.12	14.8	15.4	-0.02
Pneumonia	3.9	1.6	0.14	2.7	2.6	0.00
Psoriasis	1.1	0.9	0.02	1.1	1.0	0.00
Renal impairment	4.5	0.8	0.23	2.4	2.4	0.00
Rheumatoid arthritis	1.2	0.9	0.03	1.1	1.2	-0.01
Schizophrenia	0.1	0.1	0.00	0.1	0.1	-0.01
Ulcerative colitis	0.5	0.3	0.02	0.4	0.4	0.01
Urinary tract infectious disease	7.0	6.3	0.02	6.6	6.8	-0.01
Viral hepatitis C	0.6	0.5	0.02	0.5	0.5	0.00
Visual system disorder	16.5	15.0	0.04	16.2	16.6	-0.01
Medical history: Cardiovascular disease						
Atrial fibrillation	4.1	1.4	0.16	2.9	3.2	-0.02
Cerebrovascular disease	3.8	1.7	0.13	3.1	3.2	-0.01
Coronary arteriosclerosis	20.9	4.4	0.51	13.0	13.6	-0.02
Heart disease	45.0	16.1	0.66	33.7	35.7	-0.04

Heart failure	6.9	0.5	0.34	2.4	2.3	0.00
Ischemic heart disease	18.8	3.8	0.49	11.0	11.4	-0.01
Peripheral vascular disease	10.5	4.3	0.24	8.1	8.6	-0.02
Pulmonary embolism	0.8	0.3	0.08	0.5	0.7	-0.03
Venous thrombosis	2.4	1.1	0.10	1.7	1.8	-0.01
Medical history: Neoplasms						
Hematologic neoplasm	1.4	0.6	0.08	1.2	1.1	0.01
Malignant lymphoma	0.4	0.2	0.03	0.4	0.3	0.00
Malignant neoplasm of anorectum	0.3	0.1	0.03	0.2	0.2	0.01
Malignant neoplastic disease	6.6	4.9	0.07	6.1	6.2	0.00
Malignant tumor of breast	1.2	1.1	0.02	1.2	1.1	0.01
Malignant tumor of colon	0.4	0.3	0.03	0.4	0.4	0.00
Malignant tumor of lung	0.4	0.2	0.04	0.3	0.4	-0.01
Malignant tumor of urinary bladder	0.2	0.1	0.00	0.1	0.2	-0.01
Primary malignant neoplasm of prostate	0.6	0.5	0.01	0.6	0.7	-0.01
Medication use						
Antibacterials for systemic use	51.1	48.9	0.04	50.9	51.6	-0.02
Antidepressants	21.5	21.3	0.00	22.0	21.9	0.00
Antiepileptics	10.1	7.4	0.09	9.8	9.9	0.00
Antiinflammatory and antirheumatic products	25.5	24.5	0.02	25.5	25.8	-0.01
Antineoplastic agents	2.2	1.6	0.05	2.0	2.1	-0.01
Antipsoriatics	0.5	0.4	0.01	0.5	0.4	0.01
Antithrombotic agents	18.2	4.5	0.44	11.1	11.6	-0.01
Drugs for acid related disorders	20.0	16.7	0.09	19.1	19.3	-0.01
Drugs for obstructive airway diseases	18.9	16.1	0.07	18.5	18.6	0.00
Drugs used in diabetes	10.6	3.7	0.27	8.2	8.7	-0.02
Immunosuppressants	2.2	1.5	0.05	2.0	2.0	0.00
Lipid modifying agents	33.7	18.7	0.34	27.6	28.8	-0.03
Opioids	23.9	16.6	0.18	21.6	22.0	-0.01
Psycholeptics	27.2	23.9	0.08	26.3	26.7	-0.01
Psychostimulants, agents used for ADHD and nootropics	3.6	3.5	0.00	3.8	4.0	-0.01

CCAE, Truven MarketScan Commercial Claims and Encounters

Table S1 b. Baseline characteristics for carvedilol and atenolol new-users in the Optum database before and after propensity score matching

Characteristic	Before matching			After matching		
	Carvedilol, %	Atenolol, %	Std. diff	Carvedilol, %	Atenolol, %	Std. diff
Age group						
15-19	0.2	0.5	-0.05	0.2	0.4	-0.03
20-24	0.4	0.9	-0.07	0.5	0.6	-0.01
25-29	1.2	2.3	-0.09	1.5	1.5	0.00
30-34	2.0	4.1	-0.12	2.4	2.4	0.00
35-39	3.5	6.5	-0.14	4.3	4.2	0.01
40-44	5.7	9.2	-0.14	6.7	6.4	0.01
45-49	8.0	12.2	-0.14	9.3	9.0	0.01
50-54	10.6	13.4	-0.08	11.6	11.3	0.01
55-59	11.4	13.0	-0.05	11.8	11.6	0.01
60-64	12.0	10.5	0.05	11.6	11.7	0.00
65-69	12.6	8.6	0.13	12.0	12.1	0.00
70-74	11.5	7.6	0.13	10.3	10.3	0.00
75-79	9.5	6.3	0.12	8.5	8.8	-0.01
80-84	7.5	3.6	0.17	6.4	6.8	-0.02
85-89	4.0	1.2	0.18	2.9	2.9	0.00
Gender: female	40.0	51.6	-0.24	43.8	43.3	0.01
Medical history: General						
Acute respiratory disease	28.6	24.7	0.09	26.3	26.7	-0.01
Attention deficit hyperactivity disorder	0.9	0.9	0.00	1.0	0.9	0.01
Chronic liver disease	2.2	1.5	0.05	2.1	2.1	0.00
Chronic obstructive lung disease	13.6	4.3	0.33	9.4	9.9	-0.02
Crohn's disease	0.5	0.4	0.01	0.4	0.4	-0.01
Dementia	3.3	1.2	0.15	2.4	2.5	-0.01
Depressive disorder	12.1	10.6	0.05	11.6	11.8	-0.01
Diabetes mellitus	26.5	10.2	0.43	20.9	22.1	-0.03
Gastroesophageal reflux disease	17.5	11.7	0.16	15.9	16.4	-0.01
Gastrointestinal hemorrhage	4.1	3.0	0.06	3.5	3.6	-0.01
Human immunodeficiency virus infection	0.3	0.2	0.02	0.3	0.4	-0.02
Hyperlipidemia	62.6	44.3	0.37	58.3	59.7	-0.03
Hypertensive disorder	100.0	100.0	0.00	100.0	100.0	0.00
Lesion of liver	1.4	0.5	0.09	1.0	0.9	0.01
Obesity	10.9	7.0	0.14	9.8	10.1	-0.01
Osteoarthritis	24.4	17.1	0.18	22.9	23.3	-0.01
Pneumonia	7.3	2.4	0.23	4.6	4.8	-0.01
Psoriasis	1.1	1.1	0.00	1.1	1.1	0.00
Renal impairment	13.3	2.2	0.42	7.4	7.6	-0.01

Rheumatoid arthritis	1.8	1.4	0.03	1.7	1.7	-0.01
Schizophrenia	0.3	0.2	0.02	0.3	0.3	-0.01
Ulcerative colitis	0.5	0.4	0.02	0.5	0.5	0.00
Urinary tract infectious disease	12.2	8.4	0.12	10.7	10.8	0.00
Viral hepatitis C	0.8	0.5	0.03	0.7	0.6	0.01
Visual system disorder	31.3	26.2	0.11	29.8	30.3	-0.01
Medical history: Cardiovascular disease						
Atrial fibrillation	12.4	3.6	0.33	8.4	8.7	-0.01
Cerebrovascular disease	8.3	3.5	0.20	6.6	6.8	-0.01
Coronary arteriosclerosis	37.0	9.8	0.68	25.3	26.4	-0.02
Heart disease	64.5	25.9	0.84	51.2	53.7	-0.05
Heart failure	19.6	1.7	0.60	7.8	7.9	0.00
Ischemic heart disease	30.0	7.1	0.62	18.8	19.5	-0.02
Peripheral vascular disease	23.4	8.7	0.41	18.1	18.7	-0.02
Pulmonary embolism	1.2	0.4	0.09	0.7	1.0	-0.04
Venous thrombosis	3.8	1.7	0.13	2.7	2.8	-0.01
Medical history: Neoplasms						
Hematologic neoplasm	1.8	1.0	0.07	1.5	1.7	-0.01
Malignant lymphoma	0.9	0.4	0.06	0.7	0.7	0.00
Malignant neoplasm of anorectum	0.4	0.3	0.02	0.4	0.4	0.00
Malignant neoplastic disease	12.4	7.9	0.15	10.9	11.1	-0.01
Malignant tumor of breast	1.6	1.5	0.01	1.6	1.5	0.00
Malignant tumor of colon	0.9	0.5	0.04	0.7	0.7	0.00
Malignant tumor of lung	0.8	0.4	0.06	0.6	0.7	-0.01
Malignant tumor of urinary bladder	0.6	0.4	0.03	0.5	0.7	-0.03
Primary malignant neoplasm of prostate	2.0	1.2	0.06	1.7	1.9	-0.01
Medication use						
Antibacterials for systemic use	44.5	42.1	0.05	44.0	44.6	-0.01
Antidepressants	17.8	18.5	-0.02	18.3	18.4	0.00
Antiepileptics	9.3	6.7	0.09	8.7	9.1	-0.02
Antiinflammatory and antirheumatic products	18.6	19.0	-0.01	19.6	19.9	-0.01
Antineoplastic agents	2.8	1.8	0.07	2.4	2.6	-0.01
Antipsoriatics	0.5	0.4	0.01	0.4	0.4	0.00
Antithrombotic agents	22.6	6.3	0.48	14.9	15.3	-0.01
Drugs for acid related disorders	18.3	14.7	0.10	17.1	17.4	-0.01
Drugs for obstructive airway diseases	17.1	12.5	0.13	16.1	16.3	-0.01
Drugs used in diabetes	13.1	4.9	0.29	10.6	11.1	-0.02
Immunosuppressants	1.8	1.4	0.03	1.7	1.7	0.00
Lipid modifying agents	37.6	22.4	0.34	32.8	33.7	-0.02
Opioids	20.6	15.0	0.14	18.5	18.8	-0.01
Psycholeptics	21.5	20.2	0.03	21.0	21.1	0.00

Psychostimulants, agents used for ADHD and nootropics	1.8	2.4	-0.04	2.1	2.1	0.00
Optum, Optum ClinFormatics						

Table S1 c. Baseline characteristics for carvedilol and atenolol new-users in the PanTher database before and after propensity score matching

Characteristic	Before matching			After matching		
	Carvedilol, %	Atenolol, %	Std. diff	Carvedilol, %	Atenolol, %	Std. diff
Age group						
15-19	0.1	0.4	-0.05	0.1	0.2	-0.02
20-24	0.4	0.8	-0.05	0.5	0.6	-0.01
25-29	0.8	1.7	-0.08	1.0	0.9	0.00
30-34	1.5	2.8	-0.10	1.7	1.7	0.00
35-39	2.6	4.0	-0.08	2.9	2.8	0.00
40-44	4.2	5.9	-0.08	4.7	4.5	0.01
45-49	6.3	8.4	-0.08	6.8	6.7	0.01
50-54	9.3	11.5	-0.07	9.9	9.5	0.02
55-59	11.7	12.9	-0.04	11.9	11.7	0.01
60-64	12.7	12.5	0.01	12.8	12.5	0.01
65-69	12.7	11.1	0.05	12.5	12.6	0.00
70-74	11.4	9.1	0.08	11.0	11.2	-0.01
75-79	10.6	8.6	0.07	10.0	10.2	-0.01
80-84	11.2	7.9	0.11	10.4	10.8	-0.01
85-89	4.4	2.1	0.13	3.9	4.0	-0.01
Gender: female	47.6	57.0	-0.19	50.9	50.3	0.01
Race						
race = Asian	1.6	1.8	-0.02	1.5	1.5	0.00
race = Black or African American	11.0	6.0	0.18	9.4	9.7	-0.01
race = White	81.0	85.5	-0.12	82.5	82.1	0.01
Ethnicity						
ethnicity = Hispanic or Latino	4.0	3.4	0.03	3.8	3.7	0.00
Medical history: General						
Acute respiratory disease	11.9	11.6	0.01	11.0	10.8	0.01
Attention deficit hyperactivity disorder	0.5	0.9	-0.04	0.7	0.6	0.00
Chronic liver disease	1.4	1.3	0.02	1.3	1.3	0.00
Chronic obstructive lung disease	9.6	4.2	0.22	7.2	7.5	-0.01
Crohn's disease	0.3	0.4	-0.01	0.4	0.4	0.00
Dementia	3.3	1.8	0.09	2.7	2.7	0.00
Depressive disorder	10.5	11.6	-0.03	10.3	10.3	0.00
Diabetes mellitus	24.5	11.6	0.34	19.7	20.3	-0.02
Gastroesophageal reflux disease	15.4	14.2	0.03	14.7	15.0	-0.01
Gastrointestinal hemorrhage	2.2	1.7	0.04	1.8	1.9	0.00
Human immunodeficiency virus infection	0.3	0.2	0.01	0.2	0.2	-0.01
Hyperlipidemia	52.4	43.9	0.17	48.7	49.2	-0.01
Hypertensive disorder	95.6	97.3	-0.09	95.2	94.8	0.02

Lesion of liver	1.0	0.5	0.05	0.8	0.8	0.01
Obesity	10.4	8.8	0.06	9.6	9.7	0.00
Osteoarthritis	13.7	13.3	0.01	13.3	13.5	0.00
Pneumonia	3.9	2.1	0.10	2.7	2.8	-0.01
Psoriasis	0.7	0.8	-0.01	0.8	0.7	0.00
Renal impairment	11.6	3.2	0.32	6.7	6.8	0.00
Rheumatoid arthritis	1.5	1.3	0.02	1.5	1.4	0.00
Schizophrenia	0.5	0.4	0.01	0.5	0.4	0.01
Ulcerative colitis	0.3	0.3	-0.01	0.3	0.3	0.01
Urinary tract infectious disease	6.5	5.3	0.05	5.6	5.7	0.00
Viral hepatitis C	0.8	0.6	0.02	0.7	0.7	0.00
Visual system disorder	9.0	10.2	-0.04	8.5	8.3	0.01
Medical history: Cardiovascular disease						
Atrial fibrillation	10.2	4.3	0.23	7.7	7.9	-0.01
Cerebrovascular disease	3.6	2.0	0.10	2.9	3.1	-0.01
Coronary arteriosclerosis	30.6	9.7	0.54	22.3	23.8	-0.04
Heart disease	52.7	22.2	0.67	40.7	43.0	-0.05
Heart failure	12.1	1.1	0.45	4.1	3.9	0.01
Ischemic heart disease	17.0	3.9	0.44	9.9	10.7	-0.02
Peripheral vascular disease	13.1	6.8	0.21	10.3	10.6	-0.01
Pulmonary embolism	0.9	0.5	0.05	0.7	0.8	-0.01
Venous thrombosis	2.0	1.2	0.06	1.6	1.6	0.00
Medical history: Neoplasms						
Hematologic neoplasm	1.1	0.8	0.03	0.9	0.9	0.00
Malignant lymphoma	0.6	0.4	0.04	0.5	0.5	0.00
Malignant neoplasm of anorectum	0.2	0.2	0.00	0.2	0.2	-0.01
Malignant neoplastic disease	7.8	7.0	0.03	7.2	7.4	-0.01
Malignant tumor of breast	1.3	1.4	-0.01	1.3	1.3	0.00
Malignant tumor of colon	0.5	0.4	0.02	0.5	0.5	0.00
Malignant tumor of lung	0.5	0.3	0.03	0.4	0.4	0.00
Malignant tumor of urinary bladder	0.4	0.3	0.02	0.4	0.4	0.00
Primary malignant neoplasm of prostate	1.1	1.0	0.00	1.0	1.0	-0.01
Medication use						
Agents acting on the renin-angiotensin system	0.0	0.0	0.02	0.0	0.0	0.01
Antibacterials for systemic use	23.7	22.8	0.02	23.0	22.9	0.00
Antidepressants	21.9	23.9	-0.05	22.5	22.7	0.00
Antiepileptics	13.0	10.8	0.07	12.5	12.8	-0.01
Antiinflammatory and antirheumatic products	20.8	24.4	-0.08	22.4	22.5	0.00
Antineoplastic agents	1.5	1.3	0.02	1.5	1.5	0.00
Antipsoriatics	0.5	0.2	0.04	0.3	0.3	0.00
Antithrombotic agents	47.7	29.3	0.39	42.4	43.9	-0.03

Drugs for acid related disorders	31.3	27.3	0.09	30.3	30.8	-0.01
Drugs for obstructive airway diseases	23.9	21.0	0.07	23.2	23.5	-0.01
Drugs used in diabetes	18.0	8.4	0.29	15.0	15.5	-0.02
Immunosuppressants	2.3	1.7	0.04	2.1	2.1	0.00
Lipid modifying agents	42.7	32.5	0.21	39.9	40.9	-0.02
Opioids	25.0	19.7	0.13	22.6	23.0	-0.01
Psycholeptics	26.8	25.9	0.02	25.6	25.8	0.00
Psychostimulants, agents used for ADHD and nootropics	1.9	2.7	-0.05	2.2	2.2	0.00

PanTher, Optum® de-identified Electronic Health Record Dataset

Table S1 d. Baseline characteristics for carvedilol and atenolol new-users in the CCAE database before and after propensity score stratification

Characteristic	Before stratification			After stratification		
	Carvedilol, %	Atenolol, %	Std. diff	Carvedilol, %	Atenolol, %	Std. diff
Age group						
15-19	0.4	0.9	-0.07	0.9	0.8	0.01
20-24	1.1	1.7	-0.05	1.4	1.6	-0.02
25-29	2.3	3.0	-0.04	3.0	2.9	0.00
30-34	4.1	5.3	-0.06	6.6	5.1	0.06
35-39	6.7	8.1	-0.06	8.0	7.9	0.00
40-44	9.6	11.7	-0.07	11.6	11.4	0.00
45-49	15.0	15.7	-0.02	15.0	15.5	-0.02
50-54	18.1	18.0	0.00	17.1	18.0	-0.02
55-59	20.3	17.9	0.06	18.4	18.3	0.00
60-64	20.5	15.9	0.12	16.3	16.6	-0.01
65-69	2.0	1.5	0.03	1.6	1.6	0.00
70-74	0.0	0.0	-0.02	0.0	0.0	0.01
Gender: female	42.5	51.2	-0.18	51.3	50.0	0.02
Medical history: General						
Acute respiratory disease	28.1	24.6	0.08	26.5	25.2	0.03
Attention deficit hyperactivity disorder	1.2	1.1	0.02	1.0	1.1	-0.01
Chronic liver disease	2.1	1.4	0.05	1.2	1.5	-0.02
Chronic obstructive lung disease	5.0	1.8	0.18	2.5	2.2	0.02
Crohn's disease	0.5	0.3	0.03	0.4	0.3	0.00
Dementia	0.3	0.2	0.02	0.3	0.2	0.01
Depressive disorder	9.7	8.6	0.04	9.2	8.8	0.02
Diabetes mellitus	16.2	6.2	0.32	8.4	7.8	0.02
Gastroesophageal reflux disease	12.2	7.9	0.14	8.4	8.6	-0.01
Gastrointestinal hemorrhage	2.7	2.1	0.04	2.4	2.2	0.01
Human immunodeficiency virus infection	0.3	0.2	0.02	0.2	0.2	-0.01
Hyperlipidemia	45.9	29.6	0.34	32.7	32.3	0.01
Hypertensive disorder	100.0	100.0	0.00	100.0	100.0	0.00
Lesion of liver	0.9	0.3	0.07	0.4	0.4	0.01
Obesity	10.2	5.7	0.17	5.9	6.4	-0.02
Osteoarthritis	15.6	11.4	0.12	12.5	12.2	0.01
Pneumonia	3.9	1.6	0.14	2.1	1.8	0.02
Psoriasis	1.1	0.9	0.02	1.1	0.9	0.02
Renal impairment	4.5	0.8	0.23	1.4	1.1	0.03
Rheumatoid arthritis	1.2	0.9	0.03	1.2	1.0	0.02
Schizophrenia	0.1	0.1	0.00	0.2	0.1	0.02
Ulcerative colitis	0.5	0.3	0.02	0.4	0.3	0.01

Urinary tract infectious disease	7.0	6.3	0.02	6.7	6.4	0.01
Viral hepatitis C	0.6	0.5	0.02	0.4	0.5	-0.01
Visual system disorder	16.5	15.0	0.04	15.8	15.4	0.01
Medical history: Cardiovascular disease						
Atrial fibrillation	4.1	1.4	0.16	1.8	1.8	0.00
Cerebrovascular disease	3.8	1.7	0.13	2.1	2.0	0.00
Coronary arteriosclerosis	20.9	4.4	0.51	7.4	6.5	0.04
Heart disease	45.0	16.1	0.66	21.2	20.4	0.02
Heart failure	6.9	0.5	0.34	1.9	1.0	0.08
Ischemic heart disease	18.8	3.8	0.49	6.5	5.6	0.04
Peripheral vascular disease	10.5	4.3	0.24	5.4	5.2	0.01
Pulmonary embolism	0.8	0.3	0.08	0.3	0.4	-0.01
Venous thrombosis	2.4	1.1	0.10	1.3	1.3	0.00
Medical history: Neoplasms						
Hematologic neoplasm	1.4	0.6	0.08	0.7	0.7	0.00
Malignant lymphoma	0.4	0.2	0.03	0.2	0.3	0.00
Malignant neoplasm of anorectum	0.3	0.1	0.03	0.2	0.1	0.01
Malignant neoplastic disease	6.6	4.9	0.07	4.8	5.2	-0.02
Malignant tumor of breast	1.2	1.1	0.02	0.8	1.1	-0.02
Malignant tumor of colon	0.4	0.3	0.03	0.3	0.3	0.00
Malignant tumor of lung	0.4	0.2	0.04	0.2	0.2	-0.01
Malignant tumor of urinary bladder	0.2	0.1	0.00	0.1	0.1	-0.03
Primary malignant neoplasm of prostate	0.6	0.5	0.01	0.5	0.6	-0.01
Medication use						
Antibacterials for systemic use	51.1	48.9	0.04	50.4	49.4	0.02
Antidepressants	21.5	21.3	0.00	21.4	21.4	0.00
Antiepileptics	10.1	7.4	0.09	7.9	7.9	0.00
Antiinflammatory and antirheumatic products	25.5	24.5	0.02	26.1	24.7	0.03
Antineoplastic agents	2.2	1.6	0.05	1.9	1.7	0.01
Antipsoriatics	0.5	0.4	0.01	0.5	0.4	0.01
Antithrombotic agents	18.2	4.5	0.44	7.1	6.1	0.04
Drugs for acid related disorders	20.0	16.7	0.09	17.1	17.3	0.00
Drugs for obstructive airway diseases	18.9	16.1	0.07	16.7	16.6	0.00
Drugs used in diabetes	10.6	3.7	0.27	5.4	4.7	0.03
Immunosuppressants	2.2	1.5	0.05	1.9	1.6	0.02
Lipid modifying agents	33.7	18.7	0.34	20.8	20.9	0.00
Opioids	23.9	16.6	0.18	19.2	17.7	0.04
Psycholeptics	27.2	23.9	0.08	25.8	24.5	0.03
Psychostimulants, agents used for ADHD and nootropics	3.6	3.5	0.00	3.8	3.6	0.01

CCAE, Truven MarketScan Commercial Claims and Encounters

Table S1 e. Baseline characteristics for carvedilol and atenolol new-users in the Optum database before and after propensity score stratification

Characteristic	Before stratification			After stratification		
	Carvedilol, %	Atenolol, %	Std. diff	Carvedilol, %	Atenolol, %	Std. diff
Age group						
15-19	0.2	0.5	-0.05	0.5	0.4	0.00
20-24	0.4	0.9	-0.07	0.7	0.9	-0.02
25-29	1.2	2.3	-0.09	2.4	2.1	0.02
30-34	2.0	4.1	-0.12	3.2	3.7	-0.03
35-39	3.5	6.5	-0.14	5.7	6.1	-0.02
40-44	5.7	9.2	-0.14	9.1	8.6	0.02
45-49	8.0	12.2	-0.14	13.3	11.5	0.06
50-54	10.6	13.4	-0.08	13.1	12.9	0.00
55-59	11.4	13.0	-0.05	13.4	12.6	0.02
60-64	12.0	10.5	0.05	10.7	10.8	0.00
65-69	12.6	8.6	0.13	8.8	9.3	-0.02
70-74	11.5	7.6	0.13	7.5	8.2	-0.03
75-79	9.5	6.3	0.12	6.3	6.9	-0.02
80-84	7.5	3.6	0.17	3.8	4.4	-0.03
85-89	4.0	1.2	0.18	1.5	1.6	-0.01
Gender: female	40.0	51.6	-0.24	50.8	49.8	0.02
Medical history: General						
Acute respiratory disease	28.6	24.7	0.09	25.6	25.2	0.01
Attention deficit hyperactivity disorder	0.9	0.9	0.00	0.9	0.9	0.00
Chronic liver disease	2.2	1.5	0.05	1.5	1.7	-0.01
Chronic obstructive lung disease	13.6	4.3	0.33	6.1	5.6	0.02
Crohn's disease	0.5	0.4	0.01	0.3	0.4	-0.02
Dementia	3.3	1.2	0.15	1.2	1.5	-0.02
Depressive disorder	12.1	10.6	0.05	10.2	10.9	-0.02
Diabetes mellitus	26.5	10.2	0.43	13.2	12.9	0.01
Gastroesophageal reflux disease	17.5	11.7	0.16	12.6	12.8	-0.01
Gastrointestinal hemorrhage	4.1	3.0	0.06	2.9	3.2	-0.01
Human immunodeficiency virus infection	0.3	0.2	0.02	0.2	0.3	-0.01
Hyperlipidemia	62.6	44.3	0.37	49.5	47.6	0.04
Hypertensive disorder	100.0	100.0	0.00	100.0	100.0	0.00
Lesion of liver	1.4	0.5	0.09	0.7	0.6	0.01
Obesity	10.9	7.0	0.14	7.5	7.7	-0.01
Osteoarthritis	24.4	17.1	0.18	18.9	18.5	0.01
Pneumonia	7.3	2.4	0.23	3.7	3.1	0.04
Psoriasis	1.1	1.1	0.00	0.9	1.1	-0.01
Renal impairment	13.3	2.2	0.42	4.2	3.6	0.03

Rheumatoid arthritis	1.8	1.4	0.03	1.2	1.4	-0.02
Schizophrenia	0.3	0.2	0.02	0.2	0.2	0.00
Ulcerative colitis	0.5	0.4	0.02	0.5	0.4	0.01
Urinary tract infectious disease	12.2	8.4	0.12	10.1	9.0	0.04
Viral hepatitis C	0.8	0.5	0.03	0.5	0.5	0.00
Visual system disorder	31.3	26.2	0.11	25.7	27.2	-0.03
Medical history: Cardiovascular disease						
Atrial fibrillation	12.4	3.6	0.33	4.7	4.9	-0.01
Cerebrovascular disease	8.3	3.5	0.20	4.0	4.3	-0.02
Coronary arteriosclerosis	37.0	9.8	0.68	13.7	13.9	-0.01
Heart disease	64.5	25.9	0.84	31.0	32.3	-0.03
Heart failure	19.6	1.7	0.60	5.3	3.6	0.08
Ischemic heart disease	30.0	7.1	0.62	11.1	10.3	0.03
Peripheral vascular disease	23.4	8.7	0.41	10.7	11.1	-0.01
Pulmonary embolism	1.2	0.4	0.09	0.6	0.5	0.01
Venous thrombosis	3.8	1.7	0.13	2.0	2.0	0.00
Medical history: Neoplasms						
Hematologic neoplasm	1.8	1.0	0.07	1.1	1.2	-0.01
Malignant lymphoma	0.9	0.4	0.06	0.5	0.4	0.00
Malignant neoplasm of anorectum	0.4	0.3	0.02	0.2	0.3	-0.01
Malignant neoplastic disease	12.4	7.9	0.15	8.5	8.6	0.00
Malignant tumor of breast	1.6	1.5	0.01	1.6	1.5	0.00
Malignant tumor of colon	0.9	0.5	0.04	0.5	0.6	-0.01
Malignant tumor of lung	0.8	0.4	0.06	0.4	0.5	-0.01
Malignant tumor of urinary bladder	0.6	0.4	0.03	0.3	0.4	-0.02
Primary malignant neoplasm of prostate	2.0	1.2	0.06	1.3	1.4	-0.01
Medication use						
Antibacterials for systemic use	44.5	42.1	0.05	42.3	42.7	-0.01
Antidepressants	17.8	18.5	-0.02	18.6	18.4	0.00
Antiepileptics	9.3	6.7	0.09	7.5	7.2	0.01
Antiinflammatory and antirheumatic products	18.6	19.0	-0.01	19.3	19.2	0.00
Antineoplastic agents	2.8	1.8	0.07	1.7	2.0	-0.02
Antipsoriatics	0.5	0.4	0.01	0.5	0.4	0.01
Antithrombotic agents	22.6	6.3	0.48	8.5	8.6	0.00
Drugs for acid related disorders	18.3	14.7	0.10	14.3	15.4	-0.03
Drugs for obstructive airway diseases	17.1	12.5	0.13	14.2	13.3	0.03
Drugs used in diabetes	13.1	4.9	0.29	6.7	6.3	0.01
Immunosuppressants	1.8	1.4	0.03	1.3	1.4	-0.02
Lipid modifying agents	37.6	22.4	0.34	24.7	25.0	0.00
Opioids	20.6	15.0	0.14	16.0	16.0	0.00
Psycholeptics	21.5	20.2	0.03	21.4	20.4	0.02

Psychostimulants, agents used for ADHD and nootropics	1.8	2.4	-0.04	2.5	2.3	0.01
Optum, Optum ClinFormatics						

Table S1 f. Baseline characteristics for carvedilol and atenolol new-users in the PanTher database before and after propensity score stratification

Characteristic	Before stratification			After stratification		
	Carvedilol, %	Atenolol, %	Std. diff	Carvedilol, %	Atenolol, %	Std. diff
Age group						
15-19	0.1	0.4	-0.05	0.4	0.3	0.01
20-24	0.4	0.8	-0.05	0.8	0.7	0.01
25-29	0.8	1.7	-0.08	1.5	1.5	0.00
30-34	1.5	2.8	-0.10	2.8	2.5	0.02
35-39	2.6	4.0	-0.08	3.8	3.7	0.01
40-44	4.2	5.9	-0.08	5.6	5.3	0.01
45-49	6.3	8.4	-0.08	7.9	7.9	0.00
50-54	9.3	11.5	-0.07	11.0	10.9	0.00
55-59	11.7	12.9	-0.04	12.2	12.5	-0.01
60-64	12.7	12.5	0.01	12.3	12.5	-0.01
65-69	12.7	11.1	0.05	11.8	11.6	0.01
70-74	11.4	9.1	0.08	9.9	9.7	0.00
75-79	10.6	8.6	0.07	8.9	9.2	-0.01
80-84	11.2	7.9	0.11	8.4	8.9	-0.02
85-89	4.4	2.1	0.13	2.7	2.8	0.00
Gender: female	47.6	57.0	-0.19	56.5	54.8	0.04
Race						
race = Asian	1.6	1.8	-0.02	1.7	1.7	0.00
race = Black or African American	11.0	6.0	0.18	6.9	7.0	-0.01
race = White	81.0	85.5	-0.12	85.1	84.6	0.02
Ethnicity						
ethnicity = Hispanic or Latino	4.0	3.4	0.03	3.4	3.5	-0.01
Medical history: General						
Acute respiratory disease	11.9	11.6	0.01	11.8	11.5	0.01
Attention deficit hyperactivity disorder	0.5	0.9	-0.04	0.9	0.8	0.01
Chronic liver disease	1.4	1.3	0.02	1.4	1.3	0.01
Chronic obstructive lung disease	9.6	4.2	0.22	5.7	5.5	0.01
Crohn's disease	0.3	0.4	-0.01	0.4	0.4	0.00
Dementia	3.3	1.8	0.09	2.1	2.1	0.00
Depressive disorder	10.5	11.6	-0.03	11.8	11.3	0.02
Diabetes mellitus	24.5	11.6	0.34	14.8	14.7	0.00
Gastroesophageal reflux disease	15.4	14.2	0.03	15.0	14.6	0.01
Gastrointestinal hemorrhage	2.2	1.7	0.04	2.0	1.8	0.02
Human immunodeficiency virus infection	0.3	0.2	0.01	0.2	0.2	-0.01
Hyperlipidemia	52.4	43.9	0.17	45.4	46.1	-0.01
Hypertensive disorder	95.6	97.3	-0.09	97.4	96.8	0.04

Lesion of liver	1.0	0.5	0.05	0.7	0.6	0.00
Obesity	10.4	8.8	0.06	9.8	9.1	0.02
Osteoarthritis	13.7	13.3	0.01	13.8	13.5	0.01
Pneumonia	3.9	2.1	0.10	2.6	2.5	0.01
Psoriasis	0.7	0.8	-0.01	1.0	0.8	0.02
Renal impairment	11.6	3.2	0.32	5.4	4.8	0.03
Rheumatoid arthritis	1.5	1.3	0.02	1.3	1.3	0.00
Schizophrenia	0.5	0.4	0.01	0.4	0.4	0.00
Ulcerative colitis	0.3	0.3	-0.01	0.3	0.3	0.00
Urinary tract infectious disease	6.5	5.3	0.05	5.6	5.5	0.01
Viral hepatitis C	0.8	0.6	0.02	0.7	0.7	0.00
Visual system disorder	9.0	10.2	-0.04	9.5	9.8	-0.01
Medical history: Cardiovascular disease						
Atrial fibrillation	10.2	4.3	0.23	5.7	5.6	0.00
Cerebrovascular disease	3.6	2.0	0.10	2.4	2.4	0.00
Coronary arteriosclerosis	30.6	9.7	0.54	14.7	15.0	-0.01
Heart disease	52.7	22.2	0.67	29.4	29.7	0.00
Heart failure	12.1	1.1	0.45	4.1	2.7	0.08
Ischemic heart disease	17.0	3.9	0.44	7.3	6.8	0.02
Peripheral vascular disease	13.1	6.8	0.21	8.5	8.3	0.01
Pulmonary embolism	0.9	0.5	0.05	0.6	0.6	0.00
Venous thrombosis	2.0	1.2	0.06	1.3	1.3	0.00
Medical history: Neoplasms						
Hematologic neoplasm	1.1	0.8	0.03	0.9	0.8	0.00
Malignant lymphoma	0.6	0.4	0.04	0.5	0.4	0.01
Malignant neoplasm of anorectum	0.2	0.2	0.00	0.2	0.2	0.00
Malignant neoplastic disease	7.8	7.0	0.03	7.5	7.2	0.01
Malignant tumor of breast	1.3	1.4	-0.01	1.5	1.4	0.01
Malignant tumor of colon	0.5	0.4	0.02	0.4	0.4	0.00
Malignant tumor of lung	0.5	0.3	0.03	0.4	0.4	0.00
Malignant tumor of urinary bladder	0.4	0.3	0.02	0.4	0.3	0.01
Primary malignant neoplasm of prostate	1.1	1.0	0.00	1.1	1.0	0.00
Medication use						
Agents acting on the renin-angiotensin system	0.0	0.0	0.02	0.0	0.0	0.01
Antibacterials for systemic use	23.7	22.8	0.02	23.3	23.0	0.01
Antidepressants	21.9	23.9	-0.05	24.6	23.7	0.02
Antiepileptics	13.0	10.8	0.07	11.8	11.5	0.01
Antiinflammatory and antirheumatic products	20.8	24.4	-0.08	24.5	23.8	0.02
Antineoplastic agents	1.5	1.3	0.02	1.5	1.4	0.01
Antipsoriatics	0.5	0.2	0.04	0.3	0.3	0.00
Antithrombotic agents	47.7	29.3	0.39	34.0	34.4	-0.01

Drugs for acid related disorders	31.3	27.3	0.09	28.8	28.7	0.00
Drugs for obstructive airway diseases	23.9	21.0	0.07	22.1	22.1	0.00
Drugs used in diabetes	18.0	8.4	0.29	11.1	11.0	0.00
Immunosuppressants	2.3	1.7	0.04	1.8	1.9	0.00
Lipid modifying agents	42.7	32.5	0.21	34.6	35.4	-0.02
Opioids	25.0	19.7	0.13	21.5	21.0	0.01
Psycholeptics	26.8	25.9	0.02	27.6	26.1	0.03
Psychostimulants, agents used for ADHD and nootropics	1.9	2.7	-0.05	2.8	2.5	0.02

PanTher, Optum® de-identified Electronic Health Record Dataset

Table S2. Baseline characteristics between nebivolol and atenolol

Table S2 a. Baseline characteristics for nebivolol and atenolol new-users in the CCAE database before and after propensity score matching

Characteristic	Before matching			After matching		
	Nebivolol, %	Atenolol, %	Std. diff	Nebivolol, %	Atenolol, %	Std. diff
Age group						
15-19	0.4	1.1	-0.09	0.4	0.5	0.00
20-24	1.6	2.1	-0.04	1.7	1.7	0.00
25-29	3.3	3.6	-0.02	3.4	3.3	0.01
30-34	6.1	6.1	0.00	6.2	6.1	0.00
35-39	9.9	8.8	0.04	9.8	9.8	0.00
40-44	13.8	12.0	0.05	13.2	13.4	0.00
45-49	16.8	15.2	0.04	16.4	16.2	0.00
50-54	18.5	17.3	0.03	18.2	18.4	-0.01
55-59	16.2	16.9	-0.02	16.4	16.4	0.00
60-64	12.4	15.1	-0.08	13.2	12.9	0.01
65-69	1.0	1.4	-0.04	1.0	1.1	-0.01
Gender: female	45.7	52.6	-0.14	47.7	47.0	0.01
Medical history: General						
Acute respiratory disease	29.2	27.1	0.05	28.1	28.5	-0.01
Attention deficit hyperactivity disorder	2.0	1.7	0.02	1.9	1.9	-0.01
Chronic liver disease	1.7	1.7	0.00	1.7	1.6	0.00
Chronic obstructive lung disease	1.9	1.9	0.00	1.8	1.9	0.00
Crohn's disease	0.4	0.4	0.00	0.4	0.3	0.00
Dementia	0.1	0.2	-0.02	0.1	0.1	0.00
Depressive disorder	9.2	10.6	-0.05	9.2	9.4	0.00
Diabetes mellitus	6.3	6.9	-0.02	6.4	6.4	0.00
Gastroesophageal reflux disease	10.5	9.9	0.02	10.0	10.1	0.00
Gastrointestinal hemorrhage	1.8	1.9	-0.01	1.7	1.8	-0.01
Human immunodeficiency virus infection	0.2	0.2	0.00	0.2	0.3	-0.01
Hyperlipidemia	37.5	32.9	0.10	35.4	36.1	-0.02
Hypertensive disorder	100.0	100.0	0.00	100.0	100.0	0.00
Lesion of liver	0.3	0.4	-0.01	0.3	0.3	0.00
Obesity	8.2	8.3	0.00	8.1	8.3	-0.01
Osteoarthritis	13.4	13.3	0.00	13.1	13.4	-0.01
Pneumonia	1.5	1.6	-0.01	1.4	1.5	0.00
Psoriasis	1.0	1.0	0.00	1.0	1.0	0.00
Renal impairment	1.0	1.0	0.00	1.0	0.9	0.01
Rheumatoid arthritis	1.0	1.0	-0.01	1.0	1.0	0.00
Schizophrenia	0.0	0.1	-0.03	0.0	0.1	-0.02
Ulcerative colitis	0.3	0.4	-0.01	0.3	0.3	0.00

Urinary tract infectious disease	6.4	6.8	-0.02	6.4	6.3	0.00
Viral hepatitis C	0.3	0.5	-0.02	0.4	0.4	0.00
Visual system disorder	15.8	16.0	0.00	15.4	15.7	-0.01
Medical history: Cardiovascular disease						
Atrial fibrillation	1.1	1.7	-0.04	1.2	1.3	-0.01
Cerebrovascular disease	1.7	1.8	-0.01	1.7	1.6	0.00
Coronary arteriosclerosis	4.3	3.9	0.02	4.0	4.1	-0.01
Heart disease	19.1	16.7	0.06	16.8	17.4	-0.02
Heart failure	0.8	0.6	0.02	0.6	0.6	0.00
Ischemic heart disease	3.5	3.3	0.01	3.2	3.3	-0.01
Peripheral vascular disease	5.6	4.8	0.04	5.1	5.1	0.00
Pulmonary embolism	0.3	0.3	-0.01	0.3	0.3	0.00
Venous thrombosis	1.1	1.2	0.00	1.1	1.1	0.00
Medical history: Neoplasms						
Hematologic neoplasm	0.7	0.7	0.00	0.7	0.6	0.01
Malignant lymphoma	0.3	0.3	0.00	0.3	0.2	0.00
Malignant neoplasm of anorectum	0.1	0.1	0.00	0.1	0.1	0.01
Malignant neoplastic disease	4.8	4.8	0.00	4.7	4.8	-0.01
Malignant tumor of breast	1.0	1.0	0.00	1.0	1.0	0.00
Malignant tumor of colon	0.2	0.2	-0.01	0.2	0.2	0.00
Malignant tumor of lung	0.1	0.2	-0.01	0.1	0.2	-0.01
Malignant tumor of urinary bladder	0.1	0.1	0.00	0.1	0.1	0.00
Primary malignant neoplasm of prostate	0.5	0.5	0.01	0.5	0.6	-0.01
Medication use						
Antibacterials for systemic use	54.6	50.9	0.07	52.9	53.4	-0.01
Antidepressants	22.5	23.4	-0.02	22.2	22.2	0.00
Antiepileptics	9.0	9.0	0.00	8.9	8.8	0.00
Antiinflammatory and antirheumatic products	26.2	26.0	0.00	25.5	25.7	0.00
Antineoplastic agents	1.7	1.7	0.00	1.7	1.7	0.00
Antipsoriatics	0.4	0.4	0.00	0.4	0.4	0.00
Antithrombotic agents	4.3	4.7	-0.02	4.2	4.3	-0.01
Drugs for acid related disorders	16.7	16.5	0.00	15.9	16.1	-0.01
Drugs for obstructive airway diseases	19.8	18.6	0.03	18.7	19.0	-0.01
Drugs used in diabetes	3.6	4.0	-0.02	3.7	3.7	0.00
Immunosuppressants	1.9	1.8	0.01	1.8	1.8	0.00
Lipid modifying agents	20.8	18.7	0.05	19.1	19.4	-0.01
Opioids	18.8	19.2	-0.01	18.5	18.6	0.00
Psycholeptics	26.7	27.1	-0.01	26.2	26.3	0.00
Psychostimulants, agents used for ADHD and nootropics	5.4	4.6	0.04	5.0	5.1	0.00

CCAE, Truven MarketScan Commercial Claims and Encounters

Table S2 b. Baseline characteristics for nebivolol and atenolol new-users in the Optum database before and after propensity score matching

Characteristic	Before matching			After matching		
	Nebivolol, %	Atenolol, %	Std. diff	Nebivolol, %	Atenolol, %	Std. diff
Age group						
15-19	0.3	0.6	-0.05	0.3	0.5	-0.02
20-24	1.3	1.1	0.02	1.3	1.2	0.01
25-29	3.1	2.6	0.03	3.3	3.2	0.00
30-34	5.8	4.0	0.08	5.8	5.9	0.00
35-39	9.0	6.1	0.11	8.6	8.7	0.00
40-44	12.4	7.6	0.16	11.2	11.7	-0.01
45-49	14.2	10.3	0.12	13.3	13.7	-0.01
50-54	15.6	11.4	0.12	14.9	15.1	0.00
55-59	13.0	11.8	0.04	13.0	13.2	0.00
60-64	9.4	10.0	-0.02	9.9	9.9	0.00
65-69	6.6	11.6	-0.17	7.4	6.9	0.02
70-74	4.3	9.1	-0.19	5.0	4.6	0.02
75-79	2.4	6.5	-0.20	2.8	2.6	0.02
80-84	1.8	5.3	-0.18	2.2	2.0	0.01
85-89	0.7	1.9	-0.11	0.8	0.9	0.00
Gender: female	44.1	53.6	-0.19	46.5	45.9	0.01
Medical history: General						
Acute respiratory disease	29.5	25.9	0.08	28.0	29.1	-0.02
Attention deficit hyperactivity disorder	2.4	1.3	0.08	2.1	2.2	-0.01
Chronic liver disease	2.1	1.7	0.03	1.9	1.9	0.00
Chronic obstructive lung disease	4.1	5.3	-0.05	4.2	4.1	0.01
Crohn's disease	0.4	0.4	0.00	0.5	0.4	0.01
Dementia	0.5	1.5	-0.10	0.6	0.6	0.00
Depressive disorder	11.2	12.5	-0.04	11.0	11.2	-0.01
Diabetes mellitus	9.3	11.6	-0.07	9.3	9.2	0.00
Gastroesophageal reflux disease	13.5	14.2	-0.02	13.0	13.4	-0.01
Gastrointestinal hemorrhage	2.4	2.7	-0.02	2.2	2.3	0.00
Human immunodeficiency virus infection	0.4	0.3	0.01	0.3	0.4	-0.02
Hyperlipidemia	47.2	47.4	0.00	45.1	45.1	0.00
Hypertensive disorder	100.0	100.0	0.00	100.0	100.0	0.00
Lesion of liver	0.4	0.6	-0.03	0.4	0.4	0.01
Obesity	10.5	9.0	0.05	9.9	10.4	-0.02
Osteoarthritis	17.6	20.0	-0.06	17.7	17.8	0.00
Pneumonia	2.0	2.6	-0.04	2.0	2.0	0.00
Psoriasis	1.4	1.2	0.02	1.4	1.3	0.01
Renal impairment	2.2	3.7	-0.09	2.3	2.2	0.01

Rheumatoid arthritis	1.4	1.6	-0.02	1.3	1.4	-0.01
Schizophrenia	0.1	0.3	-0.05	0.1	0.2	-0.04
Ulcerative colitis	0.4	0.4	-0.01	0.4	0.4	-0.01
Urinary tract infectious disease	7.6	9.4	-0.06	7.8	7.7	0.00
Viral hepatitis C	0.5	0.5	0.00	0.5	0.5	0.00
Visual system disorder	21.0	28.1	-0.17	21.7	21.3	0.01
Medical history: Cardiovascular disease						
Atrial fibrillation	2.3	4.5	-0.12	2.5	2.5	0.00
Cerebrovascular disease	2.5	3.7	-0.07	2.5	2.5	0.00
Coronary arteriosclerosis	6.8	9.3	-0.09	6.7	6.7	0.00
Heart disease	26.0	26.6	-0.02	23.9	24.1	0.00
Heart failure	1.6	1.8	-0.02	1.5	1.3	0.02
Ischemic heart disease	5.4	6.2	-0.03	4.9	5.2	-0.01
Peripheral vascular disease	8.7	10.6	-0.06	8.5	8.2	0.01
Pulmonary embolism	0.4	0.6	-0.02	0.4	0.4	0.00
Venous thrombosis	1.5	1.8	-0.02	1.5	1.4	0.01
Medical history: Neoplasms						
Hematologic neoplasm	0.9	1.2	-0.02	0.9	0.8	0.01
Malignant lymphoma	0.3	0.4	-0.02	0.3	0.3	0.00
Malignant neoplasm of anorectum	0.2	0.2	-0.01	0.2	0.1	0.01
Malignant neoplastic disease	6.5	8.9	-0.09	6.7	6.5	0.01
Malignant tumor of breast	1.2	1.7	-0.04	1.2	1.1	0.01
Malignant tumor of colon	0.2	0.5	-0.04	0.3	0.3	-0.01
Malignant tumor of lung	0.2	0.5	-0.04	0.2	0.3	-0.01
Malignant tumor of urinary bladder	0.2	0.4	-0.04	0.2	0.2	-0.01
Primary malignant neoplasm of prostate	0.7	1.3	-0.06	0.8	0.8	-0.01
Medication use						
Antibacterials for systemic use	50.5	44.9	0.11	48.7	50.0	-0.03
Antidepressants	21.4	21.1	0.01	21.0	21.3	-0.01
Antiepileptics	8.9	9.0	0.00	8.8	9.1	-0.01
Antiinflammatory and antirheumatic products	23.9	21.0	0.07	23.4	23.9	-0.01
Antineoplastic agents	1.9	2.3	-0.02	1.9	1.8	0.00
Antipsoriatics	0.6	0.4	0.04	0.6	0.5	0.02
Antithrombotic agents	4.9	7.0	-0.09	5.0	4.9	0.01
Drugs for acid related disorders	14.8	15.0	-0.01	14.6	14.7	0.00
Drugs for obstructive airway diseases	18.9	15.6	0.09	17.8	18.7	-0.02
Drugs used in diabetes	4.5	5.6	-0.05	4.4	4.4	0.00
Immunosuppressants	1.9	1.7	0.01	1.9	1.7	0.01
Lipid modifying agents	23.1	24.9	-0.04	21.9	21.8	0.00
Opioids	16.0	16.9	-0.02	15.9	16.2	-0.01
Psycholeptics	24.1	22.6	0.03	23.1	23.9	-0.02

Psychostimulants, agents used for ADHD and nootropics	5.0	3.2	0.09	4.6	4.7	0.00
Optum, Optum ClinFormatics						

Table S2 c. Baseline characteristics for nebivolol and atenolol new-users in the PanTher database before and after propensity score matching

Characteristic	Before matching			After matching		
	Nebivolol, %	Atenolol, %	Std. diff	Nebivolol, %	Atenolol, %	Std. diff
Age group						
15-19	0.2	0.4	-0.03	0.2	0.3	-0.01
20-24	0.9	0.9	0.01	0.9	1.0	0.00
25-29	2.3	1.8	0.04	2.3	2.3	0.00
30-34	4.3	2.9	0.08	4.2	4.3	0.00
35-39	6.8	4.1	0.12	6.5	6.7	-0.01
40-44	9.4	5.9	0.13	9.1	9.3	-0.01
45-49	11.7	8.4	0.11	11.4	11.6	-0.01
50-54	13.9	11.5	0.07	13.8	13.8	0.00
55-59	14.3	13.0	0.04	14.4	14.3	0.00
60-64	12.2	12.6	-0.01	12.4	12.2	0.00
65-69	8.7	11.2	-0.08	8.9	8.8	0.00
70-74	6.1	9.0	-0.11	6.3	6.1	0.01
75-79	4.2	7.8	-0.15	4.3	4.1	0.01
80-84	3.8	8.3	-0.19	4.0	3.8	0.01
85-89	1.1	2.3	-0.09	1.1	1.1	0.00
Gender: female	52.3	57.0	-0.10	52.8	52.4	0.01
Race						
race = Asian	1.7	1.8	-0.01	1.7	1.8	-0.01
race = Black or African American	8.1	6.0	0.08	8.0	8.2	-0.01
race = White	84.2	85.5	-0.04	84.2	84.0	0.01
Ethnicity						
ethnicity = Hispanic or Latino	3.1	3.4	-0.02	3.2	3.1	0.00
Medical history: General						
Acute respiratory disease	13.4	11.8	0.05	12.7	12.9	0.00
Attention deficit hyperactivity disorder	1.6	1.0	0.06	1.4	1.4	0.00
Chronic liver disease	1.4	1.3	0.01	1.4	1.4	0.00
Chronic obstructive lung disease	3.7	4.3	-0.03	3.7	3.7	0.00
Crohn's disease	0.4	0.4	-0.01	0.4	0.4	-0.01
Dementia	0.8	1.9	-0.09	0.9	0.8	0.00
Depressive disorder	10.1	11.8	-0.05	9.8	9.8	0.00
Diabetes mellitus	8.6	11.5	-0.10	8.7	8.6	0.00
Gastroesophageal reflux disease	13.7	14.6	-0.02	13.5	13.7	-0.01
Gastrointestinal hemorrhage	1.2	1.7	-0.05	1.2	1.3	-0.01
Human immunodeficiency virus infection	0.2	0.2	-0.01	0.2	0.2	0.00
Hyperlipidemia	37.5	43.7	-0.13	37.4	36.8	0.01
Hypertensive disorder	97.3	97.3	0.00	97.2	97.0	0.01

Lesion of liver	0.4	0.5	-0.03	0.4	0.4	0.00
Obesity	9.8	9.0	0.03	9.6	10.0	-0.01
Osteoarthritis	11.2	13.5	-0.07	11.3	10.9	0.01
Pneumonia	1.7	2.2	-0.04	1.6	1.6	0.01
Psoriasis	0.7	0.9	-0.02	0.7	0.7	0.00
Renal impairment	2.3	3.2	-0.06	2.3	2.3	0.00
Rheumatoid arthritis	1.1	1.3	-0.02	1.1	1.1	0.00
Schizophrenia	0.1	0.5	-0.06	0.1	0.1	0.00
Ulcerative colitis	0.3	0.3	-0.01	0.3	0.3	0.00
Urinary tract infectious disease	3.7	5.3	-0.08	3.7	3.6	0.00
Viral hepatitis C	0.5	0.7	-0.02	0.5	0.5	0.00
Visual system disorder	6.9	10.3	-0.12	6.8	6.6	0.01
Medical history: Cardiovascular disease						
Atrial fibrillation	3.0	4.3	-0.07	3.1	3.1	0.00
Cerebrovascular disease	1.6	2.0	-0.03	1.6	1.5	0.01
Coronary arteriosclerosis	7.5	9.7	-0.08	7.5	7.6	0.00
Heart disease	19.9	22.3	-0.06	19.8	19.9	0.00
Heart failure	1.1	1.1	0.00	1.1	1.1	0.00
Ischemic heart disease	3.4	3.9	-0.03	3.4	3.5	-0.01
Peripheral vascular disease	5.9	6.8	-0.04	5.9	5.7	0.01
Pulmonary embolism	0.4	0.5	-0.02	0.4	0.3	0.00
Venous thrombosis	0.9	1.2	-0.03	0.9	0.9	0.00
Medical history: Neoplasms						
Hematologic neoplasm	0.6	0.8	-0.02	0.5	0.6	-0.01
Malignant lymphoma	0.3	0.4	0.00	0.3	0.3	0.01
Malignant neoplasm of anorectum	0.1	0.2	-0.02	0.1	0.1	0.00
Malignant neoplastic disease	5.2	7.0	-0.08	5.3	5.2	0.01
Malignant tumor of breast	1.0	1.5	-0.04	1.0	1.1	0.00
Malignant tumor of colon	0.3	0.4	-0.02	0.3	0.3	0.01
Malignant tumor of lung	0.2	0.3	-0.02	0.2	0.2	0.00
Malignant tumor of urinary bladder	0.2	0.3	-0.03	0.2	0.2	0.00
Primary malignant neoplasm of prostate	0.7	1.0	-0.04	0.7	0.6	0.01
Medication use						
Agents acting on the renin-angiotensin system	0.0	0.0	0.00	0.0	0.0	0.00
Antibacterials for systemic use	25.1	23.0	0.05	24.1	24.2	0.00
Antidepressants	23.5	24.2	-0.02	22.8	23.2	-0.01
Antiepileptics	10.3	11.0	-0.02	10.2	10.3	0.00
Antiinflammatory and antirheumatic products	25.4	25.0	0.01	25.0	25.1	0.00
Antineoplastic agents	1.2	1.3	-0.01	1.2	1.2	0.00
Antipsoriatics	0.2	0.2	0.00	0.2	0.2	-0.01
Antithrombotic agents	24.3	29.9	-0.13	24.6	24.3	0.01

Drugs for acid related disorders	25.6	27.6	-0.05	25.1	25.5	-0.01
Drugs for obstructive airway diseases	21.8	21.4	0.01	21.2	21.5	-0.01
Drugs used in diabetes	6.7	8.5	-0.07	6.7	6.6	0.00
Immunosuppressants	1.8	1.8	0.00	1.8	1.7	0.00
Lipid modifying agents	26.2	32.6	-0.14	26.1	25.5	0.01
Opioids	18.5	20.0	-0.04	18.4	18.4	0.00
Psycholeptics	25.9	26.2	-0.01	25.3	25.6	-0.01
Psychostimulants, agents used for ADHD and nootropics	4.3	2.8	0.08	3.9	4.1	-0.01

PanTher, Optum® de-identified Electronic Health Record Dataset

Table S2 d. Baseline characteristics for nebivolol and atenolol new-users in the CCAE database before and after propensity score stratification

Characteristic	Before stratification			After stratification		
	Nebivolol, %	Atenolol, %	Std. diff	Nebivolol, %	Atenolol, %	Std. diff
Age group						
15-19	0.4	1.1	-0.09	0.9	0.9	0.00
20-24	1.6	2.1	-0.04	1.8	1.9	-0.01
25-29	3.3	3.6	-0.02	3.4	3.5	0.00
30-34	6.1	6.1	0.00	5.9	6.0	0.00
35-39	9.9	8.8	0.04	9.1	9.2	0.00
40-44	13.8	12.0	0.05	12.5	12.7	-0.01
45-49	16.8	15.2	0.04	15.5	15.7	-0.01
50-54	18.5	17.3	0.03	17.9	17.8	0.00
55-59	16.2	16.9	-0.02	16.9	16.7	0.01
60-64	12.4	15.1	-0.08	14.8	14.2	0.02
65-69	1.0	1.4	-0.04	1.3	1.3	0.00
Gender: female	45.7	52.6	-0.14	50.9	50.1	0.02
Medical history: General						
Acute respiratory disease	29.2	27.1	0.05	28.6	28.1	0.01
Attention deficit hyperactivity disorder	2.0	1.7	0.02	1.9	1.8	0.01
Chronic liver disease	1.7	1.7	0.00	1.8	1.7	0.01
Chronic obstructive lung disease	1.9	1.9	0.00	2.2	1.9	0.02
Crohn's disease	0.4	0.4	0.00	0.4	0.4	0.01
Dementia	0.1	0.2	-0.02	0.1	0.2	-0.01
Depressive disorder	9.2	10.6	-0.05	10.7	10.1	0.02
Diabetes mellitus	6.3	6.9	-0.02	7.2	6.7	0.02
Gastroesophageal reflux disease	10.5	9.9	0.02	10.7	10.2	0.02
Gastrointestinal hemorrhage	1.8	1.9	-0.01	1.9	1.9	0.00
Human immunodeficiency virus infection	0.2	0.2	0.00	0.2	0.2	-0.01
Hyperlipidemia	37.5	32.9	0.10	35.4	34.8	0.01
Hypertensive disorder	100.0	100.0	0.00	100.0	100.0	0.00
Lesion of liver	0.3	0.4	-0.01	0.3	0.3	0.00
Obesity	8.2	8.3	0.00	8.5	8.4	0.00
Osteoarthritis	13.4	13.3	0.00	14.0	13.5	0.02
Pneumonia	1.5	1.6	-0.01	1.6	1.6	0.00
Psoriasis	1.0	1.0	0.00	1.0	1.0	0.00
Renal impairment	1.0	1.0	0.00	1.0	1.0	0.00
Rheumatoid arthritis	1.0	1.0	-0.01	1.1	1.0	0.01
Schizophrenia	0.0	0.1	-0.03	0.1	0.1	-0.01
Ulcerative colitis	0.3	0.4	-0.01	0.4	0.4	0.00
Urinary tract infectious disease	6.4	6.8	-0.02	7.1	6.7	0.02

Viral hepatitis C	0.3	0.5	-0.02	0.4	0.4	0.00
Visual system disorder	15.8	16.0	0.00	16.3	16.0	0.01
Medical history: Cardiovascular disease						
Atrial fibrillation	1.1	1.7	-0.04	1.6	1.5	0.01
Cerebrovascular disease	1.7	1.8	-0.01	2.0	1.8	0.01
Coronary arteriosclerosis	4.3	3.9	0.02	4.5	4.2	0.02
Heart disease	19.1	16.7	0.06	18.8	17.7	0.03
Heart failure	0.8	0.6	0.02	0.7	0.6	0.01
Ischemic heart disease	3.5	3.3	0.01	3.8	3.5	0.02
Peripheral vascular disease	5.6	4.8	0.04	5.5	5.1	0.02
Pulmonary embolism	0.3	0.3	-0.01	0.4	0.3	0.01
Venous thrombosis	1.1	1.2	0.00	1.2	1.1	0.01
Medical history: Neoplasms						
Hematologic neoplasm	0.7	0.7	0.00	0.8	0.7	0.01
Malignant lymphoma	0.3	0.3	0.00	0.3	0.3	0.02
Malignant neoplasm of anorectum	0.1	0.1	0.00	0.1	0.1	0.01
Malignant neoplastic disease	4.8	4.8	0.00	4.9	4.9	0.00
Malignant tumor of breast	1.0	1.0	0.00	1.0	1.0	0.00
Malignant tumor of colon	0.2	0.2	-0.01	0.2	0.2	0.01
Malignant tumor of lung	0.1	0.2	-0.01	0.1	0.2	-0.01
Malignant tumor of urinary bladder	0.1	0.1	0.00	0.1	0.1	0.00
Primary malignant neoplasm of prostate	0.5	0.5	0.01	0.5	0.5	-0.01
Medication use						
Antibacterials for systemic use	54.6	50.9	0.07	53.0	52.5	0.01
Antidepressants	22.5	23.4	-0.02	24.0	23.1	0.02
Antiepileptics	9.0	9.0	0.00	9.7	9.1	0.02
Antiinflammatory and antirheumatic products	26.2	26.0	0.00	26.7	26.2	0.01
Antineoplastic agents	1.7	1.7	0.00	1.8	1.7	0.00
Antipsoriatics	0.4	0.4	0.00	0.4	0.4	0.00
Antithrombotic agents	4.3	4.7	-0.02	5.1	4.7	0.02
Drugs for acid related disorders	16.7	16.5	0.00	17.0	16.7	0.01
Drugs for obstructive airway diseases	19.8	18.6	0.03	19.3	19.1	0.00
Drugs used in diabetes	3.6	4.0	-0.02	4.3	3.9	0.02
Immunosuppressants	1.9	1.8	0.01	1.9	1.8	0.00
Lipid modifying agents	20.8	18.7	0.05	20.0	19.4	0.01
Opioids	18.8	19.2	-0.01	20.1	19.1	0.02
Psycholeptics	26.7	27.1	-0.01	28.4	27.1	0.03
Psychostimulants, agents used for ADHD and nootropics	5.4	4.6	0.04	5.1	4.9	0.01

CCAE, Truven MarketScan Commercial Claims and Encounters

Table S2 e. Baseline characteristics for nebivolol and atenolol new-users in the Optum database before and after propensity score stratification

Characteristic	Before stratification			After stratification		
	Nebivolol, %	Atenolol, %	Std. diff	Nebivolol, %	Atenolol, %	Std. diff
Age group						
15-19	0.3	0.6	-0.05	0.3	0.5	-0.03
20-24	1.3	1.1	0.02	1.2	1.1	0.01
25-29	3.1	2.6	0.03	2.7	2.8	0.00
30-34	5.8	4.0	0.08	4.5	4.6	0.00
35-39	9.0	6.1	0.11	6.8	7.0	-0.01
40-44	12.4	7.6	0.16	8.5	9.0	-0.02
45-49	14.2	10.3	0.12	11.0	11.3	-0.01
50-54	15.6	11.4	0.12	12.4	12.6	-0.01
55-59	13.0	11.8	0.04	11.9	12.2	-0.01
60-64	9.4	10.0	-0.02	10.0	10.0	0.00
65-69	6.6	11.6	-0.17	10.2	10.1	0.00
70-74	4.3	9.1	-0.19	8.6	7.7	0.03
75-79	2.4	6.5	-0.20	5.7	5.3	0.02
80-84	1.8	5.3	-0.18	5.0	4.3	0.04
85-89	0.7	1.9	-0.11	1.4	1.6	-0.02
Gender: female	44.1	53.6	-0.19	53.1	51.0	0.04
Medical history: General						
Acute respiratory disease	29.5	25.9	0.08	27.4	27.2	0.00
Attention deficit hyperactivity disorder	2.4	1.3	0.08	1.6	1.6	0.00
Chronic liver disease	2.1	1.7	0.03	1.7	1.8	0.00
Chronic obstructive lung disease	4.1	5.3	-0.05	5.5	4.9	0.03
Crohn's disease	0.4	0.4	0.00	0.4	0.4	0.00
Dementia	0.5	1.5	-0.10	1.3	1.3	0.00
Depressive disorder	11.2	12.5	-0.04	12.9	12.1	0.02
Diabetes mellitus	9.3	11.6	-0.07	11.8	10.9	0.03
Gastroesophageal reflux disease	13.5	14.2	-0.02	14.9	14.1	0.02
Gastrointestinal hemorrhage	2.4	2.7	-0.02	2.5	2.6	-0.01
Human immunodeficiency virus infection	0.4	0.3	0.01	0.2	0.3	-0.02
Hyperlipidemia	47.2	47.4	0.00	47.8	47.3	0.01
Hypertensive disorder	100.0	100.0	0.00	100.0	100.0	0.00
Lesion of liver	0.4	0.6	-0.03	0.5	0.5	0.00
Obesity	10.5	9.0	0.05	9.3	9.5	-0.01
Osteoarthritis	17.6	20.0	-0.06	20.4	19.4	0.02
Pneumonia	2.0	2.6	-0.04	2.8	2.4	0.02
Psoriasis	1.4	1.2	0.02	1.1	1.2	-0.01
Renal impairment	2.2	3.7	-0.09	4.1	3.2	0.04

Rheumatoid arthritis	1.4	1.6	-0.02	1.4	1.6	-0.01
Schizophrenia	0.1	0.3	-0.05	0.2	0.3	-0.02
Ulcerative colitis	0.4	0.4	-0.01	0.4	0.4	0.00
Urinary tract infectious disease	7.6	9.4	-0.06	9.2	8.9	0.01
Viral hepatitis C	0.5	0.5	0.00	0.6	0.5	0.01
Visual system disorder	21.0	28.1	-0.17	27.3	26.1	0.03
Medical history: Cardiovascular disease						
Atrial fibrillation	2.3	4.5	-0.12	4.1	3.9	0.01
Cerebrovascular disease	2.5	3.7	-0.07	3.9	3.3	0.03
Coronary arteriosclerosis	6.8	9.3	-0.09	9.7	8.7	0.04
Heart disease	26.0	26.6	-0.02	28.5	26.4	0.05
Heart failure	1.6	1.8	-0.02	2.1	1.7	0.03
Ischemic heart disease	5.4	6.2	-0.03	6.5	6.0	0.02
Peripheral vascular disease	8.7	10.6	-0.06	10.9	10.0	0.03
Pulmonary embolism	0.4	0.6	-0.02	0.5	0.5	-0.01
Venous thrombosis	1.5	1.8	-0.02	1.7	1.7	0.00
Medical history: Neoplasms						
Hematologic neoplasm	0.9	1.2	-0.02	1.1	1.1	0.01
Malignant lymphoma	0.3	0.4	-0.02	0.3	0.4	-0.01
Malignant neoplasm of anorectum	0.2	0.2	-0.01	0.3	0.2	0.02
Malignant neoplastic disease	6.5	8.9	-0.09	8.2	8.2	0.00
Malignant tumor of breast	1.2	1.7	-0.04	1.5	1.5	0.00
Malignant tumor of colon	0.2	0.5	-0.04	0.4	0.5	0.00
Malignant tumor of lung	0.2	0.5	-0.04	0.4	0.4	0.00
Malignant tumor of urinary bladder	0.2	0.4	-0.04	0.4	0.4	0.00
Primary malignant neoplasm of prostate	0.7	1.3	-0.06	1.0	1.1	-0.01
Medication use						
Antibacterials for systemic use	50.5	44.9	0.11	47.7	46.8	0.02
Antidepressants	21.4	21.1	0.01	22.1	21.3	0.02
Antiepileptics	8.9	9.0	0.00	9.5	9.1	0.01
Antiinflammatory and antirheumatic products	23.9	21.0	0.07	22.8	22.1	0.02
Antineoplastic agents	1.9	2.3	-0.02	2.1	2.2	0.00
Antipsoriatics	0.6	0.4	0.04	0.6	0.4	0.03
Antithrombotic agents	4.9	7.0	-0.09	7.4	6.4	0.04
Drugs for acid related disorders	14.8	15.0	-0.01	16.2	15.1	0.03
Drugs for obstructive airway diseases	18.9	15.6	0.09	17.8	16.7	0.03
Drugs used in diabetes	4.5	5.6	-0.05	5.5	5.3	0.01
Immunosuppressants	1.9	1.7	0.01	1.9	1.7	0.01
Lipid modifying agents	23.1	24.9	-0.04	25.5	24.3	0.03
Opioids	16.0	16.9	-0.02	17.6	16.8	0.02
Psycholeptics	24.1	22.6	0.03	24.2	23.3	0.02

Psychostimulants, agents used for ADHD and nootropics	5.0	3.2	0.09	3.8	3.8	0.00
Optum, Optum ClinFormatics						

Table S2 f. Baseline characteristics for nebivolol and atenolol new-users in the PanTher database before and after propensity score stratification

Characteristic	Before stratification			After stratification		
	Nebivolol, %	Atenolol, %	Std. diff	Nebivolol, %	Atenolol, %	Std. diff
Age group						
15-19	0.2	0.4	-0.03	0.3	0.4	-0.02
20-24	0.9	0.9	0.01	0.9	0.9	0.00
25-29	2.3	1.8	0.04	1.9	1.9	0.00
30-34	4.3	2.9	0.08	3.0	3.1	-0.01
35-39	6.8	4.1	0.12	4.3	4.6	-0.01
40-44	9.4	5.9	0.13	6.0	6.5	-0.02
45-49	11.7	8.4	0.11	8.2	9.0	-0.03
50-54	13.9	11.5	0.07	11.2	11.9	-0.02
55-59	14.3	13.0	0.04	12.9	13.3	-0.01
60-64	12.2	12.6	-0.01	12.6	12.5	0.00
65-69	8.7	11.2	-0.08	11.2	10.7	0.01
70-74	6.1	9.0	-0.11	9.4	8.5	0.03
75-79	4.2	7.8	-0.15	7.4	7.1	0.01
80-84	3.8	8.3	-0.19	8.3	7.5	0.03
85-89	1.1	2.3	-0.09	2.4	2.1	0.02
Gender: female	52.3	57.0	-0.10	57.0	56.2	0.02
Race						
race = Asian	1.7	1.8	-0.01	1.7	1.8	-0.01
race = Black or African American	8.1	6.0	0.08	6.3	6.4	0.00
race = White	84.2	85.5	-0.04	85.7	85.2	0.02
Ethnicity						
ethnicity = Hispanic or Latino	3.1	3.4	-0.02	3.0	3.4	-0.02
Medical history: General						
Acute respiratory disease	13.4	11.8	0.05	11.4	12.1	-0.02
Attention deficit hyperactivity disorder	1.6	1.0	0.06	1.0	1.0	0.00
Chronic liver disease	1.4	1.3	0.01	1.4	1.3	0.01
Chronic obstructive lung disease	3.7	4.3	-0.03	4.7	4.2	0.02
Crohn's disease	0.4	0.4	-0.01	0.3	0.4	-0.01
Dementia	0.8	1.9	-0.09	2.0	1.7	0.03
Depressive disorder	10.1	11.8	-0.05	11.7	11.4	0.01
Diabetes mellitus	8.6	11.5	-0.10	12.2	11.0	0.04
Gastroesophageal reflux disease	13.7	14.6	-0.02	14.8	14.4	0.01
Gastrointestinal hemorrhage	1.2	1.7	-0.05	1.4	1.6	-0.02
Human immunodeficiency virus infection	0.2	0.2	-0.01	0.3	0.2	0.01
Hyperlipidemia	37.5	43.7	-0.13	43.5	42.5	0.02
Hypertensive disorder	97.3	97.3	0.00	96.7	97.3	-0.03

Lesion of liver	0.4	0.5	-0.03	0.5	0.5	0.00
Obesity	9.8	9.0	0.03	9.1	9.2	0.00
Osteoarthritis	11.2	13.5	-0.07	13.5	13.1	0.01
Pneumonia	1.7	2.2	-0.04	2.3	2.1	0.01
Psoriasis	0.7	0.9	-0.02	0.7	0.8	-0.02
Renal impairment	2.3	3.2	-0.06	3.4	3.1	0.02
Rheumatoid arthritis	1.1	1.3	-0.02	1.2	1.3	0.00
Schizophrenia	0.1	0.5	-0.06	0.4	0.4	0.00
Ulcerative colitis	0.3	0.3	-0.01	0.2	0.3	-0.02
Urinary tract infectious disease	3.7	5.3	-0.08	5.4	5.1	0.01
Viral hepatitis C	0.5	0.7	-0.02	0.6	0.6	0.00
Visual system disorder	6.9	10.3	-0.12	8.6	9.7	-0.04
Medical history: Cardiovascular disease						
Atrial fibrillation	3.0	4.3	-0.07	4.8	4.1	0.03
Cerebrovascular disease	1.6	2.0	-0.03	2.2	1.9	0.02
Coronary arteriosclerosis	7.5	9.7	-0.08	10.9	9.4	0.05
Heart disease	19.9	22.3	-0.06	24.1	21.9	0.05
Heart failure	1.1	1.1	0.00	1.4	1.1	0.02
Ischemic heart disease	3.4	3.9	-0.03	4.3	3.9	0.02
Peripheral vascular disease	5.9	6.8	-0.04	6.5	6.6	0.00
Pulmonary embolism	0.4	0.5	-0.02	0.6	0.5	0.02
Venous thrombosis	0.9	1.2	-0.03	1.0	1.1	-0.01
Medical history: Neoplasms						
Hematologic neoplasm	0.6	0.8	-0.02	0.5	0.7	-0.03
Malignant lymphoma	0.3	0.4	0.00	0.4	0.4	0.01
Malignant neoplasm of anorectum	0.1	0.2	-0.02	0.1	0.2	-0.01
Malignant neoplastic disease	5.2	7.0	-0.08	7.0	6.7	0.01
Malignant tumor of breast	1.0	1.5	-0.04	1.5	1.4	0.01
Malignant tumor of colon	0.3	0.4	-0.02	0.4	0.4	0.01
Malignant tumor of lung	0.2	0.3	-0.02	0.4	0.3	0.01
Malignant tumor of urinary bladder	0.2	0.3	-0.03	0.4	0.3	0.02
Primary malignant neoplasm of prostate	0.7	1.0	-0.04	1.1	0.9	0.01
Medication use						
Agents acting on the renin-angiotensin system	0.0	0.0	0.00	0.0	0.0	-0.01
Antibacterials for systemic use	25.1	23.0	0.05	23.7	23.2	0.01
Antidepressants	23.5	24.2	-0.02	25.7	24.0	0.04
Antiepileptics	10.3	11.0	-0.02	11.9	10.9	0.03
Antiinflammatory and antirheumatic products	25.4	25.0	0.01	25.3	25.0	0.01
Antineoplastic agents	1.2	1.3	-0.01	1.3	1.3	0.00
Antipsoriatics	0.2	0.2	0.00	0.2	0.2	0.00
Antithrombotic agents	24.3	29.9	-0.13	31.3	28.9	0.05

Drugs for acid related disorders	25.6	27.6	-0.05	28.3	27.2	0.02
Drugs for obstructive airway diseases	21.8	21.4	0.01	23.8	21.4	0.06
Drugs used in diabetes	6.7	8.5	-0.07	8.9	8.2	0.03
Immunosuppressants	1.8	1.8	0.00	1.9	1.8	0.01
Lipid modifying agents	26.2	32.6	-0.14	32.9	31.4	0.03
Opioids	18.5	20.0	-0.04	21.1	19.8	0.03
Psycholeptics	25.9	26.2	-0.01	27.0	26.1	0.02
Psychostimulants, agents used for adhd and nootropics	4.3	2.8	0.08	3.1	3.0	0.01

PanTher, Optum® de-identified Electronic Health Record Dataset

Table S3. Hazard ratios of carvedilol and nebivolol compared to atenolol after excluding patients with previous history of heart failure, ischemic heart disease, or atrial fibrillation (Propensity score matching, on-treatment)

Target drug	Outcome / database	Uncalibrated meta-analytic result			Calibrated meta-analytic result		
		HR	95% CI	<i>P</i>	HR	95% CI	<i>P</i>
Carvedilol	Acute myocardial infarction						
	CCAIE	1.13	0.72 - 1.73	0.578	1.14	0.74 - 1.76	0.526
	Optum	1.22	0.89 - 1.67	0.207	1.26	0.91 - 1.82	0.161
	PanTher	1.19	0.80 - 1.74	0.391	1.05	0.69 - 1.62	0.710
	Stroke						
	CCAIE	0.96	0.59 - 1.52	0.872	0.97	0.61 - 1.55	0.923
	Optum	0.94	0.69 - 1.26	0.662	0.97	0.69 - 1.35	0.833
	PanTher	1.09	0.75 - 1.57	0.638	0.98	0.65 - 1.48	0.910
	Hospitalization for heart failure						
	CCAIE	2.06	1.48 - 2.86	0.000	2.06	1.49 - 2.93	0.000
	Optum	1.67	1.36 - 2.06	0.000	1.72	1.34 - 2.35	0.000
	PanTher	2.10	1.65 - 2.68	0.000	1.70	1.24 - 2.58	0.000
Nebivolol	Acute myocardial infarction						
	CCAIE	1.12	0.62 - 1.96	0.702	1.21	0.65 - 2.27	0.532
	Optum	0.51	0.24 - 1.01	0.071	0.56	0.20 - 1.17	0.120
	PanTher	1.94	0.97 - 3.70	0.052	1.19	NA	0.127
	Stroke						
	CCAIE	1.11	0.70 - 1.75	0.646	1.20	0.73 - 2.02	0.449
	Optum	0.98	0.62 - 1.51	0.930	1.08	0.66 - 1.81	0.799
	PanTher	1.66	0.88 - 2.95	0.103	1.13	NA	0.239
	Hospitalization for heart failure						

	CCAЕ	0.36	0.16 - 0.72	0.008	0.38	0.17 - 0.83	0.014
	Optum	1.15	0.75 - 1.73	0.503	1.27	0.83 - 2.19	0.318
	PanTher	2.53	1.50 - 4.14	0.000	1.29	NA	0.003
Meta-analysis	Acute myocardial infarction	1.11	0.81 - 1.53	0.505	1.13	0.75 - 1.76	0.494
	Stroke	1.10	0.90 - 1.34	0.370	1.11	0.81 - 1.59	0.368
	Hospitalization for heart failure	1.47	0.93 - 2.32	0.097	1.49	0.90 - 2.70	0.096

Abbreviations: HR, Hazard ratio; CI, confidence interval; CCAE, Truven MarketScan Commercial Claims and Encounters; Optum, Optum ClinFormatics; PanTher, Optum® de-identified Electronic Health Record Dataset

Table S4. Meta-analytic hazard ratios of carvedilol and nebivolol compared to atenolol using propensity scores without and with baseline blood pressure adjustment in the Optum® de-identified Electronic Health Record Dataset database (Propensity score matching, on-treatment)

Target drug	Outcome / database	Uncalibrated meta-analytic result			Calibrated meta-analytic result		
		HR	95% CI	<i>P</i>	HR	95% CI	<i>P</i>
Carvedilol	Acute myocardial infarction						
	Original*	0.98	0.66 - 1.45	0.933	0.91	0.63 - 1.36	0.910
	Sensitivity†	1.01	0.66 - 1.51	0.981	0.93	0.59 - 1.42	0.750
	Stroke						
	Original*	1.01	0.69-1.45	0.964	0.93	0.66 - 1.37	0.730
	Sensitivity†	0.98	0.65 - 1.46	0.927	0.91	0.58 - 1.38	0.663
	Hospitalization for heart failure						
	Original*	1.81	1.42 - 2.31	<0.001	1.52	1.31 - 2.18	<0.001
	Sensitivity†	1.73	1.31 - 2.28	<0.001	1.46	1.08 - 2.22	0.002
	Acute myocardial infarction						
Nebivolol	Original*	2.25	1.10 - 4.35	0.021	1.52	0.92 - 2.70	0.056
	Sensitivity†	0.94	0.85 - 4.30	0.100	1.29	NA	0.173
	Stroke						
	Original*	1.39	0.69 - 2.58	0.334	1.09	0.67 - 1.84	0.570
	Sensitivity†	0.94	0.40 - 1.94	0.885	0.92	NA	0.681
	Hospitalization for heart failure						
	Original*	2.67	1.58 - 4.40	<0.001	1.72	1.15 - 2.77	0.001
	Sensitivity†	2.40	1.36 - 4.12	0.002	1.41	NA	0.008

*Estimates from original analysis were calculated based on large-scale propensity scores built without blood pressure measurements.

†Estimates from sensitivity analysis were calculated based on large-scale propensity scores additionally including blood pressure measurements.

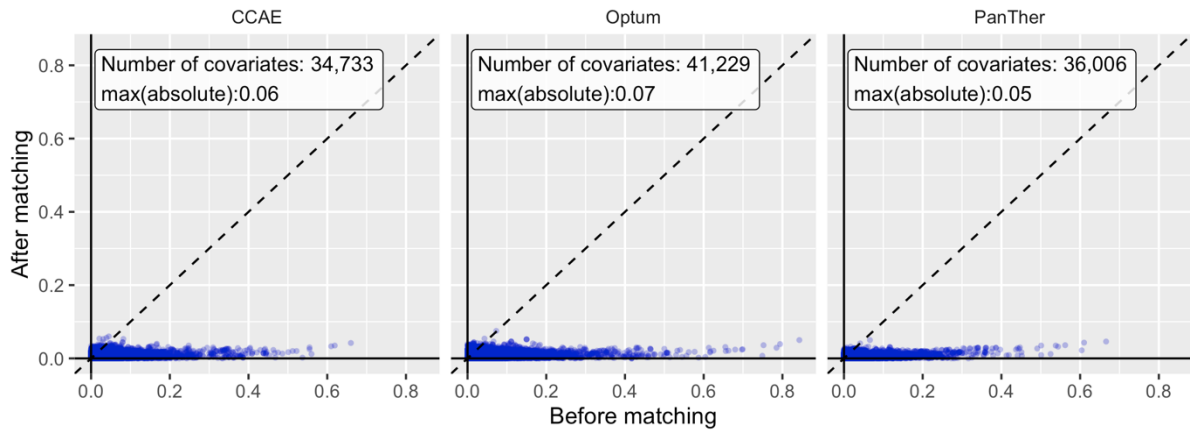
Abbreviations: HR, Hazard ratio; CI, confidence interval

Table S5. Meta-analytic hazard ratios of nebivolol compared to atenolol and other classes for primary outcomes (Propensity score matching, on-treatment)

Comparator drug	Outcome	Uncalibrated meta-analytic result			Calibrated meta-analytic result			I ²
		HR	95% CI	P	HR	95% CI	P	
Atenolol	Acute myocardial infarction	1.04	0.44 - 2.45	0.928	1.08	0.48 - 2.47	0.839	0.798
	Stroke	1.23	0.92 - 1.64	0.168	1.27	0.96 - 1.68	0.094	0.000
	Hospitalization for heart failure	1.17	0.50 - 2.74	0.721	1.21	0.54 - 2.75	0.638	0.875
ACEIs	Acute myocardial infarction	1.37	0.98 - 1.91	0.069	1.36	0.95 - 2.06	0.077	0.550
	Stroke	1.40	1.09 - 1.79	0.009	1.39	1.04 - 1.98	0.017	0.438
	Hospitalization for heart failure	1.27	0.94 - 1.71	0.126	1.27	0.91 - 1.86	0.138	0.643
ARBs	Acute myocardial infarction	1.46	1.08 - 1.97	0.013	1.42	1.01 - 2.12	0.043	0.232
	Stroke	1.33	1.06 - 1.66	0.013	1.29	0.98 - 1.81	0.072	0.035
	Hospitalization for heart failure	1.22	0.90 - 1.65	0.201	1.19	0.83 - 1.76	0.321	0.457
dCCBs	Acute myocardial infarction	1.03	0.46 - 2.32	0.935	1.07	0.48 - 2.42	0.846	0.827
	Stroke	1.37	1.07 - 1.76	0.012	1.40	1.05 - 1.97	0.008	0.000
	Hospitalization for heart failure	1.01	0.51 - 2.01	0.972	1.05	0.53 - 2.11	0.866	0.844
TDs	Acute myocardial infarction	1.24	0.70 - 2.21	0.466	1.29	0.71 - 2.41	0.393	0.548
	Stroke	1.51	1.18 - 1.93	0.001	1.56	1.17 - 2.20	0.001	0.000
	Hospitalization for heart failure	0.92	0.59 - 1.43	0.708	0.96	0.59 - 1.55	0.849	0.508

Abbreviations: HR, Hazard ratio; CI, confidence interval; ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blocker; dCCB, dihydropyridine calcium-channel blocker; TD, thiazide, or thiazide-like diuretics

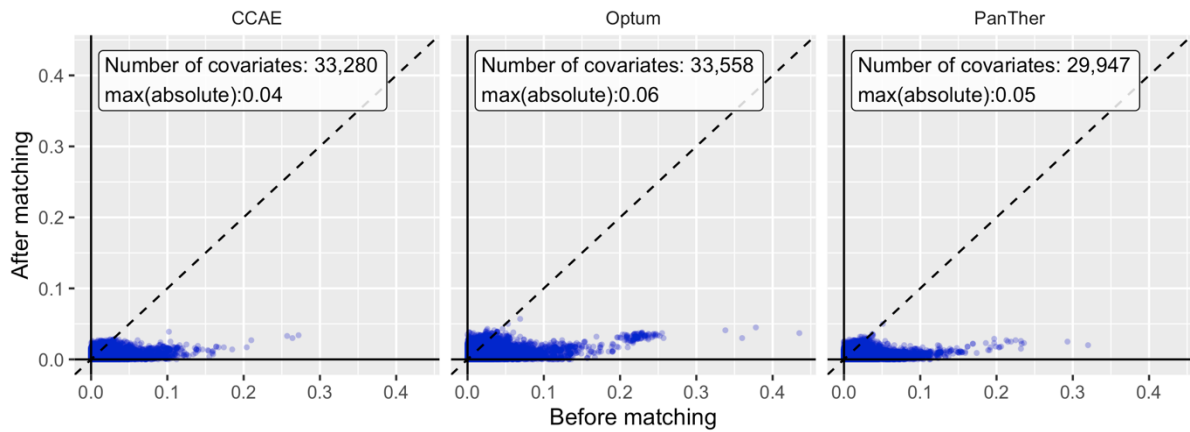
Figure S1. Covariate balance plot before and after propensity score matching between carvedilol and atenolol



The covariate balances before and after PS matching were depicted. After PS matching, every standardized mean difference from more than 30,000 covariates does not exceed 0.1.

Abbreviation: PS, propensity score; CCAE, Truven MarketScan Commercial Claims and Encounters; Optum, Optum ClinFormatics; PanTher, Optum® de-identified Electronic Health Record Dataset

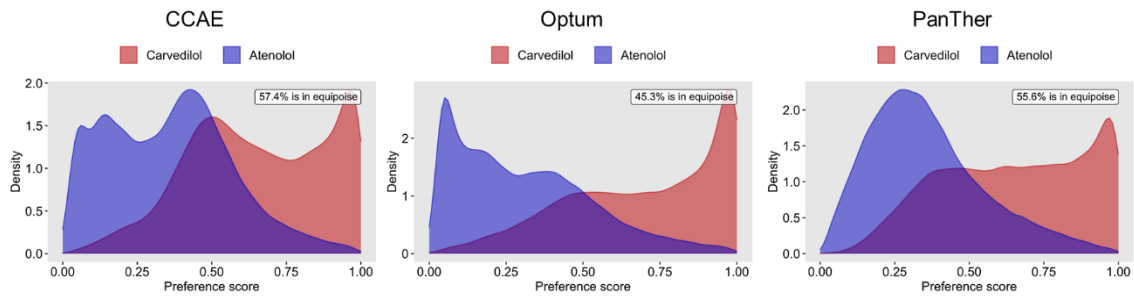
Figure S2. Covariate balance plot before and after propensity score matching between nebivolol and atenolol



The covariate balances before and after PS matching were depicted. After PS matching, every standardized mean difference from more than 20,000 covariates does not exceed 0.1.

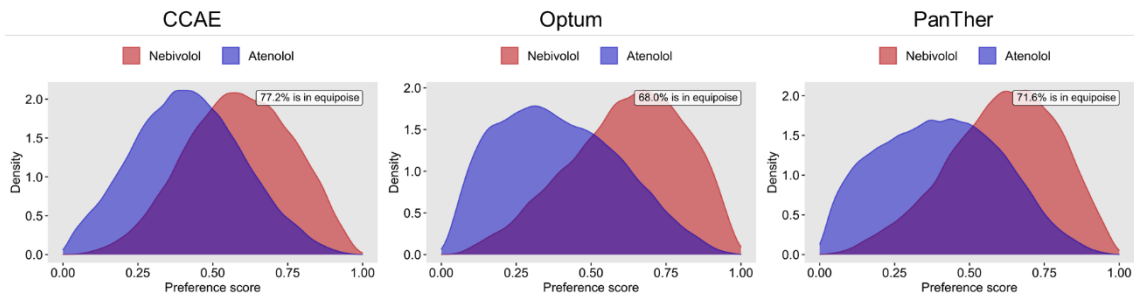
Abbreviation: PS, propensity score; CCAE, Truven MarketScan Commercial Claims and Encounters; Optum, Optum ClinFormatics; PanTher, Optum® de-identified Electronic Health Record Dataset

Figure S3. Preference score distribution before propensity score adjustment between carvedilol and atenolol



The preference score is a transformation of the propensity score that adjusts for differences in the sizes of the two treatment groups. A higher overlap indicates subjects in the two groups were more similar in terms of their predicted probability of receiving one treatment over the other. In the Optum database, only 45.3% population were in equipoise (preference score between 0.25 and 0.75), while the results in the CCAE and the PanTher shows sufficient equipoise (majority of both distributions being between 0.25 and 0.75).
Abbreviation: CCAE, Truven MarketScan Commercial Claims and Encounters; Optum, Optum ClinFormatics; PanTher, Optum® de-identified Electronic Health Record Dataset

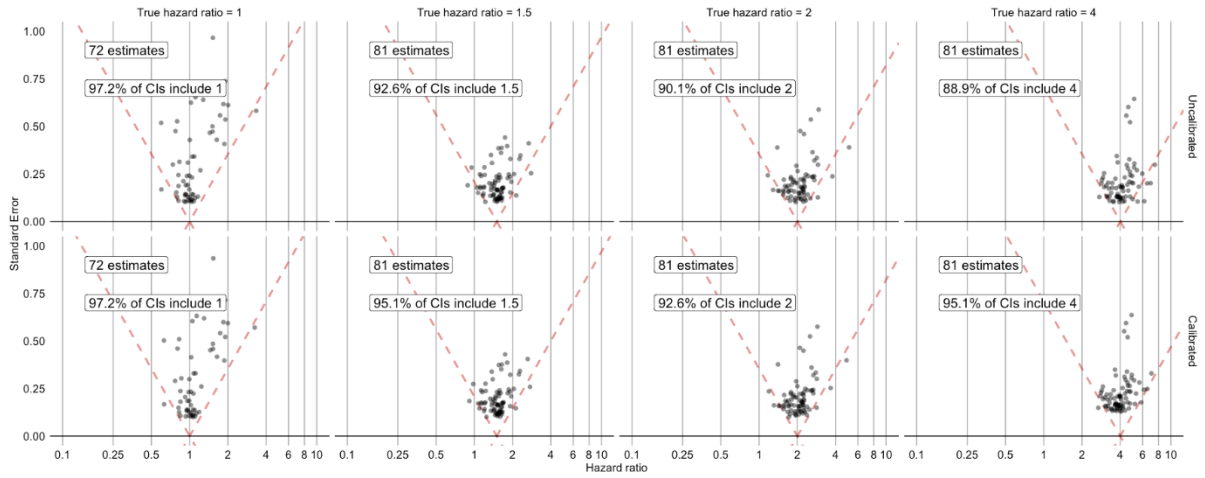
Figure S4. Preference score distribution before propensity score adjustment between nebivolol and atenolol



The preference score is a transformation of the propensity score that adjusts for differences in the sizes of the two treatment groups. A higher overlap indicates subjects in the two groups were more similar in terms of their predicted probability of receiving one treatment over the other. This plot shows sufficient equipoise (majority of both distributions being between 0.25 and 0.75) in all three databases that propensity score matching should be able to create balance without discounting a large proportion of the population, but it shows sufficient difference (non-overlap) that propensity score matching is necessary.

Abbreviation: CCAE, Truven MarketScan Commercial Claims and Encounters; Optum, Optum ClinFormatics; PanTher, Optum® de-identified Electronic Health Record Dataset

Figure S5. Systematic error control of effect estimation comparing the third-generation beta-blockers (carvedilol and nebivolol) and atenolol users in the meta-analysis under an on-treatment, PS-matching design.



The top plots hazard ratios and their corresponding standard errors before calibration for each negative and synthetic positive control. The bottom plots the same estimates after empirical calibration. The left plots with hazard ratios = 1 present negative controls, while plots with hazard ratios >1 present synthetic positive controls.

Figure S6. Kaplan-Meier plots for acute myocardial infarction between the third-generation beta-blockers users and atenolol users

Figure S6 a: Carvedilol versus atenolol in the CCAE

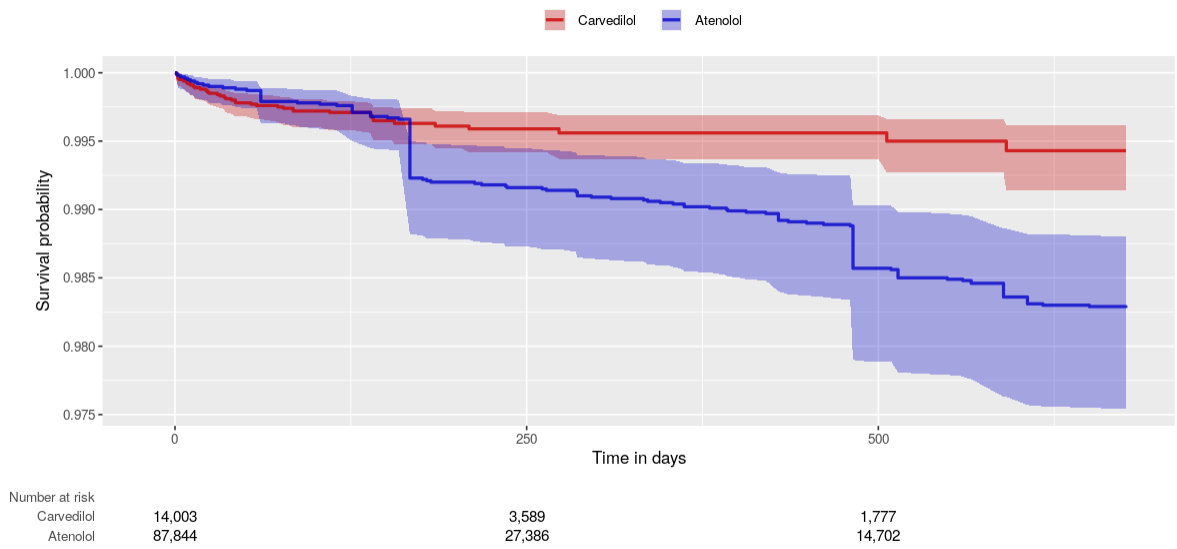


Figure S12 b: Carvedilol versus atenolol in the PanTher

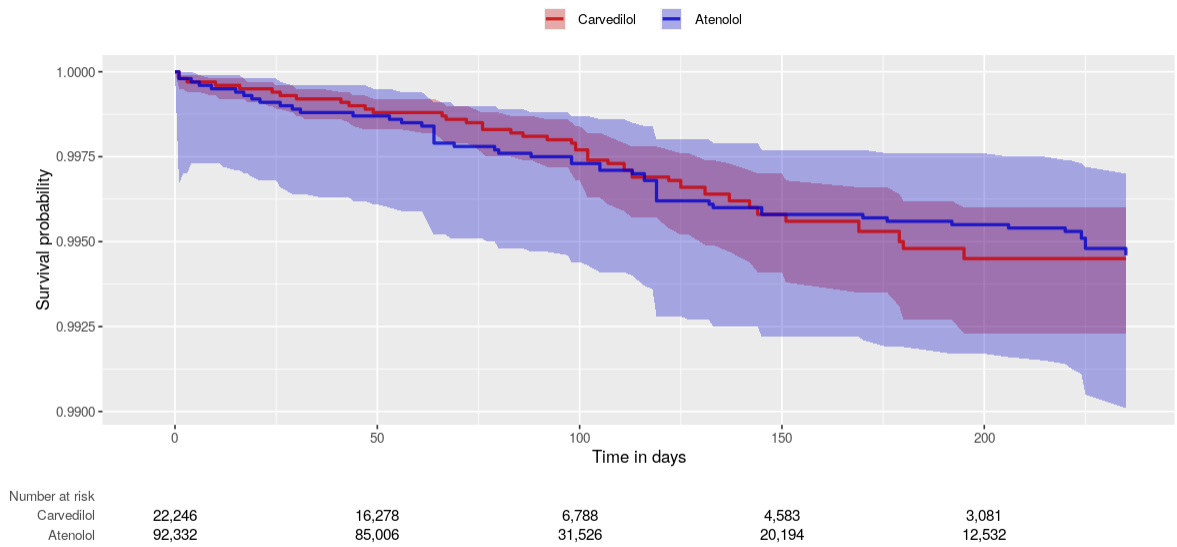


Figure S6 c: Nebivolol versus atenolol in the CCAE

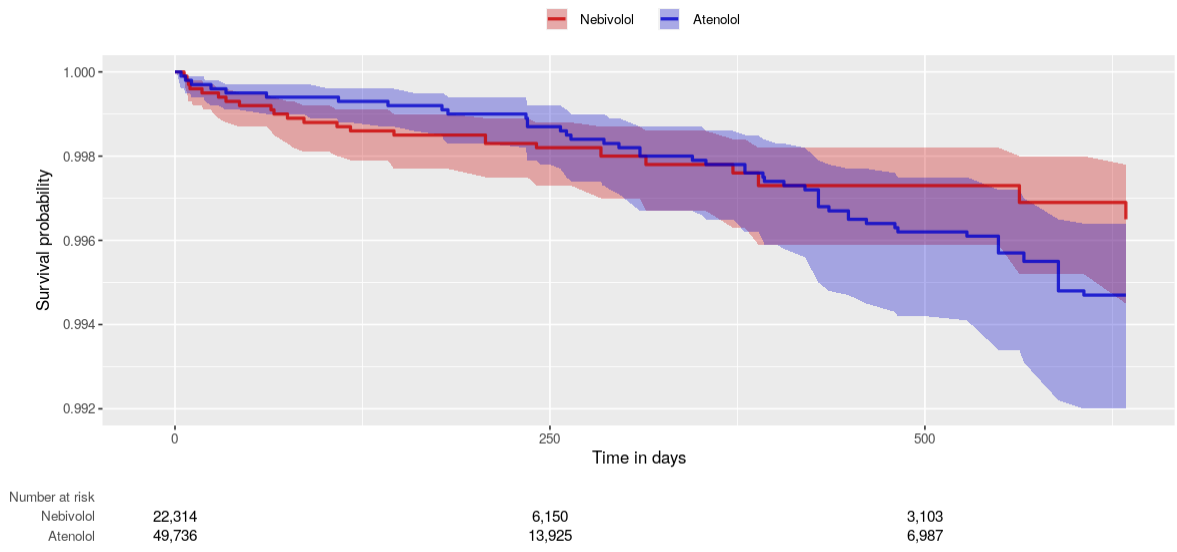


Figure S6 d: Nebivolol versus atenolol in the Optum

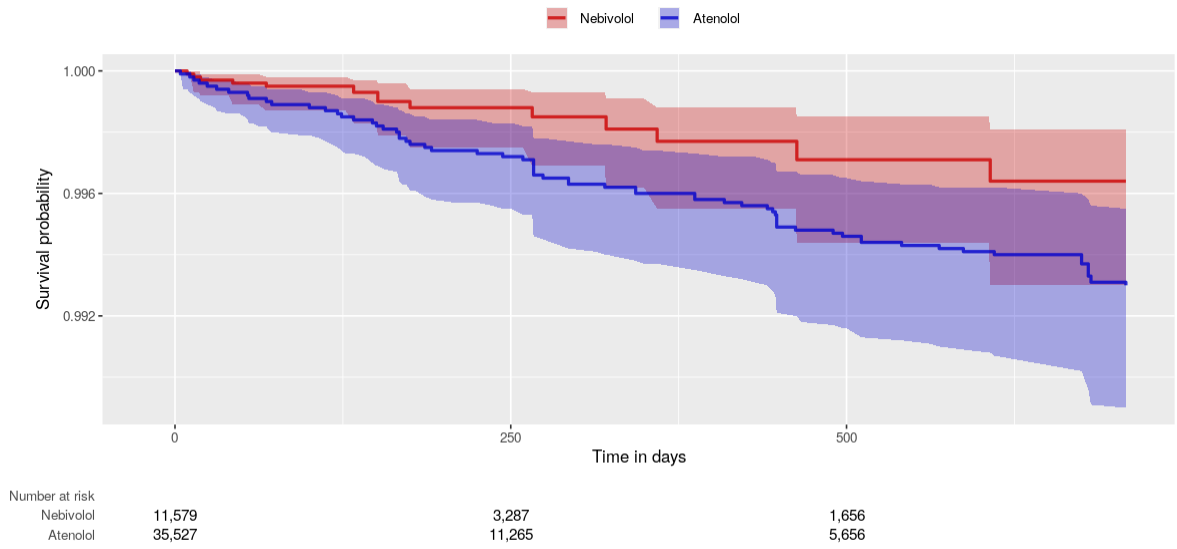
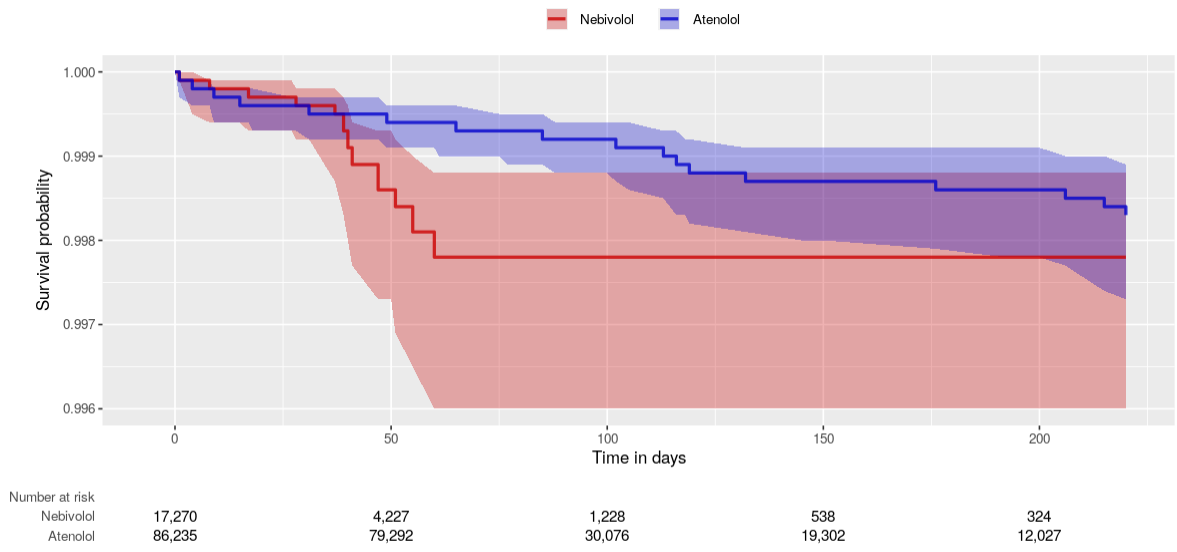


Figure S6 e: Nebivolol versus atenolol in the PanTher



Shading in survival curves represents 95% confidence intervals.

Abbreviation: CCAE, Truven MarketScan Commercial Claims and Encounters; Optum, Optum ClinFormatics; PanTher, Optum® de-identified Electronic Health Record Dataset

Figure S7. Kaplan-Meier plots for stroke between the third-generation beta-blockers users and atenolol users

Figure S7 a: Carvedilol versus atenolol in the CCAE

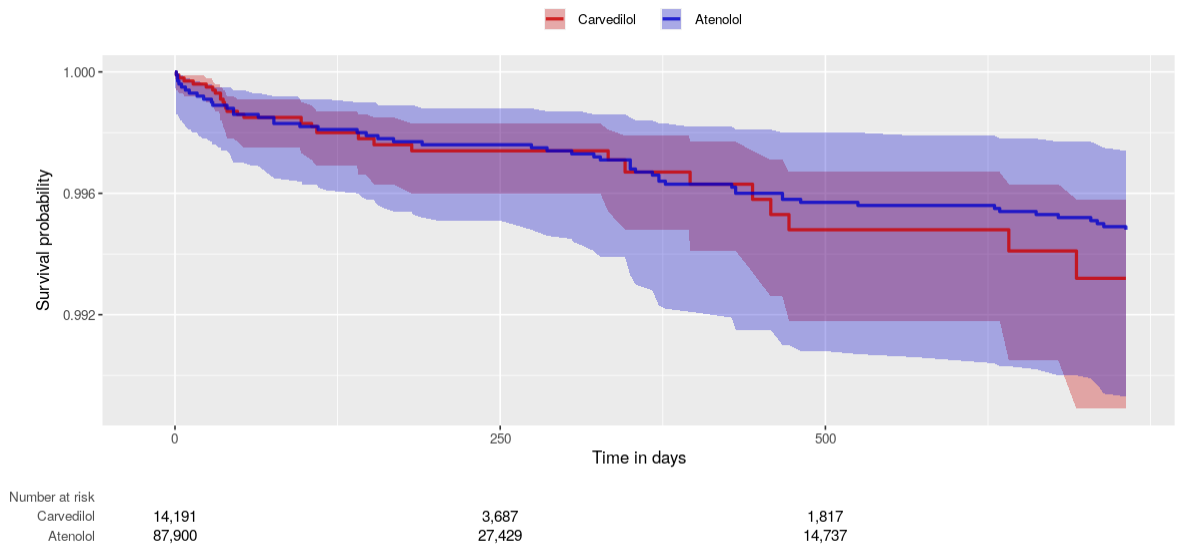


Figure S7 b: Carvedilol versus atenolol in the PanTher

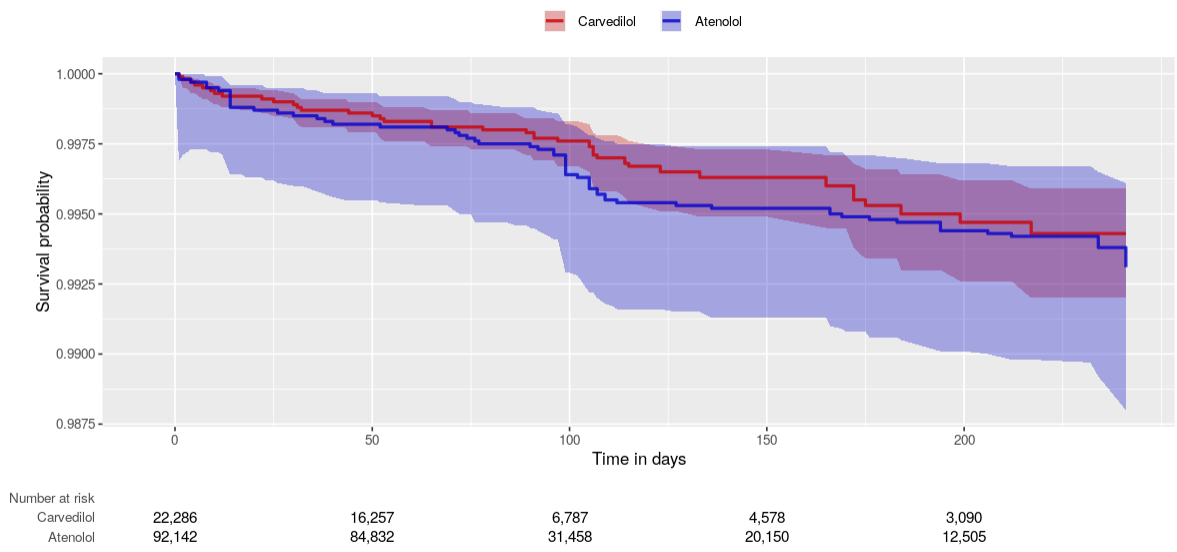


Figure S7 c: Nebivolol versus atenolol in the CCAE

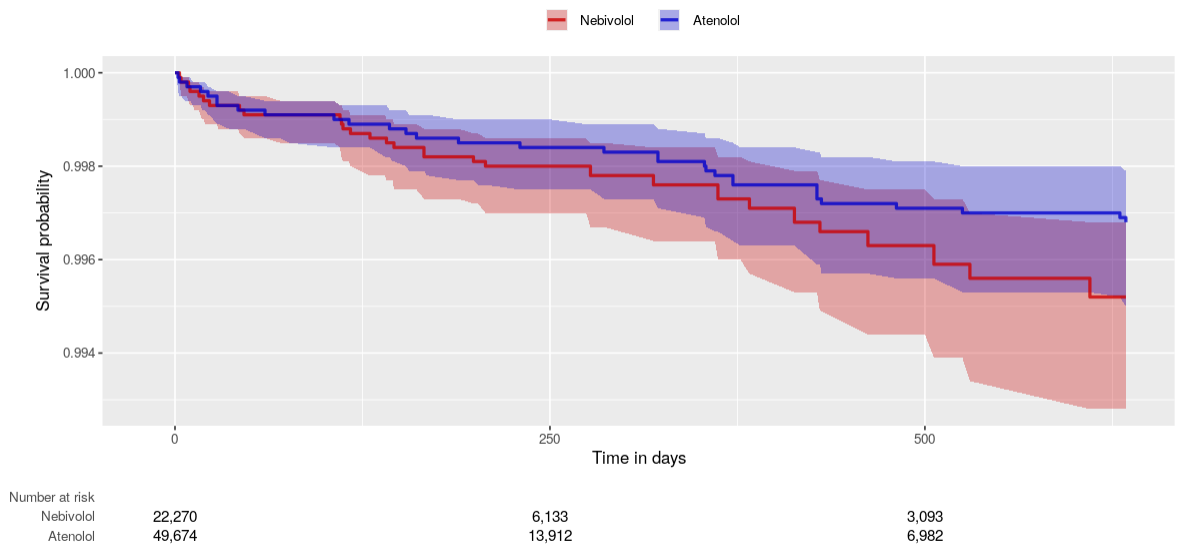


Figure S7 d: Nebivolol versus atenolol in the Optum

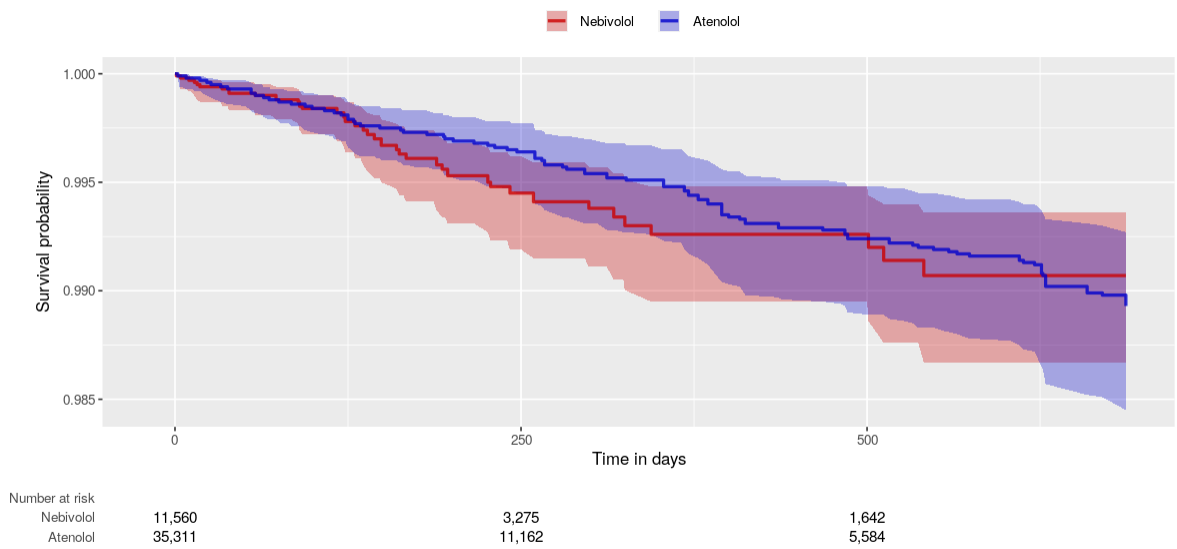
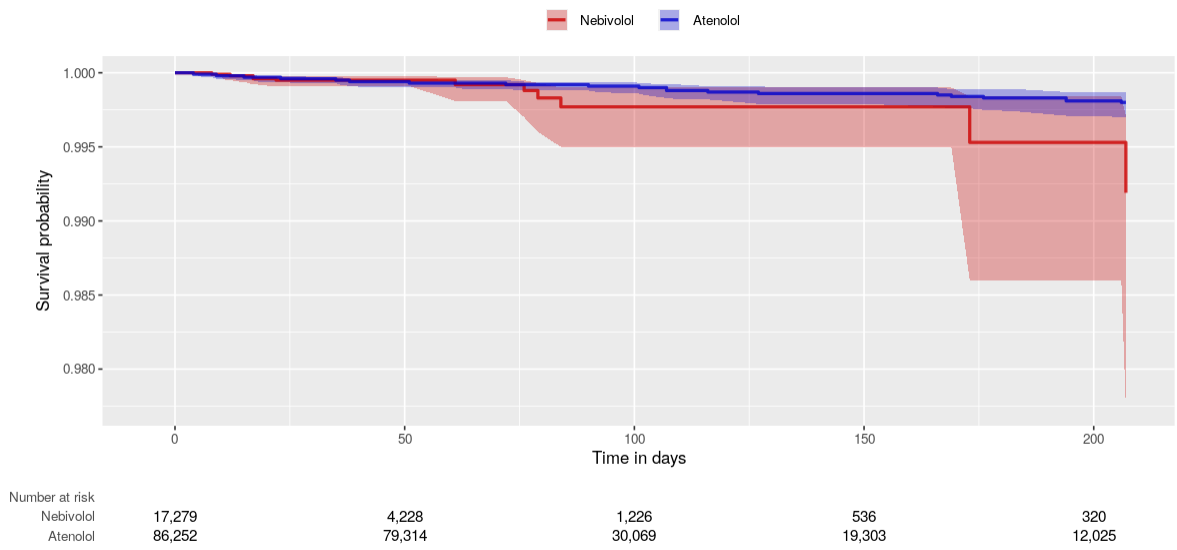


Figure S7 e: Nebivolol versus atenolol in the PanTher



Shading in survival curves represents 95% confidence intervals.

Abbreviation: CCAE, Truven MarketScan Commercial Claims and Encounters; Optum, Optum ClinFormatics; PanTher, Optum® de-identified Electronic Health Record Dataset

Figure S8. Kaplan-Meier plots for hospitalization for heart failure the third-generation beta-blockers users and atenolol users

Figure S8 a: Carvedilol versus atenolol in the CCAE

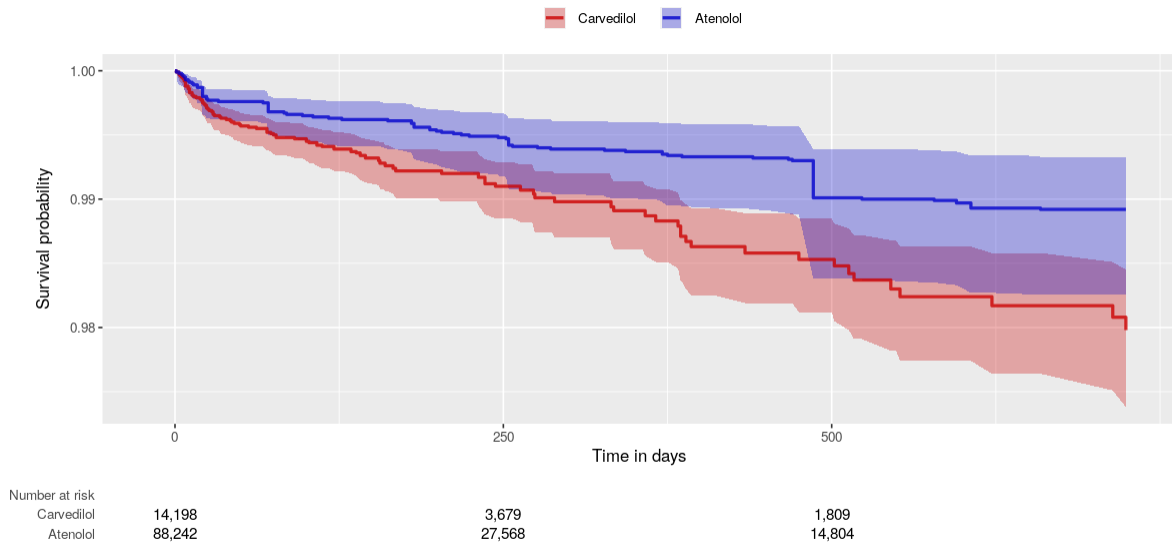


Figure S8 b: Carvedilol versus atenolol in the PanTher

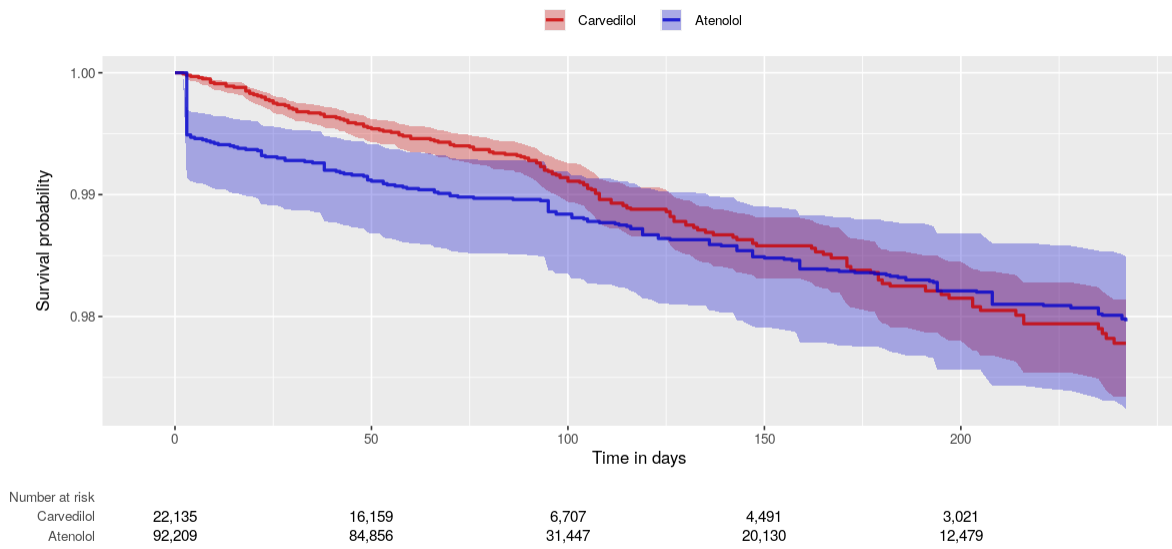


Figure S8 c: Nebivolol versus atenolol in the CCAE

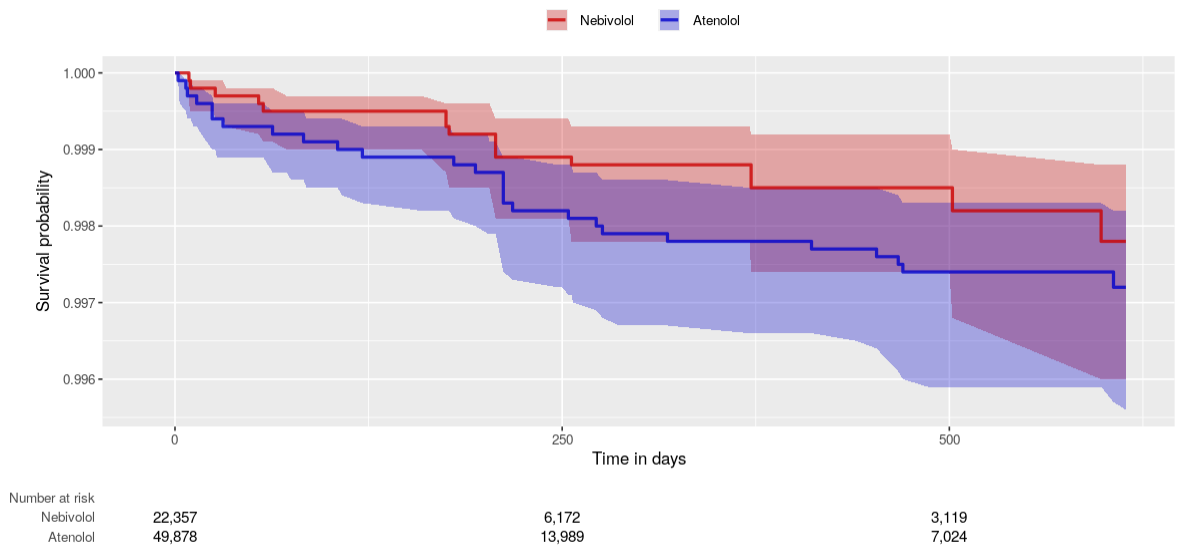


Figure S8 d: Nebivolol versus atenolol in the Optum

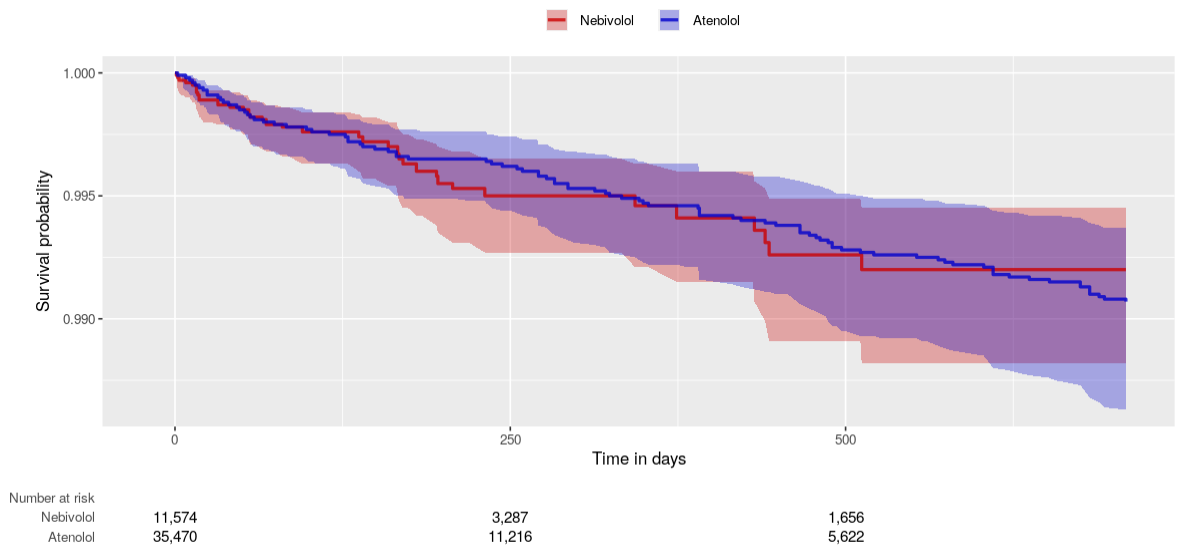
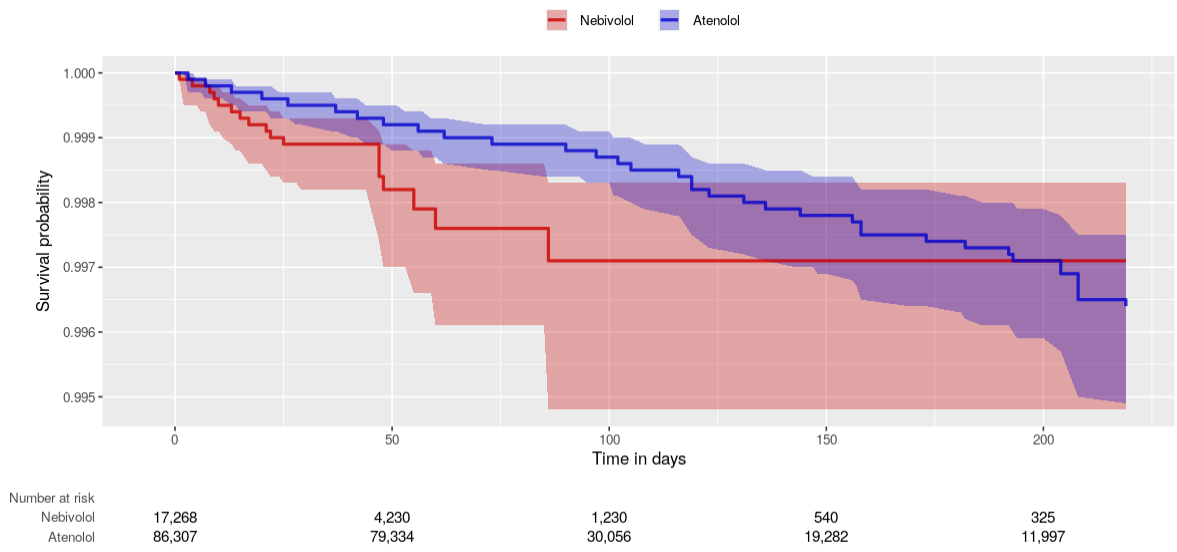


Figure S8 e: Nebivolol versus atenolol in the PanTher



Shading in survival curves represents 95% confidence intervals.

Abbreviation: CCAE, Truven MarketScan Commercial Claims and Encounters; Optum, Optum ClinFormatics; PanTher, Optum® de-identified Electronic Health Record Dataset

Figure S9. The meta-analytic HR estimates and their 95% CIs comparing the relative risk of acute myocardial infarction, stroke, and hospitalization for heart failure between third-generation beta-blockers and atenolol (PS stratification or ITT)

Figure S9 a: PS matching, ITT

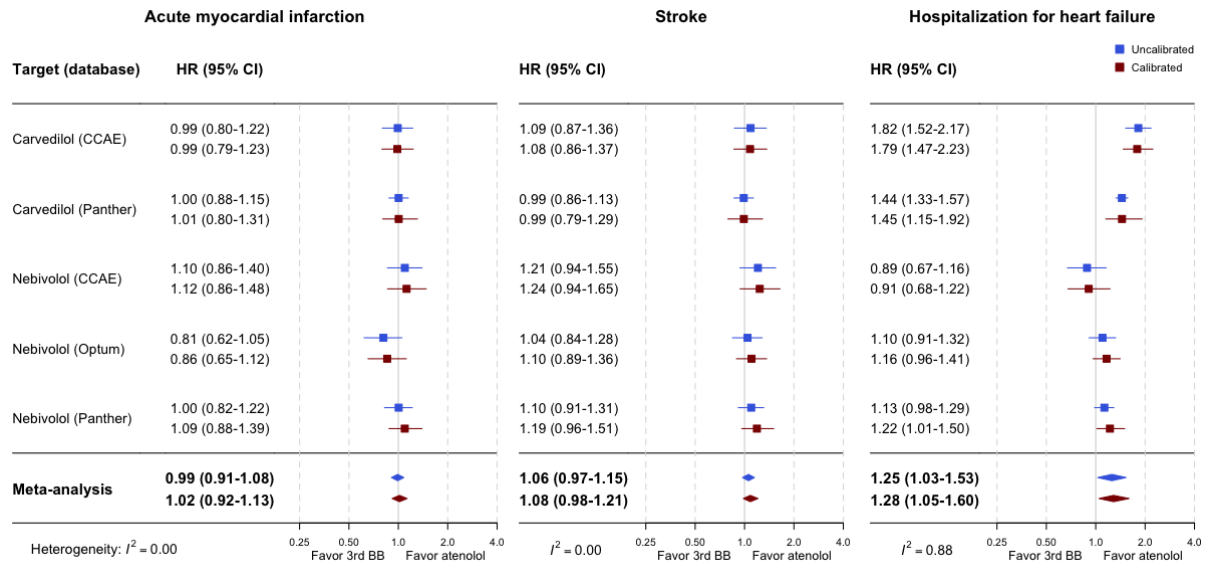


Figure S9 b: PS stratification, on-treatment

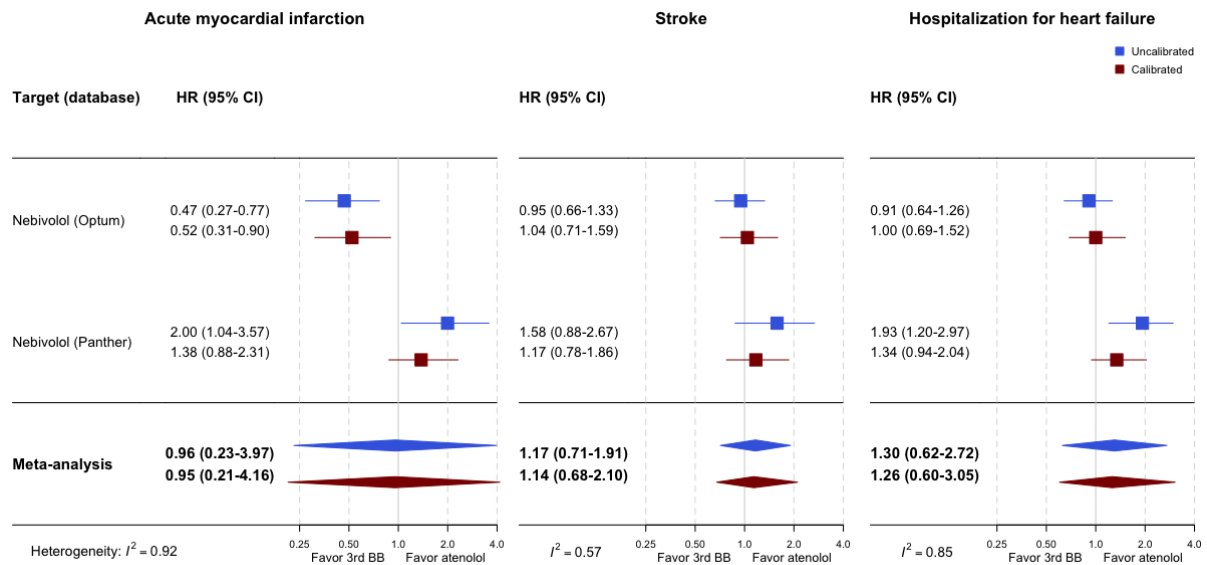
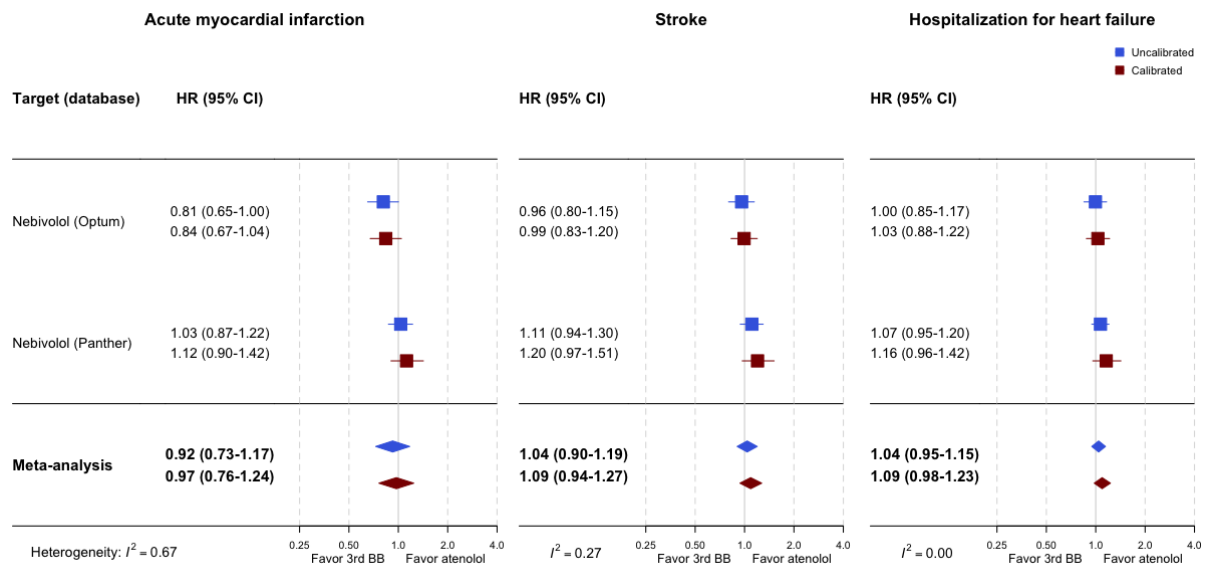


Figure S9 c: PS stratification, ITT



Abbreviation: HR, hazard ratio; CI, confidence interval; PS, propensity score; ITT, intention-to-treat; CCAE, Truven MarketScan Commercial Claims and Encounters; Optum, Optum ClinFormatics; PanTher, Optum® de-identified Electronic Health Record Dataset

Figure S10 Meta-analysis including results without sufficient balance or empirical equipoise between third-generation beta-blockers and atenolol

Figure S10 a: PS matching, on-treatment

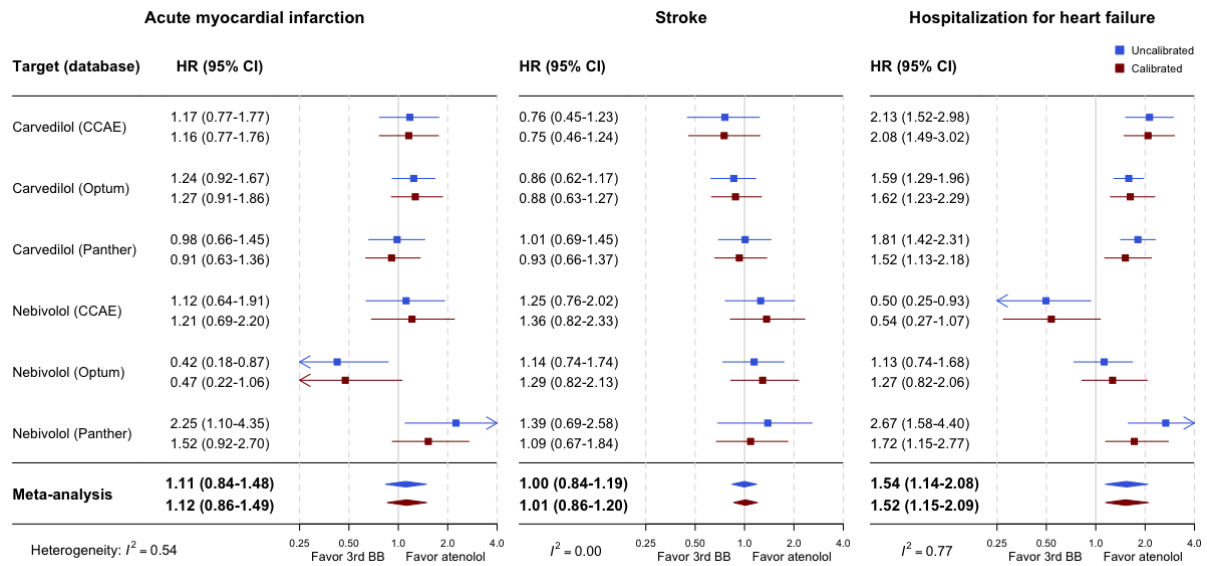


Figure S10 b: PS matching, ITT

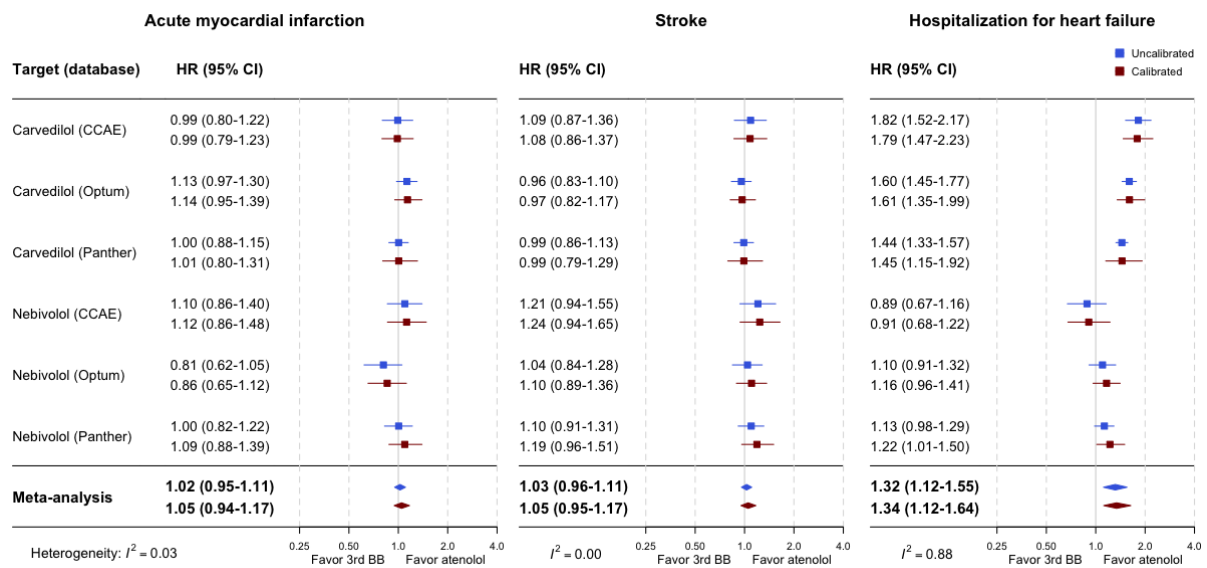


Figure S10 c: PS stratification, on-treatment

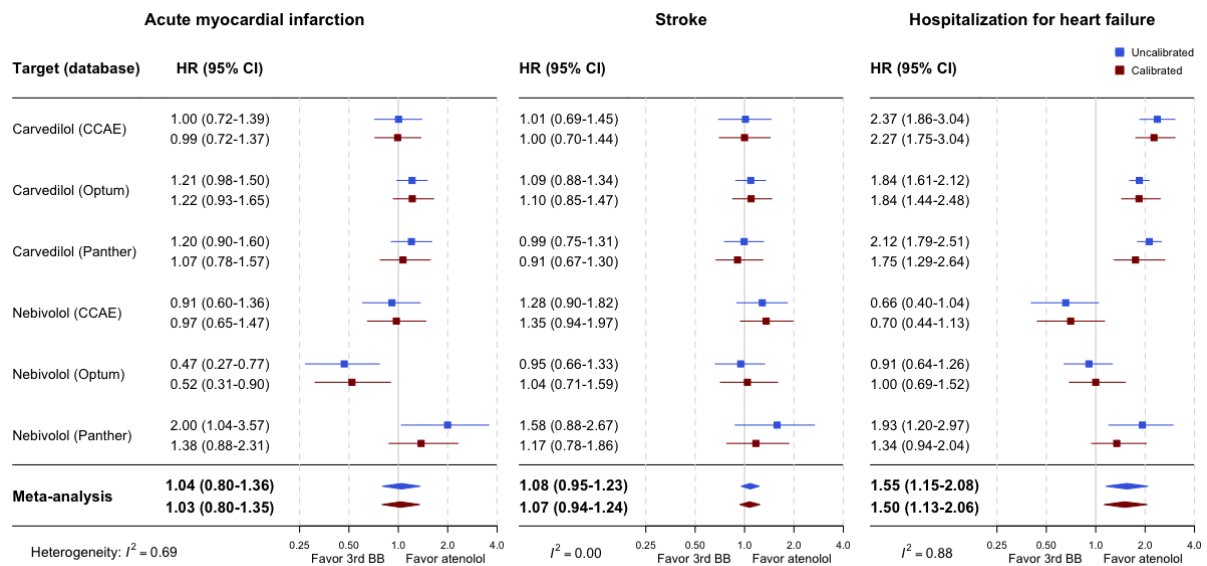
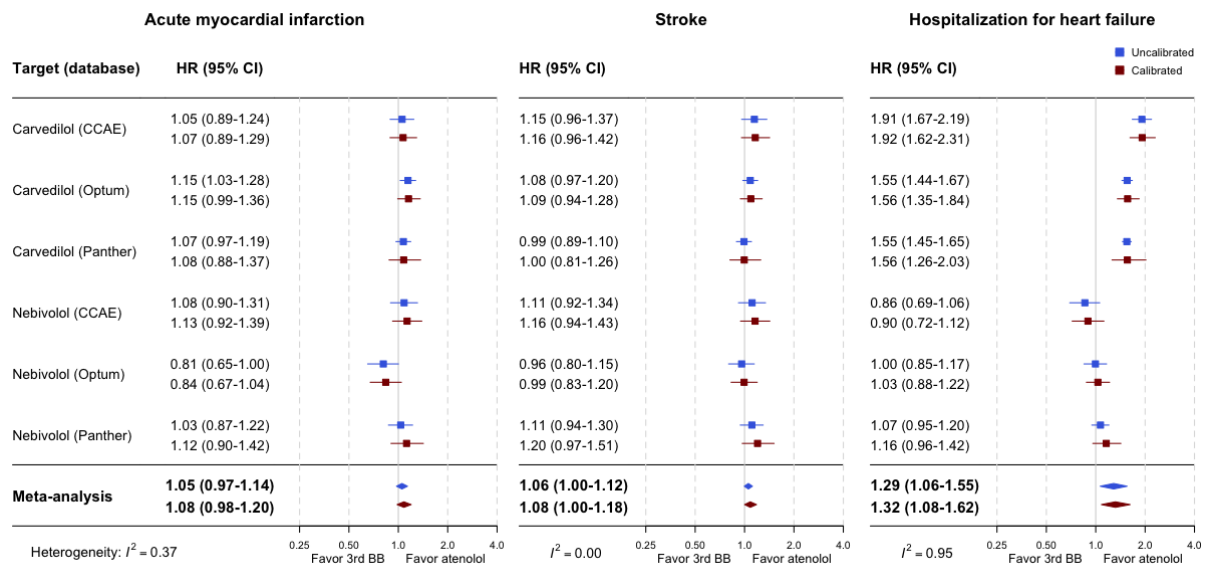


Figure S10 d: PS stratification, ITT



Abbreviation: HR, hazard ratio; CI, confidence interval; PS, propensity score; ITT, intention-to-treat; CCAEC, Truven MarketScan Commercial Claims and Encounters; Optum, Optum ClinFormatics; PanTher, Optum® de-identified Electronic Health Record Dataset

Figure S11. The meta-analytic HR estimates and their 95% CIs comparing the relative risk of acute myocardial infarction, stroke, and hospitalization for heart failure between atenolol versus other classes (PS matching, on-treatment)

Figure S11 a: atenolol versus angiotensin-converting enzyme inhibitors

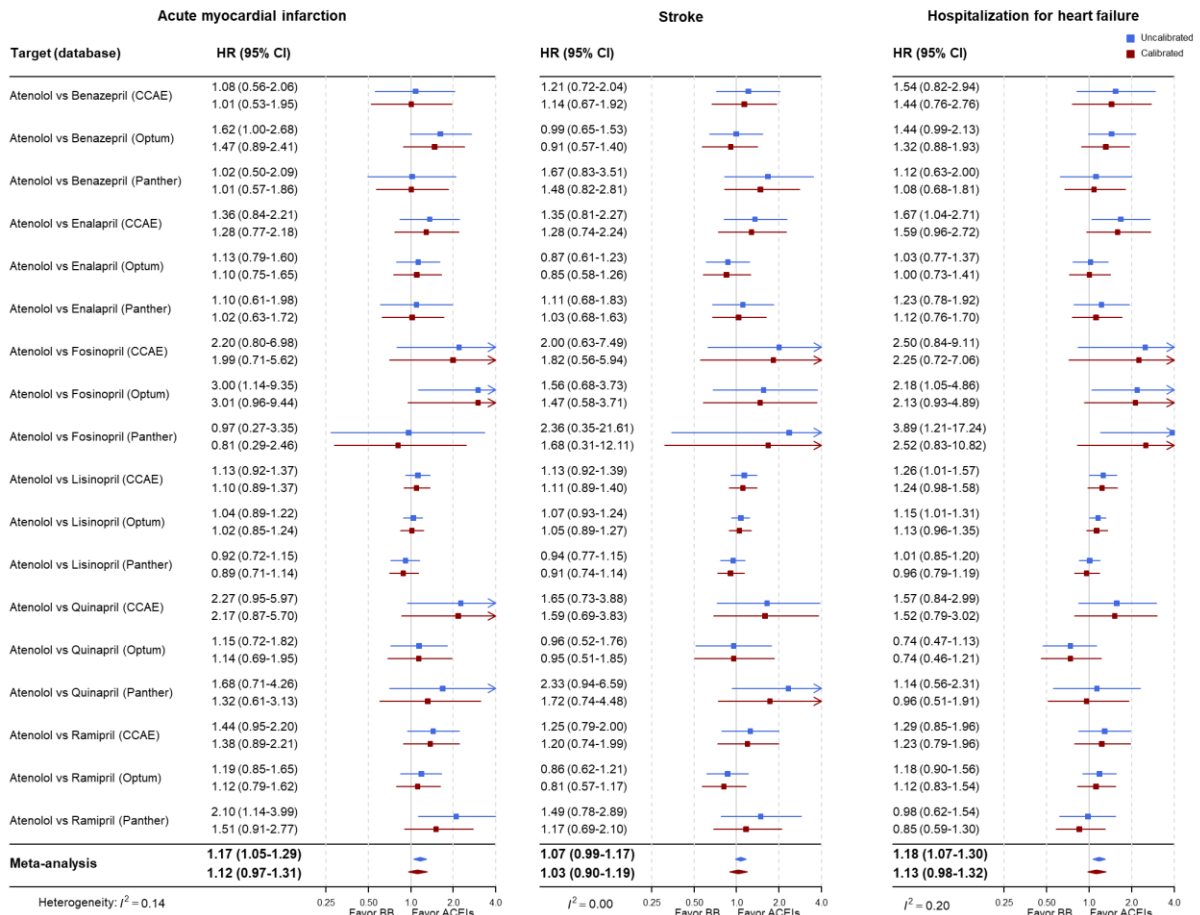


Figure S11 b: atenolol versus angiotensin receptor blockers

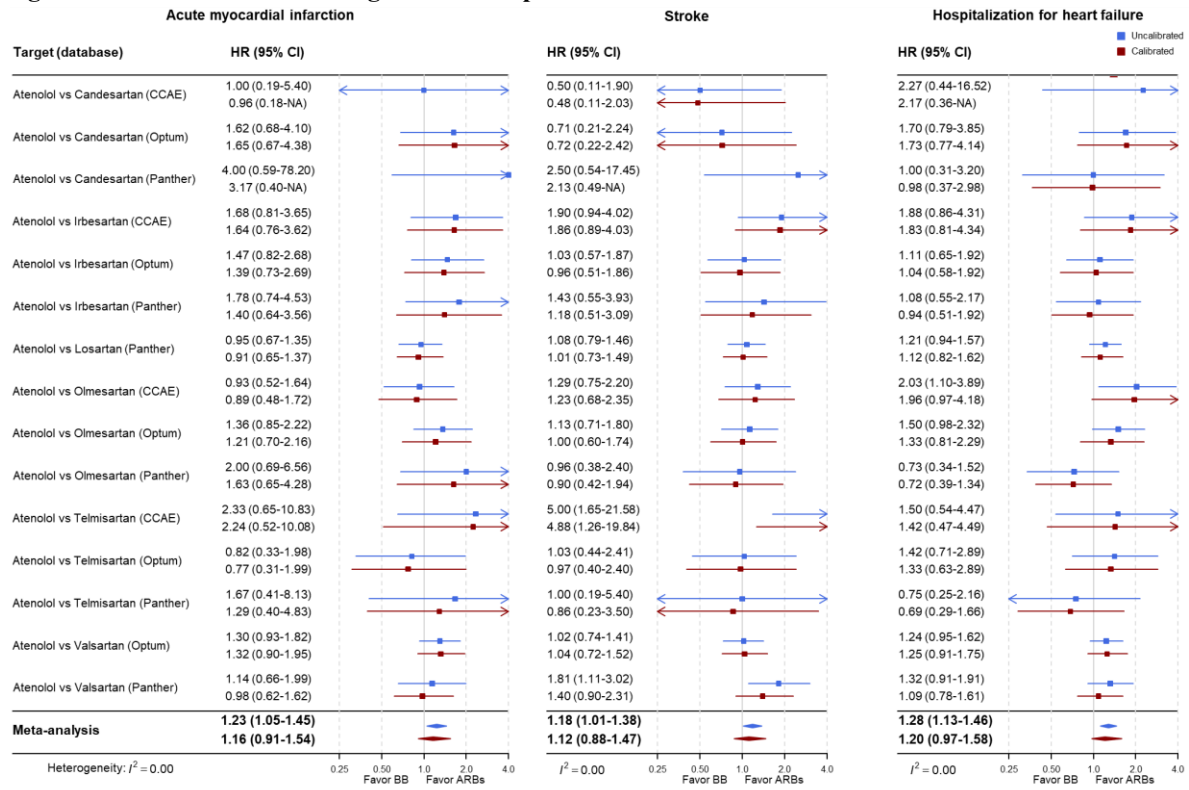


Figure S11 c: atenolol versus calcium-channel blockers

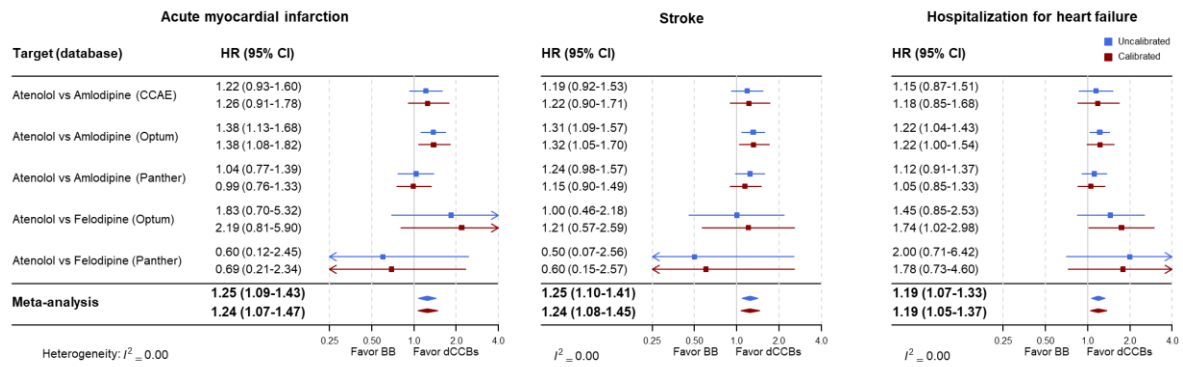
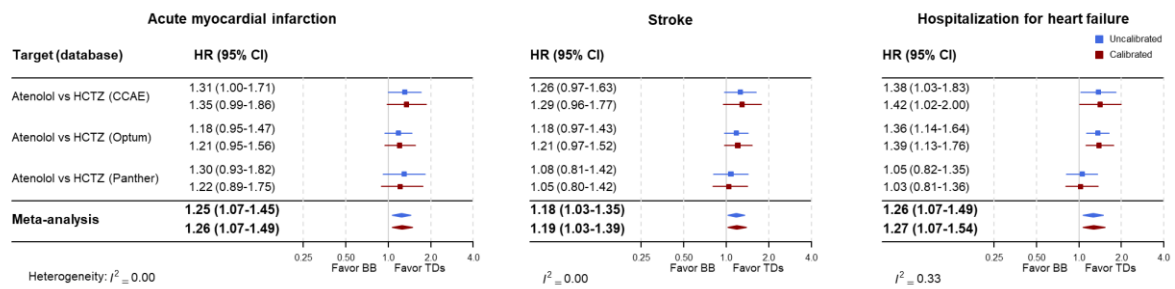


Figure S11 d: atenolol versus thiazide or thiazide-like diuretics



Abbreviation: HR, hazard ratio; CI, confidence interval; PS, propensity score; CCAE, Truven MarketScan Commercial Claims and Encounters; Optum, Optum ClinFormatics; PanTher, Optum® de-identified Electronic Health Record Dataset; HCTZ, hydrochlorothiazide

Figure S12. The meta-analytic HR estimates and their 95% CIs comparing the relative risk of acute myocardial infarction, stroke, and hospitalization for heart failure between third-generation beta-blockers versus other classes (PS matching, on-treatment)

Figure S12 a: third-generation beta-blockers versus angiotensin-converting enzyme inhibitors

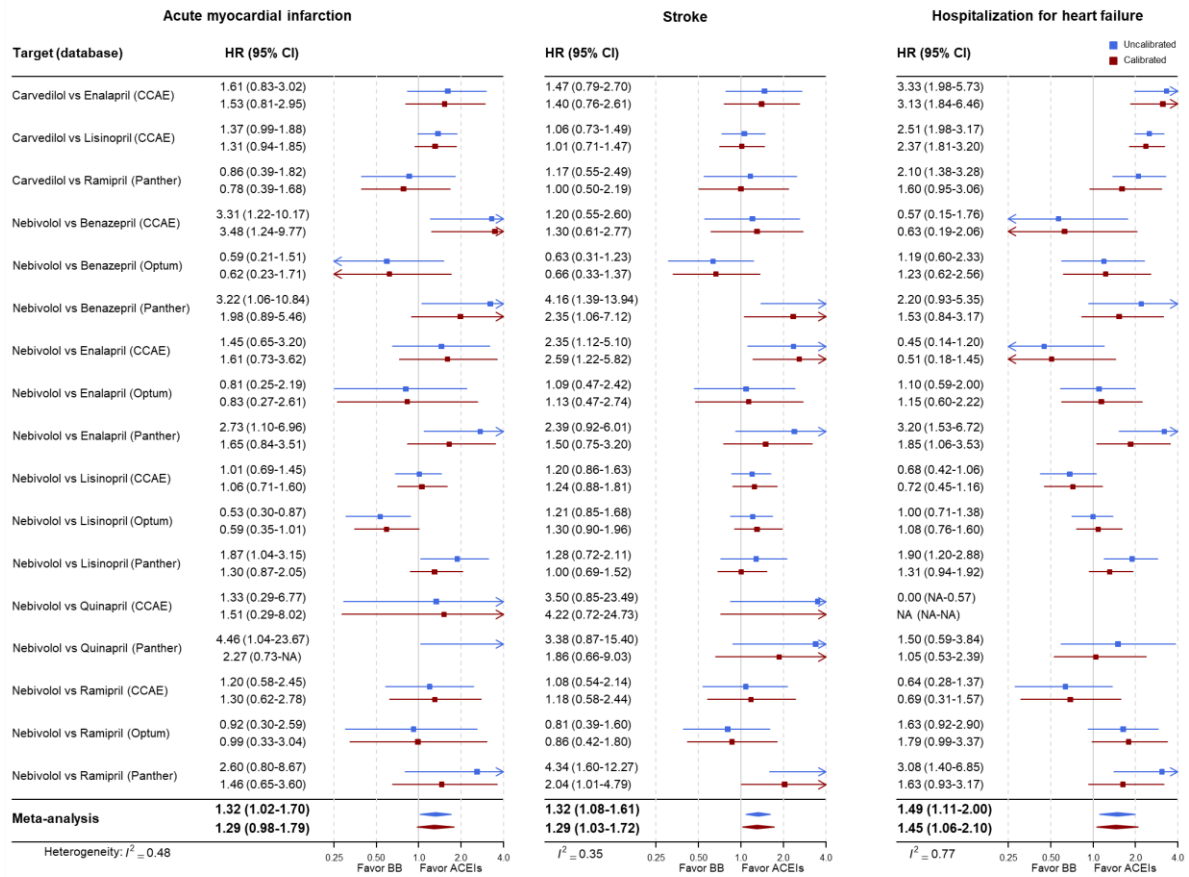


Figure S12 b: third-generation beta-blockers versus angiotensin receptor blockers

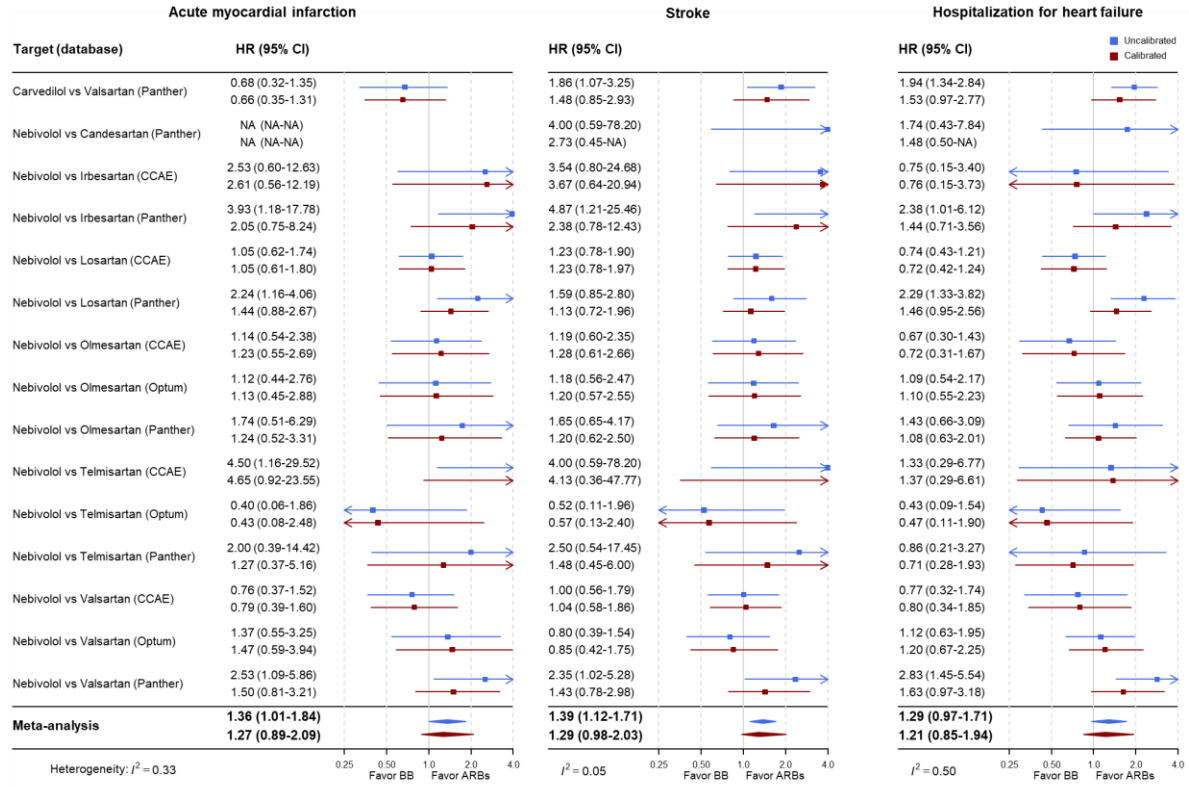


Figure S12 c: third-generation beta-blockers versus calcium-channel blockers

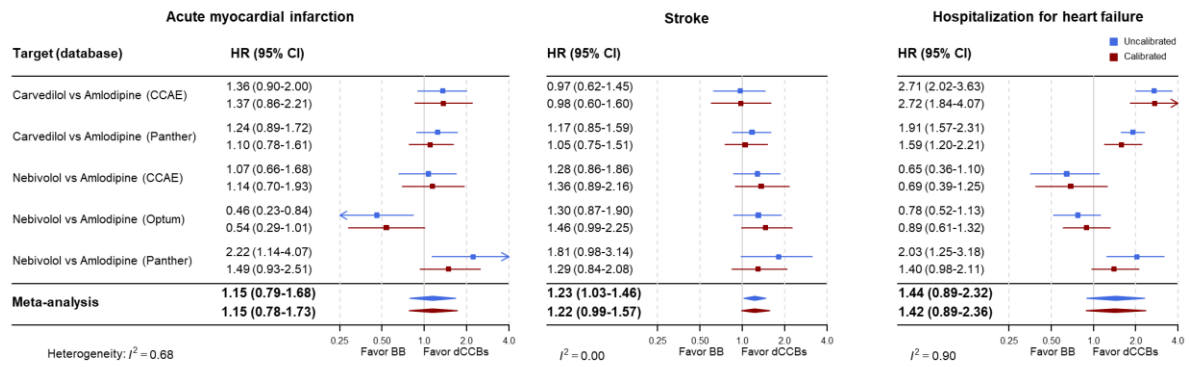
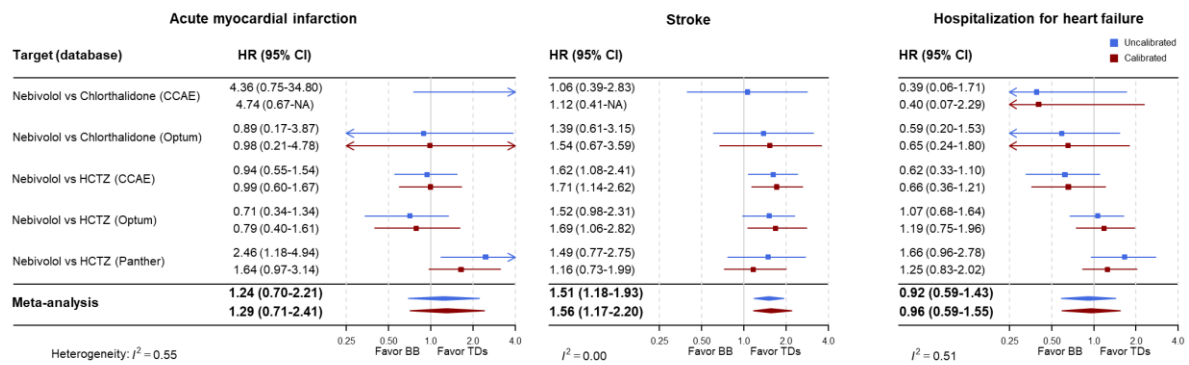


Figure S12 d: third-generation beta-blockers versus thiazide or thiazide-like diuretics



Abbreviation: HR, hazard ratio; CI, confidence interval; PS, propensity score; CCAE, Truven MarketScan Commercial Claims and Encounters; Optum, Optum ClinFormatics; PanTher, Optum® de-identified Electronic Health Record Dataset; HCTZ, hydrochlorothiazide

Figure S13. The meta-analytic HR estimates and their 95% CIs comparing the relative risk of acute myocardial infarction, stroke, and hospitalization for heart failure between metoprolol versus atenolol, carvedilol, and nebivolol (PS matching, on-treatment)

Figure S13 a: metoprolol versus atenolol

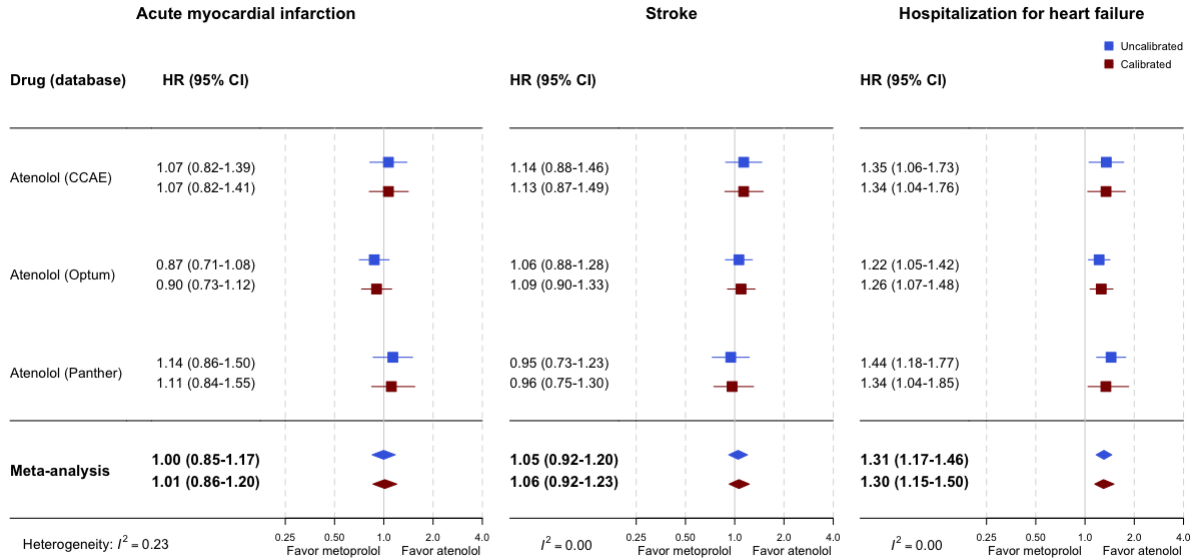


Figure S13 b: metoprolol versus carvedilol

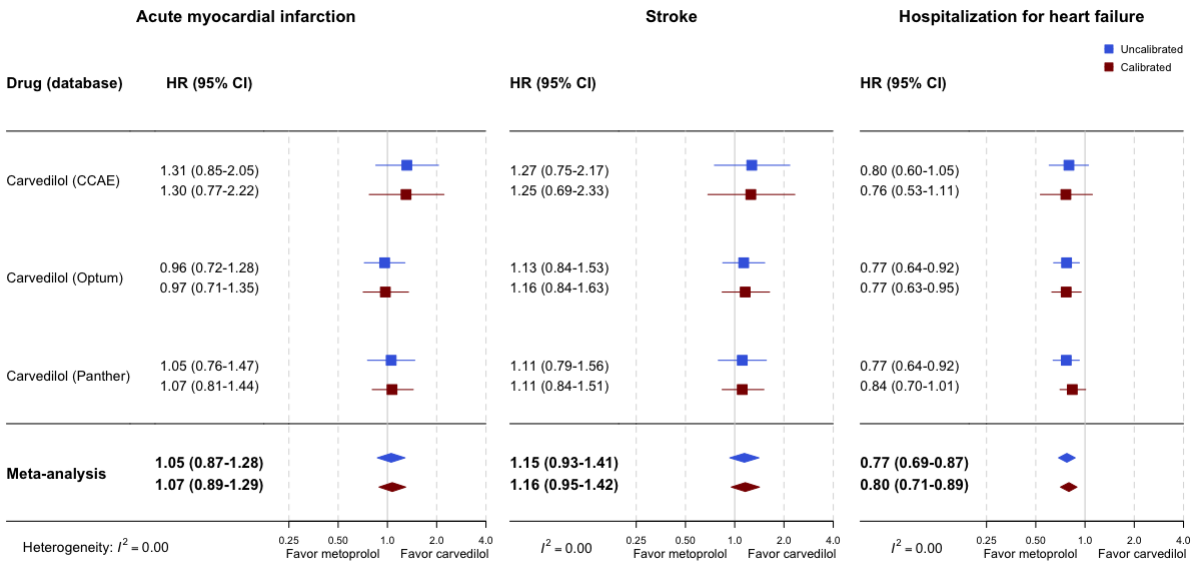


Figure S13 c: metoprolol versus nebivolol

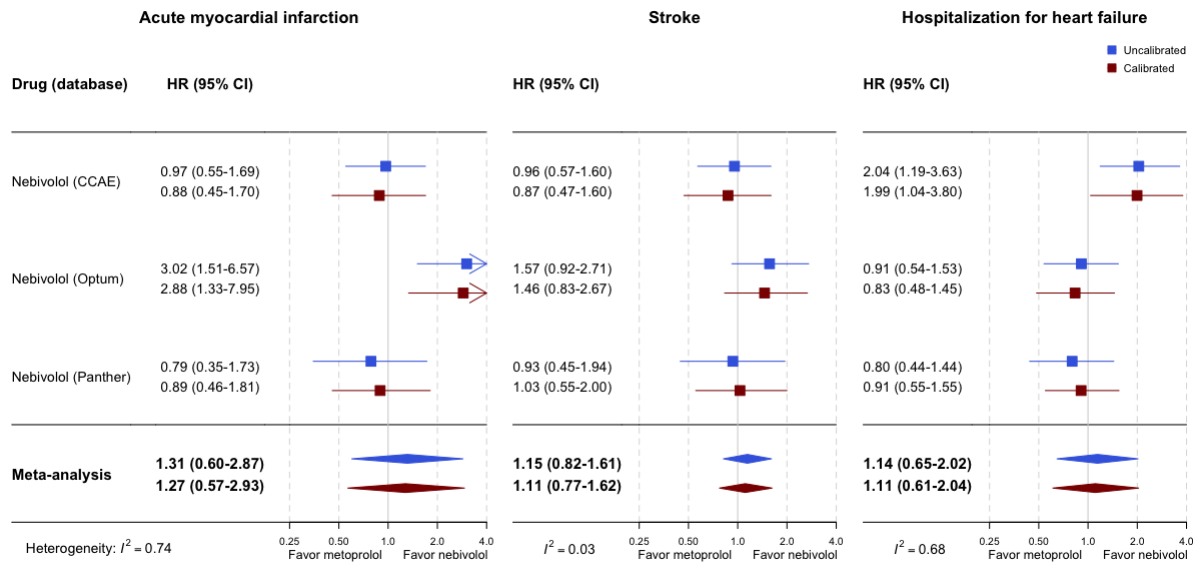


Figure S14. Meta-analytic results of secondary outcomes comparing nebivolol versus atenolol and other classes

Figure S14 a: PS stratification, on-treatment

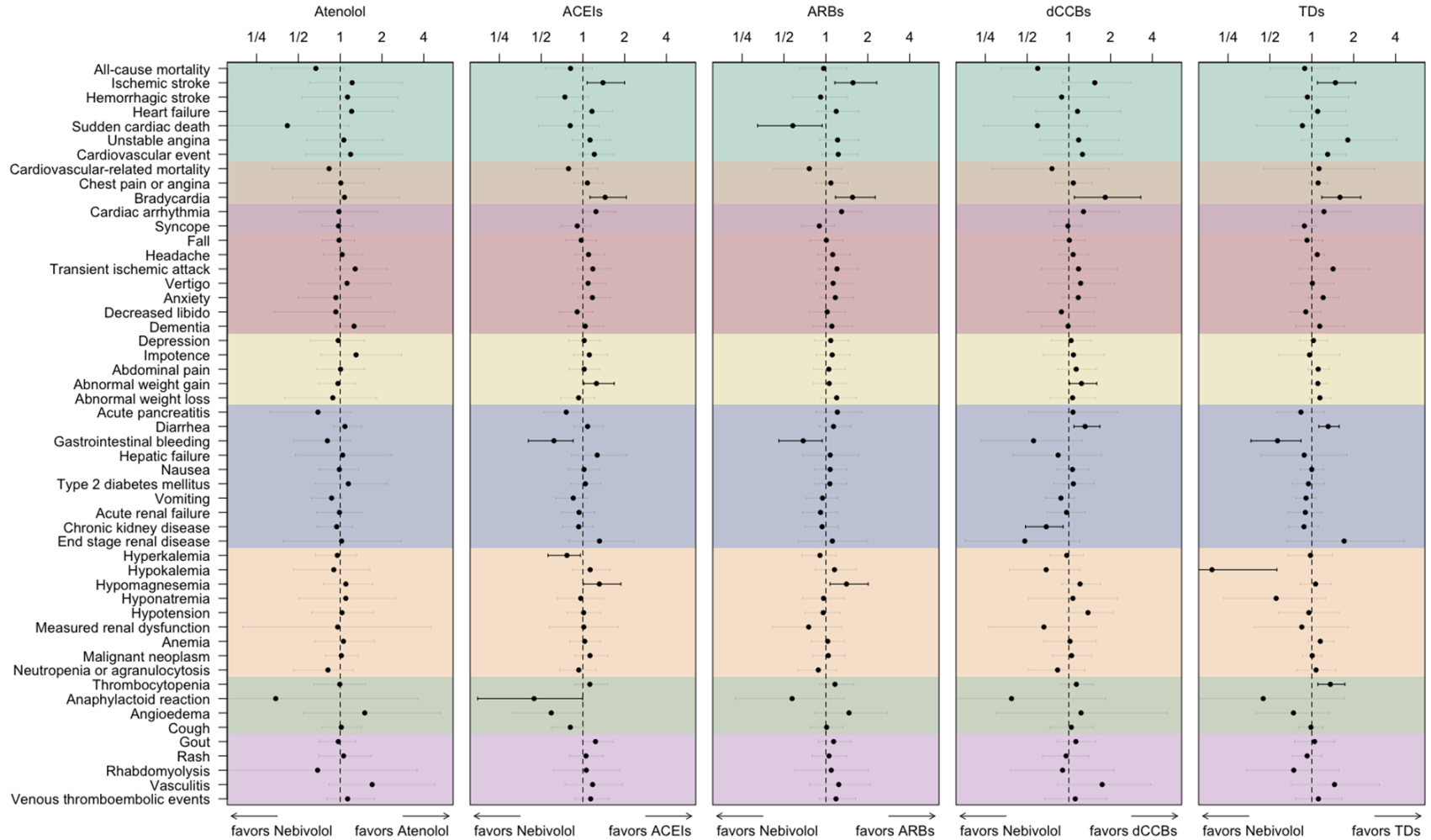


Figure S14 b: PS matching, intention-to-treat

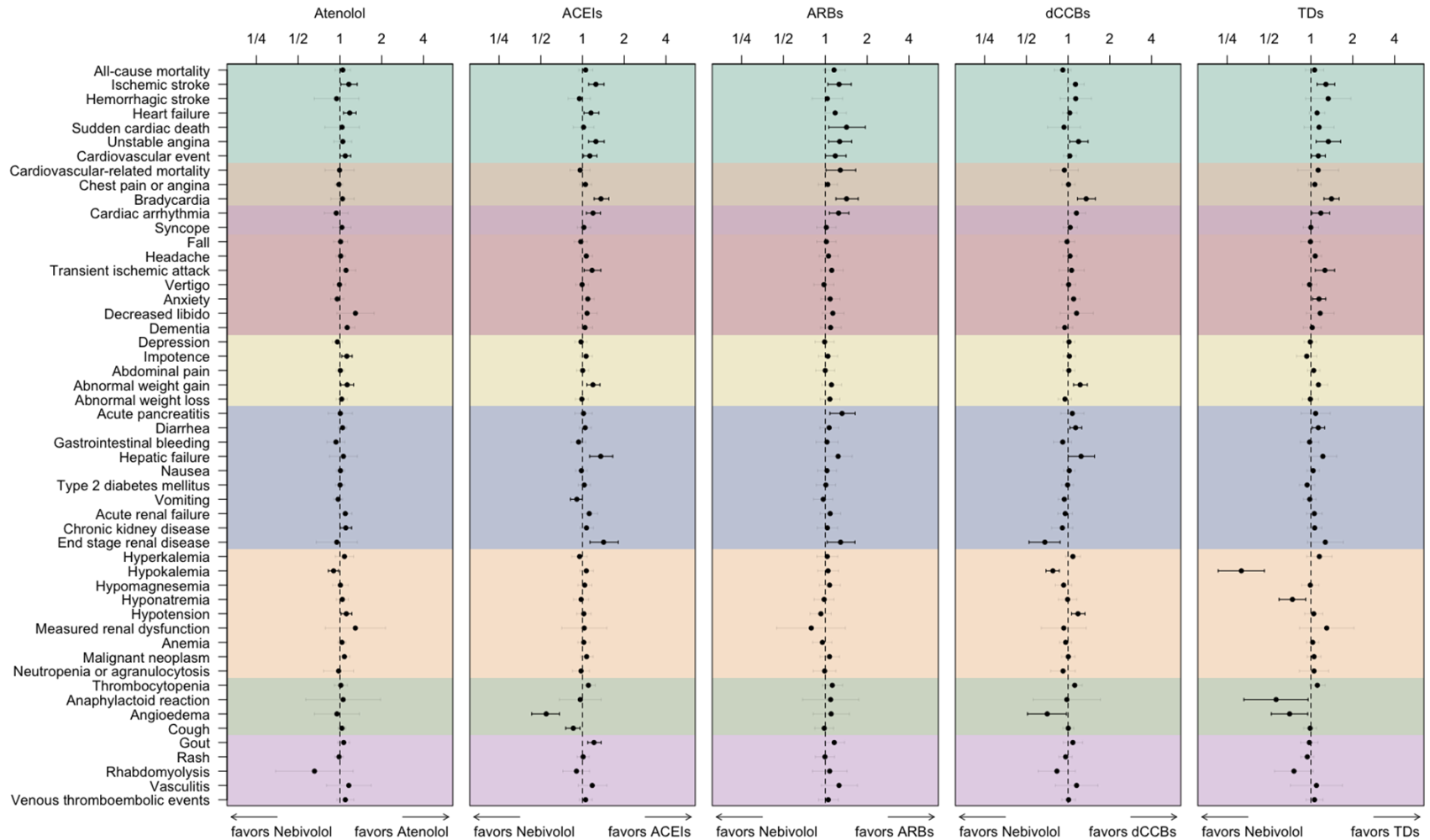
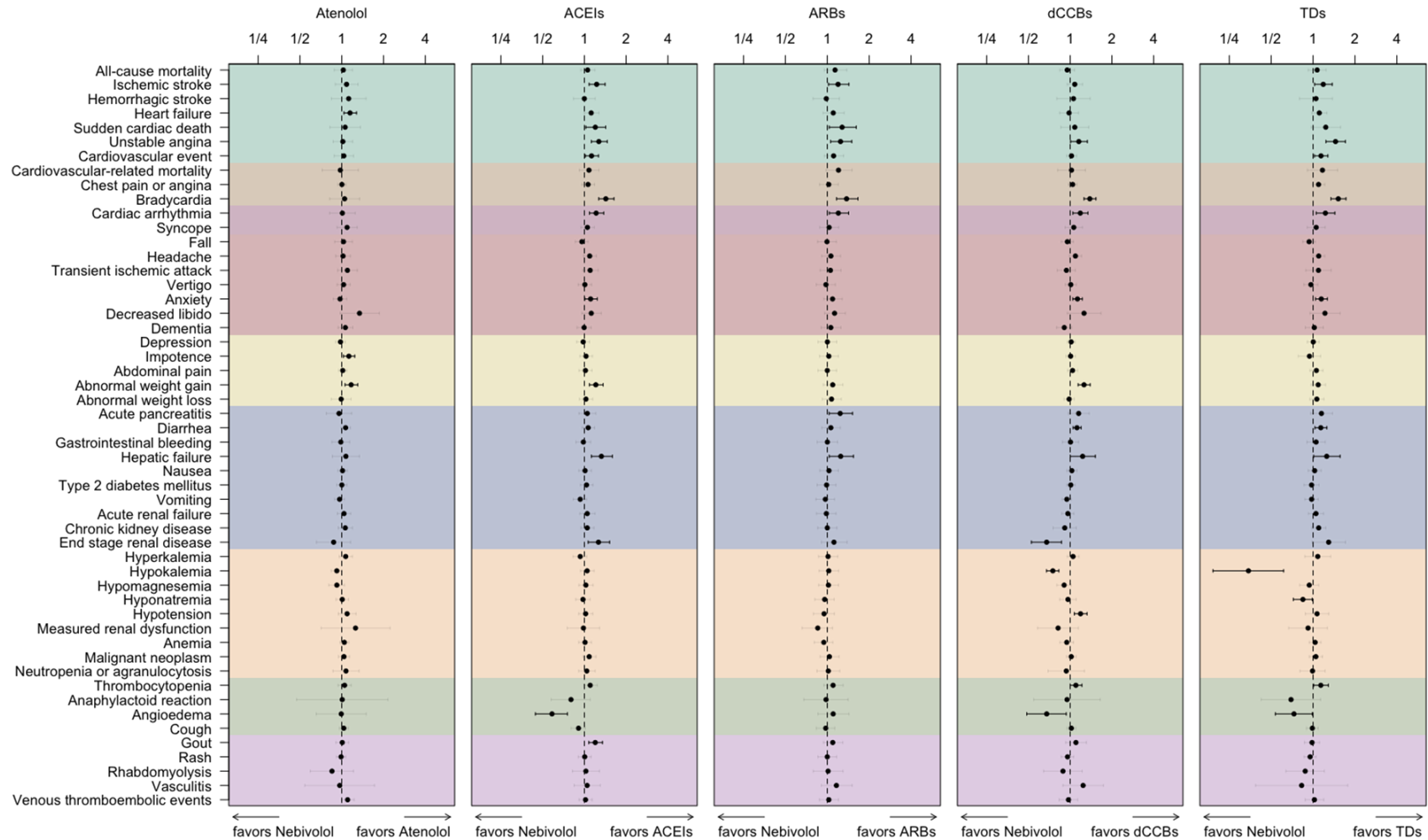


Figure S14 c: PS stratification, intention-to-treat



Meta-analytic results comparing the nebivolol versus atenolol and other classes (ACEI, ARB, dCCB, and TD) across six secondary outcomes (all-cause mortality, ischemic stroke, hemorrhagic stroke, heart failure, sudden cardiac death, unstable angina, and cardiovascular event) and 46 safety outcomes listed on product labels (PS-matching, on-treatment). Points and lines identify HR estimates with their 95% CIs,

respectively. Outcomes in grey signify that the CI covers HR of 1 (null hypothesis of no differential risk). Cardiovascular event outcome includes acute myocardial infarction, stroke, hospitalization for heart failure, and sudden cardiac death.

Abbreviations: HR, hazard ratio; CI, confidence interval; PS, propensity score; ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blocker; dCCBs, dihydropyridine calcium-channel blocker; TDs, thiazide, or thiazide-like diuretics