SUPPLEMENTARY MATERIAL

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Supplementary Table S8. Effect of the number of medication classes after excluding antiplatelet agents (beta-blockers, statins, and renin-angiotensin-aldosterone system inhibitors only) from the exposure definition (N=4,634).

Supplementary Figure S1. Flow diagram of study participant inclusion and exclusion.

Supplementary Table S1. List of Individual Beta-Blocker, Statin, Antiplatelet, and Renin Angiotensin Aldosterone System (RAAS) Medications* Considered in the Study and Details about Medication Exposure Definition

Details of the complementary approaches used to ascertain secondary prevention medication exposure, including a validation cohort using complete prescription drug dispensing data from a large, national private NH chain (HCR ManorCare, Inc., Toledo, OH), are described elsewhere.[1-3] *In brief, those approaches are important because Medicare Part D drug dispensing claims are not generated while NH residents receive care through the Skilled Nursing Facility (SNF) benefit.* [1-3]

Drug Class	**Individual Drugs**
Beta-Blockers	Acebutolol
	Atenolol
	Betaxolol
	Bisoprolol
	Carvedilol
	Labetalol
	Metoprolol
	Nadolol
	Nebivolol
	Penbutolol
	Pindolol
	Propranolol
	Timolol

Statins	Atorvastatin
	Fluvastatin
	Lovastatin
	Pitavastatin
	Pravastatin
	Rosuvastatin
	Simvastatin
Antiplatelets	Clopidogrel
Angiotensin Converting Enzyme Inhibitors	Captopril
	Benazepril
	Enalapril
	Fosinopril
	Lisinopril
	Moexipril
	Perindopril
	Quinapril
	Ramipril
	Trandolapril
Angiotensin Receptor Blockers	Candesartan
	Eprosartan
	Irbesartan
	Losartan
	Olmesartan

	Telmisartan
	Valsartan

*Only the oral formulation of all medications was considered.

Supplementary Table S2. Variables included in the propensity score estimation model.

Part A claims were also used to document characteristics of the recent AMI hospital course (including procedures), severity of cardiovascular disease, and the Elixhauser Comorbidity Index score.[4] Pre-AMI medication use was included as a marker of residents' clinically active conditions and risk of future clinical events (e.g., residents prescribed warfarin may be at higher risk of future cerebrovascular hospitalizations). A number of MDS items have been structured into reliable, valid measures of resident functional status.[5-7] The level of functional impairment for each resident was estimated with the MDS ADL score.[8] Cognitive function was measured with the Cognitive Performance Scale; scores range from 0 (intact) to 6 (severe impairment).[6] Other geriatric syndromes (weight loss, falls, presence and frequency of pain, and Changes in Health, End-Stage Disease, Signs, and Symptoms Scale (CHESS) score) and do not resuscitate (DNR) order status were also measured in the MDS. Facility characteristics and indicators of care quality were obtained from the most recent OSCAR survey before the acute AMI hospitalization.

Variable Name	**Data Source**	**Description**
chess_nh	MDS	Comorbidity index, Changes in Health, End-stage disease, and Signs and Symptoms (CHESS) Scale (0 to 5) 0=Not at all unstable,5=Highly unstable
CXBREAT_max back	MDS	Binary indicator of presence of shortness of breath in prior 7 days on last MDS assessment prior to index MI

cxdizz_maxback	MDS	Binary indicator of presence of dizziness/vertigo in prior 7 days on last MDS assessment prior to index MI
CXFL180_maxback	MDS	Binary indicator of presence of fell in the past 31 to 180 days on last MDS assessment prior to index MI
CXPAIN_maxback	MDS	Categorical variable for highest level of pain present in the prior 7 days (i.e., frequency with which resident complains or shows evidence of pain) on last MDS assessment prior to index MI
CXSYNCO_maxback	MDS	Binary indicator of presence of syncope/fainting in prior 7 days on last MDS assessment prior to index MI
dmrace	MDS	Race/ethnicity
dmsex	MDS	Gender
idage	MDS	Age at assessment
nhlos	MDS	Nursing home length of stay before MI (calculated using residential history file algorithm)
ORWTLOS	MDS	Weight loss (recent history of weight loss)
phadld	MDS	Morris additive ADL scale 0-28 (baseline)
phadld*phadld	MDS	Quadratic term for Morris additive ADL scale 0-28 (baseline)

phcps	MDS	Fries & Morris CPS index (cognitive performance score)
rhftype	MDS	Residential facility type
RXANXIE	MDS	# of days antianxiety/hypnotics
RXDEPRE	MDS	# of days antidepressants
RXHYPNO	MDS	# of days received hypnotic
RXNUMBE	MDS	Number of meds in last 7 days
RXPSYCH	MDS	# of days received antipsychotics
Dnr	MDS	Do not resuscitate order
dchrppd	OSCAR	Total direct care (RN/LPN/CNA) hrs/day/resident
lpn100t	OSCAR	Total LPN FTEs/100 beds
md100t	OSCAR	Total MD FTEs/100 beds
mdex100t	OSCAR	Total MD extender FTEs/100 beds
multifac	OSCAR	Facility is part of a chain
n_qol_def	OSCAR	OSCAR: quality-of-life deficiency score
occrate	OSCAR	OSCAR: Occupancy rate (range 0-1)
owner	OSCAR	Type of owner of nursing home

paymcaid	OSCAR	Pct Medicaid patients in nursing home
paymcare	OSCAR	Pct Medicare patients in nursing home
payoth2	OSCAR	Pct Other payer; excl Medicare residents
prov0740	OSCAR	Total number of nursing home facility beds
psychact	OSCAR	% receiving psychoactive drugs
psycha*psycha*psycha	OSCAR	Cubic term for % receiving psychoactive drugs
psychdx	OSCAR	Pct with psychiatric diagnosis
pt100t	OSCAR	Total physical therapy FTEs/100 beds
restrain	OSCAR	Pct physically restrained
rn100t	OSCAR	Total RN FTEs/100 beds
rn100t*rn100t	OSCAR	Quadratic term for total RN FTEs/100 beds
az_af	Part A	Binary indicator of presence of atrial fibrillation in 1 yr prior to index MI
az_alzheimers	Part A	Binary indicator of presence of Alzheimer's disease in 1 yr prior to index MI
az_angina_pectoris	Part A	Binary indicator of presence of angina pectoris in 1 yr prior to index MI

az_arthritis	Part A	Binary indicator of presence of arthritis in 1 yr prior to index MI
az_asthma	Part A	Binary indicator of presence of asthma in 1 yr prior to index MI
az_CHF	Part A	Binary indicator of presence of congestive heart failure in 1 yr prior to index MI
az_cop	Part A	Binary indicator of presence of chronic obstructive pulmonary disease in 1 yr prior to index MI
az_depression	Part A	Binary indicator of presence of depression in 1 yr prior to index MI
az_dm	Part A	Binary indicator of presence of diabetes mellitus in 1 yr prior to index MI
az_dyslipidemia	Part A	Binary indicator of presence of dyslipidemia in 1 yr prior to index MI
az_hypertension	Part A	Binary indicator of presence of hypertension in 1 yr prior to index MI
az_hypothyroidism	Part A	Binary indicator of presence of hypothyroidism in 1 yr prior to index MI
az_obesity	Part A	Binary indicator of presence of obesity in 1 yr prior to index MI
az_osteoporosis	Part A	Binary indicator of presence of osteoporosis in 1 yr prior to index MI
az_pvd	Part A	Binary indicator of presence of peripheral vascular disease in 1 yr prior to index MI
az_tachyarrhythmias	Part A	Binary indicator of presence of arrhythmias in 1 yr prior to index MI

az_unstable_angina	Part A	Binary indicator of presence of unstable angina in 1 yr prior to index MI
hosp_count_1yr	Part A	Number of hospitalizations in 1 yr prior to index MI, from part A inpt
ICU_CCU_group	Part A	Group: Number of days at ICU or CCU during index MI hosp stay
los_mi_stay	Part A	Number of days in the hospital during index MI hospital stay
pcicabg	Part A	Coronary revascularization or angioplasty procedures performed during the acute myocardial infarction hospitalization
max_hielix	Part A	Max of Elixhauser among hospitalizations in 1 yr prior to the index MI, from Part A inpt
d_alpha_adrenergic	Part D	Binary indicator of presence of alpha 2 adrenergic agonist drug (e.g. clonidine, guanfacine) in 1 yr prior to index MI
d_analgesic_comb	Part D	Binary indicator of presence of combination opioid analgesic drug (e.g. acetaminophen with oxycodone) in 1 yr prior to index MI
d_analgesic_opioid	Part D	Binary indicator of presence of opioid analgesic drug (e.g. oxycodone) in 1 yr prior to index MI
d_Antiarrhythmi	Part D	Binary indicator of presence of class Ib antiarrhythmic drug (e.g., lidocaine or phenytoin) in 1

c_Ib		yr prior to index MI
d_Antiarrhythmic_III	Part D	Binary indicator of presence of class III antiarrhythmic drug (e.g., amiodarone, sotalol, dofetilide) in 1 yr prior to index MI
d_Antiarrhythmic_IV	Part D	Binary indicator of presence of class IV antiarrhythmic drug (i.e., non-dihydropyridine calcium channel blockers, e.g., diltiazem or verapamil) in 1 yr prior to index MI
d_Antiarrhythmic_mis	Part D	Binary indicator of presence of antiarrthymic drug (misc) in 1 yr prior to index MI
d_Anticholinergic	Part D	Binary indicator of presence of anticholinergic drug (e.g., ipratroium, tiotropium) in 1 yr prior to index MI
d_Anticoagulant	Part D	Binary indicator of presence of anticoagulant (e.g., dabigatran) in 1 yr prior to index MI
d_Anticoagulant_cou	Part D	Binary indicator of presence of coumarin derivative anticoagulant (e.g., warfarin) in 1 yr prior to index MI
d_Antidepressant_SAR	Part D	Binary indicator of presence of antidepressant in 1 yr prior to index MI
d_Antidepressant_SNR	Part D	Binary indicator of presence of SNRI antidepressant in 1 yr prior to index MI

d_Antidepressant_SSR	Part D	Binary indicator of presence of SSRI antidepressant in 1 yr prior to index MI
d_Antilipemic_2Azeti	Part D	Binary indicator of presence of 2-azetidinone antilipemic drug (e.g., ezetimibe) in 1 yr prior to index MI
d_Antilipemic_BCS	Part D	Binary indicator of presence of bile acid sequestrant antilipemic drug (e.g., cholestyramine, colesevelam) in 1 yr prior to index MI
d_Antilipemic_Fibric	Part D	Binary indicator of presence of fibric acid antilipemic drug (e.g., gemfibrozil, fenofibrate) in 1 yr prior to index MI
d_antiparkinson_Dopa	Part D	Binary indicator of presence of dopamine agonist drug in 1 yr prior to index MI
d_Antipsychotic_atyp	Part D	Binary indicator of presence of atypical antipsychotic drug in 1 yr prior to index MI
d_Antipsychotic_typi	Part D	Binary indicator of presence of typical antipsychotic drug in 1 yr prior to index MI
d_Benzodiazepine	Part D	Binary indicator of presence of benzodiazepine drug (e.g., alprazolam, lorazepam) in 1 yr prior to index MI

d_Calcium	Part D	Binary indicator of presence of calcium channel blocker drug (e.g., amlodipine) in 1 yr prior to index MI
d_Diuretic_Loop	Part D	Binary indicator of presence of loop diuretic drug (e.g., furosemide) in 1 yr prior to index MI
d_Diuretic_Potassium	Part D	Binary indicator of presence of potassium-sparing diuretic drug (e.g., spironolactone) in 1 yr prior to index MI
d_Diuretic_Thiazide	Part D	Binary indicator of presence of thiazide diuretic drug (e.g., hydrochlorothiazide) in 1 yr prior to index MI
d_Diuretic_Thiazide_	Part D	Binary indicator of presence of thiazide-related diuretic in 1 yr prior to index MI
d_Hypnotic	Part D	Binary indicator of presence of nonbenzodiazpine hypnotic drug (e.g. zolpidem) in 1 yr prior to index MI
d_LMWH	Part D	Binary indicator of presence of low molecular weight heparin anticoagulant drug (e.g. enoxaparin) in 1 yr prior to index MI
d_nitrate	Part D	Binary indicator of presence of nitrate drug (nitroglycerin, isosorbide mononitrate, isosorbide dinitrate) in 1 yr prior to index MI
d_NSAID_cox2	Part D	Binary indicator of presence of cox-2 selective non-steroidal anti-inflammatory drug (e.g.

		celecoxib) in 1 yr prior to index MI
d_Vasodilator	Part D	Binary indicator of presence of direct-acting vasodilator drug (e.g. hydralazine) in 1 yr prior to index MI

Supplementary Table S3. Distribution of the inverse probability of treatment weights and covariate* balance between treatment groups before and after inverse probability of treatment weighting.

The inverse probability of treatment weights had a mean (standard deviation) of 1.00 (0.49) and ranged from 0.33 to 9.23.

	Absolute Standardized Mean Differences					
	2 vs 1 Meds		**3 or 4 vs 2 Meds**		**3 or 4 vs 1 Meds**	
Variable	**Before IPTW**	**After IPTW**	**Before IPTW**	**After IPTW**	**Before IPTW**	**After IPTW**
dmrace	0.00	0.01	0.06	0.04	0.06	0.05
dmsex	0.01	0.01	0.12	0.06	0.11	0.05
idage	0.15	0.06	0.18	0.05	0.33	0.10
phadld	0.10	0.05	0.10	0.03	0.20	0.08
phcps	0.09	0.01	0.13	0.06	0.22	0.07
dnr	0.01	0.05	0.11	0.03	0.20	0.08
chess_nh	0.00	0.00	0.06	0.05	0.06	0.05
rhftype	0.08	0.03	0.01	0.01	0.09	0.03
nhlos	0.08	0.03	0.07	0.00	0.16	0.03
rxpsych	0.04	0.02	0.02	0.00	0.06	0.03
rxanxie	0.05	0.04	0.04	0.05	0.01	0.01
rxdepre	0.03	0.02	0.05	0.06	0.01	0.04
rxhypno	0.04	0.03	0.01	0.02	0.03	0.01

psychdx	0.02	0.00	0.04	0.03	0.02	0.03
psychact	0.04	0.03	0.02	0.01	0.07	0.02
orwtlos	0.03	0.02	0.03	0.03	0.06	0.06
CXBREAT_maxback	0.01	0.01	0.01	0.01	0.02	0.02
CXSYNCO_maxback	0.01	0.01	0.02	0.01	0.03	0.02
cxdizz_maxback	0.02	0.02	0.00	0.01	0.02	0.00
CXFL180_maxback	0.09	0.05	0.03	0.00	0.11	0.05
CXPAIN_maxback	0.02	0.02	0.05	0.04	0.03	0.02
rxnumbe	0.07	0.05	0.04	0.01	0.12	0.06
az_CHF	0.14	0.05	0.05	0.01	0.08	0.06
az_af	0.01	0.00	0.15	0.09	0.15	0.10
az_alzheimers	0.02	0.01	0.03	0.00	0.05	0.01
az_angina_pectoris	0.11	0.03	0.07	0.05	0.17	0.08
az_arthritis	0.02	0.02	0.01	0.02	0.03	0.04
az_asthma	0.06	0.05	0.02	0.02	0.04	0.03
az_cop	0.01	0.03	0.04	0.02	0.03	0.01
az_depression	0.02	0.00	0.03	0.03	0.05	0.03
az_dm	0.07	0.04	0.15	0.06	0.22	0.09
az_dyslipidemia	0.16	0.04	0.26	0.07	0.42	0.11
az_hypertension	0.08	0.02	0.16	0.07	0.24	0.09
az_hypothyroidism	0.01	0.03	0.06	0.05	0.07	0.07
az_obesity	0.00	0.01	0.01	0.04	0.01	0.04
az_osteoporosis	0.01	0.01	0.00	0.02	0.01	0.01

az_pvd	0.02	0.02	0.07	0.04	0.10	0.06
az_tachyarrhythmias	0.01	0.02	0.02	0.02	0.01	0.00
az_unstable_angina	0.00	0.01	0.00	0.03	0.00	0.04
hosp_count_1yr	0.05	0.01	0.04	0.02	0.09	0.01
ICU_CCU_group	0.06	0.02	0.09	0.05	0.15	0.07
los_mi_stay	0.03	0.03	0.13	0.06	0.16	0.08
pcicabg	0.06	0.01	0.08	0.04	0.13	0.06
max_hielix	0.05	0.00	0.01	0.02	0.06	0.02
owner	0.02	0.00	0.00	0.00	0.02	0.01
prov0740	0.04	0.02	0.02	0.00	0.06	0.02
dchrppd	0.01	0.00	0.01	0.01	0.02	0.01
lpn100t	0.04	0.01	0.02	0.01	0.06	0.02
md100t	0.04	0.03	0.04	0.01	0.07	0.04
mdex100t	0.02	0.02	0.09	0.05	0.06	0.02
multifac	0.02	0.01	0.03	0.05	0.05	0.06
n_qol_def_wt_z	0.05	0.01	0.01	0.00	0.05	0.02
occrate	0.02	0.00	0.01	0.01	0.01	0.01
paymcaid	0.08	0.03	0.05	0.04	0.03	0.01
paymcare	0.08	0.02	0.01	0.02	0.07	0.00
payoth2	0.07	0.03	0.04	0.04	0.04	0.02
pt100t	0.07	0.05	0.06	0.06	0.00	0.01
restrain	0.02	0.01	0.01	0.00	0.03	0.01
rn100t	0.02	0.01	0.00	0.02	0.02	0.01

d_Anticoagulant	0.03	0.03	0.00	0.02	0.03	0.01
d_Anticoagulant_cou	0.13	0.06	0.03	0.01	0.16	0.08
d_Calcium	0.04	0.01	0.01	0.03	0.03	0.02
d_Diuretic_Loop	0.14	0.06	0.13	0.04	0.27	0.10
d_Diuretic_Potassium	0.02	0.01	0.13	0.10	0.16	0.09
d_Diuretic_Thiazide	0.03	0.01	0.02	0.02	0.05	0.03
d_Diuretic_Thiazide_	0.02	0.00	0.03	0.01	0.05	0.01
d_Vasodilator	0.09	0.04	0.06	0.03	0.15	0.06
d_antiparkinson_Dopa	0.03	0.00	0.06	0.06	0.09	0.06
d_analgesic_opioid	0.07	0.03	0.08	0.05	0.15	0.08
d_Antidepressant_SSR	0.12	0.05	0.07	0.02	0.20	0.07
d_Antilipemic_Fibric	0.02	0.03	0.06	0.07	0.04	0.03
d_Antilipemic_2Azeti	0.00	0.01	0.02	0.02	0.02	0.01
d_Antilipemic_BCS	0.04	0.03	0.03	0.02	0.07	0.05
d_Antipsychotic_atyp	0.00	0.03	0.05	0.03	0.05	0.00
d_Antipsychotic_typi	0.01	0.01	0.04	0.04	0.05	0.03
d_Antidepressant_SAR	0.07	0.06	0.03	0.04	0.05	0.01
d_Antidepressant_SNR	0.01	0.01	0.03	0.02	0.03	0.01
d_alpha_adrenergic	0.02	0.00	0.02	0.06	0.00	0.05
d_Benzodiazepine	0.00	0.00	0.01	0.02	0.01	0.01
d_LMWH	0.02	0.01	0.01	0.01	0.04	0.00
d_Antiarrhythmic_Ib	0.06	0.03	0.02	0.01	0.08	0.04
d_Antiarrhythmic_III	0.11	0.06	0.01	0.03	0.10	0.04

d_Antiarrhythmic_IV	0.01	0.02	0.01	0.01	0.00	0.03
d_Antiarrhythmic_mis	0.10	0.03	0.11	0.07	0.22	0.09
d_Hypnotic	0.05	0.04	0.02	0.04	0.03	0.00
d_Anticholinergic	0.08	0.04	0.09	0.03	0.16	0.06
d_NSAID_cox2	0.01	0.02	0.02	0.01	0.03	0.01
d_analgesic_comb	0.09	0.05	0.01	0.03	0.10	0.02
d_nitrate	0.08	0.02	0.05	0.02	0.13	0.05

***** A label and description for each covariate can be found in Supplementary Table S2.

Supplementary Table S4. Combinations of medication classes dispensed after acute myocardial infarction among frail, older nursing home residents.

Number of Medications	Beta-blockers	RAAS Inhibitors	Statins	Antiplatelets	n	%
4	Yes	Yes	Yes	Yes	388	8.11
3	Yes	No	Yes	Yes	317	6.62
	Yes	Yes	No	Yes	207	4.32
	Yes	Yes	Yes	No	421	8.79
	No	Yes	Yes	Yes	57	1.19
2	Yes	No	No	Yes	266	5.56
	Yes	No	Yes	No	450	9.4
	Yes	Yes	No	No	593	12.39
	No	No	Yes	Yes	91	1.9
	No	Yes	No	Yes	55	1.15
	No	Yes	Yes	No	117	2.44
1	Yes	No	No	No	1206	25.19
	No	No	No	Yes	153	3.2
	No	No	Yes	No	187	3.91
	No	Yes	No	No	279	5.83
n (%) of cohort receiving each class	3,848 (80.38)	2,117 (44.22)	2,028 (42.36)	1,534 (32.05)	Total N=4,787	Total %=100

Abbreviations: RAAS, renin-angiotensin-aldosterone system.

Supplementary Table S5. Effect of the number of medication classes on outcomes among nursing home residents after myocardial infarction stratified by age categories.

Outcome	Age Categories	No. of Medications	Events / n	Risk (%)	Crude OR (95% CI)	IPTW OR (95% CI)	P for Effect Modification*
Mortality	<=85	1	94 / 923	10.2	Reference	Reference	0.33
		2	95 / 895	10.6	1.05 (0.78-1.42)	1.16 (0.84-1.59)	
		3 or 4	57 / 886	6.4	0.61 (0.43-0.86)	0.79 (0.54-1.15)	
	>85	1	134 / 902	14.9	Reference	Reference	
		2	83 / 677	12.3	0.80 (0.60-1.08)	0.83 (0.61-1.13)	
		3 or 4	46 / 504	9.1	0.58 (0.40-0.82)	0.70 (0.48-1.04)	
Rehospitalization	<=85	1	255 / 923	27.6	Reference	Reference	0.30
		2	269 / 895	30.1	1.12 (0.91-1.38)	1.06 (0.85-1.32)	
		3 or 4	239 / 886	27.0	0.93 (0.75-1.14)	0.90 (0.70-1.17)	
	>85	1	194 / 902	21.5	Reference	Reference	
		2	144 / 677	21.3	0.94 (0.73-1.20)	0.93 (0.72-1.20)	
		3 or 4	122 / 504	24.2	1.06 (0.82-1.38)	1.08 (0.80-1.45)	

Functional Decline	<=85	1	149 / 923	16.1	Reference	Reference	0.29
		2	163 / 895	18.2	1.17 (0.91-1.50)	0.94 (0.71-1.24)	
		3 or 4	204 / 886	23.0	1.50 (1.18-1.90)	1.13 (0.85-1.49)	
	>85	1	110 / 902	12.2	Reference	Reference	
		2	111 / 677	16.4	1.37 (1.02-1.82)	1.23 (0.91-1.67)	
		3 or 4	83 / 504	16.5	1.32 (0.97-1.81)	1.11 (0.76-1.60)	

Abbreviations: OR, odds ratio; CI, confidence interval; IPTW, inverse probability of treatment-weighted.

*Presented for the IPTW estimates only.

Supplementary Table S6. Effect of the number of medication classes on outcomes among frail, older nursing home residents after myocardial infarction with weight truncation at the 1st and 99th percentiles.

In a stability analysis, we truncated the IPTW at the 1st and 99th percentiles to explore the tradeoff between bias and variance.[9]

Outcome	**No. of Medications**	**Truncated IPTW OR (95% CI)**
Mortality	1	Reference
	2	0.97 (0.78-1.21)
	3 or 4	0.75 (0.57-0.98)
Rehospitalization	1	Reference
	2	1.00 (0.85-1.18)
	3 or 4	0.95 (0.79-1.14)
Functional Decline	1	Reference
	2	1.08 (0.88-1.31)
	3 or 4	1.15 (0.93-1.42)

Abbreviations: OR, odds ratio; CI, confidence interval; IPTW, inverse probability of treatment-weighted.

Supplementary Table S7. Effect of the number of medication classes on outcomes among frail, older nursing home residents after myocardial infarction after adjustment for covariates* with absolute standardized mean differences greater than 0.08 after inverse probability of treatment weighting.

In a second stability analysis, we included covariates with absolute standardized mean differences greater than 0.08 (Supplementary Table S3) after IP weighting in the outcome models to account for any potential residual confounding bias.

Outcome	**No. of Medications**	**Covariate-Adjusted IPTW OR (95% CI)**
Mortality	1	Reference
	2	0.98 (0.78-1.22)
	3 or 4	0.74 (0.56-0.97)
Rehospitalization	1	Reference
	2	1.00 (0.84-1.19)
	3 or 4	0.95 (0.79-1.15)
Functional Decline	1	Reference
	2	1.06 (0.86-1.29)
	3 or 4	1.15 (0.93-1.44)

Abbreviations: OR, odds ratio; CI, confidence interval; IPTW, inverse probability of treatment-weighted.

*Covariates adjusted for included d_Diuretic_Potassium, az_af, az_hypertension, d_Antiarrhythmic_misc, d_Diuretic_Loop, az_dm, idage, az_dyslipidemia, az_angina_pectoris, los_mi_stay, d_analgesic_opioid, phadld, and d_Anticoagulant_cou (see Supplementary Table S2 for a label and description of each covariate).

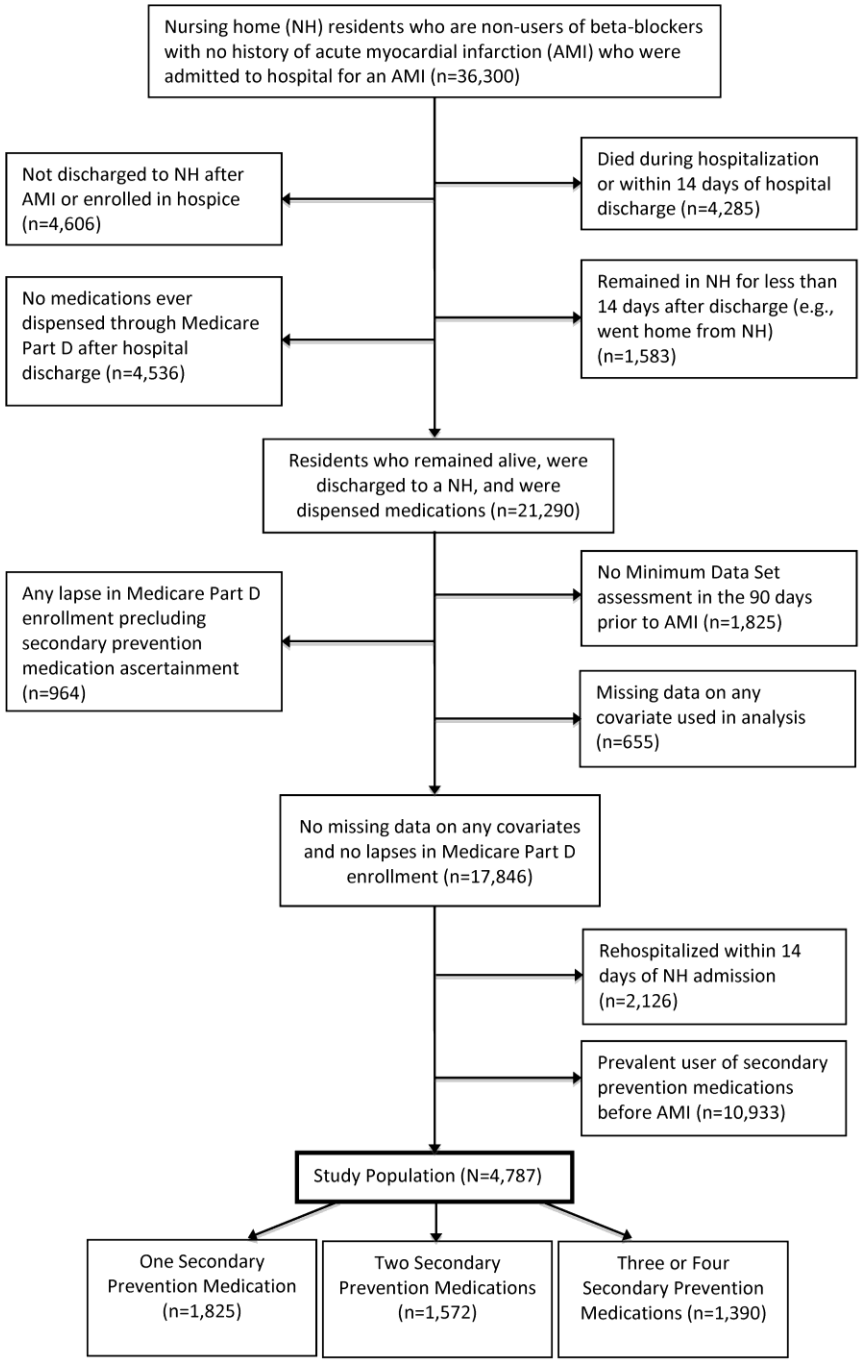
Supplementary Table S8. Effect of the number of medication classes after excluding antiplatelet agents (beta-blockers, statins, and renin-angiotensin-aldosterone system inhibitors only) from the exposure definition (N=4,634).

In a third stability analysis, we excluded users of antiplatelet agents because aspirin is a recommended antiplatelet agent (in addition to clopidogrel, or more rarely, as an alternative), but is available without a prescription and thus underascertained in Medicare claims, which could result in biased estimates.

Outcome	**No. of Medications**	**Events / n**	**Risk (%)**	**Crude OR (95% CI)**	**IPTW OR (95% CI)**
Mortality	1	254 / 2084	12.2	Reference	Reference
	2	174 / 1741	10.0	0.80 (0.65-0.98)	0.87 (0.71-1.07)
	3	61 / 809	7.5	0.59 (0.44-0.79)	0.71 (0.52-0.97)
Rehospitalization	1	521 / 2084	25.0	Reference	Reference
	2	444 / 1741	25.5	0.99 (0.86-1.15)	0.92 (0.79-1.07)
	3	220 / 809	27.2	1.05 (0.87-1.26)	0.96 (0.79-1.18)
Functional Decline	1	293 / 2084	14.1	Reference	Reference
	2	333 / 1741	19.1	1.41 (1.19-1.68)	1.27 (1.07-1.53)
	3	172 / 809	21.3	1.57 (1.27-1.94)	1.30 (1.03-1.63)

Abbreviations: OR, odds ratio; CI, confidence interval; IPTW, inverse probability of treatment-weighted.

Supplementary Figure S1. Flow diagram of study participant inclusion and exclusion.



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