**Supplementary Online Content**

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This supplementary material has been provided by the authors to give readers additional information about their work.

**eAppendix 1. Additional Information on Methods**

Development of the study cohort: additional information

We defined acute myocardial infarction (AMI) as a principal or secondary diagnosis of ICD9 code 410.XX or 411.1 on a Medicare Part A hospital discharge or admission claim between May 1, 2007 and March 31, 2010. Validation studies suggest that this approach is highly accurate for identifying Medicare patients hospitalized for AMI, with a positive predictive value of 94%.[1] Similarly, a recent systematic review found high sensitivity (76-100%) among a variety of claims-based diagnoses of AMI, most using a similar ICD9 diagnosis framework.[2]

The most common causes of exclusion were failure to return to a nursing home and remain there for 14 days, and lack of Part D data (e.g. due to lack of Part D insurance coverage) in the post-hospital period.

References:


1. Kiyota Y, Schneeweiss S, Glynn RJ, Cannuscio CC, Avorn J, Solomon DH. Accuracy of Medicare claims-based diagnosis of acute myocardial infarction: estimating positive predictive value on the basis of review of hospital records. Am Heart J. 2004 Jul;148(1):99-104.

2. Rubbo B, Fitzpatrick NK, Denaxas S, Daskalopoulou M, Yu N, Patel RS; UK Biobank Follow-up and Outcomes Working Group, Hemingway H. Use of electronic health records to ascertain, validate and phenotype acute myocardial infarction: A systematic review and recommendations. Int J Cardiol. 2015;187:705-11.


Nursing home care pathways and medication ascertainment: implications for methods.

In the immediate post-hospital period, long-stay nursing home patients who return to their nursing homes typically enter one of two care pathways. Some patients immediately re-enter the standard long-term care (LTC) pathway, in which Medicare Part D pays for medications, and other sources (typically Medicaid, private long-term care insurance, or self-pay) fund other costs. Patients with short-term rehabilitation potential or skilled nursing needs may be covered in the short term by the Medicare Part-A funded Skilled Nursing Facility (SNF) benefit. Bundled payments under the SNF benefit include medication purchases. After a short period (typically about 1 month, and at most 100 days), long-stay patients transition back to the long-term care pathway, in which Medicare Part D once again covers drug purchases. Note that both SNF-benefit care and long-term care typically occur in the same facility; the patient stays in his or her usual bed regardless, but the payment mechanism and services provided differ.

Because we were unable to directly observe beta blocker prescriptions using Part D claims while patients were on the Medicare SNF benefit, we conducted a validation study using enriched pharmacy data from a national nursing home chain (Manor Care) to evaluate the relationship between beta blocker use that occurred during the SNF-funded care and beta blocker use that occurred after those patients had transitioned back to long-term care. In this validation study, over 94% of nursing home residents who used beta blockers after transitioning to long-term care had also used these drugs during their SNF care. To evaluate comparability of Manor Care residents to residents of other facilities in our main cohort, we compared characteristics of Manor Care vs. non-Manor Care subjects (Table A1, below). Most characteristics were similar. Together, this suggests it is reasonable to use beta blocker use in the post-SNF phase to evaluate whether patients were using beta blockers while covered under the Medicare SNF benefit.

We chose a 30-day grace period for evaluating beta blocker use after resumption of Part D coverage because this allows for delays in ordering these medications through Part D. This includes time for patients to utilize the limited supply of medications that an acute care hospital may send with the patient upon their return to the nursing home before a new supply is ordered, or for the patient to utilize a supply of drug that was purchased while on SNF-benefit care and is still available to use even after transitioning to long-term care. In nursing homes, the maximum allowable days supply for a medication purchase is 30 days.

**Table A1. Characteristics of Manor Care Residents and Non–Manor Care Residents in the Main Analytic Cohort**

| Characteristic | No. (%) | |
|---|---|---|
| | Manor Care (N=218) | Non–Manor Care (N=10,774) |
| Age, mean (SD) years | 84 (8) | 83 (8) |
| Female sex | 146 (67.0) | 7,642 (70.9) |
| Race | | |
| Caucasian | 185 (84.9) | 8,797 (81.7) |
| African-American | 28 (12.8) | 1,262 (11.7) |
| Other | 5 (2.3) | 715 (6.6) |
| Chronic conditions | | |
| Diabetes | 74 (33.9) | 3,075 (28.5) |
| Heart failure | 107 (49.1) | 5,009 (46.5) |
| COPD | 75 (34.4) | 2,927 (27.2) |
| Depression | 32 (14.7) | 1,250 (11.6) |
| Elixhauser comorbidity score, median, (IQR) | 3 (2-4) | 3 (3-4) |
| ADL status prior to hospitalization * | | |
| Independent to limited assistance required | 55 (25.2) | 3,645 (33.8) |
| Extensive assistance required | 80 (36.7) | 3,499 (32.5) |
| Extensive dependency | 83 (38.1) | 3,630 (33.7) |
| Cognitive status prior to hospitalization * | | |
| Intact or borderline intact | 76 (34.9) | 3,089 (28.7) |
| Mild to moderate dementia | 133 (61.0) | 6,466 (60.0) |
| Moderately severe to very severe dementia | 9 (4.1) | 1,219 (11.3) |
| CHESS score prior to hospitalization, mean (SD) | 0.7 (0.8) | 0.6 (0.8) |
| Symptoms, geriatric prior to hospitalization | | |
| Dizziness, vertigo, or syncope | 3 (1.4) | 106 (1.0) |
| Falls | 45 (20.6) | 2,335 (21.7) |
| Dyspnea | 15 (6.9) | 901 (8.4) |
| Number of medications | 12 (9-16) | 12 (8-15) |
| Baseline medication use * | | |
| Statins | 65 (29.8) | 3,074 (28.5) |
| Antiplatelets | 46 (21.1) | 1,784 (16.6) |
| Warfarin | 34 (15.6) | 1,396 (13.0) |
| Psychotropics | 130 (59.6) | 6,899 (64.0) |
| Length of hospital stay for AMI, median (IQR) days | 6 (4-9) | 6 (4-9) |
| Number of days in ICU / CCU | | |
| None | 84 (38.5) | 4,651 (43.2) |
| 1 to 2 | 57 (26.2) | 2,715 (25.2) |
| 3 or more | 77 (35.3) | 3,408 (31.6) |
| Nursing home care pathway after hospitalization | | |
| Skilled nursing facility (SNF) benefit | 170 (78.0) | 7,591 (70.5) |
| Long-term care | 48 (22.0) | 3,183 (29.5) |

| Nursing Home Facility Characteristics | | |
|---|---|---|
| Size | | |
| <100 beds | 23 (10.6) | 3,033 (28.2) |
| 100-200 beds | 174 (79.8) | 6,252 (58.0) |
| >200 beds | 21 (9.6) | 1,489 (13.8) |
| Quality indicators | | |
| % of residents restrained, median (IQR) | 1.5 (0.0-4.0) | 3.0 (0.4-6.7) |
| No. of quality-of-life deficiencies, mean (SD) | 1.0 (1.1) | 0.7 (1.1) |
| % of residents with pressure sores, mean (SD) | 7.3 (3.9) | 7.1 (4.5) |
| Staffing | | |
| Direct care hours/resident/day, mean (SD) | 3.3 (0.6) | 3.4 (0.8) |

* ADL status was measured by the Morris 28-point ADL score, and categorized as 0-14 (independent to limited assistance required), 15-19 (extensive assistance required), and ≥20 (extensive dependency). Cognitive status was measured by Cognitive Performance Scale (CPS) and trichotomized as 0-1 (intact to borderline intact), 2-3 (mild to moderate dementia), and 4-6 (moderately-severe to very severe dementia). Psychotropics include antidepressants, antipsychotics, antianxiety medications, and sedative/hypnotics.

Assessing Functional Decline

We used the validated 28-point Morris Activity of Daily Living (ADL) scale, derived from MDS 2.0 data, to evaluate functional decline. Periodic MDS assessments by a trained assessor, typically a member of the nursing home staff, are mandated for all patients in Medicare- or Medicaid-certified nursing homes. They occur on a set schedule, occurring a minimum of every 3 months, and more often for patients with a substantial recent change in clinical status and those receiving care under the SNF benefit. During assessments, independence in each of 7 ADLs is evaluated on scale from 0 (independent) to 4 (total dependence). These are summed to create a 28-point score. To evaluate functional decline, we subtracted the baseline ADL assessment (i.e. the most recent assessment prior to the index MI) from the first follow-up assessment between 15-114 days after discharge from the AMI hospitalization. We did not evaluate MDS assessments in days 0-14 following hospitalization to be consistent with our exclusion criteria, which excluded people who died or were rehospitalized during this period. (This is because it is difficult to reliably ascertain beta blocker exposure in the post-hospitalization period among people who leave the nursing home shortly after returning to it). We also added a grace period of 2 weeks at the end of the 90-day post-hospital period to capture additional MDS assessments (i.e., days 91-114). We added this grace period because MDS assessments are conducted only intermittently, and reflect changes in clinical status that have already occurred prior to the assessment. Moreover, they are mandated to occur at least once per 90 days, thus giving a full 90 days of available followup time after day 15. We defined a decline in 3 points or greater to be a meaningful functional decline. We chose this threshold because it represents a meaningful drop in functional decline and is common enough to be present in a reasonable proportion of subjects.

Censoring in Outcomes Analyses:

We did not censor for any events other than outcome and end of follow-up period. This is because we had complete ascertainment of death regardless of residence and Medicare status, and for the outcome of hospitalization is it extremely uncommon for older adults to be disenrolled from Medicare. For the functional status outcome, leaving the nursing home could affect outcome ascertainment. We thus explored several potential approaches to censoring for this outcome, but all returned essentially identical results – in large part because only 3% of subjects in our cohort had zero MDS assessments of functional status in the first 90 days after hospitalization.

**eAppendix 2. Variables Included in Propensity Score Model**

| 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_maxback | MDS | Binary indicator of presence of shortness of breath in prior 7 days on last MDS assessment prior to index MI (LOCF) |
| cxdizz_maxback | MDS | Binary indicator of presence of dizziness/vertigo in prior 7 days on last MDS assessment prior to index MI (LOCF) |
| CXFL180_maxback | MDS | Binary indicator of presence of fell in the past 31 to 180 days on last MDS assessment prior to index MI (LOCF) |
| 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 (LOCF) |
| CXSYNCO_maxback | MDS | Binary indicator of presence of syncope/fainting in prior 7 days on last MDS assessment prior to index MI (LOCF) |
| dmrace | MDS | Race/ethnicity <IN> Identification Information |
| dmsex | MDS | Gender <IN> Identification Information |
| idage | MDS | Age at assessment |
| ORWTLOS | MDS | Weight loss <IN> Oral / Nutritional Status (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 <IN> Medications |
| RXDEPRE | MDS | # of days antidepressants <IN> Medications |
| RXHYPNO | MDS | # of days received hypnotic <IN> Medications |
| RXNUMBE | MDS | Number of meds in last 7 days, from MDS |
| RXPSYCH | MDS | # of days received antipsychotics <IN> Medications |
| dchrppd | OSCAR | Total direct care (RN/LPN/CNA) hrs/day/resident (adjusted) |
| lpn100t | OSCAR | Total LPN FTEs/100 beds (adjusted) |
| md100t | OSCAR | Total MD FTEs/100 beds |
| mdex100t | OSCAR | Total MD extender FTEs/100 beds (93b--) |
| multifac | OSCAR | Facility is part of a chain |
| n_qol_def_wt_z | OSCAR | OSCAR: State-standardized severity-weighted quality-of-life deficiency z-score, 99a-- |
| occrate | OSCAR | OSCAR: Occupancy rate (based on TOTBEDS, 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 (96a--) |
| pt100t | OSCAR | Total physical therapy FTEs/100 beds |
| restrain | OSCAR | Pct physically restrained |
| rn100t | OSCAR | Total RN FTEs/100 beds (adjusted) |
| 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 |
| max_hielix | Part A | Max of Elixhauser among hospitalizations in 1 yr prior to the index MI, from Part A inpt |
| d_ACE_inhibitor | Part D | Binary indicator of presence of angiotensin converting enzyme inhibitor drug (e.g, lisinopril) in 1 yr prior to index MI |
| 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_Antiarrhythmic_Ib | Part D | Binary indicator of presence of class Ib antiarrhythmic drug (e.g., lidocaine or phenytoin) in 1 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_Antilipemic_HMG | Part D | Binary indicator of presence of HMG-CoA reductase inhibitor antilipemic drug (e.g., atorvastatin) 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_Antiplatelet | Part D | Binary indicator of presence of antiplatelet drug (e.g., clopidogrel) 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_ARBs | Part D | Binary indicator of presence of angiotensin II receptor blocker drug (e.g., valsartan) 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 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 |

* LOCF = last observation carried forward.

* Data from OSCAR were obtained using the most recent OSCAR assessment prior to a subject's index hospitalization for AMI.

**eAppendix 3. Companion Study Using Department of Veterans Affairs Data**

Because MDS and Medicare claims files do not contain all clinically relevant data, there is the possibility of unmeasured confounding not captured in our propensity scores. To address this, we assembled a cohort of 162 older adults in Department of Veterans Affairs nursing homes who met inclusion criteria. We then used national VA and VA/MDS data to recreate propensity scores in this cohort, using parameter estimates from our main (Medicare) propensity score model. In these models we assessed beta blocker use within the first week after hospital discharge (yes/no), as there were very few people who were not dispensed a beta blocker in the first 7 days who later went on to use the drug over the following month. We then added evaluated how addition of several variables not available in our main study, including vital signs (pulse, systolic and diastolic blood pressure, body mass index), key laboratory tests (peak troponin, estimated glomerular filtration rate, serum albumin), and measures of left ventricular ejection fraction affected the relationship between beta blocker use and each of our outcomes of interest after controlling for propensity score. We measured vital signs and labs (except peak troponin) based on the first vital sign or lab recorded on the day the patient returned from the hospital to the nursing home, or the most recent prior if a given vital sign or lab was not available on that day. We measured peak troponin based on the largest value of Troponin-T or Troponin-I measured during the hospital stay. We assessed left ventricular ejection fraction using a natural language processing algorithm developed in VA's VINCI platform that incorporates data from studies such as echocardiography and nuclear medicine reports and free text notes.

Characteristics of the VA cohort are shown in Table A3-1. The biggest difference between the VA cohort and main (ie. Medicare propensity matched) cohort was the predominance of men in the VA cohort, consistent with the overall sex distribution among older VA patients. Mean age, selected comorbid conditions, and median ADL score were generally similar between the two groups, although fewer patients in the VA cohort were admitted to ICU compared with the Medicare cohort.

As shown in Table A3-2, inclusion of additional variables only available in VA data did not significantly change the relationship between beta blocker use and our outcomes of interest. This suggests that our inability to measure vital signs, laboratory test results, and possibly measures of left ventricular function in our main cohort did not create a major bias in our results. However, given the small sample size and resulting wide confidence intervals, and certain differences between the VA and Medicare cohorts (mainly the distribution of men and women, and rates of ICU utilization), we are unable to rule out non-major effects.

Table A3-2 shows results of these analyses, which we modeled in 2 ways. The first row of results shows the odds ratio for the association between beta blocker use and the outcome of interest after controlling for the original propensity score ("old PS"). This original propensity score was created using parameter estimates from our main (Medicare) propensity score models. Subsequent rows under the heading "Method 1" show the odds ratio for the association between beta blockers and the outcome of interest after adding the new variable as an additional predictor in the model (e.g. outcome = $\beta_{\text{beta blocker}} + \beta_{\text{propensity score}} + \beta_{\text{new variable}}$). Rows under the heading "Method 2" show the odds ratio for the association between beta blockers and the outcome of interest after controlling for a new propensity score that was created based on the original propensity score and the additional variables of interest. In both methods, note the wide confidence intervals. Also note that results from the left ventricular ejection fraction data had high degrees of missingness, since many patients did not have any left ventricular ejection fraction measured in VA health care settings during the assessment period. As a result, effect estimates for the left ventricular ejection fraction analyses are not reliable.

**Table A3-1. Characteristics of VA Cohort**

| Characteristic | β-blocker users N=124 No. (%) | β-blocker non-users N=38 No. (%) |
|---|---|---|
| **VARIABLES IN COMMON WITH MEDICARE COHORT (SELECTED)** | | |
| Age, mean (SD) years | 81.7 (6.4) | 82.8 (7) |
| Female sex | 5 (4) | 2 (5) |
| Race | | |
| Caucasian | 78 (63) | 22 (58) |
| African-American | 7 (6) | 1 (3) |
| Other (including Hispanic) | 39 (32) | 15 (37) |
| Chronic conditions | | |
| Diabetes | 57 (46) | 15 (40) |
| Heart failure | 60 (48) | 11 (29) |
| COPD | 50 (40) | 15 (40) |
| Depression | 18 (15) | 5 (13) |
| Elixhauser comorbidity score, median, (IQR) | 5 (3,7) | 4 (3,6) |
| ADL score prior to hospitalization, median [IQR] (range 0-28) | 10 (5,16) | 12 (6,18) |
| CHESS score prior to hospitalization, mean (SD) | 1.0 (1.0) | 0.8 (0.9) |
| Length of hospital stay for AMI, median (IQR) days | 3 (0,12) | 2 (0,10) |
| ICU during index hospitalization | 12 (10) | 6 (16) |
| **VARIABLES NOT AVAILABLE IN MEDICARE COHORT** | | |
| Vital signs (upon return to VA nursing home) | | |
| Pulse (mean, SD) | 73 (14) | 73 (16) |
| Systolic BP (mean, SD) | 129 (22) | 125 (23) |
| Body Mass Index (mean, SD) | 26 (5) | 26 (6) |
| Labs (median, IQR) | | |
| Peak troponin – TNT (n=24) | 0.5 (0.2, 3.5) | 0.2 (0.1, 2.5) |
| Peak troponin – TNI (n=109) | 3.1 (1.0 ,9.2) | 2.1 (0.5, 6.7) |
| Albumin | 2.9 (0.6) | 2.9 (0.6) |
| eGFR | 56 (38, 72) | 60 (43, 80) |
| Left ventricular ejection fraction | | |
| Most recent measurement of LVEF <40% (n=35) | 15/32 (47) | 2/5 (40) |
| Any historical measurement of LVEF <40% (n=98) | 35/80 (44) | 7/18 (39) |
| Revascularization procedure during index MI hospitalization | 1 (1) | 2 (5) |

## Table A3-2. Odds Ratio for Association Between β-Blocker Use and Outcomes With and Without Inclusion of New Variables, in VA cohort

| Additional variables in the model (All the models contain BB use variable) | Outcome | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Death within 90 days of MI discharge | Death within 180 days of MI discharge | Hospitalization within 90 days of MI discharge | Hospitalization within 180 days of MI discharge | Hospitalization or death within 90 days of MI discharge | Hospitalization or death within 180 days of MI discharge | Functional decline within 104 days of MI discharge * | Functional decline within 208 days of MI discharge * | 3-level outcome for functional decline or death within 104 days of MI discharge | | 3-level outcome for functional decline or death within 208 days of MI discharge | |
| | | | | | | | | | Functional decline vs Neither death nor functional decline | Death without functional decline vs Neither death nor functional decline | Functional decline vs Neither death nor functional decline | Death without functional decline vs Neither death nor functional decline |
| **OLD PS** | 0.65 (0.29-1.50) | 1.17 (0.54-2.54) | 2.49 (1.08-5.78) | 1.49 (0.7-3.16) | 1.39 (0.65-2.96) | 0.93 (0.41-2.11) | 1.34 (0.59-3.05) | 1.63 (0.72-3.69) | 1.48 (0.64-3.43) | 3.79 (0.37-39.28) | 2.22 (0.92-5.39) | 2.79 (0.78-10.02) |
| **Method1: Add each new VA variable** | | | | | | | | | | | | |
| **Vital Sign Variables** | | | | | | | | | | | | |
| OLD PS +Pulse | 0.64 (0.27-1.48) | 1.18 (0.54-2.56) | 2.44 (1.05-5.71) | 1.45 (0.68-3.10) | 1.36 (0.62-2.94) | 0.91 (0.40-2.07) | 1.35 (0.58-3.16) | 1.66 (0.72-3.82) | 1.51 (0.63-3.59) | 3.80 (0.37-39.10) | 2.30 (0.93-5.68) | 2.93 (0.81-10.58) |
| OLD PS +Systolic BP | 0.67 (0.29-1.52) | 1.21 (0.56-2.62) | 2.44 (1.05-5.66) | 1.46 (0.68-3.10) | 1.38 (0.65-2.94) | 0.93 (0.41-2.11) | 1.37 (0.60-3.12) | 1.67 (0.74-3.79) | 1.51 (0.65-3.50) | 4.14 (0.36-47.16) | 2.33 (0.96-5.69) | 2.94 (0.82-10.58) |
| OLD PS +Diastolic BP | 0.66 (0.29-1.51) | 1.19 (0.55-2.58) | 2.44 (1.05-5.65) | 1.46 (0.69-3.11) | 1.37 (0.64-2.92) | 0.92 (0.41-2.09) | 1.36 (0.59-3.10) | 1.66 (0.73-3.76) | 1.51 (0.65-3.51) | 3.50 (0.36-34.15) | 2.30 (0.94-5.60) | 2.88 (0.80-10.32) |
| OLD PS +BMI | 0.60 (0.26-1.38) | 1.11 (0.51-2.40) | 2.51 (1.08-5.84) | 1.48 (0.70-3.16) | 1.35 (0.63-2.89) | 0.89 (0.39-2.01) | 1.30 (0.57-2.98) | 1.59 (0.70-3.62) | 1.42 (0.61-3.29) | 3.16 (0.30-33.28) | 2.11 (0.86-5.16) | 2.58 (0.71-9.35) |
| **Lab Variables** | | | | | | | | | | | | |
| OLD PS +Maximum Troponin | 0.71 (0.29-1.75) | 1.28 (0.54-3.03) | 2.92 (1.16-7.37) | 1.71 (0.74-3.94) | 1.74 (0.76-4.00) | 1.32 (0.55-3.16) | 1.32 (0.53-3.30) | 1.76 (0.71-4.34) | 1.52 (0.59-3.90) | 3.27 (0.33-32.35) | 2.56 (0.93-7.06) | 2.73 (0.69-10.78) |
| OLD PS +Albumin | 0.57 (0.23-1.46) | 1.29 (0.52-3.22) | 3.24 (1.19-8.86) | 1.65 (0.67-4.06) | 1.53 (0.61-3.84) | 1.01 (0.37-2.77) | 1.05 (0.39-2.84) | 1.38 (0.51-3.74) | 1.15 (0.42-3.19) | 2.38 (0.21-26.76) | 1.98 (0.64-6.10) | 2.67 (0.56-12.60) |
| OLD PS +EGFR | 0.59 (0.23-1.48) | 1.35 (0.57-3.19) | 3.39 (1.29-8.94) | 1.49 (0.65-3.43) | 1.70 (0.73-3.94) | 1.05 (0.43-2.54) | 1.50 (0.59-3.78) | 1.93 (0.77-4.84) | 1.60 (0.63-4.10) | 2.62 (0.21-31.88) | 2.82 (1.01-7.87) | 3.02 (0.75-12.22) |
| **LVEF Variables** | | | | | | | | | | | | |
| OLD PS +Minimal LVEF during Index-MI hospitalization | 0.65 (0.09-4.65) | 1.85 (0.26-13.05) | 3.88 (0.37-40.4) | 1.64 (0.23-11.73) | 2.91 (0.40-21.35) | 1.72 (0.23-12.77) | 0.78 (0.09-6.66) | 1.28 (0.14-11.82) | 0.89 (0.11-7.59) | >999.999 | 2.34 (0.25-21.81) | >999.999 |
| OLD PS +Minimum LVEF (PRE-Index MI Discharge) | 0.75 (0.21-2.61) | 2.16 (0.61-7.67) | 2.35 (0.68-8.09) | 1.54 (0.48-4.91) | 2.24 (0.68-7.44) | 1.97 (0.58-6.69) | 2.14 (0.57-7.99) | 3.12 (0.82-11.80) | 2.44 (0.62-9.60) | 2.35 (0.21-26.97) | 4.64 (1.07-20.05) | 2.94 (0.46-18.71) |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| OLD PS +Minimal LVEF (Any) | 0.79 (0.24-2.61) | 2.19 (0.67-7.21) | 1.45 (0.49-4.28) | 1.06 (0.36-3.10) | 1.43 (0.49-4.16) | 1.32 (0.42-4.16) | 2.77 (0.79-9.73) | 2.84 (0.85-9.47) | 3.12 (0.86-11.40) | 2.27 (0.22-23.55) | 4.27 (1.14-16.08) | 3.40 (0.57-20.36) |

| **Method2: Create new Propensity Score using new VA variables** | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **New PS** | | | | | | | | | | | | |
| NEW PS (4 Vital Sign Variables) | 0.58 (0.25-1.33) | 1.09 (0.51-2.37) | 2.32 (1.00-5.36) | 1.42 (0.67-3.03) | 1.27 (0.60-2.70) | 0.86 (0.38-1.94) | 1.29 (0.56-2.95) | 1.59 (0.70-3.62) | 1.37 (0.59-3.18) | 2.38 (0.25-22.44) | 2.10 (0.87-5.08) | 2.57 (0.72-9.21) |
| NEW PS (3 Lab Variables) | 0.51 (0.19-1.36) | 0.98 (0.38-2.52) | 2.92 (1.04-8.20) | 1.80 (0.70-4.64) | 1.31 (0.51-3.40) | 1.04 (0.37-2.93) | 0.89 (0.32-2.52) | 1.28 (0.45-3.66) | 1.01 (0.34-2.98) | 2.19 (0.21-22.88) | 2.11 (0.59-7.56) | 2.88 (0.54-15.49) |
| NEW PS (3 LVEF Variables) | 0.72 (0.10-5.23) | 1.48 (0.21-10.48) | 4.63 (0.42-51.52) | 1.33 (0.19-9.37) | 3.58 (0.47-27.40) | 1.45 (0.2-10.45) | 0.93 (0.11-7.85) | 1.59 (0.18-13.79) | 1.11 (0.13-9.51) | >999.999 | 2.82 (0.3-26.38) | >999.999 |

PS = propensity score; BP = blood pressure; LVEF = left ventricular ejection fraction

* The time period for functional decline includes a 2 week grace period for capturing MDS functional status assessments, since MDS assessments occur only intermittently (e.g., 90 days followup = 90 days + 14 days = 104 days).

**eAppendix 4. Propensity Score Balance Within and Across Subgroups**

We evaluated the effect of beta blockers on our outcomes of interest across subgroups with different levels of baseline functional status, baseline cognitive status, age, and presence or absence of a stay in an intensive care unit (ICU) or coronary care unit (CCU) during the index hospitalization.

Within each subgroup, propensity scores were very similar between beta blocker users vs. non-users (see table below). Mean propensity scores were also very similar for patients with different levels of functional status, cognitive performance, and age. In contrast, patients who had stayed in an ICU or CCU had higher mean propensity score than patients without any ICU or CCU stay (mean propensity score 0.592 vs. 0.530).

To test whether differences in the propensity score distribution between people with or without an ICU/CCU stay would affect our subgroup analyses, we ran our effect modification models for the impact of ICU/CCU stay both with and without including the propensity score as a covariate. Results of both models were almost identical, so in the paper we present the simpler (e.g. not adjusted for propensity score) results.

**Propensity scores within and between subgroups**

| | | Propensity Score | | | | |
|---|---|---|---|---|---|---|
| **Subgroup** | **β-Blocker Status** | **No.** | **Mean** | **SD** | **Minimum** | **Maximum** |
| | | | | | | |
| **Activities of Daily Living at Baseline** | | | | | | |
| ADL Score <14 | No β-Blocker | 1866 | 0.565 | 0.113 | 0.289 | 0.770 |
| | β-Blockers | 1834 | 0.566 | 0.109 | 0.288 | 0.771 |
| ADL Score 14 to <20 | No β-Blocker | 1778 | 0.573 | 0.106 | 0.289 | 0.771 |
| | β-Blockers | 1801 | 0.571 | 0.107 | 0.288 | 0.771 |
| ADL Score ≥20 | No β-Blocker | 1852 | 0.557 | 0.099 | 0.288 | 0.771 |
| | β- Blockers | 1861 | 0.559 | 0.100 | 0.293 | 0.771 |
| | | | | | | |
| **Cognitive Performance Score at Baseline** | | | | | | |
| | | | | | | |
| CPS Score 0-2 | No β- Blocker | 2657 | 0.571 | 0.111 | 0.288 | 0.771 |
| | β-Blockers | 2642 | 0.570 | 0.110 | 0.288 | 0.771 |
| CPS Score 3-6 | No β-Blocker | 2839 | 0.558 | 0.101 | 0.288 | 0.771 |
| | β-Blockers | 2854 | 0.562 | 0.100 | 0.288 | 0.771 |
| **Age** | | | | | | |
| | | | | | | |
| Age <85 years | No β-Blockers | 2850 | 0.575 | 0.107 | 0.288 | 0.771 |
| | β-Blockers | 2833 | 0.573 | 0.107 | 0.288 | 0.771 |
| Age ≥85 years | No β-Blockers | 2646 | 0.553 | 0.104 | 0.288 | 0.771 |
| | β-Blockers | 2663 | 0.557 | 0.103 | 0.288 | 0.771 |
| **Presence vs Absence of ICU/CCU Stay During AMI Hospitalization** | | | | | | |
| | | | | | | |
| No days in an ICU/CCU | No β-Blockers | 2361 | 0.526 | 0.105 | 0.288 | 0.769 |
| | β-Blockers | 2374 | 0.533 | 0.101 | 0.288 | 0.770 |
| One or more days in ICU/CCU | No β-Blockers | 3135 | 0.594 | 0.098 | 0.291 | 0.771 |
| | β-Blockers | 3122 | 0.590 | 0.102 | 0.288 | 0.771 |

**eAppendix 5. Alternative Analytic Approaches**

To evaluate the stability of our results using different modeling techniques, we conducted our analyses using several alternate analytic approaches. To assess comparability of results from multinomial models and Cox proportional hazards models, we applied both methods to modeling the impact of beta blocker use on death (Table A5-1). We also conducted our key analyses stratifying by propensity score quintile and decile in unmatched cohorts (Table A5-2), controlling for propensity score as a continuous covariate (Table A5-3), and using inverse probability of treatment weight (IPTW)-based approaches (Table A5-4). In each case, results were similar to our main approach.

When we performed IPTW-based analyses in the original (full) cohort, the effect estimate for functional decline was attenuated with 95% confidence intervals crossing 1. However, as subjects at the margins of the propensity score distribution were trimmed – thus isolating individuals for whom there is clinical equipoise - the effect estimate converged to a value close to our main analyses (Table A5-4).

We considered the risk of immortal time bias in our study to be low. This is because more than 90% of nursing home residents who used a beta blocker after AMI started it within the first 14 days after hospitalization, and we excluded subjects who had died or were re-hospitalized within this time frame. To confirm this, we compared time-fixed vs. immortal-time corrected (i.e., time-dependent) effect estimates for a subset of subjects where they could be meaningfully compared. Results were very similar in the 2 approaches (Table A5-5).

We also explored the possibility of analyzing our data using instrumental variable approaches. To do this, we evaluated whether hospital or nursing home facility could be used as an instrument, e.g. by defining the percentage of patients treated at the institution who received a beta blocker. However, the number of patients per institution was small, such that estimates of facility-level treatment preference would be unstable. For example, the median number of patients per hospital was 7. We then tested a reduced model that included only hospitals with at least 5 patients represented in the dataset, and included a random intercept for hospital. On average, hospital accounted for only 3.5% of variation in beta blocker prescribing in the reduced model, suggesting it is a weak instrument. Given these limitations, we elected not to use facility treatment preference/pattern as an instrumental variable.

Finally, we repeated our main analyses using multinomial logistic regression to control for differences in use of other cardiovascular medications after AMI between beta blocker users and non-users (Table A5-6). This included use of statins, ACE inhibitors, and angiotensin receptor blockers, whose use was ascertained using the same methods we used to ascertain beta blocker use after AMI. We also explored evaluating differences in antiplatelet agents (aspirin and clopidogrel), but results of these analyses suggested we were not completely capturing aspirin use, which was not unexpected since it is an inexpensive, over-the-counter medication that may be dispensed as ward stock and thus not captured in Part D claims. As shown in Table A5-6, controlling for these other medications slightly attenuated the observed associations between use of beta blockers and functional decline and death, but the overall pattern of effects remained the same.

**Table A5-1. Multinomial vs. Cox Proportional Hazards models for modeling impact of beta blocker use on death.**

| Model | Impact of beta blocker use on death |
|---|---|
| Cox Proportional Hazards model | 0.74 (0.67-0.82) |
| Multinomial model | 0.72 (0.65-0.80) |

**Table A5-2. Adjusting for propensity score by stratification into propensity score quintiles and deciles**

Rather than match on the propensity score, these models adjust for the propensity score as categorical strata. In these analyses, we trimmed 1% in each tail of the distribution of propensity score to discard residents in each exposure with propensity scores outside the range of common support, leaving 15,397 subjects available for analysis.

| Adjustment strategy | Outcome | Odds Ratio (95% CI) |
|---|---|---|
| Propensity score quintiles | Death | 0.73 (0.66 – 0.80) |
| | Functional decline | 1.11 (0.96 – 1.28) |
| Propensity score declines | Death | 0.74 (0.66 – 0.80) |
| | Functional decline | 1.11 (0.96 – 1.28) |

**Table A5-3. Adjusting for propensity score as a continuous covariate**

Rather than match on the propensity score, these models adjust for the propensity score as a continuous covariate. In these analyses, we trimmed 1% in each tail of the distribution of propensity score to discard residents in each exposure with propensity scores outside the range of common support, leaving 15,397 subjects available for analysis.

| Adjustment strategy | Outcome | Odds Ratio (95% CI) |
|---|---|---|
| Propensity score as continuous covariate | Death | 0.72 (0.66 – 0.80) |
| | Functional decline | 1.11 (0.96 – 1.28) |

**Table A5-4. Analyses using inverse probability of treatment weights**

The mean (SD) IPTW was 0.999 (0.320), with range of 0.471 to 5.633. This suggests IPTW approaches may be appropriately applied to these data.

We performed our first set of IPTW analyses on the full cohort of 15,712 subjects (e.g. without any trimming). We then repeated the analyses after progressively trimming subjects at the margins of the propensity score distribution, so as to isolate individuals for whom there is clinical equipoise. As the tails were further trimmed, the effect estimates moved slightly farther away from unity.

| Adjustment strategy | Cohort | Outcome | Odds Ratio (95% CI) |
|---|---|---|---|
| Inverse probability of treatment weights | Full cohort (no trimming) | Death | 0.73 (0.67 – 0.80) |
| | | Functional decline | 1.11 (0.97 – 1.27) |
| | Trimmed bottom and top 1% | Death | 0.72 (0.65 – 0.79) |
| | | Functional decline | 1.10 (0.96 – 1.29) |
| | Trimmed bottom and top 5% | Death | 0.69 (0.63 – 0.76) |
| | | Functional decline | 1.13 (0.98 – 1.32) |
| | Trimmed bottom and top 10% | Death | 0.67 (0.60 – 0.74) |
| | | Functional decline | 1.16 (0.98 – 1.37) |

**Table A5-5. Analyses evaluating for potential immortal time bias**

We considered the possibility of immortal time bias. In our study, immortal time consists of the time between nursing home admission and the first dispensing of a beta blocker. To evaluate this, we performed a time-dependent (i.e., time-varying) analysis of time to death by beta blocker exposure status. We focused on the subset of 3,231 subjects in our propensity score-matched cohort who returned from hospital to nursing home on the long-term care (LTC) pathway, and thus had no period where new prescriptions were unobservable (because Medicare Part D resumed coverage immediately upon return to the nursing home).

The following table contrasts results from our main analytic approach in the LTC group vs. results obtained using time-varying mortality estimates that corrected for immortal time bias. The similarity of the two estimates suggests that any immortal time bias is small.

| Cohort | Time-fixed mortality estimate (main analytic approach) | Time-dependent mortality estimate (corrected for immortal/misclassified person-time) |
|---|---|---|
| Long-term Care (LTC) subset of main Medicare cohort (n=3,321) | 0.84 (0.72 - 0.98) | 0.86 (0.73 - 1.00) |

**Table A5-6. Controlling for use of other cardiovascular medications after AMI**

The following table shows the association between beta blocker use and our outcomes of interest after controlling for use of statins, ACE inhibitors, and angiotensin receptor blockers (ARBs) in the post-AMI period. Note that the observed associations for these other drugs should not be interpreted in the same way as the associations for beta blockers, since the cohort was propensity score matched based on beta blocker exposure but not on these other drugs.

| Outcome | Covariates | RRR (95% CI) |
|---|---|---|
| Functional decline | β-blockers | 1.11 (0.99 – 1.25) |
| | Other medications | |
| | ARBs | 1.16 (0.94 – 1.42) |
| | ACE inhibitors | 0.91 (0.81 – 1.03) |
| | Statins | 1.28 (1.14 – 1.44) |
| Death | β- blockers | 0.82 (0.73 – 0.92) |
| | Other medications | |
| | ARBs | 0.63 (0.49 – 0.80) |
| | ACE inhibitors | 0.73 (0.64 – 0.83) |
| | Statins | 0.55 (0.49 – 0.62) |

**eAppendix 6. Measures of Covariate Balance and Propensity Score Distribution Before and After Propensity Score–Based Matching**

This appendix contains 3 figures that illustrate covariate balance and the distribution of propensity scores in beta blocker-treated and –untreated subjects before and after matching.

**Figure A6-A. Standardized mean difference in subject characteristics among beta blocker users vs. non-users, before and after propensity score-based matching**

Prior to propensity-score matching, the biggest differences between beta blocker users and non-users were that users were less likely to have a prior diagnosis of angina pectoris (standardized mean difference [SMD} -0.22) and unstable angina (SMD -0.11), less likely to have used loop diuretics (SMD -0.11), nitrates (SMD -0.10), and vasodilators (SMD -0.10) in the year prior to hospitalization, and were more likely to have been in an ICU or CCU during the AMI hospital stay (SMD 0.14) and to return to the nursing home on the SNF-benefit care pathway (SMD 0.11). Lower use of beta blockers in nursing home residents with a history of angina pectoris and unstable angina may reflect the new-user nature of our study design: since these conditions are symptomatic manifestations of ischemic heart disease, patients with these conditions may already have already been considered for and declined beta blocker use prior to the index AMI.

After propensity score matching, the largest residual differences were that beta-blocker users were more likely to have pain at the pre-hospital baseline (SMD 0.05) and less likely to have used a class II antiarrhythmic in the previous year (SMD -0.06). All other variables had post-match standardized mean differences of 0.03 or less. This is consistent with excellent covariate balance; which is generally considered robust for SMDs of 0.10 or less (Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. *Stat Med* 2009; 28(25): 3083-107)

In the figure, blue X's represent the absolute SMD between groups prior to propensity score matching, and the red circles represent the absolute SMD after matching. The dashed line at SMD 0.10 represents a commonly-used threshold below which post-matching covariate balance is considered robust.

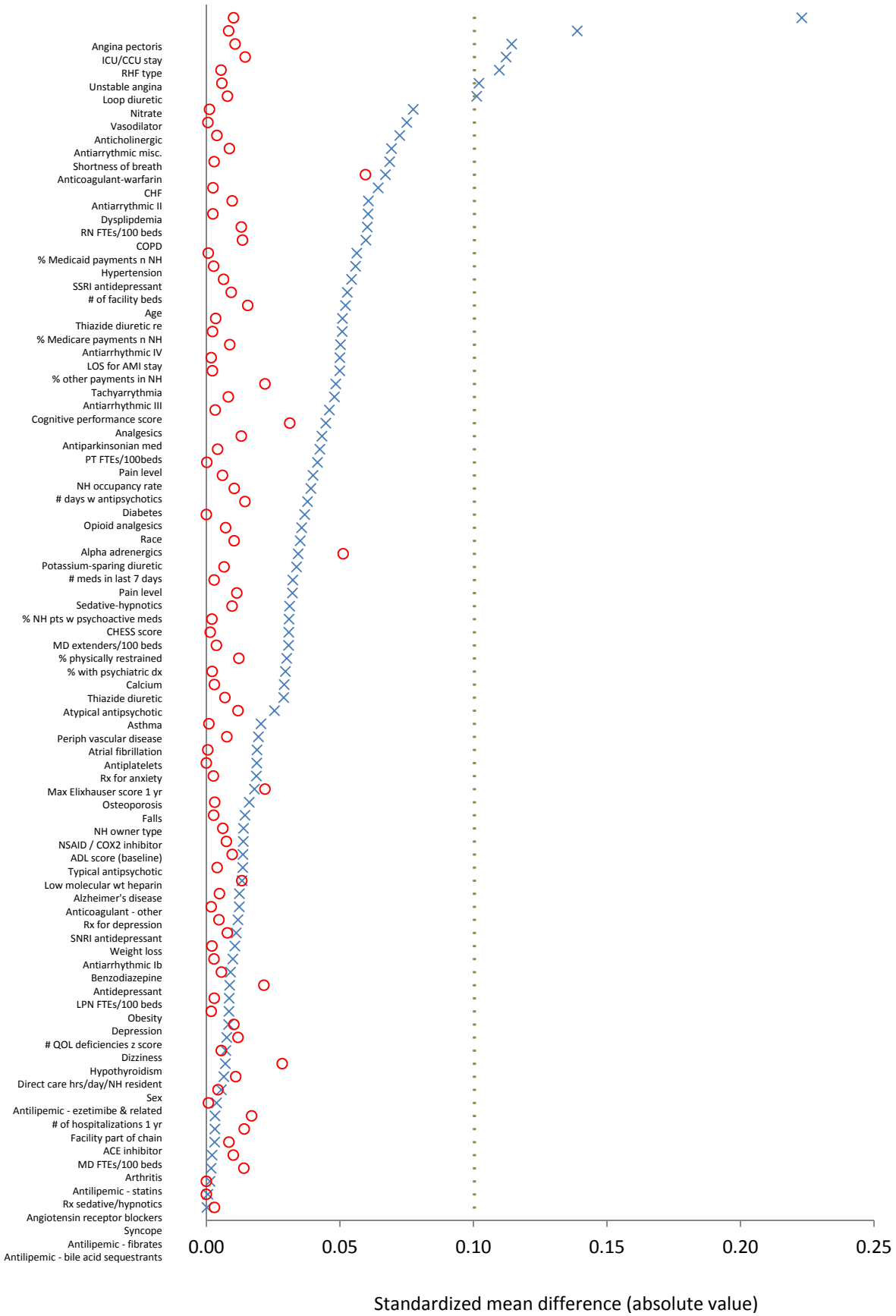
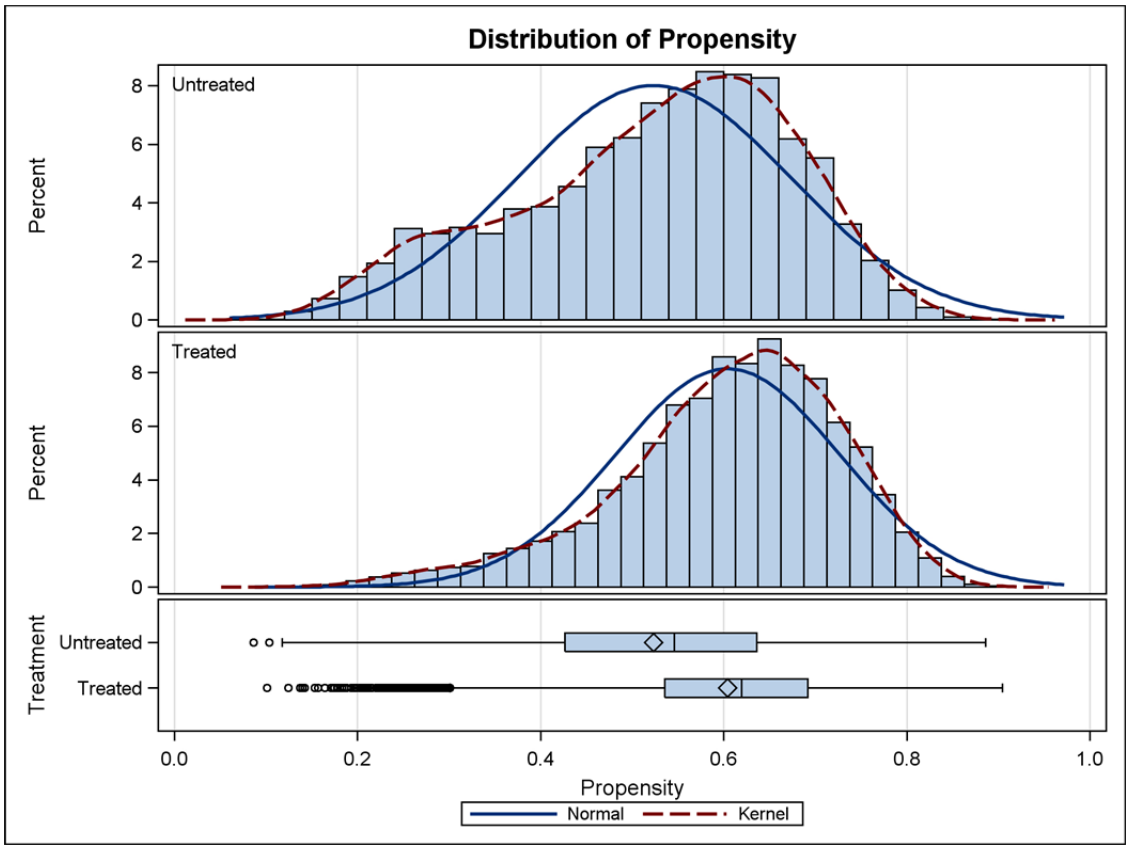
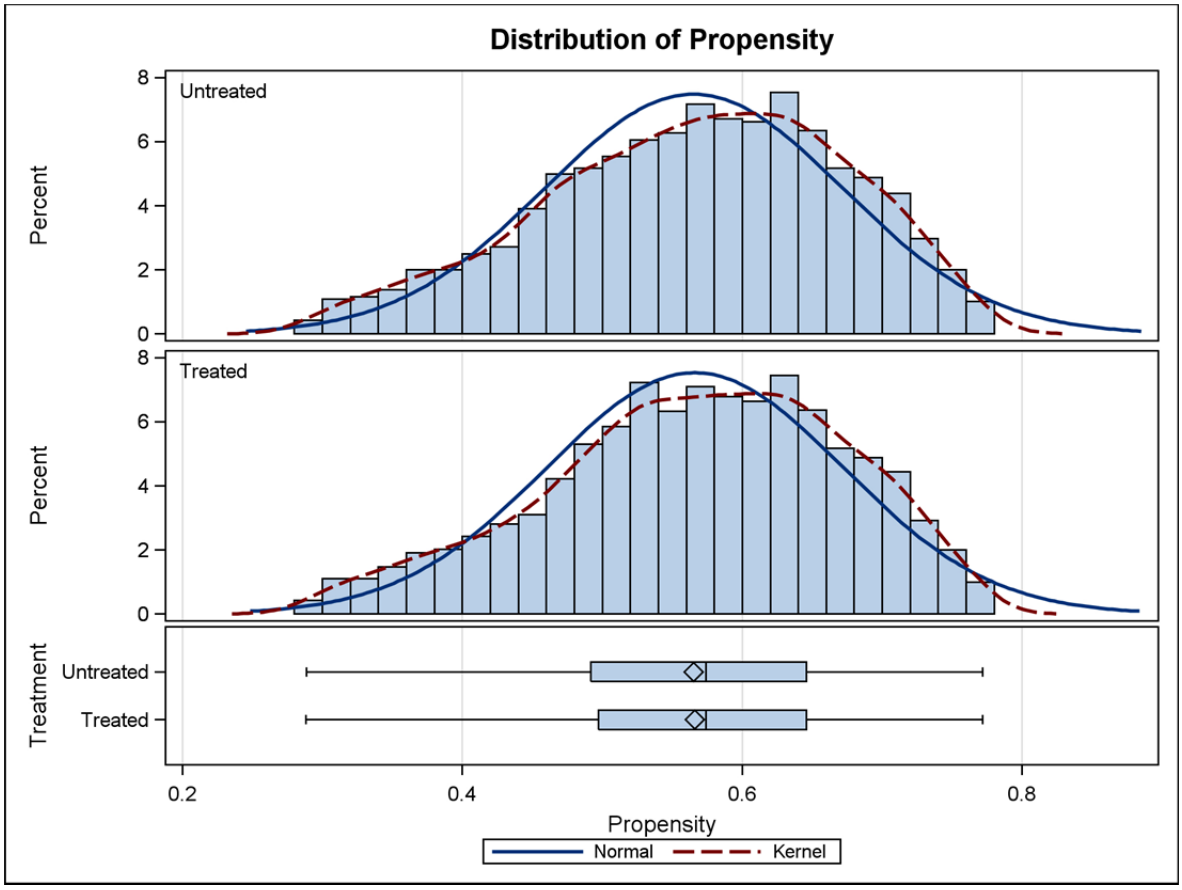


**Figure A6-B. Propensity score distribution in beta blocker users vs. non-users, before and after propensity score-based matching**

**Panel A. Prematching distribution of propensity scores in beta blocker users and non-users**



**Panel B: Post-matching distribution of propensity scores in beta blocker users and non-users**



## eAppendix 7. Detailed results from subgroup analyses, including number needed to treat (NNT) and number needed to harm (NNH)

| Overall Primary Estimates | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | |
| | Outcome Level | β- Blocker Exposed Risk | β- Blocker Exposed 95% Confidence Limits | β- Blocker Unexposed Risk | β- Blocker Unexposed 95% Confidence Limits | Risk Difference | 95% Confidence Limits | P-value | NNT or NNH (Before Rounding) | NNT or NNH (After Rounding) | 95% Confidence Limits * |
| | Functional Decline | 0.1305 | 0.1216, 0.1394 | 0.1112 | 0.1029, 0.1195 | 0.0193 | 0.0071, 0.0315 | 0.0019 | 51.8134 | 52 | 32, 141 |
| | Death | 0.1132 | 0.1048, 0.1215 | 0.1530 | 0.1435, 0.1625 | -0.0398 | -0.0525,-0.0272 | <0.0001 | 25.1256 | 26 | 20, 37 |
| | | | | | | | | | | | |
| **ADL Score** | | | | | | | | | | | |
| | | | | | | | | | | | |
| Characteristic Strata | Outcome Level | β- Blocker Exposed Risk | β- Blocker Exposed 95% Confidence Limits | β- Blocker Unexposed Risk | β- Blocker Unexposed 95% Confidence Limits | Risk Difference | 95% Confidence Limits | P-value | NNT or NNH (Before Rounding) | NNT or NNH (After Rounding) | 95% Confidence Limits |
| <14 | Functional Decline | 0.0752 | 0.0632, 0.0873 | 0.0740 | 0.0621, 0.0858 | 0.0013 | -0.0156, 0.0182 | 0.8813 | 769.2307 | 770 | NNH 55 to ∞ to NNT 65 |
| | Death | 0.0883 | 0.0753, 0.1013 | 0.1141 | 0.0997, 0.1286 | -0.0258 | -0.0452,-0.0064 | 0.0095 | 38.7596 | 39 | 23, 157 |
| 14-19 | Functional Decline | 0.1477 | 0.1313, 0.1641 | 0.1339 | 0.1180, 0.1497 | 0.0138 | -0.0089, 0.0366 | 0.2344 | 72.4637 | 73 | NNH 28 to ∞ to NNT 113 |
| | Death | 0.1138 | 0.0992, 0.1285 | 0.1665 | 0.1492, 0.1838 | -0.0527 | -0.0753,-0.0300 | <0.0001 | 18.9753 | 19 | 14, 34 |
| ≥20 | Functional Decline | 0.1682 | 0.1512, 0.1852 | 0.1269 | 0.1117, 0.1420 | 0.0413 | 0.0185, 0.0641 | 0.0004 | 24.2130 | 25 | 16, 55 |
| | Death | 0.1370 | 0.1214, 0.1526 | 0.1793 | 0.1618, 0.1967 | -0.0422 | -0.0657,-0.0188 | 0.0004 | 23.6966 | 24 | 16, 54 |
| | | | | | | | | | | | |

| CPS Score | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | |
| **Characteristic Strata** | **Outcome Level** | **β- Blocker Exposed Risk** | **β- Blocker Exposed 95% Confidence Limits** | **β- Blocker Unexposed Risk** | **β- Blocker Unexposed 95% Confidence Limits** | **Risk Difference** | **95% Confidence Limits** | **P-value** | **NNT or NNH (Before Rounding)** | **NNT or NNH (After Rounding)** | **95% Confidence Limits** |
| 0-2 | Functional Decline | 0.1567 | 0.1428, 0.1706 | 0.1468 | 0.1333, 0.1602 | 0.0099 | -0.0094, 0.0292 | 0.3143 | 101.0101 | 102 | NNH 35 to ∞ to NNT 107 |
| | Death | 0.0901 | 0.0792, 0.1010 | 0.1261 | 0.1135, 0.1387 | -0.0360 | -0.0527,-0.0193 | <0.0001 | 27.7777 | 28 | 19, 52 |
| ≥3 | Functional Decline | 0.1062 | 0.0949, 0.1175 | 0.0778 | 0.0680, 0.0877 | 0.0283 | 0.0133, 0.0433 | 0.0002 | 35.3356 | 36 | 24, 76 |
| | Death | 0.1345 | 0.1220, 0.1471 | 0.1782 | 0.1642, 0.1923 | -0.0437 | -0.0625,-0.0248 | <0.0001 | 22.8832 | 23 | 16, 41 |
| | | | | | | | | | | | |
| **Age** | | | | | | | | | | | |
| | | | | | | | | | | | |
| **Characteristic Strata** | **Outcome Level** | **β- Blocker Exposed Risk** | **β- Blocker Exposed 95% Confidence Limits** | **β- Blocker Unexposed Risk** | **β- Blocker Unexposed 95% Confidence Limits** | **Risk Difference** | **95% Confidence Limits** | **P-value** | **NNT or NNH (Before Rounding)** | **NNT or NNH (After Rounding)** | **95% Confidence Limits** |
| <85 | Functional Decline | 0.1493 | 0.1362, 0.1624 | 0.1305 | 0.1182, 0.1429 | 0.0188 | 0.0008, 0.0368 | 0.0414 | 53.1914 | 54 | 28, 1,250 |
| | Death | 0.0935 | 0.0828, 0.1043 | 0.1270 | 0.1148, 0.1392 | -0.0335 | -0.0497,-0.0172 | 0.0001 | 29.8507 | 30 | 21, 59 |
| ≥85 | Functional Decline | 0.1104 | 0.0985, 0.1223 | 0.0903 | 0.0794, 0.1012 | 0.0201 | 0.0039, 0.0362 | 0.0149 | 49.7512 | 50 | 28, 257 |
| | Death | 0.1341 | 0.1211, 0.1470 | 0.1810 | 0.1664, 0.1957 | -0.0470 | -0.0665,-0.0274 | <0.0001 | 21.2765 | 22 | 16, 37 |
| | | | | | | | | | | | |
| **ICU/CCU Use** | | | | | | | | | | | |
| | | | | | | | | | | | |
| **Characteristic Strata** | **Outcome Level** | **β- Blocker Exposed Risk** | **β- Blocker Exposed 95% Confidence Limits** | **β- Blocker Unexposed Risk** | **β- Blocker Unexposed 95% Confidence Limits** | **Risk Difference** | **95% Confidence Limits** | **P-value** | **NNT or NNH (Before Rounding)** | **NNT or NNH (After Rounding)** | **95% Confidence Limits** |
| No Use (0 days) | Functional Decline | 0.1225 | 0.1122, 0.1389 | 0.1055 | 0.0931, 0.1179 | 0.0201 | 0.0019, 0.0383 | 0.0311 | 49.7512 | 50 | 27, 526 |
| | Death | 0.1163 | 0.1034, 0.1292 | 0.1525 | 0.1380, 0.1670 | -0.0362 | -0.0556,-0.0168 | 0.0003 | 27.6243 | 28 | 18, 60 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Any Use (>0 Days) | Functional Decline | 0.1342 | 0.1223, 0.1462 | 0.1155 | 0.1043, 0.1267 | 0.0187 | 0.0024, 0.0351 | 0.0251 | 53.4759 | 54 | 29, 417 |
| | Death | 0.1108 | 0.0998, 0.1218 | 0.1534 | 0.1408, 0.1660 | -0.0426 | -0.0593,-0.0259 | <0.0001 | 23.4741 | 24 | 17, 39 |

NNT = number needed to treat; NNH = number needed to harm

* Per recommendations by Altman, confidence intervals for non-significant NNHs and NNTs are written as [NNH X to ∞ to NNT Y]. For example, 95% CIs for the non-significant NNH of beta blockers on functional decline in patients with a CPS score 0-2 could also be expressed as 35 to -107. For more information see Altman DG. Confidence intervals for the number needed to treat. BMJ. 1998 Nov 7; 317(7168): 1309–1312

**eAppendix 8. Sensitivity Analysis Using Inverse Probability of Selection Weights**

To evaluate whether the exclusion criterion that required 14 days of death- and hospital-free survival after the AMI discharge could have introduced selection bias, we repeated our main analyses using inverse probability of selection weighting. This approach weights subjects according to their similarity to individuals who were excluded due to death or re-hospitalization in the first 14 days, thus estimating treatment effects as if these people had been included in the analysis. We did this by calculating a propensity score for each subject who died or was rehospitalized in the first 14 days after hospital discharge, and using these scores as inverse probability of selection weights.

Using this approach, the mean (SD) weight was 0.998 (0.356), with a minimum weight of 0.07 and a maximum weight of 17.18.

The following table shows the effect estimate for the impact of beta blockers on mortality and functional decline using the original approach, and using the selection-weighted approach. To enhance comparability, in these analysis mortality is estimated using a multinomial logit model, not the Cox proportional hazards model used for the main analysis (however, the two methods produce very similar results). All analyses were conducted using the propensity-matched cohort of beta blocker users and non-users. Weights were stabilized, and there were no zero cells.

While inverse probability of selection weights are typically applied to non-matched rather than matched samples, applying this method to a matched sample is conceptually analogous to propensity score matching in a complex survey, where inverse probability weights are used to standardize the population to the target (see Dugoff EH et al. Generalizing observational study results: applying propensity score methods to complex surveys. *Health Serv Res*. 2014 Feb;49(1):284-303).

**Table A8.1. Effect of beta blockers on 90-day mortality and functional decline: comparison of original approach and approach applying inverse probability of selection weights**

| Outcome | Analysis | Odds Ratio (95% CI) |
|---|---|---|
| Death | Original approach | 0.720 (0.643, 0.805) |
| | Applying selection weights | 0.709 (0.628, 0.801) |
| Functional decline | Original approach | 1.142 (1.016, 1.282 |
| | Applying selection weights | 1.088 (0.957, 1.237) |

The following tables show results stratified by patient characteristics of particular interest: baseline independence in ADLs, and baseline cognition (as measured by CPS score).

**Table A8.2. Effect of β-blockers on 90-day mortality and functional decline: comparison of original approach and approach applying inverse probability of selection weights, stratified by ADL status at baseline ***

| *ADL Score* | | | |
|---|---|---|---|
| **Outcome** | **ADL Score** | **Analysis** | **Odds Ratio (95% CI)** |
| | | | |
| Death | <14 (best) | Original approach | 0.75 (0.61, 0.93) |
| | 14-19 (medium) | Original approach | 0.65 (0.53, 0.79) |
| | ≥20 (worst) | Original approach | 0.76 (0.64, 0.91) |
| | | | |
| | <14 (best) | Applying selection weights | 0.73 (0.57, 0.92) |
| | 14-19 (medium) | Applying selection weights | 0.63 (0.51, 0.78) |
| | ≥20 (worst) | Applying selection weights | 0.76 (0.63, 0.92) |
| | | | |

| | | | |
|---|---|---|---|
| Functional decline | <14 (best) | Original approach | 0.99 (0.77, 1.26) |
| | 14-19 (medium) | Original approach | 1.05 (0.86, 1.27) |
| | ≥20 (worst) | Original approach | 1.32 (1.10, 1.59) |
| | | | |
| | <14 (best) | Applying selection weights | 0.93 (0.70, 1.23) |
| | 14-19 (medium) | Applying selection weights | 1.05 (0.85, 1.29) |
| | ≥20 (worst) | Applying selection weights | 1.20 (0.98, 1.47) |

**Table A8.3. Effect of β- blockers on 90-day mortality and functional decline: comparison of original approach and approach applying inverse probability of selection weights, stratified by cognitive status at baseline ***

| *CPS Score (Cognitive Status)* | | | |
|---|---|---|---|
| **Outcome** | **CPS Score** | **Analysis** | **Odds Ratio (95% CI)** |
| | | | |
| Death | 0-2 (better) | Original approach | 0.69 (0.58, 0.82) |
| | 3-6 (worse) | Original approach | 0.74 (0.64, 0.86) |
| | | | |
| | 0-2 (better) | Applying selection weights | 0.67 (0.55, 0.81) |
| | 3-6 (worse) | Applying selection weights | 0.73 (0.63, 0.86) |
| | | | |
| Functional decline | 0-2 (better) | Original approach | 1.03 (0.89-1.20) |
| | 3-6 (worse) | Original approach | 1.34 (1.11-1.61) |
| | | | |
| | 0-2 (better) | Applying selection weights | 1.00 (0.84, 1.18) |
| | 3-6 (worse) | Applying selection weights | 1.24 (1.02, 1.52) |