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Approaches to Address Premature Death of Patients When Assessing Patterns of Use of Health Care Services After an Index Event.

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Abstract

Background: Studies of the use of health care after the onset of disease are important for assessing quality of care, treatment disparities, and guideline compliance. Cohort definition and analysis method are important considerations for the generalizability and validity of study results. We compared different approaches for cohort definition (restriction by survival time vs comorbidity score) and analysis method (Kaplan-Meier vs competing risk) when assessing patterns of guideline adoption in elderly patients.

Methods: Medicare beneficiaries aged 65 to 95 years old who had an acute myocardial infarction (AMI) in 2008 were eligible for this study. Beneficiaries with substantial frailty or an AMI in the

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prior year were excluded. We compared Kaplan-Meier to competing risk estimates of guideline adoption during the first year post-AMI.

Results: At 1-year post-AMI, 14.2% (95% CI: 14.0%, 14.5%) of beneficiaries overall initiated cardiac rehabilitation when using competing risk analysis and 15.1% (95% CI: 14.8%, 15.3%) from the Kaplan-Meier analysis. Guideline medication adoption was estimated as 52.3% (95% CI: 52.0%, 52.7%) and 53.4% (95% CI: 53.1%, 53.8%) for competing risk and Kaplan-Meier methods respectively. Mortality was 17.0% (95%CI: 16.8%, 17.3%) at 1 year post-AMI. The difference in cardiac rehabilitation initiation at 1-year post-AMI from the overall population was 0.1%, 1.7%, and 1.9% compared to 30-day survivor, 1-year survivor, and comorbidity-score restricted populations respectively.

Conclusions: In this study, the Kaplan-Meier method consistently overestimated the competing risk method. Competing risk approaches avoid unrealistic mortality assumptions and lead to interpretations of estimates that are more meaningful.

Keywords

Cardiac Rehabilitation; Guideline Concordant Care; Medicare Administrative Claims Data; Survival Analysis Method Comparison; Post-Acute MI Healthcare

Introduction

Healthcare administrative databases are increasingly used to assess quality of care and identify characteristics of patients and providers that may be indicative of sub-optimal treatment and guideline compliance (1-7). The results of these studies can be used to shape policy, identify disparities, and design quality improvement activities. An important methodological consideration in conducting observational studies is how to account for death. Restriction has been used in the study of the effect of protective treatments on mortality and morbidity to reduce biases associated with conducting these studies using observational data (8-10). Investigators can restrict the study cohort by requiring patients to survive and not be lost to follow-up for a specific time window (i.e. 30 days). However, selecting patients who survive to the end of the window limits generalizability of results when the source population is subject to high mortality during that window and/or the window interval is too long. Alternatively, cohort restriction by baseline characteristics such as a comorbidity score or predicted probability of death threshold can reduce confounding by indication but may introduce selection bias (11). In the first study aim, we employ an empirical example of post myocardial infarction initiation of guideline recommendations to compare these two cohort restriction methods to account for death.

Time-to-event analysis is another way to account for death in observational studies. In the second study aim, we use the same empirical data from the first aim to compare Kaplan-Meier survival analysis with competing risk survival analysis. A competing event is an event such as death that precludes the event of interest from occurring. Standard Kaplan-Meier survival analysis is an appropriate analysis method when death is the outcome of interest; however, this method does not appropriately account for death as a competing event (12, 13). Including death as a censoring event in a Kaplan-Meier analysis violates the assumption

that censored individuals have a similar risk of experiencing the event of interest as those individuals in which we observe the event of interest. However, not including death as a censoring event violates the assumption that an individual is at risk for the event of interest once death has occurred. The magnitude of the bias from Kaplan-Meier estimates is related to degree to which these assumptions are violated. Alternatively, competing risk models can be used to estimate the proportion of individuals experiencing the event of interest before death (14) avoiding issues arising from using the Kaplan-Meier method.

In the present paper, we use time to adoption of secondary prevention guideline recommendations from the American Heart Association (AHA) (15) among Medicare beneficiaries hospitalized for acute myocardial infarction (AMI) in 2008 as an empirical example to investigate the implication of employing different methods to account for death. We also illustrate how employing time-to-event analysis provides a fuller picture of the adoption of guidelines or treatment initiation than the traditional reporting of incidence at a single point in time.

Methods:

Study Population

We used a national sample of Medicare beneficiaries from the Centers for Medicare and Medicaid Services (CMS) to investigate AHA guideline conforming medical care after acute myocardial infarction (AMI). Medicare beneficiaries hospitalized in 2008 for AMI defined by discharge code 410.xx (excluding .x2) in first or second position; were 65 to 95 years old at the time of their index AMI; and were continuously enrolled in Medicare Part A, B, and D between January 2007 and death or end of 2009 were included in our study (Figure 1). Beneficiaries were included in this study if they survived their index hospitalization and were discharged home or left against medical advice. Beneficiaries were excluded from this study if they had an MI hospitalization in the year prior to their index event in 2008 or had evidence of substantial frailty (diagnosis of paralysis, Parkinson's disease, or bedsores; or evidence of use of a wheelchair or in-home hospital bed) in the year prior to their index event (Figure 1).

Study Design

The 12 months before the index hospitalization period were used to define baseline covariates (Figure 2). The index hospital period began with the admission date of the first AMI hospitalization in 2008 and ended when the patient was discharged. If a beneficiary remained an inpatient by being transferred to another medical facility, the index period ended when the beneficiary was discharged into the community after the final continuous transfer. Guideline concordant medical care was assessed from the end of the index hospitalization period until December 31, 2009.

Outcome Definitions

The two outcomes of interest in our study were post-AMI initiation of AHA recommendations for outpatient cardiac rehabilitation participation and combination use of 3-4 guideline recommended medications. The first date from records in the Medicare

outpatient or physician (Carrier) files with either Current Procedural Terminology (CPT) code 93797 or 93798 defined cardiac rehabilitation initiation. The first date when a beneficiary had an overlap in days supply for fills of a renin-angiotensin system actor, a beta-adrenergic receptor antagonist, and a HMG CoA reductase inhibitor (statin) defined post-AMI initiation of concordant guideline recommended medications (Supplemental Content Figure 1, Supplemental Digital Content 1, <http://links.lww.com/MLR/B585>). If a beneficiary had a revascularization procedure during the index hospitalization period, an antiplatelet fill was also required to define the medication outcome. Medications were identified in Medicare Part D records by generic medication names and/or national drug codes in each medication class. If a beneficiary started a medication before AMI hospitalization, the days supply of that medication was extended by the length of hospital stay in determining the medication outcome (Supplemental Content Figure 1, Supplemental Digital Content 1, <http://links.lww.com/MLR/B585>). Therefore, beneficiaries who had carryover pills from before their AMI hospitalization for all required study medications immediately experienced the guideline recommended medication outcome upon discharge. Aspirin is also an AHA recommendation but is not reliably captured in Part D records because of its over the counter availability so it was not included in our medication outcome definition.

Population Characteristic Definitions

Demographic characteristics (e.g., age, gender, and race) were obtained from the CMS enrollment file. International Classification of Diseases, Clinical Modification, Ninth Revision (ICD-9) codes, CPT codes, and Healthcare Common Procedure Coding System (HCPC) codes in the Medicare Standard Analytic files (Inpatient, Outpatient, and Carrier) identified comorbid conditions and procedures. We identified other relevant baseline and index period characteristics such length of stay and comorbidity score. The Gagne comorbidity score, which predicts mortality better in elderly populations than other comorbidity measures, was computed from the baseline characteristics (16). Frailty was quantified by computing the probability of diminished activities of daily living using model coefficients derived by Faurot et al (17).

Cohort Restrictions

We explored the effect of requiring varying lengths of post-AMI survival on the adoption of guideline recommendations. We considered restriction by survival to five different points in time: 30, 60, 90, 180, and 366 days post-AMI discharge. The 30, 60, and 90-day time intervals were based on the common lengths of days supply for study medications. The 180-day and 366-day (1-year) time points were chosen to represent extreme scenarios (3). We also wanted to compare the 366-day survival restricted cohort to a cohort defined by a predicted 1-year survival on the post-AMI adoption of guideline recommendations. In the derivation of their comorbidity score, Gagne et al. defined high risk of 1-year mortality as 17% which corresponded to a score ≥ 5 (16). We used this cut-off from Gagne et al. to define our predicted 1-year survival (lower risk of mortality) cohort as beneficiaries with a comorbidity score < 5 .

Statistical Analysis

Descriptive statistics (count, proportions, mean, and standard deviation) were used to summarize the characteristics of each cohort. Standardized differences were computed between the overall population and each survival and comorbidity score restricted population. Kaplan-Meier estimates were used to compute post-AMI survival. Two methods were used to estimate the cumulative incidence function (CIF) of the adoption of guideline recommendations. First, CIF estimates were computed from the complement of the Kaplan-Meier (KM) product limit estimator of the survival distribution function, $1-S(t)$ in which individuals were censored by both death and end-of-study (Appendix Equation 1, Supplemental Digital Content 2, <http://links.lww.com/MLR/B586>). This method estimates the probability (risk) of the event of interest (i.e. cardiac rehabilitation initiation) before some time t . The larger the proportion of the population that dies before cardiac rehabilitation initiation, the higher the degree to which KM assumptions are violated since death prevents the event of interest from occurring. This method was used to compute the risk of post-AMI initiation of both outcomes for all defined populations. A short example of this calculation is provided in the appendix at the end of this article (Appendix Figure 1, Appendix Table 1, Supplemental Digital Content 2, <http://links.lww.com/MLR/B586>).

The second method, the competing risk approach, estimates the joint probability of a specific event occurring before a given time point from a nonparametric estimator (Appendix Equation 2, Supplemental Digital Content 2, <http://links.lww.com/MLR/B586>). Both the probability (risk) of the event of interest (i.e. cardiac rehabilitation initiation) before death at time t and the probability of death before the event of interest at time t were computed using this method. In the competing risk approach, the population at risk at each event time excludes individuals who have had any event before time t (14). This method allows investigators to estimate the CIF for the event of interest (i.e. cardiac rehabilitation initiation) and any competing event (death) separately. SAS uses a nonparametric estimator to calculate cumulative incidence (18). This method was used to compute the risk of post-AMI initiation of both outcomes for the overall study population and the 1-year predicted survivor populations. A short example of how to calculate risk of the event of interest is provided in the appendix at the end of this article (Appendix Figure 1, Appendix Table 2, Supplemental Digital Content 2, <http://links.lww.com/MLR/B586>). All analyses were completed using SAS 9.4 (Cary, NC).

Results:

We identified 76,797 beneficiaries who met study criteria. Beneficiaries in the overall population had a mean age of 78 years old (7.5 SD), 56% were female, and 7.8% Black (Table 1). As we restricted the study cohort by increasing lengths of post-AMI survival time, the number of beneficiaries in each population decreased, however, there were very few differences in the distribution of measured baseline characteristics. Dissimilarities in the measured covariates which had greater than 10% standardized difference occurred mainly in the predicted 1-year survivor population (Table 1). The proportion of those who died in the overall population was 3% at 30 days post-AMI increasing to 17% at 1-year post-AMI (Table 1) (Supplemental Content Figure 2, Supplemental Digital Content 1, <http://>

links.lww.com/MLR/B585). In the overall population, beneficiaries experienced 11,328 cardiac rehabilitation initiation events and averaged 412 days of follow-up time for the cardiac rehabilitation initiation outcome.

Cumulative incidence estimates of post-AMI initiation of cardiac rehabilitation and concordant guideline recommended medication (Figure 3) increased with increasing amounts of survival restriction. Differences in the cumulative incidence between each consecutive survivor-restricted population were small often with overlapping confidence intervals (Supplemental Table 1, Supplemental Digital Content 1, <http://links.lww.com/MLR/B585>). When the survival requirement for population inclusion was 90 days or less, the confidence intervals for the cumulative incidence of cardiac rehabilitation for each survivor-restricted population overlapped. However, confidence intervals for the cumulative incidence of cardiac rehabilitation initiation did not overlap between the overall population and populations where at least 180 days of survival were required for population inclusion. Results were similar for guideline medications. The difference in post-AMI initiation estimates between the observed 1-year (366-day) survival population and the predicted 1-year survival population was negligible for both outcomes.

We observed that the Kaplan-Meier (KM) estimates of the post-AMI incidence of guideline initiation were consistently higher than the competing risk method estimates (Figure 4). At 1-year post-AMI discharge in the overall population, the KM method estimated that 15.2% (95%CI: 14.9%, 15.4%) and 53.4% (95%CI: 53.1%, 53.8%) of beneficiaries initiated cardiac rehabilitation and concordant guideline recommended medication respectively, however, the competing risk method estimated that 14.5% (95%CI: 14.3%, 14.8%) and 52.3% (95%CI: 52.0%, 52.7%) of beneficiaries initiated cardiac rehabilitation and concordant guideline recommended medication respectively. The magnitude of the difference in estimates between methods increased from 30 days post-AMI to 1-year post-AMI (Supplemental Table 2, Supplemental Digital Content 1, <http://links.lww.com/MLR/B585>). At 1-year post discharge, 15% of beneficiaries in the overall population had died before starting cardiac rehabilitation while 9.4% of beneficiaries died before post-AMI initiation of concordant guideline recommended medications. At 1-year post discharge, 11.3% of beneficiaries in the predicted 1-year survivor-restricted population had died before starting cardiac rehabilitation while 6.7% of beneficiaries died before post-AMI initiation of concordant guideline recommended medications. The estimates for post-AMI initiation of guideline recommendations were higher in the predicted 1-year survivor-restricted population than the overall population (Supplemental Figure 3, Supplemental Digital Content 1, <http://links.lww.com/MLR/B585>). Less than 10% of any of the populations adopted both cardiac rehabilitation and concordant guideline recommended medication within 1 year of AMI discharge (data not shown). Approximately one-half of those who initiated cardiac rehabilitation within the first year post-AMI were also concurrently using 3-4 guideline recommended medications (data not shown).

Discussion

In a population-based study of patients discharged alive after AMI, we compared different approaches to estimating the risk of patients adopting guidelines for recommended

medications or cardiac rehabilitation after hospital discharge. Restricting the study cohort by survival reduced the population size at risk and appeared to select for more guideline adoptive patients, as restriction increased the estimated risk of cardiac rehabilitation initiation or concordant guideline recommended medication possession during follow-up. The bias produced by requiring survival for a short duration in estimates of initiation may be supportable in most circumstances. However, since we demonstrated in this study that treatment adoption by comorbidity-restricted population was similar to the 1-year observed survival restricted population, we would recommend that investigators restrict cohorts by baseline prediction of survival rather than observed survival when six or more months of survival are being considered as an inclusion/exclusion criterion. Censoring patients who die is an alternative approach to requiring survival; however, implicitly censoring by death via Kaplan-Meier analysis assumes that patients who die could still go on to initiate therapy. Competing risk methods should be used as the appropriate time-to-event analyses since this method estimates the risk of an event before death. In our study, we saw relatively modest differences between the Kaplan-Meier estimates of the cumulative incidence of initiation of cardiac rehabilitation and concordant guideline recommended medication and the competing risk estimates. In studies subject to stronger mortality, these differences would be larger.

Results from our analysis have implications for outcome studies using guideline treatments as an exposure. By graphing the cumulative incidence from the time-to-event analysis, we observed that beneficiaries experienced long delays between AMI discharge and cardiac rehabilitation initiation. The proportion of cardiac rehabilitation initiators nearly doubled between 30 days and 90 days post discharge. The mean time to cardiac rehabilitation initiation of 56 days in this study was similar to what has previously been reported (7). If investigators defined an exposure window based on the median time to initiation from previous studies then half of those who would eventually initiate treatment would be misclassified as non-users since the distribution of time to initiation among initiators was skewed right (median 33 days). Defining an exposure window of 30 days instead of 60 days may overestimate the protective effect of treatment (19). Studies that aim to assess the effects of cardiac rehabilitation should consider the above factors when designing outcome studies with fixed exposure windows.

Promoting adoption of guideline recommendations remains an opportunity for public health intervention given that less than 20% of any population studied initiated cardiac rehabilitation and approximately 50% of any population studied had concordant guideline medication possession in the first year post-AMI discharge. Our estimates of cardiac rehabilitation initiation were similar to a previous study of Medicare beneficiaries at least 65 years old who survived at least 30 days post discharge and had a length of stay of 30 days or less which reported 13.9% of MI patients initiated cardiac rehabilitation within 1 year (7). In our study, we estimated 15.0% (95%CI: 14.7%, 15.2%) of beneficiaries who survived at least 30 days initiated cardiac rehabilitation within 1 year using the competing risk method. Although nearly a decade has passed between these studies, there was only a 1% increase in the adoption of this recommendation. Beneficiaries were more likely to fill prescriptions for concordant guideline medications than participate in cardiac rehabilitation. Concordant guideline recommended medication possession from this study (49.8% 95%CI: 49.4%, 50.1%) using the competing risk method at 3 months post-AMI discharge was similar to the

observed proportion of adoption (41.5%) reported for a subgroup at least 65 years old in a study of commercially insured acute coronary syndrome patients (5). In the five years between the Nichols study and our study, there was an almost 10% increase in the adoption of this recommendation. The difference may be even higher when comparing just three medication classes. Despite this increase in guideline adoption, there is still a great opportunity for public health interventions in this area.

Our large sample size was a strength of our study. It permitted us to apply several types of restrictions and maintain sufficient numbers of beneficiaries in each subpopulation to stably estimate adoption of guideline recommendations. Women, a subgroup that is often under-represented in cardiac rehabilitation trials, comprised approximately half of each population (20). Because we used both outpatient and pharmacy claims data for this study, we were able to avoid recall bias in the definition of study outcomes. However, we may have underestimated guideline recommended medication use due to some beneficiaries initiating treatment on samples or low-cost generic medications that were not recorded in the pharmacy claims (21, 22). We suspect little misclassification of cardiac rehabilitation use from outpatient claims data since providers would not be reimbursed without submitting a claim. Another limitation of this study is the unmeasured provider preference for referring patients to cardiac rehabilitation or prescribing all of the guideline recommended medications. We assumed that all beneficiaries meeting study criteria would have been referred for cardiac rehabilitation and given a prescription for all guideline recommended medication but there may be clinical or system reasons why this was not the case. We attempted to limit the impact of the violation of these assumptions with the study inclusion/exclusion criteria.

In conclusion, we discussed different approaches to accounting for death applied to a study of the use of guideline-recommended therapies after AMI. We found that restricting the population resulted in somewhat higher estimates of guideline recommended cardiac rehabilitation and concordant medication possession. Restriction by baseline covariates will produce estimates that more interpretable at the point of care than restriction by long periods of observed survival. We saw relatively modest differences between the Kaplan-Meier estimates and the competing risk estimates. In studies where mortality is more common, restricting the study to patients who survive may affect generalizability and may introduce survivor bias in the results. Competing risk approaches are preferable since they avoid these issues.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References:

1. Wilk A, Sajjan S, Modi A, et al. Post-fracture pharmacotherapy for women with osteoporotic fracture: analysis of a managed care population in the USA. *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA* 2014;25:2777–2786
2. Block AE, Solomon DH, Cadarette SM, et al. Patient and physician predictors of post-fracture osteoporosis management. *Journal of general internal medicine* 2008;23:1447–1451 [PubMed: 18584260]
3. Lee HY, Cooke CE, Robertson TA. Use of secondary prevention drug therapy in patients with acute coronary syndrome after hospital discharge. *J Manag Care Pharm* 2008;14:271–280 [PubMed: 18439049]
4. Morse RB, Hall M, Fieldston ES, et al. Hospital-level compliance with asthma care quality measures at children's hospitals and subsequent asthma-related outcomes. *JAMA* 2011;306:1454–1460 [PubMed: 21972307]
5. Nichols GA, Wang F, Pedula KL. Comparison of evidence-based versus non-evidence-based pharmacotherapy on the risk of cardiovascular hospitalization and all-cause mortality among patients with established cardiovascular disease. *Am J Cardiol* 2010;105:786–791 [PubMed: 20211320]
6. Sisler JJ, Seo B, Katz A, et al. Concordance with ASCO guidelines for surveillance after colorectal cancer treatment: a population-based analysis. *J Oncol Pract* 2012;8:e69–79 [PubMed: 23181004]
7. Suaya JA, Shepard DS, Normand SL, et al. Use of cardiac rehabilitation by Medicare beneficiaries after myocardial infarction or coronary bypass surgery. *Circulation* 2007;116:1653–1662 [PubMed: 17893274]
8. MacMahon S, Collins R. Reliable assessment of the effects of treatment on mortality and major morbidity, II: observational studies. *Lancet* 2001;357:455–462 [PubMed: 11273081]
9. McGrath LJ, Ellis AR, Brookhart MA. Controlling Time-Dependent Confounding by Health Status and Frailty: Restriction Versus Statistical Adjustment. *Am J Epidemiol* 2015;182:17–25 [PubMed: 25868551]
10. Schneeweiss S, Patrick AR, Stürmer T, et al. Increasing levels of restriction in pharmacoepidemiologic database studies of elderly and comparison with randomized trial results. *Med Care* 2007;45:S131–142 [PubMed: 17909372]
11. Hernan MA, Hernandez-Diaz S, Robins JM. A structural approach to selection bias. *Epidemiology* 2004;15:615–625 [PubMed: 15308962]
12. Bland JM, Altman DG. Survival probabilities (the Kaplan-Meier method). *BMJ* 1998;317:1572 [PubMed: 9836663]
13. Jager KJ, van Dijk PC, Zoccali C, et al. The analysis of survival data: the Kaplan-Meier method. *Kidney Int* 2008;74:560–565 [PubMed: 18596735]
14. Lau B, Cole SR, Gange SJ. Competing risk regression models for epidemiologic data. *Am J Epidemiol* 2009;170:244–256 [PubMed: 19494242]
15. Smith SC, Jr., Benjamin EJ, Bonow RO, et al. AHA/ACCF Secondary Prevention and Risk Reduction Therapy for Patients with Coronary and other Atherosclerotic Vascular Disease: 2011 update: a guideline from the American Heart Association and American College of Cardiology Foundation. *Circulation* 2011;124:2458–2473 [PubMed: 22052934]

16. Gagne JJ, Glynn RJ, Avorn J, et al. A combined comorbidity score predicted mortality in elderly patients better than existing scores. *Journal of clinical epidemiology* 2011;64:749–759 [PubMed: 21208778]
17. Faurot KR, Jonsson Funk M, Pate V, et al. Using claims data to predict dependency in activities of daily living as a proxy for frailty. *Pharmacoepidemiology and drug safety* 2014
18. Lin GS, Johnston Ying, Gordon Analyzing Survival Data with Competing Risks Using SAS® Software. *SAS Global Forum* 20122012
19. Austin PC, Mamdani MM, Van Walraven C, et al. Quantifying the impact of survivor treatment bias in observational studies. *Journal of Evaluation in Clinical Practice* 2006;12:601–612 [PubMed: 17100859]
20. Clark AM, Hartling L, Vandermeer B, et al. Meta-analysis: secondary prevention programs for patients with coronary artery disease. *Annals of Internal Medicine* 2005;143:659–672 [PubMed: 16263889]
21. Lauffenburger JC, Balasubramanian A, Farley JF, et al. Completeness of prescription information in US commercial claims databases. *Pharmacoepidemiology and drug safety* 2013;22:899–906 [PubMed: 23696101]
22. Li X, Sturmer T, Brookhart MA. Evidence of sample use among new users of statins: implications for pharmacoepidemiology. *Med Care* 2014;52:773–780 [PubMed: 24984210]

Figure 1:
Diagram of Study Population Exclusions

Figure 2:
Study Design

Figure 3:
Kaplan-Meier Complement Cumulative Incidence (%) of Cardiac Rehabilitation Initiation or Concordant Guideline Recommended Medication Use after Acute Myocardial Infarction Discharge by Restriction Method

Figure 4:

Comparison of Methods to Compute Cumulative Incidence (%) of Cardiac Rehabilitation Initiation or Concordant guideline recommended medication Use after AMI Discharge in the Overall Study Population

Table 1:**Study Population Characteristics**

Characteristics	Overall	30 Day Survivors	366 Day Survivors	Predicted 1-yr Survivors
Overall	76,797	74,487 (97.0%)	63,690 (82.9%)	63,386 (82.5%)
Demographics				
Age Group				
Aged 65-74 years	29,119 (37.9%)	28,570 (38.4%)	25,742 (40.4%)	24,643 (38.9%)
Aged 75-84 years	31,234 (40.7%)	30,346 (40.7%)	25,974 (40.8%)	25,436 (40.1%)
Aged 85+ years	16,444 (21.4%)	15,571 (20.9%)	11,974 (18.8%)	13,307 (21.0%)
Female	42,872 (55.8%)	41,594 (55.8%)	35,430 (55.6%)	35,256 (55.6%)
White	66,338 (86.5%)	64,352 (86.5%)	55,107 (86.6%)	55,417 (87.5%)
Index Hospitalizations				
Revascularization				
Angioplasty	28,555 (37.2%)	28,173 (37.8%)	26,059 (40.9%)	25,832 (40.8%)
CABG	6,956 (9.1%)	6,898 (9.3%)	6,453 (10.1%)	6,230 (9.8%)
Any ICU Stay	42,387 (55.2%)	41,162 (55.3%)	35,324 (55.5%)	34,840 (55.0%)
Hospital Transfers				
0	57,922 (75.4%)	56,205 (75.5%)	49,063 (77.0%)	48,514 (76.5%)
1	15,466 (20.1%)	15,030 (20.2%)	12,293 (19.3%)	12,332 (19.5%)
>2	3,409 (4.4%)	3,252 (4.4%)	2,334 (3.7%)	2,540 (4.0%)
Baseline Medications				
Beta-Blocker	37,002 (48.2%)	35,831 (48.1%)	30,048 (47.2%)	29,144 (46.0%)
ACEi or ARB	40,179 (52.3%)	38,969 (52.3%)	33,096 (52.0%)	32,574 (51.4%)
Statin	34,102 (44.4%)	33,133 (44.5%)	28,427 (44.6%)	27,579 (43.5%)
Calcium Channel Blocker	23,277 (30.3%)	22,533 (30.3%)	19,002 (29.8%)	18,437 (29.1%)
Antidepressant	16,011 (20.8%)	15,421 (20.7%)	12,659 (19.9%)	12,034 (19.0%)
Concurrent GRM Combination	10,697 (13.9%)	10,311 (13.8%)	8,479 (13.3%)	7,955 (12.6%)
Baseline Comorbidities				
Proxy Frailty Mean (SD)	6.3 (6.27)	6.2 (6.15)	5.7 (5.55)	5.6 (5.09)
Comorbidity Score Mean (SD)	2.3 (2.46)	2.3 (2.43)	2.0 (2.29)	1.5 (1.58)
Comorbid Conditions				
Hypertension	64,367 (83.8%)	62,490 (83.9%)	53,518 (84.0%)	53,234 (84.0%)
Hyperlipidemia	51,222 (66.7%)	49,952 (67.1%)	43,693 (68.6%)	42,748 (67.4%)
Congestive Heart Failure	35,025 (45.6%)	33,457 (44.9%)	26,243 (41.2%)	23,331 (36.8%)
Diabetes	31,688 (41.3%)	30,661 (41.2%)	25,723 (40.4%)	24,113 (38.0%)
Chronic Pulmonary Disease	26,131 (34.0%)	25,137 (33.7%)	20,317 (31.9%)	18,111 (28.6%)
Osteoporosis or Osteoarthritis	21,107 (27.5%)	20,522 (27.6%)	17,599 (27.6%)	17,113 (27.0%)
Peripheral Vascular Disease	17,606 (22.9%)	16,958 (22.8%)	13,788 (21.6%)	11,575 (18.3%)
Cancer	9,494 (12.4%)	9,027 (12.1%)	7,033 (11.0%)	5,793 (9.1%)
Cerebrovascular Disease	9,201 (12.0%)	8,848 (11.9%)	7,164 (11.2%)	6,380 (10.1%)
Depression	6,025 (7.8%)	5,820 (7.8%)	4,817 (7.6%)	4,430 (7.0%)
Renal Disease	4,718 (6.1%)	4,458 (6.0%)	3,260 (5.1%)	1,017 (1.6%)

Characteristics	Overall	30 Day Survivors	366 Day Survivors	Predicted 1-yr Survivors
Rheumatic Disease	3,771 (4.9%)	3,666 (4.9%)	3,126 (4.9%)	3,065 (4.8%)

Note: CABG - Coronary artery bypass grafting; ICU - Intensive Care Unit; ACEi - angiotensin-converting-enzyme inhibitor; ARB - angiotensin II receptor blockers; GRM - guideline recommended medication; SD - standard deviation

Note: Shaded cells have a standardized difference between the restricted population and the overall population that is greater than 10%.