Published in final edited form as:

J Card Fail. 2019 May ; 25(5): 343–351. doi:10.1016/j.cardfail.2018.10.005.

Low utilization of beta blockers among Medicare beneficiaries hospitalized for heart failure with reduced ejection fraction

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Abstract

Background: The evidence-based beta blockers carvedilol, bisoprolol, and metoprolol succinate reduce mortality and hospitalizations among patients with heart failure with reduced ejection fraction (HFrEF). Use of these medications is not well-described in the general population of patients with HFrEF, especially among patients with potential contraindications.

Objectives: Our goal was to describe the patterns of prescription fills for carvedilol, bisoprolol, and metoprolol succinate among Medicare beneficiaries hospitalized for HFrEF, as well as estimate the associations between specific contraindications for beta blocker therapy and these patterns.

Methods: Using a cohort of 15,205 Medicare beneficiaries hospitalized for HFrEF between 2007 and 2013 from the 5% Medicare random sample, we described prescription fills (30-days post discharge) and dosage patterns (1-year post discharge) for beta blockers. Using Fine and Gray competing risk models, we estimated the associations between potential contraindications (hypotension, chronic obstructive pulmonary disease (COPD), asthma, and syncope) and prescription fill and dosing patterns while adjusting for demographics, comorbidities, and healthcare utilization.

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Results: For beneficiaries who did not die or were not readmitted to the hospital, 38% of hospitalizations were followed by a prescription fill for an evidence-based beta blocker within 30 days, 12% were followed by prescription fills for at least 50% of the recommended dose of an evidence-based beta blocker within 1 year, and 9% were followed by a prescription fill for an uptitrated dose of an evidence-based beta blocker within 1 year. The prevalence of the contraindications were 21% for hypotension, 48% for COPD, 15% for asthma, and 12% for syncope. Among beneficiaries who did not fill a prescription for an evidence-based beta blocker within 30 days, 67% had at least one of these contraindications. Hypotension, COPD, and syncope were each associated with an approximately 10% lower risk of filling a prescription for an evidence-based beta blocker.

Conclusions: Prescription fill and uptitration rates for evidence-based beta blockers are low among Medicare beneficiaries with HFrEF, but contraindications explain only a minor portion of these low rates.

Keywords

Medicare Part D; competing risks

Introduction

The American College of Cardiology Foundation and the American Heart Association recommend treating patients with heart failure with reduced ejection fraction (HFrEF) with the evidence-based beta blockers bisoprolol, carvedilol, and sustained-release metoprolol succinate⁽¹⁾ in order to reduce mortality and hospitalizations.^(2–6) To avoid triggering decompensation, treatment should begin with a low dose and then be uptitrated over time.⁽¹⁾ A report from an HF registry study conducted from 2003 – 2004 that was designed to improve adherence to treatment guidelines found that 75% of patients hospitalized for HFrEF were discharged with a prescription for a beta blocker, and 93% of those participants still had a prescription for a beta blocker 60 – 90 days post discharge.⁽⁷⁾ These data were based upon a sample of hospitals that self-selected to enroll in a program to improve adherence to recommended treatment guidelines and did not account for prescriptions that were never filled. Previous research has shown that beta blocker prescription rates in other populations, such as among patients dual-eligible for Medicare and Medicaid,⁽⁸⁾ are much lower than in registry populations, potentially due to higher prevalences of contraindications, among other differences. Patients may not fill their prescriptions for beta blockers due to potential side effects including hypotension, fatigue, atrioventricular block, and worsening HF.⁽¹⁾ Although 85% of patients in clinical trials for beta blockers to treat HFrEF were able to tolerate the maximum dose after careful uptitration,⁽¹⁾ at most only 55% of older patients with HFrEF met the inclusion criteria for these trials because of potential contraindications, comorbidities, and age.⁽⁹⁾

Medicare Part D pharmacy data provide an opportunity to study a general sample of patients with HFrEF, using claims for beta blocker prescription fills that include dose. In a cohort of Medicare beneficiaries hospitalized for HFrEF, we used Medicare Part D pharmacy claims data to describe four aspects of beta blocker prescription fills: (1) filling a prescription for a beta blocker within 30 days of hospital discharge; (2) filling a prescription for an evidence-

based beta blocker (carvedilol, bisoprolol, and sustained-release metoprolol succinate) within 30 days of hospital discharge; (3) filling a prescription for at least 50% of the target dose of an evidence-based beta blocker within 1 year of hospital discharge; and (4) filling a prescription for an uptitrated dose of an evidence-based beta blocker within 1 year of hospital discharge. We chose to include an analysis of evidence-based beta blockers, given that these are the only beta blockers with evidence from randomized controlled trials to reduce mortality and readmissions among persons with HFrEF. Other beta blockers do not have as clear evidence for effectiveness in HFrEF.(1) Prescription fills for these particular beta blockers indicate an intent to treat HF and not simply a comorbidity, such as hypertension. We also tested for associations between potential contraindications for beta blocker therapy and the four outcomes to determine whether higher prevalence of contraindications in the Medicare population could explain potentially lower rates of beta blocker use relative to clinical trial participants or HF registries.

Methods

Study sample

We conducted a retrospective cohort study of Medicare beneficiaries hospitalized for HFrEF using claims data. From a 5% random sample of Medicare beneficiaries, we identified episodes of hospitalization with a primary discharge diagnosis of HFrEF between 2007 and 2013, where the beneficiary was discharged alive. HFrEF was defined as an ICD-9 diagnosis code of 428.2x (Systolic heart failure) or 428.4x (Combined systolic and diastolic heart failure). In one study, 77% of patients with these diagnoses codes had confirmed HFrEF on medical record review.(10) Follow up data was available through 2013. Beneficiaries were not included in the sample if they were not living in the US for the year prior to HFrEF admission date, did not have continuous Medicare Part A, Part B, and Part D coverage for the year prior to HFrEF admission, were not in the Medicare 5% random sample for the year prior to HFrEF admission, or were 110 years old or older on the HFrEF admission date. Beneficiaries with Medicare Advantage (Part C) were not included in this sample. We retained only the first hospitalization for HFrEF for each beneficiary during the study period.

Outcomes

Outcomes for this study were identified using pharmacy claims for patient fills of beta blocker prescriptions. The four outcomes of interest in this study were: (1) filling a prescription for any beta blocker within 30 days of HFrEF hospitalization discharge; (2) filling a prescription for an evidence-based beta blocker within 30 days of HFrEF hospitalization discharge (i.e., bisoprolol, carvedilol, or sustained-release metoprolol succinate); (3) filling a prescription for at least 50% of the recommended target dose of an evidence-based beta blocker within 1 year of HFrEF hospitalization discharge; and (4) filling a prescription for an uptitrated dose of an evidence-based beta blocker within 1 year of HF hospitalization discharge. The denominator for all outcomes was the entire cohort. For instance, we measured the outcome of filling a prescription for at least 50% of the target dose among the entire cohort, not only those who had filled a prescription for an evidence-based beta blocker. Target doses were defined in the AHA/ACC heart failure treatment guidelines.(1) Specifically, the daily target dosages were 10 mg once per day for bisoprolol,

50 mg twice per day for carvedilol, 80 mg once per day for controlled release carvedilol, and 200 mg once per day for extended release metoprolol. Each of the four outcomes were assessed independently of one another. For example, participants could reach at least 50% of the target dose of an evidence-based beta blocker without uptitrating if their first prescription for a beta-blocker was for at least 50% of the target dose or if they started on a beta blocker that was not evidence-based and then were switched to at least 50% of the target dose of an evidence-based beta blocker. Participants were censored if follow up time ended or a patient became ineligible for the study sample per the exclusion criteria described in the “Study sample” subsection above (e.g., Medicare coverage lapsed). Recurrent hospitalizations and deaths were treated as competing risks.

Potential contraindications for beta blocker therapy

We considered several potential contraindications for a beta blocker prescription: hypotension, COPD, asthma, bradycardia, syncope, and atrioventricular block (first, second, or third degree). Detection of contraindications was based upon ICD-9 diagnosis codes from combinations of inpatient, outpatient, SNF, and home health agency claims. Because of the small number of hospitalizations with evidence of bradycardia (<2%) and atrioventricular block (<1%), we focused on hypotension, COPD, asthma, and syncope. Claims for contraindications were identified during the year prior to HFrEF hospitalization (see Supplementary Methods for definitions of these contraindications).

Other variables

Potential confounders of the association between the contraindications and patterns of beta blocker prescription fills were considered. Demographic variables included were age at HFrEF hospitalization admission, race (black, white, other), gender, Medicaid eligibility, Medicare Part D subsidies, region of residence, and nursing home residence. Comorbidities included were whether the beneficiary had coronary heart disease (CHD), stroke, hypertension, hyperlipidemia, diabetes, valvular heart disease, atrial fibrillation, other arrhythmias or conduction disorders, autoimmune or inflammatory disease, cancer, malnutrition, liver disease, anemia, or depression, and were assessed during the year prior to hospitalization. We also included implantable cardiac device (cardiac resynchronization therapy – defibrillator [CRTD], cardiac resynchronization therapy – pacemaker [CRTP], defibrillator, pacemaker, or none), also assessed during the year prior to hospitalization. Indicators of health care utilization in the prior year (a hospitalization, a SNF stay, or filling a prescription for a beta blocker prior to hospitalization [evidence-based beta blocker, a non-evidence-based beta blocker, or no beta blocker]) and length of stay during an HFrEF hospitalization were also considered as potential confounders.

Statistical analysis

We calculated summary statistics of the potential confounders and four outcomes for the total sample, as well as by presence of each contraindication (hypotension, COPD, asthma, and syncope). Cumulative incidence functions were estimated for the 30-day and 1-year outcomes for the total cohort. Fine and Gray models(11) took into account the competing risks of hospitalization or death and were used to estimate hazard ratios (HRs) for the association between the contraindications with each of the beta-blocker outcomes. Given

that the competing risks of hospitalization and death are common in this population, standard Cox regression models cannot provide an unbiased estimate of the probability of filling a prescription by the specified follow up time. Fine and Gray models allowed us to estimate the probability of filling a prescription, as well as HRs for filling a prescription based upon the presence of a potential contraindication, among beneficiaries who did not die and were not hospitalized during the follow up period.

Although we initially included beneficiaries with a discharge status code that indicated a skilled nursing facility (SNF) discharge in our main analysis, we conducted a sensitivity analysis excluding these beneficiaries, given that Medicare Part D does not cover prescription benefits during episodes of Medicare-covered SNF care. In addition to the sensitivity analysis that excluded those discharged to a SNF, we also conducted three other sensitivity analyses: one that excluded participants with bradycardia or atrioventricular block (any degree), one that performed stratified analyses by beta blocker use during baseline, and one that excluded beneficiaries who had days of an evidence-based beta blocker available upon hospital admission according to previous prescription fills prior to admission. Finally, we conducted an analysis with the presence of any of the four contraindications as the exposure in a fully adjusted model in order to summarize the associations between each of the potential confounders and the beta blocker prescription fill patterns. All analyses were conducted using the R statistical software and SAS (Cary, NC).

Results

After identifying the relevant sample of HF hospitalizations from the Medicare 5% random sample, our analysis sample consisted of 15,205 beneficiaries with a hospitalization for HfrEF (See Supplemental Figure 1). Most beneficiaries had previous hospitalizations for HF. Summaries of demographic variables, comorbidities, implanted cardiac devices, and healthcare utilization variables for the entire cohort, as well as for participants with each of the contraindications, are shown in Table 1.

Figure 1 shows the cumulative incidence functions for each outcome. Approximately 51% of the hospitalizations were followed with a claim for a prescription fill for a beta blocker within 30 days, and even fewer of the hospitalizations were followed with a prescription fill for an evidence-based beta blocker within 30 days. Twelve percent of hospitalizations were followed with a claim for a prescription filled for at least 50% of the target dose of an evidence-based beta blocker within 1 year, and only 9% of hospitalizations were followed by up titration of the dose of an evidence-based beta blocker within 1 year.

Among the beneficiaries in the sample, 21% had hypotension, 48% had COPD, 15% had asthma, and 12% had syncope. Among beneficiaries who did not fill a prescription for an evidence-based beta blocker within 30 days, 67% had at least one of these contraindications. Beneficiaries hospitalized with a contraindication were more likely to have had a diagnosis code of anemia and/or depression and to have been hospitalized for any cause during the previous year compared to the entire cohort. Beneficiaries with hypotension or syncope were more likely to have filled a prescription for an evidence-based beta blocker during baseline or have a defibrillator (with or without CRT) than the entire cohort. They were more likely

to have had a diagnosis code for cardiovascular disease (CVD) (CHD or stroke) in the previous year, and have had hyperlipidemia or atrial fibrillation. Beneficiaries with COPD or asthma were more likely to be Medicaid eligible and have a Medicare Part D subsidy. Beneficiaries with asthma tended to be younger, were more likely to be black and female, and were more likely to have had hypertension and diabetes in the year prior to hospitalization compared to the entire cohort. Overall, beneficiaries with hypotension or syncope appeared to have the highest overall burden of comorbidities, treatment by beta blockers or implantable cardiac devices, and risk factors for CVD compared to the entire cohort. Finally, beneficiaries with hypotension or syncope were more likely to have had a SNF stay during the year prior to hospitalization than the entire cohort.

Figure 2 shows the HRs and 95% confidence intervals for each outcome and contraindication. Supplemental Table 1 contains the HRs and 95% confidence intervals portrayed in Figure 2. Beneficiaries with hypotension were less likely to fill a prescription for any beta blocker within 30 days (HR, 95% confidence interval: 0.90, 0.85 – 0.95), an evidence-based beta blocker within 30 days (0.92, 0.87 – 0.99), less likely to receive at least 50% of the target dose of an evidence-based beta blocker in 1 year (0.60, 0.52 – 0.68), and potentially less likely to be uptitrated within 1 year (0.97, 0.84 – 1.13) compared to those without hypotension. Compared to beneficiaries without COPD, beneficiaries with COPD had lower rates of filling a prescription for any beta blocker within 30 days (0.91, 0.87 – 0.95) and for an evidence-based beta blocker within 30 days (0.89, 0.81 – 0.97) compared to those without COPD. Beneficiaries with COPD were less likely to reach at least 50% of the target dose (0.90, 0.85 – 0.94) or uptitrated (0.84, 0.75 – 0.94) within 1 year compared to those without COPD. Beneficiaries with asthma did not have significantly lower risks of any of the outcomes compared to beneficiaries without asthma. Syncope was associated with a lower risk of filling a prescription for any beta blocker within 30 days (0.92, 0.86 – 0.99) or an evidence-based beta blocker within 30 days (0.90, 0.83 – 0.97), as well as a lower risk of filling a prescription for at least 50% of the target dose of an evidence-based beta blocker within 1 year (0.84, 0.72 – 0.98). Syncope was not significantly associated with filling a prescription for uptitrating on an evidence-based beta blocker within 1 year (0.98, 0.82 – 1.18).

The sensitivity analyses that either: (1) excluded hospitalizations with claims for bradycardia or atrioventricular block (any degree) in the year prior to the HFrEF hospitalization; (2) excluded hospitalizations with discharge codes to an SNF; or (3) excluded beneficiaries who had days of an evidence-based beta blocker available upon hospital admission found only small changes in the hazard ratios compared to the main analysis (Supplemental Figures 2, 3, and 4). However, associations between the potential contraindications and beta blocker filling patterns were stronger among beneficiaries who did not use beta blockers in the year prior to hospitalization as compared to the associations among those who had filled beta blocker prescriptions prior to hospitalization for HFrEF (Supplemental Figure 5).

Supplemental Table 2 contains the HRs for a fully adjusted model when using the presence of any of the four contraindications as the exposure, for each of the beta blocker fill pattern outcomes. Women were more likely to fill a prescription for an uptitrated dose of an evidence-based beta blocker within one year, and those with comorbidities tended to be less

likely to do so. The best predictor of reaching at least 50% of the target dose of an evidence-based beta blocker was having filled a prescription for an evidence-based beta blocker during baseline (HR, 95% confidence interval: 4.23, 3.62 – 4.94).

Discussion

The purpose of our study was to describe patterns of beta blocker prescription fills in Medicare beneficiaries hospitalized for HFrEF, and to determine whether potential contraindications may explain these patterns. We found that less than half of hospitalizations were followed by a prescription fill for a beta blocker specifically indicated in patients with HFrEF within 30 days. Approximately 1 in 10 hospitalizations for HFrEF were followed by reaching at least 50% of the target dose of an evidence-based beta blocker or by up titration of an evidence-based beta blocker within 1 year of hospital discharge. Patients with a potential contraindication were only slightly less likely to fill a prescription for an evidence-based beta blocker, or to fill prescriptions for guideline-concordant doses of these beta blockers over time. Prescription fill patterns among the Medicare population, in which comorbidities are common, may differ from the subpopulation of patients that was eligible for the randomized controlled trials for bisoprolol, carvedilol, and sustained release metoprolol succinate.

Comparisons to previous results

Our results supplement findings from HF registries to provide an understanding of whether patients with HFrEF are generally treated with beta blockers according to national guidelines. Approximately 75% of the patients in the OPTIMIZE-HF registry with HFrEF had a prescription for a beta blocker at discharge, and over 90% of them still had the prescription in 60 – 90 days.(7) However, for those on carvedilol, only one third ever had the dose of their beta blocker adjusted within that time frame.(12) This discrepancy between our results and the results from OPTIMIZE-HF could occur because registries tend to consist of hospitals that are attempting to improve patient care (e.g., improving beta blocker prescription rates). Bertoni *et al.* (2004)(8) found that among a sample of Medicare and Medicaid beneficiaries in North Carolina with HFrEF, only 48% of beneficiaries had a prescription for a beta blocker, and only 12% had a contraindication, indicating that 40% of patients might have been eligible for treatment by a beta blocker. Another explanation for the discrepancy between estimates of prescription rates and fill rates is that not all patients with HFrEF who are prescribed a beta blocker actually fill the prescription. Prescription fills are likely a better indicator of patient behavior compared to discharge prescription rates, which might be a better representation of provider behavior than patient behavior. Prescription rates for beta blockers at hospital discharge are a recommended performance measure for quality of care,(13) but the low prescription fill rates among Medicare beneficiaries compared to prescription rates in national registries suggests that prescription fill rates might be an additional factor to consider when measuring quality of care. Finally, the results of our analysis stratified by beta blocker use preceding the hospitalization that showed contraindications tended to be relevant only when the beneficiary was not using beta blockers prior to hospitalization corroborate findings from the Get With the Guidelines - Heart Failure registry, which found that the best predictor for discharge prescription for an

evidence-based beta blocker is being admitted with a prescription for an evidence-based beta blocker.(14) Further investigation of the causes of discrepancies between prescription rates and prescription fill rates for beta blockers among patients with HFrEF is warranted.

A recent study(15) using the same definition of HFrEF and Part D claims for the same beta blockers among beneficiaries discharged to a SNF estimated slightly higher prescription fill rates at 90 days (53%) than we observed at 30 days (35 – 40%). Most beneficiaries who filled a prescription for a beta blocker filled it shortly after discharge, suggesting that the difference in length of follow up between the two studies does not fully account for the difference in estimated probabilities of filling a prescription. While our study and the one by Li *et al.* had identical methods of identifying beneficiaries with HFrEF and identifying prescription fills for evidence-based beta blockers, there were differences that might explain the lower estimated probabilities in our study, including Li *et al.*'s focus on a beneficiary population that might have increased healthcare utilization compared to the entire population of beneficiaries with HFrEF(16) and exclusion of participants who died within the 90-day follow up period. Therefore, the estimated probabilities of filling a prescription from the study by Li *et al.* apply to beneficiaries discharged to a SNF and survived to 90 days post-hospitalization, while our estimated probabilities apply to a larger group of beneficiaries with multiple discharge types.

Even though 85% of patients with HFrEF in clinical trials of beta blockers are able to tolerate the target recommended dose, only approximately one quarter of Medicare beneficiaries with HFrEF and at most half of those with HFrEF would have met the inclusion criteria for those clinical trials.(9) Few Medicare beneficiaries in this study filled prescriptions that were at least 50% of the target dose or filled prescriptions that were uptitrated, which is the pattern of care recommended by national guidelines.(1) Previous studies suggest that the likelihood of reaching the target dose of a beta blocker among patients with HFrEF increased from 1999 to 2004,(17) but we do not know whether that trend has continued. There are potentially compelling clinical reasons not to prescribe or uptitrate a beta blocker for a patient with HFrEF including patient preferences, limited expected lifespan, frailty, and intolerable side effects or medication interactions during previous regimens of the medications, none of which could be assessed in this study.(18) The potential impact of these factors on evidence-based beta blocker prescription fill patterns among patients with HFrEF should be investigated.

Our study has potential implications for reimbursement policies and management guidelines. Reducing hospital readmissions for beneficiaries with HFrEF can both reduce costs to CMS and improve beneficiary outcomes, and carvedilol, bisoprolol, and sustained-release metoprolol succinate have been shown to reduce readmissions in this population. However, our findings suggest that a subset of Medicare beneficiaries with HFrEF who could benefit from taking these beta blockers are not filling prescriptions for them, given the modest associations between potential contraindications and prescription fill patterns. Therefore, reimbursement policies by CMS that better incentivize integrated inpatient and outpatient management to support use of evidence-based beta blockers among beneficiaries with HFrEF have the potential to reduce their lifetime costs of care by reducing hospital readmissions. Primary care physicians, who are responsible for much of the medical

management of patients with HF, report hypotension and other treatment effects are major barriers to use and up-titration of beta blockers.(19) This finding suggests that increasing use of these medications may require development of protocols for use of these medications that are safe and practical for use in primary care settings among patients with multiple comorbidities, including potential contraindications.

Study limitations and strengths

The results of our study must be interpreted in light of its limitations. Medicare claims do not include measures of ejection fraction; instead we relied on diagnosis codes for heart failure with systolic dysfunction. Previous studies have shown a 77% predictive value of using claims-based definitions to identify those with HFrEF,(10) indicating that the majority of beneficiaries in our study had HFrEF. Approximately 30% of Medicare beneficiaries are not enrolled in a Medicare Part D prescription drug plan (e.g., veterans or those paying out-of-pocket).(20) These individuals were not included in our study, potentially limiting generalizability. We also could not assess the relationship between other important contraindications, such as bradycardia or atrioventricular block, and likelihood of filling a prescription due to a low prevalence of these conditions in our study sample (2%). None of the conditions we examined are absolute contraindications to beta blockers. Medicare claims do not have direct measures of contraindications or indicators of contraindication severity, preventing us from determining whether contraindications with severe symptoms had stronger associations with beta blocker prescription fills than we found in our study. We did not investigate potential causes for low prescription fill rates for beta blockers beyond presence of contraindications. Our findings cannot generalize to the population of beneficiaries on Medicare Advantage ("Part C"), as claims for these participants are not included in Medicare claims data available for research. Finally, we could not determine discharge prescription status for study participants because this information is not available in claims data. Even among Medicare Part D beneficiaries discharged with a prescription for a beta blocker, medication adherence to beta blockers is approximately 60%.(21) Study strengths include the use of actual prescription fills for beta blockers instead of only receipt of prescription and the use of a large, generalizable, population-based cohort. Competing risk survival models were used to account for the competing events of hospitalization and death, which allowed us to provide unbiased estimates for the subpopulation of patients most likely to benefit from interventions that could increase adherence to beta blockers.

Conclusions

Among a cohort of Medicare beneficiaries hospitalized for HFrEF, we found that less than 40% of the hospitalizations were followed by a prescription fill for carvedilol, bisoprolol, or metoprolol succinate within 30 days, given that the beneficiary did not die and was not readmitted within 30 days. After adjusting for whether the beneficiary was taking any beta blocker before the hospitalization, demographics, comorbidities, and length of stay in the hospital, beneficiaries with hypotension, COPD, or syncope were approximately 10% less likely to fill a prescription for these beta blockers within 30 days. Contraindications had similar modest or null associations with reaching at least 50% of the target dose or uptitrating, with the exception of those with hypotension having a 40% lower risk of

reaching at least 50% of the target dose. Although there are compelling reasons to avoid beta blocker therapy in patients with HFrEF that may not be readily assessed in administrative data, our findings suggest that there are Medicare beneficiaries with HFrEF who may have lower risk of mortality and readmission with closer adherence to national treatment guidelines.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Financial support: The study was funded by Amgen Inc and NIH National Heart, Lung, and Blood Institute (5T32HL00745734). Dr. Loop received salary support from Amgen Inc. Dr. Van Dyke works in the Center for Observational Research, Amgen Inc. Dr. Chen, Dr. Brown, Dr. Durant, and Dr. Levitan have received research grants from Amgen Inc. Dr. Levitan has served on advisory boards for Amgen Inc and as a consultant for a research project funded by Novartis. Dr. Safford and Dr. Kilgore have no disclosures.

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Highlights

- The beta blockers carvedilol, bisoprolol, and sustained-release metoprolol succinate reduce readmissions and mortality among individuals with heart failure with reduced ejection fraction (HFrEF).
- At most, half of Medicare beneficiaries with HFrEF would have met inclusion criteria for the randomized controlled trials for these beta blockers.
- Less than 40% of Medicare Part D beneficiaries fill a prescription for one of these beta blockers by 30 days post discharge for a HFrEF hospitalization (given they did not die or were not readmitted).
- Potential contraindications for beta blocker therapy explain only 10% of these low prescription fill rates.

Figure 1. Cumulative incidence functions (CIFs) for outcomes.

Outcomes are receiving any beta blocker within 30 days, receiving an evidence-based beta blocker within 30 days, reaching at least 50% of the target dose of an evidence-based beta blocker, and being uptitrated on an evidence-based beta blocker within 1 year, given that the beneficiary has not died or been readmitted before the end of the follow up period. Denominator for each panel is total cohort.

Figure 2. Hazard/risk ratios (HR/RRs) for each contraindication for each outcome.

Each competing risk model was adjusted for age, race, sex, region of residence, beta-blocker use during baseline, cardiac device, Medicaid eligibility upon hospital admission, cost sharing group, nursing home residence, coronary heart disease (CHD), stroke, hypertension, hyperlipidemia, diabetes, valvular or rheumatic heart disease, atrial fibrillation, other arrhythmia or conductive disorder, inflammatory or autoimmune disease, cancer, malnutrition, liver disease, anemia, depression, hospitalization, skilled nursing facility (SNF) stay, and length of hospital stay during heart failure (HF) hospitalization. An HR/RR of 1 indicated no significant association.

Table 1.
Summary characteristics of Medicare beneficiaries hospitalized for HFrEF between 2007 and 2013, overall and in subpopulations with key contraindications.

Values are n(%) unless otherwise specified.

Variable	Overall (n=15,205)	Hypotension (n=3,257)	COPD (n=7,338)	Asthma (n=2,341)	Syncope (n=1,846)
Age at admission, years (mean(sd))	76.5(12.1)	76.5(12.1)	75.5(11.6)	74(12.9)	78.2(11.5)
Race					
Black	2,184(14)	387(12)	945(13)	422(18)	254(14)
Other	852(6)	176(5)	376(5)	151(6)	92(5)
White	12,169(80)	2,694(83)	6,017(82)	1,768(76)	1,500(81)
Women	7,869(52)	1,593(49)	3,635(50)	1,373(59)	911(49)
Dual-eligible for Medicare and Medicaid	6,146(40)	1,269(39)	3,279(45)	1,121(48)	688(37)
Medicare Part D subsidy	7,291(48)	1,513(46)	3,838(52)	1,282(55)	819(44)
US Census region					
East North Central	2,714(18)	616(19)	1,334(18)	427(18)	331(18)
East South Central	1,498(10)	296(9)	781(11)	199(9)	172(9)
Middle Atlantic	2,265(15)	460(14)	1,076(15)	404(17)	311(17)
Mountain	579(4)	125(4)	284(4)	95(4)	67(4)
New England	809(5)	183(6)	357(5)	114(5)	116(6)
Pacific	1,386(9)	303(9)	649(9)	232(10)	157(9)
South Atlantic	2,857(19)	617(19)	1,381(19)	427(18)	363(20)
West North Central	1,195(8)	262(8)	553(8)	165(7)	133(7)
West South Central	1,902(13)	395(12)	923(13)	278(12)	196(11)
Taking beta blocker during baseline					
Evidence-based	7,466(49)	1,782(55)	3,690(50)	1,152(49)	1,036(56)
Other beta blocker	3,741(25)	754(23)	1,735(24)	534(23)	417(23)
None	3,998(26)	721(22)	1,913(26)	655(28)	393(21)
Implanted cardiac device					
CRTD	1,365(9)	351(11)	644(9)	203(9)	258(14)
CRTP	75(0)	14(0)	36(0)	13(1)	17(1)
Defibrillator	1,323(9)	374(11)	653(9)	212(9)	195(11)
Pacemaker	1,565(10)	381(12)	702(10)	231(10)	305(17)
None	10,877(72)	2,137(66)	5,303(72)	1,682(72)	1,071(58)
Atrial fibrillation	7,193(47)	1,763(54)	3,563(49)	1,085(46)	980(53)
Malnutrition	1,252(8)	450(14)	725(10)	202(9)	195(11)
Liver disease	710(5)	209(6)	361(5)	125(5)	90(5)
Anemia	8,548(56)	2,158(66)	4,324(59)	1,381(59)	1,192(65)
Depression	3,499(23)	959(29)	1,963(27)	708(30)	533(29)

Variable	Overall (n=15,205)	Hypotension (n=3,257)	COPD (n=7,338)	Asthma (n=2,341)	Syncope (n=1,846)
Coronary heart disease	10,932(72)	2,600(80)	5,519(75)	1,697(72)	1,474(80)
Stroke	888(6)	271(8)	452(6)	143(6)	189(10)
Hypertension	12,337(81)	2,721(84)	6,102(83)	1,976(84)	1,617(88)
Hyperlipidemia	6,167(41)	1,558(48)	3,130(43)	1,020(44)	889(48)
Diabetes	7,439(49)	1,532(47)	3,750(51)	1,269(54)	895(48)
Valvular or rheumatic heart disease	2,242(15)	606(19)	1,019(14)	352(15)	316(17)
Other arrhythmia or conductive disorder	6,058(40)	1,607(49)	3,041(41)	1,008(43)	1,039(56)
Autoimmune or inflammatory disease	813(5)	214(7)	450(6)	168(7)	114(6)
Cancer	3,059(20)	736(23)	1,495(20)	475(20)	412(22)
Nursing home residence	2,112(14)	549(17)	1,151(16)	329(14)	306(17)
Hospitalization during baseline	4,354(29)	1,309(40)	2,448(33)	849(36)	735(40)
Skilled nursing facility stay during baseline	2,481(16)	823(25)	1,441(20)	449(19)	468(25)
Length of stay during HFrEF hospitalization, days (median(Quartile 1, Quartile 3))	5(4, 8)	6(4, 9)	5(4, 8)	5(4, 8)	5(4, 8)

COPD: Chronic Obstructive Pulmonary Disease; sd: standard deviation; CRTD: cardiac resynchronization therapy - defibrillator; CRTP: cardiac resynchronization therapy – pacemaker; LOS: length of stay; SNF: skilled nursing facility