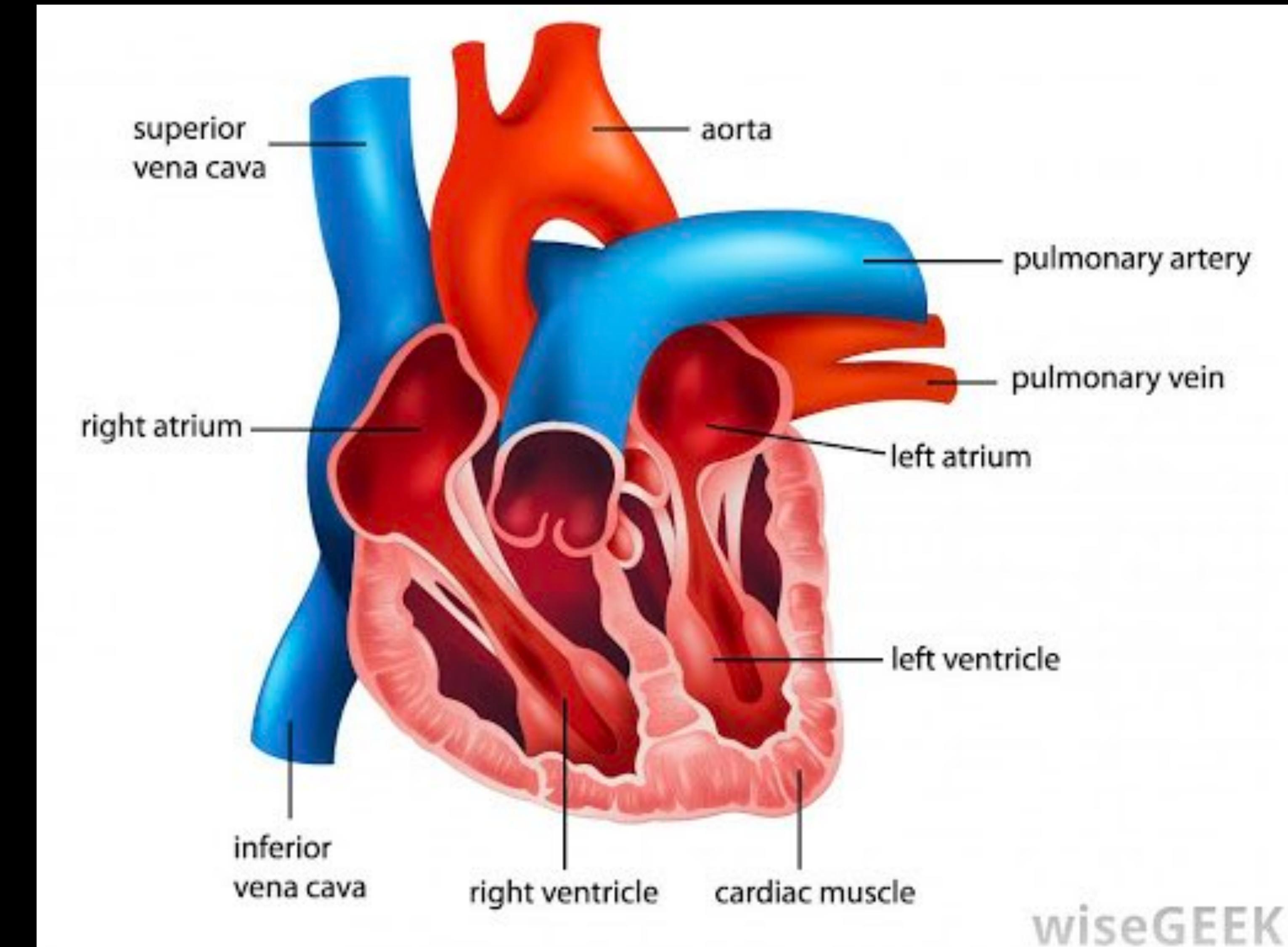


# **Beta blocker use and outcomes among Medicare beneficiaries with heart failure with reduced ejection fraction**

**Matthew Shane Loop, PhD FAHA**

**Postdoctoral work funded in part by Amgen, Inc and NHLBI (5T32HL00745734)**

# What is heart failure?



# Why should we care about heart failure?

- Heart failure has a high mortality rate and hospitalization rate.
- The prevalence of heart failure has increased. The prevalence of HF in adults at least 20 years of age increased from 5.7 million Americans in 2009 - 2012 to 6.2 million in 2013 - 2016 — an increase of 9%.
- From 1998 - 2008, the nationwide 1-year mortality among Medicare beneficiaries was 30%.

# Beta blockers improve outcomes

- Beta blockers allow the heart to relax and facilitate cardiac remodeling
- Three beta blockers have been shown to decrease mortality and hospital readmissions
  - Carvedilol
  - Bisoprolol
  - Sustained-release metoprolol succinate

# Pharmacotherapy is difficult

- Beta blockers don't make you feel very good
- Patients tend to have other comorbidities for which they are taking medication
- Some of these contraindications, such as symptomatic COPD



Despite these difficulties, increased beta blocker use should improve mortality and readmissions

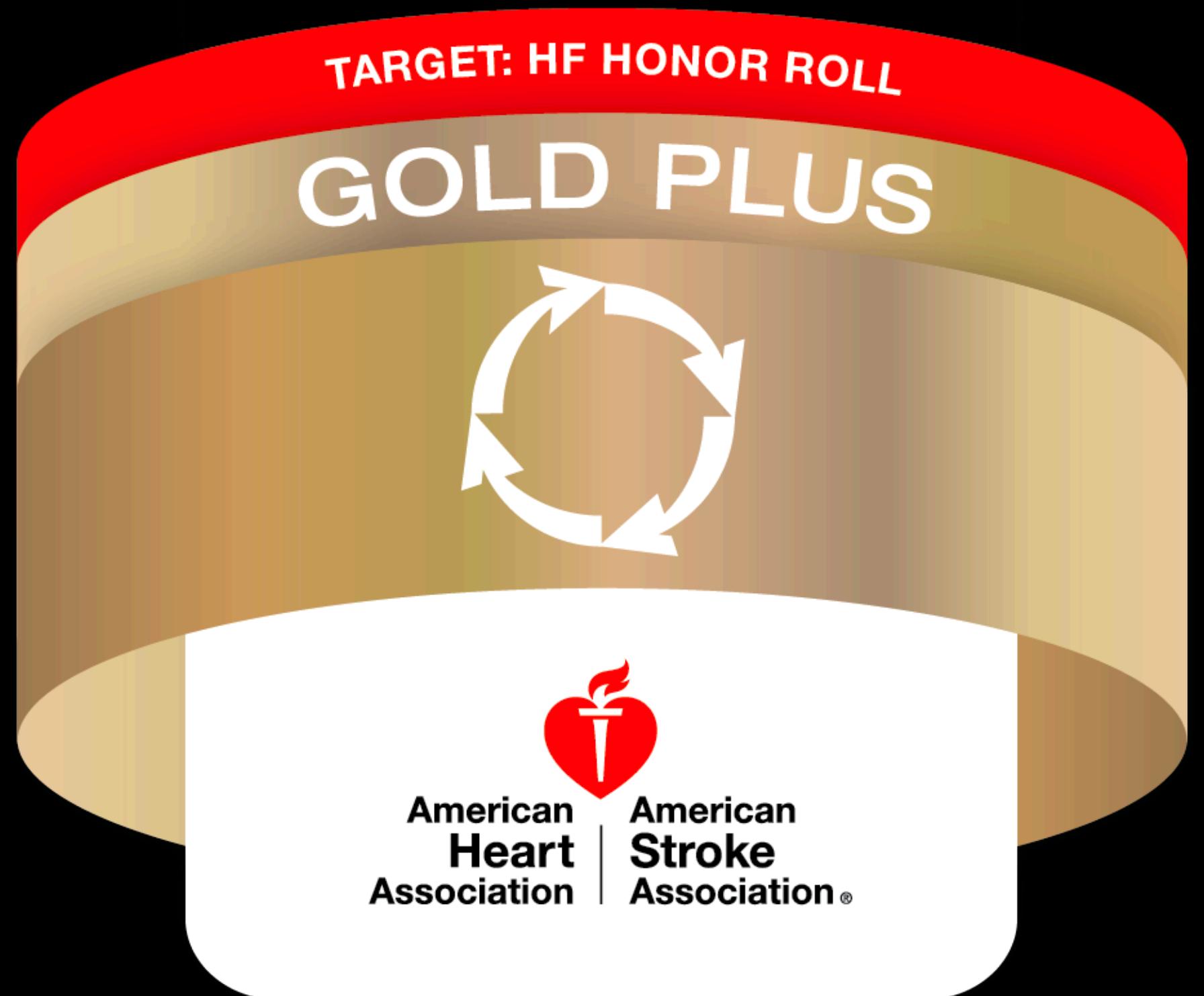
# 2018

---

## GET WITH THE GUIDELINES®

---

### HEART FAILURE



# OPTIMIZE-HF

- Enrolled 48,000 patients across 259 US hospitals
- 73% of all patients were discharged with a prescription for a beta blocker
- However, ...

**Dosing of Beta-Blocker Therapy Before, During, and After Hospitalization for Heart Failure (from Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure)**

Gregg C. Fonarow, MD<sup>a,\*</sup>, William T. Abraham, MD<sup>b</sup>, Nancy M. Albert, PhD, RN<sup>c</sup>, Wendy Gattis Stough, PharmD<sup>e,f</sup>, Mihai Gheorghiade, MD<sup>g</sup>, Barry H. Greenberg, MD<sup>h</sup>, Christopher M. O'Connor, MD<sup>i</sup>, Jie Lena Sun, MS<sup>j</sup>, Clyde W. Yancy, MD<sup>k</sup>, and James B. Young, MD<sup>d</sup>, on behalf of the OPTIMIZE-HF Investigators and Coordinators

A nighttime photograph of Duke University Hospital. The building features a modern design with a curved, illuminated entrance canopy. Large, illuminated letters spelling "DUKE UNIVERSITY" are mounted on the side of the building. A tall, rectangular tower with many windows is visible in the background. The sky is a deep purple.

DUKE UNIVERSITY



AHE  
MEMORIAL  
HOSPITAL

RCTs and registries often focus on certain populations.

Are discharge prescriptions the same  
as prescription fills?

What if we're wrong about how  
things are going for typical patients?



# Now at UNC Eshelman School of Pharmacy

- “Stati-demiologist”
- Division of Pharmacotherapy and Experimental Therapeutics
- Principal and collaborative research in adult cardiovascular disease
- Teach Quantitative Methods in Clinical Research in DPET PhD program



# Two questions for today

1. How often do Medicare beneficiaries with HFrEF fill prescriptions for beta blockers? How often does the dose of the fill change?
2. Does filling a prescription for a beta blocker have similar associations with lower mortality and hospital readmissions as seen in the clinical trials?

# Target population

- Medicare beneficiaries from 2007 - 2013
  - Only ~25% of Medicare beneficiaries would have met inclusion / exclusion criteria for beta blocker trials
- Discharged with a *primary* discharge diagnosis that indicated “systolic HF”
  - Used first admission in this time period as index admission. It almost always was not the first admission for these participants.
- Excluded some observations typical for Medicare analyses (see handout)
- For first question for today, included those discharged to a skilled nursing facility

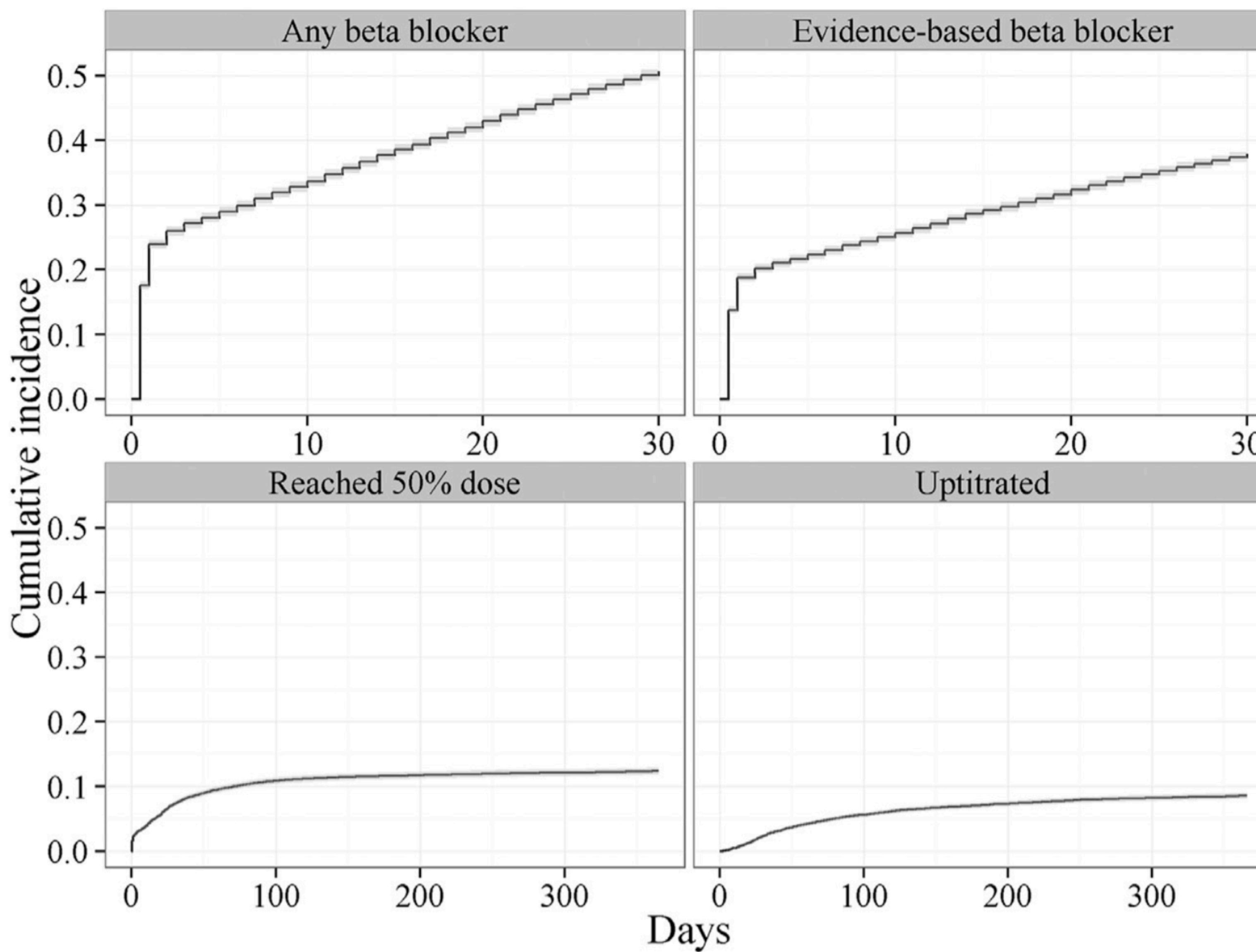
How often do Medicare beneficiaries with HFrEF fill prescriptions for beta blockers? How often does the dose of the fill change?

# Methods

- Outcomes
  - 30-day follow up for fills of carvedilol, bisoprolol, or sustained-release metoprolol succinate
  - 365-day follow up for fills for an uptitrated dose
  - 365-day follow up for fills for a dose at least 50% of guideline-recommended dose
- Exposures
  - Potential contraindications: hypotension, COPD, syncope, and asthma

# Methods

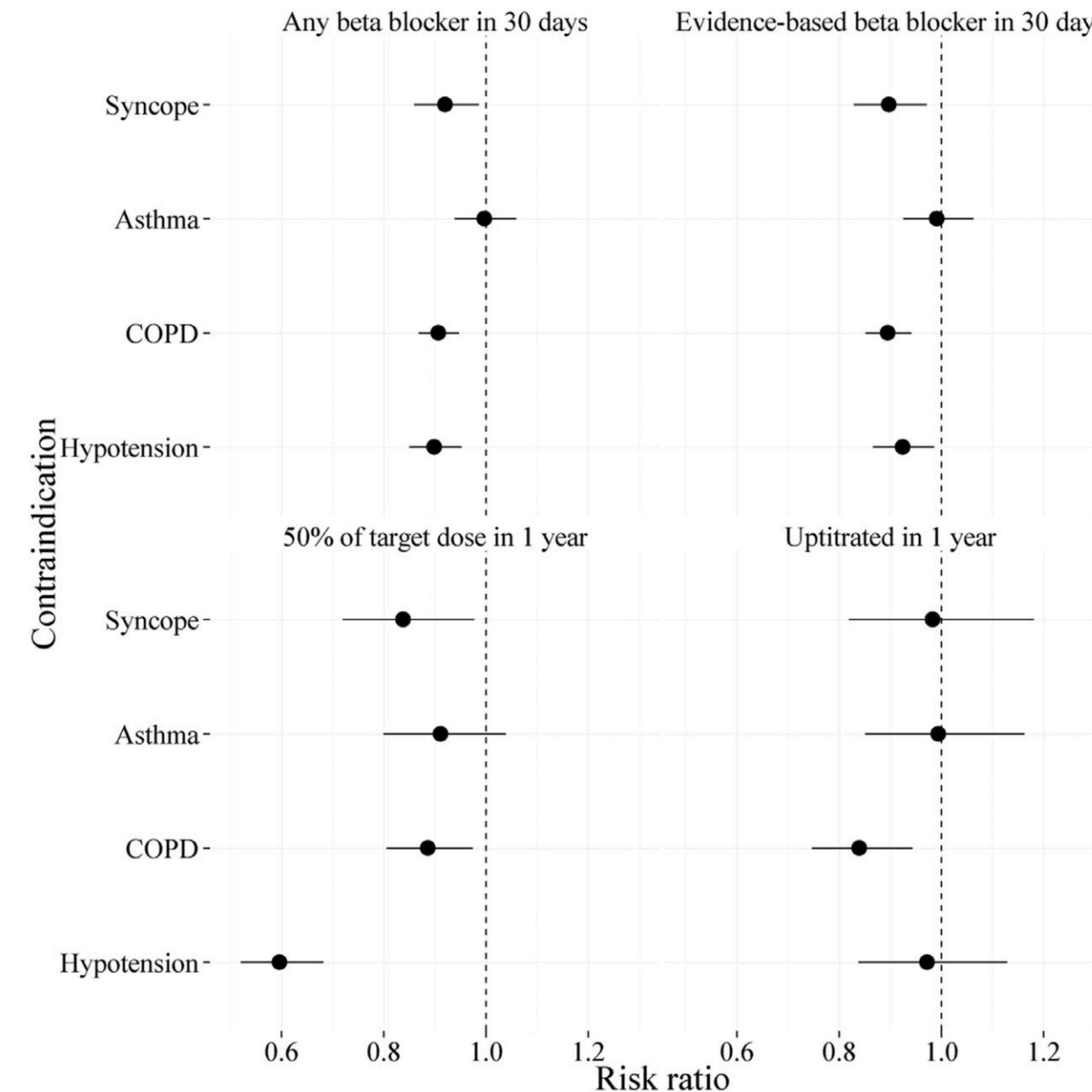
- Estimated cumulative incidence curves for fill outcomes
  - Accounted for competing risks of death and readmission using Fine and Gray method
- Estimated hazard ratios for each of the 4 contraindications, in their own models
  - Also used Fine and Gray
- Conducted sensitivity analyses that: (1) excluded those discharged to a SNF; (2) excluded those with days of a BB available at baseline; and (3) excluded participants with bradycardia or atrioventricular block
- Also performed a sensitivity analysis that stratified by beta blocker use during the year prior to admission



**Fig. 1.** Cumulative incidence functions 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 up-titrated 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.

Medicare beneficiaries are filling prescriptions at lower rates than we thought based upon registries of prescriptions.

Beneficiaries don't get treated anywhere close to the guideline-recommended doses used in the RCTs.



**Fig. 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 on hospital admission, cost-sharing group, nursing home residence, coronary heart disease, 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, and length of hospital stay during heart failure hospitalization. An HR/RR of 1 indicated no significant association. COPD, chronic obstructive pulmonary disease.

Potential contraindications do not seem to explain the size of the difference between Medicare and the OPTIMIZE-HF registry.

Does filling a prescription for a beta blocker have similar associations with lower mortality and hospital readmissions as seen in the clinical trials?

# Methods

- Outcomes
  - 30-day and 365-day mortality, all-cause readmission, and HF readmission
- Exposure
  - Fill for an evidence-based beta blocker (time-varying; helps with immortal person-time bias)
  - Hazard ratio was time-varying (0-3 days, 4-7 days, and >7 days)

The association is similar to clinical trials for mortality and HF readmissions. But the hazards are quite similar for all-cause readmissions for those that filled and didn't fill.

The hazards may have been similar for all-cause readmission because the proportion of the population that would have been kept out of the hospital by taking a beta blocker is small. Hospitalizations are caused by many things in this population.

Increase beta blocker use among older adults with HFrEF  
may not have a large causal effect on reducing overall  
hospitalizations. Then again, if the doses were higher, maybe  
it would.

# Limitations

- We focused only on beta blockers, not ACE inhibitors,e tc.
- We don't know the factors associated with received a prescription and not filling it.
- We didn't have access to quantitative measurements about beneficiary health such as ejection fraction
- Confounding by indication is always a difficult problem.

However, from a public health perspective, increasing users may not decrease all-cause readmissions. Effect of the treatment on the treated. Focusing on comorbidities may provide the greatest reduction. Want to avoid readmissions because they are costly to the patient and the health system.