HFSA 2022 ANNUAL SCIENTIFIC MEETING
WHERE HEART FAILURE TEAMS GATHER

Translating the Findings of the DELIVER Trial to Medicare Beneficiaries Hospitalized for HF in the United States

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DELIVER

Disclosures

- **Trial Sponsor:** The DELIVER trial was funded by **AstraZeneca**
- **TRANSLATE-HF** is an industry-academic collaboration overseen by an independent voluntary Steering Group and supported by **AstraZeneca**
- **Duke Clinical Research Institute (DCRI)** served as an independent data analysis center for this analysis
- **American Heart Association Get-With-The-Guidelines Heart Failure (GWTG-HF)** is powered by IQVIA, Parsippany, New Jersey
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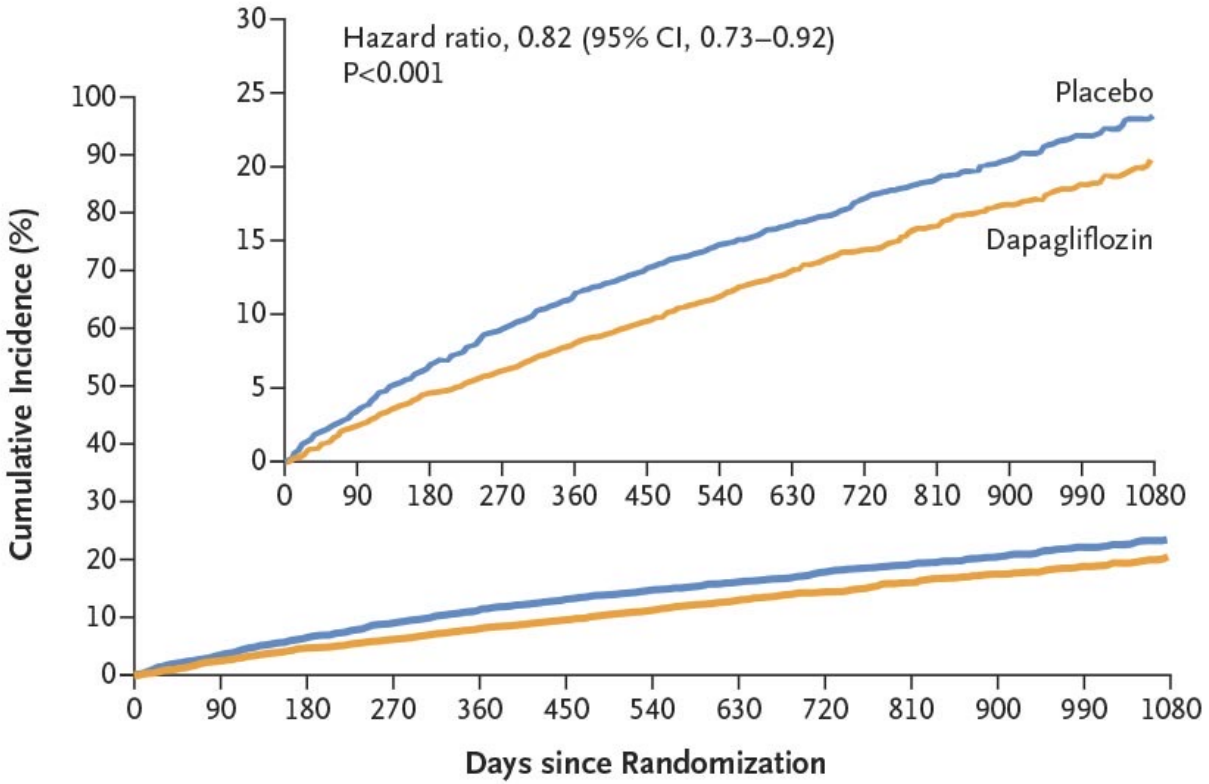
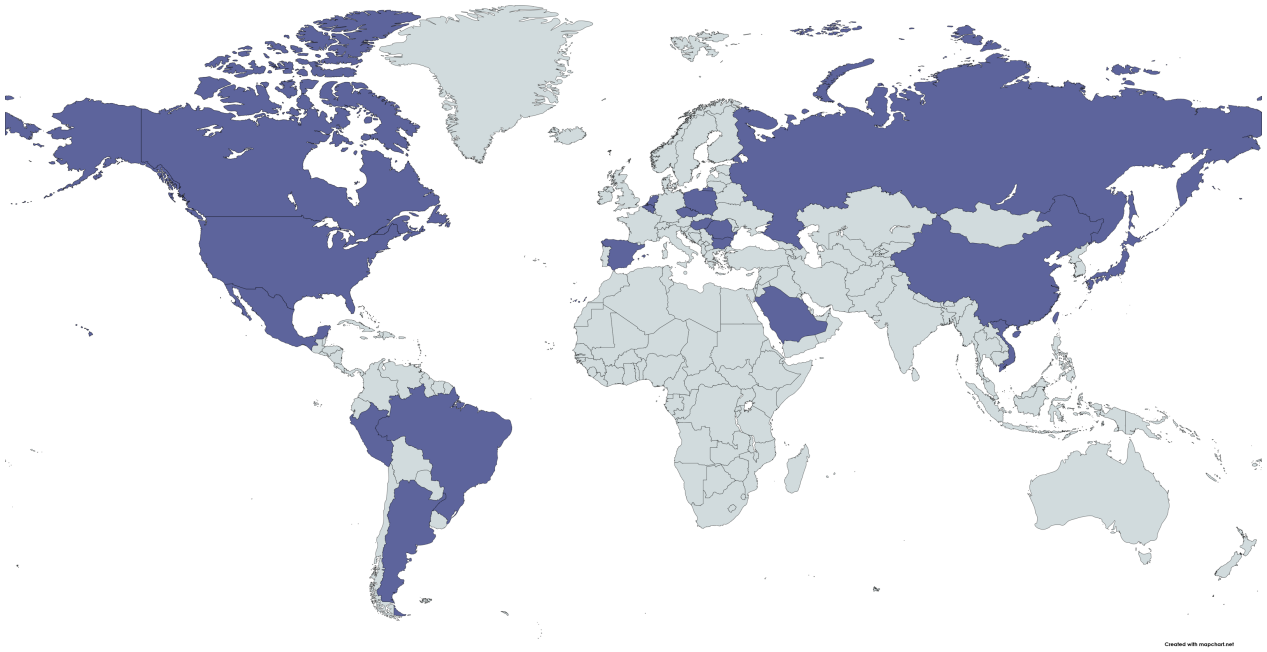
Dapagliflozin ↓ Worsening HF or Cardiovascular Death in Patients with HF with Mildly Reduced or Preserved Ejection Fraction in the Global DELIVER Trial

Primary Outcome



350 Sites across 20 Countries

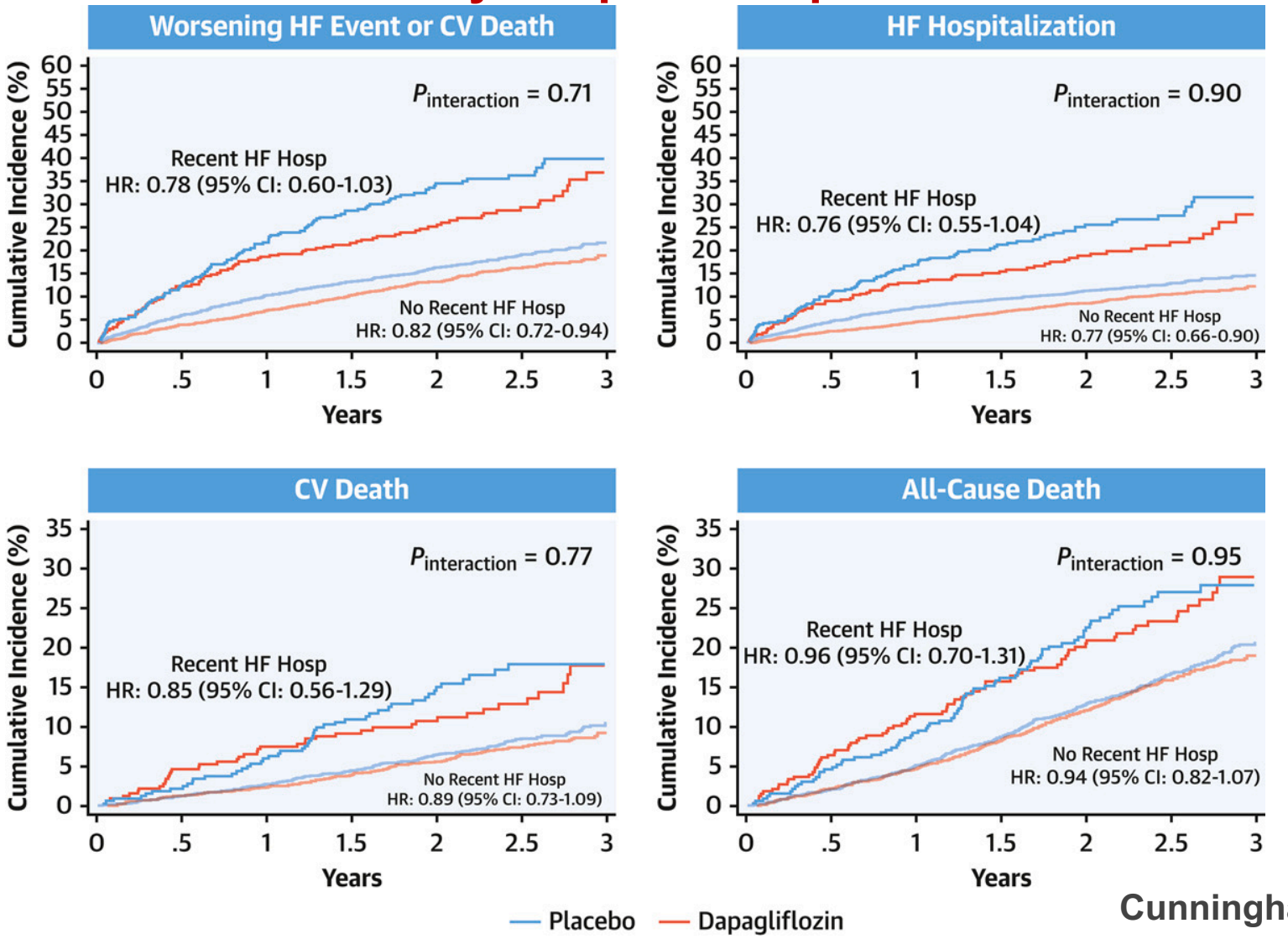


DELIVER enrolled a broad spectrum of patients, irrespective of care setting, including during hospitalization.

Solomon SD et al. *NEJM* 2022

Hospitalization as a Site for Early Implementation!

Consistent benefits irrespective of whether SGLT2i initiated in ambulatory care or in recently hospitalized patients



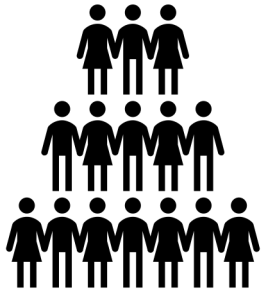
Cunningham JW et al. *JACC.* 2022

Applicability of DELIVER Trial Findings to a US Hospitalized Medicare Population?

A Prespecified Analysis in the DELIVER Academic SAP

GWTG-HF
HF & LVEF>40%
Jan 2014 to 2019

GET WITH THE GUIDELINES® HEART FAILURE



Large hospital-based quality improvement registry that prospectively collects data from patients hospitalized for HF at participating centers across the US

Eligibility in the DELIVER Trial

Comparing DELIVER Trial Participants & Dapagliflozin Treatment Candidates in GWTG-HF

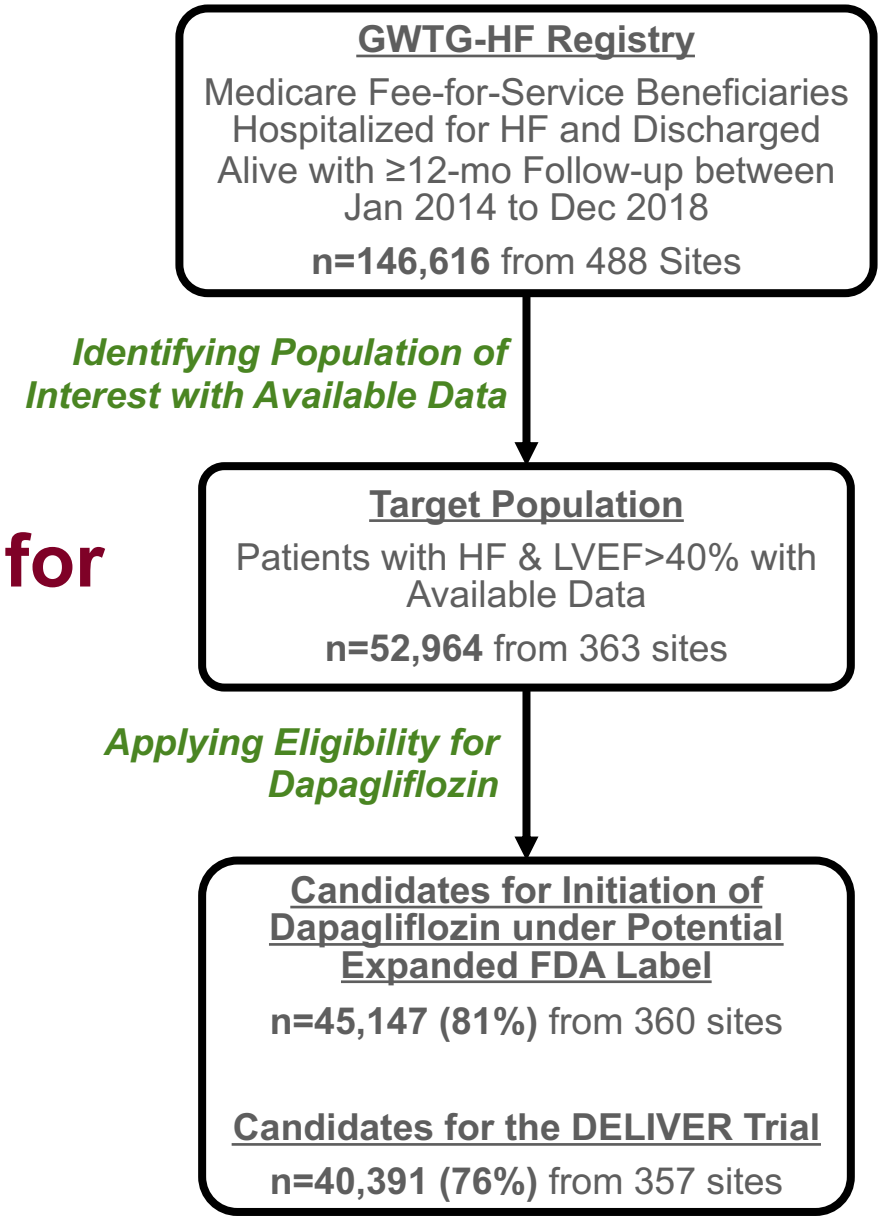
Clinical Profile and Representativeness

1-year Post-Discharge Outcomes

Potential Averted Events with Complete Implementation of Dapagliflozin

Key Objective: ***To examine eligibility for dapagliflozin, post-discharge clinical risk, and projected benefits if dapagliflozin was implemented among Medicare beneficiaries hospitalized with HF with mildly reduced or preserved ejection fraction in the US.***

Applying Eligibility for Dapagliflozin to the GWTG-HF Registry



Excluding:

- Age<65 years
- LVEF≤40% or missing LVEF
- Left AMA, transferred to acute care facility, or discharged to hospice care
- Missing critical data elements (eGFR or BP closest to discharge)

Potential Expanded Label Exclusions:

- eGFR closest to discharge <25 mL/min per 1.73 m^2
- Type 1 diabetes
- In-hospital dialysis
- History of chronic dialysis

Specific Trial Exclusions:

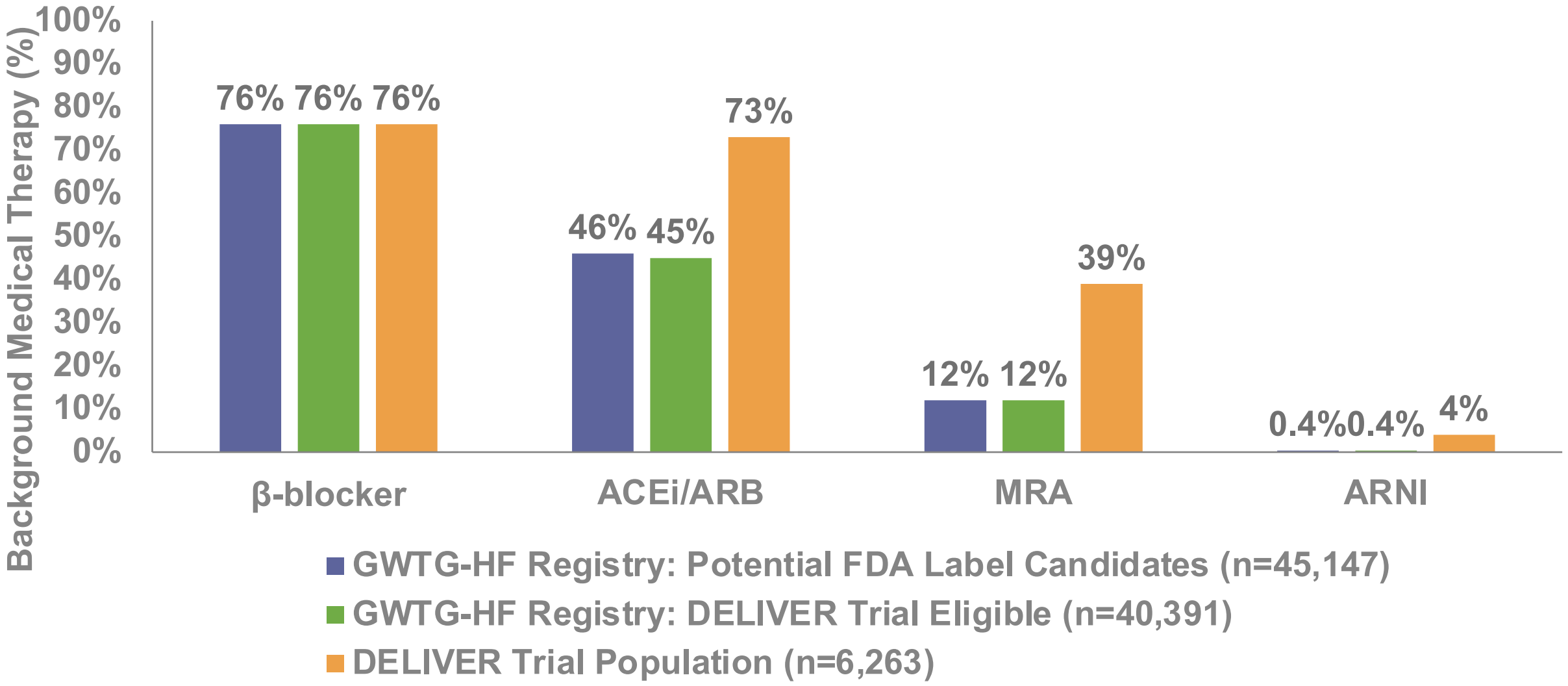
- Discharge systolic BP<95 or >180mmHg
- Non-elevated natriuretic peptide levels
- In-hospital cardiac procedure
- BMI >50kg/m^2
- Ischemia/ACS precipitating HF event

76% of Medicare beneficiaries hospitalized for HF & LVEF>40% would have been eligible for entry into the DELIVER trial

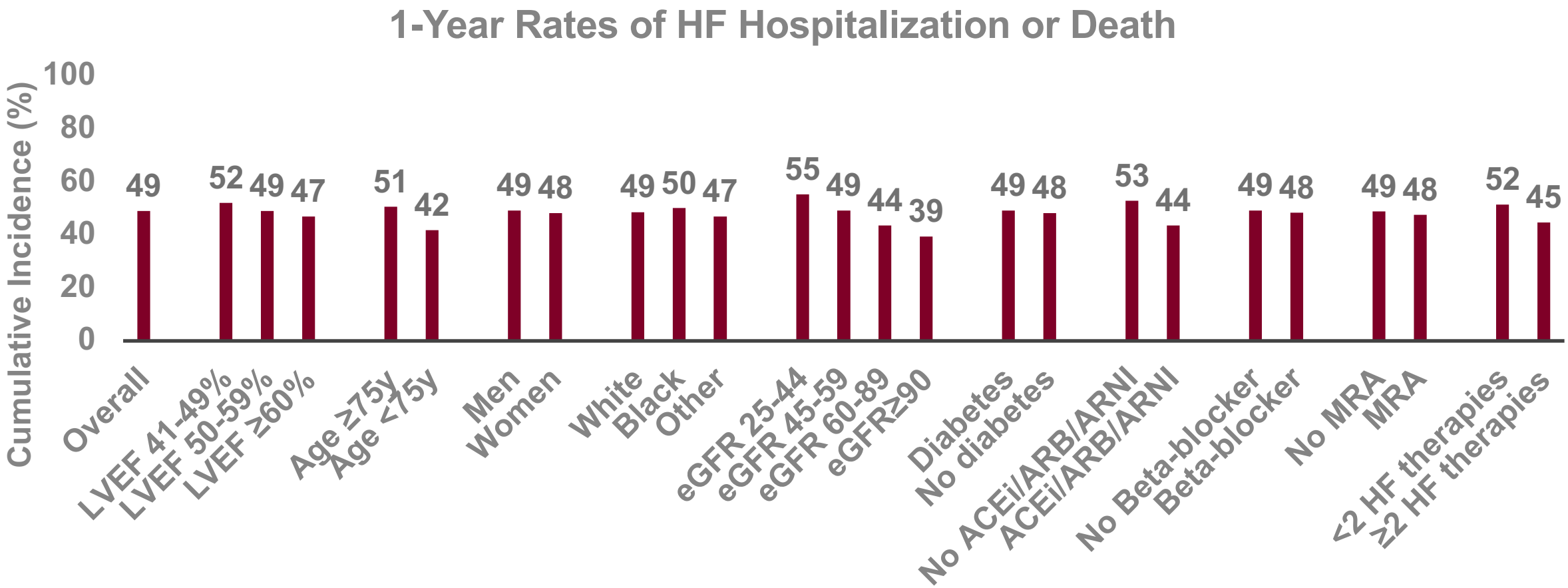
Characteristics of DELIVER Trial Participants and Dapagliflozin Treatment Candidates in GWTG-HF Registry

	GWTG-HF Registry Candidates under Potential Expanded FDA Label (n=45,147)	GWTG-HF Registry DELIVER Eligible Participants (n=40,391)	DELIVER Trial Population (n=6,263)
Age, years	82 (75-88)	82 (75-88)	72 (66-79)
Women	60%	61%	44%
White	86%	87%	71%
Black	7%	7%	3%
Atrial fibrillation/flutter	52%	52%	57%
Hypertension	86%	86%	89%
Diabetes	39%	38%	45%
Ischemic heart disease	49%	48%	51%
Smoking in prior year	7%	7%	8%
LV ejection fraction, %	57 (52-63)	57 (52-63)	54 (47-60)
Systolic BP, mmHg	143 (125-163)	143 (126-163)	128 (118-139)
BMI, kg/m^2	29 (25-35)	29 (24-34)	29 (25-33)
HbA1c, %	6.4 (5.8-7.4)	6.4 (5.8-7.3)	6.2 (5.7-7.0)
eGFR, mL/min/1.73m^2	55 (40-73)	55 (40-73)	60 (46-75)
NT-proBNP, pg/mL	3,338 (1,664-6,636)	3,521 (1,841-6,865)	1,011 (623-1,751)

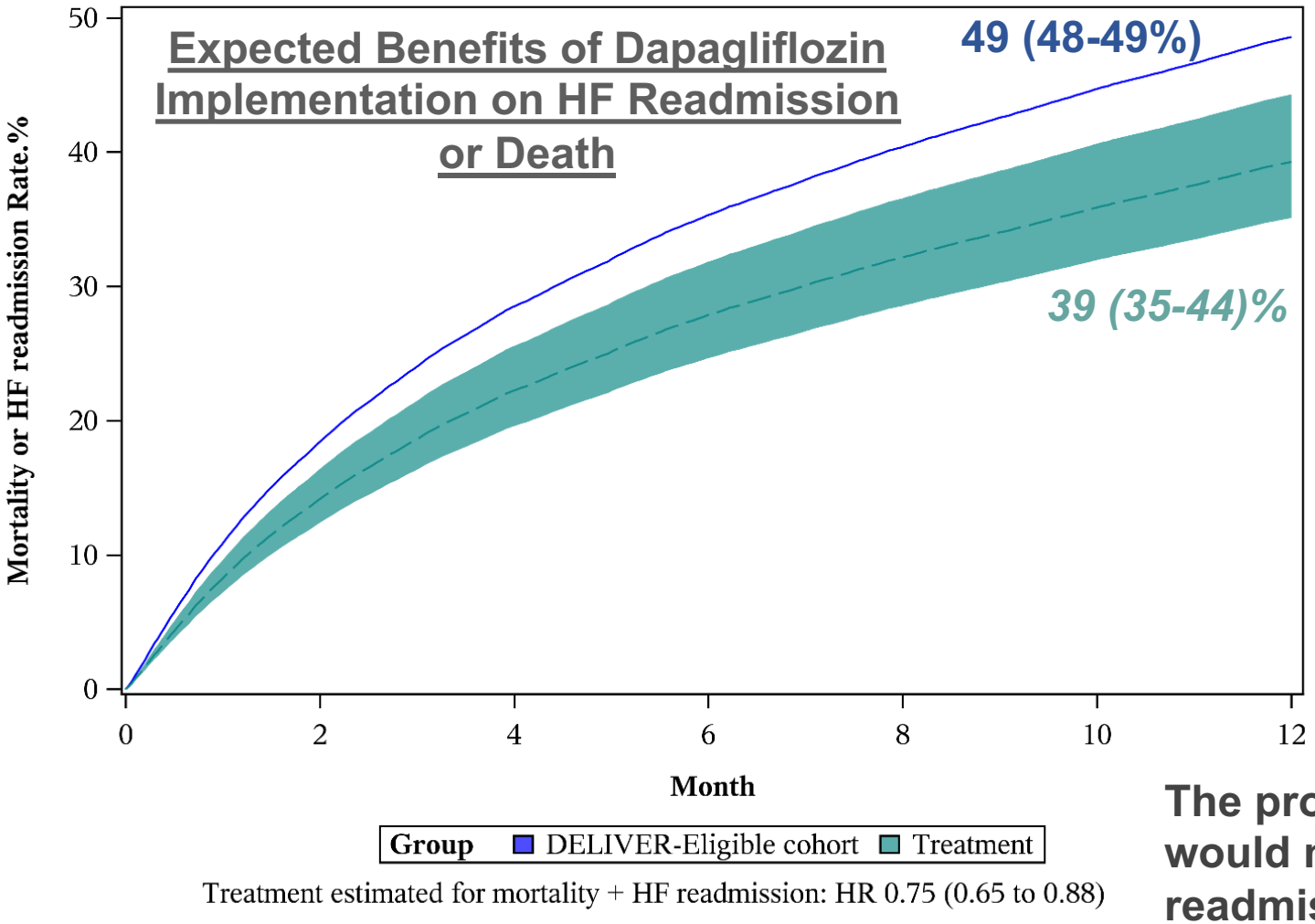
Medical Therapy among DELIVER Trial Participants and Dapagliflozin Treatment Candidates in GWTG-HF Registry



High Residual Risk in DELIVER Eligible Medicare Beneficiaries: ~50% Die or are Readmitted for HF in 1-Year



Projected Benefits of Dapagliflozin Initiation at Discharge on Post-Discharge HF Readmission or Death

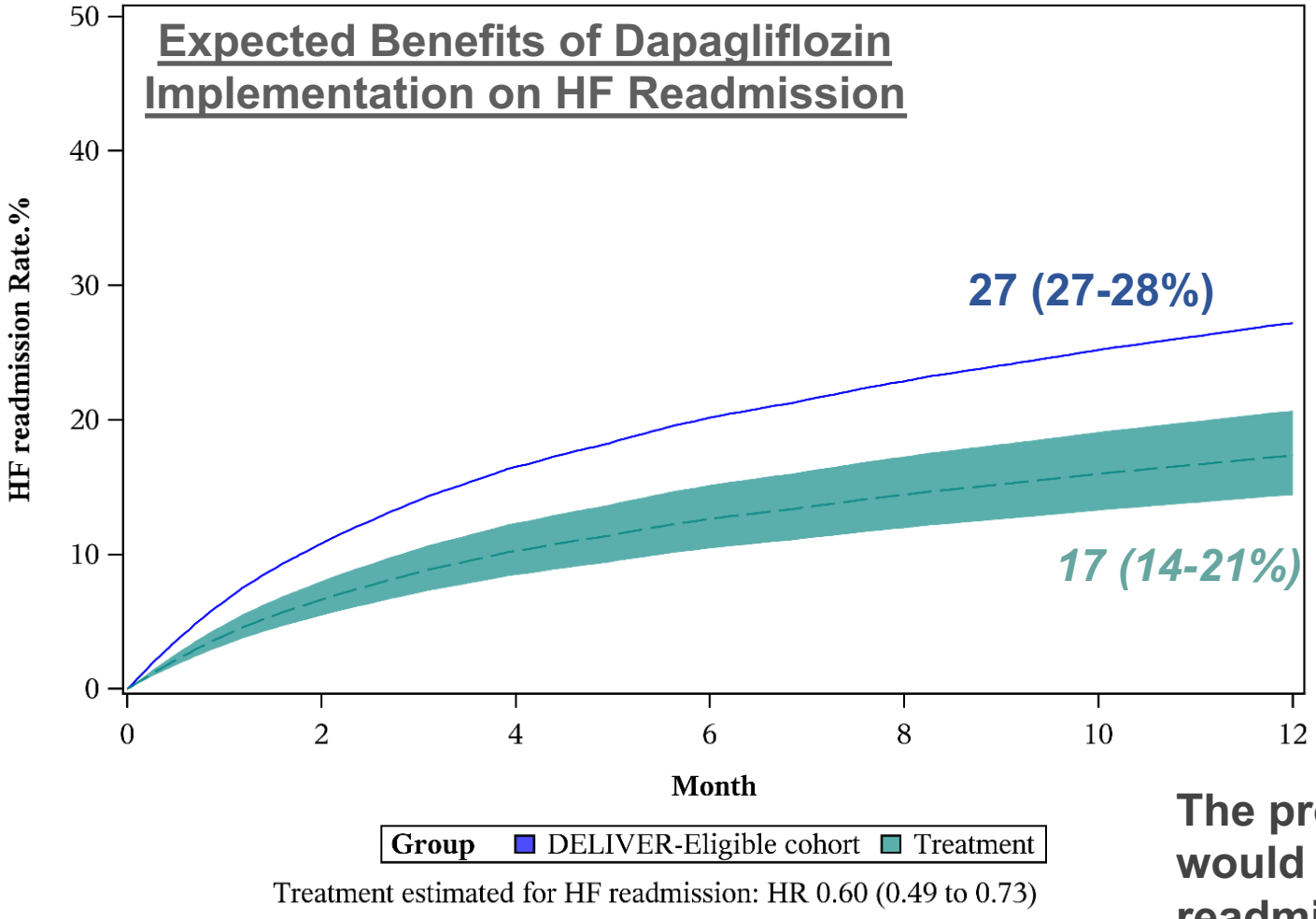


Medicare Beneficiaries in GWTG-HF who would be DELIVER-Trial Eligible

Projected 9% (4-13%) Absolute Risk Reduction with Dapagliflozin Implementation **(if Effect Sizes in Year 1 of DELIVER are Translated to Clinical Practice in Hospitalized Medicare Population)**

The projected number of Medicare beneficiaries that would need to be treated for 1 year to prevent 1 HF readmission or death is 11 (7-23).

Projected Benefits of Dapagliflozin Initiation at Discharge on Post-Discharge HF Readmission



Medicare Beneficiaries in GWTG-HF who would be DELIVER-Trial Eligible

Projected 10% (7-13%) Absolute Risk Reduction with Dapagliflozin Implementation (if Effect Sizes in Year 1 of DELIVER are Translated to Clinical Practice in Hospitalized Medicare Population)

The projected number of Medicare beneficiaries that would need to be treated for 1 year to prevent 1 HF readmission is 10 (8-15).

Study Strengths and Limitations

Study Strengths:

- GWTG-HF offers a large US contemporary registry experience
- Linked Medicare claims data to evaluate post-discharge risk trajectory
- Individual participant level data from DELIVER trial were leveraged to estimate treatment effects of dapagliflozin

Study Limitations:

- GWTG-HF registry may not represent all US HF patients, though prior studies have suggested that the patient sample is representative[1]
- Estimation of benefits in clinical practice represents a projection and assumes that the relative risk reductions with dapagliflozin would be similar to that observed in the DELIVER trial
- While patients who were actively or recently hospitalized were represented in the DELIVER trial, this represented a modest number of participants (~10%)[2]
- While potential benefits were estimated, safety, cost, and adherence were not considered

[1]Curtis LH et al. *Circ CQO* 2009 [2]Cunningham JW et al. *JACC* 2022

Conclusions

- 3 out of 4 Medicare beneficiaries hospitalized for HF with mildly reduced or preserved ejection fraction in the US would be eligible for dapagliflozin based on DELIVER clinical trial criteria.

- Potential treatment candidates in US clinical care are likely to be older, more likely to be White, and less frequently treated with concomitant HF therapies but have similarly high comorbidity burden as the global DELIVER trial population.

- Patients with HF & LVEF>40% eligible for dapagliflozin face markedly heightened risks of mortality or readmission within 1-year post-discharge.

- We estimate large and clinically meaningful absolute risk reductions with dapagliflozin if implemented during hospitalization for HF and if treatment effects in DELIVER can be fully realized in clinical practice.