Impact of Coronavirus Disease-2019 in Patients with Heart Failure with Mildly Reduced or Preserved Ejection Fraction: The DELIVER Trial

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on behalf of the DELIVER Committees, Investigators, Sponsor and Participants

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Disclosures

No relevant disclosures.

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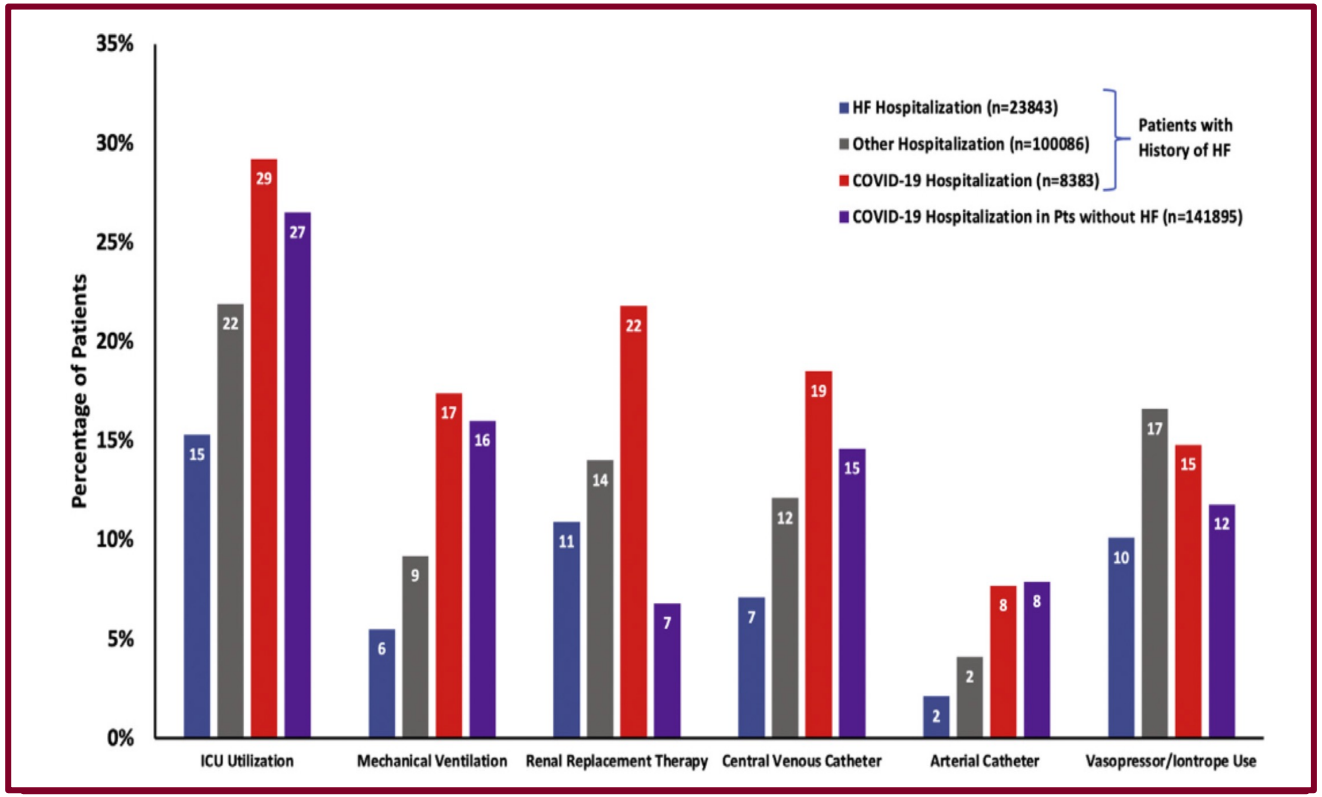
Background and Rationale

- The COVID-19 pandemic affected virtually every aspect of care delivery.
- The pandemic also created broader challenges for the conduct and interpretation of randomized clinical trials.
- Patients with heart failure may be particularly susceptible to serious complications of COVID-19.
- DELIVER is the largest trial of heart failure with mildly reduced or preserved EF and was conducted prior to and during the COVID-19 pandemic.



Therefore, we sought to examine the impact of COVID-19 in the DELIVER trial.

Bhatt AS et al. J. Am Coll Cardiol. HF 2021.
Bhatt AS et al. J. Am Coll Cardiol. 2020.

Objectives

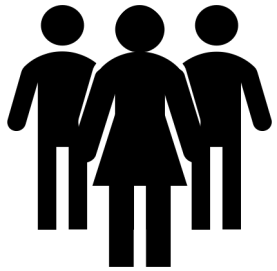
1. To describe the incidence of COVID-19 in a large, international randomized clinical trial.
2. To assess the impact of the pandemic on clinical event accrual and treatment effects.
3. To assess the health risks faced by participants with HFmrEF/HFpEF after COVID-19 diagnosis.

Design of the DELIVER Trial

Randomized, double-blind, placebo-controlled trial testing the hypothesis that dapagliflozin would reduce cardiovascular death or worsening heart failure in patients with heart failure and mildly reduced or preserved ejection fraction

Eligibility Criteria

- Age ≥ 40 years
- NYHA class II-IV
- LVEF > 40%
- Structural Heart Disease (LVH or LA Enlargement)
- Elevated Natriuretic Peptides



Dapagliflozin 10mg once daily

Double-blind Treatment period

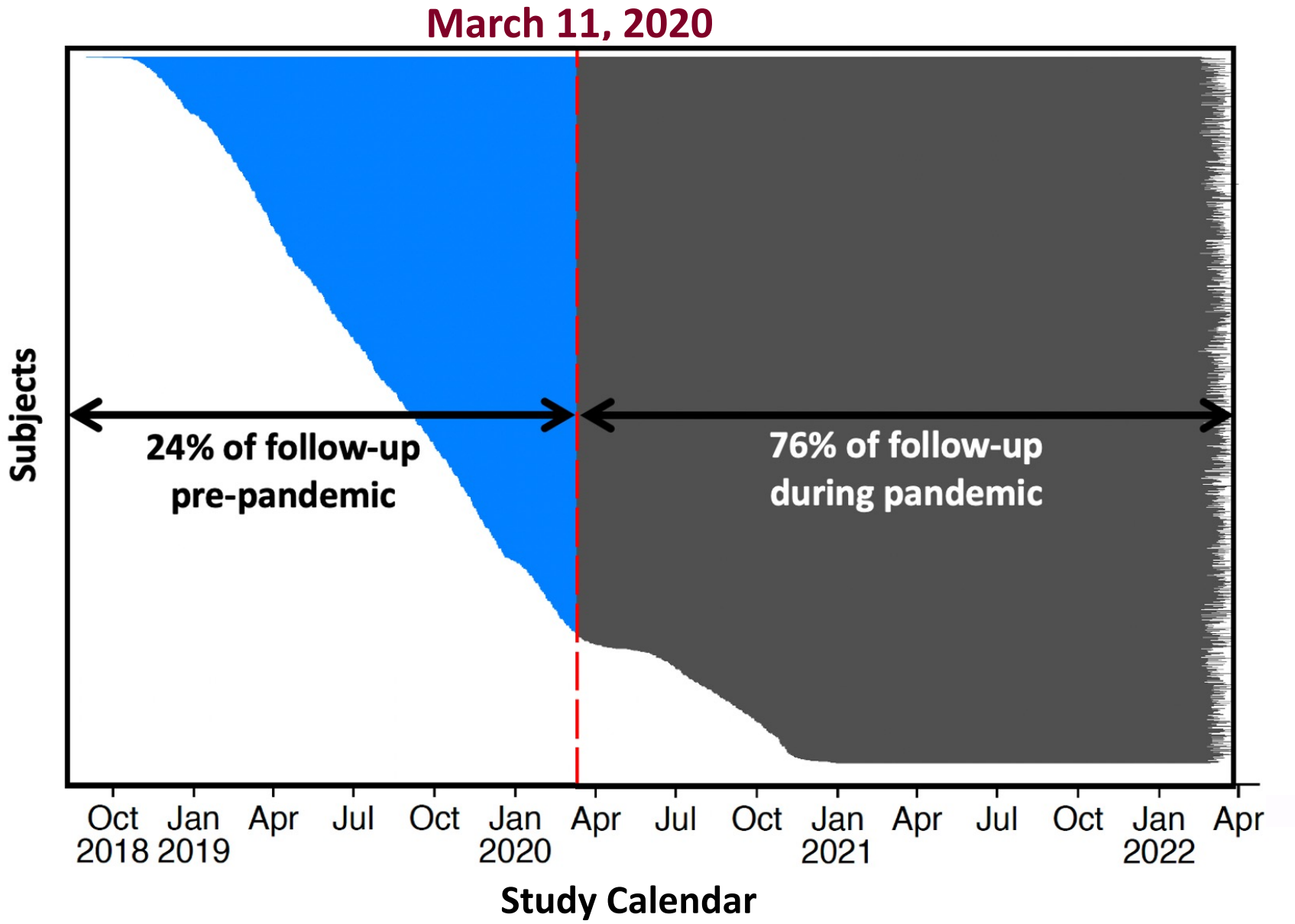
Event Driven Trial Median Follow-up: 2.3 years

Placebo

Conducted across >350 sites in 20 countries

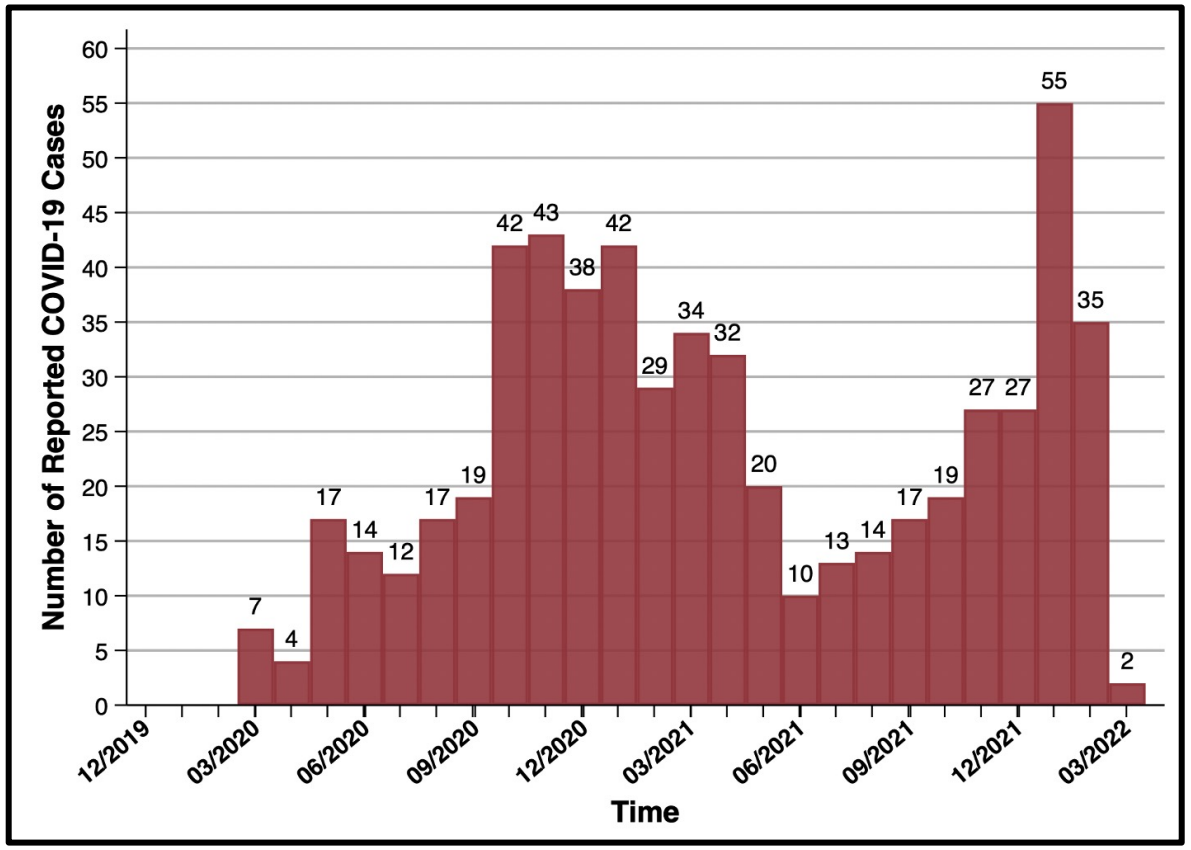
Solomon SD et al. Eur J Heart Fail 2021

Conducting DELIVER During the COVID-19 Pandemic

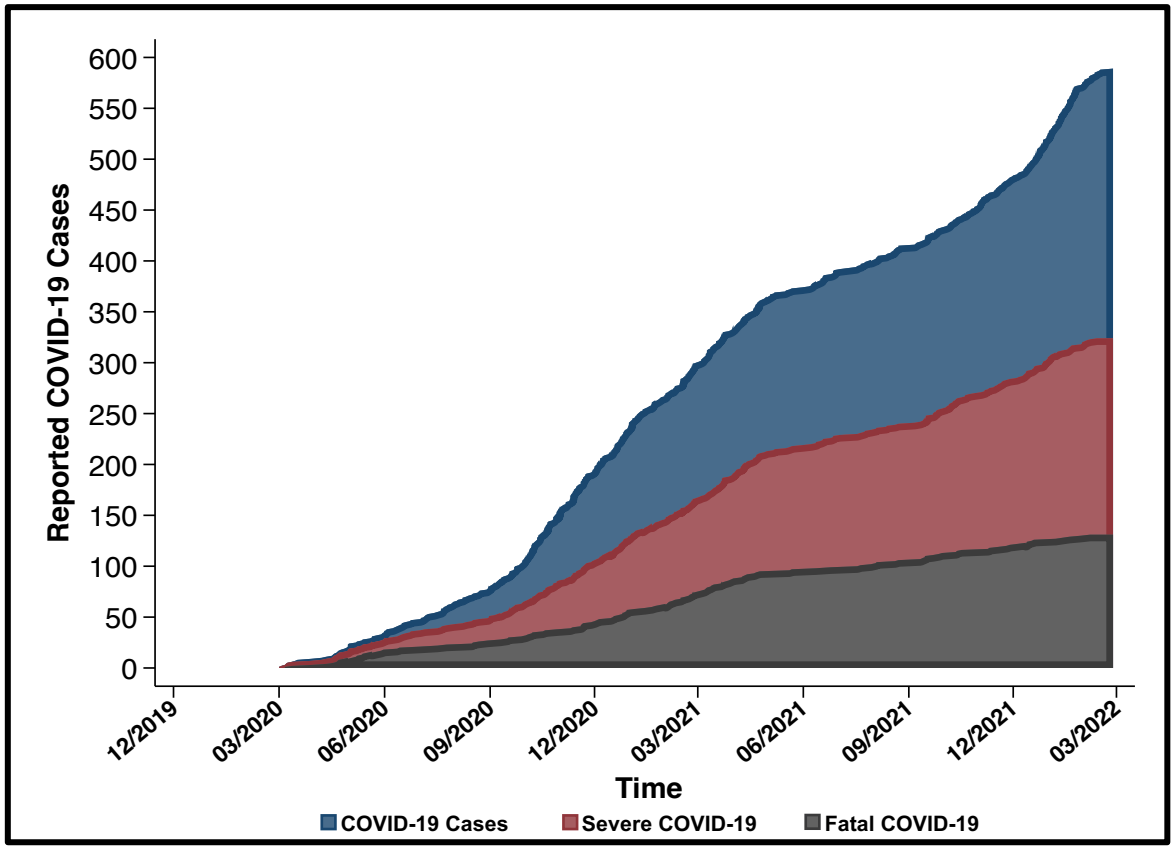


Impact of COVID-19 on Participants in DELIVER

589 (9.4%) Investigator Reported COVID-19 Infections



>50% of COVID-19 cases resulting in severe disease



Note: Severe disease = requiring/prolonging hospitalization or leading to death.
Severe disease and deaths counted based on date of onset of COVID-19 event.

Baseline Characteristics: Participants with and without COVID-19 Infection

	Developed COVID-19 n=589	Did not Develop COVID-19 n=5674	P-Value
Age (years)	71.2 ± 9.6	71.7 ± 9.5	0.17
Male Sex	54%	56%	0.31
Baseline LVEF (%)	54.1 ± 8.4	54.2 ± 8.8	0.93
Race			<0.001
White	86%	69%	
Black	4%	2%	
Asian	3%	22%	
Other	7%	6%	
Geographic Region			<0.001
Europe and Saudi Arabia	64%	46%	
Asia	3%	21%	
Latin America	22%	19%	
North America	11%	14%	
Comorbidities			
History of Dyslipidemia	70%	63%	<0.001
History of Diabetes	52%	44%	<0.001
Baseline BMI (kg/m^2)	31.9 ± 6.1	29.6 ± 6.1	<0.001

Trial Event Rates Prior to & During the Pandemic

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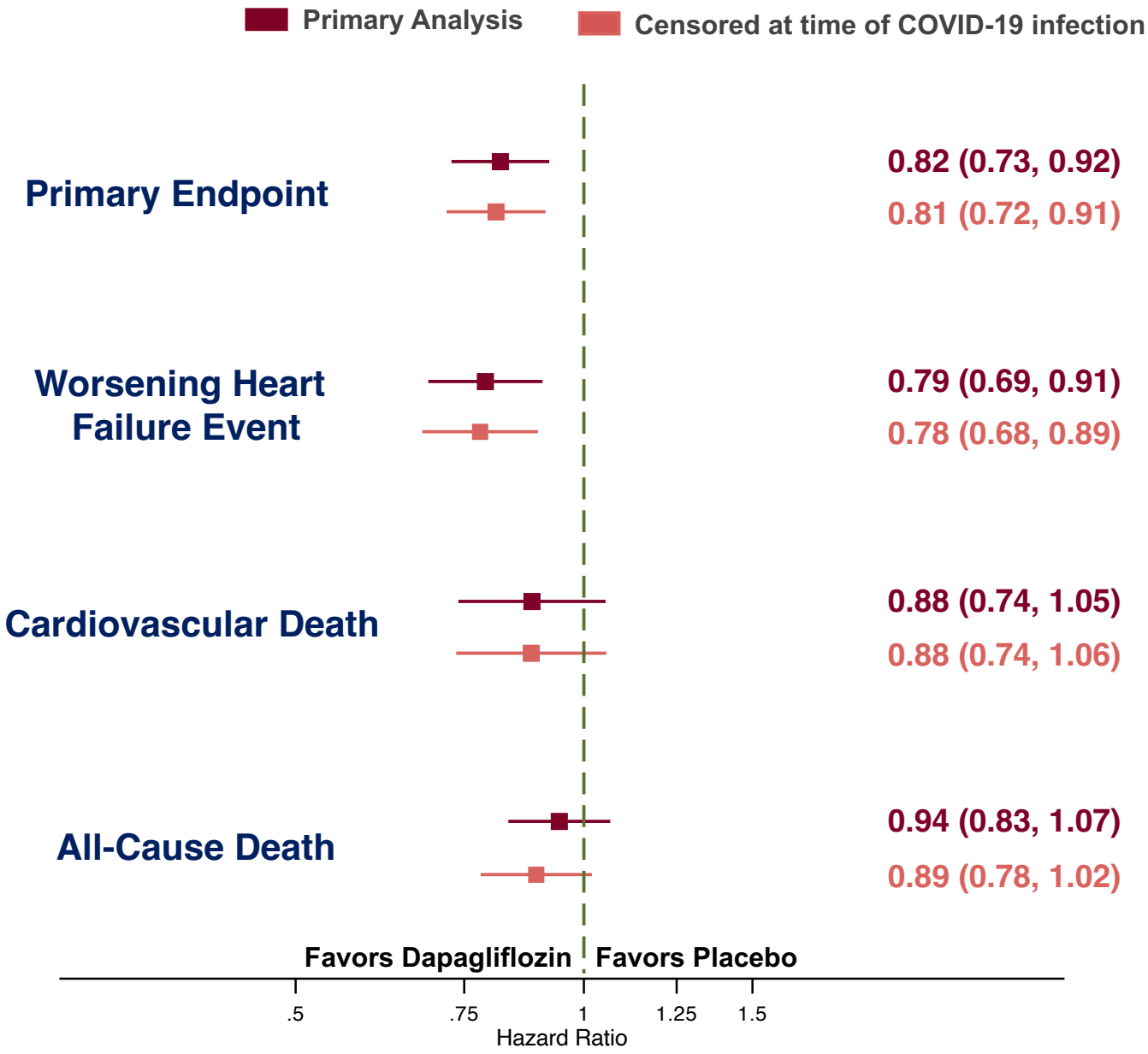
Event Rates (per 100 pt yrs, 95% CI)	Pre-Pandemic *Before March 11, 2020*	Pandemic *On or After March 11, 2020*	RR: Pandemic to Pre-Pandemic (95% CI)	P-value
Primary Composite (Worsening HF + CV Death)	11.0 (9.9, 12.2)	7.9 (7.4, 8.5)	0.93 (0.79-1.09)	0.34
All Cause Death	5.0 (4.3, 5.8)	8.2 (7.6, 8.7)	1.24 (1.00-1.54)	0.05
CV Death	2.9 (2.4, 3.5)	3.8 (3.4, 4.2)	1.10 (0.82-1.48)	0.52
Worsening HF Event	9.1 (8.1, 10.2)	5.5 (5.0, 5.9)	0.86 (0.72-1.03)	0.11
Urgent HF	1.5 (1.1, 2.0)	0.8 (0.7, 1.0)	0.59 (0.36-0.94)	0.03

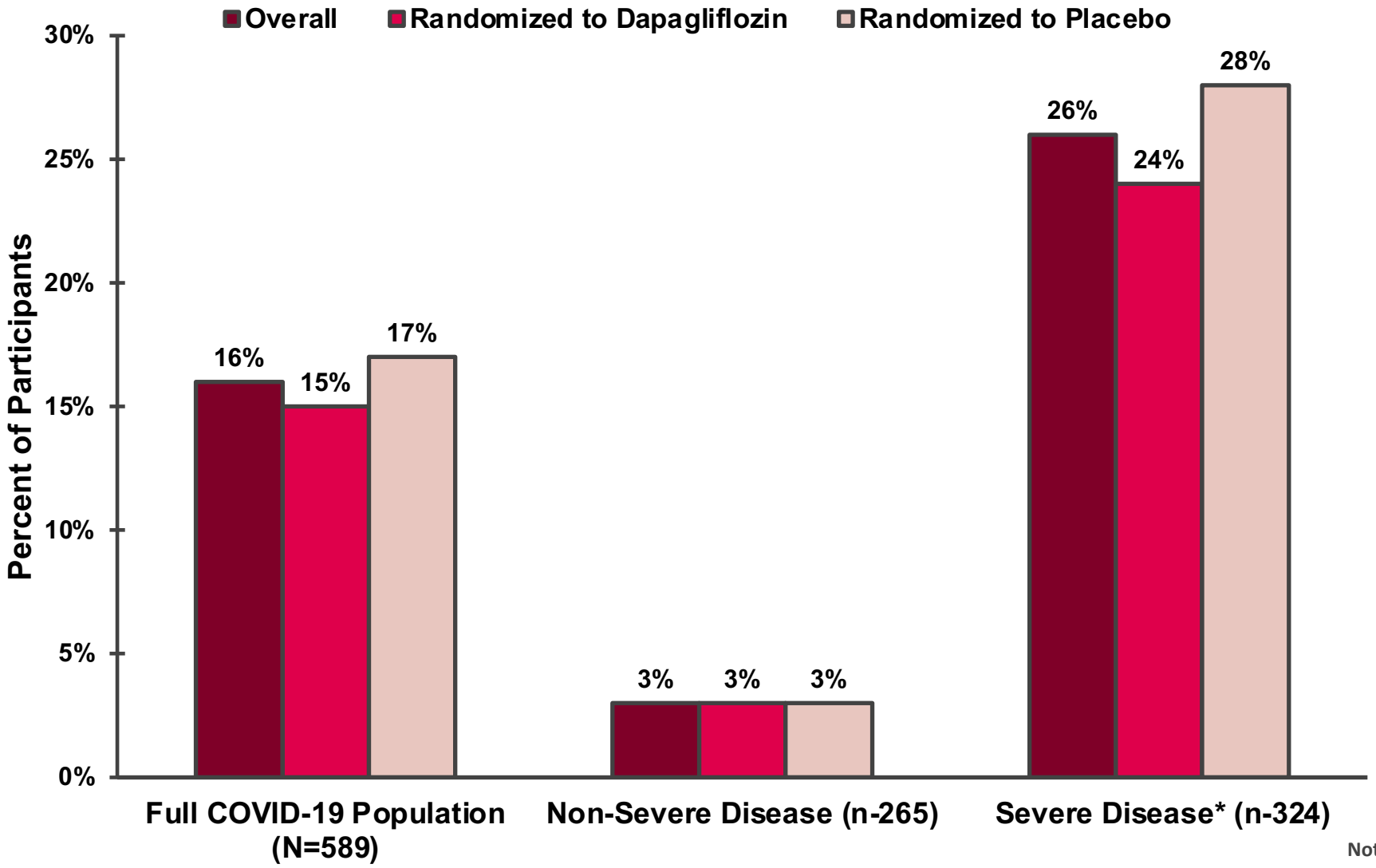
Note: The associations between COVID-19 and risks of time-to-event outcomes were estimated by creating time-updated covariates to represent pre- vs post-COVID-19 diagnosis status at the patient level.

COVID-19 Sensitivity Analysis



Presented at ESC.22 (Barcelona, Spain)

Interruption or Withdrawal of Study Drug Associated with COVID-19 diagnosis



Note: Severe disease = requiring/prolonging hospitalization or leading to death

No statistically significant differences by randomized treatment assignment

Adverse Events in the 30-days following COVID-19

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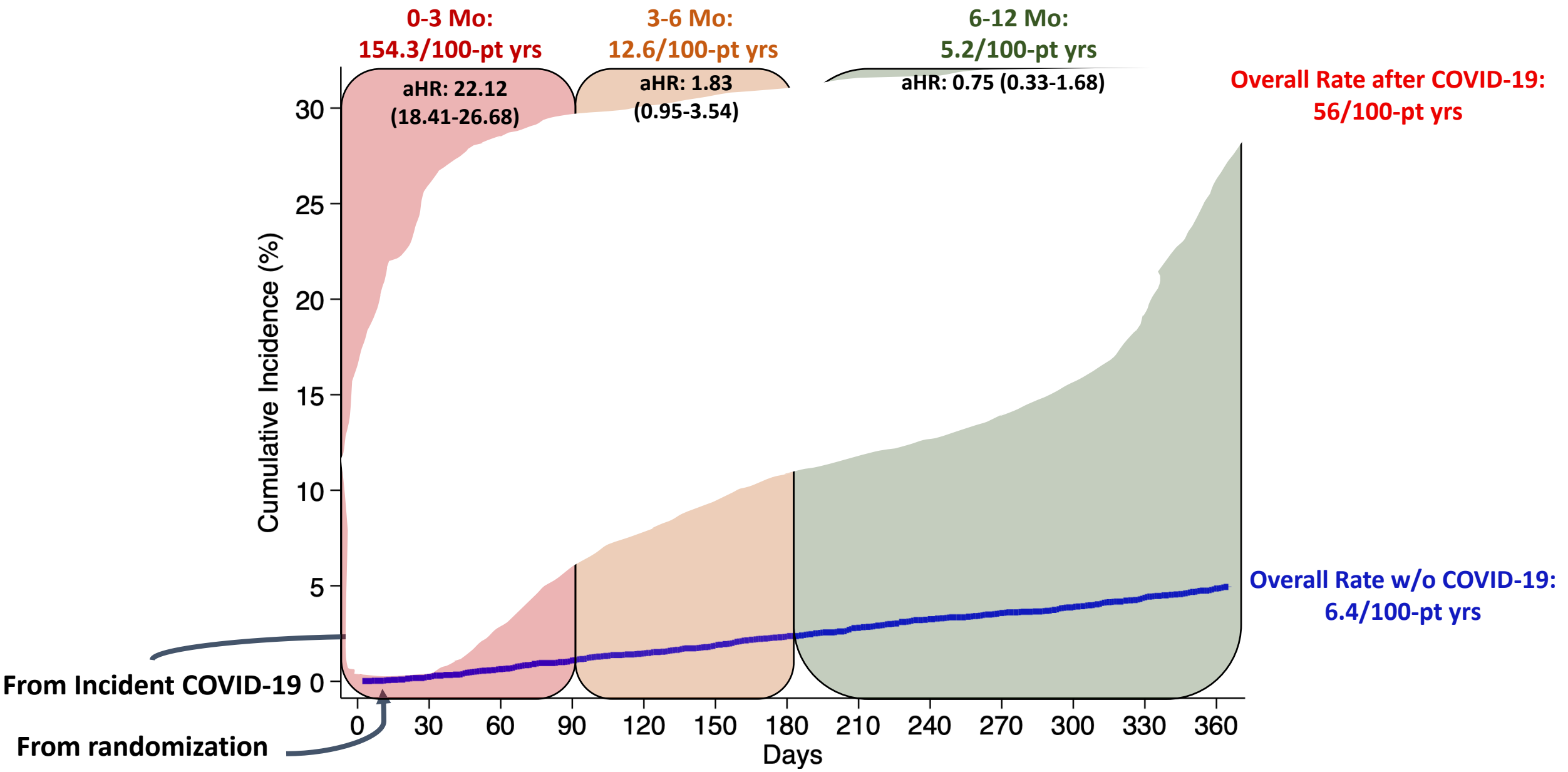
	Overall	Randomized to Dapagliflozin	Randomized to Placebo
Definite/probable DKA	0%	0%	0%
Major hypoglycemic event	0%	0%	0%
Any SAE suggestive of volume depletion	0.3%	0%	0.7%
Any renal SAE or DAE	0.7%	0.6%	0.7%
Deaths Following COVID-19			
Any death after COVID-19	31%	32%	30%
Any death in 30-days of COVID-19	27%	27%	26%
Investigator Reported COVID-19 Related Death	22%	24%	21%
CEC Adjudicated COVID-19 Related Deaths	24%	26%	23%

No statistically significant differences by randomized treatment assignment

Risk of All-Cause Death Following COVID-19



Conclusions

- DELIVER represents one of the most extensive international experiences with COVID-19 of any CV trial.
- COVID-19 was common, with >50% of diagnoses requiring/prolonging hospitalization and a high proportion leading to death.
- The pandemic period was associated a rise all-cause mortality and a reduction in urgent HF events.
- Adverse events and deaths following COVID-19 did not differ by treatment assignment.
- Treatment benefits of dapagliflozin were consistent when censoring at the time of COVID-19.
- In this analysis limited by COVID-19 as a post-randomization exposure, patients with HF surviving COVID-19 faced multifold elevations in clinical risk.

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Thank You

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