



Sex Differences in Characteristics, Outcomes and Treatment Response with Dapagliflozin across the Range of Ejection Fraction in Patients with Heart Failure:

Insights from DAPA-HF and DELIVER

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DAPA-HF



DELIVER

Disclosures

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- **Presenter Disclosures:** None.

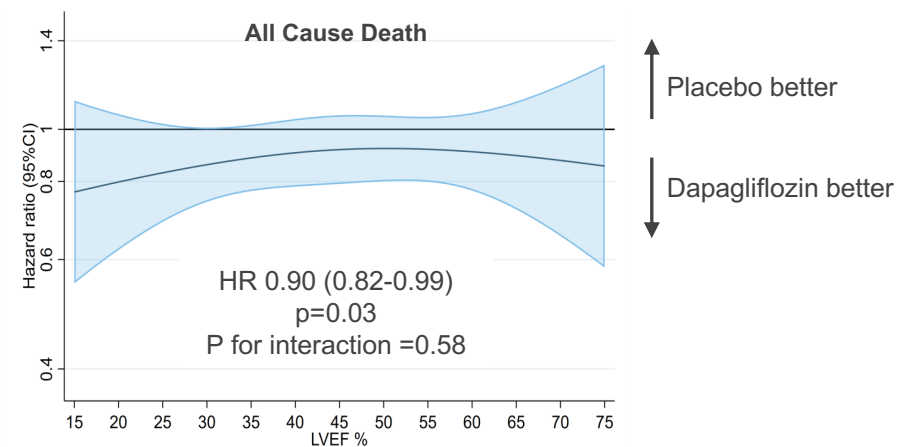
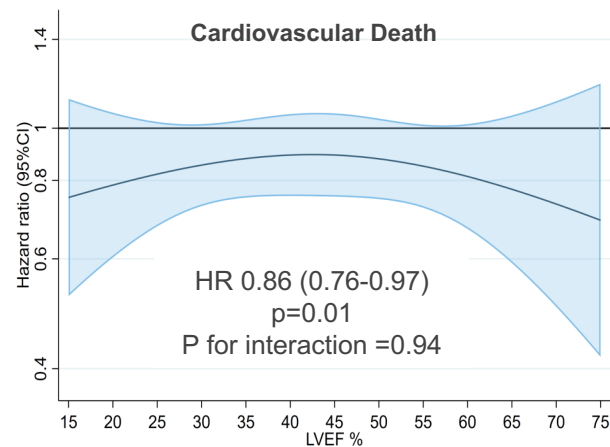
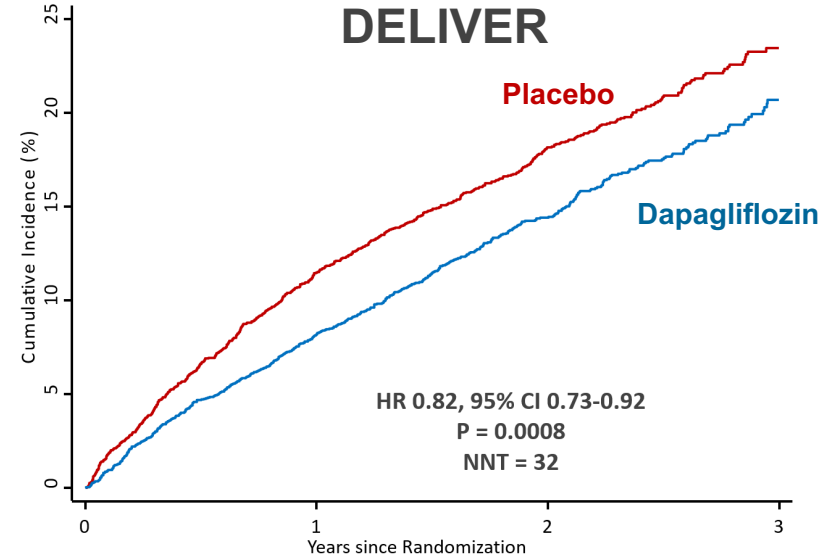
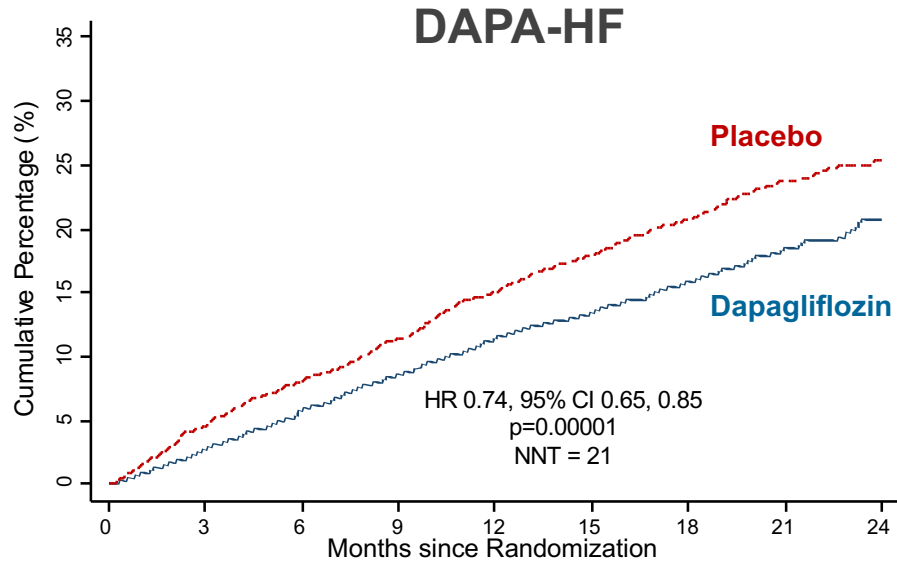
DAPA-HF and DELIVER study designs

Randomized, double-blind, placebo-controlled trials testing the hypothesis that dapagliflozin would reduce worsening heart failure or cardiovascular death in patients with heart failure and reduced (DAPA-HF) or mildly reduced or preserved ejection fraction (DELIVER).

| DAPA-HF | DELIVER |
|---|--|
| <ul style="list-style-type: none"> • Age \geq 18 years • NYHA class II-IV • LVEF \leq 40% • Elevated Natriuretic Peptides (NT-proBNP \geq600 pg/ml, or \geq400 pg/ml if hospitalized for heart failure within previous 12 months, or \geq900 pg/ml in AFF) | <ul style="list-style-type: none"> • Age \geq 40 years • NYHA class II-IV • LVEF $>$ 40% (including prior LVEF \leq 40%) • Elevated Natriuretic Peptides (NT-proBNP \geq300 pg/ml or \geq600 pg/ml in AFF) • Structural Heart Disease (LV hypertrophy or LA enlargement) • Either Ambulatory or Hospitalized for Heart Failure |



Dapagliflozin has been shown to reduce cardiovascular events in patients with heart failure



Objectives

- To assess the outcomes in women versus men in DAPA-HF and DELIVER.
- To assess the impact of sex on the safety and efficacy of dapagliflozin.
- To assess the impact of sex on the efficacy of dapagliflozin across the range of ejection fraction in patients with heart failure.

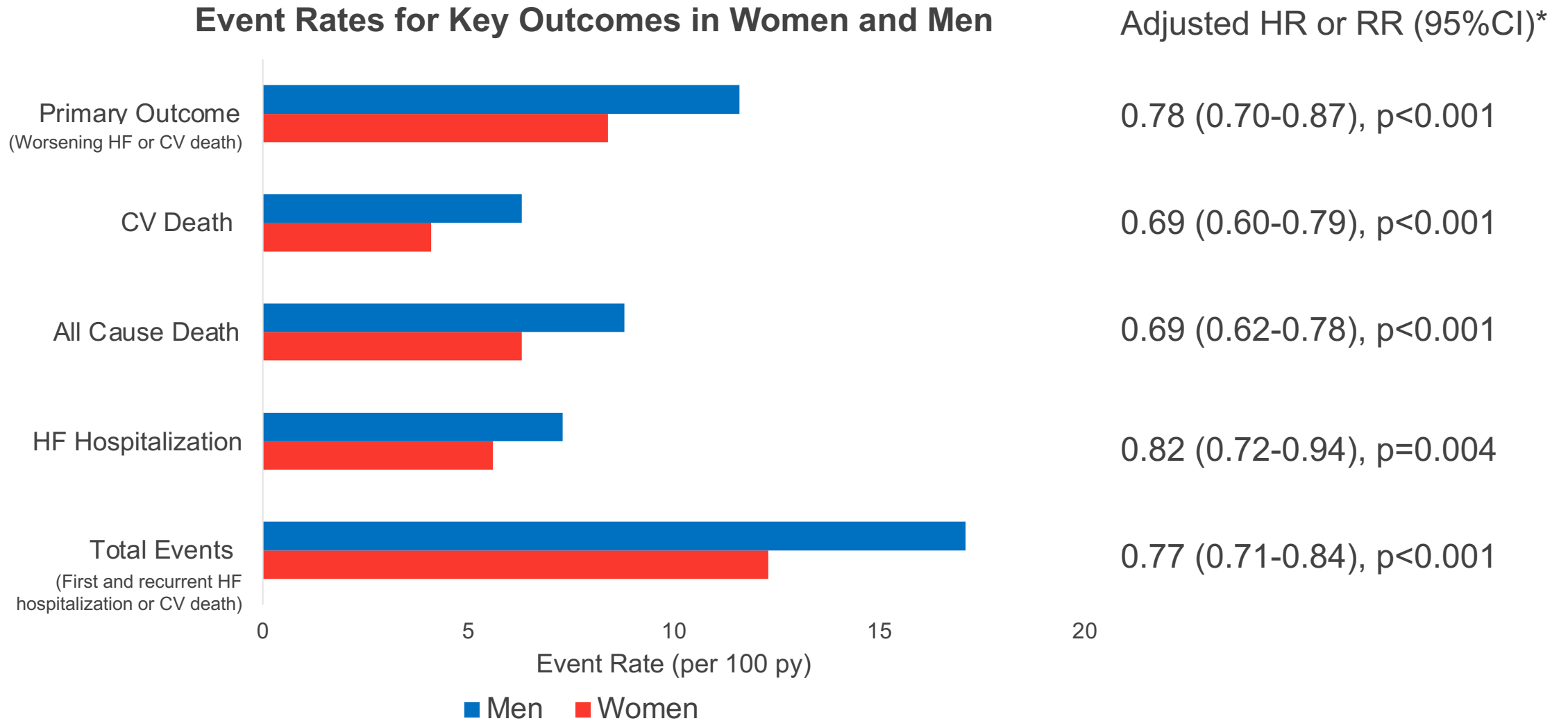
Baseline characteristics in women and men in DAPA-HF and DELIVER

| | Women | Men | |
|---------------------------------|------------------|------------------|---------|
| | N = 3856 | N = 7151 | P-value |
| Age | 71 ± 10 | 68 ± 11 | <0.001 |
| LVEF (%) | 49 ± 14 | 42 ± 13 | <0.001 |
| NT-proBNP (ng/L) | 1127 [661, 2015] | 1207 [722, 2180] | <0.001 |
| NYHA III/IV | 29.7% | 27.2% | 0.005 |
| KCCQ-TSS | 66.9 ± 22.5 | 74.0 ± 21.5 | <0.001 |
| Prior Stroke | 8.3 % | 10.4% | <0.001 |
| Prior MI | 23.5% | 39.5% | <0.001 |
| Prior HF Hospitalization | 41.9% | 44.4% | 0.011 |
| Afib/flutter | 35.9% | 33.4% | 0.010 |
| Loop diuretic | 76.6% | 79.5% | <0.001 |
| ACEi or ARB | 76.4% | 77.6% | 0.17 |
| ARNI | 4.9 % | 8.7 % | <0.001 |
| Beta-blocker | 86.0% | 89.7% | <0.001 |
| MRA | 49.6% | 57.7% | <0.001 |

DAPA-HF: 23.4% women; DELIVER: 43.9% women

ACEi = angiotensin converting enzyme inhibitor; Afib = atrial fibrillation; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor-neprilysin inhibitor; KCCQ-TSS = Kansas City Cardiomyopathy Questionnaire-Total Symptom Score; LVEF = left ventricular ejection fraction; NT-proBNP = N-terminal pro-B-type natriuretic peptide; NYHA = New York Heart Association; MI = myocardial infarction; MRA = mineralocorticoid receptor antagonist.

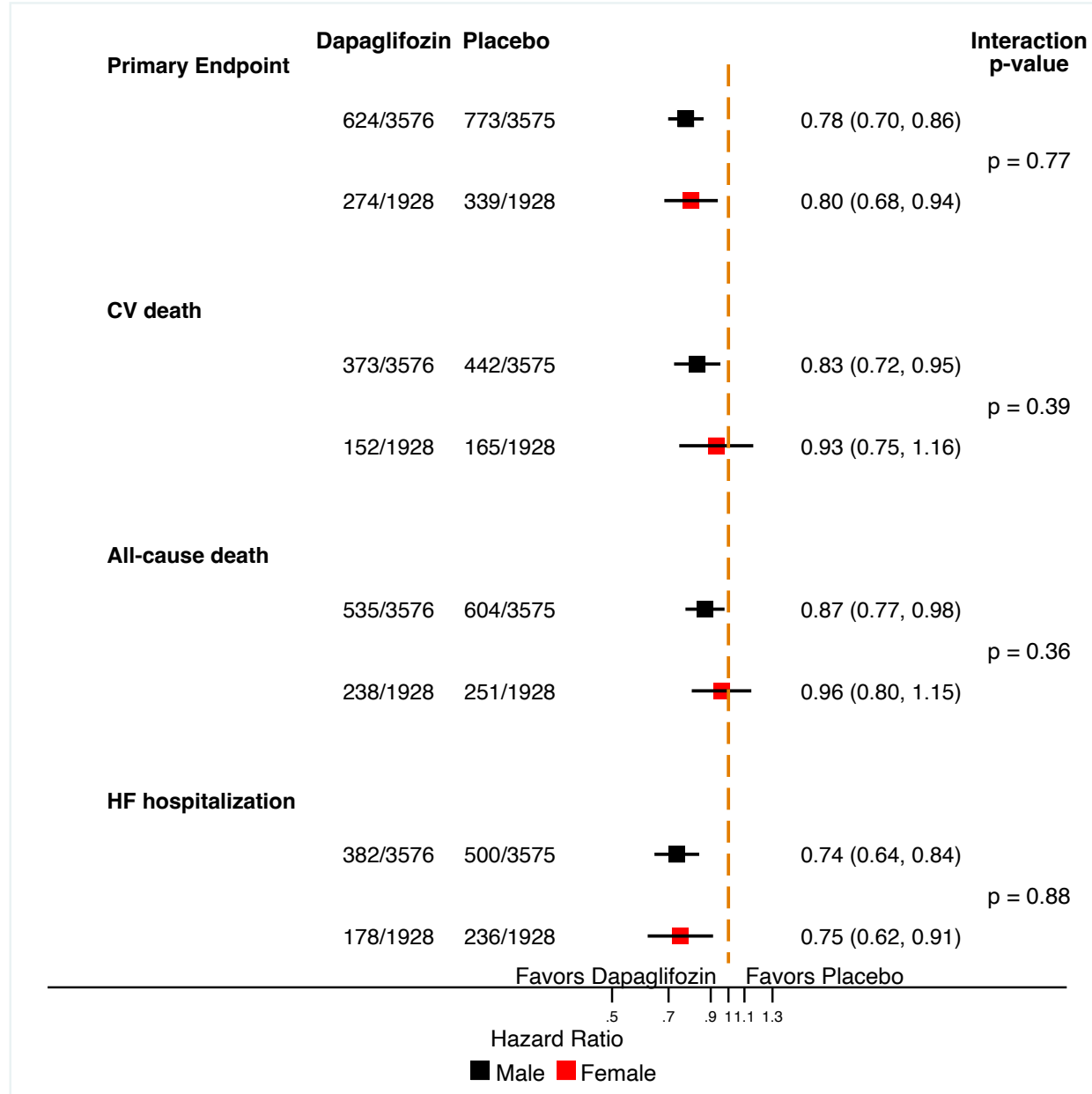
Overall, women had better outcomes compared to men



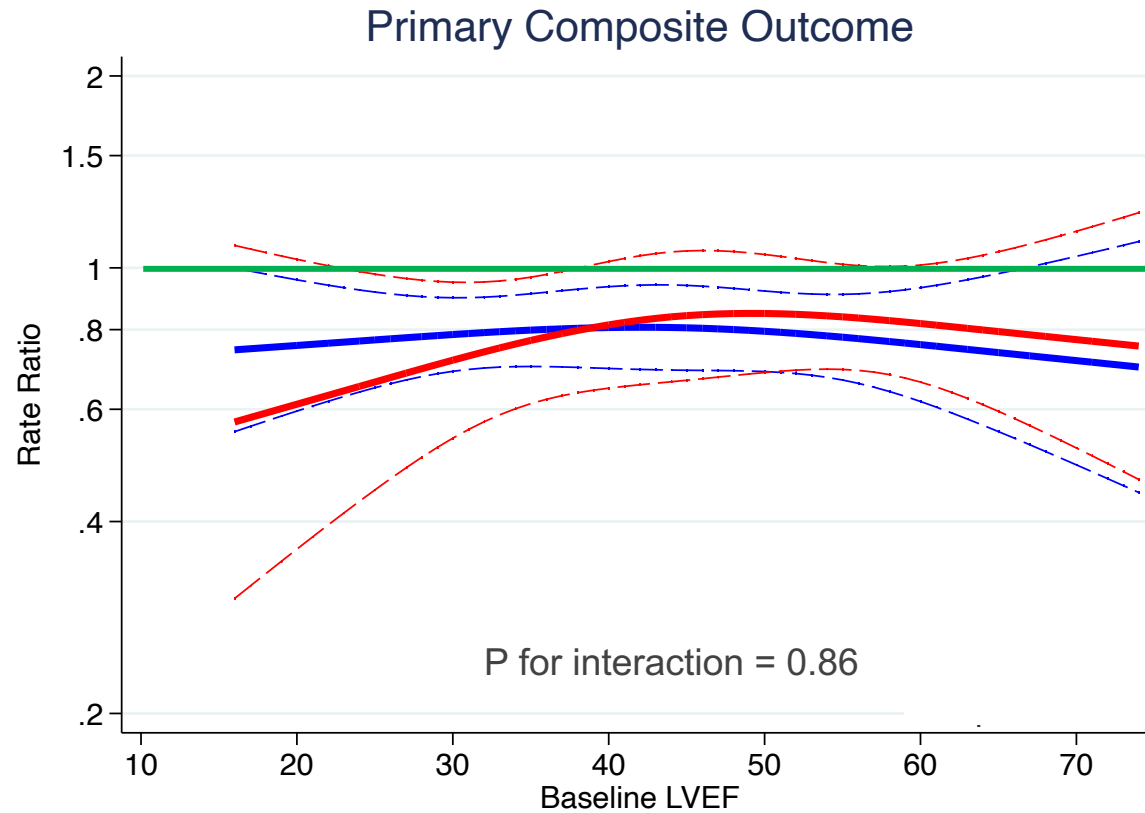
*Reference = men. Adjusted for age, heart rate, systolic blood pressure, body mass index, smoking status, NT-proBNP [log], estimated glomerular filtration rate, NYHA class, LVEF, previous HF hospitalization, myocardial infarction, diabetes mellitus, and atrial fibrillation, region; stratified by trial.

CI = confidence interval; CV = cardiovascular; HF = heart failure; LVEF = left ventricular ejection fraction; HR = heart ratio; py = person-year; RR = rate ratio.

Treatment effect of dapagliflozin in women and men



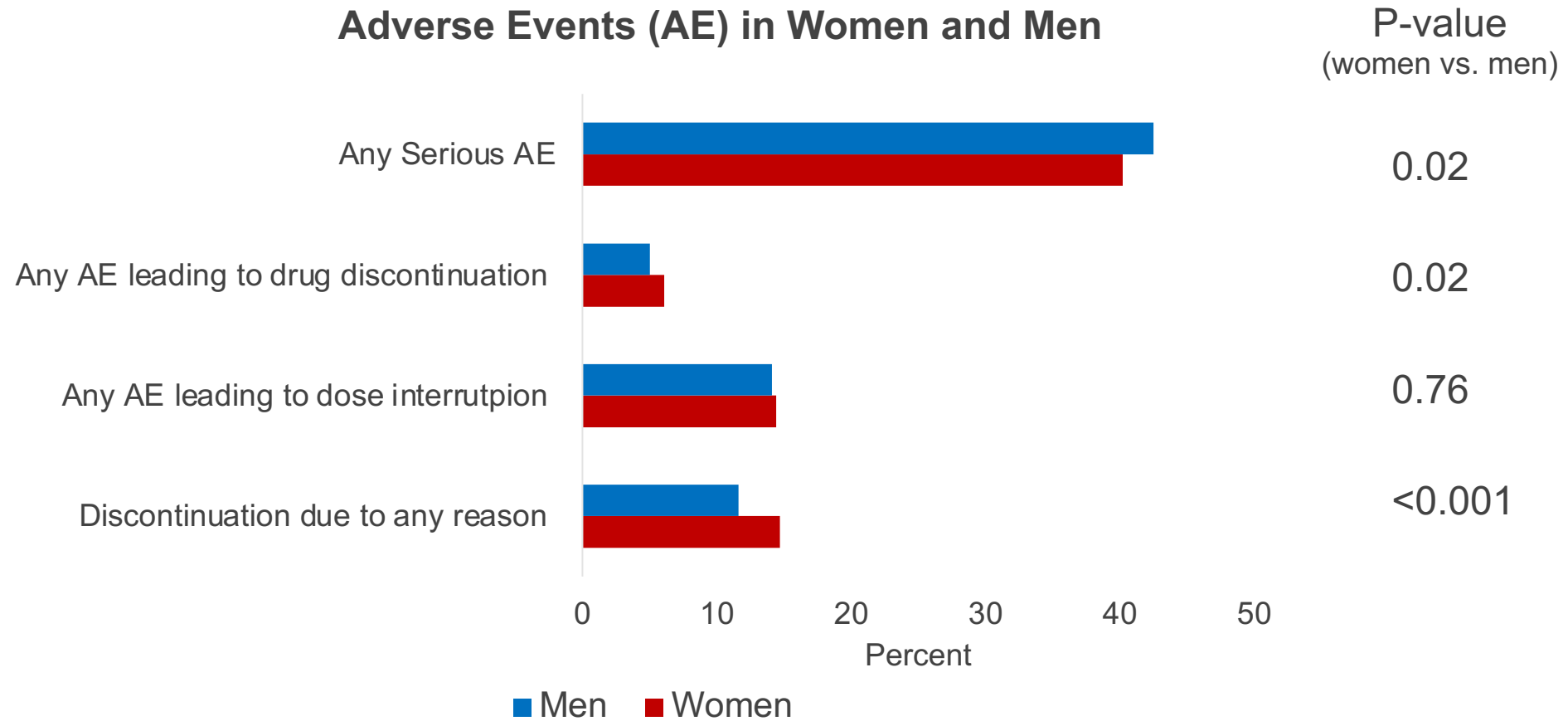
Treatment effect of dapagliflozin in women and men across left ventricular ejection fraction



Blue – Men; Red – Women

LVEF = left ventricular ejection fraction

Safety of dapagliflozin in women and men



No differential increased risk of adverse events in the dapagliflozin group in either men or women (all p-interaction > 0.10).

Limitations

- DAPA-HF and DELIVER were two large, randomized trials with strict inclusion and exclusion criteria; generalizability should consider these criteria.
- In the combined cohort, 35% were women, which reflected the lower rate of heart failure with reduced ejection in women.
- Limited data on adverse events were collected in DELIVER, given the extensive data on the safety of dapagliflozin from prior studies.

Conclusions

- In DAPA-HF and DELIVER, women had better outcomes regardless of treatment assignment.
- Dapagliflozin reduced the primary endpoint, cardiovascular death, all-cause death, heart failure hospitalization, and total events in both men and women.
- Sex did not modify the treatment effect of dapagliflozin across the range of ejection fraction.
- Dapagliflozin was well-tolerated in women and men.

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In Memory Of Lauren Gilstrap, MD, MPH



This presentation is dedicated to the memory of Lauren Gilstrap, MD, MPH, a DELIVER investigator, colleague, co-author, and friend.