

Effects of Dapagliflozin on Hospitalizations for Heart Failure According to Severity of Inpatient Treatment Course: Insights from DELIVER and DAPA-HF



Safia Chatur^{1*}, Toru Kondo^{2*}, Brian L. Claggett¹, Kieran Docherty², Zi Michael Miao¹, Akshay S. Desai¹, Pardeep S. Jhund², Rudolf A. de Boer³, MD, Adrian F. Hernandez⁴, Silvio E. Inzucchi⁵, Mikhail N. Kosiborod⁶, Carolyn S. P. Lam⁷, MBBS, Felipe A. Martinez⁸, Sanjiv J. Shah⁹, Magnus Petersson¹⁰, Anna Maria Langkilde¹⁰, John J.V. McMurray²,

Scott D. Solomon¹, and Muthiah Vaduganathan¹
¹Cardiovascular Division, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA; ²BHF Cardiovascular Research Centre, University of Glasgow, United Kingdom; ³Department of Cardiology, Erasmus MC, Rotterdam, the Netherlands; ⁴Duke University Medical Center, Durham, North Carolina, USA; ⁵Yale School of Medicine, New Haven, CT; ⁶Saint Luke's Mid America Heart Institute and University of Missouri-Kansas City, Kansas City, MO; ⁷National Heart Centre Singapore & Duke-National University of Singapore, Singapore; ⁸Universidad Nacional de Córdoba, Córdoba, Argentina; ⁹Northwestern University Feinberg School of Medicine, Chicago, IL; ¹⁰Late-Stage Development, Cardiovascular, Renal, and Metabolism, BioPharmaceuticals R&D,

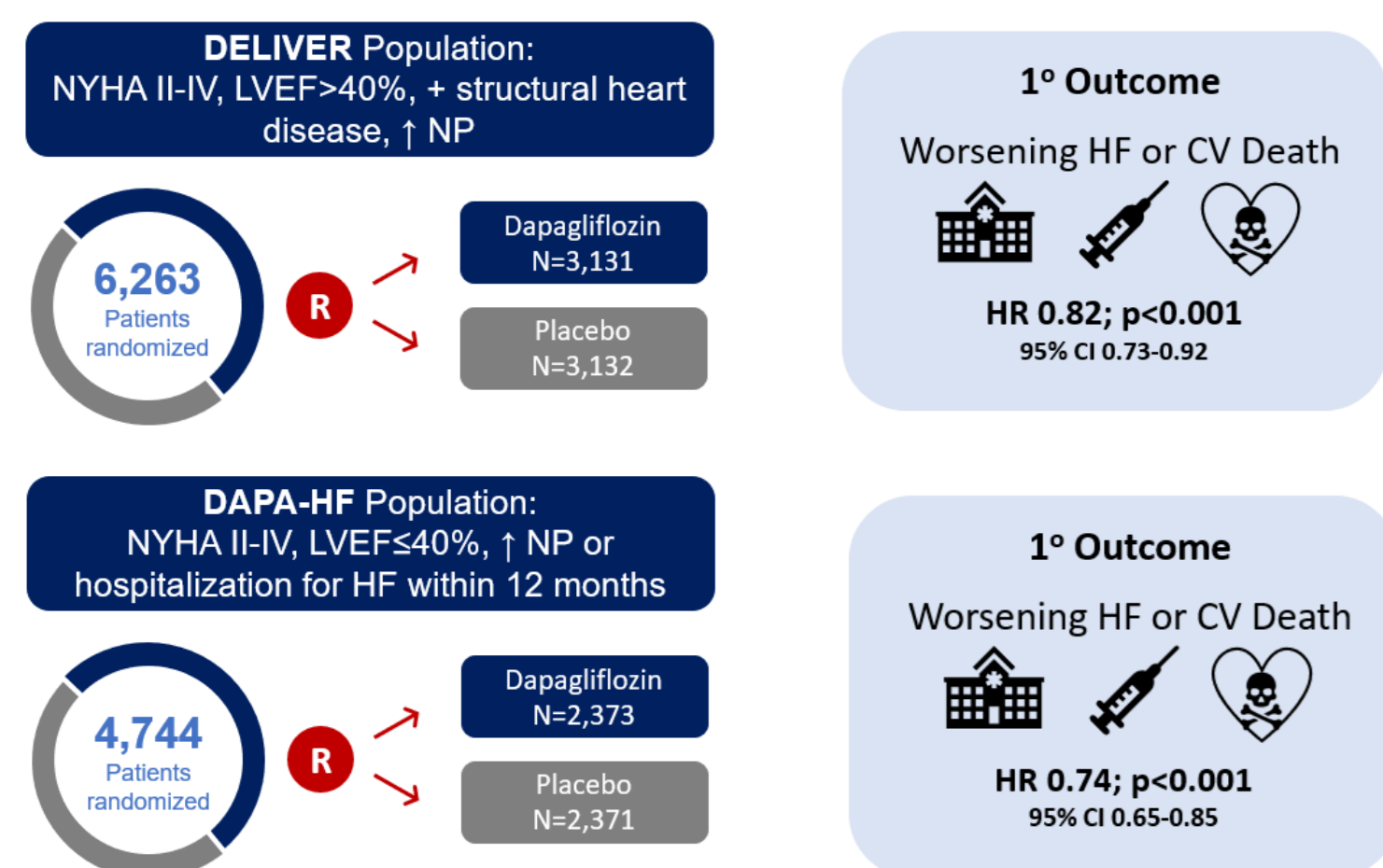
Background

- Dapagliflozin resulted in significant and sustained reductions in first and recurrent HF hospitalizations among patients with HF across the spectrum of ejection fraction.
- HF hospitalizations may vary widely with regard to their complexity, length of stay (LOS), and post-discharge trajectory
- While clinical trials have typically focused on *any* HF hospitalizations, how chronic HF treatment differentially impacts hospitalizations of varying severity is not as well studied.

Objectives

- To describe the frequency and outcomes of HF hospitalizations requiring management beyond standard intravenous diuretics
- To examine the effects of dapagliflozin on HF hospitalizations of varying complexity and LOS.

Methods



Results

Figure 1. HF Hospitalizations Requiring Escalated Care by Trial

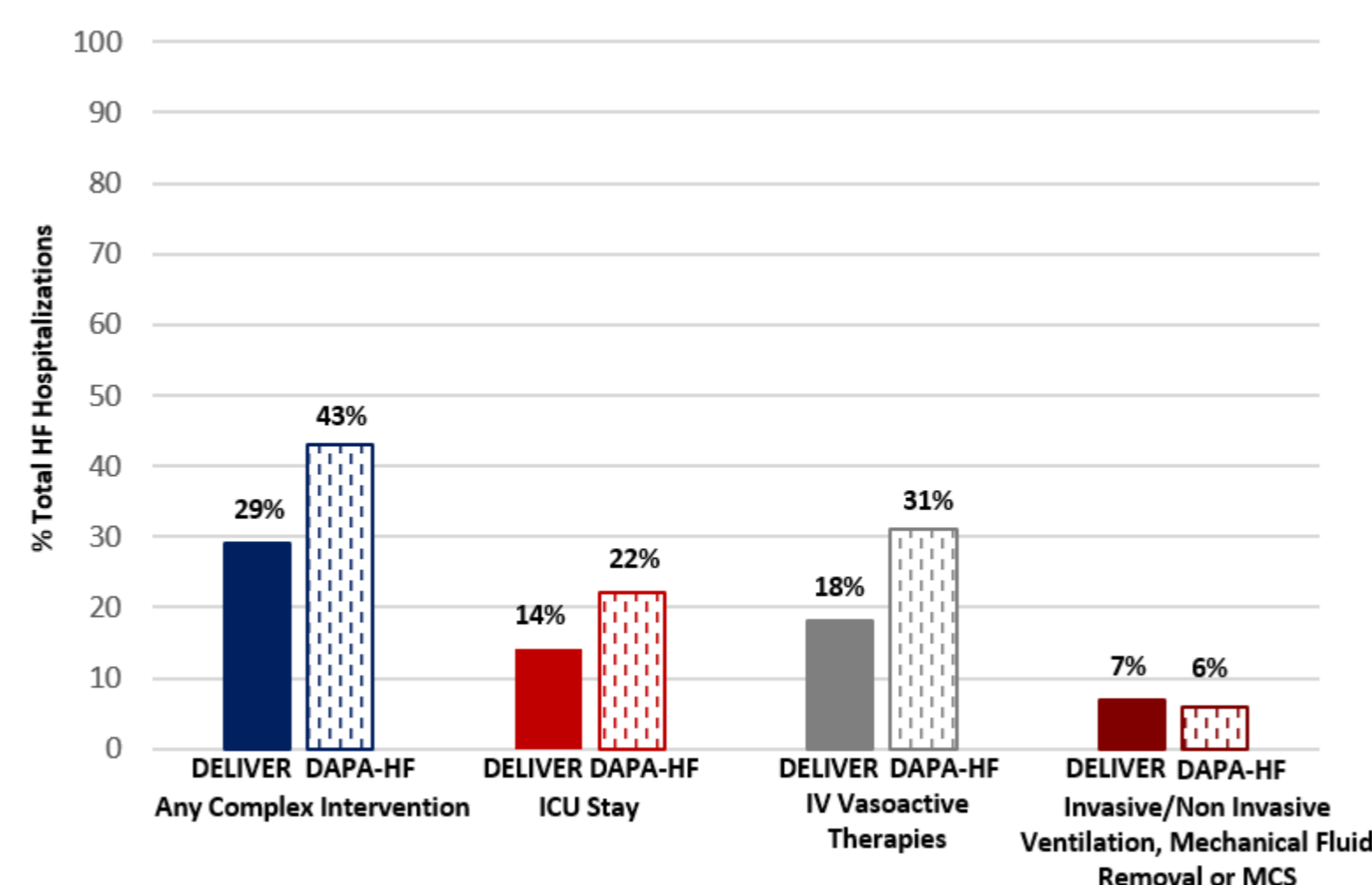


Figure 2. Geographic Distribution of Complicated HF Hospitalizations

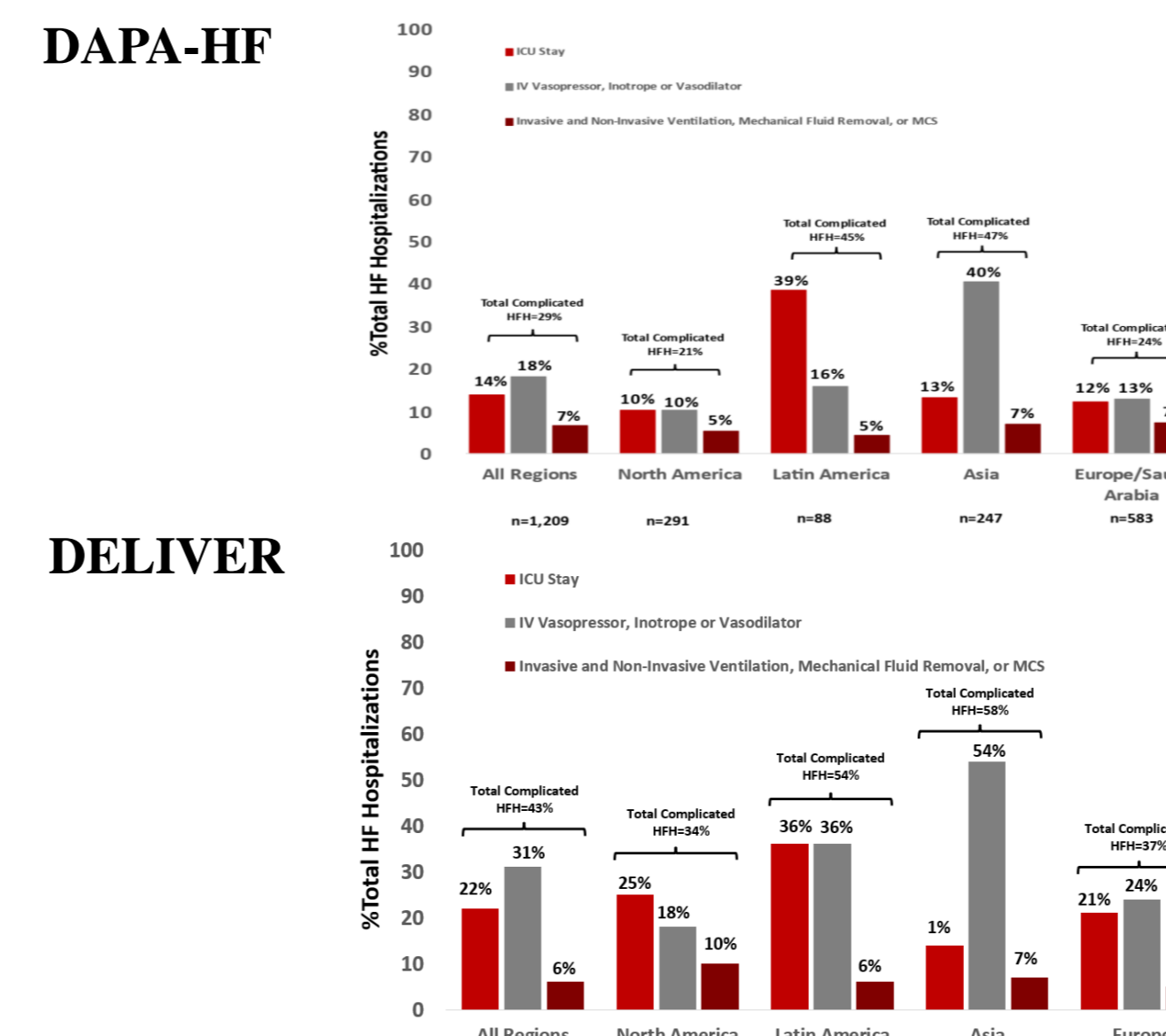


Figure 5. In-hospital Mortality by First HF Hospitalization Complexity Status

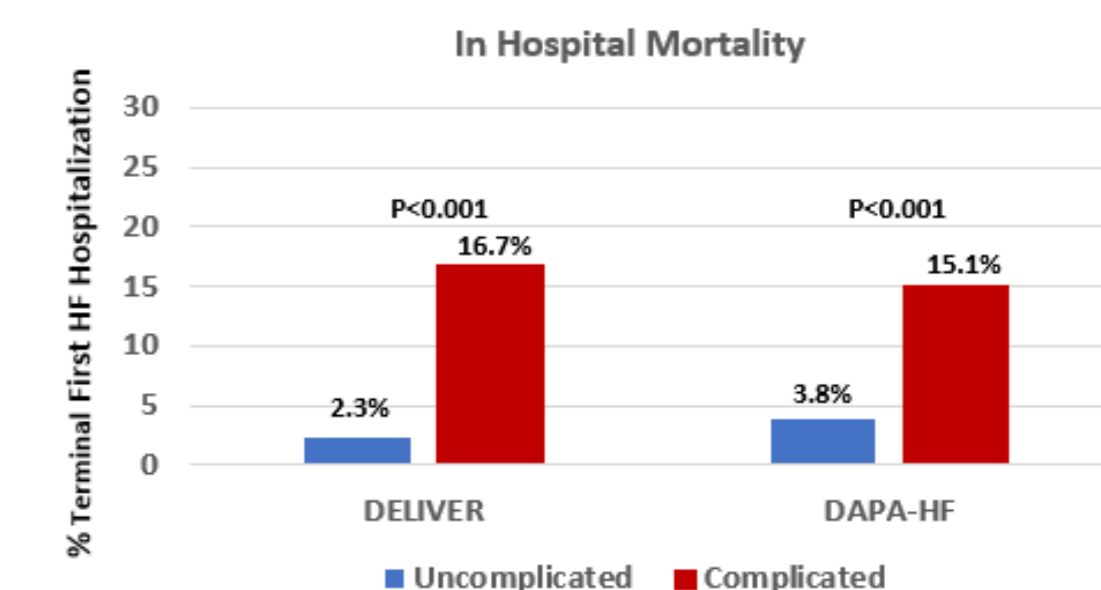


Table. Post-Discharge Mortality by First HF Hospitalization Complexity Status

Outcome	Complicated HF Hospitalization	Uncomplicated HF Hospitalization	P-Value
DELIVER			
Post-Discharge Mortality	HR 0.91; 95%CI: 0.64-1.29		0.59
DAPA-HF			
Post-Discharge Mortality	HR 1.14; 95%CI: 0.84-1.53		0.40

Figure 3. Treatment Effect of Dapagliflozin on Total (First and Recurrent) 'Uncomplicated and 'Complicated' HF Hospitalizations

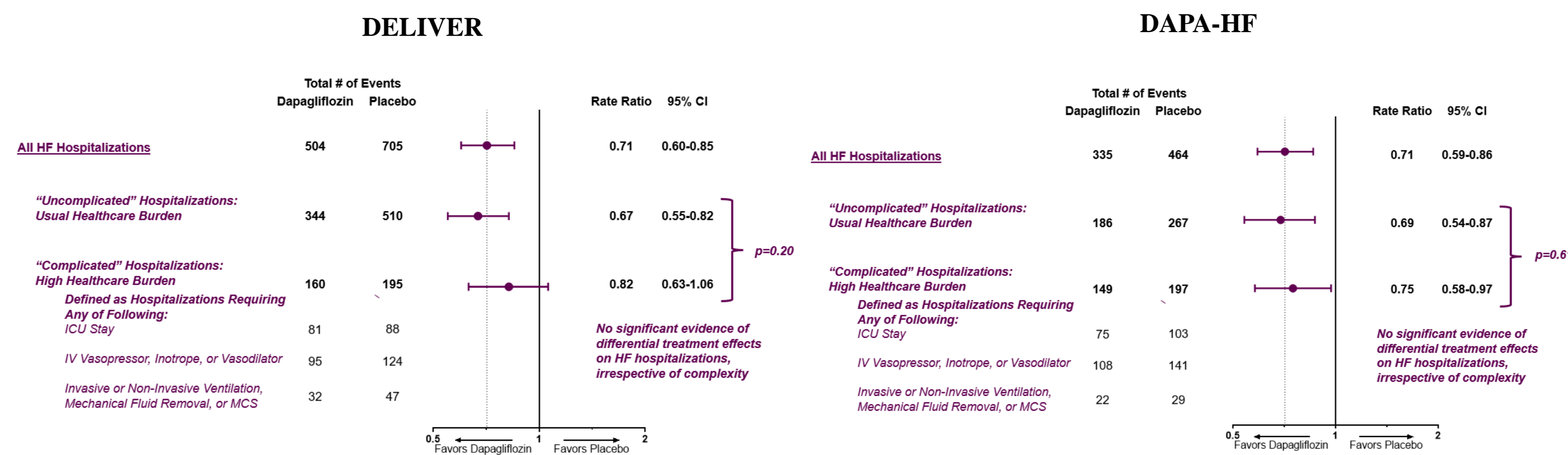
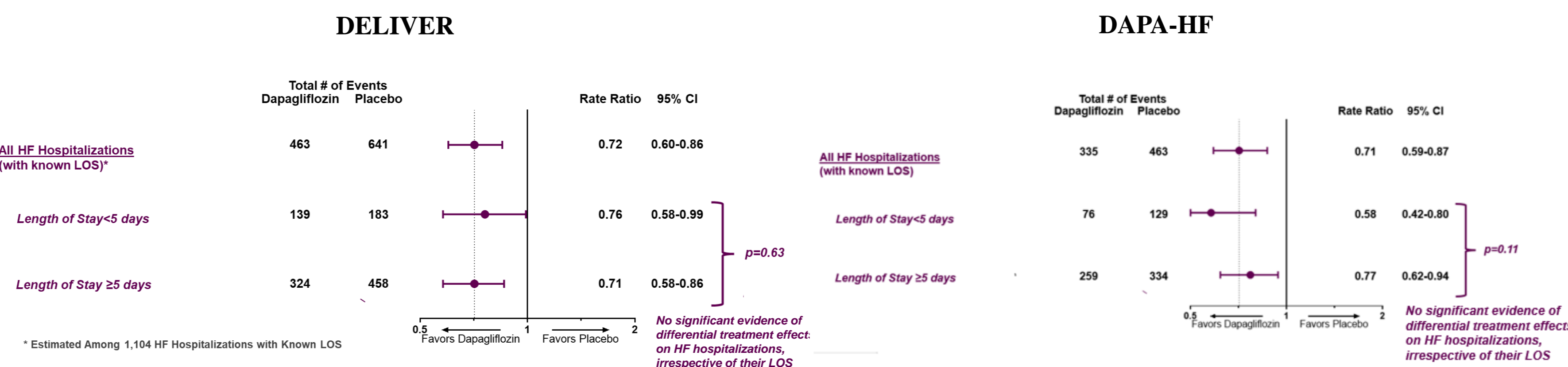


Figure 4. Treatment Effect of Dapagliflozin on Total (First and Recurrent) HF Hospitalizations According to LOS



- 'Complicated hospitalizations' were defined as those requiring intensive therapy including ICU stay, intravenous vasoactive therapies (vasopressor, inotrope or vasodilator), invasive or non-invasive ventilation, mechanical fluid removal, ultrafiltration or mechanical circulatory support (MCS). The balance were classified as 'Uncomplicated'.
- HF hospitalizations were further categorized according to their LOS: longer (≥5 days) or shorter (<5days).

Conclusions

- In 2 large contemporary trials, a substantial proportion of hospitalizations for HF (~30-40%) required escalation of treatment beyond decongestion with intravenous diuretic.
- Patients experiencing complicated HF hospitalizations had substantially higher in-hospital mortality regardless of ejection fraction.
- Treatment with dapagliflozin consistently reduced HF hospitalizations irrespective of severity of in-hospital treatment course or LOS.

Disclosures

The DELIVER and DAPA-HF trial were funded by AstraZeneca S.C., is supported by the Canadian Child's Scholarship from the Libin Institute of Alberta/University of Medicine. T.K. has received lecture fees from Abbott Medical Japan LLC, Ono Pharmaceutical Co. Ltd., Onkai Pharmaceutical Co. Ltd., Novartis Pharma K.K., AstraZeneca K.K., Bristol-Myers Squibb Co., and Abbott Japan K.K. Z.M. has nothing to disclose. B.L.C. has received consulting fees from Amgen, Cardinal, Corvia, and Novartis. A.S.D. has received research grant support from Abbott, AstraZeneca, Alnylam, Bayer, and Novartis; and has received consulting fees and/or honoraria from Abbott, AstraZeneca, Alnylam, Amgen, Astor Therapeutics, Bayer, Boston Scientific, BioPharmaceuticals, Cytokinetics, GlaxoSmithKline, Merck, Novartis, Paroel, Regeneron, Roche, and Verily. Z.M.M. reports no disclosures. P.S.J. reports support from AstraZeneca, Novartis, Alkerm, Metabolix, ProPhase Communications, Sanofi, and other activities from AstraZeneca, Boehringer Ingelheim, Novartis, research funding from AstraZeneca, Boehringer Ingelheim, Amgen, AstraZeneca, Roche Diagnostics, Pfizer, and other activities from AstraZeneca, Boehringer Ingelheim, Novartis, and Roche. D.D. has received speaker fees from AstraZeneca, Boehringer Ingelheim, Amgen, AstraZeneca, Bayer, Novartis, and Roche (outside the submitted work). A.F.H. has received research grant support from American Regent, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Merck, Novartis, Sonologic, and Verily; and has served as a consultant or on the Advisory Board for Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Boston Scientific, Bristol Myers Squibb, Cytokinetics, Eisai, Intrepid, Merck, and Novartis. S.E.I. has served on clinical trial committees or as a consultant to AstraZeneca, Boehringer Ingelheim, Novo Nordisk, Merck, Pfizer, and has given lectures sponsored by AstraZeneca and Boehringer Ingelheim. M.N.K. has received research grant support from AstraZeneca, and Boehringer Ingelheim; has served as a consultant or on an advisory board for Alnylam, Amgen, Applied Therapeutics, AstraZeneca, Bayer, Boehringer Ingelheim, Eli Lilly, Esperion Therapeutics, Janssen, Merck (Diabetes and Cardiovascular), Novo Nordisk, Sanofi, Pharmacosmos, and Vifor Pharma; has received other research support from AstraZeneca; and has received honorarium from AstraZeneca, Boehringer Ingelheim, and Novo Nordisk. C.S.P. is supported by a Clinician Scientist Award from the National Medical Research Council of Singapore; has received research support from AstraZeneca, Bayer, and Roche Diagnostics; has served as a consultant or on the advisory board/steering committee/executive committee for Actelion, Alkerm, Alnylam, Amgen, Amgen, AstraZeneca, AstraZeneca, Bayer, Boehringer Ingelheim, Boston Scientific, Cytokinetics, Derna Inc, EchoNose Inc, Eli Lilly, Impulse Dynamics, Ionis Pharmaceutical, U2L, Janssen Research & Development LLC, Medscape, Merck, Novartis, Novo Nordisk, Proscendo Inc, RealLife Group Ltd, Roche Diagnostics, Sanofi, Siemens Healthcare Diagnostics and Watson Global LLC, and serves as the cofounder and non-executive director of U2L. F.A.M. has received consulting fees and research grant support from AstraZeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Gilead, Milestone, Novartis, Pfizer, and St. Luke's University. S.J.S. has received research grants from the National Institutes of Health (54 HL100277, R01 HL127028, R01 HL140731, R01 HL19423), AstraZeneca, AstraZeneca, Corvia, Novartis, and Pfizer; and has received consulting fees from Abbott, AstraZeneca, Amgen, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Boston Scientific, Bristol Myers Squibb, Cardio, Corvia, Cytokinetics, Edwards Lifesciences, GSK, Inellus, Ionis, Inovio, Lilly, Merck, Myokardia, Novartis, Novo Nordisk, Pfizer, Prothena, Regeneron, Rivin, Sanofi, Sanofi, Shionogi, Taro, Tempus, and United Therapeutics. M.P. is an employee and shareholder of AstraZeneca. A.M.L. is an employee and shareholder of AstraZeneca. J.J.V.M. has received payments through Glasgow University for work on clinical trials, consulting and other activities from Alnylam, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, BMS, Cardiac, Cytokinetics, Dal Cor, GSK, Ionis, KIP Biosciences, Novartis, Pfizer, Theranos Personal Care for the Corvus, Abbot, Hillam, Sanofi, AstraZeneca, Medscape/Heart Org, RealLife Cardio, Servier Director, Global Clinical Trial Partners (GCTP) R.A.L.B. has received research grants from AstraZeneca, Alnylam, Amgen, Amgen, AstraZeneca, Boehringer, Bayer, BMS, Colson, Cytokinetics, Eisai, Gilead, GSK, Ionis, Lilly, Mediolan, Myokardia, NIBIB/NIH, Neuronic, Novartis, NovoNordisk, Regeneron, Sanofi/Pfizer, Theranos, U2L and has consulted for Abbott, Acton, Akros, Alnylam, Amgen, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, BMS, Cardiac, Corvia, Cytokinetics, Daiichi-Sankyo, GSK, Lilly, Merck, Myokardia, Novartis, Roche, Theranos, Quantum Genetics, Cardio, Janssen, Curis, Dimension Therapeutics, Sanofi/Pfizer, Disage, Trevena, CelPhoTher, Moderna, American Regent, Sargis, Lesion, Anacardio, Akzo, Parthenon Health. The remaining authors have nothing to disclose. M.V. has received research grant support, served on advisory boards, or had speaker engagements with American Regent, Amgen, AstraZeneca, Bayer AG, Baxter Healthcare, Boehringer Ingelheim, Chiesi, Cytokinetics, Lesion Pharmaceuticals, Merck, Novartis, Novo Nordisk, Pharmacosmos, Relpyra, Roche Diagnostics, Sanofi, and Triang Health, and participates on clinical trial committees for studies sponsored by AstraZeneca, Galmed, Novartis, Bayer AG, Octech, and Impulse Dynamics.