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Empagliflozin and Cardiovascular Outcomes in Patients With Chronic Kidney Disease: The EMPA-KIDNEY Trial

David Preiss
MRC-Population Health Research Unit,
University of Oxford

on behalf of:

EMPA-KIDNEY Collaborative Group

NDPH Renal Studies Group and **SMART-C**

Disclosures

- No personal disclosures: long-standing departmental policy to decline honoraria
- The EMPA-KIDNEY trial was initiated by the University of Oxford who led its design, analysis, and reporting with a Steering Committee of expert collaborators
- The trial was funded and sponsored by Boehringer Ingelheim with additional support from Eli Lilly and UK Medical Research Council

EMPA-KIDNEY design

Population: a broad range of patients with chronic kidney disease at risk of progression (eGFR 20-44; or 45-90 mL/min/1.73 m^2 with UACR ≥200 mg/g) in 8 countries

Intervention

Investigator-judged clinically appropriate RAS blockade, where indicated & tolerated

Empagliflozin 10 mg once daily

Placebo once daily

Primary composite outcome

CV death OR **Kidney disease progression**

- **End-stage kidney disease; Renal death**
- **eGFR change** ≥40% eGFR decline, or to <10 mL/min/1.73m^2

Key secondary outcomes

- All hospitalizations (recurrent events)
- All-cause death
- CV death or HF hospitalization

EMPA-KIDNEY Collaborative Group, *Nephrol Dial Transplant*. 2022;37:1317-29

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Baseline characteristics: 6609 participants

	Empagliflozin (n=3304)	Placebo (n=3305)
Mean age (years)	64	64
Female	33%	33%
Mean eGFR (mL/min/1.73m^2)	37	37
Diabetes	46%	46%
Cardiovascular disease	26%	27%

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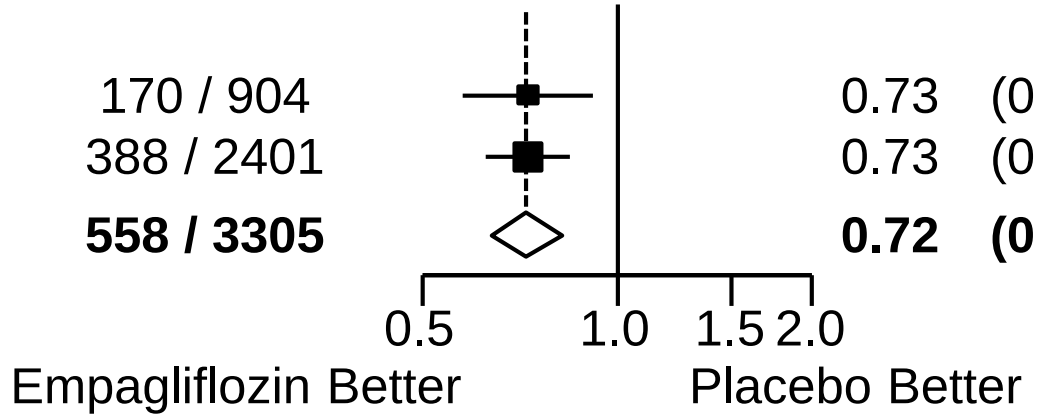
Primary outcome: by prior CV disease

	Empagliflozin events / pts	Placebo events / pts	Hazard Ratio (95% CI)		
Prior CV disease	122 / 861	170 / 904	0.73	(0.58–0.92)	
No CV disease	310 / 2443	388 / 2401	0.73	(0.63–0.85)	P_{het}=0.99
All participants	**432 / 3304**	**558 / 3305**	**0.72**	**(0.64–0.82)**	



- Average follow up: 2 years
- 128 CV deaths occurred

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Recurrent events analyses: CV outcomes

Outcome	Analysis	Empagliflozin	Placebo	HR (95% CI)
HF hospitalization	First event	88	107	0.80 (0.60-1.06)
	Total events	118	154	0.78 (0.59-1.05)
CV death or HF hospitalization	First event	131	152	0.84 (0.67-1.07)
	Total events	166	210	0.83 (0.64-1.07)
MACE*	First event	200	213	0.93 (0.76-1.12)
	Total events	251	290	0.90 (0.72-1.12)

*MACE: CV death, MI, stroke or HF hospitalization

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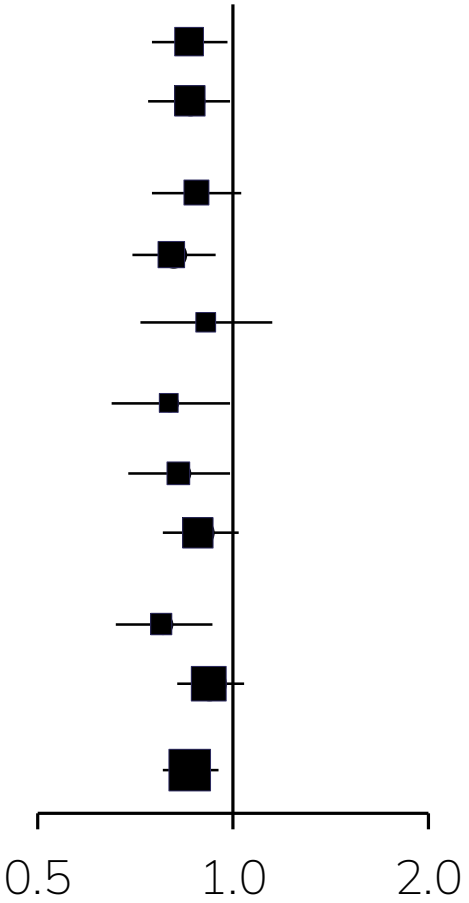
All-cause hospitalization: subgroups

Subgroup		Empagliflozin Events / 100 pt yrs	Placebo Events / 100 pt yrs	Hazard Ratio (95% CI)	
Diabetes	Yes	31.2	36.7	0.86	(0.75–0.98)
	No	19.1	22.6	0.86	(0.74–0.99)
eGFR (mL/min/1.73m^2)	<30	32.0	36.3	0.88	(0.75–1.03)
	≥30 <45	22.3	27.3	0.81	(0.69–0.94)
	≥45	18.3	21.3	0.91	(0.72–1.14)
UACR (mg/g)	<30	24.7	30.8	0.80	(0.65–0.99)
	≥30 ≤300	24.6	30.5	0.83	(0.69–0.99)
	>300	24.9	27.9	0.89	(0.78–1.02)
Prior CVD	Yes	37.8	49.1	0.78	(0.66–0.93)
	No	20.2	21.8	0.92	(0.82–1.04)
All participants		24.8	29.2	0.86	(0.78–0.95)



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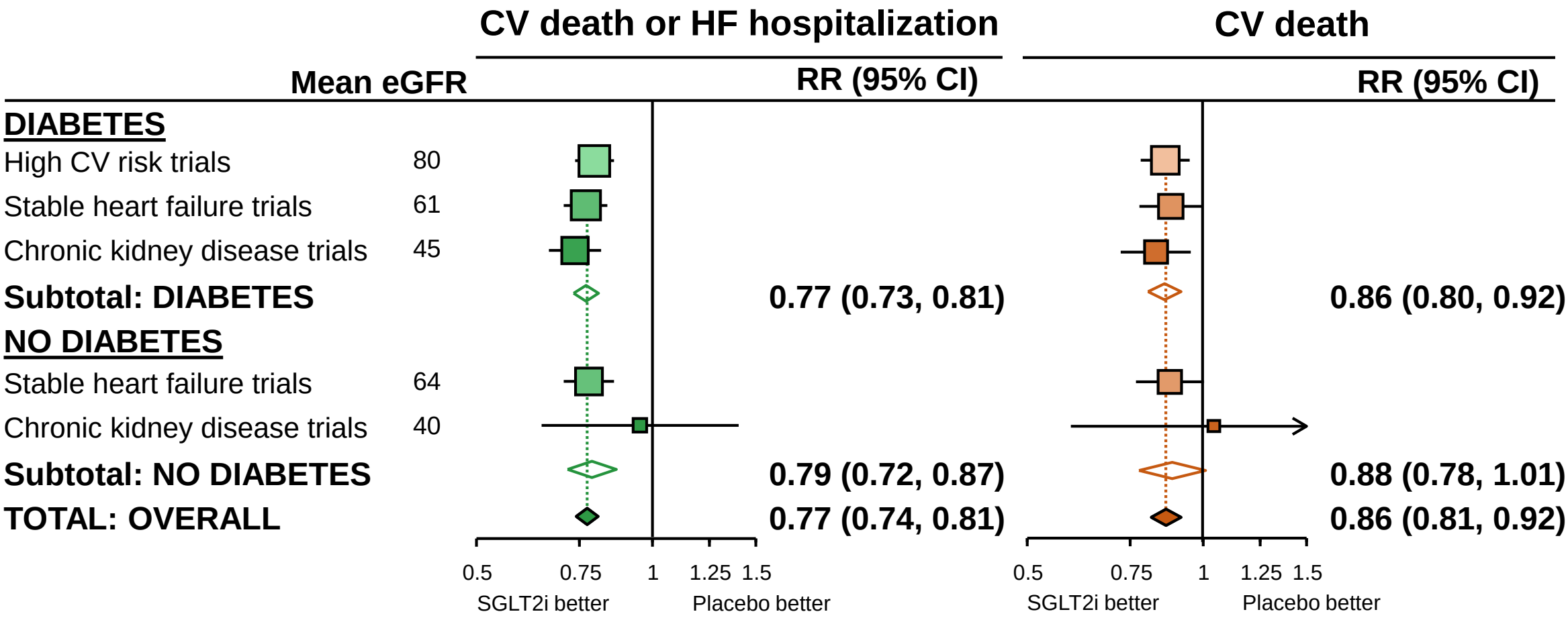
Collaborative summary meta-analysis of SGLT2i

Trials: 13 large placebo-controlled SGLT2i trials

- **T2DM + CV risk:** DECLARE-TIMI 58, CANVAS, VERTIS CV, EMPA-REG OUTCOME
- **Heart failure:** DAPA-HF, EMPEROR-Reduced, EMPEROR-Preserved, DELIVER, SOLOIST-WHF
- **Chronic kidney disease:** CREDENCE, SCORED, DAPA-CKD, EMPA-KIDNEY

Population	Trials	% with diabetes	Total nr
T2DM + high CV risk	4	100%	42,568
Heart failure	5	50%	21,947
Chronic kidney disease	4	81%	25,898
Total	**13**	**82%**	**90,413**

Cardiovascular outcomes



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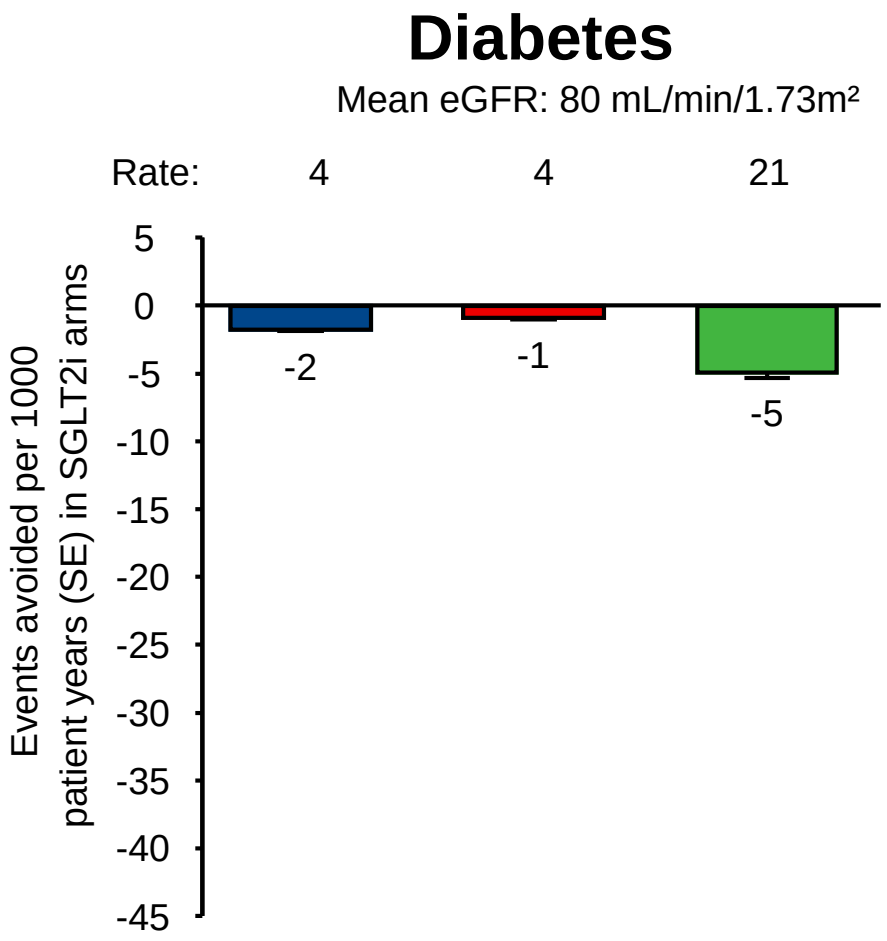
Absolute benefits: (i) T2DM + CV disease



Kidney disease progression

Acute kidney injury

CV death or hospitalization for heart failure

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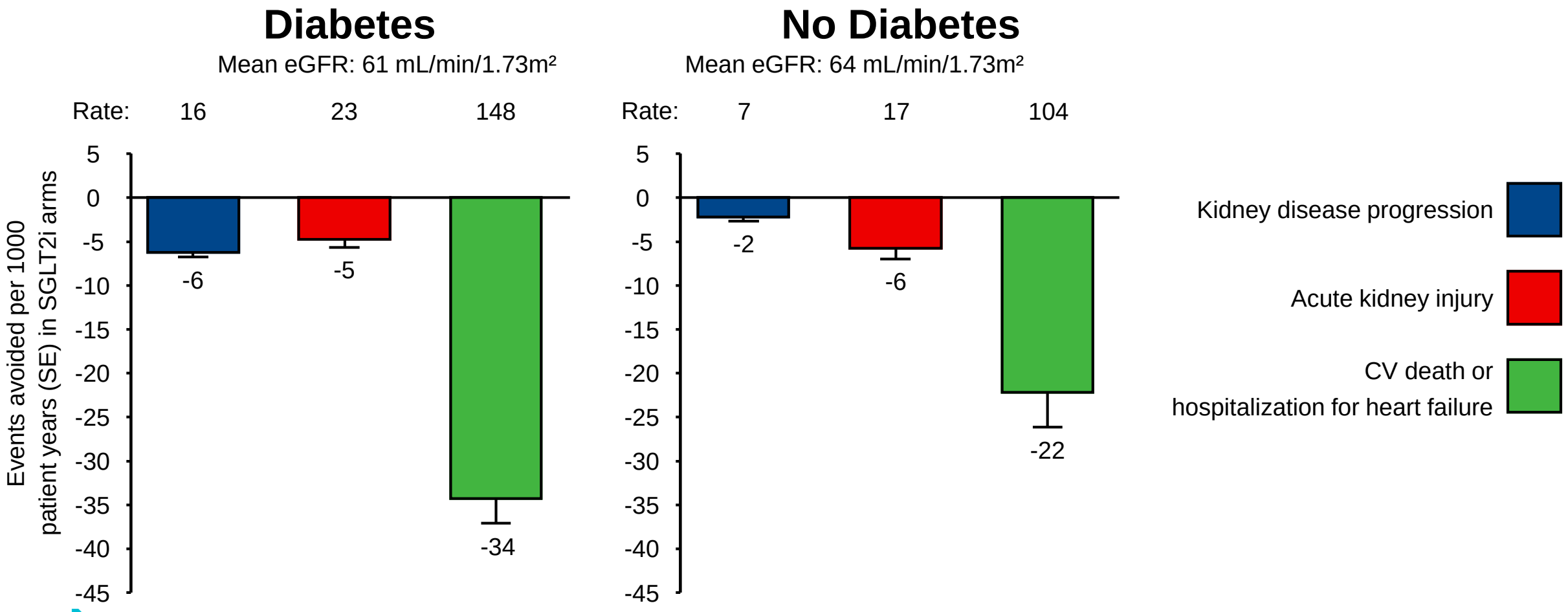
Absolute benefits: (ii) Heart failure



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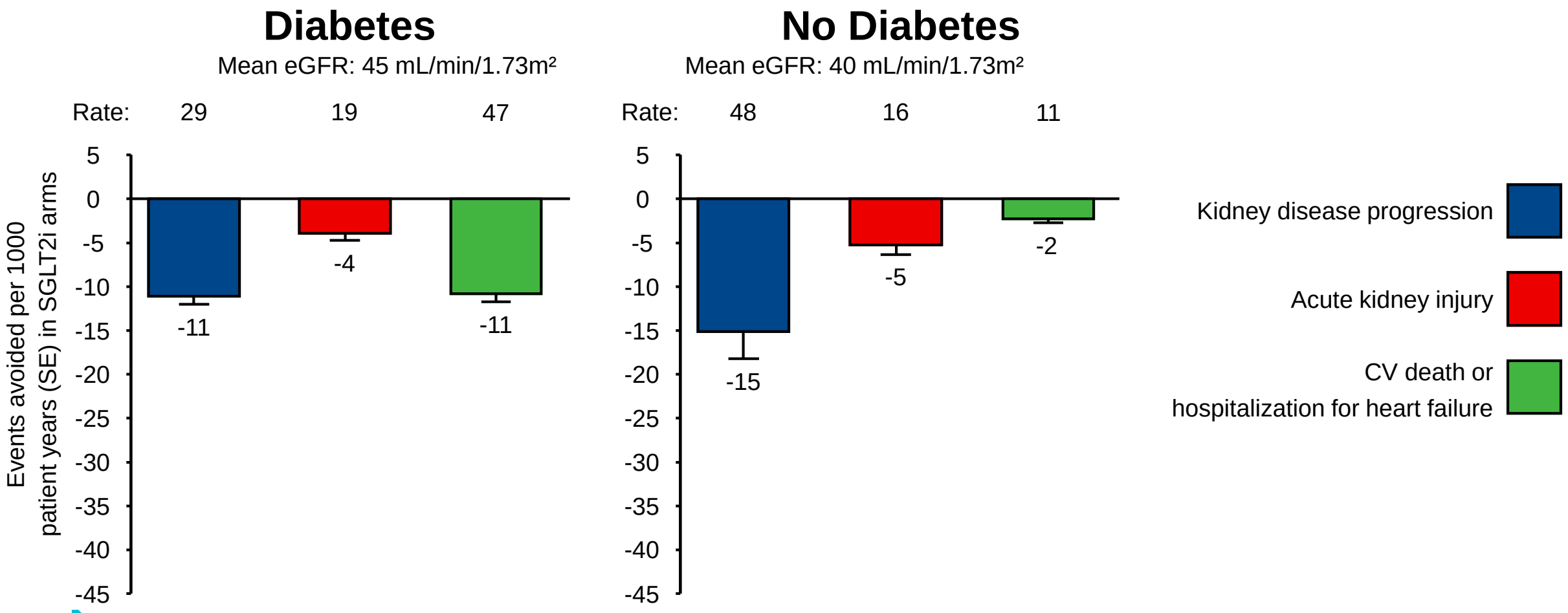
Absolute benefits: (iii) Chronic kidney disease



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Conclusions

EMPA-KIDNEY trial:

- Treatment with empagliflozin reduced (i) kidney disease progression or CV death (ii) hospitalization (similar proportional effects regardless of CV status)
- There were relatively few CV events; however, both first events and total events analyses consistent with other trials

Meta-analysis of 13 major SGLT2 inhibitor trials:

- *Diabetes*: reductions in CV death ± heart failure hospitalization in patients with high CV risk, heart failure or chronic kidney disease
- *No diabetes*: reductions in CV death ± heart failure hospitalization in participants with heart failure; less information in chronic kidney disease (but consistent with other high risk populations)

Acknowledgements

Participants, committee members, coordinating and local site staff in the **EMPA-KIDNEY Collaborative Group**

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www.empakidney.org

NDPH Renal Studies Group and **SMART-C consortium**

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