



MRC Population
Health Research
Unit



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

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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



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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 m² 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/1.73m²

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



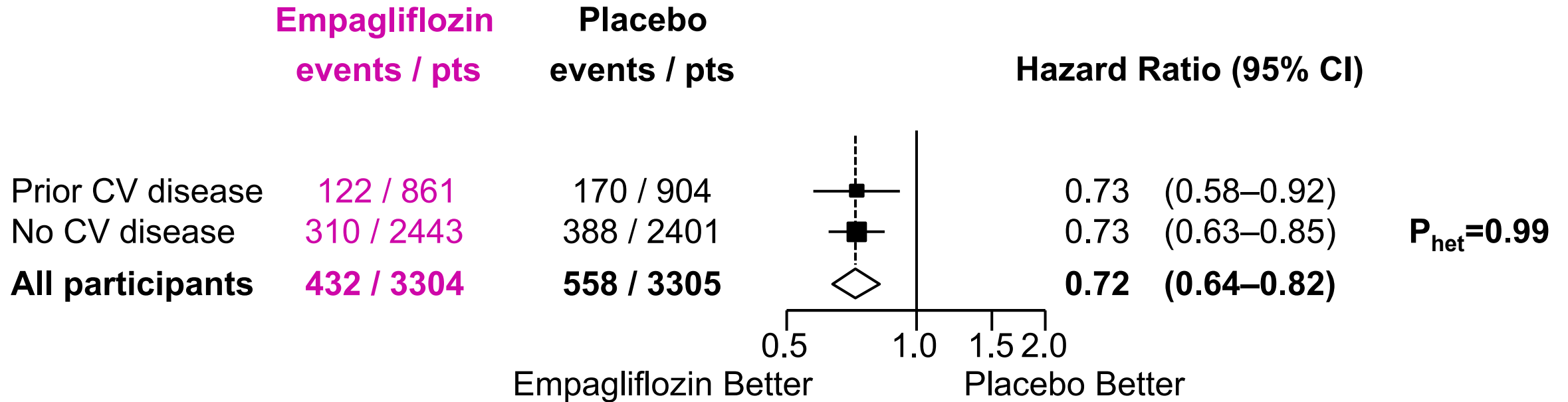
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Baseline characteristics: 6609 participants

	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%

Primary outcome: by prior CV disease



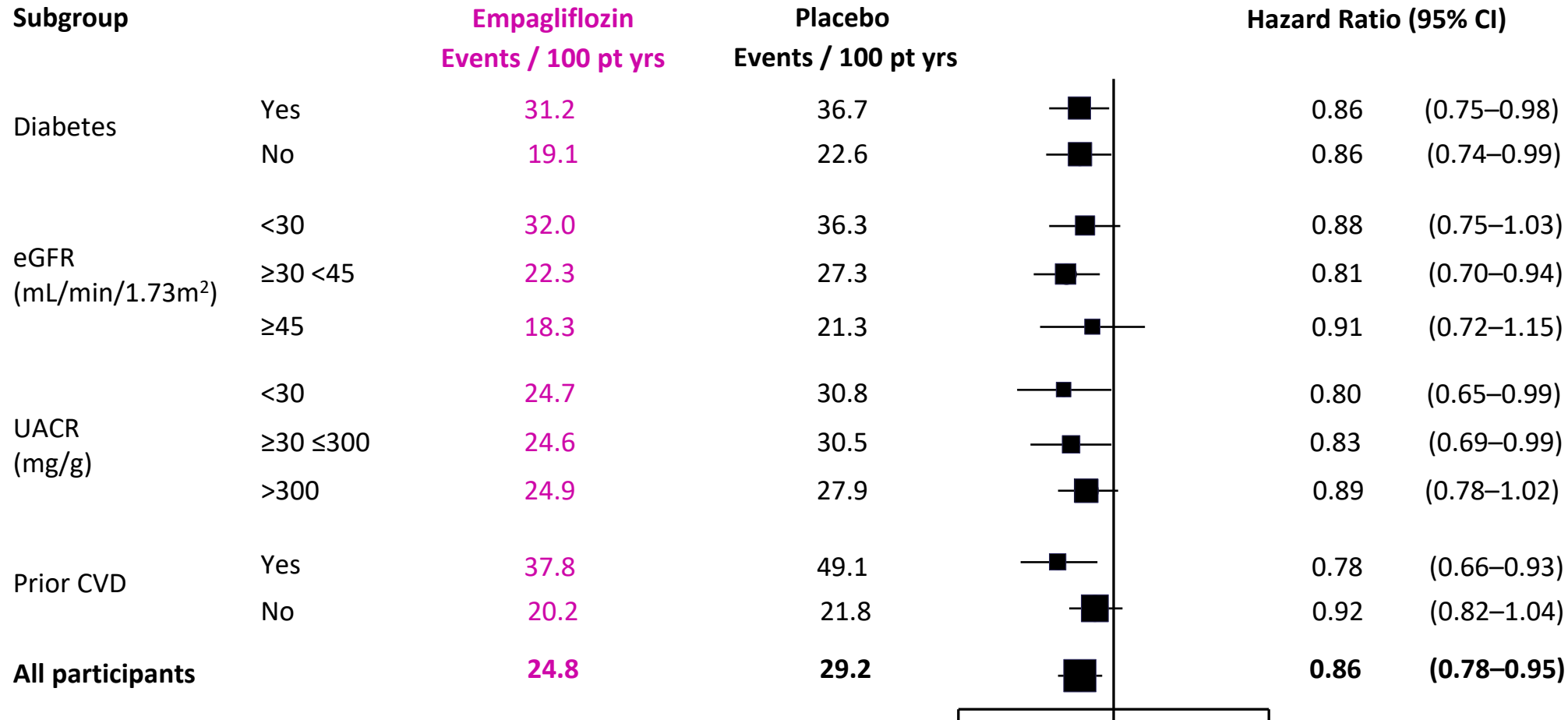
- Average follow up: 2 years
- 128 CV deaths occurred

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

All-cause hospitalization: subgroups



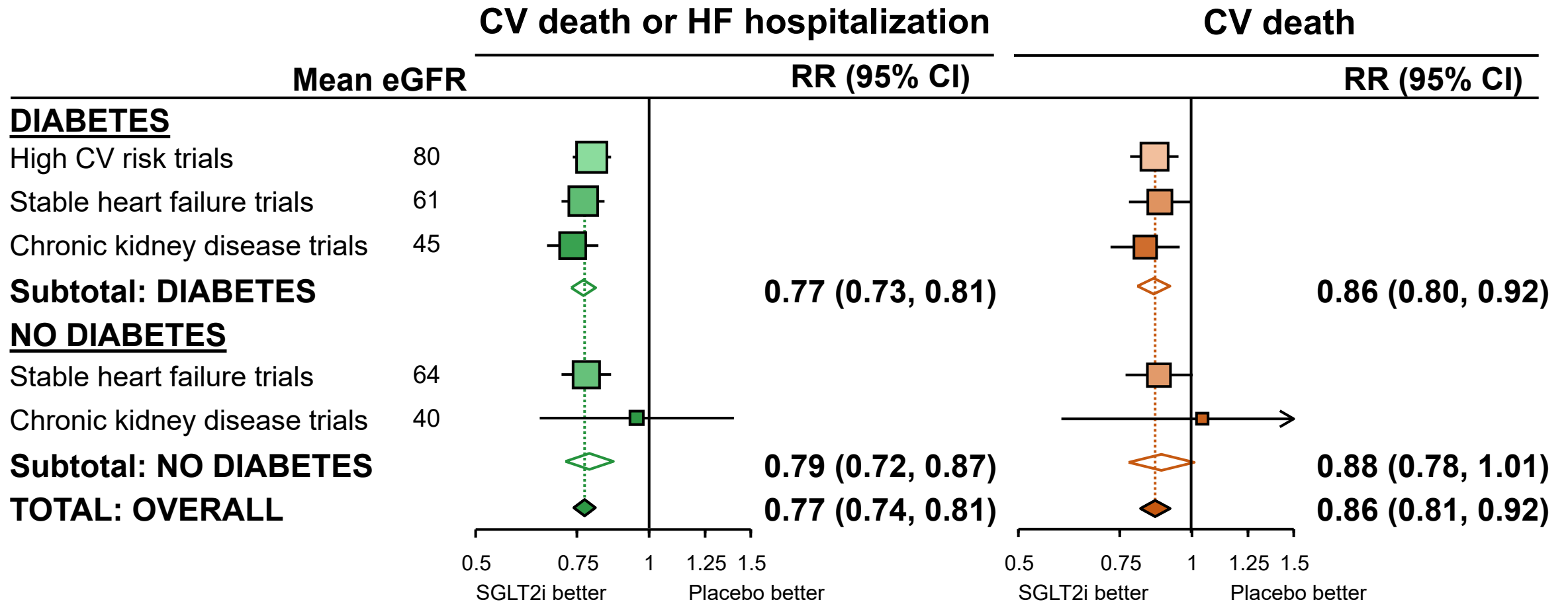
Collaborative summary meta-analysis of SGLT2i

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



Absolute benefits: (i) T2DM + CV disease

Diabetes

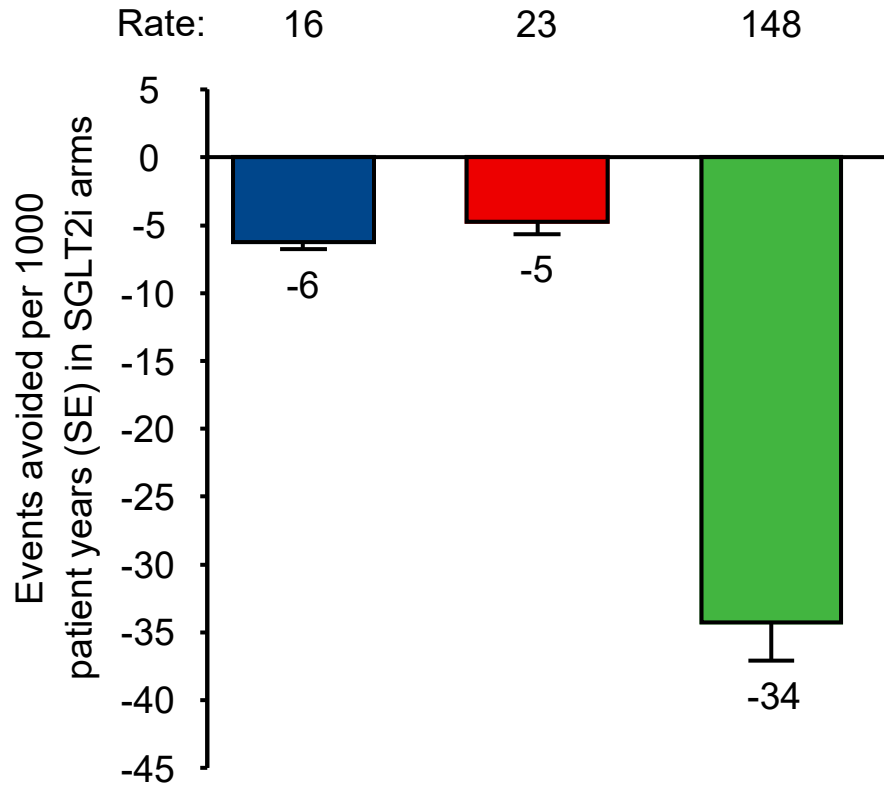
Mean eGFR: 80 mL/min/1.73m²



Absolute benefits: (ii) Heart failure

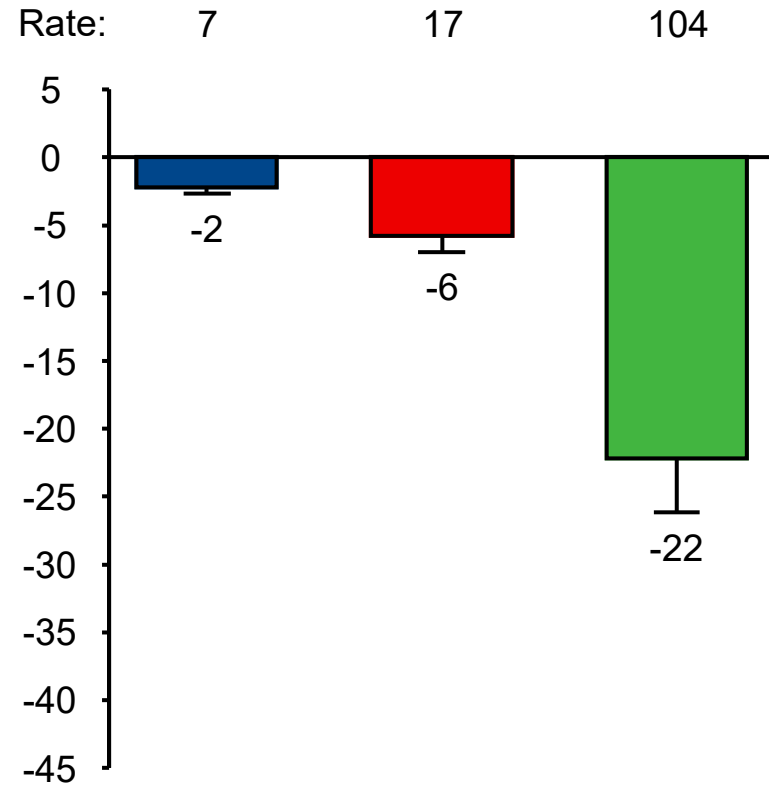
Diabetes

Mean eGFR: 61 mL/min/1.73m²



No Diabetes

Mean eGFR: 64 mL/min/1.73m²



Kidney disease progression

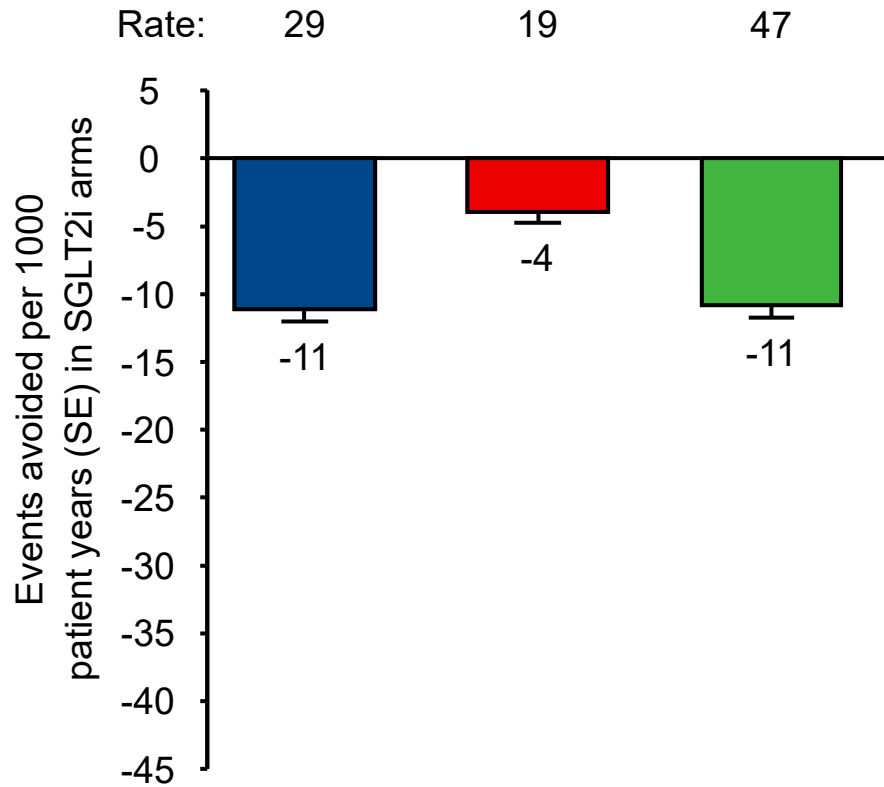
Acute kidney injury

CV death or hospitalization for heart failure

Absolute benefits: (iii) Chronic kidney disease

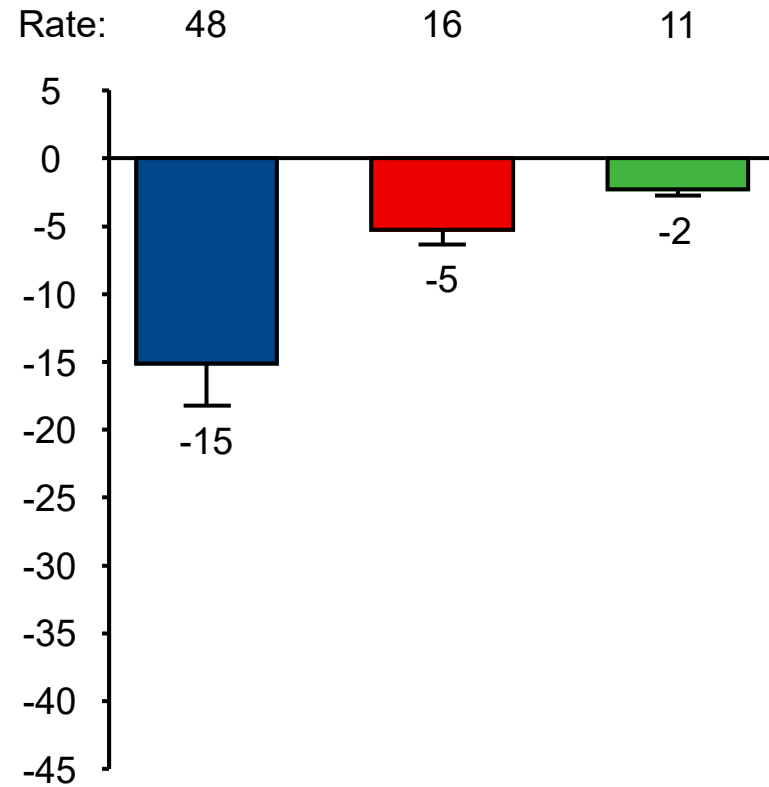
Diabetes

Mean eGFR: 45 mL/min/1.73m²



No Diabetes

Mean eGFR: 40 mL/min/1.73m²



Kidney disease progression

Acute kidney injury

CV death or hospitalization for heart failure

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 \pm heart failure hospitalization in patients with high CV risk, heart failure or chronic kidney disease
- *No diabetes*: reductions in CV death \pm 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

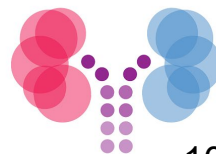


NDPH Renal Studies Group and **SMART-C consortium**

THE LANCET



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