Sodium Glucose Cotransporter-2 (SGLT2) Inhibitors Among Patients With and Without Diabetes:

Collaborative Meta-Analysis of Large Placebo-Controlled Trials

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on behalf of the
NDPH Renal Studies Group &
SGLT2 Meta-Analysis Cardio-Renal Trialists' Consortium (SMART-C)

Disclosures

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- Boehringer Ingelheim
- Eli Lilly and Company
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Aims

- Collaborative summary data meta-analysis of the effects of SGLT2 inhibitors on:
  - A common composite kidney disease progression outcome
  - Acute kidney injury events

- Main aim: comparing findings in patients with versus without diabetes
- Subsidiary aims:
  a) Any effect modification by primary kidney diagnosis (CKD trials only)
  b) Predicted absolute benefits and harms in patients with & without diabetes

Outcome definitions

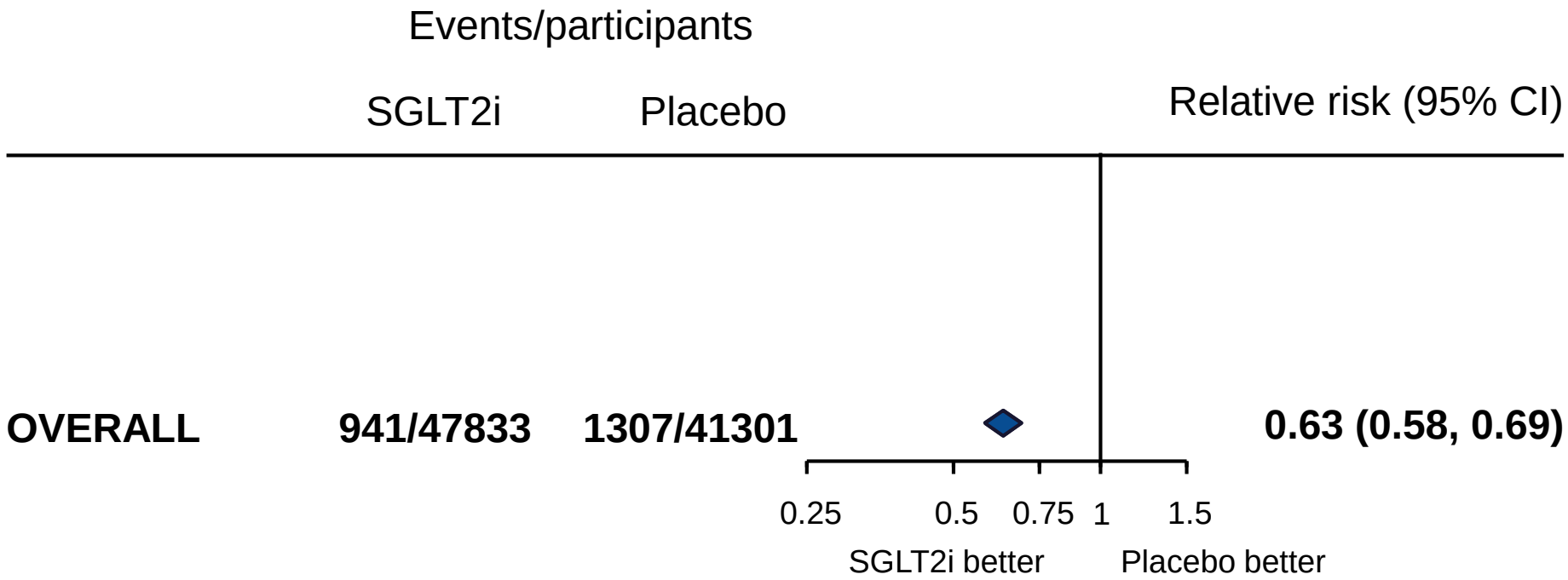
- Kidney disease progression composite outcome
  - A sustained ≥50% eGFR decline from randomisation
  - Start of maintenance dialysis or kidney transplantation
  - A sustained low eGFR (e.g. <10 or <15 mL/min/1.73m^2)
  - Death from kidney failure

- Acute kidney injury
  - Specific MedDRA Preferred Term

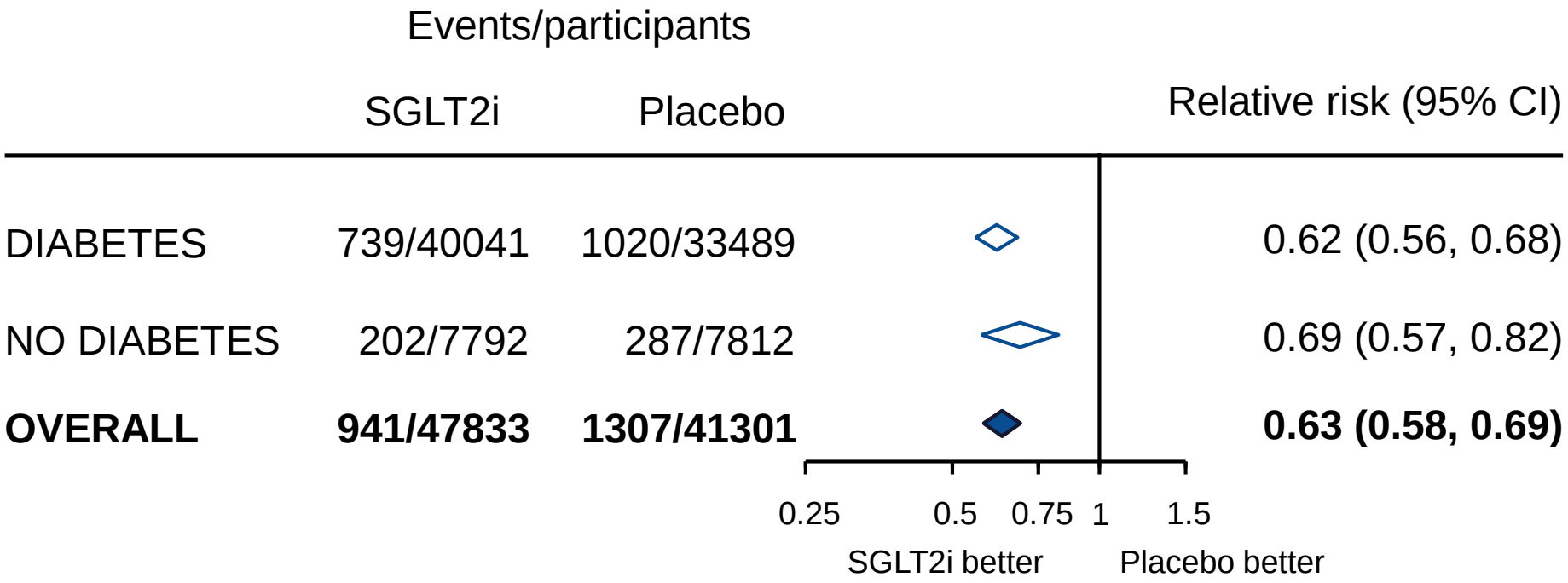
Characteristics of 13 included trials

Population	Trials	Mean eGFR, ml/min/1.73m^2 (range)	Median follow-up, years (range)	Number (%) without diabetes	Total participants
Type 2 diabetes & high CV risk	4	74-85	3.0-4.2	0 (0%)	42,568
Heart failure	5	50-66	1.3-2.6	10,985 (50%)	21,947
Chronic kidney disease (CKD)	4	37-56	0.8-2.2	4968 (19%)	25,898
TOTAL	**13**			**15,953 (18%)**	**90,413**

Kidney disease progression

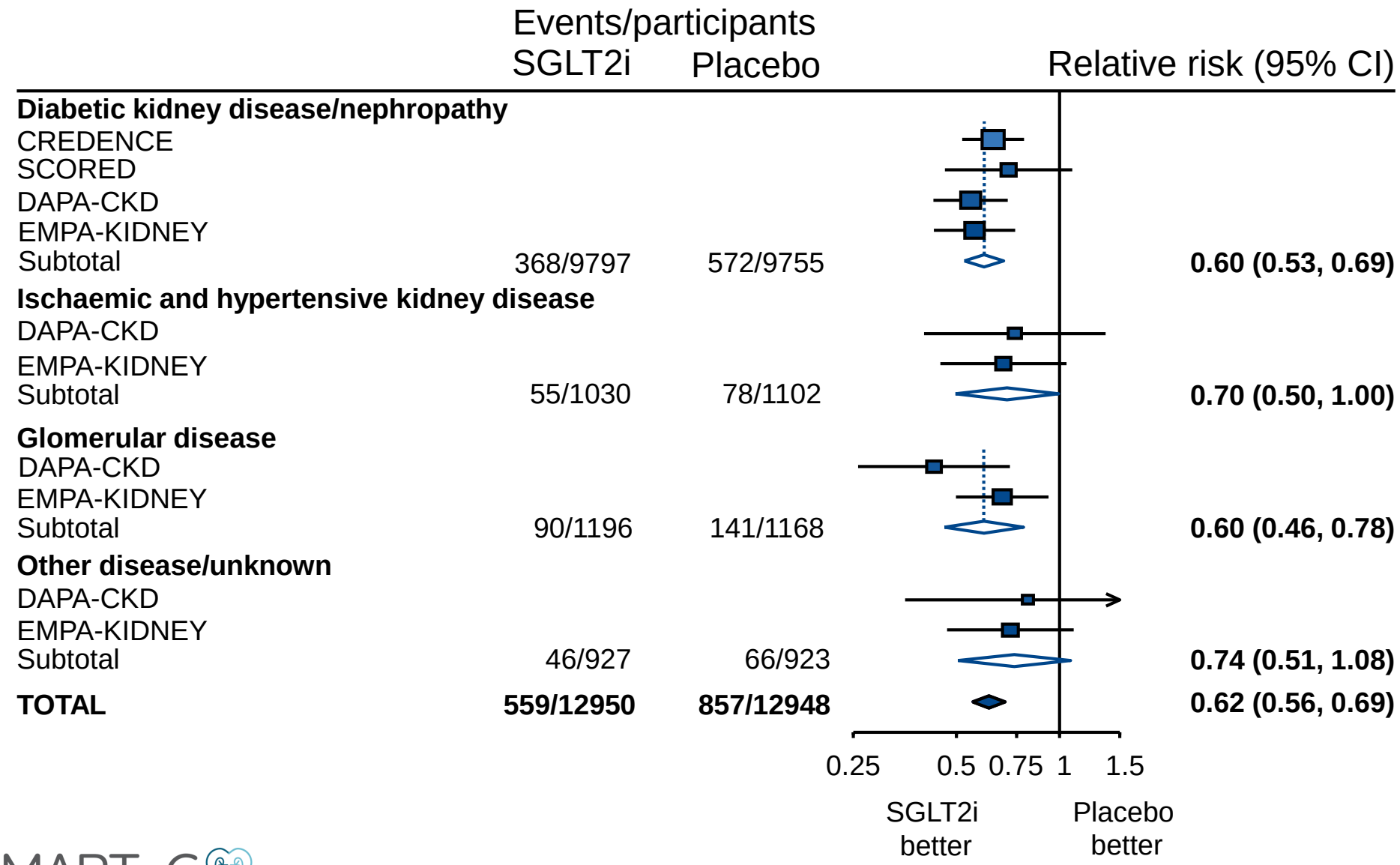


Kidney disease progression



Heterogeneity by diabetes status: p=0.31

Kidney disease progression: by DIAGNOSIS



Heterogeneity across groups of primary kidney disease: p=0.67

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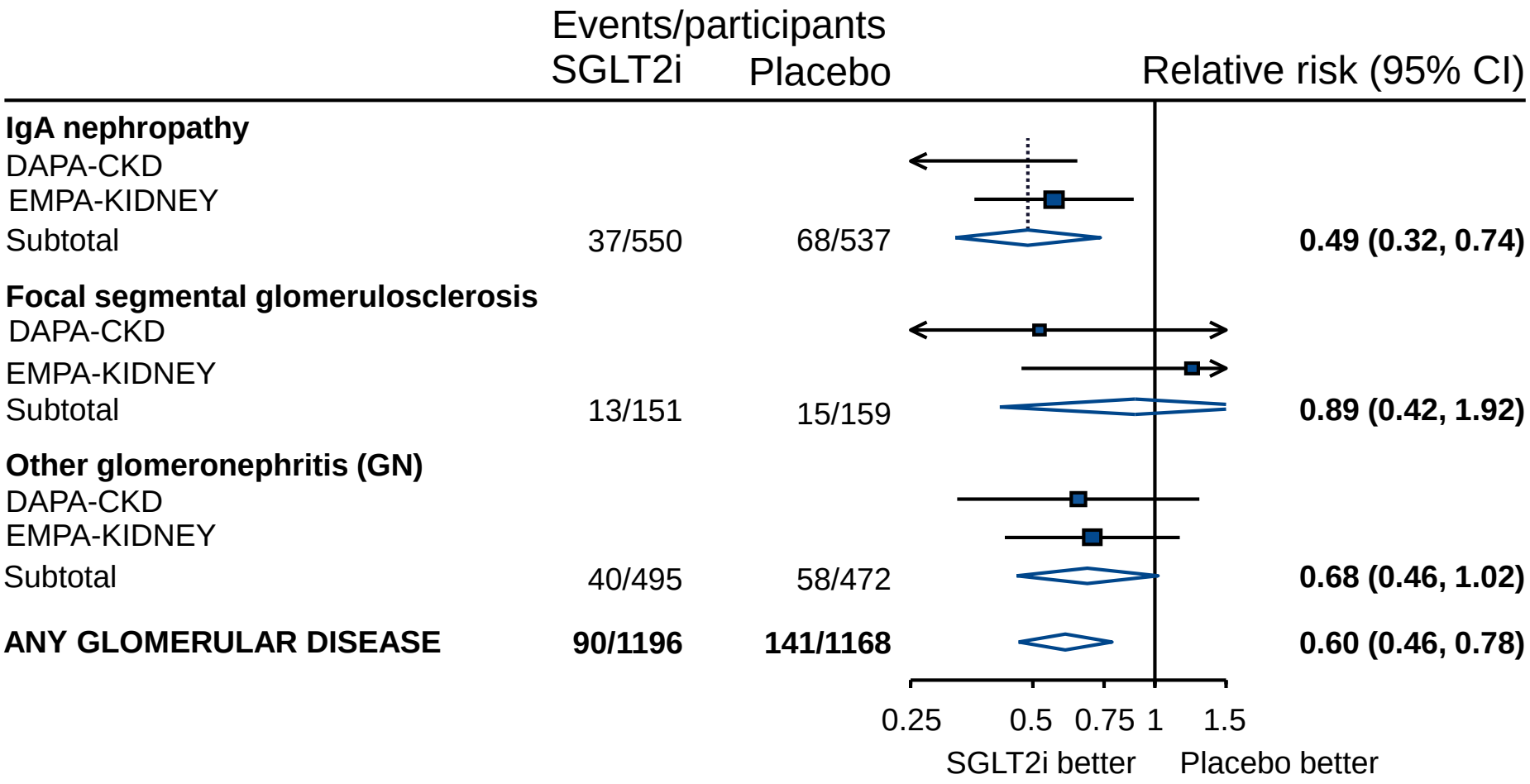
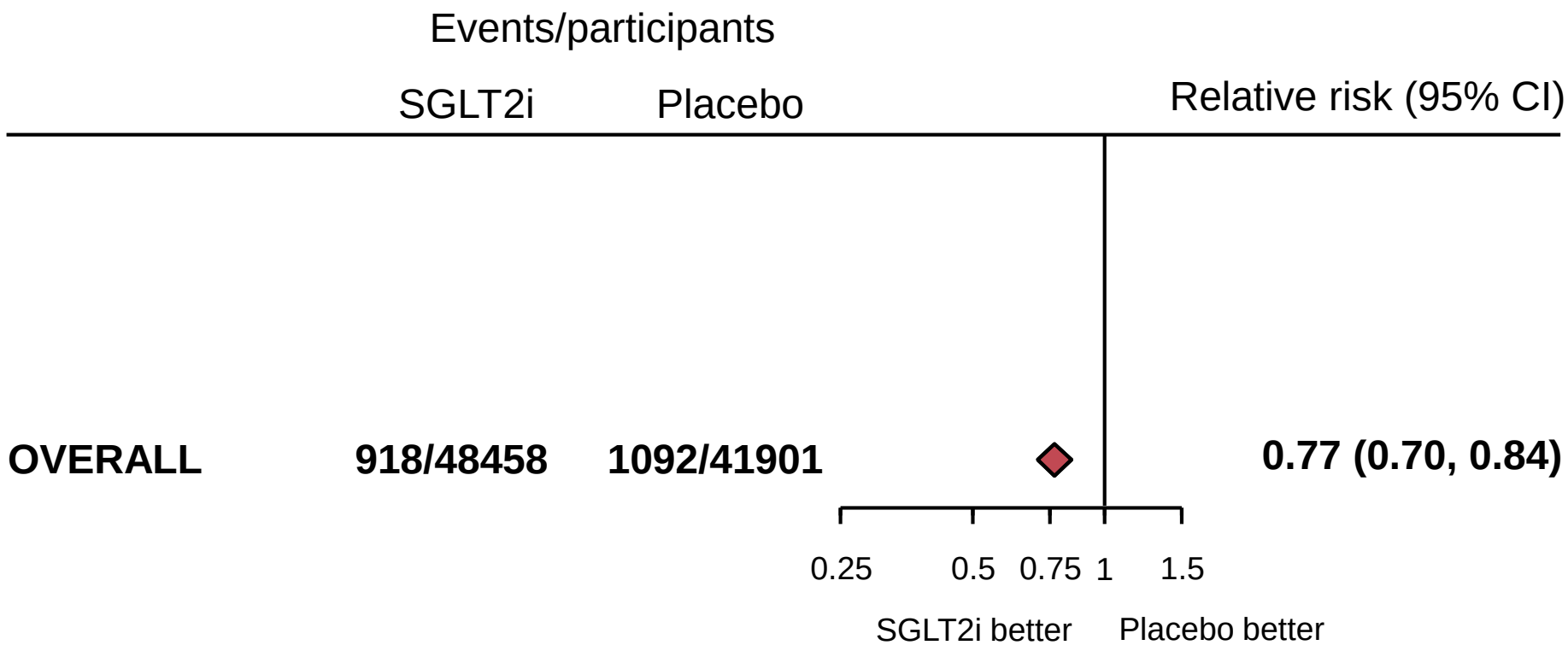
Kidney disease progression: by GN

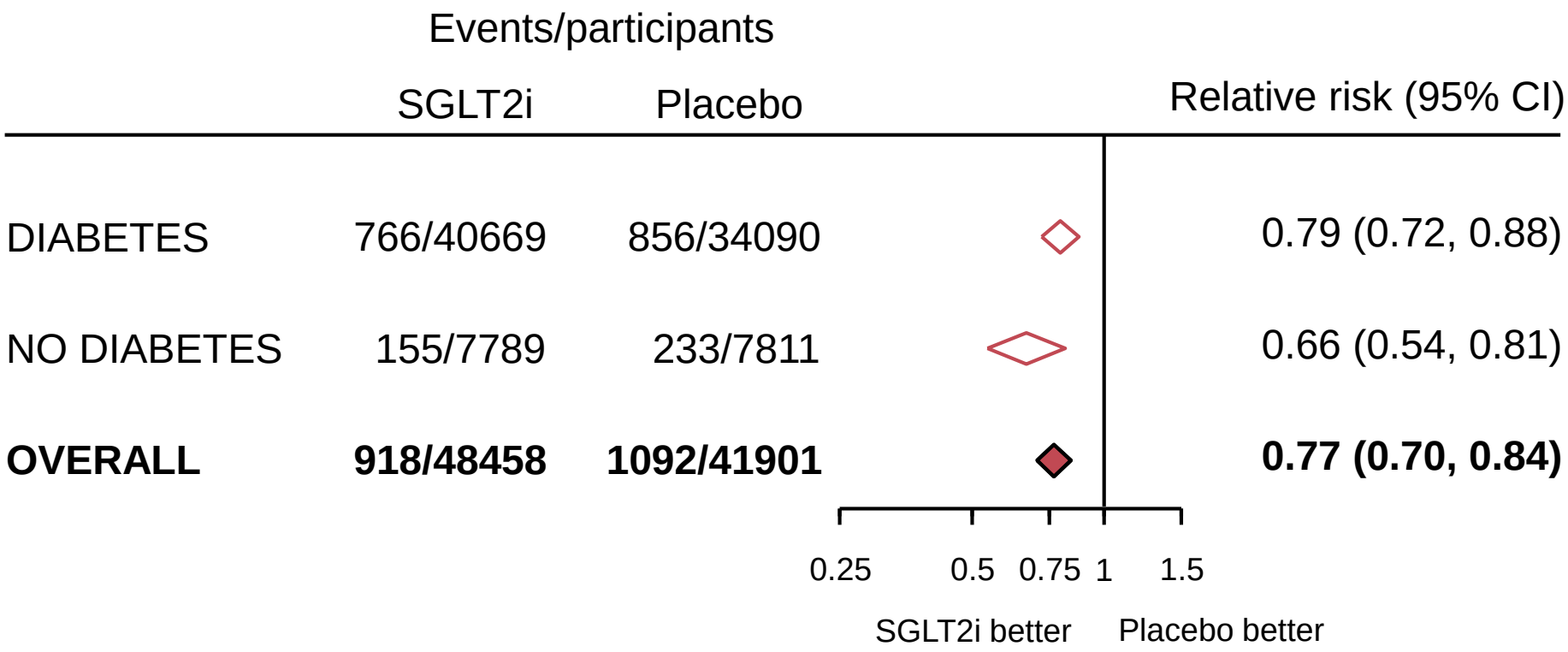


Heterogeneity across three subtypes of glomerular disease: p=0.30

Acute kidney injury

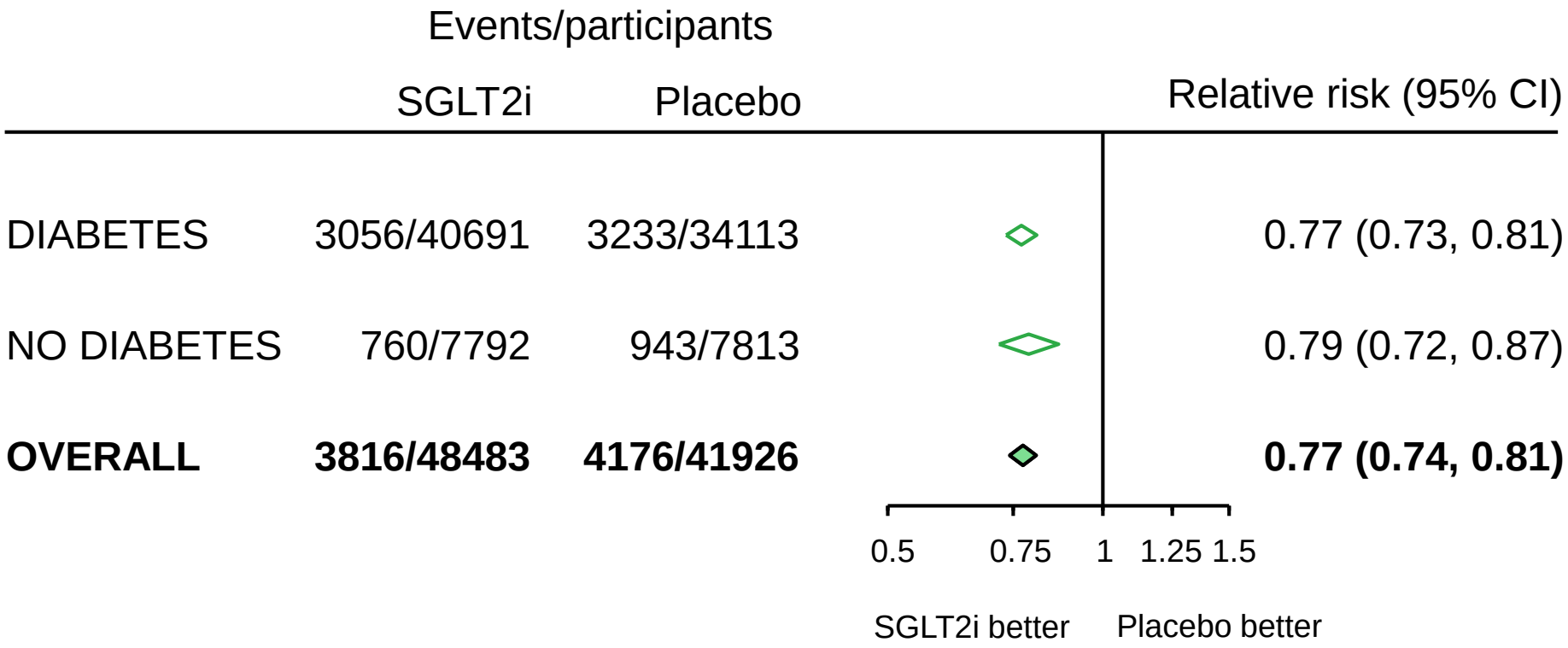


Acute kidney injury



Heterogeneity by diabetes status: p=0.12

CV death or hospitalisation for heart failure



Heterogeneity by diabetes status: p=0.67

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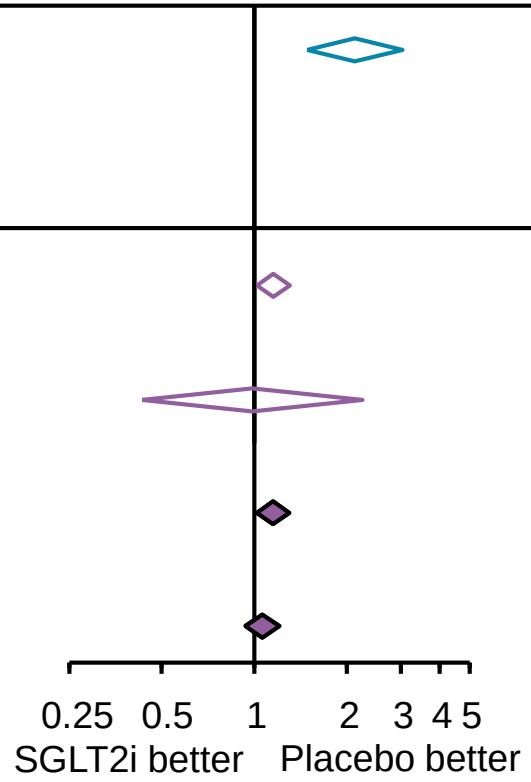
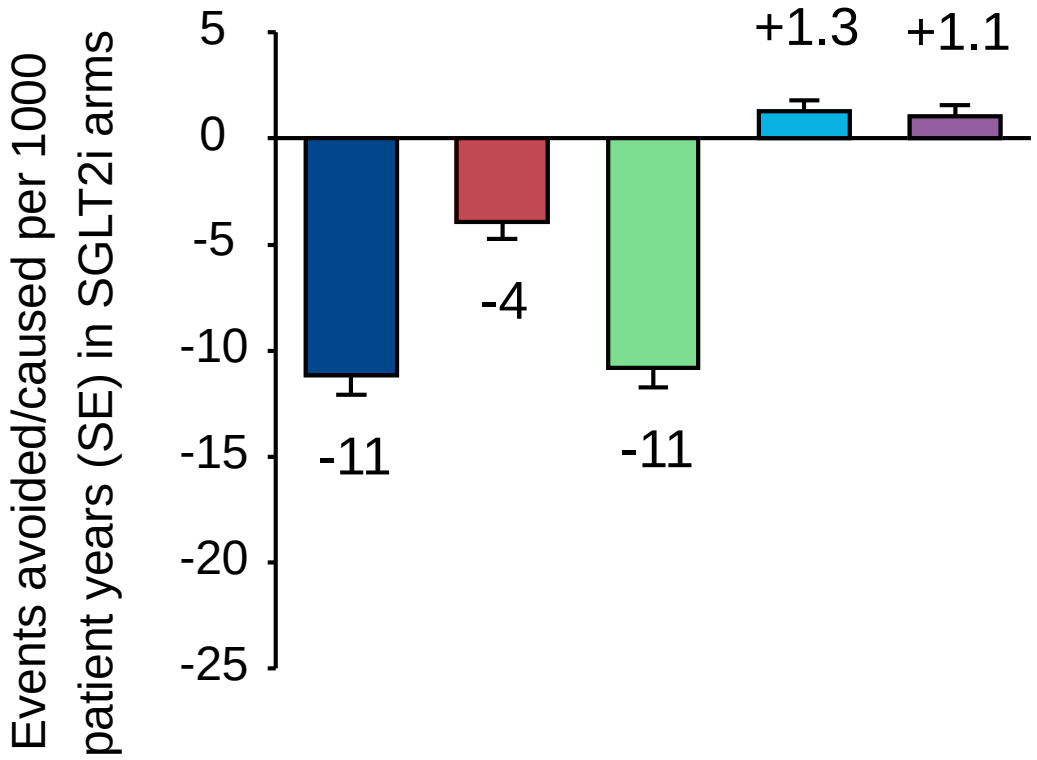
KETOACIDOSIS & AMPUTATION

		Events/participants SGLT2i	Placebo	Relative risk (95% CI)
KETOACIDOSIS	DIABETES	120/40666	47/34085	2.12 (1.49, 3.04)
	NO DIABETES	1/7788	0/7807	
LOWER LIMB AMPUTATION	DIABETES	680/40661	460/34082	1.15 (1.02, 1.30)
	NO DIABETES	12/7788	13/7807	0.98 (0.43, 2.25)
	OVERALL	**692/48449**	**473/41889**	**1.15 (1.02, 1.30)**
	OVERALL Excl. CANVAS	**552/42659**	**426/37545**	**1.06 (0.93, 1.21)**



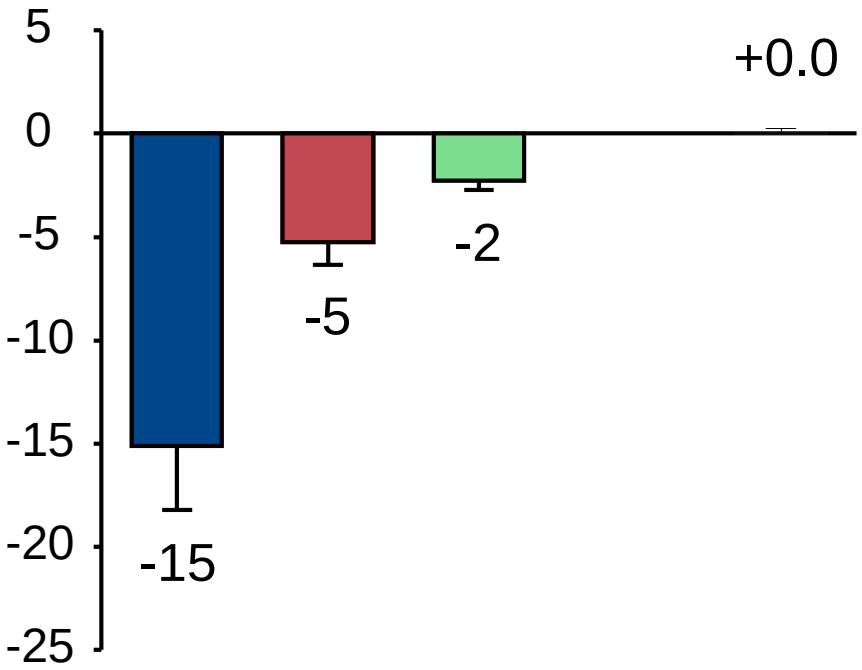
Predicted absolute effects per 1000 pt years

CKD with diabetes

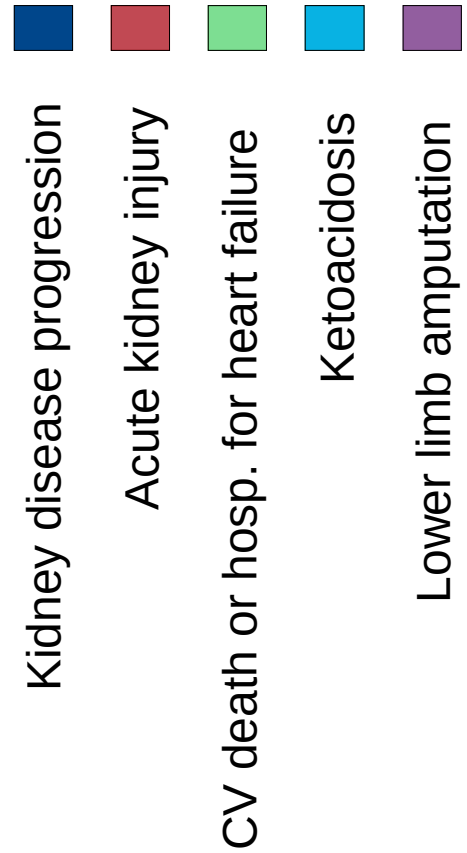


Mean eGFR: 46

CKD without diabetes



Mean eGFR: 40



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Conclusions

- In the studied populations, SGLT2 inhibitors safely reduce risk of kidney disease progression & AKI irrespective of diabetes status
- These relative benefits do not appear to be modified by primary kidney diagnosis
- Absolute benefits exceed harm in patients with CKD

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Thank you to all the trial participants and collaborators

Full details will be published on Sunday 6th November:

THE LANCET

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