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Determinants of the effects of SGLT2i on progression of CKD: Further results from the EMPA-KIDNEY trial



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On behalf of the EMPA-KIDNEY collaborative group



EMPA-KIDNEY

The study of heart and kidney protection with empagliflozin

SC-US-75881



MRC Population Health Research Unit





Disclosures

- ❧ 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
- ❧ Other financial support from:
 - ❖ Eli Lilly & the UK Medical Research Council (MRC)
 - ❖ Novo-Nordisk for the ASCEND-PLUS trial
 - ❖ Follow a long-standing departmental policy to decline honoraria

Introduction

- ✧ In EMPA-KIDNEY, the effects of empagliflozin on annual rate of change in eGFR appear to be modified by the key subgroups of baseline diabetes status, eGFR & uACR.
- ✧ However, it is not known whether some of this effect modification may be due to correlation with other key subgroups.



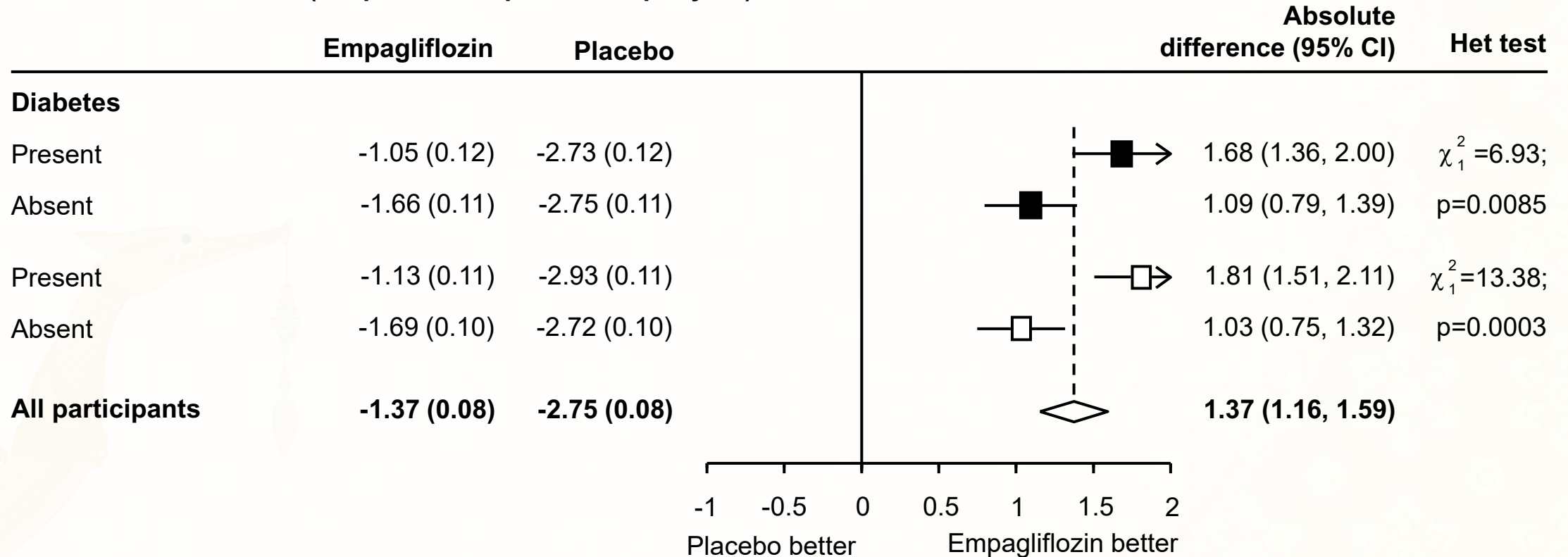
Methods

- Shared parameter models are used to estimate absolute and relative effects of empagliflozin on chronic slopes in subgroups of interest using all available eGFR values from centrally measured creatinine
- Analyses in key subgroups were conducted before and after inclusion of interactions with other key subgroups
- This allows distribution of other key subgroups to be standardised across the levels of the subgroup of interest

Absolute effects on chronic slopes – diabetes subgroup

- Before including interactions with other key subgroups
- After including interactions with other key subgroups

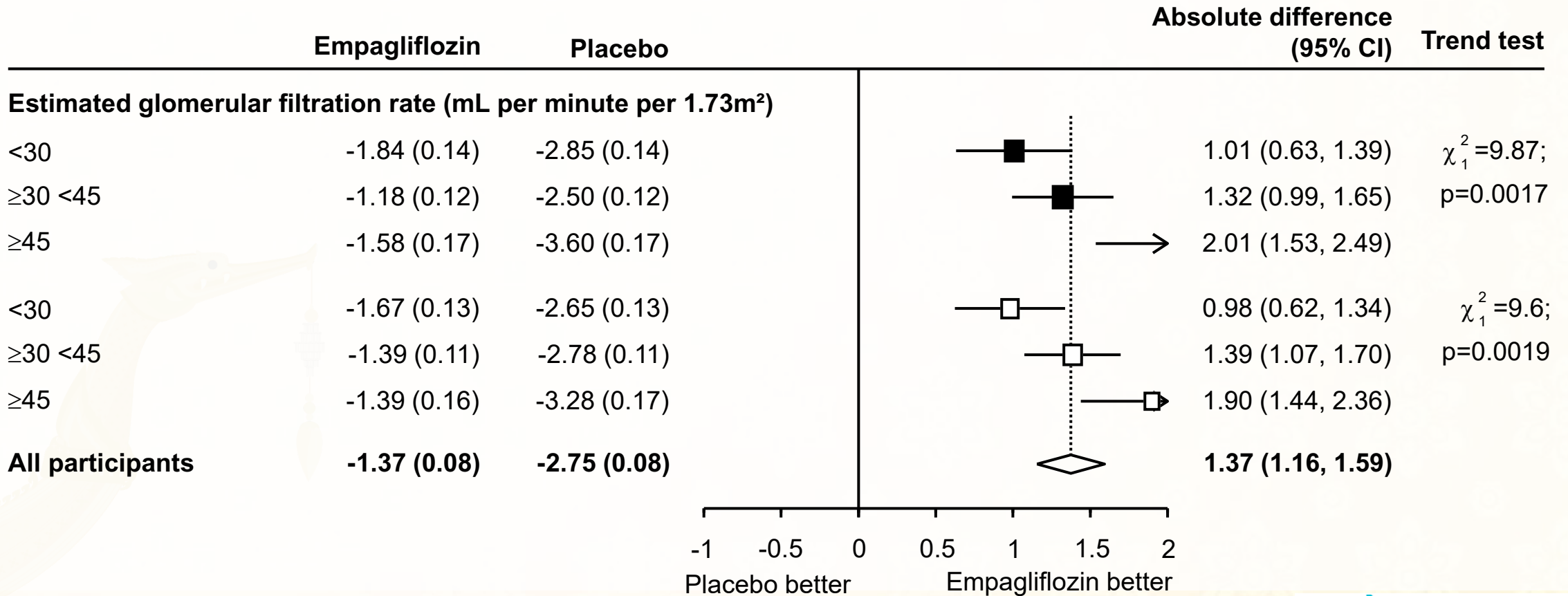
Mean/modelled slope
 (mL per minute per 1.73m² per year)



Absolute effects on chronic slopes – eGFR subgroup

Mean/modelled slope
 (mL per minute per 1.73m² per year)

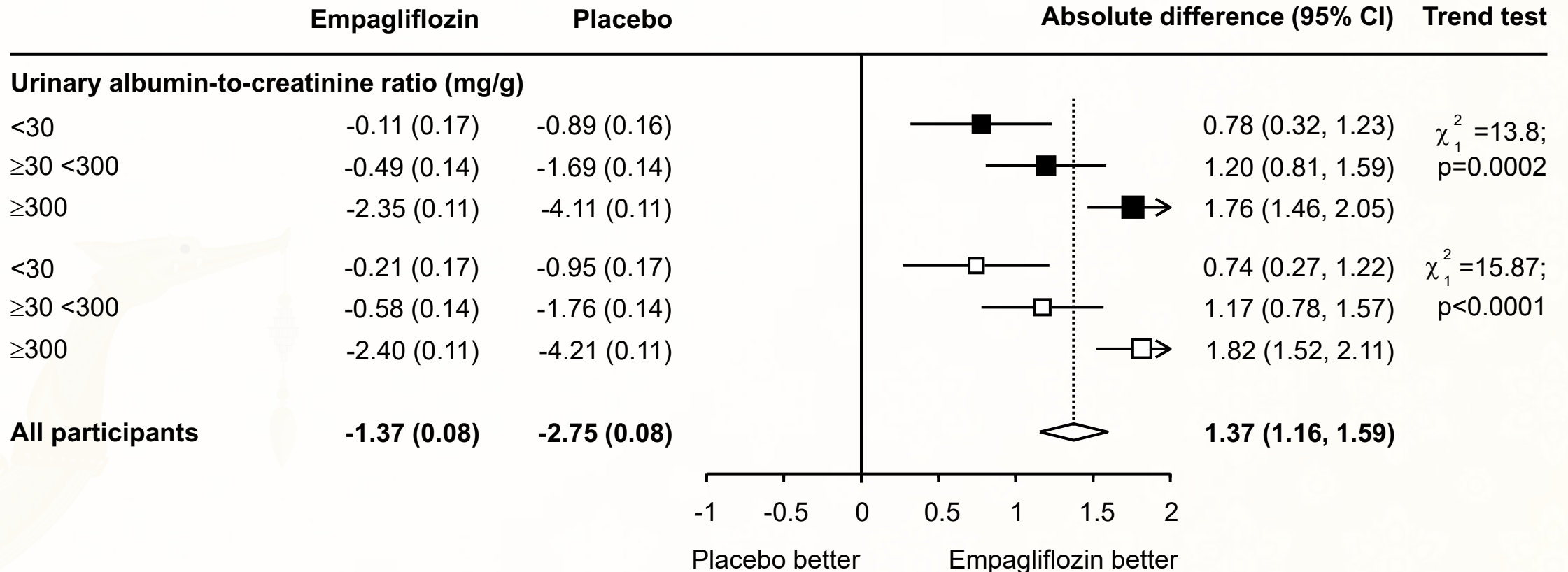
- Before including interactions with other key subgroups
- After including interactions with other key subgroups



Absolute effects on chronic slopes – uACR subgroup

Mean/modelled slope
 (mL per minute per 1.73m² per year)

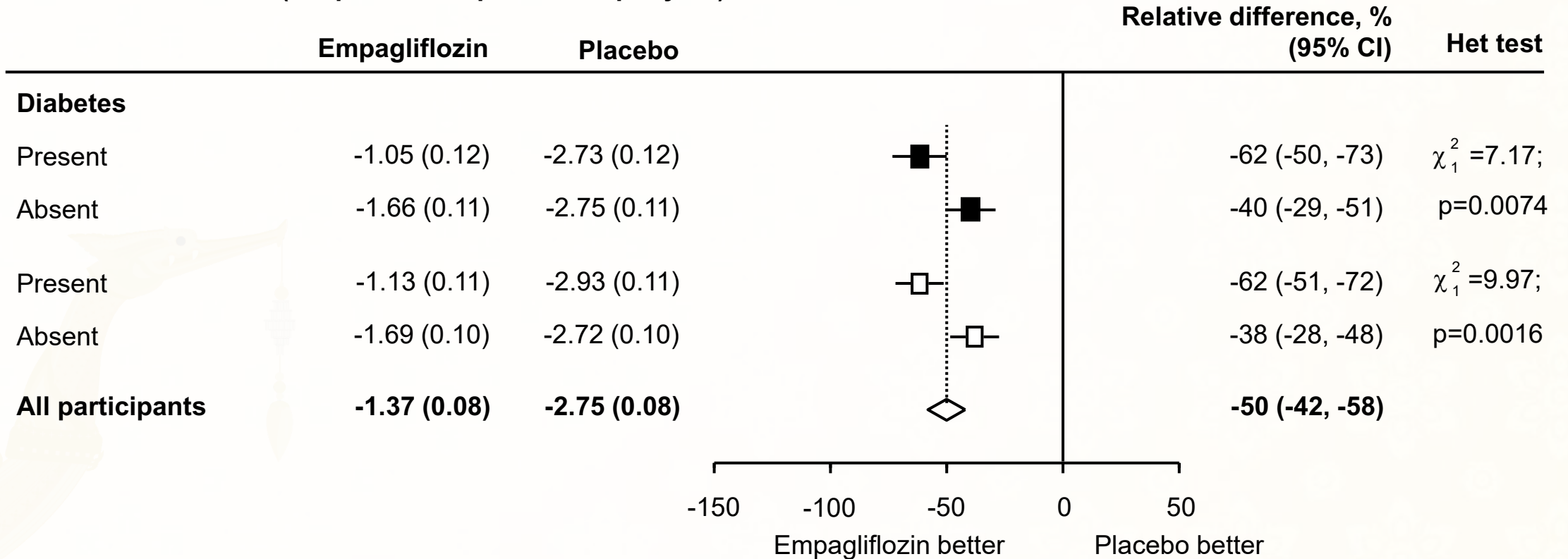
- Before including interactions with other key subgroups
- After including interactions with other key subgroups



Relative effects on chronic slopes – diabetes subgroup

Mean/modelled slope
 (mL per minute per 1.73m² per year)

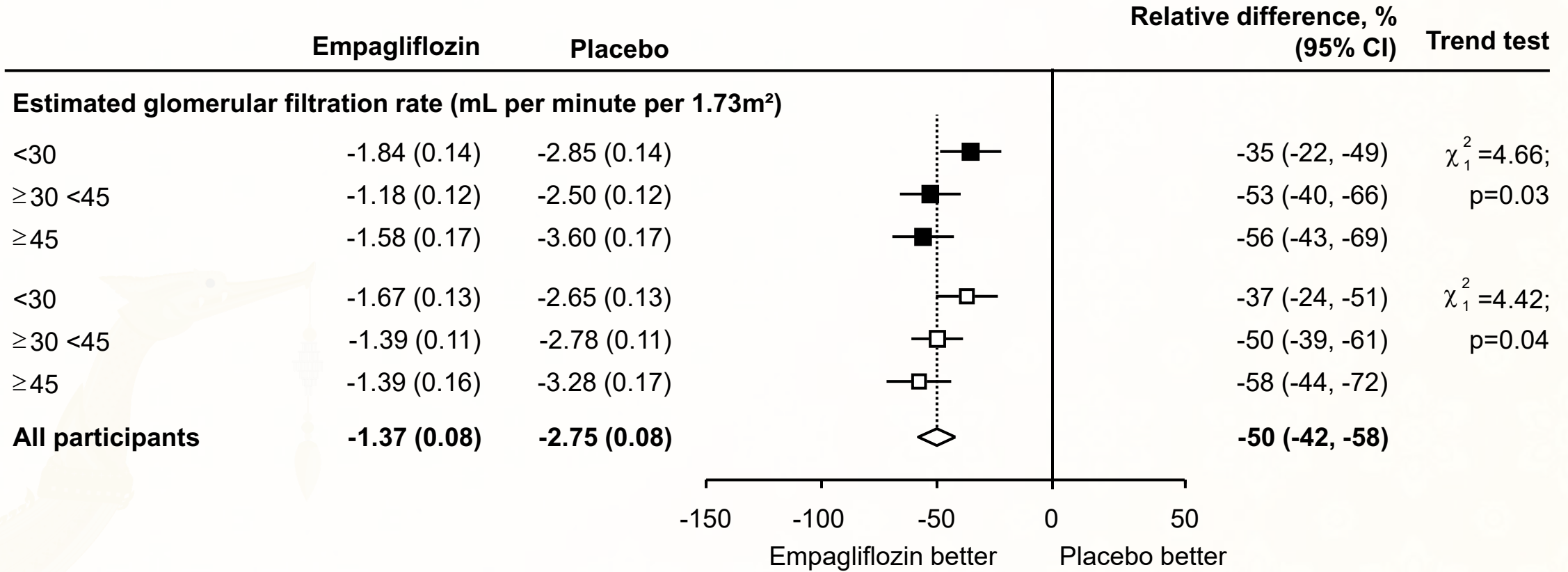
- Before including interactions with other key subgroups
- After including interactions with other key subgroups



Relative effects on chronic slopes – eGFR subgroup

- Before including interactions with other key subgroups
- After including interactions with other key subgroups

Mean/modelled slope
 (mL per minute per 1.73m² per year)

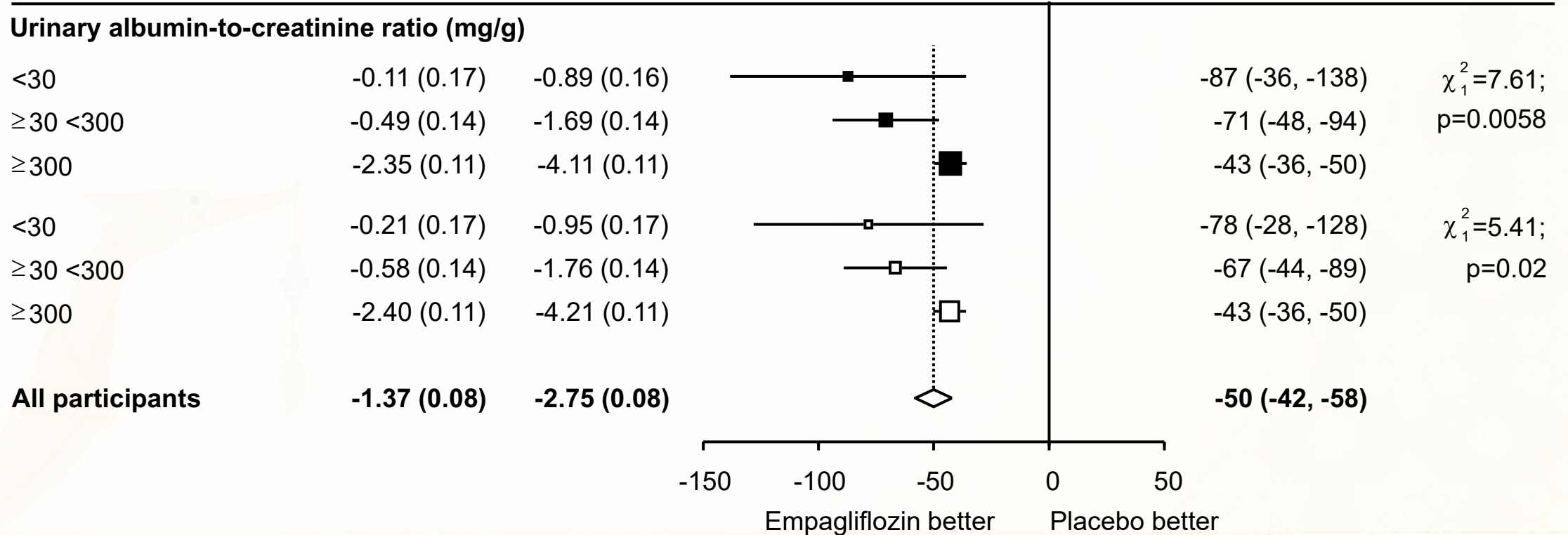


Relative effects on chronic slopes – uACR subgroup

Mean/modelled slope
 (mL per minute per 1.73m² per year)

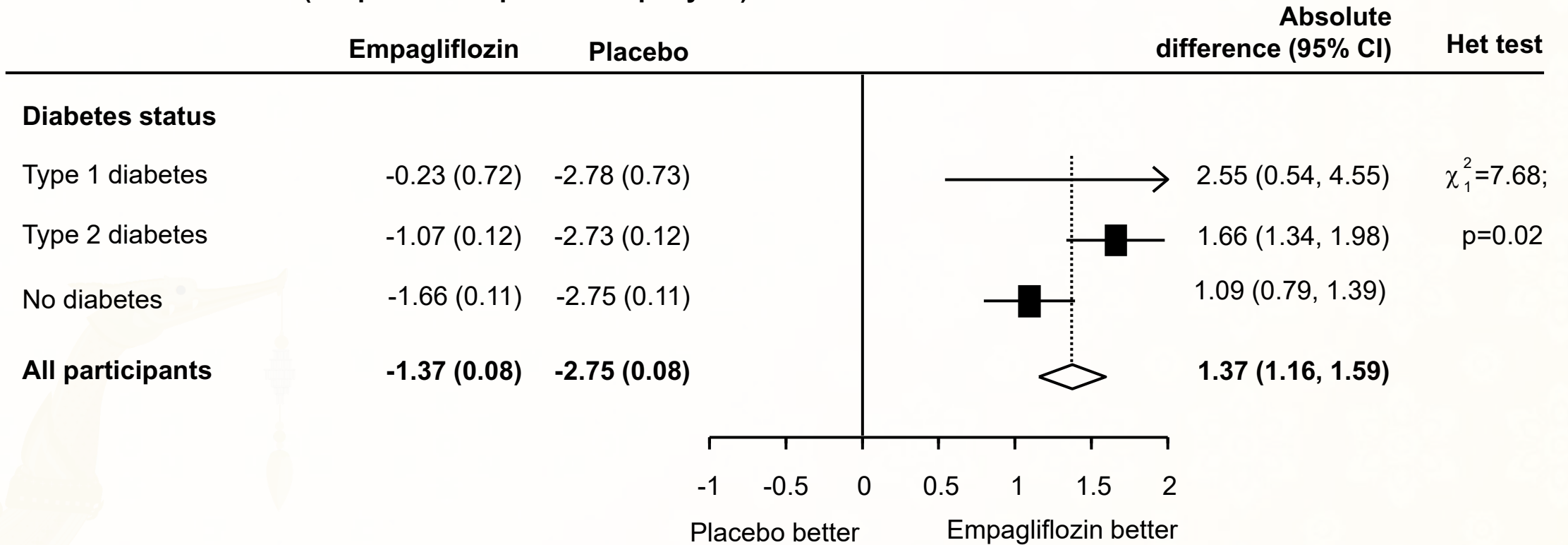
■ Before including interactions with other key subgroups
 □ After including interactions with other key subgroups

Relative difference, %
 (95% CI) Trend test



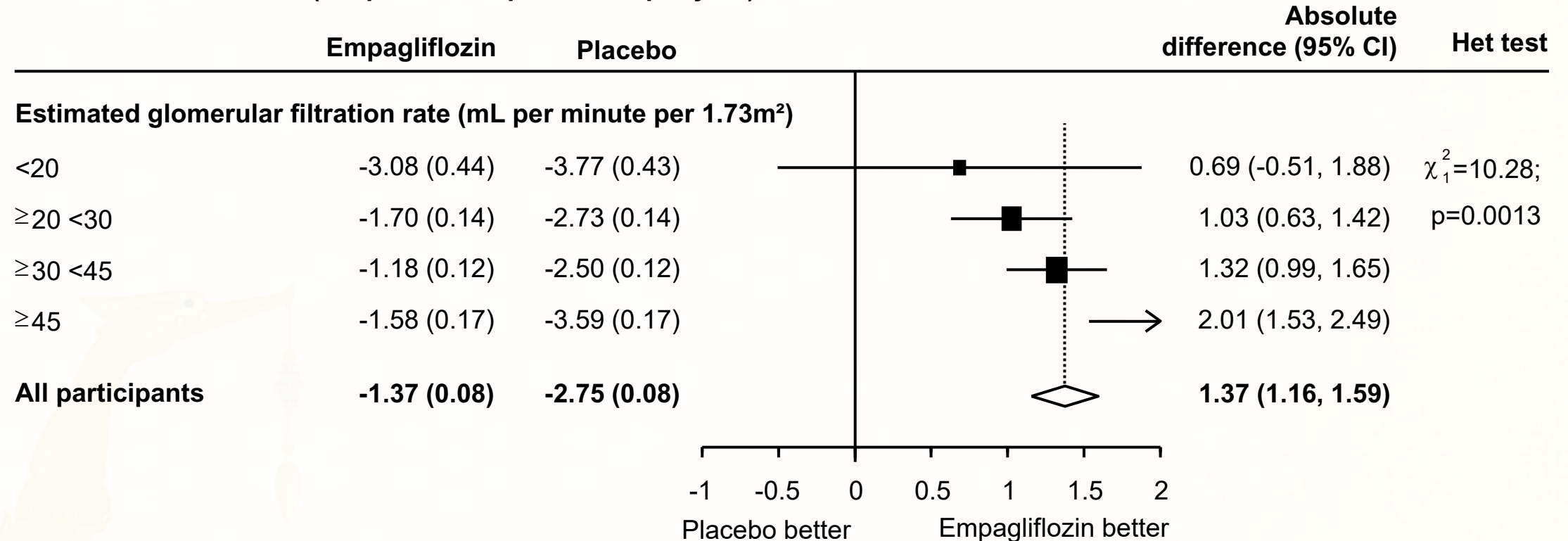
Absolute effects on chronic slopes – expanded diabetes subgroup

Mean slope
 (mL per minute per 1.73m² per year)



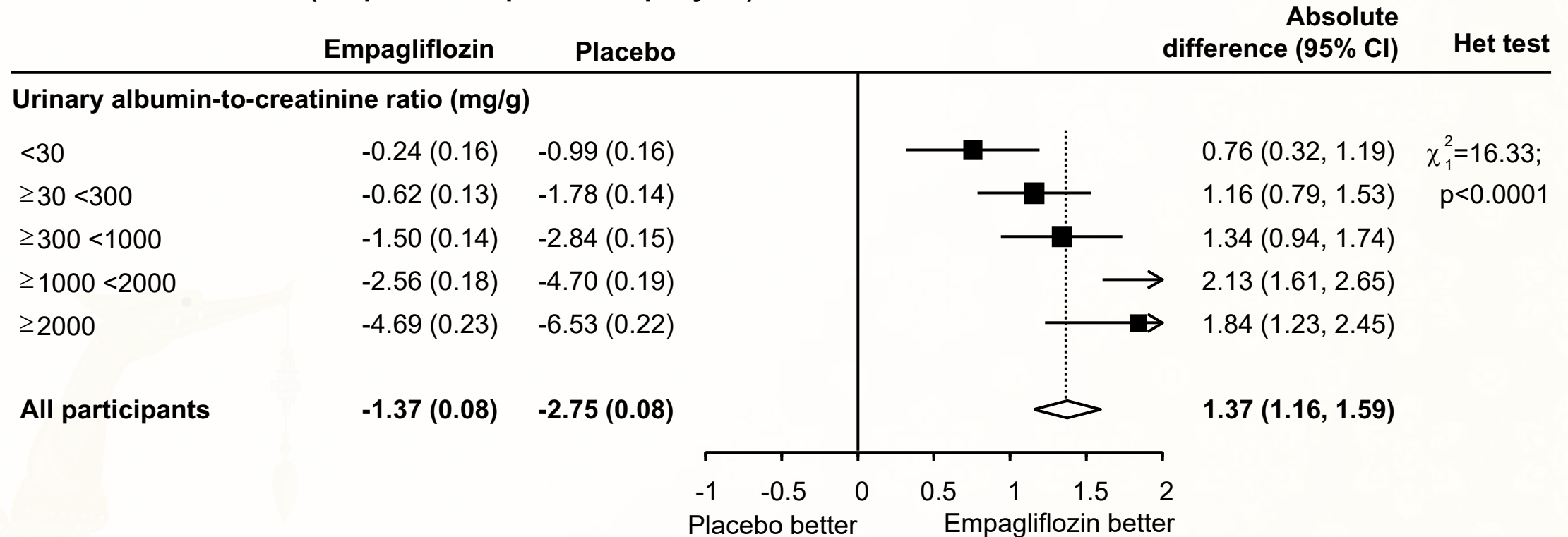
Absolute effects on chronic slopes – expanded eGFR subgroup

Mean slope
(mL per minute per 1.73m² per year)



Absolute effects on chronic slopes – expanded uACR subgroup

Mean slope
(mL per minute per 1.73m² per year)



Other subgroup analyses

No evidence of effect modification for chronic slopes for:

- ❖ Age
- ❖ Sex
- ❖ Race
- ❖ History of cardiovascular disease
- ❖ Systolic blood pressure
- ❖ Diastolic blood pressure
- ❖ Body mass index
- ❖ NT-proBNP
- ❖ Use of RAS inhibitors
- ❖ Diuretic use
- ❖ Use of lipid lowering medication
- ❖ 5 year risk of kidney failure

Sensitivity analyses

Results are not materially changed when:

- ❖ Restricted to eGFR measurements taken while patients were still on study treatment
- ❖ Using eGFR measurements based on local creatinine measurements

Conclusions

- ❧ Differences in the absolute effect of empagliflozin on chronic eGFR slope by baseline diabetes status, eGFR & uACR are not explained by baseline differences in other key baseline characteristics.
- ❧ Future work will further explore proportional effects of empagliflozin on eGFR slopes as well as seeking to further understand the relevance of the effect of uACR to the treatment effects observed.