Effects of dapagliflozin in DAPA-HF according to background glucose-lowering therapy (GLT)

Kieran Docherty

BHF Cardiovascular Research Centre, University of Glasgow

kieran.docherty@glasgow.ac.uk

Disclosures

My employer, the University of Glasgow, is paid by AstraZeneca (sponsor of DAPA-HF) for my involvement in the DAPA-HF trial.

Background

- In DAPA-HF, the SGLT2 inhibitor dapagliflozin, compared with placebo, reduced the risk of cardiovascular death or worsening heart failure, and improved symptoms in patients with heart failure and reduced ejection fraction (HFrEF), irrespective of T2D status.
- In patients with T2D, it is important to know whether the benefits of dapagliflozin were *additive* to background glucose-lowering therapy (GLT) and whether the benefit was consistent in patients who were not taking GLT, i.e. those in whom dapagliflozin was “first-line” monotherapy.
- In this *post-hoc* analysis of DAPA-HF we examined the effect of dapagliflozin according to the use/or not of background glucose lowering medications and their combinations.

McMurray JJV et al. NEJM 2019;381:1995-2008.

Methods

- The primary composite outcome was the composite of an episode of worsening HF (either an unplanned hospitalization or an urgent visit resulting in intravenous therapy for HF) or cardiovascular (CV) death, whichever occurred first.
- We compared the effect of dapagliflozin with placebo in subgroups of patients treated with GLT on the primary outcome and the individual components of CV death, HF hospitalisation, all-cause mortality and the composite endpoint of total (including recurrent) HF hospitalisations and CV death.
- Subgroups were limited to those with >200 individuals to minimize the likelihood of a Type 1 error.

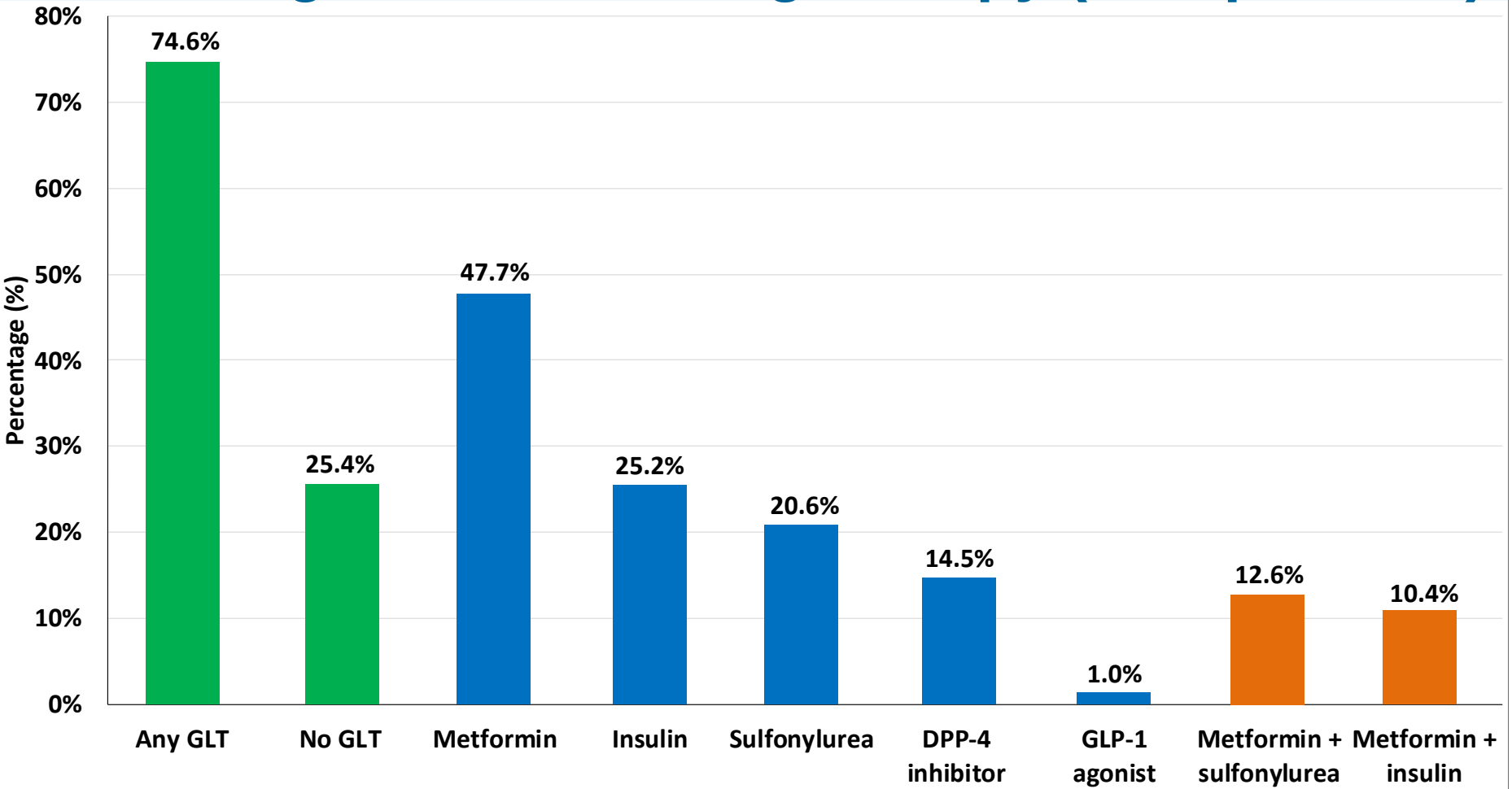
Methods

- The study population (n=2139) consisted of those with a documented history of T2D (n=1983) and those with undiagnosed T2D at baseline (n=156).
- The yes/no groups analysed were: use of any GLT, metformin, sulfonylurea, DPP-4 inhibitor and insulin. We also examined the two most frequent combinations of GLT: metformin + sulfonylurea and metformin + insulin.
- The effect of dapagliflozin compared to placebo was examined using Cox proportional-hazards models.
- Modification of treatment effect was analysed with an interaction term between the subgroup of interest and randomised treatment.

Key baseline characteristics (T2D patients)

Characteristic	No GLT (n=543)	GLT (n=1596)
Mean age (yr)	67	66
Male (%)	76	78
NYHA class II/III/IV (%)	58/40/2	66/34/1
Mean LVEF (%)	31	31
Median NT pro BNP (pg/ml)	1585	1445
Mean systolic BP (mmHg)	121	124
Ischaemic aetiology (%)	55	57
Mean eGFR (ml/min/1.73m^2)	64	63
HbA1c (%)	6.9	7.5
Median time from T2D diagnosis (yr)	0.5	8.6
BMI (kg/m$^{2)}$	28.4	29.6

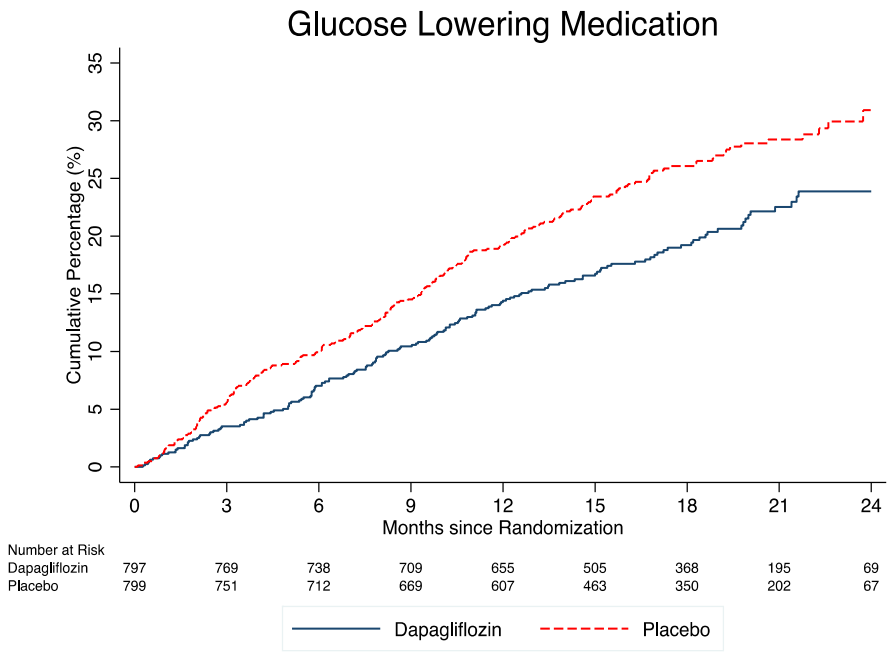
Baseline glucose-lowering therapy (T2D patients)



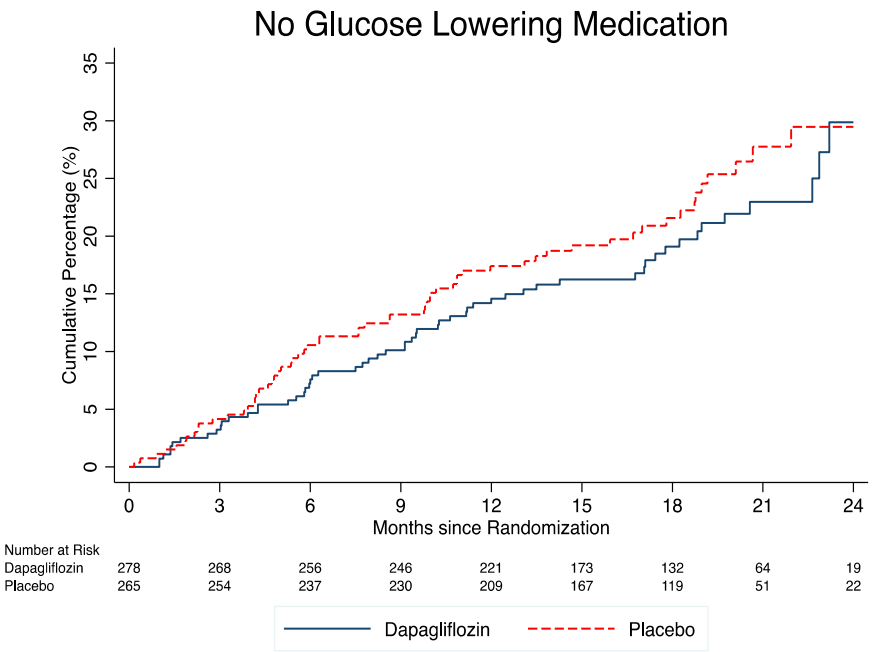
Treatment effect by background GLT (T2D patients)

Primary composite endpoint

HR 0.72 (95%CI 0.58-0.88)



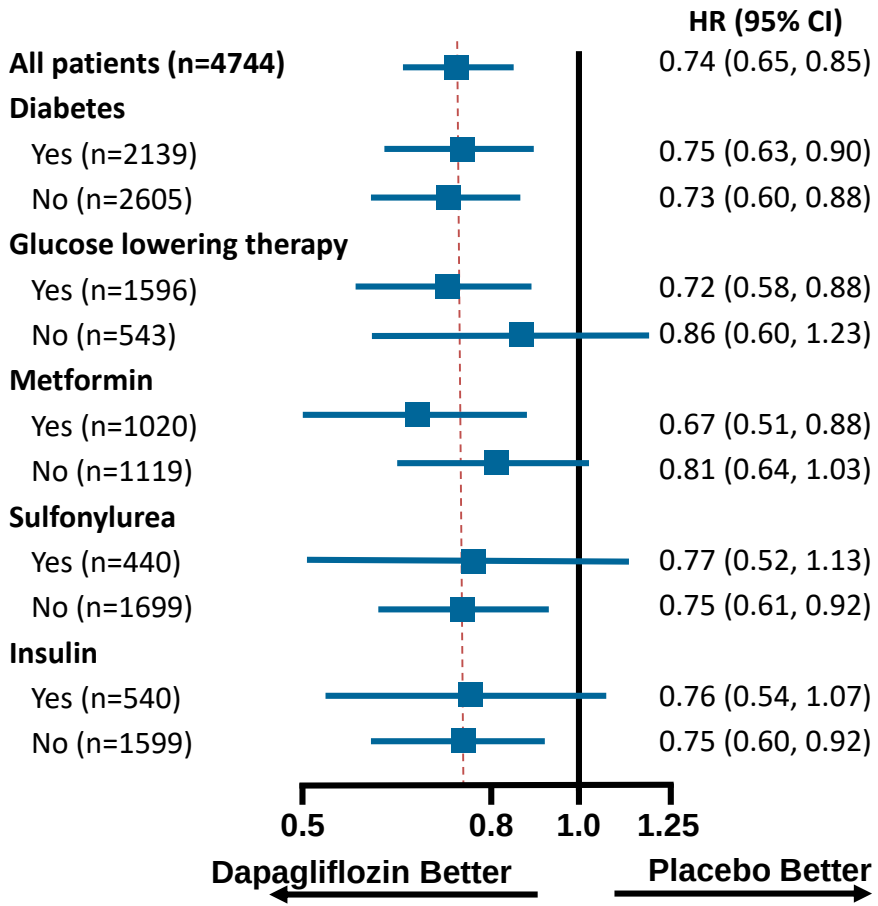
HR 0.86 (95%CI 0.60-1.23)

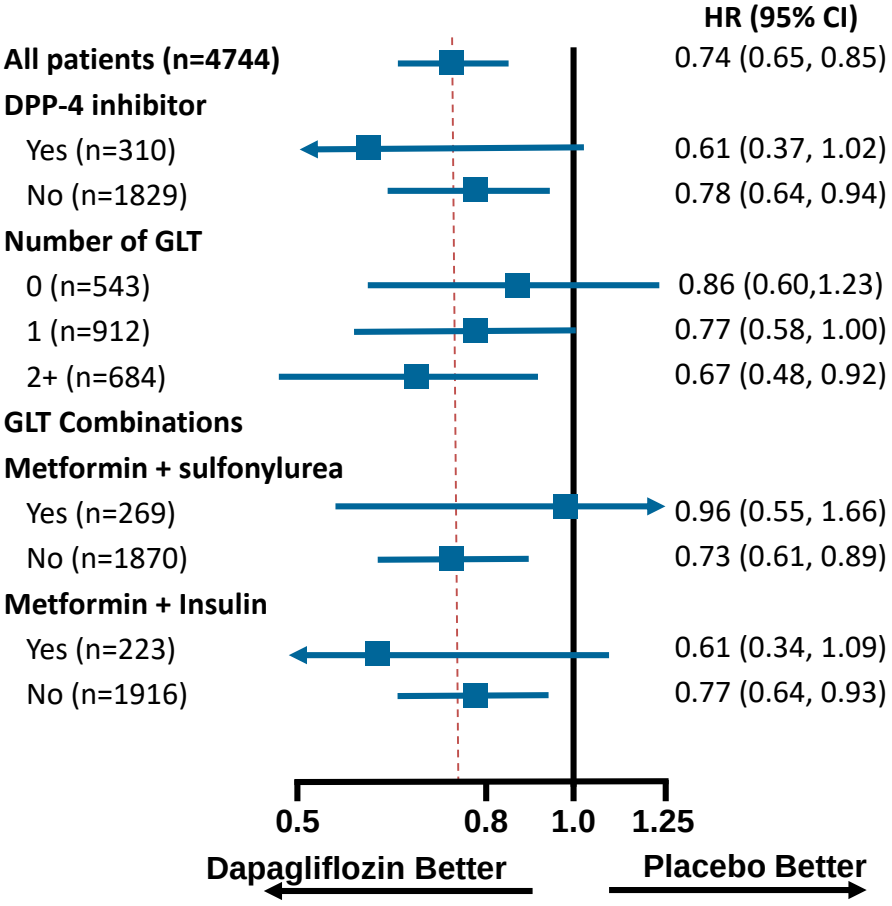


Interaction p value = 0.39

Treatment effect by background GLT

Primary composite endpoint





Summary and conclusions

- In patients with HFrEF, dapagliflozin reduced the risk of worsening heart failure events and cardiovascular death, compared with placebo, irrespective of T2D status.
- In this *post-hoc* analysis, we found a consistent benefit of dapagliflozin, over placebo, regardless of the use, or not, of GLT in patients with T2D and the type of GLT used.
- These findings suggest that the effects of dapagliflozin are incremental and complementary to other glucose lowering therapies in patients with HFrEF and T2D.
- These data support the use of dapagliflozin as first-line monotherapy in T2D, at least in patients with HFrEF.