

DELIVER: *Baseline Characteristics and Results by Glycaemic Subgroups*

Prof. Silvio Inzucchi, MD
New Haven, CT, USA

**Is HFpEF hiding in your practice?
An expert debate on the emerging role of diabetologists**



DELIVER:

Baseline Characteristics and Results by Glycaemic Subgroups

Silvio E. Inzucchi, MD

Yale School of Medicine & Yale-New Haven Hospital

New Haven, Connecticut, USA

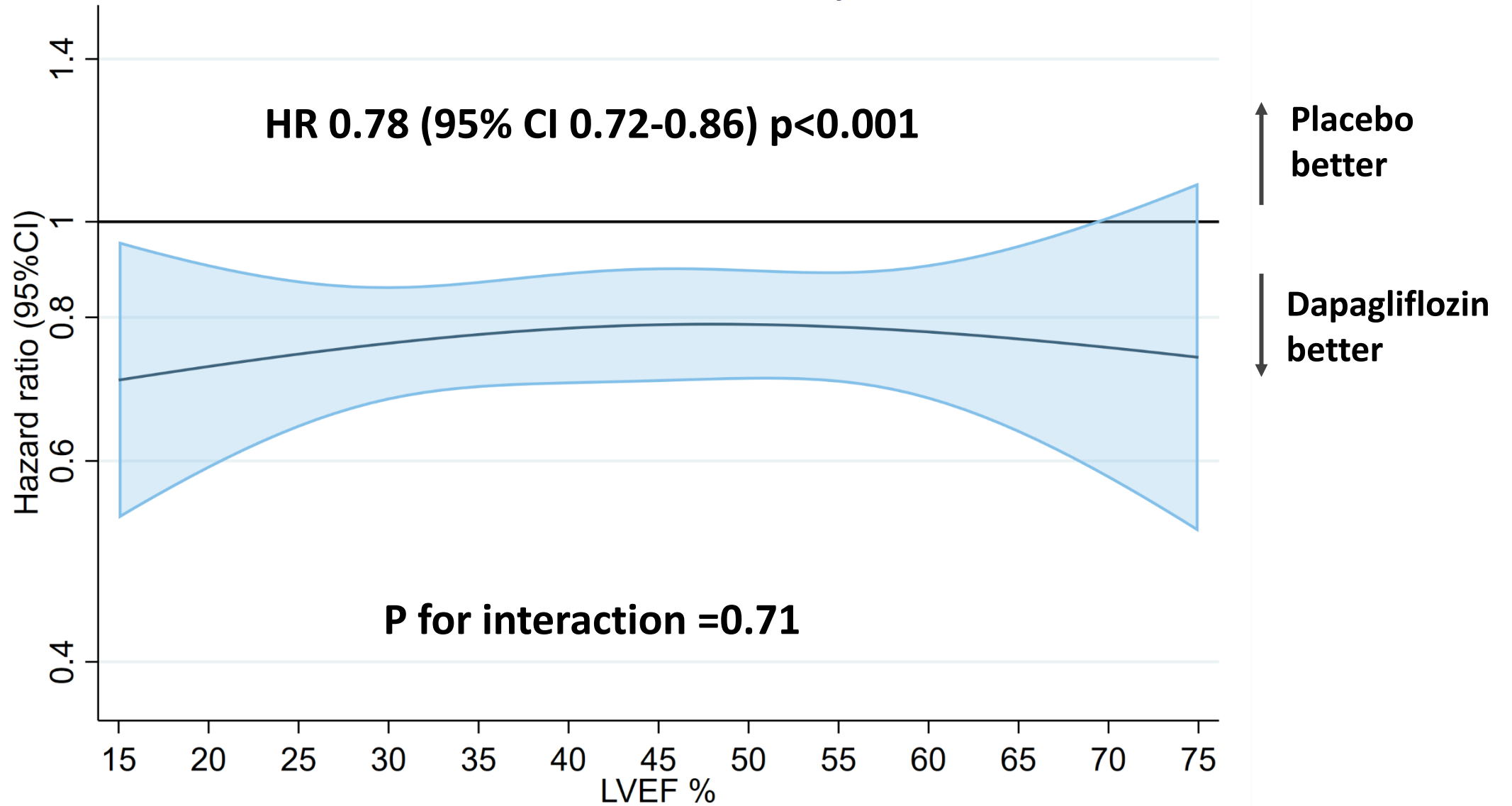
on behalf of the DELIVER Committees, Investigators, Sponsor & Participants



Disclosures

- Dr. Inzucchi has served on clinical trial committees or as a consultant to AstraZeneca, Boehringer Ingelheim, Novo Nordisk, Merck, Pfizer, Abbott, Lexicon, vTv Therapeutics and Esperion; and has delivered lectures sponsored by AstraZeneca and Boehringer Ingelheim.

DAPA-HF & DELIVER: CV death/HF hospitalisation

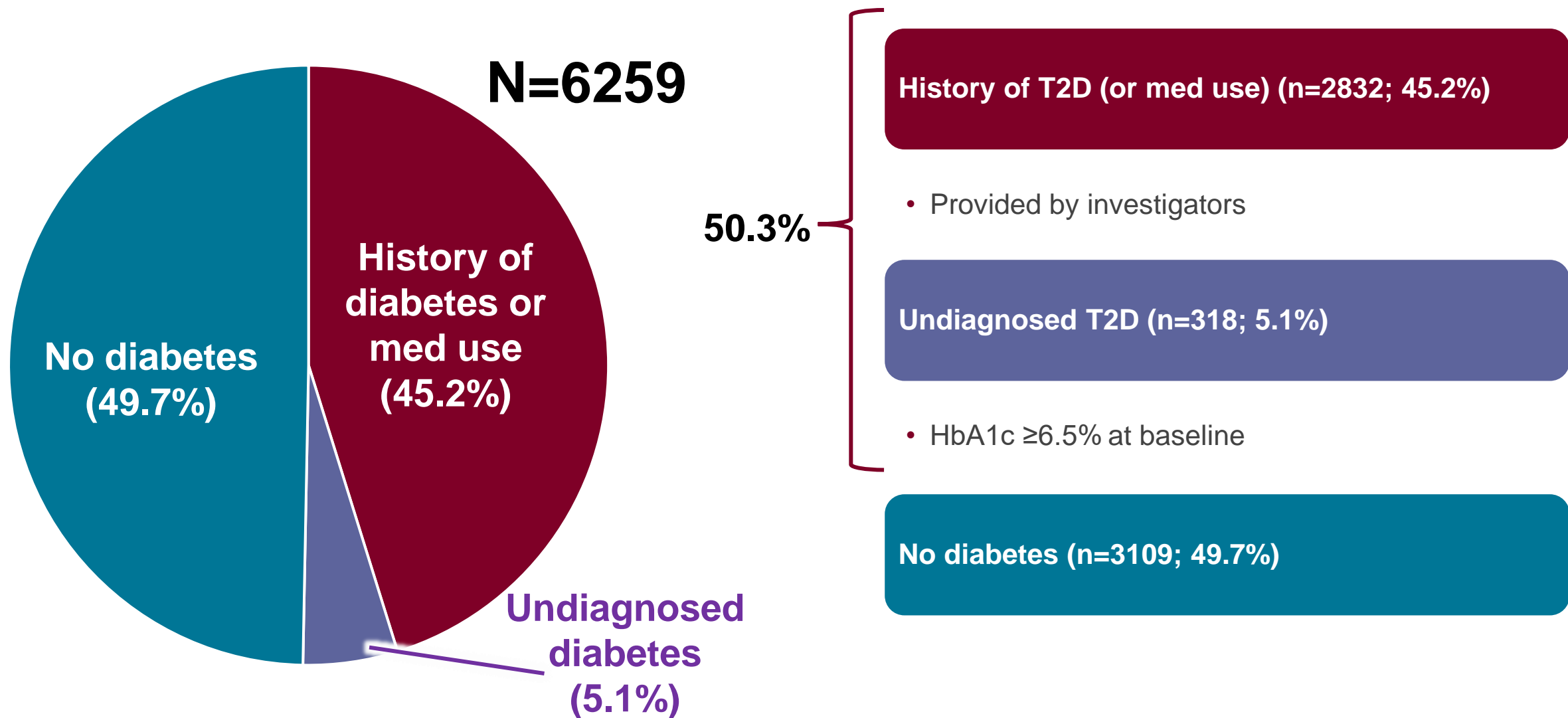


New Data: Pre-specified Analysis by Glycaemic Subgroups - Research Questions

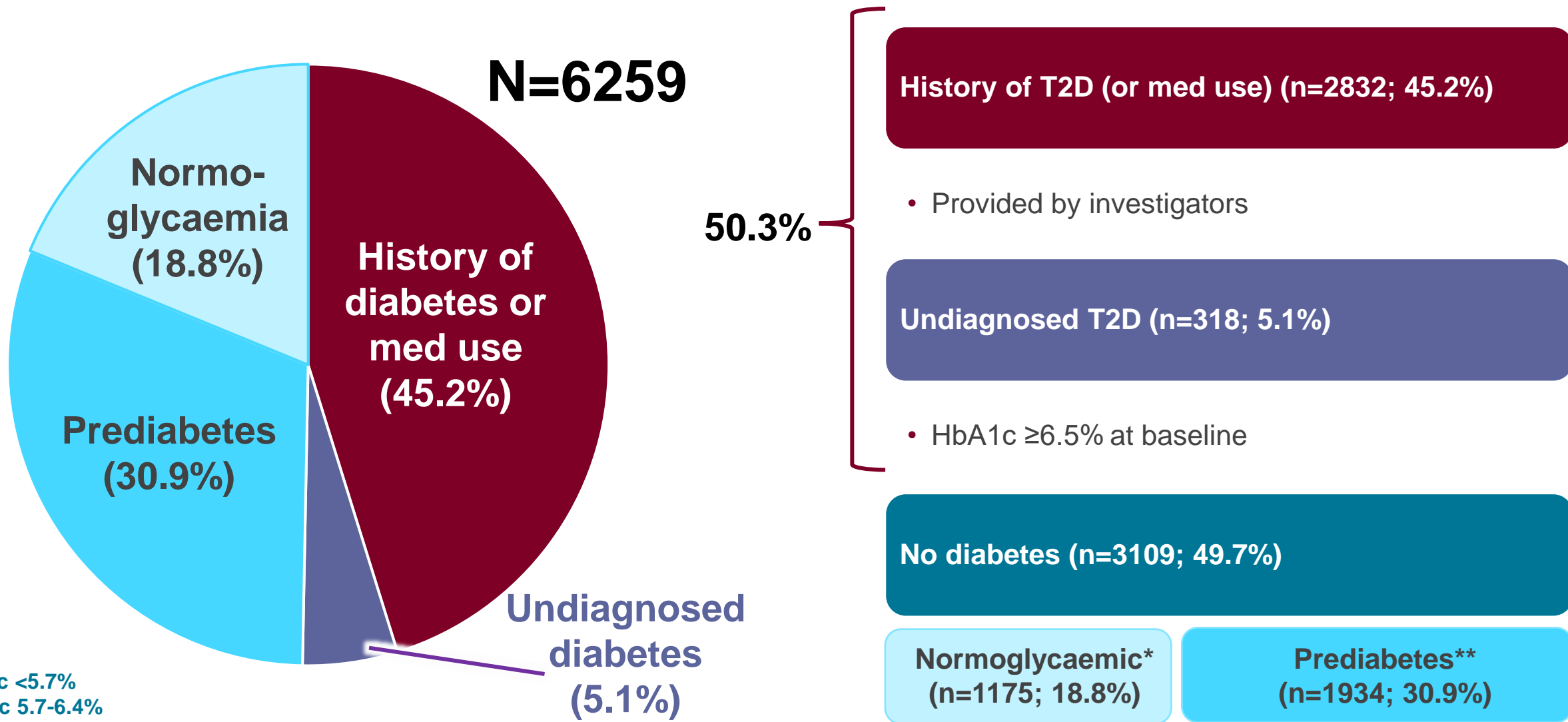


- What was the distribution of normoglycaemia vs. prediabetes vs. T2D?
- How did these individual groups behave in terms of event rates (irrespective of treatment assignment)
- What were the dapagliflozin treatment effects in each of these subgroups – did they differ?
- Any trends within these subgroups by LVEF? (*post-hoc*)
- What was the dapagliflozin treatment effect in subcategories within the T2D subgroup? (*post-hoc*)
 - By baseline diabetes duration or HbA1c
 - By baseline antihyperglycemic therapy use

Distribution of Patients by Glycaemic Status: A Typical 'HFpEF' Population



Distribution of Patients by Glycaemic Status: A Typical 'HFpEF' Population



* HbA1c <5.7%
 ** HbA1c 5.7-6.4%

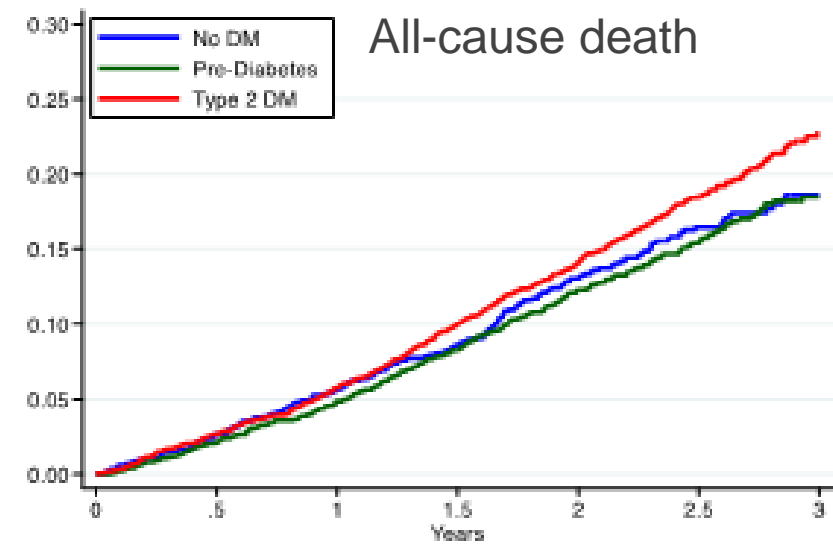
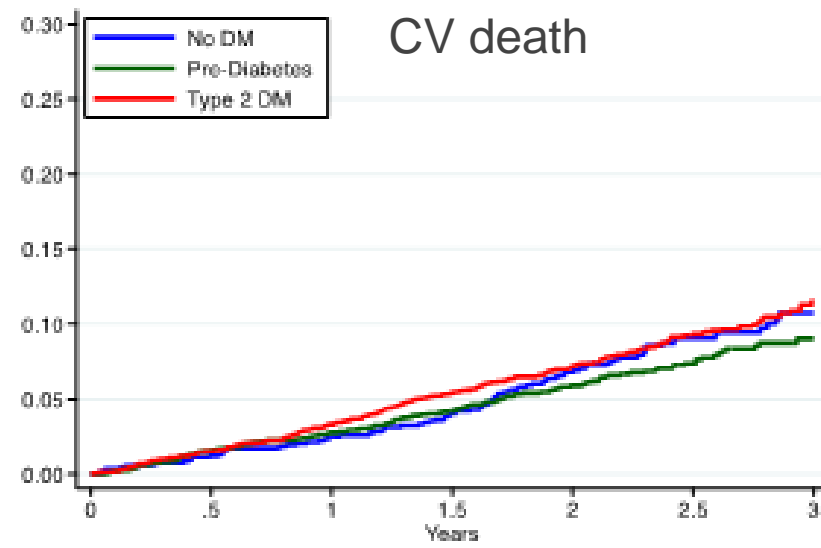
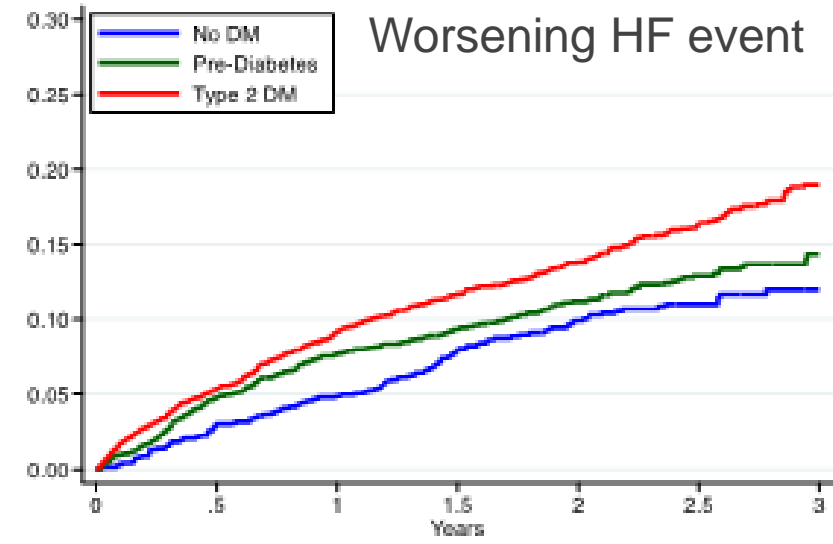
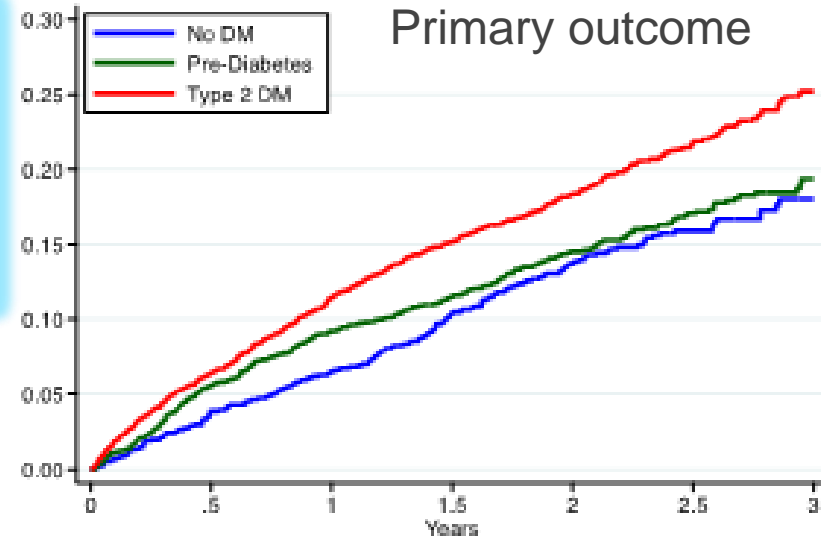
DELIVER Baseline Characteristics by Glycaemic Status



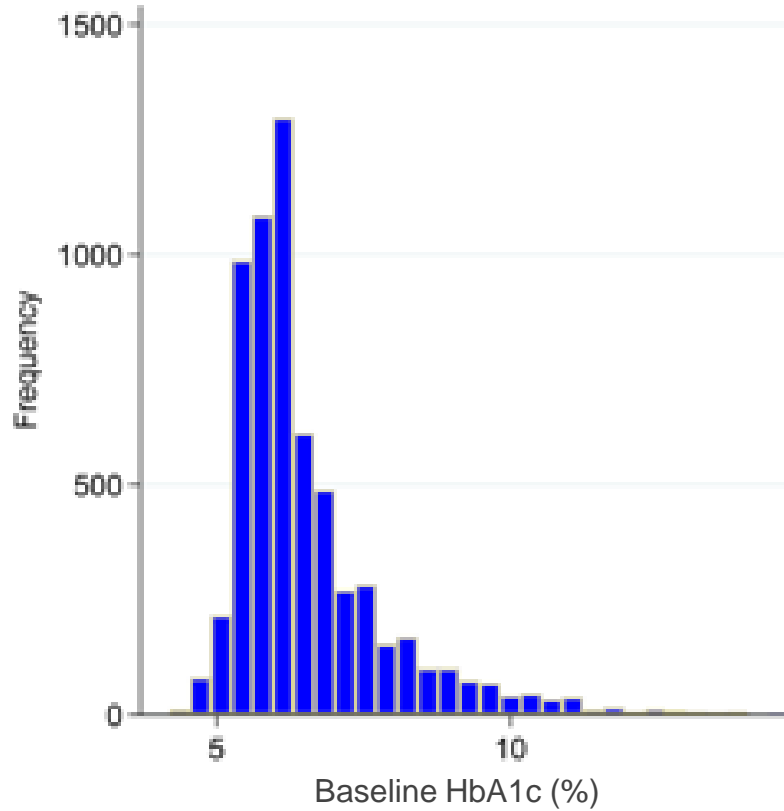
	Normoglycaemia n=1175	Prediabetes n=1934	Type 2 diabetes n=3150	p
Age (mean, SD)	71.3 ± 10.5	73.0 ± 9.5	71.0 ± 9.1	p<0.001
Men (N, %)	660 (56.2%)	1037 (53.6%)	1818 (57.7%)	p=0.017
Race: White/Asian/Black	793 (67.5%)/265 (22.6%)/29 (2.5 %)	1364 (70.5%)/422 (21.8%)/37 (1.9 %)	2278 (72.3%)/587 (18.6%)/93 (3.0%)	p<0.001
BMI	28.4 ± 5.7	29.0 ± 6.0	30.9 ± 6.2	p<0.001
History of Afib/flutter	688 (58.6%)	1198 (61.9%)	1663 (52.8%)	
History of MI	234 (19.9%)	456 (23.6%)	949 (30.1%)	p=0.006
Prior HF hosp'n	446 (38.0%)	764 (39.5%)	1327 (42.1%)	p<0.001
NYHA Class II	911 (77.5%)	1491 (77.1%)	2308 (73.3%)	
NYHA Class III	261 (22.2%)	440 (22.8%)	829 (26.3%)	p=0.002
NYHA Class IV	2 (0.2 %)	3 (0.2 %)	13 (0.4 %)	
LVEF(%)	54.3 ± 8.8	54.3 ± 8.9	54.0 ± 8.7	p=0.26
NT-proBNP (ng/L)	1012 [608, 1790]	1104 [656, 1904]	951 [606, 1673]	p<0.001
HbA1c (%)	5.4 ± 0.2	6.0 ± 0.2	7.4 ± 1.6	p<0.001
eGFR	65.4 ± 19.1	60.9 ± 18.2	59.5 ± 19.5	p<0.001

Key outcomes by Glycaemic status

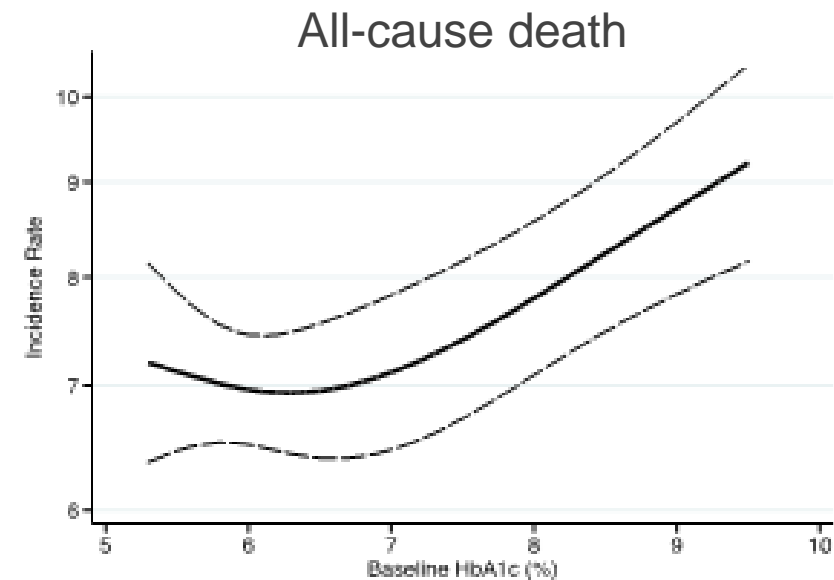
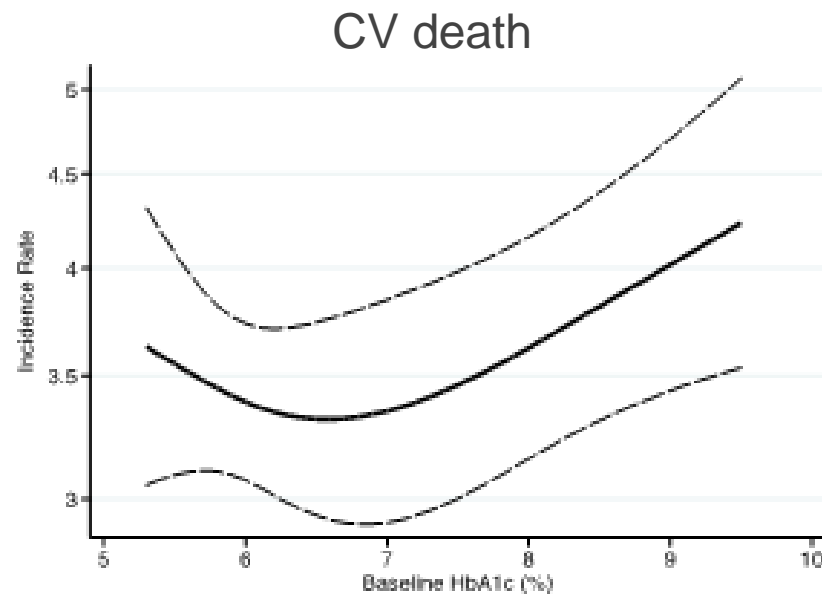
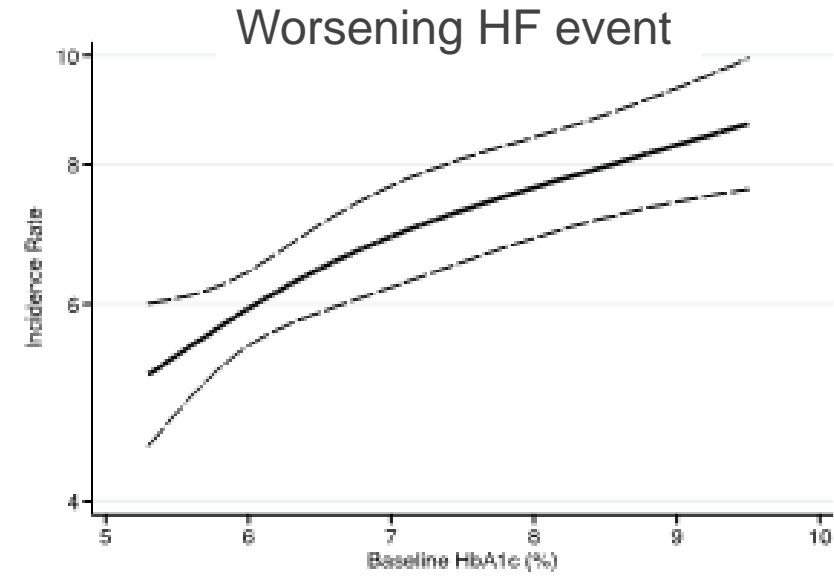
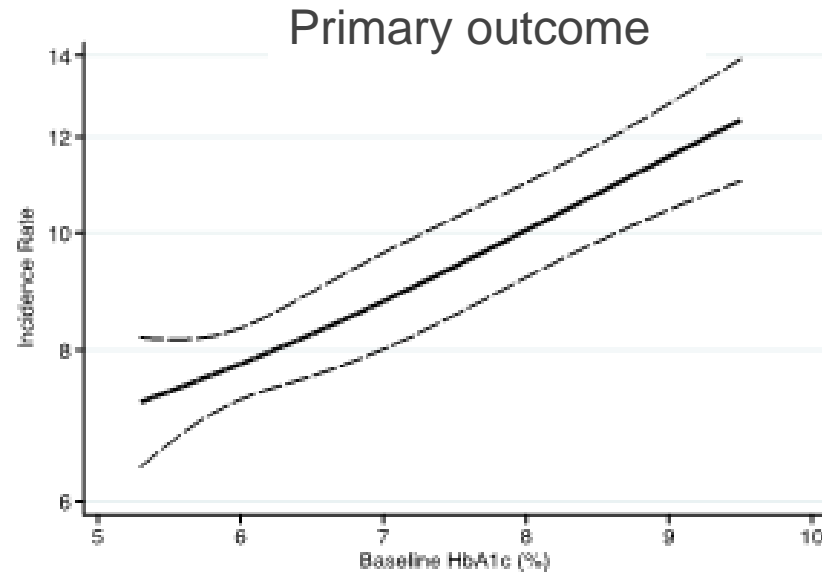
	Normal	Pre-DM	T2D
Outcome	N = 1175	N = 1934	N = 3150
Primary composite	6.9/100py [REF]	7.6 / 100py HR 1.09 (0.90, 1.31)	10.1 / 100py HR 1.46 (1.24, 1.73)
Overall p<0.001		p = 0.38	p<0.001
Worsening HF event	4.7/100py [REF]	5.7/100py HR 1.19 (0.95, 1.49)	7.5/100py HR 1.58 (1.30, 1.94)
Overall p<0.001		p = 0.13	p<0.001
CV death	3.6/100py [REF]	3.1/100py HR 0.85 (0.65, 1.11)	3.8/100py HR 1.07 (0.85, 1.36)
Overall p=0.10		p = 0.23	p = 0.56
All-cause death	6.9/100py [REF]	6.6/100py HR 0.93 (0.77, 1.12)	8.0/100py HR 1.17 (0.99, 1.38)
Overall p=0.005		p = 0.46	p = 0.07



HbA1c distribution and incidence rates by baseline HbA1c



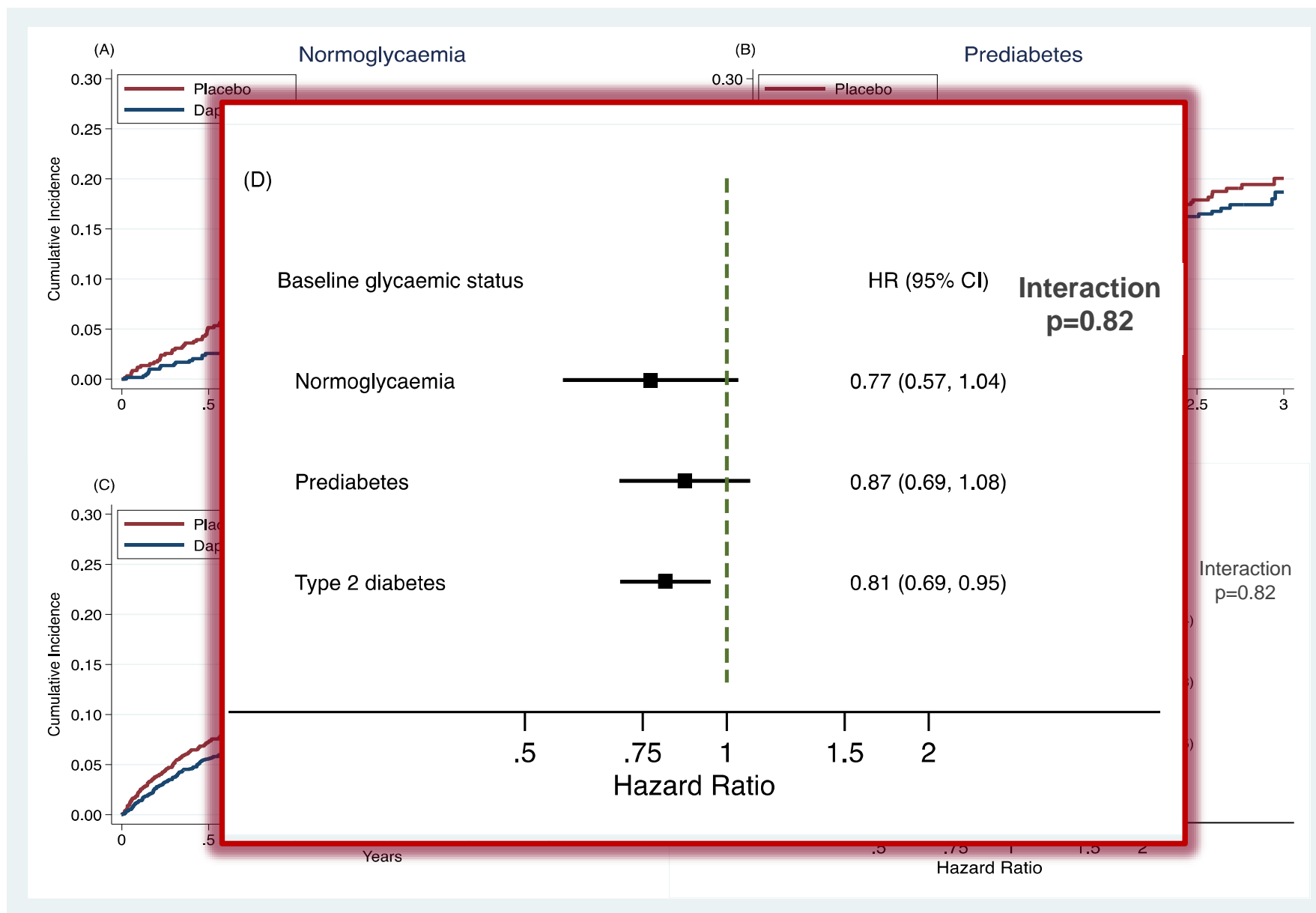
Baseline HbA1c (%)	Total
N	6247
mean	6.59
SD	1.41
min	4.2
p25	5.7
p50	6.2
p75	7
max	17.2



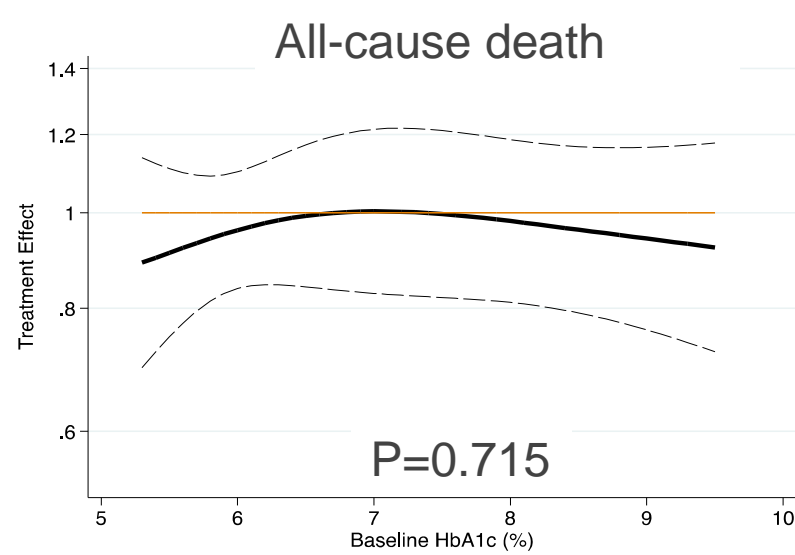
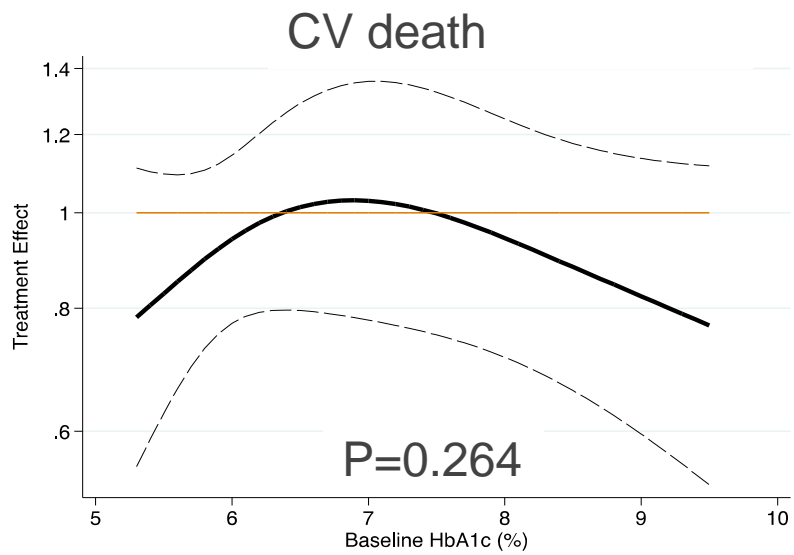
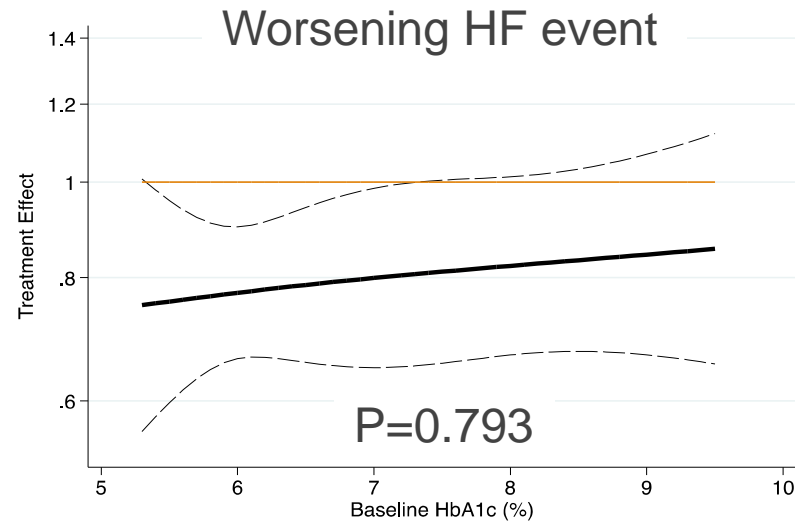
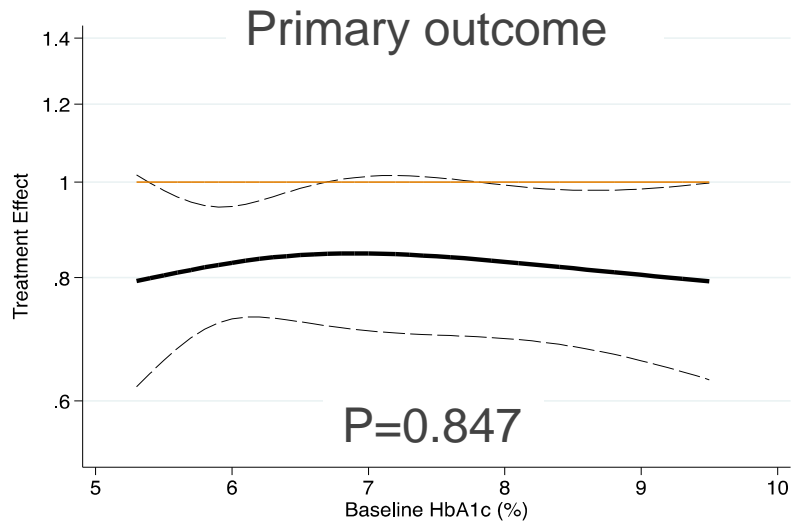
1^o Outcome by Glycaemic Status & Treatment

Worsening HF & CV Death

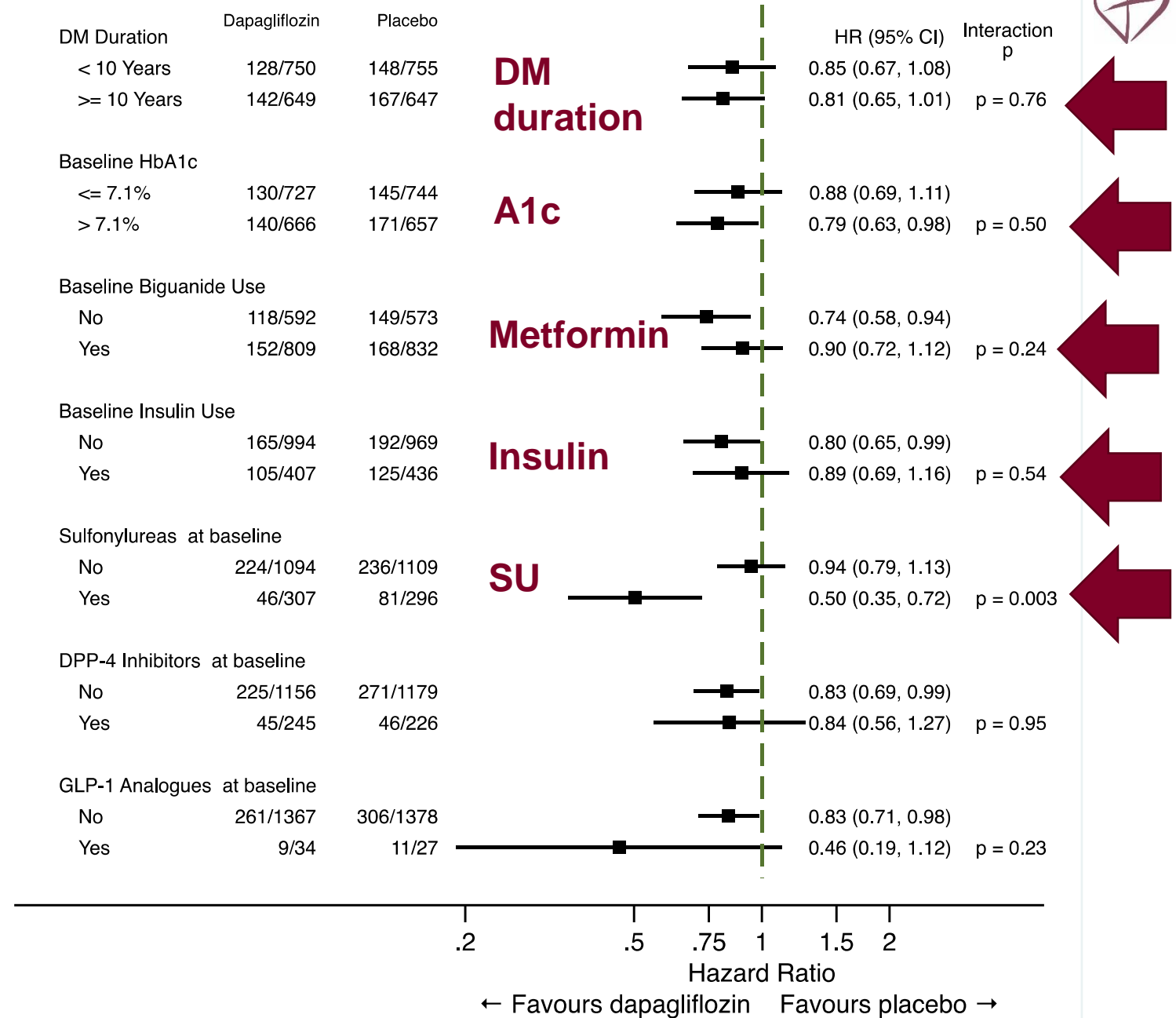
Overall result:
HR 0.82
95% CI 0.73-0.92
P = 0.0008



Treatment Effect by Baseline HbA1c (%)

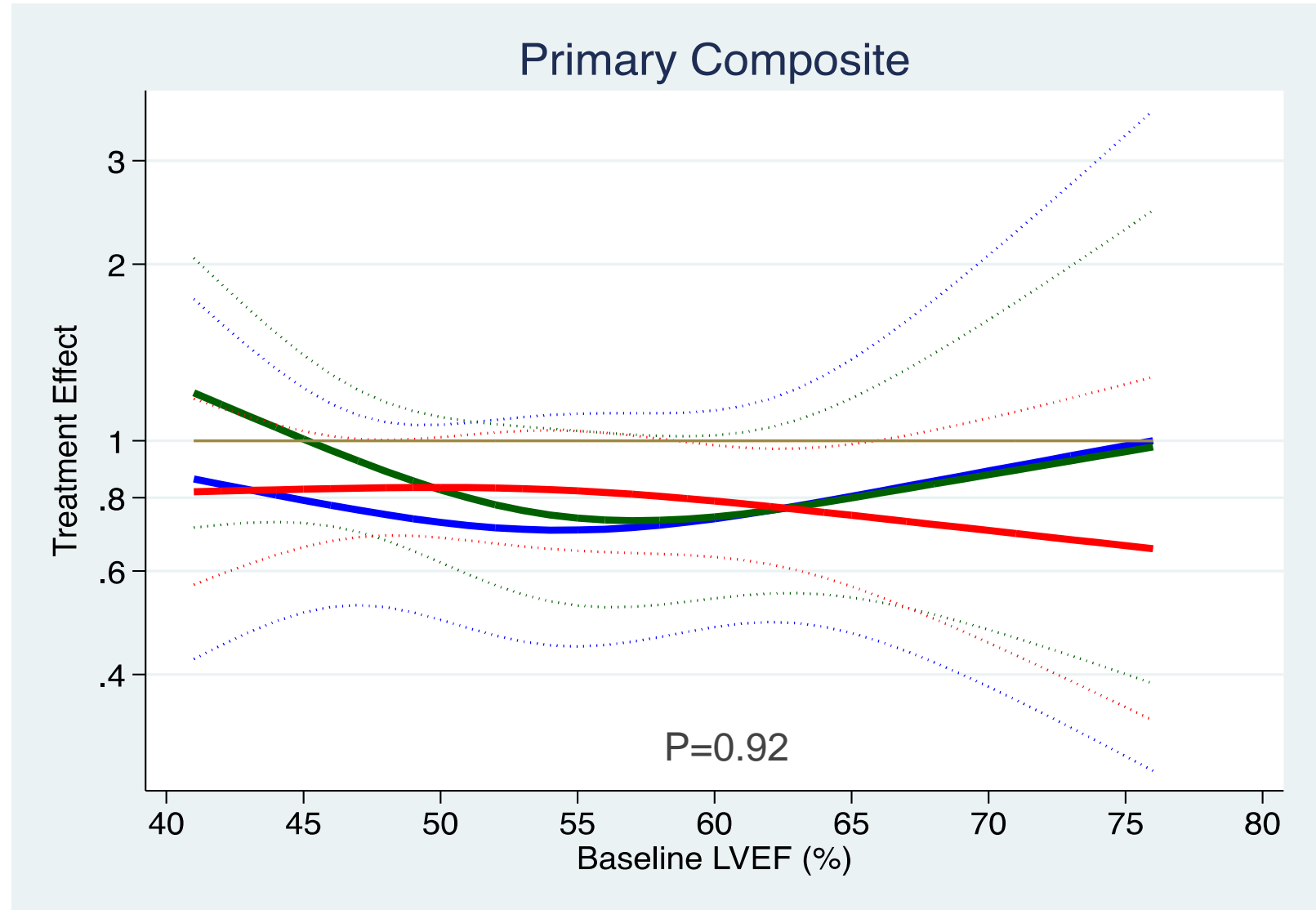


Treatment Effect by Key Variables in the Type 2 Diabetes Subgroup



Treatment effect (ratio, dapagliflozin versus placebo) by glycaemic subgroup and LVEF

- Normoglycaemia
- Prediabetes
- Type 2 diabetes



Conclusions

- Dapagliflozin reduced the risk worsening HF and CV death by 18% in patients with HFmrEF/HFpEF enrolled in the DELIVER trial.
- Dapagliflozin's benefit was consistent across the range of LVEF.
- The DELIVER population consisted of 50.3% with T2D, 30.9% with prediabetes, and 18.8% with normoglycaemia (by HbA1c.)
- In general, event rates increased with worsening glycaemic status both categorically and also using HbA1c as a continuous variable.
- There was no statistical interaction between categorical glycaemic subgrouping (nor using HbA1c) and dapagliflozin's treatment effect.
- No significant trends based on DM duration, baseline A1c or metformin or insulin therapy (in T2D) or based on LVEF across the 3 glycaemic subgroups.
- **Dapagliflozin improves HF outcomes in HFmrEF/HFpEF across the spectra of both ejection fraction and glycaemia.**