

Supplemental Material

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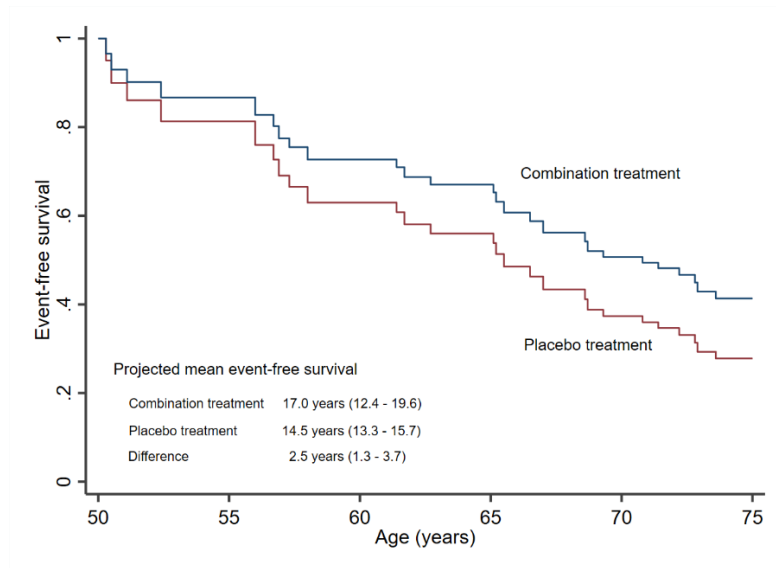
Supplemental Table 1: Baseline characteristics of non-diabetic patients by background medical therapy in DAPA-CKD

Characteristics	DAPAGLIFOZIN (N=697)	PLACEBO (N=701)
Age	56.9 (14.6)	56.0 (14.6)
Female	215 (31)	245 (35)
Race		
White	373 (54)	376 (54)
Black	28 (4)	26 (4)
Asian	268 (38)	267 (38)
Others	28 (4)	32 (5)
Systolic blood pressure	132.3 (16.4)	132.9 (16.9)
Body Mass Index (kg/m²)		
Weigh (kg)	77.9 (17.8)	78.3 (19.9)
Estimated glomerular filtration rate (ml/min/1.73m²)	41.7 (11.5)	41.8 (11.9)
Urinary albumin creatinine ratio (mg/g)	870 (472, 1533)	841 (458, 1554)
History cardiovascular disease	173 (25)	156 (22)
HbA1c (%)	5.6 (0.4)	5.6 (0.4)
Medications		
• Diuretics	210 (30)	207 (30)
• ACE inhibitors/ARBs	675 (97)	682 (97)
○ ACE inhibitors	222 (32)	238 (34)
○ ARBs	460 (66)	452 (64)
• Statin	356 (51)	356 (51)

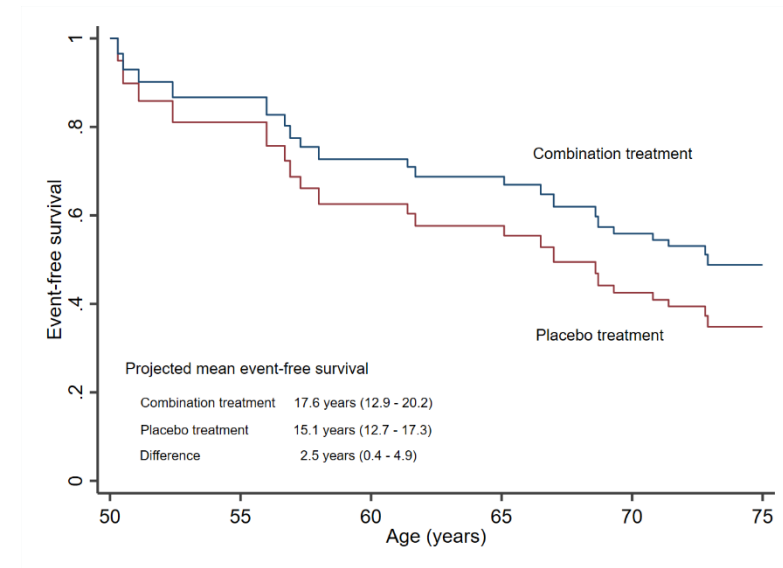
Abbreviations: DAPA-CKD= Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease; ACE= angiotensin-converting enzyme; ARB= angiotensin receptor blockers

Supplemental Figure 1: Event-free survival with combination treatment compared with RAAS inhibitor treatment for primary composite outcome i.e. doubling of serum creatinine/end-stage kidney disease/death (Panel A) and secondary composite outcome i.e. doubling of serum creatinine/end-stage kidney disease (Panel B)

A)



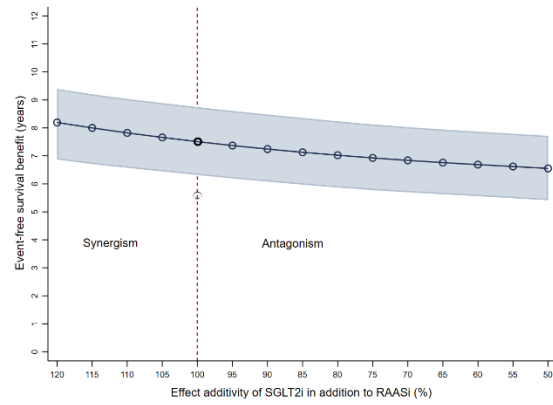
B)



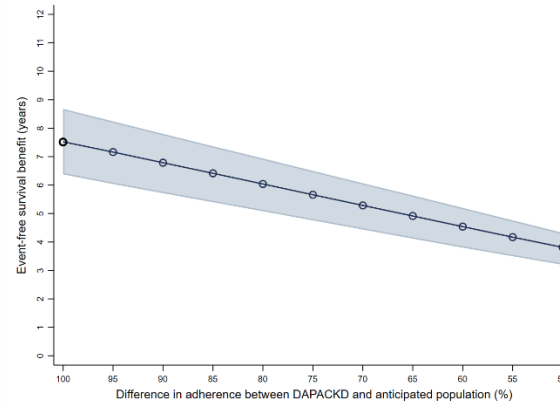
Abbreviation: RAAS=Renin-angiotensin-aldosterone system

Supplemental Figure 2: Projected event-free survival gain for the primary composite outcome by possible levels of effect additivity (Panel A), adherence (Panel B), and yearly change in efficacy of combination treatment (Panel C)*

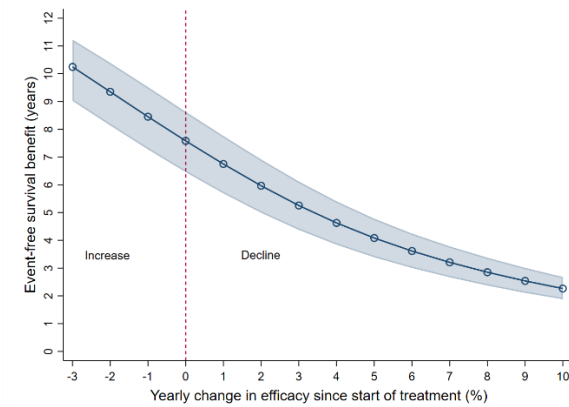
A) Effect additivity†



B) Adherence



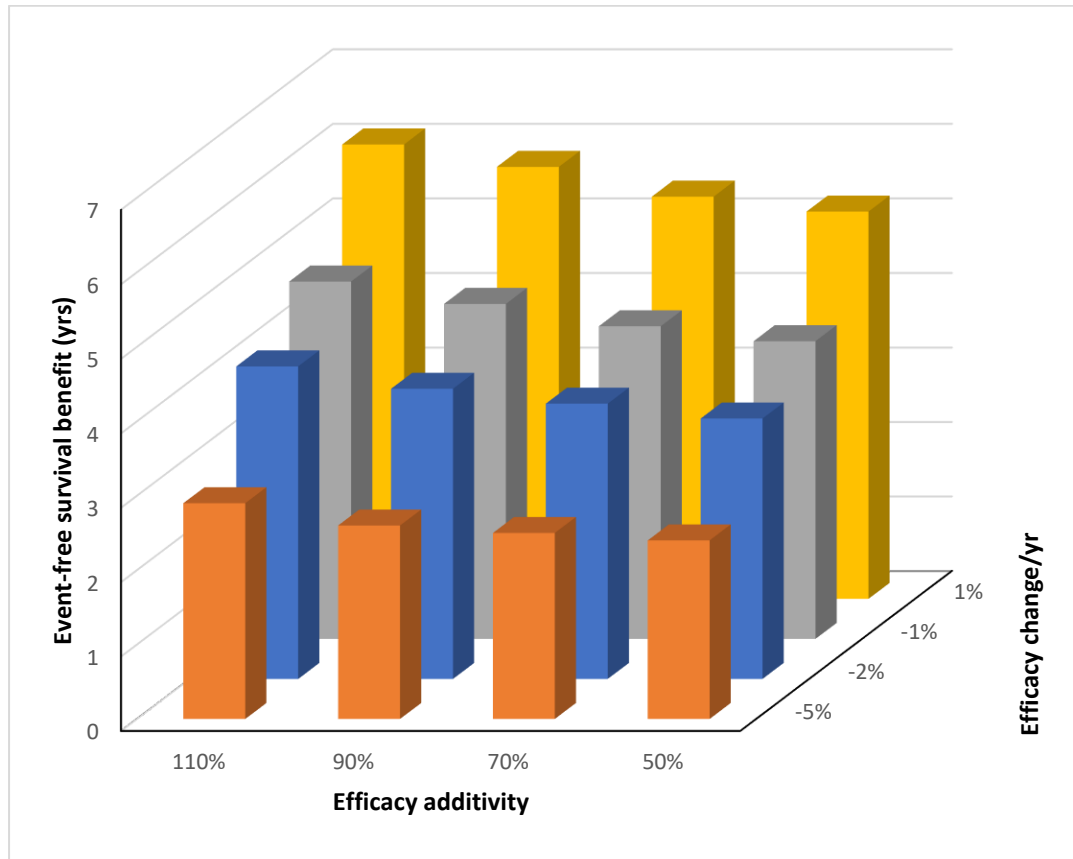
C) Yearly change in efficacy



*Average survival gain from age 50 years to 75 years

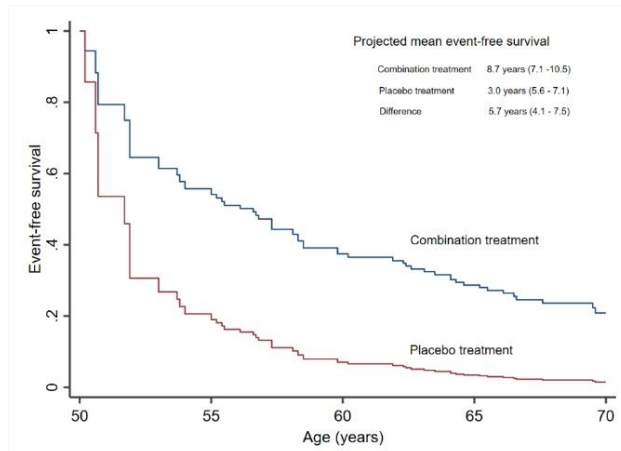
†*(Assuming 100% of the observed efficacy for ACE or ARB inhibitors and mentioned percentages of observed efficacy for SGLT2 inhibitors)

Supplemental Figure 3: Projected event-free survival gain for primary composite outcome by possible levels of efficacy additivity and decline in efficacy assuming 70% of the total adherence observed in included trials

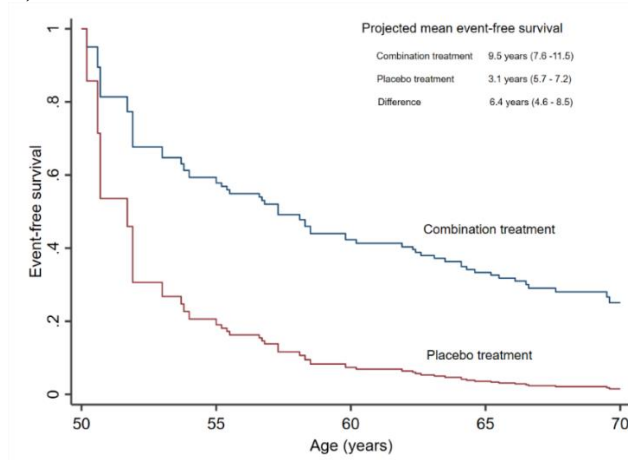


Supplemental Figure 4: Event-free survival with combination treatment vs. no treatment with either of the agents for the primary and secondary composite outcome when directly applying combination treatment effect to placebo group of REIN trial and trial from Guangzhou, China (Panels A and B, respectively) and corresponding results in DAPA-CKD trial (Panels C and D, respectively)

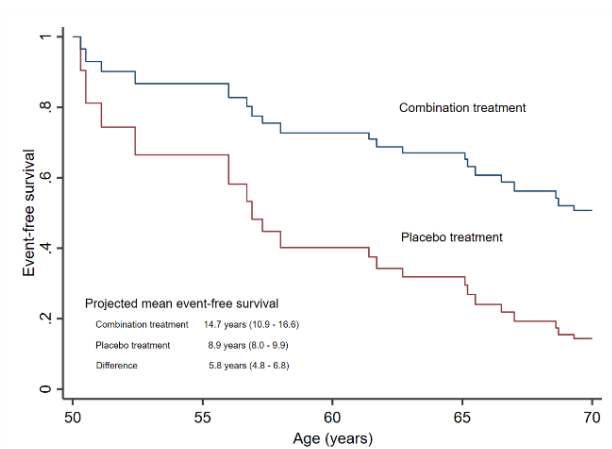
A)



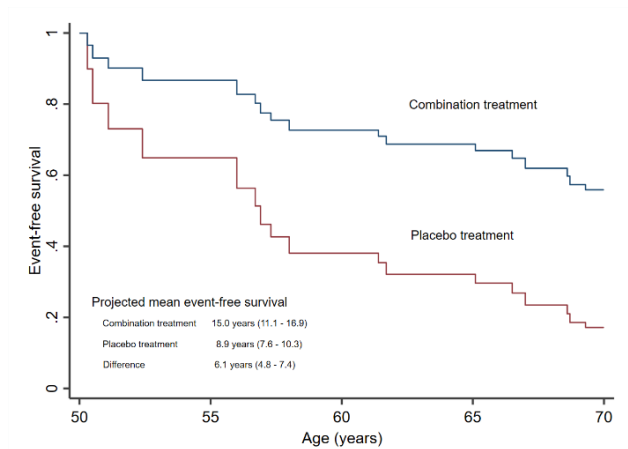
B)



C)



D)



Abbreviations: REIN= Ramipril Efficacy In Nephropathy; DAPA-CKD= Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease