Supplemental material

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Open Heart

Study or Subgroup	Sacubitril/valsartan Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
2.2.1 Valsartan							
CLCZ696B2223	0	8	0	8		Not estimable	
PRIME-HF 2019	7	60	9	58	0.4%	0.75 [0.30, 1.89]	
Subtotal (95% CI)		**68**		**66**	**0.4%**	**0.75 [0.30, 1.89]**	
Total events	7		9				
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.61 (P = 0.54)							
2.2.2 Enalapril							
AWAKE-HF 2019	5	69	4	70	0.2%	1.27 [0.36, 4.52]	
EVALUTE-HF 2019	1	231	1	232	0.0%	1.00 [0.06, 15.96]	
OUTSTEP-HF	19	309	28	310	1.2%	0.68 [0.39, 1.19]	
PARADIGM-HF 2014	1937	4203	2142	4229	94.6%	0.91 [0.87, 0.95]	
PIONEER-HF 2018	41	440	74	441	3.3%	0.56 [0.39, 0.79]	
Subtotal (95% CI)		**5252**		**5282**	**99.4%**	**0.90 [0.86, 0.94]**	
Total events	2003		2249				
Heterogeneity: Chi² = 8.54, df = 4 (P = 0.07); I² = 53%							
Test for overall effect: Z = 4.90 (P < 0.00001)							
2.2.3 Benazepril							
Li J 2019 (1)	3	62	5	64	0.2%	0.62 [0.15, 2.48]	
Subtotal (95% CI)		**62**		**64**	**0.2%**	**0.62 [0.15, 2.48]**	
Total events	3		5				
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.68 (P = 0.50)							
Total (95% CI)		**5382**		**5412**	**100.0%**	**0.89 [0.86, 0.94]**	
Total events	2013		2263				
Heterogeneity: Chi² = 8.99, df = 6 (P = 0.17); I² = 33%							
Test for overall effect: Z = 4.96 (P < 0.00001)							
Test for subgroup differences: Chi² = 0.41, df = 2 (P = 0.81), I² = 0%							

Risk Ratio axis: 0.05 0.2 1 5 20
Sacubitril/valsartan Control