Appendix 3 Supplementary forest plots

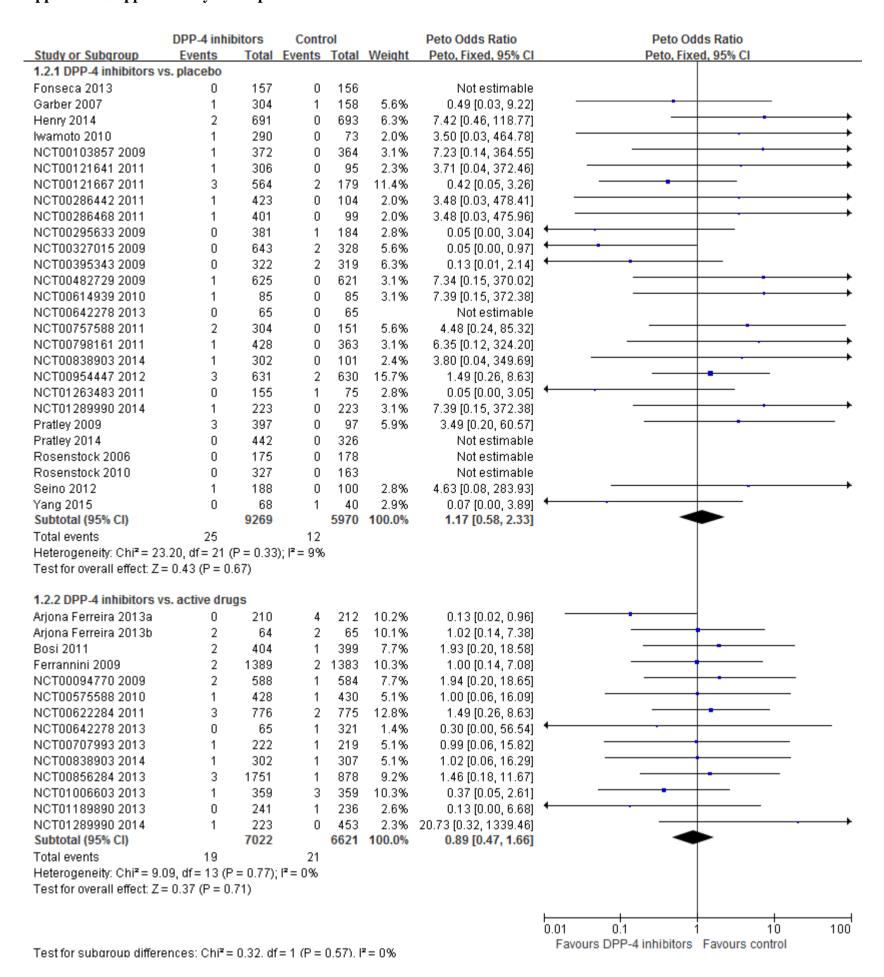


Fig A Subgroup analysis of heart failure risk by type of control in randomized controlled trials

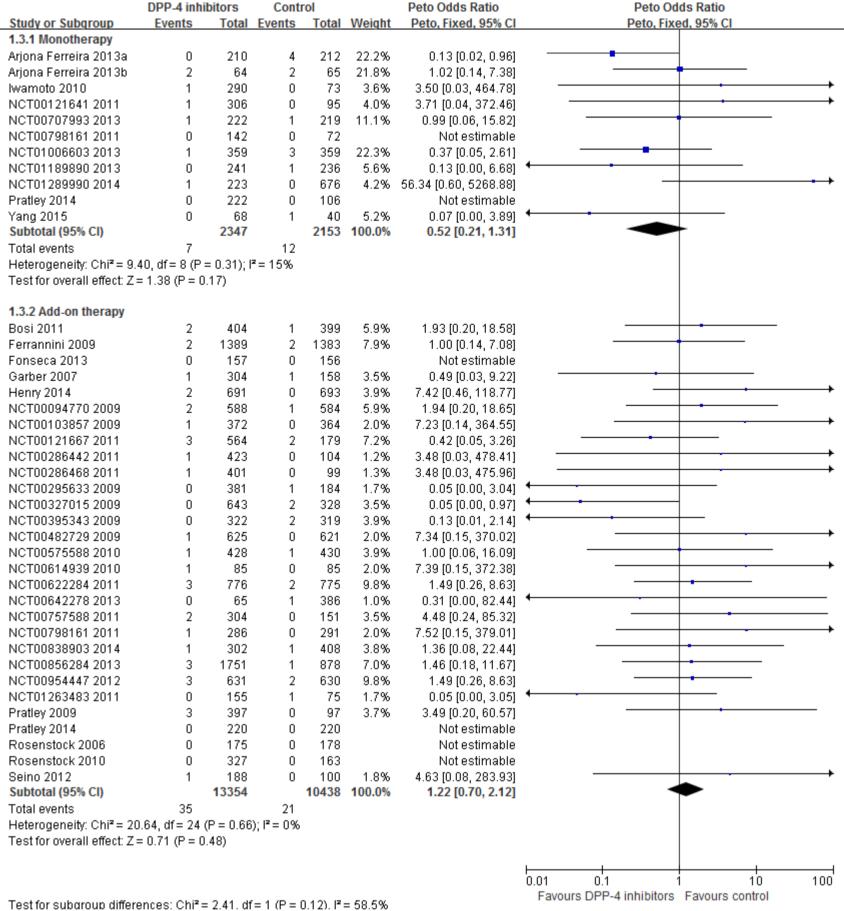


Fig B Subgroup analysis of heart failure risk by mode of therapy in randomized controlled trials

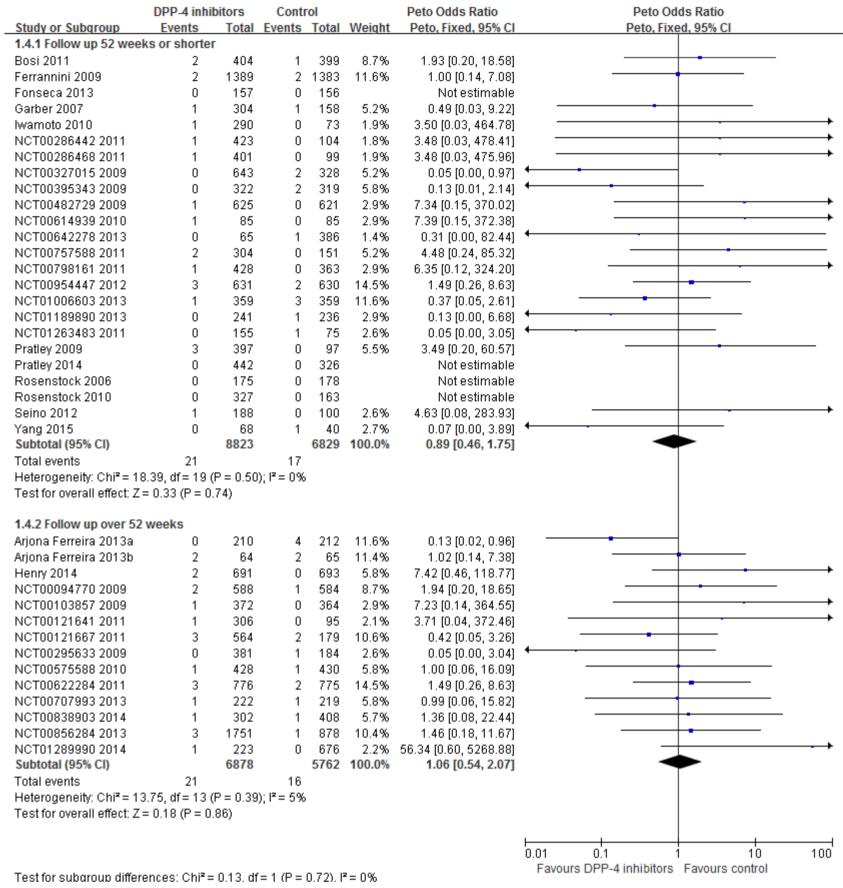


Fig C Subgroup analysis of heart failure risk by length of follow up in randomized controlled trials

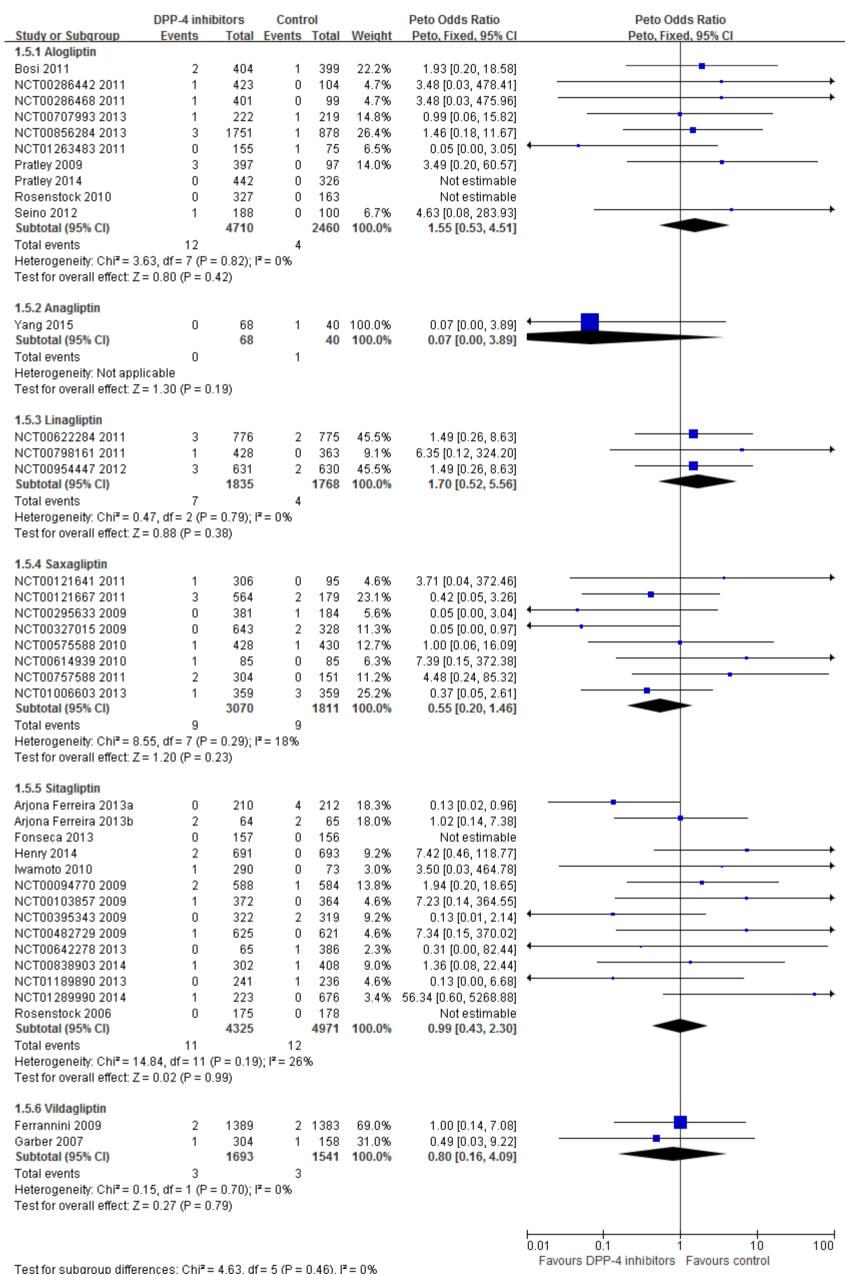


Fig D Subgroup analysis of heart failure risk by individual DPP-4 inhibitors agents in randomized controlled trials

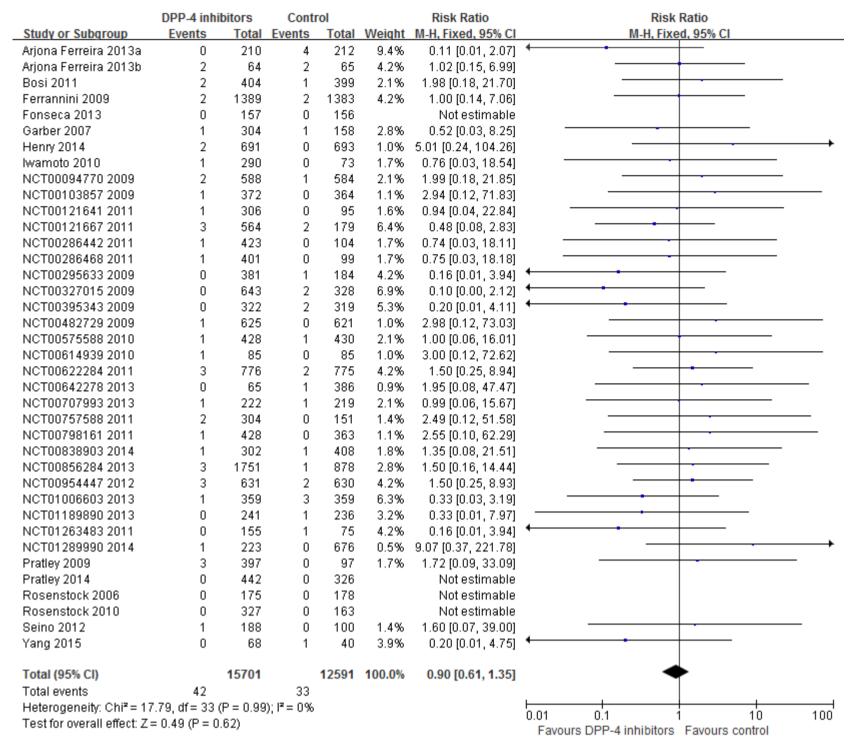


Fig E Sensitivity analysis of heart failure risk by using alternative effect measure risk ratio in randomized controlled trials

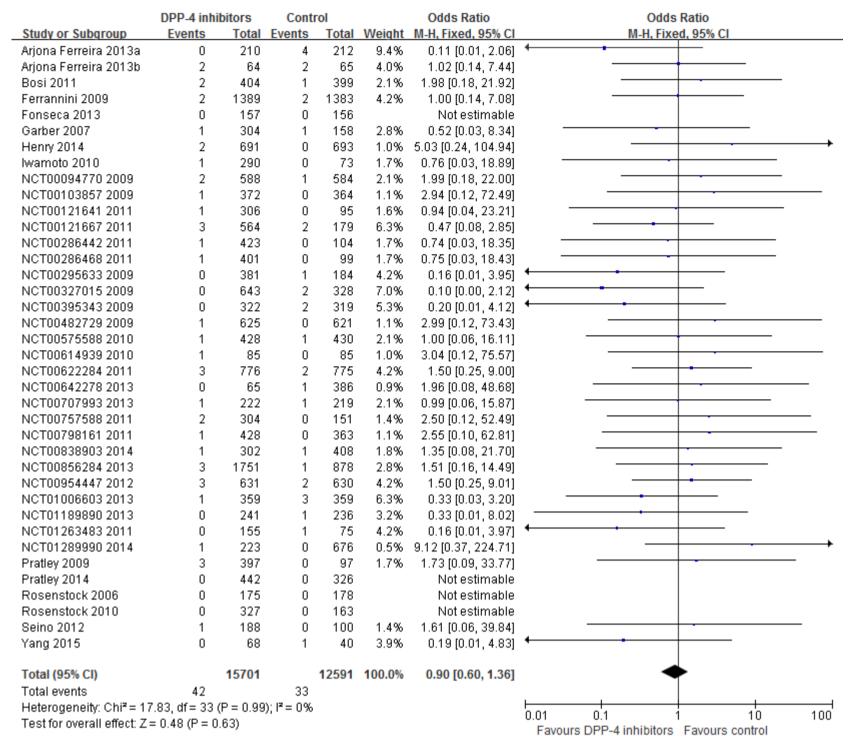


Fig F Sensitivity analysis of heart failure risk by using fixed Mantel-Hanszel statistical model in randomized controlled trials

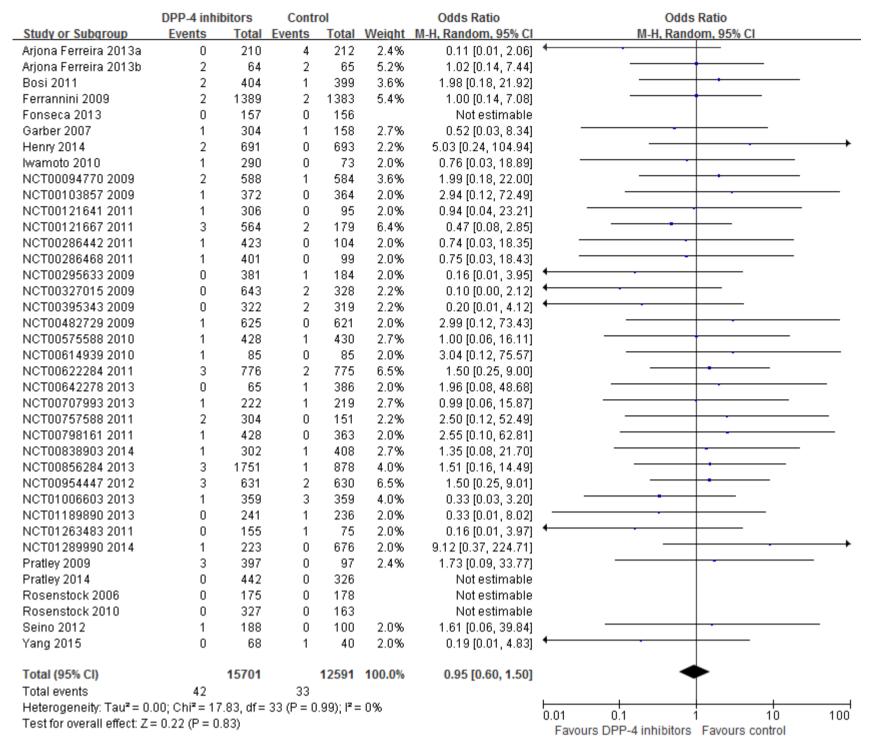


Fig G Sensitivity analysis of heart failure risk by using random effects model in randomized controlled trials

	DPP-4 inhibitors		Control		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Green 2015 (TECOS)	228	7332	229	7339	41.4%	1.00 [0.83, 1.19]	-
Krum 2014 (VIVIDD)	13	128	10	124	1.8%	1.26 [0.57, 2.77]	
Laakso 2015	7	113	6	120	1.1%	1.24 [0.43, 3.58]	
Scirica 2013 (SAVOR-TIMI 53)	289	8280	228	8212	41.4%	1.26 [1.06, 1.49]	
Zannad 2015 (EXAMINE)	85	2701	79	2679	14.3%	1.07 [0.79, 1.44]	-
Total (95% CI)		18554		18474	100.0%	1.12 [1.00, 1.26]	◆
Total events	622		552				
Heterogeneity: $Chi^2 = 3.58$, $df = 4$ ($P = 0.47$); $I^2 = 0\%$							
Test for overall effect: Z = 2.00 (P = 0.05)							0.2 0.5 1 2 5 Favours DPP-4 inhibitors Favours control

Fig H Sensitivity analysis of hospital admission for heart failure by using alternative effect measure risk ratio in randomized controlled trials

	DPP-4 inhibitors		Control		Odds Ratio		Odds Ratio		
Study or Subgroup	Events Total Even		Events	Events Total Weigh		M-H, Fixed, 95% CI	M-H, Fixed, 95% CI		
Green 2015 (TECOS)	228	7332	229	7339	41.5%	1.00 [0.83, 1.20]	-		
Krum 2014 (VIVIDD)	13	128	10	124	1.7%	1.29 [0.54, 3.06]	-		
Laakso 2015	7	113	6	120	1.0%	1.25 [0.41, 3.85]			
Scirica 2013 (SAVOR-TIMI 53)	289	8280	228	8212	41.4%	1.27 [1.06, 1.51]			
Zannad 2015 (EXAMINE)	85	2701	79	2679	14.4%	1.07 [0.78, 1.46]	-		
Total (95% CI)		18554		18474	100.0%	1.13 [1.00, 1.27]	◆		
Total events	622		552						
Heterogeneity: Chi² = 3.59, df = 4 (P = 0.46); I² = 0%									
Test for overall effect: $Z = 2.00 (P = 0.05)$							0.2 0.5 1 2 5 Favours DPP-4 inhibitors Favours control		

Fig I Sensitivity analysis of hospital admission for heart failure by using fixed Mantel-Hanszel statistical model in randomized controlled trials

	DPP-4 inhibitors		Control		Odds Ratio		Odds Ratio		
Study or Subgroup	Events Total Events Total		Total	Weight	M-H, Random, 95% CI	M-H, Rand	om, 95% CI		
Green 2015 (TECOS)	228	7332	229	7339	39.2%	1.00 [0.83, 1.20]	-	-	
Krum 2014 (VIVIDD)	13	128	10	124	1.8%	1.29 [0.54, 3.06]		<u> </u>	
Laakso 2015	7	113	6	120	1.1%	1.25 [0.41, 3.85]		•	—
Scirica 2013 (SAVOR-TIMI 53)	289	8280	228	8212	43.8%	1.27 [1.06, 1.51]			
Zannad 2015 (EXAMINE)	85	2701	79	2679	14.1%	1.07 [0.78, 1.46]		 	
Total (95% CI)		18554		18474	100.0%	1.13 [1.00, 1.27]		•	
Total events	622		552						
Heterogeneity: Tau² = 0.00; Chi²	4 (P = 0.	46); $I^2 = 0$	%		0.2 0.5	<u> </u>			
Test for overall effect: Z = 1.99 (P = 0.05)							0.2 0.5 Favours DPP-4 inhibitors	Favours control	5

Fig J Sensitivity analysis of hospital admission for heart failure by using random effects model in randomized controlled trials