

В

	Endothelin receptor antagonist		Control			Risk Ratio	Risk Ratio
Study or Subgroup	Events Total		Events	Total	Weight	M-H, Random, 95% C	M-H, Random, 95% CI
Heerspink 2019	72	1321	51	1320	70.1%	1.41 [0.99, 2.00]	-
Mann 2010	43	933	10	459	27.9%	2.12 [1.07, 4.17]	
Zeeuw 2014	1	161	1	50	2.0%	0.31 [0.02, 4.88]	-
Total (95% CI)		2415		1829	100.0%	1.53 [1.03, 2.28]	*
Total events	116		62				
Heterogeneity: Tau ² =	0.03; Chi ² = 2.37, df = 2 (P	= 0.31); I ²	= 16%				0.02 0.1 1 10 50
Test for overall effect:					Favours [experimental] Favours [control]		

С

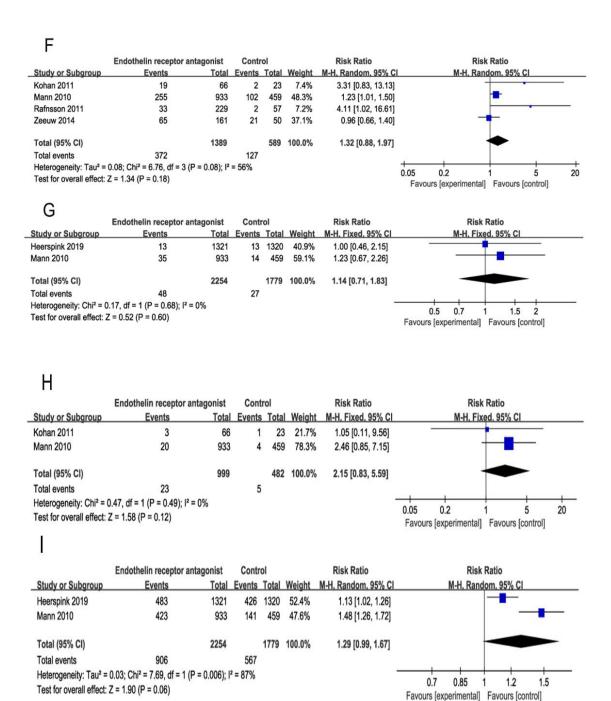
	Endothelin receptor antagonist		Control			Risk Ratio	Risk Ratio
Study or Subgroup	Events Total		Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Heerspink 2019	244	1321	136	1320	52.0%	1.79 [1.47, 2.18]	+
Mann 2010	113	933	16	459	37.1%	3.47 [2.08, 5.79]	_
Wenzel 2009	12	229	2	57	10.8%	1.49 [0.34, 6.49]	-
Total (95% CI)		2483		1836	100.0%	2.25 [1.31, 3.85]	•
Total events	369		154				
Heterogeneity: Tau ² =	0.13; Chi ² = 5.88, df = 2 (F	04 00 05 4 0 5 40					
Test for overall effect: Z = 2.95 (P = 0.003)						0.1 0.2 0.5 1 2 5 10 Favours [experimental] Favours [control]	

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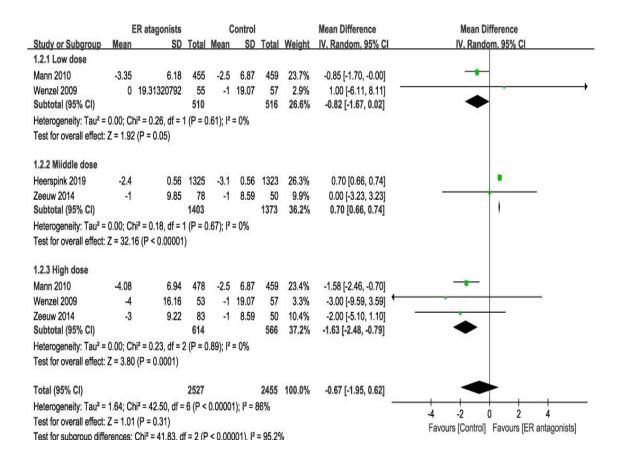
	Endothelin receptor antagonist		Control			Risk Ratio	Risk Ratio			
Study or Subgroup	Events Total		Events Total		Weight	M-H, Fixed, 95% Cl	<u> </u>	ed, 95% CI		
Heerspink 2019	14	1321	8	1320	29.7%	1.75 [0.74, 4.15]		_	-	
Kohan 2011	4	66	0	23	2.7%	3.22 [0.18, 57.68]			1000 P	- 10
Mann 2010	43	933	13	459	64.7%	1.63 [0.88, 3.00]			-	
Zeeuw 2014	1	161	0	50	2.8%	0.94 [0.04, 22.83]		7	20	
Total (95% CI)		2481		1852	100.0%	1.69 [1.04, 2.74]			•	
Total events	62		21							
Heterogeneity: Chi ² =	0.34, df = 3 (P = 0.95); l2 = 09	6					-		1 10	
Test for overall effect:	Z = 2.11 (P = 0.03)						0.02 Fav	0.1 ours [experimental]	1 10 Favours [control]	50

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	Endothelin receptor and	agonist	Contr	ol		Risk Ratio	Risk Ratio				
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C		M-H, Random, 95% CI			
Kohan 2011	5	66	0	23	15.9%	3.94 [0.23, 68.62]				•	
Wenzel 2009	11	229	1	57	31.5%	2.74 [0.36, 20.77]			_		
Zeeuw 2014	6	161	2	50	52.6%	0.93 [0.19, 4.47]		-		_	
Total (95% CI)		456		130	100.0%	1.64 [0.53, 5.13]			•	-	
Total events	22		3								
Heterogeneity: Tau ² =	= 0%				0.01	0.1		10	100		
Test for overall effect: Z = 0.86 (P = 0.39)								rs [experime	ental] Favou	irs [control]	100



Supplementary Figure 1 Forest plot of comparisons between experimental and control groups in terms of the common adverse events. A: Cardiovascular outcome; B: Cardiac failure; C: Anemia; D: Hypoglycemia; E: Headache; F: Edema; G: Hyperkalemia; H: Hypotension; I: Fluid retention.



Supplementary Figure 2 Subgroup analysis of estimated glomerular filtration rate reduction comparison between educational technology research antagonists and control. ER: Endothelin receptor; SD: Standard deviation.