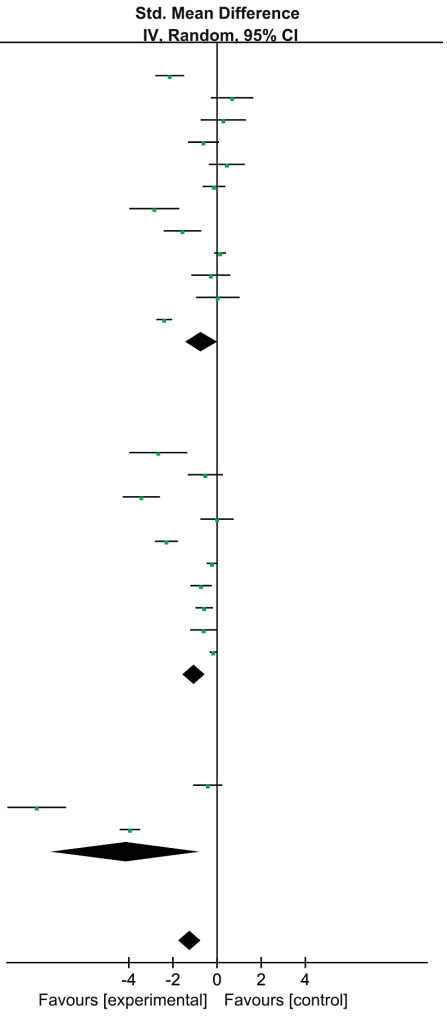
Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
1.3.1 Children									
Tari	8	1.56	30	12	2.1	28	4.1%	-2.14 [-2.80, -1.49]	1990
Hirsch	0.84	0.975	8	0.34	0.35	10	3.8%	0.68 [-0.28, 1.65]	1997
Bahçeciler	0.53	0.4	8	0.41	0.39	7	3.7%	0.29 [-0.74, 1.31]	2001
Ippoliti	0.39	0.71	18	0.82	0.65	15	4.0%	-0.61 [-1.32, 0.09]	2002
Marcucci	5.6	2.25	13	4.4	3	11	3.9%	0.44 [-0.37, 1.26]	2003
Tseng	1.72	1.78	28	1.98	1.9	31	4.2%	-0.14 [-0.65, 0.37]	2008
Yonekura	1.224	0.146	19	1.652	0.146	9	3.6%	-2.85 [-3.98, -1.72]	2010
Eifan	1.5	1	15	2.9	0.7	14	3.9%	-1.57 [-2.41, -0.72]	2010
de Bot	2.26	1.84	108	2.02	1.67	111	4.3%	0.14 [-0.13, 0.40]	2012
Yukselen	3.74	1.4	10	4.15	1.4	10	3.9%	-0.28 [-1.16, 0.60]	2012
Aydogan	3.4	2.7	7	3.3	3	9	3.8%	0.03 [-0.95, 1.02]	2013
Shao	0.41	1.535	141	3.5	0.605	77	4.3%	-2.39 [-2.75, -2.03]	2014
Subtotal (95% CI)			**405**			**332**	**47.5%**	**-0.70 [-1.43, 0.03]**	
Heterogeneity: Tau² = 1.51; Chi² = 187.15, df = 11 (P < 0.00001); I² = 94%									
Test for overall effect: Z = 1.89 (P = 0.06)									
1.3.2 Adults									
Passalacqua A	54.89	11.28	10	108.27	25.19	9	3.4%	-2.67 [-3.98, -1.36]	1998
Mungan	0.5	0.37	15	0.67	0.2	11	4.0%	-0.53 [-1.32, 0.26]	1999
Passalacqua B	1.737	0.135	28	2.281	0.175	28	3.9%	-3.43 [-4.27, -2.59]	2006
O'Hehir	36.59	22	13	36.6	29.5	14	4.0%	-0.00 [-0.76, 0.75]	2009
Bozek	2.656	0.634	47	3.977	0.501	48	4.2%	-2.30 [-2.82, -1.77]	2013
Bergmann	2.6	2.25	133	3.13	2.317	141	4.3%	-0.23 [-0.47, 0.01]	2014
Nolte	5.47	2.69	36	7.45	2.69	34	4.2%	-0.73 [-1.21, -0.24]	2015
Huang	3.89	2.01	51	5.2	2.43	52	4.3%	-0.58 [-0.98, -0.19]	2015
Potter	5.25	1.22	32	6	1.22	16	4.1%	-0.60 [-1.22, 0.01]	2015
Demoly	2.9	2.27	297	3.3	2.27	296	4.4%	-0.18 [-0.34, -0.01]	2016
Subtotal (95% CI)			**662**			**649**	**40.8%**	**-1.02 [-1.53, -0.52]**	
Heterogeneity: Tau² = 0.55; Chi² = 124.80, df = 9 (P < 0.00001); I² = 93%									
Test for overall effect: Z = 3.99 (P < 0.0001)									
1.3.3 children and adults									
Guez	2.3	1.9	25	3.2	2.4	14	4.1%	-0.42 [-1.08, 0.24]	2000
Wang	3.293	0.267	48	6.086	0.414	37	3.4%	-8.17 [-9.50, -6.84]	2013
Mosbech	0.41	0.061	120	0.745	0.107	96	4.2%	-3.95 [-4.41, -3.49]	2015
Subtotal (95% CI)			**193**			**147**	**11.7%**	**-4.13 [-7.50, -0.76]**	
Heterogeneity: Tau² = 8.67; Chi² = 131.55, df = 2 (P < 0.00001); I² = 98%									
Test for overall effect: Z = 2.40 (P = 0.02)									
Total (95% CI)			**1260**			**1128**	**100.0%**	**-1.23 [-1.74, -0.73]**	
Heterogeneity: Tau² = 1.51; Chi² = 643.59, df = 24 (P < 0.00001); I² = 96%									
Test for overall effect: Z = 4.79 (P < 0.00001)									
Test for subgroup differences: Chi² = 3.93, df = 2 (P = 0.14), I² = 49.1%									



Supplementary Figure. Subgroup analysis of efficacy according to age.