Supplementary Material

Clinical heterogeneities among *LRRK2* variants in Parkinson's disease: a meta-analysis

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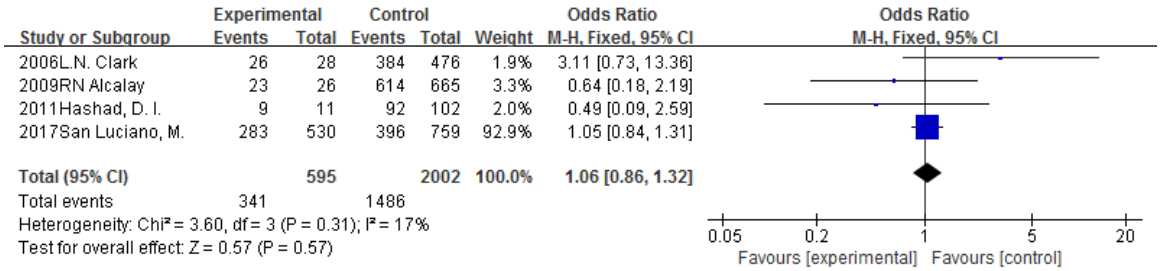
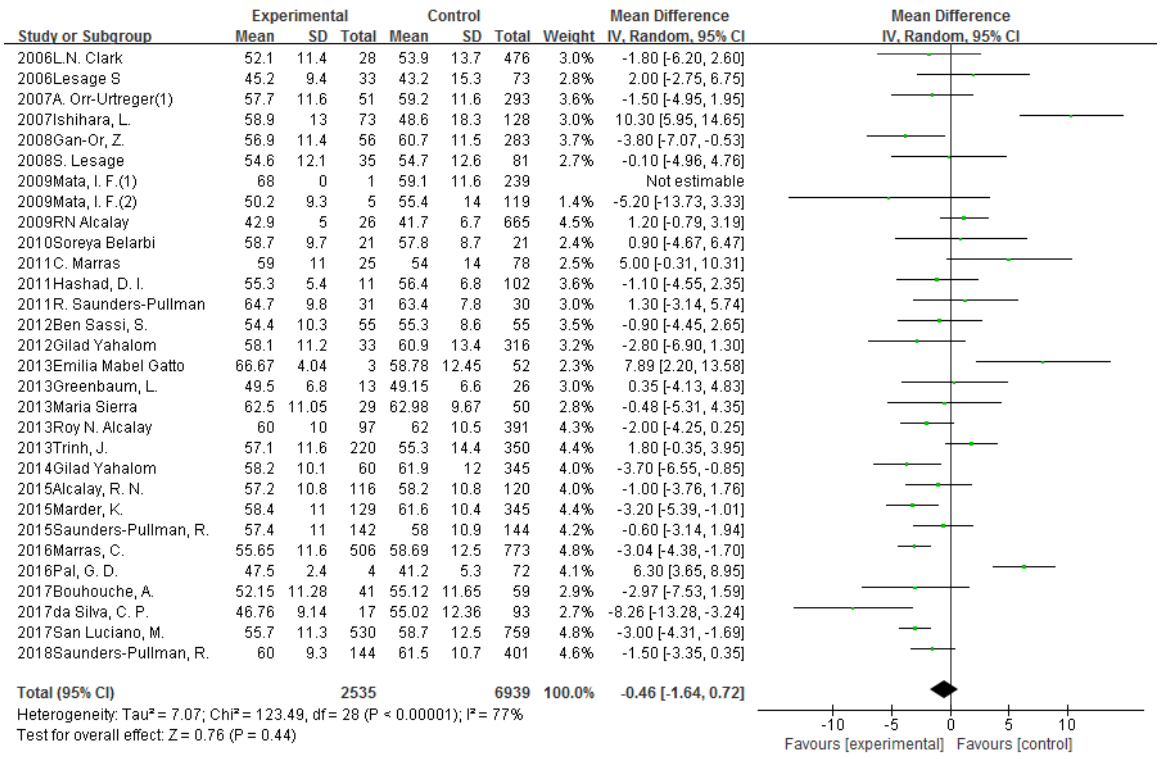
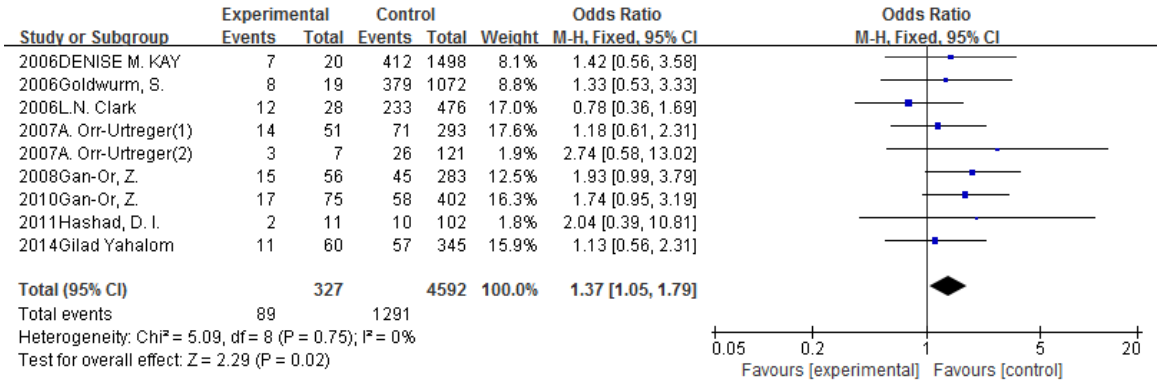


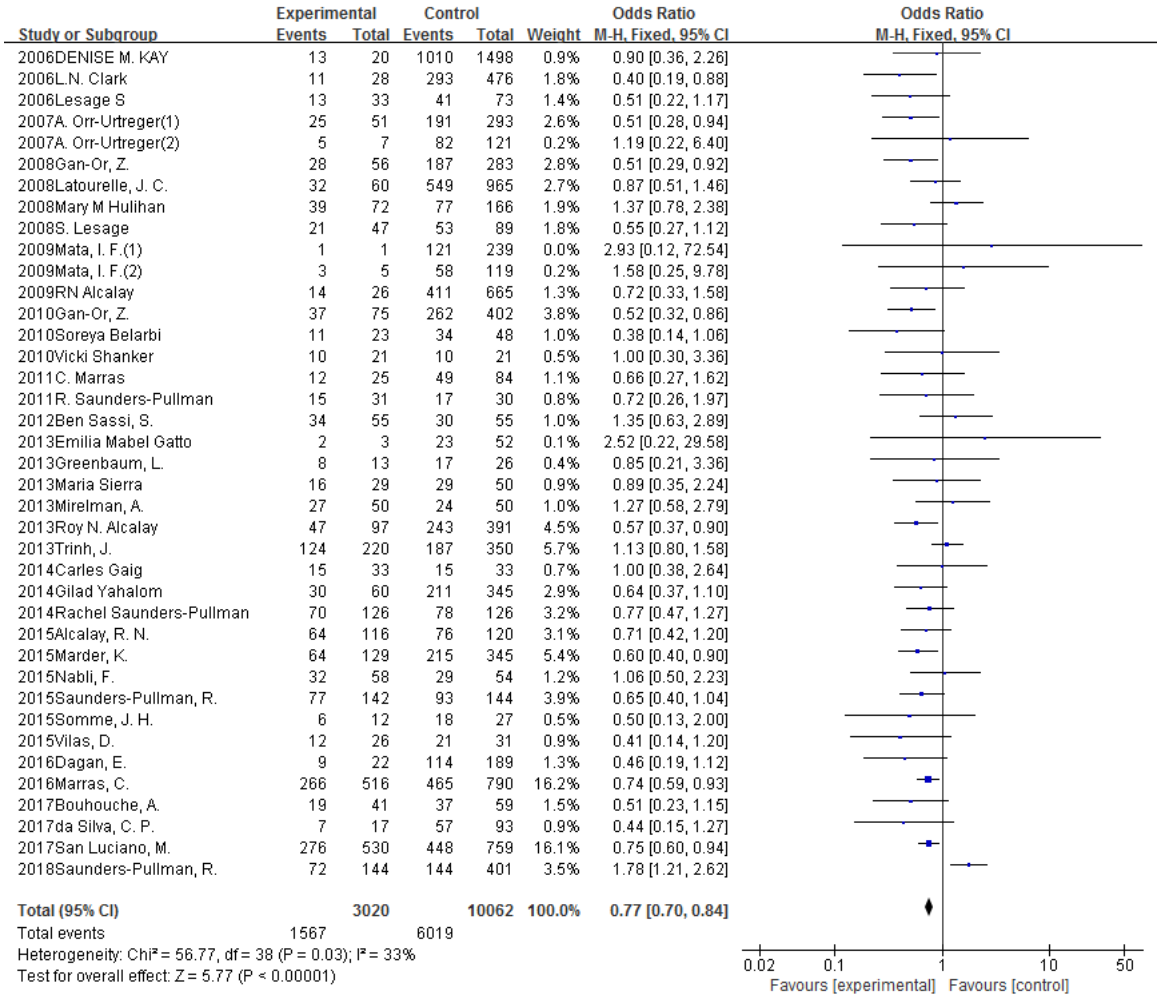
1.1 Asymmetrical onset of G2019S



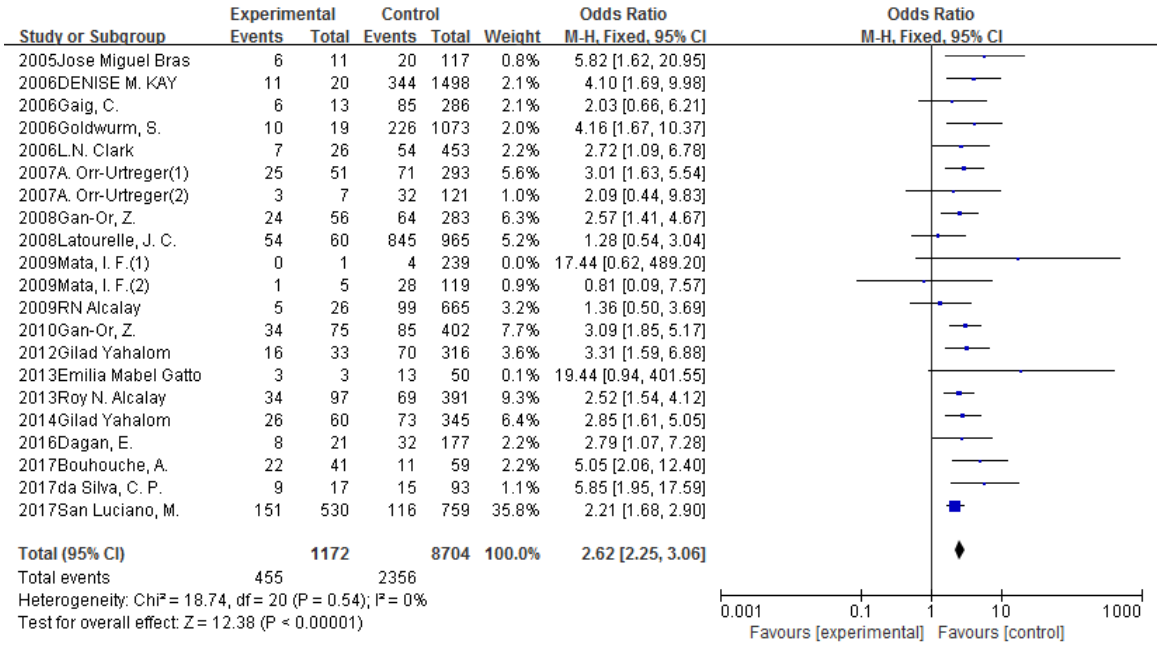
1.2 Age at onset of G2019S



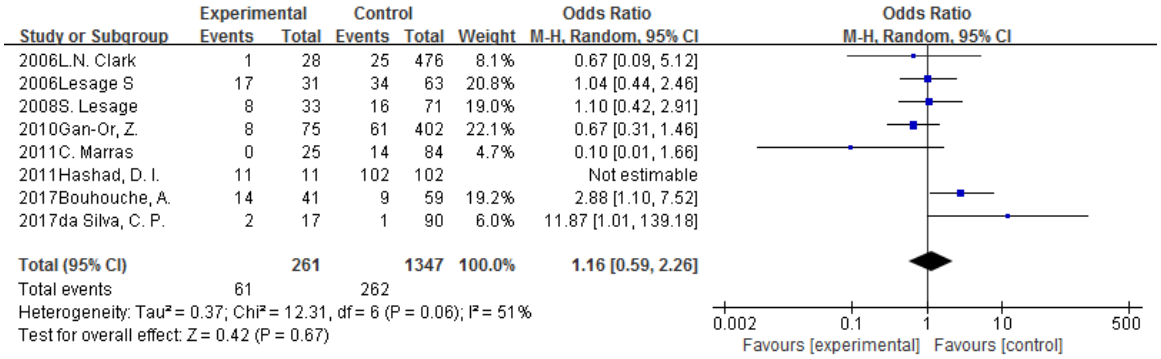
1.3 EOPD of G2019S



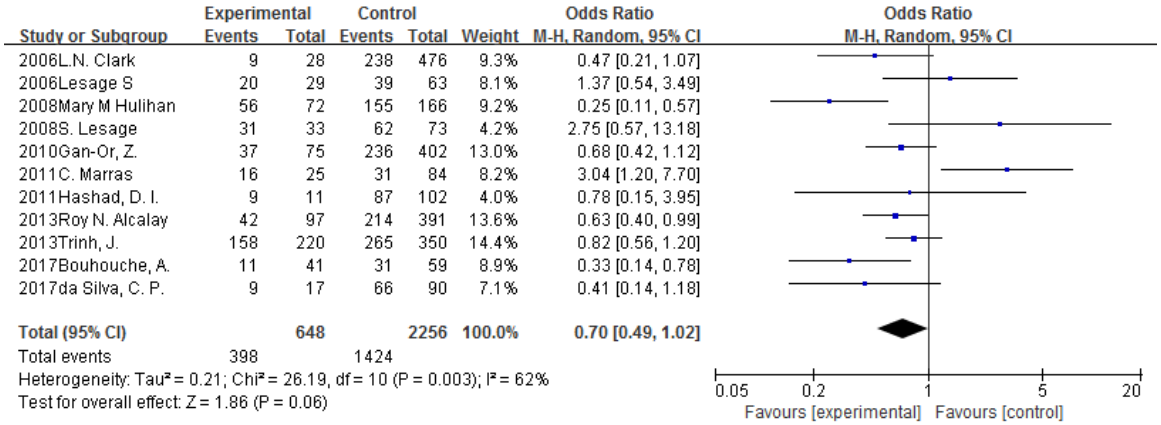
1.4 Gender-male of G2019S



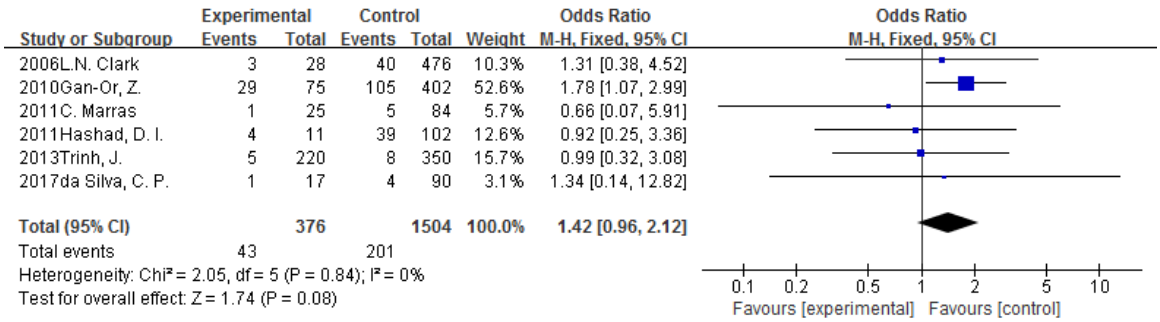
1.5 Family history of G2019S



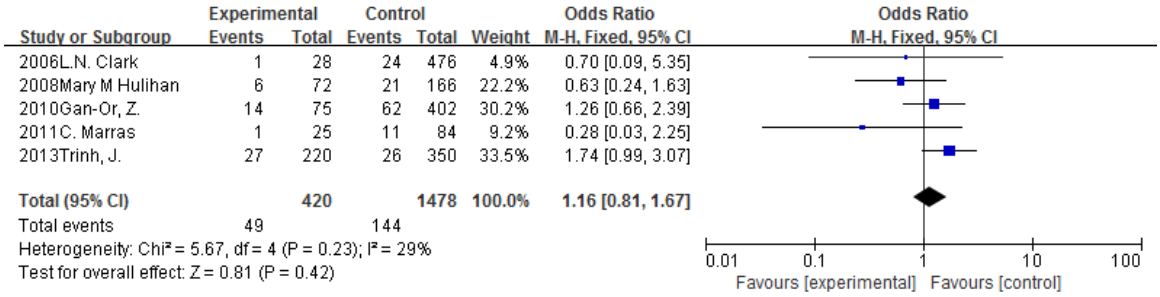
1.6 FS-bradykinesia of G2019S



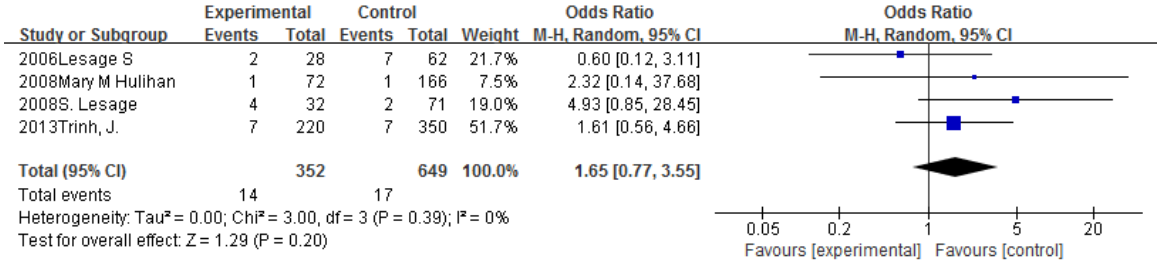
1.7 FS-resting tremor of G2019S



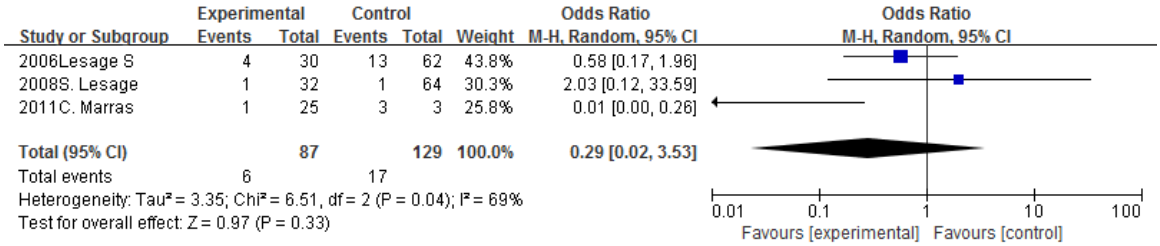
1.8 FS-rigidity of G2019S



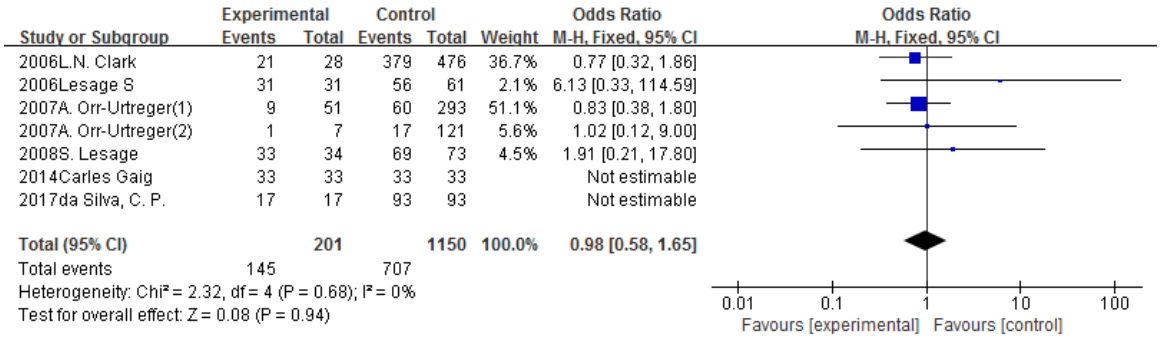
1.9 FS-Postural instability or Gait difficulty of G2019S



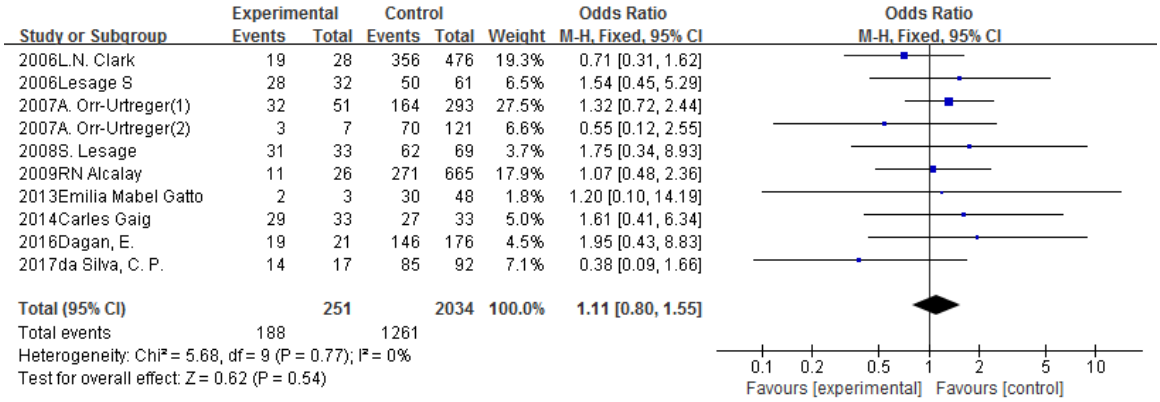
1.10 FS-Dystonia of G2019S



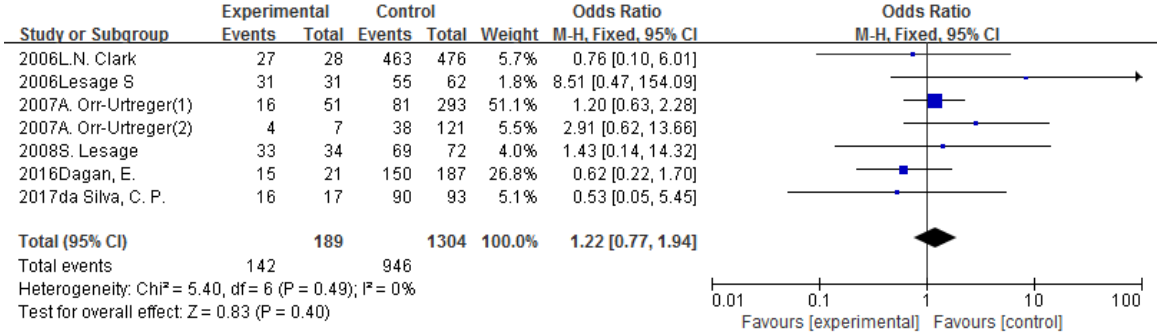
1.11 FS-Micrographia of G2019S



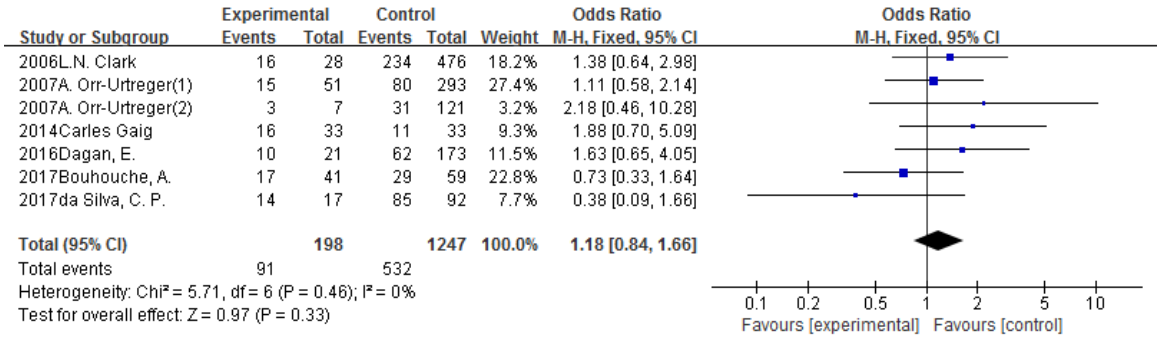
1.12 Bradykinesia of G2019S



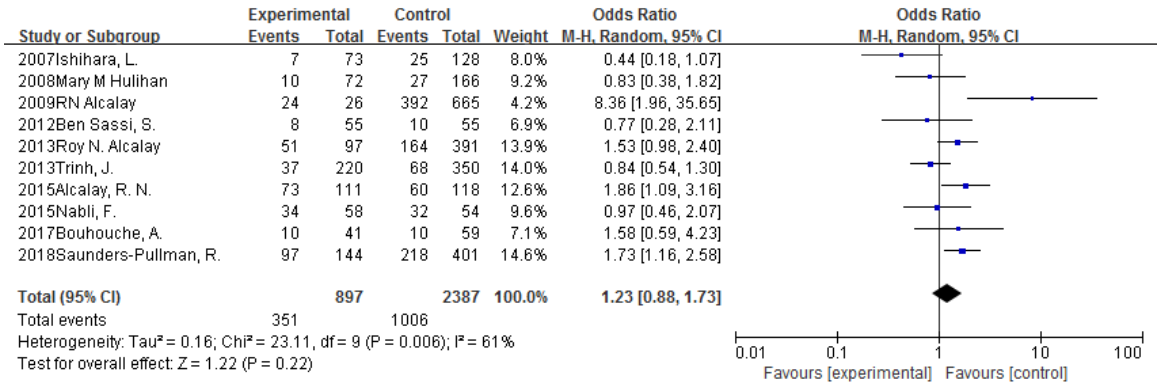
1.13 Resting tremor of G2019S



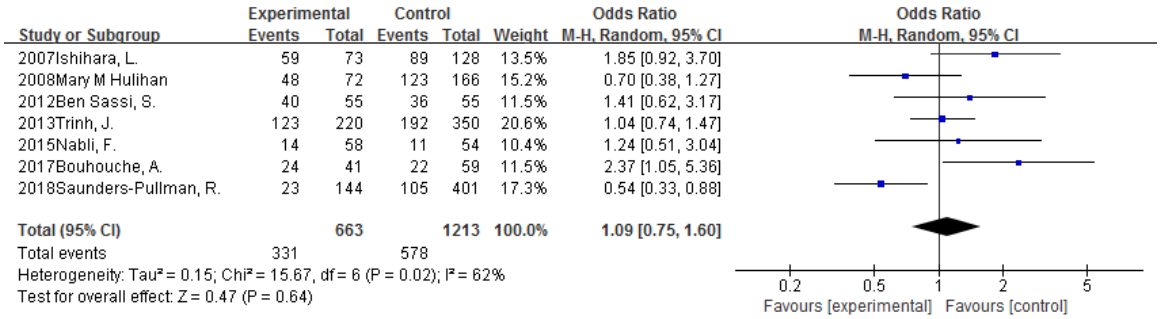
1.14 Rigidity of G2019S



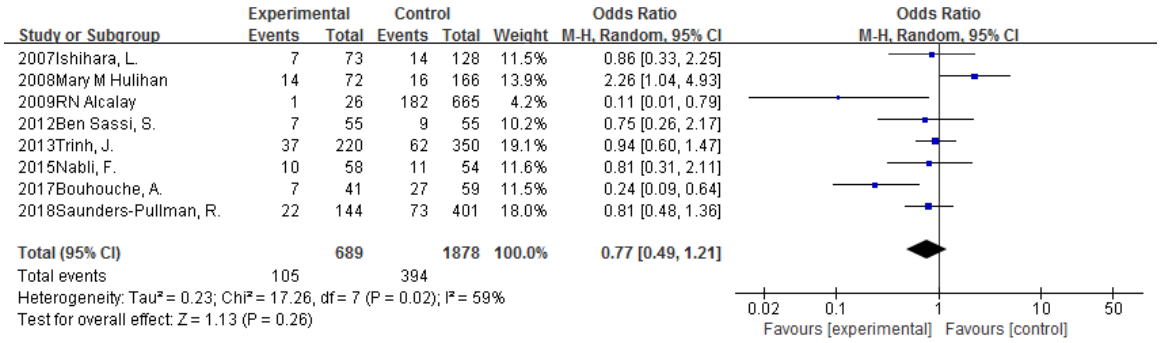
1.15 Postural instability or Gait difficulty of G2019S



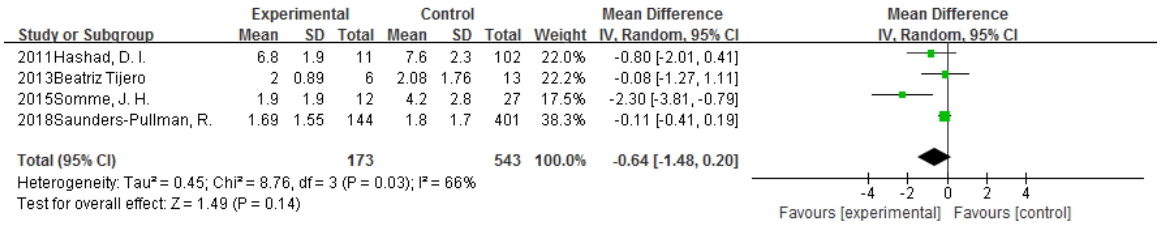
1.16 T-Akinetic-rigid/PIGD of G2019S



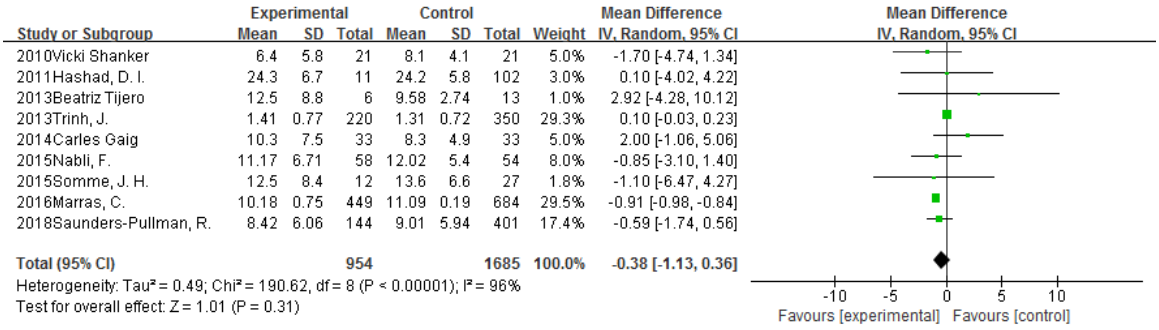
1.17 T-Mixed/Intermediate of G2019S



1.18 T-Tremor-dominant of G2019S



1.19 UPDRS Ⅰ of G2019S



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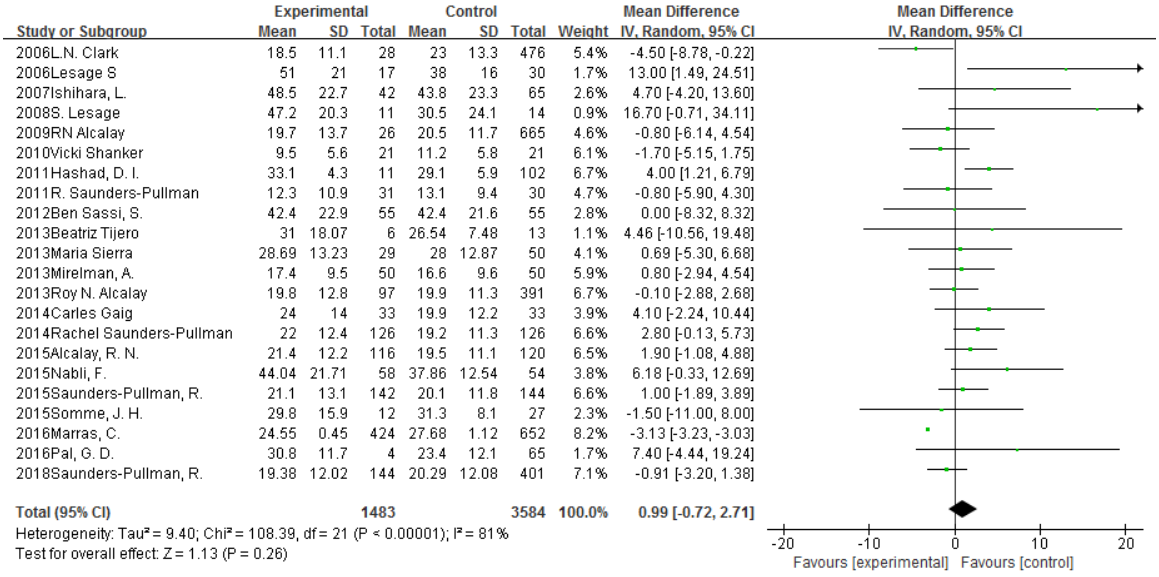
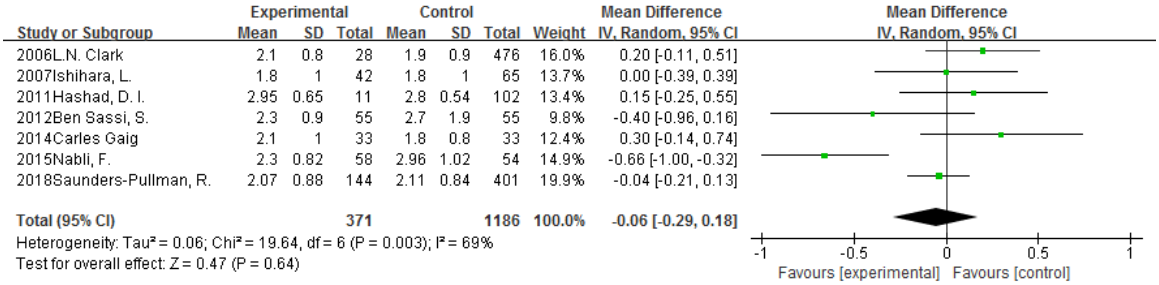
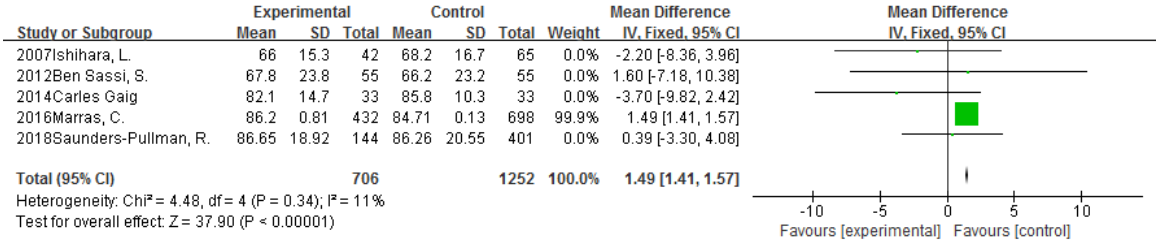


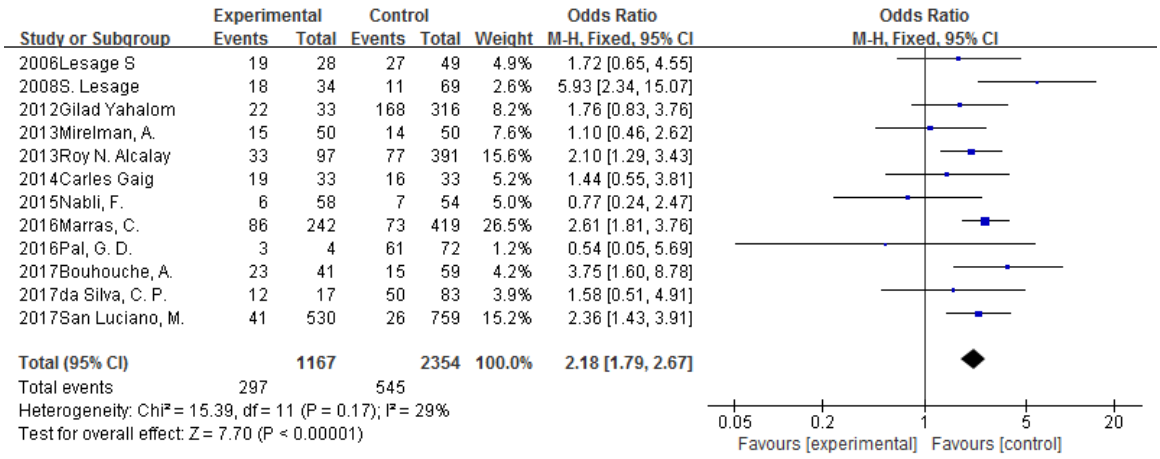
1.21 UPDRSⅢ of G2019S



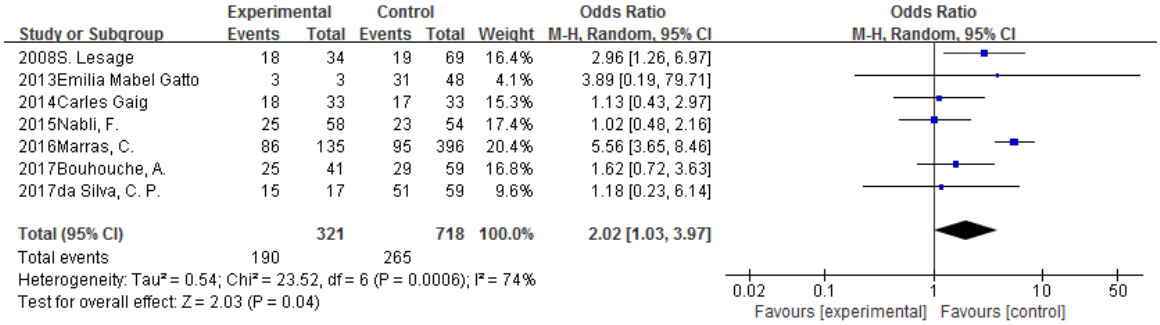
1.22 H-Y of G2019S



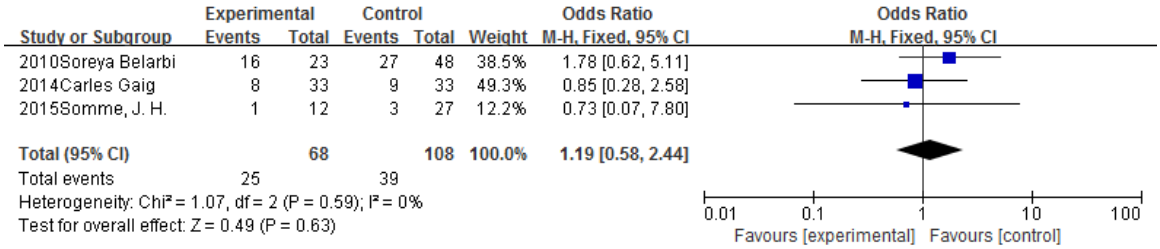
1.23 Schwab & England of G2019S



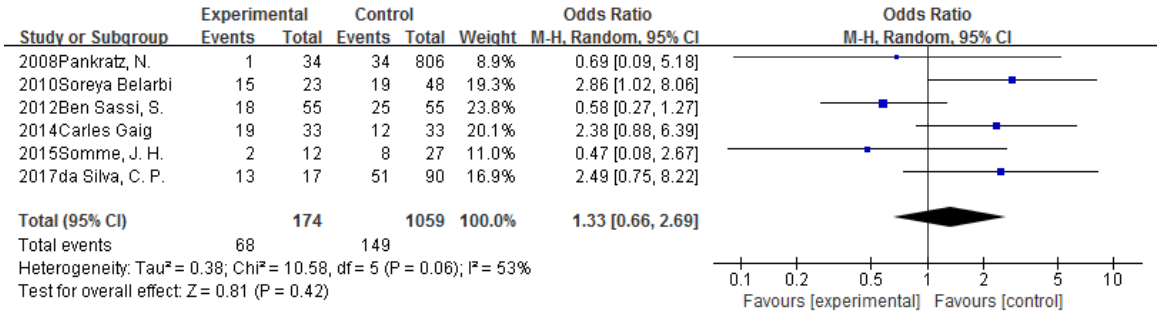
1.24 Dyskinesia of G2019S



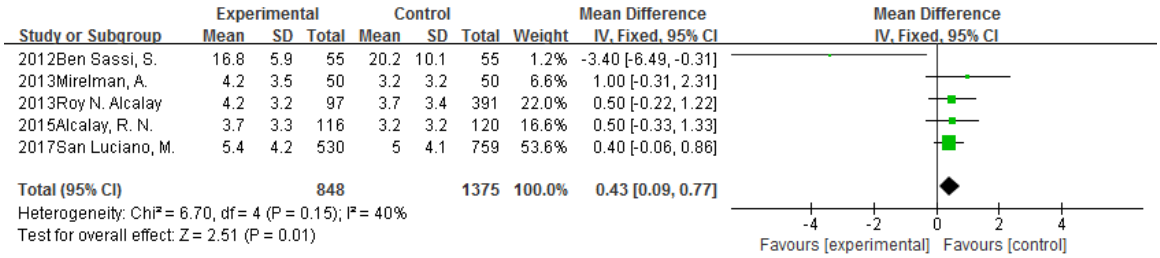
1.25 Motor fluctuations of G2019S



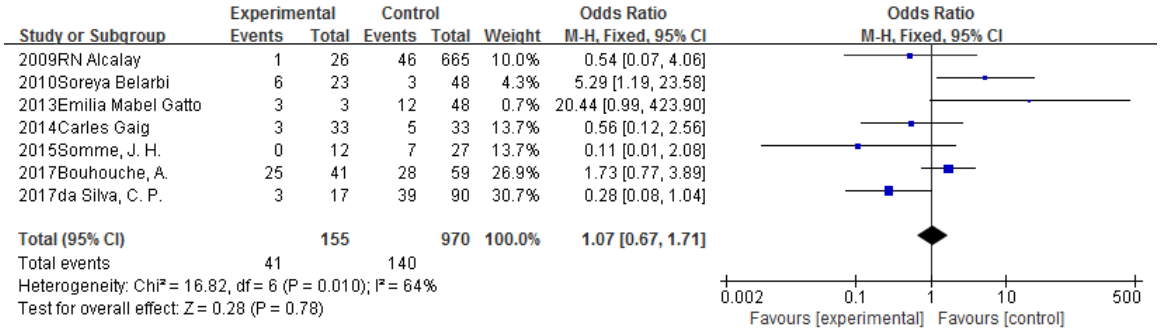
1.26 Anxiety of G2019S



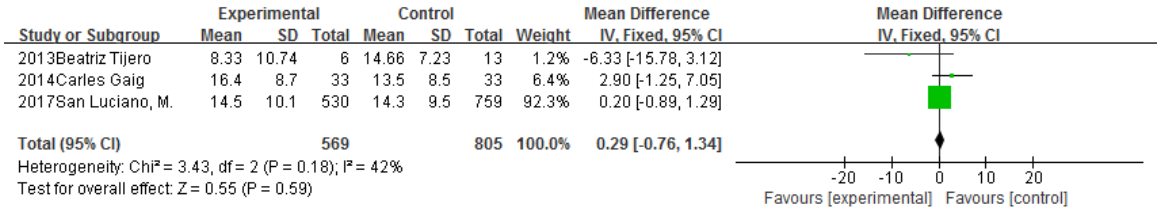
1.27 Depression of G2019S



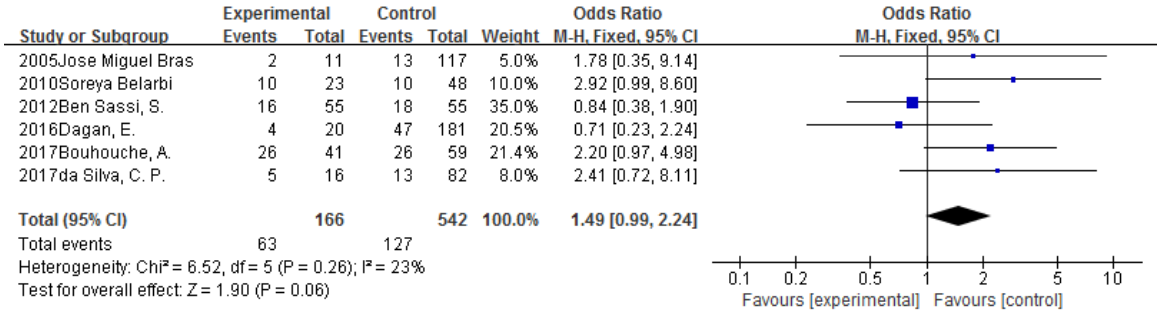
1.28 GDS15 of G2019S



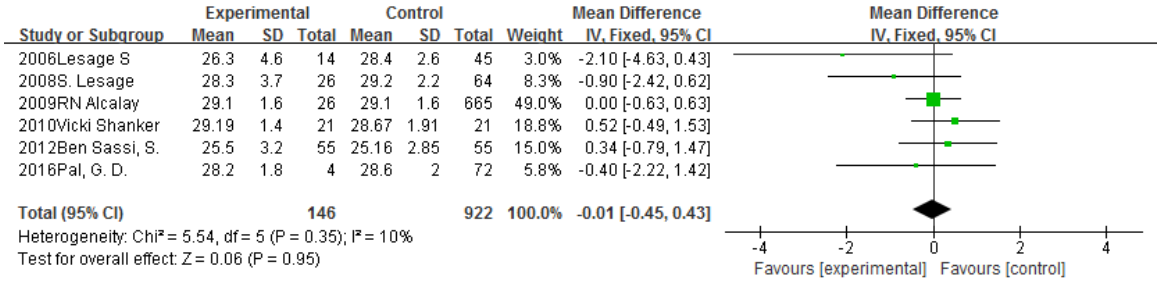
1.29 Hallucination of G2019S



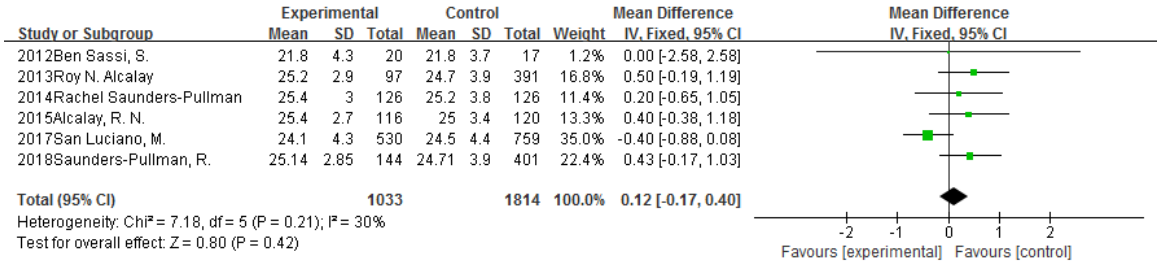
1.30 SCOPA-AUT of G2019S



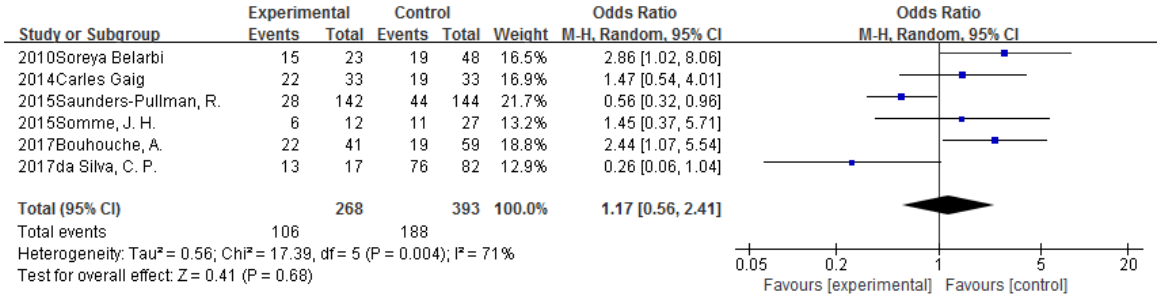
1.31 Cognitive impairments of G2019S



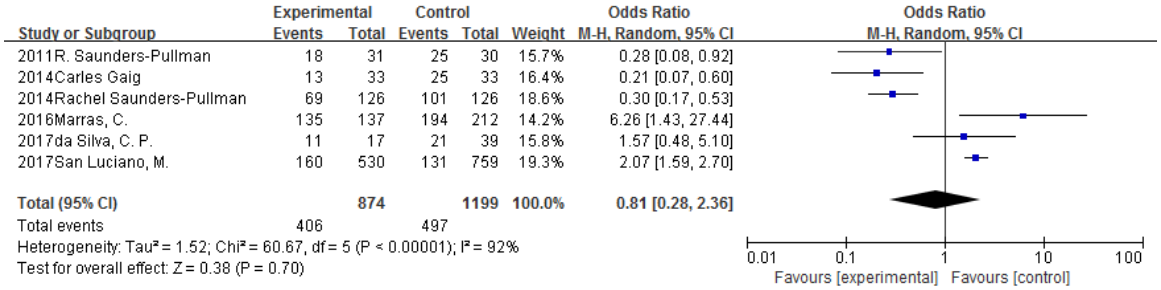
1.32 MMSE of G2019S



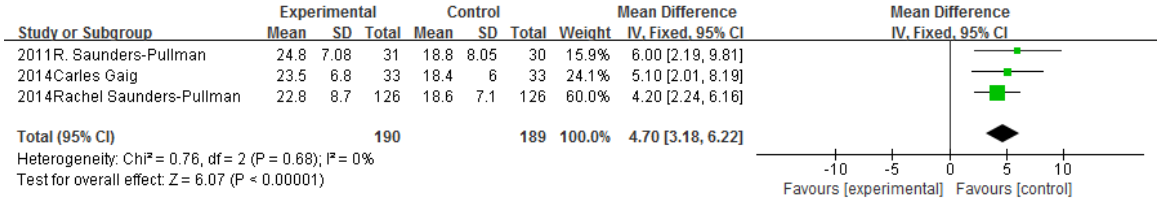
1.33 MoCA of G2019S



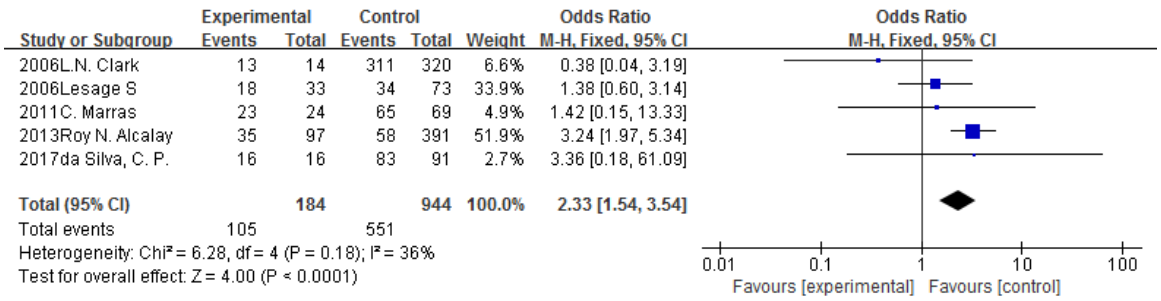
1.34 Sleep disturbances of G2019S



1.35 Olfactory disturbances of G2019S



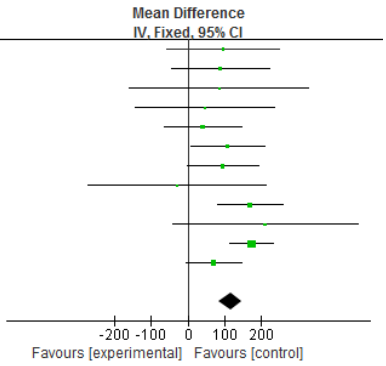
1.36 UPSIT scores of G2019S



1.37 Good response to l-dopa of G2019S

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2006Lesage S	697	322	30	601	356	48	4.0%	96.00 [-57.03, 249.03]
2008S. Lesage	580	335	31	491	245	58	5.3%	89.00 [-44.72, 222.72]
2009RN Alcalay	556	624	26	471	492	665	1.6%	85.00 [-157.75, 327.75]
2011C. Marras	631	410	25	585	423	73	2.7%	46.00 [-141.74, 233.74]
2012Ben Sassi, S.	558.1	321.7	55	517.7	229.5	55	8.7%	40.40 [-64.04, 144.84]
2013Mirelman, A.	300.1	251.9	50	191.8	262.8	50	9.3%	108.30 [7.40, 209.20]
2013Roy N. Alcalay	443	444	97	348	373	391	10.3%	95.00 [-0.78, 190.78]
2014Carles Gaig	793.7	482.1	33	823	516.4	33	1.6%	-29.30 [-270.34, 211.74]
2015Alcalay, R. N.	389	402	116	220	288	120	11.8%	169.00 [79.52, 258.48]
2015Somme, J. H.	1,066.3	388	12	857	325	27	1.5%	209.30 [-42.14, 460.74]
2016Marras, C.	539.31	578.5	516	366.13	373	527	26.9%	173.18 [113.97, 232.39]
2018Saunders-Pullman, R.	407.39	410.23	144	337.1	367.58	401	16.3%	70.29 [-5.76, 146.34]
Total (95% CI)			**1135**			**2448**	**100.0%**	**115.20 [84.47, 145.93]**

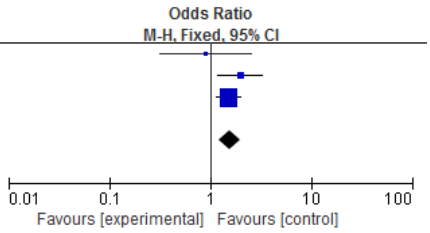
Heterogeneity: Chi² = 11.28, df = 11 (P = 0.42); I² = 2%
Test for overall effect: Z = 7.35 (P < 0.00001)



1.38 LEDD of G2019S

Study or Subgroup	Experimental Events	Total	Control Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
2011R. Saunders-Pullman	11	31	11	29	6.6%	0.90 [0.31, 2.57]
2014Rachel Saunders-Pullman	65	126	44	126	19.1%	1.99 [1.20, 3.29]
2016Marras, C.	407	498	584	783	74.3%	1.52 [1.15, 2.01]
Total (95% CI)		**655**		**938**	**100.0%**	**1.57 [1.24, 1.99]**
Total events	483		639			

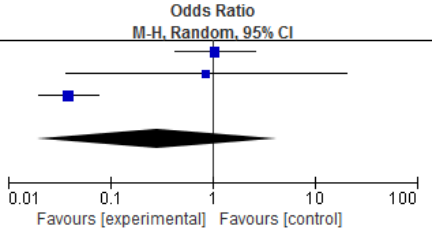
Heterogeneity: Chi² = 1.95, df = 2 (P = 0.38); I² = 0%
Test for overall effect: Z = 3.73 (P = 0.0002)



1.39 Smoke of G2019S

Study or Subgroup	Experimental Events	Total	Control Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
2006Hon-Chung Fung	20	27	203	278	37.0%	1.06 [0.43, 2.60]
2008Daniel Kam Yin Chan	3	3	28	31	25.3%	0.86 [0.04, 20.35]
2016Sun, Qian	20	76	203	225	37.7%	0.04 [0.02, 0.08]
Total (95% CI)		**106**		**534**	**100.0%**	**0.29 [0.02, 4.33]**
Total events	43		434			

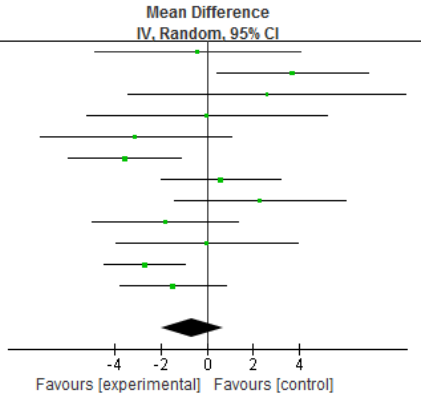
Heterogeneity: Tau² = 4.95; Chi² = 34.89, df = 2 (P < 0.00001); I² = 94%
Test for overall effect: Z = 0.90 (P = 0.37)



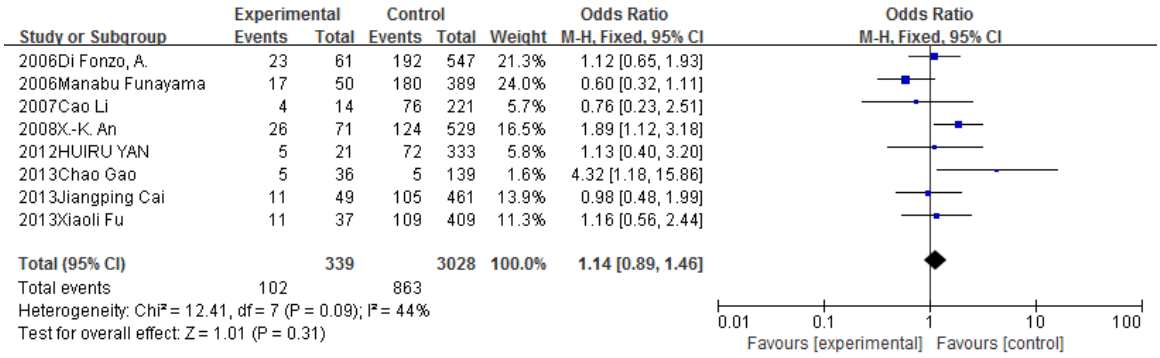
1.40 Asymmetrical onset of G2385R

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
2006Hon-Chung Fung	61.5	11.3	27	61.9	10.5	278	6.1%	-0.40 [-4.84, 4.04]
2006Manabu Funayama	54	10.6	50	50.3	14.9	389	8.6%	3.70 [0.41, 6.99]
2007Cao Li	57	11	14	54.4	13.4	221	3.9%	2.60 [-3.43, 8.63]
2007Eng-King Tan	59	11	33	59	10	29	4.8%	0.00 [-5.23, 5.23]
2007Matthew J. Farrer	54.9	11.8	34	58	11.7	376	6.6%	-3.10 [-7.24, 1.04]
2008X.-K. An	52.75	9.8	71	56.32	11	529	11.0%	-3.57 [-6.03, -1.11]
2010Jong-Min Kim	55.3	11.5	82	54.7	10.8	841	10.6%	0.60 [-1.99, 3.19]
2013Chao Gao	60.5	10.4	36	58.2	8.8	139	7.6%	2.30 [-1.40, 6.00]
2013Jiangping Cai	56.8	10.7	49	58.6	11	461	8.9%	-1.80 [-4.96, 1.36]
2013Xiaoli Fu	55	11.7	37	55	11	409	7.1%	0.00 [-3.92, 3.92]
2016Marras, C.	55.99	11.1	197	58.69	12.5	790	13.3%	-2.70 [-4.48, -0.92]
2016Sun, Qian	55.57	8.78	76	57.05	8.92	225	11.6%	-1.48 [-3.77, 0.81]
Total (95% CI)			**706**			**4687**	**100.0%**	**-0.66 [-2.01, 0.70]**

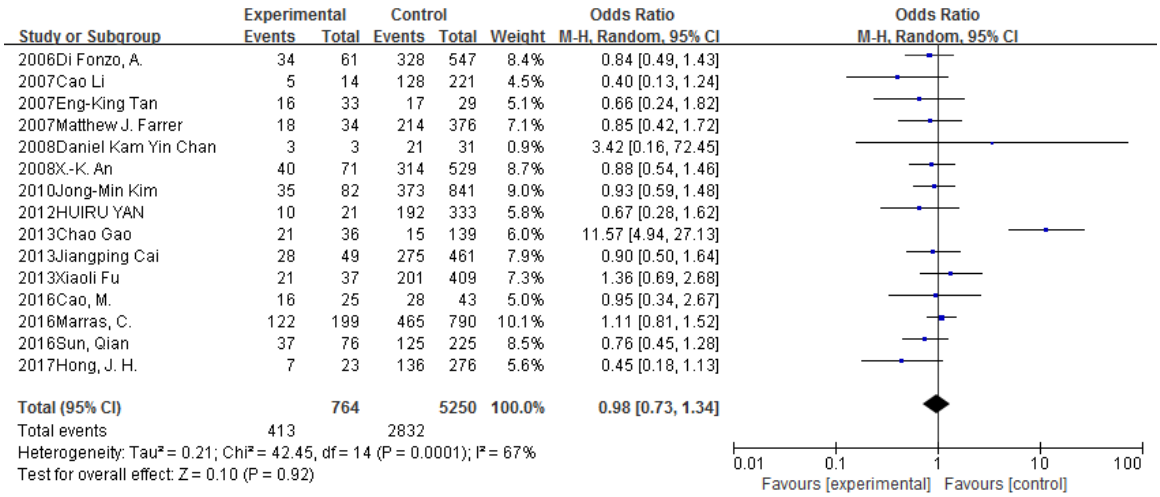
Heterogeneity: Tau² = 2.76; Chi² = 23.25, df = 11 (P = 0.02); I² = 53%
Test for overall effect: Z = 0.95 (P = 0.34)



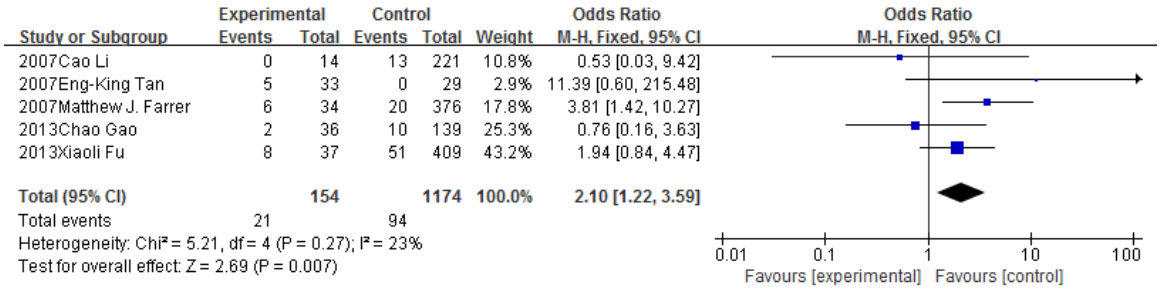
1.41 Age at onset of G2385R



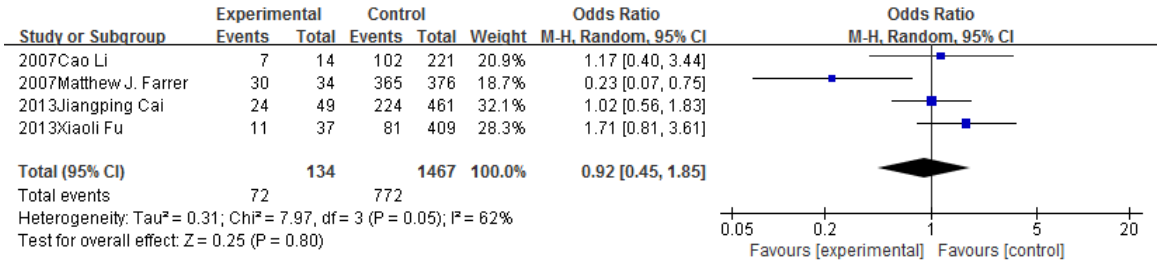
1.42 EOPD of G2385R



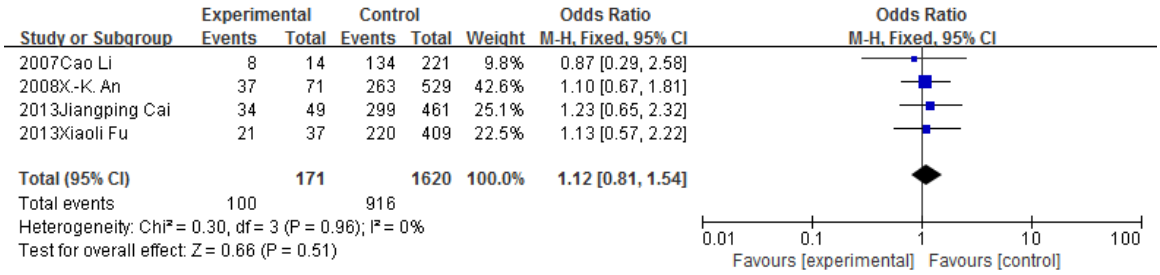
1.43 Gender-male of G2385R



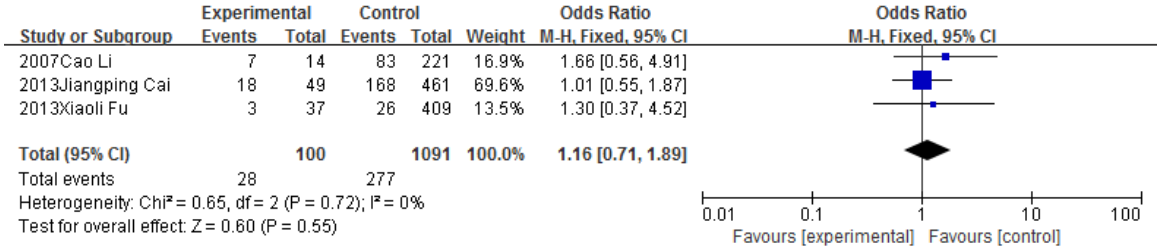
1.44 Family history of G2385R



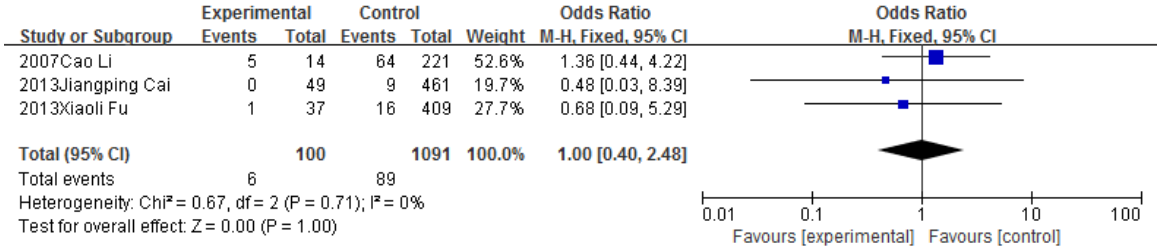
1.45 FS-Bradykinesia of G2385R



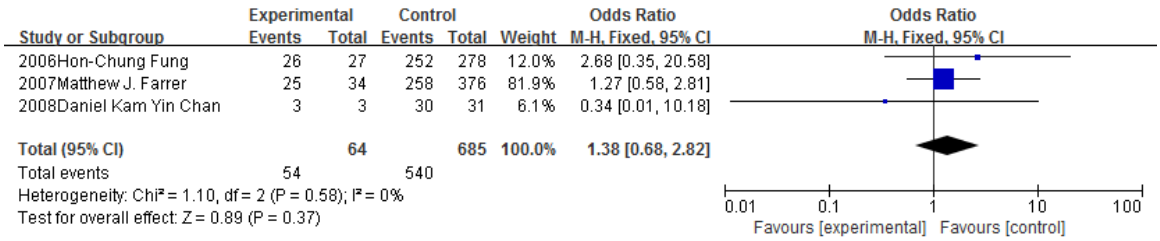
1.46 FS-Resting tremor of G2385R



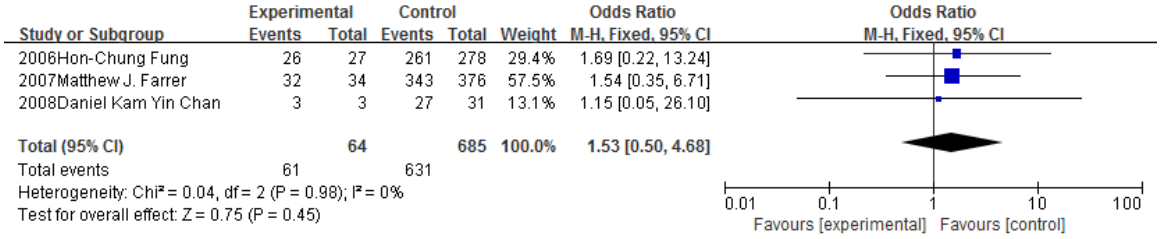
1.47 FS-Rigidity of G2385R



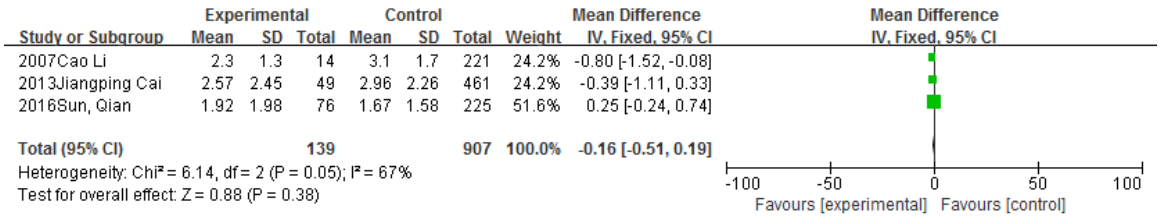
1.48 FS-Postural instability or Gait difficulty of G2385R



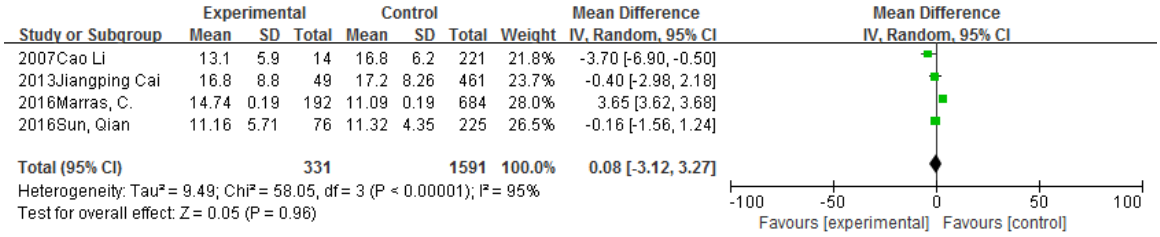
1.49 Resting tremor of G2385R



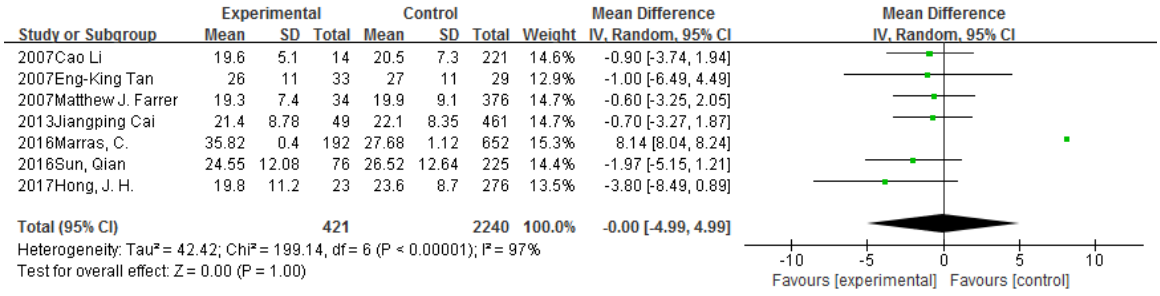
1.50 Rigidity of G2385R



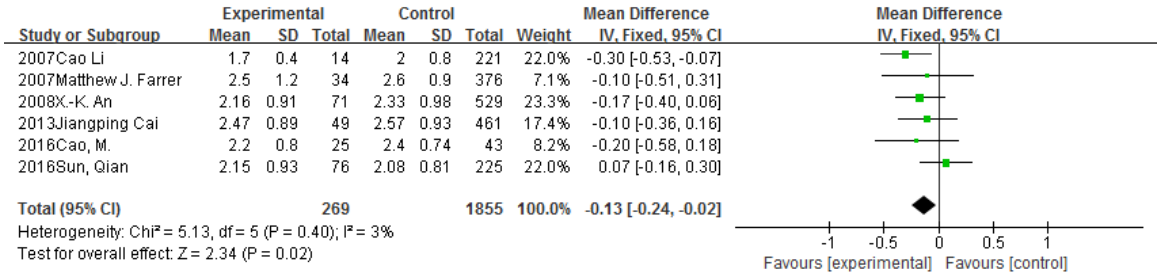
1.51 UPDRS Ⅰ of G2385R



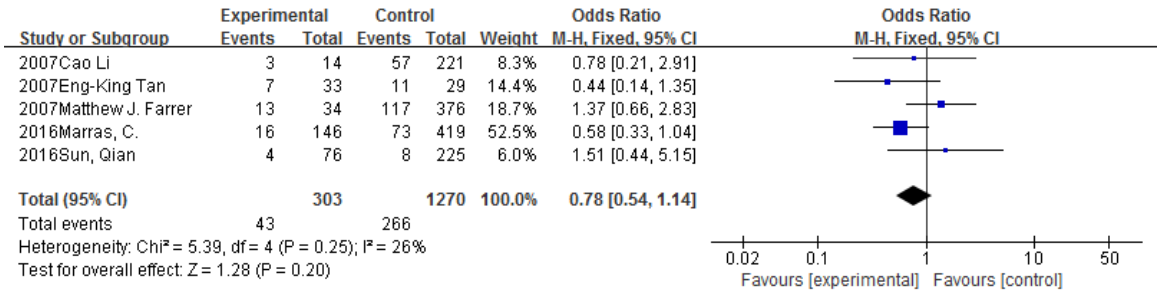
1.52 UPDRS Ⅱ of G2385R



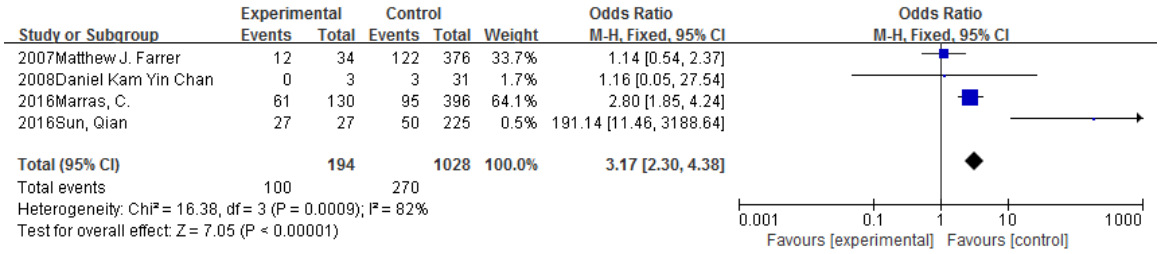
1.53 UPDRSⅢ of G2385R



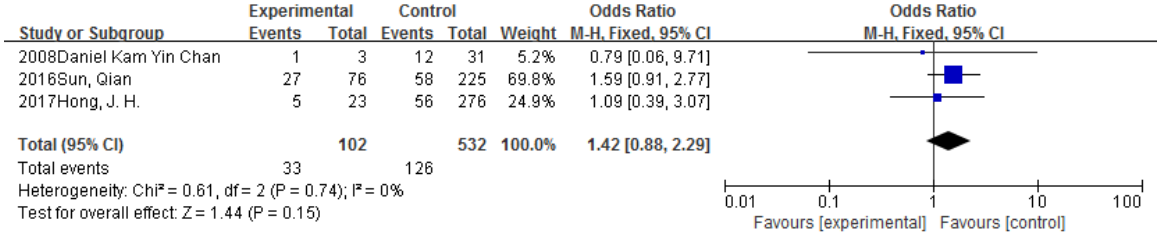
1.54 H-Y of G2385R



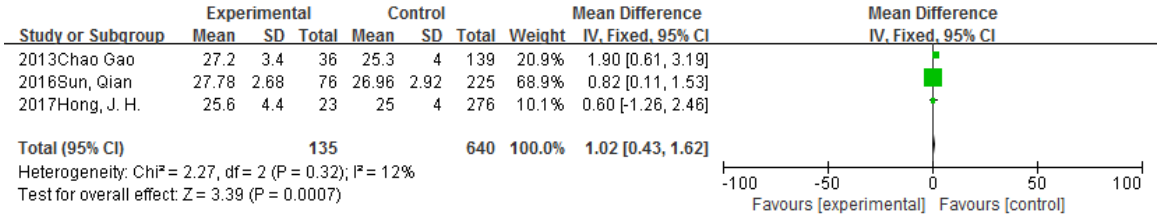
1.55 Dyskinesia of G2385R



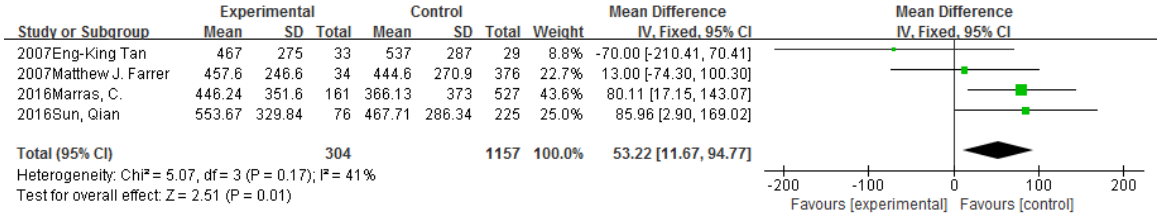
1.56 Motor fluctuations of G2385R



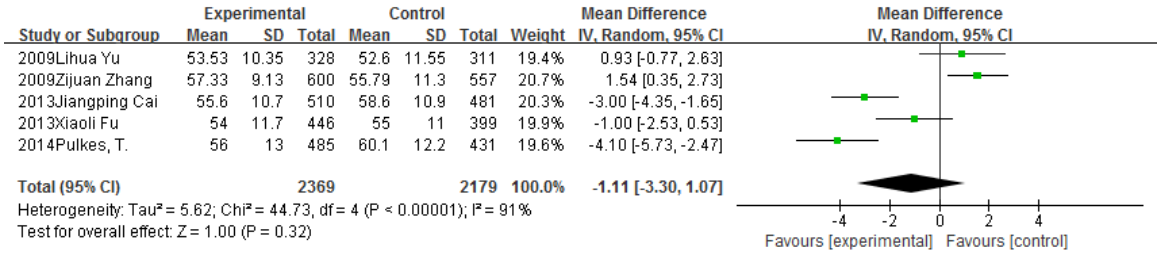
1.57 Depression of G2385R



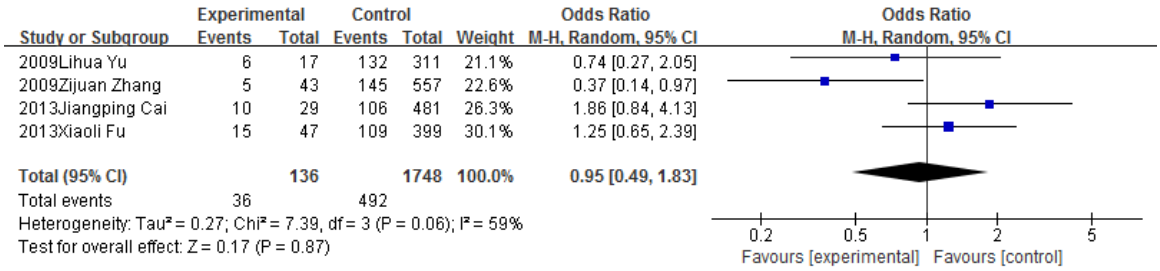
1.58 MMSE of G2385R



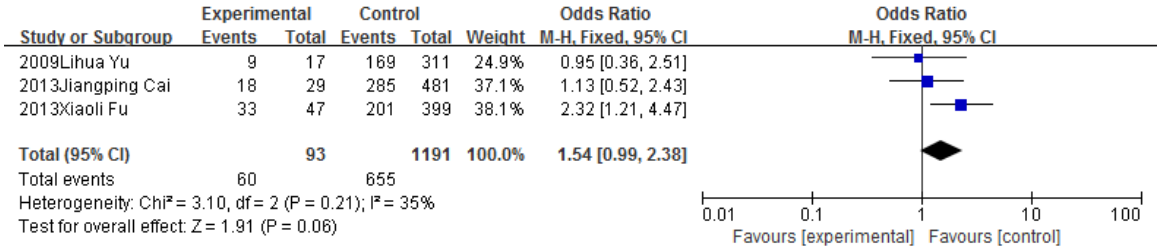
1.59 LEDD of G2385R



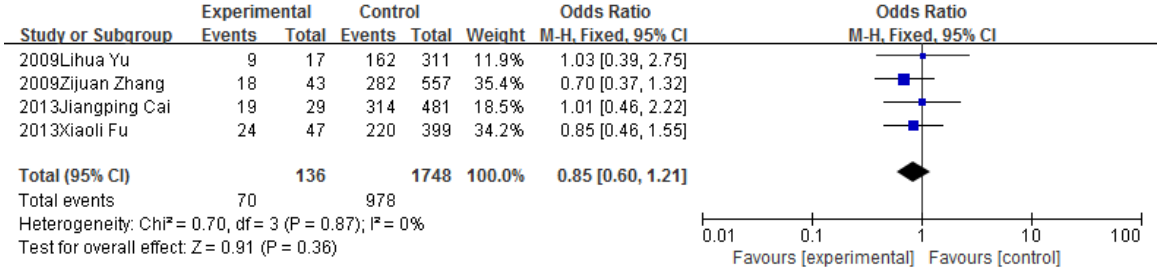
1.60 Age at onset of R1628P



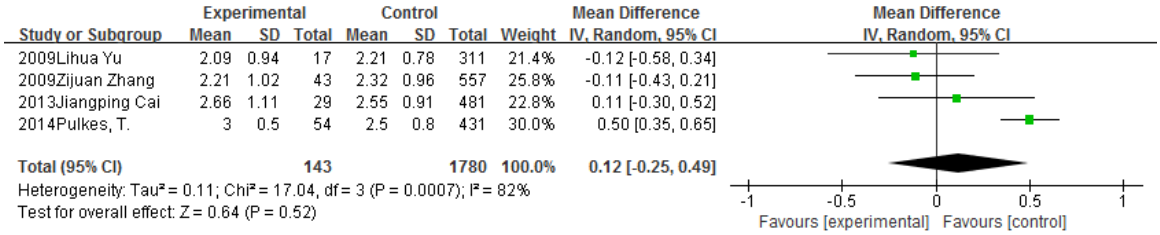
1.61 EOPD of R1628P



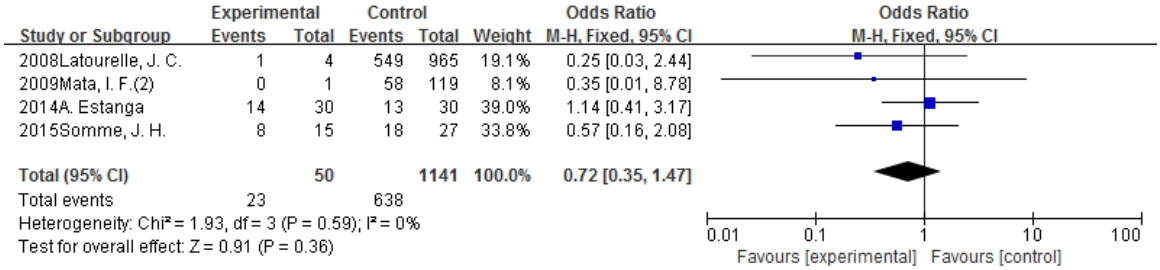
1.62 Gender-male of R1628P



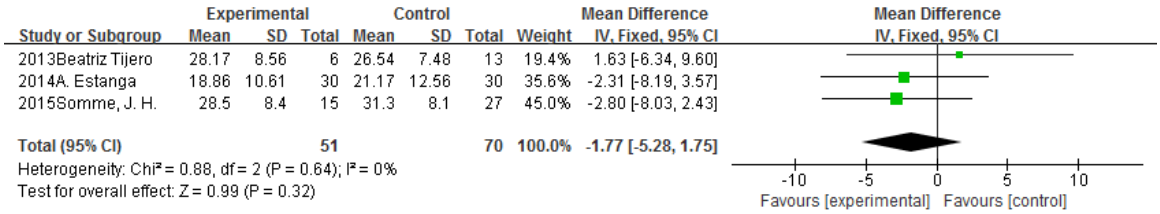
1.63 FS-Resting tremor of R1628P



1.64 H-Y of R1628P



1.65 Gender-male of R1441G



1.66 UPDRSⅢ of R1441G

Supplementary Figure 1. Forest plots of the association between specific variants in *LRRK2* and PD clinical features. 1.1-1.39 reflected the pooled results of G2019S-related clinical features.1.40-1.59 reflected the pooled results of G2385R-related clinical features. 1.60-1.64 represented the pooled results of R1628P-related clinical features. 1.65-1.66 represented the pooled results of R1441G-related clinical features.