Supplementary Material

A Comprehensive Analysis of Population Differences in *LRRK2* Variant Distribution in Parkinson's disease

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† These authors have contributed equally to this work and are co-first authors.

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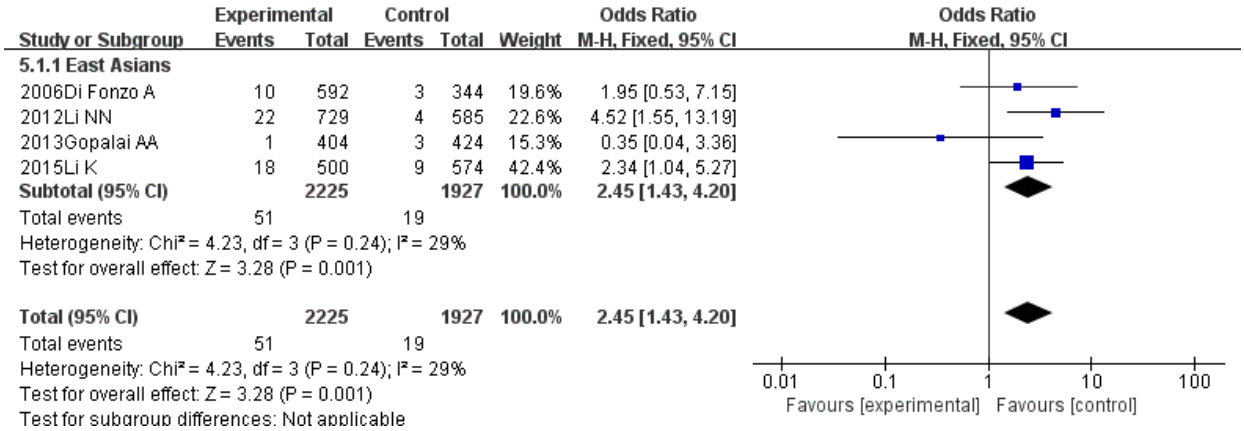
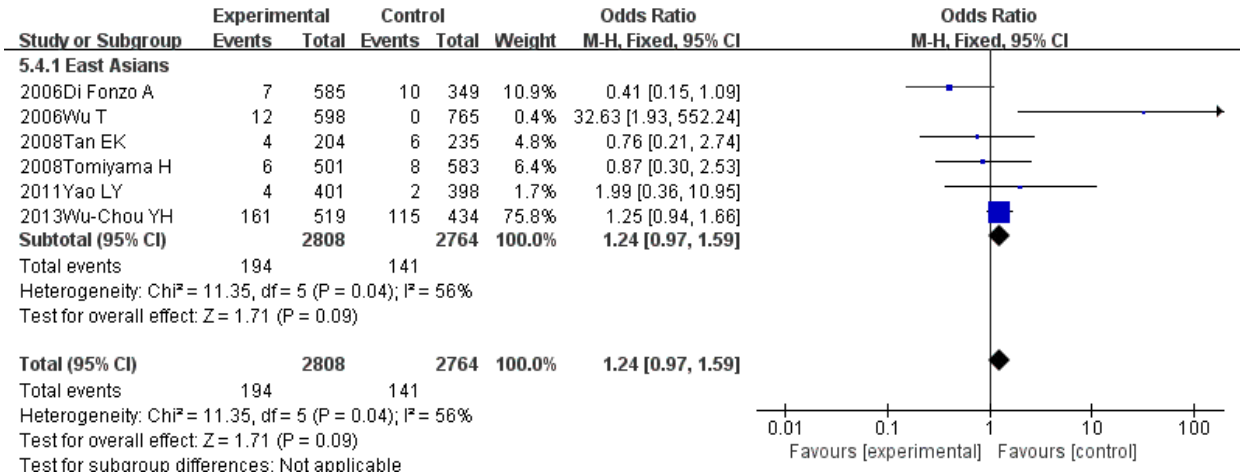
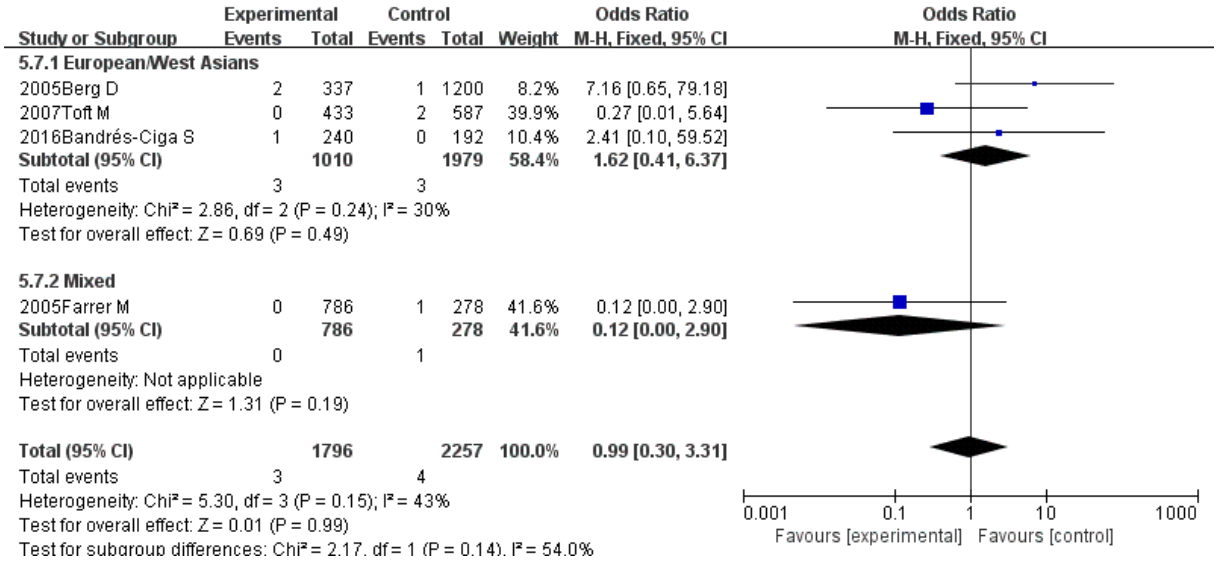
(A)



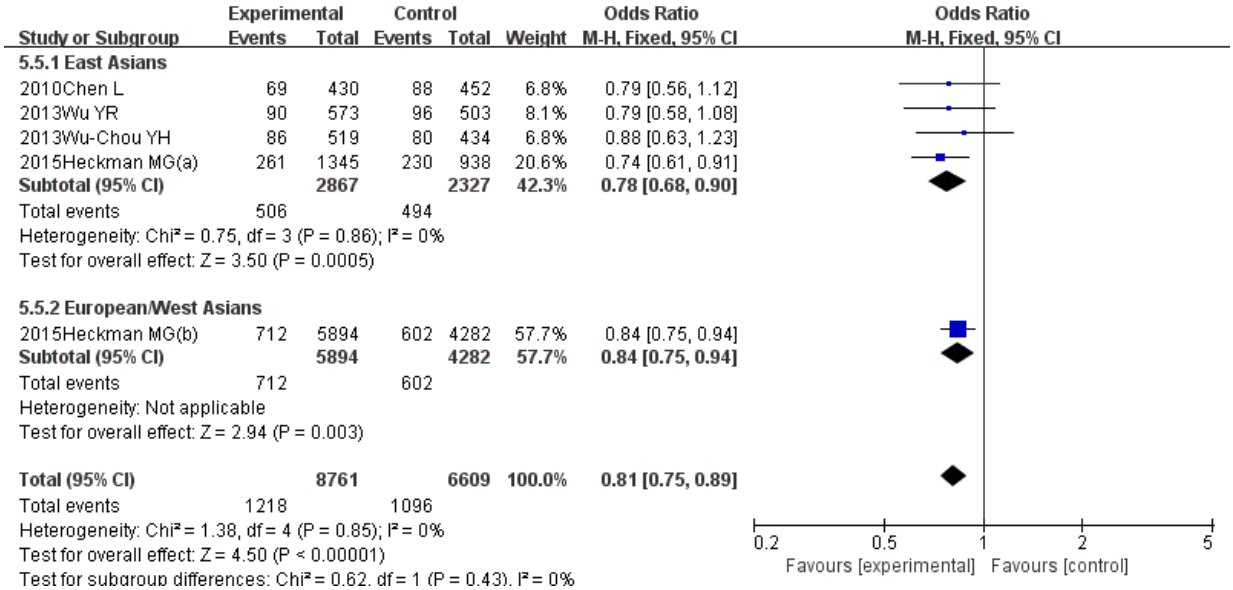
(B)



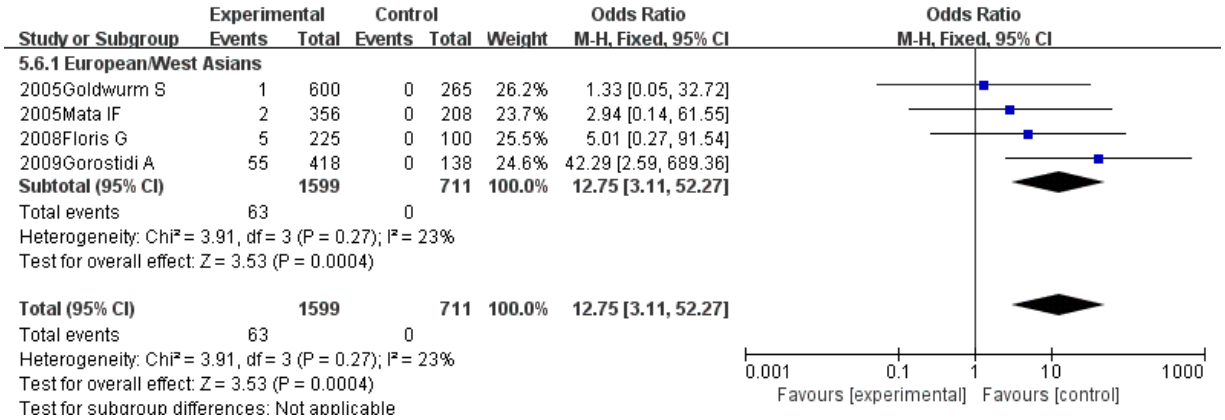
(C)


Experimental
Control
Odds Ratio
Odds Ratio
Study or Subgroup Events Total Events Total Weight M-H, Fixed, 95% CI
M-H, Fixed, 95% CI
5.7.1 European/West Asians
2005Berg D 2 337 1 1200 8.2% 7.16 [0.65, 79.18]
2007Toft M 0 433 2 587 39.9% 0.27 [0.01, 5.64]
2016Bandrés-Ciga S 1 240 0 192 10.4% 2.41 [0.10, 59.52]
Subtotal (95% CI) 1010 1979 58.4% 1.62 [0.41, 6.37]
Total events 3 3
Heterogeneity: Chi² = 2.86, df = 2 (P = 0.24); I² = 30%
Test for overall effect: Z = 0.69 (P = 0.49)
5.7.2 Mixed
2005Farrer M 0 786 1 278 41.6% 0.12 [0.00, 2.90]
Subtotal (95% CI) 786 278 41.6% 0.12 [0.00, 2.90]
Total events 0 1
Heterogeneity: Not applicable
Test for overall effect: Z = 1.31 (P = 0.19)
Total (95% CI) 1796 2257 100.0% 0.99 [0.30, 3.31]
Total events 3 4
Heterogeneity: Chi² = 5.30, df = 3 (P = 0.15); I² = 43%
Test for overall effect: Z = 0.01 (P = 0.99)
Test for subgroup differences: Chi² = 2.17, df = 1 (P = 0.14), I² = 54.0%
0.001
0.1
1
10
1000
Favours [experimental]
Favours [control]

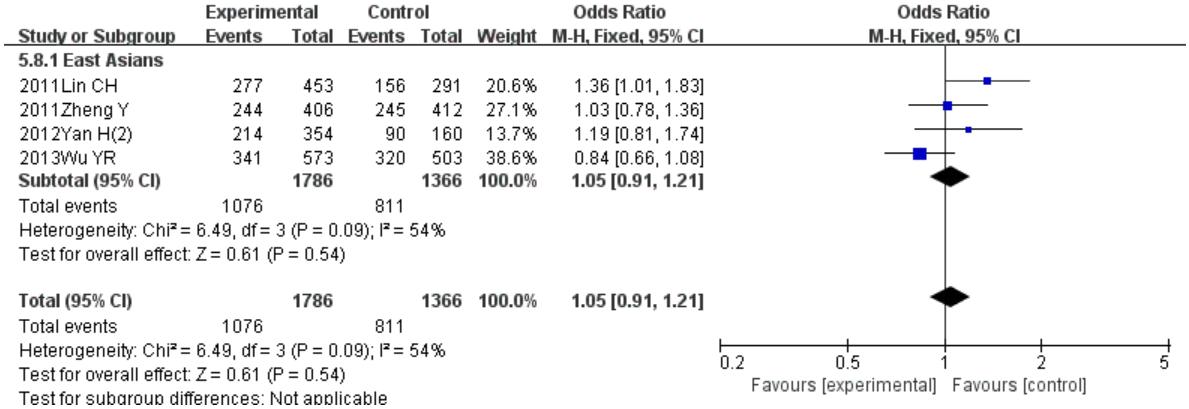
(D)


Experimental
Control
Odds Ratio
Odds Ratio
Study or Subgroup Events Total Events Total Weight M-H, Fixed, 95% CI
M-H, Fixed, 95% CI
5.5.1 East Asians
2010Chen L 69 430 88 452 6.8% 0.79 [0.56, 1.12]
2013Wu YR 90 573 96 503 8.1% 0.79 [0.58, 1.08]
2013Wu-Chou YH 86 519 80 434 6.8% 0.88 [0.63, 1.23]
2015Heckman MG(a) 261 1345 230 938 20.6% 0.74 [0.61, 0.91]
Subtotal (95% CI) 2867 2327 42.3% 0.78 [0.68, 0.90]
Total events 506 494
Heterogeneity: Chi² = 0.75, df = 3 (P = 0.86); I² = 0%
Test for overall effect: Z = 3.50 (P = 0.0005)
5.5.2 European/West Asians
2015Heckman MG(b) 712 5894 602 4282 57.7% 0.84 [0.75, 0.94]
Subtotal (95% CI) 5894 4282 57.7% 0.84 [0.75, 0.94]
Total events 712 602
Heterogeneity: Not applicable
Test for overall effect: Z = 2.94 (P = 0.003)
Total (95% CI) 8761 6609 100.0% 0.81 [0.75, 0.89]
Total events 1218 1096
Heterogeneity: Chi² = 1.38, df = 4 (P = 0.85); I² = 0%
Test for overall effect: Z = 4.50 (P < 0.00001)
Test for subgroup differences: Chi² = 0.62, df = 1 (P = 0.43), I² = 0%
0.2
0.5
1
2
5
Favours [experimental]
Favours [control]

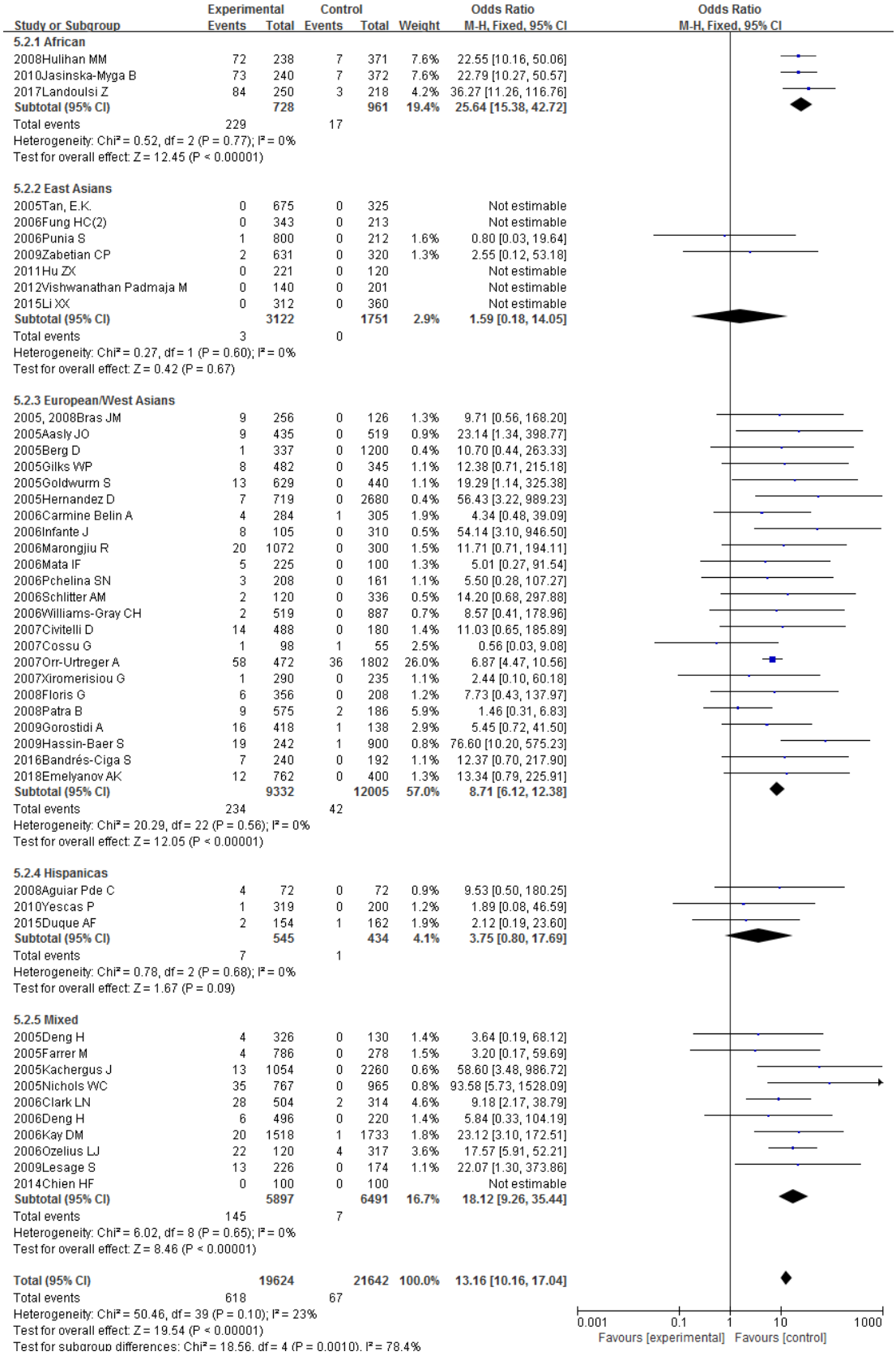
(E)


Experimental
Control
Odds Ratio
Odds Ratio
Study or Subgroup Events Total Events Total Weight M-H, Fixed, 95% CI
M-H, Fixed, 95% CI
5.6.1 European/West Asians
2005Goldwurm S 1 600 0 265 26.2% 1.33 [0.05, 32.72]
2005Mata IF 2 356 0 208 23.7% 2.94 [0.14, 61.55]
2008Floris G 5 225 0 100 25.5% 5.01 [0.27, 91.54]
2009Gorostidi A 55 418 0 138 24.6% 42.29 [2.59, 689.36]
Subtotal (95% CI) 1599 711 100.0% 12.75 [3.11, 52.27]
Total events 63 0
Heterogeneity: Chi² = 3.91, df = 3 (P = 0.27); I² = 23%
Test for overall effect: Z = 3.53 (P = 0.0004)
Total (95% CI) 1599 711 100.0% 12.75 [3.11, 52.27]
Total events 63 0
Heterogeneity: Chi² = 3.91, df = 3 (P = 0.27); I² = 23%
Test for overall effect: Z = 3.53 (P = 0.0004)
Test for subgroup differences: Not applicable
0.001
0.1
1
10
1000
Favours [experimental]
Favours [control]

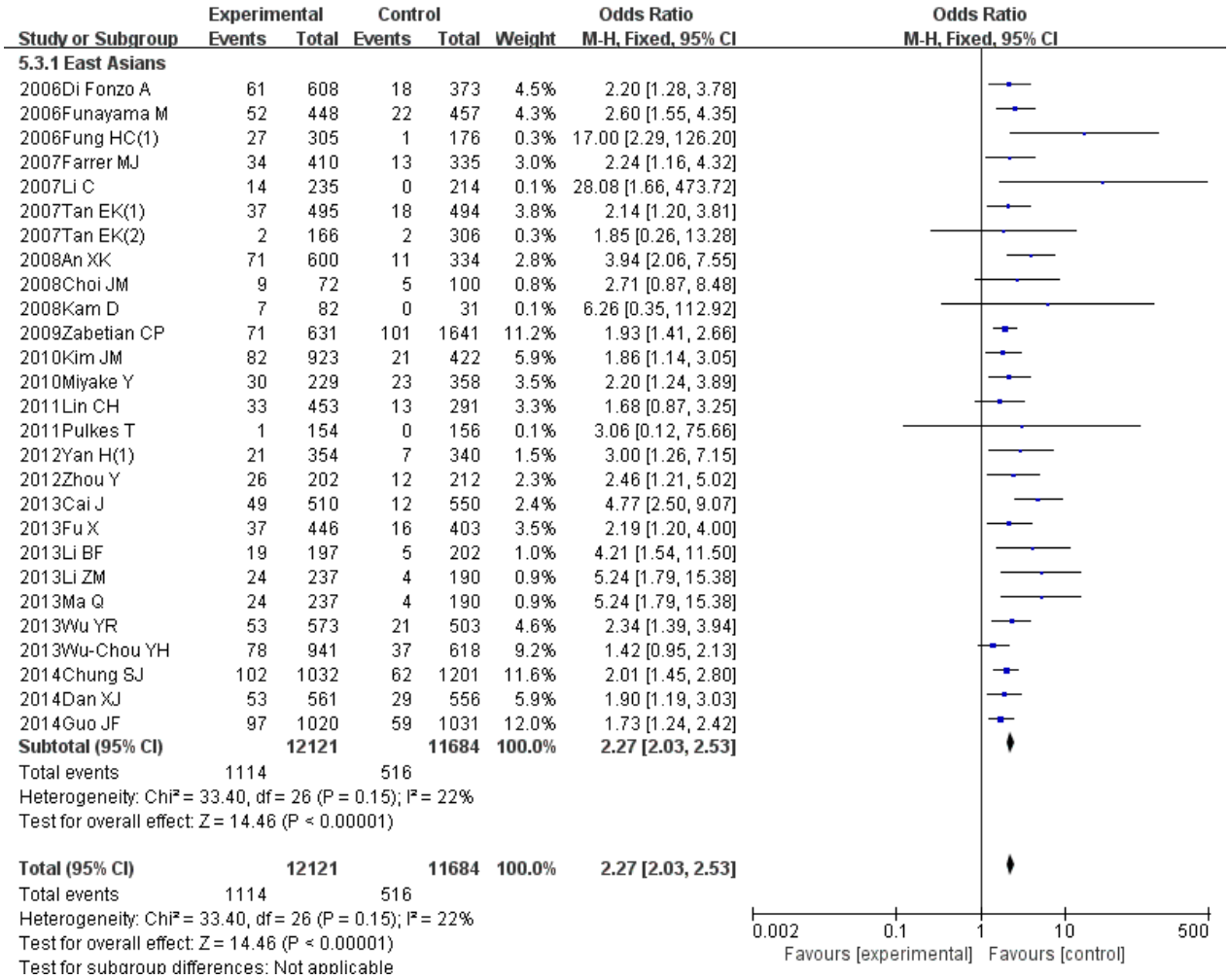
(F)


Experimental
Control
Odds Ratio
Odds Ratio
Study or Subgroup Events Total Events Total Weight M-H, Fixed, 95% CI
M-H, Fixed, 95% CI
5.8.1 East Asians
2011Lin CH 277 453 156 291 20.6% 1.36 [1.01, 1.83]
2011Zheng Y 244 406 245 412 27.1% 1.03 [0.78, 1.36]
2012Yan H(2) 214 354 90 160 13.7% 1.19 [0.81, 1.74]
2013Wu YR 341 573 320 503 38.6% 0.84 [0.66, 1.08]
Subtotal (95% CI) 1786 1366 100.0% 1.05 [0.91, 1.21]
Total events 1076 811
Heterogeneity: Chi² = 6.49, df = 3 (P = 0.09); I² = 54%
Test for overall effect: Z = 0.61 (P = 0.54)
Total (95% CI) 1786 1366 100.0% 1.05 [0.91, 1.21]
Total events 1076 811
Heterogeneity: Chi² = 6.49, df = 3 (P = 0.09); I² = 54%
Test for overall effect: Z = 0.61 (P = 0.54)
Test for subgroup differences: Not applicable
0.2
0.5
1
2
5
Favours [experimental]
Favours [control]

(G)


Experimental
Control
Odds Ratio
Odds Ratio
Study or Subgroup Events Total Events Total Weight M-H, Fixed, 95% CI
M-H, Fixed, 95% CI
5.2.1 African
2008Hulihan MM 72 238 7 371 7.6% 22.55 [10.16, 50.06]
2010Jasinska-Myga B 73 240 7 372 7.6% 22.79 [10.27, 50.57]
2017Landoulsi Z 84 250 3 218 4.2% 36.27 [11.26, 116.76]
Subtotal (95% CI) 728 961 19.4% 25.64 [15.38, 42.72]
Total events 229 17
Heterogeneity: Chi² = 0.52, df = 2 (P = 0.77); I² = 0%
Test for overall effect: Z = 12.45 (P < 0.00001)
5.2.2 East Asians
2005Tan, E.K. 0 675 0 325 Not estimable
2006Fung HC(2) 0 343 0 213 Not estimable
2006Punia S 1 800 0 212 1.6% 0.80 [0.03, 19.64]
2009Zabetian CP 2 631 0 320 1.3% 2.55 [0.12, 53.18]
2011Hu ZX 0 221 0 120 Not estimable
2012Vishwanathan Padmaja M 0 140 0 201 Not estimable
2015Li XX 0 312 0 360 Not estimable
Subtotal (95% CI) 3122 1751 2.9% 1.59 [0.18, 14.05]
Total events 3 0
Heterogeneity: Chi² = 0.27, df = 1 (P = 0.60); I² = 0%
Test for overall effect: Z = 0.42 (P = 0.67)
5.2.3 European/West Asians
2005, 2008Bras JM 9 256 0 126 1.3% 9.71 [0.56, 168.20]
2005Aasly JO 9 435 0 519 0.9% 23.14 [1.34, 398.77]
2005Berg D 1 337 0 1200 0.4% 10.70 [0.44, 263.33]
2005Gilks WP 8 482 0 345 1.1% 12.38 [0.71, 215.18]
2005Goldwurm S 13 629 0 440 1.1% 19.29 [1.14, 325.38]
2005Hernandez D 7 719 0 2680 0.4% 56.43 [3.22, 989.23]
2006Carmine Belin A 4 284 1 305 1.9% 4.34 [0.48, 39.09]
2006Infante J 8 105 0 310 0.5% 54.14 [3.10, 946.50]
2006Marongjiu R 20 1072 0 300 1.5% 11.71 [0.71, 194.11]
2006Mata IF 5 225 0 100 1.3% 5.01 [0.27, 91.54]
2006Pchelina SN 3 208 0 161 1.1% 5.50 [0.28, 107.27]
2006Schlitter AM 2 120 0 336 0.5% 14.20 [0.68, 297.88]
2006Williams-Gray CH 2 519 0 887 0.7% 8.57 [0.41, 178.96]
2007Civitelli D 14 488 0 180 1.4% 11.03 [0.65, 185.89]
2007Cossu G 1 98 1 55 2.5% 0.56 [0.03, 9.08]
2007Orr-Urtreger A 58 472 36 1802 26.0% 6.87 [4.47, 10.56]
2007Xiromerisiou G 1 290 0 235 1.1% 2.44 [0.10, 60.18]
2008Floris G 6 356 0 208 1.2% 7.73 [0.43, 137.97]
2008Patra B 9 575 2 186 5.9% 1.46 [0.31, 6.83]
2009Gorostidi A 16 418 1 138 2.9% 5.45 [0.72, 41.50]
2009Hassin-Baer S 19 242 1 900 0.8% 76.60 [10.20, 575.23]
2016Bandrés-Ciga S 7 240 0 192 1.1% 12.37 [0.70, 217.90]
2018Emelyanov AK 12 762 0 400 1.3% 13.34 [0.79, 225.91]
Subtotal (95% CI) 9332 12005 57.0% 8.71 [6.12, 12.38]
Total events 234 42
Heterogeneity: Chi² = 20.29, df = 22 (P = 0.56); I² = 0%
Test for overall effect: Z = 12.05 (P < 0.00001)
5.2.4 Hispanicas
2008Aguiar Pde C 4 72 0 72 0.9% 9.53 [0.50, 180.25]
2010Yescas P 1 319 0 200 1.2% 1.89 [0.08, 46.59]
2015Duque AF 2 154 1 162 1.9% 2.12 [0.19, 23.60]
Subtotal (95% CI) 545 434 4.1% 3.75 [0.80, 17.69]
Total events 7 1
Heterogeneity: Chi² = 0.78, df = 2 (P = 0.68); I² = 0%
Test for overall effect: Z = 1.67 (P = 0.09)
5.2.5 Mixed
2005Deng H 4 326 0 130 1.4% 3.64 [0.19, 68.12]
2005Farrer M 4 786 0 278 1.5% 3.20 [0.17, 59.69]
2005Kachergus J 13 1054 0 2260 0.6% 58.60 [3.48, 986.72]
2005Nichols WC 35 767 0 965 0.8% 93.58 [5.73, 1528.09]
2006Clark LN 28 504 2 314 4.6% 9.18 [2.17, 38.79]
2006Deng H 6 496 0 220 1.4% 5.84 [0.33, 104.19]
2006Kay DM 20 1518 1 1733 1.8% 23.12 [3.10, 172.51]
2006Ozelius LJ 22 120 4 317 3.6% 17.57 [5.91, 52.21]
2009Lesage S 13 226 0 174 1.1% 22.07 [1.30, 373.86]
2014Chien HF 0 100 0 100 Not estimable
Subtotal (95% CI) 5897 6491 16.7% 18.12 [9.26, 35.44]
Total events 145 7
Heterogeneity: Chi² = 6.02, df = 8 (P = 0.65); I² = 0%
Test for overall effect: Z = 8.46 (P < 0.00001)
Total (95% CI) 19624 21642 100.0% 13.16 [10.16, 17.04]
Total events 618 67
Heterogeneity: Chi² = 50.46, df = 39 (P = 0.10); I² = 23%
Test for overall effect: Z = 19.54 (P < 0.00001)
Test for subgroup differences: Chi² = 18.56, df = 4 (P = 0.0010), I² = 78.4%
0.001
0.1
1
10
1000
Favours [experimental]
Favours [control]

(H)



Supplementary Figure 1(A-H). Forest plots of the association between *LRRK2* variants and PD risks in total population and by ethnicity. (A)-(H) represented the pooled results of A419V, P755L, R793M, R1398H, R1441C/G/H, S1647T, G2019S, G2385R variants separately.