

Supplementary Material

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

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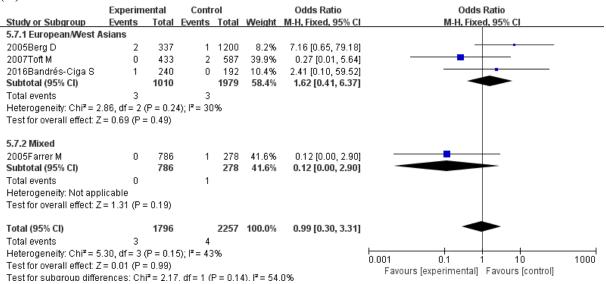
(A)

| | Experim | ental | Contr | ol | | Odds Ratio | Odds Ratio |
|-----------------------------------|-------------|----------|-----------------|-------|--|--------------------|--|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Fixed, 95% CI | M-H, Fixed, 95% CI |
| 5.1.1 East Asians | | | | | | | |
| 2006Di Fonzo A | 10 | 592 | 3 | 344 | 19.6% | 1.95 [0.53, 7.15] | |
| 2012Li NN | 22 | 729 | 4 | 585 | 22.6% | 4.52 [1.55, 13.19] | |
| 2013Gopalai AA | 1 | 404 | 3 | 424 | 15.3% | 0.35 [0.04, 3.36] | - |
| 2015Li K | 18 | 500 | 9 | 574 | 42.4% | 2.34 [1.04, 5.27] | |
| Subtotal (95% CI) | | 2225 | | 1927 | 100.0% | 2.45 [1.43, 4.20] | • |
| Total events | 51 | | 19 | | | | |
| Heterogeneity: Chi²= | 4.23, df= | 3(P = 0) | $.24); I^2 = 0$ | 29% | | | |
| Test for overall effect: | Z = 3.28 (F | P = 0.00 | 1) | | | | |
| Total (95% CI) | | 2225 | | 1927 | 100.0% | 2.45 [1.43, 4.20] | • |
| Total events | 51 | | 19 | | | | |
| Heterogeneity: Chi ² = | 4.23, df= | 3(P = 0) | $.24); I^2 = 0$ | 29% | | | 0.01 0.1 1 10 100 |
| Test for overall effect: | Z = 3.28 (F | P = 0.00 | 1) | | Favours [experimental] Favours [control] | | |
| Test for subaroup diff | erences: N | laas tok | icable | | | | ravours (experimental) ravours (control) |

(B)

| | Experim | ental | Contr | Control | | Odds Ratio | Odds Ratio | |
|--------------------------|-------------|----------|-------------|---------|--------|----------------------|--|----------|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Fixed, 95% CI | M-H, Fixed, 95% CI | |
| 5.4.1 East Asians | | | | | | | | |
| 2006Di Fonzo A | 7 | 585 | 10 | 349 | 10.9% | 0.41 [0.15, 1.09] | - | |
| 2006Wu T | 12 | 598 | 0 | 765 | 0.4% | 32.63 [1.93, 552.24] | | → |
| 2008Tan EK | 4 | 204 | 6 | 235 | 4.8% | 0.76 [0.21, 2.74] | | |
| 2008Tomiyama H | 6 | 501 | 8 | 583 | 6.4% | 0.87 [0.30, 2.53] | | |
| 2011Yao LY | 4 | 401 | 2 | 398 | 1.7% | 1.99 [0.36, 10.95] | | |
| 2013Wu-Chou YH | 161 | 519 | 115 | 434 | 75.8% | 1.25 [0.94, 1.66] | <u></u> | |
| Subtotal (95% CI) | | 2808 | | 2764 | 100.0% | 1.24 [0.97, 1.59] | • | |
| Total events | 194 | | 141 | | | | | |
| Heterogeneity: Chi²= | 11.35, df= | 5 (P = | 0.04); | : 56% | | | | |
| Test for overall effect: | Z = 1.71 (F | P = 0.09 |) | | | | | |
| Total (95% CI) | | 2808 | | 2764 | 100.0% | 1.24 [0.97, 1.59] | ◆ | |
| Total events | 194 | | 141 | | | | | |
| Heterogeneity: Chi²= | 11.35, df= | 5 (P= | 0.04); l² = | 56% | | | 0.01 0.1 1 10 | 100 |
| Test for overall effect: | Z = 1.71 (8 | P = 0.09 |) | | | | Favours [experimental] Favours [control] | 100 |
| Test for subaroup diff | ferences: N | laas tol | icable | | | | r avours [experimental] Travours [control] | |

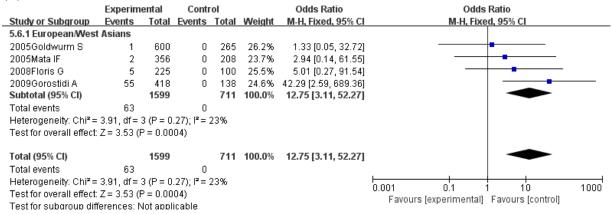
(C)



(D)

| | Experim | ental | Contr | ol | | 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 | 5); I² = 0% | 6 | | | |
| Test for overall effect: Z | = 3.50 (P = | 0.0005 | 5) | | | | |
| 5.5.2 European/West A | sians | | | | | | |
| 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 appli | icable | | | | | | |
| 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 = 0.89 | 5); I² = 0% | 6 | | | |
| Test for overall effect: Z: | = 4.50 (P < | 0.0000 | 11) | | | 0.2 0.5 1 2 5 | |
| Test for subaroup differ | ancae: Chi | i= - 0.62 | df = 1 /F | 2 – n 43 | n i≥ – nov. | | Favours [experimental] Favours [control] |





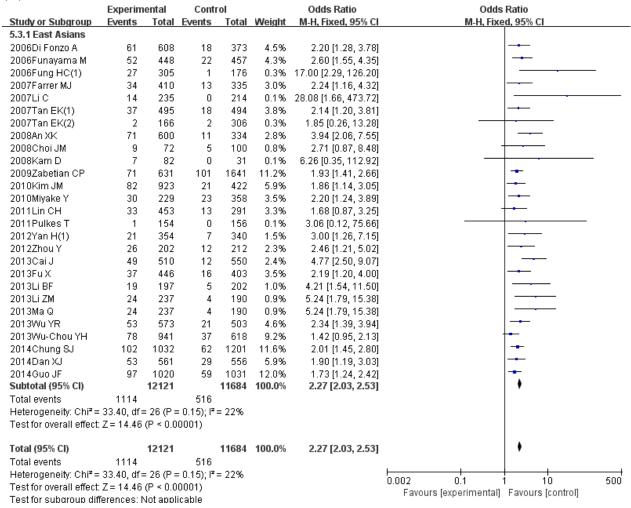
(F)

| | Experim | ental | Contr | ol | | Odds Ratio | Odds Ratio |
|-----------------------------------|-------------|-----------|--|---------------|--------|--|--------------------|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Fixed, 95% Cl | 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=1 | 3 (P = 0) | $.09$); $I^2 = 3$ | 54% | | | |
| Test for overall effect: | Z = 0.61 (F | P = 0.54 |) | | | | |
| Total (95% CI) | | 1786 | | 1366 | 100.0% | 1.05 [0.91, 1.21] | * |
| Total events | 1076 | | 811 | | | | |
| Heterogeneity: Chi ² = | 6.49, df= | 3 (P = 0. | .09); l² = : | 0.2 0.5 1 2 5 | | | |
| Test for overall effect: | Z = 0.61 (F | P = 0.54 | Favours [experimental] Favours [control] | | | | |
| Test for subaroup diff | erences: N | laas tok | icable | | | ravours (experimental) Favours (control) | |

(G)

| Combine Company Comp | (G) | | | | | | | |
|--|---------------------------------------|--------------|-------------|---------|------------|---------|----------------------|--|
| 5.2.1 African 2010 Liurionis Migo 72 230 7 371 7.6% 22.5 (1016, 50.06) 2010 Liurionis Migo 77 240 7 372 7.6% 22.5 (1016, 50.06) 2010 Liurionis Migo 77 240 7 372 7.6% 22.5 (1016, 50.06) 2010 Liurionis Migo 77 240 7 372 7.6% 22.5 (1016, 50.06) 2010 Liurionis Migo 77 240 7 372 7.6% 22.5 (1016, 50.06) 2010 Liurionis Migo 77 240 9 4 18.4% 25.6 (115.3%, 42.72) 2010 Liurionis Migo 77 24 9 4 18.4% 25.6 (115.3%, 42.72) 2010 Liurionis Migo 77 24 9 4 18.4% 25.6 (115.3%, 42.72) 2010 Liurionis Migo 77 24 18.4% 25.6 (115.3%, 42.72) 2010 Liurionis Migo 77 24 18.4% 25.6 (115.3%, 42.72) 2010 Liurionis Migo 77 24 18.4% 25.6 (115 | Chudu or Cult | - | | | | M-5-17 | | |
| 2000FunishmeNM | | Events | rotal | Events | rotal | vveight | M-H, FIXED, 95% CI | M-H, FIXEd, 95% CI |
| 29 OLD A STAN STAN STAN STAN STAN STAN STAN ST | | 72 | 220 | 7 | 271 | 7 6 96 | 22.55 (40.46.50.06) | |
| 29171-Amounts Z 94 | | | | | | | | |
| Subblack (9% CG) 78 961 19.4% 25.64 [15.38, 42.72] **Total events** Total events** Total events** Total events** Total events** Total events** Total events** **Total | | | | | | | | _ |
| Total events Fig. 23 Total versets Fig. 23 Total versets Fig. 25 Total versets Fig. 25 Total versets Fig. 25 Total versets Fig. 26 Total versets Fig. 26 Total versets Fig. 26 Total versets Fig. 27 Total v | | | | _ | | | | • |
| Test for ewarl effect \$Z = 12.45 (\$P < 0.00001) 2.00 Fan, EX | Total events | 229 | | 17 | | | | |
| 5.2.2 East Asians 2005Trag, EK. 2005Trag, EK | Heterogeneity: Chi² = 0.52, df = 2 | (P = 0.77); | l² = 0% | | | | | |
| 2005Fing EK | Test for overall effect: Z = 12.45 (F | o < 0.00001 | 1) | | | | | |
| 2005Fing EK | 5005 44: | | | | | | | |
| 2006Funish CC 0 343 0 213 Note-estimable | | | 075 | | 005 | | N - 4 40 1-1 - | |
| 2006Punis S | | | | | | | | |
| 20052-betian OP | | | | | | 1 606 | | |
| 2011 Hu Z/S | | | | | | | | |
| 2015 Harvaranthan Fadmaja M | | | | | | 1.570 | | |
| 2015LIX | | | | | | | | |
| Subtoal (95% C) | | | | | | | | |
| Heletopean/West Asians 2005, 2008/Rsa JM 9 256 0 126 1.3% 9.71 [0.56, 168.20] 2005/Assy JO 9 4.35 0 120 0.4% 17.70 [0.44, 263.33] 2005/Assy JO 9 4.35 0 120 0.4% 120 0.4% 17.70 [0.44, 263.33] 2005/Assy JO 9 4.35 0 120 0.4% 17.70 [0.44, 263.33] 2005/Assy JO 9 120 0.4% 120 0.4% 120 0.4% 17.70 [0.44, 263.33] 2005/Assy JO 9 120 0.4% | Subtotal (95% CI) | | 3122 | | 1751 | 2.9% | 1.59 [0.18, 14.05] | |
| Test for overall effect Z = 0.42 (P = 0.67) 5.2.3 European/West Asians 2005, 2008Brs a.M 9 256 0 128 1.3% 9.71 [0.56, 168.20] 2005Assy JO 9 435 0 519 0.9% 23.14 [1.34, 39.77] 2005Berg D 1 337 0 1200 0.4% 10.70 [0.44, 263.33] 2005Berg D 1 337 0 1200 0.4% 10.70 [0.44, 263.33] 2005Berg D 1 337 0 1200 0.4% 10.70 [0.44, 263.33] 2005Berg D 1 3 3 628 0 440 1.1% 12.8 [0.71, 215.18] 2005Berg D 1 3 62 0 440 1.1% 12.8 [0.71, 215.18] 2005Berg D 1 3 62 0 440 1.1% 12.8 [0.71, 215.18] 2005Berg D 1 3 62 0 440 1.1% 12.8 [0.71, 215.18] 2005Berg D 1 3 62 0 440 1.1% 12.8 [0.71, 215.18] 2005Berg D 1 3 62 0 440 1.1% 12.8 [0.71, 215.18] 2005Berg D 1 3 62 0 440 1.1% 12.8 [0.71, 215.18] 2005Berg D 1 3 62 0 440 1.1% 12.8 [0.71, 215.18] 2005Berg D 1 3 62 0 3 0 440 1.1% 12.2 [0.71, 215.18] 2005Berg D 1 3 62 0 3 0 440 1.1% 12.2 [0.71, 215.18] 2005Berg D 1 3 62 0 3 0 440 1.1% 12.2 [0.71, 215.18] 2005Berg D 1 3 62 0 3 0 440 1.1% 12.2 [0.71, 215.18] 2005Berg D 1 3 0 887 0.7% 12.8 [0.71, 215.18] 2006Berg D 1 3 0 887 0.7% 12.8 [0.71, 215.18] 2006Berg D 1 3 0 887 0.7% 12.8 [0.71, 215.18] 2006Berg D 1 3 0 887 0.7% 12.2 [0.71, 215.18] 2006Berg D 1 3 0 887 0.7% 12.2 [0.71, 215.18] 2006Berg D 1 3 0 887 0.7% 12.2 [0.71, 215.18] 2006Berg D 1 3 0 887 0.7% 12.2 [0.71, 215.18] 2006Berg D 1 3 0 887 0.7% 12.2 [0.71, 215.18] 2007Croftellian D 1 4 480 0 180 1.1% 13.0 [0.71, 215.18] 2007Croftellian D 1 4 480 0 180 1.1% 13.0 [0.71, 215.18] 2007Croftellian D 1 4 480 0 180 1.1% 13.0 [0.71, 215.18] 2007Croftellian D 1 4 480 0 180 1.1% 13.0 [0.71, 215.18] 2007Croftellian D 1 4 480 0 180 1.1% 13.0 [0.71, 215.18] 2007Croftellian D 1 4 480 0 180 1.1% 13.0 [0.71, 215.18] 2007Croftellian D 1 4 480 0 180 1.1% 13.0 [0.71, 215.18] 2007Croftellian D 1 4 480 0 180 1.1% 13.0 [0.71, 215.18] 2007Croftellian D 1 4 480 0 180 1.1% 13.0 [0.71, 215.18] 2007Croftellian D 1 4 480 0 180 1.1% 13.0 [0.71, 215.18] 200Floris D 1 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 | Total events | 3 | | 0 | | | | |
| 5.2.3 European/West Asians 2005, 2008Fras JM 9 256 0 126 1.3% 9.71 [0.56, 168.20] 2005Aasiy.JO 9 4.35 0 519 0.9% 23.14 [1.34, 398.77] 2005Brag D 1 3 37 0 1200 0.4% 10.70 [0.44, 263.33] | Heterogeneity: Chi² = 0.27, df = 1 | (P = 0.60); | l² = 0% | | | | | |
| 2005-RashyJO 9 435 0 519 0.9 2314 [13.4] 398.77 2005-RashyJO 9 435 0 519 0.9 2314 [13.4] 398.77 2005-RashyJO 9 435 0 519 0.9 2314 [13.4] 398.77 2005-RashyJO 9 435 0 519 0.9 2314 [13.4] 398.77 2005-RashyJO 9 435 0 519 0.9 2314 [13.4] 398.77 2005-RashyJO 9 435 0 519 0.9 2314 [13.4] 233.33 2005-RashyJO 9 435 0 345 1.1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 | Test for overall effect: Z = 0.42 (P | = 0.67) | | | | | | |
| 2005-RashyJO 9 435 0 519 0.9 2314 [13.4] 398.77 2005-RashyJO 9 435 0 519 0.9 2314 [13.4] 398.77 2005-RashyJO 9 435 0 519 0.9 2314 [13.4] 398.77 2005-RashyJO 9 435 0 519 0.9 2314 [13.4] 398.77 2005-RashyJO 9 435 0 519 0.9 2314 [13.4] 398.77 2005-RashyJO 9 435 0 519 0.9 2314 [13.4] 233.33 2005-RashyJO 9 435 0 345 1.1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 | E 2 2 Funny 241 | | | | | | | |
| 200569eryD 1 337 0 1200 0.4% 1070 [0.44, 263.33] 200560lks WP 8 8 492 0 345 1.1% 12.38 [0.71, 215.18] 200560lks WP 8 8 492 0 345 1.1% 12.38 [0.71, 215.18] 200560lks WP 8 8 492 0 345 1.1% 12.38 [0.71, 215.18] 200560lks WP 8 8 492 0 345 1.1% 12.38 [0.71, 215.18] 200560lks WP 8 8 492 0 345 1.1% 12.38 [0.71, 215.18] 200560lks WP 8 8 492 0 345 1.1% 12.38 [0.71, 215.18] 200560lks WP 8 8 492 0 345 1.1% 12.38 [0.71, 215.18] 200560lks WP 8 8 492 0 345 1.1% 12.38 [0.71, 215.18] 200560lks WP 8 8 492 0 345 1.1% 12.38 [0.71, 215.18] 200560lks WP 8 8 492 0 310 0.5% 54.14 [3.10, 946.50] 200560lks WP 9 8 405 0 310 0.5% 54.14 [3.10, 946.50] 20060lks WP 9 8 405 0 310 0.5% 54.14 [3.10, 946.50] 20060lks WP 9 8 405 0 30 0.5% 14.20 [0.72, 915.4] 20060lks WP 9 8 405 0 30 0.5% 14.20 [0.72, 915.4] 20060lks WP 9 8 405 0 30 0.5% 14.20 [0.72, 915.4] 20060lks WP 9 8 405 0 30 0.5% 14.20 [0.72, 915.4] 20060lks WP 9 8 405 0 30 0.5% 14.20 [0.72, 915.4] 20060lks WP 9 8 405 0 30 0.5% 14.20 [0.72, 915.4] 20060lks WP 9 8 405 0 30 0.5% 14.20 [0.72, 915.4] 20060lks WP 9 8 405 0 30 0.5% 14.20 [0.72, 915.4] 20060lks WP 9 8 405 0 30 0.5% 14.20 [0.72, 915.4] 2007Coseu G 1 98 1 55 2.5% 0.66 [0.03, 908] 2007Coseu G 1 98 1 55 2.5% 0.66 [0.03, 908] 2007Coseu G 1 98 1 55 2.5% 0.66 [0.03, 908] 2007Coseu G 1 98 1 55 2.5% 0.66 [0.03, 908] 2007Coseu G 1 98 1 55 2.5% 0.66 [0.03, 908] 2007Coseu G 1 98 1 55 2.5% 0.66 [0.03, 908] 2007Coseu G 1 98 1 55 2.20 0.20 0.20 0.20 0.20 0.20 0.20 0 | | | 250 | _ | 400 | 4.00 | 0.74 (0.50 400 000 | |
| 20056liks WP 8 842 0 345 11% 12.28 17.12 1.38 1.29 0 1.20 0.5 41.4 1.23 0.25 17.2 1.5 18 1.20 0.25 0.05 0.4 1.20 0.25 1.2 1.2 1.2 1.2 1.2 1.2 1.2 1.2 1.2 1.2 | • | | | | | | | |
| 2005Geldisw MP | , | | | | | | | |
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| 2006Matal F | | | | | | | | |
| 2008Adas F | 2006Marongiju R | | | | | | | |
| 2008-chiller AM 2 1 20 0 33 0.5% 14.20 [0.89, 297.89] 2008-chiller AM 2 1 20 0 38 0.5% 14.20 [0.89, 297.89] 2008-chiller AM 2 1 20 0 38 0.5% 14.20 [0.89, 297.89] 2007-Chiller BD 14 488 0 180 1.4% 11.30 [0.65, 186.89] 2007-Chiller BD 14 488 0 180 1.4% 11.30 [0.65, 186.89] 2007-Chiller BD 14 488 0 180 1.4% 11.30 [0.65, 186.89] 2007-Chiller BD 14 488 0 180 1.4% 11.30 [0.65, 186.89] 2007-Chiller BD 15 4 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 | - - | | 225 | 0 | 100 | | | |
| 2000Fideliams - Gray CH | 2006Pchelina SN | 3 | 208 | 0 | 161 | 1.1% | | - · · · · · · · · · · · · · · · · |
| 2007Cossu G 1 98 1 55 2.5% 0.56 [0.03, 0.08] 2007Corsu G 1 98 1 55 2.5% 0.56 [0.03, 0.08] 2007Corsu G 1 98 1 55 2.5% 0.56 [0.03, 0.08] 2007Corsu G 1 290 0 235 1.1% 2.44 [0.10, 6.018] 2007Corometisiou G 1 290 0 235 1.1% 2.44 [0.10, 6.018] 2007Corometisiou G 1 290 0 235 1.1% 2.44 [0.10, 6.018] 2008Floris G 6 356 0 208 1.2% 7.73 [0.43, 137.97] 2008Ploris G 6 356 0 208 1.2% 7.73 [0.43, 137.97] 2008Ploris G 6 356 0 208 1.2% 7.73 [0.43, 137.97] 2008Ploris G 7 2 186 5.9% 1.46 [0.31, 6.83] 2009Corostid A 16 1418 1 138 2.9% 5.45 [0.72, 41.50] 2009Gorostid A 16 1418 1 138 2.9% 5.45 [0.72, 41.50] 2009Gorostid A 16 1418 1 138 2.9% 5.45 [0.72, 41.50] 2016Bandrée-Ciga S 7 240 0 192 1.1% 1.237 [0.70, 177.90] 2016Bandrée-Ciga S 7 240 0 192 1.1% 1.3% [1.37, 177.91] 2016Bandrée-Ciga S 7 240 0 192 1.1% 1.3% [1.37, 177.92, 277.90] 2016Bandrée-Ciga S 7 240 0 192 1.1% 1.3% [1.37, 177.92] 2016Bandrée-Ciga S 7 240 0 192 1.1% 1.3% [1.37, 177.92] 2016Bandrée-Ciga S 7 240 0 192 1.1% 1.3% [1.37, 177.92] 2016Bandrée-Ciga S 7 240 0 192 1.1% 1.3% [1.37, 177.92] 2016Bandrée-Ciga S 7 240 0 192 1.1% 1.3% [1.37, 17.92] 2016Bandrée-Ciga S 7 240 0 192 1.1% 1.3% [1.37, 17.92] 2016Bandrée-Ciga S 7 240 0 192 1.1% 1.3% [1.37, 17.92] 2016Bandrée-Ciga S 7 240 0 192 1.1% 1.3% [1.37, 17.92] 2016Bandrée-Ciga S 7 240 0 192 1.1% 1.3% [1.37, 17.92] 2016Bandrée-Ciga S 7 240 0 192 1.1% 1.3% [1.37, 17.92] 2016Bandrée-Ciga S 7 240 0 120 1.2% 1.89 [0.08, 46.59] 2016Dauge-R 1 319 0 200 1.2% 1.89 [0.08, 46.59] 2016Dauge-R 2 154 1 162 1.9% 2.12 [0.19, 23.60] 2016Dauge-R 2 154 1 162 1.9% 2.12 [0.19, 23.60] 2016Dauge-R 3 1 3 1054 0 280 0 130 1.4% 3.64 [0.19, 68.12] 2005Farrer M 4 766 0 278 1.5% 3.20 [0.17, 56.89] 2005Farrer M 4 766 0 278 1.5% 3.20 [0.17, 56.89] 2005Farrer M 4 766 0 278 1.5% 3.20 [0.17, 56.89] 2005Farrer M 4 766 0 220 1.4% 5.84 [0.31, 0.19] 2006Farrer M 4 766 0 2000 1.1% 1.1% 2.17 [0.17, 56.89] 2006Farrer M 4 766 0 2000 1.1% 1.1% 2.17 [0.17, 56.89] 2006Farrer M 4 766 0 2000 1.1% 1.1% 2.17 [0.17, 56.89] 2006Farrer M 4 766 0 2000 1.1% 1.1% 2.17 [0.17, 56 | 2006Schlitter AM | 2 | 120 | 0 | 336 | 0.5% | 14.20 [0.68, 297.88] | + |
| 2007CrV-Utriger A 58 472 36 1802 26.0% 0.56 [0.03, 9.09] 2007CrV-Utriger A 58 472 36 1802 26.0% 0.56 [0.03, 9.09] 2007CrV-Utriger A 58 472 36 1802 26.0% 0.57 [4.17, 10.56] 2007CrV-Utriger A 58 472 36 1802 26.0% 0.57 [4.17, 10.56] 2008Patra B 9 575 2 186 5.9% 1.46 [0.13, 18.83] 2008Patra B 9 575 2 186 5.9% 1.46 [0.13, 18.83] 2009Grorstid A 16 418 1 138 2.9% 5.45 [0.72, 41.50] 2009Hassin-Baer S 19 242 1 900 0.0% 76.06 [0.10, 20, 575, 2.3] 2016Bandrés-Ciga S 7 240 0 192 1.1% 12.37 [0.70, 217, 90] 2016Bemelyanov AK 12 762 0 400 1.3% 13.34 [0.79, 225, 91] 2016Bandrés-Ciga S 7 240 0 192 1.1% 12.37 [0.70, 217, 90] 2016Bemelyanov AK 12 762 0 400 1.3% 13.34 [0.79, 225, 91] 2016Bemelyanov AK 12 762 0 400 1.3% 13.40 [7.9, 225, 91] 2018Crevinsov AK 12 762 0 400 1.3% 13.40 [7.9, 225, 91] 2018Crevinsov AK 12 762 0 72 0.9% 9.53 [0.50, 180.25] 2016Wescas P 1 319 0 200 1.2% 1.98 [0.08, 45.59] 2015Duoue AF 2 154 1 182 1.9% 2.12 [0.19, 23.60] 2015Duoue AF 2 154 1 182 1.9% 2.12 [0.19, 23.60] 2015Duoue AF 2 154 1 182 1.9% 3.75 [0.80, 17.69] 2015Duoue AF 2 1564 1 182 1.9% 3.75 [0.80, 17.69] 2015Duoue AF 3 26 0 130 1.4% 3.64 [0.19, 68.12] 2005Deng H 4 326 0 278 1.5% 3.20 [0.17, 58.69] 2005Michols WC 35 767 0 965 0.8% 93.88 [5.73, 1528.09] 2005Michols WC 35 767 0 965 0.8% 93.88 [5.73, 1528.09] 2005Michols WC 35 767 0 965 0.8% 93.88 [5.73, 1528.09] 2006ClarkUN 28 604 2 314 4.6% 584 [0.33, 104.19] 2006Carellus J 22 120 4 317 3.0% 18.77 [5.13, 73.79] 2006Deng H 6 496 0 220 1.4% 584 [0.33, 104.19] 2006Carellus J 22 120 4 317 3.0% 17.57 [5.17, 37.79] 2014Chien HF 0 100 0 100 Notestimable 4014Dental Protect Selection A 180 Color | 2006Williams-Gray CH | 2 | 519 | 0 | 887 | 0.7% | 8.57 [0.41, 178.96] | |
| 2007/CIV-Hurteger A 58 472 36 1802 26.0% 6.87 [4.47, 10.56] | 2007Civitelli D | 14 | 488 | 0 | 180 | 1.4% | 11.03 [0.65, 185.89] | |
| 2008Points G | 2007Cossu G | | 98 | | | | 0.56 [0.03, 9.08] | |
| 2008 Potra B 9 575 2 186 5.9% 1.46 [0.31, 13.797] 2008 Potra B 9 575 2 186 5.9% 1.46 [0.31, 16.83] 2009 Corostidi A 18 418 1 138 2.9% 5.45 [0.72, 41.50] 2009 Corostidi A 18 418 1 138 2.9% 5.45 [0.72, 41.50] 2009 Corostidi A 18 418 1 138 2.9% 5.45 [0.72, 41.50] 2009 Corostidi A 18 418 1 138 2.9% 5.45 [0.72, 41.50] 2009 Corostidi A 18 418 1 138 2.9% 5.45 [0.72, 41.50] 2009 Corostidi A 18 418 1 138 2.9% 5.45 [0.72, 41.50] 2009 Corostidi A 18 418 1 138 2.9% 5.45 [0.70, 21.90] 2018 Emelyanov AK 12 762 0 400 1.3% 12.37 [0.70, 21.90] 2018 Emelyanov AK 22 (P = 0.05); P = 0% Test for overall effect Z = 12.05 (P < 0.00001) 5.2.4 Hispanicas 2008 Aguiar Pde C 4 72 0 72 0.9% 5.70 8.71 [6.12, 12.38] 2016 You care a 19 1 319 0 200 1.2% 1.89 [0.08, 46.59] 2016 You care A 19 1 19 2 1.1% 1.1% 1.1% 1.1% 1.1% 1.1% 1.1% 1. | _ | | | | | | | |
| 2009Arbara B 9 575 2 2 186 5.9% 1.46 [0.31, 6.83] 2009Arbasin-Baer S 19 242 1 900 0.8% 76.50 [10.20, 575.23] 2009Barbara B 7 240 0 192 1.1% 12.37 [0.70, 217.90] 2018Emelyanova K 12 762 0 400 1.3% 13.34 (1.37) 12.25 91 2016Bandrés-Ciga S 7 240 0 192 1.1% 12.37 [0.70, 217.90] 2018Emelyanova K 12 762 0 400 1.3% 13.34 (1.37) 12.25 91 2016Bandrés-Ciga S 7 240 0 192 1.1% 12.37 [0.70, 217.90] 2018Emelyanova K 12 762 0 400 1.3% 13.34 (1.37) 12.25 91 2016Bandrés-Ciga S 7 240 0 192 1.1% 12.37 [0.70, 217.90] 2016Bandrés-Ciga S 7 240 0 192 1.1% 12.37 [0.70, 217.90] 2016Total events 234 42 Heterogeneity. Chi² = 20.29, df = 22 (P = 0.56); P = 0% Total events 1 319 0 200 1.2% 1.89 [0.08, 46.59] 2016Duque AF 2 154 1 162 1.9% 2.12 [0.19, 23.60] 2016Duque AF 2 154 1 162 1.9% 3.75 [0.80, 17.69] Total events 7 1 Heterogeneity. Chi² = 0.78, df = 2 (P = 0.68); P = 0% Testfor overall effect Z = 1.67 (P = 0.09) 5.2.5 Mixed 2005Farre M 4 786 0 278 1.5% 3.20 [0.17, 59.69] 2005Kachergus J 13 1054 0 2260 0.6% 56.80 [3.48, 98.72] 2005Kachergus J 13 1054 0 2260 0.6% 9.358 [5.73, 1528.09] 2005Kachergus J 2 120 4 317 3.6% 9.38 [5.73, 1528.09] 2005Clark LN 28 504 2 314 4.6% 9.18 [2.17, 38.79] 2006Clark LN 28 504 2 314 4.6% 9.18 [2.17, 38.79] 2006Clark LN 28 504 2 314 4.6% 9.18 [2.17, 38.79] 2006Clark LN 28 504 2 314 4.6% 9.18 [2.17, 38.79] 2006Clark LN 28 504 2 314 4.6% 9.18 [2.17, 38.79] 2006Clark LN 28 504 2 314 4.6% 9.18 [2.17, 38.79] 2006Clark LN 28 504 2 314 4.6% 9.18 [2.17, 38.79] 2006Clark LN 3 22 7120 4 317 3.6% 17.57 [5.91, 52.21] 2006Cage S 13 226 0 174 1.1% 22.07 [1.30, 37.386] 2014 Chien HF 0 100 0 100 Not estimable Subtotal (95% Cl) 5.897 6.897 6.90 (100) 2016 Control II 100 0 100 Not estimable Subtotal (95% Cl) 5.989 6.98 [5.72, 50.75] 2016 Control II 100 0 100 | | | | | | | | |
| 2009Gorostdi 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, 217.80] 2018Emelyanov AK 12 762 0 400 1.3% 13.34 [0.79, 225.91] 2018totai (95% C1) 9332 12005 57.0% 8.71 [6.12, 12.38] **Total events 234 42** Heterogeneity. Chi² = 20.29, df = 22 (₱ = 0.56); l² = 0% Test for overall effect Z = 1.20.5 (₱ < 0.00001) **5.24 Hispanicas 2008Aguiar Pde C 4 72 0 72 0.9% 9.53 [0.50, 180.25] 2016Vescas ₱ 1 319 0 200 12.% 1.88 [0.08, 46.59] 2016Duque AF 2 154 1 162 1.9% 2.12 [0.19, 23.60] 2015Duque AF 2 154 1 162 1.9% 2.12 [0.19, 23.60] 2015Duque AF 2 154 1 162 1.9% 3.75 [0.80, 17.69] **Heterogeneity. Chi² = 0.78, df = 2 (₱ = 0.68); l² = 0% Test for overall effect Z = 1.67 (₱ = 0.09) **5.2.5 Mixed 2005Carer M 4 786 0 278 1.5% 3.20 [0.17, 59.89] 2005Kachergus J 13 1054 0 2260 0.8% 58.60 [3.48, 986.72] 2005Kachergus J 13 1054 0 2260 0.8% 58.60 [3.48, 986.72] 2005Kachergus J 13 1054 0 2260 0.8% 93.59 [5.73, 1528.09] 2005Clark LN 28 504 2 314 4.6% 9.18 [2.17, 38.79] 2006Clark LN 28 504 2 314 4.6% 9.18 [2.17, 38.79] 2006Clark LN 28 504 2 118 1733 1.8% 23.12 [2.11, 17.25 1] 2006Core H 6 486 0 220 1.4% 58.4 [0.33, 10.4.19] 2006Cark LN 20 1518 1 1733 1.8% 23.12 [2.10, 3.73.86] 2014Chien HF 0 100 0 100 Not estimable Subtotai (95% CI) **Total (95% CI) 19624 67 **Total events | | | | | | | | |
| 2009 Hassin-Baer S 19 242 1 900 0.8% 76.80 (10.20, 575.23) 2016 Bandrés-Ciga S 7 240 0 192 1.1% 12.37 [0.70, 217.90] 2018 Emelyanov AK 12 762 0 400 1.3% 1.3.4 [0.79, 225.91] Subtotal (95% CI) 9332 12005 57.0% 8.71 [6.12, 12.38] Total events 234 42 Heterogeneity. Chi° = 20.29, df = 22 (P = 0.56); P = 0% Test for overall effect Z = 12.05 (P < 0.00001) 5.2.4 Hispanicas 2008 Aguiar Pde C 4 72 0 72 0.9% 9.53 [0.50, 180.25] 2016 Deque 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. Chi° = 0.78, df = 2 (P = 0.66); P = 0% Test for overall effect Z = 1.67 (P = 0.09) 5.2.5 Mixed 2005 Farre M 4 786 0 278 1.5% 3.20 [0.17, 59.69] 2005 Clark LN 28 504 2 314 4.6% 9.18 [2.17, 38.79] 2006 Clark LN 28 504 2 314 4.6% 9.18 [2.17, 38.79] 2006 Clark LN 28 504 2 314 4.6% 9.18 [2.17, 38.79] 2006 Clark LN 28 504 2 314 4.6% 9.18 [2.17, 38.79] 2006 Clark LN 28 504 2 314 4.6% 9.18 [2.17, 38.79] 2006 Clark LN 28 504 2 314 4.6% 9.18 [2.17, 38.79] 2006 Clark LN 28 504 2 314 4.6% 9.18 [2.17, 38.79] 2006 Clark LN 28 504 2 314 4.6% 9.18 [2.17, 38.79] 2006 Clark LN 28 504 2 314 4.6% 9.18 [2.17, 38.79] 2006 Clark LN 28 504 2 314 4.6% 9.18 [2.17, 38.79] 2006 Clark LN 28 504 2 314 4.6% 9.18 [2.17, 38.79] 2006 Clark LN 32 507 5897 67 0 655 0.89 3.58 [6.73, 1528.09] 2006 Clark LN 32 507 5897 67 0 655 0.89 3.58 [6.73, 1528.09] 2006 Clark LN 32 507 5897 67 0 655 0.89 3.89 [6.73, 1528.09] 2007 508 508 508 508 508 508 508 508 508 508 | | | | | | | | <u> </u> |
| 2018Emelyanov AIK 12 762 0 400 1.3% 12.37 [0.70, 217.90] 2018Emelyanov AIK 12 762 0 400 1.3% 13.34 [0.79, 225.91] Subtotal (95% C) 9332 42 Total events | | | | | | | | |
| 2018Emelyanov AK 12 762 0 400 1.3% 13.34 [0.79, 225.91] Subtotal (95% CI) 9332 42 | | | | | | | | |
| Subtotal (95% CI) 9332 12005 57.0% 8.71 [6.12, 12.38] | | | | | | | | |
| Total events | | 12 | | · | | | | • |
| Heterogeneity: Chi** = 20.29, df = 22 (P = 0.56); F = 0% Test for overall effect Z = 12.05 (P < 0.00001) 5.2.4 Hispanicas 2008Aguiar Pde C | | 234 | | 42 | | | | |
| 5.2.4 Hispanicas 2008Aguiar Pde C | | 22 (P = 0.5) | 6); I² = 09 | | | | | |
| 2008Aguiar Pde C | Test for overall effect: Z = 12.05 (F | P < 0.00001 | 1) | | | | | |
| 2008Aguiar Pde C | 5.2.4 Hispanicas | | | | | | | |
| 2010Yescas P | | 4 | 72 | 0 | 72 | 0.9% | 9.53 [0.50, 180.25] | |
| 2015Duque AF 2 154 1 162 1.9% 2.12 [0.19, 23.60] Subtotal (95% Cl) 545 434 4.1% 3.75 [0.80, 17.69] Total events 7 1 Heterogeneity: ChiP = 0.78, df = 2 (P = 0.68); P = 0% Test for overall effect: Z = 1.67 (P = 0.09) 5.2.5 Mixed 2005Deng H 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] 2005Kachergus J 13 1054 0 2260 0.6% 58.60 [3.48, 986.72] 2005Kachergus J 13 1054 0 2260 0.6% 58.60 [3.48, 986.72] 2006Nichols 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] 2006Clark LN 28 504 2 314 4.6% 9.18 [2.17, 38.79] 2006Clark LN 20 1518 1 1733 1.8% 23.12 [3.10, 172.51] 2006Cyelius LJ 22 120 4 317 3.6% 17.57 [5.91, 52.21] 2006Cyelius LJ 22 120 4 317 3.6% 17.57 [5.91, 52.21] 2006Cyelius LJ 22 120 4 317 3.6% 17.57 [5.91, 52.21] 2006Cyelius LJ 22 120 4 317 3.6% 17.57 [5.91, 52.21] 2014Chien HF 0 100 0 100 Not estimable Subtotal (95% Cl) 5897 6491 16.7% 18.12 [9.26, 35.44] Total events 145 7 Heterogeneity: ChiP = 6.02, df = 8 (P = 0.65); P = 0% Test for overall effect Z = 8.46 (P < 0.00001) Total (95% Cl) 19624 7 Total events 618 67 Heterogeneity: ChiP = 50.46, df = 39 (P = 0.10); P = 23% Test for overall effect Z = 9.54 (P < 0.00001) Test for overall effect Z = 9.54 (P < 0.00001) | _ | | | | | | | |
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| Section overall effect: Z = 1.67 (P = 0.09) | | 7 | | 1 | | | | |
| 5.2.5 Mixed 2005Deng H | | | r= 0% | | | | | |
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| 2005Farrer M | | | | | | | | |
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| 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); ² = 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); ² = 23% Test for overall effect: Z = 19.54 (P < 0.00001) | | | | | | | | |
| 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% Cl) 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% Cl) 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) | - | | | | | | | |
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| 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) | | | | | | | | |
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| 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); l² = 23% Test for overall effect: Z = 19.54 (P < 0.00001) Favours (experimental) Favours (controll | Heterogeneity: Chi² = 6.02, df = 8 | (P = 0.65); | | • | | | | |
| Total events 618 67 Heterogeneity: Chi² = 50.46, df = 39 (P = 0.10); l² = 23% Test for overall effect: Z = 19.54 (P < 0.00001) Favours (experimental): Favours (experimental) | restroi overan ellett. Z = 0.40 (P | ~ 0.00001) | ' | | | | | |
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| Test for overall effect: Z = 19.54 (P < 0.00001) | | | | | | | | , 1 |
| Test for overall effect: Z = 19.54 (P < 0.00001) Favours [experimental] Favours [control] | | | | 3% | | | | 0.001 0.1 1 10 1000 |
| Test for supproup differences; Chin= 18.56, at= 4 (P = 0.0010), if= 78.4% | | | | 0.00 | ov 17 - | 0.40 | | |
| | rest for suparoup differences: Ch | nr= 18.56. | ατ = 4 (P | = 0.001 | u). if = 7 | ö.4% | | |





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.