Supplementary Table 1: Results of segregation analyses incorporating mismatch repair gene and *MUTYH* mutation carrier status

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|  | No. Par | LL | AIC | *P\** | qA (95% CI) | RR Het (95% CI) | RR Hom (95% CI) | σ2p (95% CI) | q(*MLH1*) (95% CI) | q(*MSH2*) (95% CI) | q(*MSH6*) (95% CI) | q(*PMS2*) (95% CI) | q(*MUTYH*) (95% CI) |
| Base | 5 | -7296.0 | 14602.0 | 3.8x10-33 | – | – | – | – | 0.000313(0.000240,0.000407) | 0.000234(0.000177,0.000309) | 0.000701(0.000472,0.001042) | 0.000753(0.000508,0.001118) | 0.01135(0.00969,0.01330) |
| Dominant | 7 | -7229.0 | 14472.0 | 6.0x10-6 | 0.00202(0.00087,0.00468) | 28.8(17.6,47.1) | 28.8(17.6,47.1) | – | 0.000275(0.000209,0.000361) | 0.000191(0.000141,0.000258) | 0.000668(0.000450,0.000993) | 0.000712(0.000479,0.001059) | 0.01118(0.00954,0.01310) |
| Recessive | 7 | -7238.1 | 14490.2 | 6.5x10-10 | 0.1804(0.11,0.296) | 1.0 | 19.0(11.0,32.7) | – | 0.000284(0.000216,0.000372) | 0.000203(0.000151,0.000272) | 0.000667(0.000449,0.000992) | 0.000711(0.000479,0.001057) | 0. 01113(0.00950,0.01304) |
| Codominant | 8 | -7227.2 | 14470.3 | 6.2x10-6 | 0.007024(0.0032,0.0152) | 14.0(9.0,22.0) | 830.5(261.5,2637.1) | – | 0.000272(0.000206,0.000357) | 0.000189(0.000140,0.000256) | 0.000667(0.000449,0.000991) | 0.000711(0.000479,0.001057) | 0. 01114(0.00951,0.01305) |
| Polygenic | 6 | -7223.6 | 14459.2 | 0.004 | – | – | – | 1.32(1.08,1.62) | 0.000272(0.000208,0.000357) | 0.000191(0.000142,0.000257) | 0.000667(0.000449,0.000992) | 0.000705(0.000474,0.001047) | 0. 01119(0.00955,0.01311) |
| Mixed Dominant | 8 | -7217.0 | 14449.9 | 0.94 | 0.00063(0.00010,0.00398) | 40.5(13.2,124.1) | 40.5(13.2,124.1) | 0.87(0.53,1.41) | 0.000263(0.000199,0.000346) | 0.000181(0.000133,0.000245) | 0.000662(0.000445,0.000984) | 0.000701(0.000471,0.001041) | 0. 01116(0.00953,0.01307) |
| Mixed Recessive | 8 | -7221.2 | 14458.3 | 0.004 | 0.116(0.046,0.290) | 1.0 | 14.7(4.8,45.0) | 1.04(0.71,1.52) | 0.000270(0.000206,0.000354) | 0.000189(0.000140,0.000254) | 0.000664(0.000447,0.000987) | 0.000702(0.000473,0.001044) | 0. 01112(0.00949,0.01303) |
| Mixed Codominant | 9 | -7216.9 | 14451.9 | – | 0.00062(0.00009,0.00412) | 40.8(12.8,129.6) | 19.6(0,∞) | 0.87(0.53,1.41) | 0.000262(0.000199,0.000345) | 0.000179(0.000132,0.000244) | 0.000662(0.000445,0.000984) | 0.000701(0.000472,0.001042) | 0. 01115(0.00952,0.01306) |

Par, number of parameters estimated in the model; LL, log-likelihood; AIC, Akaile’s Information Criterion; qA, estimated high-risk allele frequency for the unidentified major genes; q, minor allele frequency; CI, confidence interval; hom, homozygous; het, heterozygous, RR, relative risk as compared with non-carriers; σ2p, variance of the polygenic component; –, not applicable.

\*For all models, P value refers to the comparison with the mixed codominant model using the log-likelihood ratio test.

Supplementary Table 2. Estimated population carrier frequency of a mismatch repair gene or *MUTYH* mutation from previous studies and current study

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| --- | --- | --- | --- | --- |
| **Author** | **Population** | **Gene** | **Estimate of population carrier frequency (95% CI)** | **Calculation of carrier frequency based on these assumptions.** |
| Salovaara et al. (2000) (1) | Finland | *MLH1, MSH2* | 1 in 740 | 2.7% carrier frequency in CRC × 5% lifetime risk of CRC = 0.135% |
| Dunlop (2000) (2) | Scotland (15-74 years) | *MLH1, MSH2* | 1 in 3139 (1247 - 7626) | 2.66% carrier frequency in CRC × 0.17% population prevalence of CRC ÷ 14.6% prevalence of CRC in carriers = 0.031%  |
| Terdiman (2001) (3) | USA | *MLH1, MSH2* | 1 in 800 - 1 in 1600 | 1-2% carrier frequency in CRC × 5% lifestyle risk of CRC ÷ 80% lifetime risk for carriers = 0.0625% to 0.125% |
| de la Chapelle (2005) (4) | Literature review | *MLH1, MSH2* | 1 in 660 - 1 in 2000 | 1-3% carrier frequency in CRC × 5% lifetime risk of CRC = 0.05% to 0.15% |
| Boland and Shike (2010) (5) | USA | *MLH1, MSH2, MSH6, PMS2* | 1 in 300 | 2.8% carrier frequency in CRC × 6% lifetime risk of CRC ÷ 50% lifetime risk for carriers = 0.33% |
| Hampel and de la Chapelle (2011) (6) | USA | *MLH1, MSH2, MSH6, PMS2* | 1 in 370 | 2.8% carrier frequency in CRC × 5% lifetime risk of CRC ÷ 50% lifetime risk for carriers = 0.28% |
| Win et al. (2011) (7) | Literature review | *MUTYH* | mono *MUTYH* 1 in 60bi *MUTYH* 1 in 7320 | 243 monoallelic carriers ÷ 14639 controls2 biallelic carriers ÷ 14639 controls |

CRC, colorectal cancer; CI, confidence interval

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