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 60  bi *MUTYH* 1 in 7320 | 243 monoallelic carriers ÷ 14639 controls  2 biallelic carriers ÷ 14639 controls |

CRC, colorectal cancer; CI, confidence interval

**References**

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