**Table S1**: Offspring phenotypes as reported by fathers and mothers

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Offspring phenotypes** | | **Reporting parents’ gender** | | ***P* value** |
| *Fathers*  *(N=2011 subjects, 4328 offspring)* | *Mothers*  *(N=2282 subjects, 4772 offspring)* |  |
| Never asthmaa |  | 3657 (90.5%) | 3866 (86.8%) | <0.001 |
| Early onset asthma (yes) | | 383 (9.48%) | 589 (13.2%) |  |
| Missing | | 288 (6.65%) | 317 (6.64%) |  |
| Never asthmaa |  | 3657 (91.8%) | 3866 (89.1%) | <0.001 |
| Late onset asthma(yes) | | 326 (8.18%) | 475 (10.9%) |  |
| Missing | | 345 (7.97%) | 431 (9.03%) |  |
| Hay fever | No | 3441 (79.5%) | 3446 (72.2%) | <0.001 |
|  | Yes | 848 (19.6%) | 1293 (27.1%) |  |
|  | Missing | 39 (0.90%) | 33 (0.69%) |  |
| Asthma only | | 269 (6.50%) | 339 (7.33%) | <0.001 |
| Hay fever only | | 610 (14.7%) | 854 (18.5%) |  |
| Asthma with hay fever | | 223 (5.39%) | 427 (9.23%) |  |
| No asthma/hay fever | | 3038 (73.4%) | 3004 (65.0%) |  |
| Missing | | 34 (0.79%) | 39 (0.82%) |  |

aNo asthma neither before nor after 10 years of age

**Table S2.** Association between asthma severity and clinical markers and offspring asthma and hay fever only for parents who have one child born before and one child born after ECRHS I.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | Parental disease markers assessed before conception | | Parental disease markers assessed after birth | |  |
|  | **Parental disease markers** | **Adjusted OR**  **(95%CI)a** | ***P* value** | **Adjusted OR**  **(95% CI) a** | ***P* value** | ***P* for interactions** |
| *No offspring asthma/hay fever (ref)* | | **N=565** |  | **N=625** |  |  |
|  | **Asthma score** |  |  |  |  |  |
| *Offspring* | *Asthma only* | 0.98 (0.68,1.42) | 0.92 | 1.39 (1.01,1.91) | 0.05 | 0.61 |
| *Hay fever only* | 1.36 (1.05,1.77) | 0.02 | 1.34 (1.08,1.65) | 0.007 | 0.88 |
| *Asthma with hay fever* | 1.61 (1.16,2.24) | 0.005 | 0.94 (0.65,1.36) | 0.73 | 0.06 |
|  | **BHR (N=2953)** |  |  |  |  |  |
| *Offspring* | *Asthma only* | 1.27 (0.41,3.90) | 0.68 | 4.02 (1.33,12.2) | 0.01 | 0.61 |
| *Hay fever only* | 2.14 (0.88,5.17) | 0.09 | 1.35 (0.62,2.95) | 0.45 | 0.74 |
| *Asthma with hay fever* | 3.36 (1.08,10.5) | 0.04 | 0.88 (0.26,2.96) | 0.83 | 0.02 |
| *Offspring* | **Specific IgE** |  |  |  |  |  |
| *Asthma only* | 1.09 (0.46,2.58) | 0.84 | 1.35 (0.56,3.24) | 0.50 | 0.74 |
| *Hay fever only* | 1.08 (0.57,2.05) | 0.81 | 1.59 (0.96,2.65) | 0.07 | 0.64 |
| *Asthma with hay fever* | 2.73 (1.15,6.48) | 0.02 | 1.50 (0.66,3.44) | 0.34 | 0.09 |
|  | **Total IgE** |  |  |  |  |  |
| *Offspring* | *Asthma only* | 1.26 (0.73,2.18) | 0.41 | 1.21 (0.67,2.19) | 0.52 | 0.74 |
| *Hay fever only* | 0.96 (0.61,1.51) | 0.86 | 1.44 (0.98,2.10) | 0.06 | 0.28 |
| *Asthma with hay fever* | 1.96 (1.06,3.62) | 0.03 | 1.51 (0.82,2.79) | 0.19 | 0.39 |

a Estimates were obtained with GEE multinomial regression models, adjusted for centre, type of sample, offspring age, sex and parity, and parental age and sex, smoking status and pack-years

**Table S3:** Association between parental asthma score, BHR, specific and total IgE and atopic status and asthma and allergy in children, stratified by gender of offspring and parents

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Sons (N=3067)** | | | | **Daughters (2993)** | | | |
|  | **Fathers (N=1458)** | | **Mothers (1609)** | | **Fathers (1378)** | | **Mothers (1606)** | |
|  | Adjusted RRR  (95 % CI) **a** | *P* value | Adjusted RRR  (95 % CI) **a** | *P* value | Adjusted RRR  (95 % CI) **a** | *P* value | Adjusted RRR  (95 % CI) **a** | *P* value |
| **Parental asthma score (N=3171), per unit increase in score** | | | | |  |  |  |  |
| *Offspring asthma only* | 0.98 (0.82,1.17) | 0.810 | 1.13 (0.98,1.29) | 0.080 | 1.02 (0.84,1.24) | 0.820 | 1.07 (0.92,1.23) | 0.390 |
| *Offspring hay fever only* | **1.25 (1.11,1.40)** | **< 0.001** | 1.09 (0.98,1.20) | 0.100 | 1.05 (0.92,1.20) | 0.430 | 1.07 (0.97,1.18) | 0.200 |
| *Offspring asthma with hay fever* | **1.15 (0.97,1.37)** | **0.010** | **1.22 (1.08,1.37)** | **0.001** | 1.09 (0.89,1.34) | 0.390 | 1.11 (0.98,1.26) | 0.110 |
| **Parental BHR: PD20, yes vs no (N=2679)** | |  |  |  |  |  |  |  |
| *Offspring Asthma only* | 0.91 (0.51,1.63) | 0.760 | **1.67 (1.03,2.71)** | **0.040** | 1.01 (0.51,1.98) | 0.980 | 1.00 (0.58,1.73) | 0.990 |
| *Offspring hay fever only* | **1.71 (1.15,2.54)** | **0.008** | 1.22 (0.87,1.71) | 0.250 | 1.07 (0.68,1.70) | 0.760 | 1.14 (0.78,1.67) | 0.490 |
| *Offspring Asthma with hay fever* | **1.81 (1.02,3.20)** | **0.040** | **2.00 (1.34,3.00)** | **<0.001** | **2.12 (1.12,4.01)** | **0.020** | **1.64 (1.03,2.60)** | **0.040** |
| **Parental any specific IgE (N=2852), yes vs no** | |  |  |  |  |  |  |  |
| *Offspring asthma only* | 1.01 (0.68,1.50) | 0.970 | 1.36 (0.92,2.00) | 0.120 | 1.39 (0.89,2.17) | 0.140 | **0.63 (0.40,1.00)** | **0.050** |
| *Offspring hay fever only* | **1.34 (1.02,1.76)** | **0.040** | **1.51 (1.17,1.95)** | **0.002** | **1.72 (1.29,2.31)** | **< 0.001** | **1.84 (1.40,2.41)** | **< 0.001** |
| *Offspring Asthma with hay fever* | **2.99 (1.99,4.49)** | **< 0.001** | **1.66 (1.19,2.32)** | **0.003** | **2.43 (1.51,3.91)** | **< 0.001** | **2.01 (1.42,2.86)** | **< 0.001** |
| **Parental total IgE (N=2853), per log10 (IgE) unit** | |  |  |  |  |  |  |  |
| *Offspring asthma only* | 0.91 (0.69,1.19) | 0.480 | 1.17 (0.90,1.52) | 0.250 | **1.46 (1.07,2.01)** | **0.020** | **0.89 (0.67,1.17)** | **0.400** |
| *Offspring hay fever only* | **1.27 (1.04,1.54)** | **0.020** | 1.06 (0.89,1.27) | 0.500 | **1.56 (1.26,1.94)** | **< 0.001** | **1.33 (1.10,1.62)** | **0.003** |
| *Offspring asthma with hay fever* | **2.31 (1.72,3.12)** | **< 0.001** | **1.31 (1.04,1.66)** | **0.020** | **1.99 (1.40,2.85)** | **< 0.001** | **1.37 (1.07,1.77)** | **0.010** |

a Estimates were obtained with GEE multinomial regression models, adjusted for centre, type of sample, offspring age, sex and parity, and parental age, smoking status and pack-years