### Supplementary material

Supplementary Figure 1:



Supplementary Table 1: Parameter estimates (95% CI) of best fitting trivariate models of CRP levels using only returning subjects, i.e., twins that participated in all three visits.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Model | Visit | 1 | 2 | 3 |
| 1 | 1 | **0.47 (0.35-0.57)** | 0.13 (0.00-0.27) | 0.20 (0.06-0.34) |
|  | 2 | 0.95 (0.81-1.00) | **0.49 (0.38-0.59)** | 0.25 (0.11-0.39) |
|  | 3 | 0.73 (0.58-0.88) | 0.85 (0.72-0.97) | **0.52 (0.40-0.62)** |
| 2 | 1 | **0.43 (0.31-0.54)** | 0.15 (0.01-0.28) | 0.21 (0.06-0.34) |
|  | 2 | 0.91 (0.75-1.00) | **0.43 (0.31-0.54)** | 0.25 (0.11-0.39) |
|  | 3 | 0.62 (0.43-0.79) | 0.77 (0.62-0.93) | **0.49 (0.36-0.59)** |

Note: The best fitting model for all analyses was the AE model; Genetic correlations [rg (95% CI)] are given below the diagonal and environmental correlations [re (95% CI)] above the diagonal**.** Heritability(95% CI) estimates are given on the diagonal; Model 1, adjusted for age; Model 2, adjusted for age and BMI

Supplementary Table 2:General characteristics at baseline (visit1) for ‘returning’ subjects compared to ‘non-returning’ subjects.

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| --- | --- | --- | --- | --- |
|  |  | Non-returning | Returning V2 only | Returning V2+V3 |
| Age (years) | | |  |  |
| MZ |  | 47.3±14.0 (n=2.021) | 51.6±11.5 (n=642)\*\*\* | 56.4±7.7 (n=292)\*\*\* |
| DZ |  | 47.0±13.4 (n=1.929) | 49.8±10.8 (n=1.081)\*\*\* | 52.4±9.4 (n=236)\*\*\* |
| Total |  | 47.1±13.7 (n=3.950) | 50.5±11.1 (n=1.723)\*\*\* | 54.6±8.7 (n=528)\*\*\* |
| BMI (kg/m2) | | |  |  |
| MZ |  | 25.6±4.8 (n=2.021) | 25.2±4.3  (n=642)\* | 24.7±4.0 (n=292)\*\*\* |
| DZ |  | 25.8±4.9 (n=1.929) | 25.5±4.6 (n=1.081)\* | 24.8±3.4 (n=236)\*\*\* |
| Total |  | 25.7±4.8 (n=3.950) | 25.4±4.5 (n=1.723)\*\* | 24.7±3.7 (n=528)\*\*\* |
| CRP (mg/L) | | |  |  |
| MZ |  | 1.28 (0.56-3.37) (n=2.021) | 1.16 (0.36-3.18) (n=642)\*\* | 0.80 (0.30-2.14) (n=292)\*\*\* |
| DZ |  | 1.53 (0.66-3.56) (n=1.929) | 1.41 (0.56-3.52) (n=1.081) | 1.09 (0.37-2.53) (n=236)\*\*\* |
| Total |  | 1.37 (0.60-3.43) (n=3.950) | 1.30 (0.48-3.35) (n=1.723)\* | 0.90 (0.30-2.21) (n=528)\*\*\* |

Note: Differences between returning and non-returning (reference group) twins were tested using GEE with adjustment for age (for BMI) and age and BMI (for CRP). CRP was transformed by natural logarithm; Abbreviations: BMI, Body Mass Index; CRP, C-Reactive Protein, MZ, Monozygotic twins; DZ, Dizygotic twins; n, number of subjects; Data are given in mean±SD for age and BMI, and median (IQR) for CRP; \*p<0.05; \*\**p*<0.01; \*\*\**p*<0.001.

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Supplementary Table 3. Heritability estimates of CRP from twin or pedigree studies | | | | | | | | |  |
| **Reference** | **Year** | **PMID** | **Study Design** | **N** | **Heritability** | **Age: mean (range)** | **Notes** | |  |
| Pankow *et al* | 2001 | 11257270 | Pedigree | 1.848 | 0,40 | 52.5 (25-93) | 924 sibling pairs | |  |
| Vickers *et al* | 2002 | 11922913 | Pedigree | 588 | 0,39 | 49 (19-90) | 98 nuclear families | |  |
| Austin *et al* | 2004 | 15180698 | Pedigree | 562 | 0,29 | 55 (18-94) | 68 extended kindreds | |  |
| Best *et al* | 2004 | 15711091 | Pedigree | 1.393 | 0.38; 0.46 (see notes) | M: 59 / F: 60.3 | 1,294 relative pairs; heritability calculated under the minimally and maximally adjusted models | |  |
| de Maat *et al* | 2004 | 15345506 | Twins | 482 | 0,20 | MZ: 78.1 / DZ:77.9 | 112 MZ twin pairs and 129 DZ same-sex twins | |  |
| MacGregor *et al* | 2004 | 14633907 | Twins | 620 | 0,52 | MZ: 58 (40-69.6) / DZ: 55.7 (40-70.3) | 146 MZ and 164 DZ healthy female twin pairs | |  |
| Dupuis *et al* | 2005 | 16159603 | Pedigree | 1.054 | 0,28 | M: 58 / F: 59 | 304 extended families including 348 sibships (172 sibling pairs, 114 sibling trios and 62 sibships of size ≥4). Heritability is multivariable-adjusted. | |  |
| Lange *et al* | 2006 | 17044846 | Pedigree | 461 | 0.36-0.42 | 62.2 (39-86) | 224 sibships with type 2 diabetes mellitus, heritability is the range of calculations under five adjustment levels. | |  |
| Saunders *et al* | 2006 | 17027430 | Pedigree | 10.440 | 0,10 | - (>16) | 4,938 men and 5,502 women from two-generation pedigrees | |  |
| Tang *et al* | 2006 | 16505518 | Pedigree | 702 | 0,43 | M: 50.9 / F: 52 | Nondiabetic white individuals from 349 families | |  |
| Worns *et al* | 2006 | 16900203 | Twins | 336 | 0,22 | ----- | 108 MZ and 60 same-sex DZ twin pairs | |  |
| Wessel *et al* | 2007 | 17211240 | Twins | 229 | 0,56 | 40.7 (18-81) | 76 MZ and 32 DZ pairs plus one individual from each of 13 additional twin pairs | |  |
| Fox *et al* | 2008 | 18805107 | Pedigree | 1.317 | 0,45 | 55 | 246 families from Jackson Heart Study | |  |
| Su *et al* | 2008 | 18243214 | Twins | 332 | 0,61 | 54 | 166 (88 MZ and 78 DZ) middle-aged male twin pairs | |  |
| Schnable *et al* | 2009 | 20031590 | Pedigree | 3.311 | 0,30 | 60 | 1843 individuals in 567 families, in addition to 1468 unrelated participants. | |  |
| Su *et al* | 2009 | 19073752 | Twins | 376 | 0,65 | 55 | 188 male twins including 54 MZ and 40 DZ twin pairs | |  |
| Wu *et al* | 2009 | 19238141 | Pedigree | 2.373 | White: 0.31; AA: 0.53 | Whites: 57.8 / AA: 52.9 | 1,825 whites and 548 African-Americans (AA) of the NHLBI Family Heart Study (FHS) | |  |
| Rahman *et al* | 2009 | 19456221 | Twins | 7.516 | 0,43 | M: 66.6 / F: 65.9 | 1,066 MZ, 1,340 same-sex DZ and 1352 opposite-sex DZ; from 12,000 Swedish twins | |  |
| Jermendy *et al* | 2011 | 22050728 | Twins | 202 | 0,52 | 44,3 | 63 MZ and 38 DZ adult twin pairs | |  |
| Neijts *et al* | 2013 | 23953347 | Twin-family | 7.329 | 0,45 | 44 (18-90) | 3,534 twins (1,871 MZ and 1,663 DZ), 1,568 of their non-twin siblings, and 2,227 parents from 3,095 families. | |  |
| Sas *et al* | 2014 | 24735719 | Twins | 214 | 0,52 | MZ:23.49 / DZ: 23.54 | 125 MZ and 89 DZ twins | |  |
|  |  |  |  |  |  |  |  | |  |
| Note: N indicates sample size; M, male; F, female; MZ, monozygotic twins; DZ, dizygotic twins; and AA, African-Americans. | | | | | | | |