|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **CRP (mg/L)** | | **Eosin : Lymph** | | **Sed Rate (mm/hr)** | | **Lymphocytes (mm3)** | | **Neutrophils (mm3)** | | **Eosinophils (mm3)** | |
| *Predictors* | *Estimate (95% CI)* | *p* | *Estimate (95% CI)* | *p* | *Estimate (95% CI)* | *p* | *Estimate (95% CI)* | *p* | *Estimate (95% CI)* | *p* | *Estimate (95% CI)* | *p* |
| (Intercept) | -2.74 | **<0.001** | 0.72 | **<0.001** | 5.9 | **<0.001** | 35.1 | **<0.001** | 63.37 | **<0.001** | 58.59 | **<0.001** |
| (-4.09 – -1.38) | (0.61 – 0.83) | (4.59 – 7.21) | (29.32 – 40.88) | (55.84 – 70.89) | (49.82 – 67.37) |
| APOE [E4] | -0.55 | 0.147 | -0.06 | **0.021** | -0.04 | 0.911 | 1.17 | 0.424 | -2.89 | 0.125 | -5.07 | **0.022** |
| (-1.29 – 0.19) | (-0.12 – -0.01) | (-0.69 – 0.62) | (-1.70 – 4.04) | (-6.58 – 0.80) | (-9.40 – -0.74) |
| Age [in years] | 0.01 | **<0.001** | 0 | **<0.001** | 0.01 | **<0.001** | -0.07 | **<0.001** | 0.05 | **0.003** | -0.2 | **<0.001** |
| (0.01 – 0.02) | (-0.00 – -0.00) | (0.01 – 0.02) | (-0.10 – -0.05) | (0.02 – 0.08) | (-0.24 – -0.17) |
| Sex [women] | 0.01 | 0.794 | 0 | 0.777 | 1.07 | **<0.001** | 1.03 | **<0.001** | -0.52 | 0.115 | 0.89 | **0.026** |
| (-0.09 – 0.12) | (-0.01 – 0.01) | (0.95 – 1.19) | (0.51 – 1.54) | (-1.17 – 0.13) | (0.11 – 1.67) |
| BMI | 0.89 | **<0.001** | -0.08 | **<0.001** | -0.69 | **0.001** | 5.82 | **<0.001** | 1.08 | 0.345 | -3.09 | **0.02** |
| (0.49 – 1.29) | (-0.12 – -0.05) | (-1.08 – -0.30) | (4.09 – 7.54) | (-1.16 – 3.33) | (-5.70 – -0.48) |
| Season [wet] | 0.16 | **0.018** | -0.01 | **0.002** | 0.32 | **<0.001** | -1.19 | **<0.001** | -1.02 | **<0.001** | -1.83 | **<0.001** |
| (0.03 – 0.29) | (-0.02 – -0.00) | (0.24 – 0.40) | (-1.57 – -0.81) | (-1.55 – -0.50) | (-2.40 – -1.26) |
| high WBC | 0.46 | **<0.001** | 0.05 | **<0.001** | 0.4 | **<0.001** | 8.41 | **<0.001** | 21.85 | **<0.001** | 12.25 | **<0.001** |
| (0.22 – 0.70) | (0.04 – 0.07) | (0.25 – 0.55) | (7.69 – 9.13) | (20.86 – 22.83) | (11.17 – 13.32) |
| E4 \* Age | 0 | 0.481 | 0 | 0.096 | 0 | 0.634 | -0.02 | 0.375 | 0.05 | 0.169 | 0.06 | 0.14 |
| (-0.01 – 0.02) | (-0.00 – 0.00) | (-0.01 – 0.01) | (-0.08 – 0.03) | (-0.02 – 0.11) | (-0.02 – 0.14) |
| **Random Effects** | | | | | | | | | | | | |
| Residual σ2 | 0.78 | | 0.01 | | 1.97 | | 46.72 | | 90.48 | | 103.3 | |
| τ00 | 0.01 pid | | 0.00 pid | | 0.68 pid | | 10.23 pid | | 13.11 pid | | 23.89 pid | |
|  | 0.03 community\_id | | 0.00 community\_id | | 0.11 community\_id | | 1.36 community\_id | | 3.68 community\_id | | 9.35 community\_id | |
| ICC | 0.04 | | 0.25 | | 0.28 | | 0.2 | | 0.16 | | 0.24 | |
| N | 908 pid | | 1260 pid | | 1254 pid | | 1260 pid | | 1260 pid | | 1260 pid | |
|  | 68 community\_id | | 80 community\_id | | 80 community\_id | | 80 community\_id | | 80 community\_id | | 80 community\_id | |
| Observations | 1033 | | 6121 | | 5988 | | 6136 | | 6145 | | 6130 | |
| Marginal R2 / Conditional R2 | 0.072 / 0.113 | | 0.036 / 0.273 | | 0.113 / 0.366 | | 0.107 / 0.285 | | 0.235 / 0.355 | | 0.114 / 0.329 | |

**Supplementary File 1a.** Models showing immune function and age associations, including interactive effects with *APOE* status. Results are from mixed effects linear regressions, adjusting for sex, season, and a dummy variable used as a proxy for current illness (leukocytes > 12 mm3). Results are reported as standardized betas; *CI* is the 95% confidence interval. All dependent variables were transformed and centered prior to analyses. See methods section for transformations. *APOE* genotype is coded as a categorical variable, binned as individuals that are homozygous *E3* (E3) versus those that have at least one copy of the *E4* allele (E4).

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **CRP (mg/L)** | | | **Sed Rate (mm/hr)** | | **Neutrophils (mm3)** | | **Eosinophils (mm3)** | | **Eosinophil : Lymphocyte ratio** | |
| *Predictors* | *95%CI * | | *p* | *95%CI * | *p* | *95%CI * | *p* | *95%CI * | *p* | *95%CI * | *p* |
| (Intercept) | -0.80 (-1.14 – -0.46) | | **<0.001** | -0.87 (-1.04 – -0.70) | **<0.001** | -0.27 (-0.41 – -0.13) | **<0.001** | 0.82 (0.66 – 0.99) | **<0.001** | 0.60 (0.42 – 0.77) | **<0.001** |
| *APOE4* | -0.29 (-0.44 – -0.14) | | **<0.001** | 0.06 (-0.03 – 0.15) | 0.182 | -0.03 (-0.10 – 0.04) | 0.435 | -0.16 (-0.24 – -0.08) | **<0.001** | -0.14 (-0.23 – -0.06) | **0.001** |
| Sex [women] | 0.01 (-0.11 – 0.13) | | 0.863 | 0.60 (0.53 – 0.67) | **<0.001** | -0.05 (-0.10 – 0.01) | 0.095 | 0.07 (0.01 – 0.13) | **0.032** | 0.01 (-0.06 – 0.07) | 0.859 |
| Age [years] | 0.01 (0.01 – 0.02) | | **<0.001** | 0.01 (0.01 – 0.01) | **<0.001** | 0.00 (0.00 – 0.01) | **<0.001** | -0.01 (-0.02 – -0.01) | **<0.001** | -0.01 (-0.01 – -0.01) | **<0.001** |
| high WBC | 0.43 (0.17 – 0.68) | | **0.001** | 0.23 (0.15 – 0.32) | **<0.001** | 1.82 (1.73 – 1.90) | **<0.001** | 0.98 (0.90 – 1.07) | **<0.001** | 0.37 (0.28 – 0.46) | **<0.001** |
| season [wet] | 0.15 (0.01 – 0.29) | | **0.040** | 0.18 (0.14 – 0.23) | **<0.001** | -0.09 (-0.13 – -0.04) | **<0.001** | -0.14 (-0.19 – -0.10) | **<0.001** | -0.07 (-0.12 – -0.02) | **0.004** |
| **Random Effects** | | | | | | | | | | | |
| Residual σ2 | 0.90 | | | 0.64 | | 0.63 | | 0.66 | | 0.73 | |
| τ00 | 0.04 pid | | | 0.22 pid | | 0.09 pid | | 0.15 pid | | 0.20 pid | |
|  | 0.03 community\_id | | | 0.03 community\_id | | 0.03 community\_id | | 0.06 community\_id | | 0.05 community\_id | |
| ICC | 0.07 | | | 0.28 | | 0.16 | | 0.25 | | 0.26 | |
| N | 909 pid | | | 1256 pid | | 1262 pid | | 1262 pid | | 1262 pid | |
|  | 68 community\_id | | | 80 community\_id | | 80 community\_id | | 80 community\_id | | 80 community\_id | |
| Observations | 1034 | | | 5992 | | 6149 | | 6134 | | 6125 | |
| Marginal R2 / Conditional R2 | | 0.054 / 0.125 | | 0.111 / 0.364 | | 0.235 / 0.354 | | 0.111 / 0.329 | | 0.028 / 0.276 | |

**Supplementary File 1b.** Mixed effects linear regressions assessing the association between *APOE* genotype and measures of innate immune function. The main predictor of interest, *APOE4*, is a binary variable that represents having at least a single copy of the *E4* allele. All dependent variables were transformed and centered for analyses. See methods section for transformations. Random effects are included for individual and community residence. Results are reported as standardized betas (2.5% - 97.5% confidence intervals).

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Leukocytes (1000/mm3)** | | | **Lymphocytes (mm3)** | | | **Hemoglobin (mg/dL)** | | |
| *Predictors* | *95%CI * | | *p* | *95%CI * | | *p* | *95%CI * | | *p* |
| (Intercept) | 0.23 (0.10 – 0.37) | | **0.001** | 0.51 (0.35 – 0.66) | | **<0.001** | 1.40 (1.23 – 1.57) | | **<0.001** |
| *APOE4* | -0.08 (-0.14 – -0.01) | | **0.025** | 0.01 (-0.08 – 0.09) | | 0.892 | -0.04 (-0.13 – 0.05) | | 0.400 |
| Sex [women] | 0.04 (-0.01 – 0.10) | | 0.114 | 0.13 (0.06 – 0.19) | | **<0.001** | -0.71 (-0.79 – -0.64) | | **<0.001** |
| Age [years] | -0.01 (-0.01 – -0.00) | | **<0.001** | -0.01 (-0.01 – -0.01) | | **<0.001** | -0.02 (-0.02 – -0.01) | | **<0.001** |
| high WBC | 2.01 (1.93 – 2.08) | | **<0.001** | 1.02 (0.93 – 1.10) | | **<0.001** | -0.12 (-0.20 – -0.04) | | **0.002** |
| season [wet] | -0.16 (-0.19 – -0.12) | | **<0.001** | -0.15 (-0.20 – -0.11) | | **<0.001** | -0.29 (-0.33 – -0.24) | | **<0.001** |
| **Random Effects** | | | | | | | | | | | |
| Residual σ2 | | 0.47 | | | 0.70 | | | 0.52 | | |
| τ00 | | 0.12 pid | | | 0.17 pid | | | 0.32 pid | | |
|  | | 0.04 community\_id | | | 0.02 community\_id | | | 0.02 community\_id | | |
| ICC | | 0.25 | | | 0.21 | | | 0.39 | | |
| N | | 1266 pid | | | 1262 pid | | | 1265 pid | | |
|  | | 80 community\_id | | | 80 community\_id | | | 80 community\_id | | |
| Observations | | 6229 | | | 6140 | | | 6199 | | |
| Marginal R2 / Conditional R2 | | 0.315 / 0.483 | | | 0.099 / 0.289 | | | 0.175 / 0.497 | | |

**Supplementary File 1c.** Mixed effects linear regressions assessing the association between *APOE* genotype and other measures of immune function. The main predictor of interest, *APOE4*, is a binary variable that represents having at least a single copy of the *E4* allele. All dependent variables were transformed and centered for analyses. See methods section for transformations. Random effects are included for individual and community residence. Results are reported as standardized betas (2.5% - 97.5% confidence intervals).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **CRP (< 10mg/L)** | | **CRP (< 5mg/L)** | | **CRP (< 3mg/L)** | |
| *Predictors* | *95%CI * | *p* | *95%CI * | *p* | *95%CI * | *p* |
| (Intercept) | -0.75 (-1.08 – -0.42) | **<0.001** | -0.69 (-1.01 – -0.36) | **<0.001** | -0.94 (-1.27 – -0.61) | **<0.001** |
| *APOE4* | -0.23 (-0.38 – -0.09) | **0.001** | -0.22 (-0.36 – -0.08) | **0.002** | -0.14 (-0.28 – -0.01) | **0.036** |
| Sex [women] | -0.03 (-0.15 – 0.08) | 0.603 | -0.01 (-0.12 – 0.11) | 0.918 | 0.02 (-0.09 – 0.13) | 0.739 |
| Age [years] | 0.01 (0.01 – 0.02) | **<0.001** | 0.01 (0.00 – 0.01) | **0.013** | 0.00 (-0.00 – 0.01) | 0.178 |
| high WBC | 0.36 (0.11 – 0.62) | **0.005** | 0.31 (0.10 – 0.52) | **0.004** | 0.21 (-0.03 – 0.44) | 0.087 |
| season [wet] | 0.08 (-0.06 – 0.21) | 0.271 | -0.07 (-0.20 – 0.06) | 0.296 | -0.00 (-0.13 – 0.13) | 0.963 |
| **Random Effects** | | | | | | |
| σ2 | 0.81 | | 0.57 | | 0.33 | |
| τ00 | 0.02 pid | | 0.06 pid | | 0.11 pid | |
|  | 0.03 community\_id | | 0.02 community\_id | | 0.02 community\_id | |
| ICC | 0.05 | | 0.12 | | 0.27 | |
| N | 860 pid | | 706 pid | | 510 pid | |
|  | 67 community\_id | | 65 community\_id | | 62 community\_id | |
| Observations | 979 | | 789 | | 552 | |
| Marginal R2 / Conditional R2 | 0.041 / 0.089 | | 0.034 / 0.153 | | 0.017 / 0.285 | |

**Supplementary File 1d.** Mixed effects linear regressions assessing the association between *APOE* genotype and C-reactive protein (CRP) with different cutoffs. The main predictor of interest, *APOE4*, is a binary variable that represents having at least a single copy of the *E4* allele. All dependent variables were transformed and centered for analyses. See methods section for transformations. Random effects are included for individual and community residence. Results are reported as standardized betas (2.5% - 97.5% confidence intervals).

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **BMI (kg/m2)** | | **Total Cholesterol (mg/dL)** | | **LDL (mg/L)** | | **HDL (mg/dL)** | | **oxLDL (IU/L)** | | **Troglycerides (mg/dL)** | |
| *Predictors* | *95%CI * | *p* | *95%CI * | *p* | *95%CI * | *p* | *95%CI * | *p* | *95%CI * | *p* | *95%CI * | *p* |
| (Intercept) | 0.33 (0.16 – 0.50) | **<0.001** | -0.59 (-0.83 – -0.34) | **<0.001** | -0.58 (-0.83 – -0.34) | **<0.001** | -0.50 (-0.74 – -0.26) | **<0.001** | 0.31 (-0.06 – 0.68) | 0.100 | -0.15 (-0.40 – 0.09) | 0.223 |
| *APOE4* | 0.15 (0.02 – 0.28) | **0.019** | 0.15 (0.04 – 0.27) | **0.009** | 0.08 (-0.04 – 0.19) | 0.185 | 0.05 (-0.06 – 0.16) | 0.396 | 0.16 (-0.00 – 0.32) | 0.051 | 0.07 (-0.05 – 0.19) | 0.255 |
| Sex [women] | 0.05 (-0.05 – 0.16) | 0.287 | 0.15 (0.06 – 0.24) | **0.001** | 0.19 (0.10 – 0.28) | **<0.001** | -0.07 (-0.16 – 0.01) | 0.091 | 0.08 (-0.05 – 0.21) | 0.210 | 0.11 (0.02 – 0.21) | **0.022** |
| Age [years] | -0.01 (-0.01 – -0.00) | **<0.001** | 0.01 (0.00 – 0.01) | **<0.001** | 0.01 (0.01 – 0.01) | **<0.001** | 0.01 (0.00 – 0.01) | **<0.001** | -0.00 (-0.01 – 0.00) | 0.177 | 0.00 (-0.00 – 0.00) | 0.738 |
| high WBC | -0.08 (-0.11 – -0.06) | **<0.001** | -0.13 (-0.21 – -0.05) | **0.002** | -0.31 (-0.40 – -0.22) | **<0.001** | 0.07 (-0.01 – 0.16) | 0.104 | -0.32 (-0.48 – -0.16) | **<0.001** | 0.09 (0.02 – 0.17) | **0.014** |
| season [wet] | -0.01 (-0.06 – 0.04) | 0.624 | -0.01 (-0.16 – 0.15) | 0.938 | -0.06 (-0.22 – 0.09) | 0.436 | -0.07 (-0.23 – 0.09) | 0.391 | 0.07 (-0.18 – 0.31) | 0.596 | 0.04 (-0.10 – 0.18) | 0.574 |
| **Random Effects** | | | | | | | | | | | | |
| Residual σ2 | 0.18 | | 0.70 | | 0.71 | | 0.82 | | 0.30 | | 0.57 | |
| τ00 | 0.78 pid | | 0.24 pid | | 0.18 pid | | 0.14 pid | | 0.65 pid | | 0.39 pid | |
|  | 0.02 community\_id | | 0.09 community\_id | | 0.11 community\_id | | 0.10 community\_id | | 0.11 community\_id | | 0.05 community\_id | |
| ICC | 0.82 | | 0.32 | | 0.29 | | 0.22 | | 0.72 | | 0.44 | |
| N | 1264 pid | | 1171 pid | | 1157 pid | | 1169 pid | | 909 pid | | 1176 pid | |
|  | 80 community\_id | | 71 community\_id | | 71 community\_id | | 71 community\_id | | 68 community\_id | | 71 community\_id | |
| Observations | 6225 | | 2584 | | 2393 | | 2479 | | 1034 | | 2635 | |
| Marginal R2 / Conditional R2 | 0.011 / 0.818 | | 0.021 / 0.335 | | 0.043 / 0.323 | | 0.011 / 0.233 | | 0.030 / 0.725 | | 0.006 / 0.439 | |

**Supplementary File 1e.** Mixed effects linear regressions assessing the association between *APOE* genotype and measures of lipids and BMI. The main predictor of interest, *APOE4*, is a binary variable that represents having at least a single copy of the *E4* allele. All dependent variables were transformed and centered for analyses. See methods section for transformations. Random effects are included for individual and community residence. Results are reported as standardized betas (2.5% - 97.5% confidence intervals).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **CRP (mg/L)** | | **Sed Rate (mm/hr)** | | **Neutrophils (mm3)** | |
| *Predictors* | *Estimates (95% CI)* | *p* | *Estimates (95% CI)* | *p* | *Estimates (95% CI)* | *p* |
| (Intercept) | -0.76 | **<0.001** | -1.35 | **<0.001** | -0.3 | **0.003** |
| (-1.14 – -0.38) | (-1.58 – -1.13) | (-0.50 – -0.10) |
| Total Cholesterol | -0.13 | **0.001** | -0.06 | **0.002** | 0.02 | 0.216 |
| (-0.20 – -0.05) | (-0.10 – -0.02) | (-0.01 – 0.06) |
| BMI | 0.09 | **0.011** | -0.04 | 0.06 | 0.01 | 0.785 |
| (0.02 – 0.16) | (-0.08 – 0.00) | (-0.03 – 0.04) |
| Sex [women] | 0.07 | 0.279 | 0.59 | **<0.001** | -0.05 | 0.15 |
| (-0.06 – 0.20) | (0.50 – 0.67) | (-0.13 – 0.02) |
| Age ([in yrs] | 0.01 | **<0.001** | 0.02 | **<0.001** | 0.01 | **<0.001** |
| (0.01 – 0.02) | (0.01 – 0.02) | (0.00 – 0.01) |
| Current illness | 0.65 | **<0.001** | 0.17 | **0.019** | 1.83 | **<0.001** |
| (0.37 – 0.93) | (0.03 – 0.32) | (1.70 – 1.97) |
| Season [wet] | 0.13 | 0.098 | 0.18 | **<0.001** | -0.1 | **0.009** |
| (-0.02 – 0.29) | (0.10 – 0.26) | (-0.17 – -0.02) |
| Total Cholesterol \* BMI | 0.15 | **<0.001**  **FDR p<0.001** | 0.05 | **0.008 FDR p=0.018** | 0.02 | 0.193FDR p=0.248 |
| (0.08 – 0.21) | (0.01 – 0.08) | (-0.01 – 0.05) |
| **Random Effects** | | | | | | |
| Residual σ2 | 0.92 | | 0.63 | | 0.6 | |
| τ00 | 0.00 pid | | 0.20 pid | | 0.10 pid | |
|  | 0.04 community\_id | | 0.05 community\_id | | 0.04 community\_id | |
| ICC | 0.04 | | 0.29 | | 0.19 | |
| N | 785 pid | | 1153 pid | | 1166 pid | |
|  | 65 community\_id | | 71 community\_id | | 71 community\_id | |
| Observations | 900 | | 2530 | | 2562 | |
| Marginal R2 / Conditional R2 | 0.086 / 0.120 | | 0.131 / 0.384 | | 0.220 / 0.367 | |

**Supplementary File 1f.** Mixed effects linear regression models that test direct and interactive effects of total cholesterol and BMI on inflammatory immune markers. Random effects are included for individual and community residence. Dependent and predictor variables of interest (total cholesterol, BMI, and immune markers) were transformed and centered for analyses. See methods section for transformations. Results are reported as standardized betas (2.5% - 97.5% confidence intervals).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **CRP (mg/L)** | | **Sed Rate (mm/hr)** | | **Neutrophils (mm3)** | |
| *Predictors* | *Estimates (95% CI)* | *p* | *Estimates (95% CI)* | *p* | *Estimates (95% CI)* | *p* |
| (Intercept) | -0.75 | **<0.001** | -1.35 | **<0.001** | -0.31 | **0.003** |
| (-1.13 – -0.37) | (-1.59 – -1.12) | (-0.52 – -0.10) |
| LDL Cholesterol | -0.11 | **0.006** | -0.03 | 0.139 | 0.03 | 0.098 |
| (-0.18 – -0.03) | (-0.07 – 0.01) | (-0.01 – 0.07) |
| BMI | 0.06 | 0.099 | -0.03 | 0.131 | 0.01 | 0.708 |
| (-0.01 – 0.14) | (-0.08 – 0.01) | (-0.03 – 0.04) |
| Sex [women] | 0.06 | 0.363 | 0.58 | **<0.001** | -0.05 | 0.185 |
| (-0.07 – 0.19) | (0.50 – 0.67) | (-0.13 – 0.02) |
| Age ([in yrs] | 0.01 | **<0.001** | 0.02 | **<0.001** | 0.01 | **0.001** |
| (0.01 – 0.02) | (0.01 – 0.02) | (0.00 – 0.01) |
| Current illness | 0.65 | **<0.001** | 0.16 | **0.042** | 1.82 | **<0.001** |
| (0.37 – 0.93) | (0.01 – 0.30) | (1.68 – 1.96) |
| Season [wet] | 0.09 | 0.249 | 0.17 | **<0.001** | -0.05 | 0.224 |
| (-0.07 – 0.26) | (0.09 – 0.26) | (-0.12 – 0.03) |
| LDL Cholesterol \* BMI | 0.16 | **<0.001 FDR p<0.001** | 0.03 | 0.073FDR p=0.131 | 0.01 | 0.745 FDR p=0.745 |
| (0.10 – 0.22) | (-0.00 – 0.07) | (-0.03 – 0.04) |
| **Random Effects** | | | | | | |
| Residual σ2 | 0.92 | | 0.63 | | 0.6 | |
| τ00 | 0.00 pid | | 0.21 pid | | 0.11 pid | |
|  | 0.04 community\_id | | 0.05 community\_id | | 0.04 community\_id | |
| ICC |  | | 0.29 | | 0.2 | |
| N | 779 pid | | 1138 pid | | 1152 pid | |
|  | 65 community\_id | | 71 community\_id | | 71 community\_id | |
| Observations | 895 | | 2342 | | 2381 | |
| Marginal R2 / Conditional R2 | 0.087 / 0.137 | | 0.126 / 0.384 | | 0.218 / 0.371 | |

**Supplementary File 1g.** Mixed effects linear regression models that test direct and interactive effects of LDL cholesterol and BMI on inflammatory immune markers. Random effects are included for individual and community residence. Dependent and predictor variables of interest (LDL cholesterol, BMI, and immune markers) were transformed and centered for analyses. See methods section for transformations. Results are reported as standardized betas (2.5% - 97.5% confidence intervals).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **CRP (mg/L)** | | **Sed Rate (mm/hr)** | | **Neutrophils (mm3)** | |
| *Predictors* | *Estimates (95% CI)* | *p* | *Estimates (95% CI)* | *p* | *Estimates (95% CI)* | *p* |
| (Intercept) | -0.99 | **<0.001** | -1.12 | **<0.001** | -0.44 | **0.003** |
| (-1.33 – -0.65) | (-1.45 – -0.78) | (-0.72 – -0.15) |
| Oxidized LDL | 0 | 0.963 | 0.01 | 0.825 | -0.01 | 0.607 |
| (-0.06 – 0.06) | (-0.05 – 0.06) | (-0.06 – 0.04) |
| BMI | 0.1 | **0.002** | 0.01 | 0.66 | 0.01 | 0.667 |
| (0.04 – 0.16) | (-0.05 – 0.07) | (-0.04 – 0.06) |
| Sex [women] | 0.01 | 0.929 | 0.48 | **<0.001** | -0.09 | 0.073 |
| (-0.11 – 0.12) | (0.37 – 0.59) | (-0.18 – 0.01) |
| Age ([in yrs] | 0.02 | **<0.001** | 0.01 | **<0.001** | 0.01 | **<0.001** |
| (0.01 – 0.02) | (0.01 – 0.02) | (0.01 – 0.02) |
| Current illness | 0.52 | **<0.001** | 0.25 | **0.036** | 1.9 | **<0.001** |
| (0.26 – 0.78) | (0.02 – 0.49) | (1.69 – 2.11) |
| Season [wet] | 0.15 | **0.035** | -0.19 | **0.016** | 0.19 | **0.004** |
| (0.01 – 0.30) | (-0.34 – -0.03) | (0.06 – 0.32) |
| Oxidized LDL \* BMI | 0.14 | **<0.001 FDR p<0.001** | -0.04 | 0.148FDR p=0.222 | 0.02 | 0.366  FDR p=0.411 |
| (0.08 – 0.19) | (-0.09 – 0.01) | (-0.02 – 0.07) |
| **Random Effects** | | | | | | |
| Residual σ2 | 0.92 | | 0.54 | | 0.53 | |
| τ00 | 0.01 pid | | 0.16 pid | | 0.05 pid | |
|  | 0.03 community\_id | | 0.13 community\_id | | 0.07 community\_id | |
| ICC | 0.04 | | 0.35 | | 0.19 | |
| N | 907 pid | | 845 pid | | 904 pid | |
|  | 68 community\_id | | 68 community\_id | | 68 community\_id | |
| Observations | 1032 | | 967 | | 1027 | |
| Marginal R2 / Conditional R2 | 0.077 / 0.115 | | 0.094 / 0.415 | | 0.272 / 0.409 | |

**Supplementary File 1h.** Mixed effects linear regression models that test direct and interactive effects of oxidized LDL and BMI on inflammatory immune markers. Random effects are included for individual and community residence. Dependent and predictor variables of interest (oxidized LDL, BMI, and immune markers) were transformed and centered for analyses. See methods section for transformations. Results are reported as standardized betas (2.5% - 97.5% confidence intervals).

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Total Cholesterol (mg/dL)** | | | **LDL (mg/dL)** | | | **Ox-LDL (IU/L)** | | | **HDL (mg/dL)** | | | **Triglycerides (mg/dL)** | | |
| *Predictors* | ** | *CI* | *p* | ** | *CI* | *p* | ** | *CI* | *p* | ** | *CI* | *p* | ** | *CI* | *p* |
| (Intercept) | -0.7 | -0.94 – -0.46 | **<0.001** | -0.71 | -0.95 – -0.47 | **<0.001** | 0.09 | -0.28 – 0.46 | 0.626 | -0.4 | -0.64 – -0.16 | **0.001** | -0.34 | -0.58 – -0.11 | **0.005** |
| APOE [E4] | 0.14 | 0.03 – 0.26 | **0.013** | 0.07 | -0.04 – 0.18 | 0.221 | 0.13 | -0.03 – 0.29 | 0.112 | 0.07 | -0.04 – 0.18 | 0.205 | 0.05 | -0.07 – 0.16 | 0.422 |
| BMI | 0.18 | 0.14 – 0.23 | **<0.001** | 0.2 | 0.15 – 0.25 | **<0.001** | 0.21 | 0.14 – 0.28 | **<0.001** | -0.11 | -0.16 – -0.06 | **<0.001** | 0.25 | 0.21 – 0.30 | **<0.001** |
| Sex [women] | 0.15 | 0.06 – 0.24 | **0.001** | 0.2 | 0.11 – 0.28 | **<0.001** | 0.09 | -0.03 – 0.21 | 0.158 | -0.07 | -0.15 – 0.02 | 0.117 | 0.1 | 0.01 – 0.19 | **0.023** |
| Age [in yrs] | 0.01 | 0.01 – 0.01 | **<0.001** | 0.01 | 0.01 – 0.02 | **<0.001** | 0 | -0.01 – 0.01 | 0.869 | 0.01 | 0.00 – 0.01 | **0.002** | 0 | 0.00 – 0.01 | **0.043** |
| Currently ill | 0.02 | -0.13 – 0.17 | 0.773 | -0.03 | -0.18 – 0.13 | 0.744 | 0.15 | -0.09 – 0.39 | 0.229 | -0.09 | -0.25 – 0.07 | 0.263 | 0.07 | -0.07 – 0.20 | 0.359 |
| Season [wet] | -0.12 | -0.20 – -0.04 | **0.004** | -0.29 | -0.38 – -0.21 | **<0.001** | -0.28 | -0.44 – -0.13 | **<0.001** | 0.06 | -0.03 – 0.15 | 0.168 | 0.11 | 0.04 – 0.18 | **0.003** |
| E4 \* BMI | -0.08 | -0.18 – 0.02 | 0.111 | -0.09 | -0.19 – 0.00 | 0.061 | 0.02 | -0.13 – 0.17 | 0.786 | -0.08 | -0.18 – 0.01 | 0.093 | 0.01 | -0.09 – 0.11 | 0.865 |
| **Random Effects** | | | | | | | | | | | | | | | |
| Residual σ2 | 0.7 | | | 0.71 | | | 0.3 | | | 0.82 | | | 0.58 | | |
| τ00 | 0.22 pid | | | 0.17 pid | | | 0.61 pid | | | 0.13 pid | | | 0.30 pid | | |
|  | 0.08 community\_id | | | 0.10 community\_id | | | 0.10 community\_id | | | 0.10 community\_id | | | 0.05 community\_id | | |
| ICC | 0.3 | | | 0.27 | | | 0.7 | | | 0.22 | | | 0.38 | | |
| N | 1168 pid | | | 1154 pid | | | 907 pid | | | 1166 pid | | | 1173 pid | | |
|  | 71 community\_id | | | 71 community\_id | | | 68 community\_id | | | 71 community\_id | | | 71 community\_id | | |
| Observations | 2581 | | | 2390 | | | 1032 | | | 2476 | | | 2632 | | |
| Marginal R2 / Cond. R2 | 0.049 / 0.336 | | | 0.074 / 0.326 | | | 0.070 / 0.724 | | | 0.027 / 0.239 | | | 0.072 / 0.428 | | |

**Supplementary File 1i.** Full models evaluating the moderating effects of APOE genotype on associations between BMI and cholesterols. Results report both fixed and random effects estimates from mixed effects linear regressions, which include random effects for ID and community residence. In addition to age, sex, and season, a dummy variable was used as a proxy for current illness (leukocytes > 12 mm3). Results are reported as standardized betas; *CI* is the 95% confidence interval. All dependent variables were transformed and centered prior to analyses. See methods section for transformations. *APOE* genotype is coded as a categorical variable, binned as individuals that are homozygous *E3* (E3) versus those that have at least one copy of the *E4* allele (E4).