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| eTable 1. Association of CRP with time to pregnancy in the Time to Conceive cohort. (N=717), with additional adjustment for graviditya | | |
| Variable | N | FR (95% CI) |
| CRPb | 717 | 0.99 (0.92, 1.1) |
| CRP (mg/L) |  |  |
| <1 | 373 | 1 |
| 1 - 3 | 190 | 0.95 (0.77, 1.2) |
| >3 - 10 | 109 | 1.2 (0.93, 1.6) |
| >10 | 45 | 0.83 (0.54, 1.3) |
| a “N” is the number of women. All models adjusted for age, race, education, BMI, smoking status, caffeine, alcohol, recent use of estrogen, and gravidity.  b Estimate is for a 1-natural log unit increase in CRP from the overall mean. | | |

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| eTable 2. Adjusted association of CRP with fecundability overall and by BMI, 25(OH)D level using multiple imputation to fill in missing values, and including adjustment for exercise, in the Time to Conceive cohort. (N=751) a | | | | | | | |
| Variable |  | |  |  | Overall |  |  |
| CRP b |  | |  |  | 0.98 (0.91, 1.04) |  |  |
| CRP (mg/L) |  | |  |  |  |  |  |
| <1 |  | |  |  | 1 |  |  |
| 1 - 3 |  | |  |  | 0.94 (0.77, 1.15) |  |  |
| >3 - 10 |  | |  |  | 1.21 (0.94, 1.55) |  |  |
| >10 |  | |  |  | 0.78 (0.51, 1.18) |  |  |
|  |  | | BMI <25 |  | BMI 25 - 30 |  | BMI >30 |
|  | N | FR (95% CI) | | N | FR (95% CI) |  | FR (95% CI) |
| CRP b |  | 1.02 (0.94, 1.10) | |  | 0.89 (0.69, 1.13) |  | 0.95 (0.73, 1.23) |
| CRP (mg/L) |  |  | |  |  |  |  |
| <1 | 324 | 1 | | 51 | 1.38 (1.01, 1.89) | 12 | 0.80 (0.39, 1.64) |
| 1 - 3 | 104 | 1.02 (0.81 1.28) | | 63 | 0.80 (0.57, 1.11) | 36 | 1.13 (0.77, 1.64) |
| >3 - 10 | 46 | 1.38 (0.99, 1.92) | | 33 | 1.00 (0.66, 1.53) | 35 | 1.35 (0.88, 2.07) |
| >10 | 16 | 1.02 (0.55, 1.88) | | 7 | 1.16 (0.51, 2.63) | 24 | 0.61 (0.34, 1.09) |
|  |  | | 25OHD < 30 ng/ml |  | 25OHD 30-40 ng/ml |  | 25OHD >40 ng/ml |
| Variable | N | FR (95% CI) | | N | FR (95% CI) |  | FR (95% CI) |
| CRP b |  | 0.96 (0.75, 1.24) | |  | 0.99 (0.89, 1.10) |  | 1.04 (0.82, 1.33) |
| CRP (mg/L) |  |  | |  |  |  |  |
| <1 | 98 | 1.23 (0.91, 1.67) | | 176 | 1 | 113 | 0.95 (0.71, 1.29) |
| 1 - 3 | 64 | 0.93 (0.67 1.29) | | 72 | 0.93 (0.65, 1.33) | 67 | 1.06 (0.76, 1.46) |
| >3 - 10 | 40 | 1.11 (0.77, 1.61) | | 44 | 1.12 (0.70, 1.77) | 30 | 1.98 (1.25, 3.14) |
| >10 | 12 | 0.42 (0.13, 1.34) | | 21 | 1.05 (0.57 1.95) | 14 | 0.83 (0.32, 2.16) |
| a N= number of women, models adjusted for age, race, education, BMI, smoking status, caffeine, alcohol, recent use of estrogen, and exercise.  b Estimate for a one log-unit increase in CRP from the mean value | | | | | | | |

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| eTable 3. Adjusted associations of CRP with fecundability adjusting for or stratifying by the number of cycles of attempt at the time of the blood draw, in the Time to Conceive cohort. a | | | | | | |
| Variable |  | Results presented in main text (N=727) |  | Results from main text, adjusted for attempt cycle at blood draw |  | Among women with less than 4 cycles of attempt (N=598) |
| CRP b |  | 0.98 (0.91, 1.0) |  | 0.98 (0.91, 1.0) |  | 0.98 (0.91, 1.1) |
| CRP (mg/L) |  |  |  |  |  |  |
| <1 |  | 1 |  | 1 |  | 1 |
| 1 - 3 |  | 0.93 (0.76, 1.1) |  | 0.93 (0.76, 1.1) |  | 0.91 (0.73, 1.1) |
| >3 - 10 |  | 1.2 (0.91, 1.5) |  | 1.2 (0.93, 1.6) |  | 1.2 (0.88, 1.6) |
| >10 |  | 0.78 (0.51, 1.2) |  | 0.79 (0.52, 1.2) |  | 0.88 (0.56, 1.4) |
| a Adjusted for age, race, education, BMI, smoking status, caffeine, alcohol, recent use of estrogen.  b Estimate for a one log-unit increase in CRP from the mean value | | | | | | |

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| eTable 4. Distribution of CRP across demographic and behavioral characteristics in the first cycle of the study for women in the Time to Conceive cohort whose blood was drawn within the first three cycles of attempt. (N=598) a | | | | |
| Variable | N | 25th percentile | 50th percentile | 75th percentile |
| Age |  |  |  |  |
| 29 - 33 | 369 | 0.37 | 0.89 | 2.44 |
| 34 - 37 | 158 | 0.34 | 0.89 | 2.26 |
| 38 - 39 | 35 | 0.33 | 1.39 | 5.45 |
| >40 | 36 | 0.58 | 1.19 | 3.68 |
| How would you best describe your race/ethnicity? |  |  |  |  |
| African American | 44 | 0.68 | 1.72 | 4.43 |
| American Indian/Alaska Native | 2 | 0.28 | 0.29 | 0.30 |
| Asian/Pacific Islander | 41 | 0.20 | 0.99 | 2.64 |
| White | 477 | 0.36 | 0.83 | 2.37 |
| Hispanic | 12 | 0.26 | 1.00 | 2.98 |
| Other | 22 | 0.30 | 0.99 | 2.11 |
| Education |  |  |  |  |
| Some college or less | 38 | 0.68 | 1.91 | 7.62 |
| College graduate | 113 | 0.52 | 1.37 | 3.04 |
| Some graduate school | 285 | 0.36 | 0.78 | 2.36 |
| Professional degree | 162 | 0.35 | 0.87 | 1.68 |
| BMI |  |  |  |  |
| <18.5 | 17 | 0.15 | 0.24 | 0.72 |
| 18.5 - <25 | 375 | 0.28 | 0.60 | 1.44 |
| 25 - <30 | 124 | 0.69 | 1.61 | 2.98 |
| >=30 | 82 | 1.66 | 3.67 | 7.62 |
| Gravidity |  |  |  |  |
| None | 308 | 0.35 | 0.90 | 2.34 |
| One | 170 | 0.35 | 0.79 | 2.11 |
| Two or more | 120 | 0.46 | 1.29 | 3.20 |
| Smoking |  |  |  |  |
| Never | 454 | 0.37 | 0.87 | 2.33 |
| Current | 8 | 0.49 | 1.55 | 2.94 |
| Former | 136 | 0.35 | 1.12 | 2.83 |
| Alcohol |  |  |  |  |
| 0 | 175 | 0.42 | 1.02 | 2.46 |
| >0 - <10 | 234 | 0.48 | 0.97 | 2.70 |
| >=10 | 189 | 0.28 | 0.68 | 2.21 |
| Caffeine |  |  |  |  |
| 0 | 110 | 0.37 | 0.77 | 1.96 |
| >0 - <=1 | 286 | 0.37 | 0.84 | 2.58 |
| >1 | 202 | 0.36 | 1.03 | 2.43 |
| Months since estrogen use |  |  |  |  |
| One month or less | 29 | 1.42 | 2.77 | 4.78 |
| Two months | 21 | 0.44 | 0.96 | 1.81 |
| Three months | 46 | 0.51 | 0.93 | 1.91 |
| More than 3 months | 502 | 0.34 | 0.79 | 2.35 |
| High blood pressure |  |  |  |  |
| Yes | 33 | 0.59 | 1.81 | 4.51 |
| No | 565 | 0.36 | 0.88 | 2.35 |
| Diabetes |  |  |  |  |
| Yes | 5 | 1.43 | 4.51 | 4.96 |
| No | 593 | 0.36 | 0.89 | 2.43 |
| Vitamin D |  |  |  |  |
| <30 | 121 | 0.37 | 1.12 | 2.67 |
| 30-40 | 181 | 0.33 | 0.79 | 2.46 |
| >=40 | 135 | 0.38 | 0.79 | 2.26 |

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| Table 1. Distribution of C-reactive protein across demographic and behavioral characteristics in the first cycle of the study for women in the Time to Conceive cohort. (N=717) | | | | | | |
| C-reactive protein mg/L | | | | | | |
| Variable | N | 25th percentile | 50th percentile | | 75th percentile | |
| Age |  |  |  | |  | |
| 29 - 33 | 429 | 0.37 | 0.89 | | 2.44 | |
| 34 – 37 | 194 | 0.33 | 0.90 | | 2.37 | |
| 38 – 39 | 41 | 0.52 | 1.57 | | 6.41 | |
| >40 | 53 | 0.49 | 1.04 | | 2.76 | |
| How would you best describe your race/ethnicity? |  |  |  | |  | |
| African American | 64 | 0.68 | 1.58 | | 4.42 | |
| American Indian/Alaska Native | 2 | 0.28 | 0.29 | | 0.30 | |
| Asian/Pacific Islander | 49 | 0.42 | 1.16 | | 2.36 | |
| White | 557 | 0.36 | 0.85 | | 2.43 | |
| Hispanic | 18 | 0.20 | 1.00 | | 4.51 | |
| Mixed or Unknown | 27 | 0.31 | 1.01 | | 1.81 | |
| Education |  |  |  | |  | |
| Some college or less | 54 | 0.84 | 2.64 | | 7.82 | |
| College graduate | 144 | 0.42 | 1.37 | | 3.16 | |
| Some graduate school | 330 | 0.36 | 0.78 | | 2.32 | |
| Professional degree | 189 | 0.30 | 0.85 | | 1.69 | |
| BMI (kg/m2) |  |  |  | |  | |
| <18.5 | 20 | 0.12 | 0.31 | | 0.84 | |
| 18.5 - < 25 | 445 | 0.28 | 0.60 | | 1.43 | |
| 25 - <30 | 147 | 0.74 | 1.65 | | 3.10 | |
| >=30 | 105 | 1.66 | 3.70 | | 8.58 | |
| Gravidity |  |  |  | |  | |
| None | 361 | 0.36 | 0.89 | | 2.32 | |
| 1 | 196 | 0.35 | 0.78 | | 2.22 | |
| 2 or more | 160 | 0.54 | 1.35 | | 3.20 | |
| Smoking status |  |  |  | |  | |
| Never | 551 | 0.37 | 0.88 | | 2.37 | |
| Current | 11 | 0.25 | 1.64 | | 3.70 | |
| Former | 155 | 0.34 | 1.13 | | 3.27 | |
| Alcohol (drinks per month) |  |  |  | |  | |
| 0 | 224 | 0.44 | 1.15 | | 2.84 | |
| >0 - <10 | 268 | 0.44 | 0.97 | | 2.42 | |
| >=10 | 225 | 0.26 | 0.67 | | 2.25 | |
| Caffeine (cups per day) |  |  |  | |  | |
| 0 | 132 | 0.37 | 0.80 | | 2.53 | |
| >0 - <=1 | 348 | 0.38 | 0.89 | | 2.52 | |
| >1 | 237 | 0.36 | 1.04 | | 2.52 | |
| Exercise (hours per week) a |  |  |  | |  | |
| <1 | 175 | 0.46 | 1.01 | | 2.64 | |
| 1 – 3 | 211 | 0.42 | 1.11 | | 3.11 | |
| 4 or more | 166 | 0.28 | 0.69 | | 1.98 | |
| Attempt cycle at blood draw |  |  |  | |  | |
| 1 b | 173 | 0.32 | 0.69 | | 2.11 | |
| 2 | 282 | 0.40 | 0.98 | | 2.43 | |
| 3 | 143 | 0.36 | 0.91 | | 3.17 | |
| 4 | 78 | 0.39 | 0.96 | | 3.22 | |
| 5 or higher | 41 | 0.46 | 1.40 | | 2.76 | |
| Months since estrogen use |  |  |  | |  | |
| 1 month or less | 29 | 1.42 | 2.77 | | 4.78 | |
| 2 months | 21 | 0.44 | 0.96 | | 1.81 | |
| 3 months | 46 | 0.51 | 0.93 | | 1.91 | |
| More than 3 months | 621 | 0.35 | 0.85 | | 2.43 | |
| High blood pressure |  |  |  | |  | |
| Yes | 38 | 0.52 | 1.68 | | 4.96 | |
| No | 679 | 0.36 | 0.89 | | 2.43 | |
| Diabetes |  |  |  | |  | |
| Yes | 8 | 1.43 | 4.74 | | 8.95 | |
| No | 709 | 0.37 | 0.91 | | 2.46 | |
| Use of omega-3 supplements |  |  |  | |  | |
| No | 626 | 0.37 | 0.92 | | 2.64 | |
| Yes | 90 | 0.42 | 1.01 | | 2.11 | |
| Vitamin D (ng/ml) c |  |  |  | |  | |
| <30 | 158 | 0.38 | 1.20 | | 2.85 | |
| 30 - <40 | 215 | 0.32 | 0.77 | | 2.24 | |
| >=40 | 157 | 0.38 | 0.80 | | 2.26 | |
| Number of days of the fertile window with intercourse d |  |  |  | |  | |
| 0 | 50 | 0.43 | 1.10 | | 2.44 | |
| 1 | 132 | 0.52 | 1.06 | | 2.43 | |
| 2 | 193 | 0.32 | 0.79 | | 2.53 | |
| 3 | 145 | 0.37 | 1.06 | | 2.89 | |
| 4 | 104 | 0.36 | 0.96 | | 2.69 | |
| 5 | 33 | 0.40 | 0.67 | | 1.99 | |
| 6 | 17 | 0.40 | 1.02 | | 2.97 | |
| a Exercise was not captured on the baseline questionnaire only the monthly diary, so it is more likely to be missing.  b Three women had a blood draw prior to their first cycle of attempt and are shown in the “1” category.  c Vitamin D was measured in blood spots which were not collected during the earlier years of the study and are therefore only available for a subset of participants.  d N=44 first cycles were missing frequency of intercourse information. | | | | | | |
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| Table 2. Associations of C-reactive protein (CRP) with time to pregnancy, overall and by body mass index (BMI), in the Time to Conceive cohort. (N=717) a | | | | | | | | | | | | | |
|  | Overall | | BMI <25 kg/m2 | | | | BMI 25 - <30 kg/m2 | | | | BMI ≥30 kg/m2 | | |
| Variable | N | FR (95% CI) | N | FR (95% CI) | | N | | FR (95% CI) | | N | | | FR (95% CI) |
| CRPb | 717 | 0.98 (0.91, 1.0) | 465 | 1.0 (0.95, 1.1) | | 147 | | 0.86 (0.67, 1.1) | | 105 | | | 0.95 (0.72, 1.2) |
| CRP (mg/L) |  |  |  |  | |  | |  | |  | | |  |
| <1 | 373 | 1 | 311 | 1 | | 50 | | 1.5 (1.07, 2.0) | | 12 | | | 0.86 (0.42, 1.8) |
| 1 - 3 | 190 | 0.93 (0.76, 1.1) | 95 | 1.0 (0.81, 1.3) | | 60 | | 0.78 (0.56, 1.1) | | 35 | | | 1.1 (0.77, 1.7) |
| >3 - 10 | 109 | 1.2 (0.91, 1.5) | 44 | 1.4 (1.0, 2.0) | | 30 | | 0.95 (0.60, 1.5) | | 35 | | | 1.4 (0.89, 2.1) |
| >10 | 45 | 0.78 (0.51, 1.2) | 15 | 1.1 (0.60, 2.0) | | 7 | | 1.1 (0.50, 2.5) | | 23 | | | 0.59 (0.32, 1.1) |
|  | Excluding women with high blood pressure or diabetes | | | | | | | | | | | | |
| CRPb | 675 | 0.98 (0.91, 1.1) | 450 | | 1.0 (0.96, 1.1) | | 136 | | 0.87 (0.67, 1.1) | | | 89 | 0.92 (0.69, 1.2) |
| CRP (mg/L) |  |  |  | | | |  | |  | | |  |  |
| <1 | 360 | 1 | 302 | | 1 | | 48 | | 1.5 (1.1, 2.0) | | | 10 | 0.96 (0.47, 1.9) |
| 1 – 3 | 178 | 0.94 (0.76, 1.2) | 91 | | 1.0 (0.82, 1.3) | | 57 | | 0.79 (0.56, 1.1) | | | 30 | 1.1 (0.75, 1.7) |
| >3 - 10 | 98 | 1.2 (0.88, 1.5) | 43 | | 1.4 (0.96, 1.9) | | 24 | | 0.98 (0.61, 1.6) | | | 31 | 1.2 (0.77, 1.9) |
| >10 | 39 | 0.81 (0.53, 1.3) | 14 | | 1.2 (0.68, 2.2) | | 7 | | 1.1 (0.48, 2.5) | | | 18 | 0.55 (0.28, 1.1) |
| a “N” is the number of women. All models adjusted for age, race, education, BMI, smoking status, caffeine, alcohol, recent use of estrogen.  b Estimate is for a 1-natural log unit increase in CRP from the overall mean.  FR = Fecundability ratio  CI = Confidence interval  mg/L = milligrams/liter | | | | | | | | | | | | | |