**Supplementary Table S1. Distribution of covariates and their associations with sperm concentration (SC) in the meta-regression model.a**

|  |  |  |  |
| --- | --- | --- | --- |
| Beta for covariate (95% CI) | N (%) | Covariate value | Covariate |
| NA | 244 (100) | All | Total |
| Ref.  -1.8 (-11.4 to 7.8)  -0.8 (-11.2 to 9.5) | 75 (30.2)  79 (32.4)  90 (36.9) | All men ≤ 40 years of age  Some men >40 years of age  No information | Age |
| Ref.  1.6 (-8.6 to 11.9) | 206 (84.4)  38 (15.6) | Masturbation  Incomplete information | Method of semen collection |
| Ref.  3.4 (-5.3 to 12.1) | 127 (52.1)  117 (47.9) | Haemocytometer  Incomplete information | Method of counting sperm |
| Ref.  4.2 (-9.0 to 17.4) | 226 (92.6)  18 (7.4) | None  Some | Participants: pre-vasectomy |
| Ref.  3.4 (-13.1 to 19.8) | 205 (84.0)  39 (16.0) | None  Some | Participants: semen donors |
| Ref.  -8.5 (-19.9 to 2.9) | 207 (84.8)  37 (15.2) | No  Yes | Participants: excluding men with chronic diseases or drug treatment |
| Ref.  8.0 (-2.0 to 18.0) | 177 (72.5)  67 (27.5) | No  Yes | Participants: other exclusion criteria not related to fertility |
| Ref.  0.3 (-11.6 to 12.2) | 219 (89.8)  25 (10.2) | No  Yes | Participants selected by occupation (unrelated to fertility) |
| Ref.  -12.7 (-23.3 to -2.0) | 209 (85.7)  35 (14.3) | One per man  More than one per man | Number of samples |
| Ref.  -2.3 (-15.9 to 11.3)  -0.8 (-10.1 to 8.6)  -0.5 (-11.8 to 10.8) | 133 (54.5)  15 (6.2)  56 (22.9)  40 (16.4) | Restricted by protocol  None < 3 days  Some < 3 days  No information | Abstinence time |
| Ref.  -6.5 (-21.4 to 8.4) | 173 (70.9)  71 (29.1) | No  Yes | SC estimated |
| Ref.  9.7 (-4.0 to 23.4) | 157 (64.3)  87 (35.7) | No  Yes | SE estimated |
| Ref.  2.3 (-6.2 to 10.7) | 135 (55.3)  109 (44.7) | No  Yes | Year estimated |

aAdjusted for all covariates, fertility status, region and interaction term with fertility status and region as well as indicators for studies with more than one estimate, weighted by standard error.

**Supplementary Table S2. Comparison of meta-regression models of sperm concentration (SC) over time, with and without adjustment for covariates and interaction terms by fertility and/or geographic groups.**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Adjusted for covariatesa** | **Fertility group** | **Geographic groupb** | **Slope (95% CI),**  **million/ml/year** | **P-value for slope** | **P-value for time x fertility group** | **P-value for time x geographic group** |
| **1** | No | All | All | -0.68 (-0.99 to -0.37) | <0.001 | NA | NA |
| **2** | Yes | All | All | -0.64 (-1.06 to -0.22) | 0.003 | NA | NA |
| **3** | Yes | All | Western  Other | -1.02 (-1.54 to -0.51)  0.03 (-0.64 to 0.70) | <0.001  0.93 | NA | 0.016 |
| **4** | Yes | Unselected  Fertile | All | -1.11 (-1.72 to -0.51)  -0.29 (-0.82 to 0.23) | <0.001  0.27 | 0.034 | NA |
| **5** | Yes | Unselected | Europe/Australia  North America  Other | -1.46 (-2.20 to -0.72)  -1.47 (-2.74 to -0.20)  -0.44 (-1.27 to 0.39) | <0.001  0.024  0.30 | 0.058 | Ref.  0.992  0.025 |
| Fertile | Europe/Australia  North America  Other | -0.73 (-1.39 to -0.06)  -0.73 (-2.10 to 0.63)  0.30 (-0.42 to 1.02) | 0.033  0.29  0.41 | Ref.  0.992  0.025 |
| **6** | Yes | Unselected | Western  Other | -1.38 (-2.02 to -0.74)  -0.42 (-1.24 to 0.40) | <0.001  0.31 | 0.064 | 0.027 |
| Fertile | Western  Other | -0.68 (-1.31 to -0.05)  0.28 (-0.44 to 1.00) | 0.033  0.44 |

aAdjusted for fertility group, geographic group, age, abstinence time, semen collection method reported, counting method reported, having more than one sample per man, indicators for study selection of population and exclusion criteria (some vasectomy candidates, some semen donor candidates, exclusion of men with chronic diseases, exclusion by other reasons not related to fertility, selection by occupation not related to fertility), whether year of collection was estimated, whether arithmetic mean of SC was estimated, whether standard error of SC was estimated and indicator variable to denote studies with more than one estimate.

bWestern includes studies from North America, Europe and Australia (and New Zealand). Other includes studies from all other countries (including South America, Asia and Africa).

**Supplementary Table S3. Sensitivity analyses of meta-regression models of sperm concentration (SC) over time.**

|  |  |  |  |
| --- | --- | --- | --- |
| Slope when covariate in removed from the modelb | Slope  Excluding groupa | Group excluded | Covariate |
| -1.38 | NA | - | Total |
| -1.36 | -1.10 | No information | Age |
| -1.39 | -1.66 | Incomplete information | Method of semen collection |
| -1.36 | -1.43 | Incomplete information | Method of counting sperm |
| -1.39 | -1.47 | Some | Participants: pre-vasectomy |
| -1.41 | -1.49 | Some | Participants: semen donors |
| -1.33 | -1.61 | Yes | Participants: excluding men with chronic diseases or drug treatment |
| -1.30 | -1.28 | Yes | Participants: other exclusion criteria not related to fertility |
| -1.39 | -1.56 | Yes | Participants selected by occupation (unrelated to fertility) |
| -1.33 | -1.31 | More than one per man | Number of samples |
| -1.38 | -1.34 | No information | Abstinence time |
| -1.41 | -1.25 | Yes | SC estimated |
| -1.41 | -1.32 | Yes | SE estimated |
| -1.38 | -1.52 | Yes | Year estimated |

a Slope (change of SC per year for men unselected by fertility from Europe/Australia/North America) in regression adjusted for all covariates, fertility status, region and interaction term with fertility status and region as well as indicators for studies with more than one estimate, weighted by standard error, after excluding specific group for each covariate, such as the group with incomplete information.

b Slope (change of SC per year for men unselected by fertility from Europe/Australia/North America) in regression adjusted for all covariates, fertility status, region and interaction term with fertility status and region as well as indicators for studies with more than one estimate, weighted by standard error, removing covariates one at a time from the model.