**Supplementary Online Material**

The supplementary material file includes the following sections:

**Supplementary Table 1** Correlation Matrix

**Supplementary Table 2** Models Parameters

**Supplementary Table 3** Association between paternal age at birth and risk of schizophrenia using conditional logistic regression.

**Supplementary Table 4** Association between paternal age at birth and risk of bipolar disorder using conditional logistic regression.

**Supplementary Text 1**.**The association between paternal age at birth and risk of schizophrenia in males**

**Supplementary Table 5**: The association between paternal age at birth and risk of schizophrenia in the entire male population and in the male siblings cohort

**Supplementary Table** 6: The association between paternal age at birth of first child and risk of schizophrenia in the male sibling cohort.

**Supplementary Table** 7: The association between paternal age at birth and risk of schizophrenia in the male sibling cohort stratified by sibship

**Supplementary Text 2**.**The association between paternal age at birth and risk of bipolar disorder in males**

**Supplementary Table 8**: The association between paternal age at birth and risk of bipolar disorder in the entire male population and in the male sibling cohort

**Supplementary Table 9**: The association between paternal age at birth of first child and risk of bipolar disorder in the male sibling cohort.

**Supplementary Table 10**: The association between paternal age at birth of first child and risk of bipolar disorder in the male sibling cohort stratified by sibship

**Supplementary Table 1: Correlation Matrix**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | VIF | Birth year | Paternal age at birth | Maternal age at birth | SES | Paternal age at birth of first child |
| Birth Year | 1.02 | 1 | 0.01 | 0.01 | 0.009 | -0.14 |
| Paternal age at birth | - |  | 1 | 0.46 | -0.009 | 0.79 |
| Maternal age at birth | 1.17 |  |  | 1 | -0.03 | 0.38 |
| SES | 1.00 |  |  |  | 1 | -0.05 |
| Paternal age at birth of first child | 1.20 |  |  |  |  | 1 |

All of the variables in the table are categorical: Maternal age (years; 16-19, 20-24, 25-29, 30-34, 35-39, 40-45), socioeconomic status (SES) into quartiles, year of birth (1960-1964,.1965-1969, 1970-1974,1975-1979,1980-1984,1985-1990)

**Supplementary table 2A:** Models Parameters of the main analysis in Schizophrenia

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Paternal age categories- Entire Sample** | **(model 1)**  **Crude OR**  **[95%CI]** | **SE** | **(model 2)**  **adjusted OR**  **[95%CI]1** | **SE** | **(model 3)**  **adjusted OR**  **[95%CI]2** | **SE** | **(model 4)**  **adjusted OR**  **[95%CI]3** | **SE** |
| 16-24 | 1.04  [0.94-1.14] | 0.05 | .0.98  [.0.89-1.08] | 0.05 | 0.96  [0.87-1.06 ] | 0.05 | **0.86**  **[0.77-0.95 ]** | 0.05 |
| 25-29 | 1 |  | 1 |  | 1 |  | 1 |  |
| 30-34 | 1.06  [0.98,1.14] | 0.03 | .1.06  [0.98-1.15] | 0.04 | 1.09  [1.013-1.18 ] | 0.04 | 0.93  [0.84-1.02 ] | 0.04 |
| 35-39 | **1**.**22**  **[1**.**12,1**.**34]** | **0.04** | **1.19**.  **[1.08-1.31**.**]** | **0.04** | **1.18**  **[1.08-1.30 ]** | **0.04** | 0.88  [0.77-1.01 ] | **0.06** |
| 40-44 | **1**.**44**  **[1**.**29-1**.**62]** | **0.05** | .**1.34**  **[**.**1.18-1.52]** | **0.06** | **1.29**  **[1.14-1.47 ]** | **0.06** | 0.82  [0.68-1.00 ] | **0.09** |
| 45-60 | **1**.**71**  **[1**.**49-1**.**99]** | **0.07** | .**1.54**  **[1.31-1.80**.**]** | **0.08** | **1.49**  **[1.27-1.75 ]** | **0.08** | 0.81  [0.63-1.04 ] | **0.12** |
| Maternal Age |  |  |  | **0.01** |  | **0.01** |  | **0.01** |
| SES |  |  |  | **0.01** |  | **0.01** |  | **0.01** |
| Year of birth |  |  |  |  | **]** | **0.01** |  | **0.01** |
| Paternal age at birth of 1st child |  |  |  |  |  |  |  | **0.02** |
| **Siblings Sample** |  |  |  |  |  |  |  |  |
| 16-24 | .1.05  [.0.93-1.19] | 0.06 | 1.00  [0.89-1.14] | 0.06 | 0.96  [0.84-1.09] | 0.06 | **0.86**  **[0.75-0.98]** | 0.06 |
| 25-29 | 1 |  | 1 |  | 1 |  | 1 |  |
| 30-34 | .1.03  [0.93-1.19.] | 0.04 | 1.03  [0.94-1.14 ] | 0.04 | 1.09  [0.99-1.20] | 0.04 | 0.95  [0.85-1.06] | 0.05 |
| 35-39 | **1.18**  **[**.**1.05-1.32]** | **0.05** | **1.16**  **[1.02-1.31 ]** | **0.06** | **1**.22  **[1.08-1.38]** | 0.06 | 0.93  [0.79-1.08] | 0.07 |
| 40-44 | .**1.46**  **[**.**1.25-1.71]** | **0.08** | **1.38**  **[1.17-1.64 ]** | **0.08** | **1.43**  **[1.21-1.69]** | 0.08 | 0.91  [0.73-1.14] | 0.11 |
| 45-60 | .**1.72**  **[**.**1.39-2.12]** | **0.10** | **1.57**  **[1.26-1.97 ]** | **0.11** | **1. 63**  **[1.31-2.04]** | **0.11** | 0.85  [0.62-1.16]**]** | **0.15** |
| Maternal Age |  |  |  | **0.01** |  | **0.01** |  | **0.01** |
| SES |  |  |  | **0.01** |  | **0.01** |  | **0.02** |
| Year of birth |  |  |  |  |  | **0.02** |  | **0.01** |
| Paternal age at birth of 1st child |  |  |  |  |  |  |  | **0.02** |

**Supplementary table 2B:** Models Parameters of the main analysis in Bipolar Disorder

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **paternal age categories-Entire sample** | **(model 1)**  **Crude OR**  **[CI 95%]** | **SE** | **(model 2)**  **adjusted OR**  **[CI 95%]1** | **SE** | **(model 3)**  **adjusted OR**  **[CI 95%]2** | **SE** | **(model 4)**  **adjusted OR**  **[CI 95%]3** | **SE** |
| 16-24 | 0.91  [0.72-1.14] | 0.11 | 0.93  [0.74-1.17] | 0.11 | 0.91  [0.72-1.15 ] | 0.11 | .0.86  [0.68-1.10] | 0.12 |
| 25-29 | 1 |  | 1 |  | 1 |  | 1 |  |
| 30-34 | 1.03  [0.86-1.22] | 0.08 | 1.03  [0.86-1.22 ] | 0.08 | 1.05  [0.88-1.25 ] | 0.08 | 0.97  [0.79-1.19 ] | 0.10 |
| 35-39 | 1.21  [0.99-1.48] | 0.10 | 1.24  [1.00-1.53] | 0.10 | 1.24  [1.00-1.53 ] | 0.10 | 1.06  [0.79-1.43] | 0.15 |
| 40-44 | 1.26  [0.97-1.65] | 0.13 | 1.32  [0.98-1.77] | 0.14 | 1.28  [0.96-1.72 ] | 0.14 | 1.01  [0.66-1.55 ] | 0.21 |
| 45-60 | **1**.**61**  **[1**.**16-2**.**24]** | **0.16** | **1.71**  **[1.04-2.45 ]** | 0.18 | **1.68**  **[1.17-2.39]** | 0.18 | 1.21  [0.70-2.11] | 0.28 |
| Maternal age |  |  |  | 0.02 |  | 0.02 | 0.99  [0.93-1.04] | 0.02 |
| SES |  |  |  | 0.03 |  | 0.03 |  | 0.03 |
| Year of birth |  |  |  |  |  | 0.03 |  | 0.03 |
| Paternal age at 1st child |  |  |  |  |  |  |  | 0.04 |
| **Siblings Sample** |  |  |  |  |  |  |  |  |
| 16-24 | 1.10  [0.84-1.45] | 0.13 | 1.17  [0.89-1.54 ] | 0.13 | 1.12  [0.85-1.47 ] | 0.14 | 1.02  [0.90-1.62 ] | 0.14 |
| 25-29 | 1 |  | 1 |  | 1 |  | 1 |  |
| 30-34 | 1.08  [0.89-1.34] | 0.10 | 1.10  [0.89-1.35 ] | 0.10 | 1.15  [0.93-1.42] | 0.10 | 1.04  [0.84-1.34 ] | 0.11 |
| 35-39 | **1**.**32**  **[1**.**04-1**.**69]** | 0.12 | 1.41  [1.91-1.82] | 0.13 | 1.48  [1.14-1.92 ] | 0.13 | 1.20  [0.89-1.71 ] | 0.16 |
| 40-44 | 1.11  [0.75-1.63] | 0.19 | 1.24  [0.82-1.87 ] | 0.20 | 1.28  [0.85-1.93 ] | 0.20 | 0.91  [0.56-1.69 ] | 0.26 |
| 45-60 | **1**.**60**  **[1**.**00-2**.**56]** | **0.24** | **1.86**  **[1.13-3.07 ]** | **0.25** | **1.93**  **[1.17-3.17 ]** | 0.25 | 1.16  [0.56-2.71 ] | 0.34 |
| Maternal age |  |  |  | 0.03 |  | 0.03 |  | 0.03 |
| SES |  |  |  | 0.03 |  | 0.03 |  | 0.03 |
| Year of birth |  |  |  |  |  | 0.04 |  | 0.04 |
| Paternal age at 1st child |  |  |  |  |  |  |  | 0.05 |

**Supplementary Table 3:** Association between paternal age at birth of offspring and risk of schizophrenia using conditional logistic regression. Results of families with an affected sibling are shown. Families with two or more affected siblings were removed.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Paternal age categories** | **Siblings Cohort** | **Schizophrenia Cases** | **Crude OR [CI 95%]** | **adjusted OR [CI 95%]1** |
| 16-24 | 776 | 327 | 1.18  [0.99-1.42] | **1.24**  **[1.02-1.52]** |
| 25-29 | 2452 | 936 | 1 | 1 |
| 30-34 |  | 755 | **0.78**  **[0.68-0.89]** | **0.74**  **[0.62-0.87]** |
| 35-39 | 2218 | 411 | **0.64**  **[0.54-0.77]** | **0.58**  **[0.44-0.77]** |
| 40-44 |  | 187 | **0.55**  **[0.42-0.73]** | **0.48**  **[0.31-0.74]** |
| 45-60 | 1283 | 96 | **0.50**  **[0.32—0.77]** | **0.41**  **[0.22-0.77]** |
|  | **7520** | **2712** |  |  |

OR= Odd ratio; CI=confidence of interval

Overall 613455 (98.9%) of the sample was censored before the occurrence of the first event, number of cases=2772,

1- Adjusted for maternal age at birth, socioeconomic status and year of birth

Covariate were modeled categorically: Maternal age (years; 16-19, 20-24, 25-29, 30-34, 35-39, 40-45), socioeconomic status (SES) into quartiles, year of birth (1960-1964,.1965-1969, 1970-1974,1975-1979,1980-1984,1985-1990)

**Supplementary Table 4:** Association between paternal age at birth of offspring and risk of schizophrenia using conditional logistic regression. Results of families with an affected sibling are shown. Families with two or more affected siblings were removed.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Paternal age categories** | **Siblings Cohort** | **Bipolar Cases** | **Crude OR [CI 95%]** | **adjusted OR**  **[CI 95%]1** |
| 16-24 | 185 | 198 | 1.09  [0.75-1.59] | 0.99  [0.64-1.52] |
| 25-29 | 579 | 73 | 1 | 1 |
| 30-34 | 506 | 170 | 0.84  [0.64-1.11] | 1.00  [0.70-1.43] |
| 35-39 | 268 | 98 | 0.87  [0.60-1.26] | 1.31  [0.72-2.37] |
| 40-44 | 100 | 30 | 0.66  [0.35-1.23] | 1.19  [0.47-3.00] |
| 45-60 | 61 | 19 | 0.53  [0.18—1.49] | 0.12  [0.27-4.57] |
|  | **1699** | **588** |  |  |

OR= Odd ratio; CI=confidence of interval

Overall 618,908 (99.8%) of the sample was censored before the occurrence of the first event, number of cases=590,

1- Adjusted for maternal age at birth, socioeconomic status and year of birth

Covariates appear categorically: Maternal age (years;16-19, 20-24, 25-29, 30-34, 35-39, 40-45), socioeconomic status (by quartiles) and year of birth (1960-1965,1965-1970,1970-1975,1975-1980,1980-1985,>1985).

***Supplementary Text 1: Paternal age at birth and risk of schizophrenia among males only***

Out of 559,892 males, 3699 (0.7%) were hospitalized with schizophrenia and 582 (0.1%) with bipolar disorder during the follow-up period. leaving 556,193 as a control group. Mean age at end of the follow-up was 40.34 (SD=4.80, Median=40). After randomly removing one twin from each twin-pair, there were overall 363,711 full siblings in the cohort including 2,229 (0.6%) with schizophrenia and 375 (0.1%) with bipolar disorder.

In the entire male population, there was a statistically significant increase in risk for schizophrenia with advancing categories of paternal age (**Supplementary Table 3, top panel**). Offspring of fathers aged 45-60 at birth were at the highest risk for schizophrenia (adjusted OR=1.49, 95% CI: 1.27-1.75).

Results were similar in the population of siblings: there was a statistically significant increase in risk for schizophrenia with advancing paternal age (**Supplementary Table 3, bottom panel**).

Advanced paternal age at birth of first child was also associated with increased risk of schizophrenia and remained statistically significant after adjustment for maternal age at birth, year of birth and SES (**Supplementary Table 4, models 1-3**). More importantly, when including paternal age at birth of first child as a covariate, advanced paternal age at birth of a subsequent child no longer increased the risk of schizophrenia (**Table 1, adjusted model #4**).

When taking family into account as strata in a conditional logistic regression, there was no statistically significant association between advanced paternal age at birth and risk of schizophrenia within discordant sibling pairs (**Supplementary Table3**).

**Supplementary Table 5: The association between paternal age at birth and risk of schizophrenia in the entire male population and in the male sibling cohort**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Paternal age categories** | **Male**  **Cohort** | **schizophrenia cases** | **Crude OR**  **[CI 95%]** | **adjusted**  **OR [CI 95%]1** | **adjusted OR**  **[CI 95%]2** | **adjusted**  **OR [CI 95%]3** |
| 16-24 | 77,8377 | 489 | 1.02  [0.92-1.14] | 0.98  [0.88-1.09] | 0.96  [0.86-1.07] | **0.87**  **[0.78-0.98]** |
| 25-29 | 193,121 | 1182 | 1 | 1 | 1 | 1 |
| 30-34 | 149,679 | 951 | 1.03  [0.95-1.13] | 1.03  [0.95-1.13] | 1.05  [0.96-1.14] | 0.90  [0.81-1.01] |
| 35-39 | 81,850 | 591 | **1**.**18**  **[1**.**06-1**.**30]** | **1.14**  **[1.02-1.27]** | 1.13  [1.02-1.26] | 0.87  [0.74-1.01] |
| 40-44 | 35,686 | 301 | **1**.**37**  **[1**.**21-1**.**56]** | **1.29**  **[1.12-1.48]** | **1.25**  **[1.09-1.44]** | 0.83  [0.67-1.04] |
| 45-60 | 18,020 | 185 | **1**.**67**  **[1**.**43-1**.**96]** | **1.52**  **[1.28-1**.**80]** | **1.49**  **[1.25-1.76]** | 0.86  [0.65-1.14] |
| Total | 556,193 | 3699 |  |  |  |  |
|  | **Male Siblings cohort** |  |  |  |  |  |
| 16-24 | 46,524 | 284 | 1.06  [0.92-1.21] | 1.02  [0.89-1.18] | 0.99  [0.86-1.13] | 0.89  [0.77-1.02] |
| 25-29 | 133,456 | 767 | 1 | 1 | 1 | 1 |
| 30-34 | 104,090 | 614 | 1.02  [0.92-1.21] | 1.02  [0.92-1.13] | 1.06  [0.95-1.18] | 0.93  [0.82-1.05] |
| 35-39 | 50,294 | 339 | **1.17**  **[1.03-1.33]** | 1.14  [0.99-1.31] | **1.19**  **[1.03-1.36]** | 0.91  [0.77 1.08] |
| 40-44 | 18,597 | 140 | **1**.**31**  **[1.09-1.56]** | **1**.**24**  **[1.02-1.50]** | **1.27**  [**1.04-1.54]** | 0.82  [0.63-1.06] |
| 45-60 | 8521 | 85 | **1.73**  **[1.38-2.17]** | **1**.**60**  **[1.25-2.04]** | **1.64**  **[1.29-2.09]** | 0.88  [0.62-1.24] |
| Total | 361,482 | 2229 |  |  |  |  |

OR= odds ratio; CI=confidence of interval

1=adjusted for maternal age at birth and SES

2=adjusted for maternal age at birth SES and year of diagnosis

3=adjusted for maternal age at birth, SES year of diagnosis and paternal age at birth of first child

**Supplementary Table 6** Association between paternal age at birth of first child and risk of schizophrenia in the entire male population, using logistic regression.

|  |  |  |
| --- | --- | --- |
| **Paternal age categories** | **Crude OR**  **[CI 95%]** | **adjusted OR**  **[CI 95%]1** |
| 16-24 | 1,00  [0.92-1.10] | 0.97  [0.88-1.06] |
| 25-29 | 1 | 1 |
| 30-34 | **1.24**  **[1.14-1.35]** | **1.19**  **[1.09-1.30]** |
| 35-39 | **1.43**  **[1.29-1.59]** | **1.29**  **[1.15-1.44]** |
| 40-44 | **1.64**  **[1.43-1.88]** | **1.43**  **[1.23-1.65]** |
| 45-60 | **1.77**  **[1.48-2.11]** | **1.51**  **[1.25-1.83]** |

OR= hazard ratio; CI=confidence of interval

1- Adjusted for maternal age at birth, SES and year of birth

Note: ‘sibling’s cohort’ includes the subset of siblings from the ‘entire population’. Covariate were modeled categorically: Maternal age (years; 16-19, 20-24, 25-29, 30-34, 35-39, 40-45), SES (into quartiles), year of birth (1960-1964,.1965-1969, 1970-1974,1975-1979,1980-1984,1985-1990)

**Supplementary Table 7:** Association between paternal age at birth and risk of schizophrenia in the male population, using Conditional Logistic regression. Results of siblings based stratified analysis.

|  |  |  |
| --- | --- | --- |
| **Paternal age categories** | **Crude OR**  **[CI 95%]** | **adjusted OR**  **[CI 95%]1** |
| 16-24 | **1.39**  **[1.07-1.82]** | **1.37**  **[1.01-1.85]** |
| 25-29 | 1 | 1 |
| 30-34 | **0.70**  **[0.57-0.84]** | **0.72**  **[0.57-0.92]** |
| 35-39 | **0.50**  **[0.38-0.65]** | **0.54**  **[0.36-0.82]** |
| 40-44 | **0.32**  **[0.22-0.48]** | **0.37**  **[0.20-0.67]** |
| 45-60 | **0.27**  **[0.15-0.49**] | **0.33**  **[0.14-0.78]** |

OR= hazard ratio; CI=confidence of interval

Overall 359,362 (98.8%) of the sample was censored before the occurrence of the first even, n cases=2229,

1- Adjusted for maternal age at birth, SES and year of birth

Note: ‘sibling cohort’ includes the subset of siblings from the ‘entire population’. Covariate were modeled categorically: Maternal age (years; 16-19, 20-24, 25-29, 30-34, 35-39, 40-45), SES (into quartiles), year of birth (1960-1964,.1965-1969, 1970-1974,1975-1979,1980-1984,1985-1990).

***Supplementary Text 2: Paternal age at birth and risk of bipolar disorder among males only***

In the entire male population, there was a statistically significant increase in risk for schizophrenia with advancing categories of paternal age (**Supplementary Table 6, top panel**). Offspring of fathers aged 45-60 at birth were at the highest risk for schizophrenia (adjusted OR=1.87, 95% CI: 1.24-2.81). Results were similar in the population of siblings: there was a statistically significant increase in risk for schizophrenia with advancing paternal age (**Supplementary Table 6, bottom panel**).

Advanced paternal age at birth of first child was also associated with increased risk of bipolar disorder, but this association did not remain statistically significant after adjustment for maternal age at birth, year of birth and SES (**Supplementary Table 7,**). Moreover, when including paternal age at birth of first child as a covariate, advanced paternal age at birth of a subsequent child no longer increased the risk of bipolar disorder (**Supplementary Table 6, adjusted model #4**).

When taking family into account as strata in a conditional logistic regression, there was no statistically significant association between advanced paternal age at birth and risk of schizophrenia within discordant sibling pairs (**Supplementary Table 8**).

**Supplementary Table 8: The association between paternal age at birth and risk of bipolar disorder in the entire male population and in the sibling cohort**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **paternal age categories** | **Male cohort** | **bipolar disorder (n)** | **Crude OR**  **[CI 95%]** | **adjusted OR**  **[CI 95%]1** | **adjusted OR**  **[CI 95%]2** | **adjusted OR**  **[CI 95%]3** |
| 16-24 (n=76,849) | 76,776 | 73 | 0.89  [0.68-1.16] | 0.93  [0.71-1.22] | 0.91  [0.69-1.19] | 0.84  [0.63-1.12] |
| 25-29 (n=191,185) | 190,932 | 203 | 1 | 1 | 1 | 1 |
| 30-34 (n=148,035) | 147,896 | 139 | 0.88  [0.71-1.09] | 0.88  [0.71-1.09] | 0.89  [0.72-1.11] | 0.80  [0.61-1.04] |
| 35-39 (n=80,823) | 80,737 | 86 | 0.99  [0.77-1.28] | 1.03  [0.79-1.35] | 1.03  [0.79-1.35] | 0.83  [0.56-1.123 |
| 40-44 (n=35,134) | 35,086 | 48 | 1.27  [0.93-1.74] | 1.375  [0.96 -1.94] | 1.33  [0.94-1.89] | 0.96  [0.56-1.66] |
| 45-60 (n=17,724) | 17,691 | 33 | **1.73**  **[1.20-2.50]** | **1.91**  **[1.27-2.87]** | **1.87**  **[1.24-2.81]** | 1.21  [0.60-2.42] |
| total (n=549,700) | 549,118 | 582 |  |  |  |  |
|  | **Male Sibling cohort** |  |  |  |  |  |
| 16-24 | 46,755 | 53 | 1.10  [0.80-1.52] | 1.20  [0.87-1.66] | 1.14  [0.82-1.58] | 1.03  [0.73-1.46] |
| 25-29 | 134,086 | 137 | 1 | 1 | 1 | 1 |
| 30-34 | 104,607 | 97 | 0.90  [0.70-1.17] | 0.91  [0.70-1.18] | 0.96  [0.73-1.24] | 0.85  [0.63-1.14] |
| 35-39 | 50,583 | 50 | 0.96  [0.70-1.33] | 1.06  [0.75-1.49] | 1.12  [0.79-1.57] | 0.88  [0.57-1.36] |
| 40-44 | 18,712 | 25 | 1.30  [0.85-2.00] | 1.54  [0.97-2.45] | **1.59**  **[1.01-2.53]** | 1.09  [0.58-2.04] |
| 45-60 | 8,593 | 13 | 1.48  [0.83-2.61] | **1.85**  **[1.01-3.39]** | **1.91**  **[1.04-3.51]** | 1.11  [0. 47-2.63] |
| total | 363,336 | 375 |  |  |  |  |

OR= odds ratio; CI=confidence of interval

1=adjusted for maternal age at birth and SES

2=adjusted for maternal age at birth SES and year of diagnosis

3=adjusted for maternal age at birth, SES year of diagnosis and paternal age at birth of first child

**Supplementary Table 9** Association between paternal age at birth of first child and risk of bipolar disorder in the entire male population, using logistic regression.

|  |  |  |
| --- | --- | --- |
| **Paternal age categories** | **Crude OR**  **[CI 95%]** | **adjusted OR**  **[CI 95%]1** |
| 16-24 | 1.14  [0.88-1.47] | 1.15  [0.86-1.54] |
| 25-29 | 1 | 1 |
| 30-34 | 1.23  [0.94-1.62] | 1.26  [0.91-1.74] |
| 35-39 | 1.36  [0.92-2.01] | 1.42  [0.83-2.42] |
| 40-44 | 1.51  [0.84-2.73] | 1.68  [0.76-3.74] |
| 45-60 | **1.21**  **[1.08-4.51]** | 2.72  [0.94-7.89] |

OR= hazard ratio; CI=confidence of interval

1- Adjusted for maternal age at birth, SES and year of birth

Note: ‘sibling’s cohort’ includes the subset of siblings from the ‘entire population’. Covariates were modelled categorically: Maternal age (years;16-19, 20-24, 25-29, 30-34, 35-39, 40-45), SES (into quartiles), year of birth (1960-1964,.1965-1969, 1970-1974,1975-1979,1980-1984,1985-1990)

**Supplementary Table 10:** Association between paternal age at birth and risk of bipolar disorder in the male population, using Conditional Logistic regression. Results of siblings based stratified analysis.

|  |  |  |
| --- | --- | --- |
| **Paternal age categories** | **Crude OR**  **[CI 95%]** | **Adjusted OR**  **[CI 95%]** |
| 16-24 | 1.08  [0.61-1.90] | 1.07  [0.57-2.00] |
| 25-29 | 1 | 1 |
| 30-34 | 0.51  [0.32-0.80] | 0.64  [0.35-1.14] |
| 35-39 | 0.48  [0.25-0.92] | 0.91  [0.33-2.52] |
| 40-44 | 0.91  [0.37-2.25] | 2.39  [0.55-10.40] |
| 45-60 | 0.30  [0.05-1.81] | 0.71  [0.06-8.22] |

OR= hazard ratio; CI=confidence of interval

Overall 363,001 (99.8%) of the sample was censored before the occurrence of the first even, n cases=375.

1- Adjusted for maternal age at birth, SES and year of birth

Note: ‘sibling’s cohort’ includes the subset of siblings from the ‘entire population’. Covariate were modeled categorically: Maternal age (years; 16-19, 20-24, 25-29, 30-34, 35-39, 40-45), SES (into quartiles), year of birth (1960-1964,.1965-1969, 1970-1974,1975-1979,1980-1984,1985-1990).