**Supplement**

**Supplement to: Magnus MC, Havdahl A, Morken NH, et al. Risk of miscarriage in women with psychiatric disorders**

**Content**

Supplementary methods……………………………………………………………………………..…….….…p.3

Supplementary Table 1. Diagnostic codes used to define the different psychiatric disorders in specialist care (ICD-10) and primary care (ICPC-2)……………….………………………….…………………………....…p.4

Supplementary Table 2. Diagnostic codes used to define chronic somatic diseases in specialist care (ICD-10 codes), and in primary care (ICPC- codes)……………………………………………………….……………...p.5

Supplementary Table 3. Prevalence of chronic somatic diseases prior to pregnancy among 593,009 pregnancies in Norway between 2010 and 2016)……………………………………………………….………………..…p.6

Supplementary Figure 1. Adjusted risk difference (RD) of pre-existing psychiatric disorders with risk of miscarriage…………………………………………..………………..…………….…………………….…..…p.7

Supplementary Figure 2. Unadjusted odds ratio (OR) of pre-existing psychiatric disorders with risk of miscarriage…………………………………………………………………………………………………....…p.8

Supplementary Figure 3. Adjusted\* odds ratio (OR) of pre-existing psychiatric disorders with risk of miscarriage……………………………………………………………………....…………….……………..….p.9

Supplementary Figure 4. Adjusted odds ratios (OR) of pre-existing psychiatric disorders with risk of miscarriage restricted to women who were primigravida (first pregnancies)…..…………………………………..………..p.10

Supplementary Figure 5. Adjusted odds ratios (OR) of pre-existing psychiatric disorders with risk of miscarriage stratified according to whether the miscarriage was identified in the birth or patient databases (specialist care) as opposed to the general practice database (primary care)…………………………………………………….…p.11

Supplementary Figure 6. Adjusted odds ratios (OR) of pre-existing psychiatric disorders with risk of miscarriage only looking at psychiatric disorders diagnosed in specialist care services……………………………..……...p.12

Supplementary Figure 7. Adjusted odds ratios (OR) of pre-existing psychiatric disorders with additional adjustment for substance use disorders and chronic somatic conditions…….……………………………........p.13

**Supplement methods**

**Estimation of the proportion of induced abortions for adjustment of miscarriage risk**

In 1983, Susser proposed adding 50% of induced abortions to the denominator, assuming that the gestational-week distribution of induced abortions and miscarriages are roughly similar.1With data from the Norwegian anonymous induced abortion register, we found that induced abortions in Norway occur relatively early compared with miscarriages, so that adding 50% of induced abortions would over-adjust.

A formal solution would be a life-table analysis of competing risks, which would require information on gestational-week-specific risks for both induced abortion and miscarriage. In the Norwegian data sets, we have no information on week-specific risk of miscarriage, and information on week-specific risk of induced abortion is available only for the whole population, not within disease-specific strata. In order to provide a rough adjustment for induced abortion appropriate to our data, we identified a referent set of week-specific miscarriage risks,2 and combined this with the overall week-specific risk of induced abortions from the Norwegian induced abortion register. With these two data sets, we could generate the estimated number of miscarriages that occurred among pregnancies intended for termination, and the total number of miscarriages that could have occurred in those pregnancies if no termination had occurred. The ratio of these two numbers was 20%, which serves as a rough estimate of the proportion of induced abortions needed to add to the denominator of miscarriage risk to minimize bias.

This adjustment is subject to at least two important caveats. We must assume that the published set of referent gestational-week-specific miscarriage risks provide a reasonable estimate of the risk in Norway, and that the overall gestational-week distribution of induced abortions in Norway is similar within each category of chronic disease.

To obtain estimates of the associations accounting for induced abortions, we randomly sampled 20% of the induced abortions a total of 1000 times and calculated the effect estimates as an average across these estimates. The standard errors of the effect estimates were estimated by combining the estimated variance of the betas across and between the iterations using the following equation drawing on Rubin’s rules:
$$σ^{2}= \overbar{U}+\left\{1+\frac{1}{m}\right\} B$$

, where $ \overbar{U}$ is the estimate of the variance of the beta coefficient within the iteration (calculated as the squared of the standard error), and $B$ is the estimate of the variance of the beta coefficient between the iterations.

**Supplementary Table 1. Diagnostic codes used to define the different psychiatric** **disorders** **in specialist care (ICD-10) and primary care (ICPC-2).**

|  |  |  |
| --- | --- | --- |
| **Psychiatric disorders** | **ICD-10 Code(s)** | **ICPC-2 Code(s)** |
| Schizophrenia spectrum disorders \* |  | P72, P98 |
| Bipolar disorder | F30-F31, F34.0 | P73 |
| Depressive disorders | F32-F33, F34.1 | P76 |
| Anxiety disorders | F40-F44, F93.0-F93.2 | P74, P79, P82 |
| Somatoform disorders | F45 | P75 |
| Eating disorders | F50 | P86 |
| Intellectual disability | F70-F79 | P85 |
| Autism spectrum disorders | F84 |  |
| Attention-deficit/hyperactivity disorder | F90 | P81 |
| Personality disorders | F60-F61 | P80 |
| Conduct disorder | F91-F92 |  |
| Unspecified mental disorder | F99 | P99, P77 |

\*  We did not have information available on the diagnostic codes used for this psychiatric condition from the specialist health-care services.

**Supplementary Table 2. Diagnostic codes used to define substance use disorders and chronic somatic diseases in specialist care (ICD-10 codes), and in primary care (ICPC- codes).**

|  |  |  |  |
| --- | --- | --- | --- |
| **Group of diseases** | **Diseases** | **International Classification of Diseases (ICD-10) codes**  | **International Classification of Primary Care (ICPC-2) codes**  |
| Autoimmune diseases | Type 1 diabetes | E10 | T89 |
| Celiac disease | K90.0 |  |
| Systemic lupus erythematosus | M32 |  |
| Multiple sclerosis\* |  | N86 |
| Rheumatoid arthritis/ Ankylosing spondylitis | M05-M09, M45 | L88 |
| Ulcerative colitis | K50.0, K50.1, K50.8, K50.9, K51.0, K51.1, K51.2, K51.3, K51.4, K51.5, K51.8, K51.9, K52.0 | D94 |
| Psoriasis\* |  | S91 |
| Crohn´s disease | K50 |  |
| Addison disease | E27.1, E27.2 |  |
| Haemolytic anemia | D55- D59 | B78 |
| Cardiometabolic diseases | Type 2 diabetes | E11 | T90 |
| Hypertensive disorders | I10-I15 | K85-87 |
| Atherosclerosis | I25.1, I70 |  |
| Endocrinological diseases | Hypothyroidism | E01 E03 | T86 |
| Hyperthyroidism | E05 | T85 |
| Hypoparathyroidism | E20  |  |
| Hyperparathyroidism | E21.0 , E21.1, E21.2, E21.3  |  |
| Cushing syndrome | E24  |  |
| Neurological diseases | Epilepsy | G40-41 | N88 |
| Migraine | G43 G44.1 | N89 |
| Allergic diseases | Asthma | J45 and J46  | R96 |
| Allergic rhinitis | J30 | R97 |
| Atopic dermatitis | L20 | S87 |
| Reproductive diseases | Polycystic ovary syndrome | E28.2 |  |
| Endometriosis | N80 |  |
| Substance use disorders |  |  | P15-P19 |

\*Information on these conditions were not available from the patient registry.

**Supplementary Table 3. Prevalence of substance use disorders and chronic somatic diseases prior to pregnancy among 593 009 pregnancies in Norway between 2010 and 2016).**

|  |  |  |  |
| --- | --- | --- | --- |
| **Group of diseases** | **Diseases** | **No. pregnancies**  | **%**  |
| Autoimmune diseases | Type 1 diabetes | 1808 | 0.30 |
| Celiac disease | 791 | 0.13 |
| Systemic lupus erythematosus | 246 | 0.04 |
| Multiple sclerosis | 720 | 0.12 |
| Rheumatoid arthritis/ Ankylosing spondylitis | 2559 | 0.43 |
| Ulcerative colitis | 2817 | 0.48 |
| Psoriasis | 3160 | 0.53 |
| Crohn´s disease | 1603 | 0.27 |
| Addison disease | 56 | 0.01 |
| Haemolytic anemia | 194 | 0.03 |
| Cardiometabolic diseases | Type 2 diabetes | 1951 | 0.33 |
| Hypertensive disorders | 5334 | 0.90 |
| Atherosclerosis | 66 | 0.01 |
| Endocrinological diseases | Hypothyroidism | 8372 | 1.41 |
| Hyperthyroidism | 2374 | 0.40 |
| Hypoparathyroidism | 29 | 0.005 |
| Hyperparathyroidism | 128 | 0.02 |
| Cushing syndrome | 31 | 0.01 |
| Neurological diseases | Epilepsy | 2563 | 0.43 |
| Migraine | 18594 | 3.14 |
| Allergic diseases | Asthma | 16294 | 2.75 |
| Allergic rhinitis | 23652 | 3.99 |
| Atopic dermatitis | 7674 | 1.29 |
| Reproductive diseases | Polycystic ovary syndrome | 83 | 0.01 |
| Endometriosis | 4827 | 0.81 |
| Substance use disorders |  | 6483 | 1.09 |

**Supplementary Figure 1. Adjusted\* risk difference (RD) of pre-existing psychiatric disorders** **with risk of miscarriage.**



\* Adjusted for the woman’s age at the start of pregnancy as a linear and squared term.

**Supplementary Figure 2. Unadjusted odds ratio (OR) of pre-existing psychiatric disorders** **with risk of miscarriage.**



**Supplementary Figure 3. Adjusted\* odds ratio (OR) of pre-existing psychiatric disorders** **with risk of miscarriage.**



\*Adjustment for maternal age at the start of pregnancy and year of conception.

**Supplementary Figure 4. Adjusted\* odds ratios (OR) of pre-existing psychiatric disorders** **with risk of miscarriage restricted to women who were primigravida (first pregnancies).**



\*Adjusted for the woman’s age at the start of pregnancy as a linear and squared term.

**Supplementary Figure 5. Adjusted\* odds ratios (OR) of pre-existing psychiatric disorders** **with risk of miscarriage stratified according to whether the miscarriage was identified in the birth or patient databases (specialist care) as opposed to the general practice database (primary care).**



\*Adjusted for the woman’s age at the start of pregnancy as a linear and squared term.

**Supplementary Figure 6. Adjusted\* odds ratios (OR) of pre-existing psychiatric disorders** **with risk of miscarriage only looking at psychiatric disorders diagnosed in specialist care services.**



\* Adjusted for the woman’s age at the start of pregnancy as a linear and squared term.

**Supplementary Figure 7. Adjusted\* odds ratios (OR) of pre-existing psychiatric disorders** **with additional adjustment for substance use disorders and chronic somatic conditions.**



Results are adjusted for age at the start of pregnancy, substance use disorders, autoimmune diseases (type 1 diabetes, celiac disease, systemic lupus erythematosus, multiple sclerosis, rheumatoid arthritis/ankolysing spondylitis, ulcerative colitis, psoriasis, crohn’s disease, Addison disease, haemolytic anemia), cardiometabolic diseases (type 2 diabetes, hypertensive disorders, atherosclerosis), endocrinological diseases (hypothyroidism, hyperthyroidism, hypoparathyroidism, hyperparathyroidism, cushings syndrome), neurological diseases (epilepsy, migraine), allergic diseases (asthma, allergic rhinitis, atopic dermatitis) and reproductive diseases (polycystic ovary syndrome, endometriosis).