Supplement

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

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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.[1]With 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:

$$\sigma^2 = \bar{U} + \left\{1 + \frac{1}{m}\right\} B$$

, where $\bar{U}$ 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).

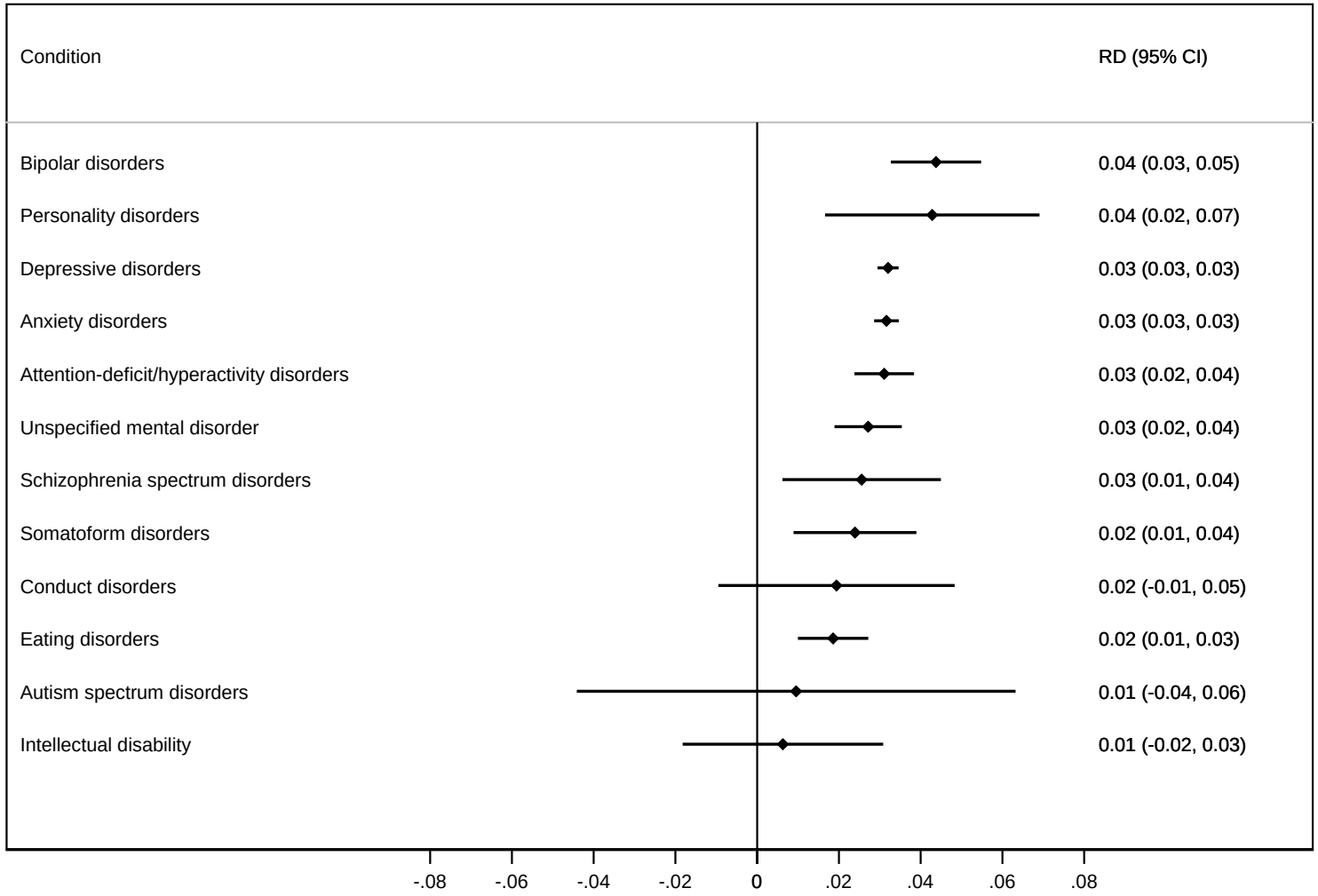
Group of diseases	Diseases	International Classification of Diseases (ICD-10) codes	International Classification of Primary Care (ICPC-2) codes
Autoimmune diseases	Type 1 diabetes	E10	T89
	Celiac disease	K90.0	
	Systemic lupus erythematosus	M32	
	Multiple sclerosis*		N86
	Rheumatoid arthritis/ Ankylosing 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).

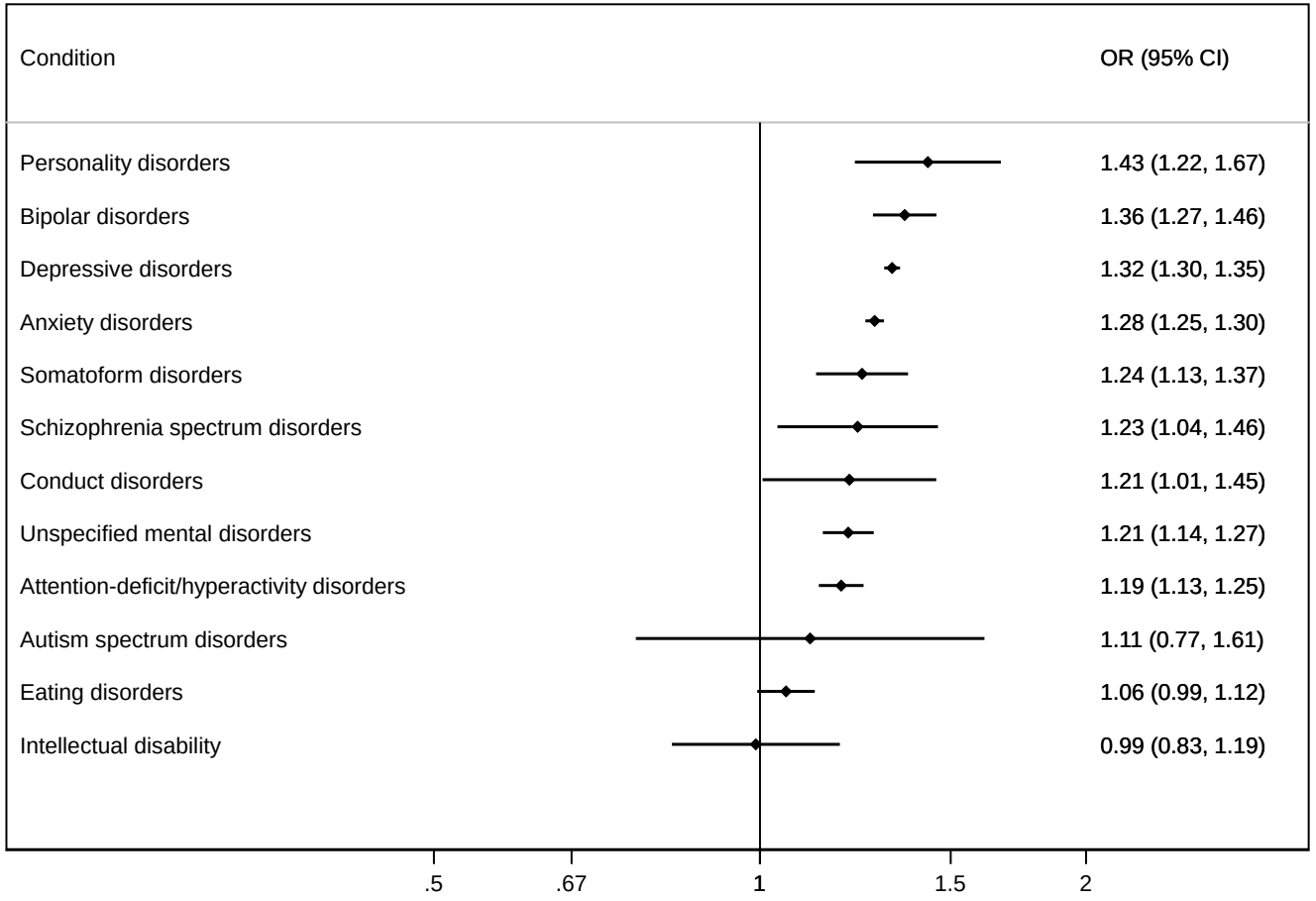
Group of diseases	Diseases	No. pregnancies	%
Autoimmune diseases	Type 1 diabetes	1808	0.30
	Celiac disease	791	0.13
	Systemic lupus erythematosus	246	0.04
	Multiple sclerosis	720	0.12
	Rheumatoid arthritis/ Ankylosing spondylitis	2559	0.43
	Ulcerative colitis	2817	0.48
	Psoriasis	3160	0.53
	Crohn´s disease	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.

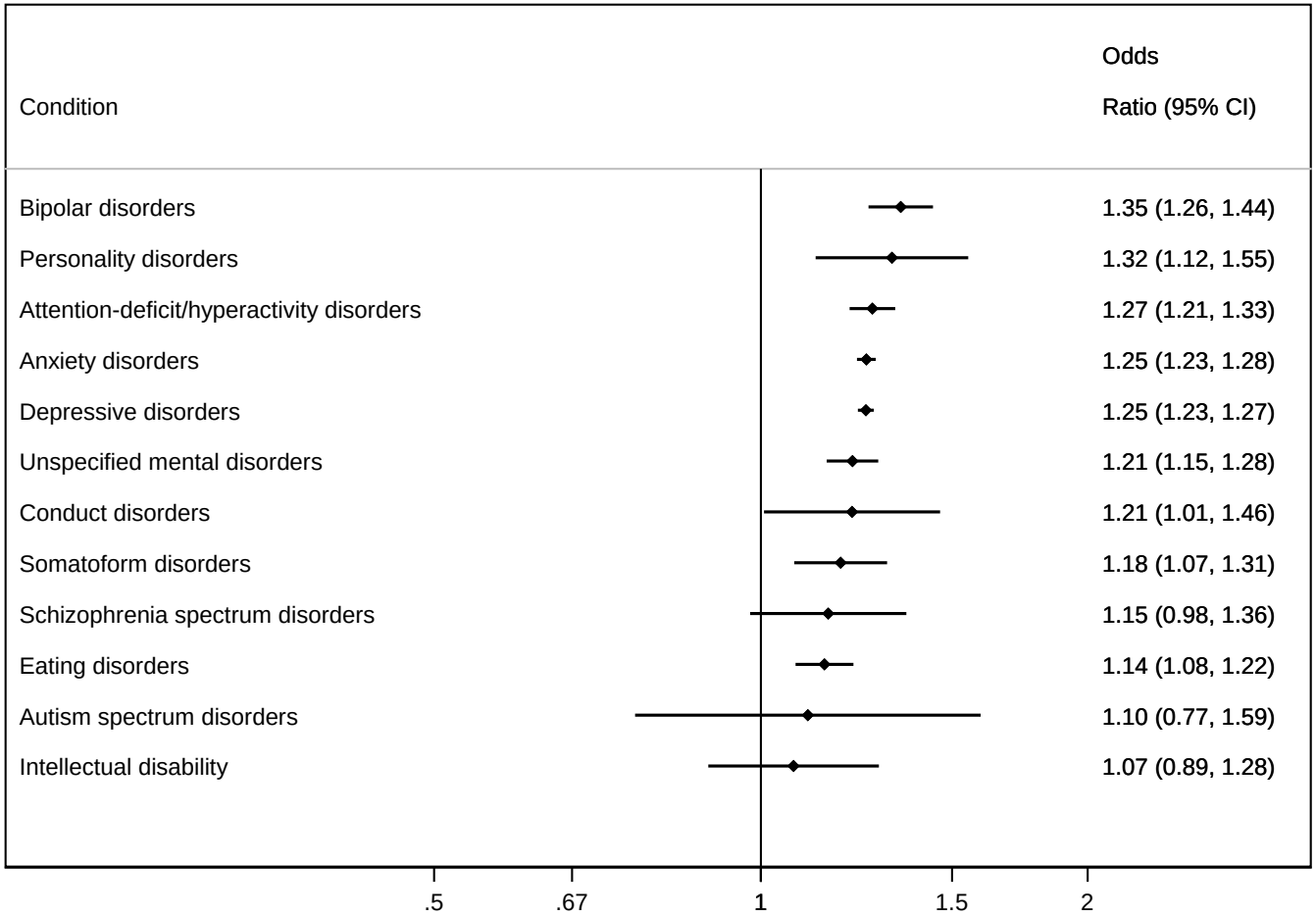


* Adjusted for the woman's age at the start of pregnancy as a linear and squared term.

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

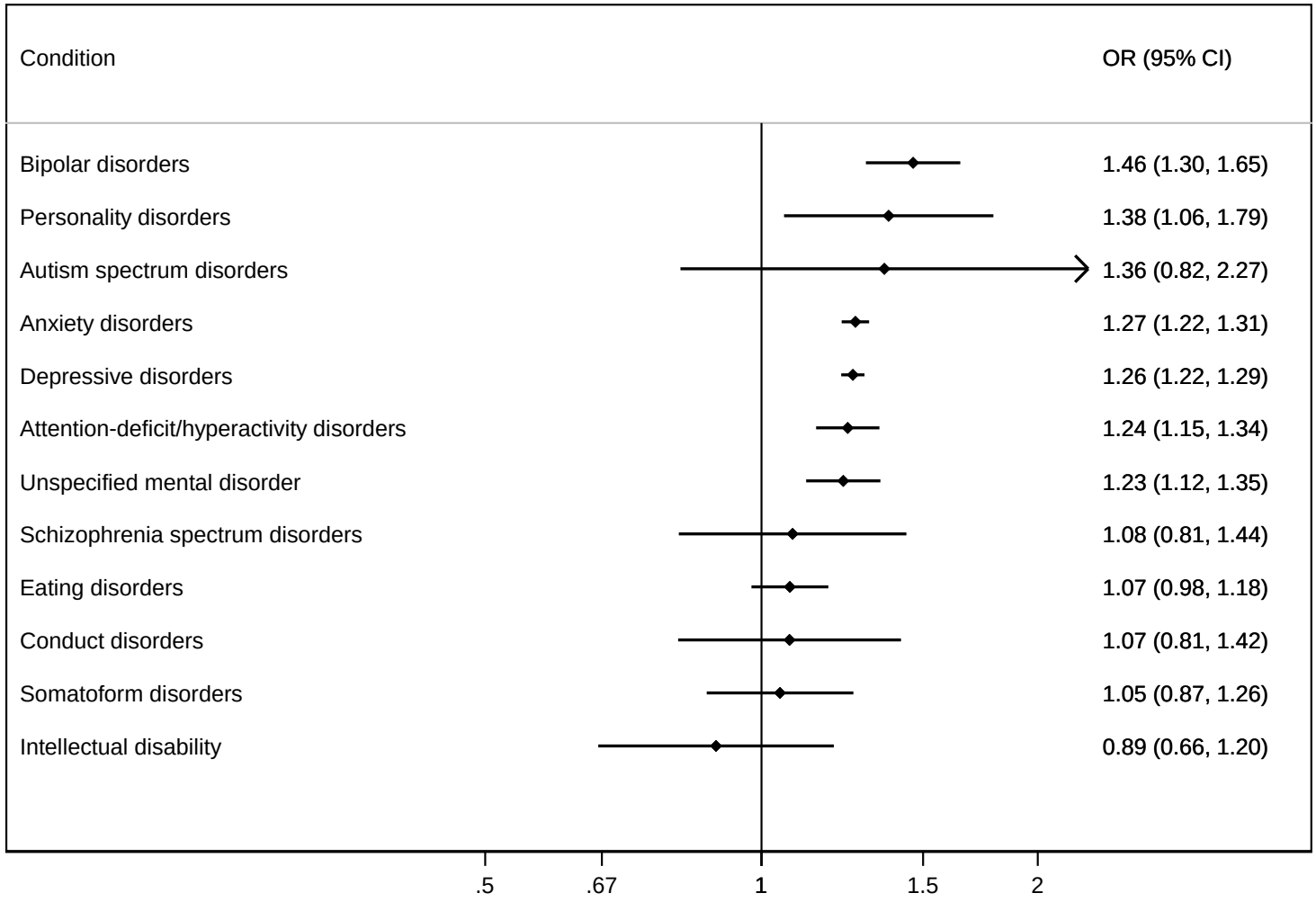


Supplementary Figure 3. Adjusted* odds ratio (OR) of pre-existing psychiatric disorders with risk of miscarriage.



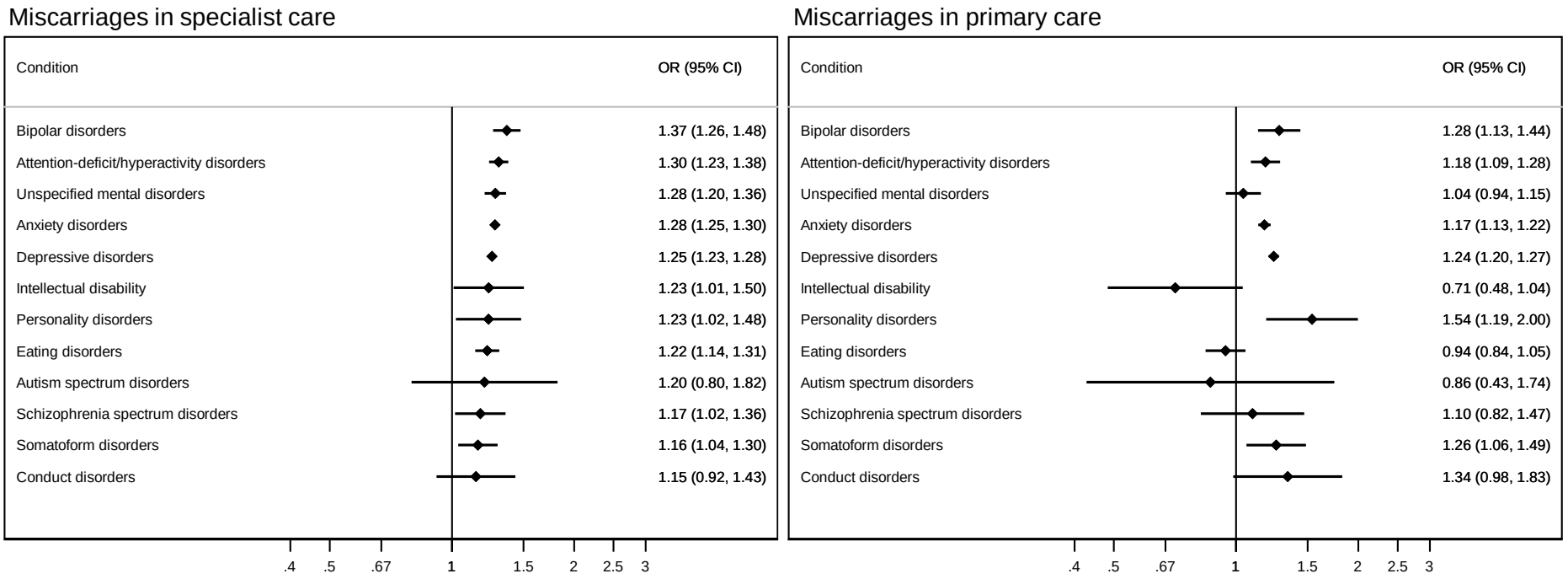
*Adjustment for maternal age at the start of pregnancy and year of conception.

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).



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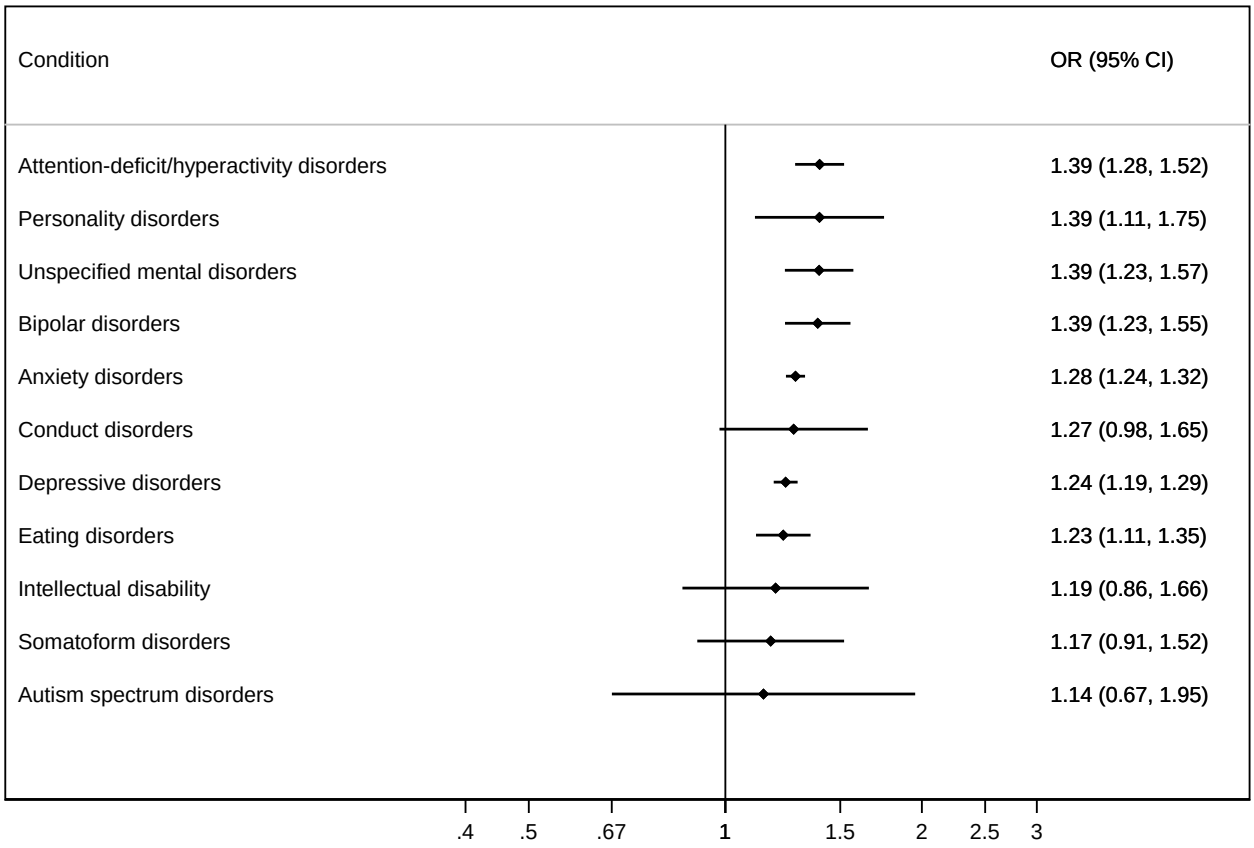
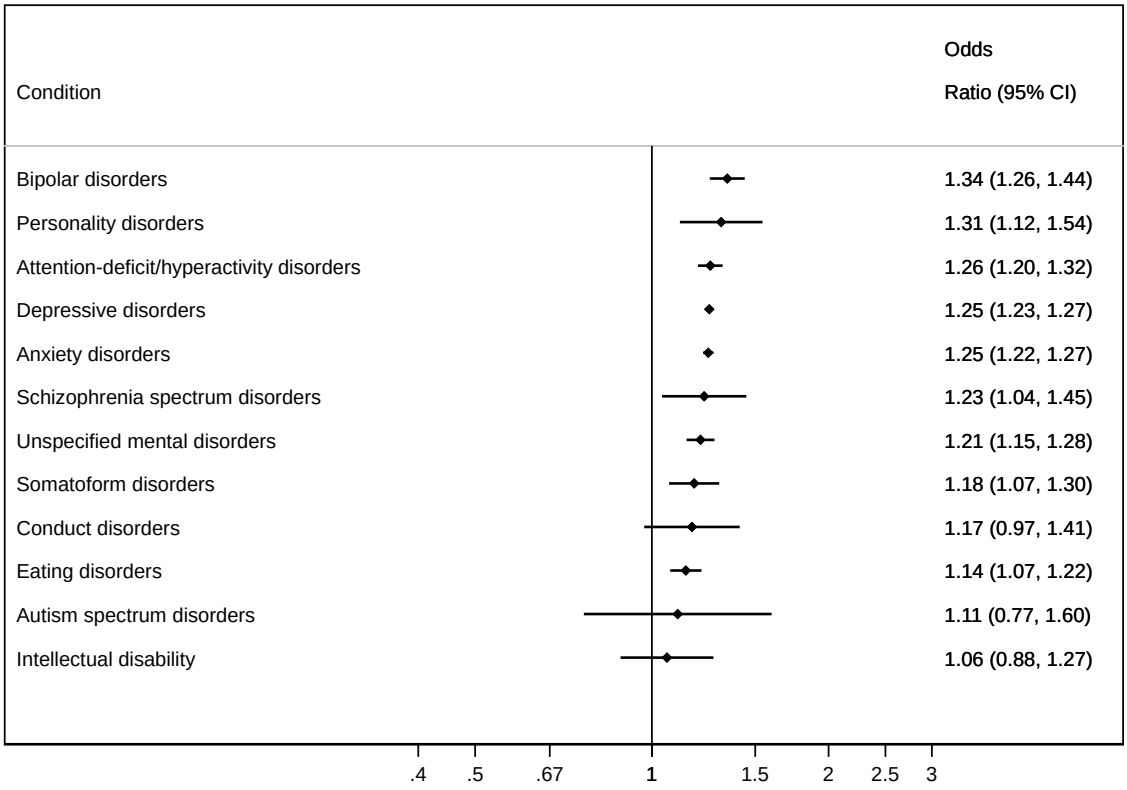
Supplementary Figure 6. Adjusted* odds ratios (OR) of pre-existing psychiatric disorders with risk of miscarriage only looking at psychiatric disorders diagnosed in specialist care services.



* 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).