

Figure S1. Outline of the consecutive stages of filtering out of likely false positive associations between maternal diagnoses around pregnancy and offspring ASD.

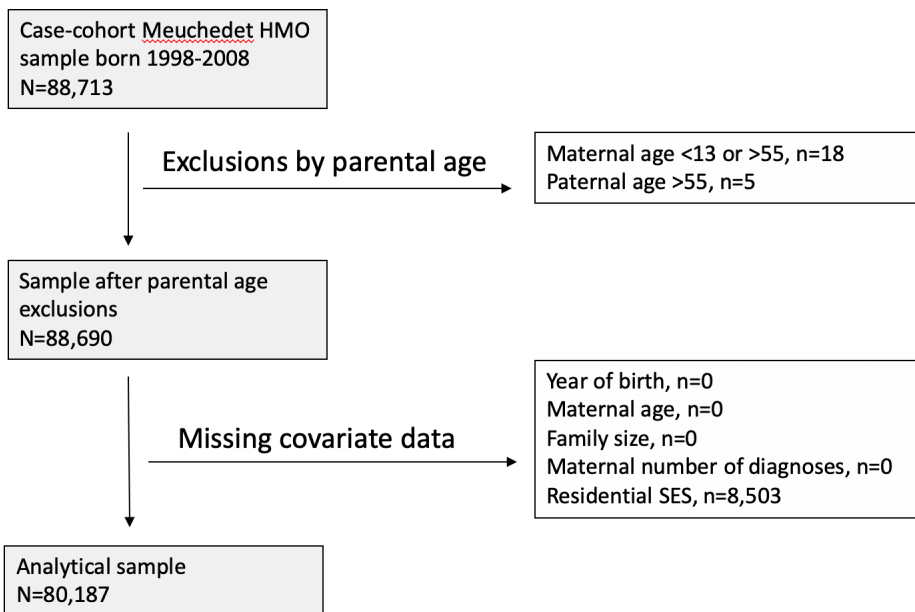


Figure S2. Population flowchart.

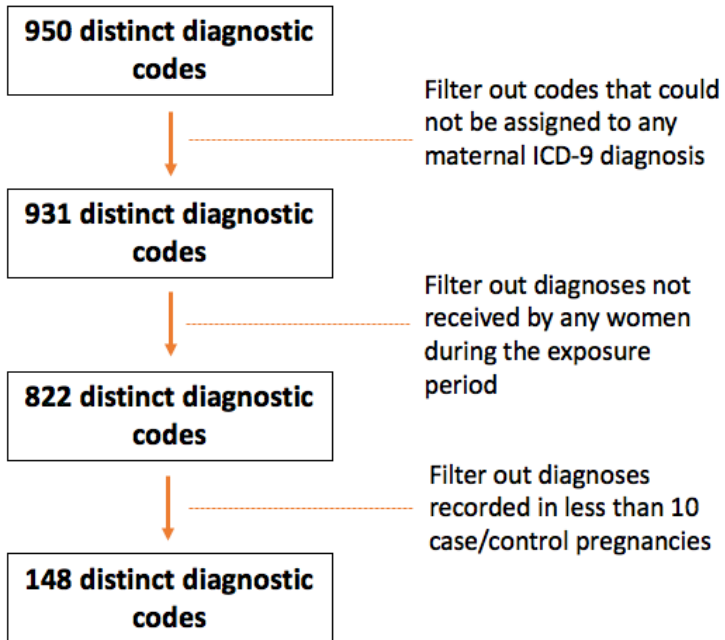


Figure S3. Selection of maternal diagnoses used in association testing.

Association of maternal diagnoses with offspring ASD

All diagnoses, by ICD group

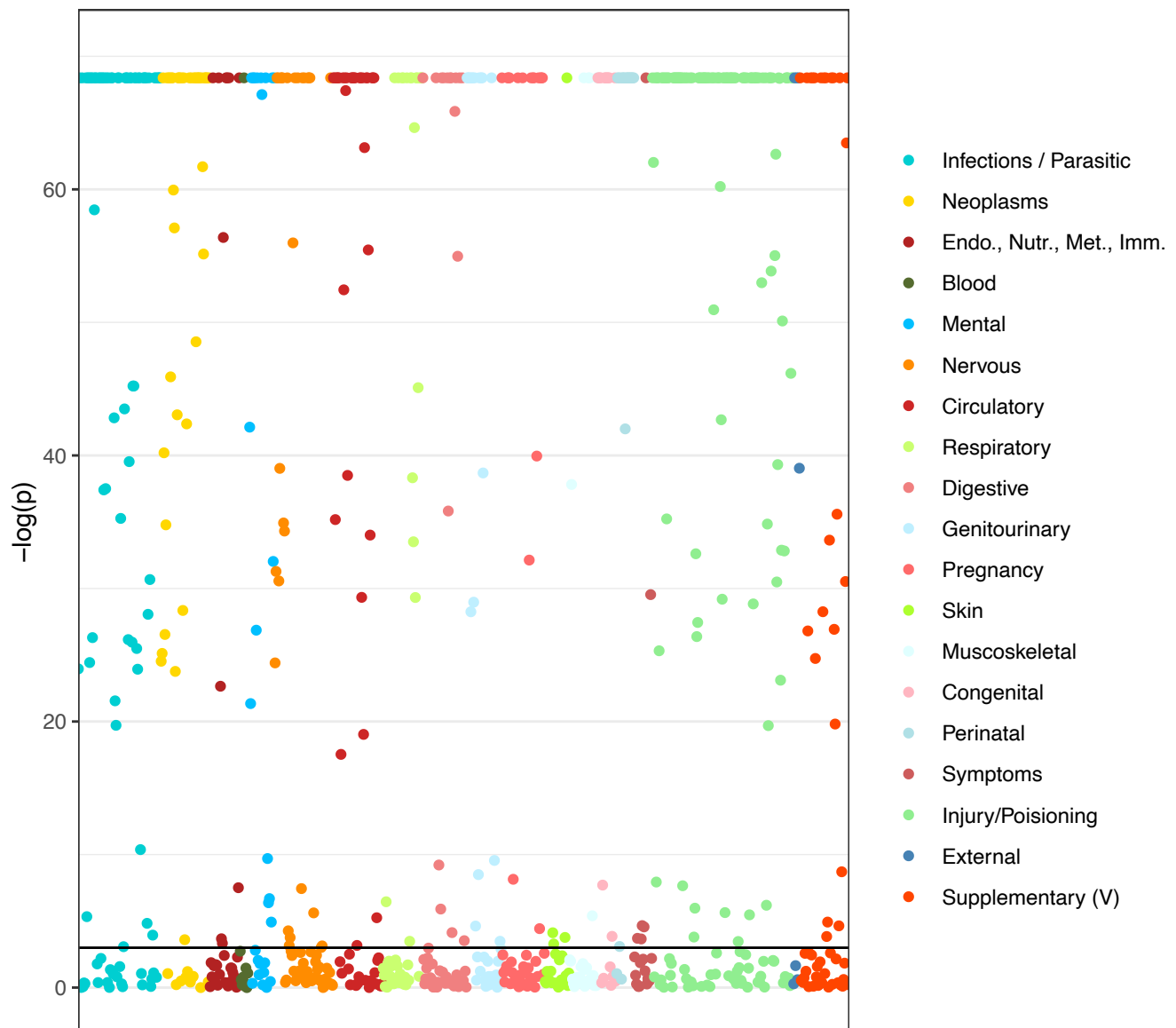
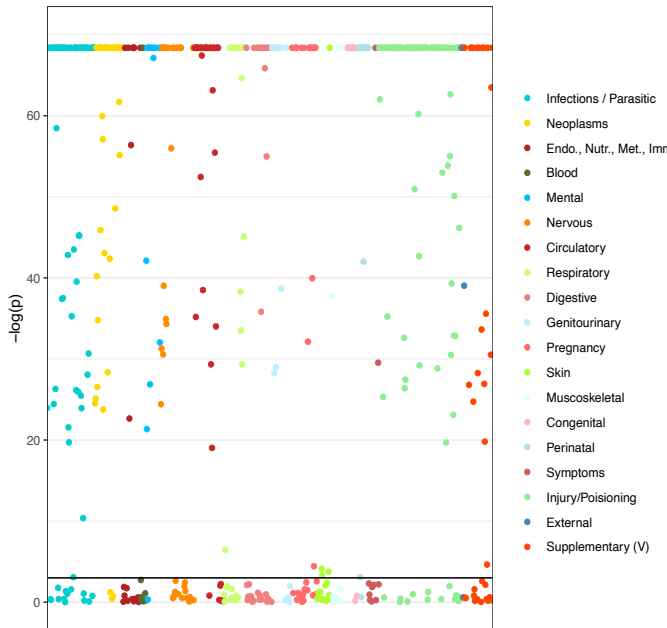


Figure S4. P-values of the associations between maternal diagnoses and ASD, for all diagnoses recorded in Meuhedet register, irrespective of their frequencies. Each dot represents a $-\log(p\text{-value})$ of an association between a distinct maternal diagnosis (level 3 of the ICD-9 codes) and offspring ASD. The results are color-coded by broad ICD-9 categories (level 1), as shown in the legend. P-values smaller than $2E^{-30}$ were capped at $2E^{-30}$ for better separation between points indicating larger p-values.

S4A)

Association of maternal diagnoses with offspring ASD
All diagnoses with HR < 1, by ICD group



S4B)

Association of maternal diagnoses with offspring ASD
All diagnoses with HR < 1, by final significance

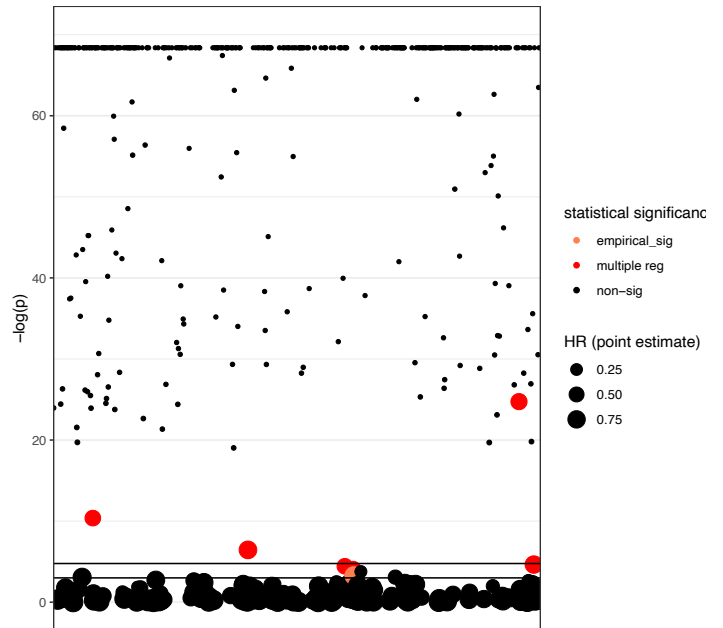
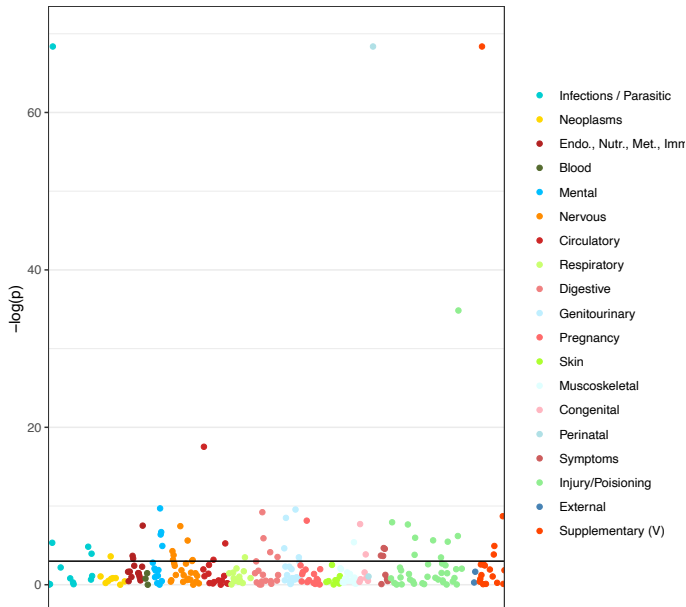


Figure S5. P-values of the associations between maternal diagnoses and ASD, for diagnoses recorded in Meuhedet register with HRs associated with ASD < 1, irrespective of their frequencies. Each dot represents a $-\log(p\text{-value})$ of an association between a distinct maternal diagnosis (level 3 of the ICD-9 codes) and offspring ASD. **Fig S3A.** Shows the results color-coded by broad ICD-9 categories (level 1), as shown in the legend. **Fig S3B.** Shows the results coded by the magnitude of the observed associations (size of the dot, with larger dots indicating smaller HRs) and whether they passed consecutive filtering stages (color).

S4A)

Association of maternal diagnoses with offspring ASD
All diagnoses with HR > 1, by ICD group



S4B)

Association of maternal diagnoses with offspring ASD
All diagnoses with HR > 1, by final significance

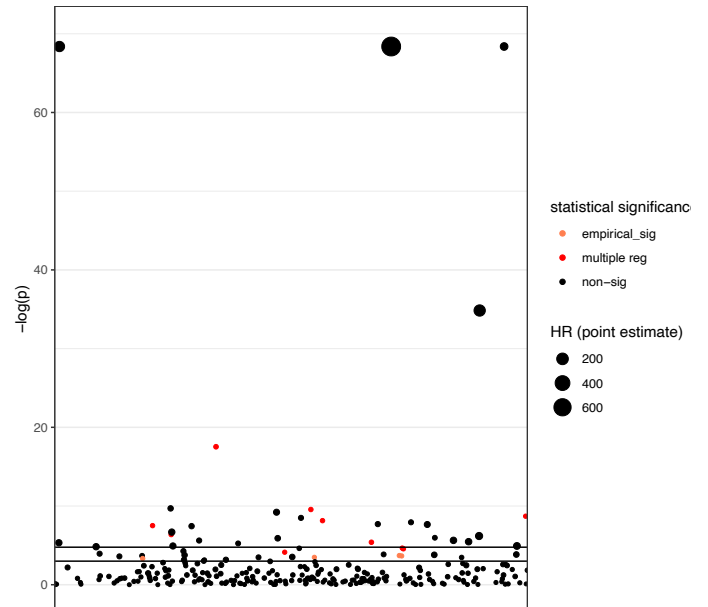


Figure S6. P-values of the associations between maternal diagnoses and ASD, for diagnoses recorded in Meuhedet register with HRs associated with ASD > 1, irrespective of their frequencies. Each dot represents a $-\log(p\text{-value})$ of an association between a distinct maternal diagnosis (level 3 of the ICD-9 codes) and offspring ASD. **Fig S4A.** Shows the results color-coded by broad ICD-9 categories (level 1), as shown in the legend. **Fig S4B.** Shows the results coded by the magnitude of the observed associations (size of the dot, with larger dots indicating larger HRs) and their whether they passed consecutive filtering stages (color).

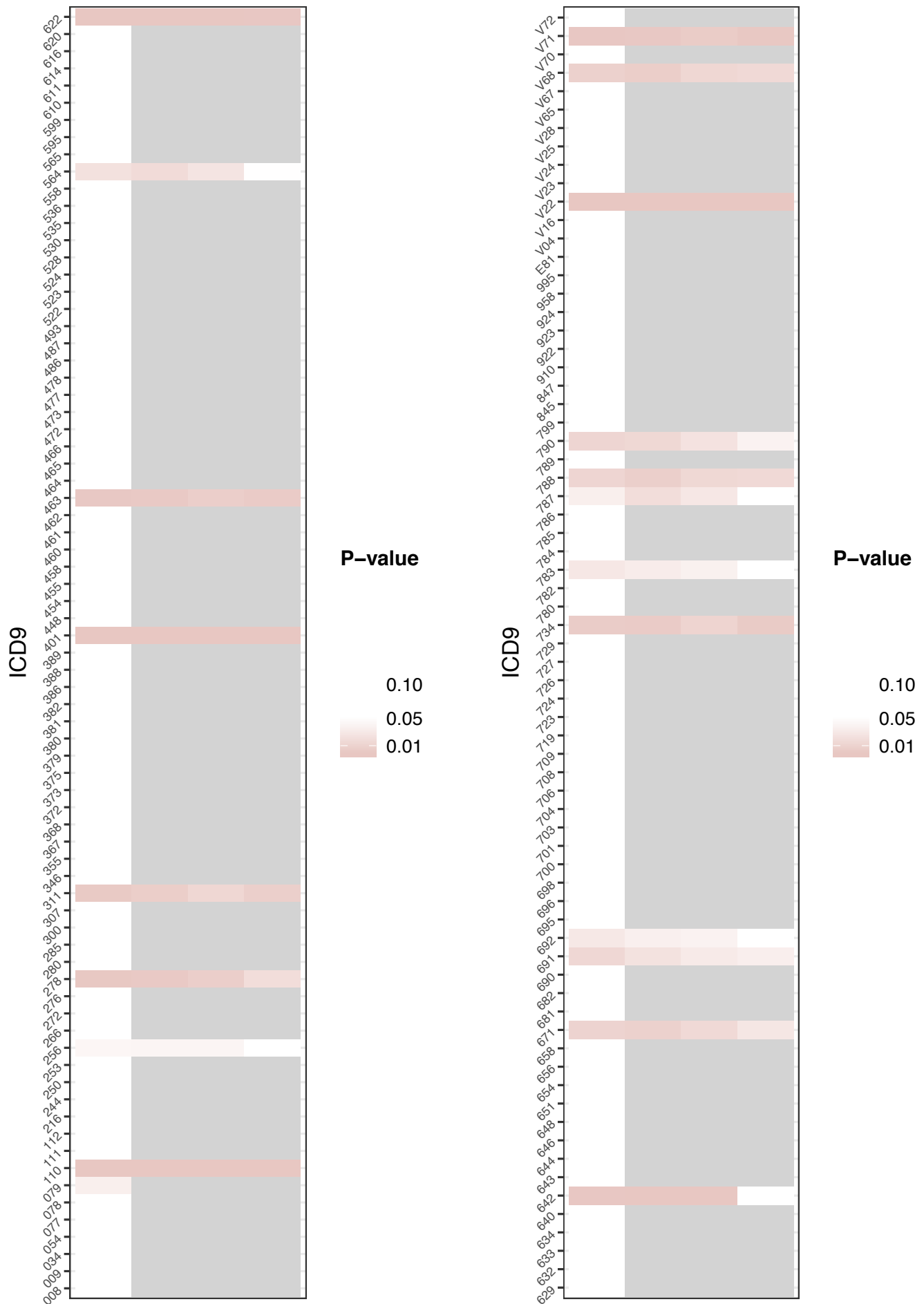
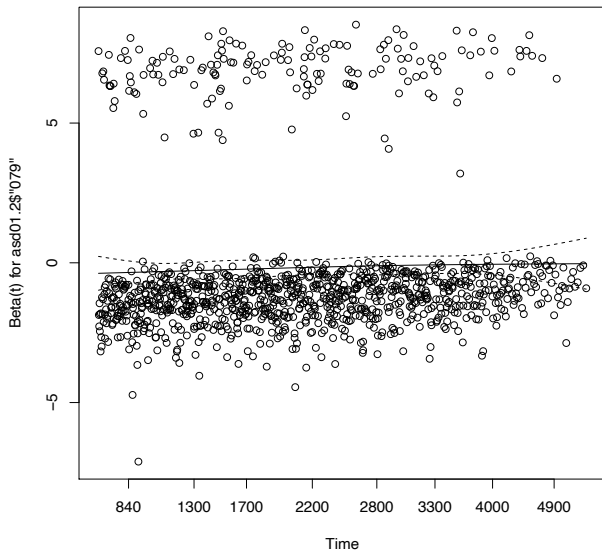


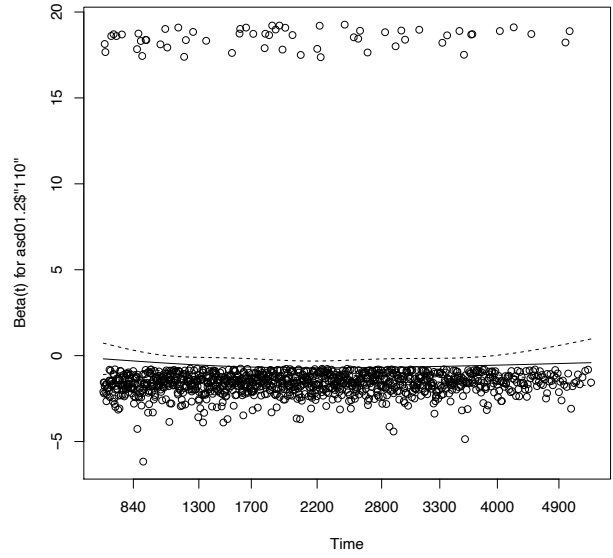
Figure S7. Levels of statistical significance of the associations between ASD and maternal diagnoses recorded in at least 10 cases and 10 controls. Each row represents a distinct diagnosis, and columns left to right the p-values in the consecutive stages of filtering. Diagnoses are shown by level-3 ICD-9 category, smallest to largest numbers (bottom to top, left to right).

Schoenefeld residuals

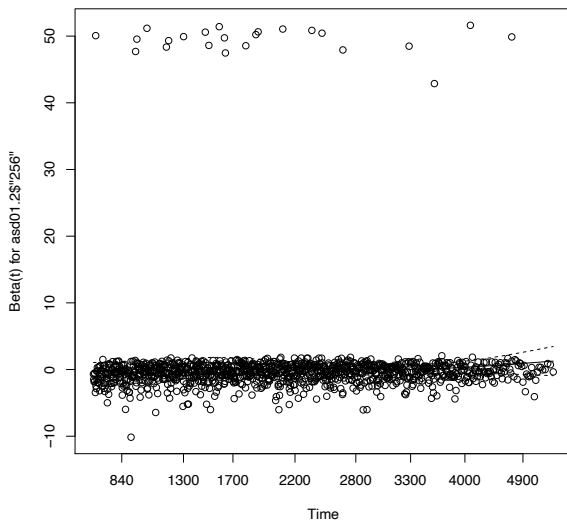
79



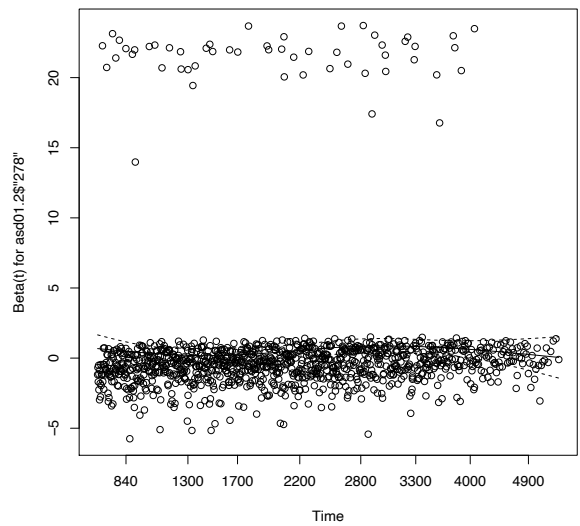
110



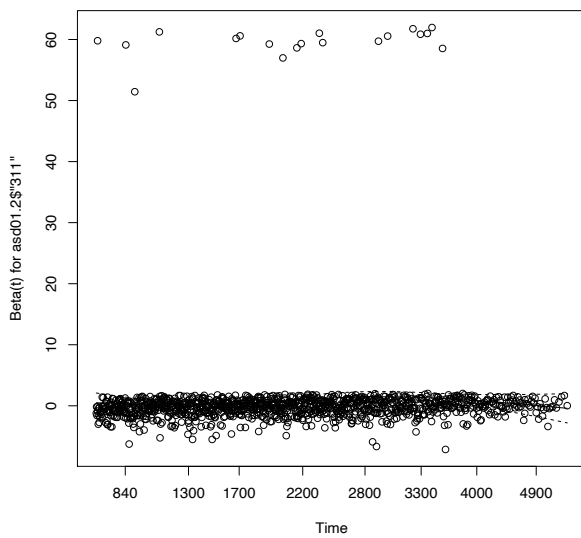
256



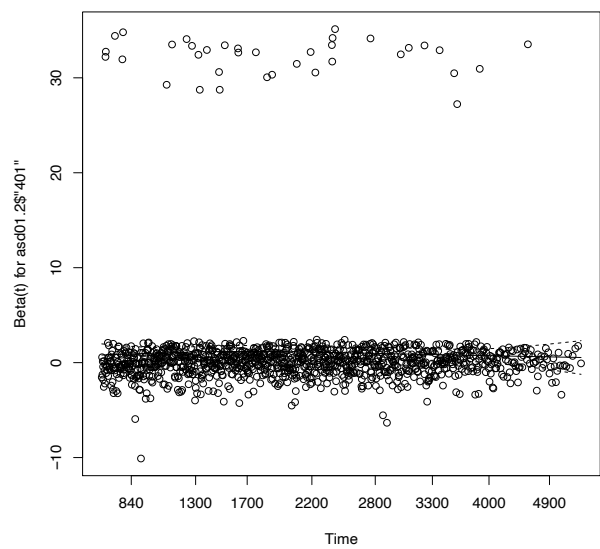
278



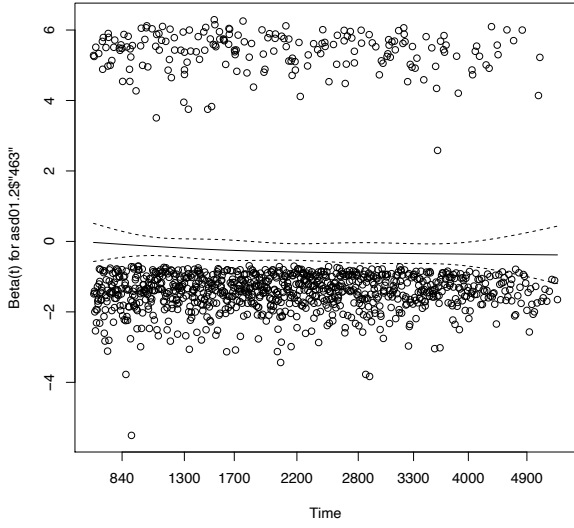
311



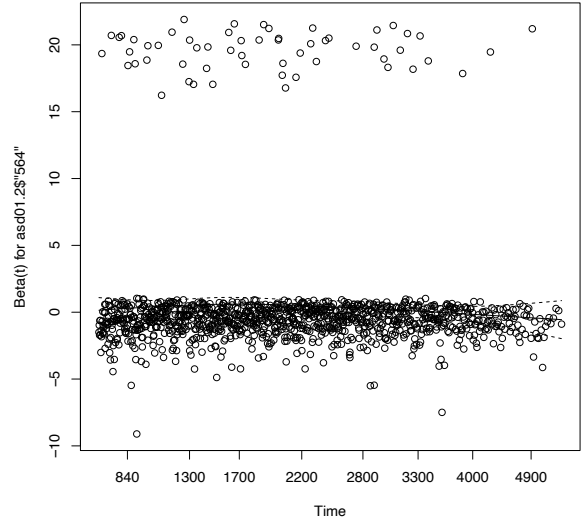
401



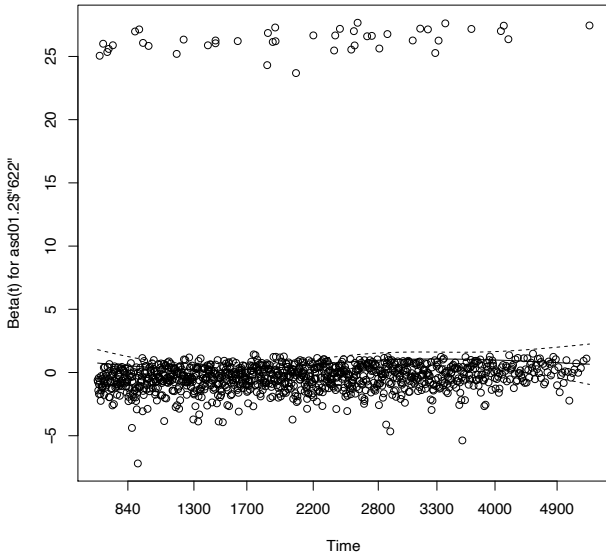
463



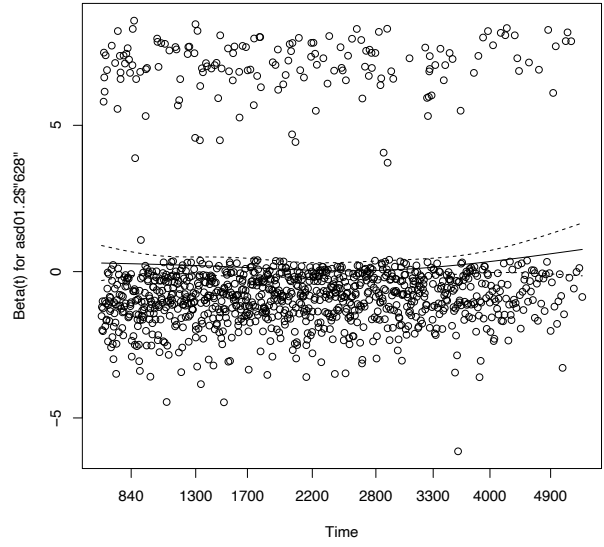
564



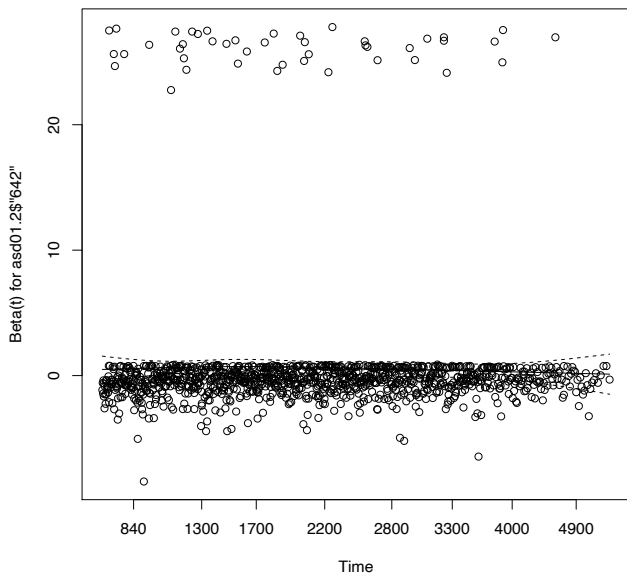
622



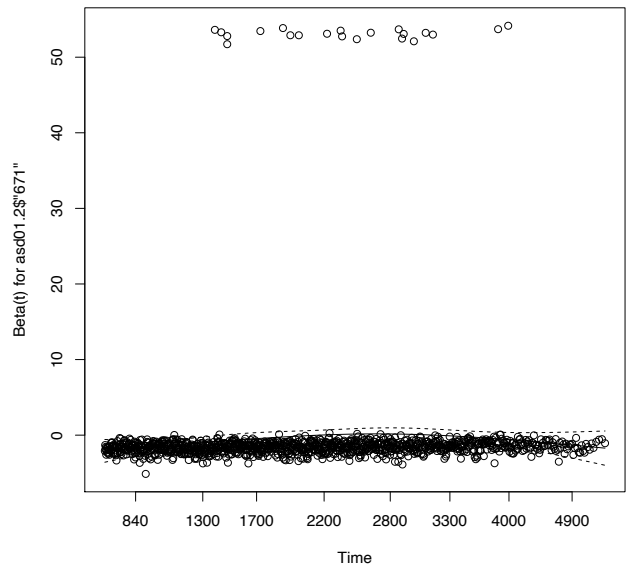
628

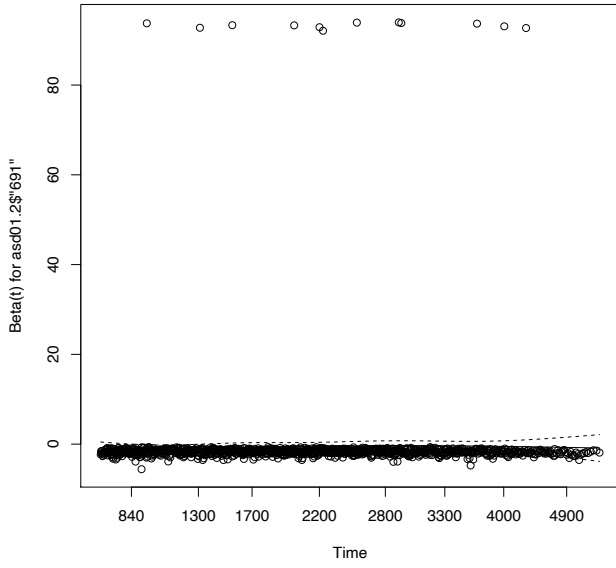
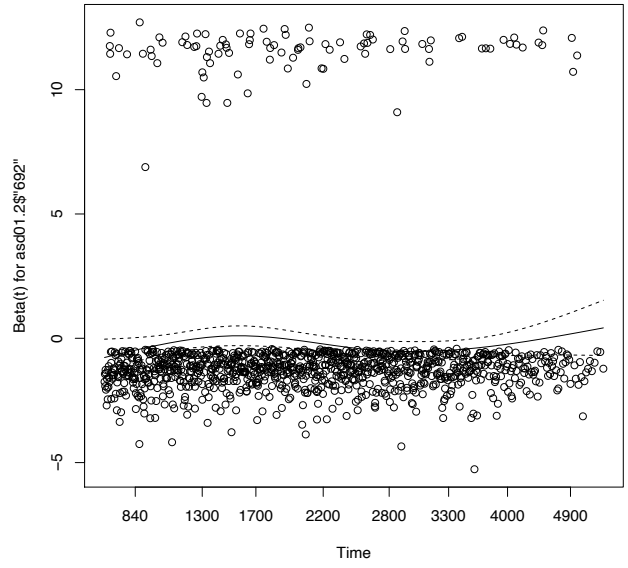
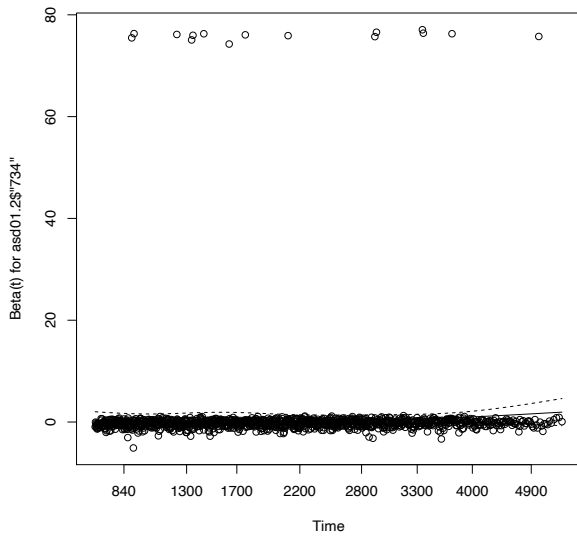
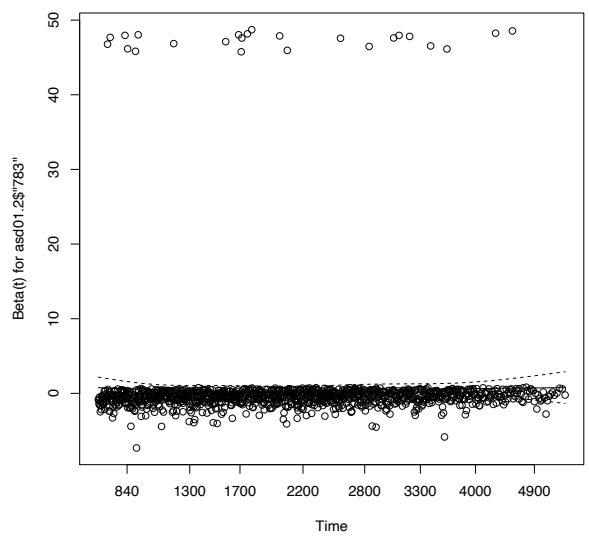
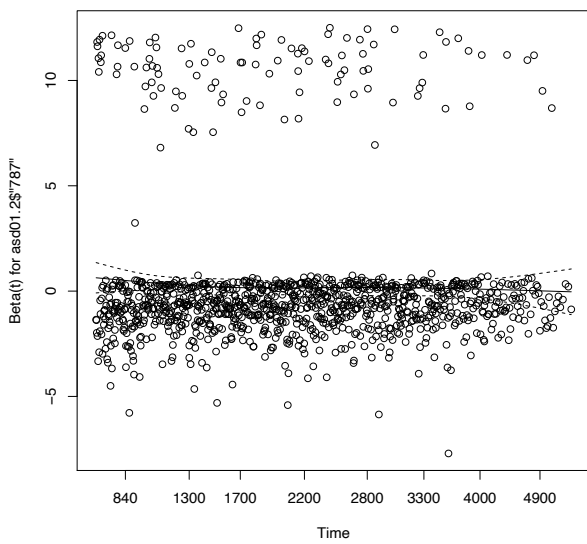
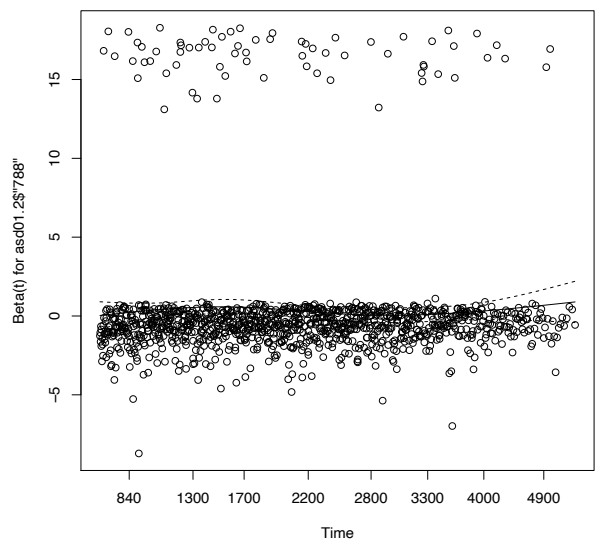


642



671



691**692****734****783****787****788**

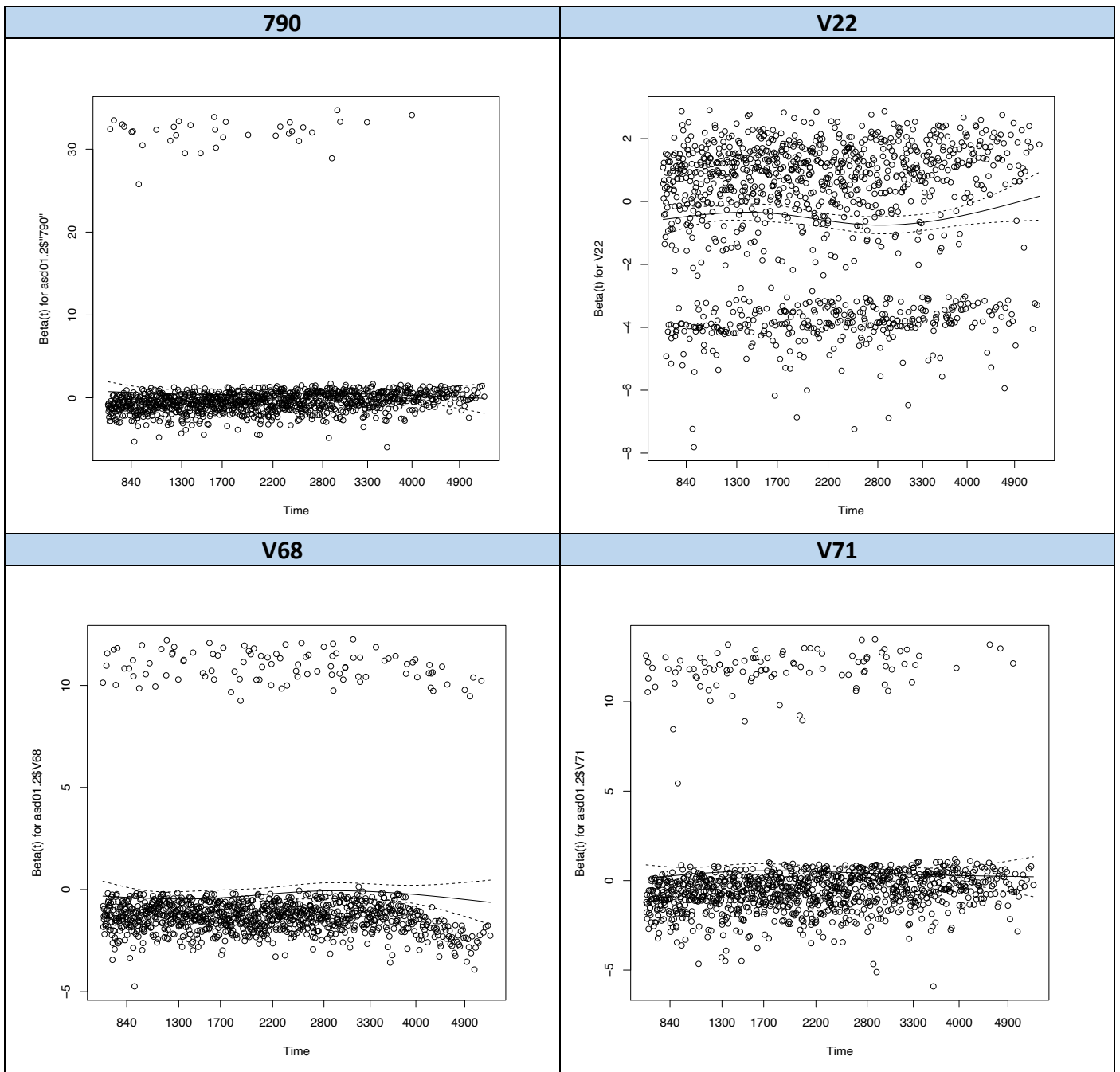


Figure S8. Distribution of the Schoenfeld residuals for all exposures nominally significant in univariate adjusted models.

ICD-10 to ICD-9 level 3 code conversion					
ICD-10 F codes				ICD-10 Z codes	
ICD-10	ICD-9	ICD-10	ICD-9	ICD-10	ICD-9
F00	290	F45	300	Z00	V70
F01	290	F48	310	Z02	V70
F02	294	F50	307	Z03	V71
F04	294	F51	307	Z04	V71
F05	293	F52	302	Z55	V62
F06	293	F53	648	Z56	V62
F07	310	F54	316	Z60	V62
F10	305	F55	305	Z61	V61
F12	305	F60	301	Z62	V61
F13	292	F61	301	Z63	V61
F19	305	F62	301	Z64	V61
F20	295	F63	312	Z65	V62
F21	301	F64	302	Z70	V65
F22	297	F65	302	Z71	V65
F23	298	F66	302	Z72	V69
F25	295	F68	301	Z73	V69
F29	298	F80	315	Z75	V63
F30	296	F81	315	Z76	V68
F31	296	F84	299	Z81	V18
F32	296	F90	314	Z82	V19
F33	296	F91	312	Z85	V10
F34	300	F92	312	Z86	V13
F39	296	F93	313	Z87	V12
F40	300	F94	313	Z91	V15
F41	300	F95	307		
F42	300	F98	313		
F43	309	F99	300		
F44	300				

Table S1. Conversion of the ICD-10 codes in the HMO records to ICD-9.

Number of children	ASD diagnosis in index child or their siblings	Probability of being included in the sample	Regression weight
Any	1	1	1
1	0	0.195	5.128
2	0	0.352	2.841
3	0	0.540	1.853
4	0	0.733	1.364
>=5	0	0.928	1.078

Table S2. Family size and ASD diagnosis-based weights reflecting inverse probability of being included in the study.

	Full sample		Excluded individuals*	
	Controls (N=87,371)	ASD (N=1,327)	Controls (N=8,310)	ASD (N=195)
% female	49.3	19.6	49.6	16.2
Mean SES (SD)	7.6 (4.3)	10.3 (4.2)	6 (3.1)	11 (4.2)
Mean maternal age (SD)	32.5 (6.1)	32.8 (6.2)	30.5 (5.3)	29.5 (6.2)
Mean paternal age (SD)	29.9 (5.4)	29.9 (5.4)	33.1 (5.8)	32.3 (6.1)
N children in the dataset born each year (% total sample)				
1999	8,847 (10.1%)	106 (8.0%)	858 (10.3%)	20 (10.1%)
2000	8,920 (10.2%)	120 (9.0%)	854 (10.3%)	29 (14.6%)
2001	8993 (10.3%)	129 (9.7%)	833 (10.0%)	18 (9.1%)
2002	9,338 (10.7%)	131 (9.9%)	907 (10.9%)	17 (8.6%)
2003	9,464 (10.8%)	173 (13.0%)	910 (10.9%)	28 (14.1%)
2004	9,316 (10.7%)	171 (12.9%)	868 (10.4%)	18 (9.1%)
2005	9,046 (10.4%)	153 (11.5%)	887 (10.6%)	18 (9.1%)
2006	8,668 (9.9%)	163 (12.3%)	848 (10.2%)	22 (11.1%)
2007	8,856 (10.1%)	147 (11.1%)	800 (9.6%)	22 (11.1%)
2008	5,917 (6.8%)	34 (2.6%)	565 (6.8%)	6 (3.0%)
% mothers with ASD	<0.1	0.3	<0.1	0.1

Table S3. Demographic characteristics in the full sample (N=88,719) and individuals excluded due to (*) lack of covariate data, maternal ages lower than 13 or higher than 55, or paternal age lower than 13 (N=8,505).

ICD-9 level 1	ICD-9 level 2	ICD-9 level 3	HR	p-value	exposed	
					ASD	controls
Infectious and Parasitic Diseases	Intestinal infectious Diseases	8	0.92 (0.61-1.39)	7.03E-01	24	1291
		9	0.95 (0.70-1.29)	7.43E-01	44	2719
	Other Bacterial Diseases	34	0.80 (0.59-1.10)	1.69E-01	44	4639
	Viral Diseases Accompanied by Exanthem	54	0.79 (0.53-1.19)	2.59E-01	27	2267
	Other Diseases Due to Viruses and Chlamydiae	77	1.10 (0.62-1.96)	7.53E-01	12	873
		78	1.01 (0.78-1.31)	9.37E-01	67	4625
		79	0.84 (0.70-1.00)	4.62E-02	156	10386
	Mycoses	110	0.57 (0.43-0.74)	3.13E-05	59	6904
		111	0.79 (0.49-1.28)	3.47E-01	19	1340
		112	0.98 (0.80-1.19)	8.15E-01	124	8593
Neoplasms	Benign Neoplasms	216	0.95 (0.73-1.22)	6.59E-01	68	4051
Endocrine, Nutritional and Metabolic Diseases, And Immunity Disorders	Disorder of Thyroid Gland	244	1.26 (0.89-1.78)	1.93E-01	39	2449
	Diseases of Other Endocrine Glands	250	1.43 (0.84-2.43)	1.89E-01	19	850
		253	1.30 (0.73-2.33)	3.73E-01	12	495
		256	1.58 (1.03-2.44)	3.58E-02	23	668
	Nutritional Deficiencies	266	0.98 (0.70-1.37)	8.90E-01	41	3247
	Other metabolic disease and immunity disorders	272	1.22 (0.83-1.79)	3.18E-01	28	1440
		276	0.99 (0.57-1.72)	9.73E-01	13	867
278		1.69 (1.25-2.27)	5.49E-04	53	2264	
Diseases of Blood and Blood- Forming Organs	Iron deficiency anemias	280	0.80 (0.63-1.01)	6.49E-02	79	7421
	Other and unspecified anemias	285	0.97 (0.65-1.46)	8.96E-01	24	2146
Mental Disorders	Neurotic Disorders, Personality Disorders, and Other Nonpsychotic Mental Disorders	300	1.33 (0.92-1.92)	1.29E-01	32	1632
		307	1.40 (0.88-2.21)	1.55E-01	19	977
		311	2.10 (1.32-3.35)	1.70E-03	19	652
	Other Disorders of the Central Nervous System	346	1.32 (0.96-1.82)	8.99E-02	43	1833

Diseases of the Nervous System and Sense Organs	Disorders of the Peripheral Nervous system	355	0.60 (0.34-1.05)	7.12E-02	13	1714
	Disorders of Eye and Adnexa	367	0.94 (0.73-1.20)	6.00E-01	66	4934
		368	1.22 (0.64-2.34)	5.51E-01	11	525
		372	0.83 (0.67-1.03)	8.81E-02	99	8117
		373	0.78 (0.51-1.19)	2.54E-01	24	2050
		375	1.37 (0.83-2.26)	2.16E-01	16	816
		379	1.00 (0.59-1.70)	9.94E-01	14	1031
	Disorders of Ear and Mastoid Process	380	0.99 (0.76-1.28)	9.24E-01	67	4975
		381	0.89 (0.61-1.29)	5.32E-01	33	2663
		382	0.95 (0.64-1.40)	7.84E-01	28	2203
		386	1.36 (0.74-2.47)	3.21E-01	11	518
		388	0.95 (0.68-1.33)	7.76E-01	39	2897
		389	1.06 (0.60-1.89)	8.41E-01	12	858
Diseases of the Circulatory System	Hypertensive Disease	401	2.74 (1.92-3.90)	2.43E-08	36	958
	Diseases of Arteries, Arterioles and Capillaries	448	1.27 (0.79-2.03)	3.26E-01	20	803
	Diseases of Veins and Lymphatics, and Other Diseases of Circulatory System	454	0.75 (0.51-1.09)	1.29E-01	30	3669
		455	0.77 (0.56-1.06)	1.07E-01	41	3527
		458	1.05 (0.60-1.82)	8.73E-01	13	808
Diseases of the Respiratory System	Acute respiratory infections	460	1.15 (0.91-1.44)	2.33E-01	85	4472
		461	0.92 (0.77-1.11)	3.95E-01	140	10281
		462	0.99 (0.84-1.17)	9.22E-01	184	14417
		463	0.78 (0.67-0.91)	1.58E-03	196	16962
		464	1.01 (0.73-1.38)	9.72E-01	42	2907
		465	0.91 (0.80-1.04)	1.58E-01	402	26814
		466	0.85 (0.68-1.05)	1.37E-01	91	7548
	Other Diseases of Upper Respiratory Tract	472	1.10 (0.75-1.63)	6.19E-01	31	1760
		473	1.17 (0.64-2.14)	6.05E-01	11	551
		477	0.93 (0.72-1.21)	6.03E-01	67	4481
		478	0.84 (0.65-1.09)	1.97E-01	62	4639
	Pneumonia and influenza	486	0.92 (0.53-1.60)	7.82E-01	13	1037
		487	0.89 (0.66-1.21)	4.57E-01	46	3220
	Chronic obstructive Pulmonary Diseases and Allied Conditions	493	0.90 (0.63-1.29)	5.75E-01	33	2377
	Diseases of the Digestive System	Diseases of Oral Cavity, Salivary Glands, And Jaws	522	0.93 (0.59-1.46)	7.52E-01	23
523			0.81 (0.43-1.52)	5.15E-01	10	955
524			1.34 (0.83-2.18)	2.31E-01	17	801
528			0.87 (0.60-1.27)	4.75E-01	31	2825
Diseases of Esophagus, Stomach and Duodenum		530	1.37 (0.88-2.14)	1.69E-01	20	1103
		535	1.01 (0.68-1.49)	9.67E-01	29	1906
		536	1.13 (0.66-1.92)	6.66E-01	14	806
Noninfective Enteritis and Colitis		558	0.96 (0.75-1.22)	7.18E-01	82	4995
Other Diseases of Intestines and Peritoneum		564	1.40 (1.07-1.85)	1.60E-02	57	2688
		565	1.13 (0.68-1.89)	6.28E-01	15	826
Diseases of the Genitourinary System	Other Diseases of Urinary System	595	1.12 (0.91-1.38)	2.92E-01	104	6416
		599	1.16 (0.97-1.39)	1.01E-01	147	8586
	Disorders Of Breast	610	1.11 (0.76-1.64)	5.83E-01	27	1280
		611	1.02 (0.76-1.35)	9.12E-01	59	4650
	Inflammatory Disease Of Female Pelvic Organs	614	1.06 (0.64-1.77)	8.15E-01	17	916
		616	1.08 (0.90-1.29)	4.34E-01	140	8192

	Other Disorders of Female Genital Tract	620	1.17 (0.75-1.83)	4.89E-01	22	976
		622	1.88 (1.38-2.57)	7.06E-05	44	1208
		623	0.93 (0.74-1.18)	5.67E-01	82	5149
		625	0.99 (0.69-1.44)	9.77E-01	30	1849
		626	0.89 (0.75-1.04)	1.38E-01	202	15276
		628	1.21 (1.02-1.44)	3.07E-02	161	7084
Complications Of Pregnancy, Childbirth, And The Puerperium	Ectopic and Molar Pregnancy And Other Pregnancy With Abortive Outcome	629	1.87 (0.99-3.55)	5.45E-02	10	331
		633	1.13 (0.66-1.92)	6.59E-01	16	806
		634	1.21 (0.87-1.69)	2.63E-01	37	2245
	Complications Mainly Related To Pregnancy	640	1.19 (0.94-1.50)	1.45E-01	79	4274
		642	1.77 (1.30-2.42)	2.91E-04	44	1549
		643	1.06 (0.76-1.49)	7.14E-01	38	2096
		644	0.87 (0.62-1.23)	4.25E-01	37	2607
		646	1.08 (0.84-1.39)	5.57E-01	66	3841
		648	0.99 (0.83-1.19)	9.43E-01	144	10040
	Normal Delivery, And Other Indications For Care In Pregnancy, Labor, And Delivery	651	0.82 (0.54-1.27)	3.80E-01	25	2283
		654	0.67 (0.35-1.25)	2.07E-01	10	1738
		656	1.40 (0.79-2.49)	2.54E-01	12	558
		658	1.04 (0.57-1.89)	9.02E-01	11	672
	Complications Of The Puerperium	671	0.56 (0.36-0.88)	1.19E-02	21	4153
Diseases Of The Skin And Subcutaneous Tissue	Infections Of Skin And Subcutaneous Tissue	681	1.09 (0.69-1.74)	7.04E-01	18	1436
		682	0.80 (0.52-1.22)	2.96E-01	22	2331
	Other Inflammatory Conditions Of Skin And Subcutaneous Tissue	690	0.90 (0.54-1.51)	6.95E-01	15	984
		691	0.50 (0.28-0.88)	1.62E-02	12	1823
		692	0.79 (0.64-0.99)	3.77E-02	95	8120
		695	0.92 (0.52-1.63)	7.65E-01	12	818
		696	0.92 (0.56-1.49)	7.27E-01	17	1204
		698	0.75 (0.52-1.08)	1.24E-01	31	2681
	Other Diseases Of Skin And Subcutaneous Tissue	700	0.94 (0.47-1.86)	8.56E-01	10	1052
		701	1.12 (0.76-1.65)	5.63E-01	27	1419
		703	0.92 (0.58-1.47)	7.35E-01	20	1738
		704	1.09 (0.81-1.47)	5.50E-01	47	2199
		706	0.91 (0.73-1.14)	4.09E-01	91	5467
708		1.03 (0.72-1.48)	8.59E-01	32	1874	
709		1.19 (0.84-1.68)	3.36E-01	38	1836	
Diseases Of Musculoskeletal System And Connective Tissue	Arthropathies And Related Disorders	719	1.06 (0.82-1.38)	6.49E-01	64	4086
	Dorsopathies	723	1.08 (0.81-1.43)	6.04E-01	55	3065
		724	0.89 (0.75-1.05)	1.65E-01	173	11536
	Rheumatism, Excluding The Back	726	0.98 (0.71-1.36)	9.10E-01	40	2707
		727	1.29 (0.83-1.99)	2.55E-01	23	1321
		729	1.06 (0.85-1.31)	6.26E-01	92	6199
Osteopathies, Chondropathies, And Acquired Musculoskeletal Deformities	734	2.10 (1.26-3.52)	4.53E-03	15	710	
Symptoms, Signs, And Ill-Defined Conditions	Symptoms	780	0.87 (0.75-1.03)	9.95E-02	197	15733
		782	0.96 (0.72-1.28)	7.65E-01	50	4065
		783	1.60 (1.06-2.41)	2.46E-02	24	1010
		784	1.01 (0.86-1.18)	9.22E-01	193	12634
		785	0.98 (0.72-1.35)	9.11E-01	45	2834

		786	0.88 (0.73-1.05)	1.55E-01	144	10853	
		787	1.27 (1.03-1.56)	2.58E-02	106	5171	
		788	1.40 (1.09-1.80)	9.47E-03	68	3504	
		789	0.89 (0.77-1.03)	1.18E-01	272	18190	
	Nonspecific Abnormal Findings	790	1.60 (1.12-2.29)	1.04E-02	35	1654	
	Ill-Defined And Unknown Causes Of Morbidity And Mortality	799	0.85 (0.70-1.04)	1.11E-01	109	9643	
Injury And Poisoning	Sprains And Strains Of Joints And Adjacent Muscles	845	0.90 (0.57-1.42)	6.58E-01	19	1551	
		847	1.11 (0.71-1.71)	6.53E-01	21	904	
	Superficial Injury	910	1.23 (0.75-2.03)	4.12E-01	16	824	
		922	1.49 (0.97-2.27)	6.74E-02	25	946	
		923	1.14 (0.71-1.84)	5.82E-01	19	1090	
		924	1.07 (0.73-1.56)	7.23E-01	28	1787	
	Certain Traumatic Complications And Unspecified Injuries	958	1.65 (0.80-3.17)	1.30E-01	11	563	
	Other And Unspecified Effects Of External Causes	995	0.88 (0.62-1.26)	4.93E-01	35	2458	
	Supplementary Classification Of Factors Influencing Health Status And Contact With Health Services	Persons With Potential Health Hazards Related To Communicable Diseases	V04	1.13 (0.63-2.02)	6.78E-01	16	753
		Persons With Potential Health Hazards Related To Personal And Family History	V16	1.77 (0.94-3.33)	7.79E-02	10	338
Persons Encountering Health Services In Circumstances Related To Reproduction And Development		V22	0.62 (0.54-0.71)	1.80E-11	827	62483	
		V23	0.92 (0.74-1.14)	4.49E-01	101	6788	
		V24	0.82 (0.60-1.11)	2.04E-01	45	5435	
		V25	0.98 (0.83-1.16)	8.53E-01	176	10939	
		V28	1.22 (0.93-1.61)	1.44E-01	56	2903	
Persons Encountering Health Services In Other Circumstances		V65	0.88 (0.75-1.03)	1.16E-01	183	13135	
		V67	0.94 (0.67-1.30)	6.94E-01	37	3170	
		V68	0.76 (0.61-0.93)	9.65E-03	100	10611	
Persons Without Reported Diagnosis Encountered During Examination And Investigation Of Individuals And Populations		V70	0.96 (0.68-1.36)	8.24E-01	34	2263	
		V71	1.53 (1.23-1.91)	1.66E-04	98	4231	
		V72	1.01 (0.88-1.16)	9.01E-01	317	22313	
Supplementary Classification Of External Causes Of Injury And Poisoning	Accidents Due To Natural And Environmental Factors	E813	1.09 (0.64-1.87)	7.52E-01	14	622	

Table S4. Associations between maternal diagnoses and offspring ASD, ordered by p-values from adjusted univariate models (child's year of birth, SES, maternal age at child's birth, total number of diagnoses in pregnancy) and exposure frequencies. Only associations with HR < 1 are shown.

ICD-9	Diagnosis / Medical code	p-value	HR	exposed	
				ASD	controls
V22	Supervision of normal pregnancy	5.75E ⁻¹¹	0.62 (0.54-0.72)	827	62483
110	Dermatophytosis	9.61E ⁻⁰⁶	0.55 (0.42-0.72)	59	6904
401	Essential hypertension	1.10E ⁻⁰⁵	2.17 (1.54-3.07)	36	958
622	Noninflammatory disorders of cervix	1.14E ⁻⁰⁵	1.99 (1.46-2.71)	44	1208
V71	Observation and evaluation for suspected conditions not found	9.85E ⁻⁰⁵	1.54 (1.24-1.92)	98	4231
671	Venous complications in pregnancy and the puerperium	2.46E ⁻⁰⁴	0.43 (0.27-0.67)	21	4153
463	Acute tonsillitis	3.13E ⁻⁰⁴	0.75 (0.64-0.88)	196	16962
642	Hypertension complicating pregnancy childbirth and the puerperium	1.57E ⁻⁰³	1.64 (1.21-2.22)	44	1549
280	Iron deficiency anemias	2.29E ⁻⁰³	0.70 (0.55-0.88)	79	7421
V68	Encounters for administrative purposes	2.36E ⁻⁰³	0.72 (0.58-0.89)	100	10611
628	Female infertility	6.76E ⁻⁰³	1.27 (1.07-1.51)	161	7084
278	Overweight, obesity and other hyperalimentation	7.68E ⁻⁰³	1.49 (1.11-2.00)	53	2264
691	Atopic dermatitis and related conditions	7.82E ⁻⁰³	0.46 (0.26-0.82)	12	1823
256	Ovarian dysfunction	8.45E ⁻⁰³	1.76 (1.16-2.68)	23	668
454	Varicose veins of lower extremities	8.48E ⁻⁰³	0.60 (0.41-0.88)	30	3669
799	Other ill-defined and unknown causes of morbidity and mortality	9.62E ⁻⁰³	0.77 (0.63-0.94)	109	9643
692	Contact dermatitis and other eczema	1.03E ⁻⁰²	0.75 (0.61-0.94)	95	8120
780	General symptoms	1.05E ⁻⁰²	0.81 (0.70-0.95)	197	15733
311	Depressive disorder, not elsewhere classified	1.16E ⁻⁰²	1.81 (1.14-2.86)	19	652
466	Acute bronchitis and bronchiolitis	2.13E ⁻⁰²	0.77 (0.62-0.96)	91	7548
654	Abnormality of organs and soft tissues of pelvis	2.62E ⁻⁰²	0.49 (0.26-0.92)	10	1738
355	Mononeuritis of lower limb and unspecified site	3.30E ⁻⁰²	0.55 (0.31-0.95)	13	1714
786	Symptoms involving respiratory system and other chest symptoms	3.30E ⁻⁰²	0.82 (0.69-0.98)	144	10853
783	Symptoms concerning nutrition metabolism and development	3.36E ⁻⁰²	1.56 (1.04-2.35)	24	1010
790	Nonspecific findings on examination of blood	3.39E ⁻⁰²	1.48 (1.03-2.13)	35	1654
734	Flat foot	3.64E ⁻⁰²	1.73 (1.04-2.88)	15	710
626	Disorders of menstruation and other abnormal bleeding from female genital tract	3.77E ⁻⁰²	0.85 (0.72-0.99)	202	15276
789	Other symptoms involving abdomen and pelvis	3.87E ⁻⁰²	0.86 (0.75-0.99)	272	18190
787	Symptoms involving digestive system	4.83E ⁻⁰²	1.23 (1.00-1.51)	106	5171
V16	Family history of malignant neoplasm	4.85E ⁻⁰²	1.89 (1.00-3.55)	10	338
V24	Postpartum care and examination	4.94E ⁻⁰²	0.74 (0.54-1.00)	45	5435

Table S5. Associations between maternal diagnoses and offspring ASD ordered by p-values from **unadjusted** univariate models (child's year of birth, SES, maternal age at child's birth, total number of diagnoses in pregnancy) and exposure frequencies. Only associations with HR > 1 are shown.

ICD-9	Diagnosis	HR (CI)* Univariate, adjusted	Analytical p-value*	HR (CI) Multiple regression, adjusted	Analytical p-value	exposed	
						ASD	controls
V22	Supervision of normal pregnancy	0.62 (0.54 - 0.71)	1.80E ⁻¹¹	0.63 (0.55-0.73)	4.71E ⁻¹⁰	827	62,483
401	Essential hypertension	2.74 (1.92 - 3.90)	2.43E ⁻⁰⁸	2.27 (1.54-3.35)	3.62E ⁻⁰⁵	36	958
110	Dermatophytosis	0.57 (0.43 - 0.74)	3.13E ⁻⁰⁵	0.59 (0.45-0.77)	9.35E ⁻⁰⁵	59	6,904
622	Noninflammatory disorders of cervix	1.88 (1.38 - 2.57)	7.06E ⁻⁰⁵	1.83 (1.33-2.51)	1.82E ⁻⁰⁴	44	1,208
V71	Observation and evaluation for suspected conditions not found	1.53 (1.23 - 1.91)	1.66E ⁻⁰⁴	1.49 (1.19-1.87)	5.37E ⁻⁰⁴	98	4,231
642	Hypertension complicating pregnancy childbirth and the puerperium	1.77 (1.30 - 2.42)	2.91E ⁻⁰⁴	1.40 (1.00-1.96)	5.00E ⁻⁰²	44	1,549
278	Overweight, obesity and other hyperalimentation	1.69 (1.26 - 2.27)	5.49E ⁻⁰⁴	1.44 (1.06-1.97)	2.00E ⁻⁰²	53	2,264
463	Acute tonsillitis	0.78 (0.67 - 0.91)	1.58E ⁻⁰³	0.80 (0.68-0.93)	3.90E ⁻⁰³	196	16,962
311	Depressive disorder, not elsewhere classified	2.11 (1.32 - 3.35)	1.70E ⁻⁰³	1.91 (1.19-3.06)	6.92E ⁻⁰³	19	652
734	Flat foot	2.10 (1.26 - 3.52)	4.53E ⁻⁰³	2.18 (1.30-3.66)	3.28E ⁻⁰³	15	710
788	Symptoms involving urinary system	1.40 (1.09 - 1.80)	9.47E ⁻⁰³	1.36 (1.06-1.76)	1.67E ⁻⁰²	28	1,106
V68	Encounters for administrative purposes	0.76 (0.61 - 0.93)	9.65E ⁻⁰³	0.77 (0.62-0.95)	1.63E ⁻⁰²	68	3,504
790	Nonspecific findings on examination of blood	1.60 (1.12 - 2.29)	1.04E ⁻⁰²	1.47 (1.02-2.11)	3.89E ⁻⁰²	100	10,611
671	Venous complications in pregnancy and the puerperium	0.56 (0.36 -0.88)	1.19E ⁻⁰²	0.60 (0.38-0.95)	2.82E ⁻⁰²	35	1,654
564	Functional digestive disorders not elsewhere classified	1.41 (1.07 - 1.85)	1.60E ⁻⁰²	1.32 (1.00-1.75)	4.91E ⁻⁰²	273	18,284
691	Atopic dermatitis and related conditions	0.50 (0.28 - 0.88)	1.62E ⁻⁰²	0.54 (0.31-0.96)	3.54E ⁻⁰²	57	2,688
783	Symptoms concerning nutrition metabolism and development	1.60 (1.06 -2.41)	2.46E ⁻⁰²	1.47 (0.97-2.23)	6.71E ⁻⁰²	584	43,286
787	Symptoms involving digestive system	1.27 (1.03 - 1.56)	2.58E ⁻⁰²	1.21 (0.98-1.50)	7.32E ⁻⁰²	24	1,010
628	Female infertility	1.22 (1.02 -1.45)	3.07E ⁻⁰²	1.15 (0.96-1.37)	1.35E ⁻⁰¹	67	3,251
256	Ovarian dysfunction	1.59 (1.03 -2.44)	3.58E ⁻⁰²	1.32 (0.85-2.05)	2.15E ⁻⁰¹	161	7,084
692	Contact dermatitis and other eczema	0.79 (0.64 -0.99)	3.77E ⁻⁰²	0.85 (0.68-1.06)	1.46E ⁻⁰¹	23	668
79	Viral and chlamydial infection in conditions classified elsewhere and of unspecified site	0.84 (0.70 -1.00)	4.62E ⁻⁰²	0.84 (0.71-1.01)	6.08E ⁻⁰²	95	8,120

* univariate models, adjusted for maternal age at child's birth, child's year of birth, SES and total number of diagnoses in pregnancy;

Table S6. Frequencies of maternal diagnoses with nominally significant associations with ASD after adjustment and present in at least 10 cases and 10 controls.

ICD-9	Schoenfeld residual p-value
79	0.750
110	0.460
256	0.524
278	0.727
311	0.360
401	0.380
463	0.201
564	0.129
622	0.304
628	0.610
642	0.321
671	0.077
691	0.334
692	0.754
734	0.756
787	0.117
783	0.959
788	0.589
790	0.282
V22	0.302
V68	0.406
V71	0.364

Table S7. Schoenfeld residuals p-values for all maternal diagnoses with nominally statistically significant associations with ASD recorded in at least 10 cases and 10 controls.

ICD-9 category	N diagnoses tested	N significant diagnoses	
		univariate, adjusted	multiple regression, adjusted
001-139: Infectious and Parasitic Diseases	10	2	1
140-239: Neoplasms	1	0	0
240-279: Endocrine, Nutritional and Metabolic Diseases, and Immunity Disorders	8	2	1
280-289: Diseases of Blood and Blood-Forming Organs	2	0	0
290-319: Mental Disorders	3	1	1
320-389: Diseases of the Nervous System and Sense Organs	14	0	0
390-459: Diseases of the Circulatory System	5	1	1
460-519: Diseases of the Respiratory System	14	1	1
520-579: Diseases of the Digestive System	10	1	1
580-629: Diseases of the Genitourinary System	14	2	1
630-677: Complications of Pregnancy, Childbirth, And the Puerperium	14	2	2
680-709: Diseases of the Skin and Subcutaneous Tissue	15	2	1
710-739: Diseases of the Musculoskeletal System and Connective Tissue	7	1	1
740-759: Congenital Anomalies	0	0	0
760-779: Certain Conditions Originating in the Perinatal Period	0	0	0
780-799: Symptoms, Signs, and Ill-Defined Conditions	24	6	5
800-999: Injury and Poisoning	8	0	0
V01-V85: Supplementary Classification of Factors Influencing Health Status and Contact with Health Services	0	0	0
E800-E999: Supplementary Classification of External Causes of Injury and Poisoning	1	0	0

Table S8. Summary of the association testing by ICD-9, level 1 category. Columns (left to right) indicate total number of ICD-9 diagnoses within each category tested for an association with ASD; (ii) number of nominally statistically significant associations (p -value < 0.05) in adjusted univariate models, and (iii) number of diagnoses statistically significantly associated with ASD (p -value < 0.05) in adjusted multiple regression.

ICD-9	HR (CI)	Analytical p-value	exposed	
			ASD	Ctrl
V22	0.62 (0.54-0.71)	3.14E ⁻¹¹	827	62,483
401	2.74 (1.92-3.90)	2.39E ⁻⁰⁸	36	958
110	0.57 (0.43-0.74)	3.31E ⁻⁰⁵	59	6,904
622	1.88 (1.38-2.57)	6.97E ⁻⁰⁵	44	1,208
V71	1.53 (1.23-1.91)	1.60E ⁻⁰⁴	98	4,231
642	1.78 (1.30-2.42)	2.83E ⁻⁰⁴	44	1,549
278	1.69 (1.26-2.27)	5.37E ⁻⁰⁴	53	2,264
311	2.11 (1.33-3.36)	1.63E ⁻⁰³	19	652
463	0.78 (0.67-0.91)	1.72E ⁻⁰³	196	16,962
734	2.11 (1.26-3.52)	4.42E ⁻⁰³	15	710
788	1.40 (1.09-1.81)	9.21E ⁻⁰³	68	3,504
790	1.60 (1.12-2.29)	1.04E ⁻⁰²	35	1,654
V68	0.76 (0.61-0.94)	1.06E ⁻⁰²	100	10,611
671	0.56 (0.36-0.88)	1.22E ⁻⁰²	21	4,153
564	1.41 (1.07-1.85)	1.56E ⁻⁰²	57	2,688
691	0.50 (0.28-0.88)	1.66E ⁻⁰²	12	1,823
783	1.60 (1.06-2.41)	2.43E ⁻⁰²	24	1,010
787	1.27 (1.06-2.41)	2.52E ⁻⁰²	106	5,171
628	1.22 (1.02-1.45)	2.84E ⁻⁰²	161	7,084
692	0.79 (0.63-0.98)	3.09E ⁻⁰²	95	8,120
256	1.59 (1.03-2.44)	3.52E ⁻⁰²	23	668
79	0.84 (0.70-1.00)	4.80E ⁻⁰²	156	10,386

Table S9. Associations between maternal diagnoses and offspring ASD, ordered by the p-values from adjusted univariate models. Maternal diagnoses significantly associated with ASD in the final multiple regression are highlighted in blue. Children of mothers who themselves had a record of an ASD diagnosis were removed from the analytical sample.

ICD-9 code	Cox PH, no imputation (N=80,817)		Logistic regression, no imputation (N=80,817)		Logistic regression with imputation (N=88,690)	
	HR	p-value	OR	P-value	OR	P-value
008	0.92 (0.61-1.39)	7.05E ⁻⁰¹	0.94 (0.62-1.41)	7.65E ⁻⁰¹	0.95 (0.64-1.41)	8.00E ⁻⁰¹
009	0.95 (0.70-1.29)	7.44E ⁻⁰¹	0.97 (0.72-1.32)	8.58E ⁻⁰¹	1.02 (0.77-1.36)	8.75E ⁻⁰¹
034	0.80 (0.59-1.10)	1.69E ⁻⁰¹	0.81 (0.60-1.10)	1.86E ⁻⁰¹	0.83 (0.63-1.11)	2.06E ⁻⁰¹
054	0.79 (0.53-1.19)	2.60E ⁻⁰¹	0.79 (0.54-1.16)	2.36E ⁻⁰¹	0.77 (0.53-1.12)	1.74E ⁻⁰¹
077	1.10 (0.62-1.96)	7.52E ⁻⁰¹	1.11 (0.62-1.97)	7.29E ⁻⁰¹	1.04 (0.60-1.80)	8.96E ⁻⁰¹
078	1.01 (0.78-1.31)	9.35E ⁻⁰¹	1.02 (0.79-1.31)	8.76E ⁻⁰¹	1.03 (0.81-1.30)	8.19E ⁻⁰¹
079	0.84 (0.70-1.00)	4.67E ⁻⁰²	0.84 (0.70-1.00)	4.53E ⁻⁰²	0.82 (0.70-0.98)	2.44E ⁻⁰²
110	0.57 (0.43-0.74)	3.16E ⁻⁰⁵	0.58 (0.45-0.76)	5.73E ⁻⁰⁵	0.63 (0.49-0.80)	1.62E ⁻⁰⁴
111	0.79 (0.49-1.28)	3.48E ⁻⁰¹	0.81 (0.51-1.28)	3.62E ⁻⁰¹	0.89 (0.59-1.35)	5.87E ⁻⁰¹
112	0.98 (0.80-1.19)	8.18E ⁻⁰¹	0.96 (0.80-1.17)	7.03E ⁻⁰¹	0.99 (0.83-1.18)	9.05E ⁻⁰¹

Table S10. Comparison of results obtained using (1) Cox proportional hazard (no imputation), (2) Logistic regression (no imputation) and (3) logistic regression with imputation, for the first 10 ICD-9 diagnoses with recorded exposure in at least 10 cases and 10 controls.