Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Methods

Directed Acyclic Graphs

We used Directed Acyclic Graphs (DAG) to make our causal model assumptions explicit and to determine which factors represented important confounders. Assumptions exist in all regression analyses, but are frequently implicit. DAG models make these assumptions explicit, which allow the reader to critique and evaluate the underlying model.

Step 1. Our DAGs were based on an extensive literature review (12,264 abstracts and articles) performed by the authors to discern causal factors related to maternal infection and separately to development of psychopathy in the child.

Step 2. Next, the relationships gleaned from the literature review were reviewed by the team of authors, who represent experts in obstetrical infections, fetal injury, perinatal epidemiology, psychiatry and child development. The causal relationships gleaned from this process were complicated given the complexities of obstetrical complications relating to infection and separately to development of psychopathy in the exposed fetus (eFigures 1-4). We have included links to manipulatable versions of the graphs in the figure legends so that readers may better understand how these assumptions informed our study.

Step 3. Based on the DAG models, we used logic rules to analyze relationships to determine which variables were confounders, colliders or neither. These logic rules established the minimally sufficient adjustment set for controlling for important factors in the regression models.

Step 4. If a disagreement developed as to the status of a variable (e.g. maternal mental health, eTable 19), the model was run with and without the variable (when possible) to determine if there was an important change in the results.

This strategy based on DAG models avoids backwards and forward step regression approaches by determining *a priori*, which factors are important, their relationships to each other and the exposures and outcomes of interest. For more information on Directed Acyclic Graphs and this modeling approach, we encourage the reader to consult the references at the end of the supplement [1,2].

Adjusted Cumulative Hazard Curves

In order to show adjusted survival plots we applied the marginal weighted approach[3]. First, data were adjusted by weighting with respect to the list of confounders (maternal age, maternal asthma, maternal diabetes, premature rupture of membranes, smoking, year) followed by simple survival analyses. Weighting was based on assigning each observation a weight equal to the ratio of the distribution of confounders in the reference population and the observed probability of each combination of confounders in both the group exposed to maternal infection and the group not exposed to maternal infection. Weighting assures that the distribution of confounders in compared groups (exposed and unexposed to maternal infection) is equivalent to the distribution of the reference population. For these analyses, we used all 4.3 million Swedish births as the reference population.

eTable 1. Maternal Infection ICD Codes

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ICD8 (1969-1986)	00001, 00010, 00097, 00099, 00197, 00199, 00200, 00210, 00220, 00297, 00299, 00300, 00301, 00302, 00303, 00304, 00305, 00306, 00307, 00309, 00390, 00391, 00392, 00393, 00394, 00395, 00396, 00397, 00399, 00400, 00410, 00420, 00430, 00440, 00480, 00497, 00499, 00500, 00510, 00520, 00580, 00597, 00599, 00600, 00690, 00697, 00699, 00700, 00710, 00720, 00796, 00797, 00799, 00800, 00810, 00820, 00830, 00880, 00898, 00900, 00919, 00920, 00921, 00998, 01099, 01101, 01102, 01103, 01104, 01105, 01106, 01107, 01109, 01200, 01210, 01211, 01212, 01220, 01230, 01290, 01291, 01292, 01296, 01297, 01300, 01390, 01397, 01399, 01400, 01401, 01407, 01409, 01500, 01510, 01520, 01588, 01597, 01599, 01600, 01601, 01602, 01603, 01604, 01605, 01606, 01607, 01608, 01609, 01701, 01702, 01703, 01708, 01709, 01710, 01718, 01719, 01720, 01721, 01722, 01723, 01729, 01731, 01732, 01739, 01791, 01793, 01794, 01795, 01796, 01797, 01800, 01810, 01898, 02000, 02010, 02099, 02100, 02101, 02102, 02106, 02107, 02109, 02297, 02299, 02300, 02310, 02320, 02397, 02399, 02499, 02599, 02600, 02601, 02610, 02699, 02700, 02701, 02708, 02709, 02710, 02798, 03000, 03010, 03020, 03030, 03097, 03098, 03099, 03199, 03297, 03299, 03300, 03310, 03390, 03396, 03397, 03399, 03400, 03410, 03417, 03419, 03599, 03600, 03610, 03611, 03612, 03680, 03697, 03699, 03799, 03800, 03810, 03820, 03880, 03888, 03897, 03899, 03900, 03910, 03990, 03991, 03992, 03993, 03998, 04000, 04001, 04007, 04199, 04299, 04397, 04399, 04499, 04500, 04510, 04597, 04599, 04699, 05000, 05010, 05097, 05099, 05199, 05200, 05201, 05207, 05209, 05300, 05301, 05302, 05306, 05307, 05309, 05400, 05401, 05402, 05403, 05404, 05405, 05406, 05407, 05409, 05597, 05599, 05697, 05699, 05700, 05710, 05788, 05797, 05799, 06000, 06010, 06097, 06099, 06197, 06199, 06200, 06210, 06220, 06230, 06240, 06297, 06298, 06299, 06300, 06310, 06320, 06397, 06399, 06499, 06590, 06599, 06600, 06601, 06602, 06608, 06609, 06700, 06710, 06720, 06738, 06740, 06750, 06790, 06800, 06810, 06820, 06898, 07001, 07002, 07003, 07004, 07007, 07009, 07199, 07200, 07201, 07202, 07203, 07204, 07206, 07207, 07209, 07399, 07400, 07401, 07410, 07420, 07421, 07498, 07499, 07501, 07502, 07507, 07508, 07509, 07699, 07799, 07800, 07810, 07820, 07880, 07899, 07900, 07910, 07920, 07930, 07940, 07950, 07951, 07959, 07980, 07981, 07988, 07997, 07999, 08099, 08100, 08110, 08120, 08197, 08199, 08200, 08210, 08220, 08299, 08300, 08310, 08320, 08388, 08397, 08399, 08400, 08410, 08420, 08430, 08440, 08450, 08488, 08497, 08499, 08500, 08510, 08520, 08597, 08599, 08699, 08799, 08899, 08900, 08990, 09100, 09110, 09120, 09130, 09188, 09197, 09199, 09200, 09297, 09299, 09300, 09391, 09392, 09393, 09398, 09399, 09400, 09401, 09402, 09408, 09409, 09410, 09490, 09491, 09498, 09499, 09500, 09501, 09509, 09699, 09700, 09710, 09797, 09799, 09800, 09802, 09803, 09804, 09805, 09806, 09808, 09809, 09810, 09811, 09812, 09813, 09814, 09815, 09816, 09818, 09820, 09821, 09828, 09829, 09839, 09888, 09899, 09909, 09919, 09929, 09990, 09991, 09992, 09996, 09997, 09999, 10000, 10088, 10099, 10199, 10299, 10399, 10400, 10498, 11000, 11001, 11002, 11003, 11004, 11005, 11006, 11007, 11008, 11009, 11100, 11110, 11120, 11180, 11188, 11199, 11299, 11399, 11499, 11599, 11600, 11610, 11620, 11699, 11700, 11710, 11720, 11730, 11740, 11788, 11799, 12000, 12010, 12020, 12030, 12088, 12097, 12099, 12199, 12299, 12300, 12310, 12320, 12330, 12340, 12350, 12360, 12398, 12399, 12497, 12499, 12597, 12599, 12699, 12700, 12710, 12720, 12730, 12740, 12750, 12799, 12899, 12999, 13000, 13010, 13020, 13099, 13197, 13199, 13299, 13300, 13390, 13398, 13399, 13400, 13410, 13420, 13430, 13498, 13499, 13601, 13602, 13603, 13604, 13607, 13608, 13609, 32000, 32010, 32080, 32088, 32099, 32100, 32109, 32200, 32201, 32202, 32203, 36000, 36001, 36100,

	36101, 36109, 36200, 36201, 36202, 36209, 36600, 36700, 36800, 36900, 36901, 38000, 38001, 38100, 38110, 38199, 38200, 38210, 38299, 38300, 38310, 38399, 38400, 38401, 38402, 39097, 39099, 39197, 39199, 39299, 39200, 39201, 39202, 39209, 39290, 42000, 42007, 42008, 42009, 42100, 42198, 42297, 42299, 46099, 46100, 46101, 46102, 46103, 46104, 46109, 46201, 46202, 46209, 46301, 46309, 46401, 46402, 46403, 46409, 46599, 46699, 47099, 47101, 47109, 47201, 47202, 47209, 47399, 47499, 48099, 48199, 48201, 48210, 48220, 48230, 48298, 48399, 48499, 48501, 48502, 48509, 48601, 48609, 49099, 50199, 50800, 50801, 50802, 50803, 51001, 51002, 51003, 51009, 51110, 51399, 52240, 52250, 52730, 52800, 52810, 52820, 52830, 54000, 54001, 54002, 54003, 54090, 54091, 54099, 54199, 54201, 56600, 56601, 56700, 56701, 56702, 56703, 56704, 56708, 56900, 56901, 56902, 56903, 56904, 57701, 59000, 59001, 59002, 59010, 59011, 59012, 59013, 59014, 59020, 59098, 59099, 59500, 59501, 59502, 59503, 59509, 59700, 59701, 59702, 59703, 59708, 59709, 61100, 61101, 61201, 61202, 61207, 61208, 61209, 61301, 61302, 61307, 61308, 61309, 61499, 61600, 61601, 61602, 61603, 62000, 62001, 62090, 62091, 62098, 62099, 62200, 62201, 62202, 62203, 62208, 62209, 62210, 62211, 62212, 62213, 62218, 62219, 62940, 63000, 63001, 63002, 63003, 63008, 63009, 63500, 63501, 63590, 63598, 63599, 63600, 67000, 67001, 67002, 67008, 67009, 67100, 67101, 67102, 67108, 67109, 67299, 67800, 67801, 67802, 67808, 68000, 68010, 68020, 68030, 68040, 68050, 68060, 68080, 68088, 68090, 68100, 68101, 68102, 68103, 68104, 68108, 68109, 68200, 68210, 68220, 68230, 68240, 68250, 68298, 68299, 68300, 68301, 68302, 68308, 68309, 71000, 71001, 71002, 71003, 71004, 71005, 71006, 71007, 71008, 71009, 72000, 72010, 72029, 72030, 72031, 72039, 68600, 68610, 68611, 68690, 68691, 68692, 68693, 68694, 68695, 68696, 68698, 73299, 76100, 76120, 76130, 76140, 76180, 76300, 99850, 99930

This table contains all infection codes available through ICD coding. We used all of these codes to capture inpatient diagnoses of infection during pregnancy. Note that Swedish ICD codes may contain a letter at the end of the code, which may differ from codes in other countries.

eTable 2. Maternal Infection ICD Codes by Infection Type

Sepsis	
ICD10	A021, A227, A267, A327, A40, A401, A402, A403, A408, A409, A41, A410, A411, A412, A413, A414, A415, A418, A419, A427, B377, O85, A241, A207, A483, O080, R572, A392, O753
ICD9	036A, 038, 038A, 038B, 038C, 038D, 038E, 038W, 038X, 112F, 670, 639A, 659A
ICD8	03610, 03800, 03810, 03820, 03880, 03897, 03898
Influenza	
ICD10	J09, J10, J100, J101, J108, J11, J110, J111, J118
ICD9	487, 487A, 487B, 487W
ICD8	47099, 47101, 47109, 47201, 47209, 47399, 47499
Meningitis or Encephalitis	
ICD10	G00, G000, G001, G002, G003, G008, G009, G01, G02, G020, G021, G028, G03, G030, G031, G032, G038, G039, G04, G040, G042, G048, G049, G05, G050, G051, G052, G058, G05, G06, G060, G060, G061, G062, G07, G08, A321, A390, A521, A170, A87, A870, A871, A872, A878, A879, B003, B051, B261, B060, B010, B021, B375, B384, B451, B574, A850, A85, A851, A852, A858, A86, B004, B050, B262, B011, B582, G008A, G008B, G008W, G042A, G042B, G048A, G048B, G048C, G048W, G049A, G049B, G061A, G061J, G061K, G061X
ICD9	320, 320A, 320B, 320C, 320D, 320H, 320W, 320X, 321, 321A, 321H, 321W, 322, 322A, 322B, 322C, 322X, 013, 013A, 013B, 013W, 013X, 036, 036A, 036B, 094C, 093E, 047, 047A, 047B, 047W, 047X, 049B, 049A, 053A, 072B
ICD8	32000, 32010, 32080, 32088, 32099, 32100, 32109, 32200, 32201, 32202, 32203, 32300, 32301, 32302, 32303, 32308, 32309, 03600, 04500, 04510, 04597, 04599, 04699, 06200, 06210, 06220, 06230, 06240, 06297, 06298, 06299, 06300, 06300, 06310, 06320, 06397, 06399, 06499, 06590, 06599, 07502, 07201, 07920, 05404, 05200, 09490, 01300, 02701, 04001, 29220, 29238, 29239
Pyelonephritis	
ICD10	N10, N11, N110, N111, N118, N119, N12, N136
ICD9	590, 590A, 590B, 590C, 590D, 590W, 590X
ICD8	59000, 59001, 59002, 59010, 59011, 59012, 59013, 59014, 59020, 59098, 59099
Pneumonia	
ICD10	J100, J12, J120, J121, 122, J123, J128, J129, J13, J14, J15, J150, J152, J153, J154, J155, J156, J157, J158, J159, J16, J160, J168, J17, J170, J171, J172, J173, J178, J18, J180, J181, J182, J188, J189, A420, A221, A548, A430, A022, A212, A010, B250, B052, B068, B012, B440, B441, B371, B380, B381, B382, B390, B391, B392, B778, B583
ICD9	480, 480A, 480B, 480C, 480W, 480X, 481, 482, 482A, 482B, 482C, 482D, 482E, 482J, 482W, 482X, 483, 484, 484A, 484B, 484C, 484D, 484E, 484F, 484G, 484H, 484W, 486, 055B, 052A
ICD8	48099, 48199, 48201, 48210, 48220, 48230, 48298, 48399, 48499, 48501, 48502, 48509, 48601, 48609
Chorioamnionitis*	
ICD10	O411, O752, O753 P027
ICD9	658E, 659C, 659D 762H
ICD8	76398, 76310
Urinary Tract Infection	
ICD10	O23, O231, O232, O233, O234, O235, O239, N300, N390, N309
ICD9	646G, 595, 595A, 595X, 599A
ICD8	63590, 59500, 59501, 59509, 59902, 78910, 78911

This table contains the maternal infection ICD codes categorized by disease used to capture inpatient diagnoses of infection during pregnancy. Note that Swedish ICD codes may contain a letter at the end of the code, which may differ from codes in other countries.

*We used codes for “fever during delivery” and “neonatal exposure to fever during delivery” as surrogates for the diagnosis of chorioamnionitis.

eTable 3. Psychopathology ICD codes

Bipolar Disorder	
ICD10	F31, F310, F311, F312, F313, F314, F315, F316, F317, F318, F319, F340, F300, F301, F308, F309, F30
ICD9	296, 296A, 298A, 298B, 296C, 296D, 296E, 296W, 296X, 298A, 298B
ICD8	29600, 29610, 29620, 29630, 29688, 29699, 29810
Psychosis, including Schizophrenia	
ICD10	F20, F200, F201, F202, F203, F204, F205, F206, F208, F209, F21, F22, F220, F228, F229, F23, F230, F231, F232, F233, F238, F239, F25, F250, F251, F252, F258, F259, F28, F29
ICD9	295, 295A, 295B, 295C, 295D, 295E, 295F, 295G, 295H, 295W, 295X, 297, 297B, 297C, 297W, 297X, 298, 298A, 298E
ICD8	29500, 29510, 29520, 29530, 29540, 29550, 29560, 29570, 29580, 29599, 29700, 29710, 29798, 29810, 29830
Autism	
ICD10	F840, F841, F844, F843, F845, F848, F849
ICD9	299A and 299B
ICD8	None*
Depression	
ICD10	F32, F320, F321, F322, F328, F329, F33, F330, F331, F332, F334, F338, F339, F341, F38, F381, F388
ICD9	296B, 300E, 298A, V79A
ICD8	29620, 29800, 30040
Suicide	
ICD10	X60, X61, X62, X63, X64, X65, X66, X67, X68, X69, X70, X71, X72, X73, X74, X75, X76, X77, X78, X79, X80, X81, X82, X83, X84
ICD9	E950, E951, E952, E953, E954, E955, E956, E957, E958, E959
ICD8	E950, E9509, E9529, E9539, E9549, E9559, E9569, E9579, E9589, E9599

This table contains the ICD codes used to capture inpatient diagnoses of psychopathology in either the child or adult born from the index pregnancy. Note that Swedish ICD codes may contain a letter at the end of the code, which may differ from codes in other countries.

*No ICD8 code for autism exists because the disorder was not assigned a code until ICD9. Therefore, our autism cohort begins in 1987 when ICD9 coding was implemented in Sweden.

Beyond ICD codes, there is no further information describing the infection available in the registries.

eTable 4. Hazard Ratios for Psychopathology Diagnosis by Infection Type in Pregnancy With Adjustment for Diagnosis of a Maternal Mental Health Disorder

Infection Type	Psychopathology Outcome	Adjusted Hazard Ratio	95% CI*	
Any Maternal Infection	Autism	1.76	1.32	2.36
	Depression	1.22	1.11	1.35
	Psychosis	1.12	0.82	1.54
	Bipolar†	0.98	0.70	1.36

The DAG models did not identify maternal mental health as a confounder that required adjustment in our analyses; therefore, we did not adjust for maternal mental health diagnoses in our main analysis. At the request of several reviewers, we ran an additional model adjusting for maternal mental health diagnosis in addition to the confounders that we had previously identified from our DAG models (maternal age, maternal asthma, maternal diabetes mellitus, premature rupture of membranes and maternal tobacco status). We used robust sandwich variance estimators due to lack of independence among sibling births. For all models, stratification was used for 10-year epoch of birth and maternal tobacco status to avoid violating the proportional hazard assumption.

*Bonferroni correction was used to adjust confidence intervals for 8 pre-specified comparisons.

†In the bipolar disorder model, stratification was also used for premature rupture of membranes and maternal age due to proportional hazards assumption violations.

eTable 5. Outcomes, Person Years and Unadjusted Rate Ratios for Maternal Infection and Autism Spectrum Disorder

	Maternal Infection		No Infection		Unadjusted Rate Ratio
	ASD	No ASD	ASD	No ASD	
N	90	18,236	3,116	1316493	
Person-Years	1,143	261,417	38,628	17,265,755	
Rate		0.000343		0.00018	**1.91**

This table shows the numbers of hospital admissions with an accompanying autism spectrum disorder (ASD) diagnosis, person years and unadjusted rate ratios with and without exposure to maternal infection in utero.

eTable 6. Outcomes, Person Years and Unadjusted Rate Ratios for Maternal Infection and Depression

	Maternal Infection		No Infection		Unadjusted Rate Ratio
	Depression	No Depression	Depression	No Depression	
N	409	25,282	20,709	1,745,120	
Person-Years	7,564	475,223	381,074	31,261,951	
Rate		0.0008472		0.000655	**1.29**

This table shows the numbers of hospital admissions with an accompanying depression diagnosis, person years and unadjusted rate ratios with and without exposure to maternal infection in utero.

eTable 7. Outcomes, Person Years and Unadjusted Rate Ratios for Maternal Infection and Bipolar Disorder

	Maternal Infection		No Infection		Unadjusted Rate Ratio
	Bipolar	No Bipolar	Bipolar	No Bipolar	
N	70	23,329	4,378	1,557,776	
Person-Years	1,194	385,538	68,459	25,025,519	
Rate		0.000181		0.000174	**1.04**

This table shows the numbers of hospital admissions with an accompanying bipolar disorder diagnosis, person years and unadjusted rate ratios with and without exposure to maternal infection in utero.

eTable 8. Outcomes, Person Years and Unadjusted Rate Ratios for Maternal Infection and Psychosis

	Maternal Infection		No Infection		Unadjusted Rate Ratio
	Psychosis	No Psychosis	Psychosis	No Psychosis	
N	75	23,325	4,274	1,557,870	
Person-Years	1,135	385,419	65,090	25,020,968	
Rate		0.000194		0.00017	**1.14**

This table shows the numbers of hospital admissions with an accompanying psychosis diagnosis, person years and unadjusted rate ratios with and without exposure to maternal infection in utero.

eTable 9. Outcomes, Person Years and Unadjusted Rate Ratios for Severe Maternal Infection and Autism Spectrum Disorder

	Severe Maternal Infection		No Severe Infection		Unadjusted Rate Ratio
	ASD	No ASD	ASD	No ASD	
N	41	10692	3165	1324037	
Person-Years	490	125,920	39,281	17,401,252	
Rate		0.000324		0.000181	**1.79**

This table shows the numbers of hospital admissions with an accompanying autism diagnosis, person years and unadjusted rate ratios with and without exposure to severe maternal infection in utero.

eTable 10. Outcomes, Person Years and Unadjusted Rate Ratios for Severe Maternal Infection and Depression

	Severe Maternal Infection		No Severe Infection		Unadjusted Rate Ratio
	Depression	No Depression	Depression	No Depression	
N	66	9,058	21,052	1,761,344	
Person-Years	883	97,594	387,755	31,639,581	
Rate		0.000670		0.000657	**1.02**

This table shows the numbers of hospital admissions with an accompanying depression diagnosis, person years and unadjusted rate ratios with and without exposure to severe maternal infection in utero.

eTable 11. Outcomes, Person Years and Unadjusted Rate Ratios for Maternal UTI and Autism

	Maternal UTI		No UTI		Unadjusted Rate Ratio
	ASD	No ASD	ASD	No ASD	
N	41	6,945	3,165	1,327,784	
Person-Years	568	109,398	39,203	17,417,775	
Rate		0.000373		0.000181	**2.06**

This table shows the numbers of hospital admissions with an accompanying autism diagnosis, person years and unadjusted rate ratios with and without exposure to maternal urinary tract infection (UTI) in utero.

eTable 12. Outcomes, Person Years and Unadjusted Rate Ratios for Maternal UTI and Depression

	Maternal UTI		No UTI		Unadjusted Rate Ratio
	Depression	No Depression	Depression	No Depression	
N	158	9,200	20,960	1,761,202	
Person-Years	2780	171,573	385,858	31,565,601	
Rate		0.000906		0.000656	**1.38**

This table shows numbers of hospital admissions with an accompanying depression diagnosis, person years and unadjusted rate ratios with and without exposure to maternal urinary tract infection (UTI) in utero.

eTable 13. Misclassification of Outcome Analysis on Autism Risk

Infection Type	Assumptions for Population Autism Prevalence				
	0.2%	0.3%	1.0%	2.0%	3.0%
Any Maternal Infection	1.6	1.5	1.2	1.0	-
Severe Maternal Infection	1.8	1.7	1.5	1.4	1.0
Urinary Tract Infection	1.8	1.7	1.3	1.1	-

We performed a bias analysis to determine the effect of misclassification of outcome, which would result if an individual was diagnosed with autism spectrum disorder, but never admitted to the hospital and therefore not captured by the Swedish inpatient population registry. Rate ratios were estimated for lifetime autism risk in the exposed fetus based on infection type (any, severe, or urinary tract infection) using different assumptions for autism prevalence in the Swedish population. This bias analysis demonstrates that population autism prevalences between 2 and 3% would nullify the effect found in our study, which is on par only with a recent and highest estimate of autism prevalence at 2.5% in Stockholm[4]. Note that prior studies in Sweden encompassing most of the study period estimated autism prevalence between 0.2 and 1%.[5] For more on this technique, see [6].

eTable 14. Misclassification of Outcome Analysis on Depression Risk

Infection Type	Assumptions for Population Depression Prevalence			
	5%	10%	20%	50%
Any Maternal Infection	1.0	0.9	0.9	0.8
Urinary tract infection	1.0	0.9	0.8	0.8

We performed a bias analysis to determine the effect of misclassification of outcome, which would result if an individual was diagnosed with depression, but never admitted to the hospital and therefore not captured by the Swedish inpatient population registry. Rate ratios were estimated for lifetime depression in the Swedish population. This bias analysis demonstrates that a population depression prevalence of only 5% would drive the effect estimate to the null. We did not perform a similar analysis with severe maternal infection, because this result was not significant in the main analysis. For more on this technique, see [6].

eTable 15. Misclassification of Exposure Analysis on Autism Risk for Any Maternal Infection

Observed RR		2.08
Sensitivity	Specificity	Corrected RR
0.46	0.99	5.05
0.75	0.99	4.99
0.95	0.99	4.96

We performed a bias analysis to determine the effect of misclassification of exposure, which would result if maternal infection was misdiagnosed or miscoded. Risk ratios were estimated for autism using different assumptions for the sensitivity of any maternal infection diagnosis during pregnancy. This bias analysis demonstrates that correction of risk ratios for decreased sensitivity and specificity resulted in greater risk ratios for autism than in the original analysis. For more on this technique, see [6].

eTable 16. Misclassification of Exposure Analysis on Depression Risk for Any Maternal Infection

Observed RR		1.36
Sensitivity	Specificity	Corrected RR
0.46	0.99	2.18
0.75	0.99	2.17
0.95	0.99	2.17

We performed a bias analysis to determine the effect of misclassification of exposure, which would result if maternal infection was misdiagnosed or miscoded. Risk ratios were estimated for depression using different assumptions for the sensitivity of a maternal infection diagnosis during pregnancy. This bias analysis demonstrates that correction of risk ratios for decreased sensitivity and specificity resulted in greater risk ratios for depression than in the original analysis. For more on this technique, see [6].

eTable 17. Misclassification of Exposure Analysis on Autism Risk for Severe Maternal Infections

Observed RR		1.6
Sensitivity	Specificity	Corrected RR
0.46	0.995	3.39
0.75	0.995	3.38
0.95	0.995	3.37

We performed a bias analysis to determine the effect of misclassification of exposure, which would result if severe maternal infection diagnoses (sepsis, influenza, chorioamnionitis, pneumonia, pyelonephritis, meningitis) were misdiagnosed or miscoded. Risk ratios were estimated for autism using different assumptions for the sensitivity of a severe maternal infection diagnosis during pregnancy. This bias analysis demonstrates that correction of risk ratios for decreased sensitivity and specificity resulted in greater risk ratios for autism than in the original analysis. For more on this technique, see [6].

eTable 18. Misclassification of Exposure Analysis on Autism Risk for Maternal UTI

Observed RR		2.47
Sensitivity	Specificity	Corrected RR
0.46	0.99	35.8
0.75	0.99	35.5
0.95	0.99	35.4

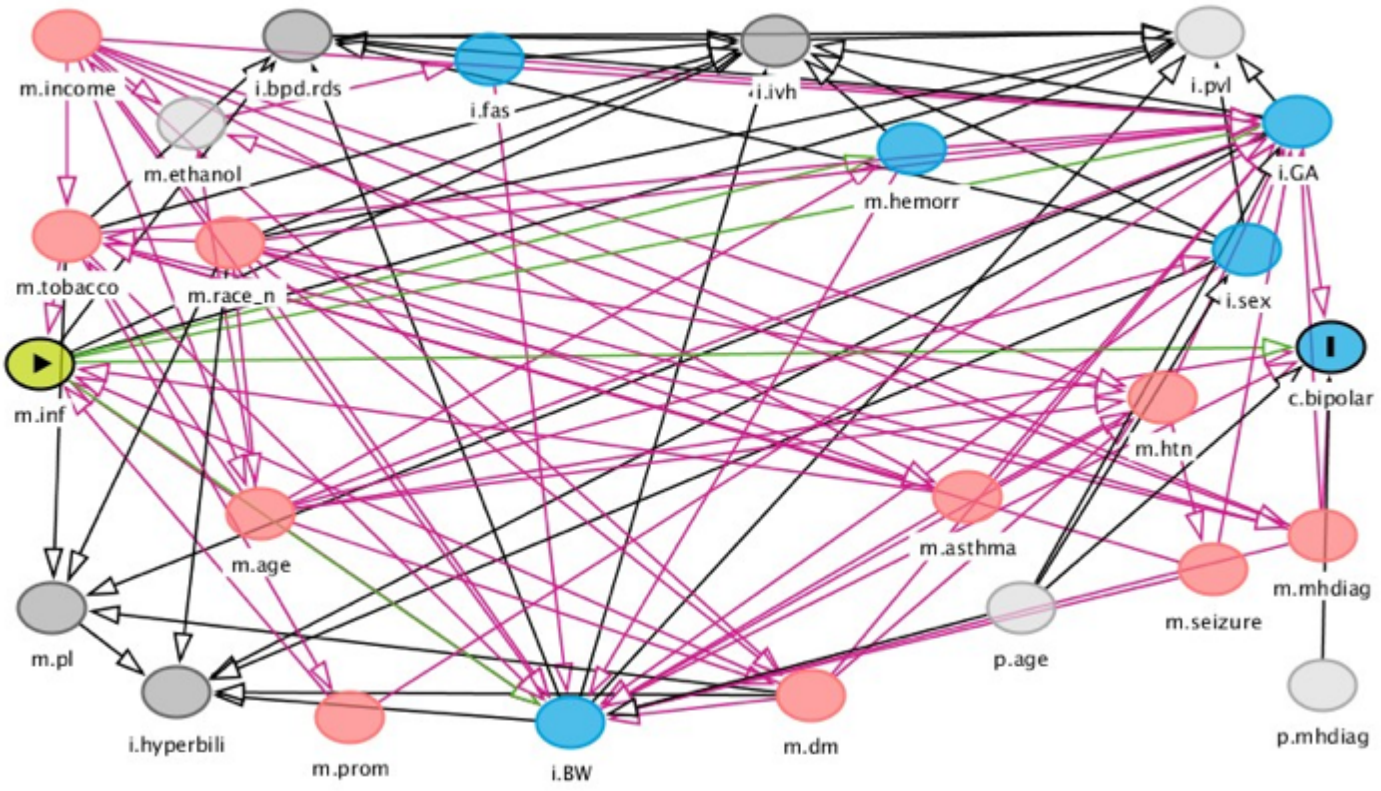
We performed a bias analysis to determine the effect of misclassification of exposure, which would result if maternal UTI was misdiagnosed or miscoded. Risk ratios were estimated for autism using different assumptions for the sensitivity of a maternal UTI diagnosis during pregnancy. This bias analysis demonstrates that correction of risk ratios for decreased sensitivity and specificity resulted in greater risk ratios for autism than in the original analysis. For more on this technique, see [6].

eTable 19. Misclassification of Exposure Analysis on Depression Risk for Maternal UTI

Observed RR		1.44
Sensitivity	Specificity	Corrected RR
0.46	0.99	11.16
0.75	0.99	11.14
0.95	0.99	11.13

We performed a bias analysis to determine the effect of misclassification of exposure, which would occur if maternal UTI was misdiagnosed or miscoded. Risk ratios were estimated for depression using different assumptions for the sensitivity of a maternal UTI diagnosis during pregnancy. This bias analysis demonstrates that correction of risk ratios for decreased sensitivity and specificity resulted in greater risk ratios for autism than in the original analysis. For more on this technique, see [6].

eFigure 1. Directed Acyclic Graph for Infection and Bipolar Disorder



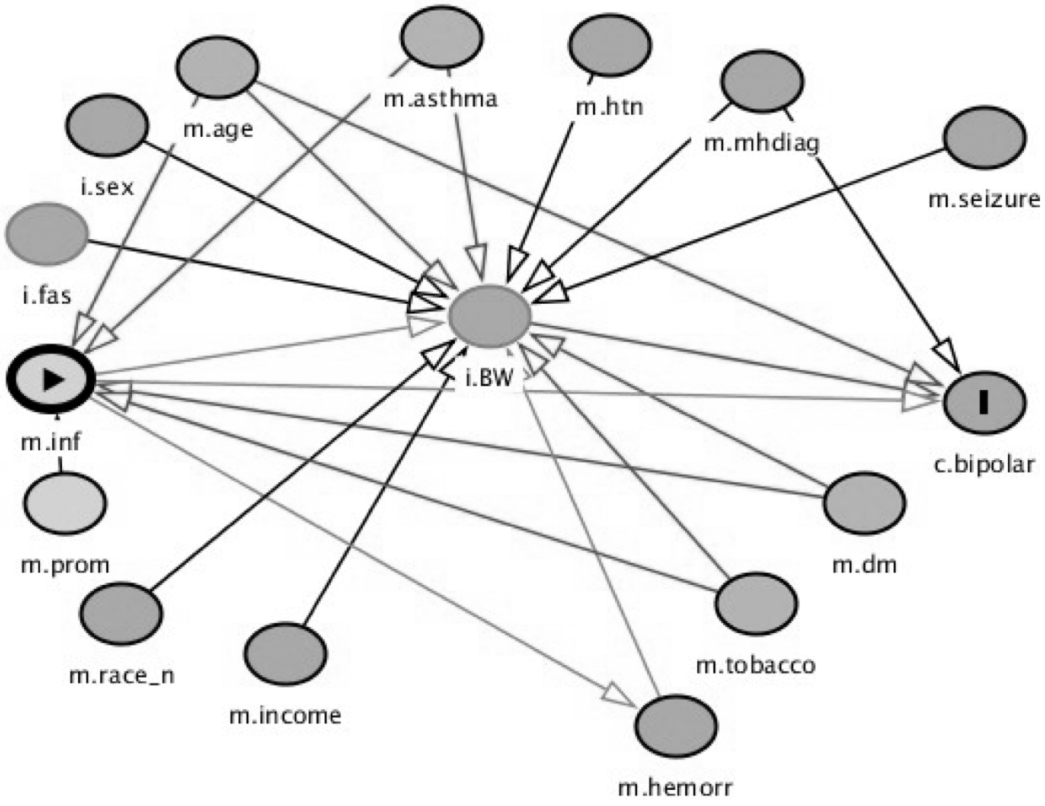
This schematic illustrates the causal relationship assumptions encoded in our DAG model for the risk for bipolar disorder in the child or adult exposed to infection *in utero*. The green circle is the exposure (maternal infection). The blue circles are either ancestors of the outcome or the outcome itself (bipolar in the child) and the red circles are both ancestors of the exposure and the outcome. The gray circles are other variables. The green, pink and grey lines are causal, biasing or other pathways, respectively.

A manipulatable version of this DAG is available at: dagitty.net/m8ARP3t

Abbreviations used in the figure are listed below:

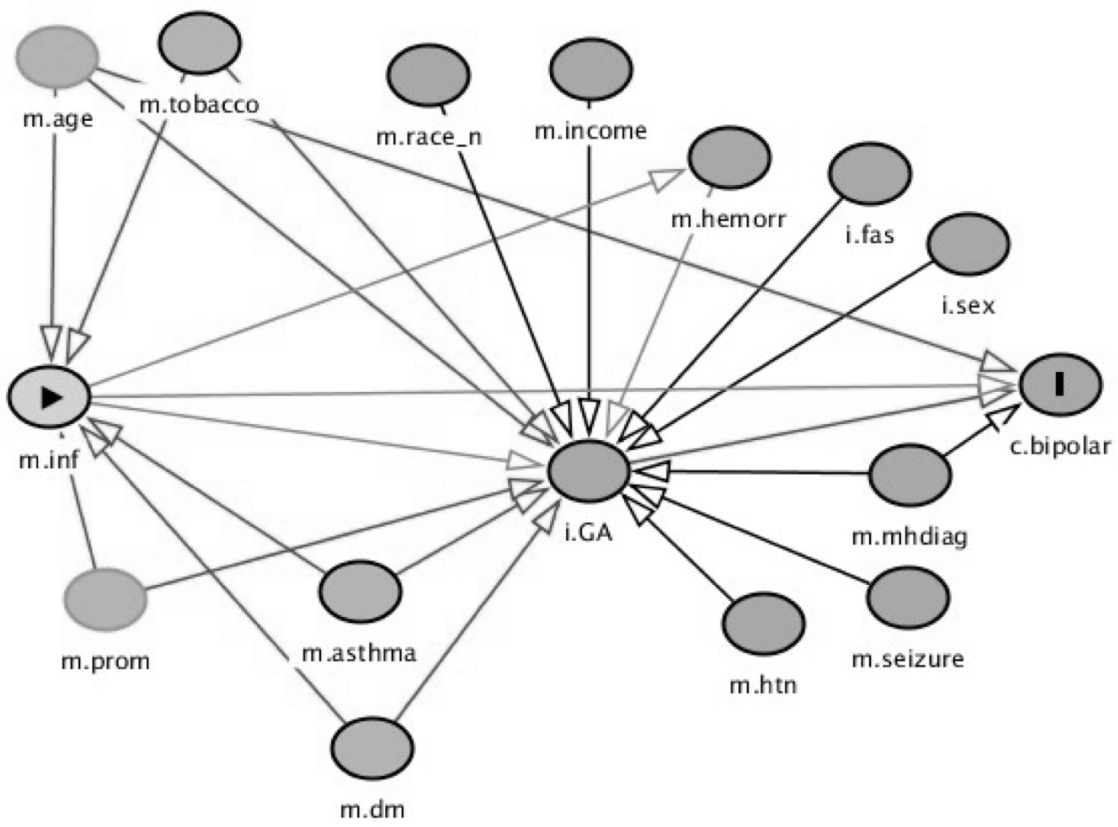
c.bipolar=bipolar disorder in the child or adult	m.hemorrh=antepartum hemorrhage
i.bpd.rds=infant bronchopulmonary dysplasia and respiratory distress syndrome	m.income=maternal income
i.BW=infant birthweight	m.inf=maternal infection
i.fas=fetal alcohol syndrome	m.mhdiag=maternal mental illness diagnosis
i.GA=gestational age at delivery	m.mhtn=maternal hypertension
i.hyperbili=infant hyperbilirubinemia	m.pl=maternal prolonged labor
i.ivh=infant intraventricular hemorrhage	m.prom=maternal premature rupture of membranes
i.pvl=infant periventricular leukomalacia	m.race_n=maternal race
i.sex=infant sex	m.seizure=maternal seizure
m.age=maternal age	m.tobacco= maternal smoking
m.asthma=maternal asthma	p.age=paternal age
m.dm=maternal diabetes mellitus	p.mhdiag= paternal mental health diagnosis
m.ethanol=maternal ethanol abuse	

eFigure 2. Portion of DAG for Infection and Bipolar Disorder with Birthweight related variables only



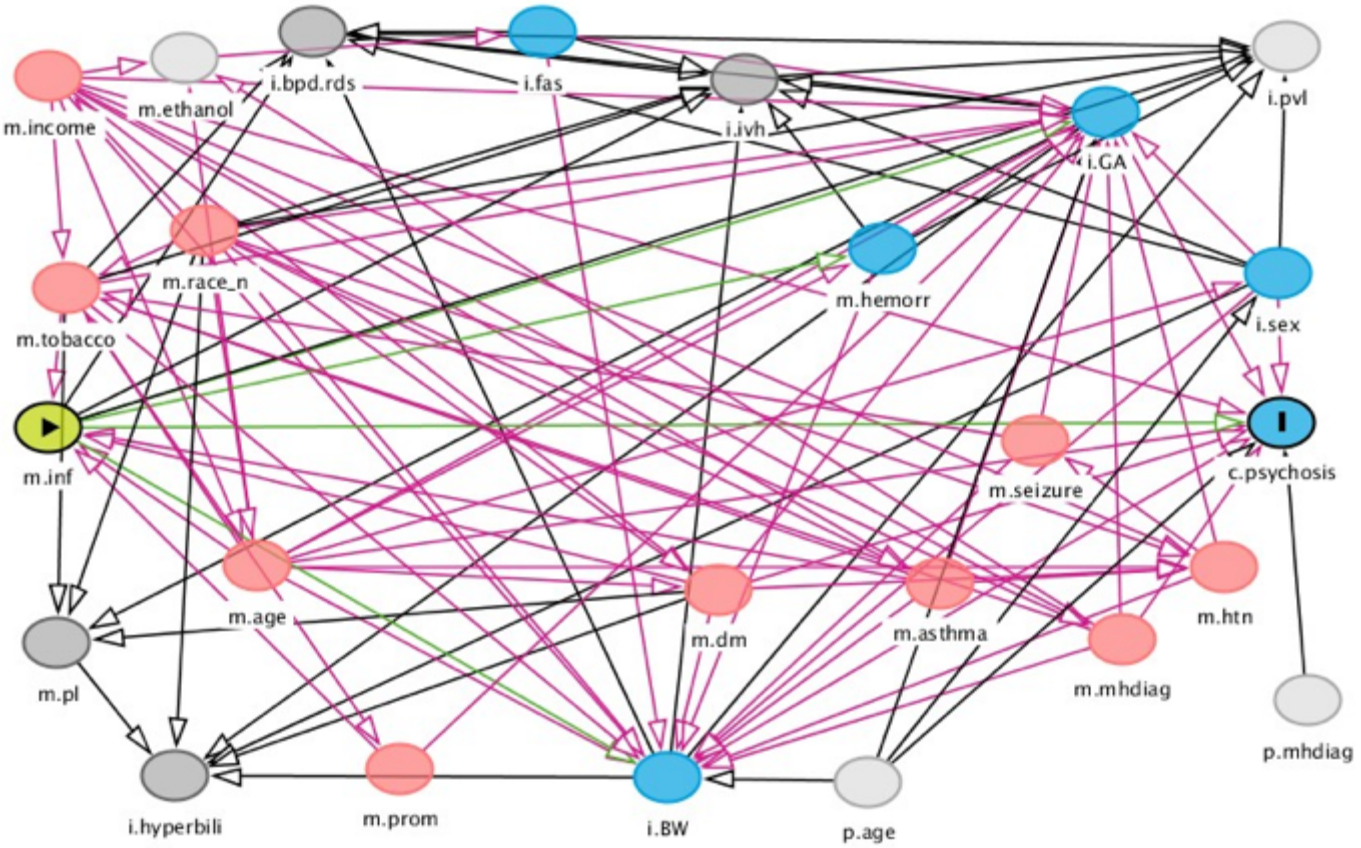
This schematic depicts a portion of the DAG from eFigure1 depicting only variables that are related to maternal infection, birthweight for gestational age and bipolar disorder in the child. All other variables and relationships among other variables are removed for clarification purposes. See eFigure1 for variable key.

eFigure 3. Portion of DAG for Infection and Bipolar Disorder with Gestational Age related variables only



This schematic depicts a portion of the DAG from eFigure1 depicting only variables that are related to maternal infection, gestational age and bipolar disorder in the child. All other variables and relationships among other variables are removed for clarification purposes. See eFigure1 for variable key.

eFigure 4. Directed Acyclic Graph for Infection and Psychosis Including Schizophrenia



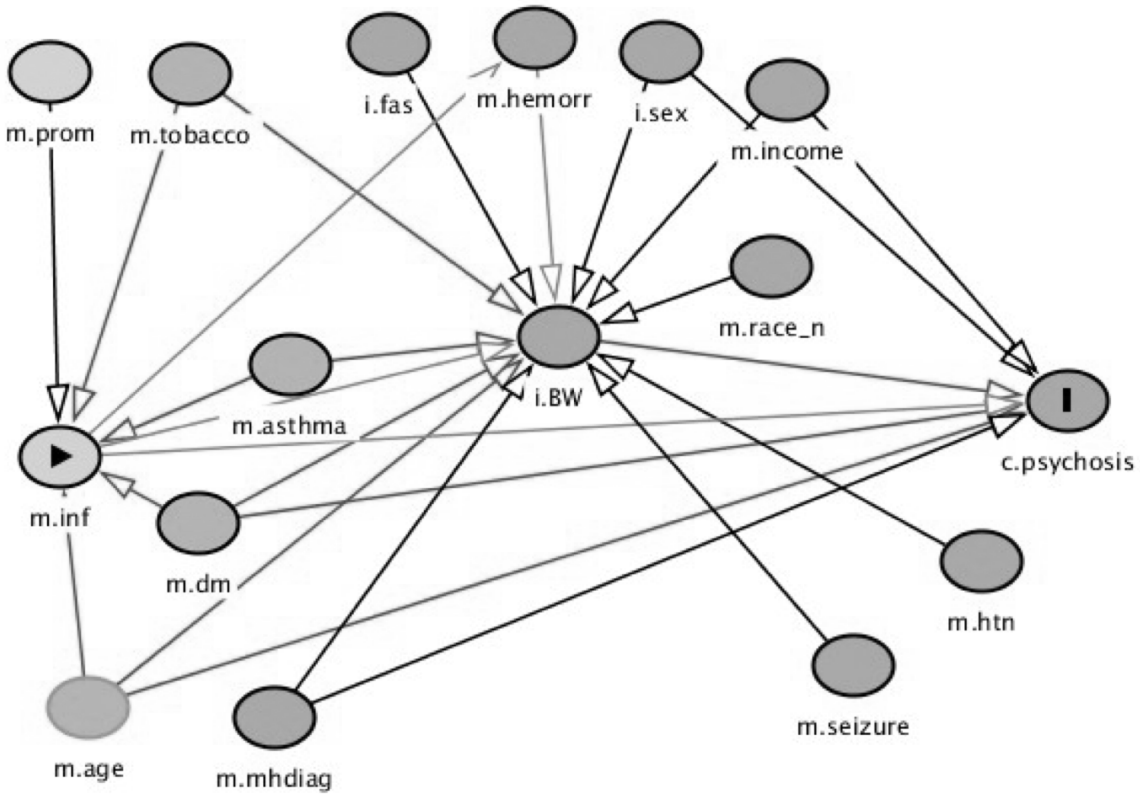
This schematic illustrates the causal relationship assumptions encoded in our DAG model for the risk for psychosis (including schizophrenia) in the child or adult exposed to infection *in utero*. The green circle is the exposure (maternal infection). The blue circles are either ancestors of the outcome or the outcome itself (psychosis in the child) and the red circles are both ancestors of the exposure and the outcome. The gray circles are other variables. The green, pink and grey lines are causal, biasing or other pathways, respectively.

A manipulatable version of this DAG is available at: dagitty.net/mc0pZP0

Abbreviations used in the figure are listed below:

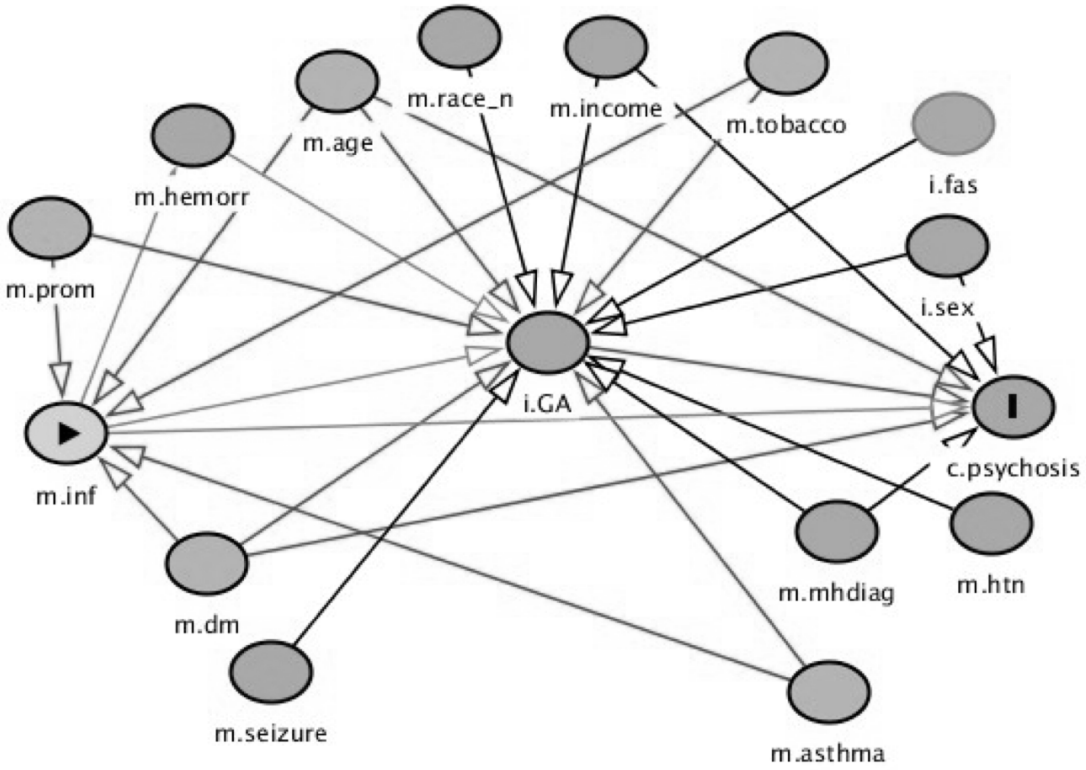
• c.psychosis=psychosis in the child or adult	• m.hemorrh=antepartum hemorrhage
• i.bpd.rds=infant bronchopulmonary dysplasia and respiratory distress syndrome	• m.income=maternal income
• i.BW=infant birthweight	• m.inf=maternal infection
• i.fas=fetal alcohol syndrome	• m.mhdiag=maternal mental illness diagnosis
• i.GA=gestational age at delivery	• m.mhtn=maternal hypertension
• i.hyperbili=infant hyperbilirubinemia	• m.pl=maternal prolonged labor
• i.ivh=infant intraventricular hemorrhage	• m.prom=maternal premature rupture of membranes
• i.pvl=infant periventricular leukomalacia	• m.race_n=maternal race
• i.sex=infant sex	• m.seizure=maternal seizure
• m.age=maternal age	• m.tobacco= maternal smoking
• m.asthma=maternal asthma	• p.age=paternal age
• m.dm=maternal diabetes mellitus	• p.mhdiag= paternal mental health diagnosis
• m.ethanol=maternal ethanol abuse	

eFigure 5. Portion of DAG for Infection and Psychosis with Birthweight related variables only



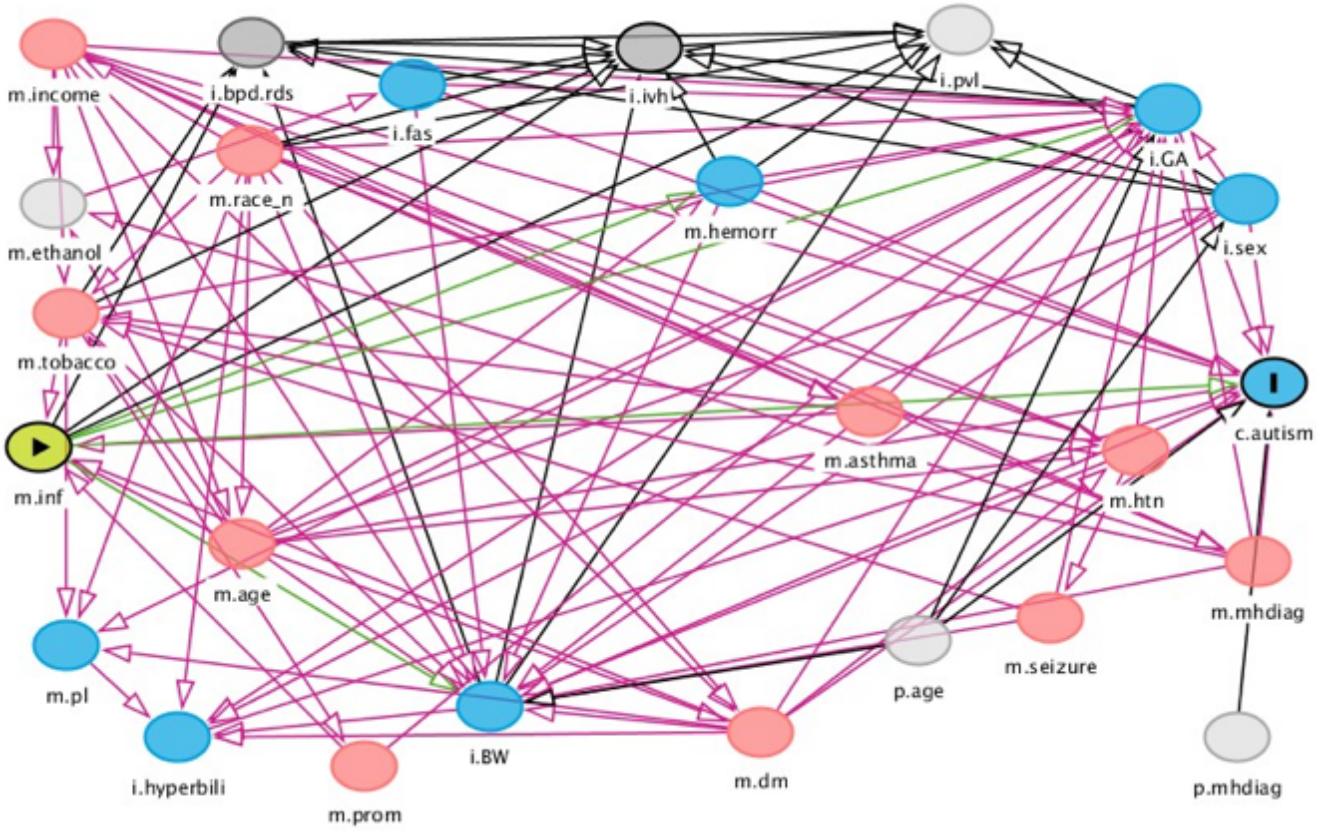
This schematic depicts a portion of the DAG from eFigure2 depicting only variables that are related to maternal infection, birthweight for gestational age and psychosis including schizophrenia in the child. All other variables and relationships among other variables are removed for clarification purposes. See eFigure2 for variable key.

eFigure 6. Portion of DAG for Infection and Psychosis with Gestational Age related variables only



This schematic depicts a portion of the DAG from eFigure2 depicting only variables that are related to maternal infection, gestational age and psychosis including schizophrenia in the child. All other variables and relationships among other variables are removed for clarification purposes. See eFigure2 for variable key.

eFigure 7. Directed Acyclic Graph for Infection and Autism



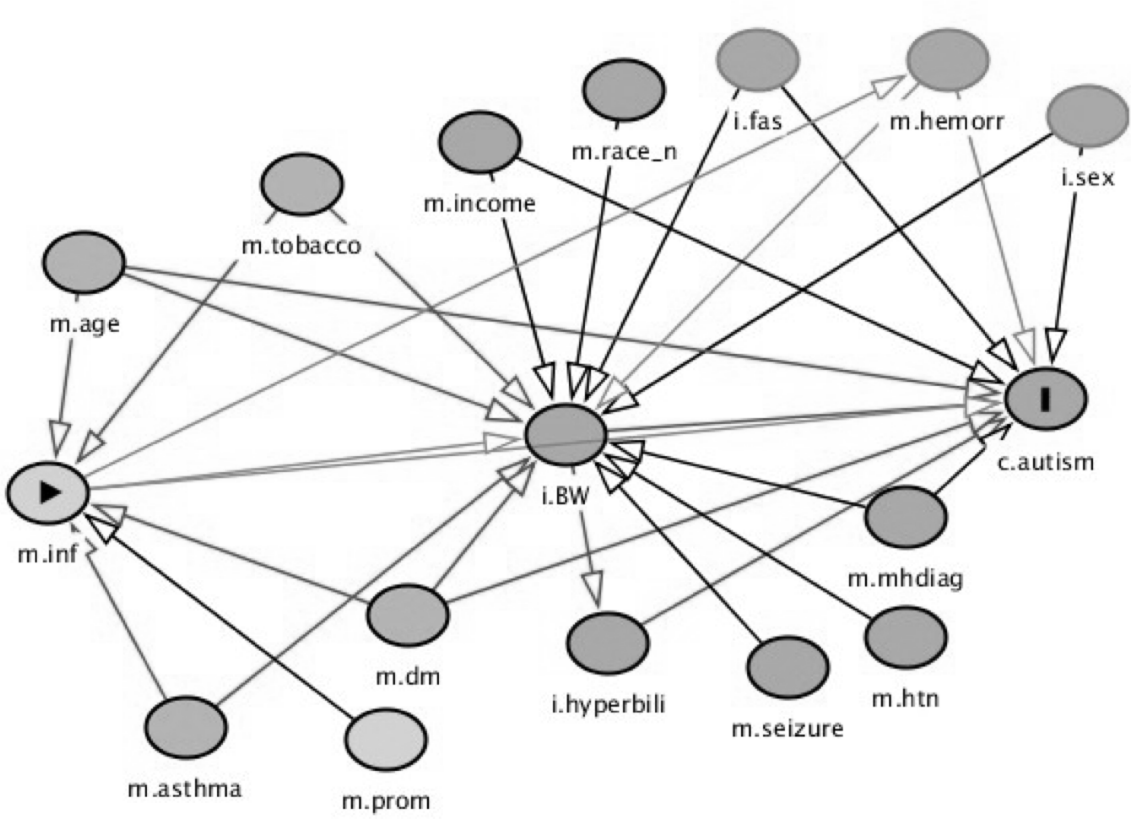
This schematic illustrates the causal relationship assumptions encoded in our DAG model for the risk for autism spectrum disorder in the child or adult exposed to infection *in utero*. The green circle is the exposure (maternal infection). The blue circles are either ancestors of the outcome or the outcome itself (autism in the child) and the red circles are both ancestors of the exposure and the outcome. The gray circles are other variables. The green, pink and grey lines are causal, biasing or other pathways respectively.

A manipulatable version of this DAG is available at: dagitty.net/mw6IFKl

Abbreviations used in the figure are listed below:

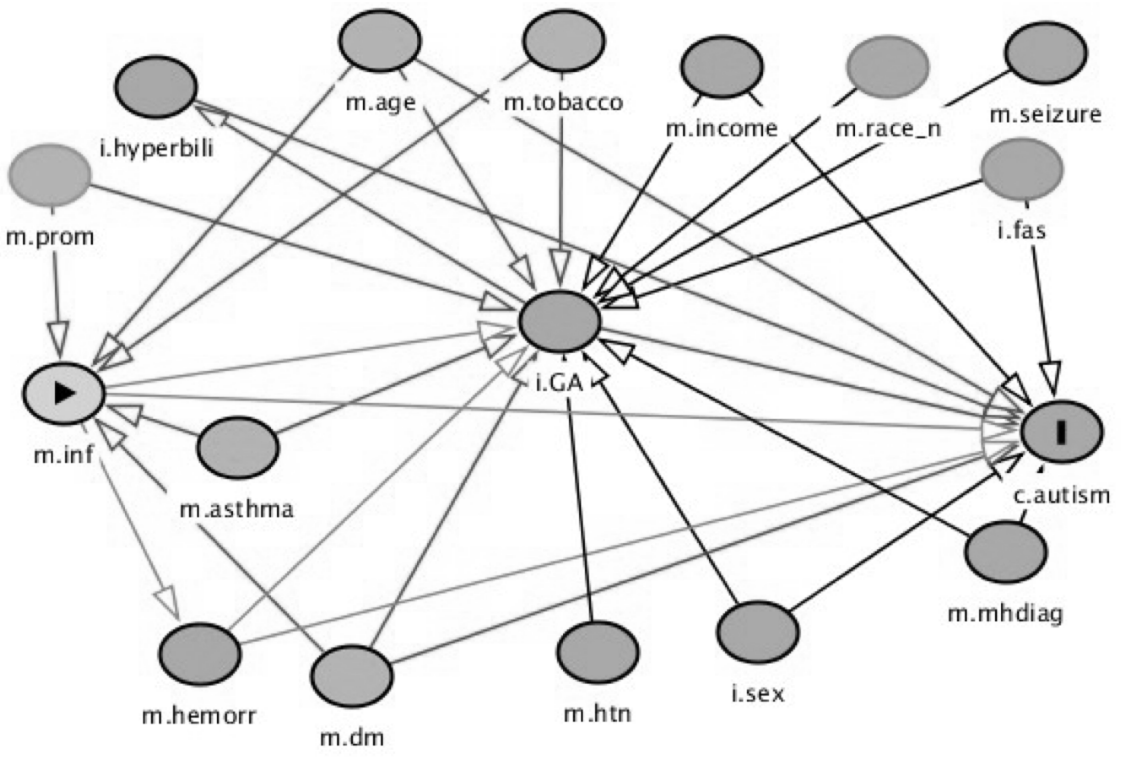
• c.autism=autism in the child or adult	• m.hemorrh=antepartum hemorrhage
• i.bpd.rds=infant bronchopulmonary dysplasia and respiratory distress syndrome	• m.income=maternal income
• i.BW=infant birthweight	• m.inf=maternal infection
• i.fas=fetal alcohol syndrome	• m.mhdiag=maternal mental illness diagnosis
• i.GA=gestational age at delivery	• m.mhtn=maternal hypertension
• i.hyperbili=infant hyperbilirubinemia	• m.pl=maternal prolonged labor
• i.ivh=infant intraventricular hemorrhage	• m.prom=maternal premature rupture of membranes
• i.pvl=infant periventricular leukomalacia	• m.race_n=maternal race
• i.sex=infant sex	• m.seizure=maternal seizure
• m.age=maternal age	• m.tobacco= maternal smoking
• m.asthma=maternal asthma	• p.age=paternal age
• m.dm=maternal diabetes mellitus	• p.mhdiag= paternal mental health diagnosis
• m.ethanol=maternal ethanol abuse	

eFigure 8. Portion of DAG for Infection and Autism with Birthweight related variables only



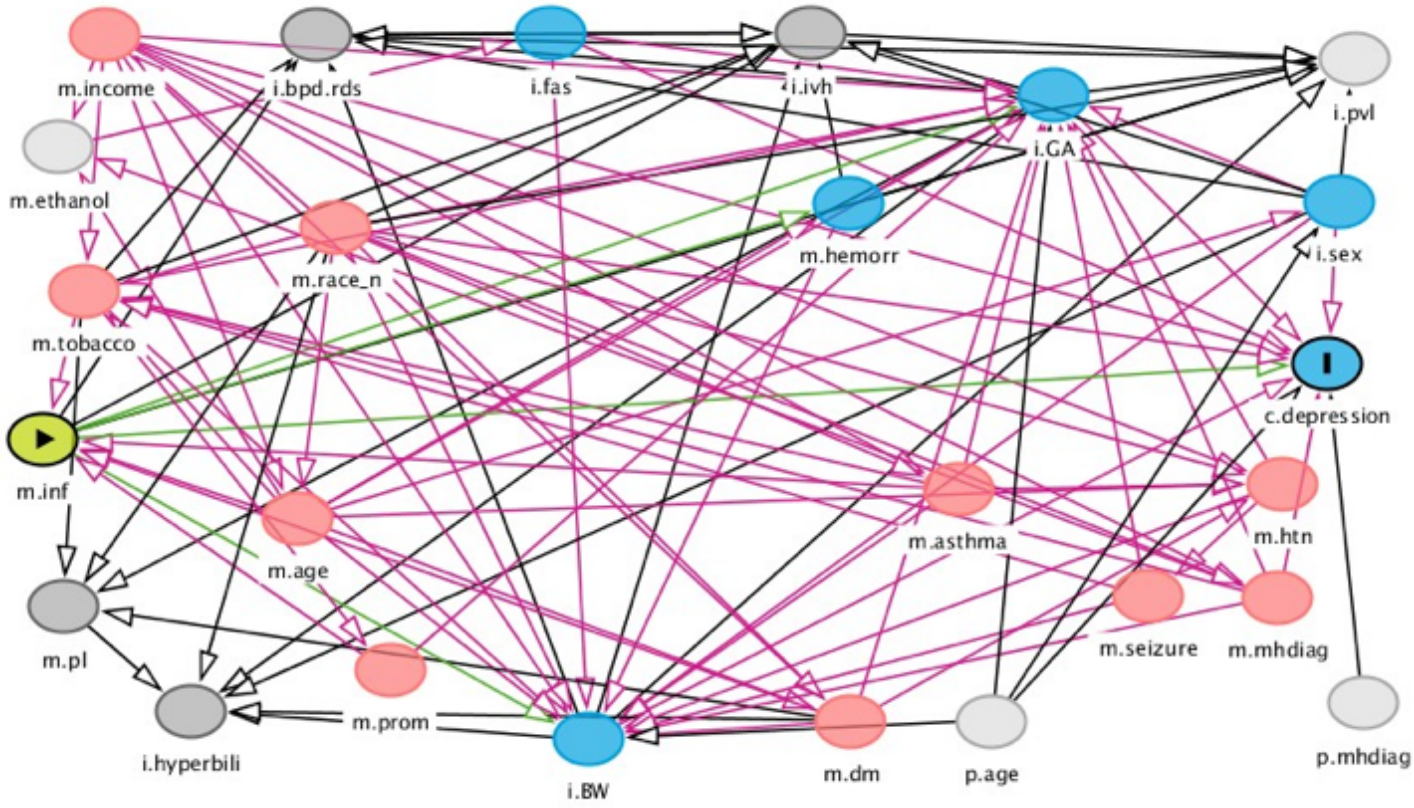
This schematic depicts a portion of the DAG from eFigure3 depicting only variables that are related to maternal infection, birthweight for gestational age and autism in the child. All other variables and relationships among other variables are removed for clarification purposes. See eFigure3 for variable key.

eFigure 9. Portion of DAG for Infection and Autism with Gestational Age related variables only



This schematic depicts a portion of the DAG from eFigure3 depicting only variables that are related to maternal infection, gestational age and autism in the child. All other variables and relationships among other variables are removed for clarification purposes. See eFigure3 for variable key.

eFigure 10. Directed Acyclic Graph for Infection and Depression



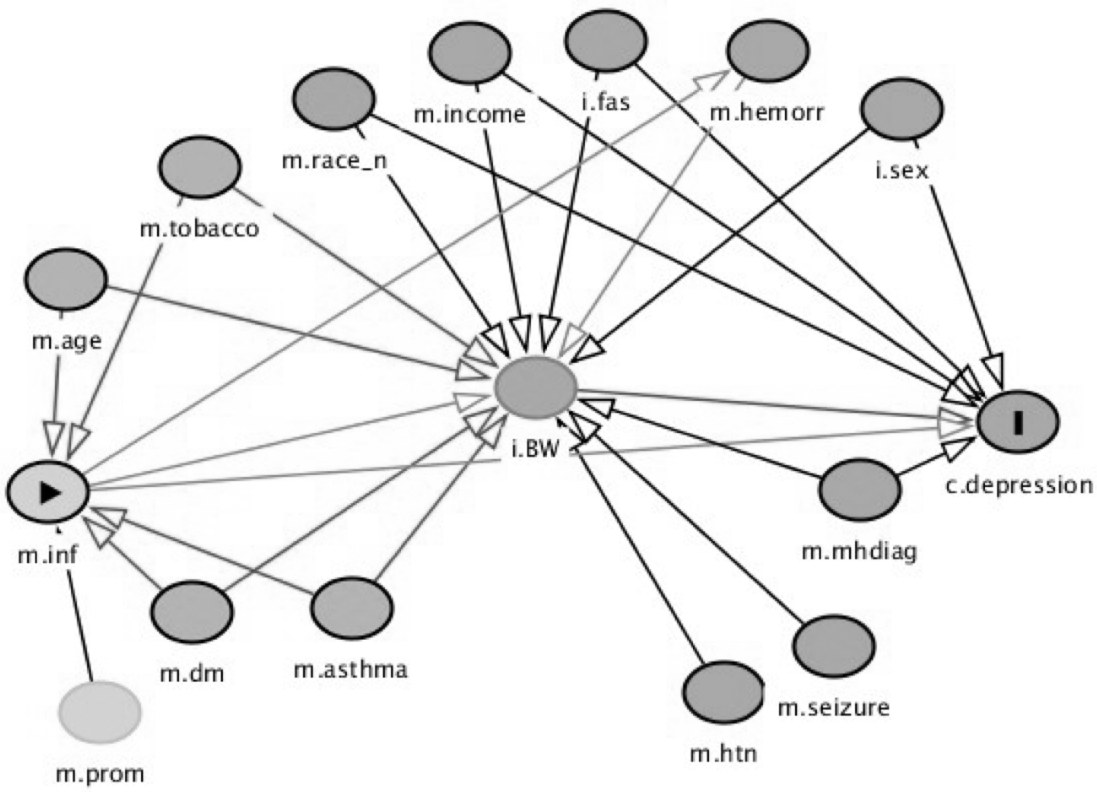
This schematic illustrates the causal relationship assumptions encoded in our DAG model for the risk for depression in the child or adult exposed to infection *in utero*. The green circle is the exposure (maternal infection). The blue circles are either ancestors of the outcome or the outcome itself (depression in the child) and the red circles are both ancestors of the exposure and the outcome. The gray circles are other variables. The green, pink and grey lines are causal, biasing or other pathways respectively.

A manipulatable version of this DAG is available at: dagitty.net/mlBjDQZ

Abbreviations used in the figure are listed below:

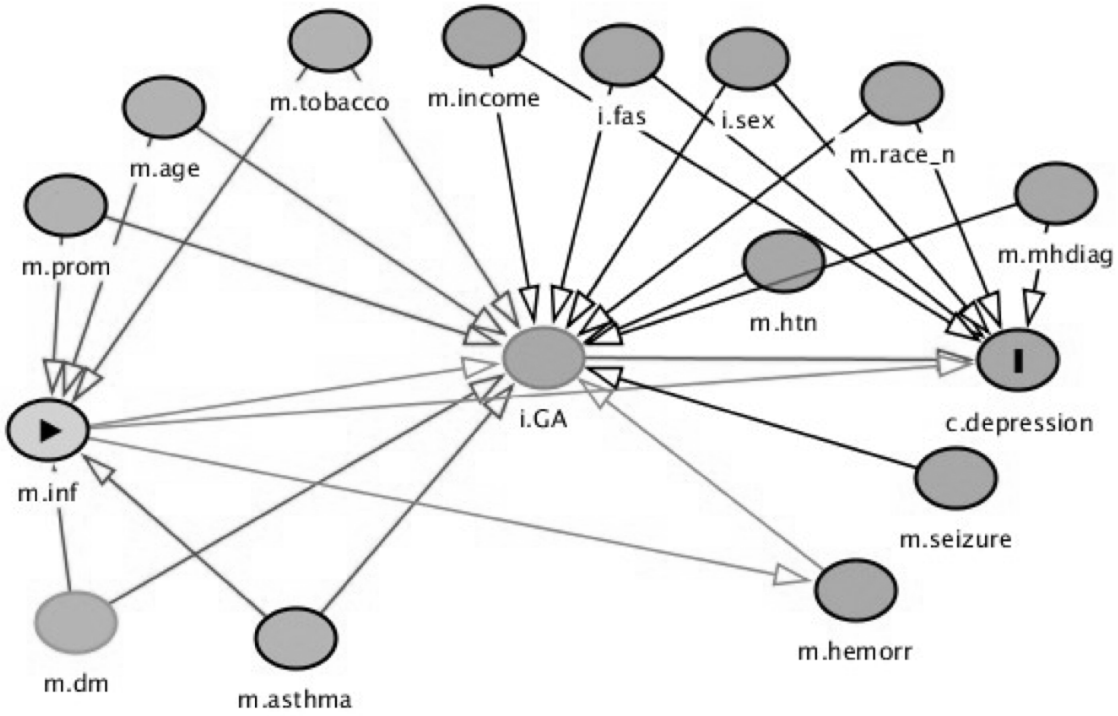
• c.depression=depression in the child or adult	• m.hemorrh=antepartum hemorrhage
• i.bpd.rds=infant bronchopulmonary dysplasia and respiratory distress syndrome	• m.income=maternal income
• i.BW=infant birthweight	• m.inf=maternal infection
• i.fas=fetal alcohol syndrome	• m.mhdiag=maternal mental illness diagnosis
• i.GA=gestational age at delivery	• m.mhtn=maternal hypertension
• i.hyperbili=infant hyperbilirubinemia	• m.pl=maternal prolonged labor
• i.ivh=infant intraventricular hemorrhage	• m.prom=maternal premature rupture of membranes
• i.pvl=infant periventricular leukomalacia	• m.race_n=maternal race
• i.sex=infant sex	• m.seizure=maternal seizure
• m.age=maternal age	• m.tobacco= maternal smoking
• m.asthma=maternal asthma	• p.age=paternal age
• m.dm=maternal diabetes mellitus	• p.mhdiag= paternal mental health diagnosis
• m.ethanol=maternal ethanol abuse	

eFigure 11. Portion of DAG for Infection and Depression with Birthweight related variables only



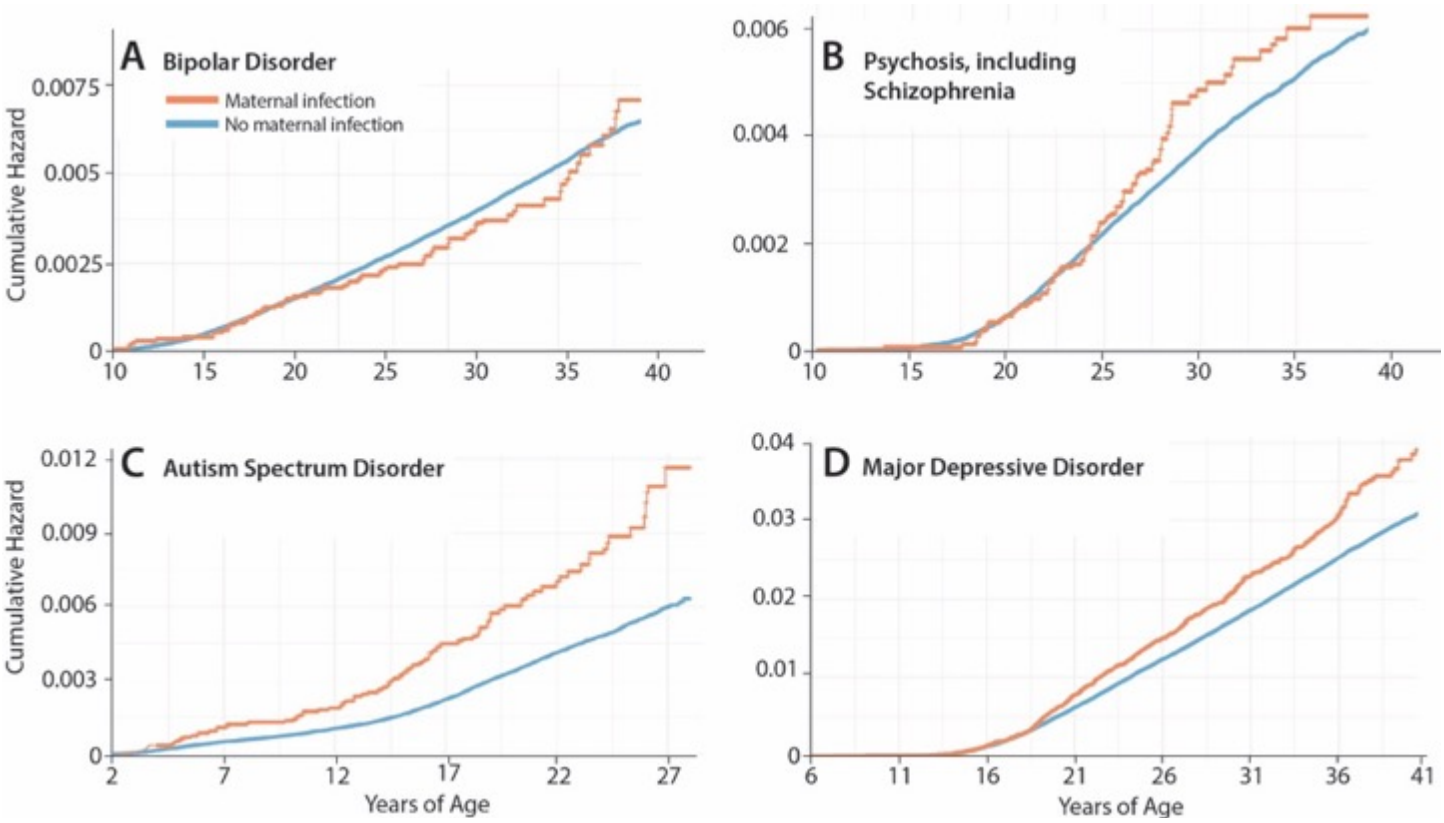
This schematic depicts a portion of the DAG from eFigure4 depicting only variables that are related to maternal infection, birthweight for gestational age and depression in the child. All other variables and relationships among other variables are removed for clarification purposes. See eFigure4 for variable key.

eFigure 12. Portion of DAG for Infection and Depression with Gestational Age related variables only



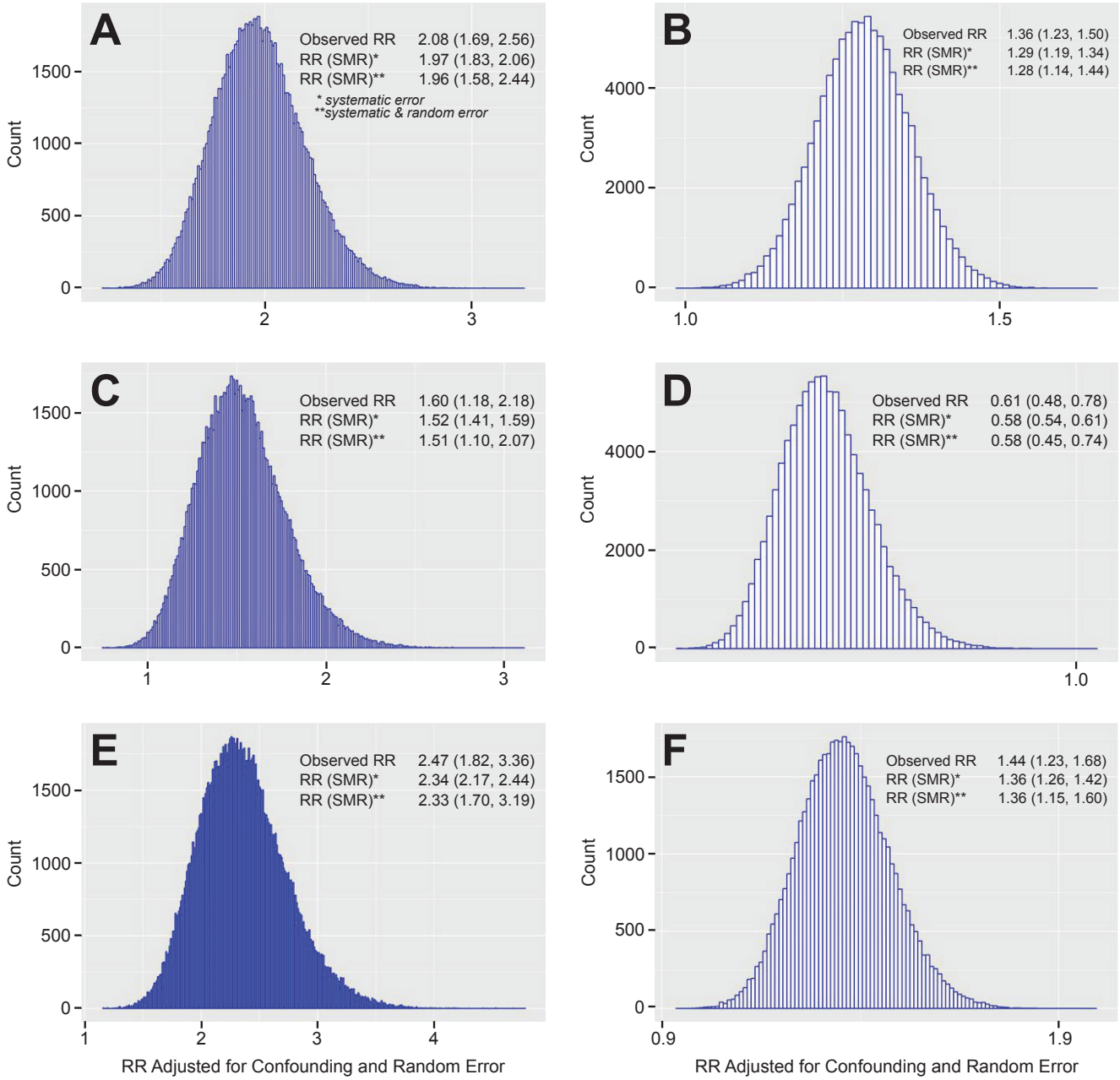
This schematic depicts a portion of the DAG from eFigure4 depicting only variables that are related to maternal infection, gestational age and depression in the child. All other variables and relationships among other variables are removed for clarification purposes. See eFigure4 for variable key.

eFigure 13. Adjusted Cumulative Hazard Curves for Maternal Infection and Development of Psychiatric Disorders in the Child



Adjusted cumulative hazard curves for the children exposed (orange line) or unexposed (blue line) to a maternal infection are shown to illustrate the relationship with (A) bipolar disorder, (B) psychosis, (C) autism spectrum disorder, and (D) major depressive disorder.

eFigure 14. Probabilistic Bias Analyses



These histograms depict Probabilistic Bias Analyses to determine the effect of an unmeasured confounder on the relative risk (RR) of hospitalization with autism among children exposed to any maternal infection (A), severe maternal infection (C) and UTI (E) during fetal life. Similarly, we examined risk of hospitalization with depression over the life course among children exposed to any maternal infection (B), severe maternal infection (D) and UTI (F) during fetal life. We used the episenr package in R with 100,000 iterations assuming trapezoidal distributions for the prevalence in the exposed (minimum = 15%, mode1 = 30%, mode2 = 35%, maximum = 50%), prevalence in the unexposed (minimum = 3%, mode1 = 10%, mode2 = 15% and maximum = 22%) and RR between the confounder and the outcome (minimum = 1.1, mode1 = 1.2, mode2 = 1.3 and maximum = 1.6)[6,7].

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