SUPPLEMENTAL MATERIAL

Supplemental Figure 1 Directed acyclic graph for the association between maternal HBV infection in early pregnancy and risk of CHD in offspring.

Supplemental Figure 2 Directed acyclic graph for the association between maternal coxsackievirus-B infection in early pregnancy and risk of CHD in offspring.

Supplemental Figure 3 Directed acyclic graph for the association between maternal HCMV infection in early pregnancy and risk of CHD in offspring.

Supplemental Figure 4 Directed acyclic graph for the association between maternal HSV infection in early pregnancy and risk of CHD in offspring.

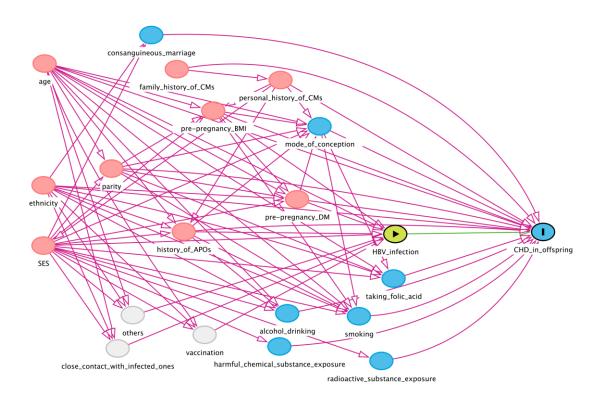
Supplemental Figure 5 Directed acyclic graph for the association between maternal rubella virus infection in early pregnancy and risk of CHD in offspring.

Supplemental Figure 6 The risks of CHD in offspring of pregnant women with viral infection in early pregnancy after excluding pregnant women whose children had non-cardiac defects.

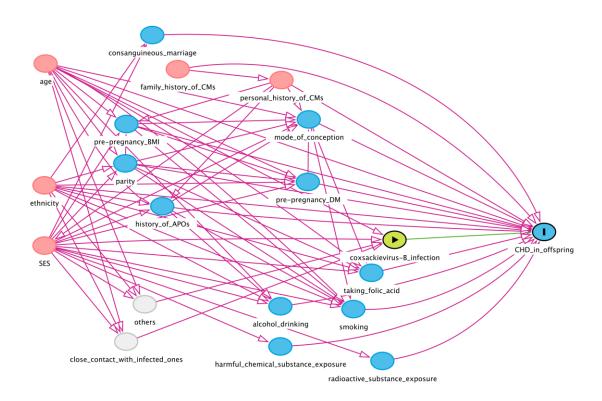
Supplemental Figure 7 The risks of CHD in offspring of pregnant women with viral infection in early pregnancy after excluding pregnant women whose children were diagnosed with more than one CHD phenotypes.

Supplemental Table 1 The distribution of maternal characteristics according to status of maternal HBV, coxsackievirus-B, and HCMV infection.

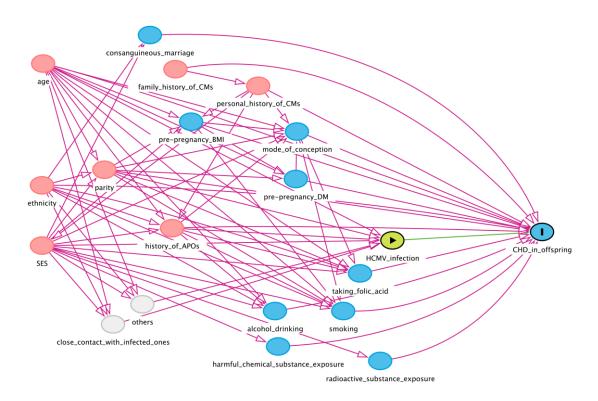
Supplemental Table 2 The distribution of baseline characteristics according to status of maternal HSV and rubella virus infection.



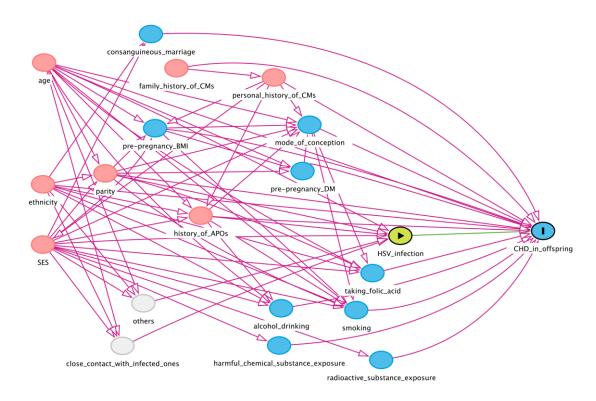
Supplemental Figure 1 Directed acyclic graph for the association between maternal HBV infection in early pregnancy and risk of CHD in offspring. Red arrows indicate biasing paths, green arrows indicate causal paths. APOs, adverse pregnancy outcomes; BMI, body mass index; CHD, congenital heart disease; CMs, congenital malformations; DM, diabetes mellitus; HBV, hepatitis B virus.



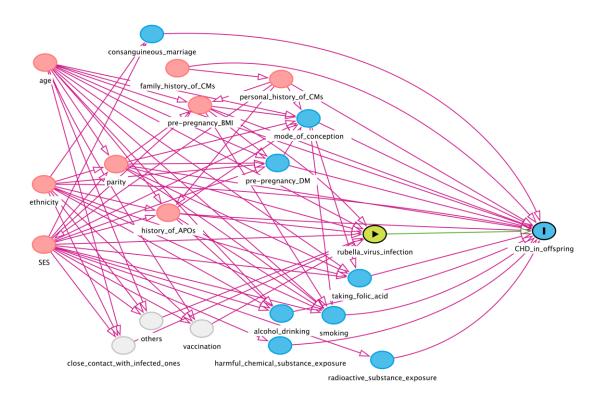
Supplemental Figure 2 Directed acyclic graph for the association between maternal coxsackievirus-B infection in early pregnancy and risk of CHD in offspring. Red arrows indicate biasing paths, green arrows indicate causal paths. APOs, adverse pregnancy outcomes; BMI, body mass index; CHD, congenital heart disease; CMs, congenital malformations; DM, diabetes mellitus.



Supplemental Figure 3 Directed acyclic graph for the association between maternal HCMV infection in early pregnancy and risk of CHD in offspring. Red arrows indicate biasing paths, green arrows indicate causal paths. APOs, adverse pregnancy outcomes; BMI, body mass index; CHD, congenital heart disease; CMs, congenital malformations; DM, diabetes mellitus; HCMV, human cytomegalovirus.



Supplemental Figure 4 Directed acyclic graph for the association between maternal HSV infection in early pregnancy and risk of CHD in offspring. Red arrows indicate biasing paths, green arrows indicate causal paths. APOs, adverse pregnancy outcomes; BMI, body mass index; CHD, congenital heart disease; CMs, congenital malformations; DM, diabetes mellitus; HSV, herpes simplex virus.



Supplemental Figure 5 Directed acyclic graph for the association between maternal rubella virus infection in early pregnancy and risk of CHD in offspring. Red arrows indicate biasing paths, green arrows indicate causal paths. APOs, adverse pregnancy outcomes; BMI, body mass index; CHD, congenital heart disease; CMs, congenital malformations; DM, diabetes mellitus.

a. Hepatitis B virus Type of CHD Negative (n=39 955) Positive (n=2 377) Model 1 Model 2 Model 3 Total CHD 514 (12.86‰) 50 (21.03‰) 1.64 (1.23-2.18) 2.22 (1.66-2.96) 2 44 (1 83-3 26) ASD 166 (4.15‰) 4 (1.68‰) 0.41 (0.15-1.09) 0.68 (0.25-1.84) 0.74 (0.28-2.01) VSD 214 (5.36‰) 32 (13.46‰) 2.51 (1.74-3.64) 4.43 (3.04-6.44) 5.11 (3.50-7.47) AVSD 52 (1.30‰) 0 (0.00%) PDA 78 (1.95%) 6 (2.52%) 1.29 (0.56-2.96) 1.29 (0.55-3.03) 1.78 (0.76-4.12) TOF 34 (0.85‰) 2 (0.84‰) 0.99 (0.24-4.11) 1.86 (0.45-7.72) 2.16 (0.50-9.34) 42 (1.05‰) 2 (0.84‰) 0.74 (0.17-3.27) PS 0.80 (0.19-3.30) 0.74 (0.17-3.28) TGA 28 (0.70‰) 0 (0.00‰) b. Coxsackievirus-B Type of CHD Negative (n=40 346) Positive (n=1 986) Model 3 Model 1 Model 2 Total CHD 516 (12.79‰) 48 (24.17%) 1.89 (1.41-2.53) 2.26 (1.67-3.07) 1.54 (1.05-2.27) ASD 161 (3.99‰) 9 (4.53‰) 1.14 (0.58-2.22) 1.15 (0.58-2.25) 0.70 (0.31-1.61) 3.19 (1.85-5.51) VSD 219 (5.43‰) 27 (13.60%) 2.50 (1.68-3.73) 3.93 (2.60-5.94) AVSD 46 (1.14‰) 6 (3.02‰) 2.65 (1.13-6.20) 3.00 (1.29-6.97) 2.24 (0.82-6.10) 80 (1.98%) 0.73 (0.27-1.97) 0.72 (0.26-1.96) PDA 4 (2.01%) 1.02 (0.37-2.77) TOF 36 (0.89‰) 0 (0.00%) PS 40 (0.99‰) 4 (2.01‰) 2.03 (0.73-5.67) 1.34 (0.47-3.76) 1.12 (0.31-3.99) 24 (0.59‰) 4 (2.01‰) 3.39 (1.18-9.75) 1.90 (0.68-5.26) 2.07 (0.74-5.79) ш-ш 012 4 6 8 10 Risk ratio 012 4 6 8 10 012 4 6 8 10 c. Human cytomegalovirus Type of CHD Negative (n=40 004) Positive (n=2 328) Model 1 Model 2 Model 3 Total CHD 482 (12.05‰) 82 (35.22%) 2.92 (2.32-3.68) 3.23 (2.52-4.13) 3.02 (2.24-4.07) 2.77 (1.72-4.47) 148 (3.70‰) 22 (9.45‰) 2.55 (1.64-3.99) 3.03 (1.74-5.26) 2.62 (1.78-3.87) VSD 2.18 (1.33-3.57) 216 (5.40%) 30 (12.89‰) 2.39 (1.63-3.49) 2.02 (0.77-5.28) AVSD 46 (1.15%) 6 (2.58%) 2.24 (0.96-5.24) 1.97 (0.82-4.76) PDA 50 (1.25‰) 34 (14.60%) 11.69 (7.57-18.03) 11.12 (6.46-19.14) 13.35 (8.08-22.08) TOF 30 (0.75‰) 6 (2.58‰) 3.44 (1.43-8.25) 7.57 (3.02-18.99) 8.36 (3.34-20.9) PS 38 (0.95‰) 6 (2.58‰) 2.71 (1.15-6.41) 2.27 (0.89-5.81) 2.3 (0.76-6.94) TGA 28 (0.70%) 0 (0.00%) d. Herpes simplex virus Type of CHD Negative (n=41 768) Positive (n=564) Model 1 Model 2 Model 3 1.07 (0.53-2.13) 0.85 (0.42-1.70) 0.65 (0.33-1.28) Total CHD 556 (13.31%) 8 (14.18‰) 2.03 (0.76-5.46) 1.87 (0.65-5.35) ASD 166 (3.97‰) 4 (7.09‰) 1.78 (0.66-4.79) 0.77 (0.31-1.90) 0.59 (0.26-1.35) VSD 241 (5.77%) 5 (8.87%) 1.54 (0.64-3.71) AVSD 50 (1.20%) 2 (3.55%) 2.96 (0.72-12.14) 2.87 (0.73-11.20) 3.79 (0.95-15.13) PDA 82 (1.96‰) 2 (3.55‰) 1.81 (0.45-7.33) 2.59 (0.63-10.76) 2.01 (0.46-8.73) TOF 36 (0.86‰) 0 (0.00‰) 44 (1.05‰) 0 (0.00%) PS TGA 28 (0.67%) 0 (0.00%) 2 4 6 8 10 Risk ratio 012 4 6 8 10 Risk ratio 012 4 6 8 10 Risk ratio e. Rubella virus Type of CHD Negative (n=41 121) Positive (n=1 211) Model 1 Model 2 Model 3 Total CHD 520 (12.65‰) 44 (36.33%) 2.87 (2.12-3.89) 2.70 (2.02-3.62) 2.88 (2.16-3.85) 153 (3.72‰) 17 (14.04‰) 3.77 (2.29-6.21) 3.38 (2.14-5.33) 3.57 (2.26-5.65) ASD VSD 226 (5.5‰) 20 (16.52‰) 3.00 (1.91-4.73) 2.29 (1.48-3.55) 2.52 (1.64-3.87) 42 (1.02‰) 10 (8.26‰) 8.08 (4.07-16.07) 2.93 (1.60-5.35) 3.67 (1.92-7.01) AVSD PDA 82 (1.99‰) 2 (1.65%) 0.83 (0.20-3.36) 0.97 (0.24-3.94) 1.12 (0.27-4.60) TOF 34 (0.83‰) 2 (1.65‰) 2.00 (0.48-8.30) 2.55 (0.69-9.47) 2.86 (0.76-10.8) 1.62 (0.39-6.67) 1.72 (0.39-7.55) 1.81 (0.41-8.01) 42 (1.02‰) 2 (1.65‰) 24 (0.58‰) 5.66 (1.97-16.29) 3.75 (1.50-9.41) 3.28 (1.29-8.35) TGA 4 (3.3%) 012 4 6 8 10 Risk ratio

Supplemental Figure 6 The risks of CHD in offspring of pregnant women with viral infection in early pregnancy after excluding pregnant women whose children had non-cardiac defects. For the five viruses analyzed, model 1 was a crude model without any variable adjusted. For HBV (a), model 2 adjusted for educational level, age, ethnicity, history of adverse pregnancy

outcomes, pre-pregnancy BMI, and pre-pregnancy diabetes mellitus, while model 3 adjusted for the variables in model 2 plus other virus infection including coxsackievirus-B, HCMV, HSV, and rubella virus. For coxsackievirus-B (b), model 2 adjusted for educational level, age, and ethnicity, while model 3 adjusted for the variables in model 2 plus other virus infection including HBV, HCMV, HSV, and rubella virus. For HCMV (c), model 2 adjusted for educational level, age, ethnicity, parity, and history of adverse pregnancy outcomes, while model 3 adjusted for the variables in model 2 plus other virus infection including HBV, coxsackievirus-B, HSV, and rubella virus. For HSV (d), model 2 adjusted for educational level, age, ethnicity, parity, and history of adverse pregnancy outcomes, while model 3 adjusted for the variables in model 2 plus other virus infection including HBV, coxsackievirus-B, HCMV, and rubella virus. For rubella virus (e), model 2 adjusted for educational level, age, ethnicity, parity, history of adverse pregnancy outcomes, and pre-pregnancy BMI, while model 3 adjusted for the variables in model 2 plus other virus infection including HBV, coxsackievirus-B, HCMV, and HSV. BMI, body mass index; CHD, congenital heart disease; HBV, hepatitis B virus; HCMV, human cytomegalovirus; HSV, herpes simplex virus.

a. Hepatitis B virus Type of CHD Negative (n=41 462) Positive (n=2 477) Model 1 Model 2 Model 3 Total CHD 408 (9.84‰) 47 (18.97‰) 1.93 (1.43-2.60) 2.20 (1.65-2.94) 2.64 (1.96-3.56) ASD 60 (1.45‰) 1 (0.40‰) 0.28 (0.04-2.01) 0.68 (0.25-1.85) 0.34 (0.05-2.43) VSD 161 (3.88‰) 32 (12.92‰) 3.33 (2.28-4.85) 4.50 (3.11-6.52) 5.44 (3.69-8.02) 0 (0.00%) AVSD 0 (0.00%) PDA 53 (1.28%) 3 (1.21%) 0.95 (0.30-3.03) 1.29 (0.55-3.00) 1.14 (0.37-3.52) TOF 25 (0.60‰) 2 (0.81‰) 1.34 (0.32-5.65) 1.91 (0.46-7.92) 3.32 (0.82-13.38) 0.74 (0.17-3.25) 29 (0.70‰) 2 (0.81‰) 1.15 (0.28-4.84) 1.18 (0.28-4.95) TGA 22 (0.53‰) 0 (0.00‰) b. Coxsackievirus-B Type of CHD Negative (n=41 863) Model 3 Positive (n=2 076) Model 2 Model 1 Total CHD 415 (9.91‰) 40 (19.27‰) 1.94 (1.41-2.68) 2.44 (1.75-3.40) 1.85 (1.23-2.80) ASD 60 (1.43‰) 1 (0.48‰) 0.34 (0.05-2.42) 0.43 (0.06-3.08) 0.47 (0.06-3.82) VSD 172 (4.11‰) 21 (10.12‰) 3.48 (1.94-6.26) 2.46 (1.57-3.86) 3.97 (2.50-6.31) AVSD 0 (0.00‰) 0 (0.00‰) 52 (1.24%) 4 (1.93%) 0.36 (0.12-1.07) PDA 1.55 (0.56-4.28) 1.04 (0.38-2.86) TOF 27 (0.64‰) 0 (0.00%) PS 27 (0.64‰) 4 (1.93%) 2.99 (1.05-8.53) 1.94 (0.67-5.62) 1.84 (0.47-7.19) 20 (0.48‰) 2 (0.96‰) 1.15 (0.28-4.77) 1.98 (0.48-8.27) 2.02 (0.47-8.62) 012 4 6 8 10 012 4 6 8 10 012 4 6 8 10 Risk ratio c. Human cytomegalovirus Type of CHD Negative (n=41 487) Positive (n=2 452) Model 1 Model 2 Model 3 Total CHD 393 (9.47‰) 62 (25.29‰) 2.67 (2.05-3.48) 3.03 (2.29-4.00) 2.69 (1.93-3.76) ASD 59 (1.42‰) 0 (0.00%) VSD 169 (4.07‰) 24 (9.79‰) 2.40 (1.57-3.68) 2.72 (1.75-4.22) 2.17 (1.26-3.72) AVSD 0 (0.00%) 0 (0.00%) PDA 32 (0.77%) 24 (9.79%) 12.69 (7.49-21.51) 10.92 (5.77-20.66) 12.65 (6.99-22.88) TOF 23 (0.55‰) 4 (1.63‰) 2.94 (1.02-8.50) 5.82 (2.05-16.58) 6.61 (2.28-19.13) 27 (0.65‰) 4 (1.63‰) 2.23 (0.68-7.33) 1.96 (0.46-8.25) 2.51 (0.88-7.16) TGA 22 (0.53‰) 0 (0.00‰) 012 4 6 8 10 Risk ratio d. Herpes simplex virus Type of CHD Negative (n=43 357) Positive (n=582) Model 1 Model 2 Model 3 Total CHD 451 (10.40‰) 4 (6.87‰) 0.66 (0.25-1.76) 0.47 (0.18-1.24) 0.40 (0.16-1.02) 61 (1.41‰) 0 (0.00‰) VSD 190 (4.38‰) 3 (5.15‰) 0.48 (0.15-1.51) 0.39 (0.14-1.07) 1.18 (0.38-3.67) AVSD 0 (0.00%) 0 (0.00%) PDA 56 (1.29%) 0 (0.00%) TOF 27 (0.62‰) 0 (0.00‰) PS 31 (0.71‰) 0 (0.00‰) TGA 22 (0.51‰) 0 (0.00%) e. Rubella virus Type of CHD Negative (n=42 660) Positive (n=1 279) Model 1 Model 2 Model 3 Total CHD 422 (9.89‰) 33 (25.80%) 2.61 (1.84-3.70) 2.47 (1.76-3.48) 2.65 (1.89-3.71) ASD 55 (1.29‰) 6 (4.69‰) 3.64 (1.57-8.44) 4.55 (2.07-10.01) 4.51 (2.06-9.87) VSD 183 (4.29‰) 12 (9.38‰) 2.19 (1.22-3.91) 1.86 (1.06-3.29) AVSD 0 (0.00%) 0 (0.00%) 1.47 (0.36-6.02) PDA 54 (1.27%) 2 (1.56%) 1.24 (0.30-5.06) 1.89 (0.46-7.75) TOF 25 (0.59‰) 2 (1.56‰) 2.67 (0.63-11.25) 3.25 (0.84-12.51) 3.61 (0.92-14.20) PS 30 (0.70‰) 1 (0.78‰) 1.11 (0.15-8.15) 1.26 (0.16-9.95) 1.28 (0.16-10.46) 18 (0.42%) 4 (3.13%) 7.41 (2.51-21.87) 4.65 (1.73-12.5) 4.07 (1.51-10.96) 012 4 6 8 10 Risk ratio 012 4 6 8 10 Risk ratio 012 4 6 8 10 Risk ratio

Supplemental Figure 7 The risks of CHD in offspring of pregnant women with viral infection in early pregnancy after excluding pregnant women whose children were diagnosed with more than one CHD phenotypes. For the five viruses analyzed, model 1 was a crude model without any variable adjusted. For HBV (a), model 2 adjusted for educational level, age, ethnicity,

history of adverse pregnancy outcomes, pre-pregnancy BMI, and pre-pregnancy diabetes mellitus, while model 3 adjusted for the variables in model 2 plus other virus infection including coxsackievirus-B, HCMV, HSV, and rubella virus. For coxsackievirus-B (b), model 2 adjusted for educational level, age, and ethnicity, while model 3 adjusted for the variables in model 2 plus other virus infection including HBV, HCMV, HSV, and rubella virus. For HCMV (c), model 2 adjusted for educational level, age, ethnicity, parity and history of adverse pregnancy outcomes, while model 3 adjusted for the variables in model 2 plus other virus infection including HBV, coxsackievirus-B, HSV, and rubella virus. For HSV (d), model 2 adjusted for educational level, age, ethnicity, parity and history of adverse pregnancy outcomes, while model 3 adjusted for the variables in model 2 plus other virus infection including HBV, coxsackievirus-B, HCMV, and rubella virus. For rubella virus (e), model 2 adjusted for educational level, age, ethnicity, parity, history of adverse pregnancy outcomes, and pre-pregnancy BMI, while model 3 adjusted for the variables in model 2 plus other virus infection including HBV, coxsackievirus-B, HCMV, and HSV. BMI, body mass index; CHD, congenital heart disease; HBV, hepatitis B virus; HCMV, human cytomegalovirus; HSV, herpes simplex virus.

Supplemental Table 1 The distribution of maternal characteristics according to status of maternal HBV, coxsackievirus-B, and HCMV infection.

Baseline characteristics	HBV			Coxsackievirus-B			HCMV		
Daseille Characteristics	Negative (n, %)	Positive (n, %)	p-value	Negative (n, %)	Positive (n, %)	p-value	Negative (n, %)	Positive (n, %)	p-value
Sociodemographic									
characteristics									
Age (years)			< 0.001			< 0.001			< 0.001
<25	4,666 (11.2%)	314 (12.7%)		4,668 (11.1%)	312 (15.0%)		4,658 (11.2%)	322 (13.0%)	
25-29.9	18,442 (44.4%)	1,282 (51.7%)		18,530 (44.2%)	1,194 (57.3%)		18,292 (44.0%)	1,432 (57.9%)	
30-34.9	13,592 (32.7%)	600 (24.2%)		13,700 (32.6%)	492 (23.6%)		13,674 (32.9%)	518 (21.0%)	
≥35	4,868 (11.7%)	284 (11.5%)		5,066 (12.1%)	86 (4.1%)		4,952 (11.9%)	200 (8.1%)	
Ethnicity			< 0.001			< 0.001			< 0.001
Han	39,350 (94.7%)	2,468 (99.5%)		39,700 (94.8%)	2,048 (98.3%)		39,428 (94.8%)	2,390 (96.7%)	
Minority	2,281 (5.3%)	12 (0.5%)		2,194 (5.2%)	36 (1.7%)		2,148 (5.2%)	82 (3.3%)	
Educational level			< 0.001			< 0.001			< 0.001
Junior high school or	6,783 (16.3%)	116 (4.7%)		6,814 (16.2%)	86 (4.1%)		6,648 (16.0%)	252 (10.2%)	
below	0,703 (10.376)	110 (4.7 %)		0,014 (10.278)	00 (4.1 /0)		0,040 (10.078)	232 (10.276)	
Senior middle school	22,276 (53.6%)	888 (35.8%)		21,826 (52.0%)	1,338 (64.2%)		21,704 (52.2%)	1,460 (59.1%)	
College	9,426 (22.7%)	1,394 (56.2%)		10,318 (24.6%)	502 (24.1%)		10,206 (24.5%)	614 (24.8%)	
Master or above	3,082 (7.4%)	82 (3.3%)		3,006 (7.2%)	158 (7.6%)		3,018 (7.3%)	146 (5.9%)	
Obstetric, clinical, and									
genetic characteristics									
Mode of conception			< 0.001			< 0.001			< 0.001
Spontaneous conception	32,638 (78.5%)	1,466 (59.1%)		32,072 (76.4%)	2,032 (97.5%)		32,012 (77.0%)	2,092 (84.6%)	
Assisted conception	8,930 (21.5%)	1,014 (40.9%)		9,892 (23.6%)	52 (2.5%)		9,564 (23.0%)	380 (15.4%)	
Consanguineous	170 (0.4%)	14 (0.6%)	0.243	152 (0.4%)	32 (1.5%)	< 0.001	158 (0.4%)	26 (1.1%)	< 0.001
marriage (yes)	170 (0.470)	14 (0.0 /0)	0.243	132 (0.4 /0)	32 (1.3 <i>/</i> 0)	< 0.001	100 (0.470)	20 (1.170)	< U.UU I

Parity			< 0.001			< 0.001			< 0.001
Nulliparous	17,954 (43.2%)	1,608 (64.8%)		19,356 (46.1%)	206 (9.9%)		18,938 (45.6%)	624 (25.2%)	
Multiparous	23,614 (56.8%)	872 (35.2%)		22,608 (53.9%)	1,878 (90.1%)		22,638 (54.4%)	1,848 (74.8%)	
History of adverse									
pregnancy outcomes	16,708 (40.2%)	1,000 (42.3%)	0.034	17,046 (40.6%)	712 (34.2%)	< 0.001	16,832 (40.5%)	926 (37.5%)	0.003
(yes)									
Family history of									
congenital malformations	62 (0.1%)	0 (0.0%)	0.054	50 (0.1%)	12 (0.6%)	< 0.001	42 (0.1%)	20 (0.8%)	< 0.001
(yes)									
Health-related factors									
Pre-pregnancy BMI			0.004			0.004			0.004
(kg/m²)			< 0.001			< 0.001			< 0.001
<18.5	7154 (17.2%)	378 (15.2%)		6,998 (16.7%)	534 (25.6%)		7,070 (17.0%)	462 (18.7%)	
18.5-23.9	27,336 (65.8%)	1,988 (80.2%)		28,018 (66.8%)	1,306 (62.7%)		27,626 (66.4%)	1,698 (68.7%)	
24-27.9	5,990 (14.4%)	72 (2.9%)		5,902 (14.1%)	160 (7.7%)		5,818 (14.0%)	244 (9.9%)	
≥28	1,088 (2.6%)	42 (1.7%)		1,046 (2.5%)	84 (4.0%)		1,062 (2.6%)	68 (2.8%)	
Pre-pregnancy diabetes	000 (0.70()	0.4 (4.40()	0.450	000 (0.00()	0 (0 00()	0.004	040 (0.00()	4.4 (0.00()	0.000
mellitus (yes)	298 (0.7%)	34 (1.4%)	0.152	332 (0.8%)	0 (0.0%)	< 0.001	318 (0.8%)	14 (0.6%)	0.268
Personal history of									
congenital malformations	394 (0.9%)	72 (2.9%)	< 0.001	466 (1.1%)	0 (0.0%)	< 0.001	426 (1.0%)	40 (1.6%)	0.005
(yes)									
Taking folic acid in 3									
months before pregnancy	20.754 (05.00()	0.040 (00.50()	0.004	40.000 (05.50()	4 004 (05 00/)	0.400	20.740 (05.00()	0.000 (04.00()	0.004
or in early pregnancy	39,754 (95.6%)	2,318 (93.5%)	< 0.001	40 088 (95.5%)	1,984 (95.2%)	0.480	39,740 (95.6%)	2,332 (94.3%)	0.004
(yes)									
Smoking in early	558 (1.3%)	46 (1.9%)	0.033	566 (1.3%)	38 (1.8%)	0.069	562 (1.4%)	42 (1.7%)	0.149

pregnancy (yes)									
Drinking in early	556 (1.3%)	9 (0 30/)	< 0.001	560 (1.3%)	4 (0.2%)	< 0.001	546 (1.3%)	18 (0.7%)	0.012
pregnancy (yes)	556 (1.5%)	8 (0.3%)	< 0.001	300 (1.3%)	4 (0.2%)	< 0.001	546 (1.5%)	10 (0.7%)	0.012
Environmental pollution									
around the dwelling place									
in three months before	880 (2.1%)	40 (1.6%)	0.088	892 (2.1%)	28 (1.3%)	0.015	884 (2.1%)	36 (1.5%)	0.024
pregnancy or in early									
pregnancy (yes)									
Exposure to radioactive									
hazardous while at work									
in three months before	1,326 (3.2%)	106 (4.3%)	0.003	1,328 (3.2%)	104 (5.0%)	< 0.001	1,372 (3.3%)	60 (2.4%)	0.017
pregnancy or in early									
pregnancy (yes)									

BMI, body mass index; HBV, hepatitis B virus; HCMV, human cytomegalovirus.

Supplemental Table 2 The distribution of baseline characteristics according to status of maternal HSV and rubella virus infection.

Baseline characteristics		HSV	Rubella virus				
baseline characteristics	Negative (n, %)	Positive (n, %)	p-value	Negative (n, %)	Positive (n, %)	p-value	
Sociodemographic							
characteristics							
Age (years)			< 0.001			< 0.001	
<25	4,824 (11.1%)	156 (26.6%)		4,796 (11.2%)	184 (14.3%)		
25-29.9	19,522 (44.9%)	202 (34.5%)		19,206 (44.9%)	518 (40.2%)		
30-34.9	14,108 (32.5%)	84 (14.3%)		13,784 (32.2%)	408 (31.6%)		
≥35	5,008 (11.5%)	144 (24.6%)		4,972 (11.6%)	180 (14.0%)		
Ethnicity			< 0.001			0.388	
Han	41,232 (94.9%)	586 (100%)		40,600 (95.0%)	1,218 (94.4%)		
Minority	2,230 (5.1%)	0 (0.0%)		2,158 (5.0%)	72 (5.6%)		
Educational level			< 0.001			0.677	
Junior high school or below	6,718 (15.5%)	182 (31.1%)		6,684 (15.6%)	216 (16.7%)		
Senior middle school	22,932 (52.8%)	232 (39.6%)		22,502 (52.6%)	662 (51.3%)		
College	10,664 (24.5%)	156 (26.6%)		10,504 (24.6%)	316 (24.5%)		
Master or above	3,148 (7.2%)	16 (2.7%)		3,068 (7.2%)	96 (7.4%)		
Obstetric, clinical, and genetic							
characteristics							
Mode of conception			0.005			0.025	
Spontaneous conception	33,622 (77.4%)	482 (82.3%)		33,072 (77.3%)	1,032 (80.0%)		
Assisted conception	9,840 (22.6%)	104 (17.7%)		9,686 (22.7%)	258 (20.0%)		
Consanguineous marriage (yes)	180 (0.4%)	4 (0.7%)	0.317	178 (0.4%)	6 (0.5%)	0.789	
Parity			< 0.001			< 0.001	
Nulliparous	19,498 (44.9%)	64 (10.9 %)		19,234 (45.0%)	328 (25.4%)		

Multiparous	23,964 (55.1%)	522 (89.1%)		23,524 (55.0%)	962 (74.6%)	
History of adverse pregnancy outcomes (yes)	17,506 (40.3%)	252 (43.0%)	0.182	17,188 (40.2%)	570 (44.2%)	0.004
Family history of congenital malformations (yes)	62 (0.1%)	0 (0.0%)	0.360	62 (0.1%)	0 (0.0%)	0.171
Health-related factors						
Pre-pregnancy BMI (kg/m²)			< 0.001			< 0.001
<18.5	7,450 (17.1%)	82 (14.0%)		7,290 (17.0%)	242 (18.8%)	
18.5-23.9	28,846 (66.4%)	478 (81.6%)		28,506 (66.7%)	818 (63.4%)	
24-27.9	6,040 (13.9%)	22 (3.8%)		5,888 (13.8%)	174 (13.5%)	
≥28	1,126 (2.6%)	4 (0.7%)		1,074 (2.5%)	56 (4.3%)	
Pre-pregnancy diabetes mellitus (yes)	332 (0.8%)	0 (0.0%)	0.034	322 (0.8%)	10 (0.8%)	0.928
Personal history of congenital malformations (yes)	466 (1.1%)	0 (0.0%)	0.012	456 (1.1%)	10 (0.8%)	0.314
Taking folic acid in 3 months before						
pregnancy or in early pregnancy (yes)	41,492 (95.5%)	580 (99.0%)	< 0.001	1,926 (4.5%)	50 (3.9%)	0.283
Smoking in early pregnancy (yes)	600 (1.4%)	4 (0.7%)	0.149	590 (1.4%)	14 (1.1%)	0.370
Drinking in early pregnancy (yes)	560 (1.3%)	4 (0.7%)	0.195	538 (1.3%)	26 (2.0%)	0.017
Environmental pollution around the						
dwelling place in three months before pregnancy or in early	908 (2.1%)	12 (2.0%)	0.945	894 (2.1%)	26 (2.0%)	0.852
pregnancy (yes)						
Exposure to radioactive hazardous while at work in three months before	1,406 (3.2%)	26 (4.4%)	0.103	1,398 (3.3%)	34 (2.6%)	0.206

pregnancy or in early pregnancy (yes)

BMI, body mass index; HSV, herpes simplex virus.