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A Propensity Score Matching Analysis of Selected Maternal Sexually Transmitted
Diseases and Preterm Birth in the United States, 2016 to 2018

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2018

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Abstract

A Propensity Score Matching Analysis of Selected Maternal Sexually Transmitted Diseases and Preterm Birth in the United States, 2016 to 2018

By Yichun Cao

Background: Preterm birth, defined as gestational age less than 37 complete weeks, is an important public health outcome. This thesis consists of fifteen substudies: each substudy examined the association between preterm birth and each of five maternal sexually transmitted diseases (STDs) acquired prior to pregnancy from 2016 to 2018. STDs examined were hepatitis B and C, gonorrhea, syphilis and chlamydia.

Methods: Data were taken from National Center of Health Statistics (NCHS) natality database. The participants of this study consisted of married and unmarried women who had a live birth from 2016 to 2018. The relative risk (RR) of preterm birth was calculated for each of the five STDs. To control for confounding, a propensity score was estimated for each STD using known confounders available in the same database, and women with similar propensity scores were matched. The analysis was conducted separately for each of the three years -- 2016, 2017 and 2018 -- to check the reliability of the RR estimate.

Results: In 2018, 11.24% of the births in the original (unmatched) population were preterm. Hepatitis C had the highest risk ratio associated with preterm birth (aRR: 1.39, 95% CI: 1.33 to 1.46), followed by syphilis (aRR: 1.34, 95% CI: 1.22 to 1.49), gonorrhea (aRR: 1.23, 95% CI: 1.16 to 1.31), chlamydia (aRR: 1.18, 95% CI: 1.15 to 1.21) and hepatitis B (aRR: 1.10, 95% CI: 1.01 to 1.20). The findings in 2016 and 2017 were similar.

Conclusions: After adjusting for confounders collected in the NCHS database, women with hepatitis B, hepatitis C, gonorrhea, syphilis or chlamydia had a higher risk of preterm birth every year from 2016 to 2018. In all three years, infection with hepatitis C had the highest risk ratio. Tailoring public health prevention strategies to individuals with STDs is needed to mitigate the risk of preterm birth.

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Introduction:

Preterm birth, defined as gestational age less than 37 full weeks, is viewed as an unpredictable and inevitable status in life. Medical efforts have concentrated on ameliorating the consequences of prematurity rather than preventing its occurrence¹. The preterm birth rate has been consistently rising in the world. Among 130 million infants born each year worldwide, there were 8 million infants who died during the first year of life, according to the estimates of World Health Organization (WHO)². In the United States, premature birth accounts for 35% of deaths in the first year of life³, and estimated annual costs exceed \$26 billion⁴. Death rate in the first year of life and gestational age at birth are inversely related. Maternal or fetal conditions are more or less related to preterm births, which are associated with a risk of preterm birth may be identified before pregnancy, at conception, or during pregnancy⁵. Some major risk factors for spontaneous preterm birth in singleton pregnancies have been identified. They include black maternal race, previous pregnancy with an adverse outcome, genitourinary infection, smoking, extremes of body weight, and social disadvantage, maternal depression, pre-pregnancy stress, poor diet, assisted fertility, and periodontal disease are also associated with preterm birth⁴.

Sexual transmitted diseases (STD) are associated with preterm birth⁶. Chronic sexually transmitted infection develops in 65% to 90% of infected infants⁷. Hepatitis C virus infected estimated 180 million people globally, which is a leading cause of chronic hepatitis, cirrhosis, and liver cancer and a primary indication for liver transplantation in the western world⁸. Hepatitis C is a major problem in high-risk pregnancy, but it is a curable

disease in young women who take antiviral regimens in the postnatal period⁹. Hepatitis B virus is carried by 300 million people globally, which is a leading cause of cirrhosis and hepatocellular carcinoma worldwide¹⁰. Mother-to-child transmission of hepatitis B virus (HBV) accounts for the majority of cases of chronic HBV infection¹¹. Chlamydia is the most common infection reported in the United States; most cases are asymptomatic. Chlamydia may convey double the risk of PTB in the presence of maternal immune response¹². Gonorrhea is the second most commonly noticeable condition in the United States. About 182.2 million dollars was spent to treat the acute infection, according to Centers of Disease Control and Prevention (CDC)¹³. Finally, syphilis had a major effect on several risk populations over time¹⁴, which all stages of syphilis in pregnant women pose a risk of transmission to the fetus, also increase infant mortality¹⁵.

Few studies have evaluated the effects of maternal sexually transmitted diseases in preterm births. In this study, we evaluated the impact of maternal risk factors and infectious disease in the United States from 2016 to 2018, using propensity score method. We then estimated the effects of five maternal sexually transmitted diseases in preterm birth in the United States from 2016 to 2018.

Methods:*Data sources and participants*

Data for this study were used by National Center of Health Statistics (NCHS) natality database, which is housed within the Center of Disease Control (CDC). The NCHS is a rich source for US people's health, which documents the population's health status, identifies the health problems and monitor the health care delivery and health status trend. The NCHS natality database begins in 2003, which contains approximately 4 million people's health status in each year. For this study, the 2016, 2017 and 2018 natality database were selected (Figure 1). In these natality databases, the variables are huge and regular, which contains baseline characteristics both mother and father, the status of mother utilizing medical and public services, mother's maternal behavior and health characteristics and infant health characteristics. All data for each participant were recorded by the electronic file, which could be automatically checked for completeness, individual item code validity, and unacceptable inconsistencies between data items. It is estimated that more than 99 percent birth data are registered in three years databases in the United States. All participants identifiers were removed from those databases, the corrections are transmitted to NCHS. We selected infants who were premature and excluded the participants who had unknown observations in the covariate factors.

Overcomes

The live birth of baby who at most 37 weeks of gestational was our primary outcome. There are plenty of infectious disease factors in mother that influence preterm birth, in this study, hepatitis B, hepatitis C, gonorrhoea, syphilis and chlamydia were calculated as primary

exposure. The major risk factors for spontaneous preterm birth in case of singleton pregnancies are race, previous pregnancy with an adverse outcome, genitourinary infection, smoking status, extremes of body weight, social disadvantage, maternal depression, pre-pregnancy stress, poor diet, assisted fertility and periodontal disease⁵. In the NCHS natality database, race of mother, WIC, previous cesarean, smoking, body mass index (BMI), infertility treatment used are the major risk factors for singleton preterm birth. WIC is a program to help low-income pregnant mother to have comprehensive nutrition, which obviously showed the diet's situation. Variables such as age of mother, infant birth order previous preterm birth, and plurality record are added in this study as the covariate factors.

Statistical analysis

Quantitative variables were summarized using mean \pm standard deviation and groups means were compared using the two samples t-test. Categorical variables were described using frequencies (percentage), and group proportions were compared using the chi-square test. Next, the propensity score of each subject was estimated using 1:1 greedy nearest neighbor matching method without replacement, and a logistic regression was fit with the disease (e.g., hepatitis C, gonorrhoea, syphilis, chlamydia and hepatitis B) as the response variable. Because complete separation or quasi-complete separation was observed, penalized maximum likelihood was employed to obtain estimates of the logistic regression parameters. The propensity scores were then used to obtain matches between exposure groups using 1:1 greedy nearest neighbor matching with caliper equal to 0.20. The success of the propensity score matching was assessed using the standardized difference. Once the demographic imbalances were minimized, outcome analysis was performed using logistic

regression, with preterm birth as the outcome. All tests were two-sided and a 0.05 level of significance was used throughout the study. All the analyses were performed in SAS 9.4 version (SAS Institute, Cary, NC).

Results:

We estimated three years follow-up databases in five sexually transmitted diseases to measure the association of five sexually transmitted diseases and preterm birth, using NCHS natality databases in 2016 (N=3,956,112), 2017 (N=3,864,754) and 2018 (N=3,801,534). Except missing and unknown value, 3,784,868, 3,709,025 and 3,659,971 maternal data are available in 2016, 2017 and 2018 (Figure 1). Maternal age, maternal race, smoking status, poor maternal diet, maternal body mass index (BMI), previous preterm birth status, previous cesarean status, infertility treatment used status, infant plurality and birth order were the covariates factors when exploring the association between sexually transmitted disease and preterm birth.

15,500 (100%), 16,882 (100%), 17,753 (100%) of the women with hepatitis C disease had an exact propensity score matching control from 2016 to 2018. Before doing 1:1 propensity score matching, BMI (2016, 0.24; 2017, 0.25; 2018, 0.25), white (2016, 0.37; 2017, 0.38; 2018, 0.37), black (2016, 0.35; 2017, 0.37; 2018, 0.37), asian (2016, 0.29; 2017, 0.29; 2018, 0.28), maternal poor diet (2016, 0.45; 2017, 0.44; 2018, 0.44), smoking status (2016, 1.42; 2017, 1.42; 2018, 1.44), previous preterm birth status (2016, 0.24; 2017, 0.24; 2018, 0.24),

previous cesarean status (2016, 0.12; 2017, 0.13; 2018, 0.15), infertility treatment used status (2016, 0.14; 2017, 0.15; 2018, 0.16), first birth (2016, 0.34; 2017, 0.34; 2018, 0.37) and second birth (2016, 0.15; 2017, 0.17; 2018, 0.16) standardized difference were larger than 0.10 from 2016 to 2018 (Table 1A, Table 2A, Table 3A and Figure 2A). After finishing 1:1 greedy nearest neighbor matching, all covariates factors' standardized differences were less than 0.10 from 2016 to 2018.

For maternal who had gonorrhea disease, there were 10,040 (100%), 10,766 (100%), 11,173 (100%) had been matched by 1:1 greedy nearest neighbor method in 2016, 2017 and 2018. During the original databases, maternal age (2016, 0.83; 2017, 0.83; 2018, 0.84), white (2016, 0.72; 2017, 0.70; 2018, 0.68), black (2016, 0.82; 2017, 0.81; 2018, 0.76), asian (2016, 0.31; 2017, 0.32; 2018, 0.30), maternal poor diet (2016, 0.60; 2017, 0.59; 2018, 0.60), smoking status (2016, 0.43; 2017, 0.42; 2018, 0.45), previous preterm birth status (2016, 0.12; 2017, 0.12; 2018, 0.14) and infertility treatment used status (2016, 0.15; 2017, 0.18; 2018, 0.17) standardized difference were larger than 0.10 from 2016 to 2018 (Table 1B, Table 2B, Table 3B and Figure 2B). All covariates factors were well balanced with matched in three years, which standardized difference were less than 0.10.

There were 3,235 (100%), 3,681 (100%), 4,157 (100%) maternal who had syphilis disease matched using an exact propensity score matching method. All confounding variables' standardized difference were less than 0.10 after matched, but maternal age (2016, 0.19; 2017, 0.21; 2018, 0.23), BMI (2016, 0.19; 2017, 0.19; 2018, 0.17), white (2016, 0.66; 2017, 0.58; 2018, 0.54), black (2016, 0.73; 2017, 0.68; 2018, 0.62), asian (2016, 0.16; 2017, 0.18;

2018, 0.20), maternal poor diet (2016, 0.51; 2017, 0.53; 2018, 0.53), smoking status (2016, 0.27; 2017, 0.28; 2018, 0.33), previous preterm birth status (2016, 0.14; 2017, 0.15; 2018, 0.17), infertility treatment used status (2016, 0.12; 2017, 0.14; 2018, 0.12), first birth (2016, 0.18; 2017, 0.16; 2018, 0.17) and second birth (2016, 0.13; 2017, 0.13; 2018, 0.12) standardized difference were larger than 0.10 from 2016 to 2018 (Table 1C, Table 2C, Table 3C and Figure 2C), also previous cesarean status standardized difference were larger than 0.10 in 2018 (0.11).

In 2016, 2017 and 2018, 68,418 (100%), 67,533 (100%) and 67,164 (100%) maternal who had chlamydia disease were matched. In the original databases, maternal age (2016, 0.94; 2017, 0.95; 2018, 0.95), white (2016, 0.39; 2017, 0.40; 2018, 0.39), black (2016, 0.48; 2017, 0.48; 2018, 0.48), asian (2016, 0.24; 2017, 0.24; 2018, 0.26), maternal poor diet (2016, 0.57; 2017, 0.56; 2018, 0.56), smoking status (2016, 0.27; 2017, 0.26; 2018, 0.25), previous cesarean status (2016, 0.15; 2017, 0.15; 2018, 0.16), infertility treatment used status (2016, 0.15; 2017, 0.16; 2018, 0.16) and first birth (2016, 0.17; 2017, 0.17; 2018, 0.18) standardized difference were larger than 0.10 from 2016 to 2018 (Table 1D, Table 2D, Table 3D and Figure 2D). All maternal covariates factors were well balanced after matched.

8,464 (100%), 8,462 (100%) and 7,808 (100%) maternal who had hepatitis B disease had been controlled by an exact propensity score matching method from 2016 to 2018. As other four sexually transmitted diseases, all covariates factors were well balanced, but for the unmatched data, maternal age (2016, 0.43; 2017, 0.41; 2018, 0.44), BMI (2016, 0.35; 2017,

0.28; 2018, 0.29), white (2016, 1.15; 2017, 1.08; 2018, 1.06), black (2016, 0.23; 2017, 0.27; 2018, 0.28), asian (2016, 1.04; 2017, 0.93; 2018, 0.90), maternal poor diet (2016, 0.15; 2017, 0.15; 2018, 0.13) and first birth (2016, 0.13; 2017, 0.14; 2018, 0.14) were not balanced from 2016 to 2018 (Table 1E, Table 2E, Table 3E and Figure 2E).

We found that in hepatitis C, gonorrhea, syphilis, chlamydia and hepatitis B disease, all matched covariate factors' standardized differences were less than 10% from 2016 to 2018. Therefore, all variables included covariates were all balanced between infectious disease and no infectious disease in all outcomes.

The results in Table 4 showed that all relative risks were larger than 1.0 from 2016 to 2018 in unmatched and matched sample, which meant that five sexually transmitted diseases were easily occurred in preterm birth. The analysis of propensity score matched sample removing selection bias according to covariates factors demonstrated that hepatitis C's risk ratio was the largest in all infectious disease in 2016 (adjusted risk ratio, 1.46; 95% CI, 1.39 to 1.54), followed by syphilis (adjusted risk ratio, 1.29; 95% CI, 1.15 to 1.45), gonorrhea (adjusted risk ratio, 1.23; 95% CI, 1.15 to 1.31), chlamydia (adjusted risk ratio, 1.14; 95% CI, 1.11 to 1.18) and hepatitis B (adjusted risk ratio, 1.06; 95% CI, 0.98 to 1.16). In 2017, hepatitis C had the highest risk in preterm birth (adjusted risk ratio, 1.41; 95% CI, 1.34 to 1.48), followed by syphilis (adjusted risk ratio, 1.19; 95% CI, 1.07 to 1.32), gonorrhea (adjusted risk ratio, 1.27; 95% CI, 1.20 to 1.35), chlamydia (adjusted risk ratio, 1.16; 95% CI, 1.13 to 1.20) and hepatitis B (adjusted risk ratio, 1.08; 95% CI, 1.09 to 1.28). Also hepatitis C had the highest risk in preterm birth in 2018 (adjusted risk ratio, 1.39; 95%

CI, 1.33 to 1.46), followed by (adjusted risk ratio, 1.34; 95% CI, 1.22 to 1.49), gonorrhea (adjusted risk ratio, 1.23; 95% CI, 1.16 to 1.31), chlamydia (adjusted risk ratio, 1.18; 95% CI, 1.15 to 1.21) and hepatitis B (adjusted risk ratio, 1.10; 95% CI, 1.01 to 1.20) (Figure 3, Table 4). Furthermore, to check whether the model is overdispersion or not, we calculated the Pearson and Deviance residuals, and the results were larger than 0.05, which represented that there was no overdispersion in the model.

Discussion:

In a nationwide natality study conducted in the United States, after adjustment for the potential confounding factors, we found that hepatitis C had the highest risk ratio among five sexually transmitted diseases in the preterm birth from 2016 to 2018. Furthermore, hepatitis B and C, gonorrhea, syphilis and chlamydia were all positively and consistently associated with preterm birth every year. Our results of covariates factors were consistent with previous study that major risks of singleton preterm birth were black maternal, had preterm birth and cesarean before, had poor diet, used tobacco and infertility treatment method⁴, but we also estimated other factors, such as the plurality and birth order, our results showed that those covariates factors were the effect to cause the rate of preterm birth infants. Missing value could influence model's accuracy, we found that except maternal race in white and black, removing missing values did not influence the model (Supplement Table 1, 2, 3), therefore we remove missing values.

Our adjusted analysis focused on the strength of association between the maternal who had hepatitis C, gonorrhea, syphilis, chlamydia and hepatitis B and preterm birth. In addition to restrict the analyses to maternal of the sexually transmitted diseases, we adjusted for potential confounding factors through propensity score matching method.

A strength of our study was the three-year follow-up analysis, which provided the strong evidence to prove the association between five infectious disease and preterm birth. Furthermore, another strength of our study was the use of NCHS natality database, which supplied a very-large population cohort, with availability of mother and farther demographic outcomes, linkable maternal and infants' health information and utilization of mother in public services. However, there are some limitations in our study. Firstly, the NCHS natality database recorded the live birth without stillbirth in the United States. We did not know the impact of stillbirth on our results. Secondly, the residuals' diagnostics by such confounding factors would not be likely explain. Data from NCHS natality database indicated that maternal who had hepatitis C disease during pregnancy were related to preterm birth, with similar residuals distributions of other four infectious disease.

In conclusions, after adjusting for confounding, hepatitis B and C gonorrhea, syphilis and chlamydia were all positively and consistently associated with preterm birth every year from 2016 to 2018. Formulation of public health prevention strategies tailored to individuals with STDs are needed to mitigate the risk of preterm birth.

Appendix:

Table 1A Baseline characteristics stratified by hepatitis C status in 2016.

Characteristics		Unmatched Population			Matched Sample		
		Hep C+ (n=15500,0.41%)	Hep C- (n=3765852,99.59%)	Standardized Difference*	Hep C+ (n=15500,50.00%)	Hep C- (n=15500,50.00%)	Standardized Difference*
Maternal Age		28.4 ± 5.0	28.7 ± 5.8	0.05	28.4 ± 5.0	28.4 ± 5.0	0.01
BMI		25.3 ± 5.8	26.8 ± 6.6	0.24	25.3 ± 5.8	25.2 ± 5.7	0.02
Maternal Race	White	13654(88.1)	2779743(73.8)	0.37	13654(88.1)	13801 (89.0)	0.02
	Black	790(5.1)	586803(15.6)	0.35	790(5.1)	839(5.4)	0.01
	Asian	195(1.3)	261353 (6.9)	0.29	195(1.3)	182(1.2)	0.00
	Other Race	13(0.1)	10467(0.3)	Reference	861(5.6)	678(4.4)	Reference
WIC**		9495(61.3)	1481735(39.3)	0.45	9495(61.3)	9598 (61.9)	0.01
Tobacco Use		9608(62.0)	261809(7.0)	1.42	9608(62.0)	9614 (62.0)	0.00
Previous Preterm Birth		1334(8.6)	114965(3.1)	0.24	1334(8.6)	1205 (7.8)	0.04
Previous Cesarean		3087 (19.9)	576543 (15.3)	0.12	3087 (19.9)	3009 (19.4)	0.01
Infertility Treatment Use		56 (0.4)	66464 (1.8)	0.14	56 (0.4)	52 (0.3)	0.00
Infants Plurality	One	14903(96.2)	3636961(96.6)	0.02	14903(96.2)	15169(97.9)	0.09
	Twice	579(3.7)	125052(3.3)	0.02	579(3.7)	323(2.1)	0.09
	Three or More	18(0.1)	3839(0.1)	Reference	18(0.1)	8(0.1)	Reference
Infants Birth Order	First	2609(16.8)	1177103(31.3)	0.34	2609(16.8)	2602(16.8)	0.00
	Second	3386(21.9)	1064798(28.3)	0.15	3386(21.9)	3278(21.2)	0.02
	Third or More	9505(61.3)	1523951(40.5)	Reference	9505(61.3)	9620(62.1)	Reference

*Unlike the p-value, the standardized difference is not affected by sample size. Standardized differences are used in observational studies to compare the distribution of baseline covariates between exposure groups. Standardized differences larger than 0.10 suggest a meaningful imbalance in the baseline covariate (Austin 2009). These relatively large standardized differences are colored blue in the table above. Notably, the standardized differences in the matched sample all suggest balance between exposure groups.

** A government program to help low-income families, which is a surrogate for socioeconomic status.

Table 1B Baseline characteristics stratified by gonorrhoea status in 2016.

Characteristics		Unmatched Population			Matched Sample		
		Gonorrhoea+ (n=10040, 0.27%)	Gonorrhoea- (n=3771312, 99.73%)	Standardized Difference*	Gonorrhoea+ (n=10040,50.00%)	Gonorrhoea- (n=10040,50.00%)	Standardized Difference*
Maternal Age		24.1 ± 5.2	28.7 ± 5.8	0.83	24.1 ± 5.2	24.1 ± 5.1	0.01
BMI		27.4 ± 7.2	26.8 ± 6.6	0.08	27.4 ± 7.2	27.3 ± 7.1	0.01
Maternal Race	White	4066(40.5)	2789331(74.0)	0.72	4066(40.5)	4080(40.6)	0.00
	Black	5158(51.4)	582435(15.4)	0.82	5158(51.4)	5171(51.5)	0.00
	Asian	99(1.0)	261449(6.9)	0.31	99(1.0)	96(1.0)	0.00
	Other Race	463(4.6)	92225(2.5)	Reference	717(7.1)	693(6.9)	Reference
WIC**		6828 (68.0)	1484402 (39.4)	0.60	6828 (68.0)	6918 (68.9)	0.02
Tobacco Use		2212 (22.0)	269205 (7.1)	0.43	2212 (22.0)	2126 (21.2)	0.02
Previous Preterm Birth		551 (5.5)	115748 (3.1)	0.12	551 (5.5)	495 (4.9)	0.03
Previous Cesarean		1413 (14.1)	578217 (15.3)	0.04	1413 (14.1)	1381 (13.8)	0.01
Infertility Treatment Use		26 (0.3)	66494 (1.8)	0.15	26 (0.3)	25 (0.2)	0.00
Infants Plurality	One	9723(96.8)	3642141(96.6)	0.02	9723(96.8)	9847(98.1)	0.07
	Twice	303(3.0)	125328(3.3)	0.02	303(3.0)	186(1.9)	0.07
	Three or More	14(0.1)	3843(0.1)	Reference	14(0.1)	7(0.1)	Reference
Infants Birth Order	First	3054(30.4)	1176653(31.2)	0.02	3054(30.4)	3083(30.7)	0.01
	Second	2453(24.4)	1065731(28.3)	0.09	2453(24.4)	2461(24.5)	0.00
	Third or More	4533(45.2)	1528923(40.5)	Reference	4533(45.2)	4496(44.8)	Reference

*Unlike the p-value, the standardized difference is not affected by sample size. Standardized differences are used in observational studies to compare the distribution of baseline covariates between exposure groups. Standardized differences larger than 0.10 suggest a meaningful imbalance in the baseline covariate (Austin 2009). These relatively large standardized differences are colored blue in the table above. Notably, the standardized differences in the matched sample all suggest balance between exposure groups.

** A government program to help low-income families, which is a surrogate for socioeconomic status.

Table 1C Baseline characteristics stratified by syphilis status in 2016.

Characteristics		Unmatched Population			Matched Sample		
		Syphilis+ (n=3235,0.09%)	Syphilis- (n=3778117, 99.91%)	Standardized Difference*	Syphilis+ (n=3235,50.00%)	Syphilis- (n=3235,50.00%)	Standardized Difference*
Maternal Age		27.6 ± 6.1	28.7 ± 5.8	0.19	27.6 ± 6.1	27.3 ± 5.9	0.04
BMI		28.2 ± 7.5	26.8 ± 6.6	0.19	28.2 ± 7.5	28.0 ± 7.2	0.02
Maternal Race	White	1398(43.2)	2791999(73.9)	0.66	1398(43.2)	1387 (42.9)	0.01
	Black	1529(47.3)	586064 (15.5)	0.73	1529(47.3)	1512 (46.7)	0.01
	Asian	108(3.3)	261440(6.9)	0.16	108(3.3)	112(3.5)	0.01
	Other Race	102(3.2)	92586(2.5)	Reference	200(6.2)	224 (6.9)	Reference
WIC**		2073 (64.1)	1489157 (39.4)	0.51	2073 (64.1)	2107 (65.1)	0.02
Tobacco Use		506 (15.6)	270911 (7.2)	0.27	506 (15.6)	481 (14.9)	0.02
Previous Preterm Birth		193 (6.0)	116106 (3.1)	0.14	193 (6.0)	183 (5.7)	0.01
Previous Cesarean		601 (18.6)	579029 (15.3)	0.09	601 (18.6)	580 (17.9)	0.02
Infertility Treatment Use		16 (0.5)	66504 (1.8)	0.12	16 (0.5)	12 (0.4)	0.01
Infants Plurality	One	3115(96.3)	3648749(96.6)	0.02	3115(96.3)	3167(97.9)	0.09
	Twice	114(3.5)	125517(3.3)	0.01	114(3.5)	68(2.1)	0.08
	Three or More	6(0.2)	3851(0.1)	Reference	6(0.2)	0(0.0)	Reference
Infants Birth Order	First	758(23.4)	1178954(31.2)	0.18	758(23.4)	755(23.3)	0.00
	Second	733(22.7)	1067451(28.3)	0.13	733(22.7)	738(22.8)	0.00
	Third or More	1744(53.9)	1531712(40.5)	Reference	1744(53.9)	1742(53.9)	Reference

*Unlike the p-value, the standardized difference is not affected by sample size. Standardized differences are used in observational studies to compare the distribution of baseline covariates between exposure groups. Standardized differences larger than 0.10 suggest a meaningful imbalance in the baseline covariate (Austin 2009). These relatively large standardized differences are colored blue in the table above. Notably, the standardized differences in the matched sample all suggest balance between exposure groups.

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Table 1D Baseline characteristics stratified by chlamydia status in 2016.

Characteristics		Unmatched Population			Matched Sample		
		Chlamydia+ (n=68418,1.81%)	Chlamydia- (n=3712934, 98.19%)	Standardized Difference*	Chlamydia+ (n=68418,50.00%)	Chlamydia- (n=68418,50.00%)	Standardized Difference*
Maternal Age		23.7 ± 5.0	28.8 ± 5.8	0.94	23.7 ± 5.0	23.6 ± 4.9	0.01
BMI		26.9 ± 6.9	26.8 ± 6.6	0.01	26.9 ± 6.9	26.8 ± 6.8	0.01
Maternal Race	White	38154(55.8)	2755243(74.2)	0.39	38154(55.8)	38680(56.5)	0.02
	Black	24144(35.3)	563449 (15.2)	0.48	24144(35.3)	23766(34.7)	0.01
	Asian	1448(2.1)	260100(7.0)	0.24	1448(2.1)	1420(2.1)	0.00
	Other Race	2674(3.9)	90014(2.4)	Reference	4672(6.8)	4552(6.7)	Reference
WIC**		45410 (66.4)	1445820 (38.9)	0.57	45410 (66.4)	45722 (66.8)	0.01
Tobacco Use		10561 (15.4)	260856 (7.0)	0.27	10561 (15.4)	10323 (15.1)	0.01
Previous Preterm Birth		2886 (4.2)	113413 (3.1)	0.06	2886 (4.2)	2500 (3.7)	0.03
Previous Cesarean		7134 (10.4)	572496 (15.4)	0.15	7134 (10.4)	6885 (10.1)	0.01
Infertility Treatment Use		175 (0.3)	66345 (1.8)	0.15	175 (0.3)	152 (0.2)	0.00
Infants Plurality	One	66535(97.3)	3585329(96.6)	0.04	66535(97.3)	67223(98.3)	0.06
	Twice	1834(2.7)	123797(3.3)	0.04	1834(2.7)	1170 (1.7)	0.06
	Three or More	49(0.1)	3808(0.1)	Reference	49(0.1)	25(0.0)	Reference
Infants Birth Order	First	26707(39.0)	1153005(31.1)	0.17	26707(39.0)	27129(39.7)	0.01
	Second	17357(25.4)	1050827(28.3)	0.07	17357(25.4)	17296(25.3)	0.00
	Third or More	24354(35.6)	1509102(40.6)	Reference	24352(35.6)	23993(35.1)	Reference

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Table 1E Baseline characteristics stratified by hepatitis B status in 2016.

Characteristics		Unmatched Population			Matched Sample		
		Hep B+ (n=8464,0.22%)	Hep B- (n=3772888, 99.78%)	Standardized Difference*	Hep B+ (n=8464,50.00%)	Hep B- (n=8464,50.00%)	Standardized Difference*
Maternal Age		31.1 ± 5.4	28.7 ± 5.8	0.43	31.1 ± 5.4	31.1 ± 5.4	0.01
BMI		24.6 ± 5.8	26.8 ± 6.6	0.35	24.6 ± 5.8	24.5 ± 5.6	0.01
Maternal Race	White	2034(24.0)	2791363(74.0)	1.15	2034(24.0)	2036(24.1)	0.00
	Black	2084(24.6)	585509(15.5)	0.23	2084(24.6)	2102(24.8)	0.01
	Asian	4046(47.8)	257502(6.8)	1.04	4046(47.8)	4042(47.8)	0.00
	Other Race	141(1.7)	92547(2.5)	Reference	300(3.5)	284(3.4)	Reference
WIC**		3957 (46.8)	1487273 (39.4)	0.15	3957 (46.8)	3974 (47.0)	0.00
Tobacco Use		490 (5.8)	270927 (7.2)	0.06	490 (5.8)	470 (5.6)	0.01
Previous Preterm Birth		320 (3.8)	115979 (3.1)	0.04	320 (3.8)	258 (3.0)	0.04
Previous Cesarean		1482 (17.5)	578148 (15.3)	0.06	1482 (17.5)	1488 (17.6)	0.01
Infertility Treatment Use		163 (1.9)	66357 (1.8)	0.01	163 (1.9)	95 (1.1)	0.06
Infants Plurality	One	8185(96.7)	3643679(96.6)	0.02	8185(96.7)	8308(98.2)	0.08
	Twice	278(3.3)	125353(3.3)	0.02	278(3.3)	156(1.8)	0.08
	Three or More	1(0.0)	3856(0.1)	Reference	1(0.0)	0(0.0)	Reference
Infants Birth Order	First	2149(25.4)	1177563(31.2)	0.13	2149(25.4)	2148(25.4)	0.00
	Second	2399(28.3)	1065785(28.3)	0.00	2399(28.3)	2424(28.6)	0.01
	Third or More	3916(46.3)	1529540(40.5)	Reference	3916(46.3)	3892(46.0)	Reference

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Table 2A Baseline characteristics stratified by hepatitis C status in 2017.

Characteristics		Unmatched Population			Matched Sample		
		Hep C+ (n=16882,0.46%)	Hep C- (n=3689315, 99.54%)	Standardized Difference*	Hep C+ (n=16882,50.00%)	Hep C- (n=16882,50.00%)	Standardized Difference*
Maternal Age		28.7 ± 5.0	28.8 ± 5.8	0.02	28.7 ± 5.0	28.6 ± 5.0	0.02
BMI		25.4 ± 6.0	27.0 ± 6.7	0.25	25.4 ± 6.0	25.2 ± 5.8	0.03
Maternal Race	White	14873(88.1)	2700854(73.2)	0.38	14873(88.1)	14903(88.3)	0.00
	Black	840(5.0)	590561(16.0)	0.37	840(5.0)	859(5.1)	0.00
	Asian	214(1.3)	258847 (7.0)	0.29	214(1.3)	217(1.3)	0.00
	Other Race	517(3.1)	94458(2.6)	Reference	955(5.7)	903(5.4)	Reference
WIC**		9977 (59.1)	1395397 (37.8)	0.44	9977 (59.1)	9981 (59.1)	0.00
Tobacco Use		10372 (61.4)	243550 (6.6)	1.42	10372 (61.4)	10374 (61.5)	0.00
Previous Preterm Birth		1521 (9.0)	119270 (3.2)	0.24	1521 (9.0)	1437 (8.5)	0.02
Previous Cesarean		3440 (20.4)	571377 (15.5)	0.13	3440 (20.4)	3279 (19.4)	0.02
Infertility Treatment Use		60 (0.4)	70106 (1.9)	0.15	60 (0.4)	44 (0.3)	0.01
Infants Plurality	One	16255(96.3)	3563416(96.6)	0.02	16255(96.3)	16493(97.1)	0.08
	Twice	615(3.6)	122185(3.3)	0.02	615(3.6)	388(2.3)	0.07
	Three or More	12(0.1)	3714(0.1)	Reference	12(0.1)	1(0.0)	Reference
Infants Birth Order	First	2801(16.6)	1143716(31.0)	0.34	2801(16.6)	2784(16.5)	0.00
	Second	3572(21.2)	1042322(28.3)	0.17	3572(21.2)	3618(21.4)	0.01
	Third or More	10509(62.3)	1503277(40.8)	Reference	10509(62.3)	10480(62.1)	Reference

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Table 2B Baseline characteristics stratified by gonorrhea status in 2017.

Characteristics		Unmatched Population			Matched Sample		
		Gonorrhea+ (n=10766,0.29%)	Gonorrhea- (n=3695431, 99.71%)	Standardized Difference*	Gonorrhea+ (n=10766,50.00%)	Gonorrhea- (n=10766,50.00%)	Standardized Difference*
Maternal Age		24.3 ± 5.3	28.9 ± 5.8	0.83	24.3 ± 5.3	24.2 ± 5.1	0.02
BMI		27.4 ± 7.3	27.0 ± 6.7	0.06	27.4 ± 7.3	27.3 ± 7.1	0.02
Maternal Race	White	4368(40.6)	2711359(73.4)	0.70	4368(40.6)	4425(41.1)	0.01
	Black	5521(51.3)	585880(15.9)	0.81	5521(51.3)	5503(51.1)	0.00
	Asian	93(0.9)	258968(7.0)	0.32	93(0.9)	86(0.8)	0.00
	Other Race	506(4.7)	94469(2.6)	Reference	784(7.3)	752(7.0)	Reference
WIC**		7099 (65.9)	1398275 (37.8)	0.59	7099 (65.9)	7187 (66.8)	0.02
Tobacco Use		2271 (21.1)	251651 (6.8)	0.42	2271 (21.1)	2168 (20.1)	0.03
Previous Preterm Birth		619 (5.7)	120172 (3.3)	0.12	619 (5.7)	528 (4.9)	0.04
Previous Cesarean		1506 (14.0)	573311 (15.5)	0.04	1506 (14.0)	1465 (13.6)	0.01
Infertility Treatment Use		15 (0.1)	70151 (1.9)	0.18	15 (0.1)	14 (0.1)	0.00
Infants Plurality	One	10411(96.7)	3569260(96.6)	0.01	10411(96.7)	10547(98.0)	0.07
	Twice	345(3.2)	122455(3.3)	0.01	345(3.2)	217(2.0)	0.07
	Three or More	10(0.1)	3716(0.1)	Reference	10(0.1)	2(0.0)	Reference
Infants Birth Order	First	3356(31.2)	1143161(30.9)	0.01	3356(31.2)	3398(31.6)	0.01
	Second	2602(24.2)	1043292(28.2)	0.09	2602(24.2)	2583(24.0)	0.00
	Third or More	4808(44.7)	1508978(40.8)	Reference	4808(44.7)	4785(44.4)	Reference

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Table 2C Baseline characteristics stratified by syphilis status in 2017.

Characteristics		Unmatched Population			Matched Sample		
		Syphilis+ (n=3681,0.10%)	Syphilis- (n=3702516, 99.90%)	Standardized Difference*	Syphilis+ (n=3681,50.00%)	Syphilis- (n=3681,50.00%)	Standardized Difference*
Maternal Age		27.6 ± 6.0	28.8 ± 5.8	0.21	27.6 ± 6.0	27.5 ± 5.9	0.01
BMI		28.3 ± 7.6	27.0 ± 6.7	0.19	28.3 ± 7.6	28.3 ± 7.6	0.01
Maternal Race	White	1691(45.9)	2714036(73.3)	0.58	1691(45.9)	1695 (46.1)	0.00
	Black	1681(45.7)	589720(15.9)	0.68	1681(45.7)	1691 (45.9)	0.01
	Asian	112(3.0)	258949(7.0)	0.18	112(3.0)	110(3.0)	0.00
	Other Race	90(2.4)	94885(2.6)	Reference	197(5.4)	185(5.0)	Reference
WIC**		2334 (63.4)	1403040 (37.9)	0.53	2334 (63.4)	2360 (64.1)	0.01
Tobacco Use		579 (15.7)	253343 (6.8)	0.28	579 (15.7)	544 (14.8)	0.03
Previous Preterm Birth		235 (6.4)	120556 (3.3)	0.15	235 (6.4)	217 (5.9)	0.02
Previous Cesarean		705 (19.2)	574112 (15.5)	0.10	705 (19.2)	678 (18.4)	0.02
Infertility Treatment Use		16 (0.4)	70150 (1.9)	0.14	16 (0.4)	14 (0.4)	0.01
Infants Plurality	One	3548(96.4)	3576123(96.6)	0.01	3548(96.4)	3602 (97.9)	0.08
	Twice	130(3.5)	122670(3.3)	0.01	130(3.5)	77(2.1)	0.08
	Three or More	3(0.1)	3723(0.1)	Reference	3(0.1)	2(0.1)	Reference
Infants Birth Order	First	881(23.9)	1145636(30.9)	0.16	881(23.9)	876(23.8)	0.00
	Second	838(22.8)	1045056(28.2)	0.13	838(22.8)	819(22.3)	0.01
	Third or More	1962(53.3)	1511824(40.8)	Reference	1962(53.3)	1986(54.0)	Reference

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Table 2D Baseline characteristics stratified by chlamydia status in 2017.

Characteristics		Unmatched Population			Matched Sample		
		Chlamydia+ (n=67533,1.82%)	Chlamydia- (n=3638664,98.18%)	Standardized Difference*	Chlamydia- (n=67533,50.00%)	Chlamydia- (n=67533,50.00%)	Standardized Difference*
Maternal Age		23.8 ± 5.0	28.9 ± 5.8	0.95	23.8 ± 5.0	23.8 ± 5.0	0.01
BMI		27.0 ± 7.0	27.0 ± 6.7	0.01	27.0 ± 7.0	27.0 ± 6.8	0.01
Maternal Race	White	37043(54.84)	2678684(73.62)	0.40	37043(54.8)	37429(55.4)	0.01
	Black	24229(35.88)	567172 (15.59)	0.48	24229(35.9)	24066(35.6)	0.01
	Asian	1381(2.04)	257689(7.08)	0.24	1381(2.0)	1326(2.0)	0.00
	Other Race	2868(4.25)	92107(2.53)	Reference	4880(7.2)	4712(7.0)	Reference
WIC**		43569 (64.5)	1361805 (37.4)	0.56	43569 (64.5)	43950 (65.1)	0.01
Tobacco Use		9842 (14.6)	244080 (6.7)	0.26	9842 (14.6)	9382 (13.9)	0.02
Previous Preterm Birth		3130 (4.6)	117661 (3.2)	0.07	3130 (4.6)	2675 (4.0)	0.03
Previous Cesarean		7136 (10.6)	567681 (15.6)	0.15	7136 (10.6)	6982 (10.3)	0.01
Infertility Treatment Use		168 (0.2)	69998 (1.9)	0.16	168 (0.2)	165 (0.2)	0.00
Infants Plurality	One	65733(97.33)	3513938(96.57)	0.04	65733(97.3)	66454(98.4)	0.06
	Twice	1777(2.63)	121023(3.33)	0.04	1777(2.6)	1066 (1.6)	0.06
	Three or More	23(0.03)	3703(0.10)	Reference	23(0.0)	13(0.02)	Reference
Infants Birth Order	First	26160(38.74)	1120357(30.79)	0.17	26160(38.7)	26369(39.1)	0.00
	Second	16925(25.06)	1028969(28.28)	0.07	16925(25.1)	16810(24.9)	0.00
	Third or More	24448(36.20)	1489338(40.93)	Reference	24448(36.2)	24354(36.1)	Reference

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Table 2E Baseline characteristics stratified by hepatitis B status in 2017.

Characteristics		Unmatched Population			Matched Sample		
		Hep B+ (n=8462,0.23%)	Hep B- (n=3697735, 99.77%)	Standardized Difference*	Hep B+ (n=8462,50.00%)	Hep B- (n=8462,50.00%)	Standardized Difference*
Maternal Age		31.1 ± 5.5	28.8 ± 5.8	0.41	31.1 ± 5.5	31.0 ± 5.6	0.02
BMI		25.2 ± 6.0	27.0 ± 6.7	0.28	25.2 ± 6.0	25.1 ± 5.7	0.02
Maternal Race	White	2186(25.8)	2713541(73.4)	1.08	2186(25.8)	2189(25.9)	0.00
	Black	2290(27.1)	589111 (15.9)	0.27	2290(27.1)	2282(27.0)	0.00
	Asian	3669(43.4)	255392(6.9)	0.93	3669(43.4)	3696(43.7)	0.01
	Other Race	174(2.1)	94801(2.6)	Reference	317(3.8)	295(3.5)	Reference
WIC**		3813 (45.1)	1401561 (37.9)	0.15	3813 (45.1)	3849 (45.5)	0.01
Tobacco Use		521 (6.2)	253401 (6.9)	0.03	521 (6.2)	483 (5.7)	0.02
Previous Preterm Birth		365 (4.3)	120426 (3.3)	0.06	365 (4.3)	276 (3.3)	0.06
Previous Cesarean		1594 (18.8)	573223 (15.5)	0.09	1594 (18.8)	1549 (18.3)	0.01
Infertility Treatment Use		211 (2.5)	69955 (1.9)	0.04	211 (2.5)	138 (1.6)	0.06
Infants Plurality	One	8152(96.3)	3571519(96.6)	0.01	8152(96.3)	8291(98.0)	0.09
	Twice	295(3.5)	122505(3.3)	0.01	295(3.5)	168(2.0)	0.08
	Three or More	15(0.2)	3711(0.1)	Reference	15(0.2)	3(0.0)	Reference
Infants Birth Order	First	2073(24.5)	1144444(31.0)	0.14	2073(24.5)	2091(24.7)	0.00
	Second	2404(28.4)	1043490(28.2)	0.00	2404(28.4)	2421(28.6)	0.00
	Third or More	3985(47.1)	1509801(40.8)	Reference	3985(47.1)	3950(46.7)	Reference

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Table 3A Baseline characteristics stratified by hepatitis C status in 2018.

Characteristics		Unmatched Population			Matched Sample		
		Hep C+ (n=17753,0.49%)	Hep C- (n=3642218, 99.51%)	Standardized Difference*	Hep C+ (n=17753,50.00%)	Hep C- (n=17753,50.00%)	Standardized Difference*
Maternal Age		29.0 ± 5.0	29.0 ± 5.8	0.00	29.0 ± 5.0	28.9 ± 5.0	0.02
BMI		25.6 ± 6.0	27.2 ± 6.8	0.25	25.6 ± 6.0	25.4 ± 5.8	0.02
Maternal Race	White	15643(88.1)	2586550(73.8)	0.37	15643(88.1)	15770(88.9)	0.02
	Black	816(4.6)	570430(15.7)	0.37	816(4.6)	849(4.8)	0.01
	Asian	220(1.2)	243768(6.7)	0.28	220(1.2)	218(1.2)	0.00
	Other Race	558(3.1)	96006(2.6)	Reference	1074(6.1)	913(5.1)	Reference
WIC**		10128 (57.0)	1301551 (35.7)	0.44	10128 (57.0)	10258 (57.8)	0.02
Tobacco Use		10922 (61.5)	225014 (6.2)	1.44	10922 (61.5)	10929 (61.6)	0.00
Previous Preterm Birth		1669 (9.4)	126749 (3.5)	0.24	1669 (9.4)	1460 (8.2)	0.05
Previous Cesarean		3794 (21.4)	569443 (15.6)	0.15	3794 (21.4)	3627 (20.4)	0.02
Infertility Treatment Use		56 (0.3)	71912 (2.0)	0.16	56 (0.3)	43 (0.2)	0.01
Infants Plurality	One	17100(96.3)	3520724(96.7)	0.02	17100(96.3)	17385(97.9)	0.09
	Twice	635(3.6)	118105(3.2)	0.02	635(3.6)	361(2.0)	0.09
	Three or More	18(0.1)	3389(0.1)	Reference	18(0.1)	7(0.0)	Reference
Infants Birth Order	First	2745(15.5)	1125525(30.9)	0.37	2745(15.5)	2783(15.7)	0.01
	Second	3735(21.0)	1023347(28.1)	0.16	3735(21.0)	3610 (20.3)	0.02
	Third or More	11273(63.5)	1493346(21.9)	Reference	11273(63.5)	11360(64.0)	Reference

*Unlike the p-value, the standardized difference is not affected by sample size. Standardized differences are used in observational studies to compare the distribution of baseline covariates between exposure groups. Standardized differences larger than 0.10 suggest a meaningful imbalance in the baseline covariate (Austin 2009). These relatively large standardized differences are colored blue in the table above. Notably, the standardized differences in the matched sample all suggest balance between exposure groups.

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Table 3B Baseline characteristics stratified by gonorrhea status in 2018.

Characteristics		Unmatched Population			Matched Sample		
		Gonorrhea+ (n=11173,0.31%)	Gonorrhea- (n=3648798, 99.69%)	Standardized Difference*	Gonorrhea+ (n=11173,50.00%)	Gonorrhea- (n=11173,50.00%)	Standardized Difference*
Maternal Age		24.4 ± 5.3	29.0 ± 5.8	0.84	24.4 ± 5.3	24.3 ± 5.2	0.01
BMI		27.5 ± 7.4	27.2 ± 6.8	0.05	27.5 ± 7.4	27.3 ± 7.0	0.03
Maternal Race	White	4686(41.9)	2697507(73.9)	0.68	4686(41.9)	4716(42.2)	0.01
	Black	5458(48.9)	565788(15.5)	0.76	5458(48.9)	5416(48.5)	0.01
	Asian	105(0.9)	243883(6.7)	0.30	105(0.9)	96(0.9)	0.00
	Other Race	598(5.4)	95966(2.6)	Reference	924(8.3)	945(8.5)	Reference
WIC**		7185 (64.3)	1304494 (35.8)	0.60	7185 (64.3)	7240 (64.8)	0.01
Tobacco Use		2440 (21.8)	233496 (6.4)	0.45	2440 (21.8)	2402 (21.5)	0.01
Previous Preterm Birth		734 (6.6)	127684 (3.5)	0.14	734 (6.6)	654 (5.9)	0.03
Previous Cesarean		1511 (13.5)	571726 (15.7)	0.06	1511 (13.5)	1470 (13.2)	0.01
Infertility Treatment Use		24 (0.2)	71944 (2.0)	0.17	24 (0.2)	20 (0.2)	0.00
Infants Plurality	One	10839(97.0)	3526985(96.7)	0.02	10839(97.0)	10960(98.1)	0.06
	Twice	331(3.0)	118409(3.3)	0.02	331(3.0)	213(1.9)	0.06
	Three or More	3(0.0)	3404(0.1)	Reference	3(0.0)	0(0.0)	Reference
Infants Birth Order	First	3567(31.9)	1124703(30.8)	0.02	3567(31.9)	3575(32.0)	0.00
	Second	2609(23.4)	1024473(28.1)	0.11	2609(23.4)	2653(23.7)	0.01
	Third or More	4997(44.7)	1499622 (41.1)	Reference	4997(44.7)	4945(44.3)	Reference

*Unlike the p-value, the standardized difference is not affected by sample size. Standardized differences are used in observational studies to compare the distribution of baseline covariates between exposure groups. Standardized differences larger than 0.10 suggest a meaningful imbalance in the baseline covariate (Austin 2009). These relatively large standardized differences are colored blue in the table above. Notably, the standardized differences in the matched sample all suggest balance between exposure groups.

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Table 3C Baseline characteristics stratified by syphilis status in 2018.

Characteristics		Unmatched Population			Matched Sample		
		Syphilis+ (n=4157,0.11%)	Syphilis- (n=3655814, 99.89%)	Standardized Difference*	Syphilis+ (n=4157,50.00%)	Syphilis- (n=4157,50.00%)	Standardized Difference*
Maternal Age		27.6 ± 6.0	29.0 ± 5.8	0.23	27.6 ± 6.0	27.5 ± 5.8	0.02
BMI		28.4 ± 7.5	27.2 ± 6.8	0.17	28.4 ± 7.5	28.2 ± 7.2	0.02
Maternal Race	White	2009(48.3)	2700184(73.9)	0.54	2009(48.3)	2023(48.7)	0.01
	Black	1765(42.5)	569481 (15.6)	0.62	1765(42.5)	1744(42.0)	0.01
	Asian	103(2.5)	243885(6.7)	0.20	103(2.5)	94(2.3)	0.01
	Other Race	146(3.5)	96418(2.6)	Reference	280(6.7)	296(7.1)	Reference
WIC**		2552 (61.4)	1309127 (35.8)	0.53	2552 (61.4)	2609 (62.8)	0.03
Tobacco Use		706 (17.0)	235230 (6.4)	0.33	706 (17.0)	678 (16.3)	0.02
Previous Preterm Birth		306 (7.4)	128112 (3.5)	0.17	306 (7.4)	268 (6.4)	0.04
Previous Cesarean		819 (19.7)	572418 (15.7)	0.11	819 (19.7)	776 (18.7)	0.03
Infertility Treatment Use		25 (0.6)	71943 (2.0)	0.12	25 (0.6)	19 (0.5)	0.01
Infants Plurality	One	4038(97.1)	3533786(96.7)	0.03	4038(97.1)	4079 (98.1)	0.06
	Twice	119(2.9)	118621(3.2)	0.02	119(2.9)	78(1.9)	0.06
	Three or More	0(0.0)	3407(0.1)	Reference	0(0.0)	0(0.0)	Reference
Infants Birth Order	First	961(23.1)	1127309(30.8)	0.17	961(23.1)	956(23.0)	0.00
	Second	957(23.0)	1026125(28.1)	0.12	957(23.0)	974(23.4)	0.01
	Third or More	2239(53.9)	1502380(41.1)	Reference	2239(53.9)	2227(53.6)	Reference

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Table 3D Baseline characteristics stratified by chlamydia status in 2018.

Characteristics		Unmatched Population			Matched Sample		
		Chlamydia+ (n=67164,1.84%)	Chlamydia- (n=3592807, 98.16%)	Standardized Difference*	Chlamydia+ (n=67164,50.00%)	Chlamydia- (n=67164,50.00%)	Standardized Difference*
Maternal Age		23.9 ± 5.1	29.1 ± 5.8	0.95	23.9 ± 5.1	23.9 ± 5.0	0.01
BMI		27.2 ± 7.0	27.2 ± 6.8	0.00	27.2 ± 7.0	27.1 ± 6.8	0.02
Maternal Race	White	37496(55.8)	2664697(74.2)	0.39	37496(55.8)	37766(56.2)	0.01
	Black	23799(35.4)	547447(15.2)	0.48	23799(35.4)	23626(35.2)	0.01
	Asian	1042(1.6)	242946(6.8)	0.26	1042(1.6)	1070(1.6)	0.00
	Other Race	2893(4.3)	93671(2.6)	Reference	4827(7.2)	4702(7.0)	Reference
WIC**		41771 (62.2)	1269908 (35.3)	0.56	41771 (62.2)	42090 (62.7)	0.01
Tobacco Use		9339 (13.9)	226597 (6.3)	0.25	9339 (13.9)	9062 (13.5)	0.01
Previous Preterm Birth		3220 (4.8)	125198 (3.5)	0.07	3220 (4.8)	2795 (4.2)	0.03
Previous Cesarean		7020 (10.5)	566217 (15.8)	0.16	7020 (10.5)	6831 (10.2)	0.01
Infertility Treatment Use		191 (0.3)	71777 (2.0)	0.16	191 (0.3)	176 (0.3)	0.00
Infants Plurality	One	65258(97.2)	3472566(96.7)	0.03	65258(97.2)	65895(98.1)	0.05
	Twice	1882(2.8)	116858(3.3)	0.03	1882(2.8)	1265(1.9)	0.05
	Three or More	24(0.0)	3383(0.1)	Reference	24(0.0)	4(0.0)	Reference
Infants Birth Order	First	26274(39.1)	1101996(30.7)	0.18	26274(39.1)	26537(39.5)	0.01
	Second	16800(25.0)	1010282(28.1)	0.07	16800(25.0)	16742(24.9)	0.00
	Third or More	24090(35.9)	1480529(41.2)	Reference	24090(35.9)	23885(35.6)	Reference

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Table 3E Baseline characteristics stratified by hepatitis B status in 2018.

Characteristics		Unmatched Population			Matched Sample		
		Hep B+ (n=7808,0.21%)	Hep B- (n=3652163, 99.79%)	Standardized Difference*	Hep B+ (n=7808,50.00%)	Hep B- (n=7808,50.00%)	Standardized Difference*
Maternal Age		31.5 ± 5.5	29.0 ± 5.8	0.44	31.5 ± 5.5	31.4 ± 5.4	0.02
BMI		25.3 ± 6.0	27.2 ± 6.8	0.29	25.3 ± 6.0	25.3 ± 5.9	0.01
Maternal Race	White	2123(27.2)	2700070(73.9)	1.06	2123(27.2)	2102(26.9)	0.01
	Black	2104(27.0)	569142 (15.6)	0.28	2104(27.0)	2133(27.3)	0.01
	Asian	3270(41.9)	240718(6.6)	0.90	3270(41.9)	3279(42.0)	0.00
	Other Race	149(1.9)	96415(2.6)	Reference	311(4.0)	294(3.8)	Reference
WIC**		3282 (42.0)	1308397 (35.8)	0.13	3282 (42.0)	3306 (42.3)	0.01
Tobacco Use		494 (6.3)	235442 (6.4)	0.00	494 (6.3)	450 (5.8)	0.02
Previous Preterm Birth		353 (4.5)	128065 (3.5)	0.05	353 (4.5)	268 (3.4)	0.06
Previous Cesarean		1449 (18.6)	571788 (15.7)	0.08	1449 (18.6)	1456 (18.6)	0.00
Infertility Treatment Use		188 (2.4)	71780 (2.0)	0.03	188 (2.4)	110 (1.4)	0.07
Infants Plurality	One	7575(96.4)	3530299(96.7)	0.02	7575(96.4)	7629(97.7)	0.07
	Twice	280(3.6)	118460(3.2)	0.02	280(3.6)	177(2.3)	0.07
	Three or More	3(0.0)	3404(0.1)	Reference	3(0.0)	2(0.0)	Reference
Infants Birth Order	First	1928(24.7)	1126342(30.8)	0.14	1928(24.7)	1918(24.6)	0.00
	Second	2162(27.7)	1024920(28.1)	0.01	2162(27.7)	2159(27.7)	0.00
	Third or More	3178(47.6)	1500901 (41.1)	Reference	3178(47.6)	3731(47.8)	Reference

*Unlike the p-value, the standardized difference is not affected by sample size. Standardized differences are used in observational studies to compare the distribution of baseline covariates between exposure groups. Standardized differences larger than 0.10 suggest a meaningful imbalance in the baseline covariate (Austin 2009). These relatively large standardized differences are colored blue in the table above. Notably, the standardized differences in the matched sample all suggest balance between exposure groups.

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Table 4. Risk ratios of preterm birth for each sexually transmitted disease from 2016 to 2018

Sexually Transmitted Disease		Unmatched Population			Matched Sample		
		2016	2017	2018	2016	2017	2018
Hepatitis C	n	15500	16882	17753	15500	16882	17753
	Hepatitis C+ Risk	3071/15500 (19.81)	3313/16882 (19.62)	3515/17753 (19.80)	3071/15500 (19.81)	3313/16882 (19.62)	3515/17753 (19.80)
	Hepatitis C- Risk	420667/3765852 (11.17)	420881/3689315 (1.41)	418441/3642218 (1.49)	2104/15500 (13.57)	2350/16882 (13.92)	2525/17753 (14.22)
	RR (95% CI)	1.77 (1.72, 1.83)	1.72 (1.67, 1.77)	1.72 (1.67, 1.78)	1.46 (1.39, 1.54)	1.41 (1.34, 1.48)	1.39 (1.33, 1.46)
Gonorrhea	n	10040	10766	11173	10040	10766	11173
	Gonorrhea+ Risk	1730/10040 (17.23)	1937/10766 (17.99)	1995/11173 (17.86)	1730/10040 (17.23)	1937/10766 (17.99)	1995/11173 (17.86)
	Gonorrhea- Risk	422008/3771312 (11.19)	422257/3695431 (11.43)	419961/3648798 (11.51)	1405/10040 (13.99)	1523/10766 (14.15)	1622/11173 (14.52)
	RR (95% CI)	1.54 (1.48, 1.61)	1.57 (1.51, 1.64)	1.55 (1.49, 1.61)	1.23 (1.15, 1.31)	1.27 (1.20, 1.35)	1.23 (1.16, 1.31)
Syphilis	n	3235	3681	4157	3235	3681	4157
	Syphilis+ Risk	540/3235 (16.69)	628/3681 (17.06)	761/4157 (18.31)	540/3235 (16.69)	628/3681 (17.06)	761/4157 (18.31)
	Syphilis- Risk	423198/3778117 (11.20)	423566/3702516 (11.44)	421195/3655814 (11.52)	419/3235 (12.95)	529/3681 (14.37)	566/4157 (13.62)
	RR (95% CI)	1.49 (1.38, 1.61)	1.49 (1.39, 1.60)	1.59 (1.49, 1.69)	1.29 (1.15, 1.45)	1.19 (1.07, 1.32)	1.34 (1.22, 1.49)
Chlamydia	n	68418	67533	67164	68418	67533	67164
	Chlamydia+ Risk	9717/68418 (14.20)	9853/67533 (14.59)	9972/67164 (14.85)	9717/68418 (14.20)	9853/67533 (14.59)	9972/67164 (14.85)
	Chlamydia- Risk	414021/3712934 (11.15)	414341/3638664 (11.39)	411984/3592807 (11.47)	8497/68418 (12.42)	8458/67533 (12.52)	8435/67164 (12.56)
	RR (95% CI)	1.27 (1.25, 1.30)	1.28 (1.26, 1.31)	1.29 (1.27, 1.32)	1.14 (1.11, 1.18)	1.16 (1.13, 1.20)	1.18 (1.15, 1.21)
Hepatitis B	n	8464	8462	7808	8464	8462	7808
	Hepatitis B+ Risk	969/8464 (11.45)	1097/8462 (12.96)	1020/7808 (13.06)	969/8464 (11.45)	1097/8462 (12.96)	1020/7808 (13.06)
	Hepatitis B- Risk	422769/3772888 (11.21)	423097/3697735 (11.44)	420936/3652163 (11.53)	912/8464 (10.78)	930/8462 (10.99)	925/7808 (11.85)
	RR (95% CI)	1.02 (0.96, 1.08)	1.13 (1.07, 1.20)	1.13 (1.07, 1.20)	1.06 (0.98, 1.16)	1.18 (1.09, 1.28)	1.10 (1.01, 1.20)

Supplement Table 1. Differences between subjects included and subjects excluded in 2016

Characteristics		Subjects Included in the Study (N=3781352, 95.58%)	Subjects Excluded in the Study (N=174760, 4.42%)	Standardized Difference*
Maternal Age		28.7 ± 5.8	28.8 ± 6.0	0.02
BMI		26.8 ± 6.6	26.7 ± 6.6	0.01
Maternal Race	White	2793397(73.9%)	116619(66.7%)	0.16
	Black	587593(15.5%)	36953(21.1%)	0.15
	Asian	261548(6.9%)	13823(7.9%)	0.04
	More than one race	92688(2.5%)	4286(2.5%)	Reference
WIC**		1491230 (39.4%)	53574 (42.8%)	0.07
Tobacco Use		271417 (7.2%)	11371 (7.3%)	0.01
Previous Preterm Birth		116299 (3.1%)	5880 (3.4%)	0.02
Previous Cesarean		579630 (15.3%)	26629 (15.6%)	0.01
Infertility Treatment Use		66520 (1.8%)	2424 (1.4%)	0.03
Infants Plurality	One	3651864(96.6%)	168172(96.2%)	0.02
	Twice	125631(3.3%)	6430(3.7%)	0.02
	More than two	3857(0.1%)	158(0.10%)	Reference
Infants Birth Order	First	1179712(31.2%)	50595(30.0%)	0.05
	Second	1068184(28.3%)	45354(26.0%)	0.05
	More than second	1533456(40.6%)	78811(45.1%)	Reference
	Hepatitis B		8464 (0.2%)	491 (0.3%)
Hepatitis C		15500 (0.4%)	1096 (0.7%)	0.03
Gonorrhea		10040 (0.3%)	521 (0.3%)	0.01
Syphilis		3235 (0.1%)	200 (0.1%)	0.01
Chlamydia		68418 (1.8%)	3170 (1.9%)	0.01

*Unlike the p-value, the standardized difference is not affected by sample size. Standardized differences are used in observational studies to compare the distribution of baseline covariates between exposure groups. Standardized differences larger than 0.10 suggest a meaningful imbalance in the baseline covariate (Austin 2009). These relatively large standardized differences are colored blue in the table above. Notably, the standardized differences in the matched sample all suggest balance between exposure groups.

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Supplement Table 2. Differences between subjects included and subjects excluded in 2017

Characteristics		Subjects Included in the Study (N=3706197, 95.9%)	Subjects Excluded in the Study (N=158557, 4.1%)	Standardized Difference*
Maternal Age		28.8 ± 5.8	28.8 ± 6.0	0.01
BMI		27.0 ± 6.7	26.9 ± 6.7	0.01
Maternal Race	White	2715727(73.3%)	104683(66.0%)	0.16
	Black	591401 (16.0%)	35260(22.2%)	0.16
	Asian	259061 (7.0%)	11546(7.3%)	0.01
	More than one race	94975(2.6%)	4105(2.6%)	Reference
WIC**		1405374 (37.9%)	47679 (42.1%)	0.08
Tobacco Use		253922 (6.9%)	11053 (7.9%)	0.04
Previous Preterm Birth		120791 (3.3%)	5841 (3.8%)	0.03
Previous Cesarean		574817 (15.5%)	23708 (15.3%)	0.01
Infertility Treatment Use		71968 (2.0%)	2009 (1.4%)	0.04
Infants Plurality	One	3579671(96.6%)	152547(96.2%)	0.02
	Twice	122800(3.3%)	5808(3.7%)	0.02
	More than two	3726(0.1%)	202(0.1%)	Reference
Infants Birth Order	First	1146517(30.9%)	45241(28.5%)	0.05
	Second	1045894(28.2%)	40963(25.8%)	0.05
	More than second	1513786(40.8%)	72353(45.6%)	Reference
Hepatitis B		8462 (0.2%)	532 (0.4%)	0.02
Hepatitis C		16882 (0.5%)	1215 (0.8%)	0.05
Gonorrhea		10766 (0.3%)	570 (0.4%)	0.02
Syphilis		3681 (0.1%)	217 (0.1%)	0.02
Chlamydia		67533 (1.8%)	3047 (2.1%)	0.01

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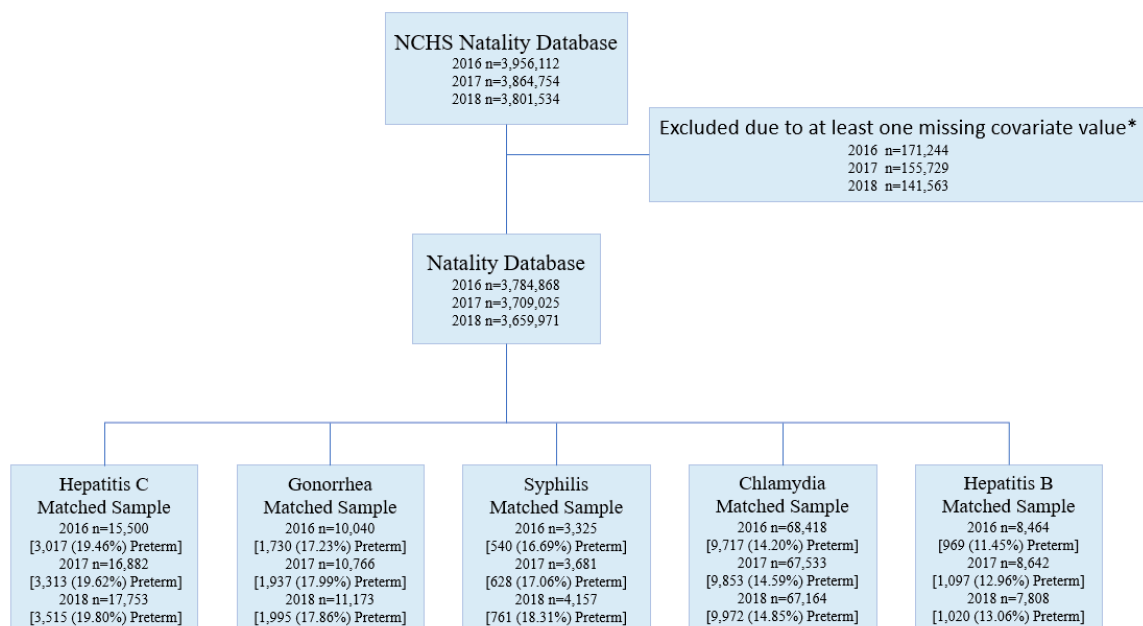
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Supplement Table 3. Differences between subjects included and subjects excluded in 2018

Characteristics		Subjects Included in the Study (N=3659971, 96.28%)	Subjects Excluded in the Study (N=141563, 3.72%)	Standardized Difference*
Maternal Age		29.0 ± 5.8	29.0 ± 6.0	0.00
BMI		27.2 ± 6.8	27.1 ± 6.8	0.01
Maternal Race	White	2702193(73.8%)	94871(67.1%)	0.15
	Black	571246(15.6%)	30352(21.4%)	0.15
	Asian	243988(6.7%)	9346(6.6%)	0.00
	More than one race	96564(2.6%)	4049(2.9%)	Reference
WIC**		1311679 (35.8%)	39899 (40.2%)	0.09
Tobacco Use		235936 (6.4%)	9424 (7.6%)	0.04
Previous Preterm Birth		128418 (3.5%)	5759 (4.2%)	0.03
Previous Cesarean		573237 (15.7%)	21635 (15.6%)	0.00
Infertility Treatment Use		71968 (2.0%)	2009 (1.4%)	0.04
Infants Plurality	One	3537824 (96.7%)	136291(96.3%)	0.02
	Twice	118740(3.2%)	5127(3.6%)	0.02
	More than two	3407(0.1%)	145(0.1%)	Reference
Infants Birth Order	First	1128270(30.8%)	40060(28.3%)	0.06
	Second	1027082(28.1%)	36351(25.7%)	0.05
	More than second	1504619(41.1%)	65152(46.0%)	Reference
	Hepatitis B		7808 (0.2%)	399 (0.3%)
Hepatitis C		17753 (0.5%)	1185 (0.9%)	0.05
Gonorrhea		11173 (0.3%)	568 (0.4%)	0.02
Syphilis		4157 (0.1%)	264 (0.2%)	0.02
Chlamydia		67164 (1.8%)	2704 (2.0%)	0.01

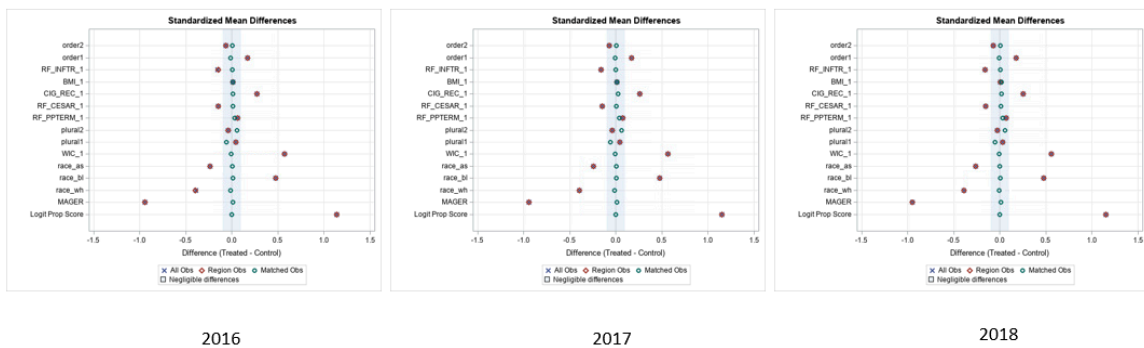
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Figure 1 Flow diagram for fifteen sub-studies

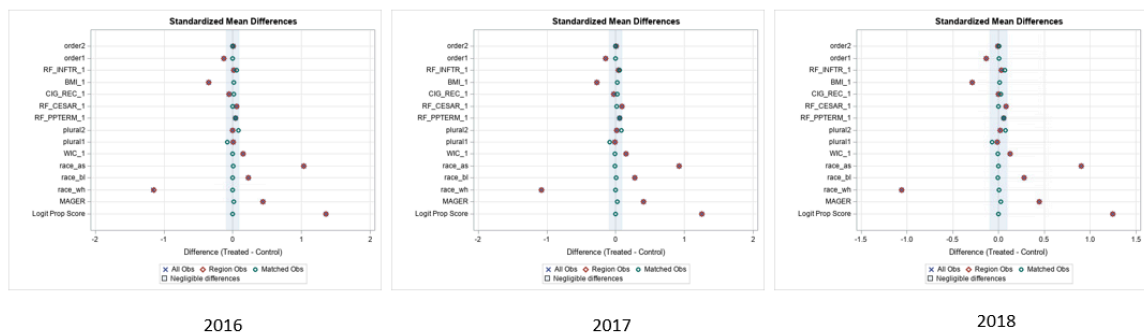
*Covariates considered in all fifteen sub-studies were maternal age, maternal race, smoking, poor maternal diet, body mass index (BMI), previous preterm birth, previous cesarean, infertility treatment used, infant plurality and birth order

Figure 2D Success of propensity score matching for chlamydia



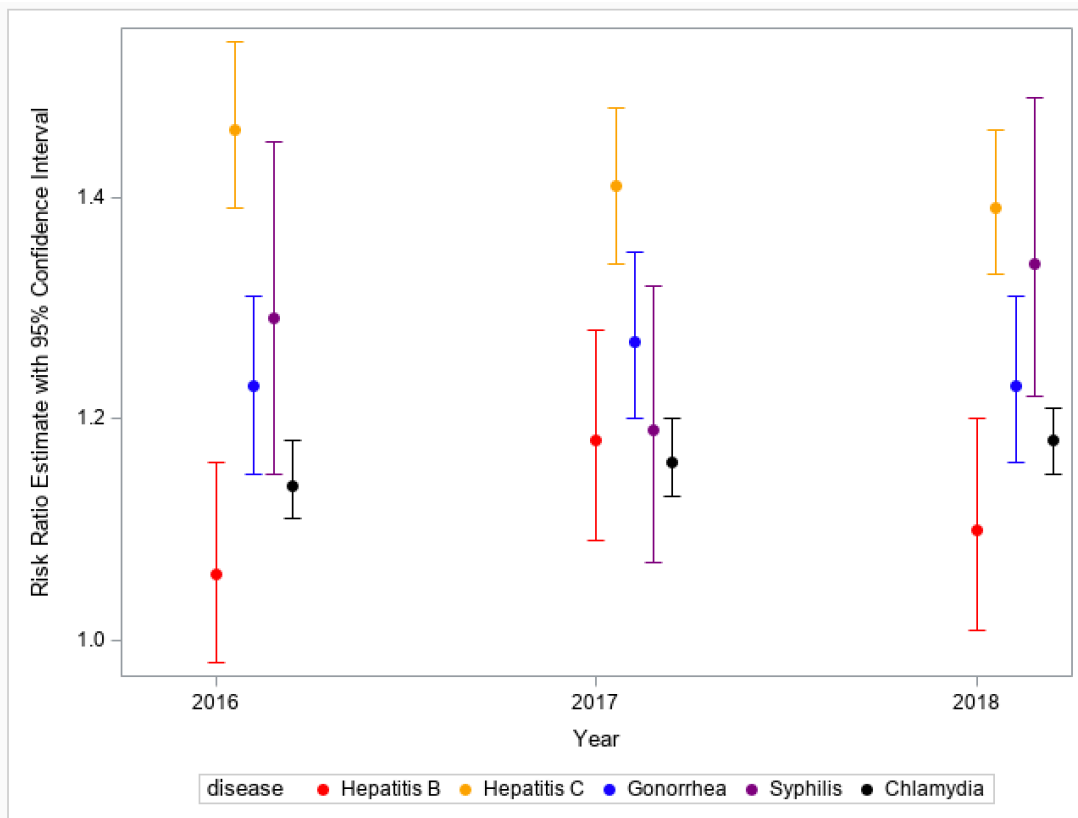
* Green circle is the matched observation, red square and cross mark the all observations

Figure 2E Success of propensity score matching for hepatitis B



* Green circle is the matched observation, red square and cross mark the all observations

Figure 3. Risk ratios of preterm birth for each of the sexually transmitted diseases, 2016 to 2018



*The error bars represent 95% confidence intervals.

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