Disclaimer

The following report(s) provides findings from an FDA-initiated query using Sentinel. While Sentinel queries may be undertaken to assess potential medical product safety risks, they may also be initiated for various other reasons. Some examples include determining a rate or count of an identified health outcome of interest, examining medical product use, exploring the feasibility of future, more detailed analyses within Sentinel, and seeking to better understand Sentinel capabilities.

Data obtained through Sentinel are intended to complement other types of evidence such as preclinical studies, clinical trials, postmarket studies, and adverse event reports, all of which are used by FDA to inform regulatory decisions regarding medical product safety. The information contained in this report is provided as part of FDA's commitment to place knowledge acquired from Sentinel in the public domain as soon as possible. Any public health actions taken by FDA regarding products involved in Sentinel queries will continue to be communicated through existing channels.

FDA wants to emphasize that the fact that FDA has initiated a query involving a medical product and is reporting findings related to that query does not mean that FDA is suggesting health care practitioners should change their prescribing practices for the medical product or that patients taking the medical product should stop using it. Patients who have questions about the use of an identified medical product should contact their health care practitioners.

The following report contains a description of the request, request specifications, and results from the modular program run(s).

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Overview for Request: tspreg_mpl2p_wp004

Request ID: tspreg_mpl2p_wp004

Request Description: In this report, we performed signal identification for selected antibiotics by monitoring maternal outcomes among pregnant patients exposed to oral macrolides, penicillins, or cephalosporins from twenty weeks of gestation to before delivery compared to pregnant patients without any antiobotic use during gestation.

Sentinel Routine Querying Module: Cohort Identification and Descriptive Analysis (CIDA) module, version 10.3.3, with Propensity Score Analysis and Signal Identification modules.
Data Source: We executed this query in the Merative™ MarketScan® Research Databases on December 9, 2022. The study period included data from October 1, 2015 through February 29, 2020 with the first valid live birth delivery of October 26, 2016 and the final valid live birth delivery date of February 29, 2020. Please see Appendix A for a list of dates of available data.

Study Design: We identified pregnant patients with use of oral macrolides, penicillins or cephalosporins from 20 weeks gestation to before delivery as our exposure group and pregnant patients without any antibiotic use during gestation as our control group. We excluded patients having preterm premature rupture of membrane diagnosis in the time from pregnancy start until index date or having used definite teratogenic drugs during any time of pregnancy. We addressed the confounding of disease severity by including only patients with mild or moderate infectious conditions. We used propensity score stratification and we monitored maternal pregnancy outcomes. This is a Type 4 analysis using the Propensity Score Analysis and Signal Identification modules in the Query Request Package (QRP) documentation.
Exposures of Interest: We identified users of macrolides, penicillins, or cephalosporins as exposed pregnant patients and non-antibiotic users as control pregnant patients. Only the first qualifying treatment episode of the exposures of interest was evaluated. See here for a list of generic and brand names of medical products used to identify oral macrolides, penicillins or cephalosporin, and here for a list of generic and brand names used to define injectable macrolides, penicillins, or cephalosporins and any use of other antibiotics for exclusion.
Cohort Eligibility Criteria: To be included in the cohort, we required pregnant patients to be continuously enrolled in health plans with medical and drug coverage for at least 391 days before delivery to delivery date during which gaps in coverage of up to 45 days were allowed. We only included qualifying members aged 10-54 with a single live birth outcome. We only included patients to have at least one respiratory tract infection (RTI) diagnosis from 143 days after pregnancy start to 8 days before delivery date. The first RTI diagnosis occurring within the RTI evaluation window was considered the indication date. A pregnant woman was classified as exposed if she has a dispensing or code for an oral macrolide, penicillin, or cephalosporin within three days before to seven days after the indication date and no previous use for any of these drugs during pregnancy. The index date was the date of the first qualifying antibiotic dispensing/code. A pregnant woman was classified as a non-antibiotic user if she has no dispensings/codes for an oral macrolide, penicillin, or cephalosporin during the entire pregnancy period. The index date among the non-antibiotic patients was assigned based on a random draw of the empirical distribution of the number of days between the fill and indication dates in the antibiotic group. We excluded patients having any antibiotic other than the study drugs, having any injectable macrolide, penicillin, or cephalosporin, having any infection other than RTI, or being hospitalized with any RTI diagnosis. We also removed patients using oral macrolides, penicillins, and cephalosporins from pregnancy start to before 20 weeks of gestation. We excluded deliveries with a preterm premature rupture of membrane-related diagnosis from pregnancy start to the date of antibiotic initiation. Any pregnancy episodes with any oral or injectable teratogenic drug from the pregnancy start date to index date are also excluded. See here for lists of generic drug names, International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM).

Follow-up Time: We followed pregnant patients from one day after index date through delivery date. We followed patients regardless of the days supply of the exposure medications in their pregnancy.

Overview for Request: tspreg_mpl2p_wp004

Propensity Score Estimation: We assessed age on the day of live birth delivery, gestational age at the time of antibiotic initiation and antibiotic related indications (ear, nose, and throat infections or lower respiratory infections) in the 7 days prior to 3 days after antibiotic initiation and included them in the propensity score model. We additionally assessed alcohol abuse, asthma, cardiac valvular disease, chronic congestive heart failure, chronic ischemic heart disease, chronic renal disease, congenital heart disease, cystic fibrosis, drug abuse, epilepsy/seizures, HIV, inflammatory bowel disease, leukemia/lymphoma, obesity, diabetes, hypertension, previous cesarean delivery, psychiatric disorders, pulmonary hypertension, rheumatoid arthritis, sickle cell disease, systemic lupus erythematosus, tobacco use, vaccine administration, screening examinations and disease management trial, PAP smear, HPV DNA test, fecal occult blood test, end stage liver disease in the 90 days before pregnancy start through the day prior to antibiotic indication and included these in the propensity score model. We assessed health service utilization intensity metrics from pregnancy start through before 20 weeks of gestation and included these in the propensity score model. The Propensity Score Analysis (PSA) module was used to calculate the propensity scores. Covariates were defined using ICD-10-CM, ICD-10-PCS, CPT-4, HCPCS, diagnosis and procedure codes as well as, NDC drug codes. For a list of codes used to defined covariates, please see here.

Stratification: After trimming non-overlap areas in the propensity score, pregnant patients were stratified into deciles of the propensity score with a two-step stratification approach. We first stratified the trimmed cohort into deciles of the propensity score and then we only stratified based on gestational age at treatment initiation (with 6 weeks gestational age cut-offs: [20-25], [26, 31], [32, 37], [38, 42] weeks) in a given propensity score stratum if we detected imbalanced distributions of that variable.

Outcome Assessment via Signal Identification: After trimming, we evaluated new health outcomes of interest (HOI). We used a hierarchical tree of ICD-10-CM diagnostic codes in the O00-O9A (Pregnancy, childbirth and the puerperium) chapter of the ICD-10 codebook.

In our analyses, we identified incident HOIs as the diagnosis to occur beginning one day after exposure initiation until the delivery date and we excluded post-partum conditions from the Maternal Outcome Tree. For an outcome to be considered incident, there were required to be no outcomes with the same first 4 digits of the ICD-10-CM code from 230 days before index date to the HOI date in inpatient or emergency department visits.

Tree-Based Scan Statistic: These data were evaluated via the TreeScan™ software (v.2.0) to determine whether there were imbalances in outcome occurrence between the two groups that rose to the level of statistical significance. TreeScan™ is a data-mining software that implements tree-based scan statistics. Under the null hypothesis, there is no position on the tree where outcomes are expected to occur in greater numbers than expected counts based on a referent rate. We used conditional Poisson tree-based scan statistic to calculate the log likelihood ratio for every node at level 3, 4 and 5 of the outcome tree. See here for list of International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) Codes Included in the Maternal Outcome Tree.

Sensitivity analyses: We conducted two sensitivity analyses by enhancing the ability of confounding control. One analysis is with 20 strata in the propensity score stratification. Another one used the high dimension propensity score in addition to the empirical-specified covariates in the propensity score model and a decile proprensity score stratification.

Please see Appendix B for the top 25 codes selected by HDPS, Appendices C and C.1 for design diagrams for this request and Appendices D and D.1 for the specifications of parameters used in this request.

Limitations: Algorithms to define exposures, outcomes, inclusion and exclusion criteria, and covariates are imperfect and may be misclassified. Therefore, data should be interpreted with this limitation in mind.

Notes: Please contact the Sentinel Operations Center (info@sentinelsystem.org) for questions and to provide comments/suggestions for future enhancements to this document. For more information on Sentinel's routine querying modules, please refer to the documentation (https://dev.sentinelsystem.org/projects/SENTINEL/repos/sentinel-routine-querying-tool-documentation/browse).

Sentinel

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Glossary of Terms for Analyses Using
Cohort Identification and Descriptive Analysis (CIDA) Module*

Amount Supplied - number of units (pills, tablets, vials) dispensed. Net amount per NDC per dispensing.
Blackout Period - number of days at the beginning of a treatment episode that events are to be ignored. If an event occurs during the blackout period, the episode is excluded.
Care Setting - type of medical encounter or facility where the exposure, event, or condition code was recorded. Possible care settings include: Inpatient Hospital Stay (IP), Non-Acute Institutional Stay (IS), Emergency Department (ED), Ambulatory Visit (AV), and Other Ambulatory Visit (OA). For laboratory results, possible care settings include: Emergency Department (E), Home (H), Inpatient (I), Outpatient (O), or Unknown or Missing (U). The Care Setting, along with the Principal Diagnosis Indicator (PDX), forms the Care Setting/PDX parameter.

- **Ambulatory Visit (AV) -** includes visits at outpatient clinics, same-day surgeries, urgent care visits, and other same-day ambulatory hospital encounters, but excludes emergency department encounters.
- **Emergency Department (ED) -** includes ED encounters that become inpatient stays (in which case inpatient stays would be a separate encounter). Excludes urgent care visits.
- **Inpatient Hospital Stay (IP) -** includes all inpatient stays, same-day hospital discharges, hospital transfers, and acute hospital care where the discharge is after the admission date.
- **Non-Acute Institutional Stay (IS) -** includes hospice, skilled nursing facility (SNF), rehab center, nursing home, residential, overnight non-hospital dialysis and other non-hospital stays.
- **Other Ambulatory Visit (OA) -** includes other non overnight AV encounters such as hospice visits, home health visits, skilled nursing facility visits, other non-hospital visits, as well as telemedicine, telephone and email

Charlson/Elixhauser Combined Comorbidity Score - calculated based on comorbidities observed during a requester-defined window around the exposure episode start date (e.g., in the 183 days prior to index).
Code Days - the minimum number of times the diagnosis must be found during the evaluation period in order to fulfill the algorithm to identify the corresponding patient characteristic.
Cohort Definition (drug/exposure) - indicates how the cohort will be defined: 01: Cohort includes only the first valid treatment episode during the query period; 02: Cohort includes all valid treatment episodes during the query period; 03: Cohort includes all valid treatment episodes during the query period until an event occurs.
Computed Start Marketing Date - represents the first observed dispensing date among all valid users within a GROUP (scenario) within each Data Partner site.
Days Supplied - number of days supplied for all dispensings in qualifying treatment episodes.
Eligible Members - number of members eligible for an incident treatment episode (defined by the drug/exposure and event washout periods) with drug and medical coverage during the query period.
Enrollment Gap - number of days allowed between two consecutive enrollment periods without breaking a "continuously enrolled" sequence.
Episodes - treatment episodes; length of episode is determined by days supplied in one dispensing or consecutive dispensings bridged by the episode gap.
Episode Gap - number of days allowed between two (or more) consecutive exposures (dispensings/procedures) to be considered the same treatment episode.
Event Deduplication - specifies how events are counted by the Modular Program (MP) algorithm: 0: Counts all occurrences of a health outcome of interest (HOI) during an exposure episode; 1: de-duplicates occurrences of the same HOI code and code type on the same day; 2: de-duplicates occurrences of the same HOI group on the same day (e.g., de-duplicates at the group level).
Exposure Episode Length - number of days after exposure initiation that is considered "exposed time."
Exposure Extension Period - number of days post treatment period in which the outcomes/events are counted for a treatment episode. Extensions are added after any episode gaps have been bridged.
Lookback Period - number of days wherein a member is required to have evidence of pre-existing condition (diagnosis/procedure/drug dispensing).
Maximum Episode Duration - truncates exposure episodes after a requester-specified number of exposed days. Applied after any gaps are bridged and extension days added to the length of the exposure episode.

Member-Years - sum of all days of enrollment with medical and drug coverage in the query period preceded by an exposure washout period all divided by 365.25.
Minimum Days Supplied - specifies a minimum number of days in length of the days supplied for the episode to be considered.
Minimum Episode Duration - specifies a minimum number of days in length of the episode for it to be considered. Applied after any gaps are bridged and extension days added to the length of the exposure episode.
Monitoring Period - used to define time periods of interest for both sequential analysis and simple cohort characterization requests.
Principal Diagnosis (PDX) - diagnosis or condition established to be chiefly responsible for admission of the patient to the hospital. 'P' = principal diagnosis, 'S' = secondary diagnosis, 'X' = unspecified diagnosis, '.' = blank. Along with the Care Setting values, forms the Caresetting/PDX parameter.
Query Period - period in which the modular program looks for exposures and outcomes of interest.
Switch Evaluation Step Value - value used to differentiate evaluation step. Each switch pattern can support up to 2 evaluation steps (0 = switch pattern evaluation start; 1 = first evaluation; 2 = second evaluation).
Switch Gap Inclusion Indicator - indicator for whether gaps in treatment episodes that are included in a switch episode will be counted as part of the switch episode duration.
Switch Pattern Cohort Inclusion Date - indicates which date to use for inclusion into the switch pattern cohort of interest as well as optionally as the index date of the treatment episode initiating the switch pattern. Valid options are the product approval date, product marketing date, other requester defined date, or computed start marketing date.
Switch Pattern Cohort Inclusion Strategy - indicates how the switch pattern cohort inclusion date will be used: 01: used only as a switch cohort entry date. First treatment episode dispensing date is used as index for computing time to first switch; 02: used as switch cohort entry date and as initial switch step index date for computing time to first
Treatment Episode Truncation Indicator - indicates whether the exposure episode will be truncated at the occurrence of a requester-specified code.
Washout Period (drug/exposure) - number of days a user is required to have no evidence of prior exposure (drug dispensing/procedure) and continuous drug and medical coverage prior to an incident treatment episode.
Washout Period (event/outcome) - number of days a user is required to have no evidence of a prior event (procedure/diagnosis) and continuous drug and medical coverage prior to an incident treatment episode.
Years at Risk - number of days supplied plus any episode gaps and exposure extension periods all divided by 365.25.

*all terms may not be used in this report

Glossary of Terms for Analyses Using Propensity Score Analysis (PSA) Module*

Covariate - requester defined binary variable to include in the propensity score estimation model (e.g., diabetes, heart failure, etc.) during requester-defined lookback period. Requester may also choose to add any of the following categorical, continuous,

1. Age (continuous)
2. Sex
3. Time period (i.e., monitoring period for sequential analyses)
4. Year of exposure
5. Comorbidity score
6. Medical utilization – number of inpatient stays
7. Medical utilization – number of institutional stays
8. Medical utilization – number of emergency department visits
9. Medical utilization – number of outpatient visits
10. Health care utilization – number of other ambulatory encounters (e.g., telemedicine, email consults)
11. Drug utilization – number of dispensings
12. Drug utilization – number of unique generics dispensed

Covariate Evaluation Window - specified number of days relative to index date to evaluate the occurrence of covariates of interest. Note: members are required to have continuous enrollment during the covariate evaluation window, regardless of the **Individual Level Data Return -** program may return individual-level, de-identified datasets to the Sentinel Operations Center (SOC). While the datasets contain a single row per patient for each specified analysis, patient identifiers such as a patient ID are not included in the output. Individual-level datasets are returned to the SOC, aggregated, and used to calculate effect estimates **Mahalanobis Distance -** provides a measure of balance across all variables while accounting for their correlation. **Matching Caliper -** maximum allowed difference in propensity scores between treatment and control patients. Requester may select any caliper (e.g., 0.01, 0.025, and 0.05). **Matching Ratio -** patients in exposed and comparator groups are nearest neighbor matched by a 1:1 or 1:n (up to 10) matching **Matched Conditional and Unconditional Analysis -** in a conditional matched analysis, a Cox model, stratified by Data Partner site and matched set, is run on the matched population. This can be done for both the both 1:1 and 1:n matched cohorts. In an unconditional analysis, a Cox model, stratified by Data Partner site only, is run on the matched population. This can be done for **Propensity Score Stratification -** option to stratify propensity scores based on requester-defined percentiles in the unmatched population. In a stratified analysis, a Cox model, stratified by Data Partner site, is run on the stratified population. Note that all **PSM Tool -** performs effect estimation by comparing exposure propensity-score matched parallel new user cohorts. Propensity score estimation and matching are conducted within each Sentinel Data Partner site via distributed programming code; data are **Risk-set Level Data Return -** alternative to the patient-level data return approach. In this approach, the PSM tool will produce de-identified, risk-set level datasets instead of or in addition to individual-level output. Whereas each observation in the patient-level datasets represents one patient in the cohort, each observation in the risk set dataset represents one event. Risk sets are created at the Data Partner site, returned to the SOC, aggregated, and used to calculate effect estimates via case-centered logistic regression. **Subgroup Analysis -** may be conducted using any requester-defined covariates. Subgroup analyses may be performed in the **Zero Cell Correction -** indicator for whether to screen variables with a zero correction added to each cell in the confounder/outcome 2x2 table. Recommended when the number of exposed outcomes is fewer than 150.

*all terms may not be used in this report

Table 1a. Unadjusted Characteristics of the Step Approach with 6-Week Gestational Age Strata and 10 for PS (Aggregated) in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

	Medical Product				Covariate Balance	
	Pregnant Exposed Group		Pregnant Unexposed Group			
Mother Characteristics[1,2]	Number/Mean	Percent/ Standard Deviation[3]	Number/Mean	Percent/ Standard Deviation[3]	Absolute Difference	Standardized Difference
Unique patients	7,494	100.0%	6,992	100.0%	N/A	N/A
Demographic Characteristics						
Age (years)	31.2	5.0	30.5	5.3	0.719	0.140
Age						
10-54 years	7,494	100.0%	6,992	100.0%	0.000	N/A
Sex						
Female	7,494	100.0%	6,992	100.0%	0.000	N/A
Race[4]						
Unknown	7,494	100.0%	6,992	100.0%	0.000	N/A
Hispanic origin						
Unknown	7,494	100.0%	6,992	100.0%	0.000	N/A
Year						
2016	328	4.4%	281	4.0%	0.358	0.018
2017	2,462	32.9%	1,991	28.5%	4.378	0.095
2018	2,216	29.6%	2,285	32.7%	-3.110	-0.067
2019	2,294	30.6%	2,258	32.3%	-1.683	-0.036
2020	194	2.6%	177	2.5%	0.057	0.004
Pregnancy Characteristics						
Pre-Term (0-258 days)	342	4.6%	307	4.4%	0.173	0.008
Term (259-280 days)	4,803	64.1%	4,287	61.3%	2.778	0.057
Post-Term (281-301 days)	1,815	24.2%	1,950	27.9%	-3.670	-0.084
Unknown Term	534	7.1%	448	6.4%	0.718	0.029
Gestational age[5] at delivery	39.8	1.4	39.9	1.4	-0.075	-0.053
Exposure Characteristics						
Gestational age[5] of first exposure (weeks)	29.3	5.2	0.0	0.5	29.325	7.953

Table 1a. Unadjusted Characteristics of the Step Approach with 6-Week Gestational Age Strata and 10 for PS (Aggregated) in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

	Medical Product				Covariate Balance	
	Pregnant Exposed Group		Pregnant Unexposed Group			
Mother Characteristics[1,2]	Number/Mean	Percent/ Standard Deviation[3]	Number/Mean	Percent/ Standard Deviation[3]	Absolute Difference	Standardized Difference
Mean number of dispensings in first trimester	0.0	N/A	0.0	N/A	N/A	N/A
Mean number of dispensings in second trimester	0.4	0.5	0.0	N/A	N/A	N/A
Mean number of dispensings in third trimester	0.8	0.6	0.0	0.0	0.793	1.872
Exposed during first trimester	0	0.0%	0	0.0%	N/A	N/A
Exposed during second trimester	2,597	34.7%	0	0.0%	N/A	N/A
Exposed during third trimester	5,281	70.5%	1	0.0%	70.455	2.183
Health Characteristics						
Ear, Nose, and Throat Infections	6,484	86.5%	5,278	75.5%	11.036	0.284
Gastrointestinal Infections	0	0.0%	0	0.0%	N/A	N/A
Lower Respiratory Infections	1,371	18.3%	1,957	28.0%	-9.694	-0.231
Sexually Transmitted Infections	0	0.0%	0	0.0%	N/A	N/A
Other Indications	0	0.0%	0	0.0%	N/A	N/A
Pelvic Inflammatory Disease	0	0.0%	0	0.0%	N/A	N/A
Skin and Subcutaneous Tissue	0	0.0%	0	0.0%	N/A	N/A
Urinary Tract and Kidney Infections	0	0.0%	0	0.0%	N/A	N/A
Alcohol Abuse	16	0.2%	15	0.2%	-0.001	-0.000
Asthma	311	4.1%	211	3.0%	1.132	0.061
Cardiac Valvular Disease	51	0.7%	30	0.4%	0.251	0.034
Chronic Congestive Heart Failure	1	0.0%	0	0.0%	N/A	N/A
Chronic Ischemic Heart Disease	6	0.1%	3	0.0%	0.037	0.015
Chronic Renal Disease	26	0.3%	29	0.4%	-0.068	-0.011
Congenital Heart Disease	31	0.4%	22	0.3%	0.099	0.016
Cystic Fibrosis	7	0.1%	5	0.1%	0.022	0.008

Table 1a. Unadjusted Characteristics of the Step Approach with 6-Week Gestational Age Strata and 10 for PS (Aggregated) in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

	Medical Product				Covariate Balance	
	Pregnant Exposed Group		Pregnant Unexposed Group			
Mother Characteristics[1,2]	Number/Mean	Percent/ Standard Deviation[3]	Number/Mean	Percent/ Standard Deviation[3]	Absolute Difference	Standardized Difference
Drug Abuse	50	0.7%	56	0.8%	-0.134	-0.016
Epilepsy/Seizures	23	0.3%	16	0.2%	0.078	0.015
HIV	0	0.0%	2	0.0%	N/A	N/A
Inflammatory Bowel Disease	25	0.3%	34	0.5%	-0.153	-0.024
Leukemia/Lymphoma	3	0.0%	6	0.1%	-0.046	-0.018
Obesity	986	13.2%	807	11.5%	1.615	0.049
Preexisting Diabetes	111	1.5%	95	1.4%	0.122	0.010
Preexisting Hypertension	241	3.2%	222	3.2%	0.041	0.002
Previous Cesarean Delivery	279	3.7%	231	3.3%	0.419	0.023
Psychiatric Disorders	992	13.2%	837	12.0%	1.266	0.038
Pulmonary Hypertension	0	0.0%	1	0.0%	N/A	N/A
Rheumatoid Arthritis	14	0.2%	18	0.3%	-0.071	-0.015
Sickle Cell Disease	8	0.1%	13	0.2%	-0.079	-0.021
Systemic Lupus Erythematosus	16	0.2%	14	0.2%	0.013	0.003
Tobacco Use	107	1.4%	105	1.5%	-0.074	-0.006
Vaccine Administration	28	0.4%	27	0.4%	-0.013	-0.002
Screening Examinations and Disease Management Training	1	0.0%	3	0.0%	-0.030	-0.018
Pap Smear	831	11.1%	729	10.4%	0.663	0.021
HPV DNA Test	0	0.0%	0	0.0%	N/A	N/A
Fecal Occult Blood Test	16	0.2%	15	0.2%	-0.001	-0.000
Teratogenic Drugs	0	0.0%	0	0.0%	N/A	N/A
End Stage Liver Disease	0	0.0%	0	0.0%	N/A	N/A
Gestational Age 20-25 weeks	2,658	35.5%	2,328	33.3%	2.173	0.046
Gestational Age 26-31 weeks	2,504	33.4%	2,293	32.8%	0.619	0.013
Gestational Age 32-37 weeks	2,113	28.2%	2,146	30.7%	-2.496	-0.055

Table 1a. Unadjusted Characteristics of the Step Approach with 6-Week Gestational Age Strata and 10 for PS (Aggregated) in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

	Medical Product				Covariate Balance	
	Pregnant Exposed Group		Pregnant Unexposed Group			
Mother Characteristics[1,2]	Number/Mean	Percent/ Standard Deviation[3]	Number/Mean	Percent/ Standard Deviation[3]	Absolute Difference	Standardized Difference
Gestational Age 38-42 weeks	219	2.9%	225	3.2%	-0.296	-0.017
Health Service Utilization Intensity Metrics						
Mean number of ambulatory encounters	5.8	4.4	5.7	4.4	0.032	0.007
Mean number of emergency room encounters	0.2	0.6	0.2	0.6	-0.004	-0.006
Mean number of inpatient hospital encounters	0.0	0.1	0.0	0.1	-0.000	-0.006
Mean number of non-acute institutional encounters	0.0	N/A	0.0	N/A	N/A	N/A
Mean number of other ambulatory encounters	2.1	2.2	2.0	2.1	0.134	0.062
Mean number of filled prescriptions	2.4	3.3	1.8	3.0	0.527	0.166
Mean number of generics dispensed	1.4	1.6	1.1	1.5	0.286	0.186
Mean number of unique drug classes dispensed	1.3	1.5	1.0	1.4	0.281	0.191

[1]Covariates in blue show a standardized difference greater than 0.1.

[2]Baseline period in reference to user defined index date (pregnancy start, exposure date, or delivery date).

[3]Value represents standard deviation where no % follows the value.

[4]Race data may not be completely populated at all Data Partners; therefore, data about race may be incomplete.

[5]Gestational age estimated using a claims-based algorithm, previously validated in the Medication Exposure in Pregnancy Risk Evaluation Program (MEPREP), to identify pregnancies ending in a live birth. ICD-10-CM diagnosis codes indicative of weeks of gestation, and ICD-9-CM and ICD-10-CM diagnosis codes for preterm and post-term deliveries, were used to calculate the length of the pregnancy episode. Codes had to occur within 7 days of a delivery date in the inpatient setting. In absence of pre-/post-term codes, pregnancy duration was set to 273 days.

Table 1b. Weighted Characteristics of Step Approach with 6-Week Gestational Age Strata and 10 for PS (Propensity Score Stratified, Aggregated), Percentiles: 10, in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

	Medical Product				Covariate Balance	
	Pregnant Exposed Group		Pregnant Unexposed Group			
Mother Characteristics[1,2,3]	Number/Mean	Percent/ Standard Deviation[4]	Number/Mean	Percent/ Standard Deviation[4]	Absolute Difference	Standardized Difference
Unique patients	7,493	100.0%	6,985	100.0%	N/A	N/A
Demographic Characteristics						
Age (years)	30.9	5.0	30.9	5.2	-0.014	-0.003
Age						
10-54 years	7,493	100.0%	6,985	100.0%	0.000	N/A
Sex						
Female	7,493	100.0%	6,985	100.0%	0.000	N/A
Race[5]						
Unknown	7,493	100.0%	6,985	100.0%	0.000	N/A
Hispanic origin						
Unknown	7,493	100.0%	6,985	100.0%	0.000	N/A
Year						
2016	339	4.5%	286	4.1%	0.435	0.021
2017	2,460	32.8%	2,003	28.7%	4.157	0.090
2018	2,221	29.6%	2,262	32.4%	-2.734	-0.059
2019	2,275	30.4%	2,259	32.3%	-1.983	-0.043
2020	198	2.6%	176	2.5%	0.125	0.008
Pregnancy Characteristics						
Pre-Term (0-258 days)	338	4.5%	313	4.5%	0.037	0.002
Term (259-280 days)	4,777	63.8%	4,286	61.4%	2.397	0.050
Post-Term (281-301 days)	1,850	24.7%	1,934	27.7%	-2.996	-0.068
Unknown Term	528	7.0%	453	6.5%	0.562	0.022
Gestational age[6] at delivery	39.8	1.4	39.9	1.4	-0.056	-0.039
Exposure Characteristics						
Gestational age[6] of first exposure (weeks)	29.5	5.2	0.0	0.5	29.481	7.971
Mean number of dispensings in first trimester	0.0	N/A	0.0	N/A	0.000	N/A

Table 1b. Weighted Characteristics of Step Approach with 6-Week Gestational Age Strata and 10 for PS (Propensity Score Stratified, Aggregated), Percentiles: 10, in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

	Medical Product				Covariate Balance	
	Pregnant Exposed Group		Pregnant Unexposed Group			
Mother Characteristics[1,2,3]	Number/Mean	Percent/ Standard Deviation[4]	Number/Mean	Percent/ Standard Deviation[4]	Absolute Difference	Standardized Difference
Mean number of dispensings in second trimester	0.4	0.5	0.0	N/A	0.354	0.970
Mean number of dispensings in third trimester	0.8	0.6	0.0	0.0	0.799	1.912
Exposed during first trimester	0	0.0%	0	0.0%	N/A	N/A
Exposed during second trimester	2,516	33.6%	0	0.0%	N/A	N/A
Exposed during third trimester	5,344	71.3%	1	0.0%	71.311	2.229
Health Characteristics						
Ear, Nose, and Throat Infections	6,085	81.2%	5,667	81.1%	0.092	0.002
Gastrointestinal Infections	0	0.0%	0	0.0%	N/A	N/A
Lower Respiratory Infections	1,721	23.0%	1,607	23.0%	-0.047	-0.001
Sexually Transmitted Infections	0	0.0%	0	0.0%	N/A	N/A
Other Indications	0	0.0%	0	0.0%	N/A	N/A
Pelvic Inflammatory Disease	0	0.0%	0	0.0%	N/A	N/A
Skin and Subcutaneous Tissue	0	0.0%	0	0.0%	N/A	N/A
Urinary Tract and Kidney Infections	0	0.0%	0	0.0%	N/A	N/A
Alcohol Abuse	17	0.2%	15	0.2%	0.005	0.001
Asthma	283	3.8%	244	3.5%	0.275	0.015
Cardiac Valvular Disease	43	0.6%	36	0.5%	0.054	0.007
Chronic Congestive Heart Failure	0	0.0%	0	0.0%	N/A	N/A
Chronic Ischemic Heart Disease	5	0.1%	4	0.1%	0.012	0.005
Chronic Renal Disease	29	0.4%	26	0.4%	0.022	0.004
Congenital Heart Disease	27	0.4%	24	0.3%	0.022	0.004
Cystic Fibrosis	6	0.1%	6	0.1%	0.001	0.000
Drug Abuse	55	0.7%	52	0.7%	-0.011	-0.001
Epilepsy/Seizures	20	0.3%	17	0.2%	0.017	0.003
HIV	0	0.0%	0	0.0%	N/A	N/A
Inflammatory Bowel Disease	31	0.4%	29	0.4%	-0.008	-0.001

Table 1b. Weighted Characteristics of Step Approach with 6-Week Gestational Age Strata and 10 for PS (Propensity Score Stratified, Aggregated), Percentiles: 10, in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

	Medical Product				Covariate Balance	
	Pregnant Exposed Group		Pregnant Unexposed Group			
Mother Characteristics[1,2,3]	Number/Mean	Percent/ Standard Deviation[4]	Number/Mean	Percent/ Standard Deviation[4]	Absolute Difference	Standardized Difference
Leukemia/Lymphoma	5	0.1%	4	0.1%	0.007	0.003
Obesity	943	12.6%	861	12.3%	0.260	0.008
Preexisting Diabetes	109	1.5%	97	1.4%	0.068	0.006
Preexisting Hypertension	246	3.3%	222	3.2%	0.110	0.006
Previous Cesarean Delivery	261	3.5%	245	3.5%	-0.028	-0.002
Psychiatric Disorders	949	12.7%	867	12.4%	0.259	0.008
Pulmonary Hypertension	0	0.0%	0	0.0%	N/A	N/A
Rheumatoid Arthritis	16	0.2%	15	0.2%	-0.003	-0.001
Sickle Cell Disease	10	0.1%	9	0.1%	0.001	0.000
Systemic Lupus Erythematosus	16	0.2%	15	0.2%	0.005	0.001
Tobacco Use	109	1.4%	99	1.4%	0.027	0.002
Vaccine Administration	28	0.4%	26	0.4%	-0.000	-0.000
Screening Examinations and Disease Management Training	2	0.0%	2	0.0%	-0.009	-0.006
Pap Smear	807	10.8%	754	10.8%	-0.028	-0.001
HPV DNA Test	0	0.0%	0	0.0%	N/A	N/A
Fecal Occult Blood Test	15	0.2%	14	0.2%	0.005	0.001
Teratogenic Drugs	0	0.0%	0	0.0%	N/A	N/A
End Stage Liver Disease	0	0.0%	0	0.0%	N/A	N/A
Gestational Age 20-25 weeks	2,574	34.4%	2,399	34.3%	0.012	0.000
Gestational Age 26-31 weeks	2,480	33.1%	2,315	33.1%	-0.052	-0.001
Gestational Age 32-37 weeks	2,209	29.5%	2,058	29.5%	0.025	0.001
Gestational Age 38-42 weeks	230	3.1%	213	3.0%	0.015	0.001
Health Service Utilization Intensity Metrics						
Mean number of ambulatory encounters	5.8	4.5	5.8	4.3	0.028	0.006
Mean number of emergency room encounters	0.2	0.6	0.2	0.6	0.003	0.005
Mean number of inpatient hospital encounters	0.0	0.1	0.0	0.1	-0.000	-0.000

Table 1b. Weighted Characteristics of Step Approach with 6-Week Gestational Age Strata and 10 for PS (Propensity Score Stratified, Aggregated), Percentiles: 10, in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

	Medical Product				Covariate Balance	
	Pregnant Exposed Group		Pregnant Unexposed Group			
Mother Characteristics[1,2,3]	Number/Mean	Percent/ Standard Deviation[4]	Number/Mean	Percent/ Standard Deviation[4]	Absolute Difference	Standardized Difference
Mean number of non-acute institutional encounters	0.0	N/A	0.0	N/A	0.000	N/A
Mean number of other ambulatory encounters	2.1	2.2	2.1	2.1	0.013	0.006
Mean number of filled prescriptions	2.2	3.1	2.1	3.3	0.105	0.033
Mean number of generics dispensed	1.2	1.5	1.2	1.6	0.049	0.032
Mean number of unique drug classes dispensed	1.2	1.5	1.2	1.5	0.055	0.037

[1]Covariates in blue show a standardized difference greater than 0.1.

[2]Weighted patient characteristics tables facilitate the assessment of covariate balance after propensity score (PS) stratification and should not be interpreted as a description of the unweighted population. Treated/control patients are weighted by the proportion of the total patient population included in their PS stratum divided by the proportion of the total treated/control patient population included in their PS stratum.

[3]Baseline period in reference to user defined index date (pregnancy start, exposure date, or delivery date).

[4]Value represents standard deviation where no % follows the value.

[5]Race data may not be completely populated at all Data Partners; therefore, data about race may be incomplete.

[6]Gestational age estimated using a claims-based algorithm, previously validated in the Medication Exposure in Pregnancy Risk Evaluation Program (MEPREP), to identify pregnancies ending in a live birth. ICD-10-CM diagnosis codes indicative of weeks of gestation, and ICD-9-CM and ICD-10-CM diagnosis codes for preterm and post-term deliveries, were used to calculate the length of the pregnancy episode. Codes had to occur within 7 days of a delivery date in the inpatient setting. In absence of pre-/post-term codes, pregnancy duration was set to 273 days.

Table 1c. Unadjusted Characteristics of Step Approach with 6-Week Gestational Age Strata and High Dimensional Propensity Score (Propensity Score Stratified, Aggregated), Percentiles: 10, in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

	Medical Product				Covariate Balance	
	Pregnant Exposed Group		Pregnant Unexposed Group			
Mother Characteristics[1,2]	Number/Mean	Percent/ Standard Deviation[3]	Number/Mean	Percent/ Standard Deviation[3]	Absolute Difference	Standardized Difference
Unique patients	7,494	100.0%	6,992	100.0%	N/A	N/A
Demographic Characteristics						
Age (years)	31.2	5.0	30.5	5.3	0.719	0.140
Age						
10-54 years	7,494	100.0%	6,992	100.0%	0.000	N/A
Sex						
Female	7,494	100.0%	6,992	100.0%	0.000	N/A
Race[4]						
Unknown	7,494	100.0%	6,992	100.0%	0.000	N/A
Hispanic origin						
Unknown	7,494	100.0%	6,992	100.0%	0.000	N/A
Year						
2016	328	4.4%	281	4.0%	0.358	0.018
2017	2,462	32.9%	1,991	28.5%	4.378	0.095
2018	2,216	29.6%	2,285	32.7%	-3.110	-0.067
2019	2,294	30.6%	2,258	32.3%	-1.683	-0.036
2020	194	2.6%	177	2.5%	0.057	0.004
Pregnancy Characteristics						
Pre-Term (0-258 days)	342	4.6%	307	4.4%	0.173	0.008
Term (259-280 days)	4,803	64.1%	4,287	61.3%	2.778	0.057
Post-Term (281-301 days)	1,815	24.2%	1,950	27.9%	-3.670	-0.084
Unknown Term	534	7.1%	448	6.4%	0.718	0.029
Gestational age[5] at delivery	39.8	1.4	39.9	1.4	-0.075	-0.053
Exposure Characteristics						
Gestational age[5] of first exposure (weeks)	29.3	5.2	0.0	0.5	29.325	7.953
Mean number of dispensings in first trimester	0.0	N/A	0.0	N/A	N/A	N/A

Table 1c. Unadjusted Characteristics of Step Approach with 6-Week Gestational Age Strata and High Dimensional Propensity Score (Propensity Score Stratified, Aggregated), Percentiles: 10, in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

	Medical Product				Covariate Balance	
	Pregnant Exposed Group		Pregnant Unexposed Group			
Mother Characteristics[1,2]	Number/Mean	Percent/ Standard Deviation[3]	Number/Mean	Percent/ Standard Deviation[3]	Absolute Difference	Standardized Difference
Mean number of dispensings in second trimester	0.4	0.5	0.0	N/A	N/A	N/A
Mean number of dispensings in third trimester	0.8	0.6	0.0	0.0	0.793	1.872
Exposed during first trimester	0	0.0%	0	0.0%	N/A	N/A
Exposed during second trimester	2,597	34.7%	0	0.0%	N/A	N/A
Exposed during third trimester	5,281	70.5%	1	0.0%	70.455	2.183
Health Characteristics						
Ear, Nose, and Throat Infections	6,484	86.5%	5,278	75.5%	11.036	0.284
Gastrointestinal Infections	0	0.0%	0	0.0%	N/A	N/A
Lower Respiratory Infections	1,371	18.3%	1,957	28.0%	-9.694	-0.231
Sexually Transmitted Infections	0	0.0%	0	0.0%	N/A	N/A
Other Indications	0	0.0%	0	0.0%	N/A	N/A
Pelvic Inflammatory Disease	0	0.0%	0	0.0%	N/A	N/A
Skin and Subcutaneous Tissue	0	0.0%	0	0.0%	N/A	N/A
Urinary Tract and Kidney Infections	0	0.0%	0	0.0%	N/A	N/A
Alcohol Abuse	16	0.2%	15	0.2%	-0.001	-0.000
Asthma	311	4.1%	211	3.0%	1.132	0.061
Cardiac Valvular Disease	51	0.7%	30	0.4%	0.251	0.034
Chronic Congestive Heart Failure	1	0.0%	0	0.0%	N/A	N/A
Chronic Ischemic Heart Disease	6	0.1%	3	0.0%	0.037	0.015
Chronic Renal Disease	26	0.3%	29	0.4%	-0.068	-0.011
Congenital Heart Disease	31	0.4%	22	0.3%	0.099	0.016
Cystic Fibrosis	7	0.1%	5	0.1%	0.022	0.008
Drug Abuse	50	0.7%	56	0.8%	-0.134	-0.016
Epilepsy/Seizures	23	0.3%	16	0.2%	0.078	0.015
HIV	0	0.0%	2	0.0%	N/A	N/A
Inflammatory Bowel Disease	25	0.3%	34	0.5%	-0.153	-0.024

Table 1c. Unadjusted Characteristics of Step Approach with 6-Week Gestational Age Strata and High Dimensional Propensity Score (Propensity Score Stratified, Aggregated), Percentiles: 10, in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

	Medical Product				Covariate Balance	
	Pregnant Exposed Group		Pregnant Unexposed Group			
Mother Characteristics[1,2]	Number/Mean	Percent/ Standard Deviation[3]	Number/Mean	Percent/ Standard Deviation[3]	Absolute Difference	Standardized Difference
Leukemia/Lymphoma	3	0.0%	6	0.1%	-0.046	-0.018
Obesity	986	13.2%	807	11.5%	1.615	0.049
Preexisting Diabetes	111	1.5%	95	1.4%	0.122	0.010
Preexisting Hypertension	241	3.2%	222	3.2%	0.041	0.002
Previous Cesarean Delivery	279	3.7%	231	3.3%	0.419	0.023
Psychiatric Disorders	992	13.2%	837	12.0%	1.266	0.038
Pulmonary Hypertension	0	0.0%	1	0.0%	N/A	N/A
Rheumatoid Arthritis	14	0.2%	18	0.3%	-0.071	-0.015
Sickle Cell Disease	8	0.1%	13	0.2%	-0.079	-0.021
Systemic Lupus Erythematosus	16	0.2%	14	0.2%	0.013	0.003
Tobacco Use	107	1.4%	105	1.5%	-0.074	-0.006
Vaccine Administration	28	0.4%	27	0.4%	-0.013	-0.002
Screening Examinations and Disease Management Training	1	0.0%	3	0.0%	-0.030	-0.018
Pap Smear	831	11.1%	729	10.4%	0.663	0.021
HPV DNA Test	0	0.0%	0	0.0%	N/A	N/A
Fecal Occult Blood Test	16	0.2%	15	0.2%	-0.001	-0.000
Teratogenic Drugs	0	0.0%	0	0.0%	N/A	N/A
End Stage Liver Disease	0	0.0%	0	0.0%	N/A	N/A
Gestational Age 20-25 weeks	2,658	35.5%	2,328	33.3%	2.173	0.046
Gestational Age 26-31 weeks	2,504	33.4%	2,293	32.8%	0.619	0.013
Gestational Age 32-37 weeks	2,113	28.2%	2,146	30.7%	-2.496	-0.055
Gestational Age 38-42 weeks	219	2.9%	225	3.2%	-0.296	-0.017
Health Service Utilization Intensity Metrics						
Mean number of ambulatory encounters	5.8	4.4	5.7	4.4	0.032	0.007
Mean number of emergency room encounters	0.2	0.6	0.2	0.6	-0.004	-0.006
Mean number of inpatient hospital encounters	0.0	0.1	0.0	0.1	-0.000	-0.006

Table 1c. Unadjusted Characteristics of Step Approach with 6-Week Gestational Age Strata and High Dimensional Propensity Score (Propensity Score Stratified, Aggregated), Percentiles: 10, in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

	Medical Product				Covariate Balance	
	Pregnant Exposed Group		Pregnant Unexposed Group			
Mother Characteristics[1,2]	Number/Mean	Percent/ Standard Deviation[3]	Number/Mean	Percent/ Standard Deviation[3]	Absolute Difference	Standardized Difference
Mean number of non-acute institutional encounters	0.0	N/A	0.0	N/A	N/A	N/A
Mean number of other ambulatory encounters	2.1	2.2	2.0	2.1	0.134	0.062
Mean number of filled prescriptions	2.4	3.3	1.8	3.0	0.527	0.166
Mean number of generics dispensed	1.4	1.6	1.1	1.5	0.286	0.186
Mean number of unique drug classes dispensed	1.3	1.5	1.0	1.4	0.281	0.191

[1]Covariates in blue show a standardized difference greater than 0.1.

[2]Baseline period in reference to user defined index date (pregnancy start, exposure date, or delivery date).

[3]Value represents standard deviation where no % follows the value.

[4]Race data may not be completely populated at all Data Partners; therefore, data about race may be incomplete.

[5]Gestational age estimated using a claims-based algorithm, previously validated in the Medication Exposure in Pregnancy Risk Evaluation Program (MEPREP), to identify pregnancies ending in a live birth. ICD-10-CM diagnosis codes indicative of weeks of gestation, and ICD-9-CM and ICD-10-CM diagnosis codes for preterm and post-term deliveries, were used to calculate the length of the pregnancy episode. Codes had to occur within 7 days of a delivery date in the inpatient setting. In absence of pre-/post-term codes, pregnancy duration was set to 273 days.

Table 1d. Weighted Characteristics of Step Approach with 6-Week Gestational Age Strata and High Dimensional Propensity Score (Propensity Score Stratified, Aggregated), Percentiles: 10, in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

	Medical Product				Covariate Balance	
	Pregnant Exposed Group		Pregnant Unexposed Group			
Mother Characteristics[1,2,3]	Number/Mean	Percent/ Standard Deviation[4]	Number/Mean	Percent/ Standard Deviation[4]	Absolute Difference	Standardized Difference
Unique patients	7,490	100.0%	6,970	100.0%	N/A	N/A
Demographic Characteristics						
Age (years)	30.9	5.0	30.9	5.2	0.018	0.004
Age						
10-54 years	7,490	100.0%	6,970	100.0%	0.000	N/A
Sex						
Female	7,490	100.0%	6,970	100.0%	0.000	N/A
Race[5]						
Unknown	7,490	100.0%	6,970	100.0%	0.000	N/A
Hispanic origin						
Unknown	7,490	100.0%	6,970	100.0%	0.000	N/A
Year						
2016	332	4.4%	288	4.1%	0.311	0.015
2017	2,456	32.8%	2,005	28.8%	4.025	0.087
2018	2,221	29.6%	2,252	32.3%	-2.661	-0.058
2019	2,285	30.5%	2,249	32.3%	-1.755	-0.038
2020	196	2.6%	177	2.5%	0.079	0.005
Pregnancy Characteristics						
Pre-Term (0-258 days)	345	4.6%	316	4.5%	0.078	0.004
Term (259-280 days)	4,753	63.5%	4,306	61.8%	1.683	0.035
Post-Term (281-301 days)	1,858	24.8%	1,901	27.3%	-2.463	-0.056
Unknown Term	534	7.1%	448	6.4%	0.702	0.028
Gestational age[6] at delivery	39.8	1.4	39.9	1.4	-0.051	-0.036
Exposure Characteristics						
Gestational age[6] of first exposure (weeks)	29.5	5.2	0.0	0.5	29.467	7.964
Mean number of dispensings in first trimester	0.0	N/A	0.0	N/A	0.000	N/A

Table 1d. Weighted Characteristics of Step Approach with 6-Week Gestational Age Strata and High Dimensional Propensity Score (Propensity Score Stratified, Aggregated), Percentiles: 10, in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

	Medical Product				Covariate Balance	
	Pregnant Exposed Group		Pregnant Unexposed Group			
Mother Characteristics[1,2,3]	Number/Mean	Percent/ Standard Deviation[4]	Number/Mean	Percent/ Standard Deviation[4]	Absolute Difference	Standardized Difference
Mean number of dispensings in second trimester	0.4	0.5	0.0	N/A	0.355	0.972
Mean number of dispensings in third trimester	0.8	0.6	0.0	0.0	0.797	1.905
Exposed during first trimester	0	0.0%	0	0.0%	N/A	N/A
Exposed during second trimester	2,523	33.7%	0	0.0%	N/A	N/A
Exposed during third trimester	5,328	71.1%	1	0.0%	71.124	2.219
Health Characteristics						
Ear, Nose, and Throat Infections	6,080	81.2%	5,676	81.4%	-0.258	-0.007
Gastrointestinal Infections	0	0.0%	0	0.0%	N/A	N/A
Lower Respiratory Infections	1,725	23.0%	1,586	22.7%	0.285	0.007
Sexually Transmitted Infections	0	0.0%	0	0.0%	N/A	N/A
Other Indications	0	0.0%	0	0.0%	N/A	N/A
Pelvic Inflammatory Disease	0	0.0%	0	0.0%	N/A	N/A
Skin and Subcutaneous Tissue	0	0.0%	0	0.0%	N/A	N/A
Urinary Tract and Kidney Infections	0	0.0%	0	0.0%	N/A	N/A
Alcohol Abuse	17	0.2%	16	0.2%	-0.003	-0.001
Asthma	274	3.7%	243	3.5%	0.167	0.009
Cardiac Valvular Disease	40	0.5%	37	0.5%	0.008	0.001
Chronic Congestive Heart Failure	0	0.0%	0	0.0%	N/A	N/A
Chronic Ischemic Heart Disease	5	0.1%	5	0.1%	-0.013	-0.005
Chronic Renal Disease	31	0.4%	27	0.4%	0.029	0.005
Congenital Heart Disease	28	0.4%	26	0.4%	-0.003	-0.001
Cystic Fibrosis	7	0.1%	7	0.1%	-0.003	-0.001
Drug Abuse	53	0.7%	51	0.7%	-0.027	-0.003
Epilepsy/Seizures	19	0.3%	17	0.2%	0.010	0.002
HIV	0	0.0%	0	0.0%	N/A	N/A
Inflammatory Bowel Disease	32	0.4%	29	0.4%	0.020	0.003

Table 1d. Weighted Characteristics of Step Approach with 6-Week Gestational Age Strata and High Dimensional Propensity Score (Propensity Score Stratified, Aggregated), Percentiles: 10, in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

	Medical Product				Covariate Balance	
	Pregnant Exposed Group		Pregnant Unexposed Group			
Mother Characteristics[1,2,3]	Number/Mean	Percent/ Standard Deviation[4]	Number/Mean	Percent/ Standard Deviation[4]	Absolute Difference	Standardized Difference
Leukemia/Lymphoma	5	0.1%	4	0.1%	0.003	0.001
Obesity	934	12.5%	863	12.4%	0.085	0.003
Preexisting Diabetes	103	1.4%	95	1.4%	0.014	0.001
Preexisting Hypertension	246	3.3%	222	3.2%	0.102	0.006
Previous Cesarean Delivery	258	3.4%	238	3.4%	0.031	0.002
Psychiatric Disorders	942	12.6%	858	12.3%	0.267	0.008
Pulmonary Hypertension	0	0.0%	0	0.0%	N/A	N/A
Rheumatoid Arthritis	15	0.2%	13	0.2%	0.012	0.003
Sickle Cell Disease	10	0.1%	10	0.1%	-0.003	-0.001
Systemic Lupus Erythematosus	14	0.2%	13	0.2%	0.008	0.002
Tobacco Use	107	1.4%	100	1.4%	-0.006	-0.001
Vaccine Administration	27	0.4%	25	0.4%	0.006	0.001
Screening Examinations and Disease Management Training	2	0.0%	2	0.0%	-0.006	-0.004
Pap Smear	805	10.7%	747	10.7%	0.030	0.001
HPV DNA Test	0	0.0%	0	0.0%	N/A	N/A
Fecal Occult Blood Test	16	0.2%	15	0.2%	-0.002	-0.000
Teratogenic Drugs	0	0.0%	0	0.0%	N/A	N/A
End Stage Liver Disease	0	0.0%	0	0.0%	N/A	N/A
Gestational Age 20-25 weeks	2,582	34.5%	2,403	34.5%	-0.002	-0.000
Gestational Age 26-31 weeks	2,482	33.1%	2,298	33.0%	0.173	0.004
Gestational Age 32-37 weeks	2,197	29.3%	2,058	29.5%	-0.199	-0.004
Gestational Age 38-42 weeks	229	3.1%	211	3.0%	0.027	0.002
Health Service Utilization Intensity Metrics						
Mean number of ambulatory encounters	5.8	4.5	5.7	4.3	0.020	0.004
Mean number of emergency room encounters	0.2	0.6	0.2	0.6	0.003	0.005
Mean number of inpatient hospital encounters	0.0	0.1	0.0	0.1	-0.000	-0.004

Table 1d. Weighted Characteristics of Step Approach with 6-Week Gestational Age Strata and High Dimensional Propensity Score (Propensity Score Stratified, Aggregated), Percentiles: 10, in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

	Medical Product				Covariate Balance	
	Pregnant Exposed Group		Pregnant Unexposed Group			
Mother Characteristics[1,2,3]	Number/Mean	Percent/ Standard Deviation[4]	Number/Mean	Percent/ Standard Deviation[4]	Absolute Difference	Standardized Difference
Mean number of non-acute institutional encounters	0.0	N/A	0.0	N/A	0.000	N/A
Mean number of other ambulatory encounters	2.1	2.2	2.1	2.1	0.007	0.003
Mean number of filled prescriptions	2.1	3.1	2.1	3.3	0.054	0.017
Mean number of generics dispensed	1.2	1.5	1.2	1.6	0.029	0.019
Mean number of unique drug classes dispensed	1.2	1.5	1.2	1.5	0.030	0.020

[1]Covariates in blue show a standardized difference greater than 0.1.

[2]Weighted patient characteristics tables facilitate the assessment of covariate balance after propensity score (PS) stratification and should not be interpreted as a description of the unweighted population. Treated/control patients are weighted by the proportion of the total patient population included in their PS stratum divided by the proportion of the total treated/control patient population included in their PS stratum.

[3]Baseline period in reference to user defined index date (pregnancy start, exposure date, or delivery date).

[4]Value represents standard deviation where no % follows the value.

[5]Race data may not be completely populated at all Data Partners; therefore, data about race may be incomplete.

[6]Gestational age estimated using a claims-based algorithm, previously validated in the Medication Exposure in Pregnancy Risk Evaluation Program (MEPREP), to identify pregnancies ending in a live birth. ICD-10-CM diagnosis codes indicative of weeks of gestation, and ICD-9-CM and ICD-10-CM diagnosis codes for preterm and post-term deliveries, were used to calculate the length of the pregnancy episode. Codes had to occur within 7 days of a delivery date in the inpatient setting. In absence of pre-/post-term codes, pregnancy duration was set to 273 days.

Table 1e. Unadjusted Characteristics of Step Approach with 6-Week Gestational Age Strata and 20 for PS (Propensity Score Stratified, Aggregated), Percentiles: 20, in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

	Medical Product				Covariate Balance	
	Pregnant Exposed Group		Pregnant Unexposed Group			
Mother Characteristics[1,2]	Number/Mean	Percent/ Standard Deviation[3]	Number/Mean	Standard Deviation[3]	Absolute Difference	Standardized Difference
Unique patients	7,494	100.0%	6,992	100.0%	N/A	N/A
Demographic Characteristics						
Age (years)	31.2	5.0	30.5	5.3	0.719	0.140
Age						
10-54 years	7,494	100.0%	6,992	100.0%	0.000	N/A
Sex						
Female	7,494	100.0%	6,992	100.0%	0.000	N/A
Race[4]						
Unknown	7,494	100.0%	6,992	100.0%	0.000	N/A
Hispanic origin						
Unknown	7,494	100.0%	6,992	100.0%	0.000	N/A
Year						
2016	328	4.4%	281	4.0%	0.358	0.018
2017	2,462	32.9%	1,991	28.5%	4.378	0.095
2018	2,216	29.6%	2,285	32.7%	-3.110	-0.067
2019	2,294	30.6%	2,258	32.3%	-1.683	-0.036
2020	194	2.6%	177	2.5%	0.057	0.004
Pregnancy Characteristics						
Pre-Term (0-258 days)	342	4.6%	307	4.4%	0.173	0.008
Term (259-280 days)	4,803	64.1%	4,287	61.3%	2.778	0.057
Post-Term (281-301 days)	1,815	24.2%	1,950	27.9%	-3.670	-0.084
Unknown Term	534	7.1%	448	6.4%	0.718	0.029
Gestational age[5] at delivery	39.8	1.4	39.9	1.4	-0.075	-0.053
Exposure Characteristics						
Gestational age[5] of first exposure (weeks)	29.3	5.2	0.0	0.5	29.325	7.953
Mean number of dispensings in first trimester	0.0	N/A	0.0	N/A	N/A	N/A

Table 1e. Unadjusted Characteristics of Step Approach with 6-Week Gestational Age Strata and 20 for PS (Propensity Score Stratified, Aggregated), Percentiles: 20, in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

	Medical Product				Covariate Balance	
	Pregnant Exposed Group		Pregnant Unexposed Group			
Mother Characteristics[1,2]	Number/Mean	Percent/ Standard Deviation[3]	Number/Mean	Standard Deviation[3]	Absolute Difference	Standardized Difference
Mean number of dispensings in second trimester	0.4	0.5	0.0	N/A	N/A	N/A
Mean number of dispensings in third trimester	0.8	0.6	0.0	0.0	0.793	1.872
Exposed during first trimester	0	0.0%	0	0.0%	N/A	N/A
Exposed during second trimester	2,597	34.7%	0	0.0%	N/A	N/A
Exposed during third trimester	5,281	70.5%	1	0.0%	70.455	2.183
Health Characteristics						
Ear, Nose, and Throat Infections	6,484	86.5%	5,278	75.5%	11.036	0.284
Gastrointestinal Infections	0	0.0%	0	0.0%	N/A	N/A
Lower Respiratory Infections	1,371	18.3%	1,957	28.0%	-9.694	-0.231
Sexually Transmitted Infections	0	0.0%	0	0.0%	N/A	N/A
Other Indications	0	0.0%	0	0.0%	N/A	N/A
Pelvic Inflammatory Disease	0	0.0%	0	0.0%	N/A	N/A
Skin and Subcutaneous Tissue	0	0.0%	0	0.0%	N/A	N/A
Urinary Tract and Kidney Infections	0	0.0%	0	0.0%	N/A	N/A
Alcohol Abuse	16	0.2%	15	0.2%	-0.001	-0.000
Asthma	311	4.1%	211	3.0%	1.132	0.061
Cardiac Valvular Disease	51	0.7%	30	0.4%	0.251	0.034
Chronic Congestive Heart Failure	1	0.0%	0	0.0%	N/A	N/A
Chronic Ischemic Heart Disease	6	0.1%	3	0.0%	0.037	0.015
Chronic Renal Disease	26	0.3%	29	0.4%	-0.068	-0.011
Congenital Heart Disease	31	0.4%	22	0.3%	0.099	0.016
Cystic Fibrosis	7	0.1%	5	0.1%	0.022	0.008
Drug Abuse	50	0.7%	56	0.8%	-0.134	-0.016
Epilepsy/Seizures	23	0.3%	16	0.2%	0.078	0.015
HIV	0	0.0%	2	0.0%	N/A	N/A
Inflammatory Bowel Disease	25	0.3%	34	0.5%	-0.153	-0.024

Table 1e. Unadjusted Characteristics of Step Approach with 6-Week Gestational Age Strata and 20 for PS (Propensity Score Stratified, Aggregated), Percentiles: 20, in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

	Medical Product				Covariate Balance	
	Pregnant Exposed Group		Pregnant Unexposed Group			
Mother Characteristics[1,2]	Number/Mean	Percent/ Standard Deviation[3]	Number/Mean	Standard Deviation[3]	Absolute Difference	Standardized Difference
Leukemia/Lymphoma	3	0.0%	6	0.1%	-0.046	-0.018
Obesity	986	13.2%	807	11.5%	1.615	0.049
Preexisting Diabetes	111	1.5%	95	1.4%	0.122	0.010
Preexisting Hypertension	241	3.2%	222	3.2%	0.041	0.002
Previous Cesarean Delivery	279	3.7%	231	3.3%	0.419	0.023
Psychiatric Disorders	992	13.2%	837	12.0%	1.266	0.038
Pulmonary Hypertension	0	0.0%	1	0.0%	N/A	N/A
Rheumatoid Arthritis	14	0.2%	18	0.3%	-0.071	-0.015
Sickle Cell Disease	8	0.1%	13	0.2%	-0.079	-0.021
Systemic Lupus Erythematosus	16	0.2%	14	0.2%	0.013	0.003
Tobacco Use	107	1.4%	105	1.5%	-0.074	-0.006
Vaccine Administration	28	0.4%	27	0.4%	-0.013	-0.002
Screening Examinations and Disease Management Training	1	0.0%	3	0.0%	-0.030	-0.018
Pap Smear	831	11.1%	729	10.4%	0.663	0.021
HPV DNA Test	0	0.0%	0	0.0%	N/A	N/A
Fecal Occult Blood Test	16	0.2%	15	0.2%	-0.001	-0.000
Teratogenic Drugs	0	0.0%	0	0.0%	N/A	N/A
End Stage Liver Disease	0	0.0%	0	0.0%	N/A	N/A
Gestational Age 20-25 weeks	2,658	35.5%	2,328	33.3%	2.173	0.046
Gestational Age 26-31 weeks	2,504	33.4%	2,293	32.8%	0.619	0.013
Gestational Age 32-37 weeks	2,113	28.2%	2,146	30.7%	-2.496	-0.055
Gestational Age 38-42 weeks	219	2.9%	225	3.2%	-0.296	-0.017
Health Service Utilization Intensity Metrics						
Mean number of ambulatory encounters	5.8	4.4	5.7	4.4	0.032	0.007
Mean number of emergency room encounters	0.2	0.6	0.2	0.6	-0.004	-0.006
Mean number of inpatient hospital encounters	0.0	0.1	0.0	0.1	-0.000	-0.006

Table 1e. Unadjusted Characteristics of Step Approach with 6-Week Gestational Age Strata and 20 for PS (Propensity Score Stratified, Aggregated), Percentiles: 20, in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

	Medical Product				Covariate Balance	
	Pregnant Exposed Group		Pregnant Unexposed Group			
Mother Characteristics[1,2]	Number/Mean	Percent/ Standard Deviation[3]	Number/Mean	Standard Deviation[3]	Absolute Difference	Standardized Difference
Mean number of non-acute institutional encounters	0.0	N/A	0.0	N/A	N/A	N/A
Mean number of other ambulatory encounters	2.1	2.2	2.0	2.1	0.134	0.062
Mean number of filled prescriptions	2.4	3.3	1.8	3.0	0.527	0.166
Mean number of generics dispensed	1.4	1.6	1.1	1.5	0.286	0.186
Mean number of unique drug classes dispensed	1.3	1.5	1.0	1.4	0.281	0.191

[1]Covariates in blue show a standardized difference greater than 0.1.

[2]Baseline period in reference to user defined index date (pregnancy start, exposure date, or delivery date).

[3]Value represents standard deviation where no % follows the value.

[4]Race data may not be completely populated at all Data Partners; therefore, data about race may be incomplete.

[5]Gestational age estimated using a claims-based algorithm, previously validated in the Medication Exposure in Pregnancy Risk Evaluation Program (MEPREP), to identify pregnancies ending in a live birth. ICD-10-CM diagnosis codes indicative of weeks of gestation, and ICD-9-CM and ICD-10-CM diagnosis codes for preterm and post-term deliveries, were used to calculate the length of the pregnancy episode. Codes had to occur within 7 days of a delivery date in the inpatient setting. In absence of pre-/post-term codes, pregnancy duration was set to 273 days.

Table 1f. Weighted Characteristics of Step Approach with 6-Week Gestational Age Strata and 20 for PS (Propensity Score Stratified, Aggregated), Percentiles: 20, in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

	Medical Product				Covariate Balance	
	Pregnant Exposed Group		Pregnant Unexposed Group			
Mother Characteristics[1,2,3]	Number/Mean	Percent/ Standard Deviation[4]	Number/Mean	Standard Deviation[4]	Absolute Difference	d Difference
Unique patients	7,493	100.0%	6,985	100.0%	N/A	N/A
Demographic Characteristics						
Age (years)	30.9	5.0	30.9	5.2	-0.041	-0.008
Age						
10-54 years	7,493	100.0%	6,985	100.0%	0.000	N/A
Sex						
Female	7,493	100.0%	6,985	100.0%	0.000	N/A
Race[5]						
Unknown	7,493	100.0%	6,985	100.0%	0.000	N/A
Hispanic origin						
Unknown	7,493	100.0%	6,985	100.0%	0.000	N/A
Year						
2016	338	4.5%	287	4.1%	0.403	0.020
2017	2,458	32.8%	2,005	28.7%	4.101	0.089
2018	2,222	29.6%	2,258	32.3%	-2.679	-0.058
2019	2,278	30.4%	2,260	32.4%	-1.957	-0.042
2020	198	2.6%	175	2.5%	0.132	0.008
Pregnancy Characteristics						
Pre-Term (0-258 days)	339	4.5%	313	4.5%	0.038	0.002
Term (259-280 days)	4,776	63.7%	4,287	61.4%	2.360	0.049
Post-Term (281-301 days)	1,853	24.7%	1,932	27.7%	-2.929	-0.067
Unknown Term	525	7.0%	452	6.5%	0.531	0.021
Gestational age[6] at delivery	39.8	1.4	39.9	1.4	-0.055	-0.039
Exposure Characteristics						
Gestational age[6] of first exposure (weeks)	29.5	5.2	0.0	0.5	29.492	7.975
Mean number of dispensings in first trimester	0.0	N/A	0.0	N/A	0.000	N/A

Table 1f. Weighted Characteristics of Step Approach with 6-Week Gestational Age Strata and 20 for PS (Propensity Score Stratified, Aggregated), Percentiles: 20, in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

	Medical Product				Covariate Balance	
	Pregnant Exposed Group		Pregnant Unexposed Group			
Mother Characteristics[1,2,3]	Number/Mean	Percent/ Standard Deviation[4]	Number/Mean	Standard Deviation[4]	Absolute Difference	d Difference
Mean number of dispensings in second trimester	0.4	0.5	0.0	N/A	0.353	0.968
Mean number of dispensings in third trimester	0.8	0.6	0.0	0.0	0.800	1.914
Exposed during first trimester	0	0.0%	0	0.0%	N/A	N/A
Exposed during second trimester	2,510	33.5%	0	0.0%	N/A	N/A
Exposed during third trimester	5,349	71.4%	1	0.0%	71.376	2.233
Health Characteristics						
Ear, Nose, and Throat Infections	6,077	81.1%	5,672	81.2%	-0.091	-0.002
Gastrointestinal Infections	0	0.0%	0	0.0%	N/A	N/A
Lower Respiratory Infections	1,728	23.1%	1,601	22.9%	0.146	0.003
Sexually Transmitted Infections	0	0.0%	0	0.0%	N/A	N/A
Other Indications	0	0.0%	0	0.0%	N/A	N/A
Pelvic Inflammatory Disease	0	0.0%	0	0.0%	N/A	N/A
Skin and Subcutaneous Tissue	0	0.0%	0	0.0%	N/A	N/A
Urinary Tract and Kidney Infections	0	0.0%	0	0.0%	N/A	N/A
Alcohol Abuse	17	0.2%	15	0.2%	0.008	0.002
Asthma	281	3.7%	246	3.5%	0.216	0.012
Cardiac Valvular Disease	43	0.6%	37	0.5%	0.048	0.007
Chronic Congestive Heart Failure	0	0.0%	0	0.0%	N/A	N/A
Chronic Ischemic Heart Disease	5	0.1%	4	0.1%	0.007	0.003
Chronic Renal Disease	30	0.4%	26	0.4%	0.022	0.004
Congenital Heart Disease	27	0.4%	24	0.3%	0.016	0.003
Cystic Fibrosis	6	0.1%	6	0.1%	0.001	0.000
Drug Abuse	55	0.7%	51	0.7%	-0.003	-0.000
Epilepsy/Seizures	20	0.3%	17	0.2%	0.021	0.004
HIV	0	0.0%	0	0.0%	N/A	N/A
Inflammatory Bowel Disease	31	0.4%	29	0.4%	0.002	0.000

Table 1f. Weighted Characteristics of Step Approach with 6-Week Gestational Age Strata and 20 for PS (Propensity Score Stratified, Aggregated), Percentiles: 20, in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

	Medical Product				Covariate Balance	
	Pregnant Exposed Group		Pregnant Unexposed Group			
Mother Characteristics[1,2,3]	Number/Mean	Percent/ Standard Deviation[4]	Number/Mean	Standard Deviation[4]	Absolute Difference	d Difference
Leukemia/Lymphoma	5	0.1%	4	0.1%	0.006	0.002
Obesity	940	12.5%	864	12.4%	0.175	0.005
Preexisting Diabetes	109	1.5%	98	1.4%	0.049	0.004
Preexisting Hypertension	246	3.3%	224	3.2%	0.077	0.004
Previous Cesarean Delivery	261	3.5%	245	3.5%	-0.026	-0.001
Psychiatric Disorders	949	12.7%	868	12.4%	0.237	0.007
Pulmonary Hypertension	0	0.0%	0	0.0%	N/A	N/A
Rheumatoid Arthritis	16	0.2%	15	0.2%	-0.003	-0.001
Sickle Cell Disease	11	0.1%	9	0.1%	0.006	0.002
Systemic Lupus Erythematosus	16	0.2%	15	0.2%	0.001	0.000
Tobacco Use	109	1.5%	99	1.4%	0.030	0.003
Vaccine Administration	28	0.4%	26	0.4%	0.003	0.001
Screening Examinations and Disease Management Training	2	0.0%	2	0.0%	-0.005	-0.003
Pap Smear	807	10.8%	754	10.8%	-0.023	-0.001
HPV DNA Test	0	0.0%	0	0.0%	N/A	N/A
Fecal Occult Blood Test	15	0.2%	14	0.2%	0.002	0.000
Teratogenic Drugs	0	0.0%	0	0.0%	N/A	N/A
End Stage Liver Disease	0	0.0%	0	0.0%	N/A	N/A
Gestational Age 20-25 weeks	2,568	34.3%	2,399	34.3%	-0.067	-0.001
Gestational Age 26-31 weeks	2,481	33.1%	2,318	33.2%	-0.078	-0.002
Gestational Age 32-37 weeks	2,213	29.5%	2,055	29.4%	0.110	0.002
Gestational Age 38-42 weeks	231	3.1%	213	3.1%	0.034	0.002
Health Service Utilization Intensity Metrics						
Mean number of ambulatory encounters	5.8	4.5	5.8	4.3	0.025	0.006
Mean number of emergency room encounters	0.2	0.6	0.2	0.6	0.004	0.007
Mean number of inpatient hospital encounters	0.0	0.1	0.0	0.1	-0.000	-0.000

Table 1f. Weighted Characteristics of Step Approach with 6-Week Gestational Age Strata and 20 for PS (Propensity Score Stratified, Aggregated), Percentiles: 20, in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

	Medical Product				Covariate Balance	
	Pregnant Exposed Group		Pregnant Unexposed Group			
Mother Characteristics[1,2,3]	Number/Mean	Percent/ Standard Deviation[4]	Number/Mean	Standard Deviation[4]	Absolute Difference	d Difference
Mean number of non-acute institutional encounters	0.0	N/A	0.0	N/A	0.000	N/A
Mean number of other ambulatory encounters	2.1	2.2	2.1	2.1	0.008	0.004
Mean number of filled prescriptions	2.1	3.1	2.1	3.3	0.082	0.025
Mean number of generics dispensed	1.2	1.5	1.2	1.6	0.037	0.024
Mean number of unique drug classes dispensed	1.2	1.5	1.2	1.5	0.043	0.029

[1]Covariates in blue show a standardized difference greater than 0.1.

[2]Weighted patient characteristics tables facilitate the assessment of covariate balance after propensity score (PS) stratification and should not be interpreted as a description of the unweighted population. Treated/control patients are weighted by the proportion of the total patient population included in their PS stratum divided by the proportion of the total treated/control patient population included in their PS stratum.

[3]Baseline period in reference to user defined index date (pregnancy start, exposure date, or delivery date).

[4]Value represents standard deviation where no % follows the value.

[5]Race data may not be completely populated at all Data Partners; therefore, data about race may be incomplete.

[6]Gestational age estimated using a claims-based algorithm, previously validated in the Medication Exposure in Pregnancy Risk Evaluation Program (MEPREP), to identify pregnancies ending in a live birth. ICD-10-CM diagnosis codes indicative of weeks of gestation, and ICD-9-CM and ICD-10-CM diagnosis codes for preterm and post-term deliveries, were used to calculate the length of the pregnancy episode. Codes had to occur within 7 days of a delivery date in the inpatient setting. In absence of pre-/post-term codes, pregnancy duration was set to 273 days.

Table 2a. Signal Identification Outcome Assessment via Conditional Poisson Tree Based Scan Statistic Among Antibiotic Users Stratified by Propensity Score Deciles and Gestational Age at Treatment Initiation in Six Week Increments. Outcomes Assessed in the Inpatient and Emergency Department Settings.

Outcome Identifier	Outcome Description	Total Outcomes Among Antibiotic Users	Expected Outcomes Among Antibiotic Users	Relative Risk	Excess Cases	Log Likelihood Ratio (Test Statistic)	P-value
O99513grp	Diseases of the respiratory system complicating pregnancy, third trimester	75	31.27	2.4	43.8	21.93	0.00001
O9951grp	Diseases of the respiratory system complicating pregnancy	106	52.42	2.03	53.72	21.13	0.00001
O6000ngrp	Preterm labor without delivery, unspecified trimester	14	1.58	8.85	12.42	18.10	0.00002
O1410ngrp	Severe pre-eclampsia, unspecified trimester	53	25.29	2.1	27.74	11.52	0.00034
O715nngrp	Other obstetric injury to pelvic organs	20	5.44	3.68	14.57	11.50	0.00034
O715ngrp	Other obstetric injury to pelvic organs	20	5.44	3.68	14.57	11.50	0.00034
O715grp	Other obstetric injury to pelvic organs	20	5.44	3.68	14.57	11.50	0.00034
O995grp	Diseases of the respiratory system complicating pregnancy, childbirth and the puerperium	324	249.15	1.31	75.83	10.41	0.00094
O700grp	First degree perineal laceration during delivery	1230	1083.4	1.14	155.36	10.09	0.00139
O700ngrp	First degree perineal laceration during delivery	1230	1083.4	1.14	155.36	10.09	0.00139
O700nngrp	First degree perineal laceration during delivery	1230	1083.4	1.14	155.36	10.09	0.00139
O9A22ngrp	Injury, poisoning and certain other consequences of external causes complicating childbirth	6	0.46	13.05	5.54	9.87	0.00190
O9A22grp	Injury, poisoning and certain other consequences of external causes complicating childbirth	6	0.46	13.05	5.54	9.87	0.00190
O99342grp	Other mental disorders complicating pregnancy, second trimester	7	1.11	6.3	5.89	7.00	0.03364
O142grp	HELLP syndrome	33	15.93	2.07	17.09	6.97	0.03440
O996grp	Diseases of the digestive system complicating pregnancy, childbirth and the puerperium	275	218.75	1.26	56.9	6.77	0.04211

Table 2b. Signal Identification Outcome Assessment via Conditional Poisson Tree Based Scan Statistic Among Antibiotic Users Stratified by 20 Propensity Score Strata and Gestational Age at Treatment Initiation in Six Week Increments. Outcomes Assessed in the Inpatient and Emergency Department Settings.

Outcome Identifier	Outcome Description	Total Outcomes Among Antibiotic Users	Expected Outcomes Among Antibiotic Users	Relative Risk	Excess Cases	Log Likelihood Ratio (Test Statistic)	P-value
O99513grp	Diseases of the respiratory system complicating pregnancy, third trimester	75	31.6	2.38	43.47	21.48	0.00001
O9951grp	Diseases of the respiratory system complicating pregnancy	106	52.68	2.02	53.47	20.87	0.00001
O6000ngrp	Preterm labor without delivery, unspecified trimester	14	1.5	9.35	12.5	18.78	0.00001
O1410ngrp	Severe pre-eclampsia, unspecified trimester	53	25.39	2.09	27.64	11.41	0.00040
O715nngrp	Other obstetric injury to pelvic organs	20	5.52	3.62	14.48	11.27	0.00047
O715ngrp	Other obstetric injury to pelvic organs	20	5.52	3.62	14.48	11.27	0.00047
O715grp	Other obstetric injury to pelvic organs	20	5.52	3.62	14.48	11.27	0.00047
O9A22grp	Injury, poisoning and certain other consequences of external causes complicating childbirth	6	0.39	15.43	5.61	10.81	0.00077
O9A22ngrp	Injury, poisoning and certain other consequences of external causes complicating childbirth	6	0.39	15.43	5.61	10.81	0.00077
O700nngrp	First degree perineal laceration during delivery	1225	1079	1.14	154.7	10.05	0.00150
O700ngrp	First degree perineal laceration during delivery	1225	1079	1.14	154.7	10.05	0.00150
O700grp	First degree perineal laceration during delivery	1225	1079	1.14	154.7	10.05	0.00150
O995grp	Diseases of the respiratory system complicating pregnancy, childbirth and the puerperium	324	251.18	1.29	73.78	9.80	0.00201
O142grp	HELLP syndrome	33	15.86	2.08	17.16	7.05	0.03114
O99342grp	Other mental disorders complicating pregnancy, second trimester	7	1.16	6.06	5.84	6.76	0.04102
O7589grp	Other specified complications of labor and delivery	207	159.01	1.31	48.39	6.67	0.04694
O7589ngrp	Other specified complications of labor and delivery	207	159.01	1.31	48.39	6.67	0.04694

Table 2c. Signal Identification Outcome Assessment via Conditional Poisson Tree Based Scan Statistic Among Antibiotic Users Stratified by High Dimension Propensity Score Deciles and Gestational Age at Treatment Initiation in Six Week Increments. Outcomes Assessed in the Inpatient and Emergency Department Settings.

Outcome Identifier	Outcome Description	Total Outcomes Among Antibiotic Users	Expected Outcomes Among Antibiotic Users	Relative Risk	Excess Cases	Log Likelihood Ratio (Test Statistic)	P-value
O6000ngrp	Preterm labor without delivery, unspecified trimester	14	1.35	10.39	12.65	20.12	0.00001
O9951grp	Diseases of the respiratory system complicating pregnancy	106	55.49	1.92	50.65	18.16	0.00001
O99513grp	Diseases of the respiratory system complicating pregnancy, third trimester	75	34.44	2.18	40.63	17.85	0.00001
O715grp	Other obstetric injury to pelvic organs	20	5.27	3.8	14.73	11.94	0.00028
O715ngrp	Other obstetric injury to pelvic organs	20	5.27	3.8	14.73	11.94	0.00028
O715nngrp	Other obstetric injury to pelvic organs	20	5.27	3.8	14.73	11.94	0.00028
O1410ngrp	Severe pre-eclampsia, unspecified trimester	53	25.07	2.12	27.96	11.77	0.00032
O9A22ngrp	Injury, poisoning and certain other consequences of external causes complicating childbirth	6	0.39	15.38	5.61	10.79	0.00069
O9A22grp	Injury, poisoning and certain other consequences of external causes complicating childbirth	6	0.39	15.38	5.61	10.79	0.00069
O995grp	Diseases of the respiratory system complicating pregnancy, childbirth and the puerperium	323	250.36	1.3	73.6	9.79	0.00189
O141grp	Severe pre-eclampsia	186	135.76	1.37	50.59	8.39	0.00800
O24420grp	Gestational diabetes mellitus in childbirth, diet controlled	17	5.61	3.03	11.39	7.46	0.02043
O141ngrp	Severe pre-eclampsia	120	83.08	1.45	37.08	7.24	0.02540
O1420ngrp	HELLP syndrome (HELLP), unspecified trimester	8	1.46	5.49	6.54	7.07	0.03116
O660grp	Obstructed labor due to shoulder dystocia	142	101.9	1.4	40.32	7.06	0.03148
O660ngrp	Obstructed labor due to shoulder dystocia	142	101.9	1.4	40.32	7.06	0.03148
O660nngrp	Obstructed labor due to shoulder dystocia	142	101.9	1.4	40.32	7.06	0.03148
O996grp	Diseases of the digestive system complicating pregnancy, childbirth and the puerperium	275	217.89	1.27	57.76	6.99	0.03406

Figure 1a. Histograms Depicting Propensity Score Distributions Before Adjustment for Step Approach with 6-Week Gestational Age Strata and 10 for PS in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

Unadjusted Propensity Score Distribution

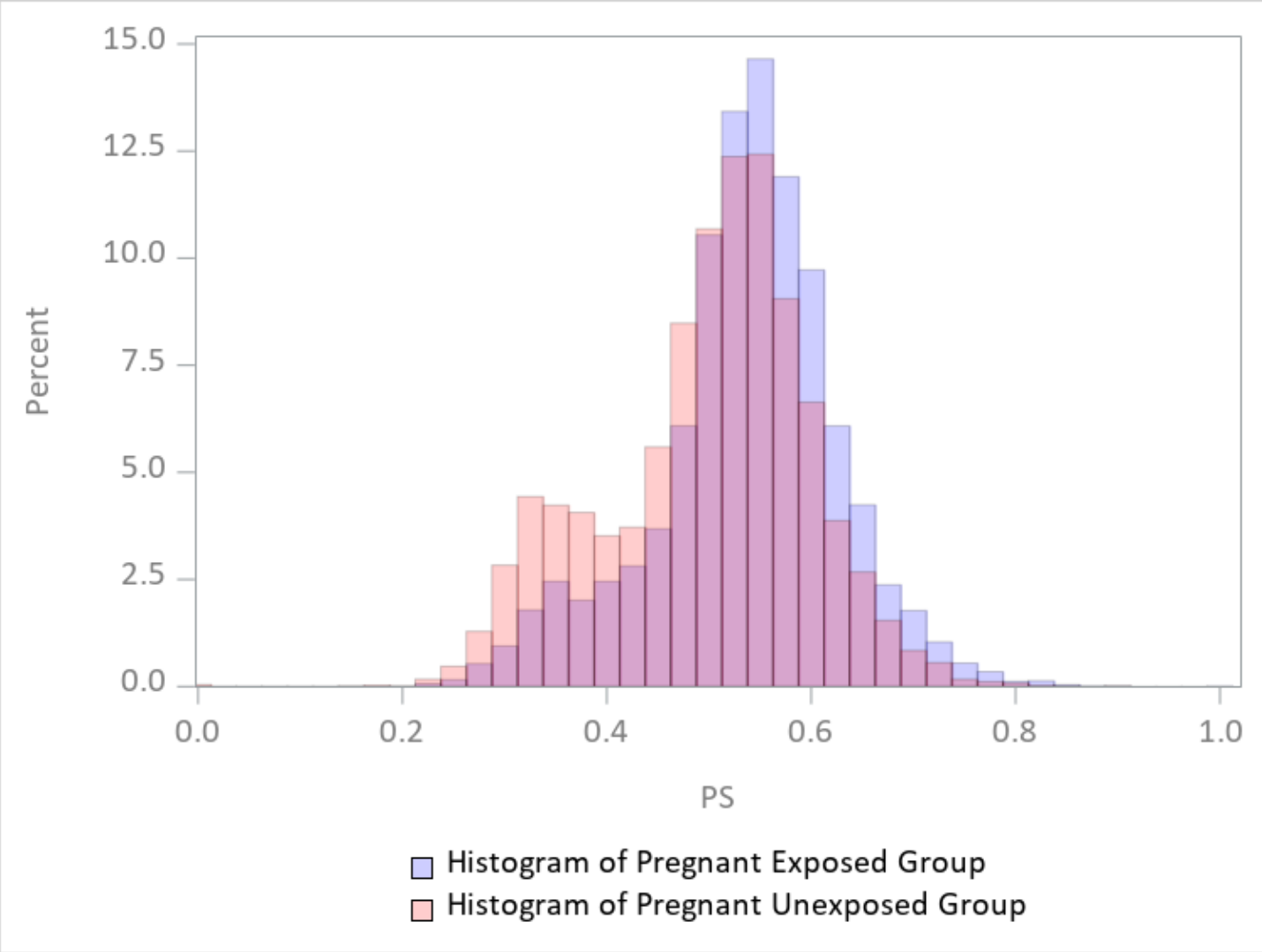


Figure 1b. Histograms Depicting Propensity Score Distributions Before Adjustment for Step Approach with 6-Week Gestational Age Strata and 20 for PS in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

Unadjusted Propensity Score Distribution

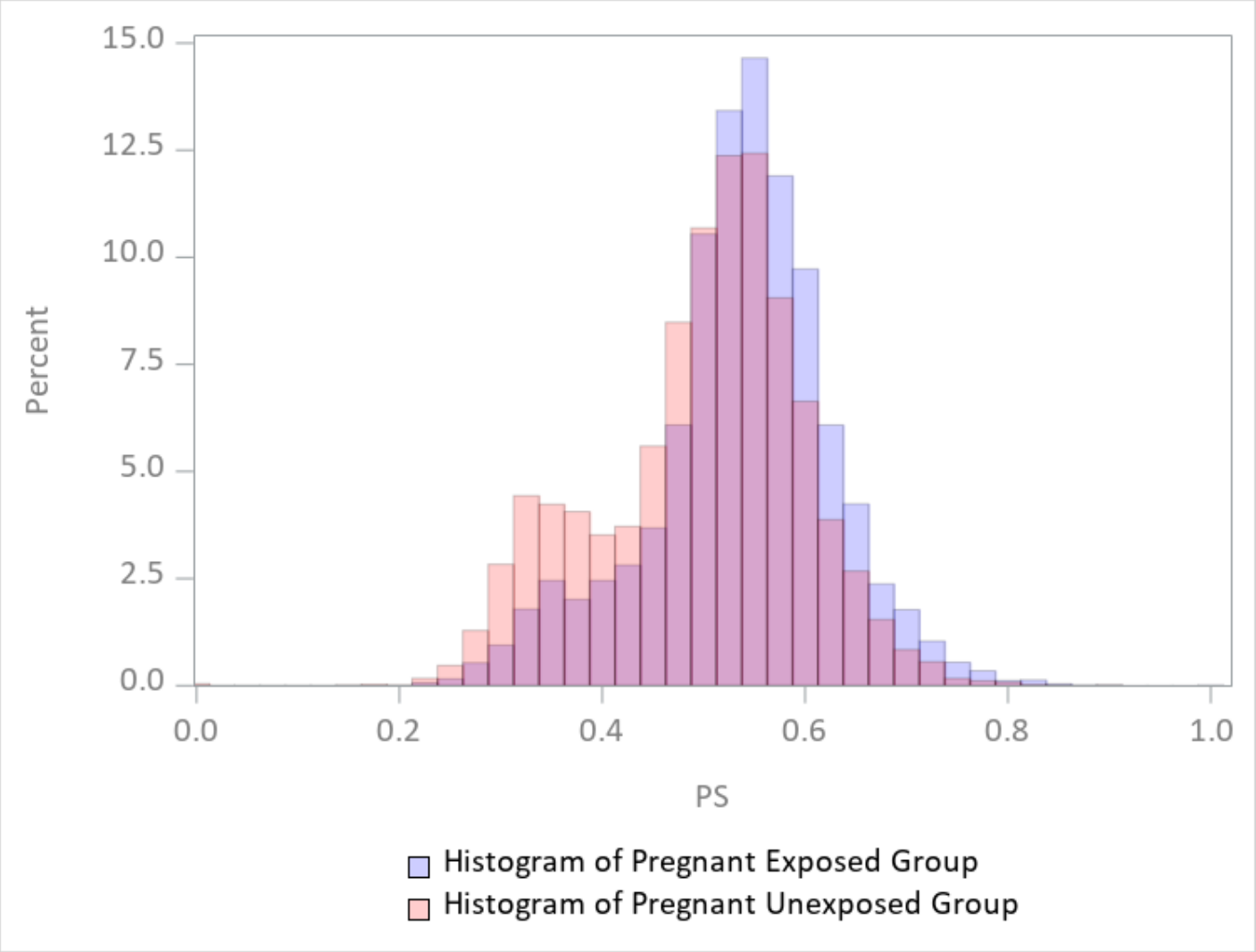


Figure 1c. Histograms Depicting Propensity Score Distributions Before Adjustment for Step Approach with 6-Week Gestational Age Strata and HDPS in the Merative MarketScan Research Databases from October 26, 2016 to February 29, 2020

Unadjusted Propensity Score Distribution

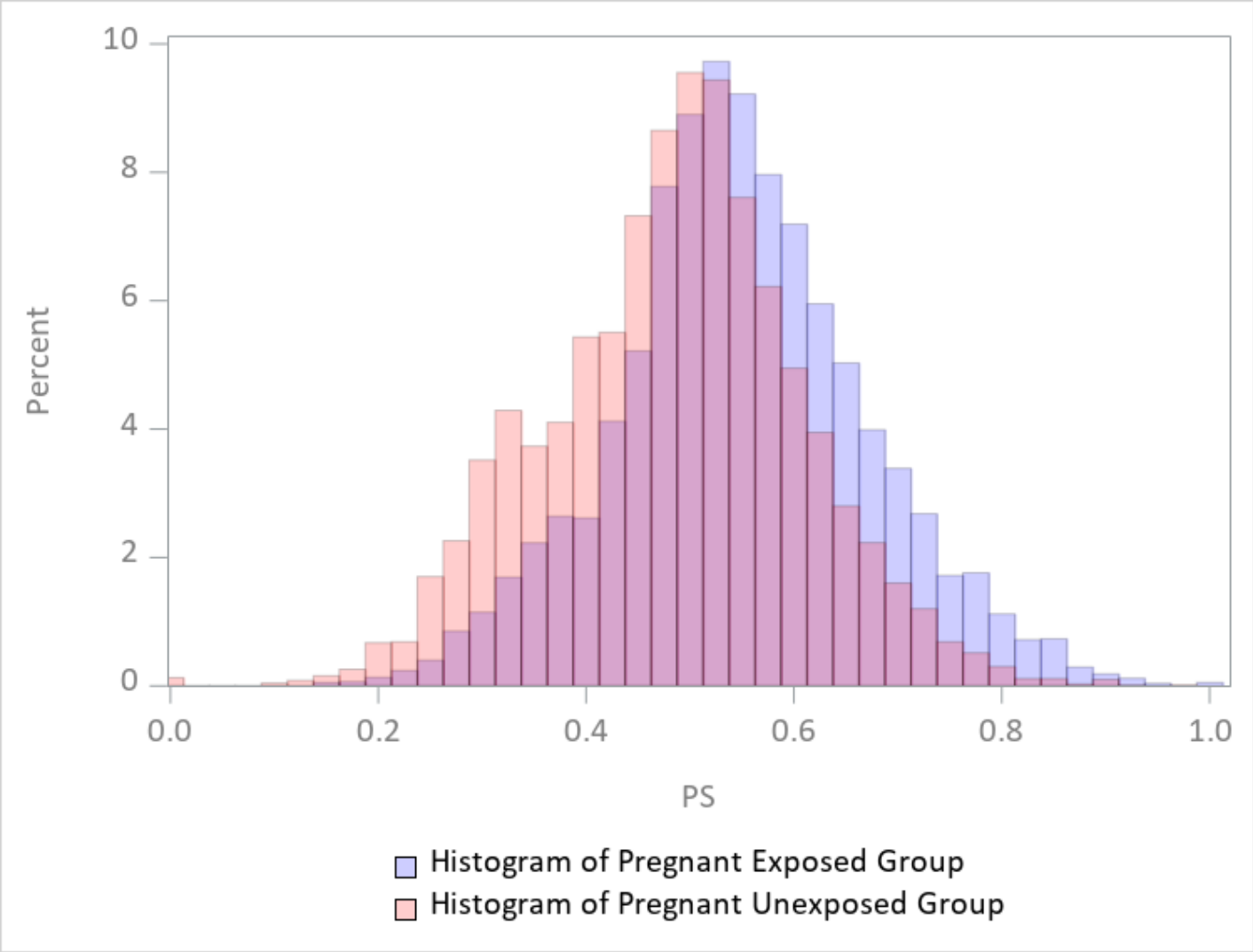
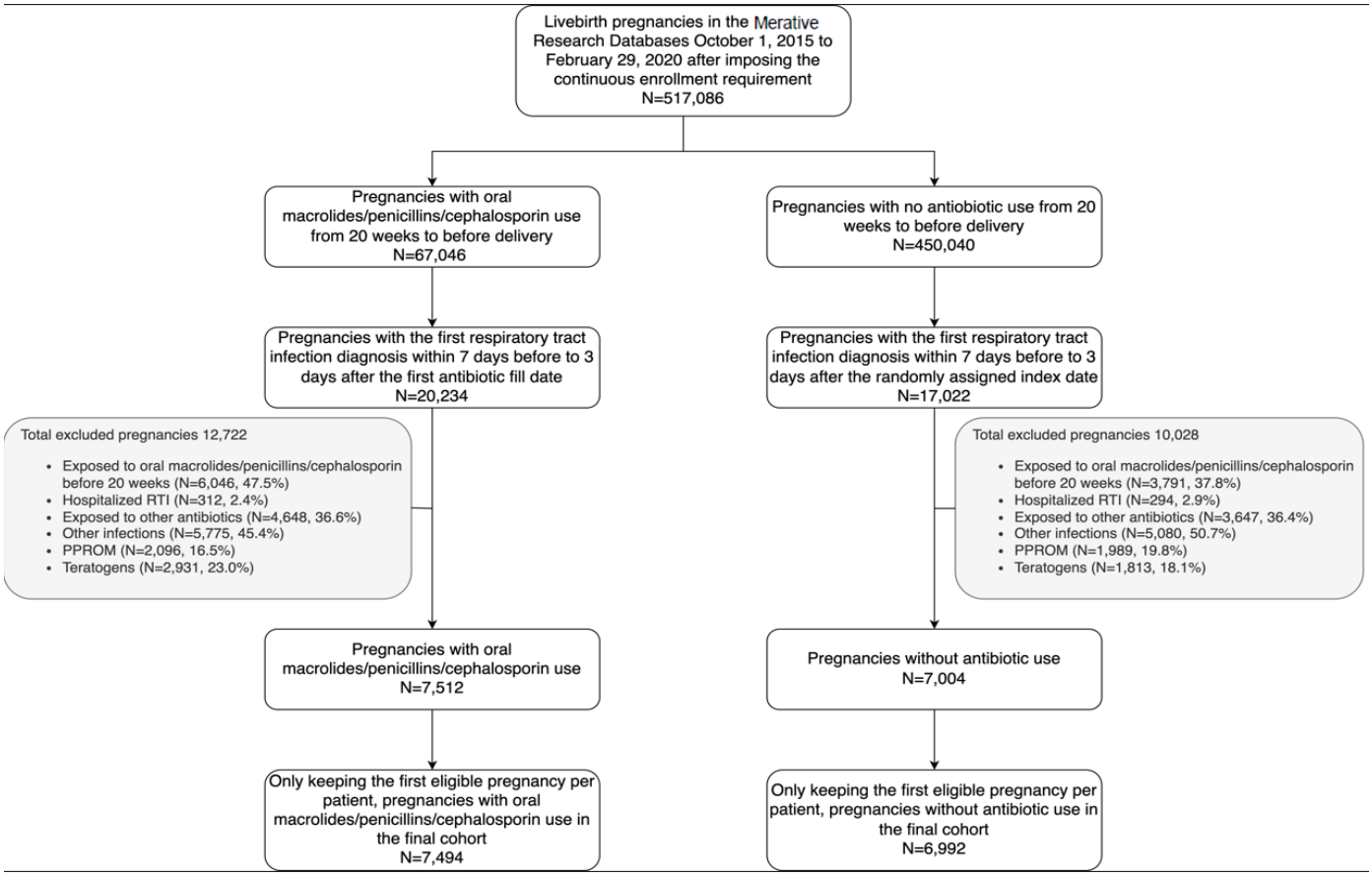


Figure 2. Attrition Table for the Antibiotic and Non-antibiotic Case Study



Appendix A. Dates of Available Data for Each Data Partner (DP) as of Request Distribution Date (09/06/2022)

Masked DP ID[1]	DP Start Date	DP End Date[2]
DP01	01/01/2010	02/29/2020

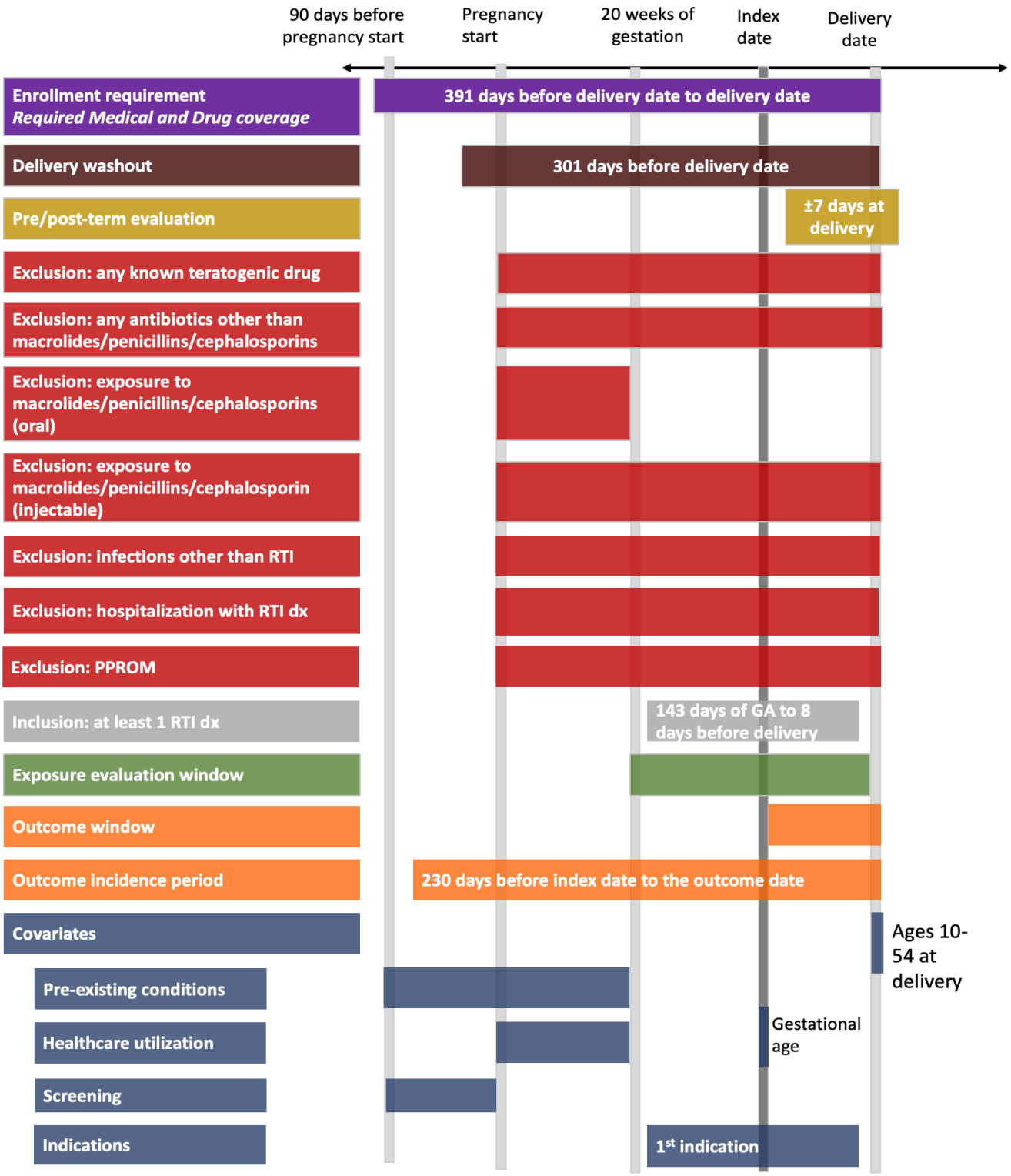
[1]Participating Data Partners include Merative MarketScan Research Databases

[2]End Date represents the earliest of: (1) query end date, or (2) most recent year-month of data for which all of a Data Partner's data tables (enrollment, dispensing, etc.) have at least 80% of the record count relative to the prior month.

Appendix B. Top 25 Codes Ranked by Exposure Association Selected by the High Dimensional Propensity Score Algorithm; step_6_10_lmp_hdps

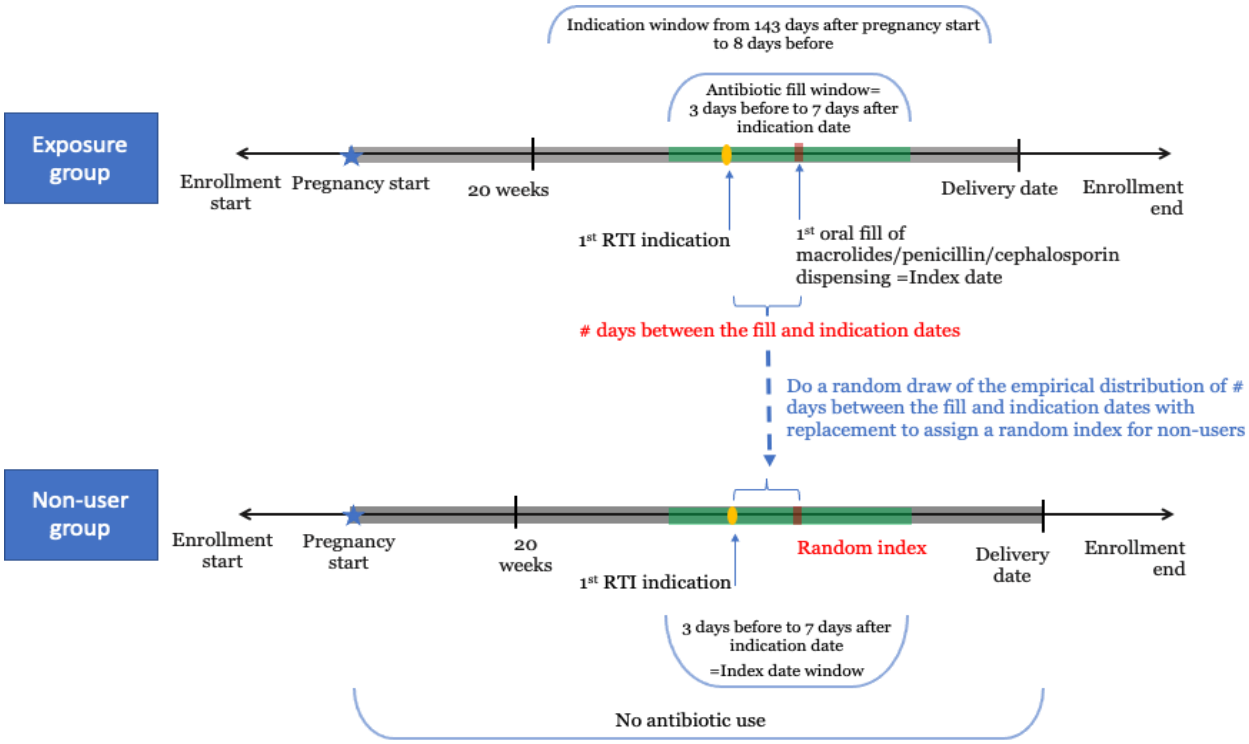
Code	Code Category	Code Type	Frequency	Ranking
C436	RX	CLASS	D02V005Spor	1.5401018504
03H00DZ	PX	ICD-10-CM	D04V002Once	1.3169582991
A7038	PX	HCPCS	D05V033Freq	1.3169582991
C167	RX	CLASS	D02V073Freq	1.2299469221
J3420	PX	HCPCS	D05V121Freq	1.1834269065
A4230	PX	HCPCS	D05V224Freq	0.9856267939
A9585	PX	HCPCS	D05V053Once	0.9422648497
L4361	PX	HCPCS	D05V441Once	0.8960146352
C328	RX	CLASS	D02V089Once	0.8469546699
J2710	PX	HCPCS	D05V055Once	0.8244818140
C167	RX	CLASS	D02V073Spor	0.7956613755
G8482	PX	HCPCS	D05V125Freq	0.7779617984
0JQ10ZZ	PX	ICD-10-CM	D04V000Once	0.7624832426
4A1HXCZ	PX	ICD-10-CM	D04V001Once	0.7624832426
0HQQXZZ	PX	ICD-10-CM	D04V025Once	0.7624832426
BQ0G0ZZ	PX	ICD-10-CM	D04V077Once	0.7624832426
BY49ZZZ	PX	ICD-10-CM	D04V089Once	0.7624832426
A4230	PX	HCPCS	D05V224Spor	0.7624832426
C383	RX	CLASS	D02V105Spor	0.7415941542
G8420	PX	HCPCS	D05V016Freq	0.7291716342
C103	RX	CLASS	D02V031Freq	0.7038538262
C874	RX	CLASS	D02V085Freq	0.7018586208
G8484	PX	HCPCS	D05V228Freq	0.6754718656
A4559	PX	HCPCS	D05V070Once	0.6615514465
G8417	PX	HCPCS	D05V020Once	0.6415106956

Appendix C. Design Diagram for the Antibiotic and Non-antibiotic Case Study



Cohort: Singleton livebirth deliveries
Query period: October 1, 2015 – February 29, 2020
First valid livebirth delivery date: October 26, 2016
Last valid livebirth delivery date: February 29, 2020

Appendix C.1. Diagram to Assign Index Date for the Exposure and Control Groups



Appendix D. Specifications for Type 4 Request: tspreg_mpl2p_wp004

Purpose: The execution of Cohort Identification and Descriptive Analysis (CIDA) Pregnancy tool [**QRP 10.3.3**] to create cohorts for analysis using the TreeScan software for comparison of macrolide and penicillin exposure.

Query period (*bound by the delivery date*): 10/26/2016 - 02/29/2020
Coverage requirement: Medical & Drug Coverage
Minimum enrollment requirement prior to delivery date: 391 Days (301 day delivery length + 90 day pre-pregnancy exposure assessment period)
Minimum enrollment requirement post delivery date: 0 days
Enrollment gap: 45 days
Pre-pregnancy period (*relative to pregnancy start date*): 90 days
Age groups (*calculated at delivery date*): 10-54 yrs
Sex: Female mothers
Stratifications: None
Output by gestational week: No
Restrictions: None
Envelope macro: Reclassify encounters during inpatient stay as inpatient
Freeze data: Yes

	Main Analysis	Sensitivity Analysis- 20 Strata Stratification
Pregnancy Cohort	preg	preg
Pregnancy Episode Creation		
Delivery Definition	Use Pregnancy Algorithm Codes	Use Pregnancy Algorithm Codes
Pregnancy Cohort Definition	Cohort includes all valid pregnancy episodes during the query period	Cohort includes all valid pregnancy episodes during the query period
Delivery Caresetting	Inpatient	Inpatient
Create Baseline Table?	Yes	Yes
Delivery washout	301 days	301 days
Pregnancy Duration Definition (Pre/PostTerm Codes)	Use Pregnancy Algorithm Codes	Use Pregnancy Algorithm Codes
Pre/Post-Term Code Evaluation Window Relative to Delivery Date	7	7
Pregnancy Duration in Absence of Pre/Post-Term Codes	273	273
Mother-infant linkage requirement	None	None

Appendix D. Specifications for Type 4 Request: tspreg_mpl2p_wp004				
Drug/Exposure				
Prevalent Exposure/Comparator	*Macrolides/penicillins/ cephalosporins (oral)*	*Non-antibiotic use*	*Macrolides/penicillins/ cephalosporins (oral)*	*Non-antibiotic use*
Incident w/ Respect to:	NA	NA	NA	NA
Incident exposure washout period	0 days	0 days	0 days	0 days
Exposure Episode Length (ITT)	1 day	1 day	1 day	1 day
Cohort Definition	Cohort includes all valid medical product exposure episodes during a pregnancy episode	Index date was assigned based on a random draw of the empirical distribution of the number of days between the fill and indication dates in the antibiotic group	Cohort includes all valid medical product exposure episodes during a pregnancy episode	Index date was assigned based on a random draw of the empirical distribution of the number of days between the fill and indication dates in the antibiotic group
Build Episodes on Point Exposure?	Yes	Yes, completed with imputed index date as described above	Yes	Yes, completed with imputed index date as described above
Treatment episode gap	NA	NA	NA	NA
Remove MOI exposure on delivery date	Exclude MOIs with a date equivalent to pregnancy delivery date	Exclude MOIs with a date equivalent to pregnancy delivery date	Exclude MOIs with a date equivalent to pregnancy delivery date	Exclude MOIs with a date equivalent to pregnancy delivery date
Care Setting/PDX	Any	Any	Any	Any
Exposure Unit	Weeks	Weeks	Weeks	Weeks
Evaluation window	(20, 42)	(20, 42)	(20, 42)	(20, 42)
Maximum Episode Duration	None	None	None	None
Stockpiling option	On	On	On	On
Forced supply to attach to code	NA	NA	NA	NA
Inclusion/Exclusion				
Inclusion/ Exclusion groups	Teratogenic drugs, penicillins (injectable), macrolides (injectable), cephalosporins (injectable), other antibiotics (any route), PPROM, hospitalization with RTI diagnosis, any infections other than RTI	Teratogenic drugs, penicillins (injectable), macrolides (injectable), cephalosporins (injectable), other antibiotics (any route), PPROM, hospitalization with RTI diagnosis, any infections other than RTI	Teratogenic drugs, penicillins (injectable), macrolides (injectable), cephalosporins (injectable), other antibiotics (any route), PPROM, hospitalization with RTI diagnosis, any infections other than RTI	Teratogenic drugs, penicillins (injectable), macrolides (injectable), cephalosporins (injectable), other antibiotics (any route), PPROM, hospitalization with RTI diagnosis, any infections other than RTI
Criteria	Exclusion	Exclusion	Exclusion	Exclusion
Care Setting/PDX	Any	Any	Any	Any
Evaluation Period Start Anchor	Pregnancy start date	Pregnancy start date	Pregnancy start date	Pregnancy start date

Appendix D. Specifications for Type 4 Request: tspreg_mpl2p_wp004				
Evaluation Period Start	0	0	0	0
Evaluation Period End Anchor	Pregnancy end date	Pregnancy end date	Pregnancy end date	Pregnancy end date
Evaluation Period End	0	0	0	0
Inclusion/ Exclusion group	Macrolides (oral), penicillins (oral), cephalosporins (oral)	Macrolides (oral), penicillins (oral), cephalosporins (oral)	Macrolides (oral), penicillins (oral), cephalosporins (oral)	Macrolides (oral), penicillins (oral), cephalosporins (oral)
Criteria	Exclusion	Exclusion	Exclusion	Exclusion
Care Setting/PDX	Any	Any	Any	Any
Evaluation Period Start Anchor	Pregnancy start date	Pregnancy start date	Pregnancy start date	Pregnancy start date
Evaluation Period Start	0	0	0	0
Evaluation Period End Anchor	Pregnancy start date	Pregnancy end date	Pregnancy start date	Pregnancy end date
Evaluation Period End	139	0	139	0
Inclusion/ Exclusion group	Respiratory tract infection (COVAR 1, 3)	Respiratory tract infection (COVAR 1, 3)	Respiratory tract infection (COVAR 1, 3)	Respiratory tract infection (COVAR 1, 3)
Criteria	Inclusion	Inclusion	Inclusion	Inclusion
Care Setting/PDX	Any	Any	Any	Any
Evaluation Period Start Anchor	Pregnancy start date	Pregnancy start date	Pregnancy start date	Pregnancy start date
Evaluation Period Start	143	143	143	143
Evaluation Period End Anchor	Delivery date	Delivery date	Delivery date	Delivery date
Evaluation Period End	-8	-8	-8	-8
Exclude evidence of days supply if inclusion/exclusion evaluation period includes dispensings	Evaluation period should search for evidence of days supply	Evaluation period should search for evidence of days supply	Evaluation period should search for evidence of days supply	Evaluation period should search for evidence of days supply
Number of instances the criteria should be found in evaluation period	1	1	1	1
Forced supply to attach to dispensings	NA	NA	NA	NA
Population to which inclusion/exclusion applies	Mother's claims	Mother's claims	Mother's claims	Mother's claims
Event/Outcome	Maternal outcome ICD-10-CM tree		Maternal outcome ICD-10-CM tree	
Index date to anchor for outcome assessment start	Exposure index date		Exposure index date	
Outcome assessment start	1		1	
Index date to anchor for outcome assessment end	Pregnancy Delivery Date		Pregnancy Delivery Date	
Outcome assessment end	0		0	

Appendix D. Specifications for Type 4 Request: tspreg_mpl2p_wp004		
Care Setting/PDX	IP/ED	IP/ED
Claims to evaluate outcome	Mother's claims	Mother's claims
Incident w/ respect to:	Level 3 codes	Level 3 codes
Incident Care Setting	Any	Any
Washout (days)	230 days before index date to outcome code date	230 days before index date to outcome code date
Blackout Period	NA	NA
Propensity Score Matching/stratification	Stratification	Stratification
Scenarios	Step model	Step model
Covariates	See Covariates tab	See Covariates tab
Covariate Evaluation Window	See Covariates tab	See Covariates tab
Index date for covariates and PS risk set	Pregnancy start date	Pregnancy start date
Matching Ratio / N strata	10	20
Trimming	Yes	Yes
Matching Caliper Settings	NA	NA
hdPS evaluation window	NA	NA
hdPS covariates considered/covariates selected	NA	NA
hdPS covariate selection method	NA	NA
hdPS exclusions	NA	NA
Zero cell correction	NA	NA
Code trunction	NA	NA
ICD-9, ICD-10, HCPCS, and CPT codes are provided by Optum360.		
NDC codes are checked against First Data Bank's "National Drug Data File (NDDF®) Plus."		

Appendix D.1. Specifications for Type 4 Request: tspreg_mpl2p_wp004		
Purpose: The execution of Cohort Identification and Descriptive Analysis (CIDA) Pregnancy tool [**QRP 10.3.3**] to create cohorts for analysis using the TreeScan software for comparison of macrolide and penicillin exposure.		
	Sensitivity Analysis- HDPS	
Pregnancy Cohort	preg	
Pregnancy Episode Creation		
Delivery Definition	Use Pregnancy Algorithm Codes	
Pregnancy Cohort Definition	Cohort includes all valid pregnancy episodes during the query period	
Delivery Caresetting	Inpatient	
Create Baseline Table?	Yes	
Delivery washout	301 days	
Pregnancy Duration Definition (Pre/PostTerm Codes)	Use Pregnancy Algorithm Codes	
Pre/Post-Term Code Evaluation Window Relative to Delivery Date	7 days	
Pregnancy Duration in Absence of Pre/Post-Term Codes	273	
Mother-infant linkage requirement	None	
Drug/Exposure		
Prevalent Exposure/Comparator	*Macrolides/penicillins/cephalosporins (oral)*	*Non-antibiotic use*
Incident w/ Respect to:	NA	NA
Incident exposure washout period	0 days	0 days
Exposure Episode Length (ITT)	1 day	1 day
Cohort Definition	Cohort includes all valid medical product exposure episodes during a pregnancy episode	Index date was assigned based on a random draw of the empirical distribution of the number of days between the fill and indication dates in the antibiotic group
Build Episodes on Point Exposure?	Yes	Yes, completed with imputed index date as described above
Treatment episode gap	NA	NA
Remove MOI exposure on delivery date	Exclude MOIs with a date equivalent to pregnancy delivery date	Exclude MOIs with a date equivalent to pregnancy delivery date
Care Setting/PDX	Any	Any
Exposure Unit	Weeks	Weeks
Evaluation window	(20, 42)	(20, 42)
Maximum Episode Duration	None	None
Stockpiling option	On	On
Forced supply to attach to code	NA	NA
Inclusion/Exclusion		
Inclusion/ Exclusion groups	Teratogenic drugs, penicillins (injectable), macrolides (injectable), cephalosporins (injectable), other antibiotics (any route), PPROM, hospitalization with RTI diagnosis, any infections other than RTI	Teratogenic drugs, penicillins (injectable), macrolides (injectable), cephalosporins (injectable), other antibiotics (any route), PPROM, hospitalization with RTI diagnosis, any infections other than RTI
Criteria	Exclusion	Exclusion
Care Setting/PDX	Any	Any
Evaluation Period Start Anchor	Pregnancy start date	Pregnancy start date
Evaluation Period Start	0	0
Evaluation Period End Anchor	Pregnancy end date	Pregnancy end date

Appendix D.1. Specifications for Type 4 Request: tspreg_mpl2p_wp004		
Evaluation Period End	0	0
Inclusion/ Exclusion group	Macrolides (oral), penicillins (oral), cephalosporins (oral)	Macrolides (oral), penicillins (oral), cephalosporins (oral)
Criteria	Exclusion	Exclusion
Care Setting/PDX	Any	Any
Evaluation Period Start Anchor	Pregnancy start date	Pregnancy start date
Evaluation Period Start	0	0
Evaluation Period End Anchor	Pregnancy start date	Pregnancy end date
Evaluation Period End	139	0
Inclusion/ Exclusion group	Respiratory tract infection (COVAR 1, 3)	Respiratory tract infection (COVAR 1, 3)
Criteria	Inclusion	Inclusion
Care Setting/PDX	Any	Any
Evaluation Period Start Anchor	Pregnancy start date	Pregnancy start date
Evaluation Period Start	143	143
Evaluation Period End Anchor	Delivery date	Delivery date
Evaluation Period End	-8	-8
Exclude evidence of days supply if inclusion/exclusion evaluation period includes dispensings	Evaluation period should search for evidence of days supply	Evaluation period should search for evidence of days supply
Number of instances the criteria should be found in evaluation period	1	1
Forced supply to attach to dispensings	NA	NA
Population to which inclusion/exclusion applies	Mother's claims	Mother's claims
Event/Outcome	Maternal outcome ICD-10-CM tree	
Index date to anchor for outcome assessment start	Exposure index date	
Outcome assessment start	1	
Index date to anchor for outcome assessment end	Pregnancy Delivery Date	
Outcome assessment end	0	
Care Setting/PDX	IP/ED	
Claims to evaluate outcome	Mother's claims	
Incident w/ respect to:	Level 3 codes	
Incident Care Setting	Any	
Washout (days)	230 days before index date to outcome code date	
Blackout Period	NA	
Propensity Score Matching/stratification	Stratification	
Scenarios	HDPS+ others	
Covariates	See Covariates tab	
Covariate Evaluation Window	[-230, -1]	
Index date for covariates and PS risk set	Exposure index date	
Matching Ratio / N strata	10	
Trimming	Yes	
Matching Caliper Settings	NA	
hdPS evaluation window	[-230,-1]	
hdPS covariates considered/covariates selected	Leave blank	
hdPS covariate selection method	exp_assoc	
hdPS exclusions	NA	
Zero cell correction	Leave blank	
Code trunction	TRUNC_10=4	

ICD-9, ICD-10, HCPCS, and CPT codes are provided by Optum360.

NDC codes are checked against First Data Bank's "National Drug Data File (NDDF®) Plus."