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

Date Run: September 19, 2018

Request Description: The purpose of this report was to compare the frequency of stillbirth diagnoses in the inpatient care setting using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes. ICD-10-CM code definitions were determined by mapping from ICD-9-CM code definitions using the Centers for Medicare and Medicaid Services (CMS) General Equivalence Mappings (GEMs). Forward-backward mapping (FBM) was used to map ICD-9-CM to ICD-10-CM codes.[1]

Sentinel Modular Program Tool Used: Cohort Identification and Descriptive Analysis (CIDA) tool, version 5.4.4

Data Source: This request was run against the IBM® MarketScan® Commercial Claims and Encounters Database and Medicare Supplemental Database, which included 127 million members. Data from October 1, 2010 to March 31, 2017 were included in this report. The report includes three separate time periods: 1) October 1, 2010 to March 31, 2017, 2) April 1, 2015 to September 30, 2015, and 3) April 1, 2016 to September 30, 2016. See Appendix A for the dates of available data used in this report.

Study Design: We examined the incidence and prevalence of stillbirth, including intrauterine death, diagnoses that occurred in the inpatient care setting across the ICD-9-CM era (October 2010 - September 2015) and ICD-10-CM era (October 2015 - March 2017) in the US. Incidence was additionally evaluated from April 2015 - September 2015 and April 2016 - September 2016. See Appendix B for specific codes used to define stillbirth.

Cohort Eligibility Criteria: Members included in the cohorts were required to be enrolled in health plans with medical and drug coverage. Individuals 12-55 years of age were included in the cohorts.

Incidence Cohort: Members included in the incidence cohort were required to be continuously enrolled in health plans with medical and drug coverage for at least 183 days prior to stillbirth diagnoses during which gaps in coverage of up to 45 days were allowed. Incident stillbirth diagnoses were defined as no previous stillbirth diagnosis in the 183 days preceding the index date with respect to ICD-9-CM and ICD-10-CM codes.

Prevalent Cohort: There was no enrollment time requirement for members in the prevalent cohort. All qualifying diagnosis codes that occurred between October 1, 2010 and March 31, 2017 were included.

Please refer to Appendix C for detailed specifications of parameters used in the analyses for this request.

Limitations: Algorithms used to define outcomes are imperfect; thus, it is possible that there may be misclassification. Therefore, data should be interpreted with this limitation in mind. The MarketScan claims databases are based on a large convenience sample. Because the sample is not random, it may contain biases or fail to generalize well to other populations. Data come mostly from large employers; medium and small firms may be underrepresented.[2]

Notes: Please contact the Sentinel Operations Center (info@sentinelsystem.org) for questions and to provide comments/suggestions for future enhancements to this document.

[1]Fung, K. W., et al. (2016). "Preparing for the ICD-10-CM Transition: Automated Methods for Translating ICD Codes in Clinical Phenotype Definitions." EGEMS (Wash DC) 4(1): 1211.

[2]IBM Watson Health (2018). [online] ibm.com. Available at: https://www.ibm.com/downloads/cas/OWZWJ0QO [Accessed 01 Mar. 2019].

Sentinel

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

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 consultations.

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.

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.

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.

*not all terms may be used in this report

Table 1. Comparison of Incident* Stillbirth Diagnoses in the Inpatient Care Setting, in the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) Eras (April 1, 2015 - September 30, 2015 and April 1, 2016 - September 30, 2016)

	Members with Diagnoses	Eligible Members	Members with Diagnosis per 100,000 Eligible Members
Stillbirth			
ICD-9-CM: April 1, 2015 - September 30, 2015			
	851	15,531,401	5.48
ICD-10-CM: April 1, 2016 - September 30, 2016			
	1,121	15,535,778	7.22

*Incidence defined by 183 day washout

Figure 1. Incidence of Stillbirth Diagnoses in the Inpatient Care Setting per 100,000 Eligible Members from October 2010 to March 2017 by Code Type, 183-Day Washout

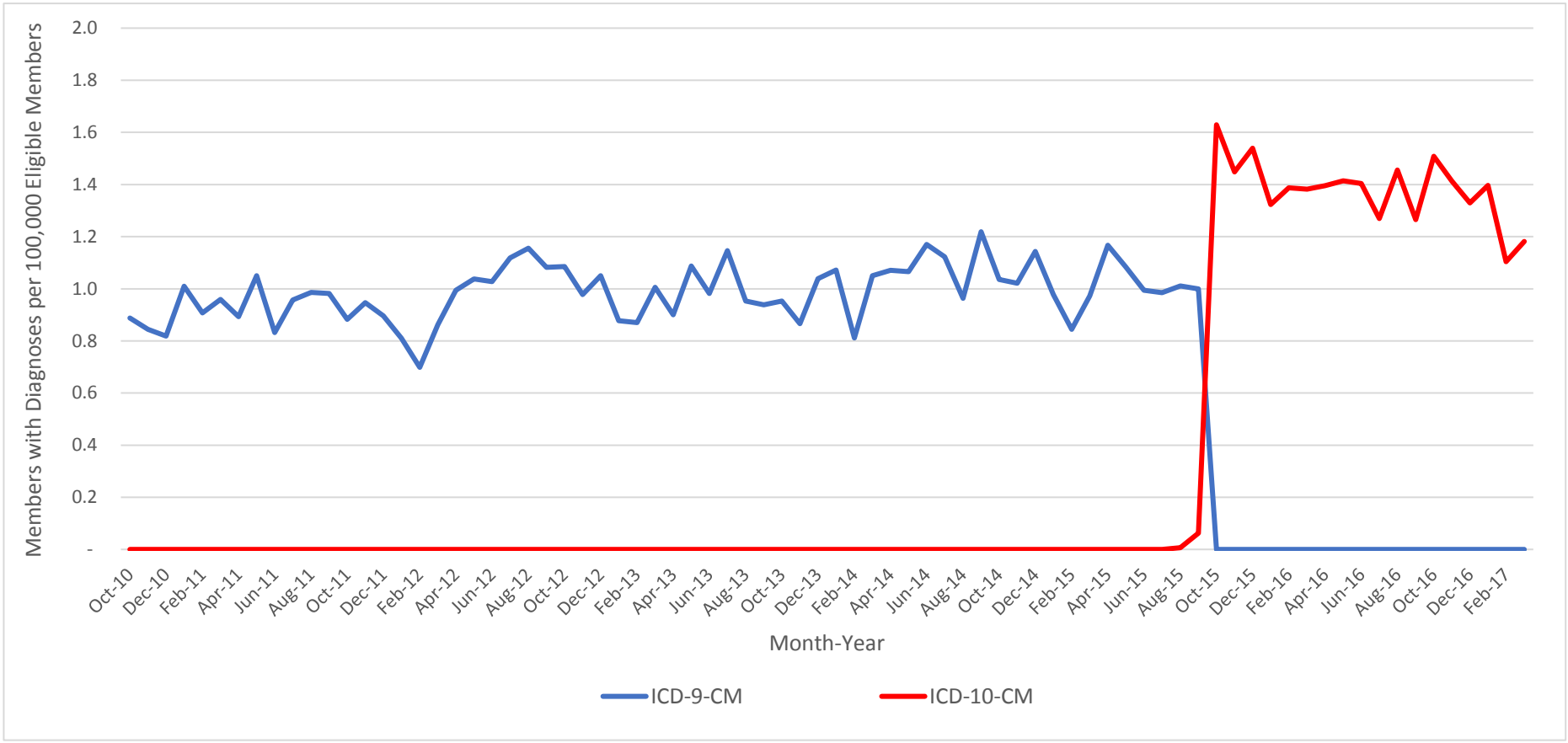
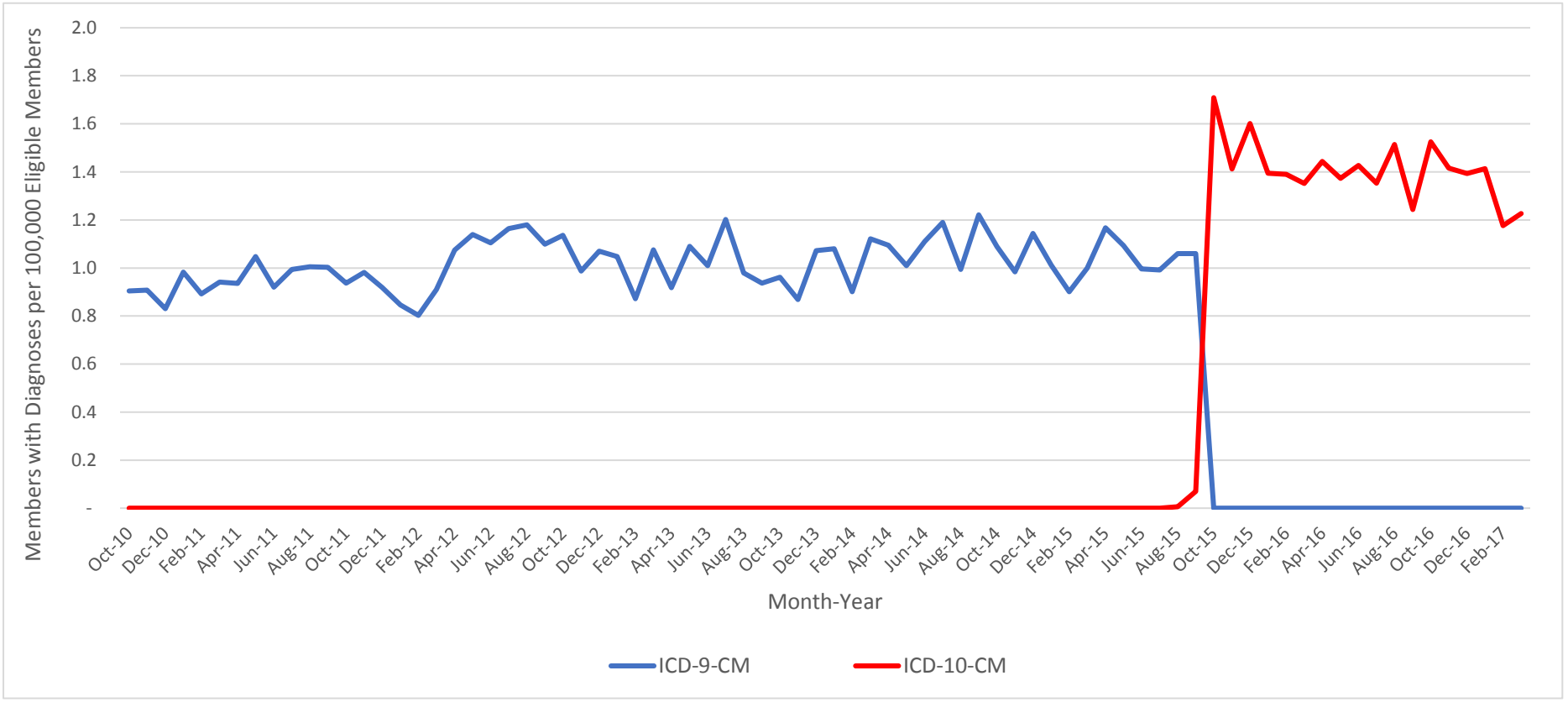


Figure 2. Prevalence of Stillbirth Diagnoses in the Inpatient Care Setting per 100,000 Eligible Members from October 2010 to March 2017 by Code Type, 0-Day Washout



Appendix A. Dates Available for IBM® MarketScan® Commercial and Medicare Supplemental Databases

Databases	DP Start Date	DP End Date
IBM MarketScan Commercial and Medicare Supplemental Databases[1]	01/01/2010	03/31/2017

[1] The IBM MarketScan Databases includes a sample of 127.2 million employees, dependents, and retirees in the United States with primary or Medicare supplemental coverage through privately insured fee-for-service, point-of-service, or capitated health plans. The IBM MarketScan claims databases are based on a large convenience sample. Because the sample is not random, it may contain biases or fail to generalize well to other populations. Data come mostly from large employers; medium and small firms may be underrepresented. For more information on the IBM MarketScan Databases, please review the White Paper here: https://www.ibm.com/downloads/cas/OWZWJ0QO

Appendix B. List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) Diagnosis Codes Used to Define Stillbirth in this Request

Code	Description	Code Type
	ICD-9-CM	
646.01	PAPYRACEOUS FETUS, DELIVERED, WITH OR WITHOUT MENTION ANTEPARTUM COND	ICD-9-CM
656.41	INTRAUTERINE DEATH, AFFECTING MANAGEMENT OF MOTHER, DELIVERY, WITH OR WITHOUT MENTION ANTEPARTUM COND	ICD-9-CM
768.0	Fetal death from asphyxia or anoxia before onset of labor or at unspecified time	ICD-9-CM
768.1	Fetal death from asphyxia or anoxia during labor	ICD-9-CM
V27.1	SINGLE STILLBORN	ICD-9-CM
V27.3	TWINS, ONE LIVEBORN	ICD-9-CM
V27.4	TWINS, STILLBORN	ICD-9-CM
V27.6	OTHER MULTIPLE BIRTH, SOME LIVEBORN	ICD-9-CM
V27.7	OTHER MULTIPLE BIRTH, ALL STILLBORN	ICD-9-CM
V32	Twin birth mate stillborn	ICD-9-CM
V32.0	TWIN, BORN IN HOSPITAL, MATE STILLBORN	ICD-9-CM
V32.00	Twin birth mate stillborn born in hospital, delivered without mention of cesarean section	ICD-9-CM
V32.01	TWIN, BORN IN HOSPITAL, CESAREAN, MATE STILLBORN	ICD-9-CM
V32.1	Twin birth, mate stillborn, born before admission to hospital	ICD-9-CM
V32.2	Twin birth, mate stillborn, born outside hospital and not hospitalized	ICD-9-CM
V35	OTHER MULTIPLE, mates stillborn	ICD-9-CM
V35.0	OTHER MULTIPLE, BORN IN HOSPITAL, mates stillborn	ICD-9-CM
V35.00	OTHER MULTIPLE, BORN IN HOSPITAL, mates stillborn	ICD-9-CM
V35.01	OTHER MULTIPLE, BORN IN HOSPITAL, CESAREAN, mates stillborn	ICD-9-CM
V35.1	Other multiple birth (three or more), mates all stillborn, born before admission to hospital	ICD-9-CM
V35.2	Other multiple birth (three or more), mates all stillborn, born outside hospital and not hospitalized	ICD-9-CM
V36	Other multiple birth (three or more), mates liveborn and stillborn	ICD-9-CM
V36.0	OTHER MULTIPLE, BORN IN HOSPITAL, mates liveborn and stillborn	ICD-9-CM
V36.00	OTHER MULTIPLE, BORN IN HOSPITAL, mates liveborn and stillborn	ICD-9-CM
V36.01	OTHER MULTIPLE, BORN IN HOSPITAL, CESAREAN, mates liveborn and stillborn	ICD-9-CM
V36.1	Other multiple birth (three or more), mates liveborn and stillborn, born before admission to hospital	ICD-9-CM
V36.2	Other multiple birth (three or more), mates liveborn and stillborn, born outside hospital and not hospitalized	ICD-9-CM
	ICD-10-CM	
O31.00X	Papyraceous fetus, unspecified trimester, not applicable or unspecified	ICD-10-CM
O31.00X	Papyraceous fetus, unspecified trimester, fetus 1	ICD-10-CM
O31.00X	Papyraceous fetus, unspecified trimester, fetus 2	ICD-10-CM
O31.00X	Papyraceous fetus, unspecified trimester, fetus 3	ICD-10-CM
O31.00X	Papyraceous fetus, unspecified trimester, fetus 4	ICD-10-CM
O31.00X	Papyraceous fetus, unspecified trimester, fetus 5	ICD-10-CM
O31.00X	Papyraceous fetus, unspecified trimester, other fetus	ICD-10-CM
O31.02X	Papyraceous fetus, second trimester, not applicable or unspecified	ICD-10-CM
O31.02X	Papyraceous fetus, second trimester, fetus 1	ICD-10-CM
O31.02X	Papyraceous fetus, second trimester, fetus 2	ICD-10-CM
O31.02X	Papyraceous fetus, second trimester, fetus 3	ICD-10-CM
O31.02X	Papyraceous fetus, second trimester, fetus 4	ICD-10-CM

Appendix B. List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) Diagnosis Codes Used to Define Stillbirth in this Request

Code	Description	Code Type
O31.02X	Papyraceous fetus, second trimester, fetus 5	ICD-10-CM
O31.02X	Papyraceous fetus, second trimester, other fetus	ICD-10-CM
O31.03X	Papyraceous fetus, third trimester, not applicable or unspecified	ICD-10-CM
O31.03X	Papyraceous fetus, third trimester, fetus 1	ICD-10-CM
O31.03X	Papyraceous fetus, third trimester, fetus 2	ICD-10-CM
O31.03X	Papyraceous fetus, third trimester, fetus 3	ICD-10-CM
O31.03X	Papyraceous fetus, third trimester, fetus 4	ICD-10-CM
O31.03X	Papyraceous fetus, third trimester, fetus 5	ICD-10-CM
O31.03X	Papyraceous fetus, third trimester, other fetus	ICD-10-CM
O36.4XX	Maternal care for intrauterine death, not applicable or unspecified	ICD-10-CM
O36.4XX	Maternal care for intrauterine death, fetus 1	ICD-10-CM
O36.4XX	Maternal care for intrauterine death, fetus 2	ICD-10-CM
O36.4XX	Maternal care for intrauterine death, fetus 3	ICD-10-CM
O36.4XX	Maternal care for intrauterine death, fetus 4	ICD-10-CM
O36.4XX	Maternal care for intrauterine death, fetus 5	ICD-10-CM
O36.4XX	Maternal care for intrauterine death, other fetus	ICD-10-CM
Z37.1	Single stillbirth	ICD-10-CM
Z37.3	Twins, one liveborn and one stillborn	ICD-10-CM
Z37.4	Twins, both stillborn	ICD-10-CM
Z37.60	Multiple births, unspecified, some liveborn	ICD-10-CM
Z37.61	Triplets, some liveborn	ICD-10-CM
Z37.62	Quadruplets, some liveborn	ICD-10-CM
Z37.63	Quintuplets, some liveborn	ICD-10-CM
Z37.64	Sextuplets, some liveborn	ICD-10-CM
Z37.69	Other multiple births, some liveborn	ICD-10-CM
Z37.7	Other multiple births, all stillborn	ICD-10-CM
P95	Stillbirth	ICD-10-CM
O36.4	Maternal care for intrauterine death	ICD-10-CM

Appendix C. Specifications for Parameters for this Request

Sentinel's Cohort Identification and Descriptive Analysis (CIDA) tool, version 5.4.4, was used to compare the frequency of diagnoses for stillbirth in the inpatient care setting using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes.

Coverage requirement: Medical and drug coverage
Enrollment requirement: 183 days for new occurrence scenarios; 0 days for prevalence scenarios
Enrollment gap: 45 days
Age groups: 12 - 55 years

			Event						
Scenario	Query Start Date	Query End Date	Event	Event Care Setting	Code Source	Event Code Type	Incidence Code Type	Washout (days)	Cohort Definition
1	4/1/2015	9/30/2015	Stillbirth	Inpatient	Algorithm (Naleway[1])	ICD-9-CM	ICD-9-CM or ICD-10-CM	183	All valid diagnoses
2	4/1/2016	9/30/2016	Stillbirth	Inpatient	Forward-Backward Mapping and reviewed code list	ICD-10 -CM	ICD-9-CM or ICD-10-CM	183	All valid diagnoses
3	10/1/2010	03/31/2017	Stillbirth	Inpatient	Algorithm (Naleway)	ICD-9-CM	ICD-9-CM or ICD-10-CM	183	All valid diagnoses
4	10/1/2010	03/31/2017	Stillbirth	Inpatient	Forward-Backward Mapping and reviewed code list	ICD-10 -CM	ICD-9-CM or ICD-10-CM	183	All valid diagnoses
5	10/1/2010	03/31/2017	Stillbirth	Inpatient	Algorithm (Naleway)	ICD-9-CM	N/A	0	All valid diagnoses
6	10/1/2010	03/31/2017	Stillbirth	Inpatient	Forward-Backward Mapping and reviewed code list	ICD-10 -CM	N/A	0	All valid diagnoses

ICD-9-CM and ICD-10-CM are provided by Optum360. ICD-10-CM codes were mapped from ICD-9-CM codes using the Centers for Medicare and Medicaid Services General Equivalence Mappings.

[1]Naleway AL, et al. Identifying pregnancy episodes, outcomes, and mother–infant pairs in the Vaccine Safety Datalink. Vaccine (2013), http://dx.doi.org/10.1016/j.vaccine.2013.03.069.