Disclaimer

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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: November 8, 2019

Request Description: The purpose of this report was to compare the frequency of diagnoses for Alzheimer's disease using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) versus International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis 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 Routine Querying Module: Cohort Identification and Descriptive Analysis (CIDA) module, version 9.0.0

Data Source: This request was run against the IBM® MarketScan® Commercial Claims and Encounters Database and Medicare Supplemental Database, which included 135 million members. Data from October 1, 2010 to September 30, 2018 were included in this report. The report includes five separate time periods: 1) October 1, 2010 to September 30, 2018; 2) October 1, 2013 to September 30, 2014; 3) October 1, 2014 to September 30, 2015; 4) October 1, 2015 to September 30, 2016; and 5) October 1, 2016 to September 30, 2017. See Appendix A for the dates of available data used in this report.

Study Design: We examined the incidence and prevalence of Alzheimer's disease across the ICD-9-CM era (October 2010 - September 2015) and ICD-10-CM era (October 2015 - September 2018) in the United States. Incidence was additionally evaluated from October 2013 to September 2014, October 2014 to September 2015, October 2015 to September 2016, and October 2016 to September 2017. See Appendix B for specific codes used to define Alzheimer's disease in this request.

Cohort Eligibility Criteria: The following age groups were included in the cohorts: 2-17, 18-44, 45-64, and 65+ years.

Incident Cohorts: Members included in the incident cohorts were required to be continuously enrolled in health plans with medical and drug coverage for at least 183 days prior to the Alzheimer's disease diagnosis of interest, during which gaps in coverage of up to 45 days were allowed. Incident Alzheimer's disease defined as no previous diagnoses of Alzheimer's disease in the 183 days preceding the index date with respect to ICD-9-CM and ICD-10-CM codes.

Prevalent Cohorts: There was no enrollment time requirement for members in the prevalent cohorts. All qualifying diagnosis codes that occurred between October 1, 2010 and September 30, 2018 were included.

Please see 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.

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.

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 consultations.

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 switch.

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

Table 1. Comparison of Incident* Alzheimer's Disease Diagnoses 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 (October 2013 - September 2014, October 2014 - September 2015, October 2015 - September 2016, and October 2016 - September 2017)

	Members with Diagnosis	Eligible Members	Members with Diagnosis per 10,000 Eligible Members
Alzheimer's Disease			
ICD-9-CM: October 2013 - September 2014			
	45,244	38,071,175	11.88
ICD-9-CM: October 2014 - September 2015			
	38,462	34,975,619	11.00
ICD-10-CM: October 2015 - September 2016			
	52,888	27,298,369	19.37
ICD-10-CM: October 2016 - September 2017			
	29,248	27,695,783	10.56

*Incidence defined by a 183 day washout

Figure 1. Incidence of Alzheimer's Disease Diagnoses per 10,000 Eligible Members from October 2010 - September 2018 by Code Type, 183-Day Washout

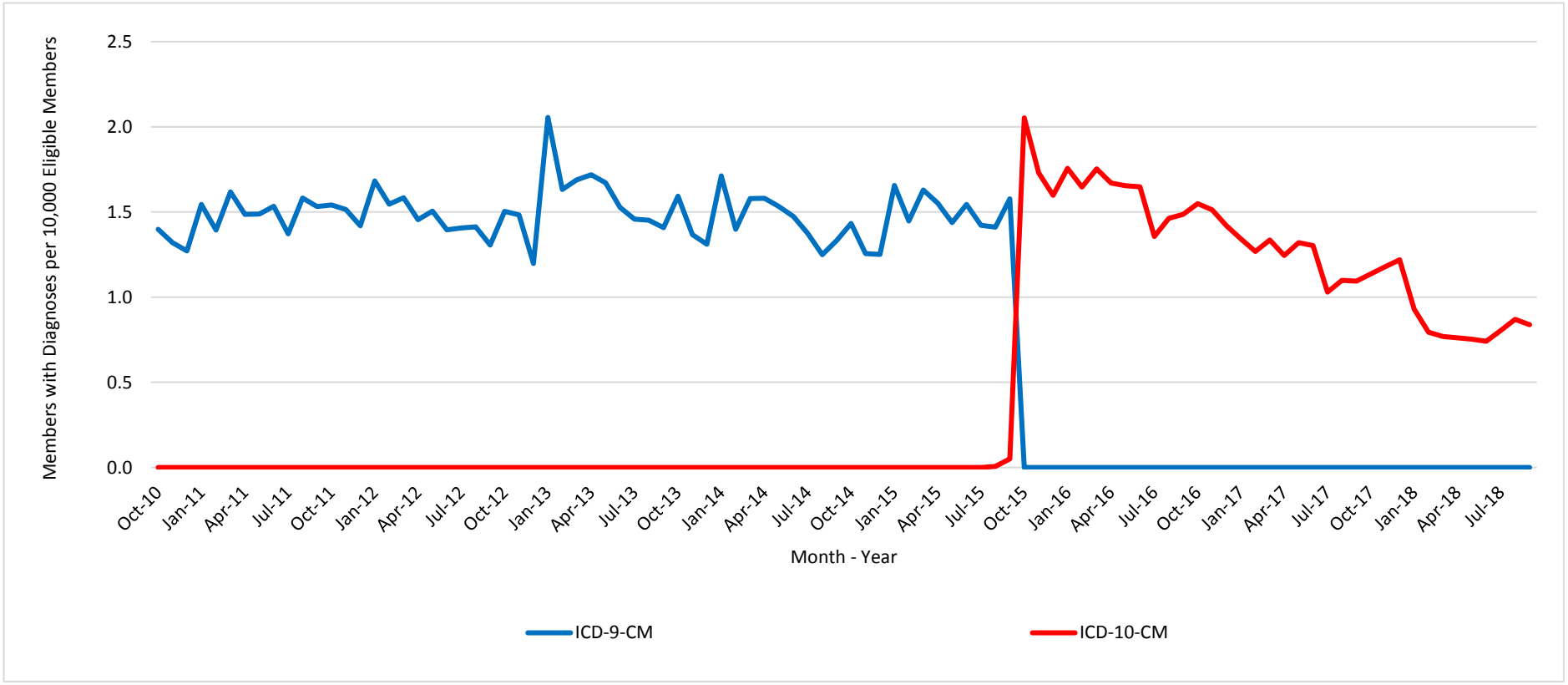
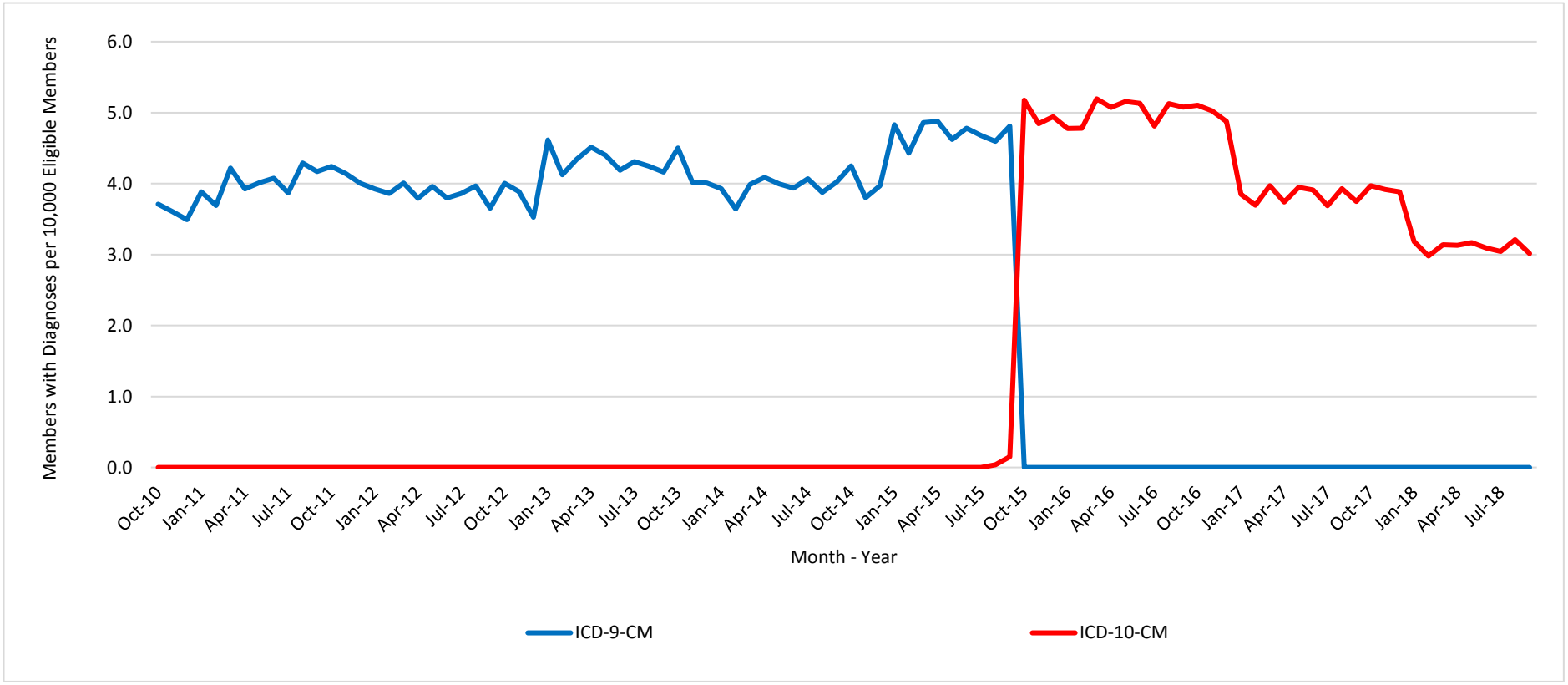


Figure 2. Prevalence of Alzheimer's Disease Diagnoses per 10,000 Eligible Members from October 2010 - September 2018 by Code Type, 0-Day Washout



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

Databases	Start Date	End Date
IBM MarketScan Commercial and Medicare Supplemental Databases[1]	1/1/2010	9/30/2018

[1] The IBM MarketScan Databases includes a sample of 135 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 Alzheimer's Disease

Code	Description	Code Type
	ICD-9-CM	
331.0	Alzheimer's disease	ICD-9-CM
	ICD-10-CM	
G30.0	Alzheimer's disease with early onset	ICD-10-CM
G30.1	Alzheimer's disease with late onset	ICD-10-CM
G30.8	Other Alzheimer's disease	ICD-10-CM
G30.9	Alzheimer's disease, unspecified	ICD-10-CM

Appendix C. Specifications for Parameters for this Request

Sentinel's Cohort Identification and Descriptive Analysis (CIDA) module, version 9.0.0 will be used to compare the frequency of diagnoses for a selection of health outcomes using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) versus International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes.

Enrollment Gap: 45 days
Age Group: 2-17, 18-44, 45-64, 65+ years
Enrollment Requirement: 183 days for incidence scenarios; 0 days for prevalence scenarios
Coverage Requirement: Medical and drug coverage
Stratifications: Calendar year by month

	Event							
Scenario	**Event**	**Query Period Start**	**Query Period End**	**Event Code Type**	**Incident with Respect To**	**Washout (days)**	**Cohort Definition**	**Care Setting**
1	Alzheimer's Disease	10/1/2013	9/30/2014	ICD-9-CM	ICD-9-CM	183	All valid events	Any
2	Alzheimer's Disease	10/1/2014	9/30/2015	ICD-9-CM	ICD-9-CM	183	All valid events	Any
3	Alzheimer's Disease	10/1/2015	9/30/2016	ICD-10-CM	ICD-10-CM	183	All valid events	Any
4	Alzheimer's Disease	10/1/2016	9/30/2017	ICD-10-CM	ICD-10-CM	183	All valid events	Any
5	Alzheimer's Disease	10/1/2010	9/30/2018	ICD-9-CM	ICD-9-CM or ICD-10-CM	183	All valid events	Any
6	Alzheimer's Disease	10/1/2010	9/30/2018	ICD-10-CM	ICD-9-CM or ICD-10-CM	183	All valid events	Any
7	Alzheimer's Disease	10/1/2010	9/30/2018	ICD-9-CM	N/A	0	All valid events	Any
8	Alzheimer's Disease	10/1/2010	9/30/2018	ICD-10-CM	N/A	0	All valid events	Any

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.