MINI-SENTINEL MODULAR PROGRAMS

MODULAR PROGRAM 4: FREQUENCY OF SELECT EVENTS DURING CONCOMITANT EXPOSURE TO DRUG/PROCEDURE GROUPS OF INTEREST

Documentation version: 5.0

Prepared by the Mini-Sentinel Operations Center

For use with Modular Program 4 version 5.0

February 7, 2014

Table of Contents

Modification History

Version	Date	Modification	By
5.0	12/17/2013	• Added Macro parameter "COVERAGE" • Added Query File parameter "ENRDAYS" • Added Concomitant Exposure, Event, Incident Event, and Dispensing Processing input files • Revised text describing primary, secondary, and concomitant episode creation • Added description of event identification and days at risk metrics	Mini-Sentinel Operations Center
4.0	5/16/2013	• Revised the way the MP4 matches codes of interest to allow either exact code match and/or wildcard match. • Added optional Output Table Selection module to instruct the MP4 to preserve only certain output tables in the final output library. • Revised various input files to allow diagnosis codes to be queried, allowing the requester to now use any type of codes in any input files.	Mini-Sentinel Operations Center
3.0	1/25/2013	• Revised former "Inclusion/Exclusion Conditions File" to be the new "Inclusion/Exclusion Conditions File" and updated functionality, file, and output descriptions. • Made clarifications to text based on user feedback.	Mini-Sentinel Operations Center
2.1	11/15/2012	• Up-versioned due to increment from mp4_2.0 to mp4_2.1	Mini-Sentinel Operations Center
2.0	11/9/2012	• Original published version	Mini-Sentinel Operations Center

I. OVERVIEW

Mini-Sentinel modular programs (MPs) allow rapid implementation of standard queries across the Mini-Sentinel Distributed Database (MSDD). MPs are designed to run against the Mini-Sentinel Common Data Model (MSCDM).[1] They are written in SAS and can be customized using various parameter settings that define exposures, outcomes, date ranges, age ranges, and other implementation details. This document describes the key program specifications and main assumptions underlying each of the query parameters for Modular Program 4 (MP4) version 5.0. Program specification requirements, formats, and default values of all parameters are defined. A sample program specification is provided along with output from a sample scenario.

II. TERMINOLOGY

For simplicity, the term "scenario" is used throughout this document to refer to a set of parameters and criteria used to define an execution of the MP. The "requester" refers to an individual (or group of individuals) who initiates the MP request and defines the scenarios. The term "request programmer" refers to an individual who creates request input files and distributes the MP to the Data Partners.

The terms "exposure" and "exposure of interest" are used to represent exposure to a medical product or procedure as defined by the MP requester. An exposure can be defined using any set of NDC, procedure and/or diagnosis codes found in the MSCDM. For example, exposure to a drug product dispensed in the outpatient setting can be defined as observation of one or more National Drug Codes (NDCs) in the pharmacy dispensing file, whereas exposure to a vaccine can be defined based on observation of specific procedure codes in the procedure file.

A "treatment episode" or "episode" is a period of continuous exposure defined using outpatient pharmacy dispensings, procedures and/or diagnoses. For dispensings, a treatment episode is a dispensing sequence that has no interruption in days supplied greater than an allowable "gap". The allowable gap is the number of days used to bridge dispensings to create a continuous treatment episode.

The terms "primary exposure" and "secondary exposure" are used to differentiate two unique exposures defined by the requester. Overlap between primary exposure treatment episodes and secondary exposure treatment episodes defines "concomitant exposure" treatment episodes.

The terms "event" and "event of interest" are used to represent the occurrence of a diagnosis, procedure and/or dispensing as defined by the MP requester. An event can therefore be defined using any set of diagnosis, procedure and/or NDCs found in the MSCDM.

The term "condition" is used to represent a medical code (or a group of codes) that identify a medical condition of interest.

The term "claim" is used to represent either an outpatient pharmacy dispensing or medical encounter/record with any of the codes for the exposure(s) or condition(s) of interest.

---

[1] See http://www.mini-sentinel.org/data_activities/ for more information about the MSCDM.

The term "member" is used to represent an individual with relevant criteria for enrollment, exposure(s), and condition(s) (as specified by the MP parameters). A member can be further defined as a "user" if evidence of use of exposure(s) of interest is observed.

Whenever a primary user is identified, the service date on the claim of the first primary exposure observed during the relevant period of interest is labeled the "primary exposure index date". Whenever a secondary user is identified, the service date on the claim of the first secondary exposure observed during the relevant period of interest is labeled the "secondary exposure index date". The date of concomitant exposure start is labeled the "concomitant exposure index date". The concomitant exposure index date will always correspond to the index date of whichever exposure – primary or secondary – was initiated last.

The execution of MP4 allows information for multiple scenarios to be generated at the same time. Results from all scenarios are included in the MP output tables and can be differentiated using "group names" defined by the requester. This document describes the process for only one scenario to be tested.

III.   PROGRAM SUMMARY

MP4 is used to characterize the frequency of select event(s) among a cohort of members with concomitant use of two exposure(s) of interest during a period defined by a start and an end date (*i.e.*, the query period). In MP4 primary exposure treatment episodes and secondary exposure treatment episodes are created independently. Overlap between primary exposure treatment episodes and secondary exposure treatment episodes defines concomitant treatment episodes. By default, MP4 generates metrics for both prevalence (*i.e.*, ever exposed during query period) and incidence (*i.e.*, newly exposed during query period) based cohorts.

MP4 has three optional modules available. One is an inclusion/exclusion feature to further restrict the analysis to members with and/or without "conditions" before or after an index date. Another allows the user to define how days supply and amount supplied on each dispensing should be processed by the MP. The third module allows the requester to output only a subset of result tables generated, reducing workload to compile and review results that are not relevant to a specific request.

One run of MP4 generates thirty-three output tables. Fifteen tables describe primary exposure, secondary exposure, concomitant exposure, exposed events, concomitance intensity, and concomitance intensity distribution for the prevalence-based cohort. An additional fifteen tables describe the same characteristics of the incidence-based cohort. Another table details the number of dispensings excluded from consideration by the MP based on user-defined parameters in the Dispensing Processing File. An additional table contains results for all possible combinations of strata (*e.g.*, by year/age group/sex). Finally, another table containing denominator information for all strata is generated. Combining the information from these last two tables allows the requester to generate population-based background rates (Section VI).

MP4 requires the specification of several parameters to define a scenario. These include program parameters that specify a request identifier, execution (run) identifier, query period, age range(s), and enrollment criteria. The names of input files (built as SAS datasets) containing several other parameters

used to identify exposure(s) of interest, incident users, events, and condition(s) of interest must also be specified.

One input file is the Primary Exposure File that defines the primary outpatient pharmacy medications, medical procedures and/or diagnoses of interest. The second file is the Incident Primary Exposure File; it is optional and is used to refine how incident users are defined. The third file is the Secondary Exposure File; it is used to describe the secondary outpatient pharmacy medications /procedures/diagnoses of interest. The fourth file is the Incident Secondary Exposure File; it is optional and is used to refine how incident secondary users are defined. The fifth file is the Concomitant Exposure File that defines how concomitant treatment episodes are constructed. The sixth file is the Event File that defines events of interest. The seventh file is the Incident Event File; it is also optional and is used to refine incident definition for events of interest. The eighth file is the Inclusion/Exclusion Conditions File, which defines the outpatient pharmacy medications, medical procedures and/or diagnoses used to restrict the cohort to members with and/or without conditions of interest. The ninth file is the Output Table Selection File, which defines the subset of MP4 output files to generate. The tenth file, the Dispensing Processing File, defines allowable ranges for days supplied and amount supplied values, and defines how multiple dispensings on the same day are handled. All parameters and input file specifications are described in Section IV.

IV.   PROGRAM PARAMETER AND INPUT FILE SPECIFICATIONS

A.   PROGRAM PARAMETER SPECIFICATIONS

There are several main program parameters that may be specified. These include a request identifier, run identifier, start and end dates for the query period, age stratifications, coverage type requirements, an allowed enrollment gap used to create continuous enrollment periods, and ten input files (the Primary Exposure File, Incident Primary Exposure File, Secondary Exposure File, Incident Secondary Exposure File, Concomitant Exposure File, Event File, Incident Event File, Inclusion/Exclusion Conditions File, Output Table Selection File, and Dispensing Processing File). Table 1 contains detailed specifications on each of these required parameters.

Table 1: Main Program Parameter Specification

Parameter	Field Name	Description
Request Identifier	REQUESTID	**Details**: a request identifier. The identifier is appended to all output file names. **Note 1:** must be 5 characters in length. The REQUESTID should start with "mpr" and include two additional digits with the assigned request number. **Defined by:** Request programmer **Input type:** Required **Format:** Alphanumeric **Example**: REQUESTID=mpr01
Run Identifier	RUNID	**Details**: a run identifier to denote each execution of the program. The identifier is appended to all output file names.

Parameter	Field Name	Description
		Note 1: must be 3 characters in length. The RUNID should start with "r" and include two additional digits with the assigned execution number. **Defined by:** Request programmer **Input type:** Required **Format:** Alphanumeric **Example**: RUNID=r01
Enrollment Gap	ENROLGAP	**Details:** sets the number of days that will be bridged between two consecutive enrollment periods to create a "continuously enrolled" period. For example, if ENROLGAP=30 and a member is eligible for medical coverage in periods 1/1/2007-3/27/2007 and 4/1/2007-12/21/2007 (*i.e.,* a 4-day gap between two consecutive enrollment episodes), the member will be considered continuously enrolled from 1/1/2007 to 12/21/2007. In this example, a gap in enrollment of greater than 30 days will result in a new enrollment period, and all the days in the gap will be considered un-enrolled. A gap of 45-days is recommended for most uses. **Named by:** Requester **Input type:** Required **Format**: Numeric **Example**: ENROLGAP=14 (gaps less than or equal to 14 days will be "bridged" to form one "continuously enrolled" sequence)
Coverage Type Requirement	COVERAGE	**Details:** an optional parameter to allow medical and drug coverage type requirements to be user-defined and not CODETYPE dependent. Valid values are: • **M:** only enrollment spells with at least medical coverage should be considered by the MP algorithm • **D:** only enrollment spells with at least drug coverage should be considered by the MP algorithm • **MD:** only enrollment spells with both medical and drug coverage should be considered by the MP algorithm (**default value**) **Note 1:** the type of coverage required is enforced for both the required Washout Period and the Minimum Enrollment Pre-Index Days features (see WASHPER and ENRDAYS parameters in the Primary Exposure File section). **Note 2:** if the COVERAGE value is left blank, or contains invalid

Parameter	Field Name	Description
		values (i.e., values other than "M", "D", or "MD"), the MP algorithm will consider only enrollment spells with both medical and drug coverage by default. **Defined by:** Requester **Input type:** Optional (default value is **MD**) **Format:** SAS character $2 **Example**: MD
Query Start Date	QUERYFROM	**Details:** date for the start of the query identification period. If QUERYFROM =03/01/2008, only treatment episodes initiated on or after this date will be considered. **Named by:** Requester **Input type:** Required **Format:** mm/dd/yyyy **Example**: QUERYFROM=03/01/2008
Query End Date	QUERYTO	**Details:** date for the end of the query identification period. If QUERYTO=03/31/2009, only treatment episodes initiated before this date will be considered. **Note:** QUERYTO only binds treatment episode start dates (*i.e.*, the index date). Treatment episodes may extend beyond QUERYTO if they start between QUERYFROM and QUERYTO. **Named by:** Requester **Input type:** Required **Format:** mm/dd/yyyy **Example:** QUERYTO=03/31/2009
Primary Exposure File	PRIMFILE	**Details:** name of the SAS dataset defining the primary exposure(s) of interest. It lists the codes of interest that define each primary exposure of interest. The file name, including its extension, must be entered. For specific details on the content of this file, see Section IV.B. **Named by:** Request programmer **Input type:** Required **Format:** **.**sas7bdat or .cport file format **Example:** PRIMFILE=prim.sas7bdat or prim.cport
Incident Primary Exposure File	INCPRIMFILE	**Details:** name of the SAS dataset refining the incident primary exposure definition(s). It contains additional codes and various parameters to further refine how incident use of each primary exposure must be defined. The file name, including its extension, must be entered. For specific details on the content of this file, see Section IV.B.

Parameter	Field Name	Description
		Named by: Request programmer **Input type:** Optional **Format:** .sas7bdat or .cport file format **Example:** INCPRIMFILE=incprim.sas7bdat or incprim.cport
Secondary Exposure File	SECFILE	**Details:** name of the SAS dataset defining the secondary exposure(s) of interest. The file name including its appropriate extension must be entered. For specific details on the content of this file, please see the "Input File Description" section. For specific details on the content of this file, see Section IV.B. **Named by:** Request programmer **Input type:** Required (cannot be left blank) **Format:** .sas7bdat or .cport file format **Example:** SECFILE=sec.sas7bdat or sec.cport
Incident Secondary Exposure File	INCSECFILE	**Details:** name of the SAS dataset refining the incident secondary exposure definition(s). The file name including its appropriate extension must be entered. For specific details on the content of this file, please see the "Input File Description" section. For specific details on the content of this file, see Section IV.B. **Named by:** Request programmer **Input type:** Optional **Format:** .sas7bdat or .cport file format **Example:** INCSECFILE=incsec.sas7bdat or incsec.cport
Concomitant Exposure File	CONCOMFILE	**Details:** name of the SAS dataset defining how concomitant treatment episodes are created. The file name including its appropriate extension must be entered. For specific details on the content of this file, please see the "Input File Description" section. For specific details on the content of this file, see Section IV.B. **Named by:** Request programmer **Input type:** Required (cannot be left blank) **Format:** .sas7bdat or .cport file format **Example:** CONCOMFILE=conc.sas7bdat or conc.cport
Event File	QUERYEVENTFILE	**Details:** name of the SAS dataset defining the query event(s) of interest. It lists the codes of interest and various parameters to specify how each code must be queried by MP3. The file name, including its extension, must be entered. For specific details on the content of this file, see Section IV.B. **Named by:** Request programmer **Input type:** Required **Format:** .sas7bdat or .cport file format **Example:** QUERYEVENTFILE=event.sas7bdat or event.cport
Incident Event File	INCEVENTFILE	**Details:** name of the SAS dataset refining the incident event

Parameter	Field Name	Description
		definition(s). It contains additional codes and various parameters to further refine how incident events must be defined. The file name, including its extension, must be entered. For specific details on the content of this file and for an example of when this file is used and how it is different from the Event File, see Section IV.B. **Named by:** Request programmer **Input type:** Optional **Format:** .sas7bdat or .cport file format **Example:** INCEVENTFILE=incevent.sas7bdat or incevent.cport
Inclusion/Exclusion Conditions File	CONDFILE	**Details:** name of the SAS dataset defining the conditions of interest. It lists the condition codes of interest and various parameters to specify how each code must be queried by MP4. The file name, including its extension, must be entered. For specific details on the content of this file, see Section IV.B. **Named by:** Request programmer **Input type:** Optional **Format:** .sas7bdat or .cport file format **Example:** CONDFILE=cond.sas7bdat or cond.cport
Output Table Selection File	OUTTABLESFILE	**Details:** name of the SAS dataset defining the output table(s) to be preserved in the output folder. The file name, including its extension, must be entered. For specific details on the content of this file, see Section IV.B. **Named by:** Request programmer **Input type:** Optional **Format:** .sas7bdat or .cport file format **Example:** OUTTABLESFILE = output.sas7bdat or output.cport
Dispensing Processing File	STOCKPILINGFILE	**Details:** name of the SAS dataset defining how dispensings, days supplied, and amount supplied are handled for primary and secondary exposure treatment episodes. The file name, including its extension, must be entered. For specific details on the content of this file, see Section IV.B. **Named by:** Request programmer **Input type:** Optional **Format:** .sas7bdat or .cport file format **Example:** STOCKPILINGFILE = stockpil.sas7bdat or stockpil.cport
Age Groups	AGESTRAT	**Details:** age group categories for reporting. Specifying this parameter will (1) restrict to certain age groups and (2) specify how age groups will be stratified in the result tables. For example, to have results stratified by 20 year increments for members 40-99 years of age, AGESTRAT=40-59 60-79 80-99 would be entered.

Parameter	Field Name	Description
		Note 1: age is determined at the index date.
		Note 2: various units of time can be used. Valid values are:
		D: days **W**: weeks **Q**: quarters **M**: months **Y**: years (default value)
		Note 3: lower value is binding. If AGESTRAT=0-5 5-10, then all 5 year olds (*e.g.*, 5.2, 5.5, 5.8) will be placed in the second age group. If AGESTRAT=0-5 6-10, then all 5 year olds will be placed in the first age group.
		For example, to have results stratified by 6 month increments for the first two years of life and then by 2 year increments until the age of 6, AGESTRAT = 00M-05M 06M-11M 12M-17M 18M-23M 02Y-03Y 04Y-05Y needs to be entered.
		Named by: Requester
		Input type: Optional (default value is **00**-**01 02**-**04 05**-**09 10**-**14 15**-**18 19**-**21 22**-**44 45**-**64 65**-**74 75+ in years**)
		Format: AA-AA BB-BB ZZ-ZZ
		Example: AGESTRAT=**40-59 60-79 80-99**

B. INPUT FILE SPECIFICATIONS

In addition to the main program parameters, several required and optional parameters need to be specified in the Primary Exposure, Incident Primary Exposure, Secondary Exposure, Incident Secondary Exposure, Concomitant Exposure, Event, Incident Event, Inclusion/Exclusion Condition, Output Table Selection, and Dispensing Processing files.

1. Primary Exposure File

The Primary Exposure File is required. It contains the comprehensive set of codes used to define the primary exposure(s) of interest. National Drug Codes (NDCs), ICD procedure and diagnosis codes, or Healthcare Common Procedure Coding System (HCPCS) codes can be used to define exposures of interest. Exposure(s) of interest can be defined using any mix of allowed code types.

The structure of the Primary Exposure File must reflect how codes should be queried to define a unique exposure. The GROUP field is used to group all codes pertaining to a given exposure of interest. For example, the GROUP "Exposure1" could be defined by all NDCs for any oral forms of anti-diabetic medications, the GROUP "Exposure2" by a mix of NDC and HCPCS codes for certain insulin products, and another GROUP "Exposure3" by only those NDCs for a recently approved oral form of anti-diabetic medication. Results will be reported for the GROUP, not individual codes, generic drug names, or procedure names. Table 2 below describes the specifications for Primary Exposure File.

Table 2: Primary Exposure File Specification

Parameter	Field Name	Description
Name of Primary Group	GROUP	**Details:** standardized name used to refer to a GROUP for primary exposure(s) of interest to be queried. **Note**: multiple primary exposure groups can be defined within the same Primary Exposure File. All groups are queried independently and results are reported separately and labeled using each primary exposure GROUP name specified. **Named by:** Request programmer **Input type:** Required **Format:** Alphanumeric; SAS character $30; no special characters (*e.g.*, commas, periods, hyphens, etc) allowed, and underscores must be used to mark spaces. **Example:** ACE_Inhibitors
Name of Primary Subgroup	SUBGROUP	**Details:** standardized name used to refer to a primary exposure SUBGROUP to be queried. **Note1:** useful when individual primary exposure groups are comprised of multiple drugs/procedures/diagnoses. For example, if GROUP= "ACE_Inhibitors", SUBGROUP may take the values "enalapril" or "lisinopril" to differentiate drugs. **Note 2:** SUBGROUP field is used by the stockpiling algorithm as group categories to adjust claim service dates. See Section V.B for more details. **Note 3**: No output will be presented by SUBGROUP. All output is presented at the GROUP level. **Named by:** Request programmer **Input type:** Required **Format:** Alphanumeric; SAS character $30; no special characters (*e.g.*, commas, periods, hyphens, etc) allowed, and underscores must be used to mark spaces. **Example:** enalapril
Primary Code Type	CODETYPE	**Details:** type of each code value included in the CODE field (below) of this file. Valid values are all those allowed by the MSCDM: • **DX09**: ICD-9-CM diagnosis • **DX10**: ICD-10-CM diagnosis • **DX11**: ICD-11-CM diagnosis • **RX11**: 11-digit NDC • **RX09**: 9-digit NDC • **PX09**: ICD-9-CM procedure • **PX10**: ICD-10-CM procedure

Parameter	Field Name	Description
		• **PX11**: ICD-11-CM procedure • **PXC4**: CPT-4 procedure (*i.e.,* HCPCS Level I) • **PXHC**: HCPCS procedure (*i.e.,* HCPCS Level II) • **PXH3**: HCPCS Level III procedure • **PXC2**: CPT Category II procedure • **PXC3**: CPT Category III procedure **Named by:** Request programmer **Input type:** Required **Format:** Alphanumeric; SAS character $4. **Example:** PX09
Primary Codes of Interest	CODE	**Details:** code values for the primary exposure(s) of interest. **Note 1:** codes are matched using exact values (i.e., 3-digit code lookup requires an exact 3-digit code match). Wildcard match (*) functionality is also available (e.g., querying "250*0" would be used to find any ICD-9-CM diagnosis codes for diabetes type II, or "250*" to find ICD-9-CM diagnosis codes for all diabetes codes that start with "250"). **Note 2**: for NDCs, either 9 or 11 digit codes can be entered. **Note 3:** remove decimal points in the code value. **Note 4**: CODETYPE must be consistent with the expected format of the CODE value (*e.g.*, MP4 will not find any valid matches in the data for CODETYPE=RX11 and a 9-digit NDC value). **Note 5**: duplicate CODETYPE-CODE combinations in a given GROUP are removed by the MP4 algorithm. **Named by:** Requester, with support from the MSOC as needed **Input type:** Required **Format:** Alphanumeric; SAS character $11. **Example:** 12345678911
Primary Incidence Type	WASHTYP	**Details:** selects how incidence for the primary exposure will be defined. As detailed in <u>Section V</u>, the incidence type can take the following values: • **MIN**: minimum incidence -- identifies and reports metrics only for the *first* valid incident primary treatment episode during the query period, and uses ALL observed claims - even those before the query period start date - to define incidence. That is, incidence is defined as the first primary treatment episode during the query period with no evidence of prior exposure using all available data. • **SING**: single incidence -- identifies and reports metrics only for the *first* valid incident primary treatment episode during the query period, and

Parameter	Field Name	Description
		uses claims observed during the specified WASHPER days to determine incidence. That is, incidence is defined as the first primary treatment episode during the query period with no evidence of prior exposure during WASHPER days. • **MULT**: multiple incidence -- identifies and reports metrics for *all* valid incident primary treatment episodes during the query period, and uses claims observed during the specified WASHPER days to determine incidence. That is, incidence is defined as any primary treatment episode during the query period with no evidence of prior exposure during WASHPER days. **Note 1:** WASHTYP parameter is used in conjunction with the Primary Washout Period (WASHPER; see below) to define a valid incident primary treatment episode. **Note 2**: the set of all primary treatment episodes reported using the single incidence case is a subset of all episodes from the multiple incidence case. **Note 3:** the MP4 algorithm may use days before QUERYFROM to ensure incidence criteria are met. **Note 4**: MIN setting should be used with caution as interpretation is complex. A primary treatment episode that meets the MIN criteria must occur during the query period and cannot be preceded by a disqualifying exposure at any time during enrollment; that is, the look-back period to define incidence is not limited to the washout period. See Section V.E for details. **Named by:** Requester, with support from the MSOC as needed **Input type:** Required **Format:** Alphanumeric; SAS character $4; case sensitive (upper case only). **Example:** MULT
Primary Washout Period	WASHPER	**Details:** length of washout period in days. The washout period is a period of time before an incident primary treatment episode index date during which a member cannot have any evidence of exposure(s) of interest or any other exposure(s) specified in the Incident Primary Exposure File. The washout period is also used to ensure that appropriate pharmacy and medical benefit coverage requirements are met (See Section V.B). In conjunction with the ENROLGAP, COVERAGE, and ENRDAYS parameters, the WASHPER parameter is used to ensure that appropriate enrollment requirements are met. Since at least WASHPER days of enrollment must be found prior to index date, the ENRDAYS parameter value is only binding if ENRDAYS > WASHPER (See Section V.A). If enrollment requirements prior to index date are not met, treatment episode incidence cannot be determined and thus the episode is excluded from output metrics. **Note 1**: length of primary washout period days must be the same within a

Parameter	Field Name	Description
		given primary GROUP. **Note 2**: required and used in conjunction with any Primary Incidence Types (WASHTYP; see above). **Note 3:** the MP algorithm may use days before QUERYFROM to determine if continuous enrollment and incidence criteria are met. **Note 4:** When WASHTYP=MIN, WASHPER is only used to assess continuous enrollment eligibility. **Named by:** Requester **Input type:** Required (0 must be entered if no washout is required) **Format:** Numeric **Example:** 183
Minimum Pre-Index Enrollment Days	ENRDAYS	**Details:** optional parameter to further restrict the number of days of continuous enrollment prior to start of new incident primary treatment episode to reach a certain minimum. **Note 1**: if not specified by the requester a default value of 0 days is used by the MP algorithm. **Note 2**: if specified must be the same within a given query GROUP. **Note 3**: in conjunction with the ENROLGAP, COVERAGE, and WASHPER parameters, the Primary Exposure File minimum pre-index enrollment days parameter is used to ensure that appropriate enrollment requirements are met. Since at least WASHPER days of enrollment must be found prior to primary episode index date, the Primary Exposure File ENRDAYS parameter value is only binding if ENRDAYS > WASHPER (See Section V.A). If enrollment requirements prior to primary index date are not met, treatment episode incidence cannot be determined and thus the episode is excluded from output metrics. **Named by:** Requester **Input type:** Optional (default value is 0) **Format:** Numeric **Example:** 365
Primary Episode Gap	EPISODEGAP	**Details:** primary exposure treatment episode allowable gap in days. For any two primary group claims, a gap of more than EPISODEGAP days between the claim date and the end of days of supply of the previous claim triggers a new primary exposure treatment episode. **Note**: If 0 is entered, no interruption in primary group days of supply will be tolerated. **Named by:** Requester

Parameter	Field Name	Description
		Input type: Required (0 must be entered if no episode gap is required) **Format:** Numeric **Example:** 10
Primary Treatment Minimum Episode Duration	MINEPISDUR	**Details:** minimum episode duration in days for the primary exposure treatment episodes. Rejects treatment episodes of fewer than MINEPISDUR days. **Note 1:** the MP algorithm considers any specified episode extensions (EXPEXTPER; below) and episode gaps (EPISODEGAP; above) in duration calculations. **Named by:** Requester **Input type:** Required (0 must be entered if no constraint is required) **Format:** Numeric **Example:** 60
Primary Treatment Minimum Days Supply	MINDAYSUPP	**Details:** minimum days of supply required for a primary exposure treatment episode. Rejects treatment episodes of fewer than MINDAYSUPP days. **Named by:** Requester **Input type:** Required (0 must be entered if no constraint is required) **Format:** Numeric **Example:** 60
Primary Treatment Minimum Follow-up Period	FOLLOWPER	**Details:** minimum number of days the member must be eligible for pharmacy and/or medical benefits after the primary exposure index date. Rejects users with fewer than FOLLOWPER days of pharmacy and/or medical benefits. **Named by:** Requester **Input type:** Required (0 must be entered if no minimum follow-up period is required) **Format:** Numeric **Example:** 60
Primary Treatment Episode Extension Period	EXPEXTPER	**Details:** extends the length of the primary exposure treatment episode by specified number of days. A primary exposure treatment episode can be extended EXPEXTPER days after the last day of supply of the primary exposure treatment episode's last claim. **Named by:** Requester **Input type:** Required (0 must be entered if no episode extension period is required) **Format:** Numeric **Example:** 10

2. Incident Primary Exposure File

The Incident Primary Exposure File is optional. If defined, the file contains the comprehensive set of codes used to refine the incidence definition of the primary exposure(s) of interest. Just like the Primary Exposure File, the file can include any mix of the following allowed code types: NDCs, ICD procedure and

diagnosis codes, or Healthcare Common Procedure Coding System (HCPCS) codes to define exposures of interest.

The GROUP structure of the Incident Primary Exposure File must match that of the Primary Exposure File. That is, for each GROUP defined in the Incident Primary Exposure File a matching GROUP must be found in the Primary Exposure File to refine the incidence definition of the primary exposure(s) of interest.

By default, for a given primary GROUP MP4 uses the list of codes included in the Primary Exposure File to determine the incident status of identified primary exposures. That is, incidence is defined as no exposure to the primary exposure of interest in the primary washout period (WASHPER). The Incident Primary Exposure File is used to define incidence based on an additional set of codes other than those used to define the primary exposure of interest. For example, the requester may be interested in examining the use of Drug A, but wants all incident users of Drug A to be free of Drug A, B and C in the 183 days before the Drug A index date. In this case, the list of codes for Drug A would be included in the Primary Exposure File, and the list of codes for Drug B and Drug C would be included in the Incident Primary Exposure File. Table 3 contains detailed specifications for the Incident Primary Exposure File.

Table 3: Incident Primary Exposure File Specification

Parameter	Field Name	Description
Name of Primary Group	GROUP	**Details:** standardized name used to refer to a GROUP for primary exposure(s) of interest to be queried. **Note**: must match GROUP values from the Primary Exposure File. **Named by:** Request programmer **Input type:** Required **Format:** Alphanumeric; SAS character $30; no special characters (*e.g.*, commas, periods, hyphens, etc) allowed, and underscores must be used to mark spaces. **Example:** ACE_Inhibitors
Name of Primary Incident Subgroup	SUBGROUP	**Details:** standardized name used to refer to a primary exposure SUBGROUP to be queried. **Note1:** useful when individual primary exposure groups are comprised of multiple drugs/procedures/diagnoses. For example, if GROUP= "ACE_Inhibitors", SUBGROUP may take the values "enalapril" or "lisinopril" to differentiate drugs. **Note 2:** SUBGROUP field is used by the stockpiling algorithm as group categories to adjust claim service dates. See Section V.B for more details. **Note 3**: No output will be presented by SUBGROUP. All output is presented at the GROUP level. **Named by:** Request programmer **Input type:** Required

Parameter	Field Name	Description
		Format: Alphanumeric; SAS character $30; no special characters (*e.g.*, commas, periods, hyphens, etc) allowed, and underscores must be used to mark spaces. **Example:** enalapril
Primary Incident Code Type	CODETYPE	**Details:** type of each code value included in the CODE field (below) of this file. Valid values are all those allowed by the MSCDM: • **DX09**: ICD-9-CM diagnosis • **DX10**: ICD-10-CM diagnosis • **DX11**: ICD-11-CM diagnosis • **RX11**: 11-digit NDC • **RX09**: 9-digit NDC • **PX09**: ICD-9-CM procedure • **PX10**: ICD-10-CM procedure • **PX11**: ICD-11-CM procedure • **PXC4**: CPT-4 procedure (*i.e.*, HCPCS Level I) • **PXHC**: HCPCS procedure (*i.e.*, HCPCS Level II) • **PXH3**: HCPCS Level III procedure • **PXC2**: CPT Category II procedure • **PXC3**: CPT Category III procedure **Defined by:** Request programmer **Input type:** Required **Format:** Alphanumeric; SAS character $4 **Example:** PX09
Primary Incident Only Codes	CODE	**Details:** code values to be used to defined additional exposure(s) to refine the incident definition for the exposure(s) of interest for this primary group. **Note 1:** codes are matched using exact values (i.e., 3-digit code lookup requires an exact 3-digit code match). Wildcard match (*) functionality is also available (e.g., querying "250*0" would be used to find any ICD-9-CM diagnosis codes for diabetes type II, or "250*" to find ICD-9-CM diagnosis codes for all diabetes codes that start with "250"). **Note 2**: for NDCs, either 9 or 11 digit codes can be entered. **Note 3:** remove decimal points in the code value **Note 4**: CODETYPE must be consistent with the expected format of the CODE value (*e.g.*, MP4 will not find any valid matches in the data for CODETYPE=RX11 and a 9-digit NDC value). **Note 5**: duplicate CODETYPE-CODE combinations in a given GROUP are

Parameter	Field Name	Description
		removed by the MP4 algorithm. **Named by:** Requester, with support from MSOC as needed **Input type:** Required **Format:** Alphanumeric; SAS character $11 **Example:** 12345678922

3. Secondary Exposure File

The Secondary Exposure File is required and used to specify the secondary drug/procedure/diagnosis codes of interest. The Secondary Exposure File allows inclusion of the following code types: NDCs, ICD procedure and diagnosis codes, or Healthcare Common Procedure Coding System (HCPCS) codes to define condition(s) of interest. GROUPs can be defined using any mix of these allowed code types. Values of the GROUP fields must match between the Primary Exposure File and the Secondary Exposure File. Table 4 contains detailed specifications for the Secondary Exposure File.

Table 4: Secondary Exposure File Specification

Parameter	Field Name	Description
Name of Primary Group	GROUP	**Details:** standardized name used to refer to a GROUP for *primary* exposure(s) of interest to be queried. This will be used to link the Secondary and Primary groups. **Note:** must match GROUP values from the Primary Exposure File. **Named by:** Request programmer **Input type:** Required **Format:** Alphanumeric; SAS character $30; no special characters (*e.g.*, commas, periods, hyphens, etc) allowed, and underscores must be used to mark spaces. **Example:** ACE_Inhibitors
Name of Secondary Subgroup	SUBGROUP	**Details:** standardized name used to refer to a SUBGROUP for *secondary* exposure(s) of interest to be queried. This is used by the stockpiling algorithm to create secondary exposure treatment episodes. **Note1:** useful when individual secondary exposures are comprised of multiple drugs/procedures/diagnoses. For example, if GROUP= "MAO_Inhibitors", secondary SUBGROUP may take the values "isocarboxazid" or "phenelzine" to differentiate drugs. **Note 2:** SUBGROUP field is used by the stockpiling algorithm as group categories to adjust claim service dates. See Section V.B for more details. **Named by:** Request programmer **Input type:** Required **Format:** Alphanumeric; SAS character $30; no special characters (*e.g.*,

Parameter	Field Name	Description
		commas, periods, hyphens, etc) allowed, and underscores must be used to mark spaces. **Example:** phenelzine
Secondary Code Type	CODETYPE	**Details:** type of each code value included in the CODE field (below) of this file. Valid values are all those allowed by the MSCDM: • **DX09**: ICD-9-CM diagnosis • **DX10**: ICD-10-CM diagnosis • **DX11**: ICD-11-CM diagnosis • **RX11**: 11-digit NDC • **RX09**: 9-digit NDC • **PX09**: ICD-9-CM procedure • **PX10**: ICD-10-CM procedure • **PX11**: ICD-11-CM procedure • **PXC4**: CPT-4 procedure (*i.e.*, HCPCS Level I) • **PXHC**: HCPCS procedure (*i.e.*, HCPCS Level II) • **PXH3**: HCPCS Level III procedure • **PXC2**: CPT Category II procedure • **PXC3**: CPT Category III procedure **Defined by:** Request programmer **Input type:** Required **Format:** Alphanumeric; SAS character $4. **Example:** PX09
Secondary Codes of Interest	CODE	**Details:** code values for the secondary exposure(s) of interest. **Note 1**: codes are matched using exact values (*i.e.*, 3-digit code lookup requires an exact 3-digit code match). Wildcard match (*) functionality is also available (*e.g.*, querying "250*0" would be used to find any ICD-9-CM diagnosis codes for diabetes type II, or "250*" to find ICD-9-CM diagnosis codes for all diabetes codes that start with "250"). **Note 2**: for NDCs, either 9 or 11 digit codes can be entered. **Note 3:** remove decimal points in the code value. **Note 4**: CODETYPE must be consistent with the expected format of the CODE value (*e.g.*, MP4 will not find any valid matches in the data for CODETYPE=RX11 and a 9-digit NDC value). **Note 5**: duplicate CODETYPE-CODE combinations in a given GROUP are removed by the MP4 algorithm. **Defined by:** Request programmer

Parameter	Field Name	Description
		Input type: Required **Format:** Alphanumeric; SAS character $11. **Example:** 12345678911
Secondary Incidence Type	WASHTYP	**Details:** selects how secondary exposure incidence will be defined. As detailed in Section V, the incidence type can take the following values: • **MIN**: minimum incidence -- identifies and reports metrics only for the *first* valid incident secondary treatment episode during the query period, and uses ALL observed claims - even those before the query period start date - to define incidence. That is, incidence is defined as the first secondary treatment episode during the query period with no evidence of prior exposure using all available data. • **SING**: single incidence -- identifies and reports metrics only for the *first* valid incident secondary treatment episode during the query period, and uses claims observed during the specified WASHPER days to determine incidence. That is, incidence is defined as the first secondary treatment episode during the query period with no evidence of prior exposure during WASHPER days. • **MULT**: multiple incidence -- identifies and reports metrics for *all* valid incident secondary treatment episodes during the query period, and uses claims observed during the specified WASHPER days to determine incidence. That is, incidence is defined as any secondary treatment episode during the query period with no evidence of prior exposure during WASHPER days. **Note 1:** WASHTYP parameter is used in conjunction with the Secondary Washout Period (WASHPER; see below) to define a valid incident secondary treatment episode. **Note 2:** the set of all secondary treatment episodes reported using the single incidence case is a subset of all episodes from the multiple incidence case. **Note 3:** the MP4 algorithm may use days before QUERYFROM to ensure incidence criteria are met. **Note 4:** MIN setting should be used with caution as interpretation is complex. A secondary treatment episode that meets the MIN criteria must occur during the query period and cannot be preceded by a disqualifying exposure at any time during enrollment; that is, the look-back period to define incidence is not limited to the washout period. **Named by:** Requester, with support from the MSOC as needed **Input type:** Required

Parameter	Field Name	Description
		Format: Alphanumeric; SAS character $4; case sensitive (upper case only). **Example:** MULT
Secondary Washout Period	WASHPER	**Details:** length of washout period in days. The washout period is a period of time before an incident secondary treatment episode index date during which a member cannot have any evidence of exposure(s) of interest or any other exposure(s) specified in the Incident Secondary Exposure File. In conjunction with the ENROLGAP and COVERAGE macro parameters and the Secondary Exposure File ENRDAYS parameter, the WASHPER parameter is used to ensure that appropriate enrollment requirements are met. Since at least WASHPER days of enrollment must be found prior to index date, the Secondary Exposure File ENRDAYS parameter value is only binding if ENRDAYS > WASHPER (See Section V.A). If enrollment requirements prior to index date are not met, treatment episode incidence cannot be determined and thus the episode is excluded from output metrics. **Note 1:** the MP4 algorithm may use days before QUERYFROM to determine if continuous enrollment and incidence criteria are met. **Note 2:** When WASHTYP=MIN, WASHPER is only used to assess continuous enrollment eligibility. **Note 3**: secondary washout period value must be the same within a given GROUP. **Note 4**: required and used in conjunction with any Secondary Incidence Types (WASHTYP; see above). **Named by:** Requester **Input type:** Required (0 must be entered if no washout is required) **Format:** Numeric **Example:** 183
Minimum Pre-Index Enrollment Days	ENRDAYS	**Details:** optional parameter to further restrict the number of days of continuous enrollment prior to start of new incident secondary treatment episode to reach a certain minimum. **Note 1**: if not specified by the requester a default value of 0 days is used by the MP algorithm. **Note 2**: if specified must be the same within a given query GROUP. **Note 3**: in conjunction with the ENROLGAP, COVERAGE, and WASHPER parameters, the Secondary Exposure File minimum pre-index enrollment days parameter is used to ensure that appropriate

Parameter	Field Name	Description
		enrollment requirements are met. Since at least WASHPER days of enrollment must be found prior to index date, the ENRDAYS parameter value is only binding if ENRDAYS > WASHPER (See Section V.A). If enrollment requirements prior to secondary index date are not met, treatment episode incidence cannot be determined and thus the episode is excluded from output metrics. **Named by:** Requester **Input type:** Optional (default value is 0) **Format:** Numeric **Example:** 365
Secondary Episode Gap	EPISODEGAP	**Details:** treatment episode allowable gap in days for the secondary exposure. For any two secondary exposure claims, a gap of more than EPISODEGAP days between the claim date and the end of days of supply of the previous claim triggers a new secondary exposure treatment episode. **Note 1**: If 0 is entered, no interruption in secondary exposure treatment episode days of supply will be tolerated. **Named by:** Requester **Input type:** Required (0 must be entered if no episode gap is required) **Format:** Numeric **Example:** 10
Secondary Treatment Minimum Episode Duration	MINEPISDUR	**Details:** minimum episode duration in days for the secondary exposure treatment episodes. Rejects treatment episodes of fewer than MINEPISDUR days. **Note 1:** the MP algorithm considers any specified episode extensions (EXPEXTPER; below) and episode gaps (EPISODEGAP; above) in duration calculations. **Named by:** Requester **Input type:** Required (0 must be entered if no constraint is required) **Format:** Numeric **Example:** 60
Secondary Treatment Minimum Days Supply	MINDAYSUPP	**Details:** minimum days of supply required for a secondary exposure treatment episode. Rejects treatment episodes of fewer than MINDAYSUPP days. **Named by:** Requester **Input type:** Required (0 must be entered if no constraint is required) **Format:** Numeric **Example:** 60
Secondary Treatment	FOLLOWPER	**Details:** minimum number of days the member must be eligible for pharmacy and/or medical benefits after the second exposure index

Parameter	Field Name	Description
Minimum Follow-up Period		date. Rejects users with fewer than FOLLOWPER days of pharmacy and/or medical benefits. **Named by:** Requester **Input type:** Required (0 must be entered if no minimum follow-up period is required) **Format:** Numeric **Example:** 60
Secondary Treatment Episode Extension Period	EXPEXTPER	**Details:** extends the length of the secondary exposure treatment episode by a specified number of days. A secondary exposure treatment episode can be extended EXPEXTPER days after the last day of supply of the secondary exposure treatment episode's last claim. **Named by:** Requester **Input type:** Required (0 must be entered if no episode extension period is required) **Format:** Numeric **Example:** 10

4.   Incident Secondary Exposure File

The Incident Secondary Exposure File is optional. If defined, the file contains the comprehensive set of codes used to refine the incidence definition of the secondary exposure(s) of interest. Just like the Secondary Exposure File, the file can include any mix of the following allowed code types: NDCs, ICD procedure and diagnosis codes, or Healthcare Common Procedure Coding System (HCPCS) codes to define exposures of interest.

The GROUP structure of the Incident Secondary Exposure File must match that of the Secondary Exposure File. That is, for each GROUP defined in the Incident Secondary Exposure File a matching GROUP must be found in the Secondary Exposure File.

By default, for a given secondary group MP4 uses the list of codes included in the Secondary Exposure File to determine the incident status of identified secondary exposures. That is, incidence is defined as no exposure to the secondary exposure of interest in the washout period (WASHPER). The Incident Secondary Exposure File is used to define incidence based on a different set of codes than those used to define the secondary exposure(s) of interest. For example, the requester may be interested in examining the use of Drug D, but wants all incident users of Drug D to be free of Drug D, E and F in the 183 days before the Drug D index date. In this case, the list of codes for Drug D would be included in the Secondary Exposure File, and the list of codes for Drug E and Drug F would be included in the Incident Secondary Exposure File. Table 5 contains detailed specifications for the file.

Table 5: Incident Secondary Exposure File Specification

Parameter	Field Name	Description
Name of Primary Group	GROUP	**Details:** standardized name used to refer to a primary GROUP for exposure(s) of interest to be queried.

Parameter	Field Name	Description
		Note: must match GROUP values from the Primary Exposure File. **Named by:** Request programmer **Input type:** Required **Format:** Alphanumeric; SAS character $30; no special characters (*e.g.*, commas, periods, hyphens, etc) allowed, and underscores must be used to mark spaces. **Example:** ACE_Inhibitors
Name of Secondary Incident Subgroup	SUBGROUP	**Details:** standardized name used to refer to a SUBGROUP for secondary exposure(s) of interest to be queried. **Note1:** useful when individual secondary exposures are comprised of multiple drugs/procedures/diagnoses. For example, if GROUP= "MAO_Inhibitors", secondary SUBGROUP may take the values "isocarboxazid" or "phenelzine" to differentiate drugs. **Note 2:** SUBGROUP field is used by the stockpiling algorithm as group categories to adjust claim service dates. See Section V.B for more details. **Named by:** Request programmer **Input type:** Required **Format:** Alphanumeric; SAS character $30; no special characters (*e.g.*, commas, periods, hyphens, etc) allowed, and underscores must be used to mark spaces. **Example:** phenelzine
Incident Secondary Code Type	CODETYPE	**Details:** type of each code value included in the CODE field (below) of this file. Valid values are all those allowed by the MSCDM: • **DX09**: ICD-9-CM diagnosis • **DX10**: ICD-10-CM diagnosis • **DX11**: ICD-11-CM diagnosis • **RX11**: 11-digit NDC • **RX09**: 9-digit NDC • **PX09**: ICD-9-CM procedure • **PX10**: ICD-10-CM procedure • **PX11**: ICD-11-CM procedure • **PXC4**: CPT-4 procedure (*i.e.*, HCPCS Level I) • **PXHC**: HCPCS procedure (*i.e.*, HCPCS Level II) • **PXH3**: HCPCS Level III procedure • **PXC2**: CPT Category II procedure • **PXC3**: CPT Category III procedure **Defined by:** Request programmer

Parameter	Field Name	Description
		Input type: Required **Format:** Alphanumeric; SAS character $4 **Example:** PX09
Secondary Incidence Only Codes	CODE	**Details:** code values used to refine the incident definition for the secondary exposure(s) of interest. For example, if a requester is examining DRUG D and requests that incidence of DRUG D be defined with respect to DRUG D *and* DRUG E, the Secondary Incident Only Codes field would include DRUG E codes. **Note 1**: Codes are matched using exact values (*i.e.*, 3-digit code lookup requires an exact 3-digit code match). Wildcard match (*) functionality is also available (*e.g.*, querying "250*0" would be used to find any ICD-9-CM diagnosis codes for diabetes type II, or "250*" to find ICD-9-CM diagnosis codes for all diabetes codes that start with "250"). **Note 2**: for NDCs, either 9 or 11 digit codes can be entered. **Note 3:** remove decimal points in the code value. **Note 4**: CODETYPE must be consistent with the expected format of the CODE value (*e.g.*, MP4 will not find any valid matches in the data for CODETYPE=RX11 and a 9-digit NDC value). **Note 5**: duplicate CODETYPE-CODE combinations in a given GROUP are removed by the MP4 algorithm. **Named by:** Requester, with support from MSOC as needed **Input type:** Required **Format:** Alphanumeric; SAS character $11 **Example:** 12345678922

5.   Concomitant Exposure File

The Concomitant Exposure File is required and used to specify how concomitant treatment episodes are created, how washout criteria are assessed, and whether concomitant use should be restricted to same-day initiation.

Values of the GROUP fields must match between the Primary Exposure File, Secondary Exposure File, and Concomitant Exposure File. Table 6 contains detailed specifications for the Concomitant Exposure File.

Table 6: Concomitant Exposure File Specification

Parameter	Field Name	Description
Name of Primary Exposure	GROUP	**Details:** standardized name used to refer to a primary GROUP for exposure(s) of interest to be queried.

Parameter	Field Name	Description
Group		**Note 1**: must match GROUP values from the Primary Exposure File. **Named by:** Request programmer **Input type:** Required **Format:** Alphanumeric; SAS character $30; no special characters (*e.g.*, commas, periods, hyphens, etc) allowed, and underscores must be used to mark spaces. **Example:** Insulin
Exposure Order Indicator	EXPORDER	**Details:** indicates whether the order of primary and secondary exposure is relevant when creating valid *prevalent* concomitant treatment episodes (e.g., primary exposure must always be initiated before secondary exposure). A value of 'Y' instructs the program to always require primary exposure to be initiated before secondary exposure; a value of 'N' will not enforce an order restriction. **Note 1:** for valid *incident* concomitant treatment episodes, if a user wants to ensure that a primary episode always precedes a secondary episode when defining concomitant episodes, the Incident Primary Exposure File must include Secondary Exposure File codes. **Named by:** Requester **Input type:** Required (default value is N) **Format:** Character $1 **Example:** N
Event Washout Extension	EVENTWASHEXT	**Details:** indicates whether the event washout period (WASHPER) should be extended to include all prior primary or secondary exposure days that were used to create the concomitant episode. "EVENTWASHEXT" parameter will take a value of 'Y' if the user wants WASHPER days for the event of interest to include all days before the concomitant index date that are exposed to either the primary or secondary exposure used to define the concomitant exposure episode. For example, if a user species a WASHPER of 183 in the Event File and EVENTWASHEXT=Y, the program will look back whichever number of days is greater: 183 or the number of days before the concomitant index date that are exposed to the primary or secondary exposure used to define the concomitant exposure. Essentially the 183 Event WASHPER value means "at least 183 days". If EVENTWASHEXT="N" the event incidence will be determined using the WASHPER days before the concomitant episode index date. **Note:** used in conjunction with the WASHPER parameter in the Event File. If WASHPER=183 and EVENTWASHEXT=Y, the program will look back at least 183 days from the concomitant exposure index date to determine incidence, but will look farther back if the days do not cover all of the prior primary or secondary exposure days used

Parameter	Field Name	Description
		to create the concomitant treatment episode. **Named by:** Requester **Input type:** Required (default value is N) **Format:** Character $1 **Example:** N
Condition Assessment Indicator	CONDEARLIEST	**Details:** indicates how the concomitant cohort should assess condition requirements (as specified in the CONDFILE). If CONDEARLIEST= Y, condition requirements will be assessed using the index date of the earliest of the primary and secondary episodes used to create the concomitant episode. If CONDEARLIEST=N, condition requirements will be assessed using the concomitant episode index date. **Named by:** Requester **Input type:** Required (default value is N) **Format:** Character $1 **Example:** N
Number of Concomitant Episodes	NUMCOM	**Details:** indicates whether one or more than one valid incident concomitant episode per member should be included in output metrics. Allowable values: • **ONE:** only one concomitant episode will be retained and reported in output metrics • **ALL:** all valid concomitant episodes will be retained and reported in output metrics **Note 1:** NUMCOM is only applicable to the incident concomitant cohort; the prevalent cohort will still retain all concomitant episodes in output metrics. **Named by:** Requester **Input type:** Required (default value is ALL) **Format:** Character $3 **Example:** ONE
Concomitant Treatment Minimum Follow-up Period	FOLLOWPER	**Details:** minimum number of days the member must be eligible for pharmacy and/or medical benefits after the concomitant episode index date. Rejects users with fewer than FOLLOWPER days of pharmacy and/or medical benefits. **Named by:** Requester **Input type:** Required (0 must be entered if no minimum follow-up period is required) **Format:** Numeric

Parameter	Field Name	Description
		Example: 60
Concomitant Treatment Episode Extension Period	EXPEXTPER	**Details:** extends the length of the concomitant exposure treatment episode by specified number of days. A concomitant exposure treatment episode can be extended EXPEXTPER days after the last day of supply of the concomitant exposure treatment episode. **Named by:** Requester **Input type:** Required (0 must be entered if no episode extension period is required) **Format:** Numeric **Example:** 10
Concomitant Treatment Minimum Episode Duration	MINEPISDUR	**Details:** minimum episode duration in days for the concomitant exposure treatment episodes. Rejects treatment episodes of fewer than MINEPISDUR days. **Named by:** Requester **Input type:** Required (0 must be entered if no constraint is required) **Format:** Numeric **Example:** 60
Concomitant Use Same Day Restriction	CONCSAMEDAY	**Details:** indicates whether the modular program should restrict concomitant episodes to those where the primary and secondary treatment episodes are initiated on the same day. Allowable values: • **Y:** restrict concomitant episodes to those where primary and secondary episodes are initiated on the same day • **N:** do not restrict episodes to those where primary and secondary episodes are initiated on the same day **Note 1:** default value is "N" **Note 2:** when CONCSAMEDAY=Y and NUMCOM=ONE, the program will include only the first valid concomitant episode where primary and secondary treatment is initiated on the same day. **Defined:** Requester **Input type:** Required **Format:** Character (1) **Example:** Y

6. Event File

The Event File is required. It contains the comprehensive set of codes used to define the event(s) of interest. NDCs, ICD-9-CM procedure and diagnosis codes or HCPCS codes can be used to define events of interest, in combination with a care setting and a principal diagnosis indicator (diagnosis codes only).

Events can be defined using any mix of allowed code types. Table 7 contains detailed specifications for the Event File.

Table 7: Event File Specification

Parameter	Variable Name	Description
Name of Primary Exposure Group	GROUP	**Details:** standardized name used to refer to a query GROUP for event(s) of interest to be queried. **Note 1**: must match GROUP values from the Primary Exposure File. **Note 2**: if multiple codes are needed to define an event, they need to be grouped using the same GROUP value. **Named by:** Request programmer **Input type:** Required **Format:** Alphanumeric; SAS character $30; no special characters (*e.g.*, commas, periods, hyphens, etc.) allowed, and underscores must be used to mark spaces. **Example:** ACE_Inhibitors
Name of Event Subgroup	SUBGROUP	**Details:** contains names of subgroups of event codes in this file. This variable is not used by the MP algorithm but it is useful for tracking purposes. **Named by:** Request programmer **Input type:** Required **Format:** Alphanumeric; SAS character $30; special characters (*e.g.*, commas, periods, hyphens, etc.) allowed and underscores must be used to mark spaces. **Example:** Angioedema
Event Code Type	CODETYPE	**Details:** type of each code value included in the CODE field (below) of this Event File. Valid values are: • **RX11**: 11-digit NDC • **RX09**: 9-digit NDC • **DX09**: ICD-9-CM diagnosis • **DX10**: ICD-10-CM diagnosis • **DX11**: ICD-11-CM diagnosis • **PX09**: ICD-9-CM procedure • **PX10**: ICD-10-CM procedure • **PX11**: ICD-11-CM procedure • **PXC4**: CPT-4 procedure (*i.e.*, HCPCS Level I) • **PXHC**: HCPCS procedure (*i.e.*, HCPCS Level II) • **PXH3**: HCPCS Level III procedure • **PXC2**: CPT Category II procedure

Parameter	Variable Name	Description
		• **PXC3**: CPT Category III procedure **Defined by:** Request programmer **Input type:** Required **Format:** Alphanumeric; SAS character $4. **Example:** DX09
Event Codes of Interest	CODE	**Details:** code values to be used to define events. **Note 1**: codes are matched using exact values (*i.e.*, 3-digit code lookup requires an exact 3-digit code match). Wildcard match (*) functionality is also available (*e.g.*, querying "250*0" would be used to find any ICD-9-CM diagnosis codes for diabetes type II, or "250*" to find ICD-9-CM diagnosis codes for all diabetes codes that start with "250"). **Note 2:** remove decimal points in the code value. **Note 3**: CODETYPE must be consistent with the expected format of the CODE value (*e.g.*, MP will not find any valid matches in the data for CODETYPE=PXC4 and a 3-digit code value). **Note 4**: duplicate CODETYPE-CODE combinations are removed by the MP4 algorithm. **Named by:** Requester, with support from MSOC as needed **Input type:** Required **Format:** Alphanumeric; SAS character $11. **Example:** J3490
Event Incidence Type	WASHTYP	**Details:** defines whether an individual can contribute at most one or more than one incident event during the query period. Only one incident event per concomitant treatment episode is allowed. The event incidence type can take the following values: • **MIN**: minimum incidence -- identifies and reports metrics only for the *first* valid incident event during the query period, but uses ALL prior observed claims to determine incidence. That is, incidence is defined as the first event during the query period with no evidence of a prior event claim using *all* available data. • **SING**: single incidence -- identifies and reports metrics only for the *first* valid incident event during the query period, and uses claims observed during the specified WASHPER days to determine incidence. That is, incidence is defined as the first event during the query period with no evidence of prior exposure during WASHPER days. • **MULT**: multiple incidence -- identifies and reports metrics

Parameter	Variable Name	Description
		for *all* valid incident events during the query period, and uses claims observed during the specified WASHPER days to determine incidence. That is, incidence is defined as any event during the query period with no evidence of an event during the prior WASHPER days. **Note 1:** WASHTYP parameter is used in conjunction with the Event Washout Period (below) to define a valid incident event. **Note 2:** the MP4 algorithm may use days before QUERYFROM to ensure incidence criteria are met. **Note 3**: MIN setting should be used with caution as interpretation is complex. An event that meets the MIN criteria must occur during the query period and cannot be preceded by a disqualifying event claim at any time during enrollment; that is, the lookback period to define incidence is not limited to the washout period. **Named by:** Requester **Input type:** Required **Format:** Alphanumeric; SAS character $4; case sensitive (upper case only). **Example:** MULT
Event Washout Period	WASHPER	**Details:** length of event washout period in days. The washout period is a period before an incident concomitant treatment episode during which a member cannot have any evidence of event(s) of interest or any other event(s) specified in the Incident Event File. The washout period is also used to ensure that enrollment requirements are met. If a member has fewer than WASHPER days of enrollment before the concomitant episode index date, the treatment episode is excluded from the incident evaluation. **Note 1**: the event washout period looks back from the concomitant episode index date. **Note 2:** used in conjunction with the EVENTWASHEXT parameter in the Concomitant Exposure File if EVENTWASHEXT=Y. If WASHPER=183 and EVENTWASHEXT=Y, the program will look back at least 183 days from the concomitant exposure index date to determine incidence, but will look farther back (to the earliest of the primary or secondary exposure index date) if the WASHPER days do not cover all of the prior primary or secondary exposure days used to create the concomitant treatment episode.

Parameter	Variable Name	Description
		Note 3: the MP4 algorithm may use days before QUERYFROM to determine if continuous enrollment and incidence criteria are met.
		Note 4: When WASHTYP=MIN, WASHPER is only used to assess continuous enrollment eligibility.
		Note 5: length of event washout period days must be the same within a given GROUP.
		Note 6: required and used in conjunction with any event incidence types.
		Named by: Requester **Input type:** Required (0 must be entered if no WASHPER is required) **Format:** Numeric **Example:** 365
Event Care Setting	CARESETTING	**Details:** contains the care settings considered for the individual diagnosis or procedure codes. If all care settings are wanted, leave the field blank. The following are valid entries; all entries must be in quotes and separated by a space: • **IP:** inpatient hospital stays • **IS:** non-acute institutional stays • **ED:** emergency department • **AV:** ambulatory visit • **OA:** other ambulatory visit **Note:** CARESETTING is allowed to vary between CODEs within the same GROUP. For example, CARESETTING is allowed to equal 'IP' for one diagnosis code and 'IP' 'ED' for another diagnosis code *in the same GROUP*. **Named by:** Requester **Input type:** Optional **Format:** Alphanumeric; SAS character $20. **Example:** 'IP' 'ED'
Principal Diagnosis Indicator	PRINCIPAL	**Details:** for a diagnosis CODETYPE (*e.g.,* DX09, DX10, DX11), if PRINCIPAL is set equal to YES, only principal diagnoses in the IP and ED settings will be chosen. However, if PRINCIPAL is set equal to NO, all diagnoses for the specified care settings will be chosen. For codes other than diagnosis codes, PRINCIPAL must be set equal to NO. **Named by:** Requester **Input type:** Required

Parameter	Variable Name	Description
		Format: Alphanumeric; SAS character $3. **Example:** YES
Event Blackout Period	BLACKOUTPER	**Details:** the event blackout period in days. The requester can specify a period at the start of a concomitant treatment episode during which valid events found by the MP4 algorithm are ignored. That is, the at-risk period starts at the end of the blackout period. Moreover, if an event occurs during the blackout period, the episode will not be considered incident with respect to the event (and thus excluded from output metrics). **Named by:** Requester **Input type:** Required (0 must be entered if no BLACKOUTPER is required) **Format:** Numeric **Example:** 7

7. Incident Event File

The Incident Event File is optional. It contains the comprehensive set of codes used to refine the incidence definition of the event(s) of interest. Just like the Event File, NDCs, ICD procedure and diagnosis codes or HCPCS codes can be used to define incident events of interest, in combination with a care setting and a principal diagnosis indicator (diagnosis codes only). Incident events can be defined using any mix of allowed code types.

By default, for a given query group MP4 uses the list of codes included in the Event File to determine the incident status of event(s) of interest. The Incident Event File is used to refine incidence based on a set of codes and/or parameters that are different than those used to define the event(s) of interest in the Event File. For example, a requester may want to evaluate the occurrence of incident principal AMI diagnoses in the inpatient and ED settings, but define incidence as *any* prior AMI diagnoses in *any* care setting. Table 8 contains detailed specifications for the Incident Event File.

Table 8: Incident Event File Specification

Parameter	Field Name	Description
Name of Primary Exposure Group	GROUP	**Details:** standardized name used to refer to a query GROUP for exposure(s) of interest to be queried. **Note**: must match GROUP values from the Primary Exposure File. **Named by:** Request programmer **Input type:** Required **Format:** Alphanumeric; SAS character $30; no special characters (*e.g.*, commas, periods, hyphens, etc) allowed, and underscores must be used to mark spaces. **Example:** ACE_Inhibitors
Name of Event	SUBGROUP	**Details:** contains names of subgroups of event codes in this file. This

Parameter	Field Name	Description
Subgroup		variable is not used by the MP algorithm but it is useful for tracking purposes. **Named by:** Request programmer **Input type:** Required **Format:** Alphanumeric; SAS character $30; special characters (e.g., commas, periods, hyphens, etc) allowed and underscores must be used to mark spaces. **Example:** Angioedema
Incident Only Event Code Type	CODETYPE	**Details:** type of each code value included in the CODE field (below) of this <u>Incident Event File</u>. Valid values are: • **RX11**: 11-digit NDC • **RX09**: 9-digit NDC • **DX09**: ICD-9-CM diagnosis • **DX10**: ICD-10-CM diagnosis • **DX11**: ICD-11-CM diagnosis • **PX09**: ICD-9-CM procedure • **PX10**: ICD-10-CM procedure • **PX11**: ICD-11-CM procedure • **PXC4**: CPT-4 procedure (*i.e.*, HCPCS Level I) • **PXHC**: HCPCS procedure (*i.e.*, HCPCS Level II) • **PXH3**: HCPCS Level III procedure • **PXC2**: CPT Category II procedure • **PXC3**: CPT Category III procedure **Defined by:** Request programmer **Input type:** Required **Format:** Alphanumeric; SAS character $4. **Example:** PX09
Incident Only Event Codes	CODE	**Details:** code values used to refine the incident definition for the event of interest. For example, if a requester is examining occurrence of DIAGNOSIS 1 but wants incidence of DIAGNOSIS 1 to be defined with respect to DIAGNOSIS 1 *and* DIAGNOSIS 2, the Incident Only Event Code fields would include DIAGNOSIS 2 codes. **Note 1:** remove decimal points in the code value. **Note 2**: CODETYPE must be consistent with the expected format of the CODE value (*e.g.*, MP4 will not find any valid matches in the data for CODETYPE =PXC4 and a 3-digit code value). **Note 3**: duplicate CODETYPE-CODE combinations are removed by the MP4 algorithm.

Parameter	Field Name	Description
		Named by: Requester, with support from MSOC as needed **Input type:** Required **Format:** Alphanumeric; SAS character $11 **Example:** J3490
Incident Event Care Setting	CARESETTING	**Details:** contains the care settings considered for the individual diagnosis or procedure codes. If all care settings are wanted, leave the field blank. The following are valid entries; all entries must be quoted and separated by a space: • **IP:** inpatient hospital stays • **IS:** non-acute institutional stays • **ED:** emergency department • **AV:** ambulatory visit • **OA:** other ambulatory visit **Note:** CARESETTING is allowed to vary between CODEs within GROUPs **Named by:** Requester **Input type:** Optional **Format:** Alphanumeric; SAS character $20. **Example:** 'IP' 'ED'
Principal Diagnoses Indicator	PRINCIPAL	**Details:** for a diagnosis CODETYPE (*e.g.,* DX09, DX10, DX11), if PRINCIPAL is set equal to YES, only principal diagnoses in the IP and ED settings will be chosen. However, if PRINCIPAL is set equal to NO, all diagnoses for the specified care settings will be chosen. For codes other than diagnosis codes, PRINCIPAL must be set equal to NO. **Named by:** Requester **Input type:** Required **Format:** Alphanumeric; SAS character $3. **Example:** YES

8. Inclusion/Exclusion Conditions File

The Inclusion/Exclusion Conditions File is optional. It is used to 1) include in the cohort only those members having evidence of certain conditions; 2) exclude from the cohort those members having evidence of certain conditions; or 3) combine inclusion and exclusion criteria to define the cohort. If defined, this file contains the comprehensive set of codes used to define the inclusion and exclusion condition(s) of interest.

The MP4 Inclusion/Exclusion Conditions File allows inclusion of the following code types: NDCs, ICD diagnosis and procedure codes, and Healthcare Common Procedure Coding System (HCPCS) codes to define condition(s) of interest. Any condition(s) can be defined using a mix of these allowed code types.

A different lookback period can be defined for each condition code specified. Values of the GROUP fields must match between the Primary Exposure File and the Inclusion/Exclusion Conditions File.

There are nine required parameters that must be specified in the Inclusion/Exclusion Conditions File; six must be specified by the requester. Table 9 contains detailed specifications for the Inclusion/Exclusion Conditions File.

Table 9: Inclusion/Exclusion Conditions File Specification

Parameter	Variable Name	Description
Name of Primary Group	GROUP	**Details:** standardized name used to refer to a primary GROUP for exposure(s) of interest to be queried. **Note**: must match GROUP values from the Primary Exposure File. **Named by:** Request programmer **Input type:** Required **Format:** Alphanumeric; SAS character $30; no special characters (*e.g.*, commas, periods, hyphens, etc) allowed, and underscores must be used to mark spaces. **Example:** ACE_Inhibitors
Name of Condition SubGroup	SUBGROUP	**Details:** contains names of subgroups of condition codes in this file. This variable is not used by the MP algorithm but it is useful for tracking purposes. **Request Programmer Note:** while not used by the MP4 algorithm, this variable must be included in the CONDFILE. **Named by:** Request programmer **Input type:** Required **Format:** Alphanumeric; SAS character $30; special characters (e.g., commas, periods, hyphens, etc) allowed and underscores must be used to mark spaces. **Example:** Diabetes
Condition Code Type	CODETYPE	**Details:** type of each code value included in the CODE field (below) of this file. Valid values are all those allowed by the MSCDM: • **DX09**: ICD-9-CM diagnosis • **DX10**: ICD-10-CM diagnosis • **DX11**: ICD-11-CM diagnosis • **RX11:** 11-digit NDC code • **RX09:** 9-digit NDC code • **DX09**: ICD-9-CM diagnosis • **DX10**: ICD-10-CM diagnosis • **DX11**: ICD-11-CM diagnosis

Parameter	Variable Name	Description
		• **PX09**: ICD-9-CM procedure • **PX10**: ICD-10-CM procedure • **PX11**: ICD-11-CM procedure • **PXC4**: CPT-4 procedure (*i.e.*, HCPCS Level I) • **PXHC**: HCPCS procedure (*i.e.*, HCPCS Level II) • **PXH3**: HCPCS Level III procedure • **PXC2**: CPT Category II procedure • **PXC3**: CPT Category III procedure **Defined by:** Request programmer **Input type:** Required **Format:** Alphanumeric; SAS character $4 **Example:** PXHC
Condition Code	CODE	**Details:** code values to define condition(s) of interest. **Note 1:** Codes are matched using exact values (i.e., 3-digit code lookup requires an exact 3-digit code match). Wildcard match (*) functionality is also available (e.g., querying "250*0" would be used to find any ICD-9-CM diagnosis codes for diabetes type II, or "250*" to find ICD-9-CM diagnosis codes for all diabetes codes that start with "250"). **Note 2:** remove decimal points in the code value. **Note 3**: CODETYPE must be consistent with the expected format of the CODE value (*e.g.*, MP4 will not find any valid matches in the data for CODETYPE=PXC4 and a 3-digit CODE value). **Note 4**: duplicate CODETYPE-CODE combinations in a given GROUP are removed by the MP4 algorithm. **Named by:** Requester **Input type:** Required **Format:** Alphanumeric; SAS character $11 **Example:** J3490
Inclusion/Exclusion Indicator	INCLUSION	**Details:** indicates whether each condition CODE specified is for an inclusion (=1) or exclusion (=0) criterion. **Named by:** Requester **Input type:** Required **Format:** Numeric **Example:** 1
Lookback Period Start	CONDFROM	**Details:** used in combination with CONDTO to define the start of the lookback period for each condition code specified, expressed in terms of "days from Index Date". For example, if Index Date=01/08/2009 and CONDFROM for a given condition code is

Parameter	Variable Name	Description
		set to -7, the MP algorithm will start looking for that condition code on 01/01/2009. **Note 1**: individual condition codes within a same GROUP are allowed to have different lookback periods and therefore have different CONDFROM and CONDTO values. **Note 2**: the index date is "day zero". Therefore, if zero is included in the CONDFROM-CONDTO interval for a given condition code, the index date is included in the lookback period. **Note 3**: if CONDFROM > 0 then the lookback period will start after the index date. **Named by:** Requester **Input type:** Required **Format:** Numeric **Example:** -180
Lookback Period End	CONDTO	**Details:** used in combination with CONDFROM to define the end of the lookback period for each condition code specified, expressed in terms of "days from Index Date". For example, if Index Date=01/08/2009 and CONDTO for a given condition code is set to -1, the MP algorithm will look for that condition code between the CONDFROM date through 01/07/2009. **Note 1**: individual condition codes within the same Query GROUP are allowed to have different lookback periods and therefore have different CONDFROM and CONDTO values. **Note 2**: the index date is "day zero". Therefore if zero is included in the CONDFROM-CONDTO interval for a given condition code the index date is included in the lookback period. **Named by:** Requester **Input type:** Required **Format:** Numeric **Example:** -1
Condition Care Setting	CARESETTING	**Details:** contains the care settings considered for the individual condition diagnosis or procedure codes. If all care settings are wanted, leave the field blank. The following are valid entries; all entries must be quoted and separated by a space: • **IP:** inpatient hospital stays • **IS:** non-acute institutional stays • **ED:** emergency department visits • **AV:** ambulatory visits

Parameter	Variable Name	Description
		• **OA:** other ambulatory visits **Note:** CARESETTING is allowed to vary between CODEs within the same GROUP. For example, CARESETTING is allowed to equal 'IP' for one diagnosis code and 'IP' 'ED' for another diagnosis code *in the same GROUP*. **Defined by:** Requester **Input type:** Optional **Format:** Alphanumeric; SAS character $20. **Example:** 'IP' 'ED'
Principal Diagnosis Indicator	PRINCIPAL	**Details:** for a diagnosis CODETYPE (*e.g.*, DX09, DX10, DX11), if PRINCIPAL is set equal to YES, only principal diagnoses in the IP and ED settings will be chosen. However, if PRINCIPAL is set equal to NO, all diagnoses for the specified care settings will be chosen. For codes other than diagnosis codes, PRINCIPAL must be set equal to NO. **Defined by:** Requester **Input type:** Required **Format:** Alphanumeric; SAS character $3. **Example:** YES

9. Output Table Selection File

The Output Table Selection File is optional. It is used to instruct the MP algorithm to preserve only a subset of all output tables generated by one run of the MP. If defined, it contains parameters used to specify which output tables generated by the MP should be kept in the output folder of the MP run.

Unlike other MP input files, the GROUP field is not part of the set of required parameters. One instance of the OUTTABLESFILE input file can be used for multiples runs of the MP no matter what GROUP values are used.

There are four required parameters that must be specified, all by the request programmer. Moreover, the input file must contain one line for each of the output files generated by each run of MP4. Table 10 contains detailed specifications for the Output Table Selection File, and a template is provided in Section IX.

Table 10: Output Table Selection File Specification

Parameter	Variable Name	Description
Name of Table in MP Documentation	DOCTABNAME	**Details:** contains the name of the table as specified in the MP documentation. **Note:** this is not the actual name used inside the program but to the name as listed in the documentation. **Named by:** Request programmer

Parameter	Variable Name	Description
		Input type: Optional, for reference only, dropped at the start of the MP execution. **Format:** Alphanumeric; SAS character $30. **Example:** Table1
Description of Table in MP Documentation	DOCTABDESCR	**Details**: contains the description of the table as specified in the table titles of the modular program documentation. **Named by:** Request programmer **Input type**: Optional, for reference only, dropped at the start of the MP execution. **Format**: Alphanumeric; SAS character $150. **Example**: Counts of Members, Incident Treatment Episodes, Total Dispensings and Days of Supply
Name of Table Generated by MP	TABNAME	**Details**: contains the name of the table generated by the modular program. **Note 1:** must be entered in lower case. **Note 2:** this is the actual table name used inside the program. **Named by:** Request programmer **Input type**: Required **Format**: Alphanumeric; SAS character $10. **Examples**: table1, table11
Table Inclusion Indicator	TABREQUIRED	**Details:** indicates whether TABNAME must be preserved. Valid values are: • **Y:** preserve table in output • **N:** remove table from output **Named by:** Request programmer **Input type**: Required **Format**: Alphanumeric; SAS character $1. **Example**: Y

10.   Dispensing Processing File

The Dispensing Processing File is optional. It is used to instruct the MP algorithm on how valid dispensings are selected and used by the stockpiling algorithm to create primary and secondary treatment episodes (Section V.B). Requesters can require restrictions on days supplied and amount supplied values for dispensings that are considered by the modular program, and determine how the program adjusts dispensing dates based on the amount of overlap between adjacent dispensings.

Note that the MP algorithm requires that stockpiling and dispensing processing for primary and secondary treatment episodes is identical.

Table 11 contains detailed specifications for the Dispensing Processing File.

Table 11: Dispensing Processing File Specification

Parameter	Variable Name	Description
Name of Query Group	GROUP	**Details:** standardized name used to refer to a query GROUP for exposure(s) of interest to be queried. **Note 1**: must match GROUP values from the Query File. **Named by:** Request programmer **Input type:** Required **Format:** Alphanumeric; SAS character $30; no special characters (*e.g.*, commas, periods, hyphens, etc.) allowed, and underscores must be used to mark spaces. **Example:** ACE_Inhibitors
Same Day Dispensing Processing Indicator	SAMEDAY	**Details**: defines how same day dispensings are processed. The first position indicates how days supplied (RxSup in the MSCDM) is handled; the second position indicates how amount supplied (RxAmt in the MSCDM) is handled. Valid values (for each position are): • **a:** adds all (amount supplied or days supplied) values for dispensings in the same GROUP/SUBGROUP on the same day • **n:** uses minimum (amount supplied or days supplied) value for dispensings in the same GROUP/SUBGROUP on the same day • **x:** uses maximum (amount supplied or days supplied) value for dispensings in the same GROUP/SUBGROUP on the same day • **m:** uses mean (amount supplied or days supplied) value for dispensings in the same GROUP/SUBGROUP on the same day **Note 1**: a total of 16 combinations are possible (e.g., aa, an, etc.). **Note 2**: default value is "aa". **Defined by:** Requester **Input type:** Required **Format:** SAS character $2 **Example:** SAMEDAY = aa
Range of Allowable Days Supplied Values	SUPRANGE	**Details:** specifies the allowable range of days supplied values (variable RxSup in the MSCDM) that are allowed for a dispensing to be used to create valid treatment episodes. Valid values are:

Parameter	Variable Name	Description
		• **x<-HIGH:** value must be > x • **y-HIGH**: value must be >= y • **LOW-<x**: value must be < x • **x-y**: value must be between x and y inclusively • **x<-y**: value must be greater than x and less or equal than y • **x-<y**: value must be greater or equal than x and less than y • **x<-<y**: value must be between x and y but not equal **Note 1**: allowable values can also be discrete, e.g., "10", "20". **Note 2**: failing to be in the specified range excludes a dispensing from consideration. **Note 3:** default is "0<-HIGH", indicating that the program will not consider days supplied values of 0 or less. **Defined by**: Requester **Input type**: Required **Format**: SAS character $40 **Examples**: SUPRANGE=5-<80; SUPRANGE = 0<-HIGH
Range of Allowable Amount Supplied Values	AMTRANGE	**Details:** specifies the allowable range of amount supplied values (variable RxAmt in the MSCDM) that are allowed for a dispensing to be used to create valid treatment episodes. Valid values are: • **x<-HIGH:** value must be > x • **y-HIGH**: value must be >= y • **LOW-<x**: value must be < x • **x-y**: value must be between x and y inclusively • **x<-y**: value must be greater than x and less or equal than y • **x-<y**: value must be greater or equal than x and less than y • **x<-<y**: value must be between x and y but not equal **Note 1**: allowable values can also be discrete, e.g., "10", "20". **Note 2**: failing to be in the specified range excludes a dispensing from consideration. **Note 3:** default is "0<-HIGH", indicating that the program will not consider amount supplied values of 0 or less. **Defined by**: Requester **Input type**: Required **Format**: SAS character $40 **Examples**: SUPRANGE=5-<80; SUPRANGE = 0<-HIGH

Parameter	Variable Name	Description
Overlap Percentage Processing	PERCENTDAYS	**Details:** the maximum percentage overlap of previous dispensing's days supply allowed for pushing dispensing dates forward. When this percentage is exceeded, the previous dispensing's days supply is truncated at the day prior to the next dispensing date. If this parameter is left blank, no truncation will occur and any overlap of supply between dispensing will be corrected by pushing overlapping days supplied forward. **Note 1**: default is 0. Defined by: Requester Input type: Optional Format: Numeric Example: PERCENTDAYS = 0.25

V.   KEY DEFINITIONS

A.   ENROLLMENT REQUIREMENTS

All claims used by the MP algorithm to select members of interest and build treatment episodes must occur during valid enrollment periods. All requirements used to build valid enrollment periods are fully customizable using a set of requester-defined input parameters.

First, the main COVERAGE parameter allows the requester to select the type of coverage required for each run of the MP based on whether medical, drug, or both medical and drug coverage are required during all enrollment periods. The default option is to require both medical and drug coverage.

Continuous enrollment periods are then constructed by bridging all enrollment records of the correct coverage type. That is, using the main ENROLGAP parameter, two (or more) consecutive enrollment periods separated by (no more) than ENROLGAP days are bridged together to form a longer, continuous enrollment episode of the relevant coverage type. Such continuous enrollment episodes are then used to confirm whether claims with query codes of interest and other characteristics can be used toward creation of incident treatment episodes, and identification of events and other inclusion/exclusion criteria.

Since each treatment episode can only be considered incident with at least WASHPER days free of exposure(s) of interest, the MP algorithm by default ensures that at least WASHPER days of continuous enrollment with the relevant coverage type are found before the index date **no matter how many minimum pre-index enrollment days are requested** (as specified by the ENRDAYS parameter of the Primary Exposure File for primary exposure episodes and the Secondary Exposure File for secondary exposure episodes). Therefore, the minimum pre-index enrollment days requirement can only be binding if it requires more days than those already requested by the required WASHPER parameter (i.e., if ENRDAYS > WASHPER). For example, if the required WASHPER is set to 183 days, a minimum number of pre-index enrollment days of ENRDAYS=183 (or less) does not impact what records are used to select the desired cohort of members.

B.   TREATMENT EPISODES

A treatment episode is defined as an uninterrupted sequence of treatment with claims of the same exposure GROUP; a treatment episode ends when this sequence is interrupted by a gap in days supply that is greater than the allowable gap (Section V.B) defined by the requester.

For claims of drug code types (*i.e.*, RX09 and RX11) the days supply used by the MP algorithm are from the MSCDM outpatient pharmacy file. For other code types used to define query groups (*e.g.*, procedure code types for vaccination or injectables), the MP algorithm assigns a default value of one day of supply. In MP4 primary exposure treatment episodes and secondary exposure treatment episodes are created independently. Overlap between primary exposure treatment episodes and secondary exposure treatment episodes defines concomitant treatment episodes.

1.   Stockpiling Algorithm

Because members may refill their drug prescriptions before the end of days supply of the current prescription, a stockpiling algorithm is used to correctly account for claims with overlapping supply of the same GROUP/SUBGROUP combination. Since this early-refill pattern can artificially reduce the length of the treatment episode, the dispensing date of the subsequent overlapping dispensing is adjusted. For example, all codes contained in subgroup "DRUG A" in primary exposure group "PrimaryExp1"will be input together in the stockpiling algorithm to adjust claim service dates. Claims in subgroup "DRUG B" in primary exposure group "PrimaryExp1" will be adjusted separately from the DRUG A claims. Once service dates have been adjusted at the SUBGROUP level, treatment episodes are created at the GROUP level using all "PrimaryExp1" claims with adjusted dates. The same applies for secondary exposure GROUP/SUBGROUP combinations.

Figure 1 illustrates the stockpiling algorithm and how the service dates of various claims of the same GROUP/SUBGROUP combination are adjusted. Note that this stockpiling process occurs before the identification of continuous treatment episodes.
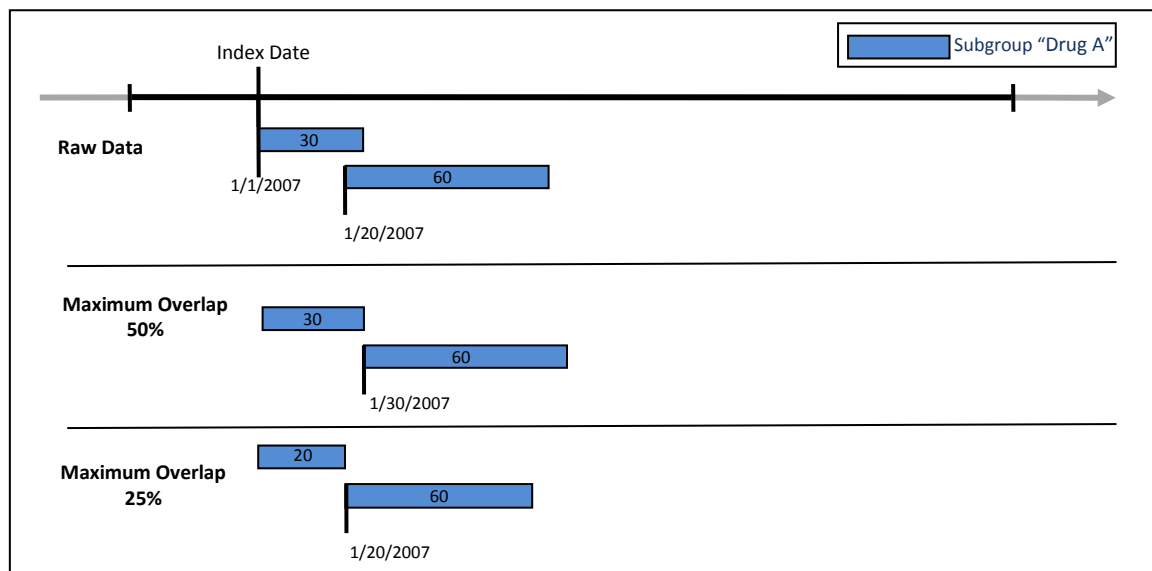
Figure 1: Stockpiling Algorithm
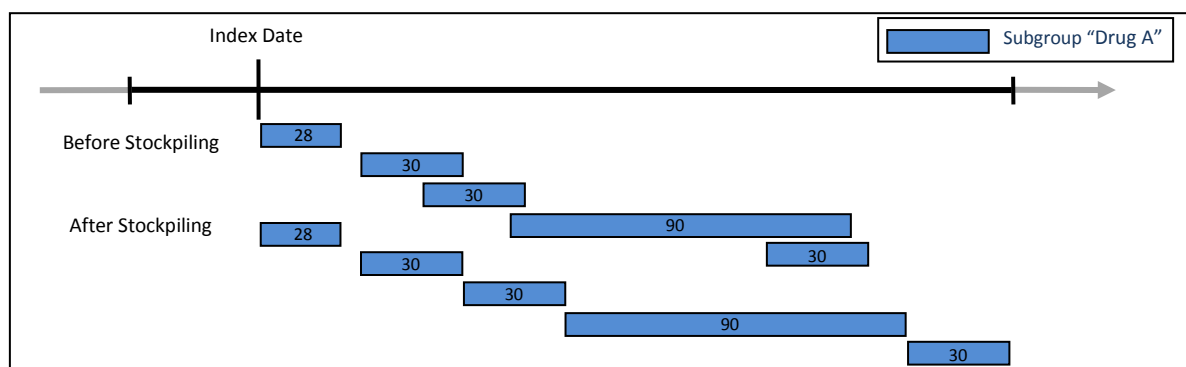
Requesters can specify which dispensings are considered by the MP and how dispensings are stockpiled. The Dispensing Processing File allows requesters to specify a range of allowable days supplied (RxSup in the MSCDM) and amount supplied (RxAmt in the MSCDM) that are considered by the stockpiling algorithm. For example, a requester could instruct the MP to only include dispensings with a days supplied < 90. Only dispensings with a days supplied <90 will then be considered by the program and used by the stockpiling algorithm.

Additionally, a requester can specify conditions under which dispensing dates are adjusted using the PERCENTDAYS parameter in the Dispensing Processing File. The PERCENTDAYS parameter sets a maximum percentage of overlap between two dispensings in order for dispensing dates to be adjusted. For example, consider the dispensing pattern in Figure 2, where the first dispensing and second dispensing overlap by 10 days.

**Figure 2: Use of Maximum Percentage Overlap in Stockpiling Algorithm**

If a requester specifies a maximum overlap of 50%, the stockpiling algorithm will only augment dispensing dates if the number of days of overlap between the two dispensing is less than (30 days * .5) = 15 days. Since the dispensings overlap by 10 days (<15 days) the start date of the second dispensing is adjusted to 1/30/2007 (30 days after the first dispensing date). However, if a requester specifies a maximum overlap of 25%, the stockpiling algorithm will only augment dispensing dates if the number of days of overlap between the two dispensing is less than (30 days * .25) = 7 days (value is rounded down). Since the dispensings overlap by 10 days (> 7 days) the start date of the second dispensing is not adjusted and the first dispensing's days supply is truncated at 20 days.

2. Allowable Gap

The allowable gap is the maximum number of days of interrupted days supply that can be found between two claims of the same group to be considered part of the same treatment episode (of either primary exposure or secondary exposure). If a gap of treatment between two claims of the same group smaller than or equal to the allowable gap occurs, the MP algorithm "bridges" these two claims to build a continuous treatment episode. If, however, the allowable gap is exceeded, the treatment episode ends at the end of the first claim and a new treatment episode starts at the beginning of the second claim. Figure 3 summarizes the treatment episode and allowable gap concepts.

Figure 3: Illustration of Treatment Episode and Allowable Gap
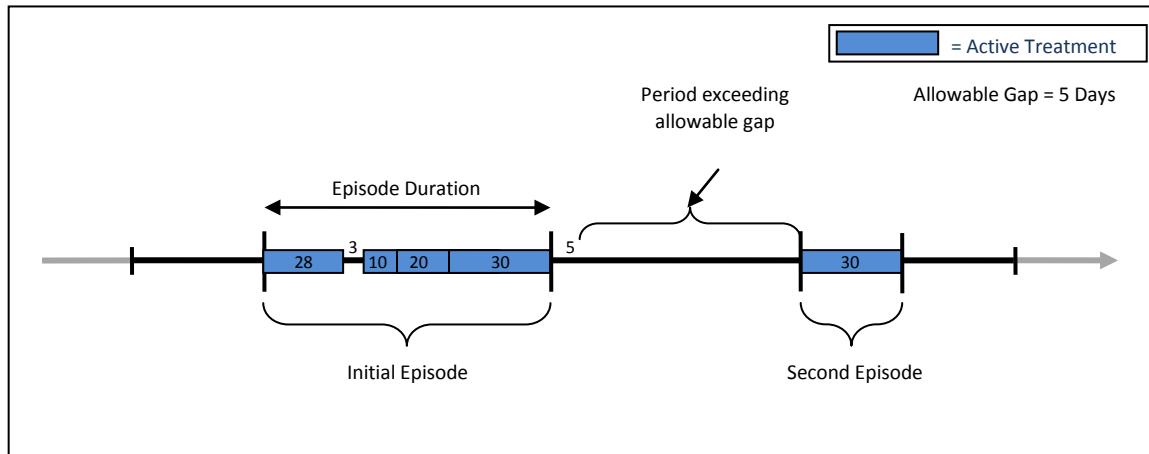
In Figure 3, an allowable gap of treatment of five days is used. The "active treatment" (in blue) corresponds to the days supply for claims of a given group. Four claims make up the first treatment episode since there is only a 3-day interruption in treatment between the first and second dispensing; that gap is "bridged" by the MP4 algorithm to create a single episode.

The treatment episode end date corresponds to the earliest of:

1. The date of the last day of supply preceding a treatment gap that is greater or equal to the "allowable gap" (as in Figure 3);

2. An interruption in the member's enrollment; or

3. The MSDD end date.

The length of a treatment episode is defined as the difference between the episode end date and the episode start date plus one.
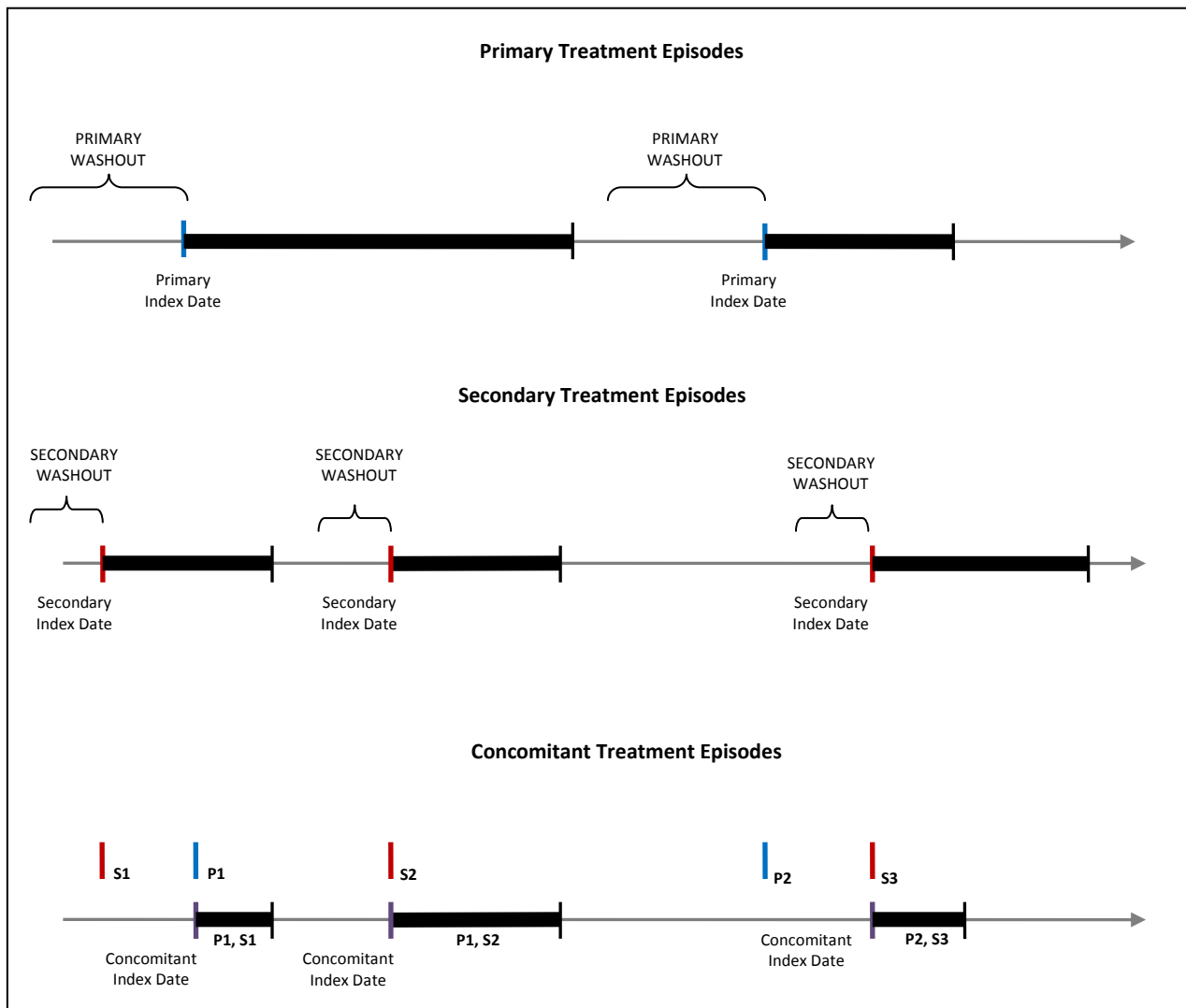
3. Primary, Secondary, and Concomitant Treatment Episode Creation

Primary and secondary exposure treatment episodes are created independently based on the parameters specified in the Primary Exposure File and Secondary Exposure File, respectively. The date of initiation of a valid primary treatment episode is the primary episode index date; the date of initiation of a valid secondary treatment episode is the secondary episode index date.

Concomitant treatment episodes are created based on overlap between primary and secondary episodes and any additional criteria specified in the Concomitant Exposure File. The start date of a valid concomitant treatment episode is the concomitant episode index date. The concomitant episode index date will always correspond to the index date of whichever exposure – primary or secondary – was initiated last.

Figure 4 illustrates the primary, secondary, and concomitant index date concepts.

Figure 4: Illustration of Primary, Secondary, and Concomitant Treatment Episodes and Index Dates

In Figure 4, primary and secondary episodes during the query period for the same member are displayed. Primary and secondary index dates (i.e., dates of treatment episode initiation) are highlighted blue and red, respectively. Three concomitant episodes are created based on overlap between primary and secondary episodes. The concomitant episode index date corresponds to the index date of the primary or secondary episode that is initiated last. The first concomitant episode index date corresponds to the first primary exposure index date; the second concomitant episode index date corresponds to the second secondary exposure index date; the third concomitant index date corresponds to the third secondary exposure index date.

4.   Minimum Requirements

For the primary, secondary, and concomitant treatment episodes, requesters can require a minimum treatment episode duration and/or follow-up period in days for the episode to be included in the cohort (using the MINEPISDUR and FOLLOWPER parameters in the Primary Exposure File, Secondary Exposure File, and Concomitant Exposure File).

Additionally, for the primary and secondary episodes, a requester can additionally specify a minimum days supply for treatment episodes (using the MINDAYSUPP parameter in the Primary Exposure File and Secondary Exposure File).

5. Concomitant Treatment Episode Options

Several additional options exist for requesters to further define the creation of concomitant treatment episodes after overlap between primary and secondary exposure is assessed:

- Require that primary treatment episode initiation always precede or start on the day of secondary exposure initiation (defined using the EXPORDER parameter in the Concomitant Exposure File)
- Require that primary and secondary exposure initiation always occur on the same day (defined using the CONCSAMEDAY parameter in the Concomitant Exposure File)
- Indicate whether one or all concomitant exposure episodes should be included in the final concomitant exposure cohort (defined using the NUMCOM parameter in the Concomitant Exposure File)
- Indicate what index date should be used to assess inclusion/exclusion and event washout requirements (defined using the EVENTWASHEXT and CONDEARLIEST parameters in the Concomitant Exposure File)

C. INCIDENT TREATMENT EPISODES

1. Incident Primary and Secondary Exposure Episodes

Incidence of primary and secondary exposure treatment episodes is determined based on the criteria specified in the Primary Exposure File and Secondary Exposure File, respectively. Valid episodes are those for which, as of the start of the episode (or index date), meet the incident exposure criteria.

Incident primary and secondary exposure are determined independently. Both primary and secondary incident exposure can be defined in three different ways by the requester, using the minimum, single, or multiple incidence type options.

a) Minimum Incidence (MIN) for Exposure

Under the minimum incidence option, members can have only one incident treatment episode during the query period and the claim used to define the treatment episode index date must be the first one observed for that member in all enrollment periods with appropriate coverage. Minimum incidence is thus defined as evidence of one claim for the exposure of interest during the query period that satisfies the two conditions below. This option should be used with caution as interpretation can be complex (*i.e.*, incidence is a function of the length of the member's available enrollment history).

1. Member is continuously enrolled at least ENRDAYS (if specified by the Minimum Pre-Index Enrollment Days parameter in the Primary Exposure File for primary exposure episodes or the Secondary Exposure File for secondary exposure episodes) and WASHPER days (specified by the Washout Period parameter) before the treatment episode index date.
2. Member has no evidence of another claim with an exposure code of interest during any enrollment period before the treatment episode index date. That is, the MP algorithm queries

the set of data available before the index claim date (regardless of the specified query period) to ensure that no claim with an exposure code of interest is observed during enrollment periods of relevant type.

b)   Single Incidence (SING) for Exposure

Under the single incidence option, members can have only one incident treatment episode during the query period, and the claim used to define the incident treatment episode must meet the following incidence conditions:

1. Member is continuously enrolled at least ENRDAYS (if specified by the Minimum Pre-Index Enrollment Days parameter in the <u>Primary Exposure File</u> for primary exposure episodes or the <u>Secondary Exposure File</u> for secondary exposure episodes) and WASHPER days (specified by the Washout Period parameter) before the treatment episode index date.
2. Member has no evidence of exposure during the WASHPER days (specified by the Washout Period parameter in the <u>Primary Exposure File</u> for primary exposure episodes or the <u>Secondary Exposure File</u> for secondary exposure episodes) before the treatment episode index date.
3. Claim is the first claim meeting conditions 1 and 2 during the query period. Under this condition, a member can only have one treatment episode during the query period.

c)   Multiple Incidence (MULT) for Exposure

Under the multiple incidence option, the MP algorithm identifies and reports metrics for all treatment episodes meeting the following two conditions:

1. Member is continuously enrolled at least ENRDAYS (if specified by the Minimum Pre-Index Enrollment Days parameter in the <u>Primary Exposure File</u> for primary exposure episodes or the <u>Secondary Exposure File</u> for secondary exposure episodes) and WASHPER days (specified by the Washout Period parameter) before the treatment episode index date.
2. Member has no evidence of exposure during the WASHPER days (specified by the Washout Period parameter in the <u>Primary Exposure File</u> for primary exposure episodes or the <u>Secondary Exposure File</u> for secondary exposure episodes) before the treatment episode index date.

The multiple incidence option is commonly used in epidemiologic assessments as it limits the period used to define incidence to a pre-index washout period that is equal for all members. A member can have multiple incident episodes as long as each episode meets both conditions above; these conditions are identical to those of the single incidence type except that the MP will report metrics on all valid episodes and not only the first one during the query period.

d)   Examples

The following examples illustrate the implications of exposure incidence type options. While the MP algorithm can evaluate multiple enrollment periods per member, for simplicity, each scenario depicted here includes members with only one enrollment period. These examples could represent either a primary or secondary exposure episode.

Figure 5 illustrates how the MP algorithm identifies an incident treatment episode using the minimum incidence option.
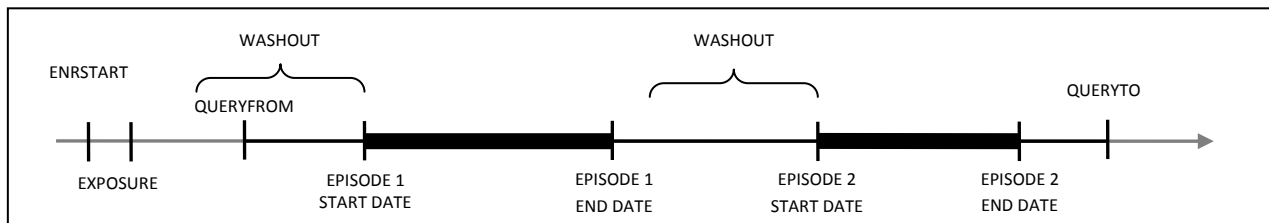
Figure 5: Incident Treatment Episode Identification Using the Minimum Incidence Option
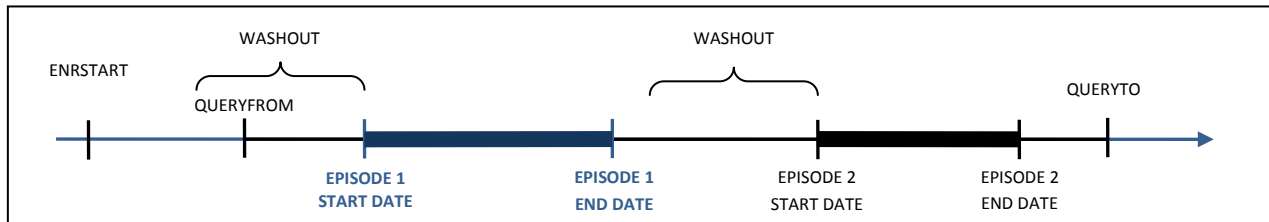
In the scenario depicted in Figure 5, ENRSTART indicates the member's start of enrollment in drug and/or pharmacy benefits (depending on the user-defined COVERAGE requirements). EPISODE 1 will be selected as the incident treatment episode in this scenario, as the member satisfies enrollment criteria and has no exposure before the EPISODE 1 start date. EPISODE 2 also satisfies enrollment criteria, but the prior treatment episode excludes this episode from being considered incident under the minimum incidence option.

Figure 6 depicts a scenario where a member does not have an incident treatment episode under the minimum incidence option.
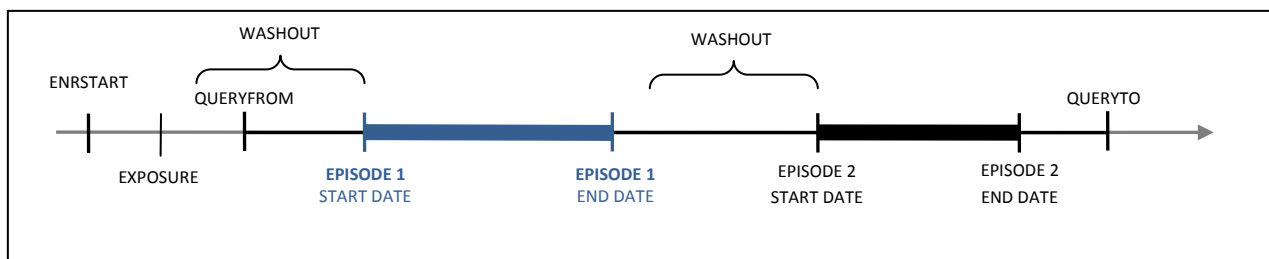
Figure 6: No Incident Treatment Episode Using the Minimum Incidence Option

In this scenario, "EXPOSURE" is not considered incident treatment since it did not occur within the query period. While treatment episodes 1 and 2 satisfy enrollment criteria, the presence of EXPOSURE before the query period, but during the member's history, excludes these as incident treatment episodes under the minimum incidence option.

Figure 7 illustrates how the MP algorithm identifies a claim using the single incidence option.

Figure 7: Incident Treatment Episode Identification Using the Single Incidence Option

In the scenario depicted in Figure 7, EPISODE 1 would be selected as the incident treatment episode, as the member satisfies the enrollment condition and has no query claim in the WASHPER days before the EPISODE 1 start date. The presence of EXPOSURE in this scenario is irrelevant, as it does not occur during the WASHPER days before the EPISODE 1 start date or during the query period. While EPISODE 2 also

satisfies the enrollment condition, the prior treatment episode excludes this episode from being considered incident under the single incidence option.

Figure 8: Incident Treatment Episode Using the Multiple Incidence Option
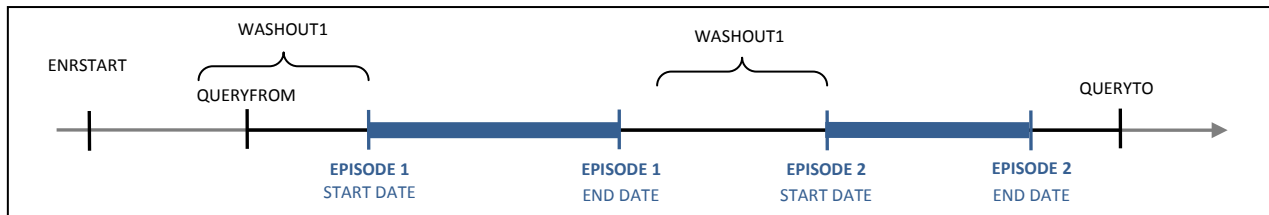
In Figure 8, EPISODES 1 and 2 will be considered incident using the multiple incidence option since a washout period free of any exposure claim of interest is observed and both satisfy the enrollment condition.

2. Incident Concomitant Exposure Episodes

Incident concomitant treatment episodes are created by assessing the overlap of incident primary and secondary treatment episodes and applying all criteria specified in the Concomitant Exposure File.

D. CONCOMITANCE INTENSITY RATIO AND TIME TO SECONDARY TREATMENT INITIATION

Several metrics are reported in MP4 that are specific to a special case implementation of MP4. In the case where a requester wants to always require that primary episode initiation precede or be initiated on the same day as secondary exposure, a concomitant intensity ratio and time to secondary initiation is calculated.

The concomitance intensity ratio is defined as the ratio of total number of overlapping days between all valid primary and secondary exposure treatment episodes to the sum of the length of all primary exposure treatment episodes (illustrated in Figure 9). A ratio of zero indicates low concomitant use where no overlap was found by the MP4 algorithm. Concomitant use increases as the ratio gets closer to one.

Figure 9: Illustration of Concomitant Use and Concomitance Intensity Ratio
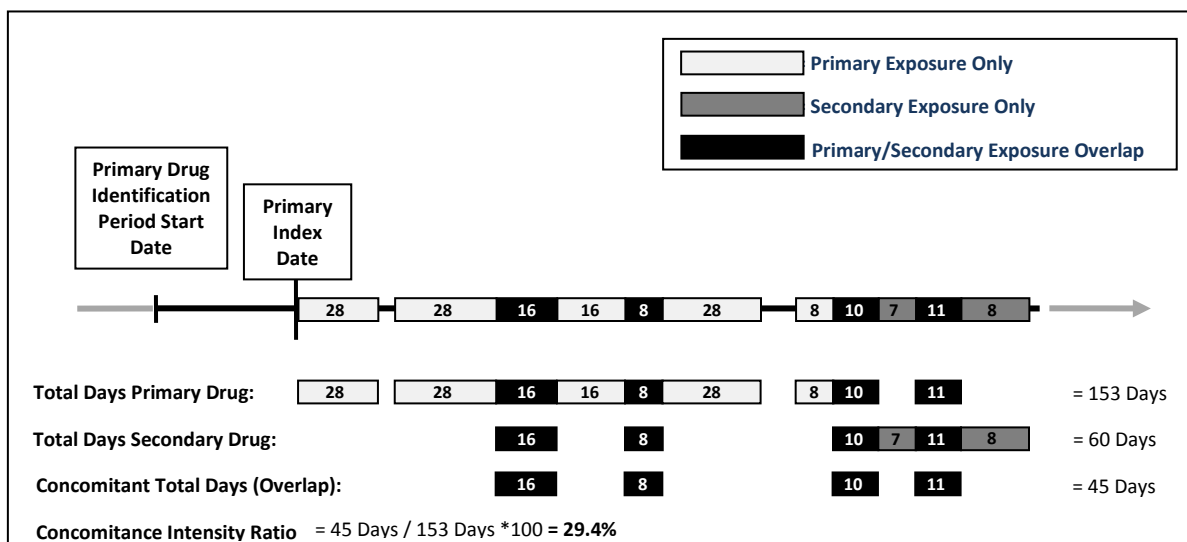
Time to secondary treatment initiation (TTI) is calculated for all primary and secondary treatment episodes used to create concomitant treatment episodes. TTI is defined as the number of days between the primary exposure index date and the secondary exposure index date. The MP4 algorithm will calculate and output mean, standard deviation, median, min, and max TTI for each GROUP.

E.   EVENTS

MP4 assesses the occurrence of events for primary exposure episodes, secondary exposure episodes, and concomitant exposure episodes. A valid exposed event is identified when the algorithm can confirm the following two conditions:

1. A claim with a medical code defining the event of interest in the Event File is identified during the treatment episode; this claim must also meet conditions set by optional parameters such as care setting - principal diagnosis indicator combinations, and episode extension and blackout periods.
2. The member must meet requester defined enrollment criteria

The number of days "at risk" for an exposed event are reported for every GROUP for each cohort (primary, secondary, concomitant). Days at risk are based on the length of treatment exposure; days at-risk during a treatment episode end upon identification of an exposed event of interest.

MP4 allows the requester to extend a treatment episode using the episode extension parameter. For example, if a treatment episode ends on December 31st, 2010 and an episode extension of 5 days is allowed, an event occurring between January 1st, 2011 and January 5th, 2011 will be considered valid (*i.e.*, exposed event).

Figure 10 illustrates the case where the allowable treatment gap and the episode extension are both set to 30 days.

Figure 10: Treatment Episode with an Episode Extension
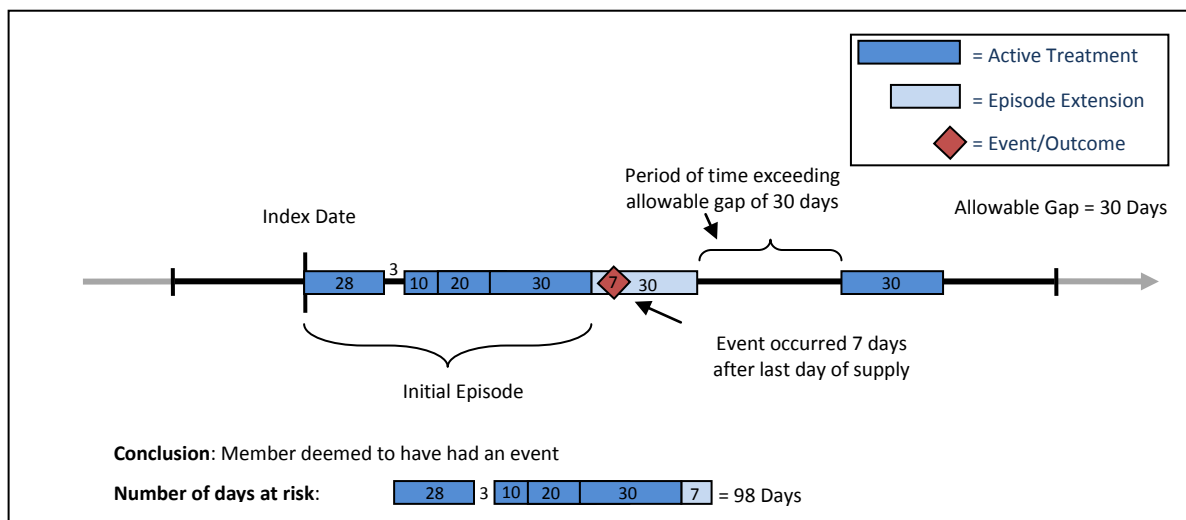
In Figure 10, the active treatment ends on the last treatment day of the fourth dispensing because a gap of more than 30 days separates this date from the fifth dispensing. Since the episode extension is set to

30 days, the event occurring 7 days after the last day of supply of the fourth dispensing is considered valid by the MP algorithm.

When an episode extension is used, the end date of the episode (and thus the episode length) is adjusted to reflect the additional days of extension. These additional days are also added to the days at risk metrics reported.

If an episode extension extends into another treatment episode (*i.e.*, episodes extension > allowable gap), the episode extension is truncated and no "bridging" of treatment episodes occurs. Under this condition, only events that occur before the start of the second treatment episode will be attributed to the first treatment episode.

MP4 permits a "blackout" period after the index date during which events are not counted. When a blackout period is defined, the effective start of the treatment episode remains the same, but the days at risk are reduced by BLACKOUTPER days.

Figure 11 illustrates the case where a blackout period of 30 days is specified.

Figure 11: Treatment Episode with Blackout Period
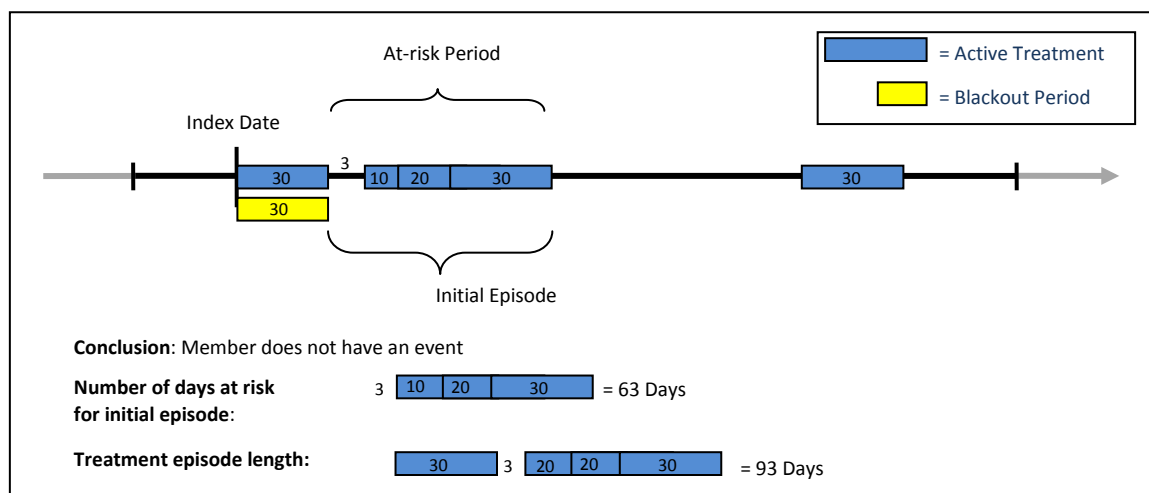
In Figure 11, the number of days at risk begins accumulating at the end of the blackout period and extends until the last treatment date of the fourth dispensing. If an event of interest occurs during the blackout period the episode is no longer incident with respect to the event and is therefore excluded from analysis.

F.   INCIDENT EVENTS

A requester may require that events observed during a treatment episode are new events, defined using requester-defined event incidence criteria that are assessed at treatment episode index date (e.g., require 365 days free of the event of interest before treatment initiation).

Incident events can be defined in two different ways by the requester, using the minimum, single or multiple incidence type options.

1. Minimum Incidence (MIN) for Event

Under the minimum incidence option, members can have only one incident event during the query period and the claim used to define the event date must be the first one observed for that member in all enrollment periods of relevant coverage type (user-defined in COVERAGE parameter). Minimum incidence is thus defined as evidence of one event claim observed during the query period that satisfies the following two conditions:

1. Member is continuously enrolled at least ENRDAYS (if specified by the Minimum Pre-Index Enrollment Days parameter in the Primary Exposure File for primary exposure episodes or the Secondary Exposure File for secondary exposure episodes) and WASHPER days (specified by the Washout Period parameter) before the treatment episode index date. Note that enrollment is not explicitly assessed for concomitant exposures, since criteria are evaluated at the primary and secondary exposure level.
2. Member has no evidence of another claim with an event code or Incident Event File code during any considered enrollment period before the treatment episode index date. That is, the MP algorithm queries the set of data available before the index claim date (regardless of the specified query period) to ensure that no claim with an event code or Incident Event File code is observed during enrollment periods of relevant type. Note that for concomitant treatment episodes, index date to assess event incidence can either be the primary or secondary exposure episode index date used to create the concomitant episode (see EVENTWASHEXT parameter in the Concomitant Exposure File).

This option should be used with caution as interpretation can be complex (*i.e.*, incidence is a function of the length of the member's available enrollment history).

2. Single Incidence (SING) for Event

Under the multiple incidence option for the event, the MP algorithm identifies and reports metrics for treatment episodes meeting the following three conditions:

1. Member is continuously enrolled at least ENRDAYS (if specified by the Minimum Pre-Index Enrollment Days parameter in the Primary Exposure File for primary exposure episodes or the Secondary Exposure File for secondary exposure episodes) and WASHPER days (specified by the Washout Period parameter) before the treatment episode index date. Note that enrollment is not explicitly assessed for concomitant exposures, since criteria are evaluated at the primary and secondary exposure level.
2. Member has no evidence of a claim with an event code or Incident Event File code meeting incidence conditions during the WASHPER days (specified by the Washout Period parameter in the Event File) before the start of the treatment episode. Note that for concomitant treatment episodes, index date to assess event incidence can either be the primary or secondary exposure episode index date used to create the concomitant episode (see EVENTWASHEXT parameter in the Concomitant Exposure File).
3. Claim is the first claim meeting conditions 1 and 2 during the query period. Under this condition, a member can only have one event during the query period.

3. Multiple Incidence (MULT) for Event

Under the multiple incidence option for the event, the MP algorithm identifies and reports metrics for treatment episodes meeting the following two conditions:

4. Member is continuously enrolled at least ENRDAYS (if specified by the Minimum Pre-Index Enrollment Days parameter in the Primary Exposure File for primary exposure episodes or the Secondary Exposure File for secondary exposure episodes) and WASHPER days (specified by the Washout Period parameter) before the treatment episode index date. Note that enrollment is not explicitly assessed for concomitant exposures, since criteria are evaluated at the primary and secondary exposure level.

5. Member has no evidence of a claim with an event code or Incident Event File code meeting incidence conditions during the WASHPER days (specified by the Washout Period parameter in the Event File) before the start of the treatment episode. Note that for concomitant treatment episodes, index date to assess event incidence can either be the primary or secondary exposure episode index date used to create the concomitant episode (see EVENTWASHEXT parameter in the Concomitant Exposure File).

a) Example

The following examples illustrate event incidence type options. While the MP algorithm can evaluate multiple enrollment periods per member, for simplicity, each scenario depicted here includes members with only one enrollment period.

Assuming the multiple incidence type was chosen in the query (exposure) group, Figure 12 illustrates the implications on the choice of valid treatment episodes using the minimum incidence option for the event. "Washout1" refers to the days specified by the Washout Period parameter for the exposure; "Washout2" refers to the days specified by the Washout Period parameter for the event.

Figure 12: Incident Treatment Episodes and the Minimum Incidence Type for Events
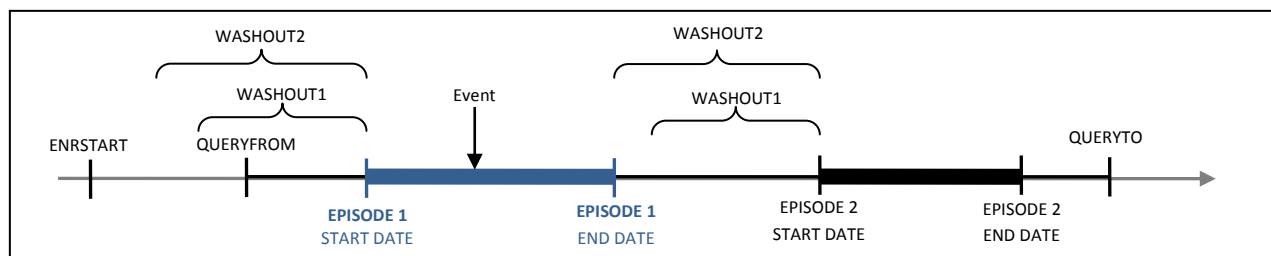
In Figure 12, the member satisfies the enrollment condition before the start of both treatment episodes 1 and 2. However, only EPISODE 1 will be considered incident as no other event claim is present before this episode. This is not the case for EPISODE 2, since an event occurred during the first treatment episode. While both EPISODE 1 and EPISODE 2 are considered incident based on the specified multiple incidence type for the query exposures of interest, selecting the minimum incidence type for the event leads the MP algorithm to retain only EPISODE 1 as a valid incident treatment episode. If the multiple incidence option was selected for the event, both EPISODE 1 and 2 would be considered incident treatment episodes.

G. COHORT INCLUSION OR EXCLUSION BASED ON CONDITIONS OF INTEREST

The requester can restrict the cohort with inclusion and/or exclusion criteria using the optional Inclusion/Exclusion Conditions File. Members can be included or excluded from the cohort if certain conditions are recorded during a specific lookback period. Conditions can be defined by any combination of valid diagnoses, procedures and/or NDCs.

The condition lookback period is defined by a combination of start and end dates (expressed in terms of days from index date, where day zero refers to the index date). Note that the start and end dates can include and go beyond the index date (Day 0 of the interval). For example, if start =-30 and end=30 the MP4 algorithm will search for conditions in the period starting 30 days before the index date and ending 30 days after.

The lookback period can also be defined at the code level. For example, the requester could require members to have a code for diabetes in the 183 days before index date OR a code for AMI in the 365 days before index date.

The presence of a claim with one of the desired inclusion condition codes is a sufficient condition to meet the inclusion criterion. However, in the case of exclusions, the absence of any claims with one of the desired exclusion condition codes is a necessary but not sufficient condition to meet the exclusion criterion. To fully satisfy the exclusion criterion the member also needs to be continuously enrolled for medical and/or drug coverage for the complete exclusion lookback period. For example, if a member is free of an exclusion claim in the -180 to -90 days before the index date, but was only enrolled from days -120 to -90, the MP algorithm cannot classify this member "free of the exclusion claims" since there is no way to know whether an exclusion claim would have been recorded during days -180 to -121.

VI.   PROGRAM STEPS

The general program steps are:

1. Process modular program parameters
2. Process modular program input files
3. Extract medical claims from the Diagnosis and Procedure tables in the MSDD
4. Recode claims that occurred during an inpatient stay as inpatient
5. Extract drug claims from the Dispensing table in the MSDD
6. Apply stockpiling algorithm to extracted claims
7. Reconcile enrollment episodes (gaps in enrollment less than ENROLGAP and coverage type)
8. Identify members having primary group and secondary group claims during the query period
9. Create all primary treatment episodes according to the criteria specified in the Primary Exposure File. Retain only treatment episodes satisfying the minimum duration, follow-up, and days of supply constraints.
10. Create all secondary treatment episodes according to the criteria specified in the Secondary Exposure File. Retain only treatment episodes satisfying the minimum duration, follow-up, and days of supply constraints.
11. Assess overlap between valid primary and secondary treatment and create concomitant treatment episodes. Retain concomitant episodes satisfying criteria specified in the Concomitant Exposure File.
12. If required, filter treatment episodes according to the specifications of the Inclusion/Exclusion Conditions File

13. Add events to primary, secondary, and concomitant treatment episodes
14. Assess prevalent and incident status of treatment episodes
15. Calculate age and identify sex for each cohort member
16. Create output tables for both prevalent and incident users

VII. PROGRAM EXECUTION

When implementing modular programs within the MSDD, the Mini-Sentinel Operations Center (MSOC) uses a uniform folder structure across Data Partners to facilitate communications between MSOC and Data Partners and to streamline file management.

Each request distributed by MSOC is assigned a unique Request ID. Upon receipt of the request, Data Partners create a folder named after the Request ID and several subfolders to organize program inputs and outputs. One of the folders contains output to be sent to MSOC and another contains intermediate files that remain with the Data Partner, but could be used to facilitate follow-up queries if necessary. Appropriate retention policies apply.

Table 12 defines the local environment variables that must be initialized by the user to execute the program (*i.e.*, defined by the Data Partner prior to execution of the program). Please note that these values cannot be left blank. Each Data Partner is required to enter user inputs at the beginning of the SAS Program sent with each request. These inputs are unique to each Data Partner.

Table 12: Environment Variable Definitions

Label	Field Name	Description
Data Partner ID	DPID	Enter the two character partner ID.
Site ID of Data Partner	SITEID	Enter the two character Site ID.
Enrollment Table Name	ENRTABLE	Enter the name of the MSCDM Enrollment table.
Demographics Table Name	DEMTABLE	Enter the name of the MSCDM Demographics table.
Dispensing Table Name	DISTABLE	Enter the name of the MSCDM Dispensing table.
Diagnosis Table Name	DIATABLE	Enter the name of the MSCDM Diagnosis table.
Procedure Table Name	PROCTABLE	Enter the name of the MSCDM Procedures table.
Encounter Table Name	ENCTABLE	Enter the name of the MSCDM Encounter table.
Vital Signs Table Name	VITTABLE	Enter the name of the MSCDM Vital Signs table.
Libname of the MSCDM	INDATA	Enter the path where the MSCDM data is saved.
Input file folder	INFOLDER	Enter the path where the input files will be saved.
Output file folder	MSOC	Enter the path where the shared output tables will be saved.
Dataset file folder	DPLOCAL	Enter the path where the local SAS datasets will be saved.

VIII. OUTPUT TABLES

Thirty-three output tables are created by MP4. Thirty output tables are created for both the incident-based cohort and prevalent-based cohort (fifteen distinct tables for each). Three additional tables are output containing the full query summary statistics and characterizing dispensings excluded by the stockpiling algorithm (based on parameters in the Dispensing Processing File). Tables can be identified by the following suffixes:

- _ITABLEX
- _PTABLEX
- _ITABLEXAG
- _PTABLEXAG
- _ITABLEXG
- _PTABLEXG
- _ITABLEXY
- _PTABLEXY
- _ITABLEXYM
- _PTABLEXYM
- _NUMCONCTABLE0
- _NUMQUERYTABLE0
- _STOCKPILING_EXCL

The "I" and "P" correspond to incident and prevalent tables, respectively, and the "X" corresponds to the table number and takes the values 1 to 7. Tables 6 and 7 metrics stratified by age group, sex, year, and year-month are included in separate tables, identified by the suffixes "AG" for age group, "G" for gender/sex, "Y" for year and "YM" for year/month. There are two tables that contain full summary statistics (NUMCONCTABLE0 and NUMQUERYTABLE0) and one table that characterizes dispensings excluded by the stockpiling algorithm (STOCKPILING_EXCL). Below are examples of incident output tables, produced using the multiple incidence type option. Prevalent tables are identical but include summary statistics for the prevalent cohort.

ITABLE1 – Primary, Secondary, and Concomitant Drug Use

Group	Primary Users	Primary Incident Episodes	Primary Dispensings	Primary Total Episode Duration	Primary Total Days Supply	Primary Total Amount Supplied	Primary Events	Primary Days at Risk
Group1	1,000	1,450	9,250	100,255	100,211	125,000	50	94,100

Secondary Users	Secondary Incident Episodes	Secondary Dispensings	Secondary Total Episode Duration	Secondary Total Days Supply	Secondary Total Amount Supplied	Secondary Events	Secondary Days at Risk
2,000	2,500	12,133	168,001	167,995	175,006	60	150,555

Concomitant Users	Concomitant Incident Episodes	Concomitant Total Episode Duration	Concomitant Events	Concomitant Days at Risk
500	520	60,991	15	51,900

<u>First row interpretation of ITABLE1</u>: Within the QUERYFROM to QUERYTO period:

 A total of 1,000 members had at least one primary exposure treatment episode in Group1. For these 1,000 members, a total of 1,450 incident primary episodes were identified and created based on 9,250 dispensings and total days supplied of 100,211. Total primary treatment episode duration was 100,255

days, and total amount supplied was 125,000 units. For a total of 94,100 days at risk, 50 events of interest were observed during primary exposure treatment episodes.

A total of 2,000 members had at least one secondary exposure treatment episode in Group1. For these 2,000 members, a total of 2,500 incident secondary episodes were identified and created based on 12,133 dispensings and total days supplied of 167,995. Total secondary treatment episode duration was 168,001 days, and total amount supplied was 175,006 units. For a total of 150,555 days at risk, 60 events of interest were observed during primary exposure treatment episodes.

A total of 500 members had at least one concomitant exposure treatment episode in Group1. For these 500 members, a total of 520 incident concomitant episodes were identified. Total concomitant treatment episode duration was 60,991 days. For a total of 51,900 days at risk, 15 events of interest were observed during concomitant exposure treatment episodes. ITABLEs 2-5 stratify ITABLE1 by age group, sex, year, and year-month.

ITABLE 6 - Concomitance Intensity

Group	Primary Users	Primary Incident Episodes	Concomitant Incident Users	Concomitant Incident Episodes
Group1	1,000	1,450	500	520

Mean Concomitant Intensity	Standard Deviation Concomitant Intensity	Minimum Concomitant Intensity	Median Concomitant Intensity	Maximum Concomitant Intensity
0.602	0.376	0.0048	0.675	1

First row interpretation of ITABLE 6: Within the QUERYFROM to QUERYTO period:

Out of 1,450 primary exposure treatment episodes, 520 overlapped a secondary exposure treatment episode. For these episodes, the mean concomitance intensity ratio was .602, the standard deviation of the ratio was .376, the minimum ratio was .0048, the median ratio was .675 and the maximum ratio was 1.

ITABLE6ag, ITABLE6g, ITABLE6y, and ITABLE6ym stratify the table by age group, sex, year, and year-month.

Note: this table is only relevant if, in the Concomitant Exposure File, EXPORDER=Y.

ITABLE7 – Distribution of Days between Primary and Secondary Exposure among Concomitant Users

Group	Concomitant Users	Mean Time to Initiation	Std Deviation: Time to Initiation	Minimum Time to Initiation	Median Time to Initiation	Maximum Time to Initiation
Group1	500	56.51	166.79	0	0	1498

First row interpretation of ITABLE7: Within the QUERYFROM to QUERYTO period:

A total of 500 members had at least one primary group treatment episode overlapping a secondary treatment episode. For these members, the mean number of days between the primary group treatment episode start and the secondary episode start (TTI = time to initiation) was 56.51 days; the

standard deviation of the TTI was 166.79, the minimum TTI was 0, the median TTI was 0, and maximum TTI was 1,498 days. The explanation above can also be applied for prevalent table interpretations.

ITABLE7ag, ITABLE7g, ITABLE7y, and ITABLE7ym stratify the table by age group, sex, year, and year-month.

Note: this table is only relevant if, in the Concomitant Exposure File, EXPORDER=Y.

Output TABLE Stockpiling Exclusions: Number of Members and Dispensings Excluded from Output Metrics due to Dispensing Processing Restrictions

Query Group	Input File	Excluded Members	Excluded Dispensings	Excluded due to RxSup Conditions Only	Excluded due to RxAmt Conditions Only	Excluded due to RxSup and RxAmt Conditions
Group1	CONDITION	100	150	75	25	50
Group1	EVENT	0	0	0	0	0
Group1	QUERY	500	675	350	250	75

Interpretation of Output TABLE Stockpiling Exclusions: In QGRP1 there were 675 dispensings excluded from the creation of valid treatment episodes due to user-defined restrictions on dispensing processing. A total of 350 of these dispensings were excluded due to restrictions on the days supplied only, 250 dispensings were excluded due to restrictions on the amount supplied only, and 75 were excluded due to restrictions on both the days and amount supplied.

IX.   EXAMPLE

Tables 13-19 below show an example of each of the five input files for MP4. Note the column headings contain the variable name, not the label.

Table 13: Example of Primary Exposure File

Code	Group	Subgroup	CodeType	EpisodeGap	MInEpisDur
11111111100	DRUGGRP1	DRUGSUB1	RX11	10	30
111111112	DRUGGRP2	DRUGSUB2	RX09	10	30
99999	PROCGRP1	PROCSUB1	PXC4	5	1
99998	PROCGRP2	PROCSUB2	PXC4	5	1

MinDaySupp	EnrDays	WashPer	WashTyp	FollowPer	ExpExtPer
1	180	180	MULT	183	10
1	180	180	MIN	183	10
1	30	30	MULT	183	10
1	360	360	MIN	183	10

Table 14: Example of Incident Primary Exposure File

Code	Group	Subgroup	CodeType
44444444401	DRUGGRP1	DRUGSUB1	RX11
66666	PROCGRP2	PROCSUB2	PXC4

Table 15: Example of Secondary Exposure File

Code	Group	Subgroup	CodeType	EpisodeGap	MInEpisDur
22222222200	DRUGGRP1	DRUGBSUB1	RX11	10	30
333333333	DRUGGRP2	DRUGBSUB2	RX09	10	30
88888	PROCGRP1	PROCBSUB1	PXC4	5	1
77777	PROCGRP2	PROCBSUB2	PXC4	5	1

MinDaysSupp	EnrDays	WashPer	WashTyp	FollowPer	ExpExtPer
1	180	180	MULT	183	10
1	180	180	MIN	183	10
1	30	30	MULT	183	10
1	360	360	MIN	183	10

Table 16: Example of Incident Secondary Exposure File

Code	Group	Subgroup	CodeType
55555555501	DRUGGRP1	CONCSUB5	RX11
55555	PROCGRP2	CONCSUB6	PXC4

Table 17: Example of Inclusion/Exclusion Conditions File

Group	SubGroup	CodeType	Code	Inclusion	CondFrom	CondTo	Principal	CareSetting
DRUGGRP1	CONDSUB1	DX09	WWW	1	-180	-1	NO	
DRUGGRP2	CONDSUB2	DX09	XXX	1	-180	-1	NO	
PROCGRP1	CONDSUB3	DX09	YYY	1	-180	-1	NO	
PROCGRP2	CONDSUB4	DX09	ZZZ	1	-180	-1	NO	

Table 18: Example of Output Table Selection File

DOCTABDESCR	TABNAME	TAB-REQUIRED
Query Numerators	numquerytable0	Y
Concomitant Numerators	numconctable0	Y
Incident Counts of Members, Episodes, Dispensing and Days of Supply stratified by Group	itable1	Y
Incident Counts of Members, Episodes, Dispensing and Days of Supply stratified by Group and Age Group	itable2	Y
Incident Counts of Members, Episodes, Dispensing and Days of Supply stratified by Group and Sex	itable3	Y
Incident Counts of Members, Episodes, Dispensing and Days of Supply stratified by Group and Year	itable4	Y
Incident Counts of Members, Episodes, Dispensing and Days of Supply stratified by Group, Year and Month	itable5	Y
Incident Concomitance Intensity Distribution stratified by Group	itable6	Y
Incident Concomitance Intensity Distribution stratified by Group and Age Group	itable6ag	Y
Incident Concomitance Intensity Distribution stratified by Group and Sex	itable6g	Y
Incident Concomitance Intensity Distribution stratified by Group and Year	itable6y	Y

DOCTABDESCR	TABNAME	TAB-REQUIRED
Incident Concomitance Intensity Distribution stratified by Group, Year and Month	itable6ym	Y
Incident Days between Query/Concomitant Dispensings Distribution stratified by Group	itable7	Y
Incident Days between Query/Concomitant Dispensings Distribution stratified by Group and Age Group	itable7ag	Y
Incident Days between Query/Concomitant Dispensings Distribution stratified by Group and Sex	itable7g	Y
Incident Days between Query/Concomitant Dispensings Distribution stratified by Group and Year	itable7y	Y
Incident Days between Query/Concomitant Dispensings Distribution stratified by Group, Year and Month	itable7ym	Y
Prevalent Counts of Members, Episodes, Dispensing and Days of Supply stratified by Group	ptable1	N
Prevalent Counts of Members, Episodes, Dispensing and Days of Supply stratified by Group and Age Group	ptable2	N
Prevalent Counts of Members, Episodes, Dispensing and Days of Supply stratified by Group and Sex	ptable3	N
Prevalent Counts of Members, Episodes, Dispensing and Days of Supply stratified by Group and Year	ptable4	N
Prevalent Counts of Members, Episodes, Dispensing and Days of Supply stratified by Group, Year and Month	ptable5	N
Prevalent Concomitance Intensity Distribution stratified by Group	ptable6	N
Prevalent Concomitance Intensity Distribution stratified by Group and Age Group	ptable6ag	N
Prevalent Concomitance Intensity Distribution stratified by Group and Sex	ptable6g	N
Prevalent Concomitance Intensity Distribution stratified by Group and Year	ptable6y	N
Prevalent Concomitance Intensity Distribution stratified by Group, Year and Month	ptable6ym	N
Prevalent Days between Query/Concomitant Dispensings Distribution stratified by Group	ptable7	N
Prevalent Days between Query/Concomitant Dispensings Distribution stratified by Group and Age Group	ptable7ag	N
Prevalent Days between Query/Concomitant Dispensings Distribution stratified by Group and Sex	ptable7g	N
Prevalent Days between Query/Concomitant Dispensings Distribution stratified by Group and Year	ptable7y	N
Prevalent Days between Query/Concomitant Dispensings Distribution stratified by Group, Year and Month	ptable7ym	N
Information on claims excluded by the stockpiling algorithm	stockpiling_excl	N

Table 19: Example of Dispensing Processing File

Group	SameDay	SupRange	AmtRange	PercentDays
DRUGGRP1	Aa	0<-HIGH	0<-HIGH	0
DRUGGRP2	aa	0<-HIGH	0<-HIGH	0

Group	SameDay	SupRange	AmtRange	PercentDays
PROCGRP1	aa	0<-HIGH	0<-HIGH	0
PROCGRP2	aa	0<-HIGH	0<-HIGH	0

In the example above, the requester additionally instructed the request programmer to use the following SAS macro parameters:

- Members must have medical and drug coverage
- Any enrollment gap of less than 30 days is considered administrative and must be ignored
- The query period spans the years 2007 to 2010
- The results should be segmented according to 5 year age groups from 10 to 49 years old
- Only certain output tables should be preserved
- Only dispensings with days or amount supplied >0 are considered by the program

For this request, the program could be executed using the following SAS Macro call:

%ModularProgram4 (

        REQUESTID=mpr01,
        RUNID=r01,
        COVERAGE=MD,
        ENROLGAP=30,
        QUERYFROM=01/01/2007,
        QUERYTO=12/31/2010,
        PRIMFILE=primaryfile.sas7bdat,
        INCPRIMFILE=incprimaryfile.sas7bdat,
        SECFILE= secondaryfile.sas7bdat,
        INCSECFILE= incsecondaryfile.sas7bdat,
        CONCOMFILE= concomfile.sas7bdat,
        QUERYEVENTFILE= eventfile.sas7bdat,
        INCEVENTFILE= inceventfile.sas7bdat,
        CONDFILE=condfile.sas7bdat,
        OUTTABLESFILE=mp_output_tables.sas7bdat,
        STOCKPILINGFILE=stockpiling.sas7bdat,
        AGESTRAT=10-14 15-19 20-24 25-29 30-34 35-39 40-44 45-49);