## OSIM 2 Optional Module 3a: Outcomes

*Drug-related Outcomes*

Increased risk of harmful outcomes following drug exposure could be indicative of potential drug adverse reactions that warrant further consideration. The simulation procedure will incorporate the relationship between drugs and outcomes by introducing additional cases of the condition into the sample based on the attributable risk of the condition due to the drug.

The osim\_drug\_outcome table can be manually populated with known condition / drug outcome effects. Running the optional outcome module will apply the rules, and either remove or insert condition eras in proportion to the specified relative risk.

Four outcome types will be added or removed from the time at risk for the person’s exposure to the drug.

***OUTCOME TYPES***

|  |  |
| --- | --- |
| **Outcome Type** | **General Description** |
| First exposure | Only first drug exposures are evaluated. The probability factor is constant (1) for any person with an initial drug exposure of at least the **minimum onset** duration.  Outcomes are injected/removed from the risk window defined by the **minimum** **onset** and **maximum** **onset** parameters applied to the first exposure. |
| Any exposure | All drug exposures are evaluated. The probability factor is constant (1) for any person with at least one drug exposure of the **minimum onset** duration.  Outcomes are injected/removed from the risk window defined by the **minimum** **onset** and **maximum** **onset** parameters applied to each drug exposure. |
| Insidious | All drug exposures are evaluated. The probability factor is the total drug exposure for any person with at least the **minimum onset** duration of total drug exposure.  Outcomes are injected/removed from the risk window defined by the **minimum** **onset** and **maximum** **onset** parameters applied to the each drug exposure. |
| accumulative | All drug exposures are evaluated. The probability factor is the power function applied to the accumulative total drug exposure for any person with at least the **minimum onset** duration of total drug exposure.  Outcomes are injected/removed **any** time after **minimum onset** duration of total drug exposure and before the **maximum** **onset** from **start** (if providied) has occurred according to the probability curve years\_of exposure**accumulative alpha** . If **minimum delay** and **maximum delay** parameters are provided, the outcome will have an additional random delay added from the uniform distribution of minimum to maximum delay. |

***OUTCOME RISK WINDOW***

The outcome risk window as defined by the additional outcome parameters establishes the time range for which a condition is considered an outcome of a drug exposure. The risk window is used for both counting existing outcomes in the data, and bounding the time in which an outcome will be inserted.

|  |  |  |
| --- | --- | --- |
| **Outcome Type** | **Risk Window Start** | **Risk Window End** |
| First exposure | Start of the first drug exposure + optional parameter **OUTCOME\_ONSET\_DAYS\_MIN**  First exposures shorter than the **OUTCOME\_ONSET\_DAYS\_MIN** have no risk window | If **OUTCOME\_ONSET\_DAYS\_MAX** = 0  Then end of first drug exposure  Else  If **OUTCOME\_ONSET\_DAYS\_MAX\_TYPE** = ‘start’  Then Start of the first drug exposure  +**OUTCOME\_ONSET\_DAYS\_MAX**  Else End of the first drug exposure  +**OUTCOME\_ONSET\_DAYS\_MAX** |
| Any exposure | Each drug exposure is assigned a risk window:  Start of drug exposure + optional parameter **OUTCOME\_ONSET\_DAYS\_MIN**  Drug exposures shorter than the **OUTCOME\_ONSET\_DAYS\_MIN** have no risk window | If **OUTCOME\_ONSET\_DAYS\_MAX** = 0  Then end of the drug exposure  Else  If **OUTCOME\_ONSET\_DAYS\_MAX\_TYPE** = ‘start’  Then Start of the drug exposure  +**OUTCOME\_ONSET\_DAYS\_MAX**  Else End of the drug exposure  +**OUTCOME\_ONSET\_DAYS\_MAX** |
| Insidious | Each drug exposure is assigned a risk window:  Start of drug exposure + optional parameter **OUTCOME\_ONSET\_DAYS\_MIN**  Drug exposures shorter than the **OUTCOME\_ONSET\_DAYS\_MIN** have no risk window | If **OUTCOME\_ONSET\_DAYS\_MAX** = 0  Then end of the drug exposure  Else  If **OUTCOME\_ONSET\_DAYS\_MAX\_TYPE** = ‘start’  Then Start of the drug exposure  +**OUTCOME\_ONSET\_DAYS\_MAX**  Else End of the drug exposure  +**OUTCOME\_ONSET\_DAYS\_MAX** |
| Accumulative | The date in the drug exposure in which the **OUTCOME\_ONSET\_DAYS\_MIN** of total exposure occurs.  The start date of subsequent drug exposures. | The end date of the drug exposure in which the **OUTCOME\_ONSET\_DAYS\_MIN** of total exposure occurs.  The end date of subsequent drug exposures.  Until the **OUTCOME\_ONSET\_DAYS\_MAX** of total drug exposure occurs. |

***OUTCOME PROBABILITY***

The outcome probability is weighted by various factors based on the outcome type and duration of drug exposure.

|  |  |
| --- | --- |
| **Outcome Type** | **Risk Window Start** |
| First exposure | Every person with at least one outcome during the first drug exposure risk window has constant probability weight of 1 (constant risk). |
| Any exposure | Every person with at least one outcome during the any drug exposure risk window has constant probability weight of 1 (constant risk). |
| Insidious | Every person with at least one outcome during the any drug exposure risk window has probability weight of the total days of drug exposure. |
| Accumulative | Every person with at least one outcome during the risk window has probability weight of (years\_of exposure+1)**accumulative alpha** |

***OUTCOME DELAY***

Any outcome may have the delay parameters set defer the outcome start date after the outcome trigger date in the risk window

***OUTCOME DELETION (BENEFIT)***

All outcomes (conditions occurring within the defined risk window) are removed for each selected person.

***OUTCOME INSERTION (RISK)***

Outcomes (conditions occurring within the defined risk window) are inserted for each selected person as follows.

|  |  |
| --- | --- |
| **Outcome Type** | **Risk Window Start** |
| First exposure | Uniform Distribution  A single outcome is inserted into the first drug exposure risk window. |
| Any exposure | Uniform Distribution  A single outcome is inserted into the one of the drug exposure risk windows. |
| Insidious | Uniform Distribution  A single outcome is inserted into the one of the drug exposure risk windows. |
| Accumulative | Accumulative probability function  A single outcome is inserted during the risk window.  The probability for the date is weighted by the function:  (years of exposure+1)**ACCUMULATIVE\_RISK\_ALPHA**   * When alpha < 0.0 the relative risk is increasing with exposure, but less than linear, making outcomes more likely earlier. * When alpha = 0.0 the risk is uniform. * When alpha > 0.0 the incidence rate ratio is actually increasing over exposure time, making outcomes more likely later.   The outcome may have an additional delay added to the randomly chosen start date. |

***TABLE OSIM\_DRUG\_OUTCOME***

|  |  |  |
| --- | --- | --- |
| **Field Name** | **Format** | **Description / Comment** |
| DRUG\_CONCEPT\_ID | Number | Outcome Drug concept ID |
| CONDITION\_CONCEPT\_ID | Number | Outcome condition concept ID |
| RELATIVE\_RISK | Float | Percentage effect to simulated drug exposures exhibiting the outcome. The value will be > 1.0 for **risk** (additional outcomes) and < 1.0 for **benefit** (outcome removal). |
| OUTCOME\_RISK\_TYPE | Text | * **first exposure** – outcomes are only added/removed to first drug exposure time at risk. The probability of an exposure being affected is proportional to the exposure time at risk. * **any exposure** – outcomes may be added/removed to any drug exposure time at risk, every exposure has an equal chance of an outcome. * **insidious** – outcomes are randomly added on a date during any exposure, exposure total time at risk is used as a probability factor * **accumulative** – outcomes are added during any drug exposure, with accumulating probability over time, ACCUMULATIVE\_RISK\_ALPHA is used to proportionally shape probability |
| OUTCOME\_ONSET\_DAYS\_MIN | Number | Risk window adjustment. Minimum days from drug exposure start date for outcome to occur; this column can be set for any outcome\_risk\_type.  For **first exposure** and **any exposure**, the days to onset is added to each drug exposure start. For **insidious** and **accumulative** the days to onset is applied to the person’s total exposure to a drug and may span several of the initial exposures. |
| OUTCOME\_ONSET\_DAYS\_MAX | Number | Risk window adjustment. Maximum days from drug exposure start or end date for outcome to occur; the value must be >= outcome\_onset\_days\_min if OUTCOME\_ONSET\_DAYS\_MAX\_TYPE = ‘start’  For **first exposure** and **any exposure**, the days to onset is added to each drug exposure start or end. For **insidious** and **accumulative** the maximum days to onset is applied to the person’s complete exposure to a drug and may span several of the initial exposures. |
| OUTCOME\_ONSET\_DAYS\_MAX\_TYPE | Text | The drug era date to which the maximum offset should be applied (‘start,’end’); ‘end’ is not valid for insidious or accumulative risk types. |
| ACCUMULATIVE\_RISK\_ALPHA | Float | Alpha adjustment for accumulative risk.  Risk will increase with the curve function:  (years of exposure)**ACCUMULATIVE\_RISK\_ALPHA**   * When alpha < 0.0 the relative risk is increasing with exposure, but less than linear, making outcomes more likely earlier. * When alpha = 0.0 the risk is uniform. * When alpha > 0.0 the incidence rate ratio is actually increasing over exposure time, making outcomes more likely later. |
| OUTCOME\_DELAY\_DAYS\_MIN | Number | Then minimum days from the chosen onset date within the risk window until the actual outcome start date.  Optional, default is no delay. |
| OUTCOME\_DELAY\_DAYS\_MAX | Number | Then maximum days from the chosen onset date within the risk window until the actual outcome start date.  Optional, must be greater than or equal to the minimum delay, if it is set. |

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### Process Function 3a: Apply Outcomes

**Process Function 3a:**

Apply Outcomes

ins\_outcomes()

OSIM 2

Outcomes

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**osim\_drug\_outcome**

OSIM 2 Process Log

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OSIM 2 Simulated CDM Tables

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**OSIM\_ Prefix Tables**

osim\_drug\_era

osim\_condition\_era

**Process Description:**

1. **Log** starting message
2. **For Each Outcome** in **osim\_drug\_outcome** table
   1. **Count Persons** with **Outcome** as defined by the outcome parameters
   2. **Log** outcome rules
   3. **Log** outcome counts
   4. **Calculate Affected Count** of persons by multiplying the actual count by **Relative Risk**
   5. **If Affected Count** < 0and **relative\_risk** < 1.0
      1. Delete all outcomes for -**Affected Count** randomly selected persons with at least one outcome
         1. If **outcome\_risk\_type** = ‘first exposure’ every person with at least one outcome in their first exposure has an equal chance of being selected
         2. If **outcome\_risk\_type** = ‘any exposure’ every person with at least one outcome in any exposure has an equal chance of being selected
         3. If **outcome\_risk\_type** = ‘insidious’ every person with at least one outcome during full drug exposure has their probability weighted by the duration of their full drug exposure.
         4. If **outcome\_risk\_type** = ‘accumulative’ every person with at least one outcome has their probability weighted by the accumulating years of drug duration.
      2. Set **outcomes\_insert\_count** = - Deleted Row Count
      3. **Log** affected row count message
   6. **If Affected Count** >= 0and **relative\_risk** > 1.0
      1. Insert an outcomes for **Affected Count** randomly selected persons with no current outcomes.
         1. If **outcome\_risk\_type** = ‘first exposure’ randomly insert a condition during the first drug exposure risk window
         2. If **outcome\_risk\_type** = ‘any exposure’ randomly insert a condition during any drug exposure risk window
         3. If **outcome\_risk\_type** = ‘insidious’ randomly insert a condition during any drug exposure risk window
         4. If **outcome\_risk\_type** = ‘accumulative’ insert a condition with the start date probability weighted by the function (years of exposure)**ACCUMULATIVE\_RISK\_ALPHA**
      2. Set **outcomes\_insert\_count** = Inserted Row Count
      3. **Log** affected row count message
   7. **Commit**
3. **Log** complete message