

Establishing a Drug Era Persistence Window for Active Surveillance

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OMOP PI Revisions/Last Revised: 25 January 2010

Background

As part of its common data model (<http://omop.fnih.org/CDMandTerminologies>), OMOP has proposed the creation of 'drug era' tables as a means to systematically apply consistent rules for all medical products to infer periods of drug exposure from available data, such as prescription dispensings, prescriptions written, and medication history lists. One important decision to make when applying drug era logic to an observational database (administrative claims or electronic health record) is to define the persistence window, or the period of tolerance for non-compliance that is allowed when constructing periods of persistent exposure. Having strict intolerance for non-compliance (and hence using a 0-day persistence window) yields periods of exposure with fewer inferences, but can result in misclassification of unexposed time. Using a 30-day persistence window, such that a gap between two prescriptions not exceeding one month over the number of days supplied or prescribed, would be considered part of one period of continuous treatment, will aggregate exposures but may be prone to greater misclassification of exposure-time. This analysis evaluates the impact of the 0-day and 30-day persistence window on the construction of drug eras across the central databases within the OMOP data community. Based on the findings, the OMOP research team recommends a 30-day persistence window assumption be consistently applied as a shared standard across the active surveillance analyses.

Methods

The OMOP common data model was developed to accommodate observational data from disparate sources, including administrative claims and electronic health records. As part of its design, the common data model contains a DRUG_EXPOSURE table, which stores all verbatim records from the source database that could be potentially used to infer drug exposure. Most source databases provide an identifier for the medical product used and an exposure start date, require inferring exposure periods based on other available records. For example, this table may contain prescription dispensings (with information such as quantity and days supply), or prescriptions written with quantity of medicine (with information such as number of refills), or medication history listings (which may provide a drug stop date). Because source databases may vary significantly in the available fields that could be used to infer exposure, a supplemental data table, DRUG_ERA, was created. The DRUG_ERA table is intended to have one common structure for maintaining periods of persistent exposure (each person can have drug exposure with corresponding start dates and end dates with exposure not dropping below 60%). DRUG_ERA is a derived table, based on the DRUG_EXPOSURE table that pre-processes the

data to make it more analysis-friendly and minimize the computational burden. The intent behind developing this framework is to establish one systematic, transparent process for building DRUG_ERAs that can be consistently applied across all drugs in a database, and potentially across multiple databases.

OMOP has 5 central databases: 4 administrative claims databases from Thomson Reuters, and 1 electronic health record database from GE Centricity. Thomson Reuter's CCAE is a large commercial claims database of a privately insured population covering 59m lives. MDCC is an 11m person database containing claims from Medicaid services. MDCR contains Medicare supplemental claims for 4.6m lives. MSLR is a 1.5m person subset of the broader population that contains medical and pharmacy claims, along with laboratory values. GE Centricity contains 11.2m lives. OMOP has developed standardized procedures for constructing drug eras that have been successfully applied against 5 central databases, and have informed the development within its distributed partners.

One parameter within the standardized procedure is the 'persistence window'. The DRUG_ERA table was developed to accommodate any persistence window. In its current work, the OMOP research team has populated the central databases with two sets of drug eras under two different persistence window assumptions, '0-day' and '30-day'. Creating eras under both scenarios have enabled exploration of the impact of the persistence window on the number of exposure records and length of exposure and its downstream effects on active surveillance analyses.

Drug era construction is a person-level data transformation that serves two purposes: 1) rolling up different medical products that contain the same active ingredient, and 2) combining records that overlap in time, subject to a persistence window. The first objective is accomplished by leveraging the hierarchy within the standardized terminology to aggregate drugs to the ingredient level of RxNorm. The second objective is achieved by deriving end dates for each drug exposure record, then evaluating whether exposure windows for the same product are sufficiently close to infer continuous use with a minimum of 60% exposure.

For claims related to pharmacy prescriptions, the dispensed date and number of days supply are used to extrapolate the end date for the period of Drug Exposure. When a Person receives recurring prescriptions for the same product and strength, the multiple prescriptions may need to be treated as a single Drug Era. To determine whether this is indeed the case, the drug's "persistence window", which is the number of days after the Person stops taking a drug and during which the Person is deemed to still be affected by the drug, must be taken into account. If the number of days between the end date of the prior Drug Exposure and the start date of the subsequent Drug Exposure falls within the persistence window, then the two exposures are considered to belong to the same Drug Era.

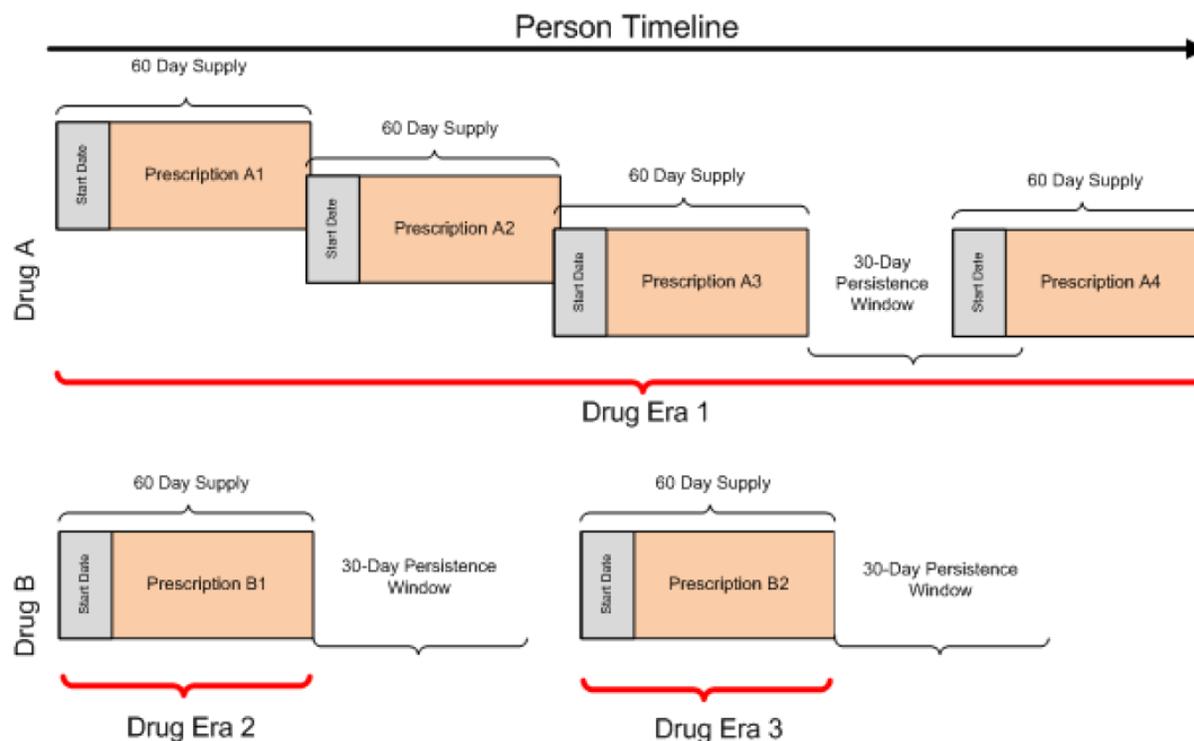


Figure 1: Example of constructing drug eras from drug exposure records

For example, as illustrated in Figure 1, consider a Person who is taking two drugs: Drug A and Drug B. The Person has had four prescriptions for Drug A (A1, A2, A3, A4), each with a sixty-day supply. The Person has also had two prescriptions for Drug B (B1, B2).

To define the Drug Era for Drug A, the timing, duration, overlap, and persistence of the Person's prescriptions for Drug A must be considered. A2 was filled before the expected completion of A1. Similarly, A3 was filled before the expected completion of A2. A4 was filled after A3 was completed, but within the persistence window for Drug A. Therefore, the four prescriptions for Drug A will be consolidated into a single Drug Era (DrugEra1), with the start for prescription A1 recorded as the start date for the consolidated record and the end date for prescription A4 recorded as the end date. As the persistence window was exceeded between filling the two prescriptions for Drug B, they are defined as two distinct Drug Eras. The start and end dates for DrugEra2 and DrugEra3 are the start and end dates for prescriptions B1 and B2, respectively.

Note, the logic for drug eras does not append overlapping exposure time to the end of the drug exposure length. That is, if a person receives a second 30-day prescription 10 days before the allotted 30-days supply for the first prescription, the resulting drug era would be 50 days long. This assumes the old prescription was completed or will be used in the future at the time of dispensing or record of the next prescription. Because drugs are rolled up to the ingredient level, this avoids misclassification of dose changes. It could be argued this conservative assumption be revised to augment the exposure length by this overlap, but these assumptions may likely vary by treatment and specific analysis.

Results

Table 1 shows the number of records created for each database using the two persistence window assumptions. CCAE is the largest database and observed 985m drug era records when using a 0-day persistence window, and 604m eras when using the 30-day persistence window. Thus, the consolidation in records was 38.7%. In other words, applying a 30-day persistence window, rather than the 0d assumption yielded 39% fewer periods of exposure. With the 0d assumption, the average era was 34.6 days long, as compared to 62 days when using the 30d window, so the average era length increased by 78%. However, in aggregate, the total person-years of exposure in the database only increased 9.2%, from 93m years to 102m years. That is, the transformation of drug exposures to drug eras, using the two different alternative assumptions for persistence window, has a significant effect on the number of exposure periods and the length of each period, but the total time exposed differs by <10% between the two alternatives. This 9.2% of exposure time reflects the amount of non-compliance time tolerated and treated as time exposed using the 30d persistence window that could have been treated as ‘non-exposure’ time when using the 0d assumption. This general phenomenon is seen fairly consistently between the claims databases (MDCD, MDCR, and MSLR); MDCR has more consolidation and longer exposures, presumably due to the characteristics of the elderly population and the increased use of medications for chronic conditions.

Table 1: Drug eras by persistence window assumption

	Era Count	Exposure Length (d)	Total exposure (yr)
CCAЕ			
0d	985,749,693	34.6	93,426,415
30d	603,949,580	61.7	102,039,970
	38.7%	78.3%	9.2%
MDCD			
0d	332,201,646	25.3	23,052,232
30d	204,821,062	46.0	25,803,386
	38.3%	81.5%	11.9%
MDCR			
0d	289,652,500	60.5	47,961,777
30d	138,551,919	135.3	51,334,597
	52.2%	123.8%	7.0%
GE			
0d	148,745,379	88.0	35,825,267
30d	132,891,479	99.8	36,323,919

	10.7%	13.5%	1.4%
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In contrast, the impact of the persistence window on GE drug exposures is much less significant. This should be expected due to the nature of exposure capture in these systems. In GE, exposure is inferred from a combination of prescriptions written and a medication history list. For prescriptions written, the length of exposure is inferred from the number of refills on the script, so much of the consolidation may already be captured from the raw data. Only when a patient completes the set of refills and gets a new prescription for the same product within 30d of the last refill would the era logic aggregate records under the 30d persistence window assumption. For the medication history list, providers have the opportunity to enter the exposure start date and end date, and commonly will enter only one record per drug. As such, it is less likely to observe multiple records for the same ingredient with multiple exposure periods that occur within 30d of one other. Across the entire database, GE has 10.7% consolidation of records, yielding an increase in era length of 13.5%; in aggregate, the 30d persistence window yields 1.4% more exposure-time than the 0d persistence window.

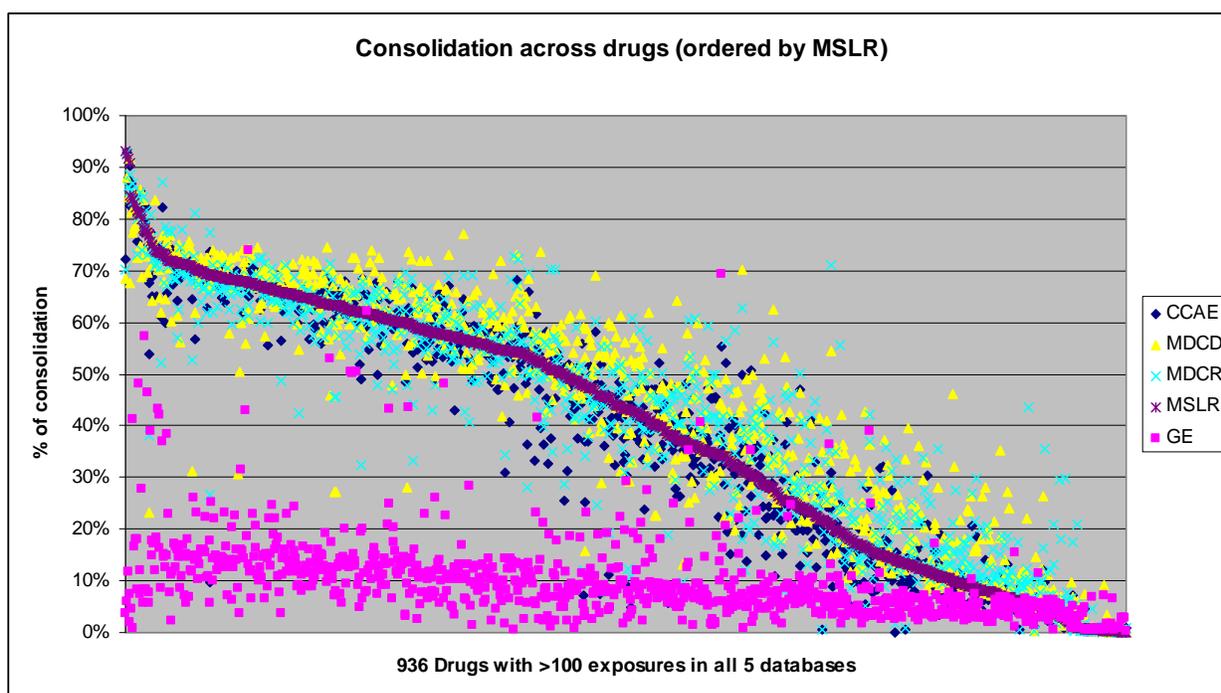


Figure 2: Era consolidation across drugs

Figure 2 shows the consolidation by drug across the 5 central databases. Here, drugs are at the RxNorm ingredient level, and are restricted to the 936 distinct ingredients with at least 100 exposures (using 0d persistence window) in each database. The four claims databases (CCAIE, MDCCD, MDCR, MSLR) follow a consistent pattern of consolidation by drug. In MSLR, 16 drugs have >80% consolidation, 413 have >50%. In general, this relative consistency makes sense since all exposures are based on prescriptions dispensed, and consolidation is largely due to refilled prescriptions, where the patient returned to the pharmacy after the first prescription completed but within 30days of the days supply. This tolerance for non-compliance allows

exposures that occurred to be considered part of one continuous period of persistent use. While this graph shows the impact does vary by drug, we see this assumption will have a >10% impact on counts of distinct exposure periods for >80% of the drugs in the database. In GE, only 8 drugs observed consolidation >50%, and only 40% of drugs aggregated >10% of the 0d drug eras.

Table 2 highlights the impact of the persistence window assumption within MDCD for the 10 OMOP drugs of interest. Eight of the drug groups (all but Amphotericin B and antibiotics) showed a consistent pattern, and observed a consolidation in records of >56%. While the average exposure length increased by greater than 160% for these eight drugs, the total impact on total exposure time ranged from 8.0% to 13.5%.

Table 2: Impact of persistence window on OMOP drugs of interest

MDCD	0d persistence window		30d persistence window		Reduction in records	Increase in exposure length	Increase in total exposure time
	Eras	Exposure length (d)	Eras	Exposure length (d)			
OMOP drug of interest							
OMOP ACE Inhibitor	4,834,363	50.9	1,252,915	212.3	74.1%	316.9%	8.0%
OMOP Amphotericin B	2,346	4.8	701	25.6	70.1%	431.7%	58.9%
OMOP Antibiotics: erythromycins, sulfonamides, and tetracyclines	2,637,818	15.5	2,264,053	19.8	14.2%	27.8%	9.7%
OMOP Antiepileptics: carbamazepine, phenytoin	1,413,869	51.6	315,764	251.9	77.7%	388.4%	9.1%
OMOP Benzodiazepines	5,812,389	42.4	2,262,601	120.0	61.1%	183.4%	10.3%
OMOP Beta blockers	3,587,753	50.5	966,989	203.0	73.0%	302.0%	8.3%
OMOP Bisphosphonates	533,913	43.8	135,459	191.5	74.6%	337.5%	11.0%
OMOP Tricyclic antidepressants	1,532,903	47.7	574,684	137.8	62.5%	189.1%	8.4%
OMOP Typical antipsychotics	984,291	35.8	428,678	93.3	56.4%	160.7%	13.5%
OMOP Warfarin	1,001,694	45.7	267,545	190.8	73.3%	317.8%	11.6%

The impact of the persistence window assumption was particularly striking for antiepileptics, where there was 77.7% reduction in the number of eras and a nearly four-fold increase in the average era length, from 52 days to 252 days.

Amphotericin B provides an interesting case study, as the average exposure length under the 0d persistence window was 4.8d, but increased to 25.6d under the 30d assumption. This can seem reasonable as individual intravenous treatments may be short, but may occur over time, particularly in an inpatient setting for fungal infections. Using the 30d persistence window increases the inferred exposure-time-at-risk by 59%.

The persistence window assumption had the least impact on antibiotic exposures, where the number of records was reduced only 14% when using the 30-day window relative to the 0-day

assumption. This also seems reasonable, as many antibiotic courses are single prescriptions and commonly less than 1 month in duration.

Table 3 provides a real de-identified person-level example from the database. Drug eras were constructed for benazepril, one of the active ingredients that is part of the ACE Inhibitor definition used for the OMOP drugs of interest. Using the 0d persistence window, one person had 35 drug eras for benazepril, with the earliest occurring in May2002, and the latest ending in Jan2008. As the pattern suggests, this individual was taking benazepril continuously, receiving regular prescriptions dispensed with 30 days supply. Periodically, the patient had the subsequent dispensing during the period of exposure (see era 16, which has an exposure length = 59). More often, this patient had the subsequent dispensing in the week or two after the prior dispensing had elapsed. In 6 instances, it appears the patient returned to the pharmacy only 1 day after the prior prescription was completed. Only once, from Jan2006-Jan2007 does the data not suggest the patient was not actively taking benazepril (during this time, the person's insurance coverage did not include pharmacy benefits so all prescriptions were unavailable).

Using the 30d persistence window assumption, these drug exposure records were consolidated into two drug eras: 1 from May2002 through Jan2006, and another from Jan2007 through Jan2008.

The overall consequence of selecting the persistence window assumption is that using '0d' yields 35 distinct periods of 'persistent exposure', totaling 1,447 days. The '30d' persistence window produces 2 distinct periods of persistence use, totaling 1,719 days. The difference in inferred time-at-risk represents the days of non-compliance. It is possible, (though unlikely in this instance given the available data), that a patient could stop taking the medicine and switch to an alternative during the drug hiatus before returning to the original drug, and thus are being incorrectly classified as a persistent user. An alternative explanation was the patient was not fully compliant with taking the medication every day or did not make it back to the pharmacy in time to have continuous exposure.

Table 3: Example from MDCD of one person with multiple exposures to benzepiril

Using 0d persistence window assumption

Era Number	Drug Era Start Date	Drug Era End Date	Exposure length	Days from last era
1	4-May-02	3-Jul-02	60	
2	6-Jul-02	5-Aug-02	30	3
3	9-Aug-02	8-Sep-02	30	4
4	27-Sep-02	27-Oct-02	30	19
5	4-Nov-02	4-Dec-02	30	8
6	11-Dec-02	10-Jan-03	30	7
7	24-Jan-03	23-Feb-03	30	14
8	25-Feb-03	27-Mar-03	30	2
9	17-Apr-03	17-May-03	30	21
10	20-May-03	19-Jun-03	30	3
11	24-Jun-03	24-Jul-03	30	5
12	25-Jul-03	24-Aug-03	30	1
13	11-Sep-03	11-Oct-03	30	18
14	24-Oct-03	23-Nov-03	30	13
15	1-Dec-03	31-Dec-03	30	8
16	15-Jan-04	14-Mar-04	59	15
17	22-Mar-04	21-Apr-04	30	8
18	26-Apr-04	18-Jul-04	83	5
19	2-Aug-04	1-Sep-04	30	15
20	7-Sep-04	5-Nov-04	59	6
21	11-Nov-04	11-Dec-04	30	6
22	17-Dec-04	16-Jan-05	30	6
23	17-Jan-05	16-Feb-05	30	1
24	17-Feb-05	19-Mar-05	30	1
25	22-Mar-05	18-May-05	57	3
26	19-May-05	14-Jul-05	56	1
27	5-Aug-05	4-Sep-05	30	22
28	6-Sep-05	3-Dec-05	88	2
29	17-Dec-05	16-Jan-06	30	14
30	2-Jan-07	2-Mar-07	59	351
31	3-Mar-07	2-May-07	60	1
32	1-Jun-07	22-Aug-07	82	30
33	28-Aug-07	27-Sep-07	30	6
34	28-Sep-07	1-Dec-07	64	1
35	4-Dec-07	3-Jan-08	30	3

Total 1447

Using 30d persistence window assumption

Era Number	Drug Era Start Date	Drug Era End Date	Exposure length	Days from last era
1	4-May-02	16-Jan-06	1353	
2	2-Jan-07	3-Jan-08	366	351

Total 1719

Figure 3 shows the distribution of era gaps that exist when applying the 0d persistence window, as observed against the 10 OMOP drugs of interest. Gaps were calculated for each person and each distinct ingredient within these drug groups as the length of time from the era end in the preceding era to the era start in the subsequent era. For all drugs except antibiotics, >75% of gaps are <30 days; these gaps represent the eras which would be combined by applying the 30d persistence window assumption. All eras with gap >30d would remain distinct.

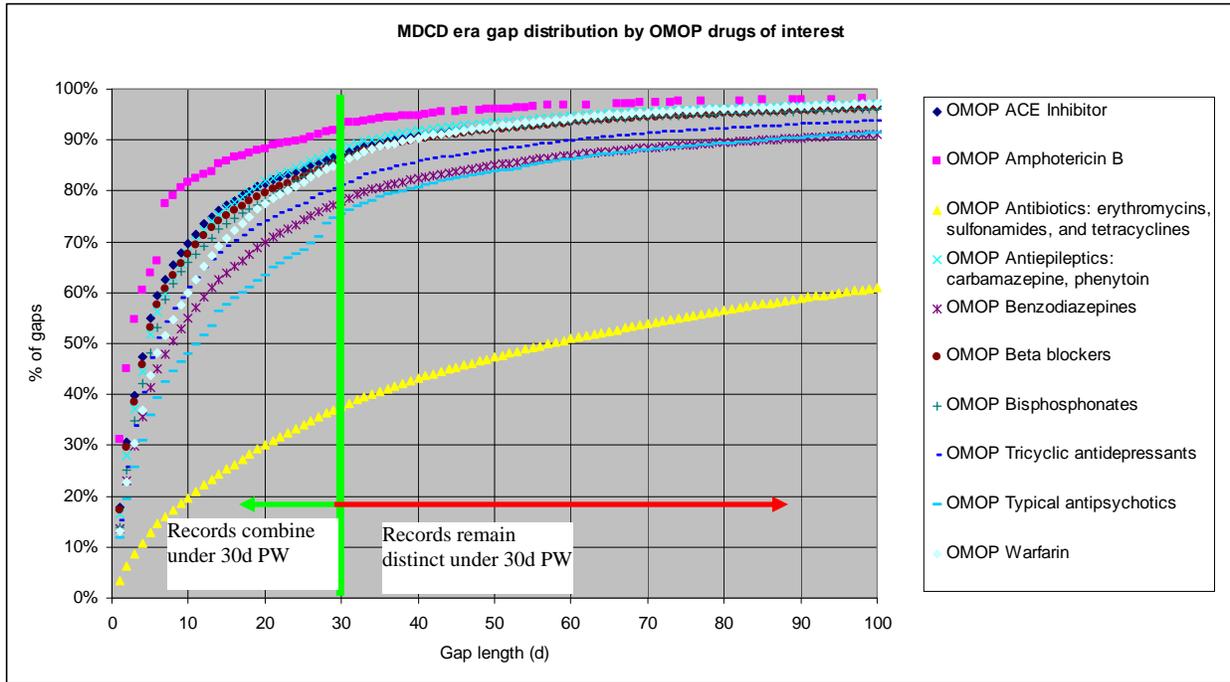


Figure 3: Era gap distribution for OMOP drugs of interest, in MDCD

As Table 4 details, among the gaps <30d (those to be aggregated under the 30d persistence window), >70% of gaps were <10d, and >89% were <20d for all drugs but antibiotics. For the OMOP Antibiotic group, 52% of the <30d gaps were less than 10 days, and 80% were less than 20 days.

Table 4: Era gap analysis for 30d persistence window in MDCD

		Among gaps <30d	
		% of era gaps <30d	% <10d
OMOP ACE Inhibitor	87.24%	79.82%	93.44%
OMOP Amphotericin B	92.57%	88.15%	95.26%
OMOP Antibiotics: erythromycins, sulfonamides, and tetracyclines	37.60%	52.48%	80.14%
OMOP Antiepileptics: carbamazepine, phenytoin	88.17%	77.03%	92.81%
OMOP Benzodiazepines	78.00%	70.41%	89.68%
OMOP Beta blockers	85.92%	78.58%	92.73%
OMOP Bisphosphonates	86.27%	76.43%	90.43%
OMOP Tricyclic antidepressants	81.14%	75.14%	91.38%
OMOP Typical antipsychotics	75.45%	63.67%	83.96%
OMOP Warfarin	85.64%	70.15%	90.52%

It seems reasonable that the pattern of era gaps for antibiotics would be different for other drugs, as these medicines are more likely to be used for acute conditions for short periods of time, and subsequent use of the medicines are more likely to be treatment for a separate disease. In contrast, many of the other OMOP drugs of interest, such as ACE inhibitors, beta blockers, antiepileptics, and bisphosphonates, are more likely to be used for long durations due to the chronic nature of the indications.

Discussion

Deriving drug eras from disparate exposure records can be a valuable component of a common data model for use in active drug safety surveillance. It creates standardized, transparent approach that can be applied consistently across any analysis. To date, all methods developed within OMOP have used drug eras, even though common data model can accommodate using raw drug exposure records. An open question is what persistence window to use: during the initial design, the OMOP advisory board requested studies using both the 0-day and 30-day assumptions.

The potential concern with applying any persistence window when defining periods of exposure is misclassification. As the tolerance level for non-compliance increases, so too does the risk of improperly combining two drug exposure records into one continuous period of exposure when they were in fact two independent treatment regimens. Also, accepting the non-compliant periods (when the patient was not in fact exposed) as time-at-risk can introduce bias into an analysis. Failure to allow tolerance for non-compliance can cause unexposed misclassification bias, as periods of time can be incorrectly classified as unexposed when in the midst of the continuous period of persistent exposure. As Table 4 reveals, even when using a 30d persistence window assumption, the large majority of aggregated eras come from non-compliance of less than 10 days. In these cases, it seems more unlikely these treatments represent independent exposures than it does that the gaps coincide with minor non-compliance.

In the context of active surveillance analyses, these periods of non-compliance can influence both the numerator and denominator of a rate ratio estimate. The question becomes whether or not adverse events that occurred during the periods of non-compliance should be included as cases, and whether the period becomes part of the exposed-time-at-risk measure for purposes of estimating the strength of the association between exposure and outcome.

Each analysis method may be parameterized to tailor the exposure window to the specific drug-condition relationship of interest. For example, the multi-set case control estimation program (<http://omop.fnih.org/MethodsLibrary>) allows the user to select the persistence window assumption (0d or 30d) and also define a surveillance window, which the period of time relative to exposure when outcomes can be considered potentially exposure-related. For example, the surveillance window allows users to specify targeting acute onset events, but specifying a window only 30d following exposure start date, or for exploring events that occur within the month following cessation of treatment (drug era end date + 30d).

However, wherever possible, when conducting first-pass analyses for active surveillance, it would be preferable to minimize the number of subjective decisions needed and to establish best practices that can be applied in many contexts, across multiple databases for different drugs and outcomes. If potential relationships are uncovered through this process, further tuning of the analysis-level parameters can be made to refine the estimate of the drug-condition association. In the extreme case, if reviewers were concerned with the potential impact of the logic used to infer exposure end dates and aggregate records into eras, the analysis could be manually reproduced by directly using the source records within the DRUG_EXPOSURE table. In this

regard, the common data model should be able to accommodate any level of analysis, from initial stages using scalable, automated exploratory processes to later stage evaluation studies.

The current approach attempts to systematically apply a common assumption across all medical products. An alternative approach would be to define a specific persistence window assumption for each drug. However, to our knowledge, there is no agreed approach for setting this assumption for active surveillance, and the assumption could vary within the same product, depending on the focus for evaluating a particular outcome. As such, it is recommended that a consistent framework for analysis be applied for all drugs and tailoring analyses for specific concerns be reserved for evaluation studies as needed.

Based on this study's findings, it is clear that selection of a persistence window can have a significant effect on the observed number of exposure periods and length of exposure per period. The interpretation of all analyses using drug eras should consider the potential impact of the assumption when drawing conclusions. As an initial assumption, it appears using the 30-day persistence window is sufficient for active surveillance. Exposure records that are aggregated under this 30-day rule appear clinically meaningful, and seem more likely to represent minor non-compliance than independent treatment episodes. Most aggregation comes from exposures whose gaps are less than 10 days.

Further study can evaluate the consistency in active surveillance analysis results based on the persistence window assumption. For example, a screening method could be run against a database using both 0d and 30d assumption, and the correlation of the results could be assessed, as well as exploration of which drug-condition pairs showed the largest differences.

Advantages and Potential Uses of Drug Eras

Drug eras are calculated in the in Common Data Model for active ingredients using Rxnorm, a standardized nomenclature for drugs and drug delivery devices. Rxnorm is developed and maintained by the National Library of Medicine (NLM). Drug eras can be used to provide an early assessment of the number of persons in a disparate data source exposed to the active ingredient of interest, the length of exposure as defined by the drug era and the number of separate drug eras the average individual is exposed to in a defined time window, without the programming complexity required to extract this information time again from the DRUG_EXPOSURE table.

In active drug safety surveillance may benefit of the drug eras, as it allows by an emerging or suspected safety signal, identify drug use pattern such as the uptake of a new drug, drug switching, characterize population exposure pattern, and convenient select the disparate data source most suitable for analysis of the safety question. Increased speed and less complexity provide convenience o a data coordinating center. If more detailed information on drug exposure is necessary than such information is accessible in the DRUG_EXPOSURE file.

Many factors may precipitate with the number and the size of the hiatus between the drug eras, with patient non-adherence the most important contributor. Others include drug stop orders documented in HER but not discernable in claims files, loss of drug coverage or eligibility while maintaining health insurance, or losing health coverage and drug coverage in one package. Loss drug eligibility while maintaining health insurance can be verified to a certain extend as a concurrent claim in the file for a medical procedure while no drug exposure claim is present.

The relationship between drug eras and Medical Possession Ratio (MPR) is interesting.¹ When the MPR is calculated across multiple refills, it is often called the continuous measure of adherence (CMA).² These measures are typically calculated using the following formula: Number of Days of Medication Supplied within the Refill Interval/Number of Days in Refill Interval. More precisely it is usually calculated by summing the number of days supplied for all but the last refill, divided by the number of days between the first and the last refill. Therefore, at least two fill dates are required to calculate this ratio. Researchers, however, may choose a fixed time frame for the refill interval, thus taking an earlier refill rather than using the last refill as the end point for the refill interval. MPRs and CMA are used not only to assess adherence in populations, but may also be used for establishing the strength of exposure, e.g. a patient with a MPR of .8 has been exposed to a twice higher dose than a patient with a MPR of .4 for the defined period of time or variable time. Thus this measure does not account for the length of neither exposure nor hiatus in exposure because of ineligibility of other reasons. Drug eras allow a minimum exposure ratio in each of the eras of .67 or higher for 30 days of supply Rx, .80 or higher for 60 days of supply Rx, and .86 or higher for 90 days of supply Rx. Drug eras are superior in defining the lower boundary in the window of exposure.

Limitations to and Considerations in the Use of Drug Eras

There are limitations to the quantification of drug exposures using drug eras. The acceptable persistence window is normative larger for 30 day dispensing than for 60 days or 90 days, as 30 days is allowed between either of these quantities of days supply. Two major drivers are that the drug era is truncated after the last day dispensed, secondly for three dispensing of thirty days, the max length of the era could be $3 \times 30 + 2 \times 29$ days = 148 days; for two dispensing of 60 days the same window of observation would be 60 days + 29 days + 30 days of the second dispensing = 119 days, for a 90 days supply prescription this would be 90 days. Most “scheduled” drugs allow for 30 days dispensing, insurance companies may place limits on the number days supplies dispensed at any given time, while others may promote 90 days of supply to reduce dispensing fees.

Drug eras derived from EHR may show pattern that overestimate exposures in the population, as prescriptions written not always reflect prescription dispensed or for that matter medications taken.

The data presented in these analyses are based on a defined window of observation defined by the data in the central data laboratory. The data available is truncated on the front as we do not know what the length of the drug era is prior to the data analyzed. In a active drug surveillance system the disparate data sources will continuously or within in small intervals download batches of data in the Common Data Model. Consequently the eras may longer in time than shown here.

Drug eras do not account in a satisfactory way for over exposure.

Queries for Health Outcomes of Interest (HOI) should not be limited to drug eras, as HOI may show latency times that surpass drug eras.

Conclusion

The definition of Drug eras as integral part of OMOP’s Common Data Model provides a significant advance in the methodological underpinnings of a system of Active Drug Safety Surveillance. In the construction of the Drug Eras a persistence window of 30 days shows superiority over the alternative.

References

1. Peterson AM, Nau DP, Cramer JA, et al. A checklist for medication compliance and persistence studies using retrospective databases. *Value Health* 2007;10(1):3-12
2. Steiner JF, Prochazka AV. The assessment of refill compliance using pharmacy records: methods, validity, and applications. *J Clin Epidemiol* 1997;50:105–16.