Creating Modified OMOP Drug Eras and Persistence Windows for Biologic Medications Using Both Pharmacy and Medical Claims

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BACKGROUND

- Analysis of medication use in automated claims databases requires identifying periods when a patient is receiving treatment, known as a **drug era**.
- Identifying drug eras is necessary for assessing drug adherence, effectiveness, and safety.
- A patient's use of certain drugs in a claims database can be identified by different types of claims.
  - **Pharmacy claims** describe drug dispensing.
  - **Medical claims** indicate when a drug was administered through a medical procedure, such as an injection or infusion.
- Some information about treatment with specific drugs is not found in claims databases but can be imputed from product labeling.
  - Recommended dose
  - Recommended dosing intervals
- A **persistence window** is defined as an allowable gap between two drug administrations occurring within the same drug era.
- The Observational Medical Outcomes Partnership (OMOP) has a common data model for defining drug eras.
  - Uses pharmacy claims only
  - Uses a 30-day persistence window

OBJECTIVE

- To identify and integrate items of information and assumptions required to create modified OMOP drug eras for biologic medications in database studies.
  - Integrate data elements for the same drug found in both medical and pharmacy claims
  - Use drug-specific persistence windows for each biologic agent, based on recommended dosing intervals found in product labeling

METHODS

Data Source

- Inpatient, outpatient, and pharmacy claims from the Truven Health Analytics MarketScan claims database for 2000 through 2010

Patient Identification

- Psoriasis patients were included if they fulfilled any of the following criteria:
  - At least 2 outpatient International Classification of Diseases, 9th Revision (ICD-9) diagnosis codes for psoriasis (696.0 or 696.1) on different days within 6 months (183 days); or
  - At least 1 outpatient psoriasis diagnosis from a specialist; or
  - At least 1 psoriasis diagnosis in any position (not necessarily primary diagnosis) from an inpatient encounter

Identification of Pharmacy and Medical Claims for Biologic Drugs

- Pharmacy claims—drug is dispensed by a pharmacy
  - National Drug Codes (NDC)
  - Date of dispensing
  - Quantity of drug dispensed
  - Days' supply of the drug
  - Items not found on a pharmacy claim
    - ICD-9 diagnosis code associated with the dispensing
    - Provider specialty associated with the dispensing
- Medical claims—drug is administered by a medical procedure
  - Healthcare Common Procedure Coding System (HCPCS) procedure codes
    - Codes beginning with "J"—Drugs administered other than oral
    - Codes beginning with "C"—Temporary codes
    - Codes beginning with "S"—Private payer codes
  - Date of procedure
  - ICD-9 diagnosis codes associated with a procedure
  - Provider specialty associated with the procedure
  - Items not found on a medical procedure claim
    - Days' supply associated with the drug procedure
    - Quantity of the drug administered through the procedure

Table 1. Biologic Medications of Interest

Category	Biologic Medication		Codes Used for Identification	
	Generic Name	Product Name	NDC Codes (Pharmacy Claims)	HCPCS Codes (Medical Claims)
Anti-interleukin (IL) 12/23	Ustekinumab	Stelara	X	X
Anti-tumor necrosis factors (TNF)	Etanercept	Enbrel	X	X
	Infliximab	Remicade	X	X
	Adalimumab	Humira	X	X
	Golimumab	Simponi	X	
Other (T-cell blockers)	Alefacept	Amevive	X	X
	Efalizumab	Raptiva	X	X

Abbreviations: HCPCS, Healthcare Common Procedure Coding System; IL, interleukin; NDC, National Drug Code; TNF, tumor necrosis factor

Recommended Dosing Intervals and Modified Persistence Window Rules

- Dosing intervals for medical procedure claims imputed from product label recommendations
- Modified persistence windows
  - Number of modified persistence window days between end date of previous medication claim and start date of next medication claim that a patient is assumed to be using treatment
  - Modified persistence windows for biologic medications equal to twice the recommended dosing interval
  - Allows for treatment effects and imperfect adherence to recommended dosing intervals

Table 2. Dosing Intervals and Modified Persistence Windows for Biologic Medications

Category	Biologic Medication			
	Generic Name	Product Name	Recommended Dosing Interval	Modified Persistence Window
Anti-IL 12/23	Ustekinumab	Stelara	12 weeks (84 days)	24 weeks (168 days)
Anti-TNF	Etanercept	Enbrel	1 week (7 days)	2 weeks (14 days)
	Infliximab	Remicade	8 weeks (56 days)	16 weeks (112 days)
	Adalimumab	Humira	2 weeks (14 days)	4 weeks (28 days)
	Golimumab	Simponi	4 weeks (28 days)	8 weeks (56 days)
Other (T-cell blockers)	Alefacept	Amevive	2 weeks (14 days)	4 weeks (28 days)
	Efalizumab	Raptiva	1 week (7 days)	2 weeks (14 days)

Abbreviations: IL, interleukin; TNF, tumor necrosis factor

Modified Drug Eras for Biologic Medications

- Period of time when patient is under treatment with a biologic medication
- Separate drug eras for each biologic drug
- A drug era for biologic medication may be defined by one or many claims
- Both types of claims for the same drug were combined to define drug eras for biologic medications
  - Pharmacy claims
  - Medical claims

Processing Pharmacy and Medical Claims

- First drug era began on date of first claim for the biologic medication
  - Pharmacy claims—dispensing date
  - Medical claims—procedure date
- Duration of claim for biologic medication
  - Pharmacy claims—"Days' supply" variable
    - Days' supply must be a positive number greater than or equal to 1 day
    - Days' supply of greater than 90 days is truncated at 90 days
  - Medical claims—impute duration from recommended dosing interval

Table 3. Summary of Processing Pharmacy and Medical Claims

Analytic Component	Pharmacy Claims	Medical Claims
Identification of drug	NDC Code	HCPCS Procedure Code
Start date of drug use in claim	Dispensing date	Medical procedure date
Duration of drug use in claim	Days' supply associated with dispensing	Imputed from recommended dosing interval (in days)
End date of drug use in claim	Derived as dispensing date + days' supply – 1 day	Derived as procedure date + imputed duration – 1 day
Allowable "persistence window days" between claims	Bridge rule	Bridge rule

Abbreviations: HCPCS, Healthcare Common Procedure Coding System; NDC, National Drug Code.

Building a Modified Drug Era from Multiple Claims

- Sort the relevant drug claims for each patient in chronologic order
- In this study, an assumption was made to count overlapping days on multiple claims only once
  - Other studies can make the assumption to concatenate days from overlapping claims
- If two claims had the same start date, use the claim with the longest duration

Figure 1. Drug Claims with the Same Start Date

- If next claim starts ***on or before*** the end of the prior claim plus the allowable number of persistence window days
  - Include the next claim as part of the continuing drug era

Figure 2. Drug Claims in the Same Drug Era

- If the next claim starts ***after*** the end of the prior claim plus the allowable number of persistence window days
  - The two claims are not part of the same drug era
  - End the prior drug era
  - Start a new drug era with the next claim

Figure 3. Drug Claims in Different Drug Eras

RESULTS

Number of Patients

- 354,856 psoriasis patients identified
- 48,736 patients had at least one pharmacy or medical procedure claim for a biologic medication used to treat psoriasis during their study period
  - 47,753 patients had a drug era for a biologic drug during their follow-up period.
  - 983 patients with at least one pharmacy or medical procedure claim for a biologic medication only had claims in their baseline period, so they had no drug eras for a biologic during their follow-up period.

Claims for Biologic Medications

- 648,193 total claims for a biologic medication of interest
  - 550,918 pharmacy claims (85%)
  - 97,275 medical claims (15%)
- Biologic medications with a majority of pharmacy claims – Ustekinumab, Etancercept, Adalimumab, Golimumab, Evalizumab
- Biologic medications with a majority of medical claims – Infliximab, Alefacept

Table 4. Claims for Biologic Medications by Type of Claim

Category	Generic Name	Year of FDA Approval	Total Number of Claims (% of Total)	Pharmacy Claims (% of Claims for Drug)	Medical Claims (% of Claims for Drug)
Anti-IL 12/23	Ustekinumab	2009	4,318 (0.7%)	4,110 (95.2%)	208 (4.8%)
Anti-TNF	Etanercept	1998	377,475 (58.2%)	365,021 (96.7%)	12,454 (3.3%)
	Infliximab	1998	78,367 (12.1%)	3,632 (4.6%)	74,735 (95.4%)
	Adalimumab	2002	155,382 (24.0%)	151,821 (97.7%)	3,561 (2.3%)
	Golimumab	2009	3,808 (0.6%)	3,808 (100%)	N/A
Other (T-cell blockers)	Alefacept	2003	7,072 (1.1%)	1,134 (16%)	5,938 (84.0%)
	Efalizumab	2003	21,771 (3.4%)	21,392 (98.3%)	379 (1.7%)

Abbreviations: FDA, Food and Drug Administration; IL, interleukin; N/A, not applicable; TNF, tumor necrosis factor

Modified Drug Eras for Biologic Medications

- Only one type of biologic agent in each drug era
- 168,881 follow-up drug eras for individual biologic agents

Table 5. Modified Drug Eras for Biologic Medications

Category	Generic Name	Patients N=47,753	Number of Drug Eras		Duration of Drug Eras, Days	
			Mean (SD)	Median (Range)	Mean (SD)	Median (Range)
Overall		47,753 (100.0%)	3.2 (3.9)	2 (1–63)	456.8 (501.9)	275 (1–3678)
Anti-IL 12/23	Ustekinumab	1,429 (3.0%)	1.0 (0.1)	1 (1–2)	154.9 (124.0)	127 (1–456)
Anti- TNF	Etanercept	29,544 (61.9%)	3.8 (4.4)	2 (1–63)	421.3 (473.6)	249 (1–3574)
	Infliximab	6,595 (13.8%)	1.1 (0.3)	1 (1–7)	467.8 (498.7)	287 (1–3433)
	Adalimumab	757 (1.6%)	1.5 (1.1)	1 (1–14)	111.5 (88.2)	91 (2–781)
	Golimumab	752 (1.6%)	1.0 (0.2)	1 (– 3)	174.3 (145.1)	129 (1–599)
Other (T-cell blockers)	Alefacept	16,495 (34.5%)	1.7 (1.4)	1 (1–26)	316.1 (334.5)	194 (1–2720)
	Efalizumab	2,255 (4.7%)	2.3 (2.4)	1 (1–26)	314.2 (348.4)	188 (1–1880)

Abbreviations: IL, interleukin; SD, standard deviation; TNF, tumor necrosis factor

Recommended Dosing Intervals Compared to Observed Dosing Intervals

- Modified persistence windows were based on recommended dosing intervals for biologic medications found in package labeling.
- A few patients had a large number (> 50) of derived etanercept drug eras.
- The actual frequency of etanercept claims for these patients was observed.
  - These patients had medical claims at regular intervals approximately every 4 weeks.
  - The duration of treatment for these medical claims was imputed to 1 week based on recommended dosing.
  - The persistence window for etanercept was derived to be 2 weeks, so claims more than 3 weeks apart would be considered to be different drug eras.
- Based on the imputed 1-week duration and 2-week modified persistence window, each regular monthly etanercept procedure ended up being counted as its own drug era.
- Patients with observed dosing intervals that were greater than the recommended dosing intervals plus the modified persistence window appeared to have a large number of drug eras of short duration rather than a single long drug era.

CONCLUSIONS

- Use of biologic medications in claims data are found in both pharmacy and medical procedure insurance claims.
- Different data elements are found in pharmacy and medical procedure claims.
- A patient's use of a specific biologic medication may be described in both pharmacy and medical procedure insurance claims.
- Information found on different types of claims needs to be integrated and combined to derive drug eras for biologic medications.
- OMOP drug eras were modified to include both pharmacy and medical procedure claims.
- Decision rules are needed to impute missing data elements in claims, such as the duration of treatment associated with a medical procedure claim.
- Decision rules can be made to address allowable persistence windows between pharmacy dispensing and medical administrations for specific biologic agents.
- These decision rules will affect the duration and number of a patient's drug eras.
- The OMOP 30-day persistence window was modified to reflect the recommended dosing intervals found in package labeling for each specific biologic agent.
- Recommended dosing intervals found in package labeling may not always be consistent with the observed dosing intervals found in claims data.

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REFERENCES

Naldi L, Raho G. Emerging drugs for psoriasis. *Expert Opin Emerg Drugs*. Mar 2009;14(1):145-163.

Observational Medical Outcomes Partnership (OMOP). Establishing a Drug Era Persistence Window for Active Surveillance. 2010; http://omop.fnih.org/sites/default/files/OMOP-Establishing%20a%20Drug%20Era%20Persistence%20Window%20for%20Active%20Surveillance-Jan%202010.pdf. Accessed October 9, 2013.

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