

The Importance of Information Extraction from Unstructured Clinical Data in Pharmacoepidemiology

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Background

Electronic health records (EHRs) and claims are an important source of real-world data used to generate real-world evidence on the safety and effectiveness of therapies. Valuable information is contained in the unstructured clinical notes and methods such as Natural Language Processing (NLP) are needed to extract the information into a structured format for analysis. Previous work focused on developing NLP methods to extract suicidality.^{1,2} However, methods to extract information on a broader array of neuropsychiatric symptoms are needed for drug safety studies and other health care use cases.

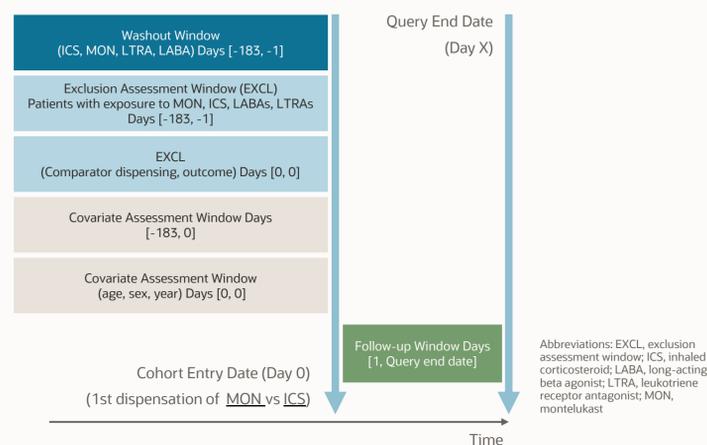
Objective

To examine the impact on outcome identification of using unstructured EHRs in a drug safety study examining neuropsychiatric events.

Methods

This retrospective study examined structured and unstructured data from the Oracle EHR Real-World Data (OERWD) linked to a national US claims data source during the study period 2015 to 2022.

Figure 1. Study Design

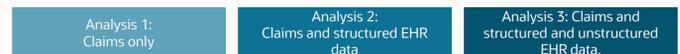


Abbreviations: EXCL, exclusion assessment window; ICS, inhaled corticosteroid; LABA, long-acting beta agonist; LTRA, leukotriene receptor antagonist; MON, montelukast

The cohort was defined as patients with a diagnosis code of asthma in either claims or electronic health record structured data and a new prescription of montelukast or inhaled corticosteroids. Prior treatment episodes were considered using a 30-day gap period (Fig 1). The covariate assessment window was the 183 days up to and including the date of prescription. For this analysis, outcomes were measured from 1 day after the prescription until query end date.

Outcomes were neuropsychiatric events based on the FDA boxed warning for montelukast (Fig 2).³ Outcomes from structured data were ascertained using diagnosis codes, hospitalization and emergency room codes, and dispensed treatments. Outcomes from unstructured data were ascertained through named entity recognition models from John Snow Labs. Guidelines for annotation were developed based on the clinical concepts in the boxed warning for montelukast and refined with the input of clinicians and trained annotations.⁴ The models were trained in four rounds, with increasing amounts of training data and enrichment of notes with mentions of rare events.

Three analytic approaches were used to examine the value of incrementally contributing sources of data for covariates and outcomes:



Propensity scores using logistic regression models were used to match montelukast initiators to the ICS referent group using a 1:1 ratio and nearest neighbor matching algorithm for each analysis group. For this study, results from the total matched cohort are presented. Statistical analyses were performed using R version 4.1.

For more information on the methods, see the protocol for the study: https://www.sentinelinitiative.org/sites/default/files/documents/MOSAIC-NLP_Protocol_v1.3.pdf

Figure 2. Outcomes of Interest: Neuropsychiatric Events

FDA's Boxed Warning	Claims/EHR Structured Data	EHR Unstructured Data
<ul style="list-style-type: none"> Agitation, including aggressive behavior or hostility Attention problems Bad or vivid dreams Depression Disorientation or confusion Feeling anxious Hallucinations Irritability Memory problems 	<ul style="list-style-type: none"> Obsessive-compulsive symptoms Restlessness Sleepwalking Stuttering Suicidal thoughts and actions Tremor or shakiness Trouble sleeping Uncontrolled muscle movements 	<ul style="list-style-type: none"> Aggressive behavior or hostility Agitation Attention problems Bad or vivid dreams Depression Disorientation or confusion Dream abnormalities Feeling anxious Hallucinations Irritability Memory problems Obsessive-compulsive symptoms Restlessness Sleepwalking Stuttering Suicidal thoughts and actions Tremor or shakiness Trouble sleeping Uncontrolled muscle movements

Results

A total of 109,076 patients with asthma who initiated montelukast or inhaled corticosteroids from 112 health systems were examined. Demographic characteristics of the propensity-matched patients are presented in Table 1.

Table 1. Demographic Characteristics of the Overall Matched Cohort According to Data Source

	Claims	Claims + Structured EHR	Claims + Structured EHR + Unstructured EHR
Number of patients	76,016	71,620	71,244
Age at treatment initiation, years, mean (SD)	29.7 (20.9)	29.7 (20.7)	29.8 (20.8)
Female, %	61.2%	61.0%	61.0%
Married or living with a partner, %	n/a	19.3%	19.4%
Race, %			
Asian, or American Indian or Alaska Native, or Native Hawaiian or Other Pacific Islander	n/a	3.0%	3.0%
Black or African American	n/a	20.2%	20.1%
White	n/a	57.7%	58.0%
Multiple races/other	n/a	12.8%	12.7%
Missing	n/a	6.3%	6.2%
Ethnicity, %			
Hispanic or Latino	n/a	24.3%	24.2%
Non-Hispanic or Latino	n/a	68.1%	68.2%
Multiple ethnicities/missing	n/a	7.6%	7.6%
Insurance status, %			
Commercial	30.5%	30.1%	30.3%
Medicaid/Medicare	68.1%	68.5%	68.4%
Other/missing	1.3%	1.4%	1.4%

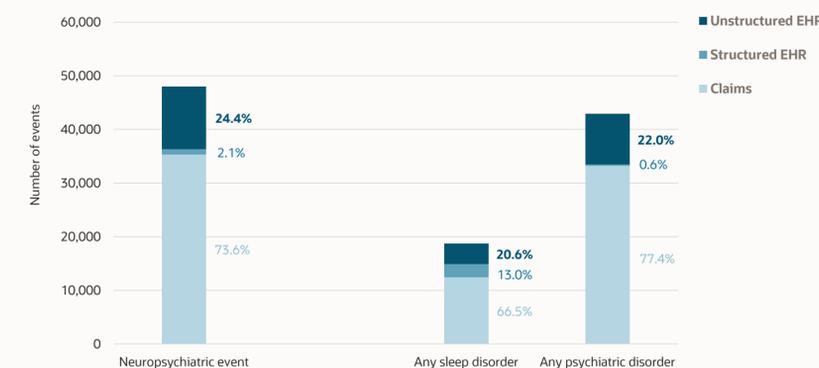
Table 2. Neuropsychiatric Events in the Overall Matched Cohort According to Data Source

	Claims	Claims + Structured EHR	Claims + Structured EHR + Unstructured EHR
Number of patients	76,016	71,620	71,244
Events per person			
Mean (SD)	2.53 (1.53)	2.64 (1.67)	2.62 (1.73)
Median (IQR)	2 (1-3)	2 (1-4)	2 (1-4)

Matched study patients had 2.5 events/person when utilizing structured data to identify outcomes, and 2.6 events/person with the addition of unstructured clinical notes (Table 2).

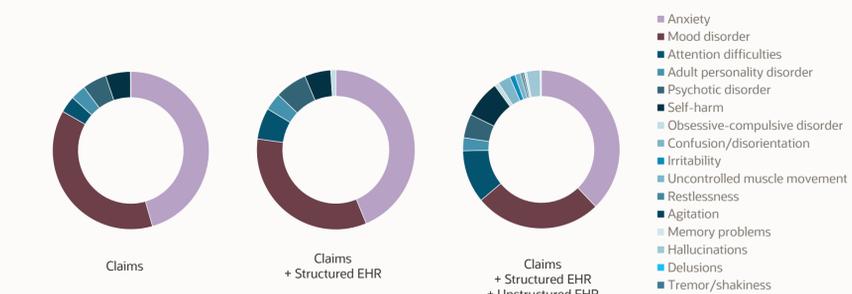
Figure 3 presents the contribution of neuropsychiatric outcomes according to data source in the final analysis that included claims and structured and unstructured EHR data. Compared to outcomes identified from claims only, adding structured EHR data resulted in only a modest increase in numbers of events identified for neuropsychiatric events, with the majority of the additional events being sleep disorders. Unstructured data added an additional 20%+ of outcome events.

Figure 3. Contribution of Neuropsychiatric Events in the Overall Matched Cohort Analysis for Claims and Structured and Unstructured EHR Data



Anxiety and mood disorder were the most frequently documented neuropsychiatric events in all sources of data. Many events, including agitation, muscle problems, hallucinations, and delusions were not identified at all in the structured data (Fig 4).

Figure 4. Distribution of Neuropsychiatric Events in the Overall Matched Cohort by Data Source



Conclusion

This study found that neuropsychiatric events may be undercounted using only structured data from EHR and claims, as the number of observed suicidality/self-harm events doubled with the addition of unstructured EHR data. Further, events such as irritability, agitation, and memory problems were only detected in unstructured data. This study illustrates the importance of unstructured data especially related to mental health outcomes.

This method is limited by the time required to annotate training data and the model's ability to identify and train on rare events, such as stuttering. Future work using large language models and hybrid methods may be able to overcome these limitation.

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