# Introduction

An adverse event is an injury to a patient. An adverse drug event (ADE) is an injury resulting from a medical intervention related to a drug. ADEs are common and occur to patients. Severe ADEs are between the fourth and sixth leading causes of death in the United States. Significant healthcare savings could be realized through preventions of ADEs and through early prevention of ADEs and through early detection and mitigation of ADEs.

When patients experience ADEs, they sometimes discuss with others on social media platforms. Unlike reports through official channels such as FDA and WHO, the information regarding ADEs in social media is in unstructured text. However, reports of ADEs in social media represent patients’ voice and may complement the reports of drug regulatory agencies. Rapid, accurate, and automated detection of ADEs in social media would provide significant cost and logistical advantages. Robust biomedical natural language processing (BioNLP) approaches that accurately detect ADEs in social media are of great interest to pharmacovigilance researchers. Studies have developed supervised learning approaches to extract ADEs from social media. To achieve this, annotation for drugs, adverse events, and adverse drug events in social media is necessary to create training data.

# Medical Entity and Relation Annotation

## Medication annotation

When an adverse event is recognized, proper measures such as adjustment the dose, or administrator an antidote could be taken. Drug and drug specific attributes are important elements to annotate. Information will be addressed to assess causal relations between an adverse event and drug administration.

**Field**: Drug name [Entity]

**Definition**: Substances for which the patient has experienced or will experience; including drug class name or medications referred with pronouns. Drug’s generic or brand name must belong to drug list under FDA’s registration. In social media discussions, consumer preferred terms often used. We refer to Consumer Health Vocabulary (<http://consumerhealthvocab.org/>) to extend the drug name coverage.

**Example**:

1. I started to use [Metformin] after I was diagnosed.
2. [Glyburide] 5 mg orally twice a day.

## Medical event annotation

Elements beyond the drug administration to annotate include: why a drug is being given, the injury resulting from a medical intervention related to a drug, and signs and symptoms.

|  |  |  |
| --- | --- | --- |
| Field | Definition | Example |
| Indication | Medical conditions for which the medication is given in the past or the present. | 1. She was diagnosed with [hypertension] and was treated with Accupril. 2. He had high cholesterol, so the doctor gave him [Lipitor]. |
| Adverse Event (AE) | Drug related injury to a patient | 1. She experienced a [hypersensitivity reaction] while injecting insulin. 2. I had [nausea] after using Metformin. |
| Signs, symptoms, findings, and diseases | Medical signs, symptoms, and diseases | 1. I have a family history of [heart disease]. 2. I was diagnosed [diabetes] 10 years ago. |

## Annotation for relations

Annotate relations (connections) between entities. Indication, signs, symptoms, diseases, and adverse event are drug attributes and are related to their drugs.

|  |  |
| --- | --- |
| Context | Relation |
| He later received chemotherapy for his lung cancer. | Indication (lung cancer, chemotherapy) |
| His death was due to the heart attack caused by Avandia. | Adverse drug event (Avandia, heart attack) |
| I didn’t have any allergy to Lantus. | None (Lantus, allergy) |

# Annotation Practice (Inter-annotator agreement)

## General considerations

* Do not make assumptions
* Do not diagnose
* Do not annotate general terms such as “problem” and “disease”. They are not informative.
* Do not annotate parts of words
* Annotate negations of adverse drug events as “None” relation type.
* Make relevant relations, regardless of distance between terms.

Choosing a span

We include most disease complements in its names. For example, annotation of medical events:

* I had [low blood glucose] very often after using this drug.
* [Women](http://www.heart.org/HEARTORG/Conditions/HighBloodPressure/UnderstandYourRiskforHighBloodPressure/High-Blood-Pressure-and-Women_UCM_301867_Article.jsp) who are taking ACE inhibitors for [high blood pressure] should not become pregnant while on this class of drugs.
* Insulin injection sometimes causes [burning sensation in injection area].

Anaphoric pronouns

Anaphoric pronouns are the pronouns that refer back to another word or phrase. We do not annotate anaphoric pronouns like it or this in examples below even though these refer to entities we do annotate:

* I had [hypoglycemia] but ***it*** was resolved after dosage change.
* I have problems with injecting [insulin]. ***It*** gave me a burning sensation.

## Drugs

* Non-drug treatment options like fluids, oxygen, and red packed cells are not annotated as drugs.
* We do not annotate the term *drug* when it does not denote a specific drug, however we annotate more specific terms like long action insulin or pain killer.
* Do not annotate social self-medication with alcohol, tobacco, IV drugs, street drugs, etc.
* Only annotate what is medically provided for an indication, or self-medication with legally obtained OTC drugs.
* Do NOT annotate the word supplement unless it is required to add meaning. For example do NOT annotate in “vitamin D supplement" or "iron supplement”, but do for “herbal supplement”.

## General Terms

* General terms are ones that are not informative. Judgment is required, but often descriptions with greater specificity follow the use of a general term and annotating those is preferred.
* Examples of general terms: concern, complaint, complication, difficulty, diffuse, disease, illness, issue, problem, drug, medication, therapy, treatment, etc.