## Frequency of Harm & Frequency of Exposure

**DDI minimum information models definitions**

<https://docs.google.com/spreadsheets/d/1dhUp496riwZ0AHqRP7I85oEvuP2jjEI0rcw1Fcm2zI8/edit#gid=0>

### Proposed User-Centered Definition (Qualtrics)

**Frequency of Harm:**

The number of individuals within a cohort that experience a drug-drug interaction clinical consequence divided by the total number of patients co-exposed to the drugs that are involved in the interaction.

**Frequency of Exposure:**

The number of individuals within a cohort that are exposed to a drug-drug interaction over a specified time period divided by the total number of patients in the cohort.

**For example:**

* **Frequency of Exposure and Frequency of Harm**: In an analysis that included 153 patients receiving antiretroviral therapy, 133 patients had any type of drug interaction, for a frequency of exposure of 86.9%. Of the 133 exposed patients, 63 patients had a clinically significant antiretroviral drug interaction, for a frequency of harm of 47.4%.
  + **Source**: Miller CD, El-Kholi R, Faragon JJ, Lodise TP. Prevalence and risk factors for clinically significant drug interactions with antiretroviral therapy. *Pharmacotherapy*. 2007;27(10):1379-86.
* **Frequency of Harm**: Among 2,427 patients co-prescribed either clarithromycin or erythromycin and a statin metabolized by CYP3A4, 47 had a clinical consequence of hospitalization for acute kidney injury, for a frequency of harm of 1.9%.
  + **Source**: Patel AM, Shariff S, Bailey DG, et al. Statin toxicity from macrolide antibiotic coprescription: a population-based cohort study. Ann Intern Med. 2013;158(12):869-76.
* **Frequency of Exposure**: Among 2712 patients age 65 or older recruited at hospital admission and exposed to at least one potential drug drug interaction, 1642 patients were exposed to at least one potentially moderate drug drug interaction, for a frequency of exposure of 60.5%.
  + **Source**: Pasina L, Djade CD, Nobili A, et al. Drug-drug interactions in a cohort of hospitalized elderly patients. *Pharmacoepidemiol Drug Saf*. 2013;22(10):1054-60.

**Background Information:**

* Gordis L. Epidemiology. 4th ed. Philadelphia, PA: Saunders; 2009:38.
  + Definition of **Incidence Rate**: “[T]he number of new cases of a disease that occur during a specified period of time in a population at risk for developing that disease.” “The denominator of an incidence rate represents the number of people who are at risk for developing the disease.”
* Suggested PDDI Categories
  + The frequency of exposure data is available
  + The frequency of exposure data is not available
  + The frequency of adverse event data is available
  + The frequency of adverse event data is not available
* Notes from Sean Hennessy:
  + When you say that 'frequency of exposure data is not available', I assume you mean frequency of concomitant use of the object + precipitant, right?
  + When you say 'not available' do you mean not published, or not calculable from health care data, or something else?
  + Similarly, when you say frequency, do you mean the frequency in the population (like % of all Americans who will receive drugs A + B together in any given year), the proportion of all prescriptions for the object that overlap with the precipitant, or something else?
  + And by frequency of the adverse event, do you mean the absolute risk or the risk attributable to the interaction?

**Suggested User-Centered Definition (Google Sheets)**

* **Frequency of Harm and Frequency of Exposure** 
  + Frequency of harm and exposure
    - "Should these be broken into two separate buckets? Freq of harm AND freq of exposure?
    - Split into two categories - one for exposure and one for harm
  + An information (content) entity....(for both frequency of harm and frequency of exposure)
* **Frequency of Harm** 
  + The incidence of severe and life-threatening clinical consequences as adverse events of drug-drug interactions among all the population who take the medications. It ranges from very common to unknown.
  + Requires us to define ""harm"". Maybe better as ""Frequency of clinically relevant consequences""?
* **Frequency of Exposure**
  + The incidence of population who take the medications?
  + Frequency or incidence of adverse drug events
  + What is the feasibility of assigning an accurate frequency of exposure when we are talking about drug pairs? I do not know that this information is readily available.
  + To the best of my knowledge, there is not any information source about frequency of exposure to DDIs, and I´m not sure anyone is trying to create such a repository. Just something that came to my mind, however, if in a hospital setting, it could be feasible at some point to gather that information from EHR? I mean, knowing the frequency of prescription of two interacting drugs in a specific Institution? Also, it is possible that some evidence resources could provide this information (such as observational studies about frequency of DDIs (see reference)). In these cases, it should be important to link the frequency of exposure to the Institution where this observation is being made.
    - Ganeva M, Gancheva T, Troeva J, Kiriyak N, Hristakieva E. Clinical relevance of drug-drug interactions in hospitalized dermatology patients. Adv Clin Exp Med [Internet]. 2013 [cited 2014 Dec 9];22(4):555–63. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/23986216>
  + It is possible to generate this evidence in clinical informatics research network like the ohdsi.org. I also have permission to work with the large claims database in the IMEDS lab (http://imeds.reaganudall.org/On-Boarding):
  + <http://imeds.reaganudall.org/sites/default/files/Boyce-IMEDS%20Research%20Lab_April%202014.pdf>
* Ideally reported using standard frequency groupings (very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); and not known)