## Contextual information/modifying factors

**DDI minimum information models definitions**

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

### Proposed User-Centered Definition (Qualtrics)

**Contextual information/modifying factors:**

Factors such as patient age, patient health conditions, treatment dosage form, or concurrent medications that might alter the risk of a drug-drug interaction clinical consequence or its seriousness.

**For example:**

* “Both corticosteroids and aldosterone antagonists have been shown to substantially increase the risk of UGIB in patients on NSAIDs, with relative risks of 12.8 and 11 respectively compared to a risk of 4.3 with NSAIDs alone (Masclee et al. *Gastroenterology*. 2014;147:784-92.)”
  + **Source**: Footnote 5 to Warfarin-NSAID Decision Table, NIH Project: R21-HS023826-01; Title: Individualized Drug Interaction Alerts; Authors: Daniel C. Malone , University of Arizona; John Horn, Philip Hansten, University of Washington
* “A number of factors have been associated with an increased risk of hyperkalemia. These include impaired renal function, diabetes mellitus, infrequent serum potassium monitoring, baseline serum potassium level, angiotensin converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs). (Henz S et al. *Nephrol Dial Transplant*. 2008;23:3939-45; Eschmann E et al. *Eur J Clin Pharmacol*. 2014;70:215-23; Indermitte J et al. *Drug Safety*. 2007;30:71-80.)”
  + **Source**: Footnote 1 to KCl + Potassoim-Sparing Diuretics Decision Table, NIH Project: R21-HS023826-01; Title: Individualized Drug Interaction Alerts; Authors: Daniel C. Malone , University of Arizona; John Horn, Philip Hansten, University of Washington

**Background Information:**

* **DINTO**:
  + In DINTO we include some of these factors as data properties related to:
    - the DDI -- has documentation level (""established"" , ""possible"" , ""probable"" , ""suspected"" , ""unlikely""), has onset ({""delayed"" , ""rapid""}),
    - the study subject – has age, has gender, has race or ethnic
    - the information source (where the DDI is described) – has subject number
    - the interacting drugs – has administration route, has concentration, has dose, has pharmaceutical form.

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

* **Contextual information/modifying factors** 
  + Information or factors that may affect individual patient’s pharmacodynamics, such as age, gender, weight, ethnicity, pharmacogenomics biomarkers, pre-existing conditions, dose (strength) and route of medications, duration of medication administration etc. Furthermore different pharmacodynamics may affect individual’s clinical consequences and their severity levels.
    - There is a category mistake in this definition, please see my comment in Column C for details:
      * When available, predisposing risk factors such as age, predisposing diseases, pharmacogenomic phenotype, and the specific drug regimen(s), such as dose, route, duration of therapy, sequence of initiating co-therapy, and timing of co-administration.
        + This probably needs some work, I am not sure that PK and PD is exhaustive here
    - Sounds like a bucket of everything that is a co-variant under the statistical context.
  + If known, genetic information, ethnicity, concomitant diseases, etc. that modify the risk of an adverse outcome
    - Patient's gender, weight, pre-existing conditions
    - Should we produce a comprehensive list of all applicable modifying factors relating to DDI's?
      * "Should include CYP inducers, inhibitors
      * Yes, as pharmacogenomic factors. Have a look to this excerpt from PharmGKB:
        + 2. EMA Label for efavirenz,emtricitabine,tenofovir and CYP2B6: The EMA European Public Assessment Report (EPAR) for efavirenz, emtricitabine and tenofovir disoproxil (Atripla) contains pharmacogenetic information related to possible increased exposure to efavirenz in patients homozygous for the CYP2B6 G516T variant (rs3745274 genotype TT), and though the clinical implications of this are unknown, the potential for an increased frequency and severity of adverse events cannot be excluded.
      * This means that if these patients are also exposed to a possible DDI between efavirenz and another drug that might increase the levels of this drug in the organism, could experience more severe consequences that other individuals.
  + I think we need to clarify what we are talking about here. Information and factors are two fairly different types of things. From the definition it is fairly obvious that we are not talking about information in the first place. Information about my age will not affect the pharmacodynamics of a drug administered to me. My age might. So, I think we are talking about information about modifying factors here.
  + In DINTO we include some of these factors as data properties related to:
    - the DDI -- has documentation level (""established"" , ""possible"" , ""probable"" , ""suspected"" , ""unlikely""), has onset ({""delayed"" , ""rapid""}),
    - the study subject – has age, has gender, has race or ethnic
    - the information source (where the DDI is described) – has subject number
    - the interacting drugs – has administration route, has concentration, has dose, has pharmaceutical form.
  + My understanding of context information includes all the information that can be used to individualize/customize medication information about a particular patient. Such as current weight information can be used to calculate dosage; a particular biomarker can be used to selecet/exclude medications. How much of such information is available right now is another issue, at least we may need to list all the possible categories, such as age, gender, weight, genetic biomarker, liver and renal functions.
* **Genus differentia**
  + An information (content) entity that is about factors known to effect the pharmacodynamics and pharmacokinetics of a drug.