

Toward an ontology-based system for the automatic detection of biases and weaknesses in drug clinical trial results

UNIVERSITÉ PARIS 13



Jean-Baptiste LAMY^a <jean-baptiste.lamy@univ-paris13.fr>,
Hélène BERTHELOT^a, Madeleine FAVRE^{b,c}, Alain VENOT^a, Catherine DUCLOS^a

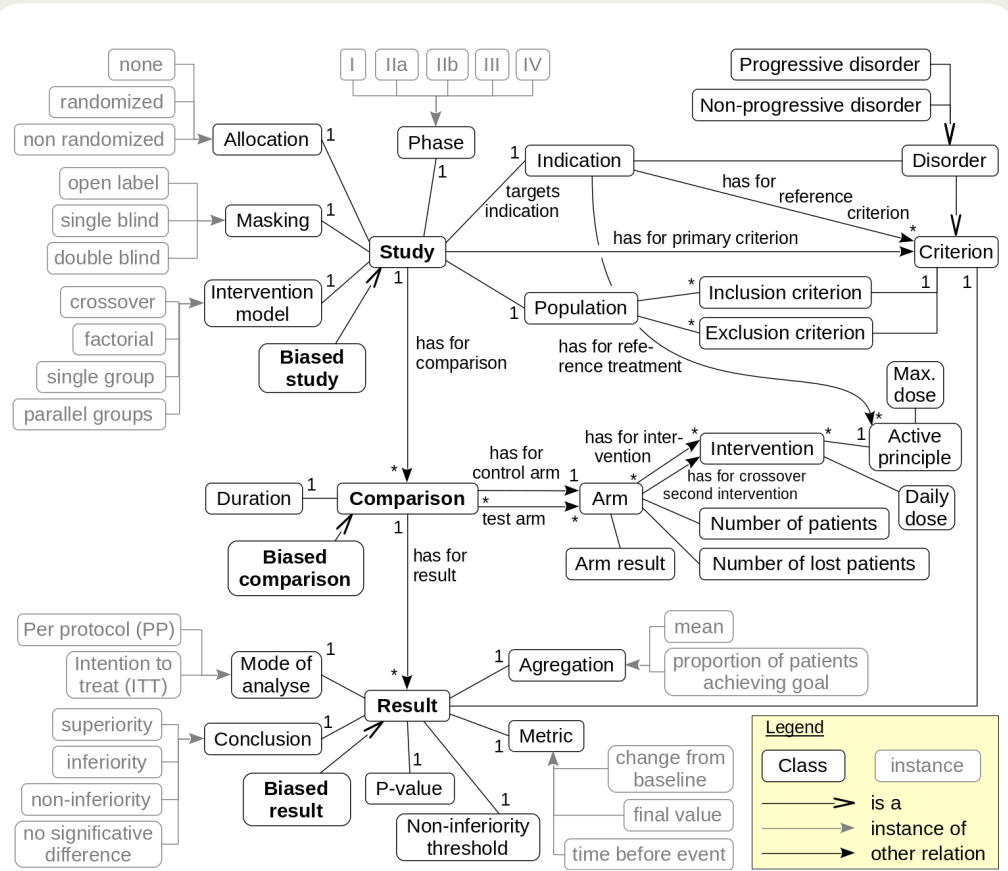
^aLIMICS (INSERM UMRS 1142), Université Paris 13, Sorbonne Paris Cité, 93017 Bobigny, France,
^{UPMC} Université Paris 6, Sorbonne Universités, Paris, ^bUniversité Paris Descartes, Paris, France,
^cSociété de Formation Thérapeutique du Généraliste (SFTG), Paris, France

Introduction

New drugs can improve patient health, but require careful evaluation and comparison with older drugs in clinical trials. But trials can be impaired by various biases and weaknesses. We present here a system for automatically detecting some biases, design flaws and weaknesses in clinical trial results.

Methods

We designed an ontology modeling the results of comparative clinical trials, using OWL (Ontology Web Language) and the Protégé editor. Then, we defined a list of weaknesses detectable from the literature and we implemented the detection of these weaknesses in OWL, SWRL rules or Python scripts. Finally, the system was evaluated on a new drug with 5 trials, and the detected weaknesses were presented to 4 experts.



The main concepts and relations in the ontology for comparative clinical trial result.

Examples of bias and weakness

Implementation

Crossover study for evolutive or non-stable disorder

OWL: Study and (has_for_intervention_model value crossover)
and (targets_indication some (has_for_disorder some Evolutive_disorder))

Study with none of the indication's reference criterion

SWRL: Study(?stud),
target_indication(?stud, ?indic),
has_for_reference_criterion(?indic, ?crit),
has_for_comparison(?stud, ?comp),
has_for_result(?comp, ?res),
has_for_criterion(?res, ?crit)
-> Study without this weakness (?stud).
Python script for asserting the weakness when its absence was not proven (negation as failure)

Comparison of non-comparable dosages (new drug at high dose vs old one at low dose)

Python script (due to the requirement of multiple negations as failure)

Results & discussion

The ontology was represented in the OWL-DL language (67 classes, 62 properties, 49 individuals, 574 axioms and 7 rules, SHOIQ(D) DL family). The detection of 13 weaknesses has been implemented. Experts agreed on the weaknesses detected during evaluation.

We have shown that it was possible to automatically detect some biases and weaknesses in clinical trial results. Our perspectives include a more comprehensive evaluation, the detection of additional weaknesses and the connection of the system to trial registries and drug databanks.