CTO: a Community-Based Clinical Trial Ontology and its Applications in PubChemRDF and SCAIView

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Agenda

• Background and overview of the Clinical Trial Ontology (Asiyah Yu Lin)
• PubChemRDF Use case (Leon Qingliang Li)
• SCAIView Use case (Stephan Gebel)
• Open research questions (Asiyah Yu Lin)
• Team and Acknowledgement (Asiyah Yu Lin)
Background

• Clinical trials are research studies conducted on human participants to evaluate medical, surgical, or behavioral interventions involving investigational drugs, devices, diagnostic products, treatments and the like.

• Registration of clinical trials is a mandate in most of the countries.
  • Declaration of Helsinki – 1964 to 2001
  • Title VIII of the Food and Drug Administration (FDA) Amendments Act of 2007 (FDAAA)
  • European Union Clinical Trials Directive 2001/20/EC
  • European clinical trials regulation (No 536/2014)
Goal: Openness and Transparency of Research

Clinical Trial Ontology - CTO

- A small set of clinical trial focused terms
- Enable the data integration, standardization and data sharing among current clinical trial registries.
- Establish a framework to link to other entities (chemicals, drugs, devices, vaccines, publications) under BFO umbrella
- Currently an OBO ontology, available at GitHub and BioPortal, can be viewed via OntoBee.
- Re-use the existing ontologies: OBI, OPMI, OCRe, ERO and many others
- 97 CTO specific terms, and 242 reused terms from 19 other ontologies.
- Ongoing work
- Aim to build an open clinical trial data science community.
CTO unique terms

- Clinical trial registry organization and registry identifiers
- Stakeholders’ roles – ‘investigation collaborator role’, ‘investigator role’, ‘contact person role’...
- Dates – ‘clinical trial start date’, ‘clinical trial completion date’...

Actively working on them. We need your input! Please provide your feedback via the issue trackers on GitHub: https://github.com/ClinicalTrialOntology/CTO
Use Case 1: PubChemRDF

PubChem is an open chemistry repository at the US National Institutes of Health (NIH).

PubChem has three inter-connected databases, **Compound**, **Substance** and **BioAssay**, which contain,
- Chemical structures,
- Identifiers,
- Chemical and physical properties,
- Biological activities,
- Patents,
- Health, safety & toxicity data,
- and more.

Use Case 1: PubChemRDF

PubChemRDF is an RDF version of PubChem supporting semantic technologies.

Use Case 1: PubChemRDF

Add *clinical trial data* to PubChemRDF by using Clinical Trial Ontology.
Use Case 2: Knowledge retrieval using SCAIView

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Terminologies
Ontologies
Use Case 2: Knowledge retrieval using SCAIView

Challenge in COVID-19 crisis
Retrieval of relevant knowledge in relation to COVID-19

Reliable source: COVID-19 related clinical trials

over 2000 clinical trials are registered in twenty different clinical trial repositories by May, 2020
Use Case 2: Knowledge retrieval using SCAIView

Clinical Trials Ontology

CORD-19 literature corpus*

search for clinical trials registry IDs

Clinical trial registry | Number of publications
--- | ---
ClinicalTrials.gov | 1823
Chinese Clinical Trial Registry | 142
Australian New Zealand Clinical Trials Registry | 25
ISRCTN registry | 23
Japan Primary Registries Network | 9
German Clinical Trials Register | 5
EU Clinical Trials Register | 3
Korean clinical trial registry (CRiS) | 3
Clinical Trials Registry - India | 3
Pan African Clinical Trial Registry | 2
Iranian Registry of Clinical Trials | 1

COVID-19 clinical trials
469 publications referring to 177 COVID-19 related trials

Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study

Without solid evidence, nearly half of the patients were given antiviral agents, and more than half were given intravenous glucocorticoids. Patients treated with immunotherapy were from an ongoing clinical trial registered on Chinese Clinical Trial Registry (NCT04244440). Remdesivir was given to the first patients with SARS-CoV-2 pneumonia in the USA. A trial on remdesivir is about to recruit both mild to moderate patients (NCT04244440) and severe patients (NCT04244440) who are infected with SARS-CoV-2. Although, intravenous glucocorticoids were extensively used in patients with severe SARS or MERS pneumonia, their efficacy remains controversial and their use to treat SARS-CoV-2 infection is also controversial. Additionally, some studies have suggested that glucocorticoids might shed some light on the safety and efficacy of these drugs as treatment.

This study has several limitations. First, only 52 critically ill patients were included. However, the population from which they were sampled was much larger than that of the three studies previously published. In conclusion, the mortality of critically ill patients with SARS-CoV-2 is likely to be set in 1-2 weeks after ICU admission, and the severity of SARS-CoV-2 resources, especially if they are not adequately staffed, is a major concern.

clinical trials identified by the parser
Open research questions

1. Ontological definition of “clinical trial”: what make it different with any other human subject researches?

2. Real World Evidence – will an observational study using retrospective data be counted as a clinical trial?

3. BFO-realism based approach introduces challenges of modeling (Rely on Community input)

4. Alignment or reuse with existing well-adopted standards (CDISC, NCTI, SNOMED CT) through outreach and collaborations
• Group Member
  • Asiyah Yu Lin (OPEQ/CDRH/FDA, NCOR)
  • Stephan Gebel, Sumit Madan, Johannes Darms, Alpha Tom Kodamullil, Martin Hofmann-Apitis (SCAI)
  • Leon Qingliang Li, Evan Bolton (PubChem, NIH/NLM/NCBI)
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