Visual Exploration of Randomized Clinical Trials for COVID-19

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The use of medications can result in severe adverse reactions, impacting the quality of life of patients. Recent studies show that adverse drug reaction events (ADRs) are associated with many causes of morbidity and mortality and bring economic losses to public health and the pharmaceutical industry. Therefore, the identification of ADRs is essential in the study of drug repurposing and pharmacology.

Qin et al. (3) presented a tool for identifying and ranking the signs of adverse reactions arising from drug interactions using association rules learning in FAERS data (FDA Adverse Event Reporting System). The authors provide a visual interface that allows users to filter the generated signals and present a network of interactions. Li et al. (1) propose a framework for real-time automatic extraction and interactive visualization for surveillance of adverse drug reactions for patients with diabetes using data from social networks and FAERS. Nguyen et al. (2) presented a survey on methods for identifying adverse reactions. Their work showed that association rule learning is commonly used to create baseline data for adverse drug reactions.

In contrast, machine learning methods are most widely used in the context of generalized prediction. Another critical point is that most of the work addresses monotherapy (administration of a single drug). There are very few models proposed for polytherapy (administration of more than one drug).

Randomized clinical trials are prospective studies in humans that aim to compare the effect and value of an intervention with a control group. These studies are randomized, as patients are randomly assigned to receive the intervention/treatment or a placebo. They can contain different data such as dosages of applied medicines, age, sex, and patients' illnesses. Adverse drug reactions can appear in many various clinical trials.

Our approach aims to identify and map information about treatments/interventions and adverse reactions in clinical trials, supported by drug data dictionaries such as DrugBank and UMLS (Unified Medical Language System) for concept extraction. This information is stored in a database, organized in a graph structure, and made available in an interactive visual interface. Users can search for terms related to drugs or adverse reactions and find clinical trials that show evidence of co-occurrences of a specific response when using a medication, check information about the effectiveness of the intervention in the treatment of COVID-19, and gain other insights.

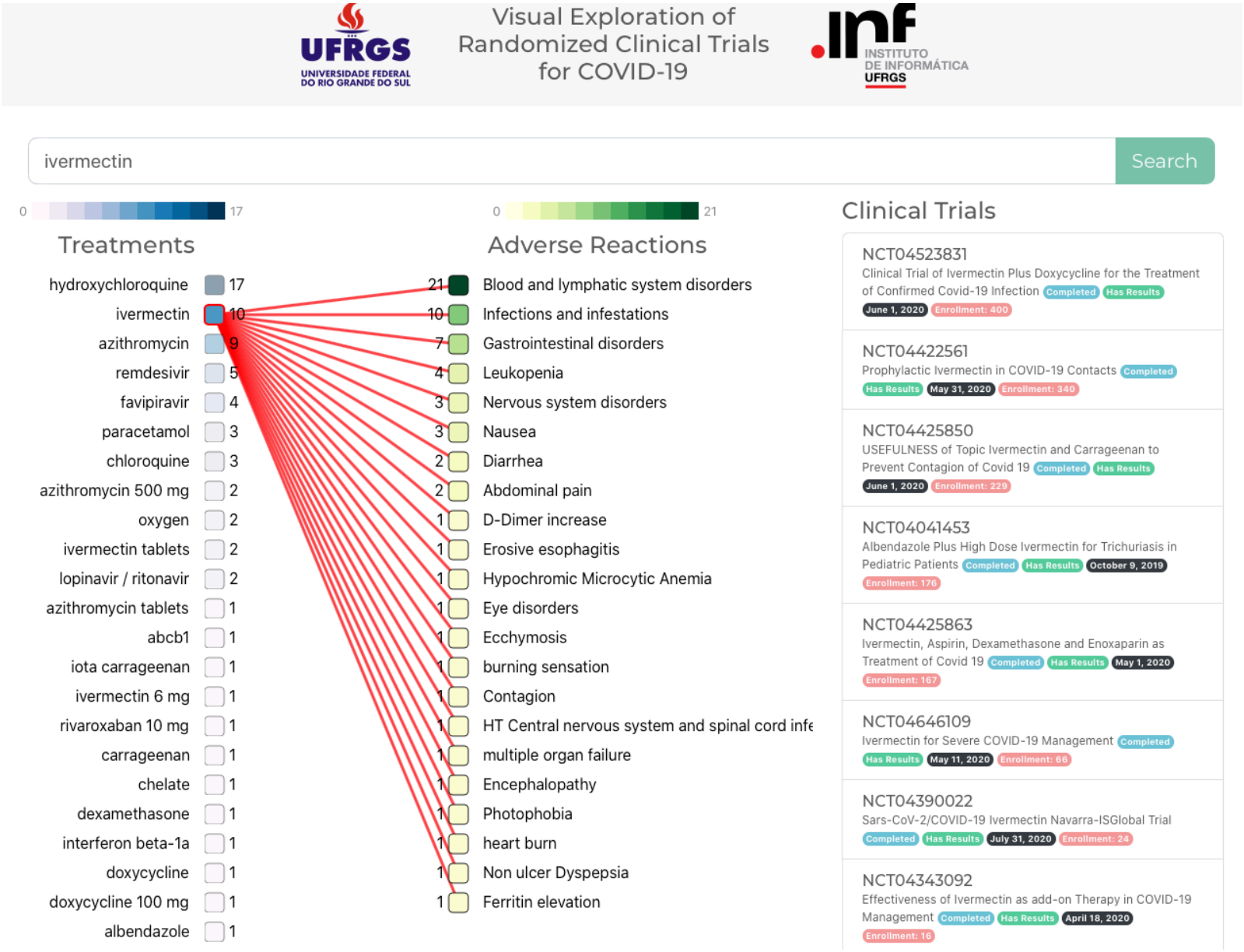
This work describes a visual analysis platform to explore randomized clinical trials applied to the treatment or prevention of COVID-19 to map the treatments and adverse reaction events observed in such interventions. We collected a set of clinical trials available on the clinicaltrials.gov platform. We used ETL techniques to extract information and build a graph-based interface to explore the observed relationships between treatments and adverse reactions.

References:

(1) Li, S., Yu, C. H., Wang, Y., Babu, Y. (2019). Exploring adverse drug reactions of diabetes medicine using social media analytics and interactive visualizations. International Journal of Information Management, 48, 228–237.

(2) Nguyen, D. A., Nguyen, C. H., Mamitsuka, H. (2021). A survey on adverse drug reaction studies: data, tasks, and machine learning methods. Briefings in Bioinformatics, 22(1), 164–177.

(3) Qin, X., Kakar, T., Wunnava, S., Maccarthy, B., Schade, A., Tran, H. Q., Zylich, B., Rundensteiner, E., Harrison, L., Sahoo, S., De, S. (2018). Mediar: Multi-drug adverse reactions analytics. Proceedings - IEEE 34th International Conference on Data Engineering, ICDE 2018, 1569–1572.



Prototype an be found at https://pitias.ufrgs.dev

Searching for "**ivermectin**" returns related treatments and adverse reactions.

Results are displayed as a bipartite graph, displayed as two columns of vertices (treatments and adverse reactions). The number of clinical trials is displayed next to each vertex

Relationships between a treatment and an adverse reaction in a clinical trial is displayed with an edge —— in the graph

The top four related adverse reactions include blood and lymphatic system disorders, infections and infestations, gastrointestinal disorders and leukopenia

The top four related treatments include hydroxycloqroquine, azithromycin, remdesivir and favipiravir

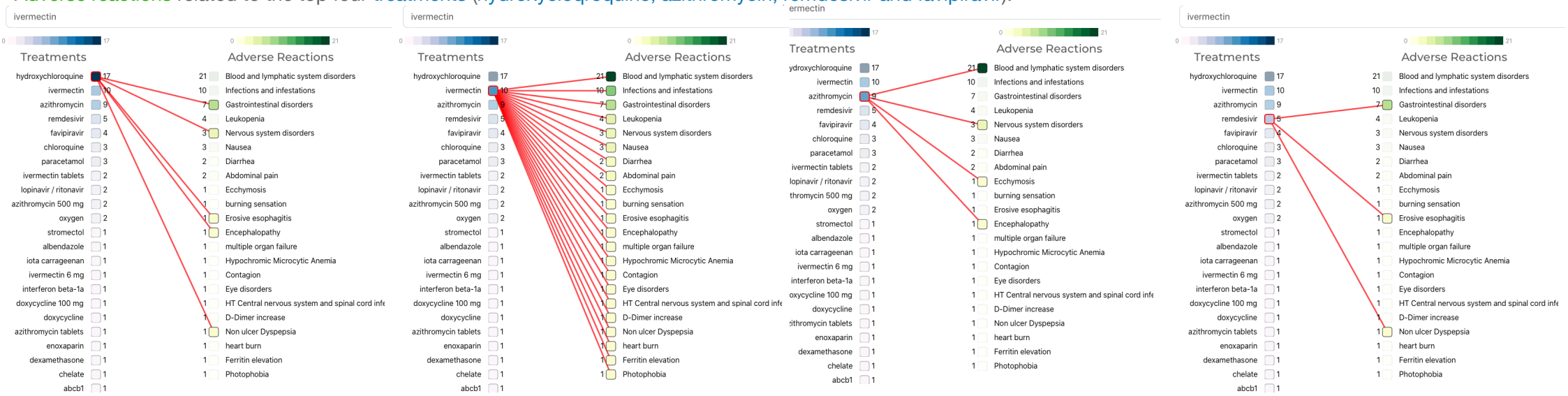
Selecting "**ivermectin**" in the treatments column returns **10** clinical trials, which can be explored in the clinical trials column

Clinical trials are ordered by trials that are **completed**, **have results** and by **enrolment size**. Clicking over the clinical trial redirects to the clinicaltrials.gov site

Figure 1

Visual exploration allows quick inspection of the relationships among treatments and adverse reactions

Adverse reactions related to the top four treatments (hydroxycloqroquine, azithromycin, remdesivir and favipiravir).



Treatments related to the top four adverse reactions (blood and lymphatic system disorders, infections and infestations, gastrointestinal disorders and leukopenia).

Figure 2