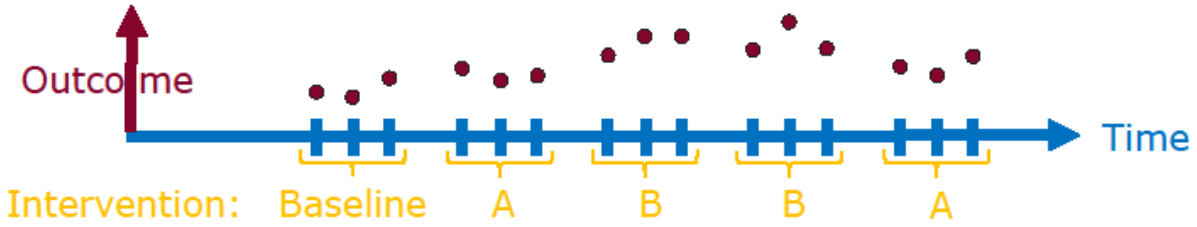
Adaptive personalized trials integrating EHR data

What is our motivation?

What can you do if you want to know which physical exercise (and in which intensity and duration) helps you best to decrease your back pain? Or if you want to know which dose of drug xyz helps you best to control your high blood pressure, given that your physician is not sure either? You could look at medical research studies that have investigated this on the population level. But they typically do not tell you whether it will work for you, they will tell you at best that a drug works in maybe 60% of the population. You could just try out whether a particular exercise helps you or which dose is best? Sure! And if you want to do this systematically to avoid biases, you can perform an experiment called N-of-1 trial to evaluate it scientifically with valid statistical inference.

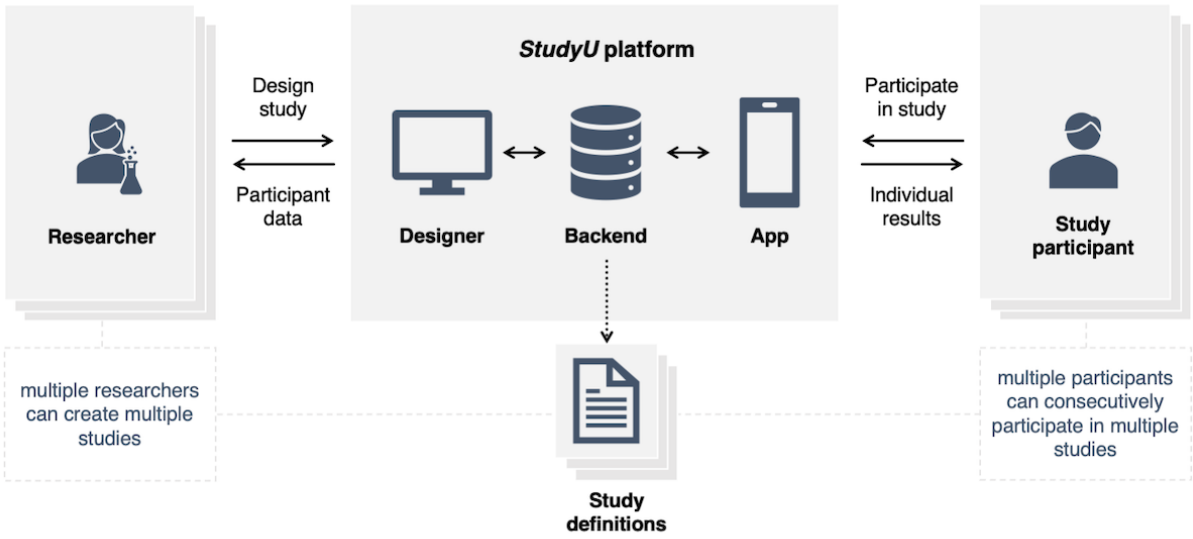
What are (traditional non-adaptive) N-of-1 trials?

More formally, N-of-1 trials are cross-over randomized controlled trials where one or more health interventions are applied sequentially in one person over time. This is illustrated below, where two interventions A and B are administered in blocks, and the outcome is measured at all time points. If multiple people perform such N-of-1 trials, you can make efficient statistical inference what might help others in the population.



What have we already developed?

In recent work, we have developed the StudyU platform (https://www.doi.org/10.2196/35884), which consists of a study designer web app (https://designer.studyu.health/) that allows researchers to design and implement N-of-1 trials, and a study app that allows study participants and patients to take part in these studies (https://app.studyu.health/). StudyU is open source (https://github.com/HIAlab/studyu) and free, the participant app is available in Android and Apple app stores and first clinical studies are running using StudyU. We have the vision to build a free resource that contains a repository of anonymized data of personalized trials and can empower users in their health behavior. StudyU has been developed and extended in three master projects, and students from the last project recently won the Best Idea Award 2022 at the HPI! The current tech stack of StudyU is Flutter/Dart, PostgreSQL/Supabase, Git/Gitlab, Jupyter Notebooks and there is ongoing work on its design. Clinical studies are ongoing or planned with UKE Hamburg, Mount Sinai, Weill Cornell, and University of Queensland that can be leveraged for clinical insights.



Description of the Master project

Currently, you can use StudyU to design and perform N-of-1 trials for patient-reported health outcomes and in ongoing work we are developing multimodal N-of-1 trials. But all these trials are for a pre-defined and fixed treatment sequence where typically two treatments are compared. If, however, multiple treatments should be compared, this is inefficient. Only by allowing an adaptive sequence, really efficient and realistic trials can be defined and give an answer much faster regarding, for example, which physical exercise (and in which intensity and duration) helps you best to decrease your back pain, or which dose of drug xyz helps you best to control your high blood pressure. This is done by finding an optimal treatment sequence and learning the next best treatment to apply based on what has been observed already.

Such adaptive N-of-1 trials have only been proposed recently. They use reinforcement learning approaches such as contextual bandits and are an exciting new area which requires novel frameworks, methodology and implementation. This will be the first working package of the master project. In a second working package, we will then work with our collaboration partners at HPI-MS to set up StudyU at Mount Sinai, set-up a pilot study, and investigate how electronic health record data can be integrated into the trial design.

Working packages of the Master project

This master project will contain 2 main work packages, and combine aspects of machine learning, app development, user-centered design and clinical applications:

(1) Concepts, models and infrastructure for adaptive N-of-1 trials

You will develop and implement methods in StudyU that allow to perform adaptive N-of-1 trials. Adaptive N-of-1 trials aim to find the optimal intervention design (e.g. allocation of treatments within treatment blocks, dosage of treatments, length of treatment blocks) and continuously adapt it during the study. Two statistical models have been recently proposed

for adaptive N-of-1 trials based on Bayesian mixed models (https://doi.org/10.1002/sim.8737, https://doi.org/10.1002/sim.8873). They provide good baseline models but are still limited in their functionality and applicability. For example, it is important for practical applications to incorporate intermediate learnings and constraints from the trial that may arise from the patient or physician's side due to side effects, treatment costs, participant preferences, and more. Another important challenge is to choose the best starting point for the trial, for example based on previously conducted trials or based on an automated suggestion tool from a literature crawl. This requires the developments of concepts, visualization in the StudyU app, and user-centric design.

(2) Implementation and clinical studies at Mount Sinai

In a second working package, you can contribute to setting up the StudyU platform and your newly developed features at Mount Sinai to allow clinical studies with Mount Sinai patients. This involves getting to know regulations that the app and its features have to satisfy, getting to know the infrastructure and any other data security/ethical considerations that are necessary for its deployment at Mount Sinai. In addition, you can contribute to the planning of a clinical pilot N-of-1 trial conducted at Mount Sinai with our collaboration partners at HPI-MS. Finally, both for cohort definition but also for warm-starting any adaptive trial algorithm and updating it, you can explore how electronic health records might be used.

What you should bring with you

The project is open to students from IT Systems Engineering, Software Systems Engineering, Digital Health, Data Engineering and Cybersecurity. To carry out this project successfully, you will need expertise in at least one of the following areas to contribute to the team:

1. App development (front end, back end)
2. Programming skills (e.g. mobile app development, web development, Python/R)
3. Interest in learning about study designs and the evaluation of interventions for personalized medicine
4. Machine learning/reinforcement learning or statistics
5. Data visualization

Further references

1. Kravitz RL, Duan N (eds), and the DEcIDE Methods Center N-of-1 Guidance Panel (2014). *Design and implementation of N-of-1 trials: a user's guide*. AHRQ Publication No. 13(14)-EHC122-EF. Rockville, MD: Agency for Healthcare Research and Quality.
2. Nikles J, Mitchell G (eds) (2015). *The essential guide to N-of-1 trials in health*. Dordrecht: Springer.

Contact

Get in touch for questions and ideas. Our offices are on the 1st floor of the Digital Health Center on Campus III, Building G2, Rudolf-Breitscheid-Str. 187, 14482 Potsdam, and you can always reach us through email and phone. See also our webpage (https://hpi.de/lippert/health-intervention-analytics-group.html) for more information.

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