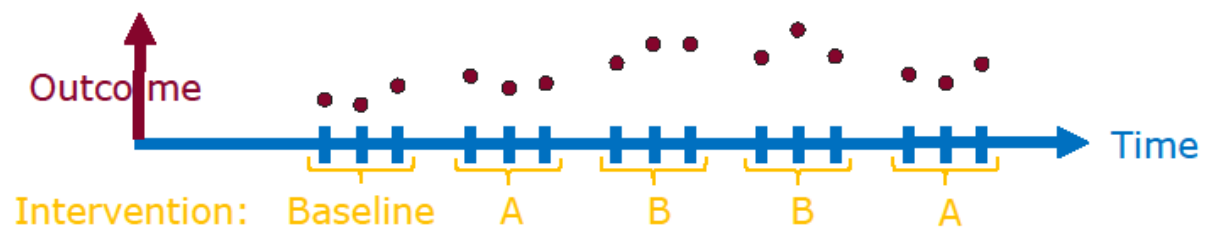


# Adaptive digital N-of-1 trials for personalizing digital health interventions

## Background

Initiated in a Master project two years ago, we have developed StudyU, a platform to evaluate the effectiveness of health interventions on an individual level [1]. For this, so-called N-of-1 trials are implemented [2-3], which are a special form of interventional study with a sample size of 1, where each study participant is exposed to different interventions over time. This is illustrated here, where two interventions A and B are administered in blocks, and the outcome is measured at all times points:



This allows investigating which intervention works better for each single participant of the study and deriving personalized medicine approaches in a clinical context. Also, N-of-1 trials of single participants can be aggregated to obtain population-level intervention estimates.

StudyU contains the StudyU Designer (<https://designer.studyu.health/>) to create the study of interest and the StudyU Health App, which participants or patients can use to take part in the studies (<https://play.google.com/store/apps/details?id=health.studyu.app>, <https://apps.apple.com/us/app/studyu-health/id1571991198>). The first clinical study using StudyU has started recently, investigating the use of open-label placebo in patients with depression. Other studies are planned on mental health, cancer and cardiovascular outcomes. StudyU is open source (<https://github.com/hpi-studyu/studyu>) and free. The current tech stack of StudyU is Flutter/Dart, PostgreSQL/Supabase, Git/Gitlab, Jupyter Notebooks.

## Description 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 implementation for clinical applications:

### (1) Getting StudyU ready for large-scale clinical applications

There are still many aspects of the existing StudyU platform that need to be developed so that it is really ready for large-scale clinical applications. In this work package, we will design and redesign, extend, and implement StudyU. This will contain the following:

- a) StudyU will be used for future studies within Germany and within the Mount Sinai health system in New York. For this, we will host StudyU on VMs at the HPI, and adapt StudyU to the requirements at Mount Sinai. This will be in collaboration with the DDP team at the Hasso Plattner Institute for Digital Health at Mount Sinai (HPI-MS) in New York (<https://www.hpims.org/research-projects/digital-discovery-program>).
- b) Important parts of redesigning and extending StudyU concern the UI/UX, statistical modeling, and visualization.
  - i) First, the current version of StudyU is not easily usable by clinicians and study participants, and requires user-centric developments. For these, we will perform user tests with physicians and potential study participants and redesign the apps.
  - ii) Second, we will implement state-of-the-art statistical and machine learning models for the analysis of the trials performed in StudyU. In the StudyU Health App, the trials of the participants are directly analyzed locally on the phone and the results are fed back to the participant. In addition, the anonymized aggregated data of all participants can be analyzed by the researchers on the StudyU designer dashboard. Currently, only simple linear regression models are available. For both analyses, we will implement Bayesian mixed models, and potentially add novel causal inference models. Potential challenges are an efficient implementation of the models so that they can run fast on participants' phones, and the implementation of a model that automatically adapts to the data of the trial and is robust against missing values or model misspecification.
  - iii) Third, what is a good visualization and communication of the results to the study participants? We will investigate different visualizations of the results and implement them.
- c) This redesign and extension of StudyU will be done with 2 concrete clinical studies in mind: investigating the effect of (i) forest therapy on cardiovascular outcomes and of (ii) fasting on side effects of drugs preventing breast cancer relapse.

## **(2) Developing and implementing adaptive digital N-of-1 trials**

In the second work package, we will develop and implement novel methods that allow to perform adaptive N-of-1 trials using StudyU. 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 [4,5]. 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. We will investigate and pursue these questions in the project, in collaboration with Prof. Girish Nadkarni from Mount Sinai. In follow-up projects, we are planning to use the results of this work package for clinical adaptive trials.

## What you should bring with you

The project is open to students from IT 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. Fundamentals of machine learning or statistics
5. Data visualization

## References

1. Konigorski S, Wernicke S, Slosarek T, Zenner AM, Strelow N, Ruether FD, Henschel F, Manaswini M, Pottbäcker F, Edelman JA, Owoyele B, Danieleto M, Golden E, Zweig M, Nadkarni G, Böttinger E (2020). StudyU: a platform for designing and conducting innovative digital N-of-1 trials. arXiv:2012.14201. <https://arxiv.org/abs/2012.14201>.
2. Kravitz RL, Duan N (eds), and the DEClIDE 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.
3. Nikles J, Mitchell G (eds) (2015). *The essential guide to N-of-1 trials in health*. Dordrecht: Springer.
4. Senarathne SGJ, Overstall AM, McGree JM (2020). Bayesian adaptive N-of-1 trials for estimating population and individual treatment effects. *Statistics in Medicine* 39(29): 4499-4518. <https://doi.org/10.1002/sim.8737>.
5. Shrestha S, Jain S (2021). A Bayesian-bandit adaptive design for N-of-1 clinical trials. *Statistics in Medicine* 40(7): 1825-1844. <https://doi.org/10.1002/sim.8873>.

## Contact

Get in touch for questions and ideas. Our offices are on the 1<sup>st</sup> 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.



Dr. Stefan Konigorski  
[Stefan.Konigorski@hpi.de](mailto:Stefan.Konigorski@hpi.de)  
0331-55094873



Juliana Schneider, M.Sc.  
[Juliana.Schneider@hpi.de](mailto:Juliana.Schneider@hpi.de)



Thomas Gärtner, M.Sc.  
[Thomas.Gaertner@hpi.de](mailto:Thomas.Gaertner@hpi.de)



Babajide Owoyele, M.Sc.  
[Babajide.Owoyele@hpi.de](mailto:Babajide.Owoyele@hpi.de)



Prof. Girish Nadkarni, MD  
[girish.nadkarni@mountsinai.org](mailto:girish.nadkarni@mountsinai.org)



Prof. Christoph Lippert  
[Christoph.Lippert@hpi.de](mailto:Christoph.Lippert@hpi.de)