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mHealth systems to advance how we understand and approach mental illness

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ABSTRACT

Fostering population mental health effectively remains a greatest ongoing challenge. A large majority of individuals with common mental disorders never seek professional treatment. Furthermore sustaining engagement with effective interventions has proven challenging with low adherence rates. One potential reason for this is that cognitive and behavioural interventions, despite being effective, require a great deal of energy and focused attention, which is made more difficult by the effect of mood disorders on individuals’ motivation and cognitive capacities. Equally at the severe end effective clinical management of individuals with severe mental illnesses outside hospitals remains challenging due to ineffective monitoring systems and fragmented care providers. This talk will present digital resources devised in Australia to overcome many of the barriers experienced by psychiatry and mental health care sector. It covers mhealth approaches to improve access, screen for symptoms early, monitor in real time, and integrate treatments into the fabric of daily lives of patient’s in a personalised manner. Equally, for more severe mental illness, opportunities afforded by administrative claims data sets to monitor risks of hospitalisation and relapse in real time are outlined.
Mobile AI for personalised healthcare

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ABSTRACT

In this talk, I will first discuss our translational research on mobile healthcare using AI, computer vision and smartphones. Then, I will discuss some of our fundamental AI research that is important for mobile healthcare, including deep model compression, generative adversarial networks and few shot learning. I will give an overview of these techniques, highlight their relevance for mobile healthcare, describe the technical challenges and discuss our work to advance state-of-the-art.
ROADMAP for precision and digital health

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ABSTRACT

Precision medicine at its core seeks to provide methodologic solutions to the challenge of patient heterogeneity and heterogeneous response to therapy. In developing mobile health applications, for example, how a user interacts with smartphone apps depends on the system recommendations (actions) in a dynamic way. While a SMART (Sequential Multiple Assignment Randomized Trial) allows for unbiased evaluation of the optimal action at each decision point, its use in practice could be limited due to the lack of guidance on how such a trial should be designed and implemented. At the same time, the notions of “N-of-1” and master protocols are very appealing to clinical researchers in precision trials. In this talk, I will compare and contrast the design issues in these two areas. I will also highlight some recent findings on SMART with regard to sample size and adaptation, and activities at the Columbia’s ROADMAP initiative for digital health.

References


Personalized data science, small data, and N-of-1 trials

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ABSTRACT

Data science has emerged in recent decades as an influential discipline to extract knowledge from data, usually applying machine learning technologies to cross-sectional big data obtained from a large number of individuals, such as electronic health records from large clinical organizations. At the same time, personalized data science (PDS) has the potential to expand existing framework for data science in several important directions, for the development and implementation of personalized healthcare. PDS provides tools to facilitate the acquisition and interpretation of individual data (small data) from individual patients acting as citizen scientists, to inform each individual’s unique healthcare decisions, both medical and lifestyle, through self-studies such as self-experimentation.

Self-experimentation made important contributions to medicine throughout history, tracing back thousands of years ago to the legendary Emperor ShenNong, who sampled hundreds of herbs to ascertain their therapeutic efficacy, laying the foundation for Chinese Medicine. In recent centuries, self-experimentation by clinical investigators has led to numerous important discoveries, including no less than eight that were awarded the Nobel Prize in Physiology or Medicine, such as the discovery of the bacterium H. pylori as a common cause for gastritis and peptic ulcer by Dr. Barry Marshall.

At the same time, self-studies such as self-experimentation by individual patients acting as citizen scientists, such as the tens of thousands of participants in citizen scientist communities such as QuantifiedSelf.com, have the potential to inform their healthcare decisions and improve their health and well-being. However, citizen scientists usually lack practical rigorous tools to conduct scientifically valid self-studies. With the advance in information and communication technologies, especially mobile technologies, PDS has the potential to fulfill this important demand, to assist citizen scientists to design their self-studies, acquired their data, and analyze/interpret their data, to inform their medical or lifestyle decisions.
An intriguing aspect of ShenNong’s legend is that he (as a divine being) had a transparent body, and thus could see the effects of different plants and herbs on himself. For mortals, modern technologies in effect begin to render our bodies transparent, approaching ShenNong’s divine power. As an example, an autotitration CPAP device is capable to sense, monitor, record, and transmit the sleep conditions for a patient with sleep apnea throughout a night of sleep, and also makes dynamic adjustments to device settings in real time to improve the patient’s sleep condition.

As an illustration of the utility of PDS in personalized healthcare, I will discuss the Personalized Research for Monitoring Pain Treatment (PREEMPT) study, led by Dr. Richard Kravitz, which studied the deployment of personalized (N-of-1) trials to inform therapeutic decisions for patients with chronic musculoskeletal pain. The study developed an mHealth app, Trialist, for patients and their clinicians to design and implement their individual personalized trials, to obtain outcome data, to analyze the data, and to produce reports to inform their therapeutic decisions. The Trialist app allows highly personalized trial design features including the therapeutic options to be compared, the number of crossovers and the duration of each therapeutic episode, etc. The study recruited 215 patients and randomized 108 to the Trialist/personalized trial condition, and 107 to the control (standard care) condition. The primary findings from the study are available in Kravitz et al. (2018 JAMA Intern Med).
Personalized lifestyle interventions – opportunities and challenges

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ABSTRACT

Promotion of healthy lifestyles, including physical activity, healthy eating, weight management and abstaining from tobacco use, is key to public health efforts for prevention of NCD. Effective NCD prevention thus requires a rigorous understanding of the patterns and determinants of these lifestyle risk factors in the general population and in patients affected by NCD. Knowledge of distribution and longitudinal trends for risk factors in the population, enables identification of the socio-demographic subgroups, and stages of life (e.g. related to ageing or changes in work status, marital status, or having children) that can be prioritized for preventive interventions. Further personalizing interventions to the individual, based on their specific behavioral risk factors, as well as their cultural, social, psychological, economic and environmental characteristics, is anticipated to enhance long-term behavior change and chronic disease management. The use of evolving technologies and digital health approaches is particularly suitable to overcome limitations of existing approaches and more deeply and continuously characterize individual’s health behaviors and contextual factors. Leveraging on these technologies the Ecological Momentary Assessment (EMA) approach can be applied for collection of comprehensive data to advance the current practice of epidemiological and clinical research and to facilitate the development of personalized lifestyle interventions. This presentation provides background for the rationale of personalized lifestyle interventions with a specific focus on physical activity and the application of EMA. It will use examples from research projects conducted in Singapore that are concerned with the development and integration of smartphones, apps, wearables and other technologies and it will illustrate practical and technological challenges in this process.
Dynamic generalized odds-ratio (dGOR): a novel approach to assess dynamic treatment regimes (DTR) with an ordinal outcome

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ABSTRACT

Sequential multiple assignment randomized trials (SMART) are used to construct data-driven optimal treatment strategies for patients based on their treatment and covariate histories in different branches of medical and behavioral sciences where a sequence of treatments are given to the patients; such sequential treatment strategies are often called dynamic treatment regimes (DTR). In the existing literature, the majority of the analysis methodologies for SMART studies assume a continuous primary outcome. However, ordinal outcomes are also quite common in clinical practice; for example, the quality of life is often measured in an ordinal scale (e.g., poor, moderate, good). In this work, first, we develop the notion of dynamic generalized odds-ratio (dGOR) to compare two dynamic treatment regimes embedded in a 2-stage SMART with an ordinal outcome. We propose a likelihood-based approach to estimate dGOR from SMART data. Next, we discuss some combinatorial properties of dGOR and derive the asymptotic properties of its estimate. We discuss some alternative ways to estimate dGOR using concordant-discordant pairs and two-sample U-statistic. Then, we extend the proposed methodology to a K-stage SMART. Furthermore, we propose a basic policy search algorithm that uses dGOR to find an optimal DTR within a finite class. A simulation study shows the performance of the estimated dGOR in terms of the estimated power corresponding to the derived sample size. We analyze data from Sequenced Treatment Alternatives to Relieve Depression (STAR*D), a multi-stage randomized clinical trial for treating major depression, to illustrate the proposed methodology. A freely available online tool using R statistical software is provided to make the proposed methodology accessible to other researchers and practitioners.
Some aspects of SMART design: methodological developments and an application in mHealth intervention

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ABSTRACT

This is really a two part talk. In the First part, we will discuss some cutting edge statistical methodology development for testing non-inferiority (NI) in the SMART setup. NI trials are becoming popular as comparative effectiveness research are becoming mainstream and fewer and fewer block-buster discoveries are made for many legacy disease areas. However, unlike traditional SMART the trial also involves a putative placebo or standard of care arm. In standard Randomized Controlled Trial (RCT) context this gives rise to three-arm NI trial consisting of Reference, Experimental and Placebo arm. However, the situation is slightly more complicated in the SMART-NI context when a third placebo arm is present as defining NI margin is not so straightforward. NI trial has other challenges such as assay sensitivity and constancy which is unique to NI-RCT (as well as for NI-SMART). In this talk we will introduce a “fraction of effect retention” based approach for designing three-arm NI-SMART. A detailed sample size and power analysis plan will be also discussed. We will show a NIH supported current ongoing trial for improvement of symptom management among cancer patients where such design could be useful.

In the Second part of the talk we will discuss a real world application of SMART design for Evaluating Implementation of Text Messaging, Cell Phone Support, and Contingency Management in Youth Non-adherent to Antiretroviral Medication. This is a current ongoing NIH funded trial where mobile device based interventions are used for increasing adherence to Antiretroviral Treatment among HIV infected youths. We will discuss the current state of the research and some of the practical challenges we have faced in implementing mHealth intervention in practice.
Hybrid statistical and mechanistic mathematical model guides mobile health intervention for chronic pain

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ABSTRACT

Nearly a quarter of visits to the emergency department are for conditions that could have been managed via outpatient treatment; improvements that allow patients to quickly recognize and receive appropriate treatment are crucial. The growing popularity of mobile technology creates new opportunities for real-time adaptive medical intervention, and the simultaneous growth of “big data” sources allows for preparation of personalized recommendations. Here we focus on the reduction of chronic suffering in the sickle cell disease (SCD) community. SCD is a chronic blood disorder in which pain is the most frequent complication. There currently is no standard algorithm or analytical method for real-time adaptive treatment recommendations for pain. Furthermore, current state-of-the-art methods have difficulty in handling continuous-time decision optimization using big data. Facing these challenges, in this study, we aim to develop new mathematical tools for incorporating mobile technology into personalized treatment plans for pain. We present a new hybrid model for the dynamics of subjective pain that consists of a dynamical systems approach using differential equations to predict future pain levels, as well as a statistical approach tying system parameters to patient data (both personal characteristics and medication response history). Pilot testing of our approach suggests that it has significant potential to well predict pain dynamics, given patients reported pain levels and medication usages. With more abundant data, our hybrid approach should allow physicians to make personalized, data-driven recommendations for treating chronic pain.
Emerging mHealth biomarkers to enable spatio-temporal precision medicine

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ABSTRACT

Wearable sensing and mobile computing are opening up unprecedented opportunities to quantify dynamic changes in an individual’s health state as well as key physical, biological, behavioral, social, and environmental factors that contribute to health and disease risk, anytime and anywhere. For example, smart watches can not only track physical activity, but they can also be used to monitor stress (from pulse rate), eating, brushing, driving, and smoking behaviors (from hand gestures). By simultaneous monitoring of changes in health status, exposures to surrounding geographical, environmental, visual, social, and digital worlds, and personal behaviors (both risky and healthy), mobile health (mHealth) can help discover new predictors of health outcomes.

By monitoring the exposure to these health risk predictors, mobile health offers an opportunity to introduce spatio-temporal precision in precision medicine, especially when mHealth data is used together with traditional sources of biomedical data (e.g., genomics, clinical). Longitudinal nature of mHealth data and the fact that it comes from the natural free-living environment allows dynamic decision making such as adapting the treatments and interventions so as to maximize the efficacy and optimize the timing of delivery. Continuous monitoring of the context surrounding the individual and monitoring of the compliance and response to treatments and interventions offers additional opportunities for dynamic optimizations.

This talk will describe the process of developing algorithms for obtaining new mHealth biomarkers and discuss design considerations when these algorithm-based biomarkers are used in designing and delivering sensor-triggered just-in-time mHealth interventions.
Interpreting step count activity patterns in an incentivized city-wide health intervention

Brian Y. Lim

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ABSTRACT

Activity trackers are being deployed in large-scale physical activity intervention programs, but analyzing them is difficult due to the large data size and complexity. As large datasets of steps become more available, it is paramount to develop analysis methods to more deeply interpret them to understand the variety and changing nature of human steps behavior. In this work, we explored ways to analyze the heterogeneous steps activity data and propose a framework of dimensions and time aggregations to interpret how activity trackers with monetary incentives influence the steps behavior of a city-wide population. We analyzed the daily step counts of 140,000 individuals walking a combined 74 billion steps in 305 days during a city-wide public health campaign. We performed data mining clustering to segment users into 16 types of users with various types of walking behaviors and demonstrate that these clusters help with interpreting how some user increased their steps level. Our findings inform how to scalably interpret large steps data to draw behavioral insights from intervention studies.
App and system for diet and lifestyle tracking for chronic diseases management and research

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ABSTRACT

The prevalence of chronic diseases such as hyperglycemia, hypertension, and hyperlipidemia (3H) becomes a major concern for public health in many countries, including Singapore and China. 3H are strongly lifestyle-related and are preventable health problems that can silently become costly diseases such as stroke, heart disease, and kidney disease. Research has shown that self-management support intervention most frequently resulted in significant improvements in patient-level outcomes; nutritional practices alone can reduce the risk of cardiovascular disease by 60%. Unfortunately, efforts to promote sustained healthy eating habits and exercise have been mostly unsuccessful, largely due to the lack of accurate and reliable ways to log an individual’s real time food intake, and other lifestyle data. We aim to tackle the problem of 3H in the population by leveraging state-of-the-art AI technologies to empower patient self-management and to support primary care practitioners using mobile apps and systems. To facilitate the tasks of lifestyle data gathering, analytics, action planning and sharing: the four key AI research technologies underpinning the whole research include: advanced AI lifestyle analytics; private and explainable machine learning; personalized nudging and influence; and incentives for data sharing and analytics.

The personal assistant App together with the backend distributed system will integrate the AI-based technologies and link up AI researchers, experienced primary care, clinical and nutritional researchers, first-line practitioners and systems architects. The infrastructure has the potential to be used to conduct various lifestyle and 3H related large-scale feasibility studies and randomized controlled trials.
Estimating time-varying causal effect moderation in mobile health with binary outcomes

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ABSTRACT

Binary outcome is common in mobile health studies. We focus on estimating the time-varying causal effect moderation for data from micro-randomized trials with binary outcomes. We give the definition of moderated treatment effect in this setting, and provide two estimation methods. One estimation method is for the proximal treatment effect conditional on the entire history; this estimator is semiparametric locally efficient. The other estimation method, based on a weighted and centered least squares approach, is for the proximal treatment effect marginal but conditional only on a subset of variables in history. Both estimators are robust in the sense that they do not require a correct control model. The methods are illustrated by simulation studies and a real data example.
Stratified micro-randomized trials with applications in mobile health

Susan Murphy

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ABSTRACT

Technological advancements in the field of mobile devices and wearable sensors make it possible to deliver treatments anytime and anywhere to users like you and me. Increasingly the delivery of these treatments is triggered by detections of vulnerability. Two challenges are that vulnerability may be impacted by prior treatment and treatment provided at time $t$ is expected to have an impact on users over a span of time during which subsequent treatments may be provided. Here we discuss our work on the design of a mobile health smoking cessation study in which the above two challenges arose. Multiple online data analysis algorithms are used for detection, for example, of physiological stress as well as forecasting the remaining number of vulnerable times in the day. These algorithms are then inputs into a randomization algorithm that ensures that each user is randomized to each treatment an appropriate number of times per day. The stratified micro-randomized trial involves not only considerations of the randomization algorithm but a precise statement of the meaning of the causal treatment effects along with primary analyses and sample size calculations.
Developing mHealth interventions to improve mood, activity, and sleep for medical interns

TIMOTHY NECAMP

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ABSTRACT

During their internship year, medical interns tend to work long hours, face difficult decisions, undergo stress, and have inconsistent sleep. They are also known to have increased rates of depression. The Intern Health Study (IHS) seeks to improve the interns’ mood, activity, sleep, and depression levels through a mobile health intervention. The intervention sends daily messages targeting one of three categories: mood, activity, or sleep. The messages contain either general advice for improving the specific category or personalized historical data summaries about that category. To evaluate, personalize, and optimize these interventions, we designed and implemented a micro-randomized trial, where interns are randomized every day to receive a particular intervention. In this talk, we give an overview of our trial, analyses of our trial data, analysis issues, and present major findings.
Perpetually enhancing technology for human learning and behavior change, through dynamic, personalized, collaborative experimentation

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ABSTRACT

There is a proliferation of websites and mobile apps for helping people learn new concepts (e.g. online courses), and learn how to change health habits and behavior (e.g. websites for reducing depression, apps for quitting smoking). How can we use data from real-world users to rapidly enhance and personalize these technologies? I show how we can build self-improving systems through three applications of MOOClets/AdapComps, a conceptual framework implemented in technology that leverages randomized A/B experiments as tools for collaboration, dynamic enhancement, and adaptive personalization.

First, a novel system that enhanced learning from K12 math problems, by crowdsourcing explanations and using machine learning to automatically experiment to discover the best explanations. Second, a system which enabled three on-campus instructors at Harvard to experimentally investigate which hints and feedback messages students found helpful, enabling more ethical experimentation by dynamically presenting the best conditions to future students. Third, I show how to boost responses to an email campaign in a MOOC, by experimentally discovering how to personalize motivational messages to a user’s activity level.

These self-improving systems use experiments as a bridge between designers, social-behavioral scientists and researchers in statistical machine learning. I’ll present future directions, such as investigating which reflection prompts help students learn, how to enhance motivation through social-psychological interventions, and how to personalize web-apps that help students set and achieve micro-goals. I will also discuss efforts to bridge education with health behavior change and marketing.
A digital community-based syndromic surveillance system for influenza and other acute respiratory infections in Singapore

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ABSTRACT

In Singapore, influenza affects nearly 20-25% of the population. About 1500 people are hospitalized and 588 die each year due to influenza. The World Health Organization (WHO) recommends a comprehensive suite of data streams for influenza surveillance ranging from a broad based community syndromic surveillance, through to district clinics and national hospitals. Traditional surveillance methods usually rely on the symptomatic person visiting a healthcare facility and such systems can be made less efficient by poor health-seeking behaviour and delays in disease notifications. As smart-phone technology gets more pervasive, it allows us an opportunity to address the base of the pyramid of disease surveillance data gathering by making community syndromic surveillance viable through a digital system. Given that Singapore is one of the more digitally connected and mobile-savvy countries in the world, a digital, community-based syndromic surveillance system for influenza can arguably complement the existing national surveillance system, making it more comprehensive and far-reaching into the population. In this presentation, we will showcase mobile applications we have developed, pilot tested and evaluated among working adults in an attempt to build a digital, community-based syndromic surveillance system in Singapore.
A gate-keeping approach to selecting adaptive interventions under general SMART designs

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ABSTRACT

Background: An objective of a sequential multiple assignment randomized trial (SMART) is to identify an optimal adaptive intervention that maximizes the expected value of certain outcomes. While this task can be performed by comparing all possible pairs of interventions with appropriate multiplicity adjustments such as the Bonferroni’s correction, the pairwise comparison approach generally suffers substantial loss in power because a SMART typically consists of many adaptive interventions. In addition, there is relatively little discussion on sample size calculation for SMARTs under general settings.

Purpose: To propose an omnibus likelihood ratio test as a gate-keeping test for selecting an optimal adaptive intervention, and to develop a sample size calculation procedure for the test.

Method: We derive the asymptotic distribution of the proposed likelihood ratio test, outline the steps to perform sample size calculation based on the asymptotic results, and evaluate the test’s finite sample performance using simulation. The method is illustrated in the context of the CODIACS trial.

Results: The simulation shows that asymptotic approximation performs well for a moderate sample size, and the test achieves the nominal significance level. In addition, the proposed omnibus test has better power than a pairwise comparison approach with Bonferroni’s adjustment, with an improvement up to 29 percentage points in our simulation scenarios. When compared to an existing omnibus test based on inverse probability weighting estimation, the proposed test reduces the required sample size by up to 17%.

Limitations: The required sample size by the proposed test increases considerably with the number of stages in a SMART. Large sample size requirement is an inherent difficulty with SMARTs as a result of curse of dimensionality.

Conclusion: The proposed omnibus test is applicable to perform intervention selection under general SMART design settings. The sample size calculation procedure provides a rigorous justification on how large a SMART should be.