

# **Personalized Data Science, Self-Experiments, and Personalized (N-of-1) Trials**

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# Outline

- Data science, self-studies, and personalized data science (PDS)
- Self-experimentation: history and future
- Personalized (N-of-1) trials for personalized decision-making
- PREEMPT Study for personalized (N-of-1) trials
- Small data and PDS
- Personalized healthcare and PDS
- Discussions

# Data Science in 20<sup>th</sup> Century

- Statistics = Data Science?
  - CFJ Wu (1997, 1998)
- Trilogy for Statistics/Data Science:
  - 1. Data Collection (experimental design, sample survey)
  - 2. Data Modeling and Analysis
  - 3. Problem Understanding/Solving, Decision Making

# Data Science in 21<sup>st</sup> Century

- Sexiest Job of the 21<sup>st</sup> Century
  - Davenport and Patil (2012 HBR)
- Data science is the study of extracting value from data.
  - <https://datascience.columbia.edu/what-is-data-science>, Jeannette Wing, Columbia University
- Often interpreted as application of data mining to big data
- Usually follows a top-down model for the knowledge enterprise

# Need for a Grassroot Model

- Demand from patients (citizen scientist) to take a more active role in knowledge enterprise
- Information and communication technologies empower citizen scientists to access clinical knowledge, and conduct self-studies to inform their own personalized health care decisions
- Knowledge produced and consumed at grassroot level, e.g...

# QuantifiedSelf.com

- A community of persons who share an interest in gaining self knowledge through self-tracking and self-experimentation, started in 2008
- 124 groups around the world
  - 4,422 in SF bay area
  - Singapore: 457 members, organizer Yau Teng Y.
    - It's a show and tell for people who are tracking data about their body and conducting their own personal investigations and research into their bodies, minds, and selves. Anything is game -- from personal genetics to ways to digitize and track information, from self-diagnosis to self-experimentation with data and statistics.

# QuantifiedSelf Conferences

- QS18, Portland, Oregon, 09/22-23/2018
- A Decade of Tracking Headaches
  - Stephen Maher started with paper and pen, and eventually developed his own app to help him learn about his headache patterns and manage his actions, medications, and expectations.
- Designing Platforms for N-of-1 Experiments
  - Mark Drangsholt, Ravi Karkar, U of Washington



# Why Bother with Self-Studies?

- Often, one size does not fit all
- Heterogeneity of treatment effects (HTE)
  - Methodological challenges in assessing HTE
  - Kravitz, Duan, Brasow (2004, Milbank Q)
- Existing studies might not apply very well to me
- Self-studies might supplement existing clinical knowledge

# Naihua's Self-Studies: APAP for Sleep Apnea



# Sleep Apnea and APAP Devices

- Sleep apnea: snoring, closure of airway, arousal
- Auto-titration continuous positive airway pressure (APAP)
- Super-smart DTR
  - Senses and records breathing status per 10 seconds
  - Built-in algorithm to anticipates events: snoring, apnea, and hypopnea, increase air pressure up to suppress event, then lower pressure afterwards (more comfortable sleep)
  - Expiratory Pressure Relief (EPR), auto on/off...
- Built-in mobile SIM to communicate with clinician
- Not comfortable, CQI self-study with new masks, devices; considering shelf life; adjust algorithm?

# Is QS Tip of a Gigantic Iceberg?

- How large is the demand for self-studies?
- Is it 1%, 5%, 10%, 25%, 50%,...?
- Personal anecdotal experience:
  - My own experience with APAP devices
  - My wife, my mother, my mother-in-law...
  - Family friend with colic infant
  - Family friend's use of glucose monitor
- Some promising signs? Kravitz et al. (2009)

# Needed: Data Science Support for Citizen Scientists

- To support citizen scientists interested in self-studies/self-experiments
- To help “pull” citizen scientists to accomplish their goals
- Hopefully leading to improved health outcomes and QOL
- Also to avoid or reduce unintended harm

# Personalized Data Science

- To support citizen scientists at the grassroots level, to help them conduct their personal investigations
- Need to emphasize data collection, design, implementation, not just analytics
- Need to *personalize* data science, to accommodate individual needs, preferences, capacity, etc.

# Self-Experimentation

- Long tradition among investigators, from Emperor ShenNong to Barry Marshall and more
- Extension to citizen scientists?

# Legendary Investigator ShenNong's Self-Experiments

- Divine Farmer, approx. 2,700 BC
- Tasted hundreds of herbs to study their therapeutic effects
- Had a transparent body, allowing him to see effects of herbs being studied
- Died of herb poisoning



# Modern Era Investigators’ Self-Experiments

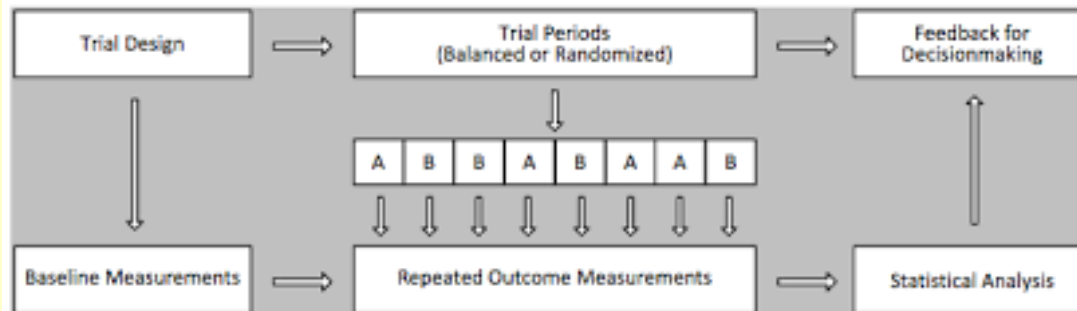
- 465 documented cases since 1800’s, leading to 8 deaths, none after 1928
- 7 Nobel Prizes in Physiology or Medicine
  - Barry Marshall, H. pylori
- Bulk email survey of 1072 prominent scientists
  - Among 52 respondents, 26 have conducted self-experiments (2.4% of total candidates)
- Hanley et al. (2018)

# Citizen Scientists' Self-Experiments

- Can some good outcome be accomplished?
- Need support to “pull” from an idea or an ad hoc experiment to a more informative rigorous scientific experiment
- Need to partner with supportive clinical provider for clinical guidance?
- Need PDS support in order to carry out a rigorous scientific experiment, and to avoid unintended harm

# Personalized (N-of-1) Trial Is a Promising PDS Application

- Within patient multiple cross-over trials
  - Experimental units: time intervals (e.g., weeks) within an individual patient
- Systematic, balanced assignment of time intervals to alternate treatment options, say, ABBABAAB....
  - Randomized or counter-balanced
- Systematic, repeated outcome assessments
  - At least once per time period, ideally more
- Compare outcomes across treatment options
- Select treatment option with preferred performance



# Indications for Personalized (N-of-1) Trial

- Stable chronic condition
- Short-acting treatments with rapid ramp-up and fast washout
- Heterogeneity of treatment effects (HTE)
- Measurable outcome

# Potential for Personalized (N-of-1) Trial

- Inform treatment decision for current patient
  - PDS application that serves the need of current patient
  - Estimates each patient's own treatment effect (ITE)
  - A most direct way to assess HTE
  - Borrow from strength to improve estimated ITE
  - Generalizable knowledge may result as a by-product
- Consistent with routine clinical practice and consumer behavior, so might have broad appeal to end users

# CONSORT Extension for Personalized (N-of-1) Trials

- Vohra S, Shamseer L, Sampson M, Bukutu C, Schmid CH, Tate R, Nikles J, Zucker DR, Kravitz R, Guyatt G, Altman DG, Moher D; CENT group. CONSORT extension for reporting N-of-1 trials (CENT) 2015 Statement. *BMJ*. 2015 May 14;350:h1738.
- Shamseer L, Sampson M, Bukutu C, Schmid CH, Nikles J, Tate R, Johnston BC, Zucker D, Shadish WR, Kravitz R, Guyatt G, Altman DG, Moher D, Vohra S; CENT group. CONSORT extension for reporting N-of-1 trials (CENT) 2015: Explanation and elaboration. *BMJ*. 2015 May 14;350:h1793.

# Challenges for Personalized (N-of-1) Trials

- Despite what appears to be a promising potential for personalized (N-of-1) trials to be utilized as a decision tool in clinical practice, numerous challenges exist
- Financing...
- Infrastructure support is needed to make applications practical
- Advances in informatic technologies, especially mobile technologies, facilitate the infrastructure support needs

# Example: PREEMPT Study

- Personalized Research for Monitoring Pain Treatment (PREEMPT)
- PI: Kravitz, UC Davis; Funding: NINR
- Personalized (N-of-1) trials using mHealth in Chronic Pain
- Infrastructure development (IT, Biostatistics)
- RCT to compare patients randomized to personalized (N-of-1) trial vs. usual care



# Personalized Design for

## Personalized (N-of-1) Trials

- Personalized selection of:
  - Treatment regimens to be compared
  - Length of episode (week or two weeks)
  - Number of Dyads (2, 3, or 4)
- Possible to personalize:
  - What to report (posterior PR, CI...)
  - Frequency/timing of assessments, reminders...
- Analogous to personalized treatment in personalized health care of personalized medicine

# Technology Supports

## Personalized (N-of-1) Trials

- “Trialist” app developed during Phase I
- Used to design trial during ‘Treatment Planning Visit’
- Conducts randomization, notifies patient of treatment to be taken, sends daily reminders for assessment data collection, provides motivational messages, present graphic summary of patient’s own data upon request, analyzed trial data and produces report, etc.

# PREEMPT Study

## Implementation and Results

- Assessed 1,092 patients for eligibility
- 460 found to be eligible
- 215 (60%) agreed to participate and be randomized to personalized (N-of-1) trial vs. standard care
- Primary outcome (6 month pain interference) fails 5% significance, CI (-2.91 to 0.19)

# PREEMPT Resources

- <https://health.ucdavis.edu/chpr/preempt/>
- Barr et al. (2015, Trials) study design
- Kravitz et al. (2018 JAMA IM) findings

# What Is Small Data?

- Small Data is the myriad of data traces we each generate everyday. Unfortunately, that data is often unavailable to us in a form that we can make sense of or act upon. Imagine a special kind of app running in the cloud that privately and securely turns your small data into big insights. (Deborah Estrin, Small Data Lab, Cornell Tech)
- Primary goal is to empower and serve the needs for individual patients/clients

# Small Data Lab at Cornell Tech

- <http://smalldata.io/>
- We're creating the apps and infrastructure to put your small data to good use for you
- Pushcart, PlateClick, Newsfie, Your Activities of Daily Living (YADL), Limbr, etc.
- Publications: <http://smalldata.io/research.html>

# Small Data, or Personalized Data Science

- Primary goal to empower and serve needs of individual patients
- Distinction from “big data” is not the *amount* of data, but rather the *purpose* to which the data are applied
- Connotation of “small data” has been disputed; “personalized data science” may be a better term

# Personalized Healthcare and PDS

- Personalized healthcare, personalized medicine
  - Taylor healthcare decisions to individual needs and heterogeneity of treatment effects (HTE)
  - Precision medicine?
- Personalization of healthcare and medicine calls for tailored data science support
  - Big data analytics are useful
  - PDS can also be useful



# Research, Quality Improvement, and Personalized Data Science

- Research aims to produce generalizable knowledge
- Quality improvement aims to produce local knowledge, to resolve needs for individual patient, specific agency, etc.
- Biostatistics and data science have focused primarily on supporting research endeavors in a top-down manner
- Personalized data science can play an important role in quality improvement endeavors in a grassroots, bottom-up manner

# Broader Implications for PDS

- Potential to pool/meta-analyze personal data to produce generalizable knowledge
- To engage more patients into clinical investigations
- To instill a cultural of empiricism

# Methodological Research Needs for PDS

- Design and causal inference for self-tracking/trigger seeking
- For personalized (N-of-1) trials:
  - Sequential stopping rules
  - Adaptive treatment assignment (multilevel?)
  - Analytic washout vs. physical washout
  - Automated model selection
  - Borrow from strength with similar trials
  - Communication with end users

# Thank You

- Questions, comments, suggestions, please!