Pragmatic clinical trials leveraging a digital research platform and passive data collection: Considerations for design and analysis

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NYU Langone Health

Pragmatic Trials
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Examples
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Summary
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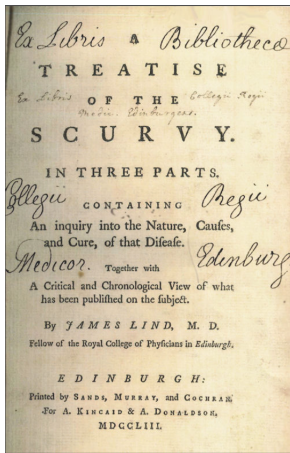## Overview

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Examples
    EMPOWER
    BE-EHR

Summary

Overview

An early pragmatic trial

An early pragmatic trial

The following are the experiments.

On the 20th of *May* 1747, I took twelve patients in the scurvy, on board the *Salisbury* at sea. Their cases were as similar as I could have them. They all in general had putrid gums, the spots and lassitude, with weakness of their knees. They lay together in one place, being a proper apartment for the sick in the fore-hold; and had one diet common to all, *viz.* water-gruel sweetened with sugar in the morning; fresh mutton-broth often times for dinner; at other times puddings, boiled biscuit with sugar, &c.; and for supper, barley and raisins, rice and currants, sago and wine, or the like. Two of these were ordered each a quart of cyder a-day. Two others took twenty-five gutts of *elixir vitriol* three times a-day, upon an empty stomach; using a gargle strongly acidulated with it for their mouths. Two others took two spoonfuls of vinegar three times a-day, upon an empty stomach; having their gruels and their other food well acidulated with it, as also the gargle for their mouth. Two of the worst patients, with the tendons in the ham rigid, (a symptom none of the rest had), were put under a course of sea-water. Of this they drank half a pint every day, and sometimes more or less as it operated, by way of gentle physic. Two others had each two oranges and one lemon given them every day. These they eat with gree-

diness, at different times, upon an empty stomach. They continued but six days under this course, having consumed the quantity that could be spared. The two remaining patients, took the bigness of a nutmeg three times a-day, of an electuary recommended by an hospital-surgeon, made of garlic, mustard-seed, *rad. raphan.* balsam of *Peru*, and gum myrrh; using for common drink, barley-water well acidulated with tamarinds; by a decoction of which, with the addition of *cremor tartar*, they were gently purged three or four times during the course.

The consequence was, that the most sudden and visible good effects were perceived from the use of the oranges and lemons; one of those who had taken them, being at the end of six days fit for duty. The spots were not indeed at that time quite off his body, nor his gums found; but without any other medicine, than a gargarism of *elixir vitriol*, he became quite healthy before we came into *Plymouth*, which was on the 16th of *June*. The other was the best recovered of any in his condition; and being now deemed pretty well, was appointed nurse to the rest of the sick.

Four features of pragmatic clinical trials

- diverse, unselected patient population
    - limited eligibility criteria
    - recruitment from diverse settings
    - low barriers to enrollment
- simple, clinically relevant interventions
    - require no specialized expertise to implement
    - widely scalable
- simple, easily measured outcomes
    - require no specialized processes to obtain
    - come from existing sources
- non-standard randomization structures
    - cluster randomization
    - unbalanced randomization ratios

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Pragmatic trials: A definition

Califf RM and Sugarman J (2015). Exploring the ethical and regulatory issues in pragmatic clinical trials. *Clin Trials* 12: 436-41.

1. An intent to inform decision makers rather than elucidate a mechanism
2. An intent to enroll a population relevant to the decision and representative of the group for whom the decision is relevant
3. An intent to either
   3.1 streamline procedures and data collection to provide adequate power
   3.2 measure a broad range of outcomes

Pragmatic trials and behavioral interventions

- Effect of selection in a trial
  - ▶ trial of drug
  - ▶ trial of behavioral intervention
- Drug trial
  - ▶ biological mechanism of action
  - ▶ unaffected by patient selection?
- Behavioral trial
  - ▶ participant motivation affects enrollment
  - ▶ participant motivation affects response to intervention
- Standard RCTs may provide high confidence answers to the wrong question

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A rapidly changing environment

- Technology
    - ▶ computers are larger, faster, and more efficient than ever
    - ▶ smartphones and tablets are prevalent
    - ▶ proliferation of wearable devices
- Changes in health care delivery

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Health information

- Electronic health records
  - ▶ outpatient
  - ▶ inpatient
  - ▶ specialty services
- Claims information
- Registry information
- Social media

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Scalability

- Scale is impossible without technology
- Technology is useless unless it engages human behavior

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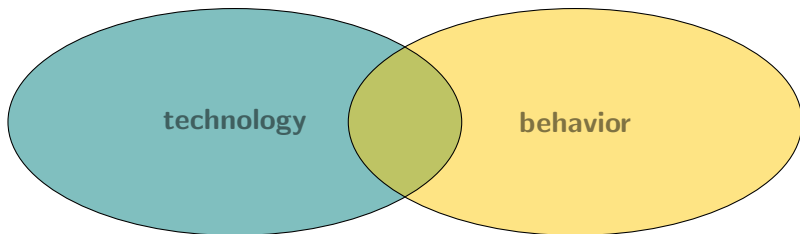
Digital platforms

- Trial implementation
    - ▶ randomization
    - ▶ participant scheduling and tracking
    - ▶ trial activity tracking
        - ▶ safety monitoring
        - ▶ DSMB reporting
- Device linkage
- Participant outreach
    - ▶ ecological momentary assessment
    - ▶ text communication
    - ▶ platform-enabled surveys
- Communication
    - ▶ patient-facing
    - ▶ provider-facing

EHR-based platforms

- Trial implementation
  - ▶ basic randomization
  - ▶ participant scheduling and tracking
  - ▶ safety monitoring
- Device linkage (?)
- Participant outreach
  - ▶ text communication
  - ▶ platform-enabled surveys
- Communication
  - ▶ patient-facing
  - ▶ provider-facing

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EMPOWER

EMPOWER

- Electronic Monitoring of Patients Offers Ways to Enhance Recovery
- Pragmatic RCT in patients with CHF

Mehta SJ, Volpp KG, Asch DA, Goldberg LR, Russell LB, Norton LA, Ianotte LG, Troxel AB. 2019. Rationale and Design of EMPOWER, a Pragmatic Randomized Trial of Automated Hovering in Patients with Congestive Heart Failure. *Circulation: Cardiovascular Quality and Outcomes* 12: 005126.

EMPOWER

- Intervention
  - ▶ lottery for patients to incentivize
    - ▶ daily weigh-ins
    - ▶ daily adherence to diuretics
  - ▶ alerts to providers of substantial weight gain

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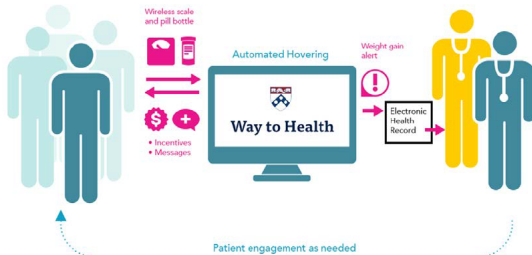
EMPOWER

EMPOWER

- Intervention delivered electronically
  - ▶ daily engagement of patients
  - ▶ extra communication when triggered by automated data
- Embedded within the health system
  - ▶ incorporate into existing clinical workflow
  - ▶ minimize burden on busy clinicians
  - ▶ enhance management within context of care
- Outcomes measured using EHR data
  - ▶ hospitalizations

BE-EHR

- Behavioral Economics in the Electronic Health Record
- Pragmatic RCT in older patients with diabetes

Belli HM, Troxel AB, Blecker S, Testa P, Anderman J, Wong C, Hegde R, Mann M. 2020. Implementation of a Behavioral Economics Electronic Health Record (BE-EHR) Module to Reduce Overtreatment of Diabetes in Older Adults. *Journal of General Internal Medicine*, in press.

BE-EHR

- nudges to providers embedded within the EHR
  - ▶ tailored advisory
  - ▶ refill protocol
  - ▶ lab result
  - ▶ peer comparison emails

BE-EHR

- Intervention delivered electronically
    - engagement with providers at opportune moment
    - communication triggered by automated evaluation of patient status
- Embedded within the health system
    - incorporate into existing clinical workflow
    - minimize burden on busy clinicians
    - enhance management within context of care
- Outcomes measured using EHR data
    - CW compliance based on recent HbA1c

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- Interventions automated and delivered electronically
    - ▶ low to no burden on providers
    - ▶ minimal reliance on research staff
- Embedded within the health system
    - ▶ incorporate into existing clinical workflow
    - ▶ minimize burden on busy clinicians
    - ▶ enhance management within context of care
    - ▶ minimize information processing by providers
- Outcomes measured using EHR data
    - ▶ reduce burden on participants
    - ▶ reduce burden on providers

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    - ▶ Penn *Way to Health* team
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        - ▶ Judd Anderman
        - ▶ Christina Wong

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Questions?