Study Design Challenges/ Lessons Learned

Patrick Heagerty, PhD
University of Washington

NIH PRAGMATIC TRIALS COLLABORATORY
Rethinking Clinical Trials®

Panelists

- Sheana Bull, PhD, MPH
  - Using Artificially Intelligent Text Messaging Technology to Improve American Heart Association's Life's Essential 8 Health Behaviors (Chat 4 Heart Health)
- Stephanie Fitzpatrick, PhD
  - Maternal OutcoMes Program: Testing Integrated Maternal Care Model Approaches to Reduce Disparities in Severe Maternal Morbidity (MOMs Chat & Care Study)
- Chenchen Wang, MD, MSc
  - Remote Tai Chi for Knee Osteoarthritis: an Embedded Pragmatic Trial (TAICHIKNEE)

Session Goals

- Learn about study design issues faced by the NIH Collaboratory Trials
- Share statistical and methodological considerations important for the planning phase and beyond

The Chat for Heart Health Study

- NIH-funded (UG3/UH3), 5-year study involving CU Anschutz Medical Campus, Denver Health, Salud Family Health Centers, and STRIDE Community Health Centers.
- Multilevel intervention using an artificially intelligent ChatBot to deliver text messages and interact with patients to help them improve their control of AHA's Life's Essential 8 (LE8) lifestyle factors: blood glucose, cholesterol, blood pressure, physical activity, weight, diet, sleep, and smoking.
- 3 arms: 1) generic informational texts only, 2) ChatBot, 3) ChatBot plus Pharmacist
- Last year, we developed the message library and piloted the intervention at each site (28-30 patients at each site).

Chat for Heart Health

Key Challenge?

- An FCC Regulatory Change that impacts our ability to use an opt-out enrollment approach

At its last open meeting of 2023, the FCC voted to adopt new rules "to protect consumers from unwanted and illegal text messages and calls." Among the changes are a new "one-to-one" consent requirement for autodialed telemarketing texts and phone calls, clarification on the applicability of the Do-Not-Call Registry to text messages

Patient identification process

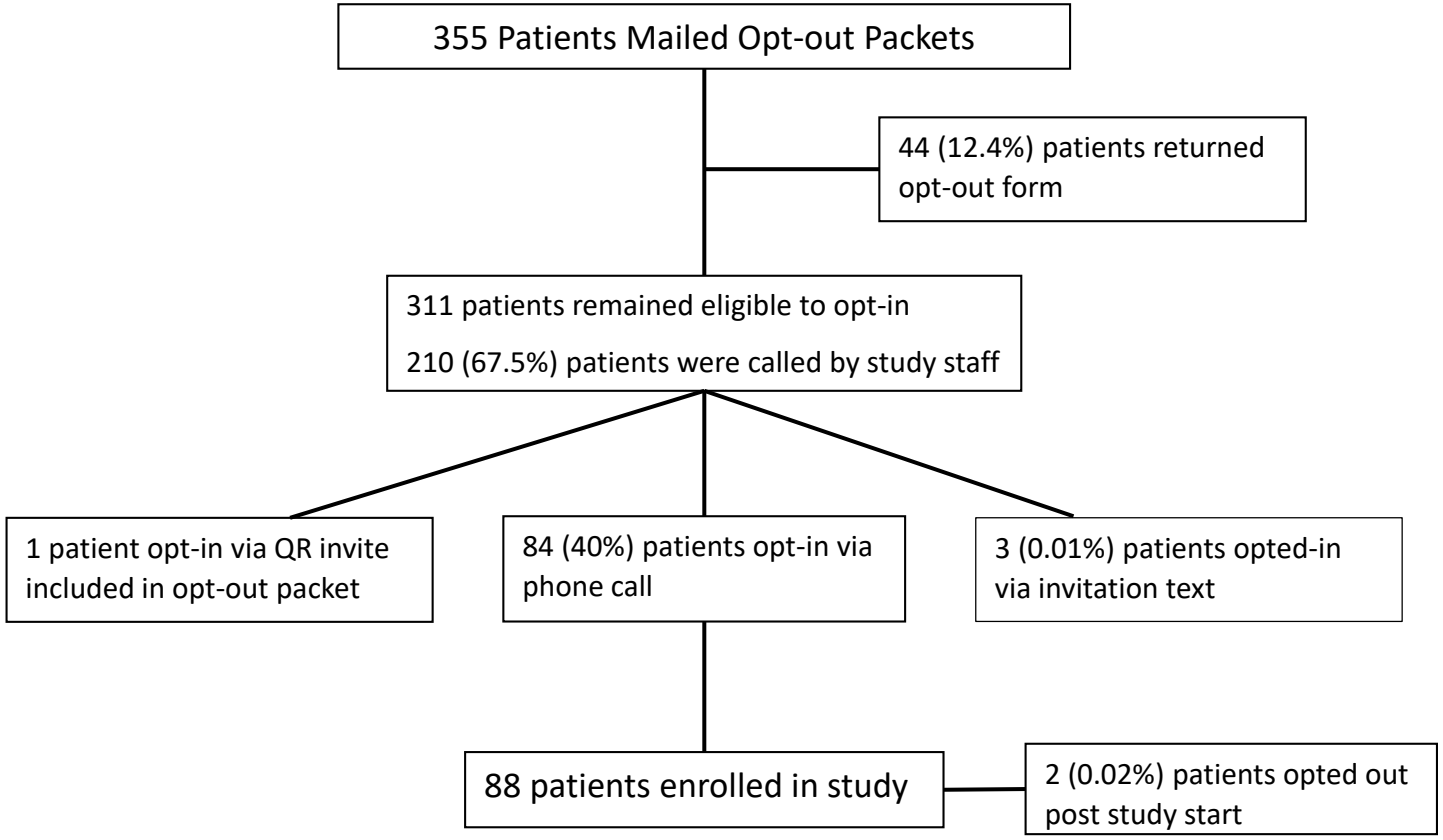
- Patients meeting inclusion criteria be identified through EHR. Staff mail each patient an opt out packet via USPS.
- The packet includes an introductory letter signed by the Site PI, "FAQ" about the study, an opt out form, a self-addressed stamped envelope
    - Patients that return opt out consent forms or have packets returned by USPS will be removed from the study
    - If patients do not return the opt out form within 2 weeks, they are considered enrolled and will be randomized to a study arm
- All enrolled patients have a secondary opportunity to opt out of the intervention by texting STOP after the first text message
- The Nudge study utilized this approach and we have consistently observed opt-out rates at or below 15% across our three health system partners.

Patient identification process

- Patients meeting inclusion criteria be identified through EHR. Staff mail each patient a packet via USPS to opt-out of the study; those not opting out must opt-in to text messages.
- The packet includes an introductory letter signed by the Site PI, "FAQ" about the study, an opt out form, a self-addressed stamped envelope
    - Patients that return opt out consent forms or have packets returned by USPS will be removed from the study
    - Patients can opt-in to texts with a QR code or by texting “Heart” to the study number
    - If patients do not return the opt out form and do not opt in to text via QR code or Text, our study team will call them to opt-in to texts and complete a baseline behavioral survey.
- All enrolled patients have a secondary opportunity to opt out of the intervention by texting STOP at any time after the first text message

Enrollment Process

- Patients mailed opt-out package – includes study information, opt-out form, opt-in form with QR code and study phone number
- Study Staff called patients who did not opt-out
- Patients not reached over the phone were texted



Implications of the FCC Regulatory Change

- Increased staff time
- Not pragmatic
- Results in lower enrollment
  - Sample bias
    - Impact on intervention effect?
  - Less diverse representation

Feinstein Institutes
for Medical Research
Northwell Health®

MOMS CHAT & CARE STUDY

NINR R01NR021134

NIH Pragmatic Trials Collaboratory
FTF Meeting
May 9-10, 2024

PURPOSE OF MOMS CHAT & CARE STUDY

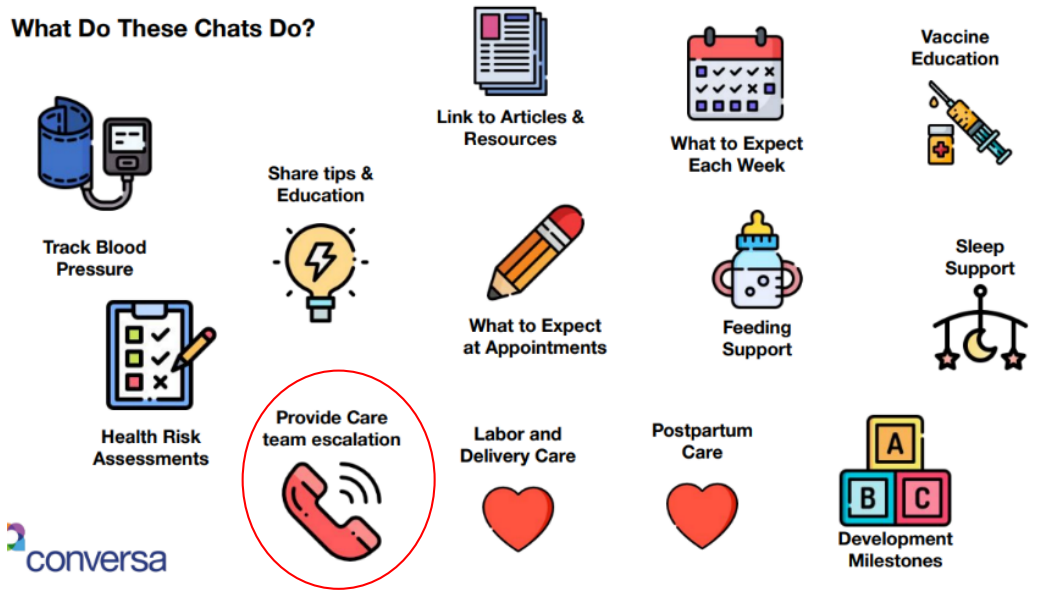
- To test the effectiveness of the Northwell MOMs Program at two different levels of intensity designed to facilitate timely, appropriate care for high-risk Black birthing people and reduce risk for severe maternal morbidity.

- Funded by the NIH, National Institute of Nursing Research (R01NR021134) – September 22, 2023 – June 30, 2028

2-ARM PRAGMATIC RANDOMIZED CLINICAL TRIAL DESIGN

MOMs Low-Touch (MOMs-LT), n = 337

- Northwell OB Chats (Prenatal to 1-year Postpartum)
- 6-weekly postpartum clinical check-ins (original MOMs program)
- Fitbit (Prenatal to 1-year Postpartum)



MOMs High-Touch (MOMs-HT), n = 337

- Northwell OB Chats (Prenatal to 1-year Postpartum)
- 6-weekly postpartum clinical check-ins (original MOMs program)
- Fitbit (Prenatal to 1-year Postpartum)

+

- 12 bi-weekly self-management support telehealth visits (Prenatal)
- Home Blood Pressure Monitoring Training

SPECIFIC AIMS/STUDY OUTCOMES

1. Compare MOMs-HT to MOMs-LT on the incidence of SMM at the time of labor and delivery.

   1a. Compare study arms on the incident rate of SMM-related hospital admissions at 1-month and 1-year postpartum.

2. Compare the two study arms on time to documented preeclampsia diagnosis and initiation of treatment (low-dose aspirin).

3. Examine the effect of the two study arms on perceived social support domains (informational, emotional, and tangible) from enrollment to 1-month and 1-year postpartum.

4. Explore the effect of each study arm on patterns of engagement in physical activity from study enrollment to 1-year postpartum and subsequent association with maternal health outcomes.

5. Examine implementation determinants and outcomes using a mixed methods approach.

INCLUSION CRITERIA (N = 674)

- Age 18 or older
- Self-identify as Black/African American
- Pregnant with gestational age no higher than 14 weeks
- OB-CMI risk score ≥ 3 and/or history of preeclampsia
- Primary language is English or Spanish
- Receive OB care at a NHPP practice site

Comorbidity	Points
Preeclampsia with severe features or eclampsia	5
Preeclampsia/gestational/chronic hypertension	2
Congestive heart failure	5
Pulmonary hypertension	4
Ischemic heart disease/cardiac arrhythmia	3
Congenital heart and/or valvular disease	4
Multiple gestation	2
Fetal death	2
Placenta previa/suspected accreta/abruption	4
Previous cesarean delivery/myomectomy	1
Autoimmune disease/lupus	2
HIV/AIDS	2
Sickle cell disease/bleeding disorder/coagulopathy/anticoagulation	3
Epilepsy/cerebrovascular accident/neuromuscular disorder	2
Chronic renal disease	1
Asthma	1
Diabetes mellitus with insulin therapy	1
Maternal age, y	
>44	3
40–44	2
35–39	1
Substance use disorder	2
Alcohol abuse	1
Body mass index, kg/m^2	
>50	3
>40	2

Easter et al. OB-CMI for maternal risk assessment. Am J Obstet Gynecol 2019.

RECRUITMENT AND ENROLLMENT PLAN

1. Will leverage MOMs Antepartum Chase List with specific MOMs-CC inclusion criteria to populate recruitment list
2. Research assistants will mail and email recruitment letters to potentially eligible patients; follow-up with recruitment phone call after 2 days (emailed letter) or 5 days (mailed letter)
    a. Recruitment will occur over 27 months; goal to recruit and enroll ~25 participants per month
3. After eligibility screening conducted and verbal informed consent obtained, participant will be randomized to either MOMs-HT or MOMs-LT
    a. Research assistants will ensure that participants have been enrolled in Northwell Pregnancy Chats and provide troubleshooting as needed
    b. Fitbit (both arms) and Home Blood Pressure Monitor (MOMs-HT) will be mailed to participant within 1 week

STUDY DESIGN

- Randomization at the patient level (1:1 ratio)
  - Stratified randomization per clinic (block randomization w/ varying block sizes (recommended by Biostats Core on Nov. 17, 2023 for possible differences in quality of care by clinic)
  - Recruiting patients from 16 Northwell OB clinics with highest number of patients meeting inclusion criteria

- Outcome data sources:
  - Electronic health record
  - Questionnaires (REDCap; Chatbot)
  - Qualitative Interviews and Focus Groups

- Interventionists are Northwell care management coordinators, RNs, and NP who will see participants in both study arms
  - MOMs Low Touch:
    - Respond to chatbot yellow and red flags (navigation)
    - Postpartum telehealth visits (clinical, behavioral health, and social health check-ins)
  - MOMs High Touch:
    - Respond to chatbot yellow and red flags (navigation)
    - Deliver 12 bi-weekly prenatal self-management support telehealth visits
    - Postpartum telehealth visits (clinical, behavioral health, and social health check-ins)

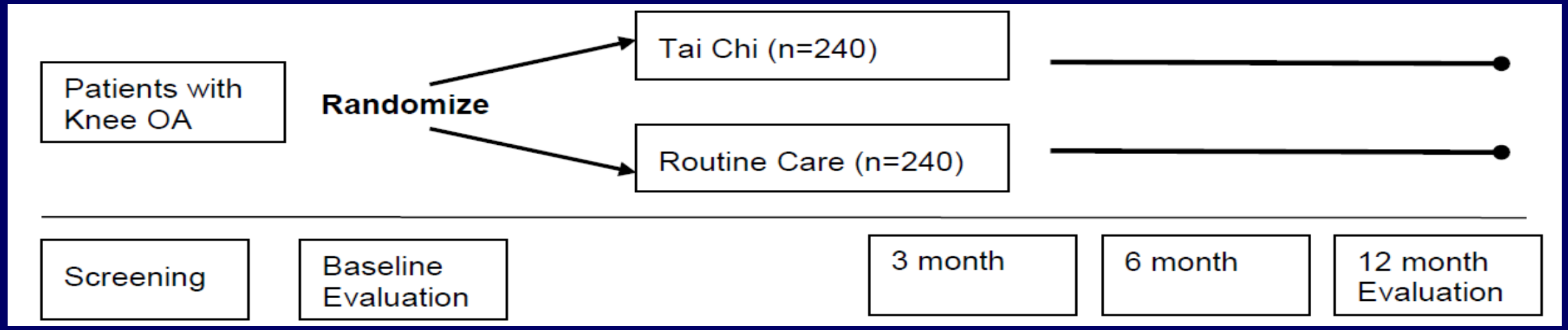
STUDY DESIGN CHALLENGES & PROPOSED SOLUTIONS

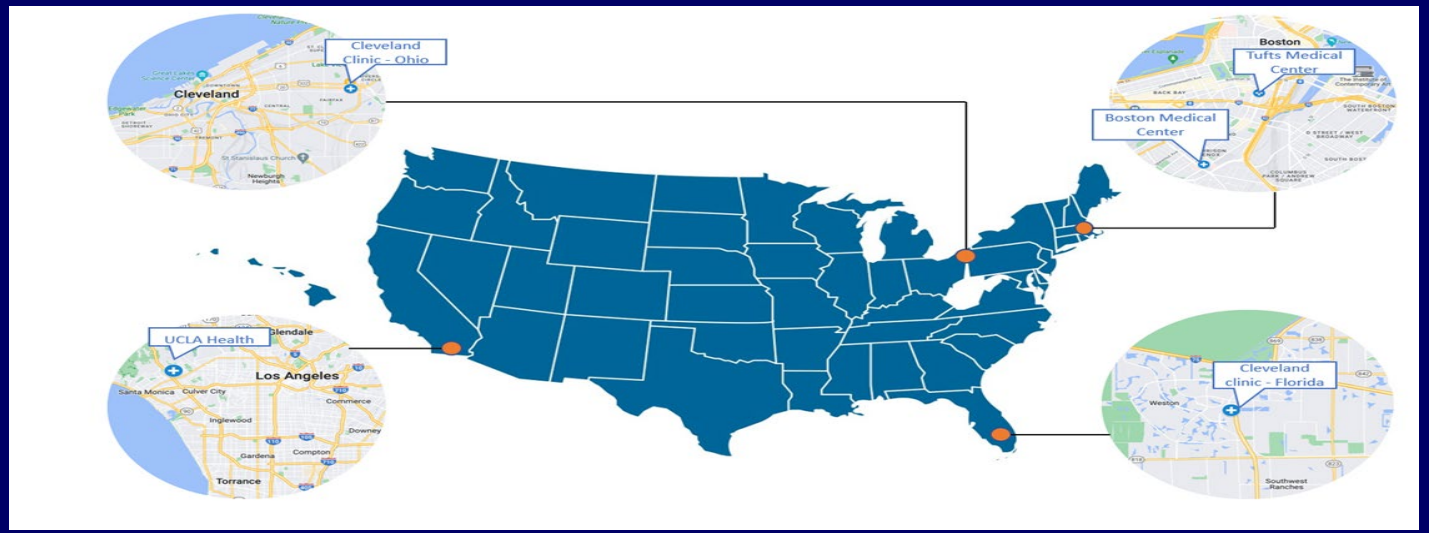
Challenge	Proposed Solution(s)
Competing maternal health studies and initiatives	▪ Communication across all teams ▪ Promote MOMs-CC health system wide ▪ Serve on maternal health boards/committees ▪ Stay up to date on local and state maternal health policy changes
Intervention staff turnover	▪ Maintain regular communication with department leadership ▪ Incentivize interventionists – additional training/skill building; acknowledge efforts
EHR system changing to Epic mid-2025	▪ Communication with all teams/departments involved in transition ▪ Create codes, processes, and workflows that make sense with Epic now

TAICHIKNEE: An Embedded Pragmatic Trial

Chenchen Wang, MD, MSc – Tufts Medical Center
Eric Roseen, DC, PhD – Boston Medical Center
Robert Saper, MD, MPH – Cleveland Clinic
Helen Lavretsky, MD, MS – UCLA Health

TAICHIKNEE Trial Overview





Major Goal: To study "real world" effectiveness and implementation of Tai Chi versus routine care for Knee Osteoarthritis across four US Healthcare Systems.

20 Years of Tai Chi Trials for Rheumatic Pain

Studies to Demonstrate Clinically Meaningful Signal

The Effect of Tai Chi on Health Outcomes in Patients With Chronic Conditions

Arch Intern Med. 2004;164:493-501

Can benefit be measured?

Intervention Development, Refinement and Standardization

Iterative process

Can the Intervention be optimized for future studies?

Tai Chi Improves Pain and Functional Status in Adults with Rheumatoid Arthritis: Results of a Pilot Single-Blinded Randomized Controlled Trial

Med Sport Sci. Basel, Karger, 2008, vol 52, pp 218–229

Feasibility and Pilot Studies

Can people adhere to protocol?

Efficacy Studies with Appropriate Comparison

Can a clinically meaningful effect be measured in an ideal design?

Tai Chi Is Effective in Treating Knee Osteoarthritis: A Randomized Controlled Trial

Arthritis & Rheumatism (Arthritis Care & Research) Vol. 61, No. 11, November 15, 2009, pp 1545–1553

Effect of tai chi versus aerobic exercise for fibromyalgia: comparative effectiveness randomized controlled trial

the bmj | *BMJ* 2018;360:k851 | doi: 10.1136/bmj.k851

Effectiveness or Comparative Effectiveness Research

Can it work in real world setting?

Annals of Internal Medicine — ORIGINAL RESEARCH

Comparative Effectiveness of Tai Chi Versus Physical Therapy for Knee Osteoarthritis

A Randomized Trial

Ann Intern Med. 2016;165:77-86. doi:10.7326/M15-2143

The NEW ENGLAND JOURNAL of MEDICINE

A Randomized Trial of Tai Chi for Fibromyalgia

N Engl J Med 2010;363:743-54.

Dissemination and Implementation Studies

Can it be used widely?

TAICHIKNEE: An Embedded Pragmatic Trial

Critical Questions

- How much of the benefit of Tai Chi is due to a placebo effect?
- What is an appropriate control for Tai Chi?
- And what do these findings mean for clinical practice?

Key Research Questions in UG3 Phase

- What are potential barriers/facilitators to “real-world” implementation of Tai Chi for knee OA in four healthcare systems?
- What potential implementation strategies appear promising?

Challenging questions in UH3 Phase

- What are appropriate recruitment strategies?
- What are appropriate blinding strategies?

Questions