TRIO STUDIO: Recruitment and Retention for the PrecISE Asthma Trial

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by Steve White, M.D.

University of Chicago

PI for the Chicagoland Asthma Consortium

Facilitators: Santosh Basapur, IIT Institute of Design and Sherry Robison, ITM

Research Assistants: Divya Jain and Luciano Annes Nunes (MDes Students)

Attendees:
PIs from University of Chicago, Northwestern and University of Illinois at Chicago were in attendance, in addition to research personnel from all six of the ITM institutions and University of Illinois at Chicago.

Summary
Steve White, M.D., University of Chicago, introduced the PrecISE severe asthma study to be conducted at University of Chicago, Northwestern Memorial Hospital and University of Illinois at Chicago. He gave background information and introduced the perceived recruitment challenges to the studio.

Steve White, M.D. and Lewis Smith, M.D. are looking for suggestions for recruitment and retention of subjects in the PrecISE severe asthma study.

Design Science Methodology and Quality Science Methodology were both used to solve the problems faced by Chicagoland site PI’s, Dr. Steve White and Dr. Lewis Smith and their teams at University of Chicago and Northwestern Memorial Hospital. Many suggestions, based on experiences at different institutions, were made.

Top 3 Actions Proposed by the Design Science Studio Participants to Dr. Steve White and Dr. Lewis Smith:

1. Citizen Scientists - Create awareness campaigns all the way from K-12 school science classes to senior citizen community programs

2. Communication plan specifically designed for explaining the complexity of this study and protocol. National level supervision works but local and customised design is much needed.

3. Explain the science of the study to the people expected to participate. Highlight the contribution they provide when they participate in this study and complete it.
Top 3 Actions Proposed by the Quality Science Studio Participants to Dr. Steve White and Dr. Lewis Smith:

1. **Registry**: Use the asthma registry for recruitment. These are patients that are already established patients and may be looking for the newest treatment or a research study to participate.

2. **Shorten Visit Times**: Use RedCap to utilize surveys for subjects to fill out prior to their appointments. Email the questionnaires/surveys a week before the appointment to help eliminate subjects having to fill them out in clinic.

3. **Non-monetary compensation/incentives**: Give subjects who participate food vouchers, parking, badges or pins, and add monetary compensation for commitment and completion of the study. Send study updates to participants in the form of a newsletter or weekly status emails.
TRIO Studio Problem Description:

Steve White, M.D. explained the goal is to recruit and retain subjects in the PrecISE severe asthma study. He defined asthma and a complex phenotypes of airway inflammation and obstruction with genetic trait x environment and is treated with inhaler medications, avoidance of triggers. Severe asthma affects 5-10% of all people with asthma with 50% of all health care costs related to asthma. It has a disproportionate effect on society with lost work/school days, etc, and patients have died from severe asthma.

Dr. White explained that the PrecISE study is an NHLBI funded, seven year study. It is a single, over-arching master protocol designed to study multiple therapies, it has an adaptive platform trial design and there are up to six novel therapies. The primary objectives of the PrecISE study are:

1. Identify novel therapies that work in biomarker-defined subgroups of severe asthmatic participants
2. Optimize the subgroups targeted for treatment by refining the biomarkers and subgroup definitions.

The secondary study objectives are:

1. Gain information about potential monitoring biomarkers for selected therapies
2. Investigate the safety and effectiveness of selected therapies in pediatric asthmatic participants

The study is looking to enroll 600 adults and 200 adolescents in site across the United States including three sites in Chicago; University of Chicago, Northwestern Memorial Hospital and University of Illinois at Chicago. The inclusion criteria includes:

1. Make or female, age >12 years
2. Meet guideline criteria for severe asthma
3. On asthma therapy with stable baseline
4. Respond to rescue inhaler

The exclusion criteria includes:

1. Current participation in an investigational drug trial or asthma clinical trial
2. Other chronic pulmonary disease
3. History of smoking
4. Pregnancy/lactation
5. Absence of medically acceptable birth control
6. Daily systemic corticosteroids above 10 mg/day
Dr. White explained the study has six arms, all subjects will be on each arm of the study. During screening, subjects will have a four week wash-out of their medications and will receive a predictive biomarker assessment. Subjects will then be randomized into one of the six arms, for period one; they will be on this treatment which is active treatment or placebo for sixteen weeks. They will then have an eight week washout period and then start period two, which will be active treatment or placebo, whichever was not selected in period one. Subjects will be in period two for sixteen weeks and then do an eight week washout. Periods 3 and following, patients will be re-randomized, at each period, they will be randomized based on their biomarkers to a new intervention or to placebo. There is a two placebo per patient maximum overall and all placebos are matched to a treatment whether patients has received the treatment or not.

The study requires substantial time and commitment from participants which include monthly visit for approximately three years and submission of electronic diaries two times a day.

Dr. White is looking for innovative way to recruit and retain subjects for such an intensive trial.
Main problem for the studio participants to solve:
The study requires substantial time and commitment from participants which include monthly clinic visit for approximately 3 years and electronic diaries submitted two times a day. What are innovative ways that the PIs can recruit and retain subjects for such an intensive trial?

Studio Methodology
Design Science approach as well as Quality Science approach were used as part of the studio to solve the problem.

Design Science Method
We used the Design Science approach with four steps:

1. Created a free form mind map of the problem and identification of issues – Mind Mapping technique
2. Actionable insights were identified
3. Generated ideas to address issues
4. Synthesized solutions from the smaller ideas – Creative integration of smaller ideas led by Design Thinking Expert facilitator was done using white boards.

Solutions were proposed and were rated by the team on implement-ability (0-4 scale)

Quality Science Method
The Six Sigma Quality Science approach was used which consisted of four steps:

1. Problem definition and mapping of actual structure of the process
2. Identify issues and analyze causality using Fishbone analysis
3. Generated ideas to address to issues – Brainstormed using SCAMPER method
4. Merged smaller ideas and scale ideas to create bigger solutions

Actionable insights and solutions were proposed and solutions were rated by the team on implement-ability (0-4 scale)
Design Thinking Based Solutions:

Problem visualized with Insights
The group first discussed the problem and its context yielding the following context diagram as well as the stakeholder map:

Figure 1. Mind map of Issues with context
Figure 2. Stakeholder Map
High level insights:
Following the context discussions, insights were generated as follows:

Figure 3. Insights discussed included Profile of participants (A), Complexity of study (B) and Retention for repeated intervention and placebo conditions (C).
Solutions Generated by Design Science Approach Team:
Five implementable solutions were created to solve the issues. The ideas were discussed to be of importance and deeper impact and hence made into these 5 solutions. The other ideas discussed but parked as being either too narrow or too light in impact have also been listed in the figure below.

The top five solutions are as follows:

1. Citizen Scientists - Create awareness campaigns all the way from K-12 school science classes to senior citizen community programs

2. Communication plan specifically designed for explaining the complexity of this study and protocol. National level supervision works but local and customised design is much needed.

3. Explain the science of the study to the people expected to participate. Highlight the contribution they provide when they participate in this study and complete it.

4. Visit optimization – Ideate to break up long visits into part home and part clinic visits such that the visit length is smaller and more pragmatic. Other ideas include home visits as well as visits to primary access clinic nearer to people’s homes in the community.

5. Retention – Optimize visits and show the data collected and data yet to be collected for the study to be successful. Maybe have stickers of landmarks as well as get togethers of participants and celebrate the people who have completed the study and helped. Develop ambassadors from the community to help retention.
### SELECTED SOLUTIONS

1. **CITIZEN SCIENTISTS**
2. **COMMUNICATION PLAN FOR COMPLEXITY OF STUDY**
3. **SCIENCE TO BE EXPLAINED + CONTRIBUTION HIGHLIGHTED**
4. **VISIT OPTIMIZATION**
5. **RETENTION - VISIT DATA OPTIMIZING EVENTS**

### OTHER SOLUTIONS

- **MODULATIZATION OF THE STUDY**
- **ONLINE FORUM (SOCIAL MEDIA)**
- **VIDEO / REMOTE VISITS**
- **CO-DESIGN STUDIES WITH PARTICIPANTS**
- **ORGANIZATION BY CENTRALIZED INSTITUTION**

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Figure 4. Top 5 solutions along with other solutions discussed.
Quality Science Based Solutions:
Problems Analysed to Identify and Define Issues.

Define the Problem

<table>
<thead>
<tr>
<th>Current State</th>
<th>Goal State</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nationwide and international centers</td>
<td>Recruit and retain subjects for a 7 year study</td>
</tr>
<tr>
<td>PRR</td>
<td>600 adults, 200 adolescents</td>
</tr>
<tr>
<td>Vacations are allowed</td>
<td>Get IRB approval</td>
</tr>
<tr>
<td>Adaptive platform</td>
<td>Start in October 2019</td>
</tr>
<tr>
<td>Upto 6 novel therapies</td>
<td>Window for a monthly visit</td>
</tr>
<tr>
<td>3 yr long participation-monthly tests + questionnaire</td>
<td></td>
</tr>
<tr>
<td>Inhaler for asthma is tied to the e-diary</td>
<td></td>
</tr>
<tr>
<td>Drug effectiveness is based on the e-diary</td>
<td></td>
</tr>
<tr>
<td>Compensation is $35-$45/hr for a 4-8 hour visit</td>
<td></td>
</tr>
</tbody>
</table>

Who is experiencing the problem
1. Study Team
2. Study PI
3. Clinicians
4. Patients
5. Moms
6. Employers
7. School Teachers

What is the scale of the problem
1. Retention Issues
2. Recruitment Team
3. Late participation can only be a part of therapies left
4. Geo location
5. 6 Consortium members all doing the same studies
6. Older people want a personal conversation while younger people prefer digital modes of communication

Why does the problem exist
1. Study team can’t screen easily
2. IRB challenges
3. EPIC not up to date
4. People reluctant to consent
5. A data point is lost when patients are on vacation
6. Weekends is not a possibility since doctors are not available
7. Visits sometimes take longer than patients expect
8. Younger people in 20s are not interested, have other responsibilities
9. Process is uncomfortable
10. Questionable safety of meds hard to communicate

Figure 5. Problem Definition
Figure 6. Flow analysis and problem occurrence location identification
Analysis of Issues and Causes

Why-Why Analysis

Figure 7. Root cause analyses and insight

Solutions Generated by Quality Science Approach Team:

Six solutions were created to solve the issue of innovative ways that the PIs can recruit and retain subjects for such an intensive trial. They are as follows in the list below and the diagram digitized from whiteboard:

1. **Registry**: Use the asthma registry for recruitment. These are patients that are already established patients and may be looking for the newest treatment or a research study to participate.

2. **Shorten Visit Times**: Use RedCap to utilize surveys for subjects to fill out prior to their appointments. Email the questionnaires/surveys a week before the appointment to help eliminate subjects having to fill them out in clinic.

3. **Non-monetary compensation/incentives**: Give subjects who participate food vouchers, parking, badges or pins, and add monetary compensation for commitment and completion of the study. Send study updates to participants in the form of a newsletter or weekly status emails.

4. **Alternative Outreach**: Educate other physicians on the study, look at rural areas (Kankakee County, Northwest Indiana, etc) for asthma patients and contact school nurses to let them know about the study and
possibly educate parents about their children participating. Use social media (Facebook support groups, Twitter, Instagram) to reach potential participants.

5. **Use ITM as a Resource:** Video testimonials, Honest Broker roll for recruitment, the New Normal Campaign, and community events to pass out IRB approved advertisements/flyers.

6. **Accessibility:** Patients can go anywhere for their follow-up appointments. If a patient is going on vacation they can have access to one of the other sites in the U.S. to do their follow-up appointment.

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**Figure 8. Solutions created and discussed along with parked solution ideas.**

<End of Document. Thank you.>
Appendix 1.
Slides used by Steve White, M.D., University of Chicago, for the studio kick off.

Appendix 2.
Actual pictures of white board from the studio session.
Problems/Issues

Reframed

* Complexity of study hard to understand by participants

* National plan of communication may not be enough—need local custom

  - Communication is too focused on the process
  - Manage participants (constrain of time/effort)
  - Participants ask for holidays from participation; it's too long
  - Concerns about injections
  - There is no opt-out from parts of the study
  - Use of engagement over time
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1. Identify Profile

   - Blood Biomarkers
   - Sputum Biomarkers
   - Urine Biomarkers
   - Nose/Throat Swab Biomarkers

2. Randomize

   - Treatment Period 1
   - Treatment Period 2

3. Repeat up to 4x

   - Placebo (1 to 3 ratio)

   - Companies don't want to compare one drug to another.

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1. Citizen Scientists - Voice to people
   - Avoid getting “fixed”

2. Communication plan for complexity of study
   - Local - blogs - forums
   - Stages - Facebook

3. Science to be explained
   - New normal campaign
   - Contribution highlighted

4. Visit optimization
   - Local clinic [Modular approach]
   - Home visit [ Videocall half/half real/digital]

5. Retention
   - Visit data and optimizing events
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Solution Ideas Parking
- add ons
- iPhones to keep our adolescents
- Modularization of the Study
- IRB issue

2. National Communication Plan - What about local?
- Diversification of Communication Channels
  - Texting
  - Survey
  - Feedback
- Stages
- Home visits
- Video visits
- Co-design studies with participants
- Outsourced
- Local clinics than Univ.
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Quality Science

DEFINE THE PROBLEM

CURRENT STATE
- Need # of participants recruited
- Need # of participants needed
- Adaptive platform
- Uptake novel therapeutics
- Inhaled X2
- Face product
- BIVK

GOAL STATE
- Recruit + retain subjects for a 7+ yr study
- 600 adults, 700 adolescents
- 80 adults + 10 children
- 800 adults = 400 to screen
- Get IRB approval
- Start in October 2019
- Window for monthly visit

Who is facing the problem?
- Patient, family, research team

What is the scale of problem?
- Recruitment goals

Why does the problem exist?
- Challenges in recruitment and retention
- Cost and feasibility

Why does the problem exist?
- Cost and feasibility
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SOLUTIONS

1. Digital (Recruitment)
   - Incentives
   - Phone Call
   - Emails

2. Social Media
   - Facebook Support Groups
   - Twitter
   - Instagram
   - Video Testimonials

3. Registry for Asthma
   - Recruitment

4. ITM
   - New Normal
   - Video Testimonials
   - Community Events
   - Event Flyers

5. Rural Outreach
   - Kankakee County
   - Northwest Indiana
   - Schools

6. Mobility
   - Patient can go anywhere
   - Summaries/briefings
   - Community Events
   - School nurse for adolescents

7. Consent
   - Phone Call
   - Email
   - In Apps

8. Community
   - Badge Pin
   - Food Voucher
   - In An Apps

9. Mobility
   - Patient can go anywhere
   - In Apps
   - Email
   - In An Apps

10. Compensation
    - Vouchers
    - Phone Call
    - Email
    - In An Apps

11. Social Media
    - Facebook Support Groups
    - Twitter
    - Instagram
    - Video Testimonials

12. Registry for Asthma
    - Recruitment
About the Institute for Translational Medicine (ITM)

The ITM is a partnership between the University of Chicago and Rush in collaboration with Advocate-Aurora Health Care, the Illinois Institute of Technology (Illinois Tech), Loyola University Chicago, and NorthShore University HealthSystem that’s fueled by about $35 million in grants from the National Center for Advancing Translational Sciences at the National Institutes of Health through its Clinical and Translational Science Awards (CTSA) Program.

We’re part of a network of more than 55 CTSA Program-supported hubs across the country working to slash the time it takes to develop and share new treatments and health approaches. We work with you and for you to make participating in health research easy, so that together we improve health care for all.

Join the movement and learn more about how we help researchers, physicians, community members, industry, government organizations, and others. Visit us at chicagoitm.org and connect with us on Facebook, Twitter, Instagram, YouTube, and LinkedIn @ChicagoITM.

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