TRIO STUDIO: Prospective Research Studies in the Adult ICU
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Facilitator: Santosh Basapur, IIT Institute of Design

Attendees:
Denise Voskuil-Marre, Rush University Medical Center (RUMC); Luis Alcantar, UChicago; Charlene Gamboa, RUMC; Siqi Zhang, RUMC; Julian Solway, MD, UChicago; Raj Shah, MD, RUMC; Ashley Lopez, ITM; Amanda Kass, ITM; and Sherry Robison, ITM.

Summary:
Anne Pohlman, MSN, APN-CNS, FCCM of University of Chicago Medicine presented the Studio topic, Prospective Studies in the Adult ICU.

Anne introduced the struggles that she and her team face in the Medical Intensive Care Unit (MICU) involving the consenting process for prospective, minimal risk, research projects spanning from enrollment to follow-up.

Design Thinking Methodology was used to solve the problem faced by the MICU research team. Many suggestions based on experiences within different departments and institutions were made.

Top 3 Actions Proposed by the Studio Participants to Anne Pohlman and the MICU Research Team:

1. Learning Healthcare System with Consent for Research at time of Care-
Creating a consent for research for all patients at any point of care in academic health centers may make it easier for prospective research studies in distinct settings such as the ICU. In fact, all ITM institutions could have same template and data sharing agreement.

2. Alteration of Consent Timeline - Targeting groups for pre-consent and delayed consent will help build flexibility in to the timeline of when consents are obtained. The team can collaborate with ITM and create templates.

3. Temporary Storage of Sample Until Patient Opt-In – Collect and hold samples until patient or family member is available for consent. If the patient does not consent, then the team can destroy the samples on hold.
CAPriCORN can also be used to get patient data.
TRIO Studio Problem Description:

Anne Pohlman, MSN, APN-CNS, FCCM of University of Chicago Medicine introduced to the Studio audience studies targeting the research population within the MICU, which consists of very sick patients who are unable to consent for themselves due to underlying conditions or interventions. In such cases, surrogates are required to offer consent for research participation on behalf of the patient. Oftentimes, surrogates are not available or do not want to talk about research upon MICU admission. The Adult MICU research team propose a new protocol in which they can prospectively enroll all MICU admissions to minimal risk studies, and then include outcomes at hospital discharge and perhaps longer.

A current proposed study involves observing alterations of the microbiome during critical illness. MICU patients are at extreme risk for alterations in their microbiome for a variety of reasons, including:

- Frequent antibiotic/analgesia administration
- Altered gut motility/change in diet
- Gut hypo-perfusion
- Impaired function of the gut’s mucosal barrier

Anne and her team propose to longitudinally sample discarded bio-specimens from subjects throughout MICU admission. The team will then correlate changes in the microbiome with de-identified clinical data, and associations found will serve as a foundation for further clinical trials to optimize the human microbiome in MICU patients.

MICU patients are admitted for services in a multitude of different avenues, such as from University of Chicago Medical Center (UCMC) in-patient services, from UCMC Emergency Department, or as a transfer from an outside hospital. All MICU admissions are screened daily by the MICU research team via the REDCap database (2019 n= 2070). RN’s within the MICU collect discarded stool specimen daily (when available) starting on Day 1 of the patient’s MICU stay.

Anne proposes that the stools, which are usually discarded, be coded and sent to a research lab for processing and storage. After one year, a list of all MICU admissions will be submitted to the Clinical Research Data Warehouse (CRDW). They will request clinical data, during the study period, be deidentified and returned for study analysis. The following factors are considered:

- Primary Endpoint: Hospital Mortality
- Secondary Endpoints:
  - Length of stay: ICU and hospital
  - ICU re-admission: sepsis, shock, other causes
  - Ventilator-free days
  - Need for RRT
  - ICU acquired weakness
  - Functional status
The stool analysis consists of the following processes:

- DNA will be extracted and purified
- 16s rRNA gene amplified by PCR
- PRC products are sequenced
- Sequence data compiled and processed
- Sequences will be evaluated for quality
- Once complete, sequences will be grouped into operational taxonomic units based on similarity
- Shotgun metagenomics will be performed in addition to metabolomic analysis

The challenges faced by the MICU team include the patients are very sick and cannot provide consent for themselves due to underlying conditions or MICU interventions, surrogates are often not available or are unwilling to talk about research upon MICU admission, enrollment rates in MICU studies are low and thus do not provide an accurate representation of the MICU population, and once discharged from the MICU, patients go to other services or to a variety of locations (e.g. other hospitals, hospice, acute rehab, skilled nursing home, home with assist, home of a family member, or home).

Anne posed a series of discussion-opening questions to the TRIO Studio audience:

- Do all prospective research projects in the MICU require consent?
- Are there alternatives to consent in studies involving minimal or no risk?
- With Electronic Medical Records (EMR), can prospective data be collected, de-identified, analyzed, and published?
- Can long-term outcomes be gathered by others not directly completing the ICU research?
Main problem for the studio participants to solve:
How to strategize options for conducting prospective minimal risk research projects in the adult MICU from enrollment to long-term follow-up?

Studio Methodology
Design Science approach was used as part of the TRIO studio to solve the problem.

Design Science Method
We used the Design Science approach with five 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.
5. Solutions were proposed and 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:

![Mind Map of Context](image)

Figure 1 Mind Map of Issues
Figure 10 Stakeholder Map
High Level Insights:
Following the context discussions, insights were generated as follows:

<table>
<thead>
<tr>
<th>Insights</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>01</strong> Middleman/entity needed between patients/data and research team</td>
</tr>
<tr>
<td><strong>02</strong> Announce sample collection on flyers and at discharge about study and follow-up/QR code</td>
</tr>
<tr>
<td><strong>03</strong> Reframe project to quality improvement of ICU system</td>
</tr>
<tr>
<td><strong>04</strong> Inform patients about research at a good point of care</td>
</tr>
<tr>
<td><strong>05</strong> Saying the study is de-identified might be a bigger barrier</td>
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<tr>
<td><strong>06</strong> “Medical waste is hospital property”</td>
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<tr>
<td><strong>07</strong> Look for broad consent and patient/community (ICU) feedback (co-design?)</td>
</tr>
<tr>
<td><strong>08</strong> Opt-In/Opt-Out ethical model</td>
</tr>
<tr>
<td><strong>09</strong> Change the approach to long term outcomes and collecting data</td>
</tr>
</tbody>
</table>
| **10** Change microstrategies to consent:  
  - pre-consent  
  - approach 24hrs+ after admission |

*Figure 11 Insights and Ideas Generated During Discussion*
Solutions Generated by Design Science Approach Team:

Five implementable solutions proposed by Design Science Team:

1. **Learning Healthcare System with Consent for Research at any Point of Care** - Creating a consent for research consideration for an entire academic health center may make it easier for prospective research studies in places such as the ICU. An example would be the Hospitalist Project at University of Chicago. In fact, all ITM institutions could have a consent template and data sharing agreements as infrastructure for translational research.
   a. **Institutes could also do a better job of** informing patients and families of research being conducted at the institute.
   b. Honest Broker could start introduction of the studies once the consent for research consideration is obtained.

2. **Alteration of Consent Timeline** - Targeting groups for pre-consent and delayed consent will help build flexibility into the timeline of when consents are obtained. The team can collaborate with ITM and see if pre-consent and delayed consent templates can be created for adoption at all ITM institutes.

3. **Temporary Storage of Sample Until Patient Opt-In** – Collect and hold samples until patient or family member is available for consent. If the patient consents then the sample can be used as data and if the patient does not consent, then the team can destroy the samples on hold. Additionally, CAPriCORN can be used to collect patient outcomes data from other hospitals incase the patient moves to other hospitals for further care or readmission.

4. **Make Collection a Standard of Care and Create Study as a De-identified Retrospective Chart Review** – Sample collection could be made part of standard of care and entered into EMR system. This allows for retrospective analysis of chart data. Sample analysis can/should be done at a CLIA certified lab. The team can also use the Clinical Research Center (CRC) lab. This further enables study team to create a MICU Microbiome Registry.

5. **Reframe the study as a Quality Improvement Project** – This is a last resort, of sorts. Prospective studies with low risk research protocols can be seen as quality improvement initiatives, if the true intent is to change how health systems/clinicians alter practice rather than a particular intervention study to directly impact a participant. This enables researchers to collect samples and work on data to improve the outcomes of care. If publishable material results from this endeavor, then IRB permission can be sought before publication.
## Solutions

<table>
<thead>
<tr>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
</table>
| **01** | Learning Healthcare System with Consent for Research at any Point of Care  
  - Create consent for research at any point of care for all ITM Institutions  
  - Inform patients and families of research being done at institute  
  - Use Honest Broker to start introduction of the study |
| **02** | Alteration of Consent Timeline  
  - Pre-consent/delayed consent  
  - Collaborate with ITM. Can this be a standard? |
| **03** | Temporary Storage of Sample Until Patient Opt-in  
  - Collect samples and hold until patient or family member consents  
  - If patient does not consent, destroy all samples  
  - Use CAProiCORN to follow patients outcomes data at other hospitals |
| **04** | Make Collection Standard of Care and Create Study as a De-Identified Retrospective Study/Chart Review  
  - Sample Analysis to be done at CLIA certified lab  
  - Use UChicago’s Clinical Research Center lab  
  - Create an ICU Microbiome Registry |
| **05** | Reframe Study as a Quality Improvement Project  
  - Low Risk prospective studies with intent to change health systems/clinicians practice can be QI initiatives  
  - Enables researchers to collect samples and data to improve outcomes  
  - Once publishable, IRB permission can be obtained |

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Figure 12 Solutions Prioritized for PI  
<End of Document. Thank you.>
Appendix 1.
Slides used by Anne Pohlman

Appendix 2.
Photos of white boards
Insights

- We need a middleman/entity between pts/death and research team
- Announce sample collection or triggers and announce discharge checklist
  - Study + follow-up / QR code
- Reframe project to Quality Improvement of ICU System
- Uniform pig death research @ a good point of care
- Scheduling the study is a identified might be a bigger burden
- Medical waste is hospital property
- Less for board consent + look for patient community (not) culture (co-design)
- Opt-in/opt-out model, make it optional
- Change the approach to long-term outcomes and
  - Long term
- Change metrics goals to consent,
  - pre-concord?
  - Pre-release?
About the Institute for Translational Medicine (ITM)

The ITM is a partnership between the University of Chicago and Rush in collaboration with Advocate 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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