Leveling the Field: Introduction to research concepts and terms

Barbara S. Gillespie, MD, MMS, FASN

Current Affiliations:
VP and Therapeutic Head of Nephrology, Covance Global Contract Research Organization (CRO)
Adjunct Professor, University of North Carolina, Division of Nephrology and Hypertension
Board of Directors, Kidney Health Initiative
Associate Medical Director, Naphcare

Disclosures: None
### Key Steps in the Dialysis Research Process

**Design**
- Identify problem(s)
- Formulate research question(s) and hypotheses
- Design strategy
  - cohort study, clinical trial, interview/focus group(s)
- Develop proposal outlining the protocol (plan)
  - recruitment, data collection, analysis, and dissemination plans
  - consider obtaining dialysis organization input
- Secure research funding
- Obtain Institutional Review Board (IRB)
- Obtain dialysis organization approval to conduct study in clinic(s) including legal contracting

**Conduct**
- Train clinic staff on protocol
- Obtain Informed Consent, then recruit study participants
- Collect study data
  - Medical record information, blood samples, interviews
- Analyze study data and interpret findings
- During conduct, consider need for re-trainings of clinic staff and/or updates to participants and facilitators

**Disseminate**
- Share key findings with important stakeholders (e.g., patients, clinicians, administrators, policymakers)
  - Manuscripts published in journals
  - Presentations, conferences, and meetings
  - Tools and resources
  - Websites, social media
- Provide follow-up to participants and facilitators
- Identify areas for future research and potential collaborators, funders

*Courtesy of Dr. Jenny Flythe*
Definitions

► **Clinical study** = research using human volunteers (aka participants, subjects) with the goal of adding to medical knowledge & public health

► **Intervention** = the thing being tested, like a new medication, procedure or program
  - If the intervention is a substance or drug, we refer to it as an Investigational Product, or IP
## Types of Clinical Studies

<table>
<thead>
<tr>
<th>Interventionsal Study (aka Clinical Trial)</th>
<th>Observational Study</th>
<th>Qualitative Research</th>
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| **Patients get assigned, or randomized, to an intervention group, and the intervention may be a:**  
  1. a drug or device  
  2. Procedure  
  3. Changes to a participant’s behavior, e.g. Diet | Assess health outcomes according to groups, who are not assigned to an intervention as part of the protocol...but they are grouped by the intervention as part of routine medical care | Uses observation to collect data in the form of truthful reporting, quotations, interviews, focus groups, surveys |
| **Goal:** determine the safety & efficacy (how well it works) | **Goal:** learn more about the effects of an intervention | **Goal:** gain a deeper understanding of behavior or patterns in a group of people |
| Ex: compare a new phosphate binder to one that is already approved, like sevelamer | Ex: we looked at the last 200 patients who got either an AVG or HD catheter placed, to understand infection rates within the first 60 days after placement | Ex: interview FSGS patients to understand their symptoms, and develop Patient Reported Outcome Measures (e.g. leg swelling) |
| Outcome of Measure: phosphorus levels | Outcome of Measure: # of infections | Outcome of Measure: symptoms |

[https://www.clinicaltrials.gov/ct2/about-studies/learn](https://www.clinicaltrials.gov/ct2/about-studies/learn) and [https://web.csulb.edu/~msaintg/ppa696/696quali.htm](https://web.csulb.edu/~msaintg/ppa696/696quali.htm) accessed on 1 April 2018
Clinical Studies

► Who conducts them?
  - Research teams (MD, RN, social workers, healthcare professionals), led by the Principal Investigator (usually an MD)

► Where are they performed?
  - Outpatient clinic, Dr.’s office, hospital, dialysis unit

► How are they performed?
  - According to the protocol, which receives input from the FDA, and must approved by IRBs (Institutional Review Boards)

https://www.clinicaltrials.gov/ct2/about-studies/learn accessed on 1 April 2018
Prior to Enrollment

Total N; **Obtain informed consent.** Screen potential participants by inclusion and exclusion criteria; obtain history

Visit 1
Time Point

Perform baseline assessments.
Administer initial study intervention

Visit 2
Time Point

Repeat study intervention *(if applicable)*

Visit 3
Time Point

Follow-up assessments of study endpoints and safety

The Protocol describes the why, who, what, and how of the study
“The Rights, Safety, and Well-being of the Trial Subjects Are the Most Important Considerations and Should Prevail Over Interests of Science and Society”

From FDA’s Guidance on Good Clinical Practice

**US Federal Agencies**
- FDA & NIH oversee most medical research
- **Inspect** institutions, individuals, research sites, drug manufacturing sites, IRBs
- Selected FDA Guidance documents that cover Good Clinical Practice & Clinical Trials: n=50 (12 just for ICF/IRB)

**Informed Consent Form (ICF)**
- Information provided by researcher
- **Explains risks & potential benefits**
- its really a **process** to ensure patient understands

**Institutional Review Board (IRB)**
- MDs, researchers, community members
- Role: ensure trial is ethical & rights and welfare of subjects are protected
- Review protocol & will suggest changes to ICF
- Risks are minimized & reasonable compared to potential benefits

**Independent Data Safety & Monitoring Boards (DSMB)**
- In many studies but not all
- Meet at pre-specified intervals to **review data on subjects** during the trial
- Can recommend if a trial needs to be stopped early

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https://www.clinicaltrials.gov/ct2/about-studies/learn accessed on 1 April 2018
Path to Drug Approval is Costly ($2.6 billion) and Long (10+ years)

"Pre-clinical", includes lab & animal testing:
- 250 drugs progress to Pre-Clinical
- 3-6 years before we expose people

"Clinical Testing", Phase 1-3:
- 5 investigational products move into Clinical Testing in humans
- 6-7 years

1 Drug to get FDA approval

Phase 4: Post Approval Research
- Includes Post Marketing Surveillance for longer term safety
- And the opportunity to study other populations (e.g. pediatrics)

5,000-10,000 substances
We conduct trials to answer questions

- New drug **safe and effective**?
- How does new intervention **compare to existing** treatment?
- **New way to use an old treatment** if easier, less side effects, more effective?
- Use of a treatment in other populations, like kids who were initially not tested

Potential **benefits** of Trial Participation?

- **Access** to novel and cutting edge research treatments
- Receive expert medical care and get **monitored more closely than usual**
- Receive care that may **not be covered** by insurance
- Empowerment: **Help other patients** like you in the future

Potential **risks** of Trial Participation?

- **Not all information is known** about investigational treatments
- Safety profile is emerging; new intervention may not be as effective as we thought
- Undergo **more tests or procedures** than usual
- **Time commitment**

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Build on the momentum

Global kidney health 2017 and beyond: a roadmap for closing gaps in care, research, and policy

As a stretch goal for the community, we propose that 30% of patients with CKD should be involved in relevant clinical trials by 2030.

Levin et al, Lancet 2017 (based on ISN’s CKD Summit in July 2016)
Ask me about a kidney clinical trial

I participated in a kidney clinical trial

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THE AMERICAS +1.888.COVANCE +1.609.452.4440 or +1.910.338.4760
EUROPE/AFRICA +00.800.2682.2682 +44.1423.500888 or +44.1763.512000
ASIA PACIFIC +800.8589.3000 +25.6.5688588

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