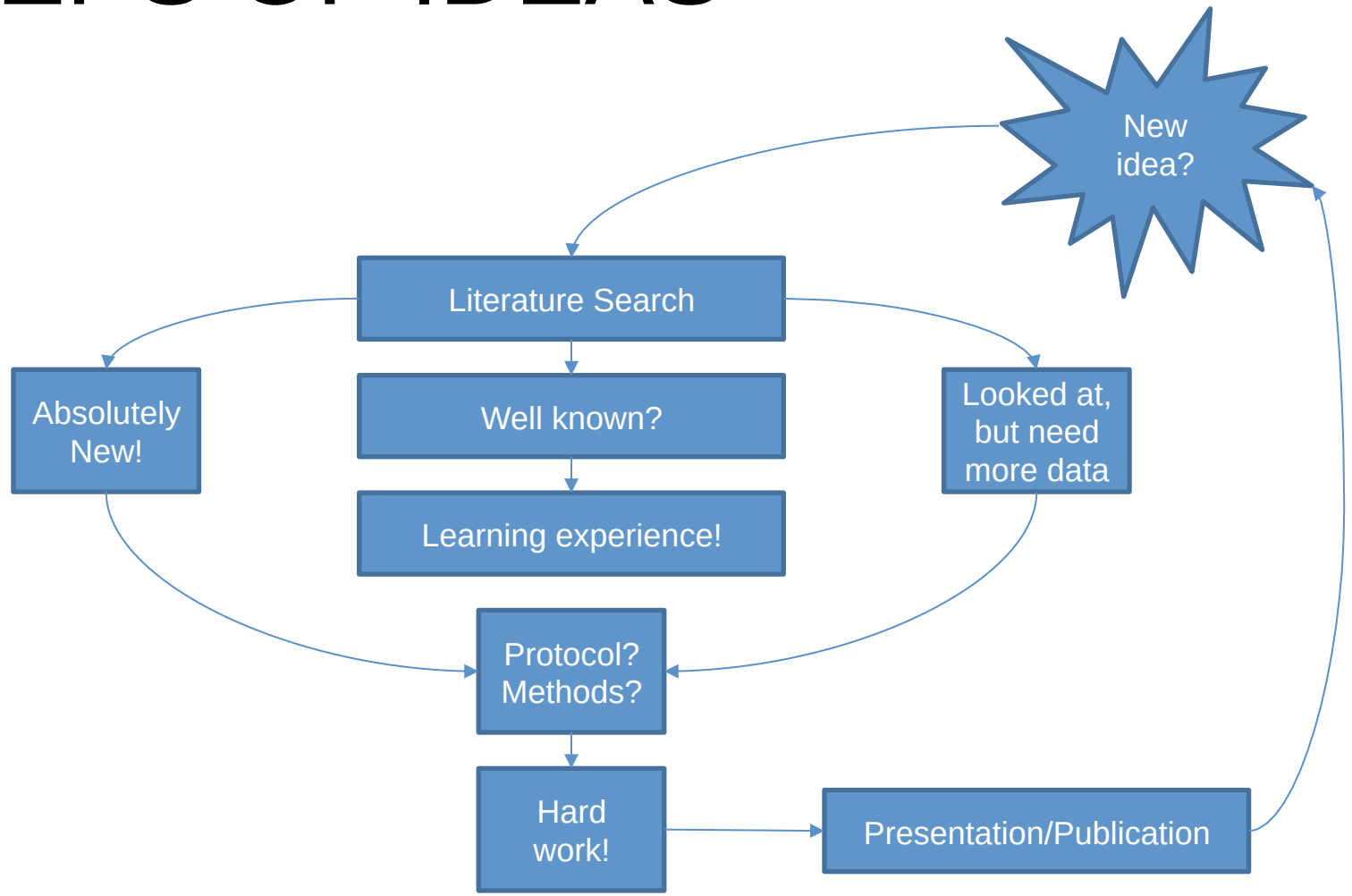
Conducting Your Research: Basic Principles of Clinical Research Project Design and Procedures

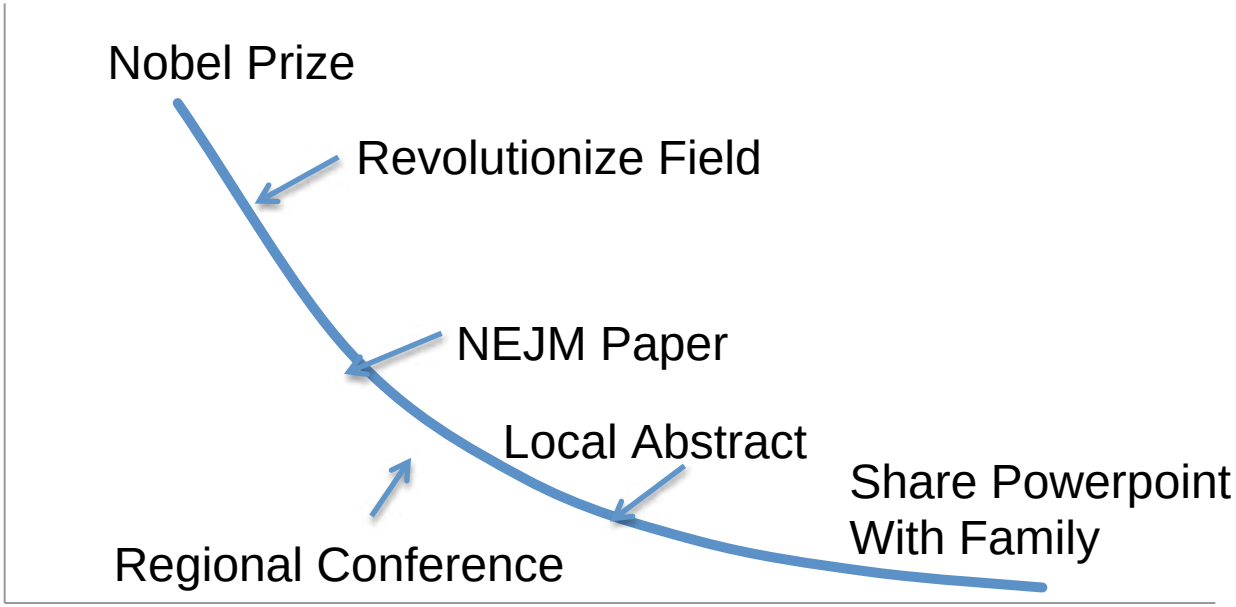
UI Health | UIC

STEPS OF IDEAS



Introduction to Clinical Research
Vasylyeva, 2012

EXPECTATIONS OVER TIME



GOOD RESEARCH QUESTIONS

- Master the literature
- Be alert to new ideas (conferences)
- Be creative
- Choose a mentor

PICOT

- Population
- Intervention
- Comparison
- Outcome
- Time

- Example: Among patients with symptomatic pulmonary hypertension [population], can sildenafil (20, 40, or 80mg) [comparison] orally 3 times daily [intervention] for 12 weeks [time] compared to placebo [comparison] improved functional status? [outcome]

FINER

- Feasibility
  - Sample size, technical expertise, time, resources/funding, scope/focus
- Interesting
  - Personal experience, asking “why?”
- Novel
  - Literature (“need for more research”), controversy, challenge evidence
- Ethical
  - Benefits > risk
- Relevance
  - Increase knowledge, influence policy or clinical practice

STUDY DESIGNS

HIERARCHY OF EVIDENCE

WHAT IS THE STUDY DESIGN?

- Researchers observed 18 patients with sarcoidosis who underwent renal transplantation.
- Subjects were identified retrospectively in 8 renal transplant departments.
- Medical charts, demographics, and transplant outcomes were reviewed.
- These data established that renal transplants may be carried out safely in transplant candidates with sarcoidosis.

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CASE SERIES

- Observational/descriptive
- Usually more than 10 patients, hypothesis-generating rather than evidence

- *Aouizerate, J et al. (2010). Renal transplantation in patients with sarcoidosis: a French multicenter study. Clinical Journal of the American Society of Nephrology, 5(11), 2101-2108.*

WHAT IS THE STUDY DESIGN?

- Researchers looked into racial disparities in motorcycle-related mortality.
- They analyzed data from the National Trauma Data Bank (2002-2006).
- They found Black motorcyclists more likely to use a helmet compared with Whites, but also more likely to die after a motor collision.

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CROSS-SECTIONAL

- Inexpensive, multiple risk factors analyzed simultaneously

- *Crompton JG et al. (2010). Racial disparities in motorcycle-related mortality: An analysis of the National Trauma Data Bank. American Journal of Surgery, 200(2), 191-196.*

WHAT IS THE STUDY DESIGN?

- Study of association between use of common psychotropic medications and traffic accidents.
- Researchers reviewed data from pharmacy prescriptions, police traffic accidents, and diving license data.
- They compared drivers with accident requiring medical assistance and those with license and no accident during 2000-2007.

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CASE-CONTROL

- Consider in retrospective chart review (inexpensive, convenient)
- Useful for rare conditions
- Watch for selection bias

- *Ravera S et al. Road traffic accidents and psychotropic medication use in the Netherlands: A case-control study. British Journal of Clinical Pharmacology, 72(3), 505-513.*

WHAT IS THE STUDY DESIGN?

- A study enrolled 3000 individuals at 7 sites with broad spectrum of renal disease severity.
- Subjects undergo extensive clinical evaluation and follow up visits including diet, activity, health behaviors, depression, cognitive function, health care utilization, CVD evaluations, and quality of life.
- The study is designed to look at risk factors of kidney disease and cardiovascular disease progression.

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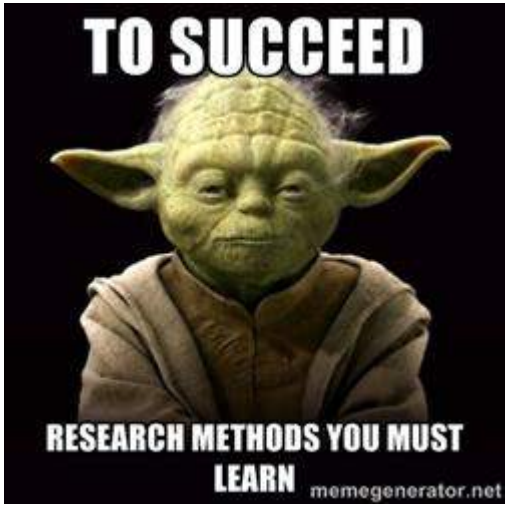
COHORT (PROSPECTIVE)

- Observational study, time-series
- No control group
- Subject loss can be an issue

- *Feldman HI et al. (2003). The Chronic Renal Insufficiency Cohort (CRIC) Study: Design and Methods. Journal of the American Society of Nephrology 14:S148-S153.*

EXPERIMENTAL STUDY DESIGNS

- Randomized Controlled Trials
  - Watch out! Strong evidence requires time, resources, and pain!
- Clinical Trials
- Cross-Over
- Quasi-Experimental
- Before-After (Pre-Post)



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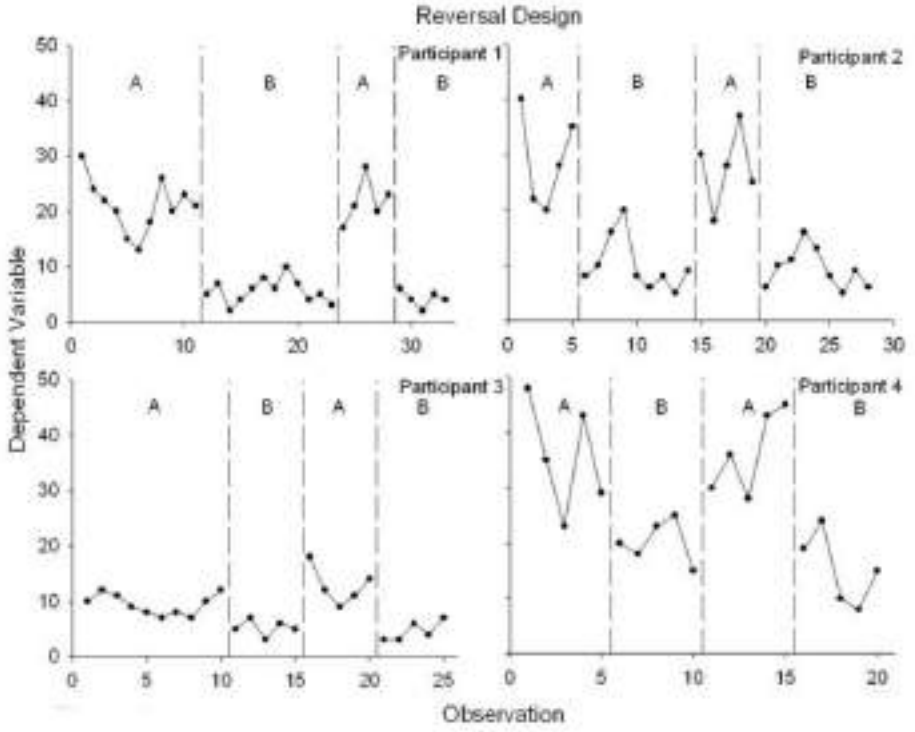

Reversal Design
Participant 1
Participant 2
Participant 3
Participant 4
A
B
Dependent Variable
Observation

OTHER QUANTITATIVE STUDY DESIGNS

- Sequential, Multiple Assignment, Randomized Trials (SMARTs)
- Multiphase Optimization Strategy (MOST)
- Factorial (full and partial) ANOVA
- Stepped Wedge
- Interrupted Time-Series
- Regression Discontinuity Design

FOCUS GROUPS

- Eight pharmacists working with community health workers described perceptions, opinions, attitudes towards them helping with medication adherence.
- Qualitative data for analysis

- *Rojas E et al. (2015). Pharmacists' perspectives on collaborating with community health workers in diabetes care. Journal of the American Pharmacy Association; 55(4):429-33.*

OTHER QUALITATIVE STUDY DESIGNS

- Phenomenological
- Ethnographic
- Grounded Theory
- Historical
- Case
- Action Research

- Methods: interviews, observation, focus groups, document review

Table 1. Comparison of quantitative and qualitative research approaches

	Quantitative	Qualitative
General framework	Seek to confirm hypotheses about phenomena	Seek to explore phenomena
	Instruments use more rigid style of eliciting and categorizing responses to questions	Instruments use more flexible, iterative style of eliciting and categorizing responses to questions
	Use highly structured methods such as questionnaires, surveys, and structured observation	Use semi-structured methods such as in-depth interviews, focus groups, and participant observation
Analytical objectives	To quantify variation	To describe variation
	To predict causal relationships	To describe and explain relationships
	To describe characteristics of a population	To describe individual experiences
		To describe group norms
Question format	Closed-ended	Open-ended
Data format	Numerical (obtained by assigning numerical values to responses)	Textual (obtained from audiotapes, videotapes, and field notes)
Flexibility in study design	Study design is stable from beginning to end	Some aspects of the study are flexible (for example, the addition, exclusion, or wording of particular interview questions)
	Participant responses do not influence or determine how and which questions researchers ask next	Participant responses affect how and which questions researchers ask next
	Study design is subject to statistical assumptions and conditions	Study design is iterative, that is, data collection and research questions are adjusted according to what is learned

Qualitative Research Methods: A Data Collector's Field Guide.
http://www.ccs.neu.edu/course/is4800sp12/resources/qualmethods.pdf

CHOOSING A STUDY DESIGN

- Discuss with mentor!
- Apply PICOT and FINER
  - State of science, Time, Resources, Limitations/bias, Patient risk
- Consult with CCTS Design and Analysis Core

IRB AND HIPAA

THE I STANDS FOR...

- Irritating?
- Impossible?

- It is necessary if Human Subjects Research

- If not sure, there's a form for that: "Determination of Whether an Activity Represents Human Subject Research"

TRAINING REQUIRED

- New investigator training
- HSPP HIPAA training (not the same as clinical HIPAA training!)

- It’s all online:
- http://research.uic.edu/compliance/irb/education-training

WHAT IS THE IRB?

- Committee composed of cross-section of community where research performed
- Protect rights and well-being of human subjects
- At least 5 members (per DHHS) and includes non-scientists, community members

- Want to know more?
- Contact the IRB and sit in on a review!

PROTOCOL CATEGORIES

- Exempt
  - Education, existing data (publically accessible), food tasting
- Expedited
  - No more than minimal risk
- Full
  - Full board review required

IRB COMMUNICATION

- Initial application
- Continuing review (each year)
- Protocol deviation
- Protocol amendment
- Adverse event
- Closure (final report)

HIPAA

- Health information that can be traced back to a particular individual (protected health information – PHI) is strictly forbidden for research unless the individual provides authorization

- HIPAA waiver may be appropriate in chart reviews
  - A study on hypertension could involve abstracting blood pressure data on 100 patients without recording other information that could identify them or link back to those patients

IRB TRICKS AND SECRETS

- Look at similar previous applications
- Keep consent forms simple with low-literacy level (use template)
- Talk to IRB personnel ahead of time about concerns
- Have mentor review application
- Create protocol following IRB's template

- Don't let yourself be frustrated!
- The IRB will always win!

BASIC PROTOCOL

- Title
- Investigators (with contact info)
- Introduction summary
- Background and justification
- Objectives and hypotheses
- Materials and methods
- Risks
- Power analysis and statistical plan
- Data management and safeguards for subjects
- References

EXAMPLE CASE 1

- 72 year old Alzheimer patient has given consent to be enrolled into a clinical study involving an investigational drug for memory.

- The patient is unable to give information about the purpose of the study or methods involved.

INFORMED CONSENT

- This case involves informed consent and probably requires a surrogate decision-maker to give consent.
- Surrogate's decision must be based on the risk-benefit ratio and what is in the best interest of the patient.

EXAMPLE CASE 2

- During a clinical trial of stem cell transplantation, a significant number of patient withdrawals occur.
- This could harm a study statistically if more drop out.
- The PI wants to modify the informed consent document to make discontinuing or withdrawing from the study a mutual decision requiring the participant and researcher to agree.

AUTONOMY

- This violates principle of autonomy.
- Consent must be voluntary, and participant must be able to withdraw from study without impediments, reprisals, or compromising future care.

EXAMPLE CASE 3

- A smoking cessation study includes 10 clinics, 5 intervention and 5 control.
- The study was presented to people in a smoking cessation program with different interventions conducted at the intervention sites.
- They were not informed it was part of a study, to prevent them from altering their responses to surveys (thus altering the results).

FULL DISCLOSURE

Subjects have the right to full disclosure prior to agreeing to participate in a study.

EXAMPLE CASE 4

- After completing a study involving collection of tissue samples, a researcher wants to do additional testing not explicitly described in the initial consent form.

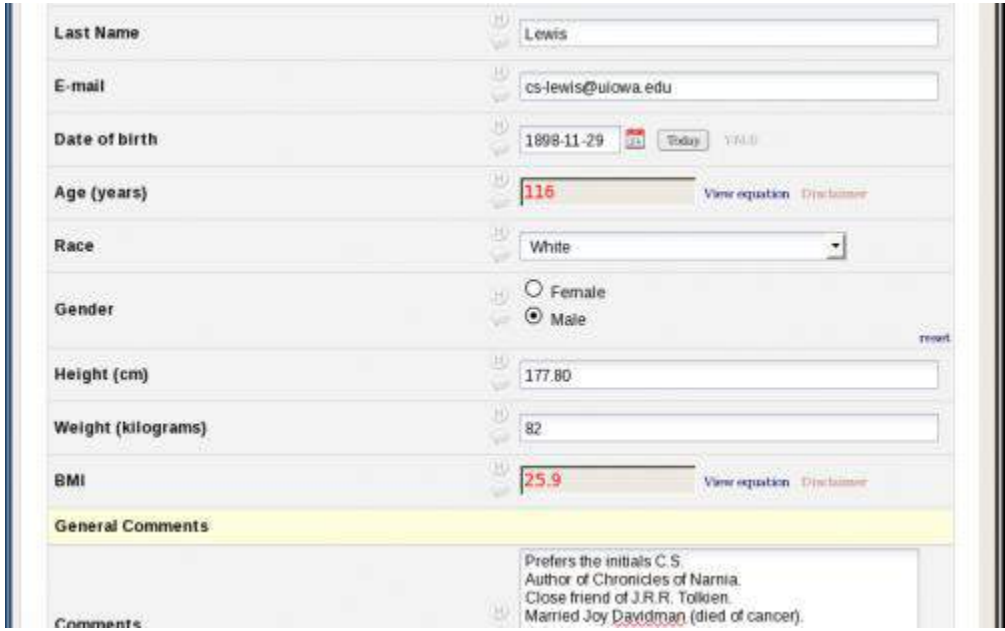
ADDITIONAL INFORMED CONSENT

- Most IRBs require an additional informed consent, or at minimum, a signed addendum to comply with the right for full disclosure.

DATA

COLLECTION

- Paper?
- Excel?
- REDCap?
- Variable definition names
- Keep a code book (dictionary)



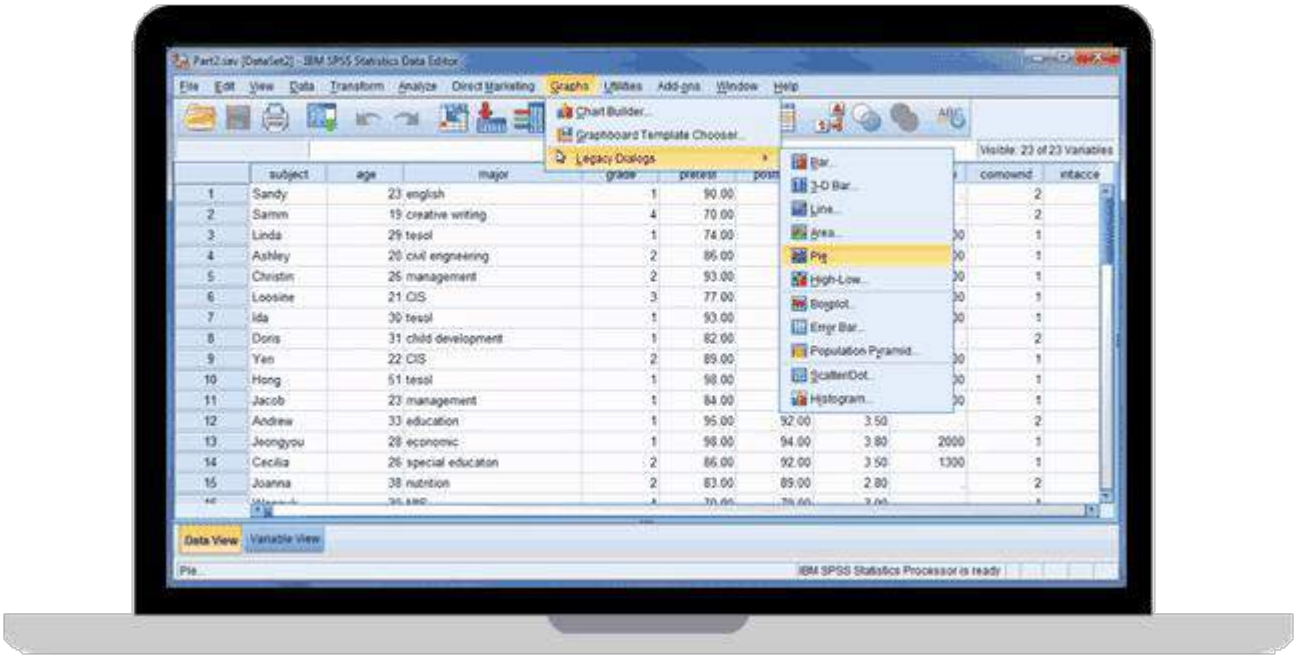
STORAGE

- Keep documents in one safe place organized
- Secure documents (lock and key)
- Keep master list with identifiers separate
- Network drive storage (routine back ups)
- Special electronic storage if HIPAA identifiers
- Know the retention policy (when to destroy records)

ANALYSIS

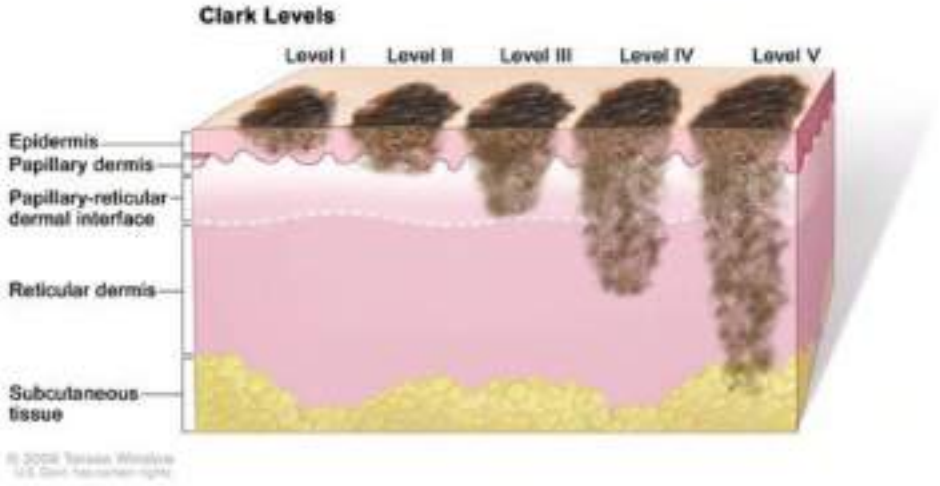
- There are alternatives to Excel!
- Get help!

- Consider:
  - SAS
  - SPSS
  - STATA
  - R



VARIABLES

- Continuous (e.g., HbA1c)
- Discrete (e.g., number of live births)
- Categorical
  - Nominal – no order
  - Ordinal – has order melanoma)



HYPOTHESES

- What are we trying to prove here?
- Null hypothesis (H_0) negative/default
  - No difference in prevalence of breast cancer between Chinese and American women.
- Alternate hypothesis (H_A) research
  - There is a difference in the prevalence of breast cancer between Chinese and American women.

GRANT WRITING

WHY WRITE A GRANT?

- You need money/resources for:
  - Statistician, data manager, research assistant, materials, participant incentives, IT
- If it is low-cost, you probably don’t need it.
- But you probably should know something about it.

GRANT COMPONENTS

- Overview, objectives, aims
- Background, needs assessment, rationale
- Personnel and environment
- Design and methods
- Budget and justification
- Timeline
- Outcomes
- References

YOUR IDEA

- Compelling
- Original (check the literature – this is your background)
- Significant
- Address problem worth addressing (question worth answering)
- Clear
- Attainable by methods
- Feasible with time and resources
- Confirm with mentors and advice on funding source

“Agreed. We fund only those proposals we can understand.”

PRESENTATION

SHARING SCIENTIFIC DATA

- Abstract
- Poster presentation
  - Scholarly Activities Day!
- Oral presentation
- Written manuscript

ABSTRACTS

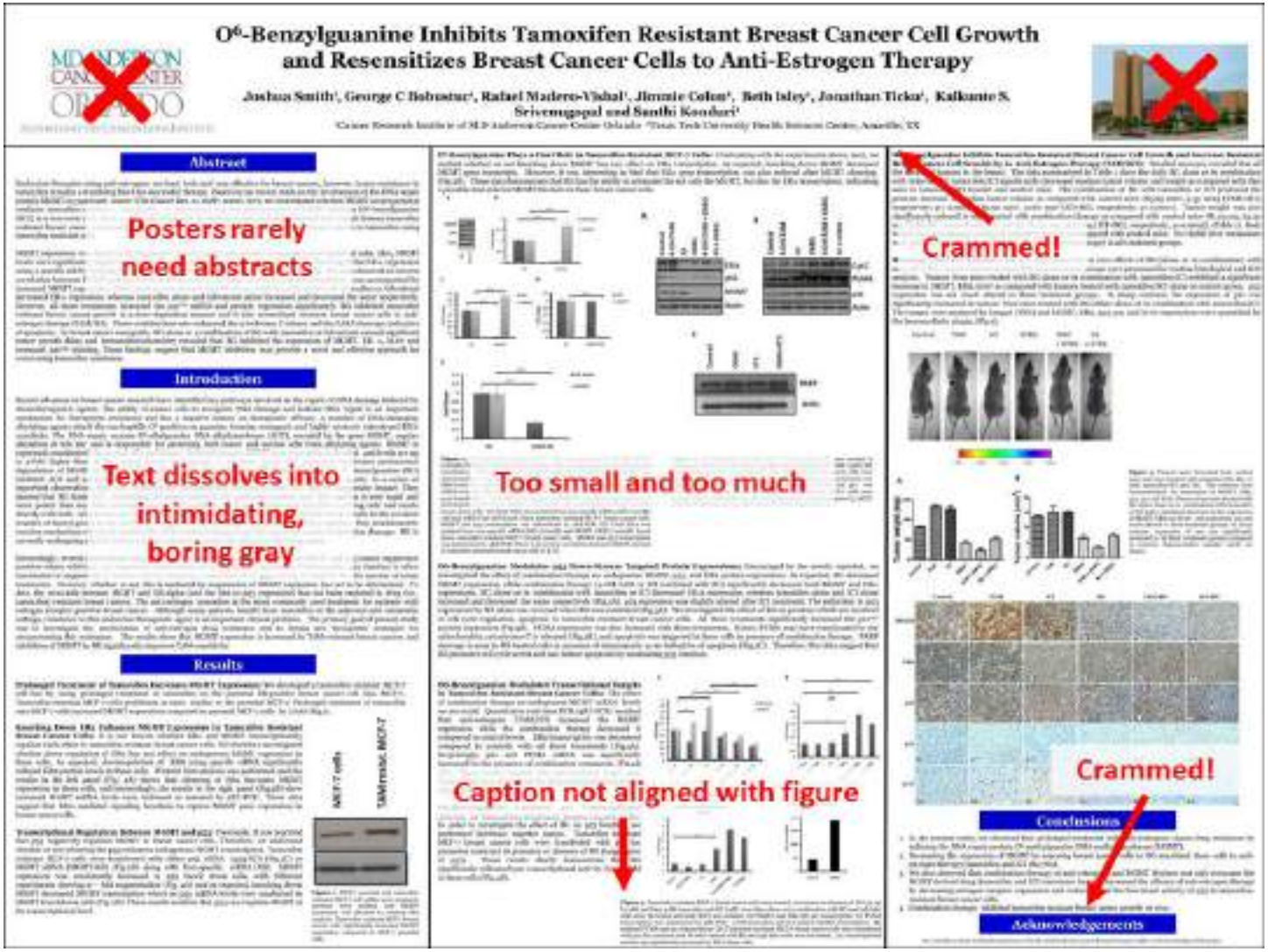
- Check the call for abstracts early!
  - Months before the meeting
- Regional meeting acceptance easier than national/larger
- Be efficient and descriptive
- Get examples!

POSTERS

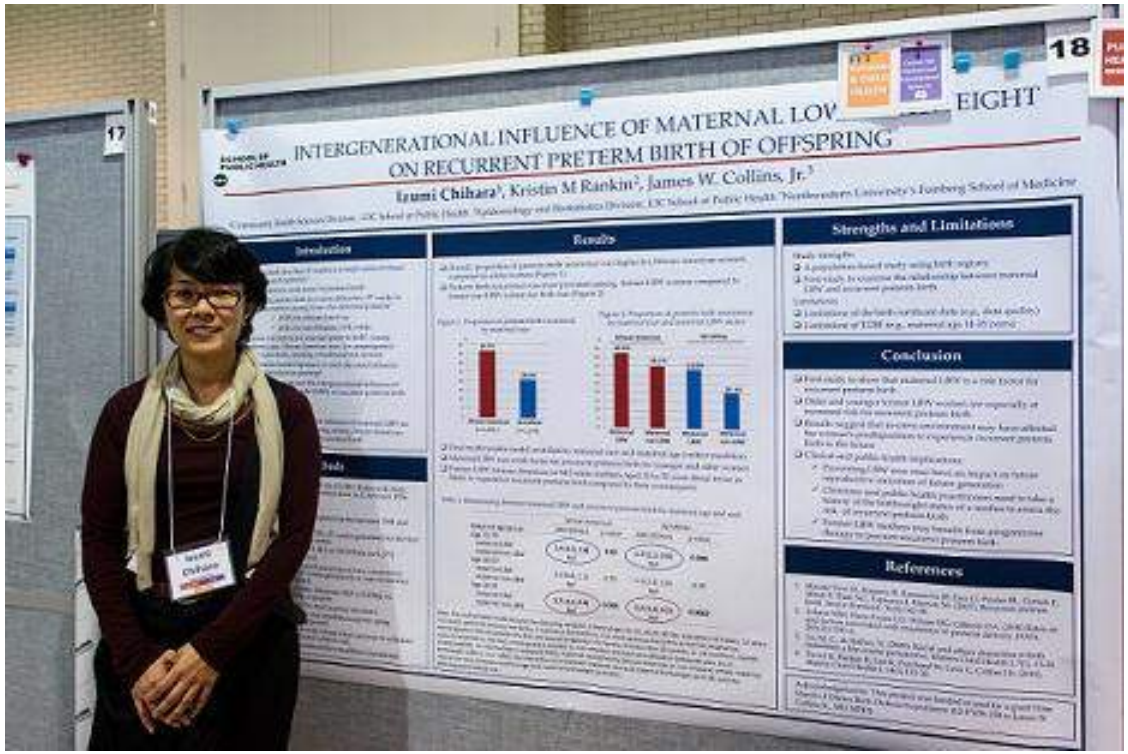
- Keep it Simple S****** (KISS)
- Clear, succinct – understood in < 1-2 minutes
- Follow guidelines for size

o Bullet points preferable

- Make sure text easy to read
- Get examples/templates!


O⁶-Benzylguanine Inhibits Tamoxifen Resistant Breast Cancer Cell Growth and Resensitizes Breast Cancer Cells to Anti-Estrogen Therapy
Joshua Smith, George C Balabanov, Rafael Madero-Vidal, Jimmie Colon, Beth Isley, Jonathan Ticku, Kalkunte S. Srivenugopal and Sunthi Kovduri
Abstract
Introduction
Results
Conclusions
Acknowledgements
Posters rarely need abstracts
Text dissolves into intimidating, boring gray
Too small and too much
Caption not aligned with figure
Crammed!
Crammed!

EXAMPLE POSTER



MANUSCRIPTS

- Get examples!

- Guidelines on what to include:

• RCT	CONSORT
• Observational studies	STROBE
• Systematic reviews	PRISMA
• Quality improvement	SQUIRE

DOM RESOURCE

http://dom-drupal.med.uic.edu/drupal