Seminar 3 Lecture

"CTS Research Project **Implementation**"

Year 1 (2012-13)

Clinical and Translational Science (CTS) Initiative

University of New England

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Outline

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2. CTS Study Implementation (Hulley and Cummings chap 14-19)
   - Chapter 14: Addressing Ethical Issues (Ross 1Nov12)
   - Chapter 15: Designing Questionnaires and Interviews (Ross 1Nov12)
   - Chapter 16: Data Management (Li 1Nov12)
   - Chapter 17: Implementing the Study and Quality Control (Li 1Nov12)
   - Chapter 18: Community and International Studies (Ross 1Nov12)
   - Chapter 19: Writing and Funding a Research Proposal (You 8Nov12)

1. Recap Lecture 2

In Lecture 2 of this year's Faculty seminar we discussed CTS Study Designs, highlighting Hulley and Cummings

- Chapter 7: Designing a Cohort Study
- Chapter 8: Designing Cross-Sectional and Case-Control Studies
- Chapter 10: Designing a Randomized Blinded Trial
- Chapter 12: Designing Studies of Medical Tests
  Chapter 13: Utilizing Existing Databases

To recap, here is a slide or two per section of Lecture 2:

Cohort Studies (H&C Chapter 7)

Cohort Studies follow groups over time.

- Two purposes:
  - To describe the occurrence of outcome/s over time
  - To analyze the associations between predictors and outcomes
- Two types:
  - Prospective cohort studies: Investigator defines sample, measures predictors, then after a follow-up period measures outcomes.
  - Retrospective cohort studies: same design but outcomes have already occurred at time of study.

Cohort Studies (H&C Chapter 7)

Prospective Cohort Study Strengths

1. Good to assess incidence (N new cases of X or Y from T1 to T2)
2. Helps to identify potential causes of X or Y
3. Establishes time sequence and prevents predictor measurement from being biased by foreknowledge of outcome
4. Allows more complete and accurate measurement of variables than in retrospective study, e.g. using medical records

Prospective Cohort Study Weaknesses

1. All observational designs: causation hard to infer, interpretation is difficult due to the influence of (unmeasured) confounders (ch 9)
2. Inefficient (therefore > cost) for studying less common outcomes which occur infrequently enough so that large numbers of people must be followed for long time periods to observe enough outcome to produce meaningful results, e.g. breast cancer

Cohort Studies (H&C Chapter 7)

Retrospective Cohort Studies Strengths

1. Same as 1 and 2 for Prospective Cohort Study, plus
2. Retrospective studies less costly and time-consuming: subjects assembled, measurements are made already.

Retrospective Cohort Studies Weaknesses

1. Investigator has limited control over sampling approach taken and the nature and quality of predictor and outcome variables and their measurement
2. Data may be incomplete, inaccurate, or measured inappropriately for the research question.
3. Possible only when adequate data on risk factors and outcomes are available on cohort of subjects already

Cross-sectional and Case-Control Studies (H&C Chapter 8)

Cross-sectional Studies

- Investigator makes all measurements on single occasion within a short time period; s/he draws a sample from a population, looks at associations of variables within that sample, designates plausible (e.g. from the literature) predictor and outcome variable relationships

Case-Control Studies

- Investigator works backward; s/he samples a patient population with the outcome (cases) and without (controls), then compares level of predictor variables in each to establish association and thus possible causality.

Cross-sectional and Case-Control Studies (H&C Chapter 8)

Cross-sectional Studies

- not longitudinal thus cannot estimate incidence (proportion of population who *get* a disease or condition over time)
- can be used to estimate population prevalence (proportion who *have* a disease or condition at time point)
- useful to health planners who need to allocate resources to care for that population and clinicians who need to estimate likelihood that a patient has that disease or condition
- used also to estimate cumulative incidence, i.e. prevalence of those who have ever done something (e.g. smoked) or ever had something (e.g. a disease or condition)

Cross-sectional and Case-Control Studies (H&C Chapter 8)

Cross-sectional Study Strengths

- no waiting for the outcome to occur, therefore fast, inexpensive, no Loss-to-follow-up
  - can be made the first step in a cohort or intervention study at little added cost
  - results may be used to define baseline demographic or clinical characteristics of a study group and to identify interesting cross-sectional associations

Cross-sectional Study Weaknesses

- difficulty establishing causal relationships
- impractical in studying rare disease or condition w/ sample of general population , e.g. stomach cancer @1 in 10,000

Cross-sectional and Case-Control Studies (H&C Chapter 8)

Case-Control Studies

- retrospective by nature, used to compare risk factors on the disease/no disease population axis and disability/no disability axis of those with disease
- provide descriptive information on characteristics of the cases and estimates of the strength of association (odds ratio) between predictor variables and disease present or absent
- do not provide disease incidence of prevalence estimates because the proportion of study subjects with disease is determined by how many cases and how many controls Investigator chooses to sample, not by proportions in the population

Cross-sectional and Case-Control Studies (H&C Chapter 8)

Case-Control Study Strengths

- rapid, high-yield information from relatively few subjects
- Used for hypothesis generation due to the retrospective approach taken and for examining large number of predictors

Case-Control Study Weaknesses

- no direct way to estimate disease incidence/prevalence
- one outcome studied (because presence or absence of the disease was how both samples are drawn) compared to any number studies by Cohort and Cross-sectional Studies.
- susceptibility to bias due to separate sampling of cases and controls (sampling bias) and retrospective measurement of predictor variables (differential measurement bias)

Randomized Blinded Trial (H&C Chapter 10)

Randomized Blinded Trial: implement intervention > observe outcomes

- Stepwise: Investigator selects sample from the population, measures baseline variables, randomizes participants, applies intervention (include blinded placebo if possible), measures outcomes during follow-up (blinded to group assignment)

RBT Strengths

- assignable causality: randomly assigning the intervention can eliminate influence of confounding variables
- blinding administration of the intervention can eliminate possibility that observed intervention effects are due to differential use of other treatments in treatment and control groups or to bias in ascertaining or adjudicating outcome

Randomized Blinded Trial (H&C Chapter 10)

Randomized Blinded Trial Weaknesses

- Trials are expensive, time-consuming, pose narrow research questions, can expose participants to harm. Accordingly
  - trails should be conducted on mature research questions when observational studies and other lines of evidence suggest that stronger evidence is required and that the intervention will be safe and effective
  - though a clinical trial design is not always indicated (e.g. when a very long-term effect of a predictor on outcome is in question), evidence based on conducting a trial should be obtained whenever possible

2. CTS Study Implementation

CTS Study Implementation (Hulley and Cummings chap 14-19)

- Chapter 14: Addressing Ethical Issues (Ross 1Nov12)
- Chapter 15: Designing Questionnaires and Interviews (Ross 1Nov12)
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Addressing Ethical Issues
(H&C Chapter 14)

Human subjects = Ethical issues. Why?

- Answer: Risk, Inconvenience to subjects

Guiding principles

1. Respect or persons, thus informed consent and the requirement of confidentiality
2. Beneficence, thus research design must be sound and risk (physical, psychosocial) acceptable relative to benefit; thus screenings out of participants, monitoring those in course
3. Justice, thus research burden/benefit to be distributed fairly
   - vulnerable populations especially must be protected, may not be capable of informed choice to participate
   - access to possible research benefits must be equitable: women, children, ethnic minorities to be represented or justify why not

Addressing Ethical Issues (H&C Chapter 14)

Federal regulations for research on human subjects

- aim to assure ethical treatment, apply to all funded federally research and to research submitted to the U.S. FDA
- enlist universities in ensuring faculty and staff compliance
- define research as "systematic investigation designed to contribute to generalizable knowledge"
- define human subjects as living individuals from whom I. obtains "data through intervention or interaction with the individual" or through "identifiable private information" that
  - a person can reasonably expect is not being observed or recorded
  - has been provided for specific purposes and that "the individual can reasonably expect will not be made public (e.g. a medical record)"

Info is identifiable if subject identity "may be readily ascertained by the investigator or associated with the information."

Addressing Ethical Issues (H&C Chapter 14)

The Office for Human Research Protections (OHRP) (at http://www.hhs.gov/ohrp/), which publishes full text of all federal regulations,

- "provides leadership in the protection of the rights, welfare, and wellbeing of subjects involved in research conducted or supported by the U.S. Department of Health and Human Services (HHS). OHRP helps ensure this by providing clarification and guidance, developing educational programs and materials, maintaining regulatory oversight, and providing advice on ethical and regulatory issues in biomedical and social-behavioral research."

Federal regulations protect human subjects by requiring 1) Institutional Review Board (IRB) approval, 2) Informed consent

Addressing Ethical Issues (H&C Chapter 14)

1. Institutional Review Board (IRB) approves a research study when it determines that 1) risks to human subjects are minimized, 2) risks are reasonable in relation to anticipated benefits and to the importance of the expected knowledge, 3) participant selection is equitable, 4) informed consent is sought from participant or legally authorized rep, and 5) confidentiality is adequately maintained. IRB system is **decentralized**, therefore

- each IRB employs forms, procedures, guidelines of its own
- there is no appeal to any higher body: a multicenter study may be approved by one, not approved by another IRB, thus require discussion or protocol modifications to be resolved

There are reasons why IRB approval should be considered only the minimum ethical standard for conducting a research study.

Addressing Ethical Issues
(H&C Chapter 14)

2. Informed Consent

- written consent forms are required to document that informed consent involving discussion between an investigator and subject has occurred
- forms must contain all information pursuant to the provisions of (OHRP) 45 CFR §46.116 of **"General requirements for informed consent" ('Common Rule')** http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.116, from the http://www.hhs.gov/ohrp/humansubjects/commonrule/
- your IRB will likely have consent language and forms that they want you to use and may require even more information to be disclosed than the Common Rule discloses.

Addressing Ethical Issues (H&C Chapter 14)

2. Informed Consent. Ethically, a participant must

- Be informed: bottom line is whether the participant understands or not the risks and benefits of the research project; therefore avoid technical jargon and complicated sentences, employ multiple ways of explaining content, gauge whether participant has actually understood the information.
- Consent voluntarily: therefore, minimize chance for coercion or undue influence, e.g. excessive payment, power differential between inviter/invited, clarify that declining to participate will not in any way compromise medical care; always ensure that participant may withdraw from the study at any time.

NB: Know when informed consent is and is not required (Table 14.3)

Addressing Ethical Issues (H&C Chapter 14)

2. Informed Consent

- legally authorized representative is required when participant not capable of giving consent; IRB will want to know if the research question can be answered otherwise
- provision to maximize benefit/minimize risk may mean to exclude those most susceptible to, and/or monitor for, adverse events, and train staff accordingly
- breach of confidentiality is always a serious risk: may lead to stigmatization or discrimination, e.g. studies of mental illness, alcohol abuse, sexual behaviors; risk may be addressed by:
  - Coding research data, locked file cabinets, protecting or destroying subject identifier keys, limiting staff access to identifiers
- NB: confidentiality may be overidden in some instances, e.g. child abuse, certain infectious diseases, threat of violence

Addressing Ethical Issues (H&C Chapter 14)

Research Participants Requiring Added Protection

- protections are to be tailored to type of vulnerability, e.g.
  - Impairment, cognitive or communicative
  - Power differences, vulnerability of the institutionalized, imprisoned, e.g. nursing home residents might feel pressure to participate; likewise a physician's patients, especially those w/ few health care alternatives
  - Socioeconomic disadvantages, e.g. people may feel more pressured to undertake risk and to participate (in order to be paid, get examined or screened) than if their income were higher; or they may not be educated or health literate enough to understand information about the study or to exercise independent judgment
- special federal regulations obtain for specific vulnerable populations including children, prisoners, pregnant women, fetuses, and embryos (H&C p. 232)

Addressing Ethical Issues
(H&C Chapter 14)

Responsibilities of Investigators

- Altering research data and/or enrolling ineligible participants constitute punishable misconduct; lead to false conclusions; and undermine public trust hence public support for federal research funding. Federal government defines misconduct as
  - Fabrication: making up results and recording or reporting them
  - Falsification: manipulating research materials, equipment, procedures, or changing or omitting data or results so that the research record misrepresents actual findings
  - Plagiarism: appropriating another person's ideas, results, or words without appropriate attribution
- This definition excludes other wrong acts (dealt with at the institutional level), e.g. double publication, failure to share research materials, sexual harassment.

Addressing Ethical Issues (H&C Chapter 14)

Responsibilities of Investigators

- Alleged research misconduct is addressed jointly by the federal funding agency and the investigator's institution,
- Punishment for proven research misconduct can involve suspension of the grant, debarment from future grants, other administrative, criminal, and civil procedures
- For issues around authorship and conflicts of interest see H&C pp. 233-35, including how to keep interests in check by:
  - blinding investigators to the intervention a subject receives
  - appointing an independent Data Safety Monitoring Board (DSMB)
  - peer reviewing grants, abstracts, manuscripts
  - in pharm trials, giving the investigator direct control over primary data and statistical analysis and freedom to publish findings no matter

Addressing Ethical Issues (H&C Chapter 14)

Ethical Issues specific to certain Types of Research

- Randomized clinical trials:
  - What if equipose, the assumption behind randomizing to test and control, is doubtable? It is unethical to withhold effective treatment.
  - What if a treating physician is able to offer that test treatment? It would unethical to expose a patient to the control condition, i.e. to withhold therapy known to be effective.
  - Dilemmas around control groups are heightened when research subjects have limited access to care and may see the research project as the only way to receive adequate treatment
  - It is unethical to continue a trial when compelling evidence comes out that one arm is more effective or when it emerges that the research question can no longer be answered due to low enrollment, high LOS, or too few outcome events, all matters which a DSMB can monitor.
  - Chapter 18 discusses added ethical dilemmas around trial work in developing countries

Addressing Ethical Issues (H&C Chapter 14)

Ethical Issues specific to certain Types of Research

- Previously collected specimens and data, e.g. DNA testing on biobanked specimens linked to clinical data may lead to id'ing genes that heighten disease risk, require no further collection of samples, and involve no physical risks to participants; but:
  - Consent for future studies is problematic since their nature cannot be known and participants may object to using samples in specific ways
  - Breaches of confidentiality may occur leading to stigma, discrimination
  - There is the record that U.S. genetics research has been used for eugenics abuse including forced sterilization
- Thus with collection of biospecimens, consent forms need to allow participants to a) to agree to or refuse broad categories of present or future research using their specimens, b) know whether their id's will be shared with other researchers and c) know whether discoveries may be patented and commercialized.

Addressing Ethical Issues (H&C Chapter 14)

Paying Research Participants

- Participants in clinical research are often paid for time and effort and reimbursed for out-of-pocket expenses such as transportation or childcare; compensation may be needed to enroll and retain participants; often, the greater the inconvenience or risk the higher the payment; but
  - Such incentives raise ethical concerns about undue inducement
  - E.g. poorer persons may be more induced to participate in riskier research by such higher compensation
  - One solution is that participants be compensated for actual time and expense and at an hourly rate for unskilled labor.

Designing Questionnaires and Interviews (H&C Chapter 15)

Designing Good Instruments: Validity of research results depends on quality of instruments!

- Open-ended questions are for when participants' own words count, e.g. *What habits do you believe increase a person's chance of having a stroke?* Participant is free to answer with fewer limits, but
  - Response may be less complete than w/ discrete list of answers
  - OE questions require qualitative methods or special programs to code/analyze responses, meaning >time, expense, subjectivity
- Open-ended questions facilitate understanding of a concept from the respondents' p.o.v. in the exploratory phase of question design; then recurrent phrases and words can become the basis for more structured items in a later phase.

Designing Questionnaires and Interviews (H&C Chapter 15)

Designing Good Instruments

- Closed-ended questions are for when measures need to be standardized: respondents choose between preselected answers, e.g. *Which of the following do you believe increases the chances of having a stroke? (check all that apply)*
- Closed-ended questions are quicker and easier to answer, and easier to tabulate/analyze; but
  - CE questions are leading, leave respondents no room to give their own, potentially more accurate answers
  - The answer set may not be exhaustive (i.e. include all possible options) hence include "Other (please explain)" or "None of the above" options
  - Answer choices may not be mutually exclusive (categories may overlap)

Designing Questionnaires and Interviews (H&C Chapter 15)

Designing Good Instruments

- Closed-ended questions
  - Avoid "Mark all that apply" (an unmarked item may represent an answer that does not apply or an overlooked item)
  - Rather use: "Mark each possible response either 'Yes' or 'No'" and add a "Don't know" option for each.
  - Visual analogue scale (VAS), using lines or other drawings, asks respondent to mark a point along a (10 centimeter) continuum (to facilitate coding) between (what must be the) extremes that represents their answer, e.g. for pain:

    None _____ Unbearable
  - VAS may be more sensitive than ratings based on categorical list of adjectives. An alternative is to give numbers across the continuum (easier to score)

Designing Questionnaires and Interviews (H&C Chapter 15)

Designing Good Instruments

- Formatting guidelines
  - Questionnaires: at start, describe purpose of study, how data will be used; same on an interview as part of obtaining consent.
  - Instruments must have instructions specifying how they are to be filled out
    - makes accurate, standardized responses more likely on self-admin q's and on forms interviewers use to record responses
    - it helps to provide a simple example of how to complete a question (see Example 15.2)
  - To aid an instrument's flow, group questions by subject areas and introduce each area with a heading or short description
  - Begin with emotionally neutral q's (e.g. name); move to more sensitive q's; end w/ q's on personal characteristics (e.g. income, sexual function)

Designing Questionnaires and Interviews (H&C Chapter 15)

Designing Good Instruments

- Formatting guidelines
  - Introduce same timeframe questions with, for example, "During the past two weeks, how many times have you …," instead of repeating the same timeframe in each question
  - Visual design matters: if too complex, r's or interviewers may skip questions, give wrong information, even refuse to complete
  - Choose roomy format: do more pages than fewer cramped ones
  - Space response scales well to avoid accidental markings
  - Give space for large handwriting for open-ended q responses
  - Use large type for elderly and for those with visual problems
  - Precede possible answers to closed-ended q with check box
  - Use branching question format for complex question, starting with a "screener," e.g. Do you smoke?
  - Consider scanning questionnaire forms technology

Designing Questionnaires and Interviews (H&C Chapter 15)

Designing Good Instruments

- Wording
  - To increase validity and reproducibility of responses, make q's simple, free of ambiguity, and invite accurate, honest responses. Questions should be clear, simple, neutral (H&C pp. 245-46)
- Time Frame
  - Goal is to ask about the shortest recent segment of time that accurately represents the characteristic over the whole time period of interest; the best length of time depends on the characteristic (H&C pp. 246-47).
  - Diaries (paper, electronic) may be a more accurate approach to track events, behaviors, or symptoms that happen episodically (e.g. falls) or vary from day to day (e.g. pain); valuable when event time or duration matters or occurrence is easily forgotten

Designing Questionnaires and Interviews (H&C Chapter 15)

Designing Good Instruments

- Pitfalls to avoid (great examples: H&C pp. 247-48) include Double-barreled questions, Hidden assumptions, Mismatched question and answer options.
- Scales and Scores to measure Abstract Variables
  - E.g. HRQoL, requires multiple not single item measures, i.e. a series of questions organized into a scale
  - Multi-item scales compared to a single item can increase range of possible responses, e.g. scores ranging 1-100 instead of 1-5
  - Likert scales, commonly used to quantify attitudes, behaviors, and domains of HRQoL, give respondents a list of statements or questions to respond to along points from Strongly agree to Strongly disagree,
  - Each item response is given a point number and scoring is additive (assuming equal weight per item, items measure same characteristic)

Designing Questionnaires and Interviews (H&C Chapter 15)

Designing Good Instruments

- Scales and Scores to measure Abstract Variables
  - Internal consistency of a scale is tested statistically using Chronbach's alpha statistic or the like calculated from correlations between scores on individual items; values above 0.70 are acceptable, 0.80 or more excellent; below 0.70 means some of the items may not be measuring the same characteristic.
- Creating New Questionnaires and Scales
  - When no adequate one exists: ranges from creating one missing but important item to measure a minor variable (*How frequently do you sneeze?*) to developing/testing a new multi-item scale for measuring a primary outcome (e.g. spiritual health status) for a major study
  - Multi-item scale construction requires a systematic approach and may take years from first draft to final product (see Example 15.3 and surrounding paragraphs)

Designing Questionnaires and Interviews (H&C Chapter 15)

Steps in Assembling the Questionnaire or Interview Instrument

1. Compose variables list of info to be collected, concepts to be measured; label each by function, e.g. predictor, outcome, or confounder
2. Collect existing measures whether single questions or full instruments; line up variables list and corresponding measures; create alternative instruments list for major variables gleaned from other investigators, reviews of instruments in books, articles, e-sources, e.g. search on "health outcomes questionnaires;" consider "SF" versions of long instruments
3. Compose first draft of instrument: include everything and format it as final draft will be formatted

Designing Questionnaires and Interviews (H&C Chapter 15)

Steps in Assembling the Questionnaire or Interview Instrument

4. Revise taking respondent role, seeking out words and phrases prone to being misunderstood
   - for non-validated q content: replace abstract words and jargon with simple, concrete words, split complex questions in two; have these reviewed by colleagues expert in questionnaire design
5. Shorten instrument set by resisting kitchen sink, appreciating respondent burden, thinking ahead to analysis and reporting phase
6. Pretest to clarify, refine, and time the instrument; to ascertain that key variables actually vary (!); and to test validity and reproducibility of the instrument

Designing Questionnaires and Interviews (H&C Chapter 15)

Steps in Assembling the Questionnaire or Interview Instrument

7. Validate instrument by assessing it for accuracy (validity) and precision (reproducibility)
   - Choose questions that have face validity for gauging characteristics of interest
   - Establish content validity and construct validity
   - Compare new instrument with gold standard approaches to measuring the characteristic of interest
   - Test predictive validity by comparing instrument's predicted to actual outcomes
   - Test instrument responsiveness by applying it to patients before and after treatments that are shown to be effective by other measures

NB: Validating a new instrument is time consuming and expensive, worthwhile only when existing instruments are inadequate for research question or population under study

Designing Questionnaires and Interviews (H&C Chapter 15)

Administering the Instruments

- Of the two approaches to collecting data about attitudes, behaviors, knowledge, health, and personal history,
  - Questionnaires, are self-administered by respondent, are more efficient and uniform (standardized) way to administer simple questions and are less expensive
  - Interviews, are conducted by an interviewer, are better for collecting answers to complicated questions that require explanation or guidance and for assuring complete answers; may be necessary when respondents have lower reading or cognitive ability; but they ere more time-consuming and costly and responses are more subject to interviewer interference
- Questionnaires are more strictly standardize-able than Interview instruments

Designing Questionnaires and Interviews (H&C Chapter 15)

Administering the Instruments

- Interviewer skill substantially affects quality of responses
  - Standardizing interview procedure across interviews maximizes reproducibility, e.g. uniform wording of questions, delivery of non-verbal signals, tone; this requires training and practice
  - Questions read verbatim must be worded in simple, common phrases to be effective
  - Follow-up probes should have standardized placement, wording
  - Interviews may be conducted in-person or by telephone
    - Computer assisted telephone interviewing (**CATI**) cuts cost
    - Interactive voice response (**IVR**) replaces interviewer with computer-generated questions that collect subject's responses by means of telephone keypad or voice recognition
  - In-person needed when physical exam or observing participants is required, or subjects lack a phone, or are with elderly or ill

Designing Questionnaires and Interviews (H&C Chapter 15)

Administering the Instruments

- Questionnaires may be administered in person, by mail or e-mail, or web-site
  - In person allows researcher to explain questionnaire before start
  - If research requires participant to visit the research site, e.g. to be examined, questionnaire may be sent in advance and checked for completeness at visit
  - E-mailed have advantages over mailed questionnaires--including off-clinic means to report data, direct entry of data into databases, automatic checking for missing and out-of-range data and correction before data are entered electronically—but they depend on participant access to and familiarity with the Internet

Community and International Studies (H&C Chapter 18)

Clinical Research may be conducted "Out There"

- Community research takes place outside university and medical center settings and is designed to meet needs of the community where it is conducted
- International research in poorer countries can involve creating a research program from scratch

Each usually involves collaboration with local investigators, which can be both

- productive and important for solving longstanding or emerging health problems, and
- challenging due to physical distance, cultural differences, funding constraints

Community and International Studies (H&C Chapter 18)

Why Community and International Research?

- Community research addresses research questions that have to do with specific settings and populations; community research priorities differ from those of medical centers
- The documented 10/90 gap in health research (just 10% of global research investment goes to 90% of global disease burden) amply justifies collaborative work that addresses low- and middle-income countries' health problems
- Local Questions may be better answered with local data, not national or state level, e.g. on disease burden or risk factors; intervention success may vary by setting, e.g. condom promotion; finding approaches that suit local needs requires local research (applies even to pathophysiology of disease)

Community and International Studies (H&C Chapter 18)

Why Community and International Research?

- Greater Generalizability of community research, e.g. document-ably, back pain presents differently at PC provider vs. Hospital sites
  - Hence practice-based research networks have arisen in which providers study research questions of mutual interest, e.g. carpal tunnel syndrome presenting in PC practices: results indicate that the PC-based and Medical center-based therapies respectively chosen (conservative vs. surgical) differ markedly!
  - Likewise, research findings from one country are not always generalizable to another, and by the same token findings from one country may generalize better to that country's displaced populations in another country.

Community and International Studies (H&C Chapter 18)

Why Community and International Research?

- Local Capacity Building results from conducting community-based research when questions of local importance are addressed rather than those strictly of medical center-based researchers oriented to their daily practice and to what they think matters scientifically or economically.
- Community participation affects what information is collected in a study and has ripple effects by
  - raising research standards,
  - building local researchers' skills and confidence as full participants in scientific work and capacity to create not just consume knowledge
  - bringing intellectual and financial resources into the community

Community and International Studies (H&C Chapter 18)

Community Research: two approaches

- Working solo
  - Start simple, i.e. not with a RCT but with small descriptive studies that yield useful local data, e.g. condom use among young men
  - Comparative advantage, i.e. what questions can you answer better than others, e.g. regarding populations which are unique to your area
  - Network, i.e. with scientists elsewhere studying same questions, who may be willing to review a draft of a research protocol, a questionnaire or a manuscript, e.g. a scientific conference is a good place to network
- Working collaboratively
  - Top-down model: studies, e.g. multi-center trials, that originate in an academic center but involve community investigators in subject recruitment and study conduct (benefit: built in senior collaborators)
  - Bottom-up model: studies where established investigator guides local I's and communities or international researchers in developing their own research agendas (but this is time-consuming and expensive)

Community and International Studies (H&C Chapter 18)

Community Research: two approaches

- Working collaboratively (cont.)
  - But community researchers can offer established Investigators incentives, e.g. access to subjects, intrinsic scientific merit of community study, co-authorship, satisfaction mentoring less experienced I's in worthy endeavor
  - Ideal option is to establish a long-term partnership between the community and an established research institution to conduct both top-down and bottom-up projects
    - E.g. Framingham Nurses Study

Community and International Studies (H&C Chapter 18)

International Research raises the same issues that come with all research collaboration and adds further challenges, including the Barriers of distance, language, and culture (p. 295) and Issues of funding (pp. 295-96) as well as Ethical issues (pp. 296-99), the same that apply to all research (chapter 14) plus the enhanced potential for exploitation that comes with international work

- What is the comparison group when testing a new treatment in a poor country where even conventional treatment is unavailable? Anti-retrovirals drug studies in poor countries have raised this question.
- What about testing treatments that, even if proven effective, are not economically accessible to the host country's population?
- Why is the study being conducted in a poor country to begin with? To help the people of that country? or to avoid obstacles to doing the research in a rich country?

Community and International Studies (H&C Chapter 18)

International Research

- Ethical Issues (cont)
  - Ethical Review Boards in both countries, for these and related reasons, need to approve studies conducted in poor countries but directed and funded from elsewhere. But
    - Poor country review boards are often weak, nonexistent, or manipulable
    - Rich country review boards can be ignorant or insensitive to issues involved in international research
  - Poor country collaborators may be mistreated: issues include Ownership of data generated, Permissions to conduct and publish results, First authorship, Poor country investigators' needs for manuscript preparation support, Time commitments on both sides

Community and International Studies (H&C Chapter 18)

International Research

- Ethical Issues (cont)
  - Local economic and political realities (as when a poor country's PM closes an approved HIV prevention study) or Local research capacity (as when local researchers, or the junior level researchers among them, are effectively excluded from attending international conferences where results are reported) can raise ethical issues (see Table 18.2 "Strategies to Improve International collaborative research")
- Risks and Frustrations confronting researchers who would work in poor countries include
  - Bureaucratic obstacles, Natural and Manmade Catastrophe, Health Risks, Safety Risks, Obstacles to Applying Findings

Community and International Studies (H&C Chapter 18)

International Research

- Rewards of conducting health research in poorer countries
  - Research need is great ("10/90" gap)
  - Investigator may have far greater impact on people's lives than by "playing it safe" at home
  - Impact comes from research itself but also from fostering international collaboration per se
  - Though funding is scarce, it goes further abroad

And:

  - There are many unintended consequences and unexpected lessons that occur which enrich an investigator's career and life

Data Management (H&C Chapter 16)

Overview of Data Management

- Managing information
  - Spreadsheets
  - Database
  - Data Warehouse
- Working with information
  - Data entry
  - Querying
  - Monitoring
  - Analysis

Data Management (H&C Chapter 16)

Data Tables

- Structuring of data is important
  - Rows vs. columns
  - Single table vs. multiple (relational database)
- Data Dictionary
  - Contains the explicit definitions for each field
  - Name, type of data, description, range of values
  - See example

Data Management (H&C Chapter 16)

Data Entry

- Methods
  - Paper forms → manual entry
    - Works for small studies
  - Machine-readable forms
  - Distributed data entry
  - Electronic data capture
- Coded responses vs. free text
  - Link back to data dictionary

Data Management (H&C Chapter 16)

Extracting Data (Queries)

- Organize, sort, filter, view, etc.
- Large dataset → analytical file
- Programs for those who don't know SQL
  - Microsoft Excel
  - Microsoft Access
  - JMP
- More advanced queries will require additional expertise

Data Management (H&C Chapter 16)

Identifying and Correcting Errors

- Identify missing data
- Examine outliers – does it make sense?
- Compare values between multiple sites

Data Management (H&C Chapter 16)

Other issues

- Data Analysis
- Confidentiality and Security
  - HIPAA
  - Certain electronic databases may not be HIPAA-compliant
  - Surveymonkey?

Data Management (H&C Chapter 16)

Final Thoughts

- Utilize a "backward design"
  1. Create empty data table shells (for publication)
  2. Conceptualize the data analytical file (rows, columns, codes, etc.)
  3. Set up the spreadsheet/database and create the data dictionary for each field
  4. Test and QA
  5. Follow steps in Chapter 17

Implementation and Quality Control (H&C Chapter 17)

Assembling Resources

- Space
- Research team
  - PI
  - Project director
  - Recruiter
  - Research assistant/clinic staff
  - Quality control coordinator
  - Data manager
  - Programmer/analyst
  - Statistician
  - Administrative assistant
  - Financial manager
  - HR manager

Implementation and Quality Control (H&C Chapter 17)

Study Start-up

- Pre-enrollment work
  - Finalize the budget
  - Administrative tasks
  - IRB approval
- Operations manual (Appendix 17.1)
  - Protocol
  - Policy and procedures
  - Data collection form

Implementation and Quality Control (H&C Chapter 17)

Finalizing the Protocol

- Pre-tests
- Pilot studies
- Protocol changes
  - Minor
  - Major
- Closeout

Implementation and Quality Control (H&C Chapter 17)

Final Thoughts

- As a PI conducting a small-scale study, you do many of these functions yourself and the process is less-formalized
- Larger studies require more manpower, and outside/additional help should be sought
- Studies utilizing existing data skip many of these steps