Evidence-Based Practice: What's The Deal? What are the Ethics?

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Learning Objectives:

- Explain the rational and ethical-legal implications of medical research and evidence-based practice.
- Describe research methods and the fundamentals of evaluating research and applying research findings to clinical practice.

Introduction

Evidence based medicine (EBM)

- Definition - "the conscientious, explicit and judicious use of current best evidence in making decisions about the care of the individual patient. It means integrating individual clinical expertise with the best available external clinical evidence from systematic research." (Sackett D, 1996)

Rationale of EBM for RCPs

- Applications to clinical practice
  - generating clinical practice guidelines
  - implementing therapeutics and medications that are effective and safe
  - implementing diagnostic procedures that are accurate and reliable
  - influencing change to more effective therapeutics and diagnostic tests

Rationale of EBM for RCPs

- Ethical implications - what are ethics of continuing with practices that have no evidence for effectiveness?
  - any research?
  - risks to patient?
  - costs?

Rationale of EBM for RCPs

- Examples of RC practices without evidence of effectiveness:
  - incentive spirometry
  - nebulized n-acetylcysteine
  - cool mist therapy

Rationale of EBM for RCPs

- Legal implications
  - patient injured because of failure to use evidence-based practice - professional liability
  - professional ought to know

Rationale of EBM for RCPs

- Example of RC practice with negative evidence:
  - large tidal volume for ALI/ARDS
  - mist tents

Barriers to evidence-based practice

- Lack of evidence
  - unethical to do the research; e.g., resuscitation efforts
  - uncommon circumstances
    - disease conditions
    - therapeutic applications
- Changing evidence - accumulation of research, often with conflicting results

Barriers to evidence-based practice

- Tradition (habit) - resistance to change
- Financial gain
- Failure to read research literature
  - lack of instruction on research
  - lack of motivation

Barriers to evidence-based practice

- Failure to believe research literature
- Arrogance - I'll do what I want!
- It's not my job!!

Research Concepts

Research concepts

- Causality
  - rationale for experimentation
  - doing 'a' (independent variable) causes 'b' (dependent variable)
- Spurious relationship
  - 'c' (confounding variable) affects relationship between 'a' and 'b'
  - commonly operational, especially in correlations

Research concepts

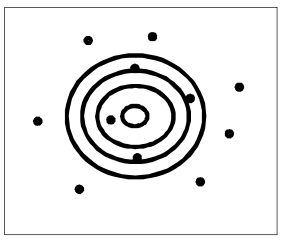
- Validity (accuracy)- measures what it purports to measure
  - internal validity of a study - within the confines of the study, the treatment produced the effect.
  - external validity - the treatment will produce the same effect within other contexts (generalizability)

Research concepts

- Reliability (precision) - measures consistently.
  - If replicated the study produces same results
  - unreliability ==> random error
  - reliability of study depends on amount of data; e.g., number of subjects.

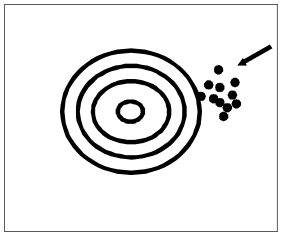
Research concepts

- Invalid and unreliable



Research concepts

- Invalid and reliable



Research concepts

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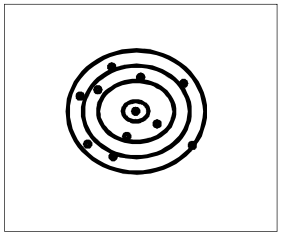

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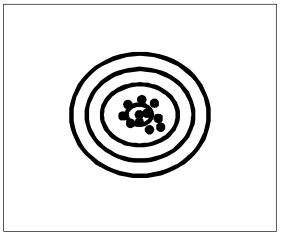

Research concepts

- Preventing bias
  - randomizing subjects - treatment assigned in manner to prevent bias
  - control groups - subjects receiving different or placebo treatment
  - blinding - researchers do not know which subject receives which treatment

Click for placebo TV
https://www.youtube.com/watch?v=QwZO9iBCVLk

Research concepts

- Preventing bias
  - multiple testing sites - increases likelihood that treatment works in more than one context - increases generalizability
  - statistical analysis - probability that effects did not occur accidentally

Research ethics

- All studies involving human subjects must receive approval from institutional review boards (IRB)
  - expedited reviews for minimal risk
  - exemptions for observations
- Human subjects of experiments must give informed consent
- Anonymity of subjects for all research must be enforced

Research ethics

- At predetermined intervals, effects of interventions are measured and experiment is stopped, if:
  - hazard of intervention is likely
  - benefit of intervention is too great to continue patients in control group.

Examples

- Tidal volumes for ALI/ARDS - it was considered unethical to continue large tidal volumes
- Aspirin for MI - it was considered unethical to deny aspirin to patients with history of MI

Evidence Sources

Information sources

- Personal experience - biased
- Textbooks - old information
- Magazines - biased
- Commercial news - biased
- Colleagues - their source?

Information sources

- Internet
  - reliability depends on specific source
  - some studies published on Internet before hard copy
- Original research reports
  - if you are serious about an issue, read these
  - time lag from completion to publication
  - multiple imperfections

Information sources

- Scientific meetings
  - often first dissemination method
  - most recent findings

Strength of cause-effect evidence

STRONG	Meta-analysis/Systematic review
	Multi-center randomized controlled trial
	Systematic review of non-RCTs
	Observational studies
WEAK	Case studies/anecdotal information

Meta-analysis of RCTs

- Definition - statistical combination of the results from all RCTs that address the same question.
- Systematic methods developed by Cochrane Collaboration

Meta-analysis of RCTs

- Strengths
  - increased statistical power
  - increased generalizability - trials conducted in different contexts
  - inexpensive, compared to trials
  - exempt from IRB review

Meta-analysis of RCTs

- Weaknesses
  - heterogeneity (differences) among trials make them not combinable
  - post-hoc analysis - data gathered before research proceeds (source of bias)
  - publication bias - not all trials are published
  - poor quality of primary trials - garbage in - garbage out

Example

- Rodrigo G, Pollack C, Rodrigo C, Rowe BH. Heliox for nonintubated acute asthma patients. Cochrane database of systematic reviews 2006.
  - 10 RCTs; 544 patients. The existing evidence does not support the administration of helium-oxygen mixtures to all ED patients with acute asthma.

Multi-center RCT

- Definition - clinical trial, conducted at several institutions, where subjects are randomized to comparison groups

Multi-center RCT

- Strengths
  - randomized - prevents several sources of bias
  - controlled - comparison groups
  - multi-center
    - increased generalizability
    - can recruit more subjects
  - Blinding adds strength

Multi-center RCT

- Weaknesses
  - very expensive
  - time consuming

Example

- Mercat A, et al. Positive End-Expiratory Pressure Setting in Adults With Acute Lung Injury and Acute Respiratory Distress Syndrome:

A Randomized Controlled Trial. JAMA. 2008;299(6):646-655.

  - In France; 37 intensive care units; 767 subjects. A strategy for setting PEEP did not significantly reduce mortality. It did improve lung function and reduced the duration of mechanical ventilation.

Randomized controlled trial (RCT)

- Definition - clinical trial with subjects randomized to comparison groups.
- Strengths
  - randomized - prevents several sources of bias
  - controlled - comparison groups
  - blinding increases strength

Randomized controlled trial (RCT)

- Weaknesses
  - may be small - statistical power concern
  - expensive
  - time-consuming
  - generalizability

Example

- Scolnik D, et al. Controlled delivery of high vs. low humidity vs. mist therapy for croup in emergency departments: a randomized controlled trial. JAMA 2006.
  - Canada. 140 pediatric patients with croup. This study does not support the use of humidity for moderate croup for patients treated in the emergency department

Systematic review of non-RCTs

- Definition - a synthesis of research literature that follows strict guidelines to prevent bias
- Methods developed by Cochrane Collaboration
- Strengths
  - control over bias
  - inexpensive
  - increased generalizability

Systematic review of non-RCTs

- Weaknesses
  - quality of primary trials
  - absence of primary trials
  - publication bias

Examples

- Bronchopulmonary hygiene physical therapy in bronchiectasis and chronic obstructive pulmonary disease: a systematic review. Heart & Lung. 2000 Mar-Apr;29(2): 125-35. Review.
  - 7 trials, poor quality, 126 subjects. Research is inconclusive.

Observational studies

- Definition - research wherein subjects are observed and variables of interest are measured.
- No manipulation of interventions
- Data are gathered
- Types:
  - case-control
  - survey

Observational studies

- Strengths
  - ethical to do when experimental research would not be ethical
  - less expensive - much data are already available
  - expedited IRB review, because there is no experimental manipulation - anonymity of subjects remains critical

Observational studies

- Weakness
  - less power than experiment for establishing cause-effect relationship

Examples

- Dongelmans DA, et al. Determinants of Tidal Volumes with Adaptive Support Ventilation: A Multi-center Observational Study. Anesth Analg 2008; 107:932-937
  - Observation in 3 Dutch intensive care units, 346 subjects. Tidal volume with adaptive support ventilation are dependent on the correctness of set body weight.

Anecdotes, case studies

- Definition - informal observational studies that report incidents, cases
- Purposes
  - communicating rare conditions, infrequently used interventions
  - instruction
  - may provide basis for formal studies

Examples

- Vihad B, Salerno DA, Marik PE. Lymphomatoid Granulomatosis: A Rare Cause of Multiple Pulmonary Nodules. Respir Care 2008.
  - Teaching case about rare occurrence.

Implications of research

- Statistical significance - relationships did not occur by chance
  - no significant differences ==> interventional group did the same as control on post-measurement.

Implications of research

- Clinical importance
  - physiologic variables for clinical interventions
  - sensitivity, specificity for diagnostic tests
  - outcomes
    - mortality
    - morbidity
    - adversity
    - cost benefits

Evaluating Research

Bias in literature

- Funding; e.g., by drug companies, equipment manufacturers
- Researchers - desire for intervention to work
- Publication bias - positive research more likely published

Things to look for

- Animal studies - useful; but, require human studies for validation to medicine
- Physiological variables - can be transient and noncontributory to outcomes
- Small studies - difficult to generalize from a few patients
- Crossover studies - each subject is counted more than once

Things to look for

- Effects of interventions may be tied to specific equipment; e.g., PCIRV, PR-2 and 900C
- Control treatment may not be appropriate for comparison

Application To Practice

Application to practice

- Formulate the question
- Search the literature to locate evidence
  - on-line resources; e.g., PubMed
  - learn to search
  - try various terms
  - search for strongest evidence

Application to practice

- Obtain research reports - medical librarian is your best friend
- Read all components:
  - abstract - summary of components
  - introduction
    - background
    - purpose of study
    - research question

Application to practice

- Read all components:
  - methods
    - context of study
    - subjects, number, description
    - procedures

Application to practice

- Read all components:
  - results
  - discussion (of results)
  - conclusion
    - implications for practice
    - implications for research

Application to practice

- Appraise the report(s)
  - quality of research methods
  - do they apply to your context (situation)?

Application to practice

- Generate conclusion for your own setting:
  - institution
  - patients
  - disease conditions
  - current practices
  - available resources

Application to practice

- Generate protocol for implementation of intervention/ diagnostic procedure, including evaluation procedures.
- Present evidence and protocol to influential parties
- Implement protocol
- Evaluate the outcomes
- Adjust, in accordance with evaluation

Conducting clinical research

- Formulate question
- Search the literature
- Identify resources
- Generate research protocol - varies with sponsoring institution
- Approvals
  - administration
  - institutional review board

Conducting clinical research

- Recruit research team
  - assistants
  - statistician
- Train research team
- Implement protocol - gather data
- Analyze data

Conducting clinical research

- Generate report - Index Medicus format
- Submit for publication

On-line reference resources

- AARC Clinical Practice Guidelines
  http://www.rcjournal.com/cpgs/index.cfm
- Medline for healthcare professionals
  http://www.nlm.nih.gov/portals/healthcare.html
- Agency for healthcare research and quality
  http://www.ahrq.gov/professionals/prevention-chronic-care/decision/clinical/index.html
- Cochrane Reviews
  http://www.cochrane.org/reviews/index.htm
- Evidence-based medicine
  http://ebm.bmj.com/
- Evidence-based practice resources (awesome)
  http://libguides.hsl.washington.edu/ebp

Additional reference sources

- Hulley SB, Cummings SR (eds.). Designing clinical research: an epidemiologic approach 2000. Williams & Wilkins; Baltimore.
- Phillips JL. How to think about statistics 1999. WH Freeman; New York.
- Donald A, Greenhaigh T. Evidence-based healthcare workbook 2000. Blackwell BMJ Books
- Greenhaigh T. How to Read a Paper: The Basics of Evidence-based Medicine 3rd Ed. 2005. Blackwell BMJ Books
- Gibson P. Evidence-based respiratory medicine 2005. BMJ Books

Summary & Review

- Introduction
  - rationale for EBM
  - ethical implications for EBM
  - barriers to EBM
- Research concepts
  - validity
  - reliability
  - bias
  - research ethics

Summary & Review

- Evidence sources
  - Cause-effect strength of research types
  - Implications of research - clinical importance
- Evaluating research
  - sources of bias
  - things to look for

Summary & Review

- Application to practice
  - DIY literature review
  - Conducting clinical research

END