Evidence-Based Practice: What's The Deal? What are the Ethics?
Arthur Jones, EdD, RRT
http://rc-edconsultant.com/

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

Example of RC practice with negative evidence:
- Large tidal volume for ALI/ARDS

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

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

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

FYI - Link to introductory article on EBM
http://www.hsl.unc.edu/Services/Tutorials/EBM/whatis.htm
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

FYI - Link to explanation of spurious relationship

- 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)

- 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

- Invalid and unreliable

- Invalid and reliable
Research concepts

- Valid and unreliable

- Valid and reliable

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

FYI - Link to Placebo Television (medical humor)
http://www.tv.com/shows/placebo/

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.

FYI - Link to Bioethics resources on the web
http://bioethics.od.nih.gov/IRB.html#policies
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?

Strength of cause-effect evidence

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### Multi-center RCT

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

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

**Weaknesses**
- very expensive
- time consuming

**Example**
  - 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.

### Meta-analysis of RCTs

**Definition** - statistical combination of the results from all RCTs that address the same question.

**Systematic methods developed by Cochrane Collaboration**

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

FYI - Link to Cochrane Collaboration
http://www.cochrane.org/
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**
- 10 RCTs; 544 patients. The existing evidence does not support the administration of helium-oxygen mixtures to all ED patients with acute asthma.
FYI - Link to article on meta-analysis
http://www.ahrp.org/COI/MetaAnalysis06.pdf

Randomized controlled trial (RCT)

**Definition** - clinical trial with subjects randomized to comparison groups.

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

**Strengths**
- randomized - prevents several sources of bias
- controlled - comparison groups
- blinding increases strength

**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

FYI - Link to article on systematic reviews
http://www.annals.org/cgi/content/full/126/5/376

Examples

  - 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

  - 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
  - online resources
  - 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

FYI - Link to guide to writing research protocol

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

FYI - Link to Respiratory Care manuscript instructions
http://www.rcjournal.com/guidelines_for_authors/preparing_the_manuscript.cfm

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**On-line reference resources**
- AARC Clinical Practice Guidelines
  http://www.rcjournal.com/cpgs/index.cfm
- Medline for healthcare professionals
- Agency for healthcare research and quality
  http://www.ahrq.gov/clinic/
- Cochrane Reviews
  http://www.cochrane.org/reviews/index.htm
- Evidence-based medicine
  http://ebm.bmj.com/
- Evidence-based practice resources (awesome)
  http://healthlinks.washington.edu/ebp

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**Additional reference sources**

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**Summary & Review**
- Introduction
  ◆ rationale for EBM
  ◆ ethical implications for EBM
  ◆ barriers to EBM
- Research concepts
  ◆ validity
  ◆ reliability
  ◆ bias
  ◆ research ethics

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**Summary & Review**
- Evidence sources
  ◆ Cause-effect strength of research types
  ◆ Implications of research - clinical importance
- Evaluating research
  ◆ sources of bias
  ◆ things to look for

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**Summary & Review**
- Application to practice
  ◆ DIY literature review
  ◆ Conducting clinical research
END