Conducting Practice-based Research to Improve Patient Care

Activity Number: 0217-0000-16-113-L04-P  1.50 hours of CPE credit; Activity Type: A Knowledge-Based Activity

Sunday, October 23, 2016
1:30 p.m. to 3:00 p.m.
Great Hall 3

This session is available for elective credit for ACCP Academy's Research and Scholarship Certificate Program. Enrollees must sign the sign-in sheet provided and claim CPE for the session to earn Academy credit.

Moderator: Travis King, Pharm. D., BCPS
Assistant Professor of Pharmacy Practice, University of Mississippi School of Pharmacy, Jackson, Mississippi

Agenda

1:30 p.m. Finding the Link Between Clinical Practice and the Research Hypothesis
   Daniel M. Witt, Pharm. D., FCCP, BCPS
   Professor and Vice Chair, Department of Pharmacotherapy, University of Utah, Salt Lake City, Utah

2:30 p.m. Designing a Quality Study to Improve Patient Outcomes
   Susan L. Davis, Pharm. D.
   Associate Professor, Pharmacy Practice Chair, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit, Michigan

Conflict of Interest Disclosures
Susan L. Davis: Consultancies: (Allergan), Grants: (Merck, Allergan)
Travis King: no conflicts to disclose
Daniel M. Witt: no conflicts to disclose

Learning Objectives
1. Identify sources of clinical practice-based research hypotheses.
2. Examine strategies for evaluating feasibility of practice-based hypotheses.
3. Discuss overcoming barriers to study execution and publication.
4. Examine quasi-experimental study design methods.
5. Select optimal data analysis tools based on study design.

Self-Assessment Questions
Self-assessment questions are available online at www.accp.com/am
Finding the Link between Clinical Practice and the Research Hypothesis

Daniel M. Witt, PharmD, FCCP, BCPS
University of Utah College of Pharmacy
Salt Lake City, UT
October 23, 2016
Conflict of Interest

• I have no conflicts of interest to disclose
Learning Objectives

• Explain how the concepts of strategic alignment and feasibility viewed within the context of clinical practice can support research hypotheses development

• Examine how the study design continuum can be used to formulate meaningful research hypotheses

• Illustrate how clinical practice can drive research hypotheses development in various settings
What makes a good research project idea?

- Clinical practice
- Strategic alignment
- Feasibility
Strategic Alignment

- Healthcare
- Profession
- Organization
- Practice site
- Care team
- Personal
- Patients/Caregivers

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Strategic Alignment

**Healthcare**
- Triple aim
  - Better health
  - Better healthcare
  - Lower cost
- Preventative care
- Patient engagement
- Reducing harm
- Expanding new delivery models

**Profession**
- Establishing credibility as clinicians
- CMM
- Contributing value to patient care
- Workforce development
Strategic Alignment

Organization
• HEDIS/Medicare 5-Stars
• Patient satisfaction
• Workforce development
• COGS/PMPM
• Triple aim
• Patient safety
• Marketing

Practice Site/Care Team
• Waiting time
• Patient safety
• Productivity
• Teamwork
• Patient satisfaction
• Staffing
Strategic Alignment

**Personal**
- Professional development
- Career goals
- Reputation
- Patient care
- Passion

**Patients/Caregivers**
- Improved health
- Healthcare experience
- Avoid harm
- Autonomy
- Concerns addressed
- Engagement
Research as a Business Imperative

The 3-Legged Stool:
• World class Rx operations
• World class Clinical Pharmacy Services
• Research & scholarship

Dennis Helling, PharmD
Demonstrating ROI to Senior Leadership

Senior leadership approved several new FTE to establish centralized, pharmacist managed anticoagulation and cardiac risk services.

How can studies aligned with the triple aim be used to demonstrate the value of this investment?
The Triple Aim

• Better health for individuals
  • Patient care experience
  • Care coordination
  • Patient Safety
  • Preventative Health
  • At risk populations

• Better healthcare for populations
  • Populations can be defined in various way

• Lower the total cost of care
  • Elimination of waste, unwanted variability
The ‘Business Plan’ Study

- Anticoagulation service patients 39% less likely to have anticoagulation therapy complications (HR 0.61 [CI 0.42-0.88])
- One complication prevented every working day of the year
- Annualized cost savings ~$1 million

Chest 2005;127:1515-1522
Excessive anticoagulation

One major bleed prevented for every 20 episodes of INR ≥6

Cardiac Risk Reduction

- Patients with any exposure to CCC program had lower mortality (CAD-related and all-cause)
- All-cause mortality HR 0.24 (95% CI 0.20-0.29)
- Early exposure to CCC was even better
- All-cause mortality HR 0.11 (95% CI 0.08-0.14)
- Also top tier HEDIS measure performance

Pharmacotherapy 2007;27:1317-78
Feasibility

- Focused study question(s)?
- Appropriate study design?
- Adequate methodology?
- Skilled research team?

- Clear pathway to data acquisition?
- Realistic timeline?
- Management support?
- Adequate resources/funding?
Developing Research Questions

<table>
<thead>
<tr>
<th>PICO</th>
<th>FINER</th>
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<tbody>
<tr>
<td>Population</td>
<td>Feasibility</td>
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<tr>
<td>Intervention</td>
<td>Interesting</td>
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<tr>
<td>Comparison Group</td>
<td>Novel</td>
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<tr>
<td>Outcome</td>
<td>Ethical</td>
</tr>
<tr>
<td></td>
<td>Relevant</td>
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</table>
Designing a Quality Study to Improve Patient Outcomes

Susan L Davis, PharmD
Twitter: @IDPharmProf
Clinical Associate Professor
Wayne State University
Infectious Diseases Pharmacy Specialist
Henry Ford Hospital
Conflict of Interest

• Received research grants from Allergan and Merck & Co.
• Served on advisory board for Allergan Inc.
Learning Objectives

1. Examine quasi-experimental study design methods
2. Select optimal data analysis tools based on study design
3. Outline limitations of quasi-experimental study methods
Hypothetical Scenario

• **Problem**: resistance to quinolone antimicrobial agents has increased in your hospital

• **Investigation**: Medication use evaluation demonstrated overuse of quinolones for a variety of indications

• **Intervention**: System-based quality improvement
  - Restriction of quinolone use
  - Prospective audit and feedback for quinolone use
Quinolone utilization

Henry Ford Health System, Internal Data
Ciprofloxacin Susceptibility

Henry Ford Health System, Internal Data

2016 ACCP Annual Meeting
#ClinicalFacultyProblems

- Intervention was a lot of work
- *Successful* as a quality improvement project
  - Improved antibiotic use
  - Improved susceptibility
- *Unsuccessful* as scholarly output
  - Not publishable
  - Difficulty linking change to any intervention

To expand the evidence for practice change, quality improvement projects must incorporate appropriate research methods.
Steps In Real Time Problem Solving

1. Observe the problem
   • See it with your own eyes, identify the right problem
2. Look for opportunities to improve, standardize
3. Involve the people directly associated with the work in designing the intervention
4. Implement and Experiment
What problems do you want to address?

• Brainstorm to yourself or in small groups
• What problem areas are there in your practice?
• What group-level outcomes are you looking to improve?
• What interventions might you implement?
Choosing a Study Design

• Are there comparator groups?
• Are the groups assigned by investigator?
• Is treatment assigned randomly?
• Is the intervention at an individual or group level?
Susan’s Resident Project Flow Chart

Does the study involve comparator groups?

No

This is a descriptive study. This could be an ecological study or MUE.

Yes

Does the investigator assign the exposure/treatment groups?

No

Congratulations, you’re doing an observational study. How are exposures and outcomes being compared?

Outcome → exposures

Case Control

Exposure → outcomes

Cohort

Cross-sectional

Both at the same time

Yes

Congratulations, you’re doing an experimental study. Is the assignment of exposure by random allocation?

No

This is probably a quasi-experiment. There are many types. Be thoughtful.

Yes

Are the random assignments made at the individual or group level?

group

This sounds like a cluster-randomized trial. This isn’t going to be easy.

individual

This sounds like an RCT. Are you sure this is necessary? It’s unlikely you’ll finish this during a residency year.
How do quasi-experimental studies fit in?

• Non-randomized allocation
  • Implementation of an intervention in a non-random sample

• Intervention is implemented on a GROUP level, not individual patient level
  • Pharmacist-directed anticoagulation service
  • Ventilator-associated pneumonia pathway
  • Emergency department culture follow-up
Notation for study designs

• **O** = observational measurement
  • Observations are made before and after interventions are made
  • Each “O” corresponds to evaluation of subjects over a specified time-period
  • Subjects in each “O” should be selected using identical inclusion/exclusion criteria with the exception of time period

• **X** = intervention being studied
• → **X** = intervention removed
The simplest design: One group, pre-test post-test

- Also known as a before-and-after study
- Goal: assess whether change in outcome occurred after intervention implemented
  - Threats to validity/causality: maturation, regression to the mean, seasonal variation, selection bias/change in patient population, controlling for confounding

Sketch out your own simple quasi-experiment

Problem: Institutional guideline recommends cefazolin for uncomplicated MSSA bloodstream infection. Nafcillin and vancomycin still commonly used.

“PRE” Group
1 year
All qualifying MSSA BSI

Intervention: pharmacist-directed therapeutic interchange with alerts, audit/feedback

“POST” Group
1 year
All qualifying MSSA BSI

Endpoints: both pre and post groups
Compliance with guideline, mortality, acute kidney injury, 30-day readmission, drug cost...
Self-assess your design

• Intervention
  • Are there multiple components, phases?
  • If the intervention a “bundle” are all components equally valid?

• Is the setting/population well defined?

• Is the time-course for observation and implementation well defined?

• Endpoints
  • Is it possible to study multiple endpoints?
  • Are there other potential differences in the pre and post intervention populations that would affect endpoints?
Quality Indicators for Stewardship

• 1 group pretest-posttest study before/after pilot of stewardship program
• to evaluate the impact of stewardship program on quality of antibiotic prescribing
  • Compliance with all quality indicators rose from 16% to 41% (p<.001)

Adequate cultures obtained (p=.093)  
87 95

Adquate empirical therapy (p=.222)  
85 91

Appropriate De-escalation (p<.01)  
72 90

Toth NR. AJHP 2010.
DMC *S. aureus* bacteremia pathway (implemented November 2007)

**Observation 1: Pre Intervention**
- 2005-2007
- All patients with MRSAB with vancomycin MIC >1 mg/L
- treated with vancomycin (prior standard of care)

**Observation 2: Post intervention**
- 2008-2010
- All patients with MRSAB with vancomycin > 1 mg/L
- Treated with daptomycin (new standard of care)

Outcomes Pre and Post Intervention

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre</th>
<th>Post</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Success</td>
<td>41%</td>
<td>75%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Length of stay (median)</td>
<td>16 days</td>
<td>14 days</td>
<td>0.04</td>
</tr>
<tr>
<td>Duration of inpatient antibiotics (median)</td>
<td>13 days</td>
<td>9 days</td>
<td>0.0001</td>
</tr>
<tr>
<td>Duration of bacteremia (median)</td>
<td>5 days</td>
<td>4 days</td>
<td>0.004</td>
</tr>
<tr>
<td>30-day readmission</td>
<td>33%</td>
<td>21%</td>
<td>0.08</td>
</tr>
<tr>
<td>Hospital Cost (median)</td>
<td>$18,385</td>
<td>$19,755</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Treatment in phase 1 was associated with failure (adjusted odds ratio 4.37, 95% CI 1.68–6.76, p<0.001), adjusting for high-risk source & comorbidities.

Limitations to Pre-Post Design

• Changes in Practice Pre and Post
  • Method of determining MIC changed between Pre and Post, study population may not be the same

• Maturation: practice, events naturally change with the passage of time
  • Did prescribers improve management of SAB naturally from 2005-2010?

• Regression to the mean: event rates following an extreme value have a tendency to return to the mean
Threats to validity

• Controlling for confounding
  • Important for any non-randomized study

• Regression to the mean
  • Extreme values may return to normal on their own

• Maturation
  • Practices can improve over time without intervention

• Seasonal variation
  • Certain problems may recur at a natural time (weather, new residents)

Minimizing limitations

- Add more observations
- Use a control group
- Take away the intervention and observe outcomes again
- All of the above together
Removing treatment

• If intervention improves, does removing intervention worsen outcome?
• Demonstrate if intervention effect is transient
• May help evaluate time-delay
• Improves evidence against maturation

• Not always feasible/ethical
Adding control group

- Improves evidence against maturation and regression to the mean
- Improves evidence of causality
- Not always feasible/ethical
### A. Without Control Groups

1. Posttest-only, single group  
   - Intervention: X O1

2. Pretest-posttest, single group  
   - Control: O1 X O2

3. Pretest-posttest using a double pretest, single group  
   - Control: O1 O2 X O3

4. Pretest-posttest using two variables, single group  
   - Control: (O1a, O1b) X (O2a, O2b)

5. Removed-treatment  
   - Control: O1 X O2 O3 removeX O4

6. Repeated-treatment  
   - Control: O1 X O2 removeX O3 X O4

### B. Control Group Without Pretest

1. Posttest-only, controlled  
   - Intervention: X O1  
     - Control: O2

### C. Control Group With Pretest

1. Pretest-posttest, controlled  
   - Intervention: O1a X O2a  
     - Control: O1b O2b

2. Pretest-posttest using a double pretest, controlled  
   - Intervention: O1a O2a X O3a  
     - Control: O1b O2b O3b

3. Pretest-posttest with sequential implementation into control group  
   - Intervention: O1a X O2a O3a  
     - Control: O1b O2b X O3b

### D. Interrupted Time-Series

1. Multiple pretest and posttest observations spaced equally  
   - Interventions X O1 O2 O3 X O4 O5 O6
How could we improve our designs?

- Increase observations?
  - “PRE” Group
    - 1 year
    - All qualifying MSSA BSI

- Remove intervention and observe again?
  - Intervention: pharmacist-directed therapeutic interchange with alerts, audit/feedback
  - “POST” Group
    - 1 year
    - All qualifying MSSA BSI

- Increase observations?

Endpoints: both pre and post groups
Compliance with guideline, mortality, acute kidney injury, 30-day readmission, drug cost...

- Add a control group?
- Add a Non-Equivalent Dependent Variable?
Statistical Analysis for Q-E Studies

• Similar to observational studies
  • T-test/ ANOVA
  • Chi-square
  • Linear/logistic/Poisson regression

• For Interrupted Time Series
  • Need to retain advantages of multiple timepoints (otherwise it’s just a pretest-posttest study)
  • Need to account for correlation and secular trends
  • Segmented regression and ARIMA* models

*auto regressive integrated moving average
Problems in the Literature

• Publications of quasi-experimental studies do not routinely...
  • Specify the type of study design used
  • Justify the use of the quasi-experimental design
  • Use appropriate nomenclature for the study design
  • Address potential limitations

Literature has evaluated quasi-experiments in infectious diseases, infection control, information technology.... What about pharmacy?

Harris AD, Lautenbach E, Perencevich E. 2005;41:77-82
Q-E Designs in Pharmacy Journals

Articles Screened (2010-12)
N=2302

Non-Research (n=1722)
- Policy/Guideline (n=20)
- Case Report/Study (n=406)
- Notes (n=403)
- Editorial/Commentary (n=232)
- Review (n=661)

Original Research Articles
n=580 (25%)

Quasi-Experiments
n = 87/580 (15%)

Duprey MS, Wagner JL, Bockelman SM, Harris AD, Davis SL. ASHP Midyear 2013 Abstract 1-301.
Types of QE studies in pharmacy journals

- 1 group posttest only: 71%
- 1 group, pretest-posttest: 14%
- Other designs included:
  - 7 type B1 (posttest only, controlled)
  - 2 type C1 (pretest-posttest, controlled)
  - 1 type A3 (pretest-posttest using a double pretest, single group)
  - 2 type D1 (interrupted time series)

Duprey MS, Wagner JL, Bockelman SM, Harris AD, Davis SL. ASHP Midyear 2013 Abstract 1-301.
## Characteristics of Pharmacy QE Studies

<table>
<thead>
<tr>
<th>Therapeutic Area</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Administration</td>
<td>17 (20%)</td>
</tr>
<tr>
<td>Ambulatory care</td>
<td>15 (17%)</td>
</tr>
<tr>
<td>Anticoagulation/Cardiology</td>
<td>19 (22%)</td>
</tr>
<tr>
<td>Critical Care</td>
<td>12 (14%)</td>
</tr>
<tr>
<td>Drug Information</td>
<td>24 (28%)</td>
</tr>
<tr>
<td>Emergency Medicine</td>
<td>5 (6%)</td>
</tr>
<tr>
<td>Hematology/Oncology</td>
<td>8 (9%)</td>
</tr>
<tr>
<td>Infectious Disease</td>
<td>29 (33%)</td>
</tr>
<tr>
<td>Internal Medicine</td>
<td>16 (18%)</td>
</tr>
<tr>
<td>Other</td>
<td>17 (20%)</td>
</tr>
</tbody>
</table>

### Quality Metrics

<table>
<thead>
<tr>
<th>Metric</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identified as a quasi-experiment</td>
<td>19 (22%)</td>
</tr>
<tr>
<td>Quasi-experiment</td>
<td>6</td>
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<tr>
<td>Pretest-posttest</td>
<td>9</td>
</tr>
<tr>
<td>Before/after</td>
<td>6</td>
</tr>
<tr>
<td>Justified the use of QE design</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Discussed at least one limitation inherent to QE designs</td>
<td>19 (22%)</td>
</tr>
<tr>
<td>Lack of randomization</td>
<td>4</td>
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<tr>
<td>Regression to the mean</td>
<td>1</td>
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<tr>
<td>Temporal confounders</td>
<td>10</td>
</tr>
<tr>
<td>Maturation effects</td>
<td>7</td>
</tr>
</tbody>
</table>

Duprey MS, Wagner JL, Bockelman SM, Harris AD, Davis SL. ASHP Midyear 2013 Abstract 1-301.
Summary: When to use Quasi-Exp Designs

• Research question investigates a group/population level effect
  • Drug use, cost, readmissions, resistance
• Intervention involves multiple components implemented at the same time
• Intervention must be applied at GROUP level
• Not ethical or feasible to randomize
Quality Improvement AND (not versus) Research

• Talk to your IRB, get approval up front
• Who is the audience?
• Make sure your data is generalizable
  • Adequate “baseline” characteristics
  • Descriptive, contextual data
• Describe the intervention roll out
• Be sure to address unique features and nomenclature if using quasi-experimental design
Read these helpful references


Steps In Real Time Problem Solving

1. Observe the problem
   • See it with your own eyes, identify the right problem
2. Look for opportunities to improve, standardize
3. Involve the people directly associated with the work in designing the intervention
4. Implement and Experiment
5. Celebrate and Spread the Success