Alternative Study Designs for Evidence-Based Practice

Making the Case for the Value of Your Device with Practice-Based Evidence

March 29, 2007

Track B

Susan D. Horn, PhD
Senior Scientist
Institute for Clinical Outcomes Research
699 E. South Temple, Suite 100
Salt Lake City, Utah  84102-1282
801-466-5595 x203 (T)     801-466-6685 (F)
shorn@isisicor.com
Presentation Overview

- *Brief description of PBE-CPI, a practice-based evidence approach to comparative effectiveness, and how it differs from other study methodologies*

- *How PBE-CPI supports device companies’ reimbursement strategies*

- *PBE-CPI examples of comparative effectiveness findings about devices and products*
Practice-Based Evidence for Clinical Practice Improvement Study Design

Analyzes the *content and timing* of individual steps of a health care process, in order to determine how to achieve:

- *superior medical outcomes* for the
- *least necessary cost* over the
- *continuum* of a patient’s care
Practice-Based Evidence for Clinical Practice Improvement Study Design

**Improve/Standardize:**

**Process Factors**
- Management Strategies
- Interventions
- Medications

**Patient Factors**
- Psychosocial/demographic Factors
- Disease(s)
- Severity of Disease(s)
  - physiologic signs and symptoms
- Multiple Points in Time

**Control for:**

**Measure:**

**Outcomes**
- Clinical
- Health Status
- Functional
- Cost/LOS/Encounters
Efficacy vs. Effectiveness

• *Efficacy* is concerned with the question of whether a treatment works (under ideal conditions).

• *Effectiveness* is concerned with the question of whether a treatment works under usual conditions of care.
Efficacy Studies

• Seek to maximize likelihood of correctly identifying an effect
  » Homogeneous patient population
  » Detailed assessments of one or two outcomes
  » Placebo comparison
  » Random assignment of treatments

• Most appropriate research design: Randomized Controlled Trial (RCT)
Effectiveness Studies

• Seek to correctly identify effects under conditions of routine clinical care
  » Heterogeneous populations
  » Multiple clinically relevant outcomes
  » Comparisons to other active treatments (comparative effectiveness)

• Appropriate research design:
  » Practice-Based Evidence for Clinical Practice Improvement
Practice-Based Evidence (PBE-CPI)

PBE-CPI Studies—7 Signature Features

1. *All interventions considered* to determine relative contribution of each.
2. *Hypotheses can be focused or broad*
3. *Minimal selection criteria* to maximize generalizability and external validity
4. *Detailed characterization of the individual* through the use of robust measures of patient acuity & functional status
Practice-Based Evidence (PBE-CPI)

PBE-CPI Studies—7 Signature Features

5. *Individual/patient/consumer differences controlled statistically* rather than through randomization

6. *Facility & clinical/consumer buy-in* through the use of a transdisciplinary Clinical/Consumer Practice Team

7. *High level of transparency* for all stakeholders.

More generalizable and transportable findings
1. All interventions considered to determine relative contribution of each. This requires:

- A detailed characterization of the care process through a well-designed point-of-care (POC) documentation system
  - User-defined and user friendly
  - Time sensitive characterization of all interventions
Practice-Based Evidence (PBE-CPI)

PBE-CPI Studies—7 Signature Features

4. *Detailed characterization of the individual* through the use of robust measures of individual acuity and functional status

- Includes Comprehensive Severity Index (CSI®)
  - Over 2,200 condition-specific signs and symptoms
  - Discrete score: 0 → 4 (most severe)
  - Continuous score: 0 → ∞
  - Admission, discharge, maximum during stay

- Includes Functional Independence Measure (FIM) and/or other measures of functional status
Practice-Based Evidence (PBE-CPI)

PBE-CPI Studies—7 Signature Features

6. *Facility & clinical/consumer buy-in* through the use of a transdisciplinary Clinical/Consumer Practice Team that:

- Develops and frames the questions
- Defines variables
- Gathers data
- Interprets data
- Implements findings
- Fosters clinical and individual buy-in (a bottom-up approach)
- Facilitates knowledge translation
Practice-based Evidence for Clinical Practice Improvement compared to Randomized Controlled Trial

**PBE-CPI**
I. Select Key Conditions to Study

**RCT**
I. Define Study
### PBE-CPI

#### II. Data Collection

**A. Patient Variables**

- Patient eligibility and stratification factors
- Use severity of illness to measure:
  - comorbidities
  - disease severity
- All patients qualify

### RCT

#### II. Data Collection

**A. Patient Variables**

- Patient eligibility and stratification factors
- Eliminate patients who could bias results:
  - comorbidities
  - more serious disease
~ 15% of patients qualify
Practice-based Evidence for Clinical Practice Improvement compared to Randomized Controlled Trial

II. Data Collection

B. Process Variables

- Methods for Stabilization
  - Measure all processes and use analysis findings to develop protocol associated with better outcomes

- Treatment Protocol
  - Specify explicitly every important element of the process of care for both treatment and control arms
Practice-based Evidence for Clinical Practice Improvement compared to Randomized Controlled Trial

### PBE-CPI

**III. Data Analysis**

*Outcome Variables*
- Dynamic improvement based on combinations of interventions

**IV. Result**
- Effectiveness research

### RCT

**III. Data Analysis**

*Outcome Variables*
- Change based on one protocol

**IV. Result**
- Efficacy research
# RCT & PBE-CPI Compared

<table>
<thead>
<tr>
<th>Dimension</th>
<th>RCT</th>
<th>PBE-CPI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of study</td>
<td>Randomized Controlled Trial</td>
<td>Prospective Observational Cohort Study</td>
</tr>
<tr>
<td>Intervention</td>
<td>1 or 2 discrete interventions</td>
<td>All interventions deemed relevant</td>
</tr>
<tr>
<td>Hypotheses</td>
<td>Well-specified</td>
<td>Focused or broad</td>
</tr>
<tr>
<td>Selection criteria</td>
<td>Extensive</td>
<td>Minimal</td>
</tr>
<tr>
<td>Sample size</td>
<td>Much smaller</td>
<td>Much larger</td>
</tr>
<tr>
<td>Control for participant differences</td>
<td>Randomization</td>
<td>Detailed characterization &amp; statistical control</td>
</tr>
</tbody>
</table>
## RCT & PBE-CPI Compared

<table>
<thead>
<tr>
<th>Dimension</th>
<th>RCT</th>
<th>PBE-CPI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blinding</td>
<td>Single, double, triple</td>
<td>No</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Few</td>
<td>Many</td>
</tr>
<tr>
<td>Effect size</td>
<td>Often small</td>
<td>Often large</td>
</tr>
<tr>
<td>Confounders</td>
<td>Not interesting; exclude them</td>
<td>Affect outcomes &amp; are interesting</td>
</tr>
<tr>
<td>Validity</td>
<td>High internal</td>
<td>High external</td>
</tr>
<tr>
<td>Causality</td>
<td>Assigned</td>
<td>Assumed</td>
</tr>
<tr>
<td>Ability to examine subgroups</td>
<td>Limited</td>
<td>More likely</td>
</tr>
</tbody>
</table>
## RCT & PBE-CPI Compared

<table>
<thead>
<tr>
<th>Dimension</th>
<th>RCT</th>
<th>PBE-CPI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td>High</td>
<td>Moderate</td>
</tr>
<tr>
<td>Culture (1)</td>
<td>Top-down; blinding</td>
<td>High transparency</td>
</tr>
<tr>
<td>Culture (2)</td>
<td>Not depend on local knowledge</td>
<td>Local knowledge contributes, valued</td>
</tr>
<tr>
<td>Knowledge translation</td>
<td>Far less buy-in</td>
<td>High level of buy-in; findings more “transportable”</td>
</tr>
<tr>
<td>Science of …….</td>
<td>Confirmation</td>
<td>Discovery &amp; innovation</td>
</tr>
<tr>
<td>Science of …….</td>
<td>Efficacy</td>
<td>Effectiveness</td>
</tr>
</tbody>
</table>
RCT & PBE-CPI Compared

“What is efficacious in randomized clinical trials is not always effective in real world of day-to-day practice…

Practice-based research provides the laboratory that will help generate new knowledge and bridge the chasm between recommended care and improved care.”

PBE-CPI and RCT

Progenitor of RCTs

RCT

Practice effects of RCT results

PBE-CPI
PBE-CPI Study

- Connects outcomes with detailed process steps
- Adjusts for severity of illness to control for patient differences/selection bias
Criteria to Select a Severity Indexing System to Control for Patient Differences

- Disease-specific
- Independent of treatments
- Comprehensive (i.e., all diseases)
- Clinically credible
- Able to measure severity at multiple points in the care process
- Statistically valid in explaining costs/outcomes
Comprehensive Severity Index (CSI®)

Severity Systems

Diagnostic/Procedure Based Systems
- AIM by Iameter
- Disease Staging by MedStat
- APR DRGs by 3m
- Patient Management Categories

Physiologic/Clinically Based Systems
- Apache (17 criteria)
- Atlas by Mediqula (300 criteria)

CSI®
Comprehensive Severity Index CSI®

- Over 2,200 individual criteria subdivided into more than 5,500 disease-specific groups
- No treatments used as criteria
- Computes disease-specific and overall severity levels on a scale of 0-4 and continuous
- Fixed times for inpatient reviews
  - Admission review--first 24 hours
  - Maximum review--any time during stay
  - Discharge review--last 24 hours
  - Each visit
### Pneumonia Criteria Set

#### 480.0-486; 506.3; 507.0-507.1; 516.8; 517.1; 518.3; 518.5; 668.00-668.04; 997.3; 112.4; 136.3; 055.1

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiovascular</strong></td>
<td>• pulse rate 51-100; ST segment changes-EKG; systolic BP ≥ 90mmHg</td>
<td>• pulse rate 100-129; 41-50; PACs, PAT, PVCs-EKG; systolic BP 80-89mmHg</td>
<td>• pulse rate ≥ 130; 31-40; systolic BP 61-79mmHg</td>
<td>• pulse rate ≤30; asystole, VT, VF, V flutter; systolic BP ≤60 mmHg</td>
</tr>
<tr>
<td><strong>Fever</strong></td>
<td>• 96.8-100.4 and/or chills</td>
<td>• 100.5-102.0 oral; 94.0-96.7</td>
<td>• 102.1-103.9; 90.1-93.9 and/or rigors</td>
<td>• ≥104.0 ≤90.0</td>
</tr>
<tr>
<td><strong>Labs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ABGs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hematology</strong></td>
<td>• pH 7.35-7.45</td>
<td>• pH &gt;7.46 7.25-7.34</td>
<td>• pH 7.10-7.24</td>
<td>• pH ≤7.09; pO₂ ≤ 50mmHg</td>
</tr>
<tr>
<td></td>
<td>• pO₂ ≥61mmHg</td>
<td></td>
<td>• pO₂ 51-60mmHg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• WBC 4.5-11.0K/cu mm; bands &lt;10%;</td>
<td>• WBC 11.1-20.0K/cu mm; 2.4-4.4K/cu mm; bands 10-20%</td>
<td>• WBC 20.1-30.0K/cu mm; 1.0-2.3K/cu mm; bands 21-40%</td>
<td>• WBC ≥30.1K/cu mm; &lt;1.0K/cu mm; bands &gt;40%</td>
</tr>
<tr>
<td><strong>Neuro Status</strong></td>
<td>• ≥12</td>
<td>• chronic confusion</td>
<td>• acute confusion</td>
<td>• unresponsive</td>
</tr>
<tr>
<td><strong>Lowest Glasgow coma score</strong></td>
<td></td>
<td>• 9-11</td>
<td>• 6-8</td>
<td>• ≤5</td>
</tr>
<tr>
<td><strong>Radiology Chest X-Ray or CT Scan</strong></td>
<td></td>
<td>• infiltrate and/or consolidation in ≤1 lobe; pleural effusion</td>
<td>• infiltrate and/or consolidation in &gt;1 but ≤3 lobes;</td>
<td>• infiltrate and/or consolidation in &gt;3 lobes; cavitation or lung necrosis</td>
</tr>
<tr>
<td><strong>Respiratory</strong></td>
<td>• white, thin, mucoid sputum</td>
<td>• dyspnea on exertion; stridor; rales ≤50%/≤3 lobes; decreased breath sounds ≤50%/≤3 lobes; positive for fremitus; stridor</td>
<td>• cyanosis present</td>
<td>• apnea absent breath sounds ≥50%/≥3 lobes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• hemoptysis NOS; blood tinged or purulent or frothy sputum</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Summary: How PBE-CPI Differs from RCT?

- Severity adjustment methodology to remove selection bias
- Three-dimensional measurement framework: patient, process, and outcomes
- Balance of rigorous science with a pragmatic operational focus
Nursing Home Study (NPULS) 1996-1997

- 6 long-term care provider organizations
- 109 facilities
- 2,490 residents studied
- 1,343 residents with pressure ulcer; 1,147 at risk
- 70% female, 30% male
- Average age = 79.8 years

Funded by Ross Products Division, Abbott Laboratories
NPULS Outcomes

- Developed pressure ulcers
- Healed pressure ulcers
- Hospitalization
- Systemic infections
Long Term Care CPI Results
Outcome: Develop Pressure Ulcer


### General Assessment
- + Age ≥ 85
- + Male
- + Severity of Illness
- + History of PU
- + Dependency in >= 7 ADLs
- + Diabetes
- + History of tobacco use
- + Dehydration
- + Weight loss

### Incontinence Interventions
- + Mechanical devices for the containment of urine (catheters)
  - Disposable briefs
  - Toileting Program

### Nutrition Interventions
- - Fluid Order
- - Nutritional Supplements
  - standard medical
- - Enteral Supplements
  - disease-specific
  - high calorie/high protein

### Staffing Interventions
- - RN hours per resident day >= 0.5
- - CNA hours per resident day >= 2.25

### Medications
- - SSRI + Antipsychotic
Long-Term Care Residents with Agitation in Dementia

Recommended Practice

• Use fewest number of medications possible (OBRA 1987)

• Minimize use of benzodiazepines

• Use atypical over typical antipsychotics

• Use SSRIs over tertiary amine antidepressants

• Avoid combination therapy
Medications from NPULS Study

Optimal Medications
Dementia & Agitation n = 803

No Psych Meds  32.5%
Anti-psychotics  31.5%
Anti-depressants  34.6%
Anti-anxiety  34.9%

Combinations in 42% of treated residents
## Medication Use and Outcomes for Elderly with Dementia with Agitation

<table>
<thead>
<tr>
<th>Medication</th>
<th>% Hospital + ER</th>
<th>% Restraints</th>
<th>% Pressure Ulcers</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Psych Medications</td>
<td>20.0</td>
<td>19.9</td>
<td>37.2</td>
</tr>
<tr>
<td>Monotherapy</td>
<td>17.2</td>
<td>24.0</td>
<td>24.0**</td>
</tr>
<tr>
<td>SSRI + Antipsychotic</td>
<td>9.9**</td>
<td>12.3*</td>
<td>12.6**</td>
</tr>
</tbody>
</table>

Monotherapy includes antipsychotic only, antidepressant only, or antianxiety only SSRI + antipsychotic medications concurrently.

*p ≤ .05  **p ≤ .01

Horn, Drug Benefit Trends 2003; 15 (Supplement 1, December): 12-18
## Effects of Nutritional Support in Long Term Care

<table>
<thead>
<tr>
<th>Nutritional Treatment Strategies</th>
<th>N</th>
<th>Pressure Ulcer Develop Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral Supplement / Standard Medical Nutritional</td>
<td>134</td>
<td>21.6%</td>
</tr>
<tr>
<td>Enteral Formula</td>
<td>210</td>
<td>23.8%</td>
</tr>
<tr>
<td>Fluid Order</td>
<td>396</td>
<td>25.0%</td>
</tr>
<tr>
<td>Snacks, House Shakes</td>
<td>403</td>
<td>27.3%</td>
</tr>
<tr>
<td>No Nutritional Risk -- No Nutritional Treatment</td>
<td>195</td>
<td>27.2%</td>
</tr>
<tr>
<td>At Nutritional Risk -- No Nutritional Support</td>
<td>323</td>
<td>35.6%</td>
</tr>
</tbody>
</table>
# Bladder Incontinence Management in Long Term Care

<table>
<thead>
<tr>
<th>Treatments</th>
<th>N</th>
<th>PU Develop Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incontinent</strong> - Use one or more of following treatments:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Briefs, disposable</td>
<td>501</td>
<td>23.6%</td>
</tr>
<tr>
<td>Toileting program</td>
<td>549</td>
<td>23.9%</td>
</tr>
<tr>
<td>Briefs, reusable</td>
<td>118</td>
<td>26.3%</td>
</tr>
<tr>
<td>Topical Treatment</td>
<td>1,159</td>
<td>29.1%</td>
</tr>
<tr>
<td>Bed pads, disposable</td>
<td>193</td>
<td>29.5%</td>
</tr>
<tr>
<td>Bed pads, reusable</td>
<td>221</td>
<td>32.1%</td>
</tr>
<tr>
<td>Use of catheter</td>
<td>195</td>
<td>51.3%</td>
</tr>
<tr>
<td><strong>Continent - No incontinence treatment</strong></td>
<td>209</td>
<td>26.3%</td>
</tr>
</tbody>
</table>
When these findings were applied, we found noteworthy results:

**Better clinical outcomes**

- CMS average pressure ulcer prevalence rate for high-risk residents went from pre-implementation of 14% to post-implementation of 8.7% and still decreasing

- Almost no in-house acquired pressure ulcers
Impact On Pressure Ulcer QMs: Achieve Better Clinical Outcomes

The combined facilities’ average shows an overall reduction of 33% in the QM % of high risk residents with pressure ulcer from pre-implementation to initial post-implementation time periods.

Source: CMS Nursing Home Compare; Facility QM data reports
Study question: Compare air-fluidized therapy with other support surfaces to treat Stage 3 and 4 pressure ulcers in nursing home residents.

- **Group 1**: Static overlays, replacement mattresses, foam, water/gel
- **Group 2**: low-air-loss, alternating pressure, powered/non-powered overlays
- **Group 3**: Air-fluidized beds
Long Term Care CPI Results
Outcome: Healing Pressure Ulcer

Findings: Mean healing rate

- Group 1: 1.5 cm² per week
- Group 2: 1.8 cm² per week
- Group 3: 5.2 cm² per week

Findings: Mean hospitalization and ER rates

- Group 1: 10.2% with mean severity 82
- Group 2: 19.0% with mean severity 108
- Group 3: 7.3% with mean severity 108

NEW: Nursing Home Study
Outcome: Healing Pressure Ulcer

Study question: What pressure ulcer treatments and products are associated with faster healing?

Device: Vacuum-assisted closure (VAC)

Funded by: Agency for Healthcare Research and Quality (AHRQ), California Health Care Foundation, Kinetic Concepts, Inc. (KCI)
Post-Stroke Rehabilitation Study
2001 - 2003

Patient Characteristics

1,161 U.S. Patients
52% Male; 58% White, 26% Black
Age range: 18.6 - 95.5 yrs
Outcome: Discharge Motor FIM
Severe Stroke (CMGs 108-114) – Full Stay

General Assessment
- Age
- Black race
+ Mild motor impairment
+ Admission Motor FIM
+ Admission Cognitive FIM

General Interventions
- Days onset to rehab
+ Enteral feeding

PT Interventions
- Formal assessment
- Bed mobility
+ Gait
+ Advanced gait

Medications
- Anti-Parkinsons
- Modafinil
- Old SSRIs
+ Atypical antipsychotics

OT Interventions
+ Home management

SLP Interventions
- Swallowing
- Orientation
+ Reading comprehension
Outcome: Discharge Motor FIM
Severe Stroke – 1\textsuperscript{st} 3 hour Therapy block only

- Age
- Severe motor impairment
+ Admission Motor FIM
+ Admission Cog. FIM
+ No Dysphagia
+ Neurotropic Impairments treated with meds

- Bed mobility time in 1\textsuperscript{st} 3 hrs
+ Gait time in 1\textsuperscript{st} 3 hrs
+ Advanced gait time in 1\textsuperscript{st} 3 hrs

- Days onset to rehab
+ LOS
+ Enteral feeding

+ Home management

- Other Antidepressant
- Old SSRIs
+ Atypical antipsychotics
Post-Stroke Rehabilitation Study

12 papers published in
Supplement to Archives of Physical Medicine and Rehabilitation
December 2005

Opening the “Black Box” of Stroke Rehabilitation
And What It Means for Rehabilitation Research

11 additional papers in other journals
NEW: JOINT Replacement Rehabilitation Study

Patient Characteristics

2,500 U.S. Patients with hip or knee replacement

- 1,500 patients in Inpatient Rehab Facilities
- 1,000 patients in Skilled Nursing Facilities

Age range: 18.3 - 100.5 yrs
NEW: 2 Spinal Cord Injury Studies

**SCI REHAB Study**
- 1,500 patients in rehabilitation with spinal cord injury
- Approximately 114-500 patients from each of six spinal cord injury centers

**Spinal Cord Injury SKIN Study**
- 900 patients with SCI or SCDisease
  » At Washington Hospital Center and/or NRH
- Goal
  - To prevent pressure ulcers in SCI or SCD patients
Discover Best Practices using PBE-CPI

- **Practitioners**: PBE-CPI data allow investigation of effects of combinations of treatments on outcomes, controlling for patient differences.

- **Insurers**: PBE-CPI data allow discovery of practices associated with better functional and clinical outcomes at lower cost.

- **Manufacturers**: PBE-CPI studies show comparative effectiveness and are less expensive to conduct.