Practice-Based Evidence Study Design for Comparative Effectiveness Research

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Objectives: To describe a new, rigorous, comprehensive practice-based evidence for clinical practice improvement (PBE-CPI) study methodology, and compare its features, advantages, and disadvantages to those of randomized controlled trials and sophisticated statistical methods for comparative effectiveness research.

Research Design: PBE-CPI incorporates natural variation within data from routine clinical practice to determine what works, for whom, when, and at what cost. It uses the knowledge of front-line caregivers, who develop study questions and define variables as part of a transdisciplinary team. Its comprehensive measurement framework provides a basis for analyses of significant bivariate and multivariate associations between treatments and outcomes, controlling for patient differences, such as severity of illness.

Results: PBE-CPI studies can uncover better practices more quickly than randomized controlled trials or sophisticated statistical methods, while achieving many of the same advantages. We present examples of actionable findings from PBE-CPI studies in postacute care settings related to comparative effectiveness of medications, nutritional support approaches, incontinence products, physical therapy activities, and other services.

Conclusions: Outcomes improved when practices associated with better outcomes in PBE-CPI analyses were adopted in practice.

Key Words: practice-based evidence, clinical practice variations, comparative treatment outcomes

(Med Care 2007;45: S50–S57)

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No commercial party having a direct financial interest in the results of the research supporting this article has or will confer a benefit upon the authors or upon any organization with which the authors are associated.

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ISSN: 0025-7079/07/4500-0050

Many researchers have written about problems with evidence from evidence-based medicine (EBM), whose main tools are randomized trials and meta-analysis.1–3 Westfall states “What is efficacious in randomized clinical trials is not always effective in the 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.” Although randomized controlled trials (RCTs) are important to confirm whether a new treatment causes an effect, they are unlikely to discover combinations of interventions or practices that are effective and efficient in routine care.

Porter and Teisberg3 call for determining the best treatments for specific types of patients. They feel that encouraging competition at the level of treatments for specific diseases or co-occurring conditions and types of patients will speed the development of the right kind of information and improve value (quality of health outcomes per dollar expended).

To rise to Porter and Teisberg’s challenge, we must develop scientifically rigorous methods that answer questions such as, “Does the treatment work in the real world of everyday practice?” or “For whom does the intervention work best?” These questions differ from typical RCT questions: “How and why does the intervention work?” or “For whom does the intervention work best?” Trials that address the latter questions are designed to maximize the chance that some effect of a new or existing treatment will be revealed by the study, and to provide a confirmatory analysis of the original study hypothesis.

In this article, we describe a practice-based evidence for clinical practice improvement (PBE-CPI) research methodology that fills gaps in information needed by clinical and health policy decision makers.1,4 As a clinical research method, PBE-CPI embraces all 4 elements of practical clinical trials (PCTs) for which the hypothesis and study design are developed specifically to answer the questions faced by decision makers. Characteristic features of PCTs are: (1) select clinically relevant alternative interventions to compare, (2) include a diverse population of study participants, (3) recruit participants from heterogeneous practice settings, and (4) collect data on a broad range of health outcomes.1 The PBE-CPI method provides a way to operationalize PCTs effectively.5 We compare RCTs, sophisticated statistical tests, and PBE-CPI research methodologies for comparative effectiveness by evaluating their relative strengths and weaknesses and present several examples of comparative effectiveness findings from PBE-CPI studies.
METHODS

Randomized Controlled Trials: Features and Challenges

RCTs are considered the gold standard for establishing causality in scientific research. The intellectual origins of RCTs lie in agriculture: in agricultural hothouses, the environment can be reasonably controlled and various interventions can be tested. Likewise, in RCTs in health services research, study participants are randomized into either a treatment or a control arm, so that participant differences can be eliminated and the effect of the treatment can be isolated. With nonrandomized comparison groups, some nontreatment effects may remain unaccounted for and the outcomes may not result from the treatment or intervention under study.

RCTs use relatively simple computations and fairly small sample sizes, which were well suited to the computational limitations of an earlier time. RCTs do not need or use the full power of multivariate statistics in which many variables can be considered simultaneously and covariates can be identified and neutralized to evaluate intervention effects. Instead they use randomization in an attempt to neutralize unmeasured confounders; measured confounders are used to exclude patients from study.

In the research world, anything less than RCT-level evidence has been considered suspect by many. However, RCTs in health services research present several major challenges. Here, we describe some of these challenges and subsequently discuss how a PBE-CPI approach is liberated from many of them.

Standardization and Artificiality

RCTs use standardized treatment protocols and hold variables constant to isolate effects of the intervention and reduce “noise” in data. Hence, the intervention setting may not reflect the real-world clinical environment. Standardized treatment protocols require extensive quality control to decrease errors in treatment delivery, but treatment purity is difficult to maintain over time, across centers, and across clinicians. If this purity is compromised, intention-to-treat analyses (which keep all participants in the study and in their assigned groups even if the treatment protocol or control is not followed as prescribed) may be the best analysis option. Unfortunately, results of ITT analyses do not reflect efficacy of the treatment being studied, because some patients in the treatment group do not receive the treatment.

Selection Criteria, Patient Recruitment, and Generalizability

To reduce variation among study participants, selection criteria are often restrictive, which limits generalizability of study findings (external validity). For example, many studies exclude subjects with comorbidities, although significant comorbidities are common in many populations and may alter outcomes. Also, due to restrictive selection criteria, clinicians sometimes dismiss RCT findings, because they believe their patients are materially different from those in a clinical trial. Restrictive selection criteria typically mean that only a small percentage of patients—usually 10% to 15%—are eligible for a trial. Often, enormous resources are expended to locate individuals who meet selection criteria and achieve desired sample sizes.

Blinding

RCTs use some degree of blinding. Ideally, the study participant, clinician, and researcher or observer should be unaware of whether the participant is in the treatment or control arm. As a practical compromise, double-blinding, defined as blinding of the participant and either the clinician or the researcher/observer, is often used. However, many interventions do not lend themselves well to blinding of any kind (eg, many physical therapy interventions, or use of certain equipment).

Cost

Elaborate protocols to screen patients, coordinate and monitor care, and collect data make RCTs expensive. For example, the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) followed 1493 patients and cost $64 million.

Summary

Because of their design characteristics, findings from RCTs do not always reflect comparative effectiveness of treatments for all types of patients in routine practice. Alternative study designs should be considered.

Observational Data and Causal Inferences

Confidence in a treatment depends on confidence in the evidence supporting a causal connection between the treatment and a patients’ improved condition. Although randomization encourages this confidence, RCT evidence can be costly to obtain, may not be broadly applicable in a real-world clinical context, and can easily be compromised by small protocol deviations. An alternative is to use data that measure characteristics of patients and their treatments. However, if these data are not obtained using participant randomization, it can be difficult to determine whether different outcomes should be attributed to different treatments or to patient differences.

To overcome these problems, methods have been developed to compute unbiased estimates of treatment effects using observational data and controlling for unmeasured confounders.6–12 Drawbacks to these methods, however, include their sensitivity to untestable assumptions and the need for sophisticated statistical knowledge to ensure appropriate adjustment for relevant factors. These drawbacks make findings less understandable to clinical decision makers. As an alternative, the method of instrumental variables was developed to estimate treatment effects using observational data when unobserved confounders are present.13 However, the treatment effect is instrument-specific, and the assumptions are again untestable.

A pragmatic way to reduce uncertainty about comparative effectiveness of treatments is to collect comprehensive patient, treatment, and outcome data that are suggested by transdisciplinary clinicians who treat the types of patients being studied. One such approach, PBE-CPI, aims to foster confidence in the generalizability of its findings, and step
over the technical concerns about assumptions that are inherent in the use of instrumental variables or unbiased estimation. PBE-CPI accepts uncertainty regarding potential alternative explanations while minimizing the likelihood of such explanations.

**Practice-Based Evidence for Clinical Practice Improvement: Features and Challenges**

Comparative features of RCTs and PBE-CPI study methodologies are listed in Table 1. PBE-CPI harnesses the complexity of patient and treatment differences in the actual practice of care. Unlike an RCT, it does not alter the treatment to evaluate efficacy of a particular intervention. Instead, it captures in-depth, comprehensive information about patient characteristics, processes of care, and outcomes to characterize the process of care and ascertain the contribution of individual processes to outcomes, controlling for patient differences. PBE-CPI is a type of observational study design with 7 significant features:

1. all interventions are considered to determine the relative contribution of each,
2. hypotheses are general,
3. minimal patient selection criteria maximize generalizability and external validity,
4. detailed characterization of patients through use of robust measures of severity of illness and functional status,
5. patient differences are controlled statistically rather than through randomization,
6. facility and clinical buy-in obtained through use of transdisciplinary Clinical Practice Team, and
7. high level of transparency for all stakeholders.

Steps used to conduct PBE-CPI studies are:

1. Establish a multisite, transdisciplinary Clinical Practice Team composed of Center medical director or lead researcher and clinicians of various disciplines to engage in an iterative process to (a) define key patient characteristics presumed to affect outcomes and/or effectiveness of therapies, (b) identify and define individual components of each discipline’s care process, (c) create discipline-specific documentation tools to quantify the delivery of those components, and (d) incorporate documentation into routine facility practices. Study clinicians select factors that may influence outcomes based on theoretical understand-

<table>
<thead>
<tr>
<th>Variables</th>
<th>Randomized Controlled Trials</th>
<th>Clinical Practice Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient variables</td>
<td>Patient eligibility and stratification factors, eliminate patients who could bias results: comorbidities, more serious disease, etc. About 10–15% of patients qualify</td>
<td>Patient eligibility and stratification factors, use severity of illness to measure comorbidities and disease severity, all patients qualify by measuring patient differences; none excluded</td>
</tr>
<tr>
<td>Process variables</td>
<td>Treatment protocol, specify explicitly every important element of the process of care for both treatment and control arms, informed consent</td>
<td>Measure or record all treatments and interventions, abstract information from charts based on existing practice, informed consent often not needed*</td>
</tr>
<tr>
<td>Outcome variables</td>
<td>Powered for primary outcome, change based on evidence</td>
<td>Many outcomes assessed, improvement based on evidence from analyses of data</td>
</tr>
<tr>
<td>Measurements/documentation</td>
<td>Limited number of patient variables, treatments, outcomes measured, variables specified precisely for all patient, treatment, and outcome measures</td>
<td>Comprehensive holistic framework, variables specified precisely for all patient, treatment, and outcome measures</td>
</tr>
<tr>
<td>Database</td>
<td>Limited to the variables needed</td>
<td>Comprehensive and detailed</td>
</tr>
<tr>
<td>Result</td>
<td>Efficacy, assigned causality</td>
<td>Effectiveness, association and assumed causality</td>
</tr>
<tr>
<td>Hypotheses</td>
<td>Typically 1 hypothesis, clearly defined at the start, narrow and focused</td>
<td>Typically many hypotheses, many and broad at the start, refined and new hypotheses generated by analytic findings</td>
</tr>
<tr>
<td>Local knowledge</td>
<td>Not dependent on local knowledge</td>
<td>Depends on local knowledge; entails participation by practicing clinicians</td>
</tr>
<tr>
<td>Confounders</td>
<td>Assumed not relevant to study or outcome—eliminated in study design</td>
<td>Do affect outcomes and are relevant to include</td>
</tr>
</tbody>
</table>

*Informed consent may not be required if there is no experimental intervention and if no data are collected beyond what is ascertained from medical records and from reports prepared by clinicians in the course of usual care.
valid measure of illness severity in multiple clinical pop-

Previous research has shown that CSI is a reliable and

for severity differences at the individual criterion level.

software application that produces disease-specific physi-

washed out by the effect of overall severity. CSI is a

helps detect differences that might otherwise be hidden or

comorbid and co-occurring conditions. This use of CSI

to balance the impact of the principal diagnosis along with

identified in earlier phases.

whether the new or modified interventions replicate results

identified in earlier phases.

Implement and evaluate findings from step 5 to determine

whether the new or modified interventions replicate results

identified in earlier phases.

In summary, PBE-CPI studies encompass all care man-

agement processes and include: (1) key patient characteristics

including disease-specific physiologic severity of illness and

psychosocial abnormalities presented at each visit or each

admission); (2) all treatment and care processes (including

medications, nutritional treatments, surgical and nonsurgical

interventions, and therapies); and (3) multiple outcome mea-

surements.

Patient Factors and the CSI

Patient factors are key characteristics of the study

population, such as demographic characteristics, indications

for treatment (eg, ruptured appendix), severity of illness,

initial functional status, and psychosocial factors. By incor-

porating detailed information about patients and accounting

for differences through statistical analyses, a PBE-CPI design

achieves some of the benefit that RCTs accomplish through

randomization of patients after excluding patients with fac-

tors that could bias the findings. Detailed patient profile data

include condition-specific physiologic data such as those in

the CSI.5,14–20 The CSI is used in data analysis as a covariate
to balance the impact of the principal diagnosis along with
comorbid and co-occurring conditions. This use of CSI
helps detect differences that might otherwise be hidden or
washed out by the effect of overall severity. CSI is a
software application that produces disease-specific physi-
ologic severity of illness scores that can be used to control
for severity differences at the individual criterion level.

Previous research has shown that CSI is a reliable and
valid measure of illness severity in multiple clinical pop-

ulations. Over 20 large, multicenter PBE-CPI studies using

CSI have been conducted.

Care Process Factors and Capturing Details About

Treatments at Point-of-Care

A process of care is a sequence of linked, usually
sequential, steps designed to cause desired outcomes. The
goal is to find measurable factors that describe each process
step. Examples include which drugs are dispensed, which
dose is used, which nutritional therapies are used and for how
long, or which physical therapy activities/interventions are
used and for how long. A data collection instrument records
the process steps in detail, including timing and dates. Front-
line clinicians characterize their interventions fully and accu-

rately. Thus, PBE-CPI studies provide a very detailed account
of processes and interventions. An example of a point-of-care
documentation form used by physical therapists in stroke
rehabilitation is presented in Figure 1. It took between 0.5 and
2 minutes to fill this out for each physical therapy session.

Outcome Factors

Commonly assessed outcomes include condition-spe-
cific complications, condition-specific long-term medical out-
comes (based on clinician assessment or patient self-report),
patient functional status, patient satisfaction, and cost. Out-

come factors are PBE-CPI analogs of assessment endpoints
in an RCT.

Analyses

Detailed data are captured in PBE-CPI studies to create
a large study database that includes all the patient, process,
and outcome variables of interest. Multivariable statistical
methods are then used to compare alternative treatments while
controlling for other variables that may drive observed dif-

ferences between treatments and outcomes. These statistical
methods allow researchers and clinicians to examine relation-
ships that are more complex than those that they could
examine if they were to use one explanatory or treatment
variable at a time (or even a few). The significant independent
variables in regression equations identify key process steps
that are associated with better or worse outcomes when
patient factors are controlled for. CPI methodology allows
important statistical associations to be identified. Controver-
sial or unexpected findings can be challenged and corrobo-
rated or disproved by examining various data subsets with
different patient and treatment characteristics. Although
causality cannot be assigned, alternate hypotheses regard-
ing possible cause and effect can be tested using the large
number of available variables to identify mediating and
moderating influences on outcomes. Results of these analy-
ses can be used to eliminate potential hypotheses regard-
ing causality, and to generate specific analytic questions.
There is no minimal effect size in PBE-CPI studies; effect
sizes change as we examine finer and finer subgroups of
patients.

PBE-CPI focuses on actionable findings that can be
implemented to improve effectiveness of care. This focus

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<table>
<thead>
<tr>
<th>Physical Therapy Rehabilitation Activities</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient ID:</strong></td>
</tr>
<tr>
<td><strong>Date of Therapy Session:</strong></td>
</tr>
<tr>
<td><strong>Therapist:</strong></td>
</tr>
<tr>
<td><strong>Time session begins:</strong></td>
</tr>
</tbody>
</table>

**INTERVENTION CODES**

**Near muscular Interventions:**
- 01. Balance training
- 02. Postural awareness
- 03. Motor learning
- 04. PNF
- 05. NDT
- 06. Gait with body weight support
- 07. Involved upper extremity addressed
- 08. Constrained induced movement therapy

**Musculoskeletal Interventions:**
- 09. Strengthening
- 10. Mobilization
- 11. PROM/Stretching
- 12. Manual Therapy
- 13. Motor Control

**Cardiopulmonary Interventions:**
- 14. Breathing
- 15. Aerobic/Conditioning exercises

**Cognitive/Perceptual/Sensory Interventions:**
- 16. Cognitive training
- 17. Perceptual training
- 18. Visual training
- 19. Sensory training

**Education Interventions:**
- 20. Patient
- 21. Family/Caregiver
- 22. Staff

**Equipment Interventions:**
- 23. Prescription/Selection
- 24. Application
- 25. Fabrication
- 26. Ordering

**Modality Interventions:**
- 27. Electrical Stimulation
- 28. Biofeedback
- 29. Ultrasound

**Pet Therapy:**
- 30. Use of dog
- 31. Use of other animal

**Assistive Device:**
- 32. Ankle dorsiflex assist
- 33. Cane - Large base
- 34. Cane - Small base
- 35. Cane - Straight
- 36. Crutches - Axillary
- 37. Crutches - Forearm
- 38. Crutches - Small base forearm
- 39. Dowel
- 40. Grocery cart
- 41. Hemirail
- 42. Ironing board
- 43. KAFO
- 44. Lite gait
- 45. Mirror
- 46. Parallel bars
- 47. Platform (parallel bars or FWW)
- 48. Standing frame
- 49. Steps (various heights)
- 50. Step ladder
- 51. Swedish knee cage
- 52. Swiss ball
- 53. Tray table
- 54. Walker - FWW
- 55. Walker - Hemiwalker
- 56. Walker - Rising Star
- 57. Walker - Standard
- 58. Wheelchair
- 59. Other
- 60. Upper Extremity
- 61. Lower Extremity
- 62. Trunk
- 63. Head/Neck

**Duration of Activity:** Enter in 5 minute increments

**Interventions:** Enter one intervention code per group of boxes.

**Pre-Functional Activity**

**Bed Mobility**

**Sitting**

**Transfers**

**Sit-to-Stand**

**Wheelchair Mobility**

**Pre-gait**

**Gait**

**Advanced Gait**

**Community Mobility**

**Intervention not related to functional activity**

**Intervention #2 not related to functional activity**

**Co-Treat:**

**Area Involved/Non-functional:**
- 60. Upper Extremity
- 61. Lower Extremity
- 62. Trunk
- 63. Head/Neck

**Patient Assessment:**
- Formal Assessment (initial, re-evaluation, discharge): minutes
- Home Evaluation: minutes
- Work Site Evaluation: minutes

**Physical Therapy Time:**

- Physical Therapist
- PT Assistant
- PT Aide/tech
- PT Student

**Group Physical Therapy Time:**

- PT Group/Divetall: minutes

**Enter the number of each that participated in the Group PT:**

<table>
<thead>
<tr>
<th>Patients</th>
<th>Therapists</th>
<th>Assistants</th>
<th>Aides/techs</th>
<th>Students</th>
</tr>
</thead>
</table>

**FIGURE 1.** A point-of-care documentation form used by physical therapists in stroke rehabilitation.
means that clinicians from all disciplines treating the study patients are involved in study design, defining study variables, study execution, data analysis, and implementation of study findings. Provider involvement at all phases of the study also facilitates buy-in from others that is needed to implement findings and improve care processes.

RESULTS

More than 20 major PBE-CPI studies have been conducted. They have demonstrated that PBE-CPI studies can reveal important comparative effectiveness associations in many diagnostic groups (eg, hip replacement) or disease states (eg, osteoarthritis) and in various clinical settings. Compari-

tative effectiveness findings from 2 studies in postacute care illustrate this.

Practice-Based Evidence for Clinical Practice Improvement in Long-term Care

The National Pressure Ulcer Long-Term Care Study (NPULS) was a PBE-CPI study to identify resident, treatment, and facility characteristics associated with pressure ulcer development in nursing home residents. NPULS differs from previous studies in the details collected about residents, treatments, and outcomes. Retrospective data were abstracted from medical records of 1524 residents (from 95 long-term care facilities) who were at risk for developing pressure ulcers. No resident started with a pressure ulcer, but 29% of residents developed one by the end of the 12-week study. Interventions identified by regression analyses to be associated with decreased likelihood of pressure ulcer development included nutritional interventions (use of oral medical nutritional supplements or tube feeding for more than 21 days), use of a combination of new selective serotonin-reuptake inhibitor (SSRI) and new antipsychotic medications, use of disposable briefs for more than 14 days, and 30–40 minutes of registered nurse direct care time per resident per day. Before the study, the nursing homes used many different treatments and products to deal with decreased nutritional intake, weight loss, incontinence, and behavior problems. After better interventions were determined by the NPULS and were implemented consistently, development of new pressure ulcers decreased up to 65%.

Practice-Based Evidence for Clinical Practice Improvement in Stroke Rehabilitation

The Post-Stroke Rehabilitation Outcomes Project (PSROP) was a PBE-CPI study that evaluated associations among stroke rehabilitation patients, processes, and outcomes. Medical directors of 6 study stroke units along with physical, occupational, recreational, and speech-language therapists, psychologists, social workers, and nurses from each site collaborated to create point-of-care documentation forms to record details about each interaction and therapy session with their stroke patients. Subsequently, the clinical teams helped with data analyses.

The activities and interventions associated with better outcomes (controlling for patient differences) included: earlier start of rehabilitation after stroke onset; more time spent per day in higher level rehabilitation activities such as gait, upper extremity control, and problem solving; use of newer psychiatric medications; and enteral feeding. Several findings contradicted conventional practice, such as starting rehabilitation with higher level, more complex activities, even for the lowest functioning patients. Also, use of newer SSRI (cita-

lopram, escitalopram), opioid analgesics (codeine, fentanyl, hydrocodone, hydromorphone, methadone, morphine, oxyc-

doane, propoxyphene), and atypical antipsychotics (cloza-

pine, olanzapine, quetiapine, risperidone) was associated with greater increases in functional levels from admission to discharge. Enteral tube feeding was significantly associated with greater increases in cognitive and motor functioning for severe stroke patients, even when the degree of dysphagia was controlled for.

PSROP regression analyses produced 2 surprising consistent findings. The first was that “earlier is better.” The more quickly a patient started inpatient rehabilitation after a stroke, the better the outcomes were, no matter how sick the patient was at admission (ie, no matter how low the admission functioning score was or how high the CSI score was). The second finding supported more aggressive therapy at the onset. For example, earlier gait activities, particularly in the first 3 hours of physical therapy, were significantly associated with better outcomes, regardless of how much additional therapy a patient received. Also, participation in higher-order or more difficult therapeutic activities seemed to improve lower-level functional activities, even when the patient did not focus direct attention on those activities. For example, gait training during the first 3 hours of therapy was strongly associated with greater independence in toilet transfers by the time of discharge, after controlling for baseline functioning.

DISCUSSION

In everyday practice, patients are assigned to different treatments based on the provider’s medical judgment, compliance is not artificially influenced, and monitoring of results is based on the provider’s need for information about a patient’s condition. Multiple interventions from multiple professionals are provided concurrently. Interaction of interventions may significantly influence outcomes. The relatively small, nonsignificant effects of a single intervention may be magnified when used in combination with other interventions. Interventions that seem effective in isolation may be antagonistic when provided together. In addition, effectiveness of combinations of interventions is likely to be different for different patients. It is impossible for a randomized clinical trial to test all possible interactions among interventions encountered in routine practice. However, the large natural variation encountered in current practice within and between facilities affords an opportunity to examine the relative effectiveness of combinations and intensities of interventions. PBE-CPI methodology provides a naturalistic view of medical treatments based on data easily documented by medical providers. This view is critical to determine comparative effectiveness of treatment alternatives. PBE-CPI analyses can be used to evaluate current practices and de-
velop evidence-based improvements based on clinical data rather than clinical opinion.

The PBE-CPI approach contrasts with the approach of traditional RCTs. Because their participants are screened, selected, and subjected to scrutiny and intervention control beyond that occurring in everyday treatment, RCTs sometimes report results that are not broadly applicable in every-day treatment.34 PBE-CPI methodology identifies medications and interventions that are associated with better outcomes for specific types of patients in real-world practice.

Another key advantage of PBE-CPI study methods is cost. Using existing data from medical records and point-of-care documentation is generally less expensive than implementing a prospective RCT. For example, PBE-CPI studies to date have had sample sizes ranging from 1000 to 2500 patients and have cost between $1 and $5 million. RCTs with similar sample sizes can cost more than 20 times as much and answer only a few questions.

In past PBE-CPI studies, patient consent has been unnecessary because the studies do not involve any change in treatment and are considered quality improvement studies. PBE-CPI studies have received expedited review from IRBs.

Observational studies do not prove causality of underlying relationships, but they can identify hypotheses that can be evaluated clinically. There are 3 approaches to causality determination from PBE-CPI studies: (1) no confounders cause a significant association to disappear; (2) a change in outcome follows a change in treatment as predicted by the PBE-CPI analyses; and (3) repeated studies on the same topic yield the same findings. PBE-CPI studies have demonstrated predictive validity: outcomes improve when practices associated with better outcomes in the PBE-CPI analyses are adopted.

Possible limitations for the PBE-CPI methodology include:

1. Data sources. PBE-CPI studies require detailed data not present in administrative claims databases. PBE-CPI studies work with front-line clinicians to determine variables to collect that either are present in existing medical charts or can be obtained using point-of-care documentation forms.

2. Missing important confounders. PBE-CPI studies attempt to identify confounders by working with front-line clinicians who define relevant patient, treatment, and outcome variables.

3. Incomplete documentation. PBE-CPI studies use site study coordinators who monitor daily documentation for data completeness.

Methodologic alternatives such as PBE-CPI do not replace RCTs; rather, they provide additional systematic outcomes information to improve clinical practice. RCTs and PBE-CPI should be considered complementary study methodologies. Effectiveness of treatments from RCTs can be tested in PBE-CPI studies and PBE-CPI can be a progenitor of new RCTs.

PBE-CPI studies enable healthcare providers, managed care organizations, payers, and individuals to compare the effectiveness of treatments in current practice and improve clinical decision making. They answer questions in the real world, where multiple variables and factors can affect outcomes.

REFERENCES


