Developing Good Research Practices for Performance-Based Risk-Sharing Arrangements

Task Force Objectives
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- What is a PBRSA?
- Distinguishing among PBRSAs
- The Four Key research questions
- Desirability of PBRSAs
- Approaching Research Design
- Timing
- Implementation
- Evaluation
- Governance
- Public vs. Private Payers

Purpose of the Session
- Provide an update on Task Force objectives and progress.
- Identify and describe key issues and challenges.
- Seek audience input and comments.

Task Force Members
Co-Chairs: Lou Garrison, PhD, University of Washington, USA  
          Adrian Towse, MA, MPhil, Office of Health Economics, UK

Task Force Members:
- Ron Akehurst, BSc (Econ) (London), Hon MFPHM, University of Sheffield, Sheffield, UK
- Andrew Briggs, MSc, DPhil, University of Glasgow, Scotland
- Gerard de Pouvourville, PhD, ESSEC Business School, France
- Jens Grueger, PhD, Pfizer Inc., USA
- Penny Mohr, MA, Center for Medical Technology Policy, USA
- Hans Severens, PhD, Erasmus University Rotterdam, the Netherlands
- Paolo Siviero, BA, AIFA, Italy
- Miguel Sleeper, GlaxoSmithKline, Inc. Guildford, UK

ISPOR Staff Liaison: Elizabeth Molsen, RN

Outlines of the Session

Presenters
Moderator: Adrian Towse MA, MPhil, Professor, Office of Health Economics, UK

Speakers:
- J.L. (Hans) Severens, PhD, Professor, Erasmus University, the Netherlands
- Jens Grueger, PhD, Vice-President, Pfizer, Inc., USA
- Gerard de Pouvourville, PhD, Professor, ESSEC Business School, France
- Lou Garrison, PhD, Professor, University of Washington, USA

To produce a report that sets out the standards that should be applied to a “good practice” PBRSA, encompassing the design, implementation, and evaluation of such an arrangement.

To provide practical recommendations for the development and application of state-of-the-art methods to be used in the design and evaluation of PBRSAs.
What is a PBRSA?

- PBRSA = Performance-Based Risk Sharing Arrangement
- Also known as:
  - outcomes-based schemes
  - risk-sharing agreements
  - coverage with evidence development
  - access with evidence development
  - patient access schemes
  - conditional licensing
  - managed entry schemes
  - pay-for-performance programs
  - innovative pricing
  - and others?

PBRSA—Working Definition (1)

1. There is a program of data collection—either by agreement between the manufacturer and payer or initiated by the payer—to reduce uncertainty about the expected effectiveness (including possible negative effects) and cost-effectiveness of the drug (or device or diagnostic) or other relevant outcome or cost impact on the health care system.

2. Data collection is typically initiated during the time period following the regulatory approval but before the full diffusion and uptake of the product, i.e., early in the commercial lifecycle.

PBRSA—Working Definition (2)

3. The price and/or revenue are either linked explicitly by formula to the outcome of this program of data collection (at a population level or at an individual patient level) or implicitly through an option to renegotiate coverage, price, and revenue later.

The arrangements are primarily concerned with reducing uncertainty about expected health outcomes (i.e., better estimates of real-world effectiveness): this can affect both uncertainty about the overall cost-effectiveness and about the utilization of the product (i.e., will the “right” numbers and types of patients get the product?).

PBRSA—Working Definition (3)

4. The uncertainty may be about:
   a. the expected outcomes of the treated population as compared to those with the use of an alternative treatment path;
   b. the size and value of cost offsets, such as fewer hospital visits;
   c. the proportion of patients who will respond, i.e., achieve a pre-set (minimum) outcome or surrogate marker;
   d. whether the patients treated are the “right” ones, i.e., matching the levels of cost-effectiveness identified in the evidence currently available?

PBRSA—Working Definition (4)

5. These arrangements provide a different distribution of risk as between the payer and the manufacturer than conventional arrangements.

6. They exclude arrangements that are primarily intended to be disguised price discounts. However, a number of the operational aspects that underpin a successful PBRSA may apply to such schemes.

A Taxonomy of PBRSAs

J.L. (Hans) Severens PhD
Professor, Evaluation in Health Care Institute
of Health Policy and Management
Erasmus University Rotterdam
Rotterdam, Netherlands
What is the source of the decision uncertainty that affects the final positive and a negative decision?

- Uncertainty in internal validity (efficacy; small sample size; inappropriate comparators)
- Uncertainty in external validity (real-world performance; compliance; link from surrogate to long-term outcomes)
- Heterogeneity—differential response/benefits among patients
- Diffusion uncertainty—(beyond initial indication) changing or appropriate population subgroups and usage over time?

Performance based risk sharing arrangements

- To manage utilization in the real world
- To provide evidence regarding decision uncertainty

Financial / Cost sharing arrangement

- Budget capping
- Utilization capping
- Discounts
- Price/volume

Risk sharing arrangement

- Outcomes guarantees
- Conditional treatment continuation
- Process of care

Intermediate endpoint
- Pre-specified agreement
- No pre-specified agreement

Clinical endpoint

Performance linked reimbursement

- Only with research
- Only in research

Intermediate endpoint
- Pre-specified agreement
- No pre-specified agreement

Key Research Questions

Jens Grueger, PhD
Vice President, Health of Global Access, Pfizer, Inc.
New York, NY
USA

Q1. Desirability: Is a PBRSA the appropriate way forward given uncertainty and alternatives to the use of a PBRSA?

The general question is whether a PBRSA can effectively and efficiently address the uncertainties remaining following marketing authorization. This is a de facto prospective value-of-information (VoI) question. What is the issue/problem? What are the alternatives to using a PBRSA to tackle the problem?
Q2. Evidence collection: Which PBRSA research design is most appropriate to collect evidence, conduct analyses of the evidence, and how should results be reported?

The answer will depend on the kind of problem the PBRSA is trying to solve:

- Uncertainty around whether the medicine will be used in the right patients, e.g., responder schemes, or via value-based pricing schemes where the price differs across indications or patient groups.
- Uncertainty at launch around clinical or economic outcomes (effectiveness vs. efficacy, final outcomes vs. surrogates, questions around the ICER).

There are many possible research designs.

Q3. Implementation: How should the PBRSA be organized / operationalised?

For a selected PRSA, how will the research (under Q2) be linked to the mechanics of the scheme, e.g., any price or revenue adjustment; rebates to be paid during the course of the scheme (in the case of responder based reimbursement), extension of restriction of the subgroups of patients who will have access to the treatment; process for review of reimbursement status? Fulfilment of adverse event reporting requirements.

Q4. Evaluation: Has the PBRSA achieved its objectives? Was it good value from a societal perspective?

This is the ex post question. It links back to expectations / assumptions in Q1. Are we more knowledgeable about the technology in question? Have patients benefited from access? How do the costs of the scheme relate to the value of the benefits?

Gerard de Pouvourville, PhD
Professor & Chair
Health Economics & Management, ESSEC Business School, Cergy Pontoise, France

When?

- A new treatment that appears to be promising, but where uncertainties question the relevance of coverage:
  - From a public health perspective: uncertain benefit/risk ratio, leading to potentially putting patients at risk
  - From a financial perspective:
    - Opportunity cost of coverage is too high
    - High uncertainty on budget impact

Why?

- A PBRSA allows access:
  - Response to patient need
- A PBRSA allows controlled access:
  - Generation of data to reduce uncertainty
  - Control of budget impact
**Payer perspective**

What are the alternatives?

- Refuse coverage, with the risk of facing political pressure …
- Frees resources for other less uncertain innovations

**Company perspective**

When?

- The development program was good enough for registration, but the payer’s resistance is anticipated:
  - Surrogate endpoints versus morbidity-mortality
  - Incompleteness of comparative data
  - Trial duration…
  - High expected budget impact:
    - High prices
    - Large target population

**Company perspective**

Why?

- PBRSAs may be a way to overcome a payer’s aversion for risk:
  - Goodwill
  - Limit public health risk
  - Limit financial risk by accepting to share the burden
  - Expected revenues over life cycle, including risk of loss, is higher than expected revenues with additional clinical development costs

**Company perspective**

What is the alternative?

- Extending the clinical development:
  - Extra cost or sometimes major difficulties (recruitment)
  - Risk of not getting positive results
  - Shorter time before LOP
  - Risk of facing competition

**Limitations**

In the case of an agreement with a pre-specified target:

- Payers may fear opportunistic pricing of companies, adjusting their price level to anticipated risk of failure:
  - Ask for a lower price upfront and agree to readjust after conclusion of the agreement
  - For companies, higher uncertainty on revenues during the test-period.

**Cross-Cutting and Other Issues**

Lou Garrison, PhD  
Task Force Co-Chair  
Professor, Pharmaceutical Outcomes Research & Policy Program, Department of Pharmacy  
University of Washington  
Seattle, WA  
USA
Begin with a systematic review and a model synthesizing all available evidence.

Identify parameter uncertainty in key drivers:
- Uncertainty in internal validity (efficacy; small sample size; inappropriate comparators)
- Uncertainty in external validity (real-world performance; compliance; link from surrogate to long-term outcomes)
- Heterogeneity—differential response/benefits among patients
- Diffusion uncertainty—(beyond initial indication) changing or appropriate population subgroups and usage over time?

Comparative effectiveness
- Prospective randomized is likely to be preferred for efficacy / treatment effect
- Need to consider feasibility (e.g. difficult to withhold covered treatments)

Link from surrogate to long-term health endpoint
- Prospective observational (pre-specified rigorous analysis; appropriately controlled, e.g., covariate; propensity, case control, etc.)

Begin discussions in pre-coverage phase to reduce time to decision, as it can take a long time to get studies up and running.

Duration of agreements should be modular rather than same for every technology.

To address dynamic uncertainty – enable multi-industry arrangements.

In long-term studies include intermediate analysis – reciprocal observations; keep contracts short.

PBRSAs need to be clear about the hypothesis that needs to be proven.

The objective(s) of the PBRSA should inform the study design.

The administrative and financial burden (transaction costs) should be proportionate to the value of the scheme and be included in the prior decision to proceed or not.

They should maintain a high level of internal integrity to ensure that the results do not misinform.

Previously established GRPs for evaluations of randomized and non-randomized studies apply.

To date, very few evaluations of PBRSAs

Evaluation should cover both process and outcomes.

Process:
- Was the information collected according to the protocol?
- Was the information analyzed according to the protocol? Was the design appropriate?
Outcomes:
- Primary endpoints, access to treatment, financial
- What consequences in terms of decision making?
- Single PBRSAs vs. Program
- Value of information framework for design
- Not applicable for evaluation

Evaluation (2)

Governance
- Some schemes need governance arrangements over and above those that would apply to good research practice for the relevant study design.
- Governance committee should have a clear charter specifying who is involved and respective roles.
- Specify aims of PBRSA, stopping rules.
- Specify who has access to data, who can publish, process for vetting manuscripts.
- Spell out process to ensure timeliness and data quality.
- Make conflict(s) of interest clear.

Public vs. Private Payers
- Most schemes to date have been with public payers.
- Should GRPs vary between arrangements with public vs. private payers? Or is “good science just good science”?
- Do PBRSAs with private payers have an ethical obligation to follow GRPs and reporting requirements?

Next steps and timetable
- Task Force internal revisions (Nov. - Dec.)
- Circulate first draft to PBRSA Review Group (mid Jan.; response early Feb.)
- Address Review Group comments (Feb.)
- Final draft manuscript (March)
- Circulate to ISPOR membership (early April)
- Submitted to Value in Health (end of April)
- Plenary presentation at the ISPOR 17th Annual International Meeting in Washington DC (June 2012)

Thank You!

For more information on the ISPOR PBRSA TF:

Please JOIN the task force as a Review Group member via the GREEN TASK FORCE PULL-DOWN MENU on the ISPOR homepage