Payers’ Use of Health Economics Data and Perceptions of Data’s Value in Formulary Decisions

Final Report

March 19, 2009

Submitted to:
Eli Lilly and Company
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Ref:  Paysers’ Use of Health Economics Data and Perceptions of Data’s Value in Formulary Decisions

Dear Dr. Ball:

Enclosed is Westat’s final report to Eli Lilly and Company, Payers’ Use of Health Economics Data and Perceptions of Data’s Value in Formulary Decisions. As you requested, we have provided you with three hard copies of the report. The report contains the following:

- The body of the report summarizes the steps we took and the results we obtained.
- The appendixes contain additional material concerning methods and substance. Specifically, the appendixes include the protocols for Phase I and Phase II interviews; a bibliography of studies selected for the literature review; highlighted abstracts of those studies; summaries of decisionmakers’ responses to the Phase II protocol questions; and other items. The summaries of responses form the basis of the findings in the body of the report.

Please note that, in addition to providing details of decisionmakers’ responses to our questions, the summaries are of independent interest. They convey the texture and tone of decisionmakers’ views on studies and models supplied to payers by pharmaceutical companies, payers’ interactions with pharmaceutical representatives and officials, and other topics of interest.

As an aid to you and your colleagues, we enclose one compact disc (CD). It contains copies of the published articles listed in Appendix D.

Westat is pleased to have had the opportunity to conduct the research reflected in this report. Our staff appreciates the collegial interactions they enjoyed with you and your colleagues and values the substantive input and guidance you and your colleagues provided.
We look forward to working with you and with Eli Lilly and Company in the future.

Sincerely,

Jonathan Ratner, Ph.D.
Senior Economist

Encl.
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**Executive Summary**

**Motivation and Objectives**

Eli Lilly and Company commissioned this study to provide up-to-date information on U.S. payers’ use of and attitudes toward pharmacoeconomic information. The research literature on this topic is not current. Much of the literature focuses on Europe, Canada, and Australia. As agreed with Eli Lilly, Westat undertook to address three objectives:

- Describe U.S. health care payers’ use of pharmacoeconomic information.
- Describe U.S. payers’ perception of pharmacoeconomic information’s value in formulary decisionmaking and characterize their attitudes toward that information.
- Identify interesting features of U.S. payers’ process of making formulary decisions and of these payers’ attitudes toward the pharmacoeconomic information that drug manufacturers provide to the payers.

**Approach and Methods**

To address the study objectives, the Westat team conducted intensive interviews with formulary decisionmakers at a judgmental sample of nine types of payers, including private insurers, employers, pharmacy benefit managers (PBM), and public payers. We decided against using a conventional survey instrument coupled with a probability sample. The intensive interview/judgmental sample approach involves a trade: give up the advantage of statistical projectability but gain substantive accuracy and meaningful responses. We decided the trade was worthwhile.

Westat undertook intensive, 1-hour interviews with formulary decisionmakers at diverse insurers and public payers. Phase I interviews were exploratory. The protocol for Phase II (full-scale research) drew on lessons from Phase I and on Westat’s systematic search of the research literature from 2001 through 2007. Our literature review identified gaps and omissions, which this study sought to fill.
Executive Summary

Findings

The study has four “meta-findings”—umbrella statements that encompass several, broadly related findings.

- Finding 1 presents themes and variation in payers’ use of pharmacoeconomic information and their attitudes toward it.

- Finding 2 looks at the many facets of payers’ interactions with pharmacoeconomic information: payers’ reactions to receiving computer models or publications, barriers to use of drug company models, the appeal and risks of real-world studies, and the direction of information-flow in payer/drug representative meetings.

- Finding 3 concerns the market for prescription drugs. It crystallizes payers’ comments on special treatment of drugs for certain disease areas, the state of the Medicare prescription drug plan (PDP) market and its prospects, and PBMs’ functions in relation to payers.

- Finding 4 sketches payers’ expectations for the future of formulary decisionmaking. The finding ends with their wish list regarding pharmacoeconomic information. Details follow.

1. Compared to 10 years ago, payers regard pharmacoeconomic information much more favorably. However, today, the variation among payers in their use and attitudes concerning such information is substantial. In particular, four points stand out:

- In the past 10 years, U.S. payers have made a major shift: they accept pharmacoeconomic information’s scientific merit in general. Nonetheless, substantial practical concerns remain, depressing payers’ use of this information considerably, relative to its potential. Payers’ concerns include manufacturers’ biased selection of data as well as difficulties payers face in translating results from randomized control trial (RCT) patients to their own populations.

- The 10-year trend aside, the use today of pharmacoeconomic information differs sharply among three broad groups of U.S. payers:

  (a) The inner ring or “bull’s eye” – a minority of payers that uses pharmacoeconomic information narrowly defined—e.g., cost-effectiveness analysis—frequently and relatively rigorously;

  (b) The middle ring – a larger group of payers that are occasional/informal users of pharmacoeconomic information narrowly defined and that regularly examine pharmacoeconomic information broadly defined—from RCT results and outcomes research to various cost measures; and
(c) The outer ring – a sizable number of payers that regularly consider such information *broadly defined* but generally process that information using professional judgment. These payers do not use an articulated, pharmacoeconomic analytic framework.

- Some payers are starting to decouple new drugs’ *clinical* evaluation from *cost* evaluation.

  In the past, pharmacy and therapeutics (P&T) committees made adoption and tiering decisions after considering both clinical effectiveness and cost. Recently, some insurers and PBMs are placing the two analytical functions in separate internal units. Still the exception, this phenomenon may be an emerging trend.

- Use of pharmacoeconomic information by payers displays unexpected features:

  As expected, *payer-type* matters (e.g., siloed Medicare Part D prescription drug plans (PDP) use such information less than do insurers that cover not just drug but medical costs). However, other factors matter too: *scale of organization* (large payers are more prone to be in the inner or middle rings); *statutory requirements* (laws that bar tiers and that require adoption of all FDA-approved drugs reduce the value to payers of pharmacoeconomic information); *idiosyncrasy* (distinctive cognitive traits and analytic stances of an influential decisionmaker affect some payers’ use of pharmacoeconomic information); *PBMs’ public face* (to placate consumers, a PBM may downplay greatly its use of cost-effectiveness criteria in communicating with the public).

2. Regarding drug companies’ presentation of pharmacoeconomic information, payers’ perceptions and reactions are disparate and at least superficially in conflict. Payers distrust pharmacoeconomic information supplied by drug companies but prefer that drug companies give them publications, not models.

  Laws that deny cost sharing and other tools to public payers may discourage their use of pharmacoeconomic information, yet a law establishing an entity to conduct impartial comparative effectiveness research could spur use of such information among all payers.

  Payers offered insights regarding real-world studies, phrases that enhance a drug’s perceived value, and whether drug company representatives misuse their time with payer decisionmakers. Highlights follow:

  - Virtually all U.S. payers interviewed look askance at drug companies and the information about new drugs they provide. The skepticism is deep-seated: payer decisionmakers see that a drug manufacturer can gain market share by selecting favorable evidence about its drugs and spinning it. To payers, their skepticism simply reflects their experience of drug marketing. In payers’ eyes, manufacturers accentuate the positive and excise the negative. In response, payers take countermeasures to level the informational playing field.
Nonetheless, most payers prefer that manufacturers supply them with publications, not models. Payers typically view drug company models as marketing tools, not impartial summaries of scientific evidence. However, a minority of payers prefers models to publications.

Payers cite two barriers to their use of drug company models:

1. Lack of transparency (black boxes inspire skepticism);
2. Selective use of data favorable to the manufacturers’ own drugs. As expected, payers prefer manufacturer-supplied information that is funded and directed independently; an editor or peer reviewer has reviewed; and a professional journal published.

Moreover, payers prefer models that can accept users’ own data, that reveal their hard-wired assumptions, and whose parameter values users can alter.

Payers fear a drug effective in an RCT may not be as effective with their own patient enrollees. Payers lack even an imperfect evidence-based method of translating results from an RCT’s population (the gold standard) into credible results for the patient population of a particular insurer or public payer.

Government can spur or reduce payers’ use of pharmacoeconomic information, depending on specifics. Payers might use more of such information if a government or independent, comparative-effectiveness research entity were created and proved impartial. Laws that, for example, mandate adoption of all drugs approved by the Food and Drug Administration may make pharmacoeconomic information less valuable to some payers.

Payers cited three interesting aspects of the information flow between pharmaceutical companies and payers:

1. Some payers acknowledge the appeal of real-world studies but discount or dismiss such studies if they show a drug to be more effective than the RCT found.
2. Most payers dismiss health-related quality of life (HRQoL) and patient-reported outcomes (PRO), while some said that the phrase “disease modifying” enhances the attractiveness of a drug.
3. Many payers find that, in meetings about new drugs, drug representatives’ canned presentations crowd out time to address formulary decisionmakers’ questions.
3. Payers cited several aspects of the market for prescription drugs of interest: special treatment of drugs for certain disease areas; a cloudy if not dark outlook for the Medicare PDP market; and PBMs’ functions in relation to payers.

- Payers increasingly are giving high-cost oncology drugs more scrutiny. (Historically, payers gave oncology drugs less stringent review than the norm.) However, for drugs in other disease areas, such as mental health and Alzheimer’s, the bar may be starting to be lowered.

- Payers interviewed said they were looking to move some specialty drugs from medical to pharmacy. In the past, drugs on the pharmacy benefit received stricter reviews than those on the medical benefit. More recently, payers report they can achieve the same effect by conducting more stringent reviews on the medical side.

- Despite the popular view that the Medicare PDP market is lucrative, some insurers doubt whether offering a PDP is profitable. Some criticize stand-alone PDPs as flawed because they institutionalize siloing of costs. These payers seem to be saying they like the MAPD model but entered the PDP market by mistake. Payers also chafe under CMS guidance they consider overly prescriptive.

- While confirming conventional views of PBMs’ functions, payers noted that PBMs sometimes aid them in managing specialty drugs; and employers sometimes request that their PBM add or remove certain drugs to their formulary (e.g., fertility drugs).

4. Looking ahead, payers foresee substantial continuity in their own organization’s formulary. But at least one payer foresees a surprising change in cooperation between payers and pharmaceutical manufacturers. Payers also expressed the wish for several changes in the supply of pharmacoeconomic information.

- For example, payers expect the trend of greater scrutiny for high-cost oncology drugs to continue. They also expect that trend and the trend toward value-based benefit design to be in tension.

- Several payers (a significant minority) cited resistance to including medical cost offsets when assessing new drugs. However, insurers attributed the resistance to employers, and employers—to insurers. Whatever the source of the situation, many agreed that there was an excessive preoccupation among stakeholders with rebates.

- One large insurer predicted that drug companies and health care payers will increasingly cooperate regarding real-world studies and improving drug companies’ dialogue with payers about the facts concerning new drugs.

- Payers hope for (but do not necessarily expect) improved pharmacoeconomic information. For example, they would like greater transparency in pharmacoeconomic information, an independent entity to supply unbiased information on new drugs’ effectiveness, and computer models that can be easily customized to the user’s specifications. Payers also included several analytical items on their wish list.
1.1 Overview

The Westat team’s work for Eli Lilly and Company on aspects of the market for health economic/pharmacoeconomic data is now complete. This final report summarizes the steps we took and the results we obtained.

The report addresses the following topics:

- The motivation for the study and the study objectives;
- The overall strategy for data collection;
- The methods used in the exploratory interviews (Phase I);
- The literature review undertaken to guide the revisions of the Phase I protocol, which were the key to the redesigned Phase II protocol;
- The methods used in the full-scale interviews (Phase II); and
- Significant findings based on these interviews.

The appendixes to the report contain additional material concerning methods and substance. Specifically, the appendixes include the protocols for Phase I and Phase II interviews; a bibliography of studies identified through the literature search; a table of topics, abstracts, and questions regarding studies included in the literature review (the table ranks studies by potential contribution to the revised protocol); and summaries of responses of decisionmakers at 9 payers to 35 questions that span 9 domains or topical areas.1 From these summaries are drawn the findings in the body of the report.

The interview summaries (see Appendix A), organized by topical area, are of independent interest for two reasons. First, the summaries contain information sufficiently detailed to convey the range of responses to any given question. In contrast, the findings characterize the typical

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1 As a complement to the text of the report, we include a compact disk that contains copies of the publications listed in the bibliography from the literature search.
response or several clusters of responses. The findings usually cannot convey the diversity of responses, but the summaries usually can. Second, Appendix A interweaves summaries of responses with quotes from individual decisionmakers. In these quotes, the payer decisionmakers sometimes express their viewpoints and perceptions in vivid or pithy ways. More generally, these quotes often possess a certain force and convey an authentic sense of how these decisionmakers view “life in the trenches,” as seen from the vantage point of their formulary/payer.

In sum, the findings and the interview summaries complement each other. The findings provide generalizations and characterize different patterns of pharmacoeconomic data use and payer perceptions. The summaries provide greater detail, combined where possible with ethnographic or journalistic detail.

### 1.2 Study Motivation

A substantial research literature on pharmacoeconomics is normative and methodological. For example, researchers assume that, in making formulary decisions, insurers and other health care payers should adopt drugs (and other treatments) that are most cost-effective. Many studies explore methodological aspects of the pharmacoeconomic toolkit—cost-effectiveness analysis, outcomes measurement, cost-utility methods of addressing multiple-outcome problems, etc. Other studies apply these tools to the assessment of particular new drugs.

A smaller literature is descriptive: it examines the use of pharmacoeconomic tools by payers and the attitudes and perceptions payers’ staff and officials have regarding pharmacoeconomic information. This literature is “positive,” not normative: it examines behavior and attitudes as they are and does not primarily seek to determine how payers should use information for new drug assessment.

Having considered the descriptive/positive literature, Eli Lilly and Company determined in 2007 that additional research in this vein was warranted. The rationale for the decision involved four points:

- Published studies of payers’ use of pharmacoeconomic information were 5 years old or more. With much else in health care changing rapidly, it was natural to explore the extent of change in payers’ use of such information and their attitudes toward it.

- Much of the descriptive/positive literature focused on countries other than the United States, such as the United Kingdom, Canada, Germany, Australia, and Scandinavia.
With the United States central to the world pharmaceuticals market, Eli Lilly decided that understanding more about the current behavior and attitudes of U.S. payers was important.

Eli Lilly recognized that much of the descriptive/positive literature, in focusing on Europe, Canada, and Australia, might have limited application to the United States. Where Europe and countries like Canada tend to finance their health care using a single payer or dominant national payer model, the United States’ system is diverse, even fractionated. The U.S. market has multiple types of payers, even within a broad category: Public payers range from idiosyncratic, Federal/state-financed but state-administered Medicaid programs to Medicare Part D private drug plans to the Veterans Affairs’ single-payer system. Private payers include national commercial insurers with indemnity, fee-for-service plans; large-scale managed care organizations; local and regional Blue Cross Blue Shield plans; and employers. Lilly conjectured payer-type matters. Specifically, given this diverse array of health financing vehicles, different types of organizations might make use of pharmacoeconomic information differently.

To understand fully the stance of payers toward such information, Lilly determined it would be helpful for new research to consider both behavior—payers’ use of this information—and attitudes—payers’ perceptions of pharmacoeconomic information’s value to them as decisionmakers.

1.3 Objectives

Lilly’s Request for Proposal (RFP) stated the initial objectives for the study. Through dialogue, Lilly staff and the Westat team refined the objectives and clarified their interpretation. Two main objectives, articulated in the RFP, are as follows:

- Describe U.S. health care payers’ use of pharmacoeconomic information.
- Describe U.S. payers’ perception of pharmacoeconomic information’s value in formulary decisionmaking and characterize their attitudes toward that information.

As a complement to these objectives, the RFP stressed Lilly’s interest in the extent to which payers’ use and attitudes/perceptions varied from payer to payer. In particular, the RFP wanted the study to devote considerable attention to the role played by type of payer. To simplify exposition, the report’s response to the two objectives above considers payer-type as an important factor, not as a separate objective.

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2 In the U.S. market, pharmacy benefits managers are important, acting for insurers and employers as their agents.
A third objective is open-ended and, to a considerable extent, cuts across the two main objectives stated above:

- Identify interesting features of U.S. payers’ process of making formulary decisions and of these payers’ attitudes toward the pharmacoeconomic information that drug manufacturers provide to the payers.

For the third objective, the rationale follows: in considering the proposal for exploratory interviews that the Westat team prepared, Lilly officials and the team recognized that many questions in the protocol had twin functions: first, payers’ responses to these questions would contribute to answering the main study questions; and second, payers’ responses would likely include information that was interesting in its own right and potentially useful to Lilly, even if a response was one step removed from the study’s central focus.³

³ In preparing the final report, we have sought to relate every item to the main objectives. In some cases, though, the report includes an item for its contextual value or its independent interest regarding the pharmaceutical marketplace.
2.1 Overview

To address the study objectives, the Westat team conducted intensive interviews with formulary decisionmakers that included a judgmental sample of payers—private insurers, employers, pharmacy benefit managers (PBM), and public payers. We considered a conventional survey instrument coupled with a probability sample (for example, a stratified random sample) but decided against it.

This section sets out the rationale for our approach. The advantages and limitations of conventional surveys are discussed, followed by an examination of the intensive interview/judgmental sample option.

2.2 Merits and Risks of Conventional Surveys

The advantages of a survey coupled with a probability sample are well-known: The estimates of key parameters calculated from sample data have desirable statistical properties, because the underlying sample represents a random draw from the entire population. In this case, the sample would be representative of the population of payers. Moreover, one could calculate estimates of parameters (such as the proportion of payers that use pharmacoeconomic information more than once a year), which could be viewed as statistically unbiased estimates of the parameters that describe the entire population.

Typically, data are collected for a random sample and the method of collection is a survey instrument. However, given the objectives of this study, as a method of collecting data from decisionmakers at payers, a conventional survey is risky. The risk lies in who responds to the survey. To see why, begin with the fact that this study seeks to answer questions related to payers making formulary decisions. It follows that those in the best position to answer such questions accurately are formulary decisionmakers—chief medical officers, pharmacy benefits directors, directors of units that evaluate drugs’ effectiveness, etc. However, conventional surveys face two related risks, given that formulary decisionmakers are senior officials. The first risk is substantial nonresponse. Busy senior officials are unlikely to fill out a survey, even on the Web. The second risk is that the task of
filling out the survey will be delegated to a junior staff member. That junior person is unlikely to be a close substitute for the senior official as an informed respondent. In part, the junior person is likely an imperfect substitute because he or she cannot report the decisionmaker’s attitudes and perceptions reliably. Such attitudes and perceptions are important to this study. Moreover, even reporting on the decisionmaker’s behavior—his or her use of pharmacoeconomic information—is problematic. In any case, the survey organization cannot readily and reliably learn who filled out a survey, regardless of its addressee.

2.3 Merits and Risks of Intensive Interviews

The strengths and limitations of the survey-plus-random sample option are mirror images of the intensive interview/judgmental sample option. By definition, a judgmental sample cannot yield estimates projectable to the population of payers. As a result, averages and other summary statistics can only describe or summarize a judgmental sample. They cannot, however, be treated appropriately as estimates of, say, the population’s mean proportion of all payers that use pharmacoeconomic information in making formulary decisions. Use of a judgmental sample risks biased estimates, precisely because it is not drawn randomly from the population.

Notwithstanding this major drawback, the intensive interview/judgmental sample option has important advantages.

- First, the intended respondents respond. Under this option, the respondents or interviewees are the formulary decisionmakers, as intended. This fact is indisputable: These individuals’ role regarding formulary decisions would be (and was) established in the initial contact and would be (and was) confirmed by the co-principal investigators in the interview. As a result, the risk of a respondent not being a formulary decisionmaker is ruled out ab initio. The “delegation bias” of a conventional survey of payers does not arise.

- Second, substantive accuracy is greater. An intensive interview with a decisionmaker increases the substantive accuracy of his or her responses. The interview format permits responses to be clarified, and followup questions to be asked about surprising responses and about allusions to unexpected or new topics. As a result, answers from an intensive interview are likely to be more meaningful than those from a conventional survey.¹

¹ Users of survey data often want to interpret the quantitative results by getting a sense of the context and shading of respondents’ answers. Consequently, discussants of conventional surveys such as the Gallup poll supplement their numerical data with informal, nonrigorous anecdotes from, for example, voters.
Third, **connections made between responses.** The interviewers can make connections between responses to different questions. This can increase the substantive accuracy of responses as recorded by the interviewers. (By remarking on apparent connections or discrepancies between responses, interviewers can spur interviewees to correct misunderstandings and misinterpretations.) It also can lead to new insights. This third advantage is generally not a feature of most surveys.

Fourth, **method suited to qualitative data.** Intensive interviews lend themselves to eliciting qualitative information, especially if the anticipated responses to a question are diverse and often difficult to anticipate. While certain qualitative questions lend themselves to Likert scales, in general the questions needed for this study are better suited to narrative responses.

Overall, the intensive interview/judgmental sample option trades away the advantage of statistical projectability (which the conventional survey offers) in order to gain substantive accuracy and meaningful responses. The Westat team decided that, for this study, such a trade is worthwhile. In effect, we deemed very valuable the greater substantive accuracy and meaningfulness we expected from our interviewees. We placed much lower value on a survey’s statistically generalizable estimates. We thought these likely to be seriously contaminated by measurement error of various sorts. In selecting our proposal, Lilly accepted our strategy.

### 2.4 Operational Aspects of Interviews

The mechanics of the interviews were straightforward: all interviews were conducted by the Westat team’s principal investigators, Daniel Mullins and Jonathan Ratner. The interviews were generally 1 hour long, although several lasted more than an hour. We requested interviews with the full complement of a payer’s formulary staff and officials. In some cases, we met with as many as a half dozen individuals. In other cases, we met with a single person, often the sole individual at an insurer or an employer who monitors the work and recommendations of the payer’s PBM. All interviewees were given an assurance of confidentiality: statements by individuals would not be attributed to the individual or his/her organization. (The one exception is if the content of a statement is already a matter of public record. For example, the content with attribution has appeared in an article written by a member of the organization.)
2.5 Two Phases of Interviews

We designed this study’s data collection to have two phases.

- **Formative research.** Phase I was “formative research,” an effort to discern the boundaries of the topic, the suitability of our initial protocol or set of questions, and so on. Phase I involved a set of exploratory interviews (see Chapter 3 for details). The responses to these interviews were analyzed and the interview experience reflected upon as part of our preparation to revise the protocol for Phase II.

- **Full-scale research.** Phase II employed a protocol revised to incorporate lessons from Phase I’s interviews as well as from a literature review (see below). Phase II used the revised protocol in interviews with a larger number of payers than in Phase I. Phase II’s set of payers corresponds to 10 major types of payers.
3.1 Objectives of Phase I Interviews

We undertook exploratory interviews of payers’ formulary decisionmakers with two aims:

- First, **to test the interview protocol we had developed, with an eye to refining it.** We sought to assess the extent to which the interview questions were understood by the interviewees or required clarification. We also wanted to establish if certain questions consistently yielded little added value, given that the literature already reported the same finding. Such questions would be candidates for deletion.

- Second, **to uncover new topics and new angles worth exploring.** We hoped the exploratory interviews would lead decisionmakers to bring to the fore concerns and issues not addressed in the Phase I protocol. Similarly, decisionmakers might volunteer facts that could point us toward new, potentially fruitful questions.

3.2 Interview Protocol for Phase I – Formative Research

For the full protocol used in Phase I of the study, see Appendix B. Highlights of this protocol, grouped by topic, are as follows:

- **Definition of Value.** Here we explore the interviewees’ conception of “value” in the context of considering a new drug for formulary adoption and tier placement; whether value is viewed differently for drugs than for devices and procedures; and how a drug’s value affects tier placement.

- **Assessment of Value.** This set of questions examines the process by which the payer organization assesses a drug’s value; the circumstances that trigger reassessment of value; and the role in value assessments of health-related quality-of-life claims.

- **Components of Effectiveness Considered.** These questions probe for how formulary decisionmakers view aspects of effectiveness: how their assessments incorporate information on secondary endpoints versus primary endpoints; whether safety is considered apart from effectiveness; the role of “real-world” studies in value assessment; and whether data on patients’ adherence/compliance enter into decisionmakers’ assessments.
Components of Costs Considered. This block of questions asks formulary
decisionmakers about whether drug costs are treated as a “silo” or whether medical cost
offsets are considered; the effect on tier placement of less conventional or hard-nosed
cost-effectiveness considerations, such as patient preferences; and the information
sources decisionmakers use regarding medical cost offsets.

Presentation of Information. We investigate payers’ preferences for cost-effectiveness
analysis versus budget impact analysis; their preferred format for viewing health
economics data; and their use of information/industry claims about patient-reported
outcomes (PROs) and quality adjusted life years (QALYs).

Time Horizon of Model and Other Issues. We ask payers about how many years out
are they willing to consider when making their assessments of new drugs; the number of
time endpoints they need or prefer when conducting their cost effectiveness and/or
budget analysis; the merits and drawbacks of pharmacoeconomic data in their recent
drug reviews; and whether they can identify best practices or worst practices regarding
the information that is brought to their pharmacy and therapeutics (P&T) committee.

The formative-research interview protocol concludes with an open-ended question to identify other
pertinent topics that the interviewees thought important.

3.3 Payers Interviewed in Phase I

In the study’s Phase I, we arranged and conducted complete interviews with seven of the eight payer
organizations we interviewed—more organizations than our proposal anticipated interviewing in the
formative research phase. (See Table 3-1.)

Table 3-1. Payer organizations interviewed in formative research (Phase I)

<table>
<thead>
<tr>
<th>Category of health care payer</th>
<th>Organization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Federal Government</td>
<td>TRICARE (U.S. Department of Defense)</td>
</tr>
<tr>
<td>State Medicaid agency</td>
<td>District of Columbia Medical Assistance</td>
</tr>
<tr>
<td>Large employer</td>
<td>Delta Airlines</td>
</tr>
<tr>
<td>Not-for-profit health insurance company</td>
<td>Select Health (subsidiary of Intermountain Health Systems)</td>
</tr>
<tr>
<td>Blue Cross Blue Shield: PPO and PDP</td>
<td>BCBS of Tennessee</td>
</tr>
<tr>
<td>Blue Cross: PPO</td>
<td>Premera&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>For-profit managed care company</td>
<td>Elder Health (now Bravo)</td>
</tr>
<tr>
<td>Medicare Advantage prescription drug plan (MAPD)</td>
<td>&quot;</td>
</tr>
<tr>
<td>Medicare prescription drug plan (PDP)</td>
<td>&quot;</td>
</tr>
<tr>
<td>Pharmacy benefit manager (PBM)</td>
<td>Express Scripts&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Source: Westat team interviews and Web research.
<sup>a</sup> Interview arranged by Brian Bresnahan.
<sup>b</sup> Interview less extensive than other exploratory interviews. For details, see this report, section 3.3, page 3-3.
In addition to interviews we arranged with the first seven payers listed in Table 3-1, we sought an interview with the P&T committee members of one pharmacy benefit manager (PBM). However, our contact there, after consulting with more senior managers, stated that we would not be allowed to interview this PBM’s P&T committee. They wanted to keep the names of the members of the committee confidential. Nonetheless, we were able to interview our contact, a senior manager who serves as the company’s liaison with its P&T committee. As a result, we succeeded in obtaining some information about the organization of the PBM’s formulary decisionmaking process.

To arrange interviews, we contacted pharmacy directors or heads of P&T committees at private and public organizations reflecting diverse payer types. Regarding one feature of the interviews listed in Table 3-1, payers’ preferences dictated a change from our plans: at each payer organization, we sought to interview multiple members of the P&T committee. Moreover, we requested a separate interview with each interviewee, because we hoped to obtain a view of each organization’s formulary decisionmaking and attitudes toward pharmacoeconomic data that was as fine-grained as possible. However, we found that most organizations preferred to schedule for us one meeting with the P&T committee as a whole or with the decisionmakers who support and interact with the P&T committee. In one case, an organization chose to schedule separate meetings, one with three committee members, the second with two members.

Nonetheless, we do not believe that the larger meetings reduced the value of our interviews substantially, although it is impossible to know this with certainty. In the group meetings, usually several members (e.g., three of five) participated actively throughout the interview. In addition, in several of the group interviews, committee members sometimes disagreed with each other or offered distinctive perspectives. As a result, we were reassured that the group interviews seemed to yield reasonably frank comments and that committee members did not seem constrained to march in lockstep.

Two additional points are worth noting:

- First, the exploratory interviews did not include community physicians. When the payer organizations set up the group meetings, they did not invite any P&T committee members who were clinicians from the community. This was true for two or three of the organizations we interviewed. In contrast, the remaining organizations often had established separate committees of community physicians to advise the payer’s P&T
committee about the perspective from “the (clinical) trenches.”

We conjecture that community physicians often play much the same advisory role, whether they serve on the P&T committee itself or on a separate advisory committee. If so, it would be unlikely that the absence of community physicians from our interviews materially changed the findings.

Second, in two organizations where we conducted interviews, a single person was responsible for formulary decisions regarding adoption and tiering of new drugs. Both of these organizations contract with PBMs and both rely heavily on their PBMs for detailed reviews of new drugs’ effectiveness and cost.

In contrast, several other organizations that we interviewed not only contract with a PBM but operate a multimember P&T committee.

1 In addition to interviewing DOD’s P&T committee, we observed a meeting of DOD’s advisory panel of community physicians and TRICARE beneficiaries. This panel receives written reports on each new drug under consideration for formulary placement. (All FDA-approved drugs must be available for their beneficiaries on DOD’s formulary.) The panel also hears a presentation by TRICARE staff on each drug, including a summary of a cost-effectiveness analysis mandated in law. The panel has an opportunity to question the staff and discuss the staff recommendation before voting on the recommendation. TRICARE is not bound to accept that recommendation.

2 One of these organizations is launching a P&T committee this fall.
4.1 Purpose

The impetus behind this study’s literature review was the desire to apply its lessons to improving the interview protocol for Phase II. More concretely, we planned, as part of the review, that we would identify gaps and omissions in published studies as well as their methodological limitations. Drawing on this list of gaps and limitations, we planned to identify promising modifications to some questions used in the Phase I exploratory interviews. We also planned to identify new questions that could strengthen the protocol and, thereby, make Phase II interviewing more effective.

We expected the literature review to serve secondary purposes too. As a by-product of the literature review, we hoped to highlight generalizations and observations about the studies reviewed that were of interest. Finally, we expected that the literature review would establish a baseline for the state of knowledge embodied in the literature. Consequently, after completion of the study, a comparison of its findings with the baseline would reveal the extent of this study’s contributions or value-added.

4.2 Literature Search: Overall Approach

In undertaking our search of the research literature, we reviewed research studies on payers’ use of and attitudes toward pharmacoeconomic data. The time span covered was recent: as specified in the RFP and in subsequent discussion with Lilly staff, we searched for studies published from January 2001 through December 2007.1 We examined only studies that met search criteria reflecting the present study’s scope. (See Appendix C.) These criteria captured 48 studies in total: some with a methodological or normative aim regarding pharmacoeconomics, and others that provide descriptive evidence on payers’ use of and attitudes regarding pharmacoeconomic data.2 We

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1 The time span of this literature review was set to begin where the 2003 ISPOR literature review ended. See Michael Drummond and others, “Use of Pharmacoeconomics Information—Report of the ISPOR Task Force on Use of Pharmacoeconomic/Health Economic Information in Health-Care Decision Making.” 2003. Value in Health. 6(4):407-416.

2 In designing search strategies, we sought to exclude technical studies with an exclusive focus on methodological issues, not pertinent to understanding descriptive studies and their limitations. We also sought to exclude studies of the cost-effectiveness or clinical effectiveness of one or more individual drugs. Such studies rarely if ever contained insights that we could discern into the use and perception of pharmacoeconomic information from the payer’s perspective. As discussed below, our final bibliography began with the results of automated searches but required expert manual review to winnow out low-value studies and articles.
reviewed the list of studies identified by the computer search. That review led to a smaller, final set of 28 studies.

4.3 Literature Search: Methods

Consistent with established methods, we undertook a sequence of literature searches. After the initial search, each iteration was guided by our review of results that emerged from previous search iterations.

These searches were defined by alternate sets of search terms. The searches involved several standard steps:

- **Obtain core search terms** by refining the core terms listed in our proposal. The core terms that we used were commonsensical:

<table>
<thead>
<tr>
<th>Core search terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>prescription drugs</td>
</tr>
<tr>
<td>decisionmaking OR attitudes OR use</td>
</tr>
</tbody>
</table>

  The terms encompassed the study’s analytic angle (cost, effectiveness), the product (prescription drugs), the locus of pharmacoeconomic information (decisionmaking, attitudes, use), and the arena that the information is intended to inform (coverage or payer).

- **Create a family of search term sets.** Using the core terms as a base, our information resources (IR) specialist devised various combinations of these terms, introduced synonyms and related words (e.g., pharmacoeconomics) into the search algorithm, and used these combinations of terms to search PubMed, EconLit, ABI/INFORM, and other databases.

- **Conduct citation-based searches.** We also tested an alternate approach: searching for studies and articles that cite key articles or sources. For example, we searched for and identified articles that cited Drummond et al.’s 2003 ISPOR literature review.³

- **Make mid-course corrections.** At several points during the search process, the project researchers reviewed the results of literature searches completed. Then, in conjunction with the IR specialist, they adjusted the search strategy to reflect lessons learned to date.

³ Specifically, we conducted a search that started from the 11 citations of Drummond’s 2003 ISPOR review. For each of these citations, we conducted a “find related articles” search for each one, limiting results to 2001-2007.
The remainder of this section provides illustrations of ways these search results yielded payoffs to the revision of the interview protocol.

### 4.3.1 Modified Search Strategy

Based on the results of our initial literature searches, we modified our strategy to rely more on manual review of the search results by the team’s research staff. This decision reflected both difficulties we encountered in the automated searching and unexpected opportunities that the automated searches afforded us.

#### Difficulties

We were unable to develop an automated search algorithm that captured publications of high relevance to the study without also sweeping in many pharmacoeconomic publications unambiguously outside the study scope. In particular, searches that used variants on the key set of relevant terms (i.e., “cost,” “prescription drugs,” “decisionmaking,” “use OR attitudes,” “effectiveness OR pharmacoeconomic”) produced many false positives: most prominently, pharmacoeconomic studies of the cost-effectiveness of a specific drug. A similar set of false-positive hits from these searches involved studies of decisionmaking regarding medical technologies and medical procedures. Generally, these studies did little to throw light on the questions raised in the present study.

#### Opportunities

Even after excluding pharmacoeconomic studies of a single new drug, we found the search results included many studies outside the study’s scope, strictly construed. They do not contain evidence on use of and attitudes toward pharmacoeconomic data. Instead, some offer prescriptions for methodology used in pharmacoeconomic studies; others comment on progress in and obstacles to the use of pharmacoeconomics. Nonetheless, these publications are still relevant as contextual inputs, potentially helpful in formulating conclusions drawn from the interviews and literature review.

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4 Our impression is that most automated literature searches require substantial manual review before a usable list can be produced.
As a result, compared to our initial plans, the computer-based searches required more manual winnowing conducted by experienced research staff. Specifically, two senior Westat staff conducted separate, independent reviews of the abstracts identified by the preferred search algorithm. Each abstract was scored on two dimensions: relevance to the present study’s scope and objectives; and quality of evidence. Discrepancies between reviewers were resolved by following the scoring of the reviewer who had placed the study in the higher-ranked category. This criterion is conservative: it errs on the side of including articles that might be relevant and high quality. The final list of studies consists of all those articles scored as relevant and high quality. (For this final list of studies, see Appendix D.)

After the selection of this final set of studies was complete, the individual studies were reviewed again. This review examined the substance of each article’s evidence and argument. The review had two goals: first, to extract lessons and useful points to guide the revision of the interview protocol; second, to identify themes in the final set of studies and to note significant observations about the studies, whether as a group, a subset, or an individual study.

The results of this review are in the appendixes. Appendix E contains the abstracts of the final list’s 28 studies. In these abstracts, interesting and noteworthy statements are bolded or underlined, where appropriate. After reviewing these abstracts, we developed potential questions (for the Phase II protocol) in response to specific points in a given abstract that our review indicated were problematic or otherwise important to pursue. (See Appendix F.) We ranked these combinations of topic, abstract, and question by potential contribution to the revised protocol. For themes and observations noted about the final set of studies in their own right, see Appendix G.

4.4 Arriving at the Phase II Protocol

We refined potential new questions for the revised protocol, based on the work described above. (See Appendix H.) However, the demand for new questions to augment the protocol exceeded the

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5 Our proposal’s expectations about the literature search were based in part on the Drummond (2003) review article that, in describing its literature search methods, was terse and elliptical. However, we recently located an unpublished report by Drummond and French (on the cost-effectiveness of substance abuse treatment). The Drummond-French report provides some detail on its literature search. Notably, the pruning of the initial computer-based search down to the final set of publications apparently was exclusively manual. Consequently, it may be that the starting point for our literature review plan, the Drummond (2003) review article, relied similarly on a manual review of a large literature search by researchers.

6 The scoring options were in, out, or other. “Other” was the category of studies or articles that did not report on payers’ use of pharmacoeconomic information (or their attitudes toward it) but provided potentially useful information (methodology, prescriptive guidance on use of pharmacoeconomics, etc.) that might have implications for the present study’s findings.

7 The scoring options for evidentiary quality were high, medium, or low.
supply of pages and time we had allotted for the interview questions. To keep each interview within the constraint of an hour, we prioritized new questions. To conserve space, we combined them when possible and trimmed away less important words and ideas. After reviewing the protocol used in the formative research phase, we eliminated several questions and condensed others.

This process yielded a revised protocol for Phase II that incorporated key parts of the protocol used in the formative research phase while augmenting that protocol substantially. (See Appendix I.) In particular, the revised protocol sharpens our focus on issues of interest, deemphasizes items that are part of the conventional wisdom regarding payers and pharmacoeconomic data, and strives to elicit comments from decisionmakers about types of pharmacoeconomic data, preferred formats for pharmacoeconomic data and evidence, etc. that are specific.
The methods for our full-scale data collection (Phase II) are straightforward: using the revised protocol to create a common frame of reference, we conducted interviews with formulary decisionmakers at nine organizations—one from each of the nine payer-types listed in our proposal.1 (See Table 5-1.) Learning from our experience in the formative research phase, we did not try, in general, to conduct separate interviews with multiple members of a payer’s pharmacy and therapeutics committee. As in the formative research phase, we conducted these interviews in person or by telephone, depending on the preferences of the interviewees.

Table 5-1. Payers interviewed in Phase II of study

<table>
<thead>
<tr>
<th>Payer category</th>
<th>Payer Interviewed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Managed care</strong></td>
<td></td>
</tr>
<tr>
<td>Medicare managed care plan with drug benefit:</td>
<td></td>
</tr>
<tr>
<td>Medicare Advantage Part D (MAPD) plan</td>
<td>XLHealth</td>
</tr>
<tr>
<td>For-profit managed care plan – for nonelderly employed</td>
<td>WellPoint</td>
</tr>
<tr>
<td>Nonprofit managed care plan</td>
<td>CareFirst BCBS</td>
</tr>
<tr>
<td><strong>Large employer/Insurer</strong></td>
<td></td>
</tr>
<tr>
<td>Large employer plan or self-insured plan</td>
<td>Coca Cola</td>
</tr>
<tr>
<td>Insurer for which union or union contract plays a large role in re: health benefit and coverage issues</td>
<td>Unable to secure an interview</td>
</tr>
<tr>
<td>National insurer</td>
<td>United Healthcare</td>
</tr>
<tr>
<td><strong>Drugs-only</strong></td>
<td></td>
</tr>
<tr>
<td>Drugs-only risk-bearing plan: Medicare Part D Plan (PDP)</td>
<td>Capital Health BCBS</td>
</tr>
<tr>
<td>For-profit pharmacy benefit manager (PBM)</td>
<td>CVS Caremark</td>
</tr>
<tr>
<td><strong>Public payer</strong></td>
<td></td>
</tr>
<tr>
<td>Medicaid programs</td>
<td>Florida Medicaid</td>
</tr>
<tr>
<td>Federal payer</td>
<td>VA</td>
</tr>
</tbody>
</table>

An important note: In the findings below, at various points we refer to individual payers with such terms as “private insurer,” “national insurer,” “public payer,” and “Medicaid program.” However, none of these terms or similar terms can be accurately linked to a specific payer. First, some payers fall under two or more payer categories. Second, whenever Phase II interviews only contained a single payer within a payer category (and no other Phase II payers could be associated with that

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1 Our proposal called for an interview with a tenth type of payer organization: a union plan (that is, a health plan in which a union, not the employer, was the principal and the health plan – the union’s agent vis a vis management of the health benefit.)
category), we automatically expanded the evidence base to include similar payers from Phase I’s exploratory interviews. As a result, for example, “Medicaid program” could refer to several state Medicaid programs, not just to a single state’s program. The same is true for other payer-types as well.
Taking the long view, since the early/mid 1990s, the degree of acceptance of pharmacoeconomic information among U.S. payers overall has risen markedly. But a close-up look at today’s landscape reveals distinct categories of payers, which vary in their use of this information in formulary decisions. The variation in the role of pharmacoeconomic information is both quantitative (e.g., how frequently?) and qualitative (e.g., how formal?) The sources of variation are in part systematic (like payer-type), in part seemingly random (like which decisionmakers are influential).

6.1 Finding One: Use of and Attitudes Toward Pharmacoeconomic Information

6.1.1 In Major 10-Year Shift, U.S. Payers Accept Pharmacoeconomic Information’s Scientific Merit, but Practical Concerns Keep Use Below Potential

From the standpoint of proponents of pharmacoeconomics and its utility for formulary decisionmaking, the threshold question has been: What are U.S. payers’ views of pharmacoeconomic information’s scientific merit and practical utility? To answer this question, this section contrasts the situation today with its counterpart a decade and a half ago. From this historical perspective, payers’ perceptions during the past 12 to 15 years have undergone a tectonic shift. In the 1990s, payers typically either dismissed most pharmacoeconomic information or granted it a grudging, minimalist acceptance. In contrast, today, the payers we interviewed give a markedly different answer. Notwithstanding this shift in perceptions, though, among U.S. payers serious, real-world concerns persist—a substantial barrier to wider, more thoroughgoing use of pharmacoeconomic information.

The Global “Aha”

Based on our recent interviews with U.S. payers, we arrived at a two-pronged answer to the threshold question.
Looking back to the 1990s revealed the large, even dramatic, change in perceptions between then and now: today (2008), a close-up look at U.S. payers’ perceptions and use of pharmacoeconomic information identifies three groupings of payers distinguished by sizable differences in their pharmacoeconomic sophistication and the frequency with which they use this information.

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**Then (The Mid/Late 1990s)**

Over a decade ago, Grabowski and Mullins (1997) found that U.S. payers—as of the mid-1990s—did not welcome pharmacoeconomic information. Relatively few payers understood pharmacoeconomic studies well. However, payers perceived studies to be scientifically weak: for example, at the time, some studies did not distinguish between costs and charges. Cost analyses often were exclusively descriptive and did not control for confounding factors by use of multiple regression analysis. (In addition, many studies evaluated clinical effectiveness against a placebo, which payers thought made the studies’ results less relevant.) Moreover, payers generally considered studies provided to them by drug companies to be biased due to the source. When asked if they would use pharmacoeconomic studies, many payers in the 1990s replied in effect, Maybe if they were transparent and unbiased. That’ll be the day!

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**Now (2008)**

In 2008, the situation is markedly different. Most decisionmakers at most U.S. insurers and public payers understand and accept pharmacoeconomic information (broadly defined) as useful, although they have a deep-seated skepticism of information supplied by drug companies.

Most payers view pharmacoeconomic studies as typically better than a decade ago. In particular, most payers consider the average scientific quality of such studies to be at least acceptable. That characterization is held more strongly when payers consider randomized controlled trials (RCT). In general, payers follow most researchers in treating RCT results as the gold standard for evidence. In addition to noting improvements in scientific quality, payers generally acknowledge some improvement in transparency: most researchers now provide more details than in the past about assumptions, data sources, and calculations that lead to the cost-effectiveness results. Finally, an

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important point of contrast: while payers interviewed generally consider the typical published study of clinical effectiveness or cost effectiveness to be less biased than similar studies of a decade ago, they still regard the studies provided by drug companies to be a skewed and misleading sample.

**The Coexistence of a Breakthrough and Major Barriers to Use**

Almost all payers now look at pharmacoeconomic studies. This is a major breakthrough, although the shift represents the accumulation of small changes in perception and use over a decade and more. (Moreover, these changes did not occur uniformly across all U.S. payers.) If the diffusion of greater acceptance and use of pharmacoeconomic information followed a logistic curve, the qualitative change or breakthrough did not occur at a discrete moment. Looking back over 15 years, however, the extent of the change is evident.

On the other hand, while payers consider many discrete pieces of pharmacoeconomic information when making formulary decisions, they assemble and arrange those pieces within a variety of frameworks. Specifically, they sometimes relate “cost” to “effectiveness” by calculating incremental cost-effectiveness ratios (ICER) as contemporary journal articles do; these payers in effect follow the prevailing academic or International Society for Pharmacoeconomics and Outcomes Research (ISPOR) standard. In contrast, other payers we interviewed related cost to clinical effectiveness in diverse ways that do not translate cleanly into conventional cost-effectiveness terms:

- Some involve structured, written analyses that employ different decision rules than “Select the drug with the smallest ICER.”
- Some involve professional judgments and unwritten “algorithms” that seem distant from ICERs and from ISPOR discussions of cost-effectiveness.²

As a result, in formulary decisionmaking, pharmacoeconomic information broadly defined is widely used, but for most payers a mixture of structured and judgmental methods—not standard cost-effectiveness analysis—drives adoption and tiering decisions.³ That said, at least among the payers

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² As discussed later in this report, payers differ in how they measure “cost,” especially concerning medical cost offsets.

³ One problem payers have in comparing ICERs between drugs is that the research literature often does not contain a head-to-head trial and does not permit a rigorous comparison of ICERs. For example, the formal use of a cost-effectiveness framework to compare two drugs’ cost and outcome, and to permit the comparison of incremental cost-effectiveness ratios between rival medications, is often honored in the breach. In addition, when making formulary decisions, payers do not necessarily use pharmacoeconomic information consistently. Often, pharmacoeconomic information and cost-effectiveness analysis do not drive the adoption or tiering decision.
we interviewed, a sizable minority often uses standard cost-effectiveness analysis as a key input into their formulary decisionmaking.

Four Factors Impede U.S. Payers’ Use of Pharmacoeconomic Information

Among U.S. insurers and public payers, the level of use of pharmacoeconomic information—especially in the narrow sense—is considerably below its potential level. This situation does not appear to stem predominantly from insufficient training, although “head count” for pharmacoeconomics was clearly an issue for several payers. Instead, use of such information is impeded by four factors:

- **Perception of biased selection.** As noted above, the movement toward broader, more consistent use of pharmacoeconomic information frequently encounters a sizable, strong, and impermeable barrier—U.S. payers’ common perception that “cherry-picking” of pharmacoeconomic studies and RCT results is widespread. When discussing drug companies’ selection of studies to support their own drug products, payers see that selection as biased. That perception, in turn, creates mistrust and distrust of information that drug companies supply about their products.

- **Answering the wrong questions.** Cost-effectiveness analyses do not address the questions that insurers and other payers want answered. These include:
  - Under what circumstances is the drug cost effective?
  - Which patients should be targeted?
  - How will this affect current drug use?

- **Difficulties translating RCT results to payer populations.** With rare exceptions, when U.S. payers, public and private, assess a new drug’s clinical effectiveness, they consider randomized controlled trials (RCT) to be the gold standard. Payers seem to understand that running head-to-head active comparator RCTs against the most commonly prescribed market drug would be prohibitively costly, yet they would like to see that type of evidence. Furthermore, payers see the results of RCTs as having limited relevance—or better, as being insufficient—when they are seeking to gauge the value of new drugs in an enrollee population. Among almost all payers we interviewed, a recurrent concern was that they could not confidently translate results drawn from an RCT’s data about a new drug to their own population. That population’s demographic characteristics and comorbidities likely differ from the RCT population. Consequently, payers fear that a new drug might work less well in one or another subgroup than in the RCT population. Moreover, payers generally know that, compared to the RCT results they seek to adapt to their populations, their own adjustments and judgments are less rigorous and less grounded in solid evidence. As a result, payers are likely to report
“looking at” RCT results—an example of use of pharmacoeconomic information *broadly* defined.

However, in the next steps of use—toward use of such information *narrowly* defined—payers’ responses splinter: some assume RCT results hold in their own populations. Others make adjustments for population differences but place considerably less weight on the adjusted results than if they came from an RCT. Still others include their reading of RCT results as part of a judgmental process that does not use a formal analytic framework. In sum, this variability in payers’ response to use of RCT and related pharmacoeconomic information stems from the perceived lack of a good RCT-payer population “dictionary”: lacking this dictionary or equivalent evidence-based rules of thumb, many payers are uneasy about translating RCT results wholesale to their own population.

- **Bifurcation of value assessment and price assessment.** Why does pharmacoeconomic information not drive decisions? For at least some payers, “There’s the value assessment and then there’s the rebating.” To proponents of pharmacoeconomics and cost-effectiveness analysis, these tools bring together value assessment and the rebate calculation (and other aspects of payers’ assessment of drug pricing). That concurrent examination of value and cost yields a formulary decision that is sound and arguably optimal. However, in our interviews, we encountered a straw in the wind that likely would distress a pharmacoeconomics proponent: some insurers are *separating* value assessment from rebate assessment. As a result, rebating gets more play than it should in a world in which formulary decisions emerge from pharmacoeconomic information, narrowly construed.

### 6.1.2 Use of Pharmacoeconomic Information Differs Sharply Among Groups of U.S. Payers

Time-lapse photography over the past 10 to 15 years would show U.S. payers making a major shift toward acceptance of the fundamental merit of pharmacoeconomic information. A close-up snapshot in 2008, though, would show that today’s pharmacoeconomic landscape displays a
noticeable “bulls-eye pattern,” in which use of pharmacoeconomic information narrowly defined falls into three groupings.  

6.1.2.1 Bull’s Eye Pattern of Pharmacoeconomic Information

The following section treats private payers and public payers separately within each of the three rings.

**The Bull’s Eye – Sophisticated Minority of Payers—Users of Pharmacoeconomic Information Narrowly Defined**

The leading edge among U.S. payers regarding pharmacoeconomics, this set of payers uses cost-effectiveness and pharmacoeconomic information frequently and, relative to most U.S. payers, with considerable rigor.

**Private Payers.** Many of the private payers we interviewed displayed a sophisticated command of and approach to pharmacoeconomic information, narrowly defined. These sophisticated users represent a significant fraction of private payers.

- Of the 12 private insurers and pharmacy benefits managers (PBMs) we interviewed in Phases I and II, a few insurers were unambiguously sophisticated in their reported use of pharmacoeconomic information, narrowly defined. Each of these insurers described its analysis and use of pharmacoeconomic studies of RCTs and of observational data in terms that revealed the insurer’s command of outcomes research and of cost-effectiveness as an analytic framework. These insurers are part of what might be termed the ISPOR Elite.

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4 The bull’s eye pattern is a useful heuristic device, when analyzing the extent of payers’ use of pharmacoeconomic information. However, the selection of boundary lines between categories is a matter of judgment. For example, the polar categories are easiest to characterize because each is in effect the negation of the other. The middle category, however, reflects decisions about where to mark the end of a polar category when payers’ use of pharmacoeconomic information is a continuous variable.
One insurer, a sizable Blue Cross Blue Shield plan, maintains a separate unit that analyzes the methodology and reported results of clinical effectiveness and other pharmacoeconomic studies of new drugs the plan is reviewing. This technical evaluation unit provides information and internal analyses to the plan’s drug assessment unit, which supports the plan’s pharmacy and therapeutics (P&T) committee. The plan’s drug-assessment decisionmakers had a good understanding of the strengths and limitations of RCTs and of observational studies. Unlike those in the first three insurers, however, these decision makers tended to discuss their assessment of drugs more in business and common sense terms, so it was not clear the extent to which this plan uses formal cost-effectiveness analysis and related tools in its formulary decisionmaking. In this case, the difference from the other three insurers may be more in the manner of expression than in substance.

At least one PBM displayed this same pair of traits: sophisticated command of pharmacoeconomic tools and research, combined with unclear statements regarding whether the PBM made decisions based on cost-effectiveness analysis. We could not determine the underlying reason for this haziness. It is possible, for example, that the PBM(s) had made a strategic decision to downplay or obscure the extent to which cost resulted in decisions that would have been different if only clinical effectiveness were the criterion for formulary adoption and tiering. By eliding the role of cost and cost effectiveness in formulary decisions, a PBM might attempt to sidestep reactions similar to the managed care backlash. In the late 1990s, patients and their advocates accused managed care plans of making decisions about care, such as those involving high-cost technologies, based on profit and financial considerations rather than on the sole criterion of individual patients’ well-being.

Public Payers. Two public payers we interviewed displayed a sophisticated command of and approach to pharmacoeconomic information. One, the Department of Defense (DOD), is required by Federal statute to conduct cost-effectiveness reviews of new drugs using formal methods. DOD holds public meetings of its Beneficiary Advisory Panel at which DOD pharmacists and other technical staff present analyses of each new drug under review, including comparative analysis of the drug’s clinical effectiveness and cost effectiveness.5 The second, the Veterans’ Health Administration (VHA), has a process for drug assessment that is described as involving sophisticated analysis of the

5 As the TRICARE web site explains, “Congress established the Uniform Formulary Beneficiary Advisory Panel (BAP) to review and comment on the recommendations from the Department of Defense Pharmacy and Therapeutics (DoD P&T) Committee. Members of the BAP include active duty family members, retirees and their family members, two clinical experts outside of the DOD, a pharmacist from the US Family Health Plan and physicians or pharmacists from the TRICARE regional contractors and the TRICARE pharmacy contractor. The DoD P&T Committee forwards recommendations, along with the comments from the BAP, to the Director, TRICARE Management Activity, for consideration prior to a final decision.” (Downloaded on October 18, 2008 from http://www.tricare.mil/mybenefit/home/Prescriptions/Medications/UniformFormulary/BeneficiaryAdvisoryPanel).
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clinical effectiveness and cost effectiveness of new drugs. VHA does not typically conduct a formal cost-effectiveness analysis of each new drug; i.e., VHA does not prepare a written report that summarizes a formal analysis of the drug’s cost effectiveness. Instead, VHA relies on “back-of-the-envelope” analyses of cost effectiveness. The VHA decisionmaker we interviewed said that VHA had found these back-of-the-envelope analyses to provide most of the analytic value that formal analyses provide—but in a fraction of the time.

The Middle Ring – Larger Group—Occasional/Informal Users of Pharmacoeconomic Information Narrowly Defined

The middle ring consists of payers who use pharmacoeconomic information narrowly defined at least occasionally during the year or who use such information informally. This middle ring of payers is larger than the bull’s eye group.

Private Payers. Among payers we interviewed, several private insurers—drawn from different segments of the commercial market—said they examine a broad array of pharmacoeconomic information, from clinical effectiveness studies and outcomes research to drug cost data and cost-effectiveness studies. In general, however, these insurers do not put that information into a formal cost-effectiveness framework. Instead, their decision process typically relies on an assessment and weighing of cost and effectiveness that is judgmental (not crystallized in an ICER or a similar analytic vehicle). Nonetheless, occasionally during a given year, these payers may focus on a formal cost-effectiveness analysis of a particular new drug. Alternatively, they may occasionally conduct a

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6 See also Sherrie L. Aspinall and others, “The evolving use of cost-effectiveness analysis in formulary management within the department of veterans affairs,” Medical Care. 2005 (43, 7): 20-26, SUP. This article, one of whose authors is a key VHA formulary decisionmaker, adds important points about cost-effectiveness analysis in VHA decisionmaking that were not emphasized in our VHA interview:

Traditionally, VHA has relied on cost-minimization analyses in formulary decisions. More recently, VHA has emphasized the use of cost-effectiveness data, especially for newer, costly drugs. In addition to including this data in drug monographs, the VHA has begun requiring formal cost-effectiveness analysis from manufacturers of selected pharmaceuticals. VHA has also requested that clinically relevant information such as quality of life plus mortality benefit be made available from industry so that internal cost analyses can be performed. It is hoped that by setting the expectation that cost-effectiveness will be formally considered in all VHA formulary decisions, the pharmaceutical industry and others will be stimulated to collect and report data that enables these analyses. We believe that if other organizations also place an emphasis on economic evaluations, industry and the public will be more accepting of decisions that incorporate cost considerations.

cost-effectiveness analysis that is informal but explicit in its use of the standard cost-effectiveness framework.

**Public Payers.** We did not interview public payers that are in the middle ring of pharmacoeconomic information users. However, we expect that at least some state Medicaid programs are in this middle category.

**The Outer Ring – Sizable Number of Payers—Users of Pharmacoeconomic Information Broadly Defined**

The third category, the outer ring of payers, does consider clinical effectiveness evidence and cost data—pharmacoeconomic information broadly defined. These payers’ distinctive trait is that their evaluation of the clinical and cost elements of a new drug does not use an articulated pharmacoeconomic framework. These payers rarely use pharmacoeconomic information narrowly defined. They do generally describe their drug assessment process as involving the weighing of cost and clinical effectiveness. However, they do not describe that weighing process in terms of an explicit analytic frame for selecting the most cost-effective drug in a class. These payers de-emphasize cost-effectiveness analysis in their decisionmaking, but this pattern does not reflect a lack of knowledge necessarily. Instead, it appears to stem from the different priorities of these organizations as opposed to those in the center ring. As a result, “the outer ring” is a characterization of these payer organizations’ behavior and rhetoric, not of the knowledge and sophistication of the decisionmakers and their staff.

The size of the outer ring is difficult to gauge with confidence. In terms of the number of payers (unweighted by covered lives), a substantial proportion of all payers, public and private, are in this category. In our view, this proportion is between one-fifth and one-third of all payers. In terms of covered lives, our guesstimate of this proportion is closer to one-fifth.

**Private Payers.** Among the dozen private payers we interviewed, only one was unambiguously in the outer ring. Although a serious user of much pharmacoeconomic information broadly defined, this commercial insurer (specifically, its pharmacy director) applied an analytic framework that is distinctive, difficult to summarize, and quite removed from conventional cost-effectiveness analysis.

**Public payers.** Of the public payers we interviewed, two examined substantial amounts of pharmacoeconomic information (broadly defined) regularly throughout the year. However, the
decisionmakers and staff at these payers did not convey to us that they regularly approached those data using an explicit cost-effectiveness framework.

As suggested above, this apparent tendency not to use such a framework may well be rooted in the statutory incentives these payers face. By statute, Medicaid programs must adopt every drug approved by the Food and Drug Administration (FDA). Moreover, Medicaid programs impose a fixed copayment (currently, $8 per prescription) and may not alter that cost sharing for other purposes. As a result, pharmacoeconomic information narrowly defined has a considerably lower payoff for these payers than it does for less constrained public payers or for private insurers and PBMs. Private payers and other public payers face real adoption decisions regarding new drugs and, likewise, have real decisions to make regarding tier placement of new drugs. In contrast, Medicaid programs are limited by law to a few tools, such as prior authorization and step therapy. Consequently, conducting cost-effectiveness analyses may appear to be a use of resources with a low payoff to a state’s program.

6.1.2.2 Caveats

The statements above in this section must be read carefully, since (as noted earlier) they are based on a judgmental sample of U.S. payers. To encourage a careful reading, we note four caveats:

- The proportion of payers we interviewed that are found in a given ring should not be viewed as a measure of the true proportion of payers not weighted by each payer’s share of covered lives.
  - Our judgmental sample likely underrepresents private payers in the outer ring and even in the middle ring, when payers are not weighted by number of covered lives.
  - Our judgmental sample likely overrepresents private payers (nationwide) that have a number of covered lives at or above the median plan’s number.

- The proportion of payers we interviewed that is found in a given ring also should not be viewed as a measure of the true proportion of payers weighted by the proportion of covered lives each payer represents.
  - Our judgmental sample likely overrepresents private payers that have a number of covered lives that is at or above the median plan’s (nationwide).

- Our judgmental sample is likely to be reasonably accurate when we consider the mean of the distribution of payers, weighted by covered lives. In effect, we believe that our
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Sample, which is tilted toward larger organizations, reflects the reality that at least half of covered lives is insured by “middle ring” or “bull’s eye” organizations.

- Our qualitative statements about the relative sizes of the three rings are both subjective or judgmental and evidence-based. In effect, these statements represent our quasi-Bayesian beliefs, conditioned on both this study’s interviews and our combined experience studying insurers and prescription drugs in the U.S. marketplace.

- Payers cannot be assigned neatly to one of the three rings based on their payer-type. Instead, regarding use of pharmacoeconomic information, payers are diverse within the same payer-type. For example, even within the category of public payers at the Federal level, we found considerable differences among DOD’s TRICARE, the VA’s Veterans Health Administration, and state-administered Medicaid programs. Similarly, we observed differences within the various types of private payers, such as national commercial insurers.

6.1.3 Signs Point to Payers Decoupling Clinical and Cost Evaluations, Creating Separate Units

U.S. payers generally assess the clinical effectiveness and cost of new drugs within a single organizational unit responsible for both clinical and cost dimensions. In particular, a P&T committee (or a formulary committee) makes these assessments. The P&T committee typically consists of a variety of physicians, from within the organization and (prescribers) from the community, as well as a limited number of pharmacists and an occasional executive with a business background. Some P&T committees also include a patient advocate. The committee makes its decisions after receiving materials provided by the staff, including memoranda, research studies, and other material pertinent to the drugs under review. In many cases, a payer’s pharmacy benefits staff—often including pharmacists, physicians, and experts in outcomes research and related fields—makes presentations to the P&T committee.

This generalization holds for most of the payers we interviewed. However, we see early signs of a possible movement away from a unitary organization responsible for both clinical and cost evaluation. Our interviews uncovered instances of payers that have decoupled cost evaluations from clinical evaluations. These payers have assigned each type of evaluation to a different organizational unit.
6.1.3.1 Bipartite Organization of Clinical Assessment and Cost Assessment of New Drugs

Among this minority of payers interviewed, the emerging procedure for assessment of new drugs is as follows:

1. **Step One**: The formulary (or P&T) committee makes one of three decisions about a new drug: Add, Do Not Add, May Add. The first two decisions are self-explanatory. The third indicates that the formulary committee considers the new drug to be an acceptable addition to the formulary on clinical grounds; however, the plan’s business managers should determine whether the new drug’s price, rebate, and other contractual features are attractive enough to warrant adding the drug to the plan’s formulary.

2. **Step Two**: A separate committee or unit examines the price, rebates, and contractual arrangements (so-called compliance programs); compares their attractiveness and drawbacks to the terms at which the drug’s competitors offer; and decides on adoption and tiering. This committee’s decision generally takes into account Step One, which is the plan’s clinical assessment of the new drug.

6.1.3.2 Observations Regarding Bipartite Organizations for Formulary Decisionmaking

Signs of future change in the organization of formulary decisionmaking are interesting, but the concrete consequences of adoption and tiering of new drugs are an open question. In this section, two aspects of the new organizational structure’s implications are discussed, in addition to a third, related point.

First, when formulary managers consider a new drug, there is no escaping the economic decision, regardless of organization chart. Consider two payers that have organized their formulary decisionmaking differently: the first payer has a traditional, single unit responsible for the assessment of new drugs and for deciding on adoption and tiering. The second payer has the bipartite organization described above.

The two payers confront the identical economic decision. Despite their organizational differences, the two payers face the same cost and clinical information, the same trade-offs, the same uncertainties, and the same complexities of pricing and rebates. At day’s end, if the drug under review is adopted, it is placed on the second, third, or fourth tier. These formulary decisions hinge on financial decisions—for example, to conclude negotiations with a drug manufacturer by, say,
accepting a slightly higher price in exchange for a larger rebate, contingent on meeting a target of x percent of plan members’ prescriptions being for the manufacturer’s new drug. In sum, creating a separate organization to evaluate cost may have virtues. Nonetheless, that organization cannot reach a minimally sensible decision about a new drug without in some manner considering cost in relation to clinical effectiveness.

Second, to date, the effects of different organizational arrangements on formulary decision are not known. (Our interviews did not yield evidence on this issue.) In principle, the results of the two hypothetical payers’ formulary decisions may differ—the first payer adopts drug A while the second payer adopts D—or they may be the same (both adopt A). Arguably, if a payer’s senior management or internal culture focuses on selecting the most cost-effective drug (say, in a therapeutic class), then the “cost” or “economic” unit in a bipartite structure should be able to follow that rule, just as a unitary formulary committee would. But will the bipartite structure produce decisions that way? The answer is a matter of facts, not analytic reasoning. Nonetheless, it is possible that payers, by setting up separate clinical and cost assessment units, create a situation in which the clinical unit is predisposed to insist that the cost unit take as given the clinical unit’s ranking of drugs in terms of clinical effectiveness. Such a procedure can have material consequences for formulary decisions, as the next point explains.

Third, organization aside, rules for dealing with criteria that conflict may differ among payers. In describing formulary decisionmaking, the casual use of the term “cost-effectiveness” can obscure potentially important differences in the way payers select a new drug that they consider most “cost-effective.” In the textbook case, a payer compares drugs and selects the drug that has the best (smallest) incremental cost-effectiveness ratio (ICER). In effect, the payer arrays drugs it is comparing, ranking them in terms of their cost-effectiveness ratios, and selects the drug with the least cost per unit of clinical effectiveness. However, as the second point above indicates, the payer’s clinical unit could rank the drugs in terms of their clinical effectiveness. Next, the clinical unit could deem “clinically acceptable” those drugs at or above a threshold level of clinical effectiveness that the clinical unit selected. Finally, the cost unit might be required to select the most cost-effective of the clinically acceptable drugs previously identified.

Under some circumstances, this rule yields a different decision—a different drug to be adopted—than the textbook cost-effectiveness analysis. In effect, this rule prevents the payer from selecting a less clinically effective drug that the manufacturer sells at a low enough price to offset its disadvantage in effectiveness. (For example, an antihistamine might be 12 percent less effective than
its competitor drug, but it might be 18 percent less expensive than the competitor and hence more cost-effective.)

Such an outcome results from fundamental strategic and analytical decisions made by a payer. In principle, both single formulary committees and bipartite structures with separate clinical and cost arms could operate according to the textbook decision rule or according to the alternative approach described immediately above. In practice, the bipartite structure may be more likely to adopt a decision rule that constrains the cost unit and that can yield a different adoption decision. Which hypothesis better describes pharmacoeconomic reality awaits pertinent evidence.

6.1.4 Use of Pharmacoeconomic Information by Payers Displays Unexpected Features

“This ain’t what you don’t know, it’s what you know that ain’t so.”
—Attributed to Mark Twain (originated by Josh Billings)

This study began with one major hypothesis—a payer’s type (e.g., national insurer, managed care organization, public payer) substantially affects that payer’s use and perceived valuation of pharmacoeconomic information. In addition, the study had several, secondary working hypotheses—for example, PBMs likely are leading users of pharmacoeconomic information. This section describes the extent to which our data support several of these hypotheses while underscoring where the data point in a different direction.

6.1.4.1 The Role of Payer-type

Regarding payers’ use of pharmacoeconomic information, payer-type matters. This is particularly true for employers, who typically hand over formulary decisionmaking to their PBMs or insurers. Nonetheless, it matters less than we had expected for different types of insurers and PBMs. To capture both the expected and the surprises, the following subsections highlight, one factor linked to payer-type; a major factor that, like payer-type, affects private insurers’ use of this information; a major factor affecting public payers’ use of pharmacoeconomic information, and an umbrella term for nonsystematic influences.
The Effect of Payer-type on the Scope of Health Care Costs Covered

As expected, private payers use more pharmacoeconomic information if their plans cover a broad range of health care expenses than if their plans cover prescription drugs only. Scope of costs covered differs by plan-type and by payer-type, but the scope of costs falls into two or three distinct groupings. Scope of costs covered does not display a smooth gradation that, in turn, differs by payer-type.

Specifically, Medicare PDPs tend to discount or ignore medical cost offsets due, for example, to decreases in hospital admissions. The statute that establishes Medicare Part D authorizes stand-alone Medicare PDPs, which are at risk only for Medicare beneficiaries’ expenses for prescription drugs. PDP decisionmakers, however, may not be inclined to take avoidance of hospitalization costs into account when choosing between “Add” and “Do Not Add.” In contrast, Medicare Advantage plans that offer a Part D drug benefit, as well as other commercial insurers, tend to consider medical cost offsets.

Scale of Payer Organization

In addition to payer-type, our interviews revealed a second major and systematic source of variation: the scale of a payer’s organization. Among private insurers, medium- and large-scale organizations tend to use (that is, review and analyze) a larger volume of pharmacoeconomic data than smaller organizations. For example, larger payer organizations are more likely to undertake an extensive search of the outcomes and cost-effectiveness literature. In addition, they are more likely to employ specialists in outcomes research, pharmacoeconomics, and cost-effectiveness analysis. Likewise, these larger payers are more likely to use pharmacoeconomic information narrowly defined (cost effectiveness analyses, etc.). In effect, as a factor explaining variation in use of pharmacoeconomic information, scale has an odds ratio greater than one. Nonetheless, large scale does not guarantee that a payer makes heavy use of pharmacoeconomic information narrowly defined.

Statutory Requirements

Within the category of public payers, disparate statutory requirements create different incentives for payers to use pharmacoeconomic information intensively or more lightly. For example, statutory differences distinguish Medicaid programs from the Veterans Health Administration program. By
law, state Medicaid programs must add to their formularies all medications approved by the FDA. Moreover, the Federal Medicaid statute bars state Medicaid programs from using different levels of copayments as a way to curb patients’ use of costly prescription drugs. In contrast, the Department of Veterans Affairs and its Veterans Health Administration (VHA) are not required to place every drug approved by the FDA on the VA formulary. As a result, while the VHA can shape its formulary in line with pharmacoeconomic information and analyses, Medicaid programs lack that latitude. It follows that pharmacoeconomic studies and analyses are considerably more valuable to VHA than they are to state Medicaid programs. In fact, our interviews bore out this hypothesis.

Medicare Part D offers another illustration: by law, Medicare PDPs must offer at least two drugs in each therapeutic class and category. Regardless of the merit of that requirement, it does reduce the incentive for PDPs to use pharmacoeconomic information. However, this disincentive to the use of such information is mild, compared to the analogous disincentive built into the Medicaid statute.

*Idiosyncrasy Matters*

The temperament and cognitive style of one or two key individuals can play a decisive role in affecting a payer’s attitude toward pharmacoeconomic information and that payer’s use of such information. In most payer organizations, a committee (typically, the P&T committee or formulary committee) makes formulary decisions. Nonetheless, even with a committee as the decisor, one or two individuals who provide staff support to the committee can influence its formulary decisions significantly.

A pharmacy director or chief medical officer who is forceful or organizationally adept can move a committee in one direction or another. For example, one Blue plan’s chief medical officer did not like the composition of the plan’s P&T committee, since it differed with the chief medical officer on various issues. The chief medical officer was able to engineer turnover in his “independent” committee and to bring in members more congenial to the chief medical officer’s quite idiosyncratic orientation to formulary decisions. “We manipulate the P&T committee,” he told us with a smile. As it happens, the chief medical officer for this payer was very skeptical of any claims of medical cost offsets. (He said that he doubted any drug’s claims of medical cost offsets could be supported.)
Quality of Care Matters (again)

A resurgence of interest in quality of care is occurring, as new initiatives aimed at report cards for insurers and public scrutiny of cost-sharing arrangements increase their reach and visibility. Insurers seem interested in being able to defend their decisions on cost-effectiveness grounds (i.e., value for money), hoping to avoid the bad publicity (and possibly legal implications) of mere cost cutting.

6.1.4.2 The Public Face of PBMs

Initially, our view of pharmacy benefit managers (PBM) was simple and conventional: in the use of pharmacoeconomic information, PBMs are leaders. However, our interviews with PBMs added nuance to that view and underlined several features of PBMs’ perceptions and use of pharmacoeconomic information.

The following hypothesis is plausible, indeed, seemingly uncontroversial: In terms of use of pharmacoeconomic information, PBMs are in the inner ring of payers. In approaching their value-conscious customers (employers and insurers), pharmacy benefit managers themselves point to their expertise at designing formularies. For example, the web site of Express Scripts, a leading PBM, states that it undertakes three steps in its assessment of clinical effectiveness and cost of alternative drug therapies, as detailed below.

Express Scripts has many years of formulary development expertise and an extensive clinical pharmacy department. Express Scripts develops formularies through a three-step process involving the work of the following committees:

- Therapeutic Assessment Committee
- Value Assessment Committee
- National Pharmacy & Therapeutics (P&T) Committee

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7 Express Scripts “Formulary,” [http://www.express-scripts.com/industryresearch/formulary/](http://www.express-scripts.com/industryresearch/formulary/) (downloaded October 6, 2008). In addition to reviewing Express Scripts’ web site, we interviewed an Express Scripts official on its process and criteria for formulary design. However, on this topic, we rely on the web site because the web content and linked documents present the basic facts regarding Express Scripts’ formulary development in a more systematic fashion.
In particular, this PBM’s web site includes the following statement:

The Value Assessment Committee (VAC) considers the value of drugs by comparing the cost of clinically equivalent products.\(^8\)

This cost comparison among products with the same clinical effectiveness is a form of cost-effectiveness analysis.\(^9\) In sum, these excerpts from PBM published statements underscore that PBMs, especially the handful of organizations with substantial market share, deploy substantial personnel skilled at assessing pharmaco-economic information broadly defined. In addition, these PBMs undertake analyses of the clinical effectiveness and costs of new drugs, compared to existing drugs.

In contrast, the PBM officials we interviewed downplayed their organization’s use of pharmaco-economic information narrowly defined in making formulary decisions. In particular, one PBM decisionmaker emphasized his organization’s focus on clinical effectiveness. Throughout our discussion, this official made little mention of the PBM assessing a new drug’s cost-effectiveness, compared to other drugs in its therapeutic class. When the PBM official did mention the cost of a drug, he indicated that his PBM made cost-related decisions about a drug after a separate unit within his organization had determined that the drug was clinically effective.

**PBMs’ bipartite structure?** From our interviews and our review of several PBM web sites, we concluded that at least several large PBMs have structured their formulary decisionmaking to keep clinical effectiveness assessment separate, at least organizationally, from assessment of a new drug’s cost. This use of separate internal organizations is consistent with the potentially emerging trend of “bipartite” structure in formulary decisionmaking that we noted among some other payers.

**PBMs’ decisionmaking rules.** PBMs’ sizable capabilities in processing and analyzing pharmaco-economic information broadly defined may not translate into an equivalently sizable propensity to base formulary decisions on pharmaco-economic information narrowly defined (conventional cost-effectiveness analysis). That is, our interviews and publicly available PBM documents suggest that at least large PBMs tend to avoid basing their decisions on textbook cost-effectiveness analysis. The textbook analysis calls for comparing the cost-effectiveness ratios of the

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\(^9\) As Express Scripts states, its procedure examines cost-effectiveness subject to the constraint that it compare only drugs deemed clinically equivalent. This analysis will select a different drug as optimal, compared to the conventional cost-effectiveness analysis, which compares all drugs, regardless of whether some are clinically superior to others.
new drug to *all* drugs in the therapeutic class. That method allows a drug with, say, 10 percent less clinical effectiveness than another to compensate by costing the payer, say, 15 percent less. Due to these lower costs, a drug that is less *clinically* effective can be the most *cost-*effective drug in its class. In contrast, the PBMs we studied, like some other payers, appear to set a threshold for clinical effectiveness. These PBMs appear to exclude drugs below the threshold of clinical effectiveness from further consideration. Consideration of a drug’s cost, relative to its competitors, is undertaken only for drugs at or above the clinical effectiveness threshold.

**PBM’s public face.** We noted a tendency for the PBMs we studied to downplay their use of conventional cost-effectiveness analysis. Moreover, they tend to acknowledge the role of costs in selecting preferred drugs only when they could obtain a lower cost drug without sacrifice of any clinical effectiveness. The PBMs’ implicit motto is “no trade-off of clinical effectiveness for (lower) cost.” We could not determine whether this rhetorical stance is matched completely by actual behavior of decisionmakers.

Nonetheless, the rhetorical stance of these PBMs is consistent with a strategy to neutralize the type of attacks that managed care organizations (MCO) drew in the mid- to late-1990s. The managed care backlash of a decade ago involved a widespread public condemnation of MCOs’ decisions to deny coverage of what many saw as life-saving procedures and treatments based on financial calculations. The PBMs we studied may have sidestepped a similar backlash by prominently featuring their own commitment to clinical effectiveness as the touchstone for their selection of preferred drugs.
6.2 Finding Two: Payers’ Perceptions of and Reactions to Presentation of Pharmacoeconomic Information by Drug Companies and Government

6.2.1 Payers—Wary of Drug Companies—Take Disparate Stances on Two Modes of Presenting Information to Them

The market for pharmacoeconomic information on new drugs is distinctive: the major supplier of such information—the pharmaceutical manufacturers—is seen by payers through two, dramatically different lenses. On the one hand, most payers rely on drug manufacturers to sponsor clinical trials (RCTs) and, frequently, to supply the payers with computer models and copies of published studies of the effectiveness of the manufacturers’ drugs. On the other hand, virtually no payers interviewed trust the manufacturers as sources of reliable information. With this tension if not paradox in mind, the remainder of this section addresses four topics:

- The source and consequences of payer wariness;
- Payer preferences regarding models and publications;
- Barriers to payers’ use of drug company models; and
- Factors that raise payers’ comfort with drug company information.

6.2.1.1 Skepticism, Cynicism, Wariness

Payers’ stance and perceptions of drug company incentives. All payers we interviewed are wary of any information provided to them by drug companies. Underlying this wariness are different mixtures of skepticism and cynicism about drug companies and their marketing. However, we did not see evidence that this wariness stems from the personality traits of formulary decisionmakers being unusually skeptical and cynical. Instead, payers’ wariness is likely a structural feature of the drug company-payer relationship. Payers recognize the incentives drug companies face when drug adoptions and rebate contracting may approximate winner-take-all contests. When stakes are high, payers reason, drug companies will try to tilt the decisionmaking table by influencing the content and message of information flowing to formulary decisionmakers.\(^\text{10}\) Moreover, payers believe their

\(^{10}\) In one interview, the analogy was made between drug companies’ push for an informational advantage and fans in a packed football stadium: When fans in lower rows stand up to see better, everyone behind them stands up as well. However, if everyone were to sit down, they all would see as well as when everyone is standing.
experience with drug company marketing confirms their view that these incentives spur drug companies to provide only information favorable to their own drugs. In addition, payers find it similarly troubling when a manufacturer exaggerates a minor therapeutic benefit or an effectiveness claim in a niche population as a claim of significant value.

**Payers’ experience with drug company marketing.** In essence, while payers perceive studies supplied by drug companies as being of higher quality than in the past, payers simultaneously believe each drug company selects studies that cast its own drugs in a favorable light. As one insurer put it, “Drug companies give us only good news!”

**Payers’ countermeasures to drug company marketing.** In response to their perception of widespread bias in the information proffered by drug companies, many insurers conduct their own literature searches. In addition, at least some payers make a point of requesting dossiers from competitors to a new drug. Finally, in some cases, payers use analyses and literature reviews conducted by national drug-review agencies in, for example, the United Kingdom (NICE) and Canada. At least some payers cite these agencies favorably, commending their reports’ quality and impartiality.

**6.2.1.2 Most Payers Prefer that Manufacturers Supply Publications, Not Models, but Still Hold Mixed Perception of Studies**

In terms of pharmacoeconomic information supplied by drug manufacturers, most payers we interviewed expressed a preference for publications over computer models. However, almost all payers interviewed had divergent reactions to research publications they receive from drug manufacturers. Most payers acknowledge that the manufacturer-supplied research studies they review are of higher quality than in the past. However, as noted above, almost all payers interviewed characterize manufacturers’ selection of studies as partial and slanted.

In response to their perception of bias in manufacturer-supplied information, many insurers undertake various strategies. One is to conduct their own literature searches. As a decisionmaker at one larger payer remarked in mock surprise, “It’s the most amazing thing—how much of the information is never presented by the drug company!” A second strategy is to request dossiers from the

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11 Drug manufacturers supply payers many if not most of the technical publications on clinical and cost effectiveness that payers receive and review regarding new drugs.
competitors of the manufacturer of a new drug. A third response is to double down on skepticism: many decisionmakers interviewed indicated that they discounted results from published, peer-reviewed research studies supplied by manufacturers. Nonetheless, results that were discounted were not necessarily dismissed. In sum, payers seek additional studies and sources to level the informational playing field; absent that, they discount information they believe is biased.

A Minority of Payers Prefers Models to Publications

When questioned about alternative modes in which drug companies present information to payers, most payers said they prefer publications to computer-based models, but some payers do prefer models. Specifically, among decisionmakers we interviewed, we noted two clusters that prefer models:

- **Sophisticated model-users.** The first cluster is a subset of those decisionmakers who are quite sophisticated in terms of pharmacoeconomic training and experience. This cluster stated a preference for computer models as a tool that aids them in working through their assessment of a new drug. They were explicit in stating that their preference holds for models provided by drug companies.

- **Hands-on learners.** A second, somewhat larger cluster consisted of decisionmakers less skilled in pharmacoeconomics. They consider models a more effective medium than conventional publications. These decisionmakers find it easier to grasp ideas from working with a model than from the printed page.

The remaining payers fall into two additional groupings:

- **Inquisitive skeptics.** A third cluster, while expressing no preference between models and publications, stated a willingness to look at a computer model supplied by a drug company. Among those payers interviewed, only a small fraction—a few payers—is in this cluster. One payer decisionmaker stated that it is a waste of time to attempt to input his own payer's data into a drug company model, “since these models are so biased.” (Emphasis in the original.). Nonetheless, despite his skepticism regarding the model's overall, bottom-line result, this decisionmaker said that he sometimes finds “a piece” of a drug-company model useful. (As he elaborated, “Data and elements are more important than the models. Having them [data and elements] helps my quantitative thinking.”) Others payers said they would look more closely at a model supplied by a drug company if the model met their conditions such as greater transparency.

- The last cluster contains the majority of payers interviewed. They consider the appeal of models to be purely notional. These payers deeply mistrust models that, in their view, drug companies create simply as marketing tools for their own drugs.
6.2.1.3 Barriers to Use of Drug Company Models

Payers we interviewed cited three features of drug companies’ pharmacoeconomic models that inhibited the payers’ use of these models. Each feature is, in principle, subject to modification by an individual drug manufacturer.

**Lack of transparency.** As formulary decisionmakers for a diverse array of payers noted, almost all pharmacoeconomic models that drug manufacturers had shown them were, in their view, black boxes. When considering any given manufacturer’s model, the decisionmakers were not sure whether a key parameter had been set at a fixed value, thereby tilting the model to yield results favorable to the manufacturer’s new drug. (One decisionmaker stated that he had discovered, in one drug company’s model, the comparison drug’s costs had been set equal to average wholesale price (AWP)—well-known to overstate the true market or transactions price substantially.) Similarly, they wondered whether, for example, the model presented only results for a time horizon favorable to the manufacturer’s drug. (For example, the results might change if the horizon were a year or two longer or shorter than whatever the model presented.) One decisionmaker at a private insurer captured the views of his colleagues at a majority of payers interviewed:

> I’ve been in this business 25 years, and I know that I can make an Excel spreadsheet come out with whatever result I want it to.

In effect, he was saying, “If I can produce results at will, the drug manufacturers certainly can as well.” He and many decisionmakers at other payers did not doubt that drug manufacturers often used such analytical ability to their marketing advantage.

**Selective use of data favorable to manufacturers’ own drugs.** These decisionmakers objected to manufacturers selecting data and parameter estimates from a particular study or studies that cast the manufacturer’s drug in a good light. They generally saw this selection as too predictable to be described plausibly as simply good professional judgment. In addition, some payer decisionmakers explicitly indicated that the models’ lack of alternative parameter values, drawn from a wider array of studies, undermined the models’ credibility. (In effect, the payer decisionmakers expressed a preference for the type of methodology used by the Social Security actuaries, who present an optimistic scenario for Social Security finances and a pessimistic scenario, which bracket the actuaries’ intermediate scenario.)
Factors that Raise Payers’ Comfort with Drug Company Information

Payers we interviewed cited several factors—all predictable—as ones that raised their level of comfort with information that drug companies provide to them. As expected, payers attribute greater credibility to drug-company-supplied information if presented in the form of:

- Manuscripts, compared to abstracts from professional meetings;
- Published manuscripts;
- Peer-reviewed articles; and
- Independently-funded research.

The first factor—information presented in a manuscript rather than an abstract—presumably enhances information’s credibility (in payers’ eyes) because readers can detect study limitations, inconsistencies, and anomalous results more readily in the full manuscript and its tables than in the narrow compass of the abstract. The next two factors reflect a publication’s value as a filter for poor quality and for bias. These two factors enhance a paper’s credibility by indicating it has passed an independent review—whether by a single editor or by peer reviewers. The last factor indicates that many payers consider independent funding as inoculating research against the research bias that (in the payers’ view) pharmaceutical companies promote.

Payers Unable to Modify Drug Company Model to Payer’s Specification

Payers interviewed said that, in principle, pharmaceutical companies could take steps that would encourage payers to use their models. However, almost no payers were optimistic that manufacturers would do so. These credibility-enhancing steps are, of course, the mirror image of the barriers—cited by payers—to their use of manufacturers’ models:

- Make explicit the key parameter values assumed by the model’s designers about important variables (number needed to treat, cost of comparator medication, length of time horizon for assessing costs, etc.) and sources (published or not) for parameter values.

- Provide information needed for a sensitivity analysis so that, for example, results from studies less favorable to a given manufacturer’s new drug can be compared to
results of studies favorable to that manufacturer’s drug—which presumably were embodied in the model.\textsuperscript{12}

- **Design models that permit much more extensive inputting of values specified by the payer/user.** In contrast, many payers interviewed maintain that the pharmacoeconomic computer models they see from drug manufacturers generally are difficult if not impossible to modify according to the user’s (payer’s) specification.

One payer observed that a manufacturer that undertook one or more of these credibility-enhancing measures would have to make its case for its preferred choice of studies, parameter values, and model specification explicit. In contrast, the payer noted, the status quo, in which each manufacturer-supplied model typically is more or less a black box, presents the model’s results in an authoritative manner. As a result, the payer suggested, it appears as if disinterested professional analysts had surveyed the literature and designed a model that produces only the results produced by the drug company’s model.

**Details on Making the Concept of “Relevance” to Payers Operational**

When they use the word “relevance,” many payers in effect are voicing an interest in credible ways of adapting RCT evidence and tailoring it to their own population. Decisionmakers at many payers interviewed, when discussing the limitations of studies and models that drug manufacturers provide to them, expressed frustration at a difficulty they face: how to determine whether these study and model results were “relevant” to their own patient base. At first, we found it difficult to see how their frustration could be relieved, aside from the funding of RCTs that study populations very similar in demographic mix and other factors to each particular payer. After further questioning, however, insurers and public payers made clear their interest in mapping RCT results to that payer’s quite different population using feasible, credible methods. These decisionmakers recognized that any such tailoring of the evidence would not have the methodological rigor and resulting persuasiveness as the RCT results. However, they also recognized that, at present, the default method is their own ad hoc judgment.

In our interviews, there were indications that payers are increasingly willing to provide limited data inputs (from their internal data systems) to manufacturer-supplied models that can accept user inputs of data. For example, payers typically can supply the demographic composition of particular

\textsuperscript{12} It was noted that a manufacturer may select favorable data not just from study A rather than study B, but from within a given study. In some cases, a study may present alternate estimates of effect size, based on different statistical procedures. If the difference in effect size is nontrivial, it would be possible to cite a widely-cited study but still selectively use its results to cast a particular drug in a better light than otherwise.
disease populations (e.g., diabetes, COPD) among their plan members. One payer agreed to the suggestion that, in effect, he was calling for “pharmaco-actuaries” to tailor the published pharmacoeconomic information to his patient/member population.

6.2.2 Government Can Spur or Reduce Payers’ Use of Pharmacoeconomic Information, Depending on Specifics

Incentives to use pharmacoeconomic information differ across Federal programs that provide health coverage. One program may treat formularies and prescription drugs quite differently than others do. As a result, some programs may make the use of pharmacoeconomic information more valuable—or less—than others. In addition, proposals exist for new legislation that also could affect payers’ incentives to use pharmacoeconomic information—specifically, proposals to establish a national center for research and assessment regarding drug effectiveness.

6.2.2.1 Statutes May Reduce Some Public Payers’ Use of Pharmacoeconomic Information

For some public payers, statutory directives limit incentives to use pharmacoeconomic information. Details follow:

- **Medicaid.** Federal law in effect requires the more than 50 state-administered Medicaid programs to place on their formularies all drugs approved by the FDA.\(^\text{13}\) As a result, Medicaid programs do not have an incentive to use pharmacoeconomic information to decide on whether a new drug should be adopted. That is a foregone decision.

Moreover, Federal law and regulation limit Medicaid programs’ use of copayments to influence beneficiaries’ choice and use of prescription drugs. The Medicaid copayment is a fixed amount—currently $8 per prescription. As a result, Medicaid programs cannot establish tiers of preferred drugs and less preferred drugs. Medicaid copayments cannot be calibrated to be in line with judgments of relative clinical effectiveness, cost effectiveness, or even drug price. As a result, Medicaid cannot use cost sharing to nudge patients toward more cost-effective drugs or, in some cases, simply less costly drugs.

In contrast, Medicaid programs have two main tools for influencing whether a patient uses a particular drug: (i) prior authorization and (ii) step therapy. The fact that these

\(^{13}\)Medicaid is a Federal-state program; each state’s program is distinct and largely administered by each state itself, within the boundaries set by the Federal statute establishing Medicaid. In every state, Federal and state funds jointly finance the program. The total number of Medicaid programs is 55: the 50 states, the District of Columbia, and four territories.
tools are available under Medicaid means that Medicaid formulary decisionmakers and pharmacy benefit managers still can derive value from pharmacoeconomic information. That said, for Medicaid decisionmakers, the incentive to use such information is considerably less than it is for, say, commercial insurers.

- **Department of Defense – TRICARE.** Federal statute requires that TRICARE, the Department of Defense (DOD) health benefits program, adopt all drugs approved by the FDA. This statutory requirement reduces TRICARE’s incentive for using pharmacoeconomic information, just as the similar Medicaid requirement affected Medicaid program’s incentive to use such information. However, the full picture for TRICARE is somewhat different, as described below.

- **Medicare Part D – Prescription Drug Benefit.** Under Medicare Part D, prescription drug plans (PDPs) must cover all drugs within a few classes. Consequently, PDPs’ incentive to use pharmacoeconomic information is lower for some drug classes than for the majority of drug classes.

### 6.2.2.2 Statutes May Spur Some Public Payers to Use Pharmacoeconomic Information

Federal law creates an incentive for the use of pharmacoeconomic information by two programs:

- By statute, VA has latitude about adopting or excluding particular, new FDA-approved prescription drugs. By retaining freedom to select some drugs over other drugs, VA potentially can save money or increase value by using pharmacoeconomic information in assessing and selecting new drugs.

- Likewise, Medicare PDPs face an incentive similar to the VA (although somewhat more limited). Medicare PDPs face no requirement to cover all drugs in most drug classes. For these drug classes, PDPs’ incentive to use pharmacoeconomic information is the same as the VA’s.

As noted earlier, our interview with VA indicated that its extensive use of pharmacoeconomic information is consistent with VA’s incentive. Pharmacoeconomic information and effectiveness analyses are potentially valuable to VA, given that its decisionmakers have latitude in selecting new drugs for its formulary. Our interviews with insurers that offer Medicare PDPs indicated that they, like VA, use this information—an unsurprising result. However, we could not determine how extensive and how sophisticated is PDPs’ use of pharmacoeconomic information.
6.2.2.3 Government-sponsored Drug Effectiveness Entity Might Increase Payers’ Use of Pharmacoeconomic Information

Proposals to establish a national center for effectiveness research and assessment are attracting attention in the political and policy arenas. (Such a center is said to hold promise as a means of curbing spending on drugs and other items with less clinical effectiveness, compared to other drugs and medical products.)\(^{14}\) A national drug-effectiveness center interests payers but elicits their skepticism as well. Such a center could alter payers’ incentives to use pharmacoeconomic information.

**Payers Interested, Skeptical about New Drug-Effectiveness Center**

Payers’ knowledge of existing effectiveness research agencies is uneven. About half of payers interviewed knew about U.S. Federal and British agencies involved in comparative effectiveness research today. (Equivalently, half of these payers did not.) Specifically, many insurers interviewed are familiar with NICE, the British government agency that gathers information on the clinical effectiveness of drugs and medical devices and that issues recommendations about their cost effectiveness. Likewise, many insurers were aware that, in the United States, an existing Federal agency (AHRQ) funds research on “comparative effectiveness.”\(^{15}\) However, only some insurers had heard about proposed legislation to create a new structure, similar to NICE, in the United States.

Payers’ conditions for interest in a drug-effectiveness center mirror their bases for skepticism. Almost all payers said that they would look at that new entity’s reviews/recommendations if that agency were “unbiased.” Some payers were explicit:

> An “unbiased” agency means an agency that sponsors sound research insulated from pressure by drug companies, patient advocacy groups, the Congress, and the Executive Branch.\(^{16}\)

Some payers expressed strong skepticism that U.S. political realities would let such an agency be established and function without its structure and operations being subtly or overtly tilted toward industry interests and patient-advocates’ demands.

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\(^{14}\) Proposals differ in their scope: Some proposals focus exclusively on prescription drugs; others include medical devices and medical procedures.

\(^{15}\) Typically, AHRQ reviews address clinical effectiveness, not cost effectiveness.

\(^{16}\) This sentence is our distillation of multiple comments made by decisionmakers we interviewed; it is not a direct quote.
New Drug-Effectiveness Center Might Spur Payers’ Use of Pharmacoeconomic Information

The implementation of a new drug-effectiveness center could affect payers’ incentives to use pharmacoeconomic information in several ways:

First, an increase in use overall: an increase in the supply of unbiased pharmacoeconomic research and evaluations would encourage payers to use such information. However, that encouragement depends on payers perceiving the research and evaluations produced or sponsored by the center to be unbiased and scientifically sound.

Second, a shift in information source. Payers might well shift the composition of the effectiveness research and evaluations they use. To the extent payers perceived less bias in the new center’s research than in studies proffered by drug manufacturers, payers might well use more of the new center’s research and less of the research provided to payers by manufacturers.17

Third, change might be modest. Payers’ incentives to use pharmacoeconomic information might not change much, if the new center’s effectiveness research were perceived to be marred by bias, similar to the bias payers often see in effectiveness and cost-effectiveness studies that manufacturers provide to them. In that case, payers’ overall use of pharmacoeconomic studies would likely not change much, nor would the composition of these studies’ sources or sponsors.

6.2.3 Payers Offer Insights about Information Flow between Pharmaceutical Companies and Payers

6.2.3.1 Real World Studies—A Double-Edged Sword?

Most payers interviewed expressed interest in what can be termed “real-world studies.” These studies use observational data on patients in “real-world” physician practices and hospital wards who receive treatment that may well differ from the protocols followed in clinical trials. In addition, real-world studies of a particular drug’s effectiveness may focus on or include patient populations with

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17 When the “price” of unbiased research and evaluation goes down, the substitution effect indicates that demand shifts toward the new center’s studies and away from the drug manufacturer’s studies. However, suppose the new center’s research and the drug manufacturer’s research are complementary; say, if the availability of the center’s unbiased studies makes it easier for payers to assess nonecenter research. In that case, it is possible for overall demand for pharmacoeconomic information and evaluations to rise.
different demographic characteristics than the population studied in the relevant RCT. Payers recognize that RCTs offer the strongest evidence regarding the causal effectiveness of a new drug and that the evidence from a real-world study is weaker. Nonetheless, payers who are proponents of real-world studies look to them as sources of empirically grounded hints or clues to how well RCT results will pass through two filters:

- Real-world imperfections in clinicians’ adherence to preferred protocols and in patients’ adherence, compliance, and persistence regarding the drug regimen their physician prescribed, and
- Clinically-relevant differences between the RCT population and each payer’s own patient population.

How payers interpret the results of a real-world study depends on the results obtained from the earlier clinical trial:

- If RCTs’ results conform to the payers’ expectations, in many payers’ eyes the RCT results are bolstered.
- If the real world results show greater efficacy than the RCT, these results are discounted if not discarded.

Consequently, for pharmaceutical manufacturers, real-world studies can appear to be a double-edged sword. In fact, that characterization is not accurate. Obviously, a real-world study of an employed population might reinforce the RCT’s findings for an elderly, Medicare population. However, if payers were to discount or dismiss a real-world study because it showed a new drug to be much more effective than did the RCT, the drug manufacturer presumably is no worse off. Whatever lesson the payer took from the RCT should still stand. If these two cases were the only ones possible or very likely, for the drug manufacturer, supporting real-world studies would have little apparent downside risk. Another case is, of course, possible: the real-world study presents evidence that the (relatively) new drug is less effective than the RCT results indicated. Interestingly, the payers interviewed did not discuss this case. If they take what some see as a conservative approach, the payers would discount the RCT results. They might assume that real-world deviations from protocol dissipate much of the effect evident when physicians and patients display fidelity to the trial protocol. Unfortunately, the decisionmakers interviewed did not address this case.

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18 The incentive for drug manufacturers to support real-world studies could set a dynamic in motion that would erode the credibility of all real-world studies. A Gresham’s Law of studies could manifest itself, if several manufacturers began sponsoring real-world studies that were less reliable and had more, presumably, hidden biases than the average study.
6.2.3.2 Types of Information that Improve Payers’ View of a Drug or Leave Them Cold

In our interviews, at least several payers indicated that they respond strongly, negatively or positively, to particular types of information or particular catchphrases intended to describe certain information. These terms or phrases include:

- **“Disease modifying.”** Drugs that are “disease modifying” are perceived as having higher value, at least by decisionmakers at some insurers. Use of the term “disease-modifying” (e.g., DMARDs) as part of the therapeutic class probably allows these drugs to obtain coverage that is more favorable.

- **HRQoL and PRO.** Payers discount “soft” measures of clinical effectiveness but exceptions exist. The payers we interviewed generally discount health-related quality of life (HRQoL) and patient-reported outcomes (PRO) as measures of clinical effectiveness. In the payers’ view, as evidence of clinical effectiveness, both types of measures are “soft.”

In their formulary decisionmaking process, private insurers who were interviewed said they consider HRQoL rarely. In contrast, some Medicaid agencies and at least one other public payer do consider HRQoL. However, given that the length of the interviews was limited, we could not establish definitively whether the various Medicaid decisionmakers interviewed meant the same thing by HRQoL as we did. (Sometimes, they seemed to mean simply that their formulary decisions take into account their enrollee/patients’ “quality of life,” broadly construed.)

Among the payers interviewed, patient-reported outcomes (PRO) drew comments that were slightly more positive. Accordingly, PROs seem to carry more weight than HRQoLs. A few plans view PROs as significant. Regarding PROs, a decisionmaker at one large payer made an interesting distinction: PROs themselves are not persuasive. However, patient-level outcomes are persuasive—if reported by the patient’s physician.

This comment exemplified a common undercurrent among payer decisionmakers: Patient-reported outcomes are difficult to validate. Payer decisionmakers believe they have little basis for assessing the extent to which patients with similar diagnoses, observable symptoms, and emotional states report their outcomes in the same way. For various reasons, decisionmakers consider physician reports on a patient’s health condition (e.g., diagnoses) to be much more credible than reports by patients themselves.
6.2.3.3 The Ear as an Organ of Marketing: Payers’ Views on Drug Companies’ Use of Their Time with Payer Decisionmakers

Payers we interviewed noted that, in the time they spend with representatives of pharmaceutical companies, these representatives generally control or dominate the agenda and discussion. In the payer decisionmakers’ view, the schedule leaves little time for the pharmaceutical representatives to answer the payer/decisionmakers’ questions. Moreover, these representatives lack the training or knowledge to respond to many of the payers’ concerns.

One decisionmaker at a large insurer elaborated on this point. He stated that the conventional visit of a drug manufacturer’s representative is stylized, like a Kabuki drama.

The representative gives a presentation that takes most of the allotted time. The payer’s pharmacy benefit and evaluation staff ask a question or two. Then pleasantries are exchanged (“Thank you for taking the time to share your information with us.” “No, it was our pleasure.”) and the meeting ends.19

However, this decisionmaker emphasized, his questions go unanswered or even unasked. He said he would greatly prefer to forgo convention. In his “fantasy scenario,” he continued, he would receive materials (studies, models) from the drug company in advance of the meeting. At the meeting, the manufacturer would send staff with appropriate training. The decisionmaker would be able to ask his questions of a knowledgeable person and engage in a serious discussion between well-informed and well-trained people. This decisionmaker thought the outcome of the meeting would be beneficial to both parties. In contrast, he maintained that the status quo often leaves the payer’s staff with more unanswered questions and more (what might be termed) free-floating skepticism about the drug manufacturer’s evidence and claims. While this particular decisionmaker is among the most sophisticated and well-trained of payer decisionmakers we interviewed, his views were similar to—though more fully articulated than—the views of some of his peers.

19 The decision maker’s statement was edited to tighten it. No edit altered meaning.
6.3 Finding Three: Payers’ Perceptions of the Prescription Drug Market Environment – Payers, Employers, PDPs, PBMs

In the course of our interviews with insurers, employers, and public payers, interviewees discussed aspects of the market for prescription drugs as seen from their vantage point. This section summarizes payers’ comments on three topics: special treatment of drugs for certain disease areas; the state of the Medicare PDP market and its prospects; and the functions of PBMs in relation to payers.

6.3.1 Payers Scrutinize Certain Drugs More, May Ease Stringency of Review for Others

*Drugs in Some Disease Areas Given Lighter Review*

Almost all insurers admit: Historically, the value threshold was not as stringent for oncology drugs as for most other drugs. Today, this historical pattern continues but is waning. Oncology drugs still get more leeway than drugs in other therapeutic areas *within the same price range*. Nonetheless, the privileged status for oncology drugs is changing to some extent. *High-cost* oncology drugs are increasingly receiving extra scrutiny due to their high prices, which pose a problem for payers.

Other disease areas also are getting a somewhat lighter review or seem likely to do so in the future. Payers interviewed indicated that they give special treatment during drug review to selected nononcology classes of drugs. Specifically, in 2008, payers sometimes give less stringent scrutiny to drugs in the disease area of mental health. This easing of stringent review is more evident for drugs used to treat patients not able to care for themselves. In the future, a similar easing of review criteria might occur for drugs in the disease area of Alzheimer’s.

From these cases of less stringent review, two conditions appear to predispose a payer to treat drugs for a given disease less stringently than the usual criteria would indicate: First, the patient population with that disease seems *vulnerable*; and second, payers recognize *a sense of “societal compassion”* toward those with the disease.

Such exemptions from intense scrutiny are uncommon. These exceptions conflict with normal business pressures within insurers and public payers: payers believe that stringent scrutiny of new
drugs tempers the perennial increases in pharmacy budgets. In addition, in managing the new drug reviews for their formulary, insurers strive for consistency across drugs.

**From Medical Side to Pharmacy Side?**

Historically, health plans and other payers have scrutinized and managed drugs covered on a health plan’s pharmacy side more closely and intensively than on the medical side. The decisionmakers we interviewed emphasized that, given the persistence of strong spending pressures, the lower bar on the medical side motivates insurers and other payers to “move drugs from medical spend to pharmacy spend.”

Increasingly, payers also are looking for opportunities to move *specialty drugs* from the medical benefit to the pharmacy benefit. This is true especially when payers had set up their information technology systems and standardized reports to focus more on pharmacy spend than on those specialty pharmaceuticals included in medical expenditures.

Recently, however, payers have targeted specialty drugs, whether the pharmacy benefit or medical benefit covers them. Compared with the past, payers’ management of specialty drugs and other drugs under the *medical benefit* has increased. Indeed, subsequent to these interviews, payers indicated to us that their management of specialty pharmaceuticals under the medical benefit has further intensified. As a result, the desire of payers to shift specialty pharmaceuticals to the medical side will be less of an issue in 2009.

**6.3.2 The Flight of the PDPs? Perceptions of and Prospects for the Medicare PDP Market**

Insurers we interviewed often expressed their opinions about the new prescription drug market and their prospects as companies offering a Medicare PDP. Payers in the Medicare PDP market questioned whether participation in that market is a sound business decision. As more than one decisionmaker noted, “It is hard to make money off a PDP.”
Insurers said managing a PDP was not a low-risk route to business success. In fact, insurers increasingly see that, as one put it, “PDPs are financial losers.” (This contention runs counter to the popular view that the Part D program is lucrative for insurers that offer PDPs.)

Insurers attribute the situation to two main factors:

- **Inadequate tools and incentives.** As one decisionmaker observed, “By managing someone’s drug expenses well, a Medicare Advantage prescription drug plan (MAPD) can make some money.” Making money with a PDP is harder because, according to the insurers interviewed, the PDP lacks both tools and incentives available to the MAPD. In particular, one decisionmaker said that “the ‘silo’ view of pharmacy budgets is inherently flawed,” yet (in his view) PDPs institutionalize the silo view as the basis of non-MAPD plan designs under Medicare Part D. Moreover, some insurers that participate in the PDP market maintain that “the value of drugs must incorporate any medical cost offsets that the drugs generate.” Acting on that belief is easier as MAPD, as noted earlier, than as a PDP.

- **CMS’s overly-prescriptive guidance.** Decisionmakers for insurers that offer Medicare PDPs said that “CMS is very prescriptive.” While some, such as consumer advocates, see as appropriate delineation of formulary features and plan design, others (especially those that offer a PDP) see as micro-managing and burdensome.

Accordingly, these insurers explained, PDPs see a Hobson’s choice:

- Provide suboptimal care and get into trouble with CMS, patients, and other institutions, or
- Spend more on these patients than premiums would bring in.

A third option, of course, is to leave the market, a course some insurers are considering.

### 6.3.3 Payers Confirm Conventional Wisdom on PBMs

In our interviews, payers confirmed the conventional wisdom about PBMs and their relationship with payers. For example, payers expect the PBM to sift through the Academy of Managed Care Pharmacy (AMCP) dossier and other information, and to provide the payer/customer with recommendations about adoption and tiering of new drugs. In addition, payers said that they challenge some recommendations by their PBM. However, such challenges are rare, especially when adopting the payer’s view would mean that the payer would incur significant costs of making a change in the formulary that the PBM provides the payer.
Payers interviewed noted two practices that are less well known:

- Providers/vendors of specialty pharmaceuticals assist with decisions that concern adoption and management of specialty drugs.

- Employers may ask their PBM for a class to be covered (or not, e.g., fertility drugs). However, generally, an employer will not select the specific drug within the class to include on the formulary. As a result, an employer’s ability to influence seems greatest for a manufacturer with a drug that is “first (and only) in class.”
6.4 Finding Four: Formulary Decisionmakers and the Future: What They Foresee, What They Wish For

In their interviews with us, formulary decisionmakers discussed the trajectory they anticipated their organizations and formularies would take over the next 3 to 5 years. These decisionmakers also identified their wish list: the changes they would like to see from pharmaceutical manufacturers, the Federal Government, and academic researchers, however likely or unlikely they may be.

6.4.1 Back to the Present? Payers Foresee Substantial Continuity in Their Own Organization’s Formulary

We all were sea-swallow’d, though some cast again,
And by that destiny to perform an act
Whereof what’s past is prologue, what to come
In yours and my discharge
-- Shakespeare, The Tempest (Act 2, Scene 1) [emphasis added]

Looking ahead 3 to 5 years and seeking to predict the future of their own organization’s formulary-related actions, the payer decisionmakers interviewed looked back to their organization’s recent history. Since they extrapolated from the recent past, their forecasts typically (and understandably) identify continuities. However, in some cases, the decisionmakers expect that two trends will likely remain in conflict.

6.4.1.1 Payers Generally Extrapolate Present Trends

Payers interviewed anticipate that three trends or patterns will continue:

- The emerging trend to scrutinize high-cost drugs more stringently;
- The (related) tendency to manage specialty pharmaceuticals more intensively; and
- The tendency for oncology drugs to receive less preferential treatment than historically.

Underlying two of these expectations is the view that cost pressures are a powerful driver of payers’ actions. This view has three elements: spending pressures—on budgets generally and on pharmacy budgets in particular—are a chronic feature of health care; the pressures are expected to continue
unabated; and insurers and public payers will persist in trying to mitigate these pressures. Consistent with this cost-centric view are greater scrutiny of high-cost drugs and more intensive management of specialty pharmaceuticals. As the latter trend has become more pronounced, a related tendency, the movement of some drugs from the medical side to the pharmacy side, seems to be waning. A particular focus is on specialty pharmaceuticals, which represent a proportion of total drug spending that is increasing.

However, the third anticipated trend stems from a different principle: consistency in drug review procedures and criteria. As those interviewed noted, formulary decisionmakers generally prefer to treat drugs consistently. At the very least, this preference holds within an established division of the benefit package (e.g., pharmacy). Consequently, we expect the decisionmakers’ desire to be consistent in their review of different drugs and drug classes to erode oncology drugs’ special status in these reviews.

**“Most Favored Nation” Status for Drugs in Certain Disease Areas**

The erosion in oncology drugs’ status does not imply that payers will exclude other disease areas from a privileged status, at least to some degree.

**Oncology.** Consider oncology drugs exclusively: as noted above, payers are beginning to review these drugs less gingerly. For many years, oncology drugs were beneficiaries of a sort of pharmaceutical “most favored nation” status. Almost all insurers admit: the value threshold was not as stringent for oncology drugs as for most other drugs. Today, oncology drugs still get more leeway than other drugs with the same price. But high-cost oncology drugs are increasingly receiving extra scrutiny, triggered by their high prices.

**Other disease areas.** While oncology drugs’ status is eroding, other drugs are candidates to assume their mantle—for example, the set of drugs available to mental health patients, especially those not able to care for themselves. In the future, drugs prescribed for Alzheimer's may be in a similar position.

In sum, a payer may treat drugs for a given disease somewhat differently if the patient population seems vulnerable and if there is a sense of “societal compassion” toward those with the disease.

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20 In our earlier interviews, decisionmakers talked about this shift to the pharmacy side as an emerging trend. More recently, though, they indicate it has been supplanted by introducing more exacting standards into the medical side.
Nonetheless, normal business pressures within insurers make such exceptions uncommon. In addition, insurers strive for consistency in their formulary decisionmaking processes.

### 6.4.1.2 Tendencies Regarding Tiering Conflict

Decisionmakers at various insurers identified two, relatively recent developments in formulary design that are both likely to continue and to be in tension:

- Many more insurers will create a *fourth tier* in their benefit design or add more drugs to the fourth tier. Patients who are prescribed drugs in their payer’s fourth tier will face cost-sharing that is especially high. In the past several years, drugs assigned to the fourth tier included very expensive oncology drugs.

- Some insurers will expand or begin to use “value-based benefit design.” A key element of value-based benefit design calls for placing each drug in a tier that corresponds to the drug’s relative *cost-effectiveness*. (In some cases, the tier corresponds to the payer’s view of the drug’s relative *clinical* effectiveness.) That is, a formulary’s decisionmakers would place a drug, which is more cost-effective than its rivals in the same drug class, in the lowest tier (with the lowest co-pays). The thrust of value-based benefit design is this: Structure patient cost-sharing so that patients face the lowest financial barriers when prescribed highly cost-effective drugs. Similarly, have patients face the strongest financial *disincentives* when prescribed the least cost-effective or least evidence-based drugs.

Taken together, these scenarios point to, in effect, worlds in collision:

- One world sees excessive health care spending on drugs and other services and seeks ways, large and small, of taming it. The more sharply the cost challenge pinches the formulary decisionmaker, the more appealing is the use of a fourth tier.

- Another world sees patients who would likely benefit from a particular, expensive drug treatment being deterred from filling a prescription or following the prescription routinely by pain in the wallet—the medication’s out-of-pocket cost to the patient. Consequently, the elimination of patient cost sharing for the medication should boost adherence, compliance, and persistence. Ideally, following the prescribed drug regimen should improve health outcomes.

On its face, the two scenarios are irreconcilable: To mitigate high costs, expensive oncology drugs should be on the fourth tier, subject to high copayments or substantial coinsurance. To improve
Findings From In-depth Interviews with U.S. Insurers and Public Payers

adherence and compliance, these oncology drugs should face copayments that are low or zero. The two scenarios can be reconciled if:

- These costly oncology drugs in fact are not as cost-effective as alternative treatments, in which case value-based design calls for high cost-sharing or

- These same drugs yield sizable medical cost offsets that render them very cost-effective, in which case these drugs would swell a payer’s overall budget less than they would its pharmacy budget.

6.4.1.3 The Silo Mentality and the Dismissal of Medical Cost Offset Claims

In a minority of our interviews, we noted one thread: During drug reviews, claims of medical cost-offsets are often dismissed. Moreover, this situation is expected to continue. According to some insurers we interviewed, their inability as insurers to consider medical cost offsets in its drug reviews is due to the employers. “The employers only care about rebates (from drug manufacturers),” one sizable insurer stated. “They can’t be bothered with evidence of, say, fewer hospitalizations. To them it’s ‘ghost evidence.’ They can’t see medical cost offsets the way they can see drug costs and rebates.” Ironically, some employers hold a mirror image. These employers blame the insurer for the reason why medical cost offsets are ignored when formulary decisions are taken.

This pattern regarding the treatment of medical cost offsets was held in the past among some payers, according to our interviewees. For those payers, they expect the pattern to continue to hold.

A coda to this point: some trends can be influenced. At one commercial insurer, several decisionmakers volunteered that one reason some employers dismiss medical cost-offsets as part of a new drug’s assessment is that, “We [the insurer] have not presented convincing cases and evidence to [the employers].” These decisionmakers indicated that they had instances of medical cost offsets in mind, but they had not been able to assemble evidence to make the case from their [the insurer’s] own claims data.21

21 In addition, this example of the insurer’s difficulty in marshalling its own claims data regarding cost offsets calls to mind other payers’ difficulty in translating RCT results to their own enrollee populations.
6.4.1.4 The Market for Pharmacoeconomic Information

Our interviews with insurers and public payers elicited comments about the market for pharmacoeconomic information that suggest the following generalizations:

- Most insurers will continue to seek pharmacoeconomic information \textit{broadly defined} (outcomes data, clinical effectiveness studies, drug costs, other cost information, etc.).

- Some insurers will increase their use of pharmacoeconomic information \textit{narrowly defined} (e.g., cost-effectiveness analysis).

- The market for such information (ICERs, formal pharmacoeconomic analyses) will continue to be latent among the majority of insurers.

- Regarding the \textit{quality and reliability of pharmacoeconomic information}, most payers will continue to believe that, for most new drugs, pharmacoeconomic information requires careful review and caution in use. These payers are on the alert for studies and information that are biased, uneven in coverage of comparator drugs, uneven in quality, or nonexistent.

- Regarding a \textit{specialized internal pharmacoeconomic capability}, a minority of payers will augment their capacity for pharmacoeconomic evaluation of new drugs in the next few years. Few payers we interviewed expressed a belief that they have a strong business case for adding staff skilled in cost-effectiveness analysis and outcomes research. This suggests that the number of payers that belong to the inner ring of pharmaceutical information users will continue to grow slowly and modestly in the next several years.

\textbf{A Break in the Trend?}

One large insurer expects a rather dramatic departure from historical trends: \textit{more dialogue and partnering between the pharmaceutical industry and insurers}. This insurer expects the two sides to find common ground in conducting “real world” studies and getting the insurer’s questions answered (rather than having the insurer or payer just hear the drug companies’ story about their new drugs).
6.4.2 Payers’ Wish List Regarding New-Drug-Related Information

When asked what changes in pharmacoeconomic information they would like to see in the next 3 to 5 years, payers’ replies fell into three categories of desired changes:

- Information on drugs produced and supplied would be independent of the drug manufacturers; as a result, the data would be unbiased;
- Computer models of new drug’s clinical and cost properties would be “driven” by the payer as model user, not by the drug manufacturer; and
- Various analytical issues would be addressed in studies and computer models more effectively.

Table 6-1 lists the items under each of the three categories. The table distinguishes potential respondents to the payers’ wishes:

- An individual drug company;
- A private consortium (presumably of payers, although potentially of drug companies);
- Consultants and academic researchers; and
- The Federal Government.

The size of a checkmark denotes our judgment of the likely relative importance of a particular actor that might respond to a particular item. For example, for the first item, greater transparency, we consider the individual drug company to be most important potentially; in contrast, we consider a private consortium, consultants and academics, and the Federal Government to be of lesser, secondary importance.
Table 6-1. Payers’ wish list regarding pharmacoeconomic information

<table>
<thead>
<tr>
<th>Item</th>
<th>Potential Respondent</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Drug Company</td>
</tr>
<tr>
<td>I. Independence and Unbiasedness</td>
<td>✓</td>
</tr>
<tr>
<td>More transparency, less bias in dossiers &amp; models that drug companies give payers</td>
<td>✓</td>
</tr>
<tr>
<td>More independent studies:</td>
<td>✓</td>
</tr>
<tr>
<td>1. Not sponsored by individual drug companies or else</td>
<td>✓</td>
</tr>
<tr>
<td>2. Conducted at arm’s length from individual drug companies</td>
<td>✓</td>
</tr>
<tr>
<td>More head-to-head clinical trials of new drugs</td>
<td>✓</td>
</tr>
<tr>
<td>II. User-driven Models as Tools for Payers</td>
<td>✓</td>
</tr>
<tr>
<td>More models that let payer modify</td>
<td>✓</td>
</tr>
<tr>
<td>(1) Demographic/Dx characteristics of patient population</td>
<td>✓</td>
</tr>
<tr>
<td>(2) Relative effectiveness of comparator drug</td>
<td>✓</td>
</tr>
<tr>
<td>(3) Cost parameters</td>
<td>✓</td>
</tr>
<tr>
<td>III. Analytical Issues</td>
<td>✓</td>
</tr>
<tr>
<td>The FDA to direct that RCTs use a particular primary endpoint for all drugs in a given drug class (Goal: facilitate comparisons across drugs)</td>
<td>✓</td>
</tr>
<tr>
<td>More information on incremental value when a product is used in combination (e.g., as “add on” therapy)</td>
<td>✓</td>
</tr>
<tr>
<td>Information on the interrelatedness of tests and drugs (p/genes)</td>
<td>✓</td>
</tr>
</tbody>
</table>

Legend:
✓ Denotes “relatively important;”
✓ Denotes “of modest or secondary importance;”
A blank cell denotes “not relevant or important.”
Concluding Observations

The body of this report examines many topics. Likewise, Appendix A distills the answers of decisionmakers at 17 payers to approximately 35 questions that span 9 topical areas. In contrast, rather than summarizing these many findings, this section presents six concluding observations—a look from the balcony, not the orchestra seats.

7.1 The Methodology Worked

By adopting a qualitative approach to this study, we identified patterns and tendencies regarding U.S. payers’ use of pharmacoeconomic information and their perception of its value. By use of intensive interviews and a structured protocol—and by creating the atmosphere of a conversation—we were also able to convey the texture of payers’ views and often sketch their underlying reasoning. Consider the preceding statements about “payers’ use of pharmacoeconomic information” and “the texture of payers’ views.” These statements are meaningful and can claim accuracy only because the term “payer” refers to an identifiable formulary decisionmaker whom we could attest to having responded to our questions.

In contrast, conventional surveys translate the term “payer” operationally as “the person who filled out the questionnaire or survey instrument.” If a survey were sent, for example, to the chief medical officer of a large Blue plan, the survey that would be returned might have been filled out by the chief medical officer or by his or her junior staff person. The survey organization and its customer may never know which it was. In the present study, the opposite is true.

7.2 A Sea Change Since the Late 1990s

Payers accept the scientific merits of pharmacoeconomic studies broadly construed. Is this dry statement worth remarking on? Yes.

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1 That is, studies of outcomes, comparative clinical effectiveness, drug and medical costs, and cost-effectiveness.
Ten or 15 years ago and more, payers generally dismissed or discounted pharmacoeconomics as an enterprise that offered much information useful to them. At most payers, formulary officials did not look to pharmacoeconomic information with eagerness when deciding whether to adopt a new drug or set its level of patient cost sharing. At the time, most payers who saw pharmacoeconomic studies tended to doubt their scientific soundness and practical relevance.

Today, most payers consider the typical peer-reviewed published article on, say, comparative clinical effectiveness of a new drug, to be acceptable—judged by scientific criteria. Whatever the focus of the study (e.g., outcomes or costs), payers take RCTs as the gold-standard source of study data. Like the sea rising from ebb tide to high tide, payers’ view of pharmacoeconomic information moved by small increments. Whatever the pace, when decisionmakers change their “default setting” for a major type of information, that shift is major.

If the default or presumption about pharmacoeconomic information is now more favorable, payers still view much pharmacoeconomic information with frustration.

The next observation suggests why.

### 7.3 Translation is a Big Issue. Other Barriers Also Hamper Payers’ Use of Pharmacoeconomic Information

Payers struggle with whether mapping RCT results to their own enrollee populations is justified. As might be expected, many barriers still inhibit the acceptance and use by many payers of specific studies on particular drugs applied to populations like theirs.

Sifting through the interviews, we identified at least four types of barriers:

- **Technical** – e.g., it is a technical challenge to make RCT results applicable to many subgroups in the population. This is particularly true for the subgroups that typify a specific payer’s population.

- **Perceived bias** – e.g., the fact that a drug manufacturer with a vested interest supplies most pharmacoeconomic information creates the perception of bias.

- **(Supply side) transparency and user friendliness** – e.g., manufacturers differ in whether their pharmacoeconomic models’ assumptions and data sources are relatively
transparent or opaque. In addition, their models differ in the amount of information that is “hard wired” into the model.

- **(Demand side) insufficient capacity** – e.g., inside many payers, formulary committees or other decisionmaking entities do not have enough trained, specialized staff to conduct high-quality pharmacoeconomic assessments of new drugs. Moreover, these payers do not see a strong business case for a major expansion of this capability.

### 7.4 Who’s Listening?

From our interviews with formulary decisionmakers, we drew two implications that relate to the notion that “the ear is an organ of marketing.”

- First, **opportunities exist for pharmaceutical manufacturers to improve communications with payers.** Specifically, payer officials consider it important that drug company representatives listen to them. When that occurs, drug company representatives have received information from payers—facts, opinions, questions, requests. When the directional arrow points toward the drug company representatives, this flow of information matters (to those payer officials) at least as much as the reverse flow of information—the transmission of information by those drug company representatives to the payer officials.

  Furthermore, the number of PowerPoint slides presented and talking points conveyed is not the metric of effective information transmission. Rather, the meaningful metric is the extent to which the payer officials and decisionmakers are engaged; whether they pay real attention to what is being said and process it in a constructive manner. Finally, as one formulary decisionmaker noted, “‘Information transmission’ sounds like a power line. But I need a dialogue, not an electric current. I need to ask questions of someone knowledgeable and to get things clarified and to get answers.”

- Second, **disagreement and trust are not necessarily mutually exclusive.** Consider a presentation by a pharmaceutical company representative: The more structured and inflexible the presentation is, the more likely the payer decisionmaker senses that the drug representative and his or her company lack confidence in their ability to respond directly and cogently to questions and concerns that the payer officials have. As a result, as one payer decisionmaker put it, “It’s different when you leave a meeting with a drug company and say ‘I learned something,’ than when you leave a meeting and say ‘I was sold something.’”
7.5 **Pharmacoeconomic Champions?**

The formal tools of pharmacoconomics, pharmacoeconomic models, and cost effectiveness analyses have penetrated the leading edge of payers (e.g., Premera BCBS). In contrast, the median payer does not have internal leaders who look at drugs through ICER lenses. Insurers and other payers that want their formulary decisions framed and perhaps driven by formal pharmacoeconomic tools have two options: (1) Contract out new drug assessment to a PBM, particularly one that is willing to spell out how it uses these tools, and alternatively, (2) Undertake a multiyear process of organizational change and investment in suitably trained staff. The first option is less likely to call for an internal champion of pharmacoconomics. The second option is not likely to make meaningful progress without such a champion. In turn, payers would have to select and develop trained staff with leadership and change-agent skills. Such leaders or champions would foster a broader diffusion of the formal tools of pharmacoconomics and of their integration into formulary decisionmaking.

7.6 **Are Cases of a Split Between Value and Business Assessment More Form or Substance?**

Our interviews regarding payers’ review of new drugs uncovered several cases of bifurcation of value assessment and business decisions. How much of this is a change in form, how much a change in actual decision results? Based on our interviews, we conjecture that much of the impetus toward any value/business assessment split was due to external factors that unsettled the managers of certain payers. In particular, some insurers and PBMs may believe that, by segregating value assessment and business assessment in separate organizations, they can sidestep a pharmaceutical analogue to the managed care backlash of the 1990s. Nonetheless, once organizational changes occur, unintended consequences may ensue. For example, when new drug assessment was conducted under the umbrella of a single formulary organization, staff oriented toward “cost” may have worked out a rough-and-ready collaboration with “clinical” staff. In contrast, when clinical evaluation is separated from cost effectiveness evaluation, collaboration might become more difficult to achieve. Accordingly, we believe that cases of a value/business bifurcation call for monitoring and for fact gathering.
**Coda**

The ancient Greek poet Archilochus observed that “The fox knows many things, but the hedgehog knows one big thing.” For those readers who want to know many things, we offer our findings and our topic-by-topic summary of the interviews (see Appendix A). For those readers who want to know one big thing regarding the state of pharmacoconomic information and its use in the United States, we offer one long sentence:

> U.S. payers have crossed a threshold in their consideration of such information as scientifically acceptable, but major barriers hamper its use, particularly when pharmaceutical manufacturers are its source.

Each perspective has its place. Our suspicion is that, in this case, the starting point for effective action is the specifics. For us as students of pharmacoeconomic information and its use, the fox gets the nod.
Appendixes
Appendix A

Narrative Summaries of Phase II Interviews – By Topical Area
SECTION ONE
How Do Payers Define “Value”?
Elements of Value; Role of Medical/Pharmacy Side, Disease State, etc.

1.1 Imagine a new molecule has just been launched. When it is considered for formulary adoption and tier placement, its “value” gets discussed. That “value” is often described as a balancing of safety, effectiveness, and cost. Is that description the way you see it?

a. If so, how does your organization balance those three elements when assessing value?

b. Do you consider any factor other than safety, effectiveness, and cost as part of value?

c. Suppose that newly launched molecule has entered a crowded therapeutic class. What information other than price is necessary for that molecule to be placed on second tier?

Definition of value

All payers interviewed accepted the conventional formulation—the value of a drug depends on its safety, clinical effectiveness, and cost characteristics.

Balancing of safety, effectiveness, and cost

Payers’ answers to this question follow two or three different threads. Some insurers and at least one PBM assess safety, effectiveness, and cost sequentially: first safety and effectiveness, then cost. In contrast, one insurer trades off safety, effectiveness, and cost in one step. A public payer began by saying that it assesses all three value elements concurrently with equal weight and then added: “But it depends on the class of drugs and the impact on the beneficiaries.” The remaining payers interviewed did not provide answers that were clear-cut.

From an analytic standpoint, assessment that is sequential and hierarchical can yield a different decision than concurrent assessment that involves tradeoffs among safety, effectiveness, and cost. From the standpoint of suppliers of drug assessment data—i.e., academic researchers and pharmaceutical manufacturers—it is noteworthy that some payers look at cost effectiveness in a pure fashion, reminiscent of a journal article or International Society for Pharmacoeconomics and Outcomes Research (ISPOR) monograph. In contrast, some payers rank drugs by safety and effectiveness; only then do they trade off cost against increments of the drug’s safety and effectiveness ranking.

The role of safety in the balancing process is highly variable. During some periods, safety is taken for granted, so its role in the assessment process is not prominent. In other periods, public concerns
about safety are high, so payers move a new drug’s safety to the front of their assessment process. In these periods of high visibility, the usual stimuli to heightened concerns are, as expected, new reports of safety concerns and action by the Food and Drug Administration (e.g., removing a drug from distribution due to safety concerns). As one insurer put it,

But there’s a threshold: When safety becomes important, it becomes “too important”—because of safety’s affective component and because of risk perceptions.

Comments of individual decisionmakers

- One decisionmaker at a commercial insurer noted that “There is no formal method to evaluate safety and effectiveness rigorously.” Instead, assessments that balance safety and effectiveness are judgmental. While this situation may not have obvious operational implications for drug manufacturers, it does help explain why various payers may arrive at different assessments of the same drug or seemingly comparable drugs.

- The pharmacy director at another private insurer noted that, in assessing value, it was important to evaluate effectiveness in terms of the long-term outcome. Similarly, the pharmacy director distinguished near-term costs (drug costs) from longer-term costs (fewer hospitalizations and lower medical costs), which accrue when the drug affects the patient’s longer-term outcomes. The point is obvious: long-run cost offsets are predicated on long-run outcomes gains. In practice, it may be ignored (e.g., one may be asserted without evidence of the other).

- Commenting on balancing the elements of value, a decisionmaker at an employer remarked that “When a generic is available, its lower price is a stronger driver [of the value assessment] than most gains in effectiveness.”

1.1b. Do you consider any factor other than safety, effectiveness, and cost part of value?

Most payers did not cite other factors. One insurer mentioned, as an additional element of value, “ease of use.” An employer cited the patient’s view or perception of on-the-job productivity.

1.1c. Suppose a newly-launched molecule enters a crowded class. Other than price, what information is necessary for that drug to be placed on the second tier?

On this core, even pivotal, question for formulary decisionmakers, their responses were very different.

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1 The statement is significant because this decisionmaker has a strong background in pharmacoeconomics.
Two payers (an insurer and a PBM) said that they considered information needed to make a more or less conventional cost-effectiveness assessment. (They implied that the price of drug A versus the price of drug B was not the central consideration for tiering.)

- A Blue plan indicated that while it looked at cost-effectiveness information, cost effectiveness can be trumped by safety concerns, by cost concerns, and by rebates.
- Another commercial insurer stressed that cost effectiveness can get trumped by rebates.
- For two public payers, the question was moot, because the statutes establishing their programs forbid or militate against significant cost sharing and tiering.

1.2 Do you assess specialty pharmaceuticals differently than traditional drugs (under the pharmacy benefit)? If so, how?

Again, payers interviewed had diverse responses:

Same assessment

Three payers (a public payer, a PBM, and a large insurer) said that the process for assessing specialty and traditional drugs is the same. For example, the large insurer stressed that it used “the same grading criteria for studies and the same modeling of total cost of care.” The public payer observed that “We could do a prior auth [authorization] for specialty drugs, just as we would for regular drugs.” Focusing on the consequences of its process, the PBM noted that the same process can yield different rates of adoption: “Because specialty drugs have fewer me-too or comparable drugs, specialty drugs tend to get placed on the formulary.”

Greater scrutiny of specialty drugs

The high cost of a drug is a magnet for greater scrutiny. Among our interviewees, two payers (an employer and a regional insurer) said they are subjecting specialty drugs to more scrutiny than traditional drugs due the specialty drugs’ high cost. The insurer acknowledged the need to weigh some increment of greater effectiveness against a very large increment in cost but did not say how that trade-off was made.

The stimulus to greater scrutiny was cost. As one large, sophisticated insurer put it, “As the number and cost of these specialty meds increased, [our company] experienced shock in dealing with these very high-cost drugs. That spurred [the company] to put many specialty drugs on the third tier (high

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2 Recall that any decisionmaker's statement cannot be traced back by the reader to any specific payer. (This is true whether the statement is in this appendix or in the body of the report.) A Phase II payer-type may include only one payer interviewed in Phase II. In that case, we automatically expand the evidence base to include other payers of the same type that were part of the Phase I exploratory interviews. As a result, every payer-type cited here refers to at least several payers, not just one.

3 This decisionmaker mentioned several significant caveats: Safety trumps cost effectiveness. Lower cost trumps greater clinical effectiveness for a minority of cases. (The rationale for the latter case was not made explicit.)

4 This insurer uses a panel of physicians to deal with difficult cases involving specialty drugs. This panel obviously is called upon after the insurer’s formulary committee has made its adoption decision; consequently, the panel deals with the cases of individual patients, not with drug adoption policy.
As a result of the increase in scrutiny, some specialty drugs are placed on the fourth tier. For example, “[Our company] found that, for two rheumatoid arthritis drugs, one costing $40,000 and the other $16,000, the differential in copay was small. As a result, [we] put these drugs on a fourth tier with a higher copay.”

However, we lacked the time to probe further. For example, it is not clear what receives “greater scrutiny.”

- Do the decisionmakers examine the evidence of a new drug’s clinical effectiveness more critically, perhaps by reviewing more non-U.S. studies and more real-world studies than usual?

- Do decisionmakers require that specialty drugs offer a larger increment of clinical effectiveness, compared to existing drugs?

- Do decisionmakers require greater certainty (less uncertainty) about improved clinical effectiveness, compared to the level of (un)certainty they consider acceptable for less expensive drugs?

- Are standards for cost-effectiveness set higher than they are for conventional (nonspecialty) drugs?

For each one of these questions, at least some payers would likely agree with the question. However, the specific actions that translate into greater scrutiny may be less important than the simple fact that specialty drugs tend to be scrutinized more than other, less costly drugs.

**Payer A:** One large insurer had a similar, though more elaborate, response: The insurer has shifted from less scrutiny to more scrutiny of specialty drugs than previously. In addition, the insurer is conducting more relative (clinical) effectiveness analysis. Finally, the insurer is using high-copay third and fourth tiers, as well as renewing or increasing its use of prior authorization and step therapy. The key decisionmaker at this insurer noted that “[Our company’s] approach is not yet mature.”5 Moreover, initially, it was hard for [our company] to deal with these specialty drugs because there were very few in the market. [Our company] had moved away from prior authorization and step therapy likely in response to the managed care backlash. As a result, it was hard to get physicians and patients to use regular drugs before trying a very costly biological.

Now, (1) [we] reintroduced prior authorizations and step therapy. (2) [We also] started looking at relative effectiveness and the value of specialty drugs.

**Payer B:** One public payer had a distinctive approach for specialty drugs: In assessing these drugs’ safety, effectiveness, and cost, the payer reorders the three elements, with safety last. The rationale is that the risk of premature mortality is sufficiently great for oncology patients to warrant trading off...
greater safety for greater effectiveness. In effect, greater effectiveness against the disease—fewer deaths due to a cancer—justifies some collateral damage, in which some patients succumb to the toxicity of the treatment.

**Less scrutiny of specialty drugs**

One commercial plan was an outlier. This plan treats more leniently and gives less scrutiny to specialty and oncology drugs regarding adoption and tiering. This insurer attributed its leniency to physicians’ pressure:

> With an oncology drug, there’s a fear factor (patients fear a quick and painful death). Doctors manipulate this. So we are pushed toward “let the docs buy and bill.”

This insurer said that it “cannot move epo [Erythropoietin] to Drugs from Medical due to pushback from physicians.” This example illustrates, according to the insurer, “[the tension] between the insurer’s self-interest as a business and the initial mission of the Blues—pay the provider.” In contrast, this insurer believes a for-profit insurer would not buckle to physicians’ pressure.

1.2a. Are drugs on the medical side assessed differently re: value than traditional drugs on the pharmacy benefit side?

**Conventional wisdom**

Of the nine payers interviewed in Phase II, three provided support to the conventional wisdom: they said that their organization’s review is more rigorous or strict on the pharmacy side.

**Identical review processes**

One national insurer said that its review processes on the medical side and the pharmacy side are identical.

**Other**

A public payer indicated that its review on the medical side differs from its pharmacy side review but did not characterize how the reviews differed. (The remainder (four) did not answer or respond on point.)

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6 Note that a change in formulation (from infusion to oral) can change copays from zero to the usual level that plan enrollees pay out-of-pocket.
1.2b. Are drugs on the medical side assessed differently re: value than traditional drugs on the pharmacy benefit side?

Drug regulation and review— stricter

As expected, payers reported that, compared to their review of medical services, procedures, and devices, their organizations’ review of drugs is more thorough, more strict, or both. According to the payers who provided answers (about half of those interviewed), regulatory pressures push insurers and other payers to adopt medical procedures and devices. In contrast, regulatory pressures on insurers to compel adoption of drugs are lighter. (This view is at odds with the tenor, if not the logic, of much academic and think tank criticism of the regulatory pressures on drugs and their manufacturers.)

The remaining payers did not respond or did not respond on point.

1.3a. How is your assessment of a new drug’s value affected by the specific disease state?

Disease state affects value assessment

Six payers said that disease state does affect value assessment, at least under some circumstances. Examples follow:

Public payers and employers reported the following:

- One decisionmaker cited three examples of disease states that affect his/her organization’s value assessment: HIV/AIDS, heart disease, and oncology. The decisionmaker added detail on each disease category:
  - HIV/AIDS: Lack of alternatives, resistance issues, etc. led this public payer to adopt every drug there is in the category.
  - Oncology: In the past, this organization followed the “adopt every new drug” approach to oncology drugs. Now, it is distinguishing between new and old drugs.
  - If the therapeutic class is crowded, the effectiveness and safety evaluations are affected. The tier structure is not affected by a crowded therapeutic class. (This latter statement is counterintuitive.)

- A disease-modifying drug that did not affect survival (say, for multiple sclerosis (MS) or rheumatoid arthritis (RA)) might be a better value than an oncology drug that increased survival a bit. (This is an example of a payer stating that a material improvement in quality of life can trump an increase in survival time without an improvement in quality of life.)

7 The technical health economics literature makes a similar point: “In older populations, current methods overstate the cost-effectiveness of interventions which extend life compared to interventions which improve the quality of life.” Abstract for David
same decisionmaker noted that the situation regarding drugs in certain disease states has changed recently. Five years ago, drugs for a category of disease considered “bad” received less strict scrutiny. Today (as noted elsewhere in this report), the high cost of drugs for some of these once-favored disease categories are undergoing greater scrutiny.

Commercial insurers (large and not-so-large) reported the following:

- **Insurer A**: Key disease states that affect this commercial organization’s value assessment include heart disease and oncology.

- **Insurer B**: The lead decisionmaker for this insurer cited three disease categories that his/her organization treated differently in the drug assessment process:

  - *Behavioral health* category: Drugs for these conditions are reviewed more carefully because the insurer’s formulary committee does not want to destabilize patients.

  - *HIV Category*: Its formulary covers all drugs in the HIV category.

  - Oncology Category: Of all drugs in the oncology category, only oral oncology drugs are reviewed by the insurer’s P&T committee.

  - Oncology is still distinctive and receives special treatment.

   Asked, “Do oncology drugs get more preference?” the decisionmaker at this insurer replied, “While the marginal gain of life-years or months is low, the emotional impact of the situation trumps cost-effectiveness analysis. We decided to cover these drugs but put them in a higher tier. Now, though, our organization accepts that demand is not responsive to the copay.”

  - This same insurer made a more general point that is important:

    When assessing a drug’s value, this insurer does not look across disease states. Instead, the insurer looks at drugs for a given disease state. For example, the formulary committee does not look at Quality Adjusted Life Years (QALYs) across disease states for different drugs. It compares QALYs only for drugs that treat a given disease state. As a result, disease state necessarily affects valuation.

    A second reason that assessment varies by disease state: “It’s difficult to explain to physicians and patients that you put a particular drug on a given tier because of cost/utility analysis. You hope they won’t say, ‘What’s that?’”

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Insurer C: Oncology is the only disease state that gets treated differently.

- In general, Medicare directs insurers to look at 20 different references. In contrast, Medicare allows much more leniency for oncology drugs.
- This decisionmaker cited rheumatoid arthritis drugs, which generally require prior authorization before the prescription can be filled, as a pertinent point of comparison with drugs in the oncology category.

In contrast, one private insurer said that disease state did not affect assessment.

1.3b. How is your assessment of a new drug’s value affected by the specific patient population?

No effect

Three private payers said that consideration of one specific patient population versus another did not affect their assessments of new drugs. Nonetheless, decisionmakers noted that this conclusion held for covered lives in their commercial plans’ only. In contrast, they did take into account the nature of the patient population (largely, the elderly) when assessing new drugs for their Medicare covered lives. (One insurer was explicit that a separate division of its organization is responsible for coverage of its plan enrollees who are Medicare beneficiaries.8)

1.3c. How is your assessment of a new drug’s value affected by alternative therapies?

Conventional wisdom confirmed

Two private payers said that, when a new drug is being assessed and another drug is in the therapeutic class, the new drug (as expected) faces a higher hurdle. For reasons of time, the remaining payers did not respond to this question.

1.3d. How is your assessment of a new drug’s value affected by politics, patient advocacy, and community physicians?

Patient advocates can affect decisions

Of all the payers interviewed, only one indicated unambiguously that patient advocates can affect formulary decisions. Specifically, this payer said that politics could affect a large employer’s decision. For example, if an employer has thousands of workers in Africa, a decision not to cover antiretroviral drugs to treat HIV would “look bad to the workers, African governments,…” [and others in the international community.]

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8 Apparently, this insurer limits the purview of the unit responsible for pharmacoeconomic evaluation to the insurer’s commercial side; this unit apparently has little interaction with the Medicare division. This example underlines the fact that the use of pharmacoeconomic information and analysis is uneven, not only between payers but sometimes within a given payer.
No effect of patient advocates

Payers, private and public, generally made the point: Patient advocacy groups do not affect decisions made by the payer organization; although, as one public payer put it, “There’s a lot of it (patient pressure).” One insurer that operates in the Medicare market said simply, “Evidence trumps pressure.” This insurer’s key decisionmaker added, “[Our organization] does not change its decision unless they [patient advocates] cite literature to back their claims.” The pharmacy benefits director at a large insurer said, “Patient advocates have no effect usually. They present very slanted views not based on evidence.” One formulary decisionmaker demurred from answering, saying “Those phone calls [from patient advocates and irate patients] go to higher levels in our company than mine.”

Other

Several payers did not make a clear statement one way or the other about patient advocates’ effect. Instead, these payers tended simply to describe their processes for obtaining public input.

Little effect of physician/prescribers on formulary

Generally, payers said that physicians’ telephone calls and other communications with the payer do not alter formulary decisions, unless the physician presents credible evidence to the payer. As one insurer put it, “They are influential only if they get all their documentation in order.” The pharmacy benefits manager of a large insurer said that “With community docs, it’s the money motive, not the evidence.” In addition, he noted that “the … drug company representatives push the doctors [to pressure the insurer or payer].”

At one large insurer, the lead decisionmaker presented a detailed picture of his company’s decision process and highlighted where advocacy by patients and by physicians enters that process:

One group focuses on clinical evidence regarding a new drug and its therapeutic equivalents. (This group compares clinical effectiveness, acquisition cost, and deferred cost (i.e., future med cost offset).) Another group in the chain looks at the contracting aspects. [Finally,] there’s a PBL management committee: The policy side [of our company] is sensitive to patient advocates and specialty societies. The PBL committee also has business types and clinicians as members. If the evidence is strong and supports a particular decision, [our company] has to explain it well—that it’s based on evidence and relative value.

[This decisionmaker added that there has been] a big change in the past 3 or 4 years: [our company] communicates with external groups better. [We go] to [a particular] specialty society [whose patients would take our drug or its competitors]—in advance of the formulary decision—to begin a dialogue.
SECTION TWO
Assessment of Value

2.1 **What is the process** by which that drug’s value gets assessed within your organization? Specifically, how much do you rely on information **from outside your organization** versus information **internal to your organization**? Similarly, do you do the analysis and assessment of the new drug largely within your organization or do you rely mostly on assessments conducted outside your organization?

In assessing new drugs, payers differ in the extent to which the information they rely on they produce themselves or they acquire from outside sources and suppliers of drug assessments.

- **Internal staff.** About half of the payers we interviewed relied exclusively on assessments researched and prepared internally. (This proportion very likely overstates the situation among U.S. payers generally, because we tended to select for our study organizations that are larger and have more resources, pharmacoconomic or otherwise.) As expected, PBMs of course rely exclusively on their own staffs for literature search and review, for secondary analysis of information in journal articles, and for primary analysis of the PBMs’ own databases. In addition, however, other payers have developed a critical mass of internal staff capability for reviewing and analyzing pharmacoeconomic information. These more technically-equipped and sophisticated payers include a public payer, a national insurer, a large managed care insurer, and a smaller insurer/MA plan. Details of the assessment process used by the public payer – the Department of Veterans Affairs (VA) – are part of the public record.9 [Among these payers, the common denominator is large scale. However, that statement is limited in two ways: First, many large health insurers and public payers do not rely exclusively, and perhaps even predominantly, on their internal pharmacoeconomic resources. Large scale is not a sufficient condition for exclusive reliance on internal resources. Second, occasionally, smaller insurers rely on their internal resources, despite their organization not being large scale.

- **External sources.** Two employer(s) [from Phase I as well as Phase II interviews] told us they rely exclusively (“100 percent”) on their insurer for assessment of new drugs and for pharmacoeconomic information in particular. The employers we interviewed tended to have a

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small staff, effectively one senior person, responsible for liaison with the insurer and for monitoring formulary decisions. One employer noted that it reserves the right to alter a formulary, as it did regarding whether to include Viagra as a covered drug.

- **Mixed** We encountered instances of payers not at either end of the spectrum. For example:

  - **Support to payer.** One smaller insurer we interviewed uses its PBM to support the insurer’s staff, its pharmacy and therapeutics committee, and a separate committee “that does cost modeling.”

  - **Outsourcing literature search and analysis.** One Medicaid agency has an elaborate assessment process, but it outsources key inputs to the assessment that involve pharmacoeconomic information. In addition to soliciting the views of its stakeholders, this agency routinely meets with industry representatives, who provide it with information on the new drugs soon to be reviewed. To conduct literature searches and pharmacoeconomic analyses, this Medicaid agency uses both its own staff and its contractor (a PBM?). The agency provides the results of these searches and analyses to its independent pharmacy and therapeutics committee (composed of community physicians and pharmacists).

But this particular ‘mixed’ model differs considerably from the insurer’s mixed model both in the specifics of procedure and in the role of the payer’s own staff. One plausible reason for the difference is that the Medicaid agency’s process is structured by statute and influenced by the norms of administrative due process, of open access of stakeholders to public bodies, and of transparency. Accordingly, the agency promotes input from the public, physicians, and industry, and permits the selection of well-trained pharmacists and physicians for the pharmacy and therapeutics committee. The agency’s internal staff does not appear to attempt to provide the P&T committee with a preliminary, technical evaluation of the information the staff provide to the committee members. We could not gauge the extent to which the staff’s role as information-gatherer and transmitter reflects their interpretation of statute, a less-assertive stance of the agency’s senior managers, the staff’s comparative advantage in the assessment process, or direction provided by the P&T committee.

- **Outsourcing complementary research.** Another sizable regional insurer directs its consultant to prepare a monograph, which the P&T committee reviews. The insurer prepares its own literature search and usually does not get other information from outside sources. Nonetheless, P&T committee members bring in outside information.

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10 The Medicaid pharmacy benefit officials we interviewed did not spell out whether they and their staff simply transmit the information they receive from industry representatives about a new drug to the state Medicaid P&T committee, or whether the Medicaid staff presents to that committee the industry’s information accompanied by the staff’s technical evaluation of that information.
2.3 Have you conducted alternative analyses using *a drug company's pharmacoeconomic model* that permitted you to modify the model’s assumptions?

a. How often did that occur in the past year?

### Alternative Analyses with Drug Company PE Models

Of payers that we interviewed, a minority (about one-third) cite cases in which drug companies’ models affected payer decisions. These payers use models if they can modify them to some extent or otherwise correct for perceived biases. In contrast, the other payers we interviewed either indicated that they did not use drug company models or cited their own internal PE analyses.

**Details**

Only two payers, a smaller Blue plan and a large MCO, stated that their use of a drug company’s PE model had affected formulary decisions frequently. The two payers differed considerably in the scale and PE training of their staff devoted to drug assessment.

The Blue plan had a distinctive strategy for using drug company models. As the plan’s pharmacy director commented, “It depends on the model. [I] do not use a drug company’s model to analyze that company’s own product. [Instead,] I will use drug company A’s model to investigate B’s product, and vice versa.” (In effect, the pharmacy director treated B’s estimate of the effectiveness of A’s product as a lower bound on A’s effectiveness and treated A’s estimate of the effectiveness of B’s product as a lower bound on B’s effectiveness.)

The MCO’s pharmacy evaluation staff are sophisticated users of PE models, and they drew on their PE skills when using drug company models. A senior MCO executive with pharmacy responsibilities explained the MCO’s approach this way:

Drug company models are *very* biased though still worth looking at briefly. So [we] let the drug companies come in and show their [PE] models. After the drug company presents its model, there’s a back-and-forth about what we want changed. Usually that doesn’t happen. So we take the models as is, since they’re so biased that inputting our own data wouldn’t be a good use of company time! [But] then we do a back-of-envelope calculation of relative effect size.

Typically, the MCO’s staff undertake due diligence to assess the extent of bias in the drug company model due to its incorporating (according to the MCO staff) only those research results favorable to the drug company's new product. As a result, we conclude that, for this payer, the drug company model is a useful, relatively low-cost vehicle, which helps it organize information about a new drug. However, it is highly unlikely that this MCO’s decision about the new drug is altered materially by the model as presented by the drug company.
Among the other payers we interviewed, none cited any instances in which a drug company model affected the payers’ formulary decisions. Note that at least some of these payers had seen drug company models from time to time. Whatever effect these models had on the views of the payers’ formulary staff and decisionmakers, it was not one that the decisionmakers either recognized or were willing to acknowledge.

2.4 Have you constructed your own cost-effectiveness analysis or pharmacoeconomic model that incorporated data on clinical effectiveness and drug costs, plus assumptions or data on medical cost offsets? How often did that occur in the past year?

More than two-fifths of the payers interviewed construct their own cost-effectiveness analysis or PE model – that is, a formal analysis that incorporates data on clinical effectiveness and acquisition costs of a new drug and its competitors and that introduces data on or assumptions about medical cost offsets. Three of nine payers interviewed conduct their own PE models or formal cost-effectiveness analyses. Of these payers, two (a Blue plan and an MCO) conduct their own analyses frequently (e.g., for a dozen drugs per year). Another payer (an insurer in the Medicare market) does its own cost-effectiveness analyses occasionally (e.g., whether ACE inhibitors are cost-effective for 85-year-olds). A fourth payer (a public payer) neither constructs its own PE model nor carries its own formal cost-effectiveness analysis. Nonetheless, this payer frequently carries out back-of-the-envelope or simple spreadsheet analyses of a new drug’s cost-effectiveness.

Some additional payers (among our interviewees, a Blue plan and an employer) rely on their PBMs for drug assessments, so it is possible that the agents of these payers – the PBMs – use PE models and cost-effectiveness analysis on behalf of the payers. Recall, however, that one PBM interviewed stated that it never used PE models, “because our P&T committee doesn’t assess costs.” (The latter comment is somewhat remarkable on its face. A possible explanation is the following: We were not able to establish if this PBM has a bifurcated drug assessment process. However, if it does, then the P&T committee would be the PBM’s evaluation arm for clinical-effectiveness, and a separate committee would assess the cost aspects of new drugs and presumably would combine the P&T committee recommendations and clinical information to make a cost-effectiveness assessment. If so, then this PBM, which disavows using PE models in its P&T committee, may use them in a second, separate stage of its assessment process.)

It is notable that payers that do not use or rarely use PE models include large organizations, e.g., a national insurer and a public payer.

Two payers (a smaller Blue and an MCO): do their own CE analyses or PE model fairly frequently (e.g., a dozen times per year) One payer (an MA plan) does its own CE analysis occasionally, although it wasn’t clear if the insurer looked at a specialized issue (whether ACE inhibitors are cost-effective for 85 yr. olds) using a drug company model or did its own analysis from scratch. Two payers (public payer and national insurer) rarely use PE models. Three payers never use PE models: a PBM, b/c its P&T committee doesn’t assess costs (!) [P&T committee may not assess costs, but PBM was silent on whether other units within the company assess costs]; a Blue and an employer, both of which leave PE models to their PBMs.
2.5 When you assess value, when would you consider health-related quality-of-life issues? Are you more likely to consider quality of life under particular circumstances?

Health-Related QoL Often Dismissed

In their assessments of new drugs, most (but not all) payers interviewed state that they do not consider health-related quality of life (QoL) frequently if at all. For example,

- A Blue plan declared, “We give no consideration to quality of life. No one pays me for QoL. Quality of life is not a benefit!” “That is, according to this plan’s pharmacy director, its insurance contract with the patient does not commit the plan to providing services that improve a patient-member’s quality of life.11 As the pharmacy director elaborated, “It’s not a cure for a disease so it’s not a benefit.” This pharmacy director kept Retin A off the plan’s formulary for a long time because it is not curative.

- A PBM attributed its lack of interest in QoL to its customers: “[They] see QoL as ‘soft,’” so the PBM has no incentive to consider QoL when assessing new drugs.”

Other payers downplayed health-related quality of life: For example, a national insurer discounts “on-the-job productivity” and QoL claims made by drug companies but budgets for internal research on QoL – research that the insurer considered credible. An MA plan generally discounts QoL information (“Our plan doesn’t have much confidence in these QoL tools”) but would consider QoL if all else were equal between two drugs. A PBM stated that, “[If] QoL refers to the number of times per day a patient takes a pill or to productivity in the workplace,” then its clients [employers] still consider these to be ‘soft savings.’ An employer echoed the PBM’s comments: “[Our] staff lack familiarity with and intuition about QoL scales. Is a two-point change big or small? QoL scales are not intuitive or readily interpreted.”

At another Blue plan, two officials disagreed sharply about the facts concerning whether they dismiss or consider QoL: One pharmacy benefit official (a non-MD) was firm in his/her view: “Never! It’s too subjective. You can’t correlate QoL with anything objective.” The second official (a physician) said, “Yes, we consider it all the time!”12 (This disagreement elicits a note of caution: It sometimes can be misleading to ascribe a single behavior or view to a payer as a corporate body. That payer’s decisionmaking process involves individuals who do not necessarily share the same view or even the same perception of how their organization’s decisionmaking process operates.)

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11We asked, “What about pain?” The pharmacy director replied, “No. Otherwise there’s no limit.” Then, after a pause, “Well, if a drug helps with normal functioning, then maybe it’s OK.”

12This physician noted that s/he does not count drug X’s “one dose per day” vs. drug Y’s “two doses per day” as an important difference in health-related QoL.
As many as a third of payers interviewed were much more open to considering QoL:

- Two public payers considered QoL frequently – one cited hypertension drugs, while the other cited oncology drugs and ED drugs (for which QoL was the only factor).

- A third payer (an MCO) identified features of the evidence and its presentation that raise QoL’s appeal: “QoL can be useful if evidence about it is intuitive – if the evidence has meaningful detail. For example, it’s not meaningful to say “5 of 7 indicators of QoL were statistically significant and in the right direction. That’s NOT useful b/c it’s not intuitive. “

- Furthermore, even payers that are very skeptical of drug company-supplied QoL information sometimes are open to considering such information. For example, the skeptical national insurer referred to above “…requires QoL data, if available, [to be included] in a drug company’s dossier.” In addition, this insurer reported that, “In the past year, QoL mattered in one of our formulary decisions.” ¹³

In sum, our interviews point to two sources of payers’ resistance to QoL information:

1. Skepticism about drug companies. Payers’ perception of self-interested bias in the information drug companies supply to payers extends to QoL information.

2. Lack of intuitive evidence presented on health-related QoL. For example, some payers find scales that quantify improvements in quality of life not to be meaningful or intuitive.

In principle, a drug company can address the second issue by making meaningful its evidence about a new drug’s QoL properties. The data presented need to be intuitive measures with commonsense interpretations. For example, “43 percent of patients receiving treatment A were able to leave the house and do ordinary activities such as grocery shopping, compared to 27 percent of patients receiving treatment B who were able to do the same activities.”

2.6 If you did not consider health-related quality of life, are there specific patient-reported outcomes (PROs) that you find valuable?

As with the QoL measures, payers’ comments on the use of patient-reported outcomes (PRO) were diverse but generally more favorable than to QoL. While one payer stated that PROs had no effect on its formulary decisions, four payers considered PROs under at least one of these conditions:

- when reduction in pain boosted normal functioning (a Blue plan and an MCO listed this);
- for certain mental illnesses (a PBM emphasized this condition);

¹³The insurer added, “But it’s probably only been a year or two that these data have been available!”
when developing criteria for use of a new drug (a smaller insurer stressed this);
when the information supporting the PRO claim complemented traditional data on new drugs
(a smaller insurer).
Two additional payers stated that PROs occasionally enter the assessment but were vague about the
circumstances.

Reasons for being open to PROs varied.

- An intuitive measure. Several payers commented that PROs are easier to grasp than QoLs. An
  employer observed, “QoL is fuzzy. PROs are more concrete. A PRO that ‘the patient got out
  more and got to work more easily’ is intuitive.”
- Importance of clinical differences. A Blue plan was open to considering PROs because “significant
  clinical differences matter.” As an example of this, the insurer pointed to epo: “[The patients] feel
  better with an epo shot.” However, a moment later, in a humorous comment tinged with
  skepticism, this insurer observed: “Of course, a B12 shot and a shot of Red Bull all have the same
  effect.”
- Independent supporting evidence. A smaller insurer stated, “If evidence that is patient reported were
  in addition to traditional, physician-based evidence, we would consider the PRO. For example: A
  patient got no relief from NSAID 1 or NSAID 2 but did get relief from NSAID 3.” The insurer
  added an important proviso, “Without evidence from a physician, though, we wouldn’t consider a
  PRO on its own.”
- Patients know their pain level. An MCO stated, “The individual patient would know best about his
  or her own pain level.”

With regard to payers’ reluctance to use PROs more in their assessments, a Blue plan
identified an additional cause that is interesting and plausible: The rarity of head-to-head
comparisons of drugs in regard to PROs. The chief medical officer of this insurer elaborated on this:
Consider a one-point change in the SF-36 score associated with Drug A, compared to Drug
B. [We] never have seen that comparison made. Instead, the drug company reports the result
for its own drug, and it doesn’t say much more.
A second factor behind reluctance to use PROs reprises similar payers’ concerns about health-
related QoL measures: As an MCO put it, “The question is, what does pain going from 8 to 7 or
from 8 to 6 mean in terms of activity?”
SECTION THREE
What Concretely Do Payers Consider to Be “Effectiveness”?
Endpoints, Real-world Studies, Adherence/Compliance

3.1 How significant are primary endpoints versus secondary endpoints?

Endpoints

How significant are primary endpoints versus secondary endpoints? The short answer is
obvious: Much more significant. All but one payer said, as one would expect, that they much
preferred primary endpoints to secondary endpoints. Two insurers observed that primary
endpoints are essential to making effectiveness comparisons among drugs. One of these insurers
added that it appreciated it when the FDA selected the primary endpoint, since that facilitated
rigorous comparisons across drugs.

The primary-endpoint rule did not garner universal support. One employer argued that it was more
important, not to be primary per se, but to be pre-specified. Another payer noted that the question
is often moot because “Most of the time, the FDA dictates the endpoint.”

The secondary endpoint received unenthusiastic reviews, which ranged from icy to lukewarm: One
large national insurer dismissed it, asking, “Why look at the secondary endpoint if the RCT was not
designed for it?” Another large insurer [Caremark] indicated that it would look at the secondary
endpoint. However, this insurer was not clear about whether it would do so if the drug failed its
primary endpoint. A third insurer stated that it would look at the secondary endpoint evidence more
skeptically than if the evidence pertained to the primary endpoint.

3.2 What weight do you give “real world” studies when the clinical trials of the drug you’re
assessing either are not head-to-head trials or are non-inferiority studies?

- When do you find “real world” studies to be particularly helpful? When — of little help?

Real-world studies

Important. Many payers (six of nine in our Phase II interviews) said real-world (RW) studies
are important or very important. As one large insurer said, “When aren’t they helpful?” Some payers
stressed that RW studies cast light on both successes and problems with new drugs. As one insurer
observed, “[RW studies are] important: It has to be real.” Going beyond other payers in our study,

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14 A senior official at one public payer was not familiar with the terms “primary endpoint” and “secondary endpoint.” While the training of officials
and staff at this public payer was uneven, its pharmacy and therapeutics committee evidently contains private-sector individuals with strong training.
For example, the P&T committee included a community pharmacist at a sizable teaching hospital. This pharmacist appears to be proficient in
assessing prescription drugs in relation to clinical considerations.
one public payer stated that “The real world study would weigh more heavily than a clinical trial.” (Emphasis added.)

**Insights from RW studies.** Several payers and one employer looked to RW studies for insight into adherence/compliance issues. As the employer observed, “There’s no one in the real-world, community setting to make sure that the patient takes the drug on time.” A smaller insurer agreed: “[RW studies are] “very worthwhile. With them, you can compare clinical trials’ adherence with your own adherence data.” The employer made a related but distinctive point: “If the real-world study is done as part of a Phase III trial, then it has more value.”

{The employer cited very favorably a study circa 2002, the Diabetes Prevention Program (DPP).[Daniel: However, my understanding is that the DPP was a clinical trial, not a “real world” study. So this interviewee’s comment would be off-point, if I’m right.]} Beyond adherence/compliance issues, a wider range of insights was identified by one PBM, which finds that “real-world studies give increased credibility to [a claim of] real-world effectiveness or problems.” In this regard, the PBM cited the examples of Regalin and Vioxx. This PBM added, “When we seem more than one study saying the same thing, we go back to the P&T committee and show them the problems. We have taken a drug off the formulary before the FDA put a black box warning on it or pulled the drug.”

In contrast, this same PBM provided our one case in which the “unfolding of real world information” led the PBM to move a drug to a better position on the PBM’s formulary. Initially, the PBM was “very hesitant [about Crestor] because of initial safety concerns. However, as that situation has been clarified, [the PBM has] given Crestor more of a role [on the PBM formulary].”

**Internal RW studies.** Just as payers differ in their assessment of externally-produced RW studies, they differ in the extent to which they study their own data for clues on utilization and outcomes regarding particular drugs. At one extreme, the public payer that stressed the value of RW studies did not provide examples of it examining its own claims data to augment a drug assessment. At the other, another payer (also public) “does a lot of data mining on [its own] data.”

**Conditionally important.** In the view of one sophisticated insurer, RW studies are important if they meet certain conditions. This insurer noted that the definition of “real world” is not obvious and not simple to specify and operationalize. As a result, s/he posed him-/herself the question, “How much bias can I eliminate in the clinical trial data from not capturing ‘real world’ compliance and adherence patterns?” To answer the question, s/he starts with the randomized clinical trial (RCT) and compares its population to an available RW registry study. If the RW study’s population is different than the RCT’s population (i.e., the two populations do not overlap), then the registry study results can be compared to the RCT study’s results. “If the registry study has a broader population, then (we) ask, ‘What information is added by including those additional segments of the population?”

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15 DPP is a major, 3-year clinical trial that examined the extent to which (a) diet and exercise or (b) the oral diabetes drug metformin (Glucophage) could delay or prevent the onset of type-2 diabetes in people with impaired glucose tolerance (IGT). The DPP found that diet and exercise markedly lowered the chances that a person with IGT would develop diabetes. Metformin also reduced risk but by less. (This summary paraphrases a description of the DPP on the NIDDK Clearinghouses Reference Collection web site, [http://www.catalog.niddk.nih.gov/resources/results.cfm?searchterms=diabetes+prevention+program&databases=1](http://www.catalog.niddk.nih.gov/resources/results.cfm?searchterms=diabetes+prevention+program&databases=1), accessed June 29, 2008.)
Not important. Not all payers like RW studies, though. The pharmacy director at one Blue plan said s/he had “never seen a RW clinical study that (convincingly) showed an improvement in cost-benefit or cost-effectiveness, compared to the existing drug(s).” As a result, s/he maintained, “When a grievance or an appeal comes up, I can’t use that real-world study.” One national insurer focused on the source of most RW studies: S/he “doesn’t trust the drug companies regarding [RW studies]”; as a result, this insurer effectively only looks at RW studies that it itself prepares or sponsors. Despite different emphases, both of these payers are intensely skeptical of the methodology used in available RW studies.

### 3.3 How do data on adherence/persistence/compliance enter your assessment of value?

When assessing a drug’s value, most payers interviewed (more than three-quarters) consider adherence an important dimension to evaluate. Nonetheless, a minority of payers interviewed spend little time on it. For example, a public payer considers adherence data to be mostly “background information.”

**Caveats to Payers’ Consideration of Adherence**

Even payers that consider adherence typically do so subject to at least one of several caveats or conditions.

- **Same outcomes.** According to one payer, “[The drugs for which better adherence is claimed] must show the same path for most drugs in a given class. So there is a smaller magnitude [of _____?] for some drug than another.”

- **Presumption of lack of adherence.** Skepticism about the durability of any change in adherence predisposes many to discount evidence that a particular drug improves adherence and compliance. A national insurer’s skepticism reflects its view that “50 percent of patients drop off their meds within six months!” A public payer’s senior pharmacy manager shares that view and “is skeptical that switching drugs leads to a big change in adherence because people don’t stay with most drugs over the long haul. {I’m} pessimistic that changing from pill A to B leads to a big change in adherence.”

- **Good data.** Absent credible data on adherence, compliance, and persistence, payers tend to ignore adherence claims.

- **Data on side-effects.** To make adherence claims credible, data on side-effects are necessary. For example, evidence of lower toxicity ends credibility to an adherence claim. As one insurer stated, “Adherence claims without data on side-effects are not meaningful.” Moreover, the insurer continued, it is worth establishing “How important is that side-effect in your population?” The national insurer’s pharmacy director concurred: “[We] need to drill into the toxicity or tolerability issue. That would lead to a better or worse adverse event profile. That’s important [to establishing the strength of adherence claims].”

In the same vein, at another insurer, the chief medical officer noted, “The old hypertension drugs caused drowsiness, which reduced compliance. The new, non-drowsy drugs increased
compliance.” Here, clinical evidence of fewer side-effects reinforced the new drugs’ claims of greater compliance – in the chief medical officer’s eyes. However, the same insurer’s formulary manager was unmoved: Asked how much weight adherence received in the assessment process, s/he replied, “Not a whole lot.”

- **Condition-dependent.** Adherence is judged more important or less depending on the condition:
  - One insurer contrasted “an allergy vs. [high] cholesterol.” (Presumably, according to this payer, improved adherence is more important clinically in a statin than in an antihistamine.)
  - Some payers emphasize adherence for patients with severe mental illnesses. As one insurer explained, “[We] focus on side-effects of psychotropic drugs because these patients can’t handle themselves without the drug.”  
  - {That is, patients with mental illness can’t function without the drug. Consequently, it’s important to identify side-effects of drugs, so that the drug with the least side effects can be selected. In turn, the mentally ill patients will display greater adherence and hence better functioning.}

While one MCO incorporates adherence, etc. into its value assessment, a senior official of the MCO emphasized that “…it’s a very difficult process. Looking at adherence, etc. is another way to evaluate RW effectiveness.” This payer takes a systematic, quantitative approach to the assessment dimension of value.\(^\text{17}\)

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16 Note that the insurer moved from discussing adherence to discussing side-effects that affect adherence.

17 To analyze adherence and compliance, the senior official drew an analogy to a dose-response curve. When a difference in RW adherence is suspected for two drugs, for each drug, “we order the patients by their compliance levels” and plot each patient’s effectiveness or outcomes measure.” Doing this produces a compliance-outcomes curve. As the MCO official put it, “We expect the drug with greater compliance to yield better outcomes” – and that comparison of the compliance-outcomes curves for the two drugs demonstrates this.” S/he added, “If enough data on these dimensions (persistence, adherence) are available, the evaluation of a new drug should incorporate them.”
SECTION FOUR
Components of Costs Considered

4.1 When you consider Direct Medical Costs, which components most influence your formulary decisionmaking and tier-placement: Drug costs or Health services and other medical costs?

Note: The payers interviewed sometimes gave answers to a question related to but different than the one asked. Instead of stating whether drug costs or all medical care costs influence their formulary decisions more, several payers reported on whether they consider total medical costs or just the costs of prescription drugs. Nonetheless, we can report the responses of about half the payers interviewed concerning whether non-drug costs are important in their formulary decisionmaking.

Major Cost Influence on Formulary Decisions

Several payers, including a national insurer and a Blue plan, stated that total health care costs are the major cost influence on their decisions concerning formulary adoption and tiering.

Several other payers reported that the major cost influence on their formulary decisions is a subset of drug and medical costs. For example,

• An MA plan identified three elements of cost as key: “(1) drug (acquisition) costs, (2) costs of the side-effect of the drug, and (3) cost of hospitalization (since that’s what we’re trying to prevent).” In effect, this plan excluded ambulatory costs not related to the drug’s side-effects as not being a major cost driver of formulary decisions.

• In contrast, one public payer focuses on true variable costs (drug and medical). Unlike most payers, for which all medical costs are variable and hence potentially avoidable by use of the appropriate drug, this public payer provides a considerable amount of health care directly through its own hospitals and medical staff. As a result, a substantial fraction of its hospital costs and physician costs is fixed, at least in the economist’s short run.

Extent of Cost Siloing

Siloing – in this context, making formulary decisions based on no cost components other than drug costs – is often cited as a widespread phenomenon in U.S. health care and an economic tunnel vision that leads insurers and other health care organizations to leave money on the table. Is it a figment of the imagination? Perhaps: Almost all payers that responded report they consider both drug costs and medical care costs. This tally includes employers we interviewed, who reported that they consider all costs – drug and non-drug. All public payers interviewed stated that they consider at least some non-drug costs. For example, a Medicaid program affirmed that it considers hospitalizations. All other public payers interviewed stated they consider either total health care costs or drug costs plus a subset of non-drug medical costs. (See discussion above of major influences on
One public payer noted that the stability of its patient base predisposes this payer to consider total health care cost: “[We] have our patients for several decades, enough time to make it pretty likely [that hospitalizations and sizable amounts of ambulatory care services will occur, at least absent appropriate medications].”

**Specifics on Considering Total Costs**

Payers elaborated on their approach to assessing drugs in relation to total health care costs. For example, a Blue plan noted that its assessment process deals with such cases as when Drug A reduces hospitalization while drug B is “more effective clinically but information on related hospitalization costs is lacking.” A large employer articulated a sophisticated view of costs: According to the physician responsible for monitoring the company’s PBM, it is important to “address total health care costs, not simply the health care costs linked most directly to the diagnoses [the drugs] are treating.”

**Testimonial Evidence on Siloing’s Prevalence**

Notwithstanding the unanimous response about these payers’ own focus on total costs, several payers reported that siloing persists – elsewhere. A large Blue plan and a smaller one both characterized employers as often if not always focused on drug costs and rebates to the exclusion of medical cost offsets. The smaller Blue plan insisted that its employer-customers are single-minded about rebates and drug costs. The large Blue plan reported its numerous attempts to persuade employer-customers to view costs more comprehensively; furthermore, it candidly suggested that employers’ resistance might be due to the plan’s own inability to present convincing examples of avoided costs of hospitalization and other medical services due to the use of a new drug by an employer’s workers and retirees.

Our interviews left open a key issue: How insurers resolve the tension between their own orientation toward considering all health care costs and the predilection of at least some of their customers for having formulary decisions made based on a silo treatment of drug costs. When it comes to formulary decisions by insurers, who rules?

### 4.2 To what extent do you consider medical cost offsets?

**What information sources regarding these offsets do you use?**

**Medical Cost Offsets**

Most payers interviewed stated that they consider medical cost offsets. Many of the responses reproduce elements of the payers’ answers to the previous question or are implicit in those answers. The responses were uneven in revealing how significant the payers typically found offsets to be in their assessments of a new drug’s cost effectiveness.

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18 Presumably, this view is concerned that a cost analysis is misleading if it focuses exclusively on avoided hospitalizations due to a new drug but that ignores ambulatory care costs to treat dizziness, gastrointestinal symptoms, etc. induced by the drug.
Payer Comments

• Importance of offsets and benchmarks. A smaller insurer, which offers a Part D prescription drug plan (PDP) and another Medicare product, reports that “We always think about offsets.” The insurer’s pharmacy director maintained that

[Employers often focus on rebates] but rebates can never offset medical cost savings foregone by not using a better drug. But you can’t just look at the literature and get benchmarks that are at all useful. [We] work with actuaries to get benchmarks.

• Thin U.S. literature on offsets. A Blue plan that takes medical cost offsets into account had these comments regarding sources of information on medical cost offsets:

We don’t see information in the American literature on medical cost offsets.19 [Instead, we] look to the European and Canadian literature, since some information is better than no information. Still, there’s the issue that the patient population in the literature is not the same as “our” population.

• Number of cost items vs. effect on CE. Most payers did not relate back their discussion of medical cost offsets to the core issue: The incremental cost-effectiveness of the new drug under review. An MCO we interviewed is an exception. While discussing the MCO’s efforts to construct internal PE models, a senior pharmacy manager observed that many cost items are included in these models: “That’s a good thing, despite many having only a small impact on cost effectiveness.” (Emphasis added.)

• Program costs; Checking claims of offsets. Regarding medical cost offsets, a Medicaid agency stated that it considers “anything that reduces Medicaid’s costs.” The agency’s pharmacy officials gave an example: “Drug companies claim that asthma drugs reduce hospitalizations.” To check the claim, “[the agency staff] looked at the utilization data. [However,] it’s not often that that [offset] occurs.”

• Frequency of a drug’s use and offsets’ importance. An employer, which considers medical cost offsets during its new-drug assessments, gave an example of a self-administered drug vs. an IV-administered drug. The employer’s generalization was, “The more frequent the drug’s use, the more important are medical cost offsets.”

• Variable costs and medical cost offsets. As seen above, one public payer limits its consideration of medical cost offsets to its variable costs. For a traditional insurer, which reimburses allowed charges (or, for ambulatory care, 80 percent of allowed charges), all these medical cost reimbursements are variable costs. This easy equation of medical cost offsets and variable costs does not hold for payers that also operate health care facilities and employ staff. These atypical payers include Kaiser-type staff-model HMOs and public payers like DOD and VA that, in whole or in part, are integrated health systems.

• Dismissing medical cost offsets. One Blue plan is an outlier in its dismissal of medical cost offsets. Though atypical, the pharmacy director’s reasoning is clear:

19 We are not aware of a systematic review of the U.S. literature that assesses the extent to which that literature includes estimates of medical cost offsets associated with particular drugs.
If I can see it (the medical cost offset), then OK. But all the data regarding medical cost offsets are based on assumptions. [So] generally, no. I don't take into account medical cost offsets.

When a plan like this one adopts an “I’m from Missouri: Show me” stance, chains of reasoning do not persuade it. In the following statement, this pharmacy director underlines his/her view that the crucial link between results for a study population and results for a particular payer's population is uncertain:

Medical cost offsets are based on the assumption that the hospital will cooperate. If the hospital does not kick out patients on time, then [I] can’t believe (the cost estimate). Unless the drug company representative shows me data from another Blue plan, it’s a very high bar for me to believe the medical cost offset numbers.

The pharmacy director supplied an example that reinforced his/her skepticism: “Prilosec was supposed to be a cost saver in terms of hospitalization. It never happened.”

4.3 When do you consider the following factors relevant to tier placement?

   a. Patient preferences
   b. Effect on (i) ability to work and (ii) patient productivity on the job
   c. Caregiver issues

a. Patient Preferences

Apparently, patient preferences per se scarcely register on a conscious level in many formulary assessments, according to over one-third of payers interviewed. In part, this statement is misleading, because formulary assessment processes take for granted that formulary decisions are broadly compatible with patient preferences. In part, the statement is not misleading, because “patient preferences” is generally taken to mean “patients’ tastes about aspects of drugs that clinicians deem second-order, compared to clinical effectiveness in treating a given condition.” Given that interpretation, payers tend to pass by patient preferences regarding, say, taking a drug two times a day rather than three, since the payers have considered and dismissed such preferences in years past.

   Detailed Payer Comments on Patient Preferences

No free lunch. The pharmacy director of an MA plan stated firmly a related point: “If they (the patients) want it, they can pay for it. That sounds callous. But ....” In effect, the incremental cost-effectiveness of drug A compared to drug B drives the insurer's formulary decisions. Patient preferences between drug A and drug B carry no independent weight with the insurer. This view is widespread among payers: If patients want drugs or drug formulations the superiority of which are not supported by evidence of clinical effectiveness and cost-effectiveness, such patients always may choose to pay out-of-pocket to obtain products that better fit their preferences.
Preferences by osmosis. A PBM stated that its P&T committee “gets exposed to patient preferences via clinicians who care for these patients and MDs who prescribe these drugs.” This position is a corollary to the generalization above that often patient preferences scarcely register on a conscious level.

An influence at the margin. An employer indicated that, “When the costs of two therapies do not differ significantly, then patient preferences may enter.”

b. Ability To Work and On-The-Job Productivity

Among our interviewees, claims that a particular drug increases patients’ ability to work as well as their productivity when working received little support. Payers interviewed find evidence advanced for such claims to be thin. A Medicaid agency blandly stated that its “contractor gives our staff copies of articles on these topics,” adding that job productivity and ability to work are part of quality-of-life considerations. According to a national insurer, productivity on the job is “pushed by the drug companies, but data are scarce.” According to an employer, ‘ability to work’ is hard to measure and the “differential in patient productivity is hard to believe.” Moreover, “insurers don’t care since it’s the employers’ money, not theirs (the insurers’). Work costs are not their money.” This view of insurers impervious to the interests of their employer-customers is striking, since it suggests the market for group health insurance fails even large, institutional buyers.20 Regarding patient productivity, the employer stated that it would consider the argument if the cost offset (patient productivity) were believable.

A public payer offered mild support for the ‘ability to work’ claim. The payer’s pharmacy director recalled that, “Occasionally, perhaps rarely, [we] have added a drug to increase patients’ ability to work.” For example, s/he recalled the payer’s decision to put non-sedating antihistamines on its formulary to help its beneficiaries who work. Nonetheless, this individual also remarked that the ‘ability to work’ and ‘job productivity’ arguments are less important for his/her organization, since its patient population is typically elderly and less likely to be working.

c. Caregiver issues

A minority of payers interviewed give caregiver issues some attention. For example, a Medicaid agency seemed open to getting information on caregiver issues as part of its drug assessment. (In addition, having had personal experience as a caregiver to family members evidently made some of the agency’s pharmacy staff more open to considering these issues.) A national insurer was willing to consider caregiver issues as an aspect of quality-of-life considerations, but viewed caregiver issues as even less of a factor than quality of life. This insurer also reported that it had used data on caregiver burden for an Alzheimer drug.

An employer identified a novel angle: While the issue had not come up to date, the employer commented that “The Family Medical Leave Act has implications for drug assessment. If a new

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20 The degree to which economic analysis supports this contention is debatable. It implies insurers have considerable market power vis a vis their employer-customers and, by refusing to better satisfy their employer-customers, stubbornly take less of their monopoly profit than they could. While possible, it is not a foregone conclusion.
drug reduces the patient’s use of FMLA, then that’s a plus for the employer. And it should be a plus for the insurer.”

Other payers interviewed gave caregiver issues a cool reception. An insurer in the PDP and Medicare Advantage markets stated without qualification that it “would not look at caregiver gain or benefit when making a formulary decision.” However, the insurer had had caregiver issues arise for individual patients and dealt with them without changing the formulary. For example,

A patient with dementia had failed on other drugs. Lack of sleep led to a big increase in other medical problems, which in turn created problems for the daughter as caregiver. [The patient was prescribed] Ambien CR, which is not the plan’s formulary. This was dealt with by the pharmacy group as an individual case.

The remaining payers interviewed, both private and public, did not offer examples of ‘caregiver issues’ affecting their formulary decisionmaking. (However, a Blue plan noted that the issue had come up before – for example, with injectables.)
SECTION FIVE
Presentation of Information

5.1 In what kinds of situations do you prefer to see cost-effectiveness analysis (CEA) versus Budget Impact Analysis (BIA) and vice versa?

In effect, this question asked payers whether they would prefer that drug companies give them CEA or BIA, when providing the payers with information about their new drugs. As with several other topics, in this case payers split – between those who were negative toward cost-effectiveness analysis (CEA) and budget impact analysis (BIA) and those who were open to one or both tools supplied by drug companies.

Both CEA and BIA Ignored

Some payers are indifferent between CEA and BIA because they mistrust such information that drug companies provide. A Blue plan was particularly adamant in stating that drug company models are not credible. At the Blue plan, a senior formulary manager maintained that they never had seen either a CEA or BIA that was credible: “There’s no way to validate the model.” This same position was presented in a more nuanced fashion by the plan’s chief medical officer:

We rarely if ever see convincing cases of drug A being greatly superior to drug B. One example that was convincing: The first statins were much more effective than the alternatives.

A public payer also rejected CEA from drug companies, drily remarking that “[we] are not enamored with the CEA capabilities at the drug companies.” Regarding BIA, this payer stated, “No. [It’s] not a huge factor. If a drug is medically necessary and appropriate, it will be added to the formulary.” This payer makes a sharp distinction between tools like CEA and BIA as used by drug companies and the same tools used internally. The payer pointed to several examples (such as Avandia) in which “in-house analysis developed cost drivers for our budget office.” The payer added that “The analysis was done after the decision was made to include Avandia on the formulary.”

5.2 Health economics data are presented in various formats. Which are you most comfortable using?

a. Computer interface models – What types of these models are useful?
b. Formulary dossiers – How do you use information within these dossiers?
c. Models vs. publications vs. dossiers – Which do you prefer?
d. Face-to-face interaction with medical/HO?

Preferences among models, publications, and dossiers

Regarding information about new drugs, our interviewees did not state a clear-cut preference for one presentation mode over the others. Although not willing to state a single preference, a
sizable minority of payers mentioned their willingness to look at drug companies’ computer models, at least if certain conditions were met.

- A Medicaid agency declared that it had no preference among computer models, publications, and dossiers:

  A senior pharmacist looks at all these materials. The staff will look at whatever the drug companies give them.

- A Blue plan was enthusiastic about drug company models:

  I prefer PE models from the drug companies! I can use them. I want the drug company representative to walk me through the model.

- At an employer, the physician responsible for the pharmacy benefit prefers the drug company models if their assumptions concerning population characteristics can be modified. Specifically,

  I like to simulate [the employer’s] population’s likely use of drugs and then look at the cost implications. I like models because I’m more left-brained. My budget people often do not agree.

**Payers’ Comments on Individual Modes of Presenting Drug Information**

**Computer models**

Almost half of the payers interviewed at least look at computer models provided by drug companies. For example, a Blue plan uses the models without imposing any conditions. In contrast, a PBM has its staff look at the drug company models but does not give them or their results to its P&T committee. As noted above, an employer looks at the drug company models if and only if the payer’s own data can be introduced into the model. An MCO “does not use the drug company models” but does get value from looking at the elements of the model and the data it uses. The MCO staff added, “Having them (data and elements) help our quantitative thinking.”

The remaining payers interviewed either do not use computer models from drug companies or in effect did not respond to the question. For example, a public payer ignores drug company models because “they are hard-coded,” which prevents the payer from modifying the model’s population characteristics or other assumptions.

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21 The pharmacy manager for this employer is referring only to drug company models for which the characteristics of the population can be modified by the model user.
Dossiers

Payers expressed a spectrum of views regarding dossiers provided by drug companies about their new drugs. Many payers appreciate the convenience of the dossiers but some object to bias in the dossiers’ selection of studies.

Tolerance. Five payers are at least tolerant of dossiers from drug companies.

- A PBM commented that it “Like to get written material because it saves time on the literature search. It’s fine if the manufacturer saves us the time of obtaining copies of studies in the literature.”
- A Medicaid agency stated that “[We] will read whatever the drug companies give us.”
- Another public payer had a simple message: “Send us the dossier!”
- An MCO’s comment was more measured: “We consider dossiers generally pretty useful. But they can be incomplete and cherry-picked.” In part for that reason, the MCO prefers to have a discussion with drug company representatives about the evidence in the dossier.

We prefer the drug company reps do not come in first. Instead, their sending us stuff first is ideal. Then they [the reps] should come in, do a presentation, and spend time discussing [their information and points] with our staff.

However, the reality is different, according to this MCO:

Most drug companies take up all the time. It’s not very effective communication – pro forma and ritualized. The drug company rep says: “Thank you for your time.” We say, “Thank you for your information.” But later, near decision time, we need to go back to the drug company to have a better exchange. Sometimes that happens. Sometimes it doesn’t.

- Like the MCO, a national insurer’s view was tempered:

We prefer our own dossier format. The AMCP dossier meets about 85 percent of our needs. We also prefer to have the drug company send the dossier electronically.

Not useful. A Blue plan has a decided objection to the conventional dossier:

The AMCP dossier is too detailed. Neither the P&T committee nor the pharmacy benefit group manager has time to read them.

Models vs. publications vs. dossiers

Payers vary greatly in ranking models, publications, and dossiers in order of preference. As a result, compared to the payers’ broader comments about ranking, the payers’ comments about specific modes (embedded within the broader comments) are often more useful.
Randomized clinical trials. Several payers made a point of citing RCTs as “the gold standard.” For example, a public payer stated that “We strongly prefer to use RCT publications. Usually, there aren’t many.” So, until they become available, “we set tight limits on use” of the new drug.

Individual papers from drug companies. Asked if it prefers to get one or two papers from a drug company, an MCO responded that it does its own search to identify bias in whatever the drug company provides.

If the drug company selected them, it’s not that useful. [Confronted with those one or two papers,] we would do a search based on the references. [If given one or two papers, or] if the dossier has been cherry-picked, that [leads us to do] a deep dive into the drug class of the drug under review.

In the past, we have always been skeptical. Over the past four or five years, we have been more able to identify bias, challenge bad stuff, etc. in a more professional manner.

Model preferred. An employer expressed a cautious preference for models:

A model may be better than the publications. The model lets you work in your population as it is – the numbers who would be using the drug and what you consider the likely medical cost offsets to be.

Drug Company Representatives

As they did with other modes of presenting information about new drugs, payers expressed disparate views of face-to-face interactions w/ drug companies’ medical scientists, clinicians, and representatives. A small minority of those interviewed were unwilling to meet with drug company representatives, regardless of the representatives’ training and background. Almost half of payers interviewed at least tolerate meeting with such representatives, and some of these payers see the dialogue with drug company staff as valuable. The remainder of payers interviewed did not respond or respond substantively concerning this presentation model.

Payers’ Comments

The contrast between payers’ responses concerning representatives was sometimes striking. For example, a Blue plan is not inclined to turn to drug company representatives:

Show me the journal an article is published in, not the dossier.

We look more at peer-reviewed articles. We’re always just skeptical.

Taking a similar tack – expressed with force – a public payer with considerable pharmacoeconomic expertise declared: “We do not want to hear from their medical scientists.” The diametrically opposite stance was taken by a PBM, which insisted, “The drug company better bring in a clinician, not a drug rep type!” Elaborating, the PBM explained that “Presentations allow our clinicians to ask questions.”
An MCO’s stance was similar to the PBM’s:

We want to question the reps, interact with them, and try to push them to provide information that we think is important to our assessment.

An employer prefers a mixed strategy: On the one hand,

If the same information came from a CE program [i.e., model] or a medical liaison, I’d prefer the CE program.

On the other hand,

If a drug has a high cost impact, I’d want to get as much information as possible. So I’d use the drug company’s rep to get me up to speed. The more people in the room, the better the dialogue.

5.3 How do you use claims regarding patient-reported outcomes (PROs)? Similarly, what about QALYs?

What types of PROs are meaningful?

When are PROs viewed as primary versus supplemental information?

Our interviews with most payers skipped this question due to limited time and to having obtained some QALY and PRO information as responses to earlier questions.

The tenor of payers’ comments throughout the interviews is that QALYs are unappealing because they are seen as neither intuitive nor useful. As the pharmacy director of an insurer with Medicare PDP and SNP plans remarked,

I do not like QALYs. They don’t mean a lot to me. I like NNTs much more.22

PROs are seen as a cousin to quality-of-life measures and information. The more anchored in recognizable behavior and the more supported by independent observation of a physician, the more open at least some payers are to PROs. A national insurer finds most PROs unpersuasive:

[Patient-reported outcomes have] zero effect on drug decisions because we are skeptical of these types of data.

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22 NNT is the number needed to treat in order to avoid one adverse event. It measures the amount of therapeutic effort needed to produce a therapeutic outcome.
SECTION SIX
Time Horizon of MODEL

Question 6.1

6.1 Insurance companies are often stereotyped as considering costs and outcomes over a horizon of only one or two years because the turnover among health-plan members is high.
Under what circumstances would you consider a time horizon beyond two years?

Length of Time Horizon

Our interviewees answered this question in several ways. In part, they provided their view of the horizon their organization generally considers. In part, they discussed circumstances associated with a longer horizon. In part, they commented on related matters. More specifically, most payers cited a particular number of years or range of years that constitutes their time horizon. A minority of payers said that their horizon depends on the drug or the condition being treated. One payer stated that “it depends on whom you ask: Finance or Clinical.”

The number of years cited as the organization’s time horizon is as follows:

<table>
<thead>
<tr>
<th>Time horizon of payer</th>
<th>Examples of payers</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 to 5 years</td>
<td>• Employer</td>
</tr>
<tr>
<td></td>
<td>• PBM</td>
</tr>
<tr>
<td>5 years</td>
<td>• National insurer</td>
</tr>
<tr>
<td>20 to 30 years</td>
<td>• Public payer</td>
</tr>
<tr>
<td>Depends on the condition</td>
<td>• Public payer (Medicaid)</td>
</tr>
<tr>
<td></td>
<td>• Medicare Advantage plan</td>
</tr>
<tr>
<td>Depends on whether decisionmaker is in Finance or Clinical</td>
<td>• Managed care organization</td>
</tr>
</tbody>
</table>

Specific Comments by Payers

- A 3-to-5-year horizon was proposed by both an employer and a PBM. This similarity in horizons is plausible if the employer’s horizon is typical of employers generally and given that the PBM’s customers are generally employers. Both the employer and the PBM also commented on populations that call for shorter horizons: For example, the PBM observed:

  Shorter horizons make sense for employer-clients with custom formularies. Custom formularies are found more often in the health plan world. Often, these custom formularies are extremely narrow (e.g., generics only or where the health plan does not care about disrupting patients’ treatment plans).

Similarly, the employer recognized that “shorter horizons are appropriate for high-turnover populations.”
A national insurer opted for a 5-year horizon, which it characterized as “a pretty good dart throw.” This insurer has many employer-customers, and its horizon is at the upper limit of the range described by the employer and the PBM above.

The long-horizon outlier is the public payer that reported an horizon of 20 to 30 years. This payer’s population is unusual because it generally remains with this payer for many years.

Specific medical conditions determine the appropriate time horizon, according to the staff of an insurer with a PDP plan and a Medicare Advantage plan. This situation is reflected in the following table:

<table>
<thead>
<tr>
<th>Condition or set of conditions</th>
<th>Time horizon in years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure (CHF)</td>
<td>1 year</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2 to 3 years</td>
</tr>
<tr>
<td>Hip fractures</td>
<td>No more than 10 years. But HEDIS requirements push them toward a longer horizon</td>
</tr>
<tr>
<td>Special needs</td>
<td>1 to 5 years</td>
</tr>
</tbody>
</table>

An MCO offered a sophisticated take on the issue of time horizon. According to the MCO, the appropriate horizon is one year, based on the principles of welfare economics, on which pharmacoconomics rests. However, the MCO stated, “in the U.S. health care system, the employer has a longer-term perspective, and the insurer has a shorter-term perspective.” The MCO added, The Finance people focus on the payback time and the initial outlays. The MCO summarized the Finance Department view as follows:

- If the initial outlay is large and the payback is 25 years, then they’ll say that they can’t get the numbers to work.
- If the initial outlay is smaller and the payback time is within 5 years, then the Finance people might accept it.
- If the initial outlay is smaller and the payback time is within 10 years, then a favorable response from the financial side is iffier.
- If the initial outlay is smaller and the payback time is within 30 or 40 years, then the question is: when will UHC realize its hoped-for reduction in HC costs?

The MCO observed that “uncertainty about when savings or cost offsets will materialize is a real issue.” The expectation is that, after three or five years, members will leave [the MCO]. [We] did this analysis a number of years ago. Obviously, assumptions become more uncertain as the horizon approaches 20, 30, or 40 years.
SECTION SEVEN
Pharmacoeconomic Models in Practice

7.1 Think about a recent therapeutic-class review where you believed there are actual differences across agents.

a. What was informative about the pharmacoeconomic data/models you reviewed?

b. What about these data and/or models seemed confusing or hard to use?

Informative Aspects of PE Data/Models Reviewed

Only two examples of helpful/informative PE data or models were offered by any payer interviewed: A Blue plan cited “an example on the medical side – Procrit vs. Aranesp – as informative,” although the plan did not elaborate on what made the PE information in this case notably useful. An MCO made a broader point, stating that “PE models sometimes help me identify things overlooked on my short list of key items.” (These key items include cost items, relative effect sizes, and quantitative assessment of safety issues.) In addition to this heuristic value of the PE models reviewed, the MCO noted that “the models we see are improving.”

This MCO made other points that were relatively positive about drug company models:

First, “Models are getting better – by and large.”

Second, the MCO – specifically, a senior pharmacy manager skilled in pharmacoeconomics – identified a recent improvement in the MCO’s interactions with drug companies regarding their PE models:

Companies now are bringing in half-finished models and ask me whether I think that’s OK or what other things I think should be included. I appreciate their doing this (since it makes it more likely that the model will be useful to us). However, [my company’s] finance people might ask for something else later!

This comment illustrates an important point: When a payer locates different parts of formulary decisionmaking in different units or with different individuals, there is no single corporate view of what that payer wants from a PE model. No unit within that payer is the unique owner of the payer’s preferences regarding PE models and information. As a result, the job for drug companies is harder, purely from a technical standpoint. In effect, a drug company ideally would have a portfolio of models, each tuned to the generic preferences of particular functional groups within payers (e.g., clinical, finance, cost-effectiveness evaluation).

When there is no single corporate view of what the payer wants, it is hard if not impossible to determine which of the several views within a payer is decisive at the margin. A simple nose-count of decisionmakers’ views does not identify which decisionmaker or set of decisionmakers was decisive in a particular drug evaluation – let alone in successive evaluations of other new drugs.
Negative aspects of PE Data/Models Reviewed

Payers identified three aspects of pharmacoeconomic models and information that bothered them during their reviews or that they found to be unsatisfactory:

1. **Not knowing what’s behind the screen**

Several payers voiced dissatisfaction with the opaqueness of PE models that drug companies give them. A pharmacy manager at a Blue plan elaborated on this point:

> What are the defaults? The thought process involved? Are there overriding values [that are hard-coded and drive the results]? Was the study stopped at a certain time [so that the results would appear more favorable]? Were patients excluded and why? What other studies were done that were thrown away?

Underscoring why mistrust of black box models is widespread and deep, the pharmacy manager added, “I can make Excel show whatever I want to. I have 20 or 25 years in the industry [so I’ve seen everything].”

2. **Unsupported extrapolation of one year’s worth of RCT data**

An employer indicated s/he was unpersuaded by claims based on one year of RCT data:

> [I don’t like it when I see] claims that [take] a drug that reduces ER visits in the first year [of an RCT] and then that extrapolate those utilization and cost changes out to ten years, in order to claim big savings. I’m very skeptical of such claims.

3. **Cherry-picking studies**

An MCO focused on the evidentiary basis for drug companies’ PE models:

> What’s irritating? When drug companies cherry pick data [for their models]. The companies include or incorporate one or two studies where their drug looks good. As a result, the model makes their drug look good. But when all the (relevant) studies are included, then the new drug looks not so good.

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23 One payer even asserted that ‘nothing was [either] informative or uninformative.’ This payer also revealed that “We have a good P&T committee. Nothing really influenced the [formulary] decision.”
SECTION EIGHT
Assessment of Drugs after
The Initial P&T Committee Review

8.1 After your Pharmacy and Therapeutics (P&T) committee makes its recommendation about a drug’s formulary positioning, does your organization make a final determination that takes into account contracting agreements re: pricing?

Final decision made *after* review of pricing

Five payers we interviewed make their final decision about a new drug’s formulary position after reviewing of its pricing. In practice, this sequencing means that the P&T committee makes its decision; then, a different unit within the payer makes a business decision about the new drug, taking into account pricing and contracting. For example, two payers (a commercial plan and a public payer) agreed that they make the final decision about drug adoption and/or tiering only *after* their assessment of a new drug’s clinical effectiveness. In this final stage, the payer reviews the pricing provisions of its contracts with the manufacturers of the new drug and its rivals.

Three payers went further, saying that they organize their drug assessment processes in ways that effectively separate the clinical from the business:

- One private payer stressed it separates the clinical effectiveness decision from any consideration of cost and pricing.
- Another payer (a large commercial insurer) noted it had recently modified its assessment process by introducing a third committee into that process. This insurer had charged this new committee with assessing the business/pricing aspect of drug adoption and tiering.
- A third payer (a commercial insurer) indicated that, while the decisionmaker we interviewed heads the company’s pharmacoeconomic evaluation group, other units addressed other aspects of drug adoption. Evidently, one such unit dealt with the contract pricing issues regarding adoption of new drugs.

However, it is an open question whether the organizational separation of clinical and business assessment affects a payer’s decisions about a specific drug in a material way. The issue is whether some unit within the payer judges the new drug’s clinical and business merits *concurrently, without that unit’s hands being tied by prior judgments of other units earlier in the process*. An example begins with the P&T committee’s ranking of alternative drugs by their effectiveness. Suppose the payer requires that no drug be adopted with clinical effectiveness below a clinical cut-off for a category of drugs, regardless of how low its acquisition cost. Then, as a result, the sequencing and hierarchy of assessment decisions will affect the ultimate decisions to adopt new drugs and place them in tiers. (If a payer uses a clinical cut-off that constrains cost-effectiveness analysis, the payer will assess the cost-effectiveness of only those drugs with clinical effectiveness *above* the cut-off. As a result, less clinically effective drugs are ignored, regardless of how large the cost advantage may be of a drug below the clinical cut-off.)
As payers reminded us, adoption decisions often wrestle with incorporating prices of a new drug and its competitors in future years. Decisions that take into account contract prices are complicated when a particular drug’s patent life will expire in the next few years. For example, one public payer takes into account contract provisions routinely, as in this case:

[The public payer took into account the] time left on patent exclusivity for [a] statin. [The payer] decided against a long-term contract because it bet that a drug in the therapeutic class would lose patent exclusivity.24, 25

(Four payers did not respond to this question and one payer’s answer was not on-point.)

8.2 That way does your organization reassess the formulary position of a drug when new information becomes available (e.g., new indications, new safety concerns, etc.)?

Positive response to new information

When new information becomes available regarding a drug’s safety, clinical data, or clinical guidelines, this triggers a reassessment of the drug in question, according to two payers (one commercial insurer, one public payer). In particular, the public payer will change its formulary “if the clinical data changed” or (in most cases) if new American Diabetes Association (ADA) guidelines change or NHANES next generation changes. However, this public payer will not change its formulary if these new guidelines are “consensus-based” or are from an advocacy group. As for the commercial insurer, it noted,

When Januvia was added to the formulary, we revisited all the orals. It’s the PBM’s job to add new drugs or [have them] taken them off. We can only make a “negative change” in the formulary twice a year.

The insurer also noted that “we do not simply (i.e., automatically) cover anything that the FDA allows and [we] look at evidence itself.”

A commercial insurer made a related but more far-reaching point: When a new drug comes on the market, this event initiates a reassessment of the whole class of drugs that includes the new drug. Another public payer focused on pricing (not on formulary adoption and tiering): this payer stated it responds to an increase in the number of drugs in a class by negotiating a lower price with the manufacturer of an incumbent drug on the formulary.

24 This example pertains to the payer’s first statin contract. “The contract drugs cost more than the drugs that [the payer] had access to before the contract.” Why did the payer adopt the new drugs? “They had better lipids-reducing ability and better documented outcomes (regarding metabolism, potency, outcomes). It came down to dollar cost per incremental reduction in LDL...” This case is an example of explicit but informal cost-effectiveness analysis.

25 The advantages of a lower price due to a long-term contract must be weighed against the lower price of a generic that will become available once the originator drug’s patent expires.
Neutral/delayed-positive response

Several payers reported that, when new information about a drug appears, they do not respond quickly. Instead, they choose not to alter the pace of their planned, periodic reassessment of a drug or drug class. As one public payer noted, “We wait until the next scheduled review of this drug [about which new information has emerged].” One commercial insurer was emphatic that “a new indication does not lead to a reassessment” [that is out of the usual sequence].

Negative response

A commercial insurer said that,

> When FDA sends out a black box notice, we do not take those drugs off the formulary. [Instead,] we send a letter to our patients who are on that drug. We also send a letter to the physicians treating those patients.

One payer’s response to new information was unexpected: In response to a new indication for a drug on its formulary, this insurer tightens its limits on utilization of that drug. As its pharmacy director commented,

> [I] struggle to rein in the resulting increase in utilization.

In a similar vein, the pharmacy director elaborated:

> When a new indication comes in for drug A, that is not an advantage. [I] will try to disadvantage it as much as possible. [I] will try to manage the drug as much as possible. All these drugs will be pulled together (Rituxin, etc.). [Then the new drug will be compared with the existing drugs. Its cost-effectiveness will be scrutinized. It will have to provide a big advantage in clinical effectiveness to get favorable treatment.]

In effect, this pharmacy director has a strong “lean-against-the-wind” approach to managing prescription drug utilization. His/her assumption is that many prescribers respond to fads and fashions in prescribing. In this view, the new indication is the seedbed in which a fad will sprout.

Other

Not surprisingly, one employer did not know whether the pharmacy benefits manager (PBM) made its decisions after considering the implications of contract pricing.

> As [the employer’s] pharmacy guy, I haven’t been part of the P&T committee of their insurer, so I don’t have first-hand knowledge of this.

In general, employers may make judgments about the reputation of a PBM, the cost of its services, and its ability to generate high satisfaction among the employee-patients. The details of process may not be an issue unless a problem casts a searchlight on the formulary decisionmaking process.

(Four payers did not respond to this question or their answers were not on-point.)
SECTION NINE
Changes in Assessment of Value

9.1 Looking back a bit, what has been the biggest change in your company’s approach to assessing the value of pharmaceuticals within the past 12 months?

Organizational Change within Payer

Within the prior 12 months (roughly mid-2006 through 2007), two private payers changed aspects of the organizational structure used in making their formulary decisions:

- Insurer A added a third committee (in addition to a clinical evaluation committee (a national P&T committee) and a formulary review and benefit design committee). The third committee takes into account rebate and contracting information, in addition to clinical efficacy and cost-effectiveness.

- Insurer B split P&T committee in two so that physicians would have less (no?) say re: managing cost.

Insurer A’s case merits elaboration: At the urging of the pharmacy director, this insurer split its P&T committee in two, in order to take power away from the physicians on the committee. Under the new organizational structure, one committee makes the “must add/may add/don’t add” decisions. The second, ‘pharmacy management workgroup,’ is charged with managing costs. The pharmacy director explained the underlying impetus for the change: He had decided both of his company’s PDP and MAPD products “were spending too much;” now they manage drugs “very aggressively,” and the new committee is the vehicle that enables him to pursue his policy goal.

Of less interest, during the same period one public payer experienced very substantial management turnover (ranging from the agency head to the head of the pharmacy department). This is a case of organizational change without any structural change. However, this public payer’s staff noted in passing a change in operating policy: For some unspecified reason, “the P&T committee is stricter in conducting its review and takes more time to make the right decision.” Meanwhile, the payer’s P&T committee continued with its membership untouched by the turnover among senior executives.

Change in Factors Considered in Formulary Decisionmaking

Two private payers expanded the category of costs considered in their formulary decisionmaking to include medical costs beyond the cost of drugs.

- An insurer operating in the Medicare market added “hospitalization” as a factor to consider.

- A commercial insurer shifted its cost focus from the drug silo to an umbrella encompassing all medical costs.
This insurer reported the following:

“Five years ago, our approach to value assessment was very silo’d. Now, it’s a major umbrella. We consider all costs, not just drug costs.”

The insurer then attributed its own silo’d approach to value assessment to the stance taken by its customers: the employers who adopt the insurer’s health plan.

“But our customers just don’t get it. They don’t understand that not just drug costs but all costs should be considered.”

Another insurer, also with a medium-large number of covered lives, had a similar complaint. However, this second insurer acknowledged that it had not educated its customers effectively enough.

“We [the insurer] don’t show [or explain to] our customers well enough that carve-outs lead to higher costs. We haven’t developed case studies or examples that show in a way they’d understand how siloing costs them [the customers] money.”

The insurer then identified what it sees as a solution to this pressure from employers:

“There needs to be a third party to do the analysis that shows a narrow formulary ends up costing more [than a formulary that is not driven by cost siloing].”

One private payer *broadened its focus* from medical costs exclusively to include *various noncost factors*. Such factors considered now include (1) worker (patient) on-the-job productivity, (2) “disease-modifying” as a criterion; and (3) treatment of risk, not the diagnosis.

**Change in Approach to Formulary Decisionmaking**

In its review of new prescription drugs, one national insurer *added* to its categories for formulary decision a new category: “lack of data.” The rationale: to distinguish adoption decisions based on data that are adequate (“adopt,” “do not adopt”) from decisions to not adopt a new drug because the information available is not yet sufficient to reach an evidence-based conclusion.

Another large commercial insurer noted two changes in its approach for formulary decisionmaking:

- First, this insurer had instituted in the prior 12 months “a more quantitative approach to each specific review.”

- Second, this insurer had begun “sharing with drug companies new information that [it] had extracted from the literature.”

One public payer observed that, while no significant changes had occurred in the past 12 months, the current situation differed sharply from the situation 10 years ago.
Back then, cost minimization for prescription drugs was the goal. No medical cost offsets were considered. [In contrast, today, the formulary decisionmakers’ emphasis is on maximizing value. In addition, cost offsets are taken into account routinely.]

9.2 Now, looking ahead, what changes to assessing the value of pharmaceuticals do you see as likely in the next 3 years?

Anticipated Changes

In their interviews with us, decisionmakers at private insurers and public payers said they anticipated a range of diverse changes in the next several years. These anticipated changes follow:

- Diverse changes will be made by one or more payers:
  - Increase rebates to retain employers as customers;
  - Assess injectables separately – that is, as a distinct category between traditional pharmaceuticals and medical procedures/devices;
  - Increase dialogue with drug companies, specialty societies, and patient advocates; and
  - Add an ethicist to deal with genomics revolution.26

- Public programs will continue their incremental transformation—a morphing or evolution from single payer of providers to single payer of health plans.

One public payer stressed its view that, over the next 3 years and beyond, public programs will rely more on private managed care organizations. As a result, these programs would continue their shift toward private health plans with their own formularies. Consequently, Medicaid programs in particular will become like other managed care plans—less fee-for-service, more HMO. This payer underlined one consequence: in these public programs, each health plan will have its own formulary and process for making formulary decisions.

- The trend among payers toward greater reliance on evidence-based decisionmaking will continue.

- Some payers will improve their own pharmacoeconomic analysis.

In part, they will strengthen this capability due to internal demands for greater usefulness of analytic products, in part due to the spread of very costly biotech and genomic drugs.

- One insurer stated that it wanted to provide its P&T committee with analytic products that are much more comprehensive, thorough, and tight.

26 This payer continued as follows: “An ethicist can help address new questions, such as: When to pay for new technology? The genomics revolution will arrive relatively soon. [We] expect to add an ethicist to [our] P&T committee in the next year. An example of the potential problems: A new drug works for 0.001% of the population but can add 5 years to such a patient’s life. Should it be covered?”
Another insurer commented as follows:

- The emergence of costly new biotech and genomic drugs—they are increasingly important—demands much better data and analysis to show whether these very costly new drugs are worth it. [Furthermore, this insurer continued,] the big increase in money spent on biotech and genomic drugs will lead to a stronger analytic response than seen to date.

S/he illustrated her/his point by referring to a recent alternative to coumadin:

The company shot itself in the foot and destroyed its credibility due to its claim about survivability “doubling”—from 6 days to maybe 12 days!

After considering cautionary tales like this one, the insurer stressed that:

[There] will have to be really good data to show why these new, very expensive drugs are worth adopting.

Along the same lines, this insurer cited the need for more internal analyses—“clinical informatics.”

When discussing what it meant to improve its own pharmacoeconomic analyses, one insurer observed,

- [We all want] really good drugs that really improve outcomes. But ... were the Vioxx studies good or not? Were the initial RCTs flawed in design? In implementation? [Or were the problems enough outside the norm of clinical trial experience that they could not have been readily anticipated and prevented?] No slice of drug companies or therapeutic classes or researchers is immune to these problems.

Changes Desired but Not Necessarily Anticipated

In addition to anticipating certain changes, payers expressed the desire for certain changes that they did not necessarily expect to occur. Viewed broadly, one such change stands out:

- Payers want/expect someone—academics, drug companies—to produce better data and more transparent models

Payers gave two examples of such data improvements:

- First, some payers expressed interest in more evidence that a new drug has a medical-outcome value as used in the real world. (That is, the new drug should produce a better health outcome, given real-world patterns of physician practice and patient adherence.)

  Are people getting to treatment goals? You have to go back to [a] the drug and [b] the physician treating the patient.

  In this same vein, a greater stress on productivity on the job was also cited.
• Second, more rigorous data on specialty drugs will be provided—as one insurer wryly observed, a hope, not a forecast.

Pivotal role of drug companies

Payers did not expect much change over the next 3 years (regarding pharmacoeconomic information) to occur “without [as one insurer put it] a shift by drug companies toward more transparent and more usable pharmacoeconomic models.” Moreover, as another insurer indicated,

The potential for greater use of pharmacoeconomics is undermined by [the insurers’ and payers’] suspicion of bias [on the part of the drug companies] and by bad data.

Promise and pitfalls of national comparative effectiveness center

Payers consider a national comparative effectiveness center as a good idea in principle.

However, both public and private payers do not believe it will help them in assessing new drugs unless key features are in place, such as the center being independent of drug companies and other interested parties.

Several insurers’ and public payers’ comments follow:

• A U.S. comparative effectiveness center would help if it were free from outside influence.

• A comparative effectiveness center is a possible change. It would be worthwhile—if it built in public/private collaboration and if its staff had proper credentials.

• A comparative effectiveness center is a good idea, but the FDA’s history is not promising:
  – Look at how the drug companies harass the FDA!
Appendix B

Protocol for Exploratory Interviews (Formative Research)
Commitment to Confidentiality

For this project, we (the Westat team) will report on patterns across payers or payer-types.

The Westat team recognizes and respects the potentially proprietary nature of the procedures and practices of any company whose executives and employees we interview.

- Specifically, the Westat team is committed to preserving and protecting the confidentiality of the conversations we have with your company’s representatives. No report that we deliver and no article that we might publish will contain information that would permit identifying a health care payer at which we conducted an interview or would permit identifying an individual employed by that payer.

- Moreover, the Westat team treats its internal work products, such as interview notes and summaries, as confidential. We will not share or reveal confidential information about an individual company such as yours to anyone outside the Westat team.
Questions for Payer Decisionmakers about Use and Valuation of Pharmacoeconomic Data in Coverage Decisions on Drugs

1. Definition of Value
   - 1.1 How do you define “value” when considering drugs for formulary adoption?
   - 1.2 Is “value” defined differently for drugs than it is for health services/procedures?
   - 1.3 How do the following impact your assessment of value?
     a. The specific disease state
     b. The specific patient population (e.g. pediatrics, elderly)
     c. Alternative therapies
     d. Politics and patient advocacy
   - 1.4 What is the relationship between a drug’s value and its formulary-tier placement?

2. Assessment of Value
   - 2.1 How does value get assessed within your organization?
   - 2.2 Is value assessed internally or based upon publications/information provided?
   - 2.3 How does the concept of “risk” enter the value equation?
   - 2.4 How do you reassess value after a new drug is used by your prescribers?
   - 2.5 When would you accept predicted costs from pharmacoeconomic models?
   - 2.6 When would you consider health-related quality-of-life issues in assessing value?

3. Components of Effectiveness Considered
   - 3.1 How significant are primary endpoints versus secondary endpoints?
     a. Are single or composite endpoints (all cause mortality) preferred?
     b. How are post hoc analyses viewed?
   - 3.2 How much emphasis is placed on effectiveness versus safety?
   - 3.3 What weight is given to clinical trials versus “real world” studies?
   - 3.4 How are “real world” studies assessed?
3.5 When would you accept predicted outcomes from epidemiologic models?

3.6 How do data on adherence/persistence/compliance enter your assessment of value?

4. **Components of Costs Considered**

4.1 When you consider Direct Medical Costs, which of the following components are most influential for formulary decisionmaking and tier placement?

   a. Drug *versus* health services and other medical
   b. Inpatient *versus* outpatient

4.2 When are the following (Indirect costs) considered relevant?

   a. Patient preferences
   b. Patient productivity issues
   c. Caregiver issues

4.3 Are the specific costs examined driven by enrollee or employer (perspective)?

4.4 How do you calculate costs?

4.5 How do you consider medical cost offsets?

5. **Presentation of information**

5.1 When do you want to see cost-effectiveness analysis (CEA) versus Budget Impact Analysis (BIA)?

   a. For CEA, should there be a single denominator or multiple metrics?
   b. For BIA, PMPM (per member per month) vs. PPPY (per patient per year)?

5.2 What is your preferred format for viewing health economics data and claims?

   a. What types of computer interface models are useful?
   b. How important are peer-reviewed abstracts and publications?
   c. How do you use information within formulary dossiers?

5.3 How do you use claims regarding patient reported outcomes (PROs) and QALYs?

   a. What types of PROs are meaningful?
   b. When are PROs viewed as primary versus supplemental information?
c. What is required for you to believe the quality adjustment in QALYs?
d. Would you always want to see life years saved (LYS) in addition to QALYs?

5.4 The statistical rigor of complex analytical models lead to more accurate projections, but are more difficult to comprehend and interpret. What is the appropriate balance between statistical rigor and transparency when conducting pharmacoeconomic models?

6. Time horizon of model
   6.1 When examining CEAs and BIAs, how many time endpoints are needed?
   6.2 What range of time endpoints (6 vs. 12 months; minimum and maximum values) is preferred and which are the ones that drive your formulary decisions?
   6.3 To what extent does the time horizon depend on the disease to be treated?

7. Non-traditional aspects of value
   7.1 Can you describe one or two examples of “best practices” where “non-traditional aspects of value” influenced your decisionmaking process?
   7.2 Similarly, can you describe an example or two of “worst practices” – or “less-desirable practices” – where non-traditional aspects of value influenced the decisionmaking process?

8. Think about a recent review therapeutic class review where you believe there are actual differences across agents
   8.1 What was informative about the pharmacoeconomic data/models?
   8.2 What appeared to just add “clutter and confusion?”

9. Was there anything that we didn’t cover that you believe we should have discussed?
Appendix C

Bibliography of 48 Studies
Identified in Literature Search
Reference List

Studies Listed by Year of Publication


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The numbering in this Reference List corresponds to the abstract numbers in Appendix F.


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**Addendum to Bibliography:**

**Articles Identified by Eli Lilly Staff**


**Abstract:**

There are three known criteria that underlie drug reimbursement decisions: therapeutic value, cost-effectiveness, and burden of disease. However, evidence from recent reimbursement decisions in several jurisdictions points to residual, unexplained variables, among which is budget impact. Budget impact refers to the total costs that drug reimbursement and use entail with respect to one part of the health care system, pharmaceutical care, or to the entire health care system, taking into account the possible reallocation of resources across budgets or sectors of the health care system. The economic and equity rationale for carrying out budget impact analyses is opportunity cost, or benefits forgone, measured in terms of utility or equitable distribution, by using resources in one way rather than another. In other words, by choosing to draw down the budget in one way, decision makers forgo other opportunities to use the same resources. Under a set of
unrealistic assumptions, cost-effectiveness analysis accounts for opportunity cost while conveying to the decision maker the price of maximizing health gains, subject to a budget or resource constraint. However, the underlying assumptions are implausible, particularly in the context of pharmaceutical care. Moreover, budget impact analysis is more useful to the decision maker than cost-effectiveness analysis if the objective is not to maximize health gains subject to a budget or resource constraint, but to reduce variance in health gains. With respect to equitable distribution, budget impact analyses lay bare the individuals or groups who lose out — those who bear the opportunity cost of spending resources in accordance with one decision rule rather than another.


**OBJECTIVE:** To explore decision-making and the use of economic evaluation at the local health care decision-making level in England (UK).

**METHODS:** Data collection was over a 16-month period (January 2003 to April 2004). Data collection comprised 29 in-depth interviews with a range of decision makers, 13 observations of decision-making meetings, and analysis of documents produced at meetings. A constant comparative approach was used to identify broad themes and sub-themes arising from the data. Data were analysed using Microsoft Word.

**RESULTS:** National Institute for Health and Clinical Excellence (NICE) guidance provides the main way in which economic evaluation is used at a local level in the UK, although following NICE guidance is often regarded as detrimental to pursuing local priorities. Other than through NICE, economic evaluation is not considered at the local level; we found no evidence for use at the meeting group (by individuals). Although decision makers appear to understand notions of scarcity, with some also referring to value for money, the process of decision-making departs from these principles in practice. Disinvestment decisions are not made nor are decisions weighted against pre-defined criteria. Options appraisal is conducted, but it does not embody the principles of economic evaluation, since options are not considered in terms of their costs and benefits and opportunity cost is not accounted for. There appear to be two reasons why economic evaluation is not used at the local level: (1) the nature of management decisions concerned with the employment of extra staff and new equipment, rather than the choice of medicines or specific interventions usually assessed in published economic evaluation; (2) lack of awareness of the economic evaluation approach to decision-making. These two factors point to a lack of freedom in decision-making at the local level and a lack of understanding of how priority setting can be achieved in practice.

**CONCLUSION:** A more detailed and rigorous approach to prioritisation at the local level is required. Whilst, PCTs have been given greater responsibility for priority setting, they lack the necessary power and understanding of the ways in which long term solutions to problems in health care can be achieved. Economics can be a valuable asset to priority setting and has already filtered into the jargon used by decision makers. Whilst most concepts are understood, the leap to adopting these concepts into the practice of decision-making needs to be made.

**OBJECTIVES:** In view of resource scarcity, decisions have to be made on the optimal allocation of resources and one possible option in health care is economic evaluation. Little is known, however, about the use of economic evaluation. The objectives of this review were to assimilate the empirical evidence on this topic, discuss the main findings, and explore the possible need for further work needed in this area.

**METHODS:** A total of 40 studies were included in the review from a range of countries. A systematic search strategy was used and data from papers were extracted in a systematic way.

**RESULTS:** Pharmacists and clinicians in the US are the most frequently sampled group and postal surveys was the most commonly used method. Despite some positive findings, in most cases there appear to be obstacles to the extensive use of economic evaluation in decision-making. Obstacles can be linked to three factors: (1) institutional and political; (2) cultural; (3) methodological factors associated with economic evaluation itself.

**CONCLUSION:** There has clearly been an increase in the use of economic evaluation over time, especially in the UK, whereas the US appears to have a deep rooted disfavour of the approach. However, there is still little known about the exact influence of economic evaluation at the local level. Whilst work conducted to date has been valuable in providing information about use and barriers to use, further qualitative work is needed to enrich and explain some of the findings from this review.


**OBJECTIVES:** To determine the extent to which health economic information is used in health policy decision-making in the UK, and to consider factors associated with the utilisation of such research findings.

**DATA SOURCES:** Major electronic databases were searched up to 2004.

**REVIEW METHODS:** A systematic review of existing reviews on the use of economic evaluations in policy decision-making, of health and non-health literature on the use of economic analyses in policy making and of studies identifying actual or perceived barriers to the use of economic evaluations was undertaken. Five UK case studies of committees from four local and one national organisation [the Technology Appraisal Committee of the National Institute for Health and Clinical Excellence (NICE)] were conducted. Local case studies were augmented by documentary analysis of new technology request forms and by workshop discussions with members of local decision-making committees.

**RESULTS:** The systematic review demonstrated few previous systematic reviews of evidence in the area. At the local level in the NHS, it was an exception for economic evaluation to inform technology coverage decisions. Local decision-making focused primarily on evidence of clinical benefit and cost implications. And whilst information on implementation was frequently requested, cost-effectiveness information was rarely accessed. A number of features of the decision-making environment appeared to militate against emphasis on cost-effectiveness analysis. Constraints on the capacity to generate, access and interpret information, led to a minor role for cost-effectiveness analysis in the local decision-making process. At the national policy level in the UK, economic analysis was found to be highly integrated into NICE’s technology appraisal programme. Attitudes to economic evaluation
varied between committee members with some significant disagreement and extraneous factors diluted the health economics analysis available to the committee. There was strong evidence of an ordinal approach to consideration of clinical effectiveness and cost-effectiveness information. Some interviewees considered the key role of a cost-effectiveness analysis to be the provision of a framework for decision-making. Interviewees indicated that NICE makes use of some form of cost-effectiveness threshold but expressed concern about its basis and its use in decision-making. Frustrations with the appraisal process were expressed in terms of the scope of the policy question being addressed. Committee members raised concerns about lack of understanding of the economic analysis but felt that a single measure of benefit, e.g. the quality-adjusted life-year, was useful in allowing comparison of disparate health interventions and in providing a benchmark for later decisions. The importance of ensuring that committee members understood the limitations of the analysis was highlighted for model-based analyses.

CONCLUSIONS: This study suggests that research is needed into structures, processes and mechanisms by which technology coverage decisions can and should be made in healthcare. Further development of 'resource centres' may be useful to provide independent published analyses in order to support local decision-makers. Improved methods of economic analyses and of their presentation, which take account of the concerns of their users, are needed. Finally, the findings point to the need for further assessment of the feasibility and value of a formal process of clarification of the objectives that we seek from investments in healthcare.


The American College of Physicians recently highlighted the need to provide increased information comparing the effectiveness of health care interventions to ensure the rational and effective practice of medicine. Comparative effectiveness refers to the evaluation of the relative clinical effectiveness, safety, and cost of 2 or more medical services, drugs, devices, therapies, or procedures used to treat the same condition. The College further recommended the establishment of an adequately funded, trusted national entity that should prioritize, sponsor, or produce both comparative clinical and cost-effectiveness data. This article addresses the need for the proposed entity to develop cost-effectiveness information. It examines the current reluctance to develop and use cost-effectiveness in the United States; it argues for the importance of this information for all health care stakeholders; and it makes specific recommendations regarding how this information can best be made available and used for the good of the public and our patients.


**Abstract:**

Knowledge about the cost-effectiveness of innovative technologies or new guidelines in health care is more and more a necessary condition for implementation in common practice. However, there are situations where implementation of a new technology that is found more effective and cost effective and is strongly advocated by the medical profession stagnates. The reason for this is the discrepancy between long-run efficiency, on which cost effectiveness is based, and short-run efficiency. This paper addresses the potential paradox between long-term and short-term efficiency in health care and explores possibilities to overcome hurdles to implementation due to that paradox.

**Excerpt of interest:**

"A step further would be if the aim of economic evaluation of innovations in health care adds to the CEA-based research question another research question, namely: "what is the additional value of technology X for organization W when X is implemented in common practice?" The last question explicitly deals with the investment necessary to embed the technology in the organization, how this technology interferes with existing technologies in the organization and consequently whether diseconomies of scale, scope, and learning occur on the short run."


**Abstract:**

Despite the growing activity in the field of health economics very little is known about the influence of economic evaluation studies on health care decision making in the EU member states. Several investigations about the impact of health economic studies on decision making have been performed, but most of them did not involve decision makers themselves. In this paper the results of the EUROMET survey are reported and discussed. Different types of decision makers in nine European countries were surveyed by postal questionnaires, semi-structured interviews and focus group discussions. Questions include issues about the extent of knowledge about economic evaluation, the actual and potential use of study results as well as barriers and incentives in the use of studies. It is concluded that despite the general positive attitude knowledge about the formal methodology is rather limited. Accordingly, results of economic evaluation studies are not widely used in decision making. The results show that institutional dimensions, such as difficulties in transferring budgets, are viewed as important barriers. Also, the lack of credibility of studies is assigned a high relevance. Moreover, decision makers wish for a better explanation of the practical relevance of studies and feel that there is a need for more training in health economics. Considering these requirements a number of recommendations for enhancing the value of health economic studies are given.

Appendix D

Bibliography of
28 Studies from Literature Search Considered Relevant and High Quality
Literature Search

Sources Listed by Date of Publication


**NOTE:** These 28 studies represent an extract from a literature search that yielded 48 studies.

- The literature search aimed at capturing studies on the payers’ use of pharmacoeconomic information (e.g., cost-effectiveness analyses) in relation to formulary and coverage decisions.

- The 28-study extract consists of those studies scored by independent reviewers as (i) “relevant” to the present study’s scope and objectives and (ii) “high quality” in terms of the strength of evidence presented.

- The review and scoring of studies erred on the side of including potentially relevant studies. Only a subset of even these 28 studies unambiguously addresses the present study’s scope and objectives.
Appendix E

Abstracts of 28 Articles
Considered Relevant and High Quality,
2001 through 2007
Abstracts

NOTE: Portions of the abstracts below considered significant or interesting have been bolded or underlined

   Ref ID: 53
   **Abstract**: Authorities in a number of countries rely increasingly on cost-effectiveness analysis to determine reimbursement status or clinical guidance for pharmaceuticals. This study compared the use of health economic evidence across five reimbursement committees (Australia, Ontario and British Columbia in Canada, Finland, and France) and one clinical guidance committee (England and Wales). Health economic evidence was found to support decision making, although cost-effectiveness is less important in some identifiable situations. Since the relative importance of cost-effectiveness varies, it will be difficult to implement a single explicit threshold. Further research may make patterns of decision-making, distributional concerns, and the importance of different criteria more transparent, which would help to narrow the gap between the theory and practice of health economic evaluations. While the use of health economic evidence and the outcome of decision-making are similar across committees, there is presently only limited knowledge to what extent prescribing patterns are influenced by decisions.

   Ref ID: 19
   **Abstract**: The Veterans Health Administration (VHA) runs the largest integrated healthcare system in the nation. Formulary management within VHA primarily involves 3 national groups: the Medical Advisory Panel, the Veterans Integrated Service Network Formulary Leaders, and the Pharmacy Benefits Management Strategic Healthcare Group. Together, these groups manage the VHA national drug formulary with a goal of providing a comprehensive, safe, and cost-effective pharmacy benefit for veterans.

   Traditionally, VHA has relied on cost-minimization analyses in formulary decisions. More recently, VHA has emphasized the use of cost-effectiveness data, especially for newer, costly drugs. In addition to including this data in drug monographs, the VHA has begun requiring formal cost-effectiveness analysis from manufacturers of selected pharmaceuticals. VHA has also requested that clinically relevant information such as quality of life plus mortality benefit be made available from industry so that internal cost analyses can be performed. It is hoped that by setting the expectation that cost-effectiveness will be formally considered in all VHA formulary decisions, the pharmaceutical industry and others will be stimulated to collect and report data that enables these analyses.

   We believe that if other organizations also place an emphasis on economic evaluations, industry and the public will be more accepting of decisions that incorporate cost considerations.

Ref ID: 195

**Abstract:** Finding ways of curbing government expenditure on the Pharmaceutical Benefits Scheme (PBS) while maintaining social equity and access to ‘essential rsquo; medicines is at the centre of ongoing public debate. This article describes a microsimulation model of the PBS that simulates current and future use and costs of PBS medicines under existing and different PBS policy settings, and estimates the distributional effects of policy changes. The article outlines future developments that will extend the current model to include health outcomes. Adding health outcomes will enable the debate on PBS sustainability to be advanced beyond the prevailing cost-containment mentality to consider not only the costs of pharmaceutical use but also the benefits that result from the use of these medicines.


Ref ID: 43

**Abstract:** Resource scarcity is the raison d’etre for the discipline of economics. Thus, the primary purpose of economic analysis is to help decisionmakers when addressing problems arising due to the scarcity problem. The research reported here was concerned with *how cost-effectiveness information is used by the National Institute for Health & Clinical Excellence (NICE) in national technology coverage decisions in the UK*, and how its impact might be increased. The research followed a *qualitative case study methodology with semi-structured interviews*, supported by observation and analysis of secondary sources.

Our research highlights that the technology appraisal function of NICE represents an important progression for the UK health economics community: *new cost-effectiveness work is commissioned for each technology and that work directly informs national health policy.*

However, accountability in policy decisions necessitates that the information upon which decisions are based (including cost-effectiveness analysis, CEA) is accessible. This was found to be a serious problem and represents one of the main ongoing challenges.

**Other issues** highlighted include *perceived weaknesses in analysis methods* and the *poor alignment between the health maximization objectives assumed in economic analyses and the range of other objectives facing decisionmakers in reality.*


Ref ID: 42

**Abstract:** This article *reviews the development of economic evaluation of health technologies in the UK and its impact on decision-making*. After a long period of limited impact from studies mainly carried out as academic exercises, the advent of the National Institute for Health and Clinical Excellence (NICE) in 1999 provided a transparent decision-making context where economic evaluation plays a central role. *This article reviews some of the key characteristics about the way NICE works*, for example, the way NICE has defined the form of analysis that it requires, reflecting its objective of maximizing health gain (QALY’s) from the predetermined and limited UK NHS budget.

Several broad *areas of widespread concern* are noted.
The first relates to the cost-effectiveness thresholds that NICE uses and the basis for them. The second is the patchy implementation of NICE guidance and the possible reasons for this. But even within the UK, NICE is the exception in making extensive and explicit use of economic evaluation and this article goes on to suggest that if there is to be a more widespread and consistent use of economic evaluation at both central and local levels, then health economists and others need to address three issues. The first is to be clear about what is the correct conceptual basis for determining the cost-effectiveness threshold and then to ensure that NICE has the empirical evidence to set it appropriately.

The second is to recognize that even using the limited view of costs adopted by NICE, economic evaluations imply temporal and cross-service budgetary flexibility that the NHS locally does not in practice enjoy.

The third issue is that with academic pressures for ever-increasing sophistication of ‘state of the art’ economic evaluation analysis, the NHS has more and more precise understanding of the cost effectiveness of just a few new technologies and little or no analysis of most. This limits the value of the former by reducing further the scope for appropriately disinvesting from cost-ineffective technologies to meet the additional costs of investing in cost-effective new ones. Whilst NICE stands out as an example of a context where high-quality economic evaluation plays a major role in decision making, the process is far from perfect and certainly is not representative of the use made of economic evaluation by the NHS as a whole.

Health economists need to engage with the public and the health service to better understand their perspectives, rather than focusing on academic concerns relating to details of theory and analytical method.


Ref ID: 4

Abstract: OBJECTIVE: To explore pharmacists’ perceptions on the use of economic evaluations in decision-making within Medicine Management Committees (MMCs), identify factors that influence the uptake of economic evidence and examine the usefulness of different presentations of economic evidence.

METHOD: This two-stage qualitative study was carried out in July and August 2004 in two hospitals in northwest England. First, a researcher observed the decision-making process at two MMCs. Handwritten notes were made during observation, which were later transcribed. Subsequently, in-depth semi-structured interviews were conducted with a purposive sample of pharmacists involved in the MMCs. The interviews explored pharmacists’ views on the usefulness of economic evaluations in decision-making, the factors influencing the uptake of economic evidence by the MMCs, and the optimal presentation of economic results. The interviews were audio taped and transcribed verbatim. All the transcribed data were thematically analyzed using the constant comparison approach.

RESULTS: In all, six new drug applications were observed and ten pharmacists were interviewed. Pharmacists were observed to play an important role in decisions about drug formularies in hospitals. Although interviewees considered that timely economic evaluations would be useful in reviewing new medicines, the actual use of economic evidence in decision-making within MMCs was limited. The barriers to using economic evaluations included pharmacists’ lack of initiative to search for and difficulty in understanding economic evaluations, and the perceived availability, credibility and transferability of economic studies. However, the main barrier to
implementing economic evidence was the decisionmakers’ concern about the impact of the medicines on the hospitals’ drug budgets. Interviewees felt that they understood and trusted disaggregated economic results better than aggregated ones.

CONCLUSION: This study found the use of economic evidence in decision-making at both MMCs was limited. To improve the usefulness of economic evaluations in MMCs, members of MMCs will need more training in accessing, understanding and appraising economic evidence; researchers need to improve the credibility and transferability of economic studies, and present the results in clear and understandable ways. However, due to the restricted focus of local, short-term drug budgets, evidence-based decision-making remains a challenge for local MMCs.

Ref ID: 58
Abstract: OBJECTIVE: To identify economic and organizational characteristics that affect the likelihood that health maintenance organizations (HMOs) include new drugs on their formularies.

DATA SOURCES: We administered an original survey to directors of pharmacy at 75 HMOs, of which 41 returned usable responses. We obtained drug-specific data from an industry trade journal.

STUDY DESIGN: We performed multivariate logistic regression analysis, adjusting for fixed-drug effects and random-HMO effects. We used factor analysis to limit the number of predictors.

DATA COLLECTION METHODS: We held initial focus groups to help with survey design. We administered the survey in two waves. We asked respondents to report on seven popular new drugs, and to describe a variety of HMO organizational characteristics.

PRINCIPAL FINDINGS: Several HMO organizational characteristics, including nonprofit status, the incentives facing the director of the pharmacy, size and make-up of the pharmacy and therapeutics committee, and relationships with drugs makers, all affect formulary adoption.

CONCLUSIONS: There are many organizational factors that may cause HMOs to make different formulary adoption decisions prescription drugs.

Ref ID: 29

Ref ID: 28
Abstract: OBJECTIVES: Health decisionmakers involved with coverage and payment policies are increasingly developing policies that seek information on “real-world” (RW) outcomes. Motivated by these initiatives, the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) created a Task Force on Real-World Data to develop a framework to assist health-care decisionmakers in dealing with RW data, especially related to coverage and payment decisions.
METHODS: Task Force cochairs were selected by the ISPOR Board of Directors. Cochairs selected chairs for four working groups on: clinical outcomes, economic outcomes, patient-reported outcomes, and evidence hierarchies. Task Force members included representatives from academia, the pharmaceutical industry, and health insurers. The Task Force met on several occasions, conducted frequent correspondence and exchanges of drafts, and solicited comments on three drafts from a core group of external reviewers and from the ISPOR membership.

RESULTS: We defined RW data as data used for decision-making that are not collected in conventional randomized controlled trials (RCTs). We considered several characterizations: by type of outcome (clinical, economic, and patient-reported), by hierarchies of evidence (which rank evidence according to the strength of research designs), and by type of data source (supplementary data collection alongside RCTs, large simple trials, patient registries, administrative claims database, surveys, and medical records).

Our report discusses eight key issues: 1) the importance of RW data; 2) limitations of RW data; 3) the fact that the level of evidence required depends on the circumstance; 4) the need for good research practices for collecting and reporting RW data; 5) the need for good process in using RW data in coverage and reimbursement decisions; 6) the need to consider costs and benefits of data collection; 7) the ongoing need for modeling; and 8) the need for continued stakeholder dialogue on these topics.

CONCLUSIONS: Real-world data are essential for sound coverage and reimbursement decisions. The types and applications of such data are varied, and context matters greatly in determining the value of a particular type in any circumstance. It is critical that policymakers recognize the benefits, limitations, and methodological challenges in using RW data, and the need to consider carefully the costs and benefits of different forms of data collection in different situations.


Ref ID: 63

Abstract: OBJECTIVE: The principle aim of this study was to generate a league table of drugs considered by the Australian Pharmaceutical Benefits Advisory Committee (PBAC) for reimbursement. The table was used to test the hypothesis that decisions made by the PBAC are consistent with the maxim of economic efficiency. In addition, we explored whether the past decisions by the PBAC revealed a threshold incremental cost-effectiveness ratio beyond which the PBAC is not prepared to recommend reimbursement of a drug.

METHODS: All 355 submissions made to the PBAC between January 1991 and June 1996 were reviewed. Submissions using cost per life-year gained (26 submissions) or the cost per quality adjusted life-year (QALY) gained (9 submissions) were ranked in a league table and compared with advice given by the PBAC about that drug. The confidentiality restrictions for the submissions require that the individual drug details cannot be revealed in this article.

RESULTS: There was a statistically significant difference between the cost per life-year gained for drugs that were recommended for listing and those that were not, suggesting that the PBAC has been broadly consistent with the use of economic efficiency as a criterion for decision-making. We did not find an explicit threshold beyond which the PBAC was unwilling to pay for additional life years gained. However, between 1992 and 1996 the PBAC appears to have been unlikely to recommend a drug for listing if the additional cost
per life-year exceeded 76 000 Australian dollars [AUD] (1998/1999 values) and was unlikely to reject a drug for which the additional cost per life-year gained was less than AUD42 000. The cost-effectiveness ratio was not the only factor determining the reimbursement decision.

CONCLUSIONS: The results of this preliminary study indicate that decisions to recommend a drug for listing by the PBAC in the last few years have, by and large, been consistent with the notion of economic efficiency.


Abstract: OBJECTIVE: The objective of this study is to review the concept of the ‘Hannover Costing Study’ and to present and discuss the major insights generated during the course of the project.

The costing study was performed in conjunction with a randomized controlled prospective trial assessing the effectiveness of a disease management module in rheumatoid arthritis (RA). A full set of clinical and cost data both from patient-reported and payer-derived cost data was developed. In particular the study included (1) the development of a matrix of cost domains which might be used as a common taxonomy in costing studies, (2) the descriptive analysis of payer derived cost data, (3) the analysis of cost data in patients with uncertain diagnosis; (4) the development and validation of a patient-reported costing instrument, and (5) an assessment of productivity costs.

The following are the results (1) the developed matrix of cost domains included 16 separate cost domains: 7 outpatient, 3 inpatient, 4 other disease related, and 2 productivity domains; (2) the micro-costing analysis showed total direct costs of <euro>3,815 per patient-year (standard error of mean, SEM: <euro>267) and RA-related direct costs were <euro>2,312 per patient-year; (3) in patients with uncertain diagnosis of RA and no treatment with ‘Disease Modifying Antirheumatic Drugs’ (DMARD) costs were significantly lower; (4) the comparison of patient-reported with payer-reported cost data generally supports the use of highly aggregated items to assess health care utilization in RA; (5) productivity costs in patients that are gainfully employed and in patients who receive RA-related retirement payments exceed RA-related direct costs. Furthermore, RA-patients reported their productivity losses adequately. The study added some additional insights to the following questions: What costs should be collected, what level of detail is required for that task, what patients should be analyzed, and what data sources should be used in further studies in RA.


Abstract: OBJECTIVE: To determine if a pre-assessment can be used to establish whether cost-effectiveness results would meet the actual information needs of Dutch healthcare decisionmakers.

METHODS: Two recent studies in rehabilitation medicine served as study material. Based on Wholey, a limited pre-assessment was performed in which the potential impact of cost-effectiveness analysis (CEA) results on intended users’ decision-making was assessed. Desk research and semi-structured interviews with several intended users of CEA results were
performed. These included general practitioners, representatives of health insurance companies, the Health Care Insurance Board (CvZ), and medical guidelines committees.

RESULTS: In day-to-day decision making of the interviewed decisionmakers, a cost-effectiveness criterion seemed to be of limited importance. Instead, results from clinical effectiveness studies and budget impact studies appeared to be sufficient. CvZ, however, preferred relative cost-effectiveness to be a criterion for inclusion in future reimbursement guidelines. In both cases, the limited pre-assessments changed the expectations of the investigators regarding decision-making impact of an economic evaluation.

CONCLUSION: This study revealed that the use of CEA results for Dutch micro- and meso-level healthcare decision-making is not self-evident. The main purpose of CEA results is to support health policy making and planning at a macroeconomic level. Pre-assessment can be a valuable tool in designing a CEA to support the actual information needs of the decisionmakers.


Abstract: BACKGROUN: Provincial governments are responsible for administering publicly-funded anti-cancer drug benefit programs in Canada. This study examines inter-provincial variations in not only the content of such programs, but also the policies/processes used when considering a new drug for coverage.

METHODS: Pharmaceutical manufacturers and provincial/regional cancer boards were surveyed to identify the drugs covered by public drug benefit plans. Kappa coefficients were calculated to determine inter-provincial coverage variations. The comprehensiveness of availability of anti-cancer drugs across the country was also assessed. A semi-structured survey of all 10 provincial/regional cancer board pharmacy and therapeutics (P&T) committees were employed to examine decision-making policies/procedures. It included questions on committee composition and processes and on factors influencing decisions regarding the introduction of new drugs. Completed surveys were analyzed using qualitative and quantitative techniques.

RESULTS: All cancer boards and 75% of manufacturers contacted provided information on drugs covered in each province. Where lists were obtained from both sources, there was full agreement on content. Kappa values calculated ranged from -0.403 to 0.594, indicating poor to moderate agreement on anti-cancer drug coverage between provinces. Only 7 of the 115 drugs were available in all 10 provinces. Regarding decision-making processes, while ratings for both the relative importance and use of factors involved in decision-making (clinical effectiveness, patient preference, etc.) were similar across provinces, those for the relative importance and use of different information types (clinical trials, expert opinion, etc.) varied.

CONCLUSION: Access to anti-cancer drugs clearly varies across the country. In part, this may be due to differences in the views of P&T committees on the usefulness of information they use in their deliberations.

**Abstract:** Previous research indicates that in order to make pharmacoeconomic information applicable and useful for pharmaceutical benefit management (PBM) companies, several aspects need to be considered and improved. These include [six items]: timely availability of information, head-to-head comparators, peer-reviewed publications, independent sponsorship of pharmacoeconomic studies, use of relevant populations in research and published pharmacoeconomic models, and pharmacoeconomics training for pharmaceutical companies’ sales personnel. In addition to these measures, guidelines have been playing an important role in improving the applicability of pharmacoeconomic information.

This paper examines the progress to date in enhancing the applicability of pharmacoeconomics for optimal PBM decision making. The greatest improvements have been made in enhancing the quality of pharmacoeconomic research and the quality of peer-reviewed publications. Direct comparator studies are starting to emerge, but in limited numbers. The need for additional training of pharmaceutical representatives and PBM staff members remains a critical issue.


**Abstract:** OBJECTIVE: To investigate the extent to which preferred drug lists and tiered formularies reflect evidence of value, as measured in published cost-utility analyses (CUAs).

METHODS: Using 1998-2001 data from a large registry of cost-effectiveness analyses, we examined the 2004 Florida Medicaid preferred drug list and the 2004 Harvard Pilgrim Pharmacy Program 3-tier formulary, and compared cost-utility ratios (standardized to 2002 US dollars) of drugs with *preferred* and *nonpreferred* status.

RESULTS: Few drugs on the formularies had any cost-utility data available. Of those that did, median cost-utility ratios were somewhat higher (less favorable) for Florida's preferred drugs compared with the nonpreferred drugs (25,465 dollars vs 13,085 dollars; \(P = .09\)). Ratios did not differ for drugs on tiers 1 and 2 of the Harvard Pilgrim formulary, although they were higher for tier 3 and for excluded drugs (18,309 dollars, 18,846 dollars, 52,119 dollars, and 22,580 dollars, respectively; \(P = .01\)). Among therapies reported to be cost-saving or to have cost-utility ratios below 50,000 dollars, 77% had favored status in Florida Medicaid and 73% in Harvard Pilgrim. Among dominated drug interventions (reported to be more costly and less effective than alternatives), 95% had favored status in Florida Medicaid and 56% in Harvard Pilgrim.

CONCLUSIONS: This study underscores the paucity of published cost-utility data available to formulary committees. Some discrepancies prevail between the value of drugs, as reflected in published cost-utility ratios, and the formulary placement policies of 2 large health plans.
Ref ID: 31
Abstract: In this paper we consider the evolving American healthcare landscape and what it means for the use of economic evaluation of health interventions. We emphasize that use of economic evaluation in the US is unlikely to follow the European, Canadian or Australian models, which use cost effectiveness openly and explicitly, given the decentralized manner in which American healthcare is organized, financed and delivered, as well as different political systems and traditions, and cultural expectations and attitudes surrounding healthcare.

However, this does not mean that considerations of value are absent. On the contrary, measurement of value remains near the top of the agenda among US policymakers. With a few exceptions, it just isn’t playing out explicitly. In the American context, it means in part heightened debate over clinical evidence, and cost sharing. In some cases, payers are also considering economic evaluation more directly in coverage and reimbursement decisions and indirectly for clinical practice guidelines and best practice recommendations. A dramatic shift in policy towards cost effectiveness seems unlikely in the near future. Change will likely come in incremental fashion through experimentation and perhaps in selected circumstances with public and private leaders willing to take the political risks. Conceivably, more substantial change will occur with a major shift in the political leadership in Washington, DC in the legislative or executive branches, and/or with an economic downturn and severe pressures on federal and state health budgets. However, a more likely outcome is the ongoing indirect use of cost-effectiveness information.

Ref ID: 17
Abstract: BACKGROUND: In recent years, there has been more emphasis on determining the total value of a drug product, which includes safety and efficacy information and clinical and economic value relative to other therapies. The Academy of Managed Care Pharmacy (AMCP) Format for Formulary Submissions was intended as a tool to assist health care providers in evaluating and selecting drug products.

OBJECTIVE: The purpose of this research was to gain the perspectives of a sample of managed care organizations (MCOs) and pharmaceutical manufacturers regarding the AMCP Format submission and evaluation process, as well as their comments on possible future direction for these guidelines as an important part of the formulary decision-making process.

METHODS: A random sample of large (>1 million lives) and small (<1 million lives) MCOs was generated using telephone numbers from the National Directory of Managed Care Organizations’ database. Pharmaceutical manufacturer respondents were identified from the Pharmaceutical Research and Manufacturers of America (PhRMA) Foundation’s Health Outcomes Committee. Telephone interviews were conducted by 2 researchers between September 2004 and October 2005. Respondents from both pharmaceutical manufacturers and MCOs nationwide were familiar with the AMCP dossier preparation and review process, allowing us to compare perspectives from each group. The interview was designed to assess the following key areas: economic models, organizational
burden, confidentiality, overall value, and future expectations.

RESULTS: Representatives from 20 MCOs and 7 pharmaceutical manufacturers completed the interview; 21 MCO representatives refused to participate, citing company policy. Nearly all (87.5%) of the MCO personnel contacted reviewed dossiers within their organization. However, MCO respondents indicated that only 40% of all drugs they reviewed included dossiers from the manufacturers. For drug evaluation at the level of the pharmacy and therapeutics committee, we found that drugs were compared with a variety of products, with 11 respondents reporting comparisons with a placebo, and all respondents reporting a comparison with at least 1 other branded product. On average, 53.5% of the dossiers MCOs received included budget-impact models, and 39.3% included cost-effectiveness analyses (CEAs) or cost-benefit analyses. Of the dossiers with economic models, less than half (46.2%) were deemed adequate. Nearly two thirds of MCO respondents reported that they modified the provided model with their own population statistics, as many reported that manufacturers do not make models directly applicable to their health plan population. The perspectives of the pharmaceutical manufacturers varied dramatically from the MCO respondents with regard to the inclusion of economic models. Five of the 7 respondents indicated that their companies always included an economic model in the submitted dossiers. One respondent indicated that 85% of company dossiers included models, and another reported that 50% of dossiers included CEA models. Both MCOs and pharmaceutical manufacturers commented that organizational burden was high, with 70% of both groups reporting the use of outside consultants to assist in the dossier process.

CONCLUSIONS: Overall, findings for this study suggest that awareness of the AMCP Format is high among MCOs and pharmaceutical manufacturers, but aligning objectives between the 2 organization types is necessary. Conceptually, proving a drug value beyond what the U.S. Food and Drug Administration requires is a reasonable request, something most respondents agreed on. However, less than half of all drugs reviewed had a dossier. In contrast to MCO respondents, pharmaceutical manufacturers appear to have a more positive outlook on the role of the AMCP Format in effectively communicating the value of a new drug product. Further steps need to be taken to improve acceptance and integration of the AMCP Format.

Ref ID: 153
Abstract: BACKGROUND: Access to new therapies in hospitals depends upon both clinical trial evidence and local Pharmacy and Therapeutics (P&T) committee approval. The process of formulary evaluation by P&T committees is not well-understood.

OBJECTIVES: To describe the formulary decision-making process in Canadian hospitals for cardiovascular medications recently made available on the Canadian market.

METHODS: Postal survey of hospital pharmacy directors in all Canadian hospitals with more than 50 beds. Target drugs included abciximab, enoxaparin, dalteparin, clopidogrel, eptifibatide and tirofiban.

RESULTS: Of 428 surveys mailed, responses were received from 164 P&T committees representing 350 hospitals for an effective response rate of 82%. While physicians make up the largest proportion of committee membership, pharmacists play an influential role. Information most commonly cited as influencing formulary decisions included
published clinical trials (97%), regional guidelines (90%), pharmacoeconomic data (84%),
decisions at peer hospitals (73%) and local opinion leaders (60%). However, this information
was often not required on formulary applications. Approval timelines varied widely for target
medications but there were no regional, hospital or P&T committee characteristics that were
independent predictors of early formulary application or approval.

CONCLUSIONS: There is wide variability in the time taken for Canadian institutions
to adopt new cardiovascular therapies, which is not explained by regional, hospital or P&T
committee characteristics. Standardization of the formulary application and evaluation processes,
including sharing of information amongst institutions, would lead to broader understanding of
the applicable issues, more objectivity and improved efficiency.

20. Spath, H. M., Charavel, M., Morelle, M., Carrere, M. O. “A qualitative approach to the use of
economic data in the selection of medicines for hospital formularies: a French survey.”
Ref ID: 35
Abstract: OBJECTIVE: Qualitative interviews were conducted with pharmacists in hospitals
and clinics in the Rhone-Alpes region of France to determine the role of economic data when
selecting medicines for formularies, to identify barriers to the use of this information and to
study to what degree a healthcare establishment’s financing system influences the use of this
data.

METHOD: A stratified sample of healthcare establishments with over 100 short-stay beds was included: (1) thirteen public and semi-private hospitals financed through annual
global budgets and (2) six private clinics financed on a fee-for-service basis. Interviews were
carried out between October 1999 and January 2000, and coded independently by two
researchers.

MAIN OUTCOME MEASURE: A multiple correspondence analysis was performed
to compare the two groups of healthcare establishments.

RESULTS: The influence of economic data in the decision-making process is limited, for other factors appear to have greater weight: (1) efficacy and safety of
medicines (2) relations between decisionmakers and the pharmaceutical industry and
(3) patient quality of life. Economic data used was mainly related to medication prices
and quantities consumed. This data was used in a large number of decisions and seemed to
have more importance in hospitals than in clinics. Information related to resources that
could be saved by the inclusion of a new medicine on formularies was seldom used
and apparently considered less important in hospitals than in clinics. Pharmacoeconomic
evaluations were very rarely used.

Six barriers to the use of economic data were raised by the pharmacists, including: lack of
time, which limits the collection and analysis of such information; insufficient health
economics training, an obstacle to decisionmakers’ analytical capacity; and closed budgets
within hospitals.

CONCLUSION: Economic data concerning ‘medication budgets’ appears to have a
greater impact in public and semi-private hospitals than in private clinics. Obstacles linked to
the decision-making context itself were particularly highlighted, and it can be concluded that
in order to increase the use of economic data, it is first necessary to create an environment
that is more favorable to its application.

Ref ID: 37

**Abstract**: PURPOSE: The distribution, content, timeliness, use, and influence of pharmacoeconomic assessments (PEAs) of drugs in New Zealand public hospitals were examined.

METHODS: In April 2005, a questionnaire-based, cross-sectional survey was sent to chief pharmacists at all 29 New Zealand hospitals employing a pharmacist. The questionnaire asked pharmacists about the use and influence of PEAs in their hospitals’ formulary decision-making process. Answers were given using a scale of 1 to 6, with 1 being the most positive response.

RESULTS: Of the 29 surveys mailed, 24 (83%) were completed. Data on 12 PEAs were analyzed. Assessments were seen and summaries read in most hospitals (median, 77% and 65%, respectively). Full documents were read in fewer hospitals (35%). In general, the PEAs were considered moderately easy to understand, provided a concise summary, and contained adequate detail of the methodology. Of the 24 respondent hospitals, 21 had assessment processes for new medicines; hence, a total of 252 hospital evaluations of Pharmaceutical Management Agency (PHARMAC)-assessed drugs were possible. A total of 132 possible evaluations (52%) were undertaken. More evaluations (106 [42%]) took place before PHARMAC’s PEAs were distributed and fewer (26 [10%]) after distribution. Where used, the PEAs appeared to have a modest effect on hospital decisions.

CONCLUSION: The provision of 12 PEAs by PHARMAC to hospitals in New Zealand had only a modest influence on their formulary decision-making process, mostly due to the lack of timeliness of the PEAs. The timely delivery of centrally developed PEAs may be essential to generating a greater effect on the formulary decisions at a wider level.


Ref ID: 12

**Abstract**: Given the potential role of economic information in healthcare decision making, it is of interest to assess its influence on decisions at a national or regional level (macro level), at a healthcare facility level (meso level) and at the healthcare provider level (micro level). This literature review summarizes 36 empirical studies that examined the influence of economic evaluations on these three healthcare decision-making levels.

Economic evaluations are considered useful and important; however, their direct influence on decision making (instrumental use) is moderate, especially at the macro and micro levels. A major influence was observed at the meso level, leading to the conclusion that economic evaluations have the most pronounced influence on decision making within healthcare organizations. However, unexpectedly, our literature search did not reveal an empirical study analyzing the considerable influence of economic evaluations on decisions by the National Institute of Health and Clinical Excellence in the UK.

Our findings indicate that results of economic evaluations cannot be considered the dominant decision criterion for healthcare decisionmakers at either the macro, meso or micro levels.

Enlightenment use (where scientific evidence provides a background of information, ideas
and concepts that affect the way policymakers view problems and solutions) of economic evaluations in decision making remains to be proven.


Abstract: In the face of significant real healthcare cost inflation, pressured budgets, and ongoing launches of myriad technology of uncertain value, payers have formalized new valuation techniques that represent a barrier to entry for drugs. Cost-effectiveness analysis predominates among these methods, which involves differencing a new technological interventions marginal costs and benefits with a comparator’s, and comparing the resulting ratio to a payer’s willingness-to-pay threshold. In this paper we describe how firms are able to model the feasible range of future product prices when making in-licensing and developmental Go/No-Go decisions by considering payer’s use of the cost-effectiveness method. We illustrate this analytic method with a simple deterministic example and then incorporate stochastic assumptions using both analytic and simulation methods. Using this strategic approach, firms may reduce product development and in-licensing risk. SUBJECT(S).


Abstract: BACKGROUND: Faced with high drug expenditures in an environment of cost containment, drug formulary systems, particularly in managed care, have become more dependent on pharmacoeconomic evaluations to assess the value of new products. Within pharmacoeconomics (PE), cost-effectiveness analysis (CEA) is the most commonly used method. However, current methodological concerns about CEA have limited its practical contribution to the formulary process. Advances in analysis are likely to improve the relevance of CEA over time.

OBJECTIVE: The purpose of this paper is to review CEA, its limitations, and its applications in formulary decision making in order to promote greater utility of CEA for managed care pharmacists.

SUMMARY: Enhancements to CEA, such as the development of modeling software, rank-order stability analysis, cost-consequence analysis (CCA), and budget impact analysis are discussed. A combined method of CCA-CEA and standardized guidelines are suggested to improve the impact of CEA in the drug formulary process.

CONCLUSION: Along with advances in its methodology and relevant standardized guidelines, CEA will gain increased importance in formulary decision making, helping to assure the goal of cost containment while ensuring quality of care.


Abstract: BACKGROUND: Promoting use of pharmaco-economic models by formulary reviewers is a goal of the Academy of Managed Care Pharmacy (AMCP) Format for Formulary Submissions, but relatively few decisionmakers use such models, and many doubt
that they provide meaningful input.

OBJECTIVE: To demonstrate how sophisticated disease-based pharmaco-economic models can aid formulary decisionmakers when long-term outcomes data are lacking.

METHODS: The Center for Outcomes Research (CORE) Diabetes Model (CDM), a published, validated Markov pharmaco-economic model that projects clinical and economic endpoints, was used to model the cost-effectiveness of exenatide, a new injectable antidiabetic agent that enhances glucose-dependent insulin secretion, in a standard cohort of type 2 diabetes patients (mean body mass index [BMI] = 27.5 3 kg/m2), compared with a modified obese cohort (mean BMI = 35 3 kg/m2) that was otherwise demographically identical at baseline to the standard cohort. The standard cohort was assumed to maintain baseline weight during treatment, and the modified obese cohort was assumed to experience weight loss of approximately 9% (mean = 3 kg/m2), with corresponding improvements in blood pressure, low density lipoprotein cholesterol, and triglycerides. We selected a 30-year time horizon because it was the time interval during which the CDM predicted most of the subjects would have died, and the costs obtained thus reasonably projected lifetime total direct medical costs for these cohorts. While treatment options certainly will change over a 30-year period, our goal was to estimate the incremental effect of exenatide over other available therapies.

RESULTS: The model predicted reduced long-term treatment costs in obese patients, driven by an 11% decrease in cardiovascular disease burden and derived from the presumed weight loss. The incremental cost-effectiveness ratio (ICER) for adding exenatide over 3 years was 35,000 dollars/quality-adjusted life-year (QALY). Using a 30-year horizon, ICER values were 13,000 dollars/QALY versus insulin, 32,000 dollars versus generic glyburide, and 16,000 dollars versus no additional treatment. Exenatide dominated pioglitazone. By comparison, the 30-year ICER for exenatide versus insulin in the nonobese cohort was 33,000 dollars. These results were presented to the pharmacy and therapeutics (P&T) committee and influenced its decision to add exenatide to the drug formulary. While our modeling assumed certain patient characteristics (e.g., obesity, need of further A1c reduction at baseline, motivation to lose weight), the P&T committee imposed only a step-therapy requirement to try either metformin or a sulfonylurea before trying exenatide and did adopt a nonspecific requirement for physician reauthorization of refills before the fourth pharmacy claim for exenatide.

CONCLUSIONS: Disease-based pharmaco-economic models may help third party payers project costs and be particularly useful when only data from short-term clinical trials are available. In the present case, the pharmacy staff of a health plan used a pharmaco-economic model for drug treatment of type 2 diabetes provided by the manufacturer as part of the AMCP Format dossier process to project cost outcomes for exenatide, adjunct injectable therapy for patients taking metformin and/or sulfonylurea. The P&T committee approved the drug for inclusion in the drug formulary based in part on the results of the pharmaco-economic model produced from the cost inputs entered into the model by the health plan pharmacists.

Ref ID: 2

Abstract: In a context of rapid technological advances in health care and increasing demand for expensive treatments, local formulary committees are key players in the management of scarce resources. However, little is known about the information and processes used when making decisions on the inclusion of new treatments. This paper reports research on the use of economic evaluations in technology coverage decisions in England, although the findings
have a relevance to other health care systems with devolved responsibility for resource allocation. It reports a study of four local formulary committees in which both qualitative and quantitative data were collected.

Our main research finding is that it is an exception for cost-effectiveness analysis to inform technology coverage decisions. Barriers to use include access and expertise levels, concerns relating to the independence of analyses and problems with implementation of study recommendations. Further barriers derive from the constraints on decisionmakers, a lack of clarity over functions and aims of local committees, and the challenge of disinvestment in medical technologies.

The relative weakness of the research-practice dynamics in this context suggests the need for a rethinking of the role of both analysts and decisionmakers. Our research supports the view that in order to be useful, analysis needs to better reflect the constraints of the local decision-making environment. We also recommend that local decision-making committees and bodies in the National Health Service more clearly identify the ‘problems’ which they are charged with solving and how their outputs contribute to broader finance and commissioning functions. This would help to establish the ways in which the routine use of cost-effectiveness analysis might become a reality.


Ref ID: 41

Abstract: BACKGROUND: In the National Health Service in England and Wales, technology coverage decisions are taken by the National Institute for Health and Clinical Excellence (NICE). The intention formally to apply cost-effectiveness analysis to the decision-making process distinguishes NICE from most other bodies making similar policy recommendations. We carried out a case study of the NICE Appraisals Committee to explore the influence and use of economic evaluation in the decision-making process.

METHODS: Qualitative case study methodology. This involved analysis of all relevant secondary sources, observations of Appraisals Committee deliberations and interviews with a cross-section of Committee members.

FINDINGS: Economic evaluation is integrated into the Committee’s work. There are two main ways in which the use of economic analysis is understood by Committee members: an ordinal approach, whereby cost-effectiveness is only considered if the technology has passed a clinical effectiveness hurdle; and a framework approach, whereby the economic evaluation and model provide a structure for considering the decision problem and the evidence. These two approaches appear to operate simultaneously but are, in essence, inconsistent.

CONCLUSIONS: The NICE ‘experiment’ has seen cost-effectiveness analysis move to the centre-ground of UK national policy deliberations regarding technology coverage. However, our case study implies that there may be room for further refinement of the appraisal process in order to resolve the observed tension between two different ways of incorporating cost-effectiveness analysis in NICE’s decisionmaking.
Abstract: BACKGROUND: The extent to which the increased volume of available health-related quality of life (HRQOL) information and heightened education has increased the acceptance and use of HRQOL remains unclear. Likewise, the value of HRQOL information in the formulary decision-making process continues to be undefined.

OBJECTIVE: To investigate the perceptions and use of HRQOL by managed care decisionmakers in the formulary development process.

METHODS: A mail survey was sent to a nationwide sample of 108 Academy of Managed Care Pharmacy (AMCP) members who were involved in formulary management. Survey candidates were identified according to their job titles listed in the 1999-2000 AMCP membership directories. The survey process began in May 2000 and ended in August 2000. The main outcome measures included (a) managed care formulary decisionmakers’ assessment of HRQOL as a treatment outcome, (b) the existing role and future use of HRQOL information in formulary decisions, and (c) the level of understanding of HRQOL concepts and the benefits attributable to favorable HRQOL results.

RESULTS: A response rate of 51.9% was obtained. Most of the respondents (>70%) believed that patients consider HRQOL as an important treatment outcome. Fewer respondents (43%) felt that payers view HRQOL outcomes as an important quality indicator. Most respondents (95%) considered HRQOL data in making formulary decisions, and many (73%) believe that HRQOL outcomes will play a more important role in future formulary decisions. Respondents indicated a better understanding of disease-specific and generic HRQOL measurements than utility measurement and interpretation of results. A minority of respondents (34%) would be willing to pay a higher price for a product with better HRQOL outcomes. When asked which factors would lead to increased use of HRQOL information, respondents indicated that health care cost savings and increased productivity were considered important (77% and 65%, respectively).

CONCLUSIONS: A drug product with better HRQOL outcomes alone will not command a favorable listing on managed care formularies. HRQOL information needs to be made more applicable to managed care decision-making. Future studies should focus on the link between positive HRQOL outcomes, health care cost savings, and increased productivity.
Appendix F

Topics, Abstracts, and Questions
Ranked by Potential Contribution to the Revised Protocol
### Topic/Abstract/Question Combinations – Ranked by Likely Contribution to the Revised Protocol

Based upon Abstracts from Literature Search for Studies of Payers’ Use of Pharmacoeconomic Information

<table>
<thead>
<tr>
<th>Topic</th>
<th>Author / Abstract # (Appendix D)¹</th>
<th>Questions or Summary Comments</th>
</tr>
</thead>
</table>
| ✓ Evaluation of all new drugs or some?     | Lyles 30                          | • Q: Do you evaluate all new drugs?  
“57% of plans studied evaluate at least half of new drugs                                                                                                                                  |
| ✓ What “using PE” means concretely         | Bloom 42                          | Q: If you “use” PE, what does “use” mean – read a PE study? Analyze the quantitative implications of a PE study for your payer’s patient mix? Conduct a formal meta analysis of PE studies of a drug or drug class? ___? |
| ✓ Frequency of PE use                      | Olson 14                          | Q:  
• Have you had at least one experience where a PE model of some type played a role in tier placement or other positioning in a formulary?  
• In the past year/review cycle, how often did that occur?  
  • In this study, 95% of respondents had seen a PE model play a role in optimizing the formulary positioning of a product at least once (!). |
| ✓ Frequency of PE use                      | Weinstein 16                      | Q: How often do you see a PE model presented in your organization?  
Every P&T Comm mtg <----------------------> Once in 3 years                                                                                                                                                                                                                                               |
| ✓ Methods of using PE data                | Sanchez 25                        | Q: Do you and your colleagues use PE data in any of the following ways:  
1. At face value  
2. In a sensitivity analysis  
3. As part of a meta analysis (or literature synthesis)  
4. By incorporating the data into a PE model By reproducing the study on a smaller scale [Does that ever happen? What does this really refer to?? ] |

¹ These abstract numbers correspond to the numbering in Appendix E
<table>
<thead>
<tr>
<th>Topic</th>
<th>Author / Abstract # (Appendix D)</th>
<th>Questions or Summary Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use and source of formal CE</td>
<td>Lyles 30</td>
<td>Q: Do you use a formal, structured cost-effectiveness study from the literature? From a PBM? Or do you conduct a quantitative CE analysis of your own, drawing on available studies? Or both? Q: Does your organization’s use of formal, quantitative CE vary with circumstances? If so, how?</td>
</tr>
<tr>
<td>Reliance on PE/CE varies w/ cost &amp; outcomes impact of drug</td>
<td>Sanchez 25</td>
<td>Q: Do you vary the analysis you undertake, depending on whether the product’s impact on costs and outcomes is large or relatively small?</td>
</tr>
<tr>
<td>Different PE models’ effectiveness</td>
<td>Olson 14</td>
<td>Q: When you listen to the following list of PE models, which in your experience is most effective? Least effective? (Assume the same quality of work, data, etc. goes into each model type)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>◦ Spreadsheet [Note: 7 of 20 favored spreadsheets]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>◦ Markov models</td>
</tr>
<tr>
<td></td>
<td></td>
<td>◦ “Decision analytic tools” [What exactly are these?]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>◦ Multivariate regression</td>
</tr>
<tr>
<td>Transparency of assumptions/Availability of sensitivity analyses</td>
<td>Weinstein 16</td>
<td>Q: In the PE models you’ve seen, how often are key assumptions and parameters reported explicitly and clearly? Q: How often do you see sensitivity analyses that convey adequately that the relationship b/w inputs and results is conditional on various factors?</td>
</tr>
<tr>
<td>Topic</td>
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<tr>
<td>Adjusting CE results for patient mix</td>
<td>Grabowski/Mullins 29</td>
<td>Q: Since most CE/PE studies do not analyze therapeutic substitution in populations w/ characteristics similar to most insurers/payers, do you routinely adjust the reported results to match your patient mix? If not, or not regularly, do most of these studies give you enough information to do so?</td>
</tr>
<tr>
<td>Informal and formal CE</td>
<td>West 18</td>
<td>Q: In your organization, do you weigh cost &amp; effectiveness even if you do not calculate or cite an ICER? How do you do that weighing? What info are you drawing on? <strong>Premise</strong> Canadian provincial decisionmakers said: Efficacy info is generated in a scientifically rigorous way. But cost effectiveness info is subject to biases &amp; judgment.</td>
</tr>
<tr>
<td>Bias of efficacy and CE info</td>
<td>West</td>
<td>Q: Do you think that generally efficacy [clinical effectiveness?] information is generated and presented in a scientifically rigorous and unbiased way? Would you say that generally efficacy information is less biased and less subject to spin than information on cost-effectiveness?</td>
</tr>
<tr>
<td>Product superiority indicated by studies in addition to clinical trials</td>
<td>Clouse 19</td>
<td>Q: Can an indication of product superiority be derived from different types of studies – clinical trials, basic science, retrospective PE analyses – in a variety of patient settings? <strong>Premise</strong>: Randomized trials are usually placebo-controlled, not comparisons of medications in the same class. Randomized naturalistic studies can yield valuable info but are rarely performed</td>
</tr>
<tr>
<td>Noncompliance-related factors</td>
<td>Hughes 20</td>
<td>Q: When you see evidence about noncompliance, do any of the following factors matter to you: the type of noncompliance? The drug being considered? The disease that the drug would treat? Q: Are there cases where the particular type of noncompliance, drug, and disease made or make a difference?</td>
</tr>
<tr>
<td>PROs and willingness to pay</td>
<td>Longo 27</td>
<td>Q: Suppose you obtained studies of how much patients would be willing to pay to, say, avoid major side-effects of chemo. <strong>Would having solid studies that quantified patients’ willingness to pay overcome your skepticism about studies of patient-reported outcomes (PRO)&amp;QoL?</strong></td>
</tr>
<tr>
<td>Budget cost dominates CE</td>
<td>Kolassa 28</td>
<td>Q: Suppose two drugs are equally cost-effective but one drug’s price point is high and the other is low. Would the difference in price points affect your decision in formulary and tier placement?</td>
</tr>
<tr>
<td>Topic</td>
<td>Author / Abstract # (Appendix D)</td>
<td>Questions or Summary Comments</td>
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</tr>
</tbody>
</table>
| Reliance on CE varies with uncertainty, burden of target disease, net cost of drug | Devlin 33 | Q: Do you have a dollar threshold for a CE analysis? (E.g., maximum = $50,000 per QALY)  
Q: How does uncertainty about the CE-result affect your decision?  
Q: How about the burden of the disease that the new drug is directed at?  
Q: How about the net cost of the drug to your organization? |
| Max CE or other goal in picking drug for best placement | Bryan 36 | Q: Is your organization’s goal to pick the drug with the maximum effectiveness per unit of cost (when you compare a new drug to others in its class)? Or does your organization have, in addition to CE, other objectives as well? Do these come into play in your evaluations of most new drugs, or only for certain types of drugs? |
| CE/PE flawed in implementation or as methods in themselves | Bryan 36 | Q: Do you think the concepts & methods of PE and CE are fine but you sometimes find they are not applied well or in an unbiased manner?  
Q: Or do you think that the methods themselves have weaknesses and limitations? |
| Analytic Quality | Hahn 4 | Four factors are correlated with an index of analytical quality:  
1. One author or more affiliated w/ a university  
2. Publication in a journal w/ experience/track record in publishing similar articles  
3. The intervention/product (here, a life-saving invention) is in (delivered in) the US  
4. The analysis considers a measure of “social costs or benefits”  
Abstract not explicit re: what US PHS panel thought “quality” was |
| CE thresholds vary | Barbieri 6 | 1. Cost effectiveness (CE) estimates vary from country to country in W. Europe  
2. Nonetheless, if the conventional $50,000 threshold for cost per QALY were applied, in most cases the results (adopt—Y/N) would be the same! |
| Timing of generic entry | Shih 8 | Q: Do payer decisionmakers take into account the likely timing of future generic drug entry?  
* Generic entry in near term can affect CE-ness of drug A vs drug B a lot |
Appendix G

Themes and Observations Regarding Studies Considered Relevant and High Quality: 2001 Through 2007
Themes and Observations

In reviewing selected studies we had identified as pertinent to the present study, our primary purpose was to extract lessons from studies on the same topic to guide our revision of the interview protocol. (The Phase II interviews used the revised protocol.) A second purpose of the literature review was to identify themes, findings, and observations concerning this slice of the pharmacoeconomic literature that were significant or interesting in their own right. What follows highlights several such points regarding the literature on payers, their use of pharmacoeconomic information, and their attitudes toward it. The literature reviewed spans 2001 through 2007. (See Appendix D.)

- **Amount of evidence on payers’ use of pharmacoeconomic information, especially in the United States**

  The Drummond *et al.* 2003 ISPOR review foreshadowed what seems to be true in the post-2000 literature: The volume of studies that focus on decisionmakers’ use of and attitudes toward pharmacoeconomic data is relatively small. Moreover, in terms of national markets and decisionmakers, this literature tends to be at least as much about the European and non-U.S. situation – particularly the situation in the United Kingdom, Canada, and Australia – as about the situation in the United States.

- **Formal pharmacoeconomic analysis and public payers**

  Public payers and their associated agencies that review new drugs and have a national purview are more likely to have formal procedures and use pharmacoeconomic data explicitly, compared to private payers. For example, a national comparative effectiveness agency is more likely to consider a formal cost-effectiveness analysis and to calculate an incremental cost-effectiveness ratio (ICER), compared to a private insurer or (in the U.S.) a state agency.

  The public/private distinction overlaps with the non-U.S./U.S. distinction, in part because private health care payers are generally not as prominent in other industrialized countries as in the United States.

- **Traits of evidence favored by payers**

  Concerning evidence considered when they assess new drugs, payer-decisionmakers express a preference for clinical trials, peer-reviewed publications, and models and studies with transparent methods. These findings confirm commonsense and conventional wisdom.
- **Role of cost versus cost-effectiveness**

  Some studies leave the impression that decisionmakers – despite not seriously considering a new drug’s ICER, let alone calculating one – do consider cost-effectiveness of a new drug in an informal or judgmental way.

  In contrast, one study suggests that ‘cost’ enters some payers’ decisionmaking in a manner inconsistent with cost-effectiveness analysis. For example, one study reported that a sample of decisionmakers, presented with hypothetical data that indicated drugs A and B were equally cost-effective, chose drug A over drug B because drug A’s price point was half that of drug B.

- **Possible disjunction between methodological studies and payers’ analytic needs**

  In some studies, decisionmakers report that they find the available pharmacoeconomic studies of new drugs to be inadequate for their purposes. The decisionmakers point to various real-world concerns that make a clinical trial's results less helpful or even irrelevant to the payer’s decision.

  In contrast, most methodological studies captured in our review seem to talk past the concerns of formulary decisionmakers. Many methodological studies provide refinements of standard cost-effectiveness and cost-utility methodologies or present critiques that question those standard methodologies’ soundness.
Appendix H

Potential New Questions for Revised Protocol
Potential Questions for Revised Protocol  
Based upon Search of Pharmacoeconomic (PE) Literature

**PE Model: Frequency and Type of Use**

- Have you had *at least one* experience where a PE model of some type played a role in tier placement or other positioning in a formulary?
  - In the past year/review cycle, how often did that occur? (Every P&T Comm mtg?)
  - In the past three years, how often did a PE model play a role in formulary decision making? Once a year? Once in 3 years?

- Have you conducted alternative analyses using a drug company’s pharmacoeconomic model that permitted you to modify its assumptions?
  - How often did that occur in the past year? In the past three years?

- Have you constructed your own cost-effectiveness analysis or pharmacoeconomic model that incorporated data on clinical effectiveness and drug costs, plus assumptions or data on medical cost offsets?
  - How often did that occur in the past year? In the past three years?

**Using PE Results without Necessarily Using a PE model: Details and Frequency**

- Some organizations use results of a pharmacoeconomic analysis without using a pharmacoeconomic model itself. Is this true of your organization?
  - *If so* (If you use pharmacoeconomic (PE) or cost-effectiveness analysis): What does “use” mean?
    - Read a PE or cost-effectiveness study? (Usually from a PBM? The literature? A pharmaceutical manufacturer?)
    - Compare new drugs to their therapeutic substitutes by examining ICERs?
    - Adjust the results of someone else’s pharmacoeconomic or cost-effectiveness study to account for your organization’s patient mix?
      - Do most of the studies that you review present enough information for you to make that adjustment if you wanted to?
  - How often do you use pharmacoeconomic/cost-effectiveness results in these ways?
When Use of CE / PE is More Likely/Less Likely

- Are you more likely to use a formal cost-effectiveness analysis under some circumstances – or much less likely to do that under other conditions?
  - (Follow-up Q: ) Do you vary your use of formal cost-effectiveness (or pharmacoeconomic) analysis depending on whether the product affects costs and outcomes a lot or a little?

“NICE-TO-HAVE” BUT NOT ESSENTIAL QUESTIONS

Method and manner of presenting PE results

- When you listen to the following list of PE models, which in your experience is most effective? Least effective? (Assume the same quality of work, data, etc. goes into each model type)
  - Spreadsheet
  - Markov models
  - “Decision analytic tools”
  - Multivariate regression

- In the PE models you’ve seen, how often are key assumptions and parameters reported explicitly and clearly?

Informal cost-effectiveness analysis

- Does your organization weigh cost & effectiveness even if you do not calculate or cite an ICER? How do you do that weighing? What information are you drawing on?

Bias in clinical effectiveness studies vs. cost-effectiveness studies

- Do you think that generally efficacy [clinical effectiveness??] information is generated and presented in a scientifically rigorous and unbiased way? Would you say that efficacy information is generally less biased and less subject to spin than information on cost-effectiveness?

Noncompliance issues

- When you see evidence about noncompliance, do any of the following factors matter to you: the type of noncompliance? The drug being considered? The disease that the drug would treat?
  - Are there cases where the particular type of noncompliance, drug, and disease made or make a difference?
Drug cost/price point

- Suppose two drugs are equally cost-effective but one drug’s price point is high and the other is low. Would the difference in price points affect your decision in formulary and tier placement?

Uncertainty, disease burden, net cost of drug

- How is your formulary decision affected by each of these factors:
  - Uncertainty about the CE-result?
  - The burden of the disease that the new drug is directed at?
  - The net cost of the drug to your organization?

Cost-effectiveness versus other goals?

- Is your organization’s goal to pick the drug with the maximum effectiveness per unit of cost (when you compare a new drug to others in its class)? Or does your organization have, in addition to CE, other objectives as well?
  - Do these come into play in your evaluations of most new drugs, or only for certain types of drugs?

Merits of pharmacoeconomics and cost-effectiveness analysis in principle and in practice

- Do you think the concepts & methods of PE and CE are fine but you sometimes find they are not applied well or in an unbiased manner?
  - Or do you think that the methods themselves have weaknesses and limitations?
Appendix I

Protocol for Full-Scale Data Collection (Phase II)
Commitment to Confidentiality

For this project, we (the Westat team) will report on patterns across payers or payer-types.

The Westat team recognizes and respects the potentially proprietary nature of the procedures and practices of any company whose executives and employees we interview.

- Specifically, the Westat team is committed to preserving and protecting the confidentiality of the conversations we have with your company’s representatives. No report that we deliver and no article that we might publish will contain information that would permit identifying a health care payer at which we conducted an interview or would permit identifying an individual employed by that payer.

- Moreover, the Westat team treats its internal work products, such as interview notes and summaries, as confidential. We will not share or reveal confidential information about an individual company such as yours to anyone outside the Westat team.
1. **Definition of Value**

1.1 Imagine a new molecule has just been launched. When it is considered for formulary adoption and tier placement, its “value” gets discussed. That “value” is often described as a balancing of safety, effectiveness, and cost. Is that description the way you see it?

   a. If so, how does your organization balance those three elements when assessing value?

   b. Do you consider any factor other than safety, effectiveness and cost as part of value?

   c. Suppose that newly-launched molecule has entered a crowded therapeutic class. What information other than price is necessary for that molecule to be placed on second tier?

1.2 Let’s consider *specialty pharmaceuticals*. Do you assess their value like that differently than traditional drugs (covered under the pharmacy benefit)? [If so, how does this differ?]

   a. What about *drugs on the medical side* – do you assess their value differently than traditional drugs (covered under the pharmacy benefit)?

   b. Do you assess the value of *drugs* differently than *medical services and procedures*? [If so, how does this differ?]

1.3 How is your assessment of a new drug’s value affected by the following factors?

   a. The specific disease state (that the drug is aimed at)

   b. The specific patient population (e.g. pediatrics, elderly)

   c. Alternative therapies

   d. Politics, patient advocacy, and community physicians/prescribers

2. **Assessment of Value**

2.1 Let’s stay with that new molecule entering a crowded therapeutic class. What is the *process* by which that drug’s value gets assessed within your organization?

   a. Specifically, how much do you rely on information *from outside your organization* versus information *internal to your organization*? Similarly, do you do the analysis and assessment of the new drug largely within your organization or do you rely mostly on assessments conducted outside your organization?
2.2 Pharmacoeconomic models are designed to present cost-effectiveness information about the value of drugs. Have you had at least one experience in which a pharmacoeconomic model or cost-effectiveness article played a role in formulary adoption or tier placement?

   a. In the past year, how often did that occur? (E.g., every P&T Committee meeting? Once? A few times?)

   b. In the last time or two that pharmacoeconomic information affected your formulary decisions, what was the value message conveyed by that pharmacoeconomic information? What exactly did that information affect the coverage of that drug within the pharmacy benefit? (Adoption of the drug? Step edit? Tier placement?)

2.3 Have you conducted alternative analyses using a drug company's pharmacoeconomic model that permitted you to modify the model's assumptions?

   a. How often did that occur in the past year?

2.4 Have you constructed your own cost-effectiveness analysis or pharmacoeconomic model that incorporated data on clinical effectiveness and drug costs, plus assumptions or data on medical cost offsets?

   a. How often did that occur in the past year?

2.5 When you assess value, when would you consider health-related quality-of-life issues? Are you more likely to consider quality of life under particular circumstances?

2.6 If you did not consider health-related quality of life, are there specific patient-reported outcomes (PROs) that you find valuable?

3. Components of Effectiveness Considered

3.1 How significant are primary endpoints versus secondary endpoints?

3.2 What weight do you give “real world” studies when the clinical trials of the drug you’re assessing either are not head-to-head trials or are noninferiority studies?

   a. When do you find “real world” studies to be particularly helpful? When — of little help?

3.3 How do data on adherence/persistence/compliance enter your assessment of value?
4. **Components of Costs Considered**

4.1 When you consider Direct Medical Costs, which components most influence your formulary decision making and tier-placement: **Drug costs** or **Health services and other medical costs**?

4.2 To what extent do you consider **medical cost offsets**? What information sources regarding these offsets do you use?

4.3 When do you consider the following factors relevant to tier placement?
   a. Patient preferences
   b. Effect on (i) ability to work and (ii) patient productivity on the job
   c. Caregiver issues

5. **Presentation of information**

5.1 In what kinds of situations do you prefer to see cost-effectiveness analysis (CEA) versus Budget Impact Analysis (BIA) and vice versa?

5.2 Health economics data are presented in various formats. Which are you most comfortable using?
   a. **Computer interface models** – What types of these models are useful?
   b. **Formulary dossiers** – How do you use information within these dossiers?
   c. **Models vs. publications vs. dossiers** – Which do you prefer?
   d. **Face-to-face interaction with medical/HO**?

5.3 How do you use claims regarding patient-reported outcomes (PROs)? Similarly, what about QALYs?
   a. What types of PROs are meaningful?
   b. When are PROs viewed as primary versus supplemental information?

7. **Time horizon of model**

7.1 Insurance companies are often stereotyped as considering costs and outcomes over a horizon of only one or two years because the turnover among health-plan members is high. Under what circumstances would you consider a time horizon beyond two years?
8. Pharmacoeconomic models in practice

8.1 Think about a recent therapeutic-class review where you believed there are actual differences across agents.

   a. What was informative about the pharmacoeconomic data/models you reviewed?

   b. What about these data and/or models seemed confusing or hard to use?

9. Assessment of Drugs after The Initial P&T Committee Review

9.1 After your P&T Committee makes its recommendation about a drug’s formulary positioning, does your organization make a final determination that takes into account contracting agreements re: pricing?

9.2 In what way does your organization reassess the formulary position of a drug when new information becomes available (e.g., new indications, new safety concerns, etc.)?

10. Changes in assessment of value

10.1 Looking back a bit, what has been the biggest change in your company’s approach to assessing the value of pharmaceuticals within the past 12 months?

10.2 Now, looking ahead, what changes to assessing the value of pharmaceuticals do you see as likely in the next 3 years?

11. Have we missed anything that you believe we should have discussed?

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Thank you very much for your time.

NOTE: Be sure to request the following information (“As a token of our appreciation, we have one more favor to ask. Could you send us a few non-identifying characteristics of your organization, such as number of covered lives? Before we say that the payers we talked with were diverse, we need a little confirmation.” (Hand over short list.) [“Again, nothing will be given to anyone outside our team and nothing will be published that permits identifying your organization.”]

Non-identifying demographics for stratification such as

- Number of lives covered
- Number of drugs reviewed in past year
- Type of population/program financially at risk for: Medicare, Medicaid, or private
- If your organization is an insurance plan:
– Not-for-profit/For-profit;
– HMO/POS/PPO/Indemnity; and
– Medicare PDP (yes/no)

Questions Dropped from Phase I Protocol

1. Definition of Value
   1.1 How do you define “value” when considering drugs for formulary adoption?
   1.2 Is “value” defined differently for drugs than it is for health services/procedures?
   1.4 What is the relationship between a drug’s value and its formulary-tier placement?

2. Assessment of Value
   2.3 How does the concept of “risk” enter the value equation?
   2.4 How do you reassess value after a new drug is used by your prescribers?
   2.5 When would you accept predicted costs from pharmacoeconomic models?

3. Components of Effectiveness Considered
   3.1a. Are single or composite endpoints (all cause mortality) preferred?
   3.1b. How are post hoc analyses viewed?
   3.2 How much emphasis is placed on effectiveness versus safety?
   3.5 When would you accept predicted outcomes from epidemiologic models?

4. Components of Costs Considered
   4.1b When you consider Direct Medical Costs, which of the following components are most influential for formulary decision making and tier placement?
   Inpatient versus outpatient
   4.3 Are the specific costs examined driven by enrollee or employer (perspective)?
   4.4 How do you calculate costs?
5. **Presentation of information**

5.1a. For CEA, should there be a single denominator or multiple metrics?

5.1b. For BIA, PMPM (per member per month) vs. PPPY (per patient per year)?

5.2b. How important are peer-reviewed abstracts and publications?

5.3c. What is required for you to believe the quality adjustment in QALYs?

5.3d. Would you always want to see life years saved (LYS) in addition to QALYs?

5.4 The statistical rigor of complex analytical models lead to more accurate projections, but are more difficult to comprehend and interpret. What is the appropriate balance between statistical rigor and transparency when conducting pharmacoeconomic models?

6. **Time horizon of model**

6.1 When examining CEAs and BIAs, how many time endpoints are needed?

6.2 What range of time endpoints (6 vs. 12 months; minimum and maximum values) is preferred and which are the ones that drive your formulary decisions?

6.3 To what extent does the time horizon depend on the disease to be treated?

7. **Non-traditional aspects of value**

7.1 Can you describe one or two examples of “best practices” where “non-traditional aspects of value” influenced your decision-making process?

7.2 Similarly, can you describe an example or two of “worst practices” – or “less-desirable practices” – where non-traditional aspects of value influenced the decision-making process?