An Inside Look at Managed Care Executive Conversations within the Health Payer Council: What Is Evidence?

By Enid W. McDonough, JD, and Roger Green, MBA
Ms McDonough is Executive Director and Mr Green is President and Chief Executive Officer, Roger Green and Associates

In 2010, the payer landscape was changing rapidly, with no central place for medical and pharmacy directors to exchange ideas and to expand the ways in which they viewed the ever more complex daily choices and decisions with which they were faced. In addition, there are challenges regarding speaking one’s mind publicly. Some payer organizations chaste their directors for giving their personal opinions in any setting, claiming that everything the director says reflects on the company as a whole.

From these realizations, after a year of development, the Health Payer Council (HPC) was launched by Roger Green on April 11, 2012. HPC is comprised of 105 members, including a few retired members. The working member, on average, represents a plan that covers more than 6 million lives combined (Table). The members include 48 active pharmacy directors and 54 active medical directors—14% from national plans, 32% from regional plans, 24% from state plans, and less than 1% from local plans.

Most significantly, participation in HPC is anonymous. Members do not know the identity of the colleagues with whom they engage in online conversations.

The result of this carefully guarded anonymity is a community with rich, in-depth weekly exchanges, plus a forum for biopharmaceutical companies and others to purchase open, detailed, blinded research.

What Is Evidence? The Payer’s Perspective

A recent discussion focused on the thorny question, “What is evidence?” Kim D. Slocum, President of KDS Consulting, LLC, in West Chester, PA, posed the following questions:

1. What is evidence to you?
2. What is the proper balance between the definitive, but narrow information provided by randomized trials and the quicker, more real-world but less-definitive insights provided by observational studies?
3. How do you make decisions when the available information is incomplete or even contradictory?
4. Given the uncertainties that almost always accompany the launch of new medical technologies, what can developers do to help you make these difficult choices?

The medical and pharmacy directors evaluated these questions by breaking down their observations into 4 distinct buckets: randomized clinical trials (RCTs), head-to-head trials, comparative effectiveness research (CER), and real-world data. The participants made it clear that currently there is no conversation about science that does not include money and politics, with economics trumping science almost every time when the conversation evolves from idealism to reality.

Randomized Clinical Trials

Although many today have considered RCTs the “gold standard” for clarifying basic safety and efficacy issues, slightly more than 50% of the participants find the time-honored RCT model of limited value in today’s world. One national pharmacy director finds these studies to be “good for FDA [the US Food and Drug Administration] approval and nothing more.” Other participants were not so extreme, and still find value in RCTs, particularly for evaluating (1) new compounds, (2) new mechanisms of action, or (3) agents that address an unmet need or are directed toward a disease that had been undertreated or untreated.

Beyond these types of drugs, the participants perceive RCTs to be of marginal use to establish any value proposition for other agents. This is particularly so for drugs released into a mature market, in determining efficacy

<table>
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<tr>
<th>Covered lives per plan</th>
<th>Members (N = 105)</th>
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<tbody>
<tr>
<td></td>
<td>Commercial plan</td>
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<tr>
<td>Average lives, by type of plan, Nb</td>
<td>5,277,576</td>
</tr>
<tr>
<td>Average total lives, Nb</td>
<td>6,300,869</td>
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*There are some overlapping numbers, because some members are in multiple buckets.
*Each average calculated for members who cover >0 lives in the category.
HPC indicates Health Payer Council.
and/or safety for any subpopulation, or to aid in formu-
lary placement for drugs with similar mechanisms of ac-
tion and those brought to market by a pharmaceutical
industry that focuses more on “follow-on patent plays”
than on innovation, according to a pharmacy director at
a state pharmacy benefit management (PBM).

Although the medical and pharmacy directors assess
the value proposition of RCTs as strictly defined and
marginal from an evidentiary standpoint, they deem
RCTs necessary because of economic realities, a method-
ology they must accept as a result of political pressure.
Although 20 participants agree that RCTs are an effec-
tive baseline for new drugs, and that they provide basic
essential information, 6 members feel that the FDA’s
strict adherence to and acceptance of RCTs demonstrate
acquiescence to the biopharmaceutical companies,
which they believe do not want to fund more valuable
studies nor want to risk undesirable outcomes.

Payers both accept and resent the role of RCTs in the
approval process. Their view reflects people seeking to fix
any problem from the middle rather than having the
luxury of returning to the starting point. When adopting
a purely scientific approach, payers discuss the needs for
normative judgments, application of Bayesian logic and
analysis, and a nationally standardized electronic medi-
cal records (EMRs) system.

In reality, RCTs, when well designed, provide informa-
tion on a “class effect” for similar mechanisms of ac-
tion, but they often leave providers with a broad range of
products from which they randomly prescribe one drug
to their patients, without clear evidence which drug
provides the maximum benefit. One national medical
director equated this approach to “throwing objects
against the wall to see what sticks best.” However, as
long as RCTs are all that are required, every real deter-
mination, past basic safety and efficacy, can often be left
to real-world data, which often means a random trial-
and-error approach.

**Head-to-Head Trials**

Half of the HPC participants specifically state that
they view head-to-head trials as important when other
agents are available in the same drug class or agents with
similar mechanisms of action. The perceived reasons for
the shortage of these studies vary. Some payers flat out
blame biopharmaceutical companies’ refusal to risk pub-
lic failure. One national pharmacy director surmises that
such studies are “vexing” for drug manufacturers because
of the small difference between new and older treat-
ments. Payers assert that incremental improvement does
not merit a premium price, making head-to-head trials
not only monumentally expensive, but also potentially
worthless if the results do not mirror manufacturer
claims. In the absence of head-to-head trials, payers
adopt negative assumptions regarding new agents in a
class that already has a current market leader.

Even in a perfect world, HPC members would most
likely not view head-to-head trials as a panacea. By the
time such studies are completed, if properly conducted,
the “gold standard” used by the manufacturer may have
become obsolete. Approximately 25% of participants
specifically state that they see head-to-head trials as the
best option. Yet few addressed the costs to the biophar-
maceutical industry. Only 1 participant acknowledges
the costs of these studies to be exorbitant; 2 others rec-
ognize them as expensive but valuable. The medical and
pharmacy directors have little sympathy for any econom-
ic burdens that biopharmaceutical companies may face.
Overall, they perceive biopharmaceutical companies as
adamantly avoiding head-to-head studies—not because
of monetary pressures, but because they fear the results.

Payers express frustrations with the limitations of any
controlled trials. For patients who do not match the
study sample (eg, subpopulations, patients with comor-
bidities, geriatric patients, or patients on complex drug
regimens), variations in study results can become appar-
tant quickly. Some payers refer to the applications of
studies as an art rather than a science, and they call for a
standardized EMR system. They call for partnership be-
tween payers and manufacturers to truly obtain accurate
data over time.

One medical director observed that in advisory board
meetings, grading the level of evidence was a consistent
theme. Advisory board members, they note, often concur
that this is dependent on the maturity of the particular
disease state of research. HPC’s medical and pharmacy
directors agree that providing and managing care must
be based on evidence, but they made clear that it is chal-
lenging at best to agree on a definition, as this discussion
demonstrates.

**Real-World Data**

Real-world data draw even more varied definitions.
Some refer to “postmarketing surveillance,” as a subjective
term, or to evidence that “must be considered practically.
It cannot be black and white,” one participant noted.
Others find real-world data less valuable because of impre-
cision in the collection of the data and because clinicians
have their own biases, of which they are unaware.

Those who seek more empirical data talk of mining
medical and pharmacy claims to evaluate clinical real-
world responses. Also, they wish for a coalition of similar
plans to track off-label use of medications. To make any
of these wishes a reality, a national EMR system is a necessity.
Otherwise, the available data are often incomplete, obso-
lete, or too slow to be applied to real-life decision-making.
The Payer’s Challenge

However payers choose to evaluate and define evidence, their view of the data source skews each payer’s reading and interpretation, depending on their trust level. One national pharmacy director admitted to automatic skepticism any time a drug manufacturer tries to “ease MCOs’ [managed care organizations] and PBMs’ concerns,” regardless of the merits of their claims or the rigor of their data. Another pharmacy director is compelled to consider the public’s perception of his decisions, even when he seeks to consider the source impartially.

As one senior medical director summed it up, no evidence can directly demonstrate to payers how to weigh benefits, harms, and costs. He noted, “These are not questions that can be answered in the absence of normative judgments. I fully agree with those who have indicated that we are in a position to provide guidance and direction to the studies that are needed for evidence-based decision-making, and that those involved with developing these studies would be well served to obtain input regarding the optimal trial designs and to be certain that the right questions are asked to enable the desired decisions to be made. As [HPC members] have indicated…, there would be great value in a consortium-type approach designed with academic, scientific principles and appropriate input, which would provide a better chance for getting us...the data we need to make informed decisions in the presence of uncertainty.”

The participants offered several examples of RCT data leading to bad decisions. Two payers discussed a “lifesaving” bone marrow transplant procedure for breast cancer. The evidence showed that over time the procedure was not only not lifesaving, but was causing more harm than good. Payers were vilified in the press for withdrawing coverage for the procedure, which was ultimately discredited by further evidence. Public pressure also plays a part in some ill-advised approvals, causing payers to give new products or procedures unwarranted benefit of the doubt.

In other cases, the RCT data were disproved by real-world data over time or led to conjectures that did not hold up over time. Several participants made reference to cyclooxygenase-2 drugs, especially rofecoxib (Vioxx), that illustrate the first problem, and ezetimibe (Zetia) for the second.

Ezetimibe’s approval provided challenges based on accurate RCTs reviewed with faulty assumptions. Although clinical trials accurately reported ezetimibe’s impact on high-density lipoprotein levels, the ENHANCE trial established that the drug nonetheless had no positive impact on cardiovascular morbidity or mortality.1 A head-to-head trial would not have helped here, because the outcomes would have led to the same false assumptions as the initial trials did.

The consistent themes throughout this discussion centered on timing and trust. Payers do not receive data early enough in the evaluation and approval process, and they have little faith in its source—biopharmaceutical companies. One pharmacy director discussed the case of ramipril (Altace), based on the HOPE trial,2 noting that, “Data helped in the placement of Altace on formulary in the face of multiple ACE [angiotensin-converting enzyme] inhibitors on the market. The HOPE trial demonstrated a reduction in morbidity and mortality in patients on Altace and the P & T [Pharmacy & Therapeutics] committee approved the move to preferred tier after that data was [sic] published. This was at least 5 years after the product had initially launched into the market.”

Bridging the gaps between FDA requirements, the types of evidence available, and payers’ needs and perceptions regarding the data needed to bring agents to market is critical. One national medical director noted, “Science evolves with data, and what is believed today as evidence can be disproved over time with more data.”

Conclusion

According to the HPC payers, RCTs may be sufficient for products to gain market approval, but they do not provide the range and type of data on which payers rely. Head-to-head data provide superior guidance but usually cover only a short period of time. Over a more extended period, real-world data can provide these answers. As the discipline of CER matures, CER studies may provide the most robust evidence on whether a drug has new value for patient care. Urgency and transparency are keys. If manufacturers lack the funds or the patient pools to create large head-to-head trials, collaboration with payers can support trials in offering data that payers can use to determine the value of a new medicine. A regional medical director proposed “that the game changer in most of this (drug and otherwise) will be the existence of very large EMR-based data that will (albeit postlaunch) make large population outcome research much easier.” The collection of data is a science and the application is an art. Therein lies the challenge.

Author Disclosure Statement

Mr Green is a stockholder of AccuSphyg, LLC. Ms McDonough has reported no conflicts of interest.

References