How to Reward Innovation and Value in Comparative Effectiveness Research

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“…the companies that will survive and thrive in this new environment will be those that embrace **Comparative Effectiveness Research** as the next logical step in the progression of requiring evidence and recognize it as a necessary input for a value-driven healthcare system.”

– Biopharma Executive
The Role of CER in Innovation

Innovation is an investment that needs to be rewarded
Pharma faces a critical need to increase value of their innovative products by means of comparative effectiveness

*R2009 values are estimated*
CER Role in Innovation

Availability of CER Data

Between 2000-2010, approximately 51% of NME’s had CER data available at the time of drug approval in the U.S. – data was more common for some therapeutic areas than others.

**Study Background**

**Objective**
- Quantify availability of CER data for NME approval in the U.S.

**Data**
- Approval packages through the online database of drug products approved by the U.S. FDA

**Results**
- Of 197 NMEs identified, 100 met criteria for having comparative efficacy data

**Note**
- The results are in line with a similar study based on European approvals

**CER Data for Specific Therapeutic Indications**

- **Diabetes**: 89%
- **Infectious Diseases**: 73%
- **HIV/AIDS**: 64%
- **Arthritis and Rheumatism**: 60%
- **Cancer**: 35%

NMEs = new molecular entities

Source: Goldberg et al, 2011.
Several stakeholders have to do more to ensure that innovation will improve health outcomes.

Overall, do you approve of the job each of the following are doing to improve health outcomes in the United States?

- High Approval
- Low Approval

% who approve

Sums may not add to 100% or be equal to components due to rounding.
Pharma companies traditionally focus on innovation derived from scientific research, but they broaden their focus to include addressing unmet needs and adding value for patients.

What is the most important role that biopharmaceutical companies play today in improving health outcomes? Please rank each using consecutive numbers between 1 and 5, where 1 is the most important.

<table>
<thead>
<tr>
<th>Role</th>
<th>Percentage</th>
<th>Mean Rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>Translating scientific research into new medications</td>
<td>43%</td>
<td>1.8</td>
</tr>
<tr>
<td>Bringing new medications to market</td>
<td>36%</td>
<td>2.2</td>
</tr>
<tr>
<td>Identifying unmet health needs</td>
<td>10%</td>
<td>3.3</td>
</tr>
<tr>
<td>Supporting research in basic science</td>
<td>10%</td>
<td>3.7</td>
</tr>
<tr>
<td>Providing value-added services for patients</td>
<td>2%</td>
<td>4.0</td>
</tr>
</tbody>
</table>

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CER Role in Innovation

Biopharma’s Changing Role

As biopharma adapts to the changing influence of other stakeholders, and reacts to pressure to more clearly demonstrate the value of its products, the industry finds itself torn between establishing long-term relationships at the expense of short-term gains.

Do you think biopharmaceutical companies should invest more in long-term relationships and long-term outcomes data at the expense of short-term gains?

- 78% Yes
- 14% No
- 8% I’m not sure

What barriers do you think biopharmaceutical companies would encounter to more investment in long-term relationships and long-term outcomes data at the expense of short-term gains? (Select all that apply) (n=194)

- Lack of investor support: 71%
- Weak financial position: 48%
- Need greater commitment internally: 46%
- Regulatory barriers: 37%
- No industry consensus: 36%
- Information or knowledge gaps: 31%
- Other: 8%
- I’m not sure: 2%
Various stakeholders are regulating the road to market access, with the patients serving as the final decision maker in rewarding innovation.

“The initial FDA approval of a drug should be the beginning of an intensive period of assessment, not the end.”

CER and Value

Innovation can only be rewarded if it adds value for each stakeholder.
CER and Value
Decision Makers’ Perceptions

However, these stakeholders have different definitions of value and one third of patients has difficulty with defining the value for healthcare products.

In your own words, how would you define “value” in healthcare?

**Biopharma**
- 38% Mentions both cost & outcomes
- 30% Mentions cost
- 23% Mentions outcomes
- 10% Mentions neither
- 0% Not sure

**Managed Care**
- 23% Mentions both cost & outcomes
- 43% Mentions cost
- 13% Mentions outcomes
- 19% Mentions neither
- 1% Not sure

**Physicians**
- 19% Mentions both cost & outcomes
- 40% Mentions cost
- 10% Mentions outcomes
- 28% Mentions neither
- 2% Not sure

**Patients**
- 2% Mentions both cost & outcomes
- 30% Mentions cost
- 30% Mentions outcomes
- 33% Mentions neither
- 31% Not sure

Opportunity to move from highly silo’d and fragmented healthcare market... …to create integrated Evidenced-Based healthcare ecosystem

CER offers the prospect of overcoming the disjointed healthcare market, and rather, creating an integrated evidence based healthcare network
Recent attention on CER provides stakeholders with a unique opportunity and responsibility to build innovative and sustainable CER structures.

“In presenting the outlines of this concept, Janet Woodcock drew an analogy to the interstate highway system and national electricity grid. Such large public works require sustained government support because the market is unlikely to provide the interconnecting pieces necessary for the whole to work efficiently.”

“The analogy aptly suggests the scale of the federal research infrastructure that would be needed to close the enormous gap in clinical evidence in decision making....One can imagine, for example, the challenge of using grants to build the interstate highway system. The result would probably be stretches of highway where the gains to local interests are clear, but with no interstitial linkages.”
CER and Value
Prioritizing Systems Analysis

IOM recommended CER review of the top 100 topics most important to the health of the US population

Focus on *how* or *where*, rather than *which* services are provided

CER and Value

*HTA Agencies in other Healthcare Systems*

Various other agencies globally already influence CER by considering economic evaluations in their coverage decisions or recommendations

<table>
<thead>
<tr>
<th>Country</th>
<th>Review Body</th>
<th>Function/Role</th>
<th>Evaluation Tendencies</th>
<th>Relation to Government</th>
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</thead>
<tbody>
<tr>
<td>Denmark</td>
<td>DKMA</td>
<td>Coverage/Regulatory</td>
<td>Budget Impact</td>
<td>Integrated</td>
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<td>Coverage/Regulatory</td>
<td>Health Economics</td>
<td>Arms-Length</td>
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<td>TLV</td>
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<td>Health Economics</td>
<td>Arms-length</td>
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<tr>
<td>Australia</td>
<td>PBAC</td>
<td>Pricing/Advisory</td>
<td>Health Economics</td>
<td>Independent</td>
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As a result, pricing deals that hinge on clinical value are becoming more prevalent, highlighting the necessity for CER in Europe.

Glaxo offers NHS rebate if latest cancer drug fails to outperform Pfizer rival

26 December 2010

“...price is driven by value and value is driven by evidence, and therefore we can start to construct different sorts of arrangements where we can balance this off.... The Government...outlined plans for a radical shake-up of its drugs policy and the introduction of a “value-based” pricing model...”
CER and Value

Building Partnerships to Exhibit Value

In the US, partnerships can be an efficient CER mechanism that stakeholders can construct in a mutual effort to understand the real-world value of innovative products.

AstraZeneca and WellPoint the Latest to Focus on Value in Care

AstraZeneca and WellPoint’s HealthCore subsidiary have teamed up to study which treatments for chronic and other diseases give the best value for money. AZ says it will use the data to help make R&D decisions and in talks with payers about covering available drugs.
The partnership between Medco and Sanofi-Aventis brings the payer view to R&D

Medco, Sanofi drug deal brings payor view to R&D

- Medco may consult for sanofi-aventis on CER studies
- For drugs designed for a condition with no approved treatments, Medco might gather data on the disease’s prevalence, hospitalizations from the disease, and its total costs
- Medco can also help frame data in a way that is more useful to payers

Linking Innovation to Value

CER needs to be integrated with clinical development to optimize market access
Integrated CER starts during clinical development and continues post-launch with observational research. It requires involvement from commercial, market access, and clinical teams.
CER encompasses investigating the real-world practice patterns, understanding patient populations, comparing the relative effectiveness of products, and communicating the results.
Coordination between agencies may streamline government efforts and improve efficiency in evaluating the value of a new innovative product.

**Provenge Case**
Expected Provenge cost is $93,000

- **Median Survival**
  - Months: 20, 22, 24, 26, 28
  - Patients receiving Provenge: 25.8 months
  - Patients not receiving Provenge: 21.7 months

- **Parallel Review**
  - FDA
  - CMS

- Enhanced Communication between regulators, reimbursement authorities, and manufacturers
- Reduce administrative burden
- Provide more rapid access to new technologies
- Provide feedback to companies about study design and endpoints needed to justify reimbursement

**A proposed “parallel review” process between the FDA and the CMS would mark a landmark change in market access in the U.S.**

CMS = Centers for Medicare and Medicaid Services; FDA = Food and Drug Administration

Evidence Based Medicine (EBM) links stakeholders and evidence, providing patients with targeted, real-world, and cost-effective care.

EBM = Evidence Based Medicine

Evidence Based Medicine (EBM)

- Real-time, Real world Point of Care
- Observational Research
- Retrospective Real World Data Analytics
- RCTs

Comparative Effectiveness Research

- Risk-Benefit Analysis

Health Technology Assessment

- Cost-Benefit Analysis

Safety, Efficacy, and Quality

Pharma | Payers | Providers | Patients

Stakeholder
Baseball and Healthcare

*Billy Beane, Newt Gingrich and John Kerry*

– “A doctor today can get more data on the starting third baseman on his fantasy baseball team than on the effectiveness of life-and-death medical procedures.”

– “America’s health care system behaves like a hidebound, tradition-based ball club that chases after aging sluggers.”

– “To deliver better health care, we should learn from the successful teams that have adopted baseball’s new evidence-based methods. The best way to start improving quality and lowering costs is to study the stats.”
CER Cases

Innovation to be rewarded when value is demonstrated
### CER Case Studies

**Four Key Examples**

The following cases demonstrate the value that CER can bring to patients, payers, physicians, policymakers, and the biopharma industry

#### CATIE
- Clinical antipsychotic trials of intervention effectiveness
- The CATIE study showed that first-generation antipsychotics still have a role in schizophrenia

Source: [http://www.catie.unc.edu/schizophrenia/about-public.html](http://www.catie.unc.edu/schizophrenia/about-public.html), 2003

#### GeCCO
- Genotype guided comparison of clopidogrel & prasugrel outcomes
- The GeCCO study will show if a large patient subgroup will have better outcomes with prasugrel

Source - Medco Launches Plavix, Effient Comparative Effectiveness Study Examining Role Of Genetics, 2009

#### OAD
- Comparison of metformin, sulfonylureas, and thiazolidinediones
- This study on antidiabetic drugs showed that metformin was performing better in real practice than sulfonylureas, though did not (yet) publish its results for thiazolidinediones

Source: Huizinga Pharmacoepid. Drug Safety, 2010

#### CATT
- Comparison of Age-related Macular Degeneration (AMD) Treatments
- The CATT Trail concluded that Lucentis (ranibizumab) and Avastin (bevacizumab) had equal effects on visual acuity in AMD

Source - Press Release, NIH, National Eye Institute, 2008
Closing Remarks

- Pharma faces a critical need to increase value of their innovative products by means of comparative effectiveness, so they should broaden their focus to address unmet needs and adding more value for patients.

- Pharma should take an integrated approach on CER that starts during early clinical development and continues post-launch with observational research, which requires involvement from various teams.

- Pharma is actively conducting CER studies to demonstrate value for innovative products, though it may be too early to measure their effect on market access, drug utilization and coverage decisions.