When Is Evidence “Enough” to Make a Health Care Decision?

National Pharmaceutical Council
IMS Health
July 31, 2013
Fracking healthcare big data: Drilling for value or just hot gas?


Want to Cut Healthcare Costs? Peer Into the Data

Forbes Healthcare Summit: Using Big Data To Make Patients Better

Using Big Data To Make Patients Better And Help Guide Doctors Part 1
Forbes  Dec. 12, 2012
What is the Greatest RWE Fear?

It Will Be Used?

It Won’t Be Used?
Agenda

• Introductions

• When Is Evidence Sufficient for Decision-Making? A Framework for Understanding the Pace of Evidence Adoption

• RWE Market Impact on Medicines: A Lens for Pharma

• Question and Answers
Speakers

Dr. Robert W. Dubois
Chief Science Officer, National Pharmaceutical Council

Dr. Ben Hughes
Senior Principal, Real World Evidence Solutions, IMS Health

Dr. Eleanor M. Perfetto
Professor, Pharmaceutical Health Services Research, School of Pharmacy, University of Maryland

Marla Kessler
Vice President, IMS Consulting Group
2 Ways to Ask a Question

To Submit Questions
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Existing Resources for Real-World Evidence

- Demystifying CER
- Making Informed Decisions
- CER Principles
- GRACE and GRACE 2.0
A Preview of Coming Attractions

Stakeholder surveys of RWE value
- Payer survey of CER
- Clinical Practice Guidelines

Tools to evaluate and synthesize evidence
- GRACE 2.0
- AMCP/ISPOR/NPC CER Collaborative

Frameworks: from evidence to action
- Fit for purpose
- Impact of CER on Patient Utilization
- RWE: When Will the Emperor Have Clothes
When Is Evidence Sufficient for Decision-Making? A Framework for Understanding the Pace of Evidence Adoption

Robert W. Dubois, MD, PhD
Michael Lauer, MD
Eleanor Perfetto, PhD, MS

A Tale of TWO SETS of Evidence

Pace of Evidence **Adoption**  
Pace of Evidence **Formulation**
Pace of Evidence Adoption

• To understand the pace of evidence adoption, a conceptual framework was proposed

• The framework was applied to three case studies:
  – Statins
  – Drug Eluting Stents
  – Bone Marrow Transplantation for Breast Cancer

• The goal was to identify possible critical factors that affect adoption and optimize translation into routine clinical practice so that those factors can be considered in future work
Five Factors Influenced the Rate of Adoption (Conceptual Framework)

1. Validity, reliability, and maturity of the science
2. Communication of the science
3. Applicability
4. Economic Drivers
5. Rapid (or slow) incorporation into practice guidelines
Case Study #1: Statins
Timeline of Evidence & Market Considerations

**Market & Guidelines**
- Lovastatin approved by FDA 1987
- Pravastatin and simvastatin approved by FDA 1991
- Lovastatin recommended as a 2nd line therapy 1993
- ATP III guidelines commented that statins were generally safe 2002
- Cerivastatin withdrawn 2001
- FDA warning: statin therapy may cause memory loss or develop diabetes 2011

**Evidence**
- 1961 Framingham Study identifies cholesterol and CAD link
- 1996 - 1998 Large morbidity & mortality trials conducted (LIPID, CARE, WOSCOPS) show:
  - ↑ survival among patients with CAD
  - ↓ risk among patients with CAD and elevated cholesterol
- 1999 Meta-analysis confirms benefits of previously conducted trials
- 2005 Meta-analysis reports prolonged statin treatment should be considered patients at high risk of major vascular events
- 2010 Meta-analysis reports intensive ↓ of cholesterol beyond current target levels may provide additional benefits

CAD = Coronary artery disease
Case Study #1: Statins
Timeline of Use

Targeted Use Among Patients

- 1992: Drug therapy recommended in only 20% of ambulatory visits involving a diagnosis of hyperlipidemia.
- 1999: 39% of adult patients with high cholesterol reported using cholesterol-lowering medications.
- 2000: >50% of ambulatory visits involving a diagnosis of hyperlipidemia were treated with statins, accounting for 90% of Rx.
- 2006: 54% of adult patients with high cholesterol reported using cholesterol-lowering medications.

All Patients

- 1992: 3% of all American adults used cholesterol-lowering medications.
- 2010: 16% of all American adults used cholesterol-lowering medications.

CAD = Coronary artery disease
Case Study #1: Statins

Influential Factors

- Maturity of the Science
- Economic Drivers
- Communication of the Science
- Slow incorporation into practice guidelines
Case Study #1: Statins

Influential Factors

- Maturity of the Science
- Economic Drivers
- Communication of the Science
- Slow incorporation into practice guidelines
Case Study #2: Drug Eluting Stents
Timeline of Evidence & Market Considerations

Market & Guidelines

1970s
- Percutaneous option only available treatment
- Early 1970s

Early 1970s
- CABG ↑ survival for patients with CAD

Late 1970s
- Balloon angioplasty introduced
- DES approved by FDA 2003

1986
- BMS introduced

1995
- Guidelines suggest DES as an alternative to BMS 2005

2003
- Guidelines updated to reflect risk of thrombosis
- CMS DRG initiated for stents 2008

2005
- Hospitals find ↓ rate of repeat procedures 2010

2007
- Guidelines: DES should not be performed if the patient is unlikely to tolerate and comply with DAPT 2011

Evidence

2002
- RAVEL trial ↓ CV events in European Study

2004
- TAXUS IV trial ↓ CV events in US

2007
- COURAGE trial question use of stents at all in stable diseases

2009
- SYNTAX trial questions use of stents in patients w/ extensive blockage

CAD = Coronary artery disease
BMS = Bare Metal Stents
DES = Drug Eluting Stents
CABG = Coronary artery bypass grafting
DAPT = dual antiplatelet therapy
Case Study #2: Drug Eluting Stents
Timeline of Adoption

2002
Drug Eluting Stents (DES) approved by FDA

2003
More than 50% of all PCI involved the implementation of DES

2005
~90% of all PCI involved the implementation of DES

2007
DES use ↓ to 60% after reports of late risk of life-threatening thrombosis

PCI = percutaneous coronary interventions || DES = drug eluting stents
Case Study #2: Drug Eluting Stents
Influential Factors

Validity, Reliability, and Maturity of the Science

Ability to Apply Published Scientific Findings

Economic Drivers

Communication of the Science
Case Study #2: Drug Eluting Stents

Influential Factors

Validity, Reliability, and Maturity of the Science

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Economic Drivers

Communication of the Science
Case Study #3: Bone Marrow Transplantation (BMT) for Breast Cancer

Timeline of Evidence & Market Considerations

Market & Guidelines

- **1970s**
  - BMT used in leukemia

- **1980s**
  - Use of BMT for breast cancer continues to rise due to enthusiasm by key opinion leaders, lobbying efforts and legal challenges **1980s-1990s**
  - Patients with metastatic breast cancer begin to receive BMT

- **1980s-1990s**
  - Lawsuits ensure coverage 1990

- **1990**
  - Raised awareness and media prior to ASCO annual meeting

- **1994**
  - OPM requires coverage

- **1999**
  - Aetna withdraws reimbursement 2000
  - 3 of 4 randomized trials presented at ASCO annual meeting show no net benefit

Evidence

BMT = Bone Marrow Transplantation | OPM = Office of Personnel Management
Case Study #3: Bone Marrow Transplantation (BMT) for Breast Cancer
Timeline of Adoption

Throughout the 1980s and early/mid '90s, 2,000 - 4,000 a year women underwent BMT for breast cancer.
Timeline of Adoption

Throughout the 1980s and early/mid ‘90s, 2,000 - 4,000 a year women underwent BMT for breast cancer

3 of 4 randomized trials presented at ASCO annual meeting show no net benefit*

*Study that demonstrated a net benefit was later determined to be fraudulent and subsequently retracted
Case Study #3: Bone Marrow Transplantation (BMT) for Breast Cancer

Timeline of Adoption

Throughout the 1980s and early/mid ‘90s, 2,000 - 4,000 a year women underwent BMT for breast cancer

3 of 4 randomized trials presented at ASCO annual meeting show no net benefit*

1980s

1999

2002

Only 118 women receive BMT treatment, a 97% fall from its peak annual use

*Study that demonstrated a net benefit was later determined to be fraudulent and subsequently retracted
Case Study #3: Bone Marrow Transplantation (BMT) for Breast Cancer Influential Factors

Validity & Reliability of the Science

Ability to Apply Published Scientific Findings

Economic Drivers

Communication of the Science
Case Study #3: Bone Marrow Transplantation (BMT) for Breast Cancer Influential Factors

Validity & Reliability of the Science

Ability to Apply Published Scientific Findings

Economic Drivers

Communication of the Science
Implications

• This was an exploratory study with a limited sample
• However, it indicates that these conceptual factors may be useful to understanding and accelerating research translation
• Dissemination and translation may be improved by considering experiences with how and when past research was adopted
• Continued development of our proposed framework with additional case examination will further understanding in this area
• Federal support of CER through the Patient-Centered Outcomes Research Trust Fund will continue to grow and can benefit from this type of research
RWE Market Impact On Medicines: A Lens for Pharma
We are excited to share our views of the evolving availability and use of RWE

The white paper we are discussing today is part of our ongoing commitment to enabling pharmaceutical companies to leverage RWE effectively.
Lack of clarity on RWE impact: Nexium case study

- Prilosec becomes OTC
- AHRQ first CER review: PPIs equally effective (based on systematic review)
- UHC drops Nexium. Supports decision w/ RWE – “no statistically significant adverse impact, including ER and hospital visits” (claims analysis, 2006)
- Ripple effect to TriCare
- Wellpoint (BCBS GA): costly PPIs (including Nexium) to be excluded from coverage
- AZ claims analysis shows increased cost per patient following Switch from Nexium in a major health plan
- WellPoint’s Pharmacy and Therapeutics Committee (P&T) reassessed Nexium and approved it
- Additional support for esomeprazole 40 mg (non-RWE)?
- AHRQ CER Update: RWE focused on surgical evaluation and safety
  - Did not review (no peer review published) UHC and AZ analyses
- AZ publishes study
  - Used United Healthcare (Ingenix LabRx) data

Selected events and approximate timings

NPC Webinar: RWE Market Impact On Medicines • July 2013
Despite this increased attention paid to RWE, stakeholders are split on the value it brings to medicines

**Skeptics**

See RWE narrowly – supporting safety or mandatory submissions

**Evangelists**

See RWE as a broad lever to engage stakeholders
We wanted to inform the discussions with a fact base focused on ten key markets.

100+ Impacted Products in IMS Proprietary RWE Database

- Oncology: 42%
- Other Specialty: 27%
- Primary Care: 31%

>50 Discussions with payers, HTA experts and clients

- Canada
- Denmark
- France
- Italy
- Germany
- Netherlands
- Spain
- Sweden
- UK
- US
This enabled us to address misconceptions surrounding RWE

**MISCONCEPTIONS**

- Impact mainly pharmacovigilance (PV)
- Only payers set the RWE agenda
- Payers RWE agenda focused on cost containment
- RWE strategies have to be different in every country

**IMS VIEW**

- >100 non PV/Safety case studies observed
- Manufacturer-generated RWE influenced > 25% of observed decisions
- Payers want value, which can mean expanding use of medicines
- Four fundamental market archetypes can focus RWE strategy for pharma

NPC Webinar: RWE Market Impact On Medicines • July 2013
We started by assessing RWD supply in terms of data usefulness and access

- **USEFUL data** has extensive coverage, illustrates the full patient journey and has clinical depth and quality

- **ACCESSIBLE data** is available and transparent to all stakeholders

Bubble size indicates total journal publication output

NPC Webinar: RWE Market Impact On Medicines • July 2013
Case study breadth and volume demonstrate existing RWE demand

Number of case studies

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<th>UK</th>
<th>Sweden</th>
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NPC Webinar: RWE Market Impact On Medicines • July 2013

Focus for today
We quantified each market’s supply and demand to enable us to compare countries.

**RWE assessment scale**

<table>
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<th>Supply</th>
<th>Demand</th>
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<td>Application</td>
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<td>Frameworks</td>
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We overweight demand to focus on where the evidence is actually applied or most likely to be used.
To date, no country exceeded a score of 11 out of 20

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Low scores indicate that RWE is either less available or more costly to generate, with less consistent or transparent use in decision-making.
The US has a strong commercial market for healthcare data covering a large section of the population.

**Data supply**

- **Usefulness**
  - Coverage
    - EMR penetration at 69% in primary care, but significantly lower in secondary care
    - Data covers large proportion of US population
    - Data sets likely to be further extended due to private and national investment
  - Depth, Linkage and Quality
    - Value enhanced by incorporation of selected clinical data such as lab values
    - Further non-traditional data types (e.g. purchasing and biobanks) expected to be integrated into the date
    - Substantial RWE research output

- **Access**
  - Data readily available from many private vendors and payers

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The US demand framework is highly limited by stakeholder fragmentation and associated differing attitudes and approaches.

**Demand Frameworks**

- **USA**
  - Highly variable amongst fragmented stakeholder base
  - Landscape comprises leaders, followers and non-engagers

- **Evaluation**
  - No national framework or HTA body, use varies by payer
  - CER using RWE (e.g., AHRQ reviews) focus on non-pharmaceutical interventions

- **Measurement**
  - National quality indicators (HEDIS) limited for prescribing (as in most countries)

- **Dissemination**
  - Limited by restrictions on directly communicating RWE study results to physicians
Application in the US is limited by payer preference for their own RWE data and its usage for high budget impact areas only

**Application**

- High frequency of RWE application (21 case studies identified with only Italy showing more case studies at 22)
- Frequency limited as RWE is application is focused on high budget impact areas (primary care and oncology)

**Volume**

- Medium variety as 4 out of 5 types of application were identified (A price specific application is missing)
- Distribution skewed towards “Ongoing Access”: 13 out of 21 cases

**Variety**

- Impact limited by fragmentation of RWE application given that payers have a strong preference for their own rather than competitor data

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What does this mean for pharma’s RWE strategy?
Four clusters of markets have emerged
What could you do differently

- Develop evidence platforms and tools that support multiple internal stakeholders
- Develop a differentiated engagement approach

What excellence looks like

- All relevant datasets in oncology
- Developed different internal customer tools to exploit datasets
- Produced multiple peer-reviewed publications
- Improved sales forecasting accuracy
Example of excellence: Novartis’s VERO (integrated Datamart for MS)

A number of different data sources are being linked via one backbone

This integrated data mart has already yielded a number of studies

Evidence is being actively disseminated and used to inform decisions

Pharmacy Data

Insurance Claims Data

Hospital Data

EMR Data

Integration Backbone

RCT Data

Observational Study Data

PRO Data

Standardised reports and dashboards of real world market and disease trends

Outcomes Publications

Exploratory analysis / hypothesis generation

Company internal dissemination of RWE generation capabilities and result metrics to inform business decisions

Proactive and nuanced external dissemination of study results (conferences, scientific papers, scientific exchange)
What excellence looks like

**Explorers**
- Manufacturer developed a high quality evidence platform in France
- No access to payer data, but to EMR and MoH datasets
- Manufacturer partnered with commercial vendors to optimize data usage
- Now gathering supplementary data to develop reference cohort

**Pioneers**
- Manufacturer developed a mobile (iPad) evidence platform to support a drug launch in the UK
- Used RCTs and RWD sources to build models of prescribing patterns, cost and outcomes for GPs
- Trained sales representatives to use RWD in detailing visits

**Laggards**
- Dialogue with regional stakeholders
- A clear value proposition
- Local RWE capabilities
Thank you very much for participating!

Suggested Further Reading

Questions, Thoughts, Ideas?

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Marla Kessler
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Thank You

• The webinar will be archived and posted on NPC’s website in coming days.

• For further information, contact:
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