Welcome to....
The 7th Annual Meeting of ISMPP

Anticipating Change in Medical Publications: Leading Now for the Future
The Evolving Landscape for Health Economics and Outcomes Research: Implications for Medical Publications Professionals

Alan Lyles, ScD, MPH, RPh

Henry A. Rosenberg Professor of Public, Private and Nonprofit Partnerships, University of Baltimore
Docent, University of Helsinki

AlanLyles@comcast.net
Why Are Health Economics & Outcomes Research Needed?

(1) The evolution of comparative effectiveness research & the Patient Centered Outcomes Research Institute’s (PCORI's) potential impact on medical publications,

(2) A vision for the future of medical publications in a market-driven health care system, and

(3) Core competencies for medical publications professionals in this new world.
“The right context is worth 50 IQ points.”

- Alan Kay

Inventor of Object Oriented Programming

Visionary: Laptop Computer
<table>
<thead>
<tr>
<th>%</th>
<th>USA</th>
<th>China</th>
<th>Russian Federation</th>
<th>Finland</th>
<th>Germany</th>
<th>Canada</th>
<th>UK</th>
<th>France</th>
</tr>
</thead>
<tbody>
<tr>
<td>Life Expectancy at Birth (2008)</td>
<td>78</td>
<td>74</td>
<td>68</td>
<td>80</td>
<td>80</td>
<td>81</td>
<td>80</td>
<td>81</td>
</tr>
<tr>
<td>Health expenditures as % GDP</td>
<td>15.7</td>
<td>4.3</td>
<td>5.4</td>
<td>8.2</td>
<td>10.4</td>
<td>10.1</td>
<td>8.4</td>
<td>11.0</td>
</tr>
<tr>
<td>Government expenditures as % Health expenditures</td>
<td>45.5</td>
<td>44.7</td>
<td>64.2</td>
<td>74.6</td>
<td>76.9</td>
<td>70.0</td>
<td>81.7</td>
<td>79.0</td>
</tr>
<tr>
<td>Private expenditures as % Health expenditures</td>
<td>54.5</td>
<td>55.3</td>
<td>35.8</td>
<td>25.4</td>
<td>23.1</td>
<td>30.0</td>
<td>18.3</td>
<td>21.0</td>
</tr>
<tr>
<td>Government health exp as % All Government expenditures</td>
<td>19.5</td>
<td>9.9</td>
<td>10.2</td>
<td>12.9</td>
<td>18.2</td>
<td>18.1</td>
<td>15.6</td>
<td>16.6</td>
</tr>
</tbody>
</table>

Distribution of National Prescription Drug Expenditures by Source of Payment, 1998-2008

Notes: Percentages may not total 100% due to rounding.

National Health Care Expenditure Cost Components, United States, 1960-2005

# USA National Health Expenditures & Sources of Funds 1966-2006

Source: Centers for Medicare & Medicaid Services, Office of the Actuary: Data from the National Health Statistics Group.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total ($USD B)</td>
<td>2,106</td>
<td>1,069</td>
<td>0.471</td>
<td>0.152</td>
<td>0.046</td>
</tr>
<tr>
<td>Per Capita ($USD)</td>
<td>7,026</td>
<td>3,938</td>
<td>1,932</td>
<td>687</td>
<td>230</td>
</tr>
<tr>
<td>Private (%)</td>
<td>54</td>
<td>54</td>
<td>59</td>
<td>58</td>
<td>70</td>
</tr>
<tr>
<td>Public (%)</td>
<td>46</td>
<td>46</td>
<td>41</td>
<td>41</td>
<td>30</td>
</tr>
<tr>
<td>Federal (%)</td>
<td>33</td>
<td>33</td>
<td>28</td>
<td>28</td>
<td>16</td>
</tr>
<tr>
<td>State &amp; Local (%)</td>
<td>13</td>
<td>13</td>
<td>13</td>
<td>13</td>
<td>14</td>
</tr>
</tbody>
</table>
Persons Enrolled in HMOs, 1976 through 1997

Source 1: The data for 1976 through 1985 are for June of the year specified; those for 1986 through 1991 are for December. Data are from Hoy et al and Group Health Association of America, with the permission of the publisher.

Generic Prescriptions as a Percentage of the U.S. Pharmaceutical Market


Drugs expected to come off-patent 2005-2006:
http://www.gphaonline.org/AM/Template.cfm?Section=Resources1&CONTENTID=1597&TEMPLATE=/CM/HTMLDisplay.cfm
Figure 1. Evolution of Pharmaceutical Product Communications and Prescribing Decisions

A. Before Rx Insurance

- Patients
  - Physicians
    - Pharmaceutical Manufacturers

B. After Managed Care

- Patients
  - Physicians
    - Pharmacy and Therapeutics Committee
      - Pharmaceutical Manufacturers

Frequency of Economic Impact Studies

Number of Studies

Year


* Devices and procedures
** Education, behavior, other

*  Devices and procedures
**  Education, behavior, other
Pharmacoeconomics

“… identifies, measures, and compares the costs and consequences of pharmaceutical products and services.”

---

Distribution is statistically different from distribution for the previous year shown (p<.05).

‡ No statistical tests are conducted between 2003 and 2004 or between 2006 and 2007 due to the addition of a new category.

Note: Fourth-tier drug cost sharing information was not obtained prior to 2004.

Changing Patterns of Pharmaceutical Innovation*


- 65% used active ingredients previously approved
- 35% New Molecular Entities (NMEs)
  - 58% Standard Drugs (No significant clinical improvement)
  - 42% Priority drugs (Provide Clinical Improvement)

\[\sum = 153 \text{ (15\%)} \text{ used new active ingredients & represented significant clinical improvement}*\]

PUSHING PILLS
How Big Pharma Got Addicted To Marketing

ALSO
THE MYSTERIOUS LBO POWERHOUSE
INDIA'S NEW OIL MONEY
Pharmacoeconomics (an Alternate Definition)

“… a pseudodiscipline … conjured into existence by the magic of money.”

- Evans RG.

Underutilization of Recommended Services: How Effective Can Pharmaceuticals Be in Usual Community Practice?

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of Indicators</th>
<th>No. of Participants Eligible</th>
<th>Total No. of Times Indicator Eligibility Was Met</th>
<th>Percentage of Recommended Care Received (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall care</td>
<td>439</td>
<td>6712</td>
<td>98,649</td>
<td>54.9 (54.3–55.5)</td>
</tr>
<tr>
<td>Type of care</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preventive</td>
<td>38</td>
<td>6711</td>
<td>55,268</td>
<td>54.9 (54.2–55.6)</td>
</tr>
<tr>
<td>Acute</td>
<td>153</td>
<td>2318</td>
<td>19,815</td>
<td>53.5 (52.0–55.0)</td>
</tr>
<tr>
<td>Chronic</td>
<td>248</td>
<td>3387</td>
<td>23,566</td>
<td>56.1 (55.0–57.3)</td>
</tr>
<tr>
<td>Function</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Screening</td>
<td>41</td>
<td>6711</td>
<td>39,486</td>
<td>52.2 (51.3–53.2)</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>178</td>
<td>6217</td>
<td>29,679</td>
<td>55.7 (54.5–56.8)</td>
</tr>
<tr>
<td>Treatment</td>
<td>173</td>
<td>6707</td>
<td>23,019</td>
<td>57.5 (56.5–58.4)</td>
</tr>
<tr>
<td>Follow-up</td>
<td>47</td>
<td>2413</td>
<td>6,465</td>
<td>58.5 (56.6–60.4)</td>
</tr>
</tbody>
</table>
Medical Guesswork
From heart surgery to prostate care, the medical industry knows little about which treatments really work
BY JOHN CAREY (P. 72)
Concentration of Health Spending in the Total U.S. and Family Populations, 2002*

Source: Kaiser Family Foundation. Trends and Indicators, 2005 Update, Exhibit 1.11.
Geographic Variation in Medicare Drug Spending*

Zhang Y, Baicker K and Newhouse JP. NEJM 2010;

Figure 1. Quintiles of Adjusted Annual Drug Spending per Beneficiary, According to Hospital-Referral Region.
Definition:
Comparative Effectiveness Research (CER)

CER is the generation and synthesis of evidence that compares the benefits and harms of alternative methods to prevent, diagnose, treat, and monitor a clinical condition or to improve the delivery of care.

The purpose of CER is to assist consumers, clinicians, purchasers, and policy makers to make informed decisions that will improve health care at both the individual and population levels.

Comparative Effectiveness: What Can It Do?

Major Outcomes in High-Risk Hypertensive Patients Randomized to Angiotensin-Converting Enzyme Inhibitor or Calcium Channel Blocker vs Diuretic
The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT)

JAMA 2002;288:2981-2997
Context  Antihypertensive therapy is well established to reduce hypertension-related morbidity and mortality, but the optimal first-step therapy is unknown.

Objective  To determine whether treatment with a calcium channel blocker or an angiotensin-converting enzyme inhibitor lowers the incidence of coronary heart disease (CHD) or other cardiovascular disease (CVD) events vs treatment with a diuretic.

Design  The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), a randomized, double-blind, active-controlled clinical trial conducted from February 1994 through March 2002.

Setting and Participants  A total of 33,357 participants aged 55 years or older with hypertension and at least 1 other CHD risk factor from 623 North American centers.

Interventions  Participants were randomly assigned to receive chlorthalidone, 12.5 to 25 mg/d (n=15255); amloidipine, 2.5 to 10 mg/d (n=9048); or lisinopril, 10 to 40 mg/d (n=9054) for planned follow-up of approximately 4 to 8 years.

Main Outcome Measures  The primary outcome was combined fatal CHD or non-fatal myocardial infarction, analyzed by intent-to-treat. Secondary outcomes were all-cause mortality, stroke, combined CHD (primary outcome, coronary revascularization, or angina with hospitalization), and combined CVD (combined CHD, stroke, treated angina without hospitalization, heart failure [HF], and peripheral arterial disease).

Results  Mean follow-up was 4.9 years. The primary outcome occurred in 2956 participants, with no difference between treatments. Compared with chlorthalidone (6-year rate, 11.5%), the relative risks (RRs) were 0.98 (95% CI, 0.90-1.07) for amloidipine (6-year rate, 11.3%) and 0.99 (95% CI, 0.91-1.08) for lisinopril (6-year rate, 11.4%). Likewise, all-cause mortality did not differ between groups. Five-year systolic blood pressures were significantly higher in the amloidipine (0.8 mm Hg, P=.03) and lisinopril (2 mm Hg, P<.001) groups compared with chlorthalidone, and 5-year diastolic blood pressure was significantly lower with amloidipine (0.8 mm Hg, P<.001). For amloidipine vs chlorthalidone, secondary outcomes were similar except for a higher 6-year rate of HF with amloidipine (10.2% vs 7.7%; RR, 1.38; 95% CI, 1.25-1.52). For lisinopril vs chlorthalidone, lisinopril had higher 6-year rates of combined CVD (33.3% vs 30.9%; RR, 1.10; 95% CI, 1.05-1.16); stroke (6.3% vs 5.6%; RR, 1.15; 95% CI, 1.02-1.30); and HF (8.7% vs 7.7%; RR, 1.19; 95% CI, 1.07-1.31).

Conclusion  Thiazide-type diuretics are superior in preventing 1 or more major forms of CVD and are less expensive. They should be preferred for first-step antihypertensive therapy.

JAMA. 2002;288:2981-2997  www.jama.com
## Comparative Effectiveness Research & US Health Care Reform

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>CER under AHRQ</td>
<td>CER under Federal Coordinating Council</td>
<td>Creates a <strong>new</strong> Public-Private entity</td>
<td>CER under AHRQ</td>
<td>CER under AHRQ</td>
<td>Existing policies &amp; Process for COI</td>
<td>New Public-Private entity (Patient-Centered Outcomes Research Institute)</td>
</tr>
<tr>
<td>IOM Determine Funding Priorities</td>
<td>Governing Board (15) 3 from industry</td>
<td>Peer Review decides actions</td>
<td>Governing Board (19) incl: <em>private payers, pharm’, device, &amp; diagnostic manufacturer</em> s &amp; developers</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Patient Centered Outcomes Research Institute
(PCORI http://www.pcori.org/aboutus.html)

The purpose of the Institute is to assist patients, clinicians, purchasers, and policy-makers in making informed health decisions by advancing the quality and relevance of evidence … through research and evidence synthesis that considers variations in patient subpopulations,

…

identifying effective strategies for organizing, financing, or delivering public health services in real world community settings, including comparing State and local health department structures and systems in terms of effectiveness and cost.

The purpose of the Institute is the dissemination of research findings with respect to the relative health outcomes, clinical effectiveness, and appropriateness of the medical treatments, services, ...
Prohibited:

- Insurance coverage decisions/recommendations
- Producing clinical practice guidelines
- Developing or using metrics that provide a value threshold (QALYs)

Principles

- Transparency
- Public-Private entity, i.e., non-governmental
- 21 member board: broad stakeholder representation
- Stable funding
- Priority setting
- Methodology committee

*Sources: Patient Protection and Affordable Care Act of 2010. PL 111-148, sec. 6301
Part II

1) The evolution of comparative effectiveness research & the Patient Centered Outcomes Research Institute’s (PCORI's) potential impact on medical publications,

2) A vision for the future of medical publications in a market-driven health care system, and

3) Core competencies for medical publications professionals in this new world.
Four Principles of Comparative Effectiveness Analyses*

1) “Real-world” setting: usual community practice, with placebo comparators generally not an option

2) **Representative populations**: less restrictive than RCTs

3) Personalized health care: **Patient-specific & preferences**

4) **Full information**: multiple outcomes, particularly patient concerns such as AEs, side effect risks

ePublishing & Beyond

- Comparative effectiveness results (PCORI) will support improved private sector cost effectiveness analysis (Garber & Sox, 2010)

**Futuristic, but is the future now?**

- Actual real-time global readership
- Rapid TAT, with no page limit(s)
- Peer Reviewed Communications > text alone
- Post-publication review (Rennie & Luft, 2000)
- Social media (pending FDA guidance)
- Comprehensive publication strategies
- Richer metrics than Impact Factor alone

Part III

1) The evolution of comparative effectiveness research & the Patient Centered Outcomes Research Institute’s (PCORI's) potential impact on medical publications,

2) A vision for the future of medical publications in a market-driven health care system, and

(3) Core competencies for medical publications professionals in this new world.
Medical Publication Professionals’ Competencies: More Than Health Economics

Core Competencies

- RCT and pragmatic clinical trials
- Phase IV (post-marketing) methodologies
- Pharmacovigilance
- Health economics’ core concepts
- Quantitative reasoning & modeling concepts
- Personalized medicine
Medical Publication Professionals’ Competencies: More Than Health Economics

Professional Practice

• Good Research for Comparative Effectiveness (GRACE) Principles ¹
• Systematic reviews per PRISMA (http://www.prisma-statement.org/) ²
• Process and hierarchy of evidence-based practice
• Guidelines for Good Pharmacoepidemiologic Practices ³
• ICMJE Uniform Disclosure Form for Potential COI (JAMA 2010)
• Cochrane Risk Bias Tool (Lundh & Gøtzsche)⁴
• ISPOR’s Health Economic Publication Guidelines Task Force
  (http://www.ispor.org/taskforces/EconomicPubGuidelines.asp)

Medical Publication Professionals’ Competencies: More Than Health Economics

**Critical Competitive Edge:** General systems thinking that integrates clinical, economic, humanistic and policy considerations for feasible recommendations.
Survival and Success

“In our view, the companies that will survive and thrive in this new environment will be those that embrace comparative effectiveness research (CER) as the next logical step in the progression of requiring evidence and recognize it as a necessary input for a value-driven healthcare system.”*

Welcome to….
The 7th Annual Meeting of ISMPP

Anticipating Change in Medical Publications:
Leading Now for the Future
SUPPLEMENTAL MATERIAL
Filibuster & Cloture: United States Senate

Filibuster: Informal term … any attempt to block or delay Senate action on a bill … by offering numerous procedural motions, or by any other delaying or obstructive actions.

Cloture: The only procedure by which the Senate can vote to place a time limit on consideration of a bill … and overcome a filibuster.

Under the cloture rule (Rule XXII), the Senate may limit consideration of a pending matter to 30 additional hours, but only by vote of three-fifths of the full Senate, normally 60 votes.

Senate Action on Cloture Motions
(Source: United States Senate http://www.senate.gov/pagelayout/reference/cloture_motions/clotureCounts.htm )

Motions Filed
Votes on Cloture
Cloture Invoked
Patient Centered Outcomes Research Institute (PCORI [http://www.pcori.org/aboutus.html])

PCORI Governing Board
[http://www.gao.gov/about/hcac/patientcentered_outcomes.html]
Outcomes Variation from Efficacy to Effectiveness of Pharmacotherapy (OVERxTx©):
A Post-Marketing Systems Perspective

A diagnostic search for gaps, discontinuities, conflicts and/or redundancies.
November 15th, 1941
On the cusp of change

---

### TAMAQUA MEDICAL SOCIETY

**FEE SCHEDULE**

Effective November 15, 1941

<table>
<thead>
<tr>
<th>Service</th>
<th>Fee</th>
</tr>
</thead>
<tbody>
<tr>
<td>Office Consultation — Minimum</td>
<td>$1.50</td>
</tr>
<tr>
<td>Extra Charge for Medicine</td>
<td></td>
</tr>
<tr>
<td>First Surgical Office Visit — Minimum</td>
<td>$3.00</td>
</tr>
<tr>
<td>Subsequent Dressings</td>
<td>$2.00</td>
</tr>
<tr>
<td>Pre-Marital Health Examination</td>
<td>$6.00—$11.00</td>
</tr>
<tr>
<td>Health Certificate</td>
<td>$1.00</td>
</tr>
<tr>
<td>Home Visit — Town 8 A.M. to 9 P.M.</td>
<td>$3.00</td>
</tr>
<tr>
<td>Home Visit — Town 9 P.M. to 12 Midnight</td>
<td>$4.00</td>
</tr>
<tr>
<td>Home Visit — Town 12 Midnight to 8 A.M.</td>
<td>$5.00</td>
</tr>
<tr>
<td>Home Visit — Requested during Office Hours</td>
<td>$4.00</td>
</tr>
</tbody>
</table>

This Schedule does not apply to Services rendered on
Sundays and Holidays.
Money Flow in The Pharmaceutical Distribution Chain*

*Source: CMS, Office of Research, Development & Information
Cost of Drug Development

Cost ~ $500 - $800 million to develop a drug

Why is it so expensive?

• Average length of time is 15 years
• Cost of capital for R&D
• Companies are exposed to a lot of risks and uncertainties

Tufts Center for the Study of Drug Development:
http://csdd.tufts.edu/InfoServices/Publications.asp

by Sean D. Sullivan, Alan Lyles, Bryan Luce, and Joseph Grigar

A Private Sector, Demand Driven Approach
Annual Meeting, San Diego October 2000

Public-Private Arrangements

• “Any arrangement between government and the private sector in which partially or traditionally public activities are performed by the private sector.” (Savas, 2004)

• Distinguished from *Outsourcing* and *Privatization*, Public Private Partnerships are long term

• Accountability implications (Forrer, et al. 2010)

### Public-Private Partnerships in Healthcare: Complementary Circumstances

<table>
<thead>
<tr>
<th>Public Sector</th>
<th>Private Sector</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ Safety net</td>
<td>+ Innovation</td>
</tr>
<tr>
<td>+ Standards &amp; Enforcement</td>
<td>+ Payment Systems</td>
</tr>
<tr>
<td>+ Collective societal goods</td>
<td>+ Efficiency</td>
</tr>
<tr>
<td>+ Managing COI</td>
<td>+ Insurance options</td>
</tr>
<tr>
<td>- Innovation</td>
<td>- Medically Uninsurable</td>
</tr>
<tr>
<td>- Payment Systems</td>
<td>- Setting standards</td>
</tr>
<tr>
<td>- Productivity</td>
<td>- Enforcement / Accountability</td>
</tr>
<tr>
<td>- Options &gt; basic insurance</td>
<td>- Limited Funds</td>
</tr>
<tr>
<td>- Limited Funds</td>
<td>- Limited Funds</td>
</tr>
</tbody>
</table>

**Source:** Morlock LL, Waters HR, **Lyles A**, Ozsari H, and Aktulay G. Health Care Reform in Turkey – Charting the Way Forward. The Turkish Industrialists’ and Businessmen’s Association (TÜSIAD). August 31, 2004.
Comparative Effectiveness: MMA (2003) Section 1013

• authorizes the Agency for Healthcare Research and Quality (AHRQ) to conduct research, demonstrations, and evaluations designed to improve the quality, effectiveness, and efficiency of Medicare, Medicaid, and the State Children's Health Insurance Program (SCHIP)

• The goals of Section 1013 are:
  To develop valid evidence about the comparative effectiveness of different treatments and appropriate clinical approaches to difficult health problems. To make the information easily accessible and understandable to decisionmakers.

Source: Agency for Healthcare Research and Quality (AHRQ)
http://effectivehealthcare.ahrq.gov/aboutUs/faq.cfm
Welcome to....
The 7th Annual Meeting of ISMPP

Anticipating Change in Medical Publications:
Leading Now for the Future