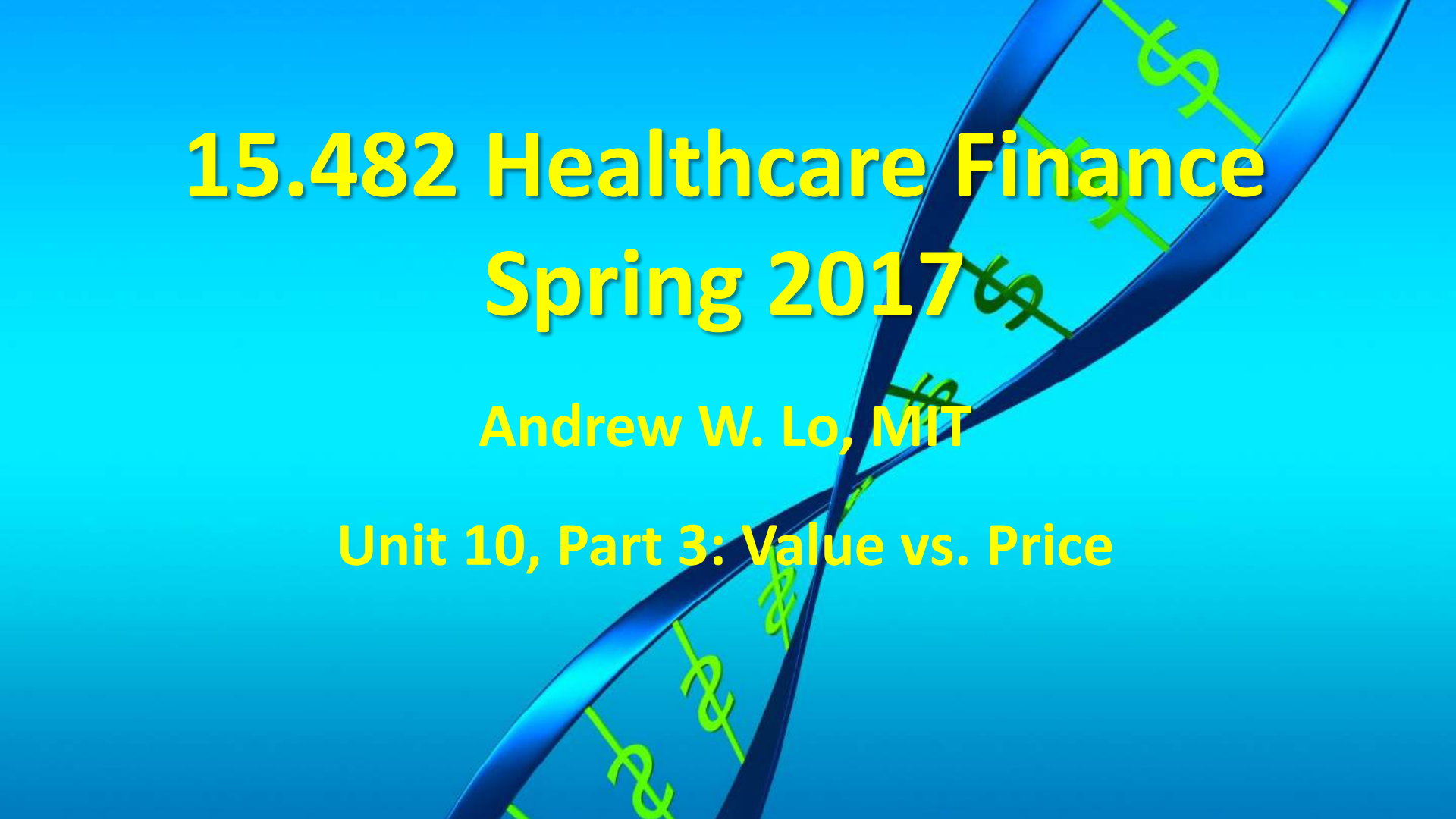
15.482 Healthcare Finance
Spring 2017

Andrew W. Lo, MIT

Unit 10, Part 3: Value vs. Price



Unit Outline

- Pricing
- Ethics
- Pricing Issues for Cancer Drugs
- Price vs. Value
- Questcor Pharmaceuticals

Value vs. Price

Why Is Medicine Different?

- Consumers are not the decision makers
- Doctors have no incentive to manage costs (Hippocratic oath)
- Life-and-death issues mean that economic analysis is not the only thing that matters—policymakers must be involved ("your money or your life?")
- Complexity reduces transparency (multi-payer system, regulation, international market, etc.)

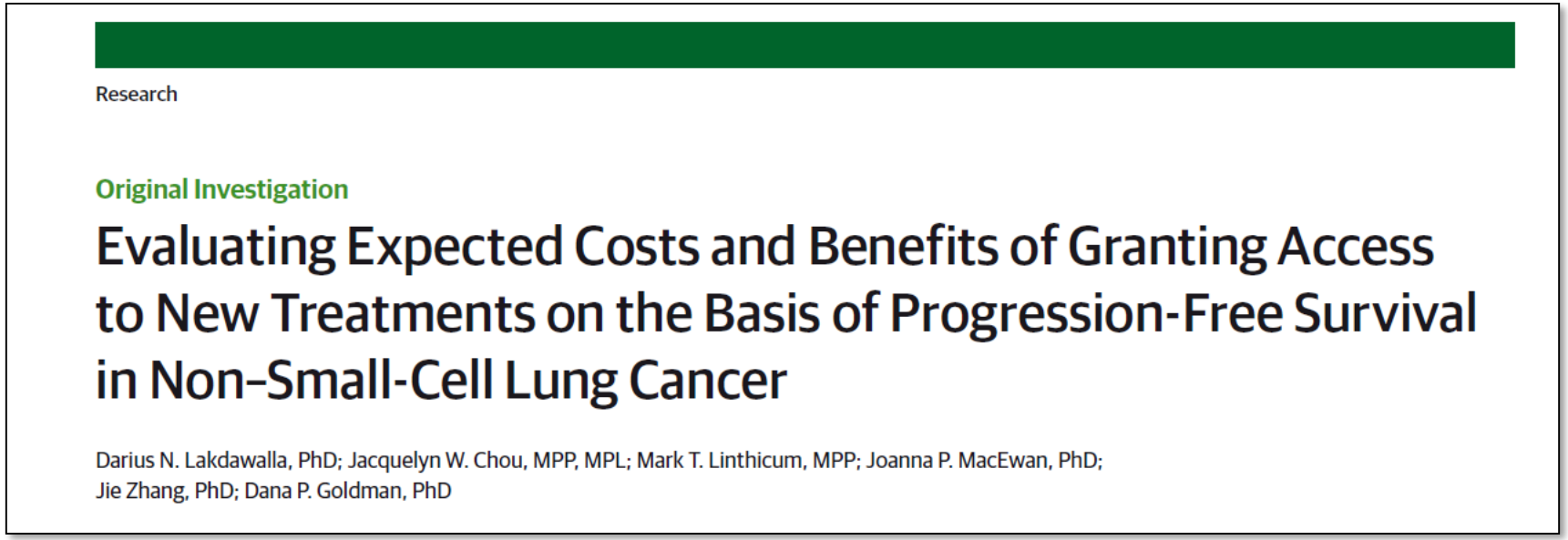
Why Not Create "Consumer Reports"?

- Measure "quality adjusted life years" (QALYs) for each new drug and pay according to value
- "Cost effectiveness" or "cost/benefit" studies
- "Value-based pricing"
- "Health technology assessment"
- "Pharmacoeconomics"

$$\text{ICER} \equiv \frac{\Delta\text{Cost}}{\Delta\text{Health}} = \frac{\text{Cost}_{\text{new}} - \text{Cost}_{\text{old}}}{\text{Health}_{\text{new}} - \text{Health}_{\text{old}}}$$

Sensible, But Ultimately Leads To Saying "No" To Certain Drugs (and Patients)

Cost/Benefit Analysis



Research

Original Investigation

Evaluating Expected Costs and Benefits of Granting Access to New Treatments on the Basis of Progression-Free Survival in Non–Small-Cell Lung Cancer

Darius N. Lakdawalla, PhD; Jacquelyn W. Chou, MPP, MPL; Mark T. Linthicum, MPP; Joanna P. MacEwan, PhD; Jie Zhang, PhD; Dana P. Goldman, PhD

Cost/Benefit Analysis

OBJECTIVE To present a framework for evaluating the expected net benefit or cost of providing early access to new treatments on the basis of evidence of PFS benefits before OS results are available, using non–small-cell lung cancer (NSCLC) as an example.

DESIGN, SETTING, AND PARTICIPANTS A probabilistic decision model was used to estimate expected incremental social value of the decision to grant access to a new treatment on the basis of PFS evidence. The model analyzed a hypothetical population of patients with NSCLC who could be treated during the period between PFS and OS evidence publication. Estimates for delay in publication of OS evidence following publication of PFS evidence, expected OS benefit given PFS benefit, incremental cost of new treatment, and other parameters were drawn from the literature on treatment of NSCLC.

Cost/Benefit Analysis

RESULTS For "medium-value" model parameters, early reimbursement of drugs with any PFS benefit yields an incremental social cost of more than $170 000 per newly treated patient per month. In contrast, granting early access on the basis of PFS benefit between 1 and 3.5 months produces more than $73 000 in incremental social value. Across the full range of model parameter values, granting access for drugs with PFS benefit between 3 and 3.5 months is robustly beneficial, generating incremental social value ranging from $38 000 to more than $1 million per newly treated patient per month, whereas access for all drugs with any PFS benefit is usually not beneficial.

CONCLUSIONS AND RELEVANCE The value of providing access to new treatments on the basis of surrogate end points, and PFS in particular, likely varies considerably. Payers and clinicians should carefully consider how to use PFS data in balancing potential benefits against costs in each particular disease.

But This Is Not A Perfect Science

Health Affairs, 27, no.6 (2008):1577-1586

COST-EFFECTIVENESS

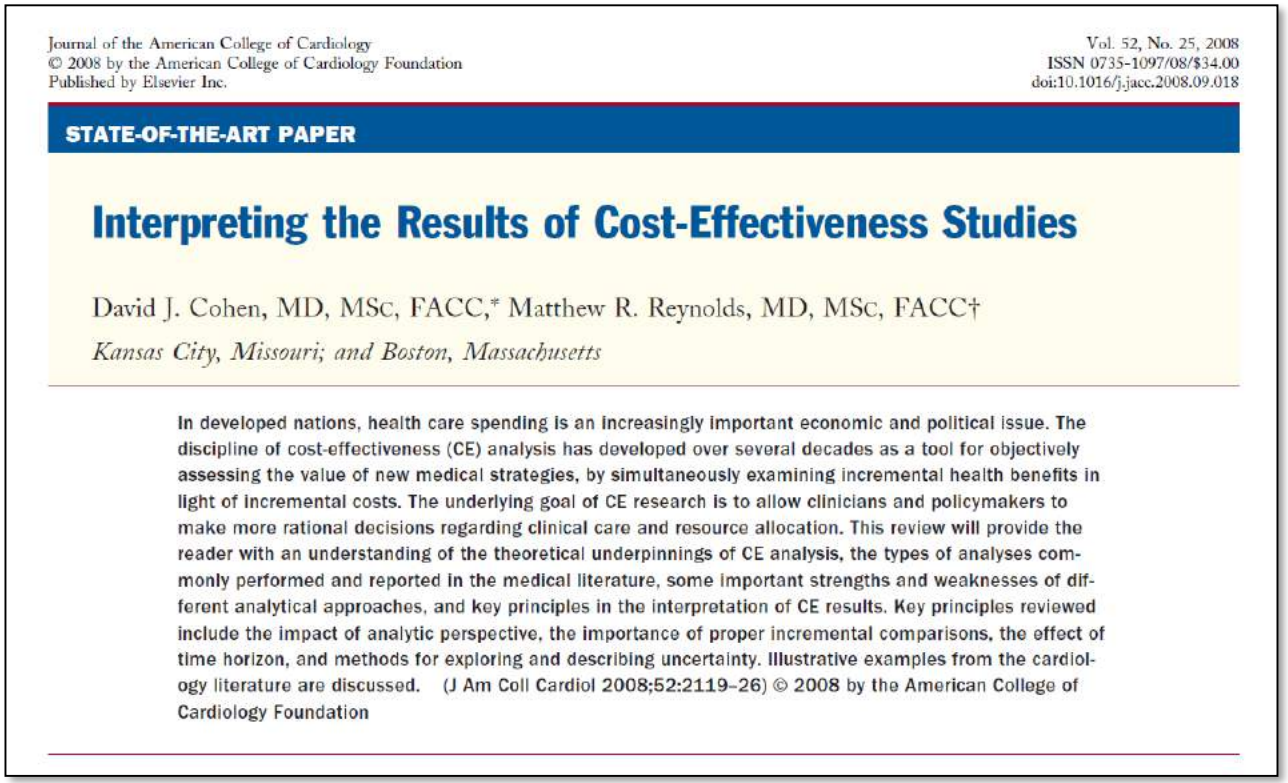
The Appropriate Role Of Cost-Effectiveness In Determining Device Coverage: A Case Study Of Drug-Eluting Stents

Cost-effectiveness analysis is not in itself sufficient for making major policy decisions.

by Brian Garriock Firth, Liesl M. Cooper, and Steve Fearn

ABSTRACT: The use of incremental cost-effectiveness ratios based on quality-adjusted life-years (QALYs) as a critical determinant of what should be covered by a health system is a growing trend. This presents challenges when applied to rapidly evolving technologies. The case study here focuses on the example of drug-eluting stents and the four-year change in cost-effectiveness as determined by the U.K. National Institute for Health and Clinical Excellence (NICE). We contend that classic cost-effectiveness as a blunt instrument for determining what should be covered may lead to erroneous conclusions when a broader perspective and the impact on health outcomes and costs are considered. [*Health Affairs* 27, no. 6 (2008): 1577–1586; 10.1377/hlthaff.27.6.1577]

But This Is Not A Perfect Science



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doi:10.1016/j.jacc.2008.09.018

STATE-OF-THE-ART PAPER

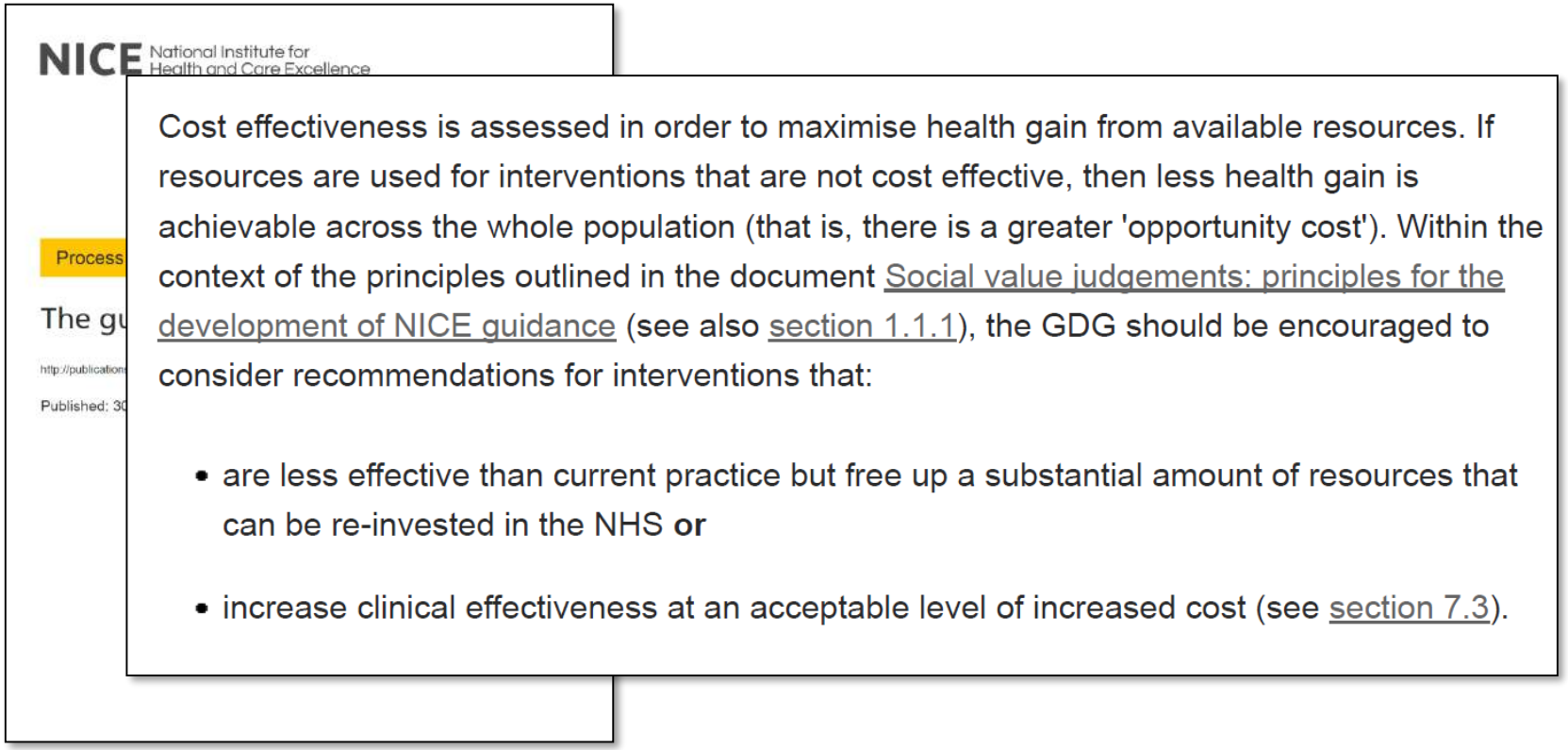
Interpreting the Results of Cost-Effectiveness Studies

David J. Cohen, MD, MSc, FACC,* Matthew R. Reynolds, MD, MSc, FACC†

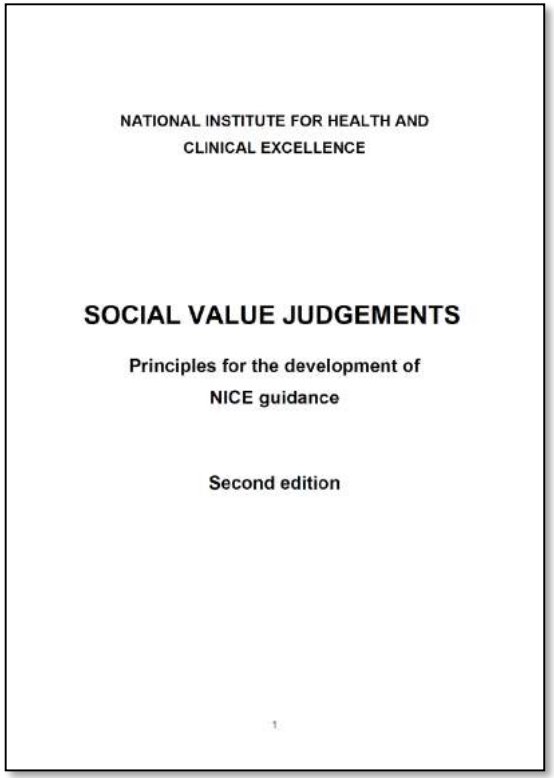
Kansas City, Missouri; and Boston, Massachusetts

In developed nations, health care spending is an increasingly important economic and political issue. The discipline of cost-effectiveness (CE) analysis has developed over several decades as a tool for objectively assessing the value of new medical strategies, by simultaneously examining incremental health benefits in light of incremental costs. The underlying goal of CE research is to allow clinicians and policymakers to make more rational decisions regarding clinical care and resource allocation. This review will provide the reader with an understanding of the theoretical underpinnings of CE analysis, the types of analyses commonly performed and reported in the medical literature, some important strengths and weaknesses of different analytical approaches, and key principles in the interpretation of CE results. Key principles reviewed include the impact of analytic perspective, the importance of proper incremental comparisons, the effect of time horizon, and methods for exploring and describing uncertainty. Illustrative examples from the cardiology literature are discussed. (J Am Coll Cardiol 2008;52:2119–26) © 2008 by the American College of Cardiology Foundation

UK's NICE



UK's NICE



NATIONAL INSTITUTE FOR HEALTH AND
CLINICAL EXCELLENCE

SOCIAL VALUE JUDGEMENTS

Principles for the development of
NICE guidance

Second edition

1

UK's NICE

2.3 Procedural justice

Procedural justice provides for 'accountability for reasonableness'. For decision-makers to be 'accountable for their reasonableness,' the processes they use to make their decisions must have four characteristics [15]: publicity, relevance, challenge and revision, and regulation.

Publicity

Both the decisions made about limits on the allocation of resources, and the grounds for reaching them, must be made public.

Relevance

The grounds for reaching decisions must be ones that fair-minded people would agree are relevant in the particular context.

UK's NICE

Challenge and revision

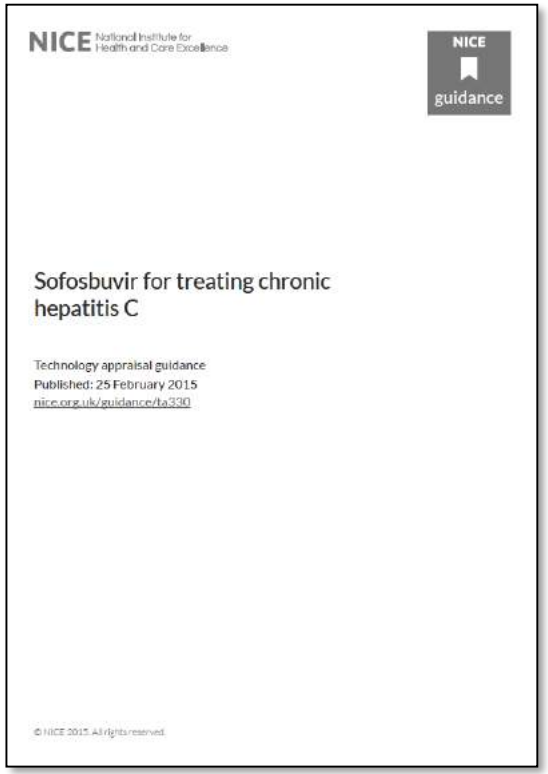
There must be opportunities for challenging decisions that are unreasonable, that are reached through improper procedures, or that exceed the proper powers of the decision-maker. There must be mechanisms for resolving disputes; and transparent systems should be available for revising decisions if more evidence becomes available.

Regulation

There should be either voluntary or public regulation of the decision-making process to ensure that it possesses all three of the above characteristics.

It is particularly important for NICE to be 'accountable for its reasonableness' because it provides advice to the NHS. The NHS is funded from general taxation, and it is right that UK citizens have the opportunity to be involved in the decisions about how the NHS's limited resources should be allocated.

NICE Sovaldi Report


NICE National Institute for Health and Care Excellence

NICE guidance

Sofosbuvir for treating chronic hepatitis C

Technology appraisal guidance
Published: 25 February 2015
nice.org.uk/guidance/ta330

Table 1 Sofosbuvir for treating adults with chronic hepatitis C

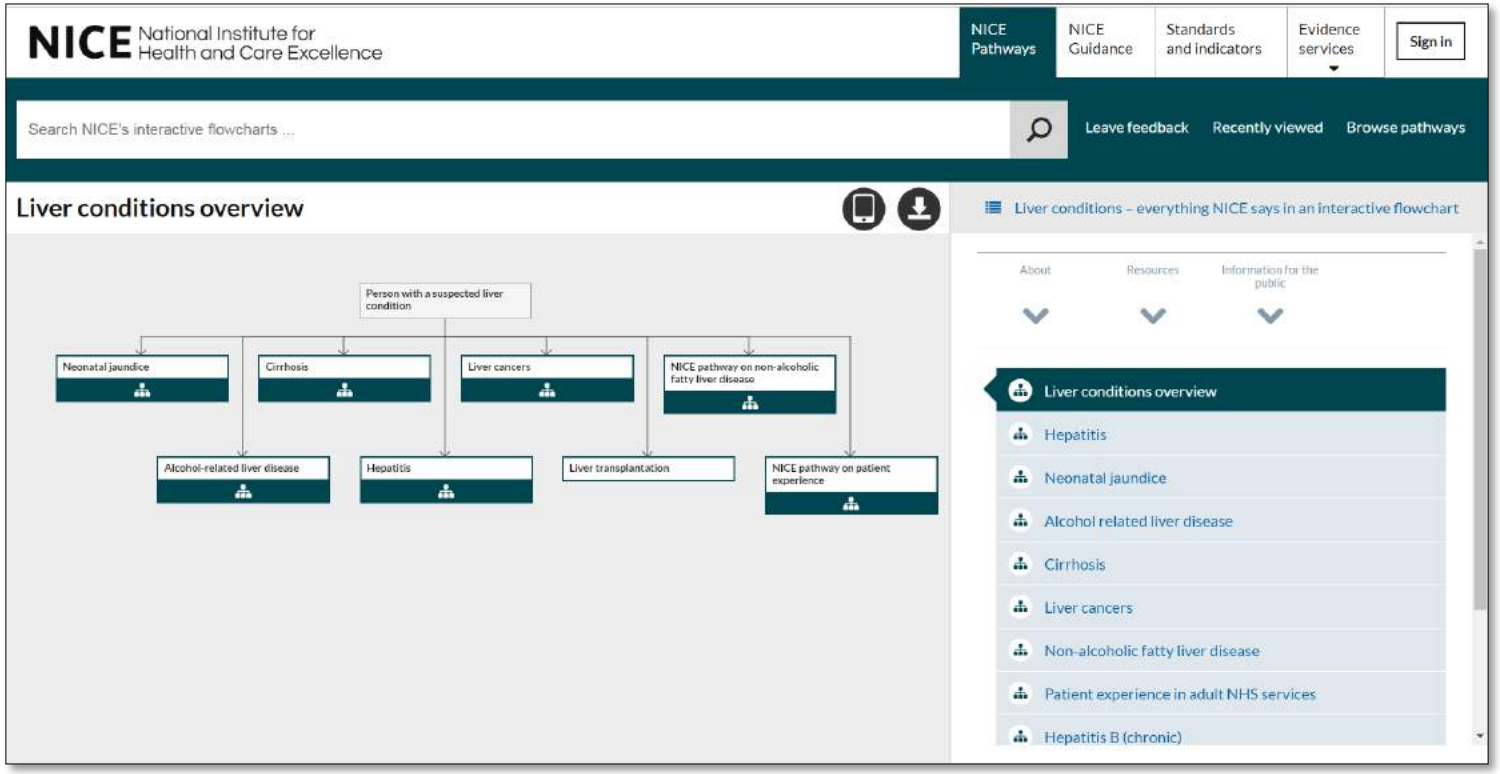
	Sofosbuvir in combination with peginterferon alfa and ribavirin		Sofosbuvir in combination with ribavirin	
Genotype	**Treatment history**	**Recommendation**	**Treatment history**	**Recommendation**
Adults with genotype 1 HCV	All	Recommended	All	Not recommended
Adults with genotype 2 HCV	All	Not licensed for this population	Treatment-naive	Only recommended for people who are intolerant to or ineligible for interferon
			Treatment-experienced	Recommended
Adults with genotype 3 HCV	Treatment-naive	Only recommended for people with cirrhosis	Treatment-naive	Only recommended for people with cirrhosis who are intolerant to or ineligible for interferon
	Treatment-experienced	Recommended	Treatment-experienced	Only recommended for people with cirrhosis who are intolerant to or ineligible for interferon
Adults with genotype 4, 5 or 6 HCV	All	Only recommended for people with cirrhosis	All	Not recommended

HCV – hepatitis C virus

Treatment-naive – the person has not had treatment for chronic hepatitis C

Treatment-experienced – the person's hepatitis C has not adequately responded to interferon-based treatment

NICE Sovaldi Report



NICE Says "No" To Kadcyla

NICE National Institute for Health and Care Excellence

1 Guidance

1.1 Trastuzumab emtansine is not recommended, within its marketing

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Breast cancer

Breast cancer drug rejected for NHS use on cost-benefit grounds

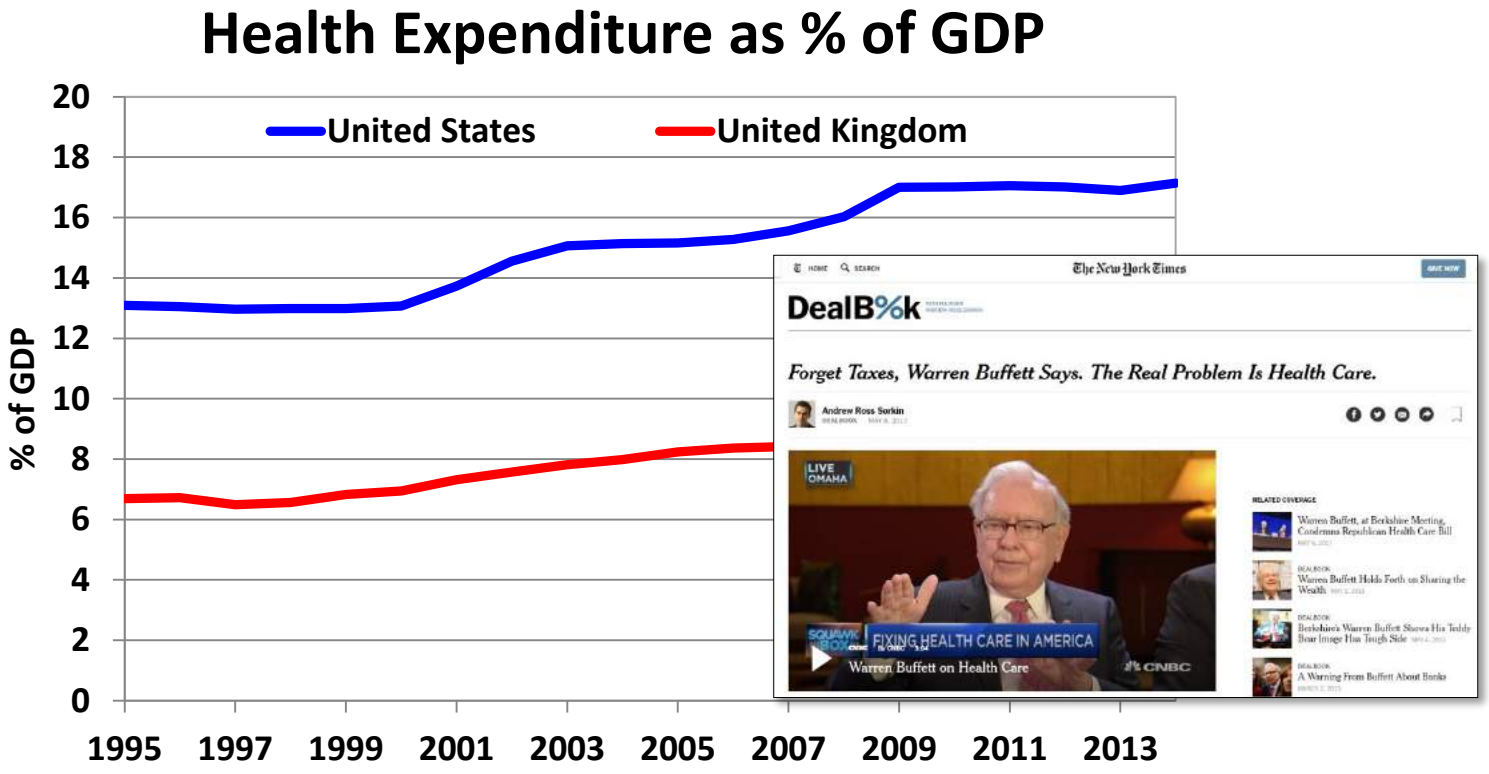
Charities angered by guidance on Kadcyla, which costs £90,000 per year per patient and gives extra nine months on average

Why Don't We Have NICE In the US?

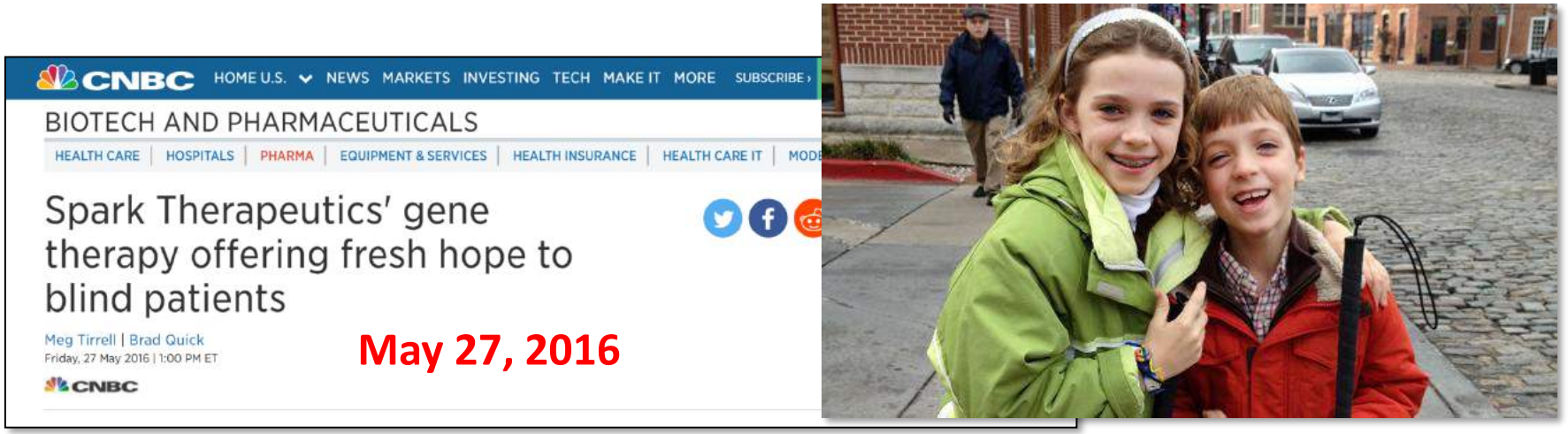
ICER
INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

The Institute for Clinical and Economic Review (ICER) is a non-profit organization that evaluates evidence on the value of medical tests, treatments and delivery system innovations and moves that evidence into action to improve the health care system. To accomplish this goal ICER performs analyses on effectiveness and costs; develops reports using innovative methods that make it easier to translate evidence into decisions; and, most distinctively, fills a critical gap by creating sustainable initiatives with all health care stakeholders to use evidence to drive improvements in both practice and policy. Through all its work, ICER seeks to play a pivotal role in creating a future in which collaborative efforts to move evidence into action provide a foundation for a more effective, efficient, and just health care system.

We Need A New Approach



We Need A New Approach



- How do we choose?
- **Who** do we choose?

"I went outside when it was snowing, and I was like, 'Oh! I can see the snowflakes!'" Caroline said. "It was really cool to actually see something that I've never seen in my life before."

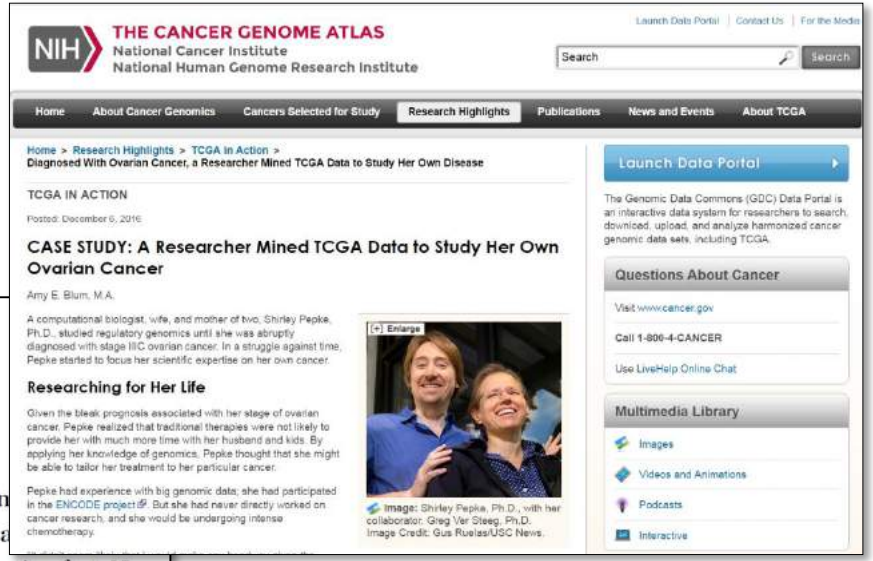
One Possibility

July 7, 2012

In Gene Sequencing Treatment for Leukemia, Glimpses of the Future

By GINA KOLATA

ST. LOUIS — Genetics researchers at Washington University, one of the world's leadin
work on the human genome, were devastated. Dr. Lukas Wartman, a young, talented a
colleague, had the very cancer he had devoted his career to studying. He was deteriorating fast. No known treatment could save him. And no one, to their knowledge, had ever investigated the complete genetic makeup of a cancer like his.



The Last Resort Clinic (LaRC)

- Focus exclusively on wealthy terminally ill cancer patients
- Take cases one at a time, 24/7/365 no-holds-barred effort
- Use every available means to save each life
  - DNAseq, RNAseq, ATACseq, ChIPseq, off-label medication, experimental therapies, high-throughput screening, etc.
- Hedge fund fee structure:
  - if successful (more than 2σ versus standard-of-care), pay 2.5% of your net worth; if unsuccessful, pay time and materials only
- Then make the therapy public-domain for other patients
- Where is this clinic?

CROWD INNOVATION LAB at HARVARD UNIVERSITY

MIT Laboratory for Financial Engineering

global cures

CancerCommons

Last Resort Clinic (LaRC) Working Group

Session 1: March 11, 2015

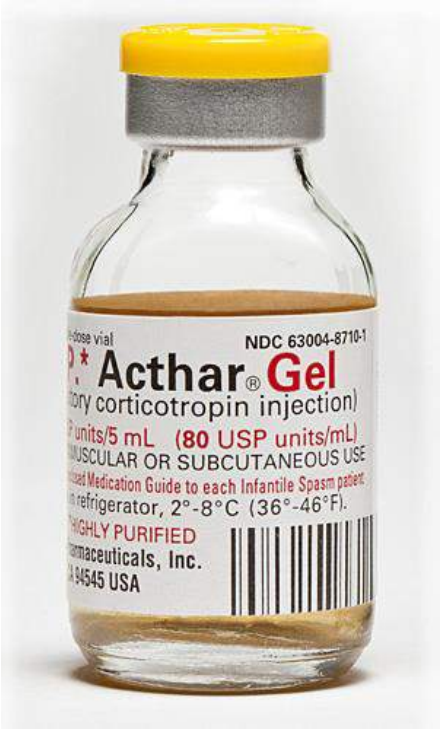
http://lastresortclinic.mit.edu

Pricing for Survival in the Biopharma Industry: Questcor Pharmaceuticals

(Burnham, Huang, and Lo, 2017)

Acthar Gel Is An Anti-Inflammatory Drug

- Adrenocorticotropic hormone (ACTH)
- Derived from purified pig pituitary glands
  - Manufacturing is protected trade secret to this day (**monopoly power)**
- Approved by the FDA in 1952 for 50 inflammatory diseases



Used Off-Label To Treat Infantile Spasms

- Severe form of epilepsy
- Impacts 2,000 infants per year
- Life-saving drug
- Without treatment: death or severe mental retardation

Acthar Pricing History

Questcor acquires Acthar

Above average price increases

Most controversial price hike

Below average price increases

Acthar Price over Time			
Year	Price Increase	Acthar Price ($USD)	Source
2000	N/A	50	(Pollack 2012)
2001	1300%	700	(Pollack 2012)
2002	26%	879	Approximated
2003	26%	1,104	
2004	17%	1,292	(10-K 2004)
2005	14%	1,473	(10-K 2005)
2006	12%	1,650	(10-K 2006)
2007	1310%	23,269	(10-K 2007)
2008	4%	24,153	
2009	4%	25,071	Approximated
2010	4%	26,024	
2011	4%	27,013	
2012	4%	28,000	(Pollack 2012)

Focus On Pricing


Harvard Business Review

POLICY

Price Gouging and the Dangerous New Breed of Pharma Companies

by A. Gordon Smith

JULY 06, 2016

"Questcor bought the rights to Acthar Gel [in 2001]…a company that did not contribute to the medicine's creation raised the **price of a vial from $50 to $23,000** [over 2001 to 2007]." **460X increase**

Focus On Pricing


WIRED GEAR SCIENCE ENTERTAINMENT BUSINESS SECURITY

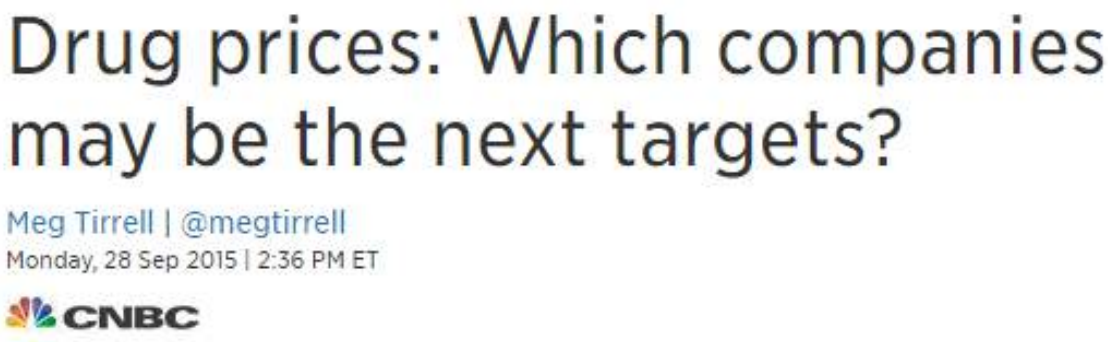
Drug Companies Get Healthy, but at Whose Expense?

By Russ Mitchell, Portfolio.Com 07.23.08

"The Joint Economic Committee will open hearings in Congress on dramatic price hikes for drugs used in children, with a focus on companies such as Questcor."

"Trevor would end up mentally retarded for life without treatment. His mother, Danielle, will join those who testify against companies like Questcor"

Focus On Pricing



Drug prices: Which companies may be the next targets?

Meg Tirrell | @megtirrell

Monday, 28 Sep 2015 | 2:36 PM ET

CNBC

"Bernstein analyst Ronny Gal pointed out many companies ratchet up drug prices when the market presents an opportunity."

"Gal pointed to three examples: Jazz Pharmaceuticals, Questcor, and Mylan"

A Different Narrative

- After 1980s, Acthar was extremely unprofitable at $50/vial

- Synthetic steroids replaced Acthar for most diseases except **Infantile Spasms**

A Different Narrative

- Companies did not want the responsibility of making Acthar
- Public health crisis in 1995 when **Rhone Poulenc Rorer** discontinued Acthar
- By 2001, its manufacture was in the process of discontinuation

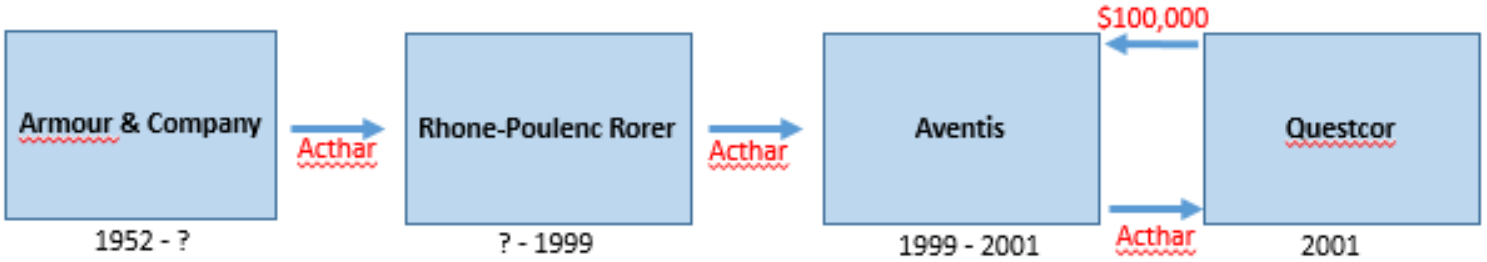


Figure 1: Acthar Ownership from 1950s to 2001

A Different Narrative

- Questcor acquired Acthar in 2001 yet struggled to stay afloat
- 2001 Acthar Price: $700
- 2005: $23.5M asset divestiture
- 2006: Questcor focused on Acthar
- 2006 Acthar Price: $1,650

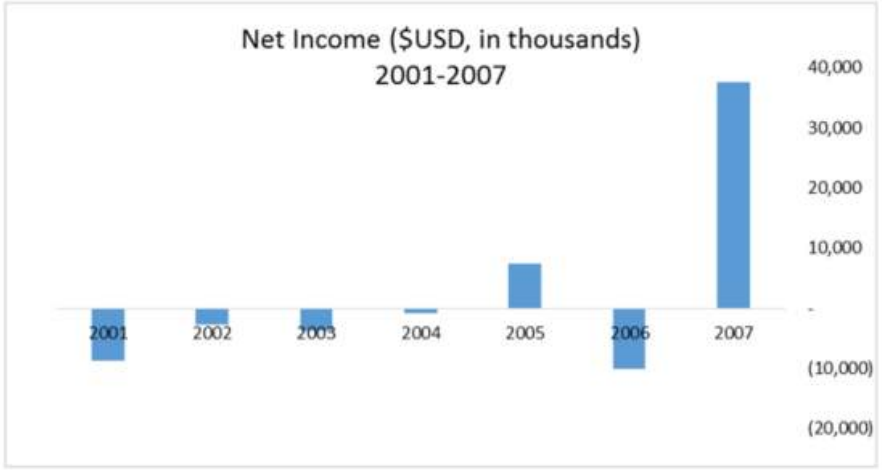


Figure 2. Questcor's net income leading up to 2007 when the price of Acthar was increased.

A Different Narrative

Questcor's Operational Challenges In 2006

Line Item	$ (000's)	% of Revenue
Revenue	$ 12,788	
COGS	$ 3,000	23%
SG&A	$ 17,282	135%
R&D	$ 3,033	24%
Net Income	$ (10,109)	

Figure 3: Key items from Questcor's 2006 income statement

A Different Narrative

- Acthar was not FDA-Approved for IS, even though it was the **standard of care** for the disease
- 2006 R&D costs preparing sNDA to get Acthar approved for Infantile Spasms: **$3M**
- SG&A costs trying to sell Acthar: **$17M**

A Different Narrative

- **Directly advertising drugs off-label is illegal**
- Marketing drugs for on-label indications
  - Sales teams can **initiate** discussions with doctors
- Marketing drugs for off-label indications
  - Sales teams of "medical science liaisons" can only respond to inquiries **from** doctors
- Generating Acthar prescriptions was difficult and expensive

A Different Narrative

Problematic For Patients

- Many neurologists unaware of Acthar's benefits for Infantile Spasms
- **No FDA-approved label/ guidelines**
  - Indications
  - Optimal Dosage
  - Administration
  - Contraindications
  - Safety

DOSAGE AND ADMINISTRATION

- In the treatment of infantile spasms, the recommended dose is 150 U/m^2 divided into twice daily intramuscular injections of 75 U/m^2. After 2 weeks of treatment, dosing should be gradually tapered and discontinued over a 2-week period. (2.1)

CONTRAINDICATIONS

- H.P. Acthar Gel should never be given intravenously.
- H.P. Acthar Gel is contraindicated in patients with scleroderma, osteoporosis, systemic fungal infections, ocular herpes simplex, recent surgery, history of or the presence of a peptic ulcer, congestive heart failure, uncontrolled hypertension, or sensitivity to proteins of porcine origin.
- Administration of live or live attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of H.P Acthar Gel.
- H.P. Acthar Gel is contraindicated in children under 2 years of age with suspected congenital infections. (4)
- Treatment of conditions listed within the INDICATIONS AND USAGE section is contraindicated when they are accompanied by primary adrenocortical insufficiency or adrenocortical hyperfunction. (4)

Figure 4: Sections of FDA-Approved Acthar Label from 2015
http://www.acthar.com/pdf/acthar-pi.pdf

A Different Narrative

Suppose You Are Questcor Senior Management in 2006

1. Acthar's revenues did not even pay for SG&A, let alone R&D
2. Your operations netted $10M in losses as a result
3. You have $18M cash left, with 1-2 years of run time
4. You aren't in a position to raise capital
5. Your sNDA submission to get Acthar FDA-approved for infantile spasms was rejected

What To Do??

A Different Narrative

Possible Actions:

1. Close down Questcor operations and stop manufacturing Acthar
2. Divest Acthar to another company
3. Raise the price to make the business sustainable

A Different Narrative

Questcor Increased Price From $1,650 to $23,000

- Higher cost burden on healthcare system, but at this price Acthar is a sustainable business, **ensuring continued availability**
- Expanded sponsorship and co-pay assistance programs
- Questcor was “not aware of a single patient” in need of Acthar without access, which was not the case prior to the strategy change (Questcor 10-K 2008).
- In 2010, Questcor finally achieved FDA-approval for infantile spasms

Conclusions

- An old drug can become “mispriced” due to evolving market conditions
- Profit motive can be aligned with patient benefit
- We must distinguish **unacceptable price-gouging behavior** from **legitimate business decisions** that benefit patients
- Health technology assessment may be helpful