A Vision for Large Simple Trials in Learning Health Care Systems

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Institute of Medicine
Large Simple Trials in a Learning Health Care System

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When I was a Teenager…

In 1976 Kodak claimed

90% film
85% cameras

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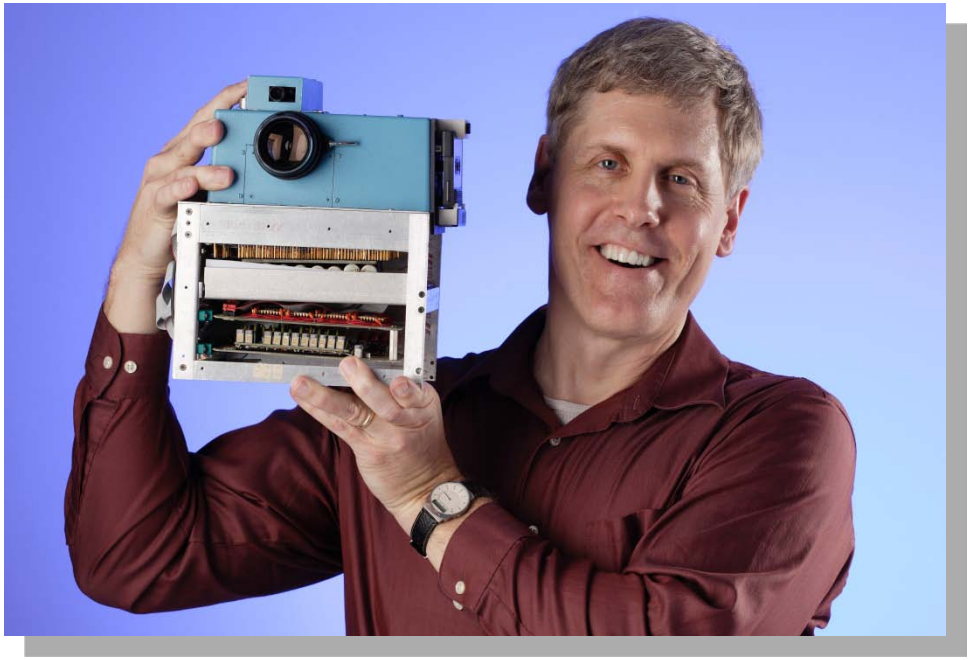
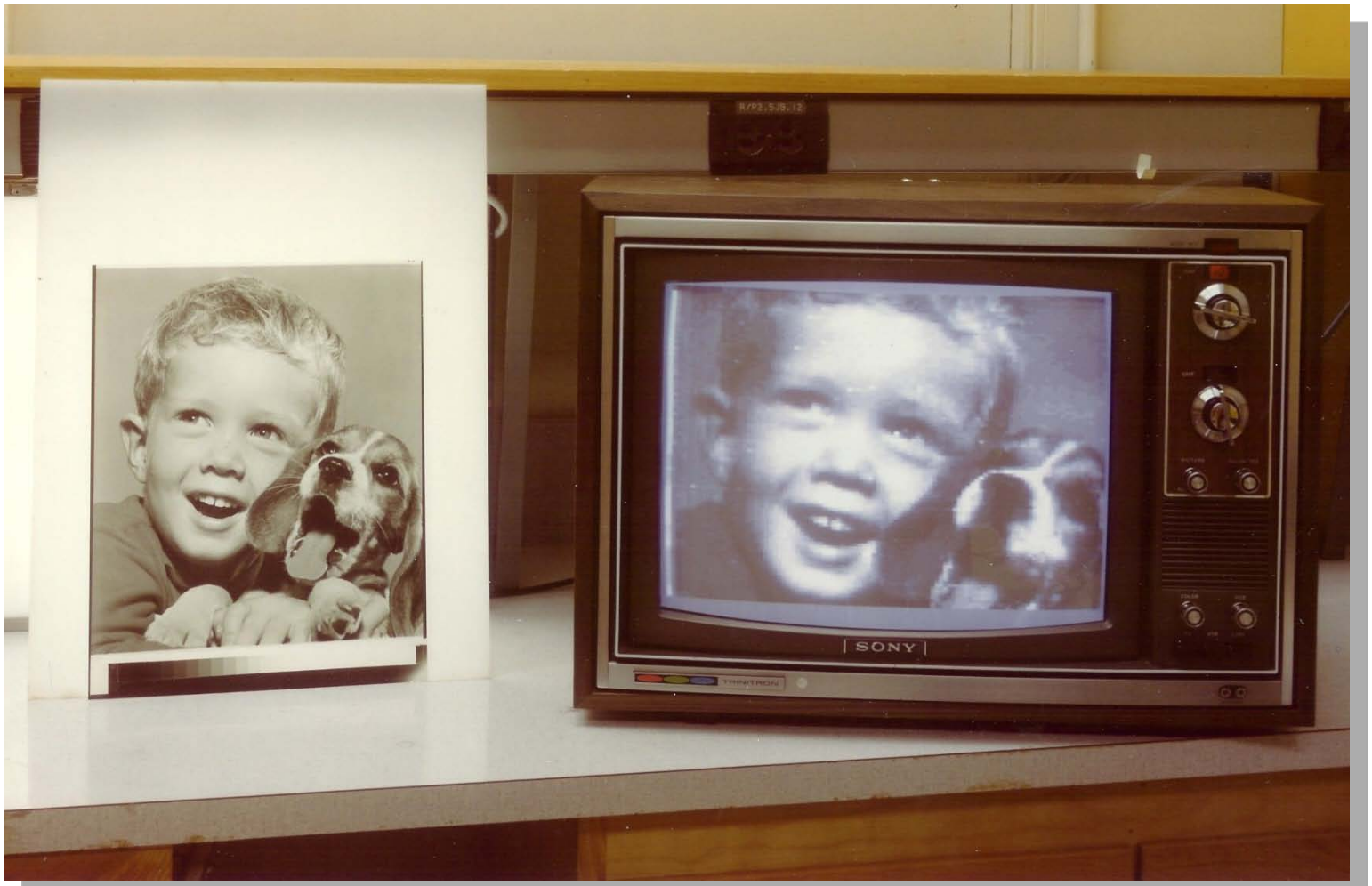
An Invention



“But it was filmless photography, so management’s reaction was, ‘That’s cute, but don’t tell anyone about it.’”

Steve Sasson, quoted in the *NY Times*, May 20, 2008

Obviously Inferior Technology



http://pluggedin.kodak.com/pluggedin/post/?id=687843

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And The Rest is …

http://www.forbes.com/sites/chunkamui/2012/01/18/how-kodak-failed/

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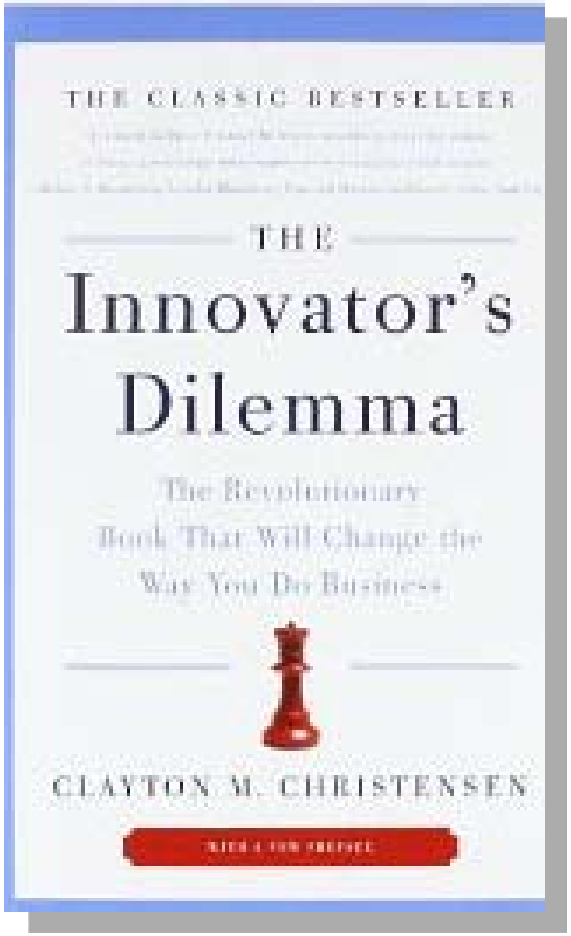
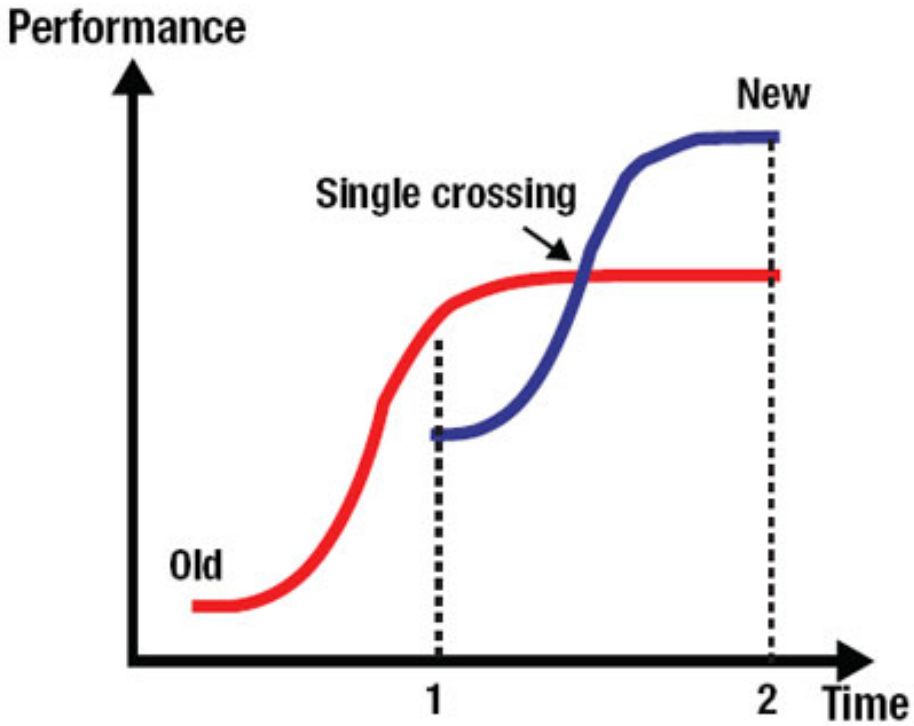
A Recurring Pattern





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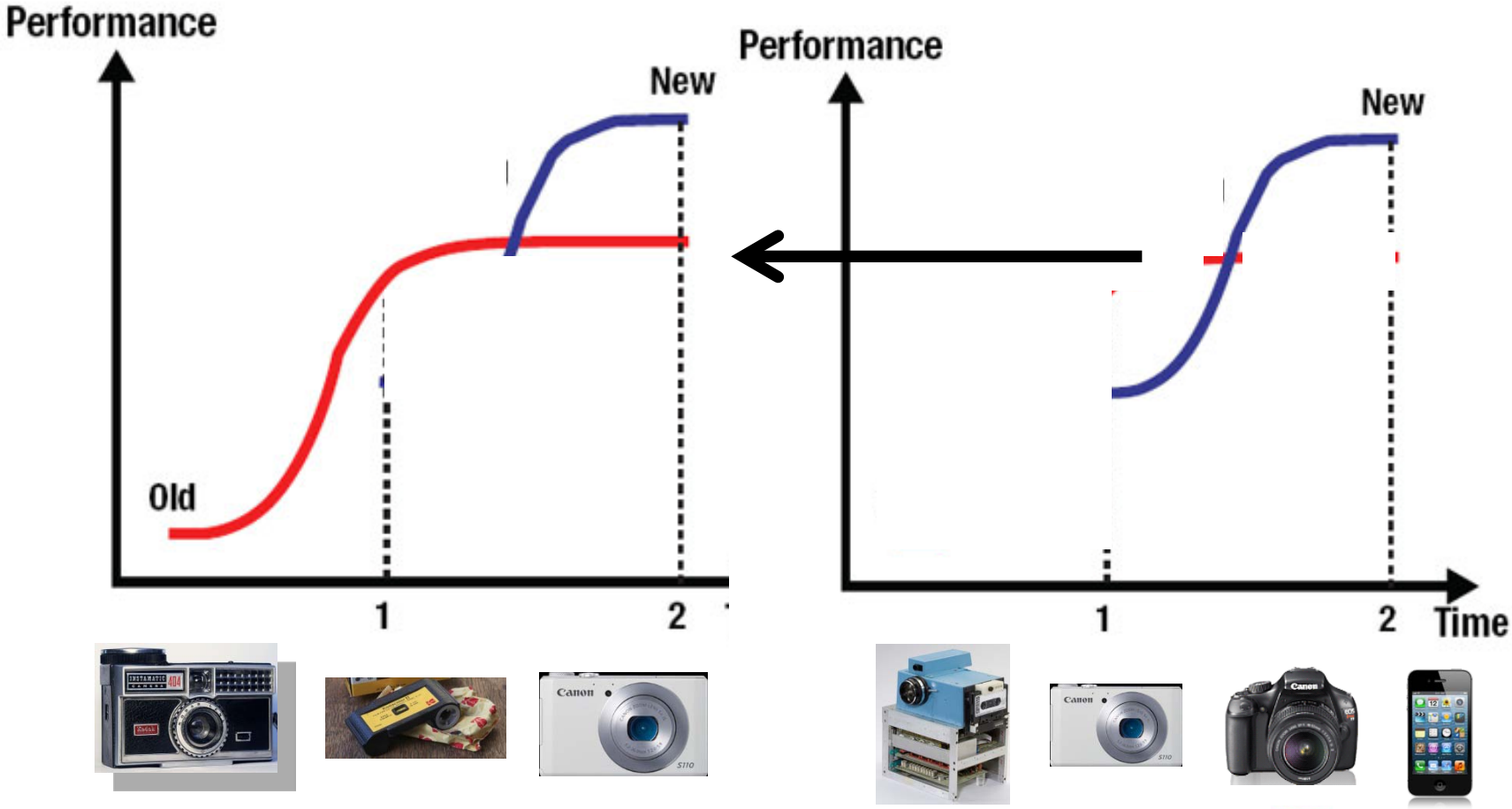
Enter the Disruptive Technology

Market A with Metric A

Market B with Metric B



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“Classic” Clinical Trial Business Model

Size

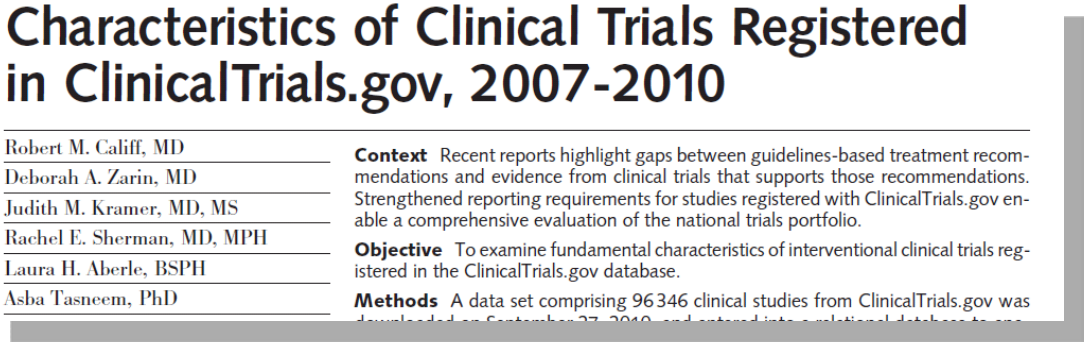
- Mostly small N
- Huge budgets

Endpoints

- Mostly surrogate
- Clinical trials employ adjudication

Setting

- Research enterprise – “parallel universe”
- “High-grade” data – audited, monitored



Characteristics of Clinical Trials Registered in ClinicalTrials.gov, 2007-2010

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Context Recent reports highlight gaps between guidelines-based treatment recommendations and evidence from clinical trials that supports those recommendations. Strengthened reporting requirements for studies registered with ClinicalTrials.gov enable a comprehensive evaluation of the national trials portfolio.

Objective To examine fundamental characteristics of interventional clinical trials registered in the ClinicalTrials.gov database.

Methods A data set comprising 96 346 clinical studies from ClinicalTrials.gov was

Califf RM et al. JAMA 2012;307:1838-47

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Looking Back at a Disruptive Technology

EFFECTIVENESS OF INTRAVENOUS THROMBOLYTIC TREATMENT IN ACUTE MYOCARDIAL INFARCTION

GRUPPO ITALIANO PER LO STUDIO DELLA STREPTOCHINASI NELL'INFARTO MIOCARDICO (GISSI)*

Summary In an unblinded trial of intravenous streptokinase (SK) in early acute myocardial infarction, 11 806 patients in one hundred and seventy-six coronary care units were enrolled over 17 months. Patients admitted within 12 h after the onset of symptoms and with no contraindications to SK were randomised to receive SK in addition to usual treatment and complete data were obtained in 11 712. At 21 days overall hospital mortality was 10·7% in SK recipients versus 13% in controls, an 18% reduction (p=0·0002, relative risk 0·81). The extent of the beneficial effect appears to be a function of time from onset of pain to SK infusion (relative risks 0·74, 0·80, 0·87, and 1·19 for the 0–3, 3–6, 6–9, and 9–12 h subgroups). SK seems to be a safe drug for routine administration in acute myocardial infarction.

The Lancet · Saturday 22 February 1986

"It started with no funding and skepticism in some quarters but today GISSI is recognized as an Italian achievement that has changed cardiology treatment worldwide."

http://eurheartj.oxfordjournals.org/content/31/9/1023.full

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More Disruptive Thoughts

Practical Clinical Trials

Increasing the Value of Clinical Research for Decision Making in Clinical and Health Policy

Sean R. Tunis, MD, MSc
Daniel B. Stryer, MD
Carolyn M. Clancy, MD

Decision makers in health care are increasingly interest
quality scientific evidence to support clinical and health po
ever, the quality of available scientific evidence is often

JAMA®

AHJ American Heart Journal

Thrombus Aspiration in ST-Elevation myocardial infarction in Scandinavia (TASTE trial). A multicenter, prospective, randomized, controlled clinical registry trial based on the Swedish angiography and angioplasty registry (SCAAR) platform. Study design and rationale

Ole Fröbert, MD, PhD,[a] Bo Lagerqvist, MD, PhD,[b] Thórarinn Gudnason, MD, PhD, FESC,[c] Leif Thuesen, MD, PhD,[d] Roger Svensson, MSci,[e] Göran K. Olivecrona, MD, PhD,[f] and Stefan K. James, MD, PhD[b] *Örebro, Uppsala and Lund, Sweden; Reykjavik, Iceland; and Aarhus, Denmark*

Tunis SR et al. JAMA 2003;290:1624-32
Frobert O et al. AHJ 2010;160:1042-8

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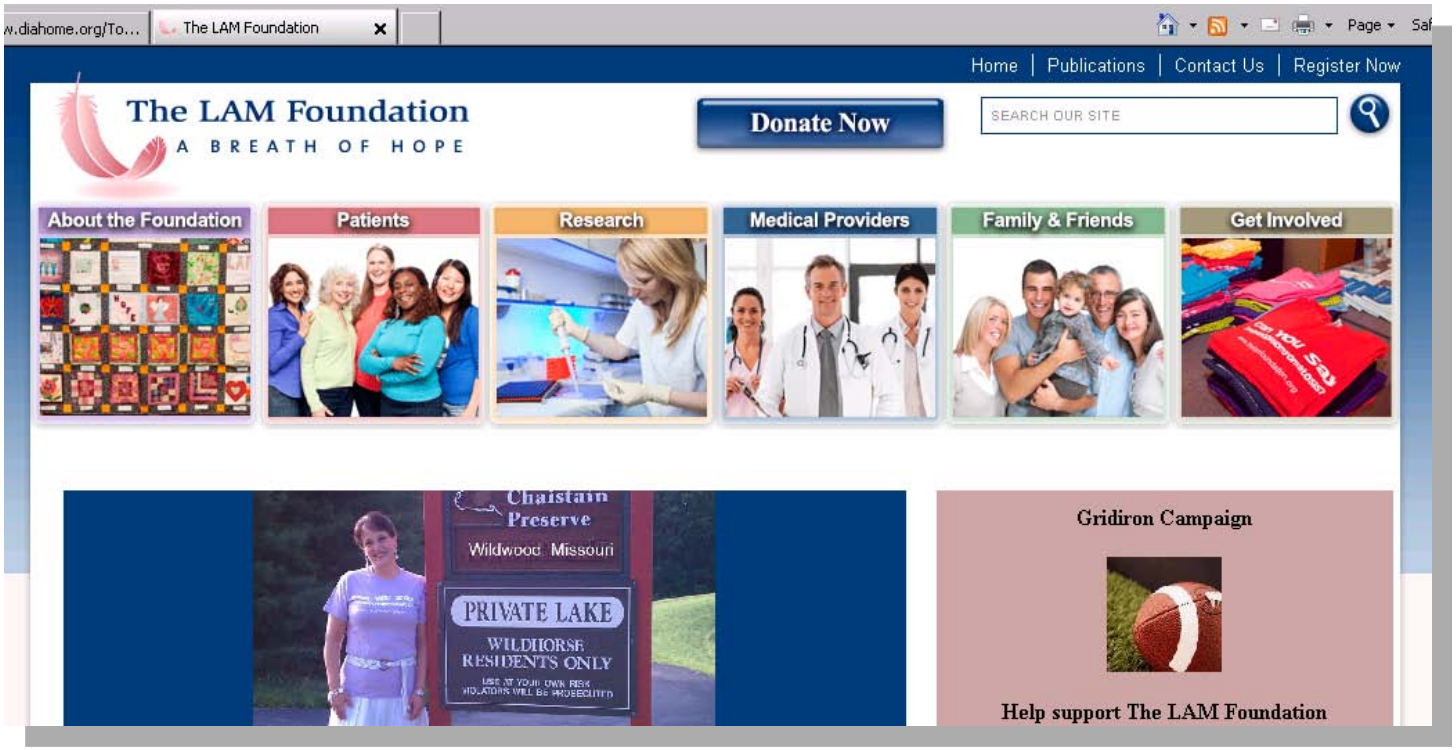
Another Disruptive Technology: Patients



"The LAM Foundation urgently seeks safe and effective treatments, and ultimately a cure, for LAM through **advocacy and the funding of promising research**. We are dedicated to serving the scientific, medical and patient communities by offering information, resources and a worldwide network of hope and support."

http://www.thelamfoundation.org/

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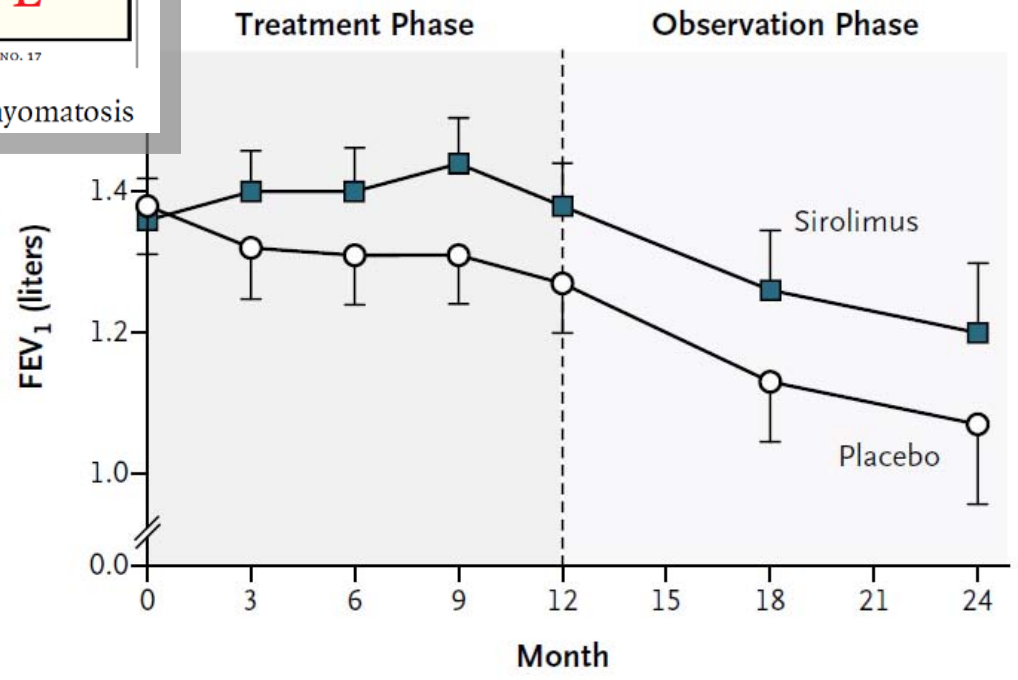
Lessons from a Rare Disease Trial

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 APRIL 28, 2011 VOL. 364 NO. 17

Efficacy and Safety of Sirolimus in Lymphangioleiomyomatosis

NIH Office of Rare Diseases
FDA
CIHR
Pfizer
Japanese MOH
LAM Foundation
Tuberous Sclerosis Alliance
Cincinnati Children's Hospital
Adler Foundation
NHLBI (DIR)



Improved QOL and functional performance (P=0.03 both)

McCormack FX et al. N Engl J Med 2011;364:1595-606

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“New” Models for Clinical Trials

Size – both bigger and smaller

- Huge N – robust estimates, heterogeneity
- Streamlined budgets – grows a bigger pie

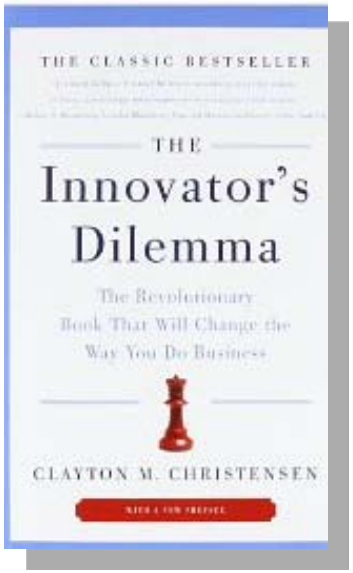
Endpoints – what really matters

- Patient-oriented with minimal adjudication

Setting – increasingly integrated world

- Within patient-care units and communities
- Leverage digital data sources
- ALL Patients as partners, not subjects

How to Approach Disruptive Technologies



Embed into existing projects

Create "small sub-organizations"

- Generate excitement
- Thrilled with "small wins"

Fail early, often, and inexpensively

Utilize resources, but not processes/values

Look for new markets, compete elsewhere

- Existing markets can mislead us

Christensen C. Harper Business 2000.

Final Thoughts

Back to the Future – trials that are

- Huge, simple, pragmatic, robust
- Inexpensive
- Integrated into medical care, public health

We look to you for disruptive approaches

- Digital revolution
- Integration of clinical medicine
- Appeals to different clinical trial “markets”
- Willingness to experiment and learn