

Some Perspectives on Trials, Pragmatic and Otherwise

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NIH Collaboratory Steering Committee Meeting

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Congressional Ballroom, Bethesda Marriott (Pooks Hill Road)

Disclosures: None



A Pragmatic Airline



The Best Breakfasts in America

PLUS
THE MOST
IMPORTANT
MEAL?
BREW
BETTER
COFFEE
THE
CELEBRITY
BREAKFAST
CLUB
SCRAMBLE
BETTER EGGS
BACON,
JUSTIFIED

And an unforgettable
tale about crab cakes

JANUARY 2016

Mission Unchanged

“... same Mission and Purpose as we did in 1971 – to deliver People where they want to go, safely, ontime, with their bag, and with a smile ... With low fares and no hidden fees.”

Gary Kelly
CEO

<http://swamedia.com/magazine>

Quantitative, Meaningful, Simple, and Transparent

- Where they want to go: % non-stops
- Safely: 0% major incidents
- On time: % of flights on time
- With their bag: % of checked bags lost
- With a smile: rate of complaints
- Low fares: comparable measure



“Recent performance in our clinical trials program is not acceptable: recruitment is too slow, registration in public databases is not consistent, and reporting takes too long to meet the needs of the public.”



Tom Insel

<http://www.nimh.nih.gov/about/director/2014/a-new-approach-to-clinical-trials.shtml>



A Personal Story Starts 4+ Years Ago...



EDITORIAL

A Threat to Medical Innovation

“The ... current situation ... is putting truly excellent laboratories out of business. In the spirit of ‘never waste a good crisis,’ a serious evaluation of ... NIH ... policies and programs is warranted. They include ... large collective funding efforts [like] ***expensive clinical and epidemiological research.***”


BMJ

BMJ 2011;344:d7292 doi: 10.1136/bmj.d7292 (Published 3 January 2012)

Page 1 of 10

RESEARCH

Publication of NIH funded trials registered in ClinicalTrials.gov: cross sectional analysis

 OPEN ACCESS

Joseph S Ross *assistant professor of medicine*^{1,2}, Tony Tse *program analyst at ClinicalTrials.gov*³, Deborah A Zarin *director of ClinicalTrials.gov*³, Hui Xu *postgraduate house staff trainee*⁴, Lei Zhou *postgraduate house staff trainee*⁴, Harlan M Krumholz *Harold H Hines Jr professor of medicine and professor of investigative medicine and of public health*^{2,5,6}



The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE

Publication of Trials Funded by the National Heart, Lung, and Blood Institute

David Gordon, M.D., Ph.D., Wendy Taddei-Peters, Ph.D., Alice Mascette, M.D.,
Melissa Antman, Ph.D., Peter G. Kaufmann, Ph.D., and Michael S. Lauer, M.D.

ABSTRACT

BACKGROUND

Rapid publication of clinical trials is essential in order for the findings to yield maximal benefits for public health and scientific progress. Factors affecting the speed of publication of the main results of government-funded trials have not been well characterized.

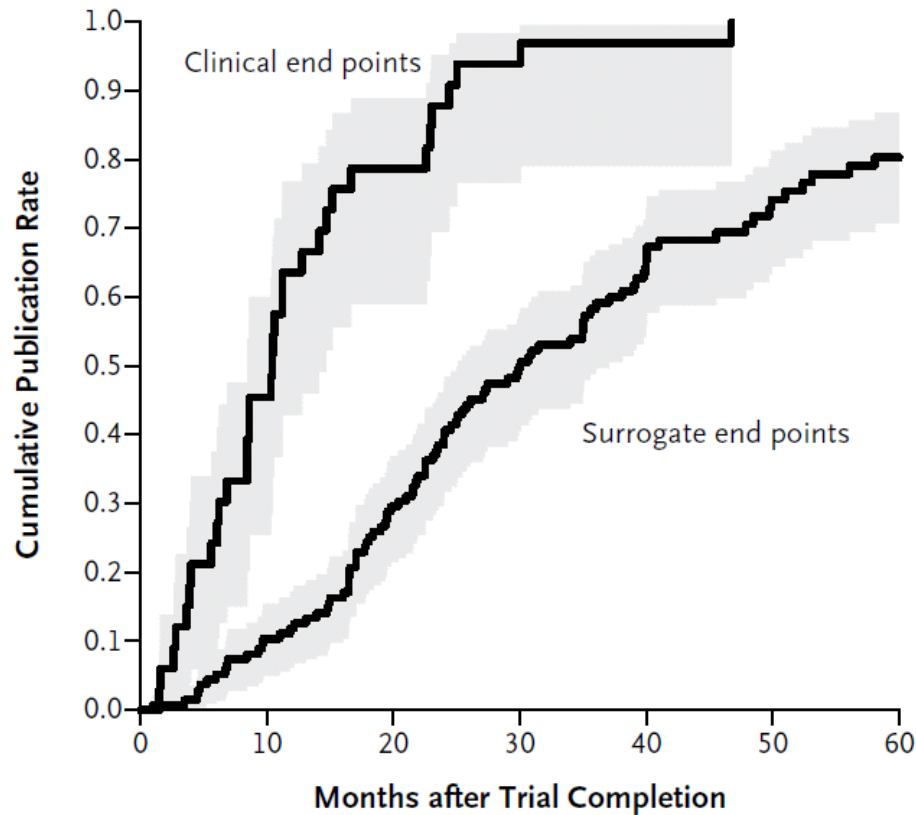
METHODS

We analyzed 244 extramural randomized clinical trials of cardiovascular interventions that were supported by the National Heart, Lung, and Blood Institute (NHLBI). We selected trials for which data collection had been completed between January 1, 2000, and December 31, 2011. Our primary outcome measure was the time between completion of the trial and publication of the main results in a peer-reviewed journal.



Confirmation ... With a Twist

Unadjusted rate ratio, 5.47 (95% CI, 3.74–7.98); P=0.001
 Adjusted rate ratio, 2.11 (95% CI, 1.26–3.53); P=0.004



No. at Risk

Surrogate end points	199	158	110	67	40	24	16
Clinical end points	45	22	7	2	1	0	0



When It Comes to Trials, Do We Get What We Pay For?

P.J. Devereaux, M.D., Ph.D., and Salim Yusuf, M.B., B.S., D.Phil.

Table 1. Barriers to Rapid Publication and Potential Solutions.

Barriers	Potential Solutions
Not enough large trials focused on clinical end points	Change in priorities of funders, an appreciation from review panels of the importance of such trials, and avoidance of inefficient and unimportant aspects of trial design

Barrier: Not enough large trials focused on clinical endpoints.

Solutions: Change priorities of funders; appreciation from review panels; avoidance of inefficient and unimportant aspects of trial design.

Reporting Takes Too Long ...

Publication and reporting of clinical trial results: cross sectional analysis across academic medical centers

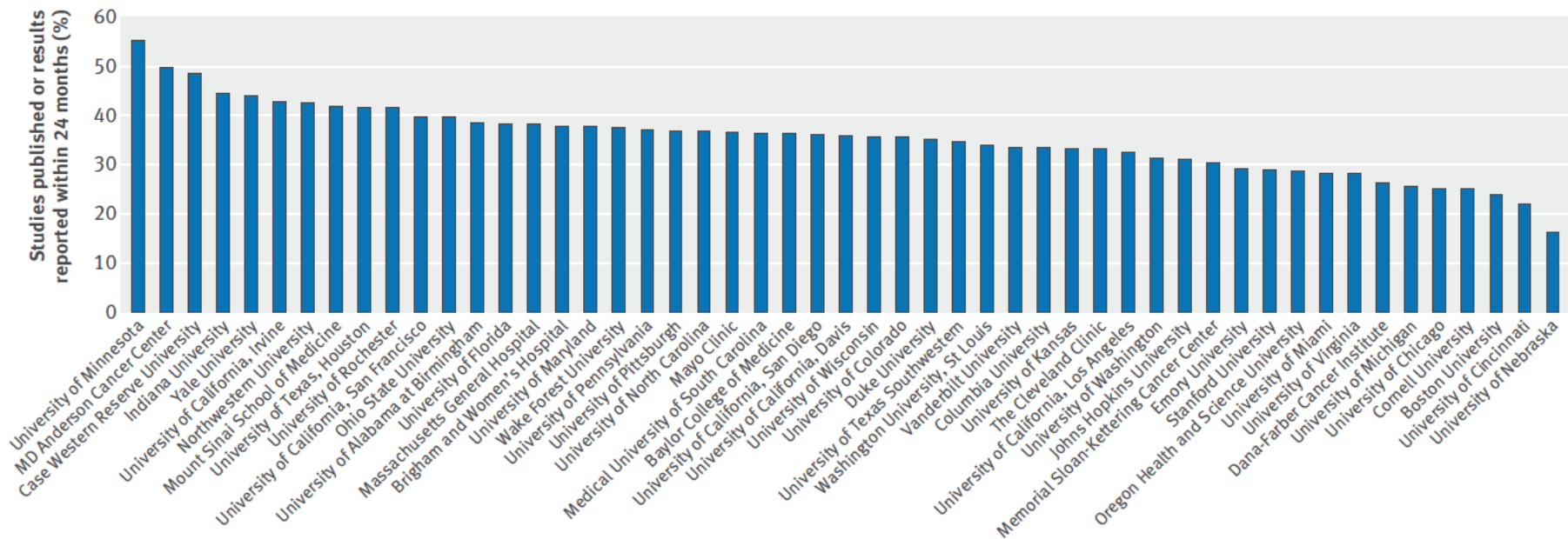


Fig 2 | Rates of dissemination of clinical trial results (publication of results or reporting of results on ClinicalTrials.gov) within 24 months across academic institutions. Of 4347 completed clinical trials, this figure excludes trials without dissemination of results (n=1455) as well as those with publication date and results reporting date <0 (n=216)

Krumholz H et al. BMJ 2016;352:i637

Academic Medical Centers Get An F In Sharing Research Results

Updated February 24, 2016 · 9:43 AM ET
Published February 23, 2016 · 1:59 PM ET
Commentary

HARLAN KRUMHOLZ

Meaning ...



SHARE



Who will check the study results if they aren't made public?

Simone Golob/Corbis

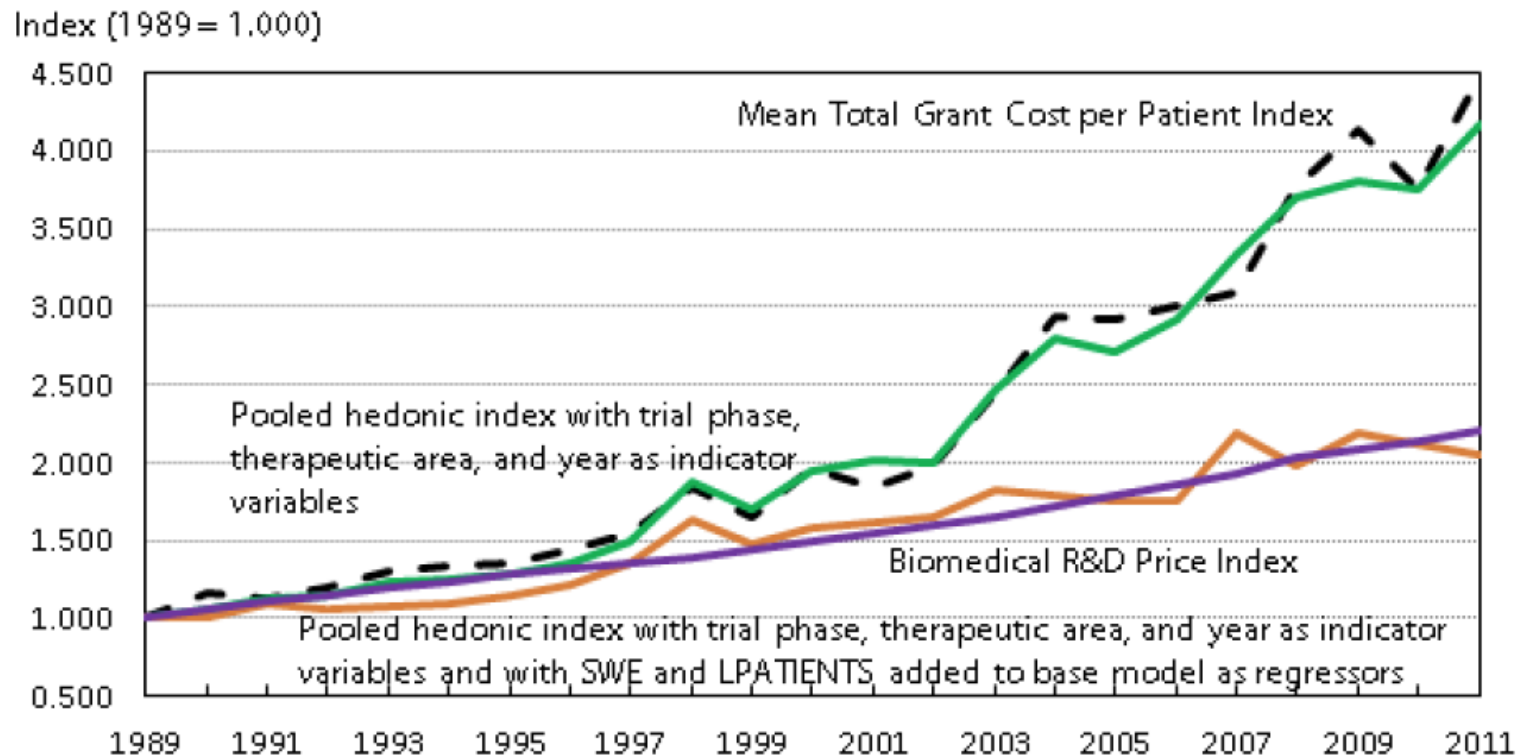
<http://www.npr.org/sections/health-shots/2016/02/23/467712481/academic-medical-centers-get-an-f-in-sharing-research-results>



NIH National Institutes of Health
Office of Extramural Research

Insights from an Unexpected Source ...

Figure 3. Mean Total Grant Cost per Patient Index, Biomedical R&D Price Index, and pooled hedonic indexes, 1989–2011

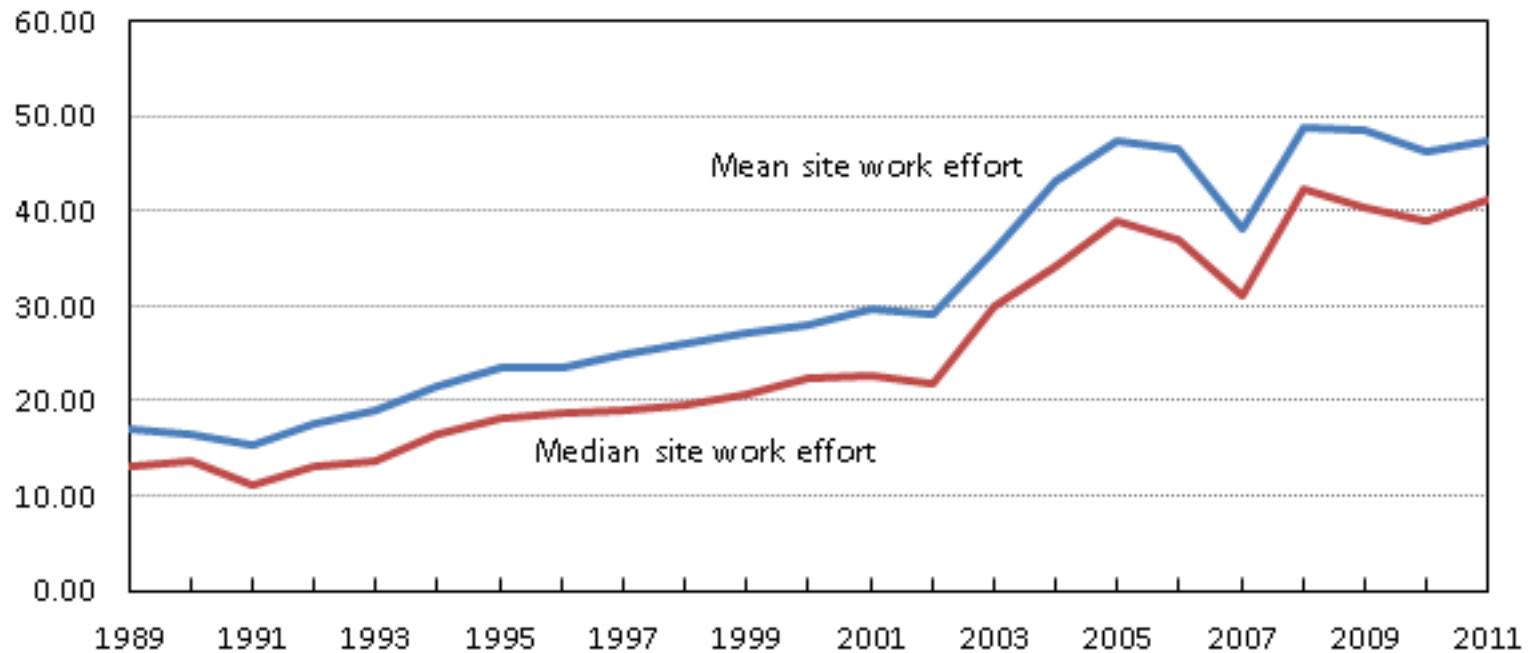


Source: Authors' calculations based on Medidata Solutions, Inc.'s, PICAS[®] database.



One Driver is Complexity

Figure 1. Mean and median site work effort, 1989–2011



¹ RVUs = relative value units (see text); WEUs = work effort units (see text).

Source: Authors' calculations based on Medidata Solutions, Inc.'s, PICAS[®] database.

Berndt E, Cockburn I. Monthly Labor Review, June 2014



Serious Barriers to Progress

TASK ORDER No. HHSP23337007T
CONTRACT No. HHSP23320095634WC

EXAMINATION OF CLINICAL TRIAL COSTS AND BARRIERS FOR DRUG DEVELOPMENT

FINAL

Eastern Research Group, ASPE Report, 2014



- Use of electronic health records
- Fewer enrollment restrictions
- Simplified protocols, fewer amendments
- Reduced source data verification
- mHealth, electronic data capture
- Lower cost facilities
- More efficient priority review, regulations

Eastern Research Group, ASPE Report, 2014

Good News – Lots Happening!

- NIH Collaboratory, task forces
- CTSA: Networks, metrics, RICs and TICs
- CTSA: IRB-Reliance
- FDA, CTTI, NAM
- PCORnet, Societies, registry trials