## ClinicalTrials.Gov and HHS Final Rule

Jodi Black, PhD
Office of Extramural Research
National Institutes of Health

Federal Demonstration Partnership

NIH Clinical Trials Policy

January 9, 2017

Hyatt Regency Capital Hill, Washington, DC

Disclosures: None



## All is Not Well ...

"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, MD



# Underreporting Research Is Scientific Misconduct

Iain Chalmers, FRCOG

"Substantial numbers of clinical trials are never reported ... Failure to publish is a form of scientific misconduct that can lead to inappropriate treatment decisions.

Investigators, ethics committees, funding bodies, and scientific editors all have responsibilities to reduce underreporting of clinical trials."

JAMA 1990;263:1405-8



## A Dozen Years Ago ...



# Factors Associated With Failure to Publish Large Randomized Trials Presented at an Oncology Meeting

Monika K. Krzyzanowska, MD, MPH Melania Pintilie, MSc Ian F. Tannock, MD, PhD

**Context** Large clinical trials are the criterion standard for making treatment sions, and nonpublication of the results of such trials can lead to bias in the liter and contribute to inappropriate medical decisions.

Objectives. To determine the rate of full publication of large randomized trial

26% of large cancer trials unpublished after 5 years!





## **FDITORIAL**

## 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*."

## A Few Months Later ...



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

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## RESEARCH

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

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Joseph S Ross assistant professor of medicine <sup>12</sup>, Tony Tse program analyst at ClinicalTrials.gov<sup>3</sup>, Deborah A Zarin director of ClinicalTrials.gov<sup>3</sup>, Hui Xu postgraduate house staff trainee <sup>4</sup>, Lei Zhou postgraduate house staff trainee <sup>4</sup>, Harlan M Krumholz Harold H Hines Jr professor of medicine and professor of investigative medicine and of public health<sup>256</sup>



## Can't Ignore This Any Longer ...

FRED UPTON, MICHIGAN
CHAIRMAN

HENRY A. WAXMAN, CALIFORNIA
RANKING MEMBER

ONE HUNDRED TWELFTH CONGRESS

## Congress of the United States

House of Representatives

COMMITTEE ON ENERGY AND COMMERCE 2125 RAYBURN HOUSE OFFICE BUILDING WASHINGTON, DC 20515–6115

> Majority (202) 225–2927 Minority (202) 225–3641

February 14, 2012

The Honorable Francis S. Collins Director National Institutes of Health 9000 Rockville Pike Bethesda, Maryland 20892

"This study raises concerns whether NIH is adequately implementing...

Dear Dr. Collins:

We are writing to express our core ern over a recent report documenting the underreporting of results of clinical arug trials. The most recent issue of the British Medical Journal contains a study by researchers from the University of Nottingham that finds that researchers and pharmacer acal companies routinely fail to publish data from clinical drug trials in a timely fashion. This study raises concerns whether NIH is adequately implementing the law

### So We Looked ...

#### 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**

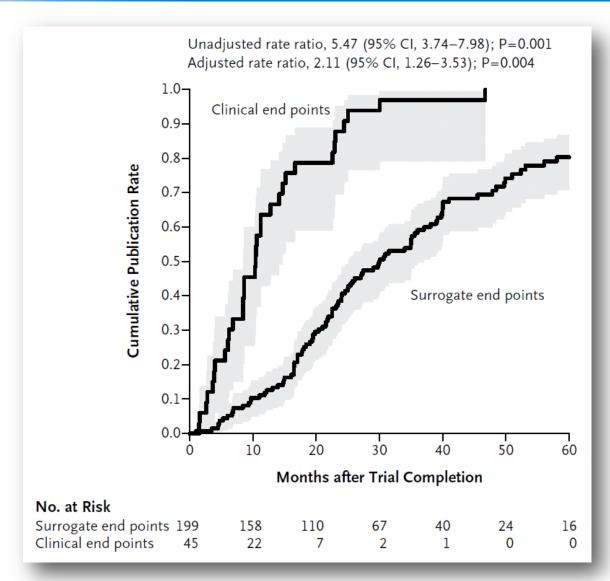
We analyzed 244 extramural randomized clinical trials of cardiovascular interventions that were supported by the National Heart, Lung, and Blood Institute (NHLBI). We selected trials for which data collection had been completed between January 1, 2000, and December 31, 2011. Our primary outcome measure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







## Confirmation ... With a Twist







## At Your Institution? ...

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

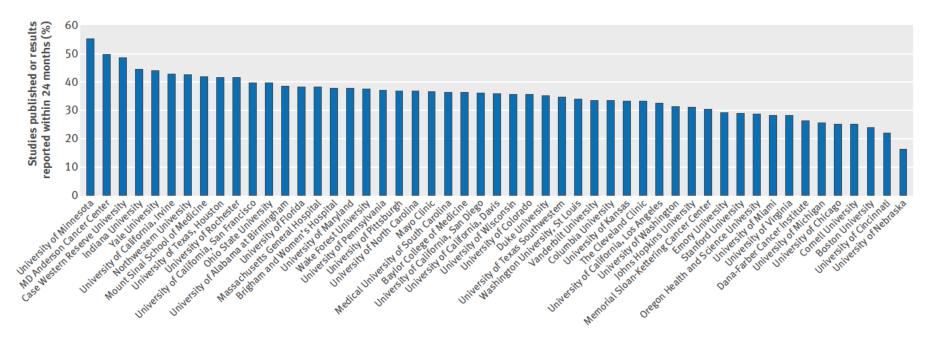


Fig 2 | Rates of dissemination of clinical trial results (publication of results or reporting of results on ClinicalTrials.gov) within 24 months across academic institutions. Of 4347 completed clinical trials, this figure excludes trials without dissemination of results (n=1455) as well as those with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

### Not reporting results:

- Violates a basic principle of the scientific method
- Harms patients, society and science
- Dishonors the study participants who gave consent and bore the risk

SHARE



Who will check the study results if they aren't made public? Simone Golob/Corbis

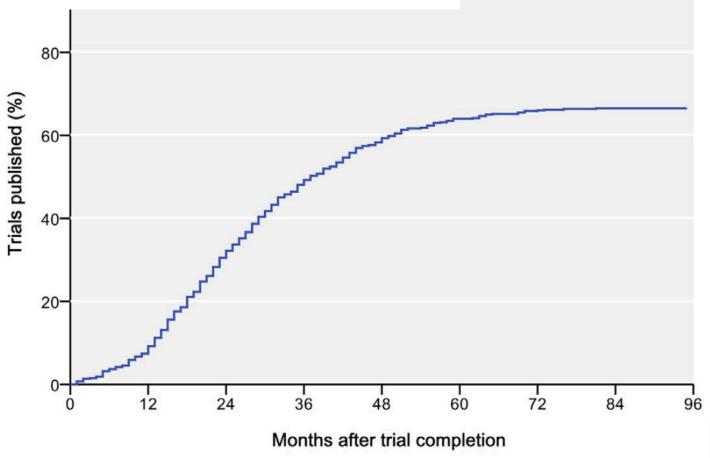




## And It Goes On...

Publication status of contemporary oncology randomised controlled trials worldwide

Yu-Pei Chen <sup>a,1</sup>, Xu Liu <sup>a,1</sup>, Jia-Wei Lv <sup>a,1</sup>, Wen-Fei Li <sup>a</sup>, Yuan Zhang <sup>a</sup>, Ying Guo <sup>b</sup>, Ai-Hua Lin <sup>c</sup>, Ying Sun <sup>a</sup>, Yan-Ping Mao <sup>a,d</sup>, Jun Ma <sup>a,\*</sup>





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## A New Policy ...



Toward a New Era of Trust and Transparency in Clinical Trials

Kathy L. Hudson, PhD National Institutes of Health, Bethesda, Maryland.

Michael S. Lauer, MD National Institutes of Health, Bethesda, Maryland.

Francis S. Collins, MD, PhD National Institutes of Health, Bethesda, "To realize the benefits of a clinical trial, the data must be broadly shared quickly. The DHHS has released a regulation for registration and summary results reporting..."

Maryland.

## **NIH Trials Reporting Policy**

## Applies to <u>all NIH-funded trials</u>, except

- Trials where NIH funded infrastructure only
- Trials initiated before January 18, 2017

## Applications address trial reporting

- Mention in informed consent
- Register trial in ClinicalTrials.gov by 21 days after first participant enrollment
- One record per trial
- Submit results in ClinicalTrials.gov within one year of completion



## What Results Information to Report

- Participant flow
- Demographic and baseline characteristics
- All primary and secondary outcomes
- Adverse events
- Full protocol and statistical analysis plan

## Open Mike

https://nexus.od.nih.gov/all/2016/09/16/visibility-of-clinical-trial-activities-and-results/



## Consequences ...



## Toward a New Era of Trust and Transparency in Clinical Trials

Kathy L. Hudson, PhD National Institutes of Health, Bethesda, Maryland.

Michael S. Lauer, MD National Institutes of Health, Bethesda, Maryland.

Francis S. Collins, MD, PhD National Institutes of Health, Bethesda, "To realize the benefits of a clinical trial, the data must be broadly shared quickly. The DHHS has released a regulation for registration and summary results reporting. The NIH will withhold clinical trial funding if the agency is unable to verify adequate registration and results reporting..."

Maryland.

## Transparency is Not a New Idea! ...



The Year was 1543...

http://ads.harvard.edu/books/1543droc.book/ Packer, M, BMJ, September 2016

Thanks also to Sarah Carr and Jeremy Brown



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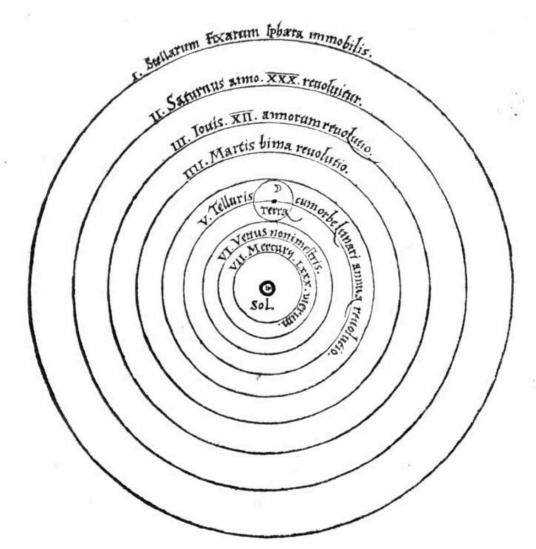
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http://ads.harvard.edu/books/1543droc.book/

## The Most Famous Picture ...







## But Also ... Lots of ....

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## **Back to the Future...**

