Industry Support for RCT
Food for Thought

Zeev Kain, MD, MBA
Associate Dean Clinical Operations
Chair and Professor
Department of Anesthesiology & Perioperative Care

February 28, 2014

UC Irvine Health

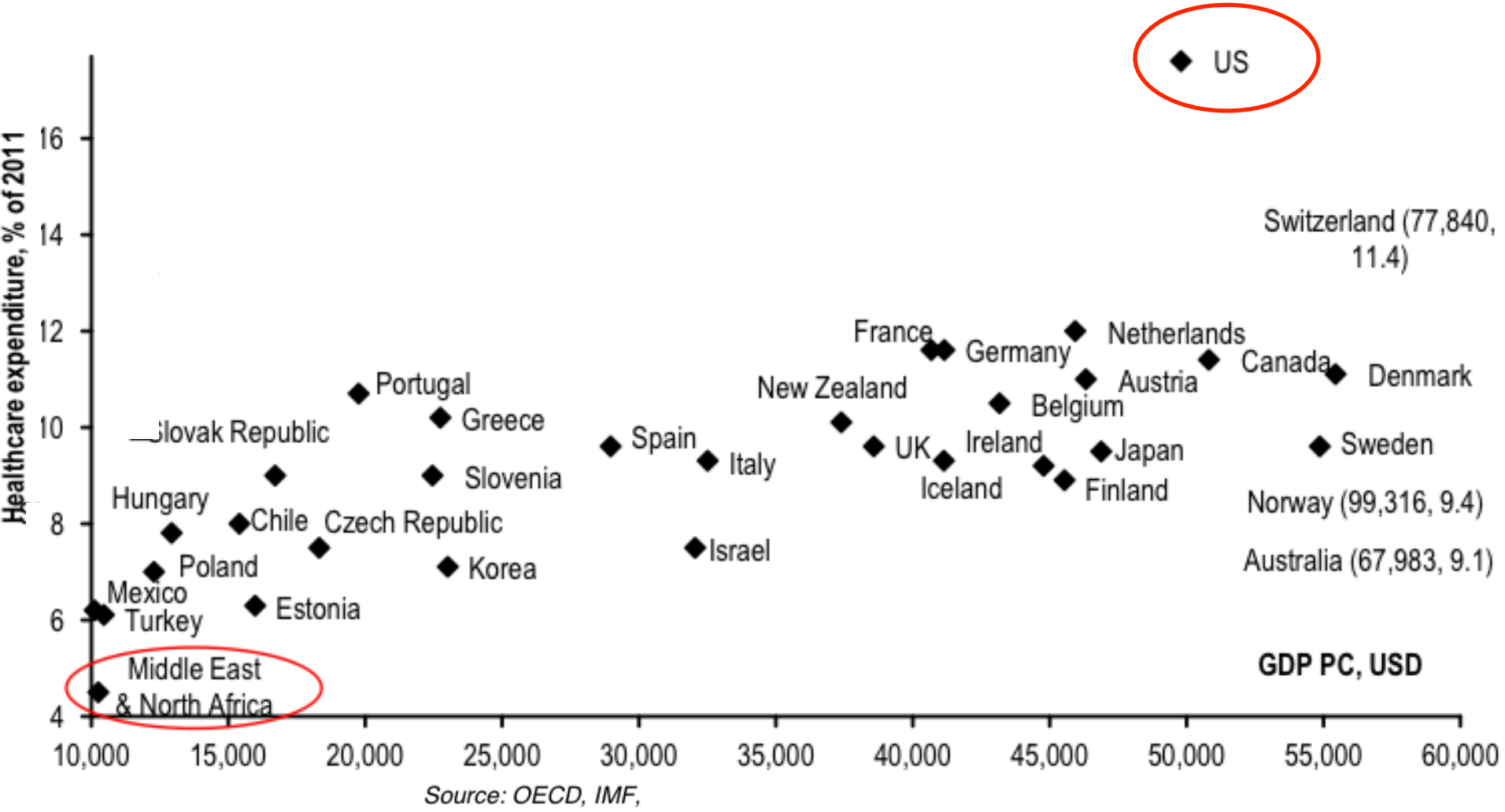
Disclosures

- Pharma:
  - Investigator initiated research*: Roche, Anesta, Aspect (2001 last support)
  - Speaker (Crew Resources Management, Merck)
- NICHD: Continuously funded since 1996
- Past Member of Editorial boards:
  - Anesthesiology
  - Pediatrics
  - Journal of Clinical Anesthesiology
  - Journal of Pediatric Psychology
  - Anesthesiology News

The Pharmaceutical Industry in the US

- Big Pharma responsible for over 90% of new chemical entities approved by FDA
- Significantly advance our scientific knowledge
- Increased life span
- $ for treatment of diseases in developing countries
- Huge research budgets
- A high stakes game

Spending on Healthcare in the US



Source: OECD, IMF,

UC Irvine Health

One Hundred Dollars

Ten thousands Dollars

One Hundred Million Dollars

UC Irvine Health

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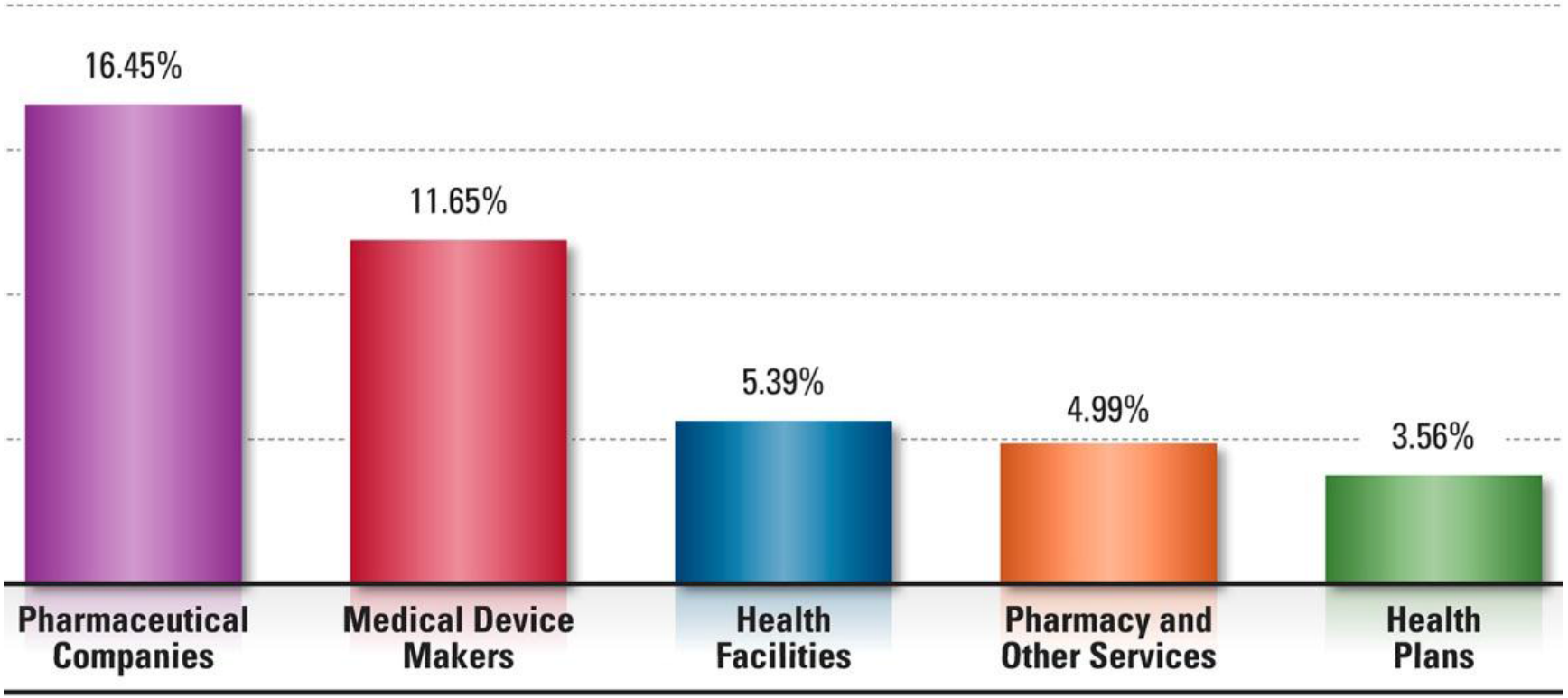
Profit Margins By Industry Group (2010)



US Healthcare costs. Medmutual.com. Acessed 02/27/2014

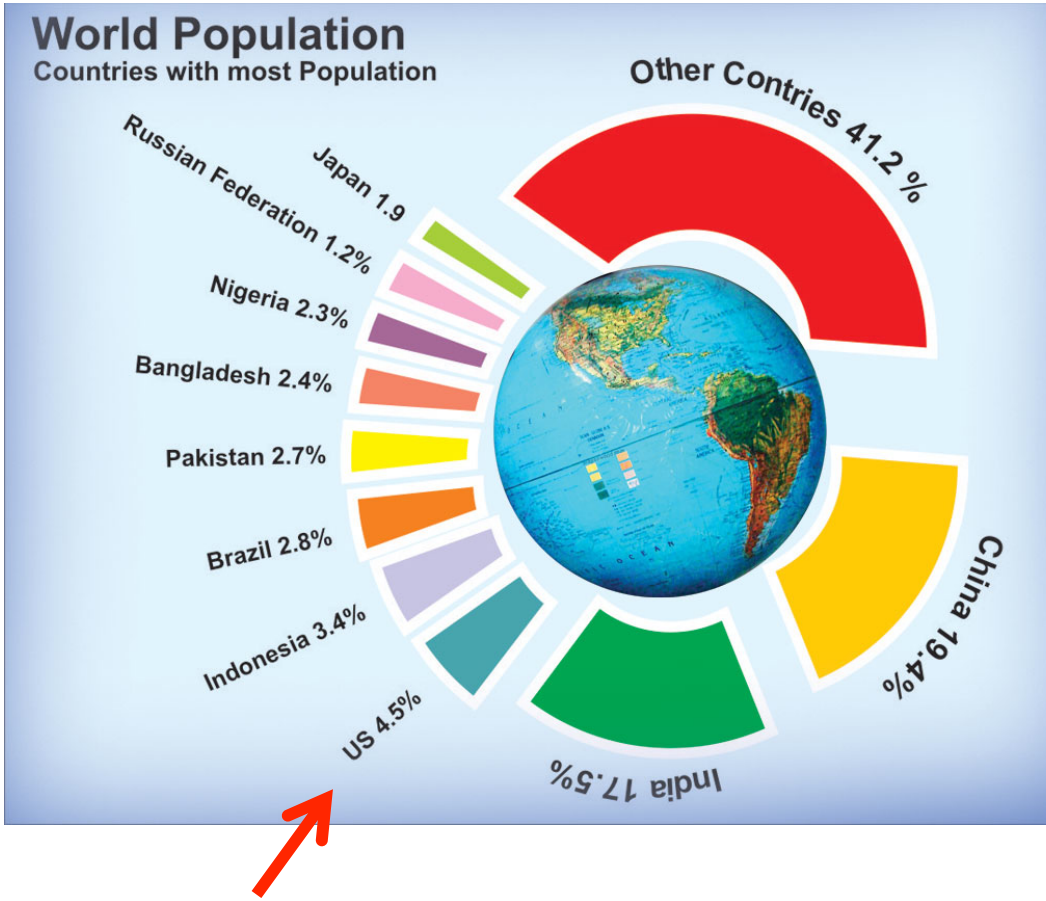
Key Global Markets vs. Population:

KEY GLOBAL MARKETS

With 41% of sales, the U.S. dominates the pharmaceutical market

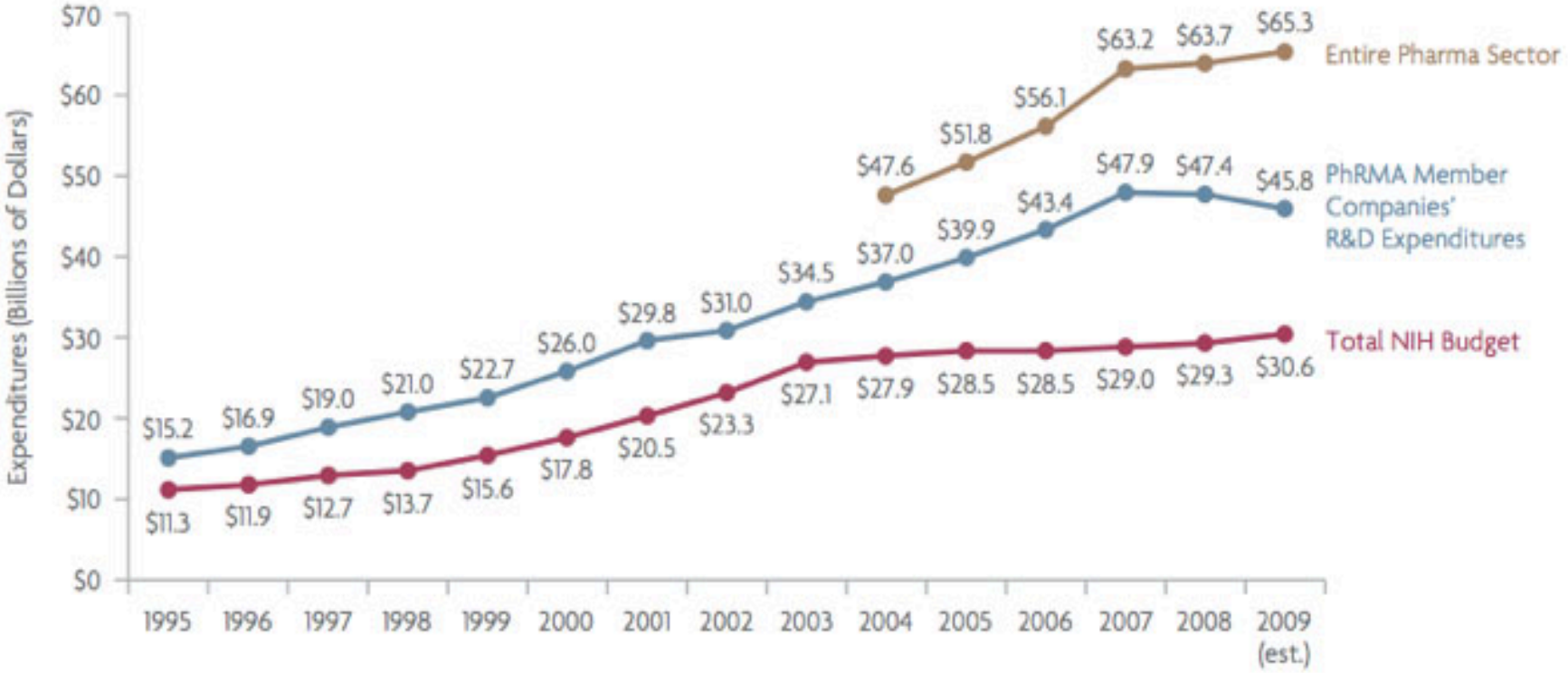
	SALES TO JUNE 2008 ($ BILLIONS)	SHARE OF GLOBAL SALES	12-MONTH CHANGE IN SALES
U.S.	$288.9	40.7%	1.5%
Japan	63.5	8.9	4.6
France	42.5	6.0	5.0
Germany	40.4	5.7	6.9
Italy	25.1	3.5	3.4
U.K.	23.5	3.3	2.8
Spain	21.6	3.0	8.1
Canada	19.1	2.7	6.1
China	16.8	2.4	28.4
Brazil	11.9	1.7	9.8
Top 10 markets	**$553.4**	**77.9%**	**4.0%**

NOTE: Sales are in U.S. dollars for the 12 months ending June 2008. **SOURCES:** IMS Health, MIDAS



Private and Public R&D Spending

Total biopharmaceutical company R&D, PhRMA member R&D, and NIH operating budget: 1995-2009



Source: Burrill & Company, PhRMA, NIH Office of Budget[10]

NIH DIRECTOR'S BLOG

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Editor: Bijal Trivedi

If you have comments or questions not related to the current discussions, please direct them to olib@od.nih.gov

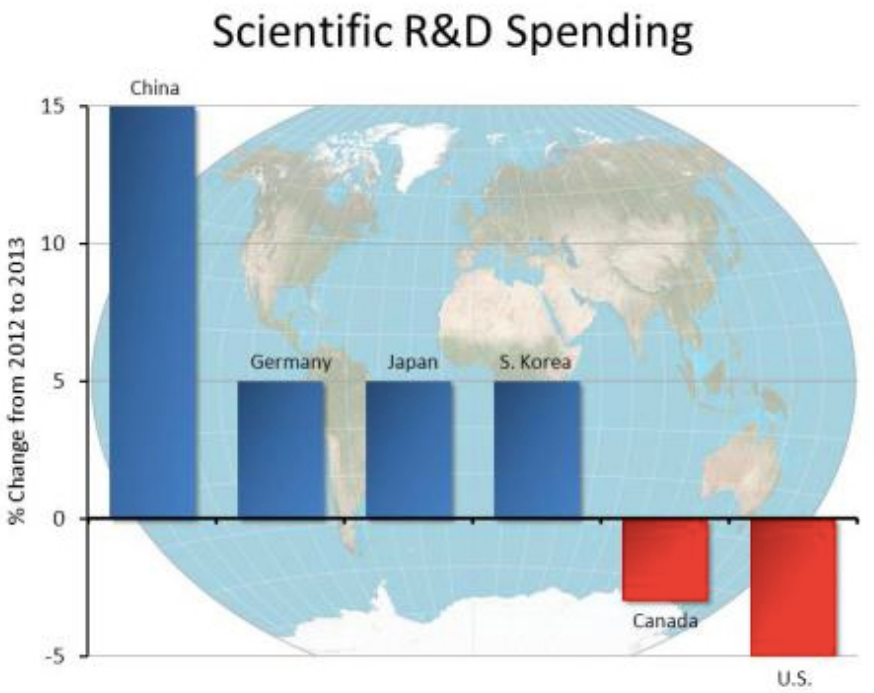
If you are looking for general information about the National Institutes of Health, or the 27 Institutes and Centers, please visit http://www.nih.gov/

Recent Posts

Rare Disease Sleuths Uncover New Clues to Stroke February 25, 2014

One Nation in Support of Biomedical Research?

Posted on September 24, 2013 by Dr. Sally Rockey and Dr. Francis Collins



PHARMA & HEALTHCARE | 1/14/2013 @ 7:00AM | 28,523 views

Congress Is Killing Medical Research

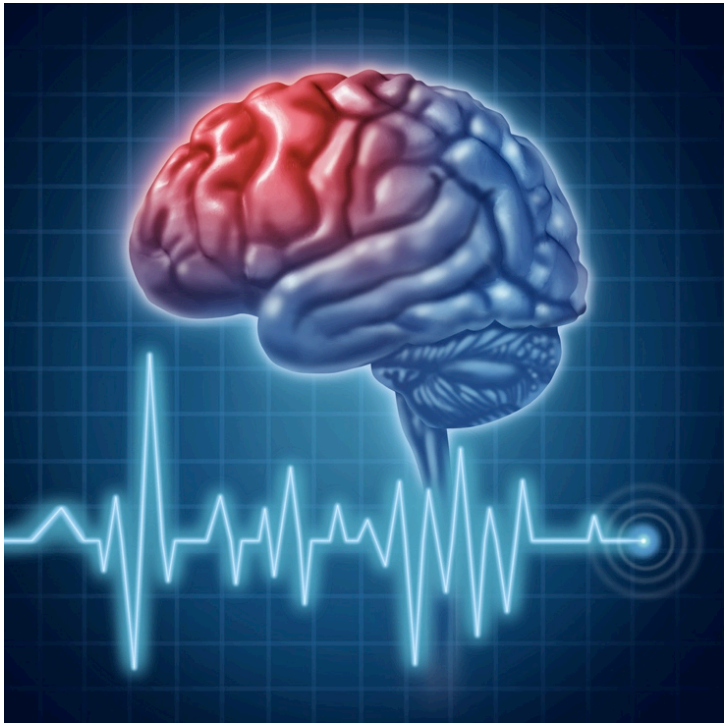
The Mark O. Hatfield Clinical Research Center on the NIH campus (Photo credit: Wikipedia)

Congress is killing medical research. The tragedy is that they don't want to, but they may do it anyway.

While the ridiculous posturing about the U.S. budget deficit drags on, seemingly without end, biomedical research in the U.S. is crumbling. Congress's chronic inability to pass a

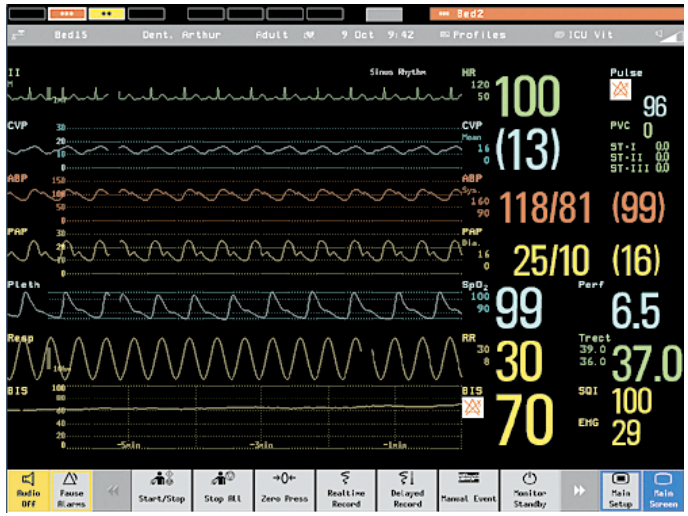
A Bedtime Story: Awareness

- Frequency of Anesthesia in the US
  - 21 Million per year in NA
- Incidence of Awareness
  - 1-2 per 1000?
  - define, measure
- Outcomes
  - Psychological
    - Immediate
    - Delayed
- Solutions
  - Old - HR, BP
  - New - BIS



Depth-of-Anesthesia Monitor: BIS

"The global market leader is the bispectral index system (BIS, Aspect Medical Systems), which relies on a proprietary algorithm for processing an EEG and alerts the anesthesiologist if the depth of anesthesia is inadequate."



Bispectral Index During Isoflurane Anesthes
Pediatric Patients

Simon D. Whyte, MB, BS, FRCA, and Peter D. Booker, MB, BS, MD, FRC
Jackson-Rees Department of Anesthesia, Royal Liverpool Children's Hospital and the Li
Anesthesia, United Kingdom

PEDIATR
OFFICIAL JOURNAL OF THE AMERICAN ACADE

Validation of the Bispectral Index Monito
and Deep Sedation in Children

Nicole Brown McDermott, MD, Tamitha VanSickle, MD, Domi
Robert H. Friesen, MD
Department of Anesthesiology, The Children's Hospital and the University of Col
Denver, Colorado

In this study, we tested the validity of the bispectral index (BIS) monitor during conscious and deep sedation of children by comparing it with the University of Michigan Sedation Scale (UMSS), a validated observational pediatric sedation scale. Eighty-six children <12 yr of age were enrolled in this observational study. The subjects underwent conscious or deep sedation administered by non-

during sedation; per
cations and perform
the BIS and UMSS s
BIS scores and UMS
0.0001), including in
-0.761, $P < 0.001$).
amine or an oral

Hundreds of Aspect Supported Trials!

Bispectral Index as a G

Karen S. Powers, Emily B. N
Elise W. van der La

British Journal of Anaesthesia **86 (2)**: 209–12 (2001)

EEG bispectral index and hypnotic component of anaesthe
induced by sevoflurane: comparison between children and a

C.-S. Degoute[1]*, C. Macabeo[1], C. Dubreuil[2], R. Duclaux[3] and V. Banssillon[1]

*[1]Department of Anaesthesiology and Intensive Care, [2]Department of ENT Surgery and [3]Depart
Physiology (CNRS UPRESA 5020), Centre Hospitalo-Universitaire Lyon-Sud, France*

**Corresponding author: Service d'Anesthésie-réanimation, Centre Hospitalo-Universitaire Lyon-Sud, F-6949
Bénite Cedex, France*

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 13, 2008 VOL. 358 NO. 11

Anesthesia Awareness and the Bispectral Index

Michael S. Avidan, M.B., B.Ch., Lini Zhang, M.D., Beth A. Burnside, B.A., Kevin J. Finkel, M.D., Adam C. Searleman, B.S., Jacqueline A. Selvidge, B.S., Leif Saager, M.D., Michelle S. Turner, B.S., Srikar Rao, B.A., Michael Bottros, M.D., Charles Hantler, M.D., Eric Jacobsohn, M.B., Ch.B., and Alex S. Evers, M.D.

- Results not reproducible for studies that reported lower anesthesia awareness with BIS monitoring
- Awareness occurred even when BIS values within target ranges
- Findings do not support routine BIS monitoring as part of standard anesthesia practice

The Stock Market….

UC Irvine Health

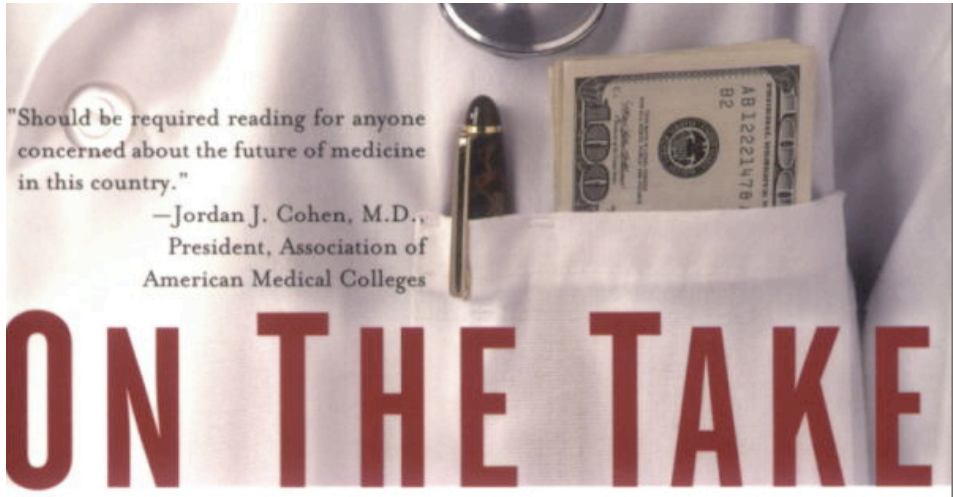
The Truth About the Drug Companies

HOW THEY DECEIVE US AND WHAT TO DO ABOUT IT

MARCIA ANGELL, M.D.

Former editor in chief of *The New England Journal of Medicine*
Winner of the Polk Award

The NEW ENGLAND JOURNAL of MEDICINE



"Should be required reading for anyone concerned about the future of medicine in this country."
—Jordan J. Cohen, M.D., President, Association of American Medical Colleges

ON THE TAKE

HOW MEDICINE'S COMPLICITY WITH BIG BUSINESS CAN ENDANGER YOUR HEALTH

JEROME P. KASSIRER, M.D.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Glycemic Durability of Rosiglitazone, Metformin, or Glyburide Monotherapy

Steven E. Kahn, M.B., Ch.B., Steven M. Haffner, M.D., Mark A. Heise, Ph.D., William H. Herman, M.D., M.P.H., Rury R. Holman, F.R.C.P., Nigel P. Jones, M.A., Barbara G. Kravitz, M.S., John M. Lachin, Sc.D., M. Colleen O'Neill, B.Sc., Bernard Zinman, M.D., F.R.C.P.C., and Giancarlo Viberti, M.D., F.R.C.P., for the ADOPT Study Group *

ABSTRACT

BACKGROUND

The efficacy of thiazolidinediones, as compared with other oral glucose-lowering medications, in maintaining long-term glycemic control in type 2 diabetes is not known.

METHODS

We evaluated rosiglitazone, metformin, and glyburide as initial treatment for recently diagnosed type 2 diabetes in a double-blind, randomized, controlled clinical trial involving 4360 patients. The patients were treated for a median of 4.0 years. The primary outcome was the time to monotherapy failure, which was defined as a confirmed level of fasting plasma glucose of more than 180 mg per deciliter (10.0 mmol per liter), for rosiglitazone, as compared with metformin or glyburide. Prespecified secondary outcomes were levels of fasting plasma glucose and glycated hemoglobin, insulin sensitivity, and β-cell function.

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TECHNOLOGY

Glaxo in $3 Billion Settlement

Email Print Save 38 Comments A A

By JEANNE WHALEN, DEVLIN BARRETT and PETER LOFTUS

Updated July 3, 2012 12:01 a.m. ET

Drug maker GlaxoSmithKline GSK.LN +0.96% PLC agreed to plead guilty to criminal charges of illegally marketing drugs and withholding safety data from U.S. regulators, and to pay $3 billion to the government in what the Justice Department called the largest health-care fraud settlement in U.S. history.

Pharmaceutical maker GlaxoSmithKline has agreed to plead guilty and pay $3 billion to resolve criminal and civil liability over drug marketing and other issues, the U.S. Department of Justice said Monday. Devlin Barrett has details on Lunch Break. Photo: Getty Images.

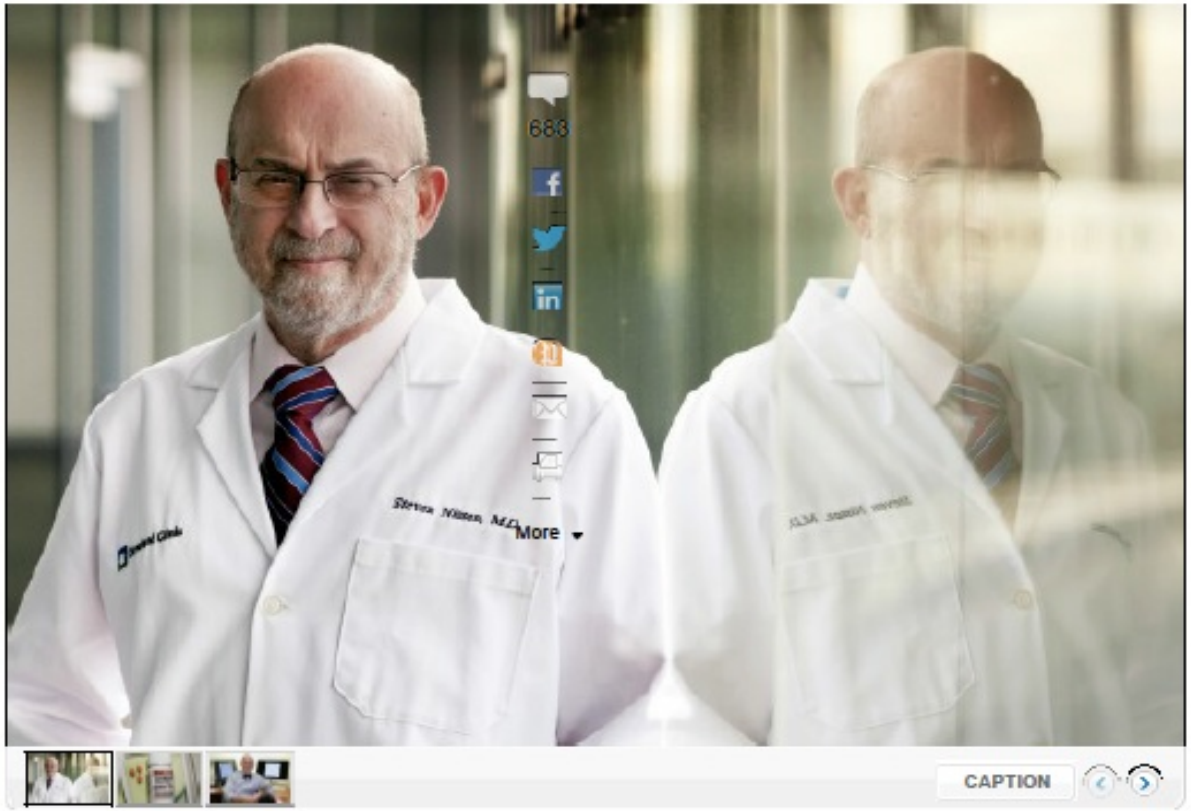
Under the deal, which requires court approval, Glaxo will plead guilty to criminal charges involving three drugs—the antidepressants Paxil and Wellbutrin and the diabetes drug Avandia. The settlement includes $1 billion in criminal fines and $2 billion to resolve civil liabilities owed to the federal government and the states, the Justice Department said. Glaxo had announced the settlement's size in November.

Is this a Unique case?

BUSINESS

The Washington Post with Bloomberg

As drug industry's influence over research grows, so does the potential for bias



By **Peter Whoriskey**, Published: November 24, 2012 E-mail the writer

For drugmaker GlaxoSmithKline, the 17-page article in the New England Journal of Medicine represented a coup.

Cite this article as: BMJ, doi:10.1136/bmj.38973.444699.0B (published 6 October 2006)

Research

BMJ

Cochrane reviews compared with industry supported meta-analyses and other meta-analyses of the same drugs: systematic review

Anders W Jørgensen, Jørgen Hilden, Peter C Gøtzsche

Abstract

Objective To compare the methodological quality and conclusions in Cochrane reviews with those in industry supported meta-analyses and other meta-analyses of the same drugs.

Design Systematic review comparing pairs of meta-analyses that studied the same two drugs in the same disease and were published within two years of each other.

Data sources Cochrane Database of Systematic Reviews (2003, issue 1), PubMed, and Embase.

Data extraction Two observers independently extracted data and used a validated scale to judge the methodological quality of the reviews.

Results 175 of 1596 Cochrane reviews had a meta-analysis that supported systematic reviews. We aimed to compare Cochrane reviews with other meta-analyses of the same drugs, which we divided into those that had industry support, those with undeclared support, and those that had non-profit support or no support.

Methods

We searched for pairs that consisted of a Cochrane review and a similar review in a paper based journal. A Cochrane review was eligible if it used meta-analysis to compare at least two different drugs or classes of drugs; was published in the *Cochrane Database of Systematic Reviews* 2003, issue 1; could be matched with a meta-analysis of the same drugs and diseases published in full in a paper based journal within two years before or after the most

Other Studies?

Djulbegovic B, et al. The uncertainty principle and industry-sponsored research. *Lancet* 2000; 356: 635–38.
(136 trials in multiple myeloma found that more than 75% of IST reported results that favor the new therapy over standard therapy)

Davidson RA. Source of funding and outcome of clinical trials. *J Gen Intern Med* 1986; 1: 155–58.
(pharmaceutical company were about three times more likely to report in favor of the experimental therapy)

Cho MK, Bero LA. The quality of drug studies published in symposium proceedings. *Ann Intern Med* 1996; 124: 485–89.
(trials with drug company support were much more likely to report in favour of the experimental therapy, 98% vs 79%).

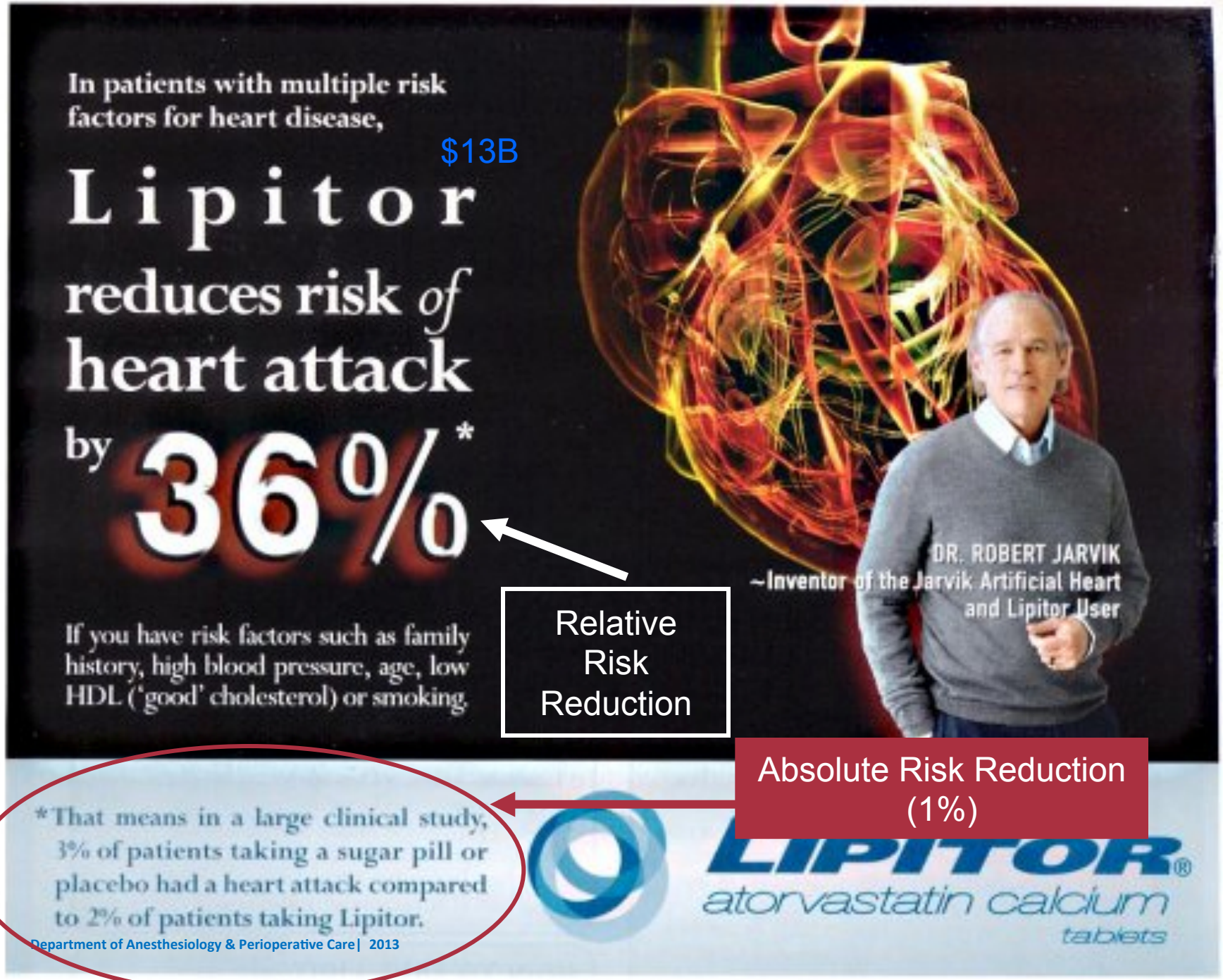
Friedberg et al.. Evaluation of conflict of interest in economic analyses of new drugs used in oncology. *JAMA* 1999; 282: 1453-7.
(only 5% of industry-supported analyses reported unfavorable conclusions compared with 38% of not-for-profit sponsored studies)

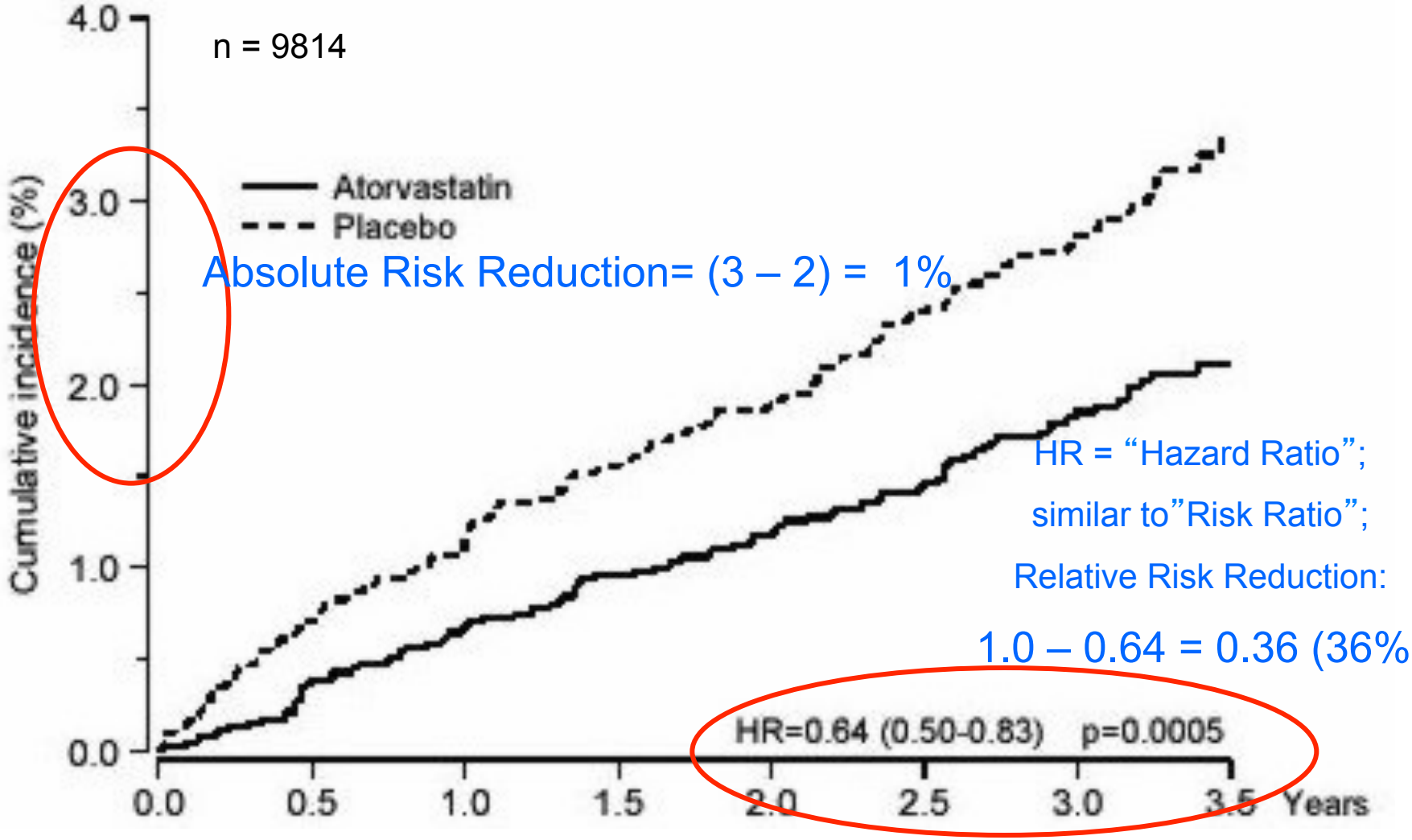
Medical Journals Are an Extension of the Marketing Arm of Pharmaceutical Companies

PLoS Medicine | www.plosmedicine.org May 2005 | Volume 2 | Issue 5 | e138

Some study design issues

- Present results that are most likely to impress—for example, reduction in relative rather than absolute risk.
- Conduct a trial of your drug against a treatment known to be inferior.
- Trial your drugs against too low a dose of a competitor drug.
- Conduct a trial of your drug against too high a dose of a competitor drug (making your drug seem less toxic).
- Conduct trials that are too small to show differences from competitor drugs.
- Use multiple endpoints in the trial and select for publication those that give favourable results.
- Do multicentre trials and select for publication results from centres that are favourable.
- Conduct subgroup analyses and select for publication those that are favourable.


In patients with multiple risk factors for heart disease,
$13B
Lipitor
reduces risk of heart attack
by 36%*
If you have risk factors such as family history, high blood pressure, age, low HDL ('good' cholesterol) or smoking.
DR. ROBERT JARVIK
~Inventor of the Jarvik Artificial Heart and Lipitor User
Relative Risk Reduction
Absolute Risk Reduction (1%)
*That means in a large clinical study, 3% of patients taking a sugar pill or placebo had a heart attack compared to 2% of patients taking Lipitor.
LIPITOR®
atorvastatin calcium
tablets



Absolute Risk Reduction= (3 – 2) = 1%

HR = "Hazard Ratio";

similar to"Risk Ratio";

Relative Risk Reduction:

1.0 – 0.64 = 0.36 (36%)

THE NUMBER NEEDED TO TREAT

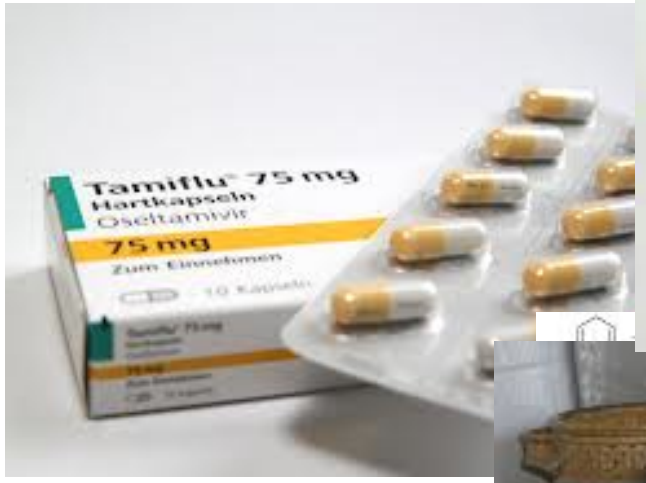
How well do drugs work? Ads and news stories usually say that a medicine slashes the risk of, say, heart attacks by a big number, like 50%. But that often overstates the benefit, because it fails to provide the absolute risk. If only 2 people in a group of 100 are expected to have a heart attack, then a drug that cuts the rate by 50% prevents just 1 heart attack when taken by all 100 people. That's why researchers favor using the "number needed to treat" (NNT). It shows how many people must take a drug for one person to benefit.

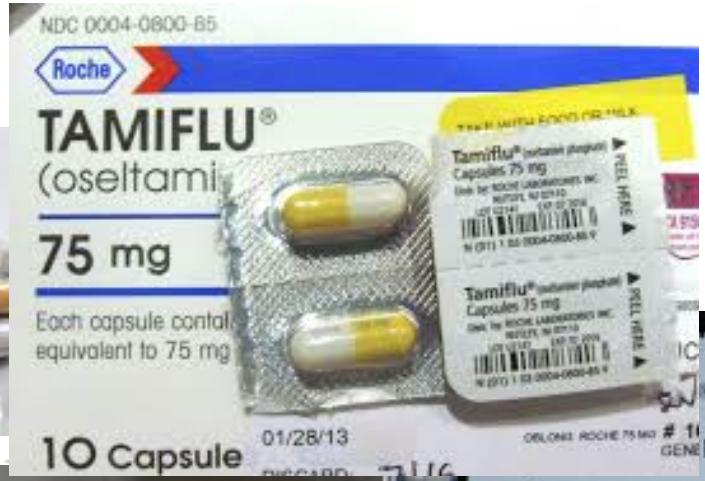
"What if you put 250 people in a room and told them they would each pay $1,000 a year for a drug they would have to take every day, that many would get diarrhea and muscle pain, and that 249 would have no benefit? And that they could do just as well by exercising? How many would take that?

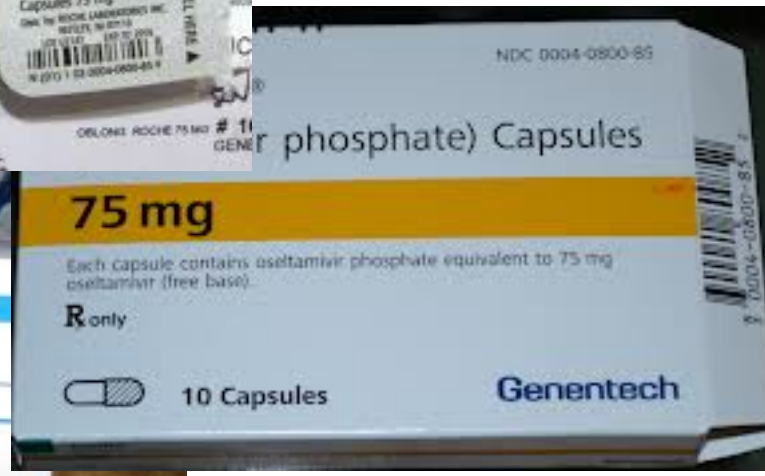
Dr. Jerome R. Hoffman

	fects of diabetes	kidney failure, nerve damage, amputations.
Zetia, which lowers cholesterol	**1,000+** to prevent heart disease	Companies admit that it has not been shown to reduce heart disease or heart attacks.

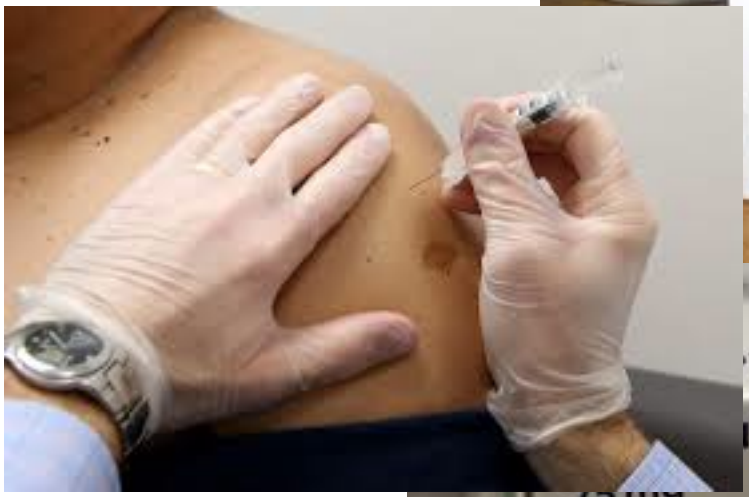
Data: Bandolier, Therapeutics Initiative, *BusinessWeek*


Tamiflu 75 mg
Hartkapseln
Oseltamivir
75 mg
Zum Einnehmen


NDC 0004-0800-85
Roche
TAMIFLU®
(oseltami
75 mg
Each capsule contai
equivalent to 75 mg
10 Capsule
01/28/13


NDC 0004-0800-85
r phosphate) Capsules
75 mg
Each capsule contains oseltamivir phosphate equivalent to 75 mg oseltamivir (free base).
℞ only
10 Capsules
Genentech


TAMIFLU
(oseltamivir phosphate) Capsules
75 mg
10 Capsules
℞ only




10 capsules
Tamiflu®
75 mg
10 capsules


Tamiflu
75 mg
Tamiflu
75 mg
Tamiflu
75 mg

Neuraminidase inhibitors for preventing and treating influenza in healthy adults and children (Review)

Jefferson T, Jones MA, Doshi P, Del Mar CB, Heneghan CJ, Hama R, Thompson MJ

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2012, Issue 1

THE COCHRANE COLLABORATION®

Cochrane is a global independent network of health practitioners, researchers, patient advocates and others, responding to the challenge of making the vast amounts of evidence generated through research useful for informing decisions about health.

The Cochrane Collaboration

- We found a high risk of publication and reporting biases in the trial programme of oseltamivir.

- We expect full clinical study reports containing study protocol, reporting analysis plan, statistical analysis plan and individual patient data to clarify outstanding issues. These full clinical study reports are at present unavailable to us.

House of Commons

Committee of Public Accounts

Access to clinical trial information and the stockpiling of Tamiflu

Thirty-fifth Report of Session 2013–14

Report, together with formal minutes, oral and written evidence

Ordered by the House of Commons to be printed 18 December 2013

The UK government spent around $695 billion dollars—to stockpile Tamiflu in case of a flu epidemic, even though there is only limited evidence on how well the drug works and disagreement among experts as to how helpful it would be in that situation.

+AllTrials

All Trials Registered | All Results Reported

home | why this matters | news | get involved | comments | organisations | about | contact

It's time all clinical trial results are reported.

Patients, researchers, pharmacists, doctors and regulators everywhere will benefit from publication of clinical trial results. Wherever you are in the world please sign the petition:

Thousands of clinical trials have not reported their results; some have not even been registered.

Information on what was done and what was found in these trials could be lost forever to doctors and researchers, leading to bad treatment decisions, missed opportunities for good medicine, and trials being repeated.

All trials past and present should be registered, and the full methods and the results reported.

We call on governments, regulators and research bodies to implement measures to achieve this.

The petition has also been translated into many different languages. If you would like to sign the petition on behalf of an organisation then please contact us. Data will be held by Sense About Science. Read our privacy policy here.

LATEST NEWS:

NEWS

All trials registered and results reported

Sign the petition

First Name ** | Last Name **

Email **

Country | Occupation

I signed this because... (add your comment for the wall here)

Sign Now

63626 signatures

Share this with your friends:

facebook | twitter

theguardian

Bad Pharma™

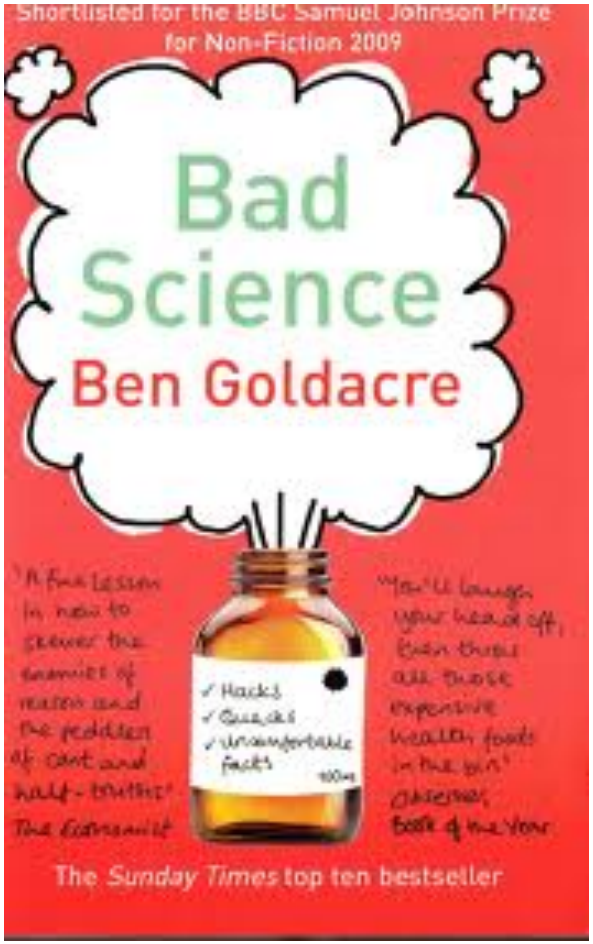
Ben Goldacre

Bestselling author of Bad Science

How drug companies mislead doctors and harm patients

364 pages

4th



So how are we going to fix this?

- Appropriate controls
  - Control dosing issues
  - External validity (age, gender, SES)
- Surrogate endpoints
  - Short term vs. Long term
  - Clinically relevant
- The role of academic CROs
- Tight control of study data, analysis, and interpretation by the commercial sponsor is undesirable
- TRANSPARENCY

JAMA®

Reporting Conflicts of Interest, Financial Aspects of Research, and Role of Sponsors in Funded Studies

Phil B. Fontanarosa, MD, MBA
Annette Flanagin, RN, MA
Catherine D. DeAngelis, MD, MPH

RESEARCH STUDIES IN BIOMEDICAL JOURNALS ARE INcreasingly scrutinized, not only for their scientific findings and clinical and public health implications, but also because of concerns related to conflicts of interest of investigators[1] and concerns about misleading reporting of industry-sponsored research.[2] The perception that conflicts of interest or financial concerns may have potentially detrimental effects on medical science has prompted medical journals to critically examine and more vigorously enforce policies for disclosure of potential conflicts and for reporting of relationships with industry.[3]

The need for transparency in reporting the financial conflicts of interest of authors and the relationships between investigators and funding sources has never been greater and is essential to help maintain confidence and trust in the scientific integrity of medical research articles. In this editorial, we review and update our policies for authors reporting conflicts of interest and disclosing financial support and other paid contributions for their work, as well as the requirements for reporting of industry-sponsored studies. Much of this information and the rationale for these policies have been described in previous editorials[4] and are detailed in the current *JAMA* Instructions for Authors.[3]

the time of publication. Authors also must report other financial interests that represent potential future financial gain, such as relevant filed or pending patents or patent applications in preparation. Although many universities and other institutions and organizations have established policies and thresholds for reporting financial interests and other conflicts of interest, *JAMA* requires complete disclosure of all relevant financial relationships and potential financial conflicts of interest, regardless of amount or value. Authors who are uncertain about what might constitute a potential financial conflict of interest should always err on the side of full disclosure and should contact the editorial office if they have questions or concerns.

To report this information, each author is required to sign and submit the following disclosure statement on the *JAMA* authorship form: "I certify that all my affiliations with or financial involvement, within the past 5 years and foreseeable future (eg, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, royalties) with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript are completely disclosed."[3] Authors may include these disclosures on the *JAMA* financial disclosure form or should indicate that the disclosures are included in an attachment to the form or in the manuscript. In addition, authors who have no relevant financial interests should provide a statement indicating that they have no financial interests related to the mate-

JAMA Published Fewer Industry-Funded Studies after Introducing a Requirement for Independent Statistical Analysis

Elizabeth Wager[1]*, Rahul Mhaskar[2], Stephanie Warburton[2], Benjamin Djulbegovic[2,3]

1 Sideview, Princes Risborough, Buckinghamshire, United Kingdom, **2** Center for Evidence-based Medicine and Health Outcomes Research, University of South Florida, Tampa, Florida, United States of America, **3** H. Lee Moffitt Cancer Center & Research Institute, Tampa, Florida, United States of America

Abstract

Background: *JAMA* introduced a requirement for independent statistical analysis for industry-funded trials in July 2005. We wanted to see whether this policy affected the number of industry-funded trials published by *JAMA*.

Methods and Findings: We undertook a retrospective, before-and-after study of published papers. Two investigators independently extracted data from all issues of *JAMA* published between 1 July 2002 and 30 June 2008 (i.e., three years before and after the policy). They were not blinded to publication date. The randomized controlled trials (RCTs) were classified as industry funded (IF), joint industry/non-commercial funding (J), industry supported (IS) (when manufacturers provided materials only), non-commercial (N) or funding not stated (NS). Findings were compared and discrepancies resolved by discussion or further analysis of the reports. RCTs published in *The Lancet* and *NEJM* over the same period were used as a control group. Between July 2002 and July 2008, *JAMA* published 1,314 papers, of which 311 were RCTs. The number of industry studies (IF, J or IS) fell significantly after the policy ($p = 0.02$) especially for categories J and IS. However, over the same period, the number of industry studies rose in both *The Lancet* and *NEJM*.

Conclusions: After the requirement for independent statistical analysis for industry-funded studies, *JAMA* published significantly fewer RCTs and significantly fewer industry-funded RCTs. This pattern was not seen in the control journals. This suggests the *JAMA* policy affected the number of submissions, the acceptance rate, or both. Without analysing the submissions, we cannot check these hypotheses but, assuming the number of published papers is related to the number submitted, our findings suggest that *JAMA*'s policy may have resulted in a significant reduction in the number of industry-sponsored trials it received and published.

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SUBMIT STUDIES

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Why Should I Register and Submit Results?

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What Is the Purpose of Trial Registration and Results Submission?

Registering clinical trials when they begin, providing timely updates, submitting summary results, and making this information publicly available fulfills a number of purposes and benefits a variety of people.

Trial Registry Purposes for Various Groups

Registry Purpose	Group That Benefits
Fulfill ethical obligations to participants and community	Patients, general public, research community
Provide information to potential participants and referring clinicians	Patients, clinicians

Trial Publication after Registration in ClinicalTrials.Gov: A Cross-Sectional Analysis

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Abstract

Background: ClinicalTrials.gov is a publicly accessible, Internet-based registry of clinical trials managed by the US National Library of Medicine that has the potential to address selective trial publication. Our objectives were to examine completeness of registration within ClinicalTrials.gov and to determine the extent and correlates of selective publication.

Methods and Findings: We examined reporting of registration information among a cross-section of trials that had been registered at ClinicalTrials.gov after December 31, 1999 and updated as having been completed by June 8, 2007, excluding phase I trials. We then determined publication status among a random 10% subsample by searching MEDLINE using a systematic protocol, after excluding trials completed after December 31, 2005 to allow at least 2 y for publication following completion. Among the full sample of completed trials ($n = 7,515$), nearly 100% reported all data elements mandated by ClinicalTrials.gov, such as intervention and sponsorship. Optional data element reporting varied, with 53% reporting trial end date, 66% reporting primary outcome, and 87% reporting trial start date. Among the 10% subsample, less than half (311 of 677, 46%) of trials were published, among which 96 (31%) provided a citation within ClinicalTrials.gov of a publication describing trial results. Trials primarily sponsored by industry (40%, 144 of 357) were less likely to be published when compared with nonindustry/nongovernment sponsored trials (56%, 110 of 198; $p < 0.001$), but there was no significant difference when compared with government sponsored trials (47%, 57 of 122; $p = 0.22$). Among trials that reported an end date, 75 of 123 (61%) completed prior to 2004, 50 of 96 (52%) completed during 2004, and 62 of 149 (42%) completed during 2005 were published ($p = 0.006$).

BMJ

BMJ 2013;347:f6104 doi: 10.1136/bmj.f6104 (Published 29 October 2013)

RESEARCH

Non-publication of large randomized clinical trials: cross sectional analysis

Christopher W Jones *attending physician*[1], Lara Handler *school of medicine liaison librarian*[2], Karen E Crowell *clinical information specialist*[2], Lukas G Keil *research assistant*[3], Mark A Weaver *assistant professor*[4], Timothy F Platts-Mills *assistant professor*[3]

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Give The People the Data

"While the U.S. has required the registration of clinical trials since 1997, drug makers still have wide latitude on deciding what data from those tests they will disclose to the public. That created an opportunity to hide failures and lackluster results that advocacy groups said may have been useful to ensuring patient safety".

Bloomberg News, January 31, 2014

YODA Project

Yale University Open Data Access (YODA) Project

A New Approach to Evaluation and Transparency

Each day, patients and their physicians make treatment decisions with access to only a fraction of the relevant clinical research da
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Objectives of the YODA Project

The YODA Project is rooted in the view that patients, providers, and industry will be better informed when academic investigators are able to facilitate the independent assessment and dissemination of data relevant to the benefits and harms of industry products. These assessments will allow physicians and patients to base their decisions on the most comprehensive and contemporary evidence available.

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Traditionally, patient-level data that can be used to assess medical treatments have not been made available to researchers outside of industry. As a result, independent researchers who are interested in evaluating a product have relied on data summaries and published manuscripts, which often provide an incomplete picture because much of the data is not published. The YODA Project model aims to make all patient-level clinical research data available for analysis by other external investigators.

Change is in the Air…

- Medtronic Inc. was the first medical company to ask Yale to review a trial of its bone graft product (infuse)
- GlaxoSmithKline was the first major drug company to make its trial data available. Glaxo has received 16 requests for data, approving 12

BloombergBusinessweek
News From Bloomberg

J&J Sets Drug Data Free in 'YODA' Collaboration With Yale

By Drew Armstrong | January 31, 2014

Johnson & Johnson (JNJ:US) will give academics access to data on clinical trials, a move that may prompt more companies to do the same.

BMJ

BMJ 2014;448:g213 doi: 10.1136/bmj.g213 (Published 15 January 2014)

EDITORIALS

Improving, and auditing, access to clinical trial results

All trials should be registered, with their full methods and results reported, and routine audit on the extent of information withheld

Ben Goldacre *Wellcome research fellow in epidemiology*[1], Carl Heneghan *professor*[2]

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The House of Commons Public Accounts Committee delivered a remarkable report on 3 January. Its initial remit was the United Kingdom's £424m (€510m; $697m) stockpile of oseltamivir (Tamiflu), but the committee soon broadened out—with evident surprise—into the ongoing problem of clinical trial results being

There have also been extensive new proposals for greater transparency from European Union legislators, the European Medicines Agency (EMA),[10] and industry bodies.[11] All, however, share the same loophole—they all propose improved access to information on trials conducted from 2014 onwards. This means

nature International weekly journal of science

NATURE | EDITORIAL

Data sharing will pay dividends

As public pressure builds for drug companies to make more results available from clinical trials, the industry should not forget that it relies on collective goodwill to test new therapies.

07 January 2014

Readers of *Nature* who are familiar with recent controversies surrounding clinical trials and medical practice may find it bizarre that anyone could be "surprised and concerned to discover that information is routinely withheld from doctors and researchers about the methods and results of clinical trials", as stated in a UK government report last week.

After all, campaigning doctors have warned for years that pharmaceutical companies have in the past concealed data that reflected poorly on their drugs. Regulators — notably the London-based European Medicines Agency — have pushed for more information to be released into the public

Clinical trials: clearer rules, better protection for patients

ENVI Press release - **Public health** – 20-12-2013 - 12:09

Pharmaceutical companies and academic researchers will be obliged to upload the results of all their European clinical trials to a publicly accessible database, under a provisional agreement reached between Parliament and Council of ministers on EU rules on clinical trials of medicines.

The draft, designed to encourage research whilst protecting patients' rights is to replace an existing directive with simpler, more uniform rules. The new text makes specific provision for low-intervention trials, clarifies the role of ethics committees in the authorisation process, and details how to obtain informed consent from patients.

"For too long, unflattering studies on new medicines have gone undisclosed. Around half of all trials are never published, usually those with negative or disappointing results. It is vital we know about negative outcomes, otherwise trials can be conducted repeatedly before it becomes public knowledge they are ineffective, or even dangerous", said Glenis Willmott (S&D, UK) who is steering the legislation through Parliament.

THE WALL STREET JOURNAL. ≡ OPINION

Zeev's Jou

The FDA Wants You for Sham Surgery

There are better ways to test medical devices than [illegible] patients be placebos who get fake operations.

By SCOTT GOTTLIEB

Feb. 18, 2014 7:17 p.m. ET

In a landmark study of a new cardiovascular device unveiled last month, patients received anesthetics, had a large-bore catheter inserted through a cut into one of their major arteries, and had dye injected into their bloodstream. Their surgeons worked on them for about an hour, with unnecessary pokes and prods, while a monitor displayed the false progress using radioactive fluoroscopy.

The patients weren't being treated. They had agreed to undergo the angiogram procedure without knowing if they'd get the real treatment. They were part of a Food and Drug Administration-approved study of a new medical device from Medtronic MDT -1.21% to treat serious high blood pressure that is resistant to conventional medicines. Some patients were randomly assigned to this sham surgery. They were placebos.

But the spring is not here yet…

Let's not throw the baby out with the bath water.

R&D Spending

Year	PhRMA members[7]
2012	$48.5 billion (*est.*)
2011	$48.6 billion
2010	$50.7 billion
2009	$46.4 billion
2008	$47.4 billion
2007	$47.9 billion
2006	$43.4 billion
2005	$39.9 billion
2000	$26.0 billion
1990	$8.4 billion
1980	$2.0 billion

Value of Medicines

- **Cancer:** Since 1980, 83% of life expectancy gains for cancer patients are attributable to new treatments, including medicines.[19] Another study found that medicines specifically account for 50% to 60% of increases in survival rates since 1975.[20]
- **Cardiovascular Disease:** According to a 2013 statistics update by the American Heart Association, death rates for cardiovascular disease fell a dramatic 33% between 1999 and 2009.[21]
- **HIV/AIDS:** Since the approval of antiretroviral treatments in 1995, the HIV/AIDS death rate has dropped by 85%.[22,23]

Myth:

Industry sponsored research is always valid

Reality:

We need more data transparency