Transparency and access to medical research

Dr. Wim Weber
European editor, BMJ
Present medical research has a credibility problem
Development timeframe of a medical intervention

- Discovery/Synthesis
- Preclinical
- Phase 1
- Phase 2
- Phase 3
- FDA Review
- Phase 4
- Ongoing Safety Surveillance

Years
What happened to:

Monoclonal antibody therapy
Gene therapy
Stem cell therapy

Personalised medicine
Proteomics
Translation of medical research

- 25,000 papers
- 6 major basic research journals (1979-83)
- Claimed to have clear clinical potential
- Had 1 positive trial done by 2002
- With a clinical license by 2003
- Widely used

*Am. J. Med. 114, 477 (2003).*
What is the problem?
Examples in basic science
Functional MRI in neuroscience

Cortical Activity during Hand Movement

Contralateral Hemisphere

Ipsilateral Hemisphere

Healthy Subjects (Right Hand)

Stroke Patients Affected Hand (Right Hand)
What happens when you scan a dead fish?
Most studies are not reproducible

Amgen researchers were able to replicate only 6 of 53 landmark cancer studies

What causes this bias?

In 4455 animal studies

3x positive studies

Overestimates of effect size
What causes this bias?

Survey among basic researchers:

They said they publish 90% of experiments

But thought that less than 50% of other animal experiments are published.

Employees of for-profit organizations estimated that 10% are published.

*PLoS ONE 2012: 0043404*
for many current scientific fields, claimed research findings may often be simply accurate measures of the prevailing bias.
Studying Up
The number of journal articles published world-wide

TOTAL, in millions

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BY SUBJECT

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Sources: U.K. Department for Business, Innovation and Skills; Elsevier
Money allocated to basic research
Is clinical research less biased?
Evidence in Vioxx Suits Shows Intervention by Merck Officials

By ALLEN RUBINSON
Published: April 19, 2006

In 2000, amid rising concerns that its painkiller Vioxx posed heart risks, Merck overruled one of its own scientists after he suggested that a patient in a clinical trial had probably died of a heart attack.

In an e-mail exchange about Vioxx, the company’s most important new drug at the time, a senior Merck scientist repeatedly urged the researcher to change his views about the death “so that we don’t raise concerns.” In later reports to the Food and Drug Administration and in a paper published in 2003, Merck listed the cause of death as “unknown” for the patient, a 73-year-old woman.

Regulators Scuttle Drug for Diabetes

WASHINGON—U.S. regulators put tight curbs on the diabetes drug Avandia and European authorities said they were stopping its sales, effectively ending widespread use of a medicine that was once a multimillion-dollar-a-year seller.

By ALICIA MUNDY, JENNIFER CORBETT DOOREN and JEANNE WHALEN

The Food and Drug Administration and European regulators said they were taking action on Avandia, made by GlaxoSmithKline PLC, because of data tying it to increased risk of heart attacks.

The FDA move marks a tougher stance by the agency’s leadership, named last year President Barack Obama, and signals to pharmaceutical makers and patients that mass-marketed drugs with troublesome side effects are getting closer scrutiny.

The New York Times

Business

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Open a Vanguard mutual fund account.

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Some of the problems

- Trials measure outcomes not relevant to patients
- Failure to acknowledge earlier research
- **Non-publication of negative results**
Non-publication

Bad Pharma
Ben Goldacre
Bestselling author of Bad Science
How drug companies mislead doctors and harm patients
364 pages
Cochrane review 2006:

Oseltamivir 150 mg daily prevented lower respiratory tract complications
2009: Cochrane review updated, but:

- Only 2 / 10 RCTs published
- The pooled analysis was done by Roche
- Obtaining the original data has been very difficult
After 5 years Roche made all data available: and the new meta-analysis is published this week:

- There were 83 RCTs
- There is no evidence for effect on complications
- There are substantial side effects: nausea and psychiatric symptoms
New EU legislation

Trials must be registered

Results must be published
We need less basic research, but more epidemiologic research:

- Observational work validating patient-relevant outcomes
- RCTs
- Meta-analyses
Scientific excellence in Europe
Scientific excellence in Europe in 2034
Thanks

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