

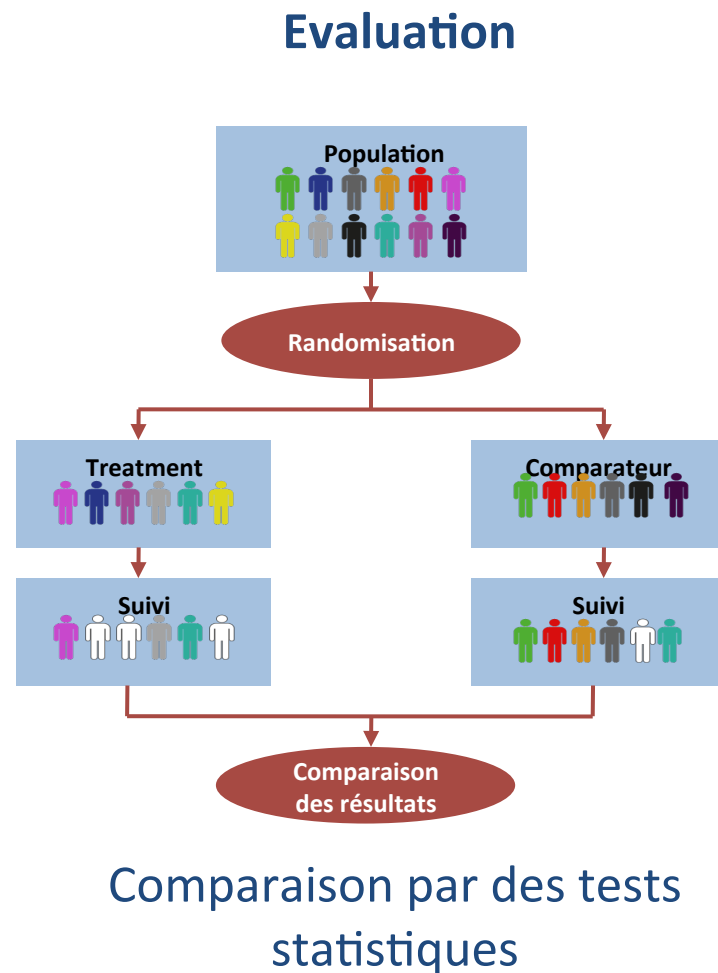
Qualité et transparence de la recherche médicale

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Centre EQUATOR (Enhancing the QUALity and Transparency Of health Research) France

Distorsion des résultats de la recherche clinique?



Interprétation des résultats

- ✓ Le traitement est plus efficace que le comparateur
 - Différence statistiquement significative en faveur du traitement expérimental ($P < 0.05$) (essai positif)

- ✓ Le comparateur est plus efficace que le traitement
 - Différence statistiquement significative en faveur du comparateur ($P < 0.05$)

- ✓ Pas de preuve en faveur de l'efficacité du traitement
 - Pas de différence statistiquement significative entre les 2 groupes ($p > 0.05$) (essai neutre [ex_négatif])

Open access, freely available online

Essay

Why Most Published Research Findings Are False

John P. A. Ioannidis

THE LANCET

A new Lancet Series



increasing value
reducing waste
in research

OPEN ACCESS Freely available online

PLOS MEDICINE

Essay

Why Current Publication Practices May Distort Science

Neal S. Young*, John P. A. Ioannidis, Omar Al-Ubaydli

This essay makes the underlying assumption that scientific information is an economic commodity, and that scientific journals are a medium for its dissemination and exchange. While this exchange system differs from a conventional

Summary

The current in biomedical a distorted view of scientific data laboratory and be studied by

OPEN ACCESS Freely available online

PLOS MEDICINE

Perspective

Bias, Spin, and Misreporting: Time for Full Access to Trial Protocols and Results

An-Wen Chan

Although randomized trials provide key guidance for how we practice medicine

Linked Research Article

This Perspective discusses the

Bero and colleagues also identified important discrepancies between the primary outcomes, statistical

presented in majority of sponsor's used reporting. the FDA

W Avoidable waste in the production and reporting of research evidence

Iain Chalmers, Paul Glasziou

Lancet 2009; 374: 86-89
Published Online

Without accessible and usable reports, research cannot help patients and their clinicians. In a published disir

Conclusions and recommendations

Although some waste in the production and reporting of research evidence is inevitable and bearable, we were surprised by the levels of waste suggested in the evidence we have pieced together. Since research must pass through all four stages shown in the figure, the waste is cumulative. If the losses estimated in the figure apply more generally, then the roughly 50% loss at stages 2, 3, and 4 would lead to a greater than 85% loss, which implies that the dividends from tens of billions of dollars of investment in research are lost every year because of correctable problems. Although we have mainly used

Résultats des essais non disponibles

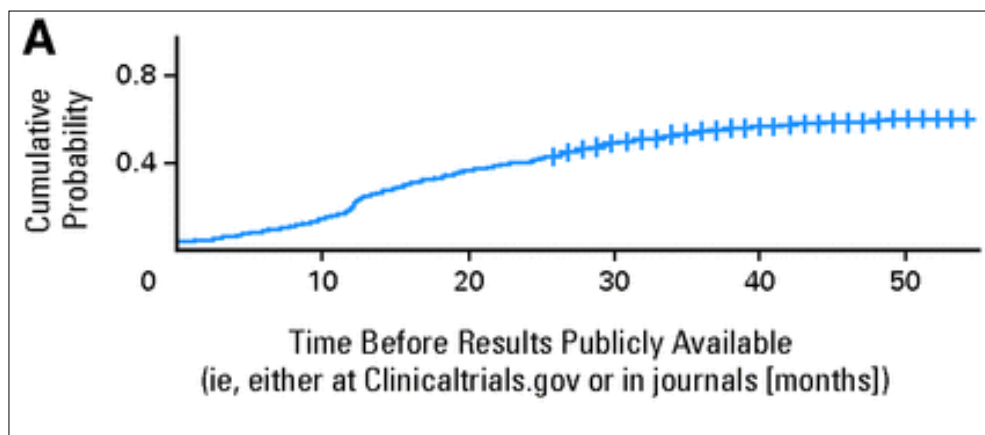
VOLUME 31 · NUMBER 24 · AUGUST 20 2013

JOURNAL OF CLINICAL ONCOLOGY

Public Availability of Results of Trials Assessing Cancer Drugs in the United States

Thi-Anh-Hoa Nguyen, Agnes Dechartres, Soraya Belgherbi, and Philippe Ravaud

209 essais dans le domaine du cancer



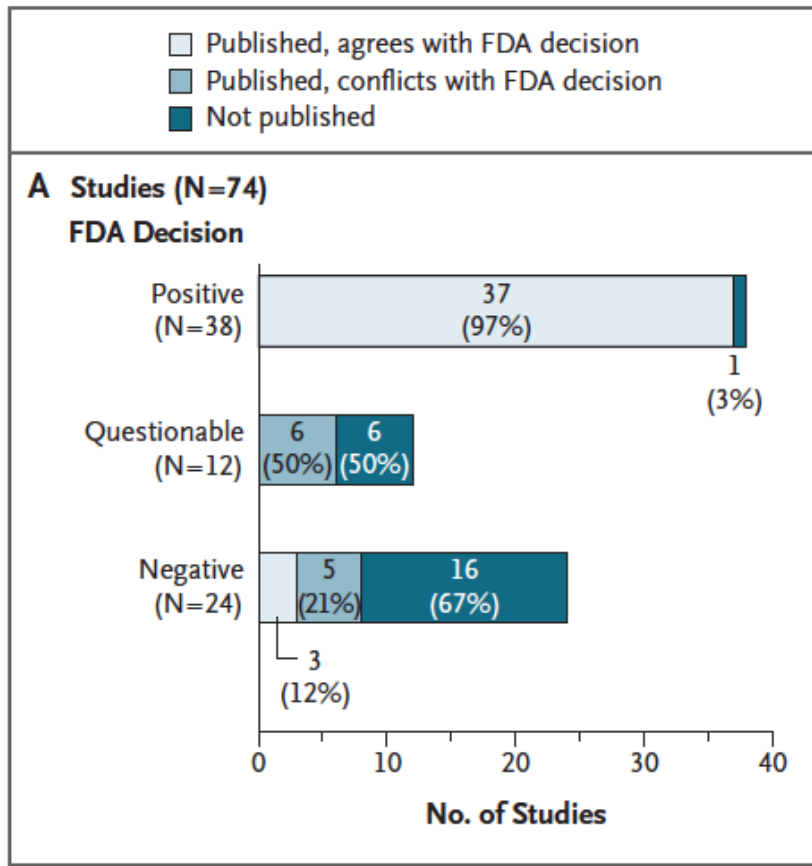
**3 ans après la fin de l'étude,
45 % n'ont aucun résultat
disponible**

Biais de publication

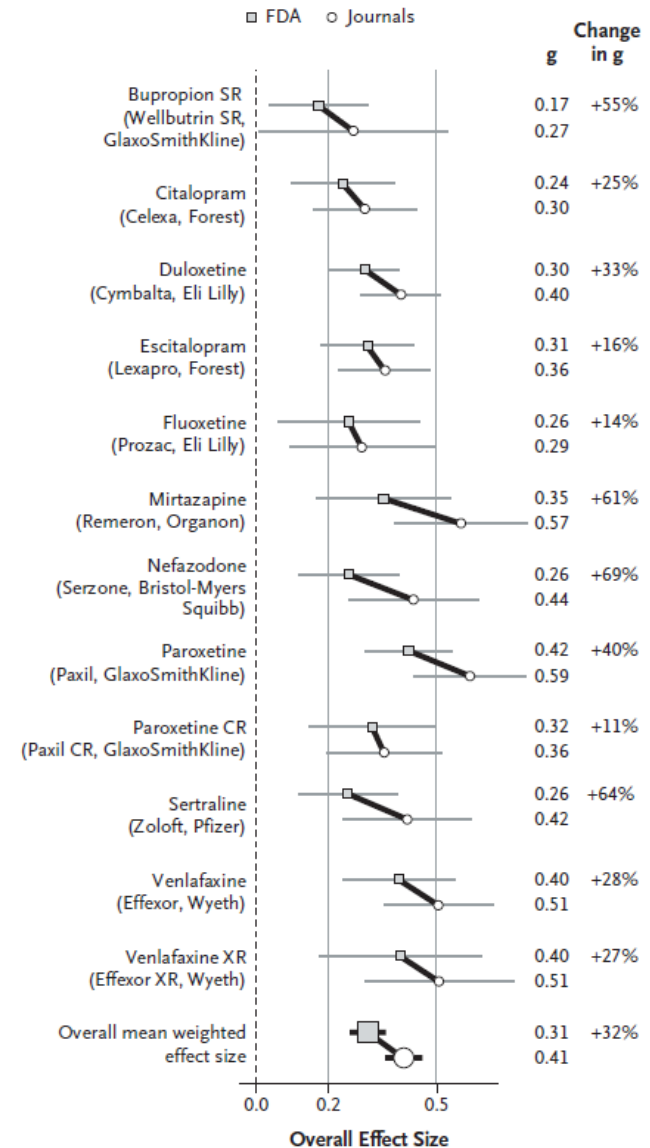
The NEW ENGLAND JOURNAL of MEDICINE

Selective Publication of Antidepressant Trials and Its Influence on Apparent Efficacy

Erick H. Turner, M.D., Annette M. Matthews, M.D., Eftihia Linardatos, B.S., Robert A. Tell, L.C.S.W., and Robert Rosenthal, Ph.D.



5



Sélection des résultats publiés

JAMA *JAMA. 2004;291:2457-2465*

Empirical Evidence for Selective Reporting of Outcomes in Randomized Trials Comparison of Protocols to Published Articles

An-Wen Chan, MD, DPhil

Asbjørn Hróbjartsson, MD, PhD

Mette T. Haahr, BSc

Peter C. Gøtzsche, MD, DrMedSci

Douglas G. Altman, DSc

- 102 essais (3736 critères de jugement) avec un [protocole disponible](#)
- 62% des essais ont au moins un critère de jugement principal qui a été changé, omis ou rajouté.
- Les critères positifs sont plus souvent publiés que les négatifs (OR=2.4 [1.4-4.0])

JAMA *JAMA. 2009;302:977-984*

Comparison of Registered and Published Primary Outcomes in Randomized Controlled Trials

Sylvain Mathieu, MD

Isabelle Boutron, MD, PhD

David Moher, PhD

Douglas G. Altman, DSc

Philippe Ravaud, MD, PhD

- 147 essais [enregistrés sur ClinicalTrials.gov avant leur fin](#)
- Discordance entre les critères de jugement enregistrés et publiés: 31% des essais
- Discordance en faveur des critères positifs (83%)

Interprétation des résultats: SPIN

JAMA *JAMA. 2010;303:2058-2064*

Reporting and Interpretation of Randomized Controlled Trials With Statistically Nonsignificant Results for Primary Outcomes

Isabelle Boutron, MD, PhD

Susan Dutton, MSc

Philippe Ravaud, MD, PhD

Douglas G. Altman, DSc

- 72 articles analysés
- Distorsion des résultats **en faveur de l'efficacité ou de la sécurité**
- Dans le résumé
 - Résultats: 27%
 - Conclusions: 42%
- Dans le texte de l'article
 - Résultats: 21%
 - Discussion: 31%
 - Conclusions: 36%

Prévenir les biais de dissémination: un enjeu majeur

- Prévenir les biais de publication et la sélection des résultats
 - Enregistrement préalable des études et résultats publics
 - Initiative des éditeurs de revues médicales en 2005 (ICMJE)
 - FDA Amendment Act (2007): enregistrement et **résultats** des essais cliniques (< 1 an après la fin) sur ClinicalTrial.gov
 - Directive UE (≥ 2016): résumé des résultats posté sur un registre < 1 an après la fin de l'essai
- Prévenir les rapports incomplets
 - *Reporting guidelines* décrivant quoi rapporter dans toute publication (et comment)

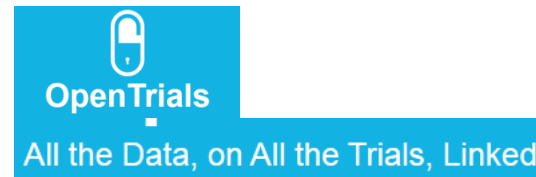
The screenshot shows the EQUATOR network website. At the top left is the EQUATOR network logo with the tagline "Enhancing the QUALity and Transparency Of health Research". To the right is a globe icon and the text "Visit the EQUATOR Spanish Website". Below the logo is a navigation menu with links: Home, Library, Toolkits, Courses & events, News, Blog, About us, Contact. A green banner below the menu reads "The resource centre for good reporting of health research studies". The main content area is divided into three columns. The left column features a "Library for health research reporting" section with a description and two buttons: "Search for reporting guidelines" and "Visit the library for more resources". The middle column is titled "Key reporting guidelines" and lists several guidelines with links to "Full Record", "Checklist", and "Flow Diagram": CONSORT, STROBE, PRISMA, STARD, COREQ, ENTREQ, SQUIRE, CHEERS, CARE, and SAMPL. The right column contains a photograph of a large, ornate classical building with a dome, likely a historical or institutional building.

Une dynamique vers *l'Open data*

- Importance de la **transparence** et de la **disponibilité** des informations sur les essais cliniques



All Trials Registered | All Results Reported



- Utiliser d'autres sources d'information que les publications
 - EMA policy 0070 (2015): rapports cliniques soumis rendus publics
 - Partage des données sources, protocoles, rapports cliniques, ... en particulier par les laboratoires pharmaceutiques



Transparence et accès aux documents de la recherche

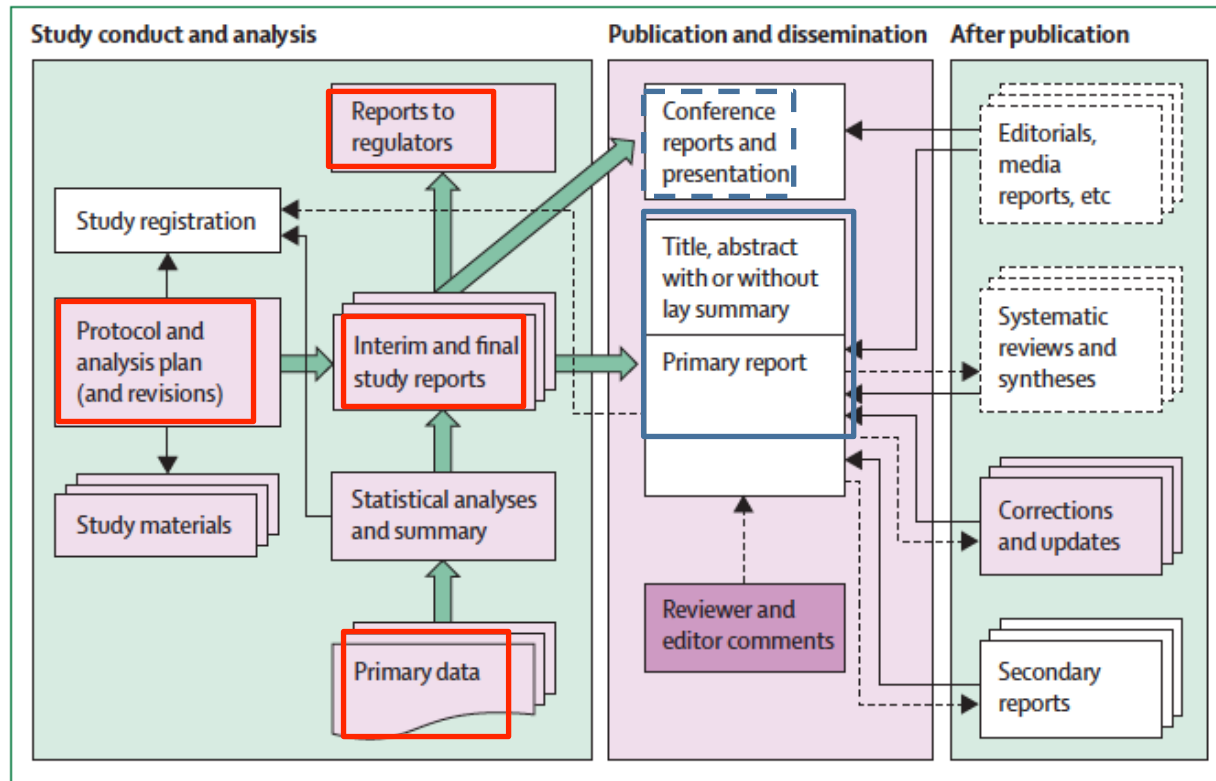


Figure 1: Inefficiency of research reporting due to information being presented in multiple formats, inadequate linkage between information sources, and inaccessibility of documents
 Many documents are unavailable; dark purple boxes indicate those that are rarely available, light purple boxes those that are sometimes available, and white boxes those that are usually publicly available. Block green arrows indicate flow of data, thin lines references or links. Many documents are poorly linked; solid arrow indicates those that are usually linked, and dashed arrow those that are rarely linked.

Utilisation des données de la FDA vs publications

Impact of Reporting Bias in Network Meta-Analysis of Antidepressant Placebo-Controlled Trials

Ludovic Trinquart^{1,2,3,4,5}, Adeline Abbé^{1,2,3,4,5}, Philippe Ravaud^{1,2,3,4,5*}

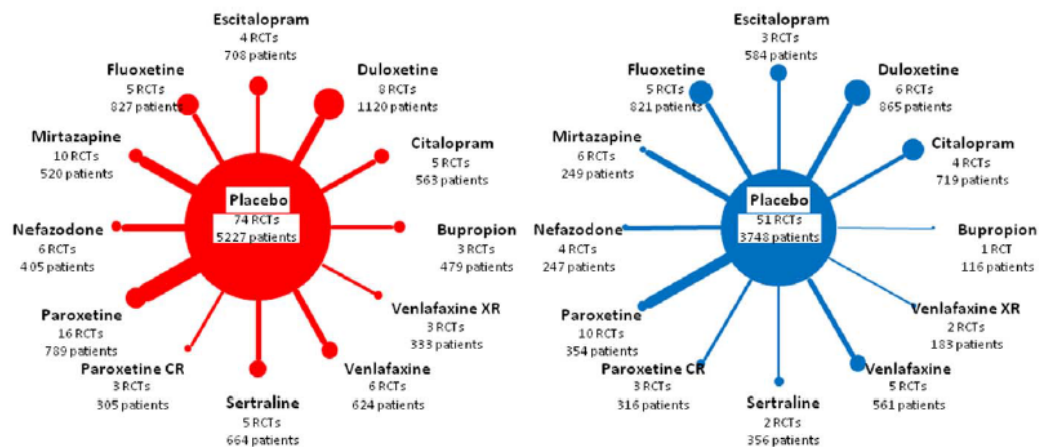


Figure 1. Star-shaped networks of comparisons of data from 74 US Food and Drug Administration (FDA)-registered trials of 12 antidepressants and their 51 related publications. The central node represents the placebo, and each leaf node represents an antidepressant agent. Each node diameter is proportional to the number of patients who received the antidepressant agent; each connecting line width is proportional to the number of trials that addressed the comparison. doi:10.1371/journal.pone.0035219.g001

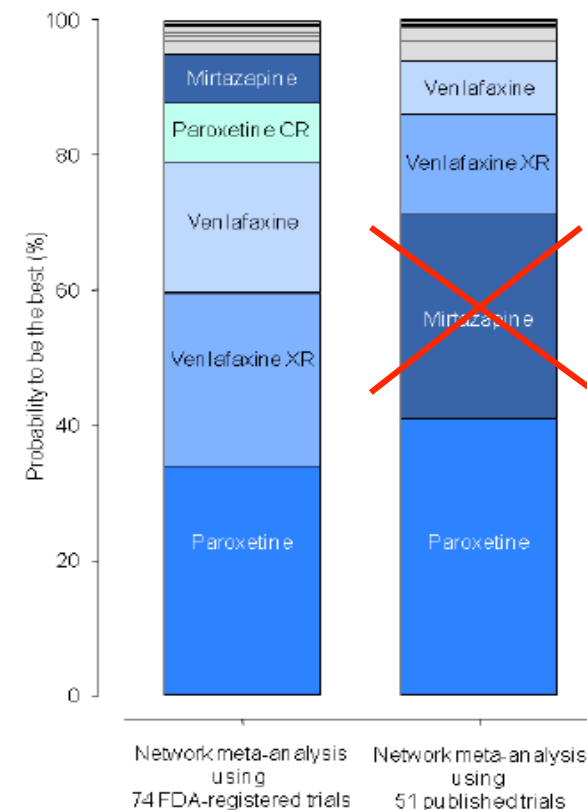



Figure 3. Probabilities that each antidepressant drug is the best according to network meta-analyses of data from 74 FDA-registered trials or 51 published trials with published effect sizes. For instance, for mirtazapine, the probability of being the best was 7.3% and 30.2% according to network-meta-analysis of the 74 FDA-registered trials and 51 published trials with published effect sizes.

Réanalyse d'un essai

 OPEN ACCESS



Restoring Study 329: efficacy and harms of paroxetine and imipramine in treatment of major depression in adolescence

Joanna Le Noury,¹ John M Nardo,² David Healy,¹ Jon Jureidini,³ Melissa Raven,³ Catalin Tufanaru,⁴ Elia Abi-Jaoude⁵

- Réanalyse des données de l'essai à partir des rapports cliniques et des données individuelles obtenues auprès de GSK


Article original (Keller, 2001)

nearly one third did so because of adverse cardiovascular effects. **Conclusions:** Paroxetine is generally well tolerated and effective for major depression in adolescents. *J. Am. Acad. Child Adolesc. Psychiatry*, 2001, 40(7):762–772. **Key Words:**

Réanalyse (Le Noury, 2015)

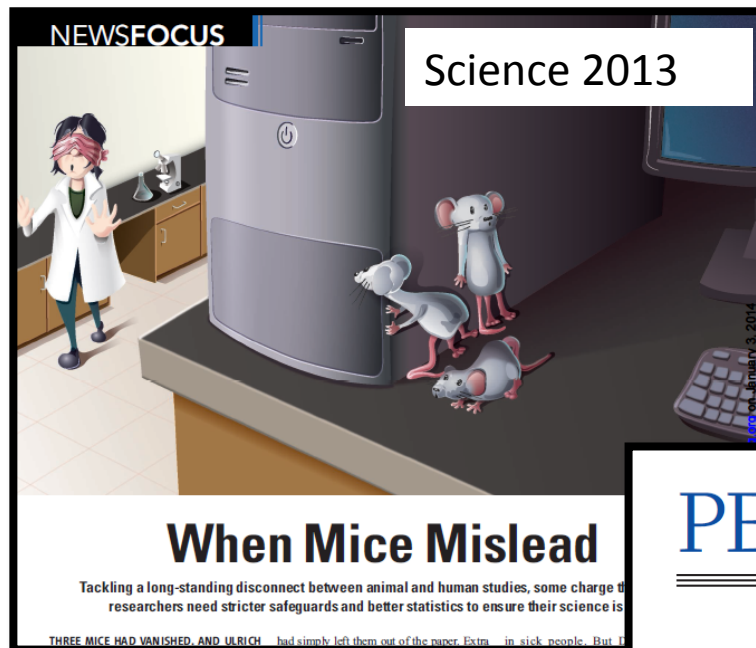
Neither paroxetine nor high dose imipramine showed efficacy for major depression in adolescents, and there was an increase in harms with both drugs. Access to

Restoring invisible and abandoned trials: a call for people to publish the findings

 OPEN ACCESS

Unpublished and misreported studies make it difficult to determine the true value of a treatment. **Peter Doshi and colleagues** call for sponsors and investigators of abandoned studies to publish (or republish) and propose a system for independent publishing if sponsors fail to respond

Pas uniquement le problème de la recherche clinique ...



Nature 2013

ANNOUNCEMENT

Reducing our irreproducibility

Over the past year, *Nature* has published a string of articles that highlight failures in the reliability and reproducibility of published research (collected and freely available at go.nature.com/huhbyr). The problems arise in laboratories, but journals such as this one compound them when they fail to exert sufficient scrutiny over the results that they publish, and when they do not publish enough information for other researchers to assess results properly.

From next month, *Nature* and the Nature research journals will introduce editorial measures to address the problem by improving the consistency and quality of reporting in life-sciences articles. To ease the interpretation and improve the reliability of published results we will more systematically ensure that key methodological details are reported, and we will give more space to methods sections. We will examine statistics more closely and encourage

we will commission statisticians as consultants on certain papers, at the editor's discretion and at the referees' suggestion.

We recognize that there is no single way to conduct an experimental study. Exploratory investigations cannot be done with the same level of statistical rigour as hypothesis-testing studies. Few academic laboratories have the means to perform the level of validation required, for example, to translate a finding from the laboratory to the clinic. However, that should not stand in the way of a full report of how a study was designed, conducted and analysed that will allow reviewers and readers to adequately interpret and build on the results.

To allow authors to describe their experimental design and methods in as much detail as necessary, the participating journals, including *Nature*, will abolish space restrictions on the methods section.

To further increase transparency, we will encourage authors to provide tables of the data behind graphs and figures. This builds on our established data-deposition policy for specific experiments and large data sets. The source data will be made available directly from the figure legend, for easy access. We continue to encourage authors to share detailed methods and reagent descriptions

PERSPECTIVE

Nature 2012

doi:10.1038/nature11556

A call for transparent reporting to optimize the predictive value of preclinical research

Story C. Landis¹, Susan G. Amara², Khusru Asadullah³, Chris P. Austin⁴, Robi Blumenstein⁵, Eileen W. Bradley⁶, Ronald G. Crystal⁷, Robert B. Darnell⁸, Robert J. Ferrante⁹, Howard Fillit¹⁰, Robert Finkelstein¹, Marc Fisher¹¹, Howard E. Gendelman¹², Robert M. Golub¹³, John L. Goudreau¹⁴, Robert A. Gross¹⁵, Amelie K. Gubitzi¹, Sharon E. Hesterlee¹⁶, David W. Howells¹⁷, John Huguenard¹⁸, Katrina Kelner¹⁹, Walter Koroshetz¹, Dimitri Krainc²⁰, Stanley E. Lazic²¹, Michael S. Levine²², Malcolm R. Macleod²³, John M. McCall²⁴, Richard T. Moxley III²⁵, Kalyani Narasimhan²⁶, Linda J. Noble²⁷, Steve Perrin²⁸, John D. Porter¹, Oswald Steward²⁹, Ellis Unger³⁰, Ursula Utz¹ & Shai D. Silberberg¹

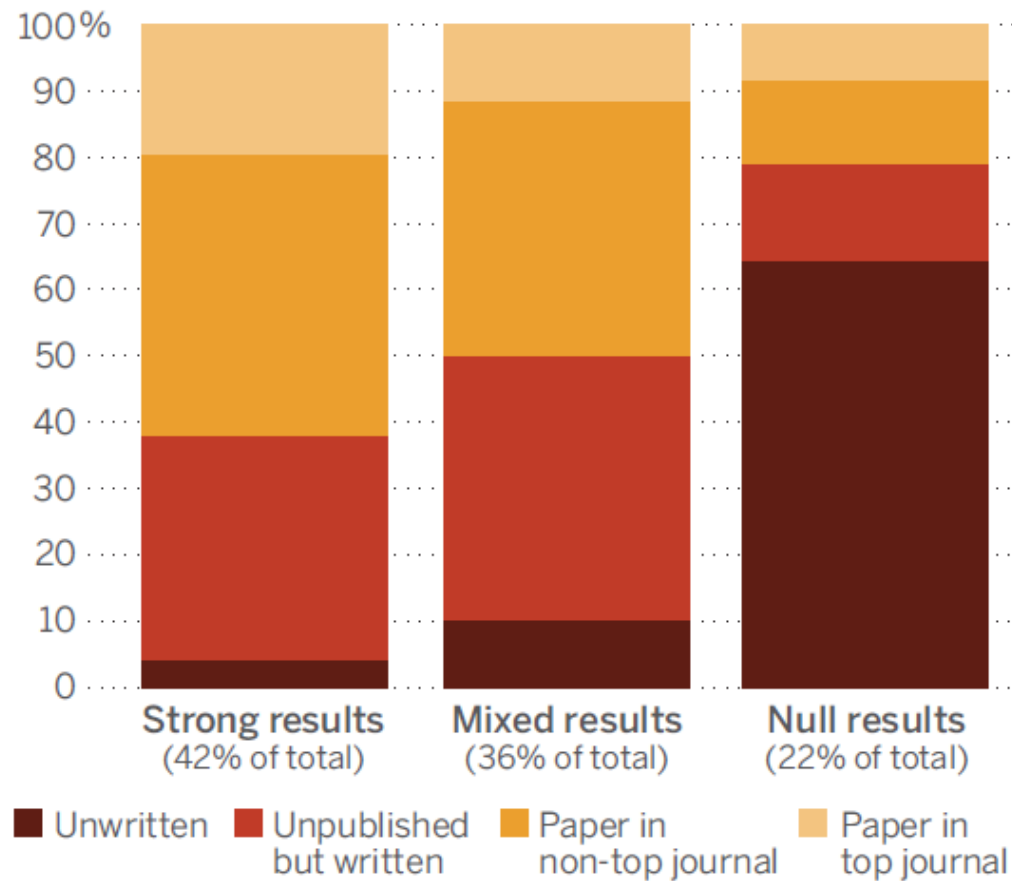
The US National Institute of Neurological Disorders and Stroke convened major stakeholders in June 2012 to discuss

Ni un problème de la recherche en santé

Biais de publication dans les sciences sociales

Most null results are never written up

The fate of 221 social science experiments



Recherche financées par la *National Science Foundation*

Source: A. Franco *et al.*, *Science* (28 August)

Remerciements

Centre EQUATOR / Equipe de recherche

- Pr Philippe Ravaud (directeur)
- Pr Isabelle Boutron (directrice-adjointe)
- Agnès Dechartres
- Ludovic Trinquart
- Amélie Yavchitz
- Gabriel Baron
- Carolina Riveros
- Doctorants: I. Atal, P. Créquit, R. Haneef, Y. Yordanov

Réseau EQUATOR

<http://www.equator-network.org>

- Lancé en Juin 2008 à Oxford
- Objectif principal : Améliorer la qualité et la transparence de la recherche en santé
 - Amélioration de la transparence de la recherche en assurant la promotion d'une présentation claire, complète, transparente et exacte des articles publiés
 - Développement de « reporting guidelines »
 - Diffusion et implémentation des « reporting guidelines »
 - Amélioration de la planification, de la mise en oeuvre et analyse des projets de recherche en santé



Essential resources for writing and publishing health research



Library for health
research reporting

The Library contains a comprehensive searchable database of reporting guidelines and also links to other resources relevant to research reporting.



Search for reporting
guidelines



Not sure which reporting
guideline to use?

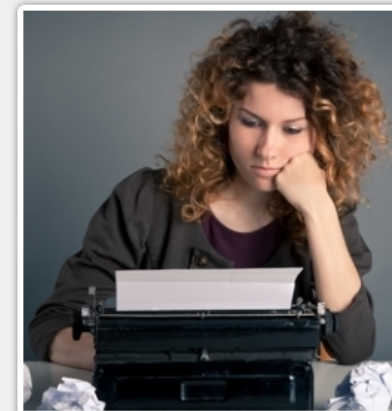


Reporting guidelines
under development



Reporting guidelines for main
study types

| | | | |
|---|-------------------------|----------------------------|-----------------------|
| Randomised trials | CONSORT | Extensions | Other |
| Observational studies | STROBE | Extensions | Other |
| Systematic reviews | PRISMA | Extensions | Other |
| Case reports | CARE | | Other |
| Qualitative research | SRQR | COREQ | Other |
| Diagnostic / prognostic studies | STARD | TRIPOD | Other |
| Quality improvement studies | SQUIRE | | Other |
| Economic evaluations | CHEERS | | Other |



EQUATOR toolkit for authors

Library for health research reporting



The Library for health research reporting provides an up-to-date collection of guidelines and policy documents related to health research reporting. These are aimed mainly at authors of research articles, journal editors, peer reviewers and reporting guideline developers.



Search for reporting guidelines



Reporting guidelines under development



Translations of reporting guidelines



Guidance on scientific writing

Authors



Information and resources for authors

Editors



Information and resources for editors and peer reviewers

Developers



Information and resources for guideline developers

Librarians



Information and resources for librarians

Teachers



Information and resources for teachers