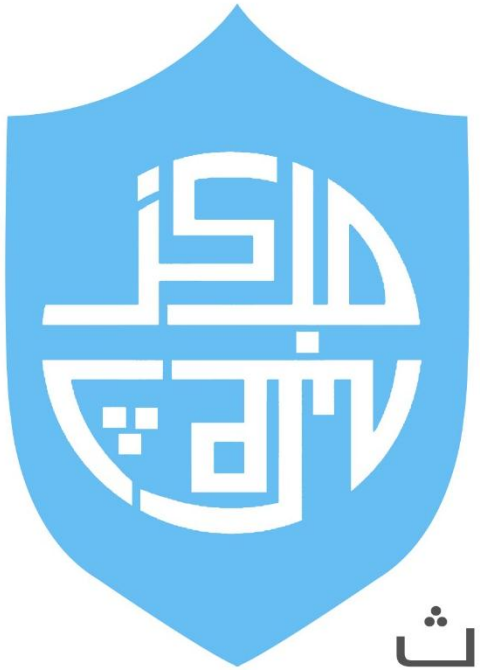


مركز بحوث
الدراسات العلمية و الطبية
RESEARCH CENTER
FOR FEMALE SCIENTIFIC AND MEDICAL COLLEGES

عمادة البحث العلمي

جامعة الملك سعود

البحث العلمي المنشور بين الجيد والرديء

سيناء عبد المحسن العقيل
استاذ مشارك بقسم الصيدلة الاكلينكية
كلية الصيدلة

Salageel@ksu.edu.sa

@alaqeels

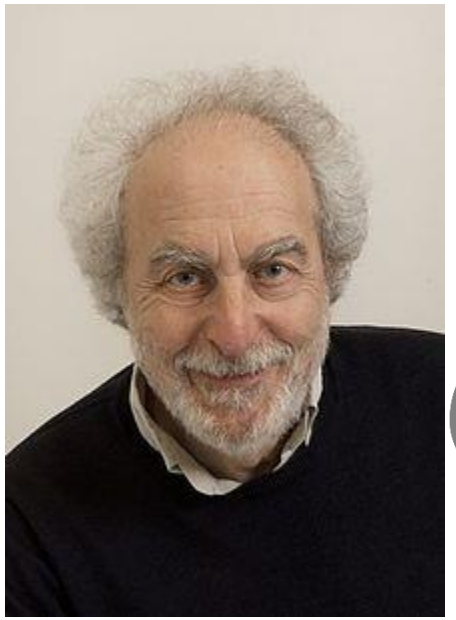

A
B
C
simulation
√1000
X+Y=Z
Collecting data
A
test
B

Peer Review Process

William Whewell, peer-review pioneer
Source: N AT U R E, VO L 5 3 2 . 2 0 1 6

BMJ

LONDON, SATURDAY 29 JANUARY 1994



Douglas Altman (1948 –2018)

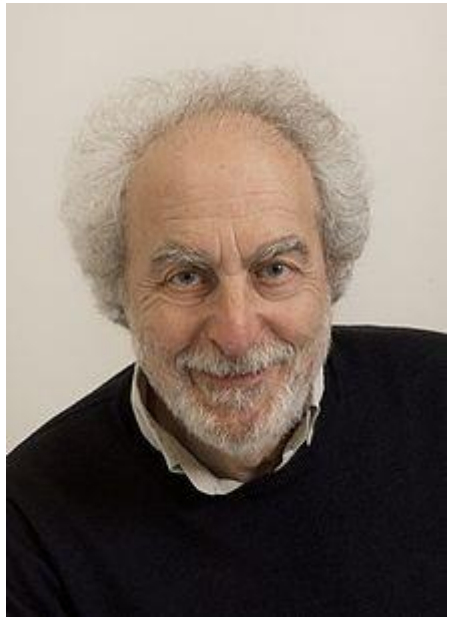
The scandal of poor medical research

We need less research, better research, and research done for the right reasons

"What should we think about a doctor who uses the wrong treatment, either wilfully or through ignorance, or who uses the right treatment wrongly (such as by giving the wrong dose of a drug)? Most people would agree that such behaviour was unprofessional, arguably unethical, and certainly unacceptable."

BMJ

LONDON, SATURDAY 29 JANUARY 1994



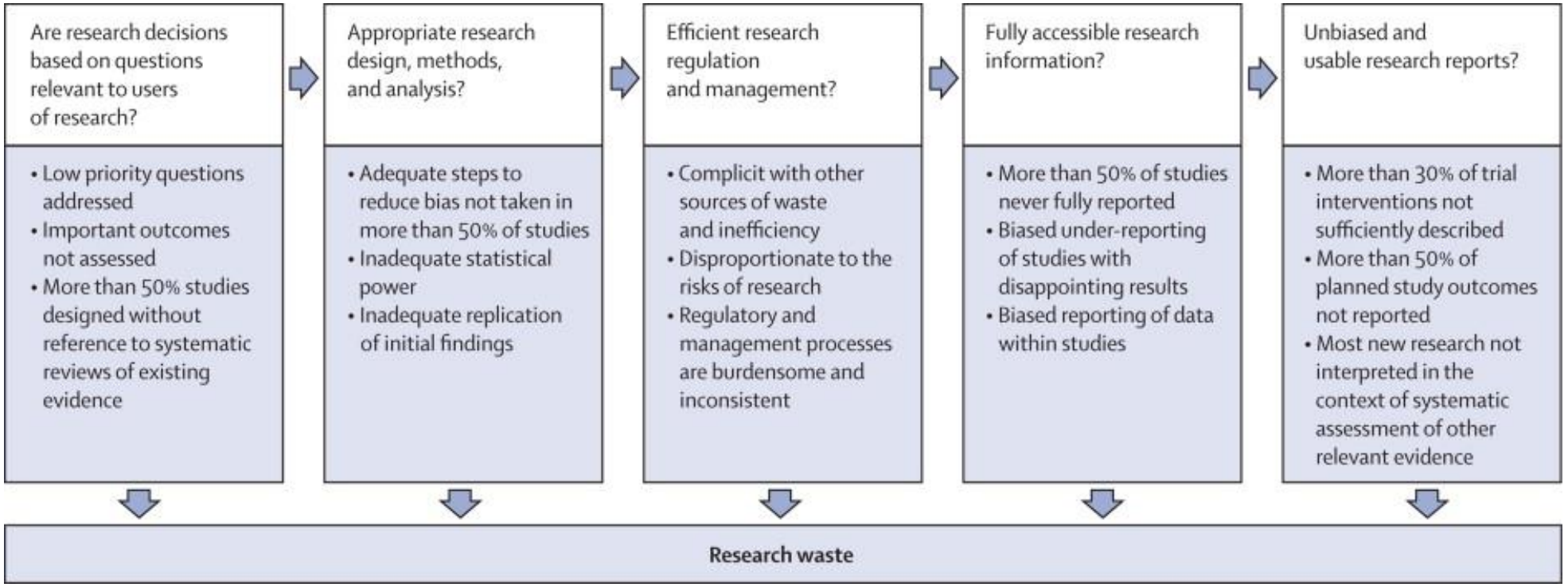
Douglas Altman (1948 –2018)

The scandal of poor medical research

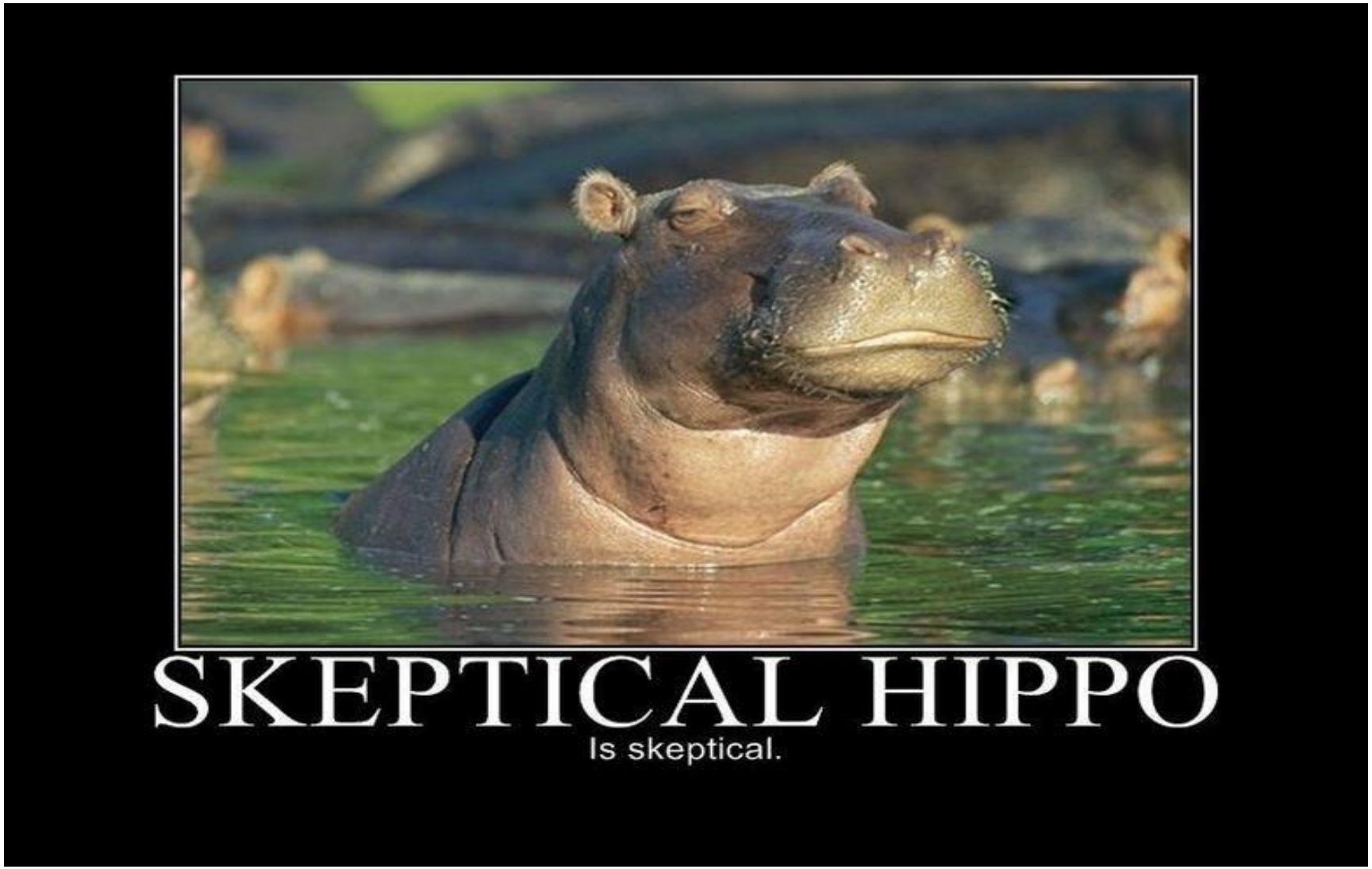
We need less research, better research, and research done for the right reasons

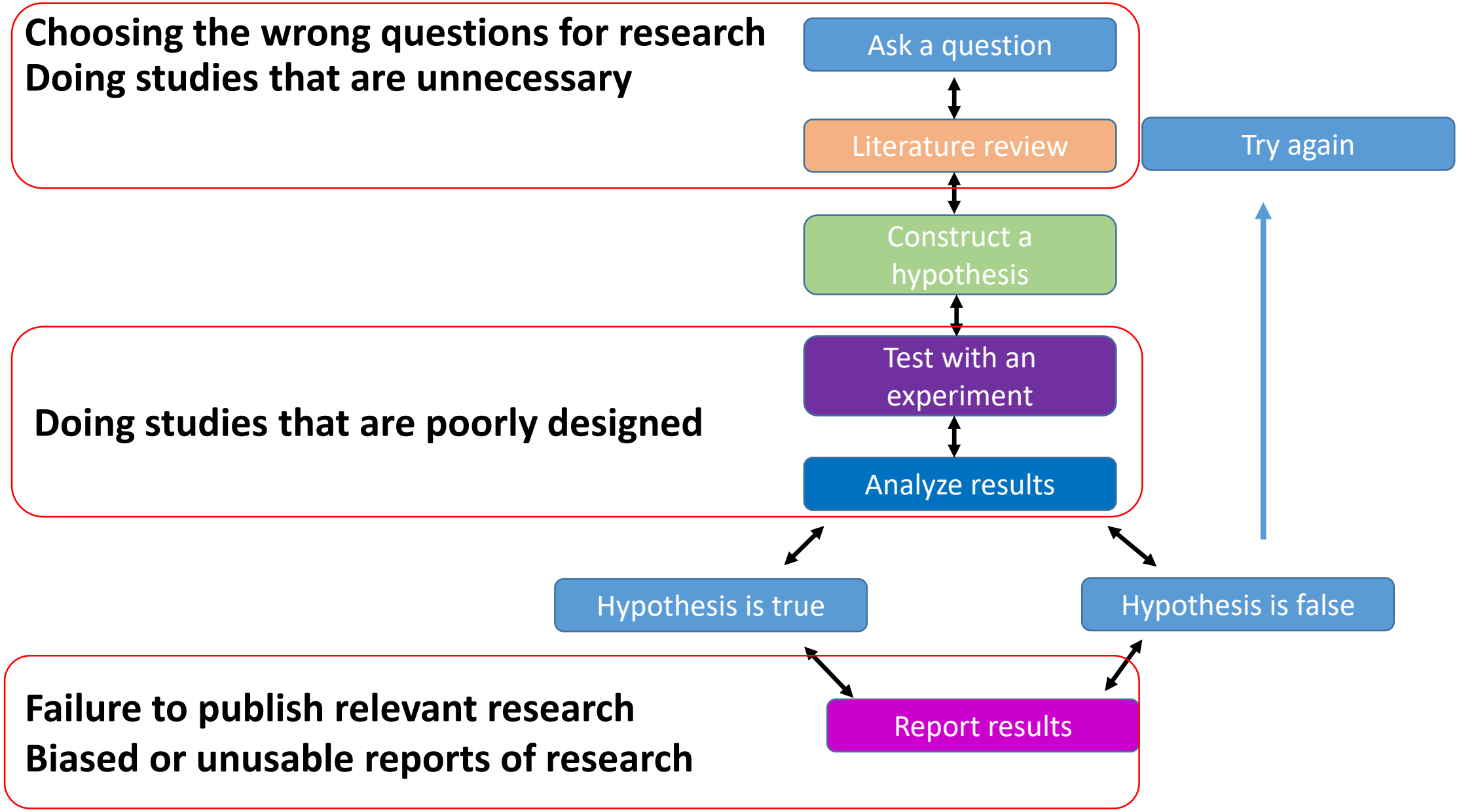
"What, then, should we think about researchers who use the wrong techniques (either wilfully or in ignorance), use the right techniques wrongly, misinterpret their results, report their results selectively, cite the literature selectively, and draw unjustified conclusions? We should be appalled. Yet numerous studies of the medical literature, in both general and specialist journals, have shown that all of the above phenomena are common.[1-7] This is surely a scandal."

An estimated $200 billion —85% of global spending on research — is routinely wasted on poorly designed and redundant studies. (2010)



Lancet 2009; 374: 86–89


SKEPTICAL HIPPO
Is skeptical.


Choosing the wrong questions for research
Doing studies that are unnecessary
Ask a question
Literature review
Try again
Construct a hypothesis
Doing studies that are poorly designed
Test with an experiment
Analyze results
Hypothesis is true
Hypothesis is false
Failure to publish relevant research
Biased or unusable reports of research
Report results

Bias

Any trend in the collection, analysis, interpretation, publication or review of data that can lead to conclusions that are systematically different from the truth. (Last J. *A dictionary of epidemiology*, 2001)

Risk of bias.

Bias

- Allocation bias
- Ascertainment bias
- Attention bias
- Attrition bias
- Chronological bias
- Co-intervention bias
- Contamination bias
- Diagnostic access bias
- Diagnostic suspicion bias
- Detection bias
- Detection-signal bias
- Expectation bias
- Exposure bias
- Hawthorne effect
- Incorporation bias
- Insensitive measurement bias
- Intervention bias
- Lead time bias
- Measurement bias
- Membership bias
- Neyman bias
- Non-respondent bias
- Observer bias
- Prevalence-incidence bias
- Proficiency bias
- Publication bias
- Recall bias
- Referral bias
- Reporting bias
- Response bias
- Sampling bias
- Selection bias
- Spectrum bias
- Survival bias
- Time lag bias
- Timing bias
- Unmasking bias
- Verification bias (or partial verification bias)
- Volunteer bias

DEMO

Catalogofbias.org

Doing studies that are poorly designed

Failure to publish
Biased or unusable reports

Attrition (drop out) bias

Reporting bias

Channeling bias

Detection bias

Confirmation bias

Selection bias

Performance bias

Publication bias

Recruitment/Allocation

Implementation

Analysis/Publication

Research Misconduct

Doing studies that are poorly designed

	Attrition (drop out) bias	Reporting bias
Allocation bias	Detection bias	Confirmation bias
Selection bias	Performance bias	Publication bias
Recruitment/Allocation	Implementation	**Analysis/Publication**

Research Misconduct

Selection bias

COFFEE AND CANCER OF THE PANCREAS

BRIAN MACMAHON, M.D., STELLA YEN, M.D., DIMITRIOS TRICHOPOULOS, M.D., KENNETH WARREN, M.D., AND GEORGE NARDI, M.D.

Abstract We questioned 369 patients with histologically proved cancer of the pancreas and 644 control patients about their use of tobacco, alcohol, tea, and coffee. There was a weak positive association between pancreatic cancer and cigarette smoking, but we found no association with use of cigars, pipe tobacco, alcoholic beverages, or tea. A strong association between coffee consumption and pancreatic cancer was evident in both sexes. The association was not affected by controlling for cigarette use. For the sexes combined, there was a significant dose-response relation ($P \sim 0.001$); after adjustment for cigarette smoking, the relative risk associated with drinking up to two cups of coffee per day was 1.8 (95 per cent confidence limits, 1.0 to 3.0), and that with three or more cups per day was 2.7 (1.6 to 4.7). This association should be evaluated with other data; if it reflects a causal relation between coffee drinking and pancreatic cancer, coffee use might account for a substantial proportion of the cases of this disease in the United States. (N Engl J Med. 1981; 304:630-3.)

Selection bias: the classic example

630 THE NEW ENGLAND JOURNAL OF MEDICINE March 12, 1981

COFFEE AND CANCER OF THE PANCREAS

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Abstract We questioned 369 patients with histologically proved cancer of the pancreas and 644 control patients about their use of tobacco, alcohol, tea, and coffee. There was a weak positive association between pancreatic cancer and cigarette smoking, but we found no association with use of cigars, pipe tobacco, alcoholic beverages, or tea. A strong association between coffee consumption and pancreatic cancer was evident in both sexes. The association was not affected by controlling for cigarette use. For the sexes combined, there was a significant dose-response relation ($P \sim 0.001$); after adjustment for cigarette smoking, the relative risk associated with drinking up to two cups of coffee per day was 1.8 (95 per cent confidence limits, 1.0 to 3.0), and that with three or more cups per day was 2.7 (1.6 to 4.7). This association should be evaluated with other data; if it reflects a causal relation between coffee drinking and pancreatic cancer, coffee use might account for a substantial proportion of the cases of this disease in the United States. (N Engl J Med. 1981; 304:630-3.)

OVER the past few decades, cancer of the pancreas has emerged as one of the most important neoplasias in human beings. It now accounts for approximately 20,000 deaths annually in the United States. Causative factors have been sought in several previous studies, but only cigarette smoking has emerged as a consistent, though relatively weak, exogenous risk factor. We report the results of a study that was planned to reevaluate the relation of this disease to smoking and to examine the role of alcohol consumption as a possible confounding variable. Data were also obtained on intake of tea and coffee — factors that have not been adequately investigated in this disease.

METHODS

We conducted a case-control interview study. The cases were patients with histologic diagnoses of cancer of the exocrine pancreas who were in any of 11 large hospitals in the Boston metropolitan area and Rhode Island between October 1974 and August 1979. Patients with tumors of the islet cells, periampullary duodenal mucosa, or ampulla of Vater were not included. We identified 578 patients and interviewed 485 of them. Twenty patients died and 35 were discharged before an interview could be arranged; 78 were too sick to be interviewed, 14 had language difficulties, and 26 refused the interview. Also excluded from the analysis were eight nonwhite patients, four residents of countries other than the United States, eight patients older than 79 years, and 16 patients whose interview information was judged by the interviewer to be of questionable reliability. The analysis is based on data from the remaining 369 patients.

To assemble a control series, the interviewers also attempted to question all other patients who were under the care of the same physician in the same hospital at the time of an interview with a patient with pancreatic cancer. Either before the interview (if the information was known) or afterward, patients with diseases of the pancreas or hepatobiliary tract or diseases known to be associated with smoking or alcohol consumption were excluded. The principal diagnostic categories excluded (in addition to diseases of the biliary tract or pancreas) were cardiovascular disease, diabetes mellitus, respiratory or bladder cancer, and peptic ulcer. From a total of 1118 eligible patients, we interviewed 708; nine died and 131 were discharged before the interview, 179 were too ill, 26 had language problems, and 73 refused. After exclusion of 17 nonwhites, five foreign residents, four persons older than 79 years, and 30 persons whose interviews were judged to be unreliable, the control series used for the analysis consisted of 644 patients. Minor differences between tables in the stated numbers of cases and controls resulted from absence of specific items being analyzed in a few questionnaires.

The control series was composed of two principal diagnostic groups: 273 patients with cancer other than cancers of the pancreas and biliary tract, respiratory tract, or bladder and 371 patients with other disorders. Of the control patients with cancer, the tumor was in the breast in 65 patients, colon in 60, rectum in 25, stomach in 24, small intestine in nine, ovary in eight, prostate in eight, and cervix in seven; there were also 16 with melanoma and 13 with lymphoma. No other cancer was found in more than four subjects. Diagnoses in the controls without cancer were of a wide variety, although because of the nature of the practices of many of the physicians who were responsible for patients with cancer of the pancreas, patients with gastroenterologic conditions were probably overrepresented in relation to a general hospital population. The principal diagnoses were hernia in 70 patients; colitis, enteritis, or diverticulitis in 41; bowel obstruction, adhesions, or fistulae in 26; gastritis in 17; other gastroenterologic conditions in 47; benign tumors in 29; varicose veins or phlebitis in 21; genitourinary disorders in 20; neurologic disorders in 20; gynecologic disorders in 16; and other conditions in 54.

In the analyses, the patients with pancreatic cancer were compared with the control patients with cancer and independently with the control group without cancer. The findings were quite similar, and only the results with the combined control group are presented here.

Several questions in the interview probed the duration and intensity of smoking of cigarettes, cigars, and pipes. Questions on alcoholic beverages asked about the frequency of use before the onset of illness, the age span over which such use occurred, and the type of beverage used most frequently. The questions on tea and coffee were limited to the number of cups consumed in a typical day before the current illness was evident.

Tests of significance and estimates of adjusted relative risks and their confidence limits were derived with the method of Mantel and Haenszel[5] and its extension.[6] The data were stratified by age in 10-year groups and by sex where appropriate. All confidence limits are 95 per cent intervals. Most analyses were performed with the calculator programs developed by Rothman and Boice.[7]

RESULTS

Tobacco

There was no difference between cases and controls in the use of cigars or pipe tobacco. Among men, the

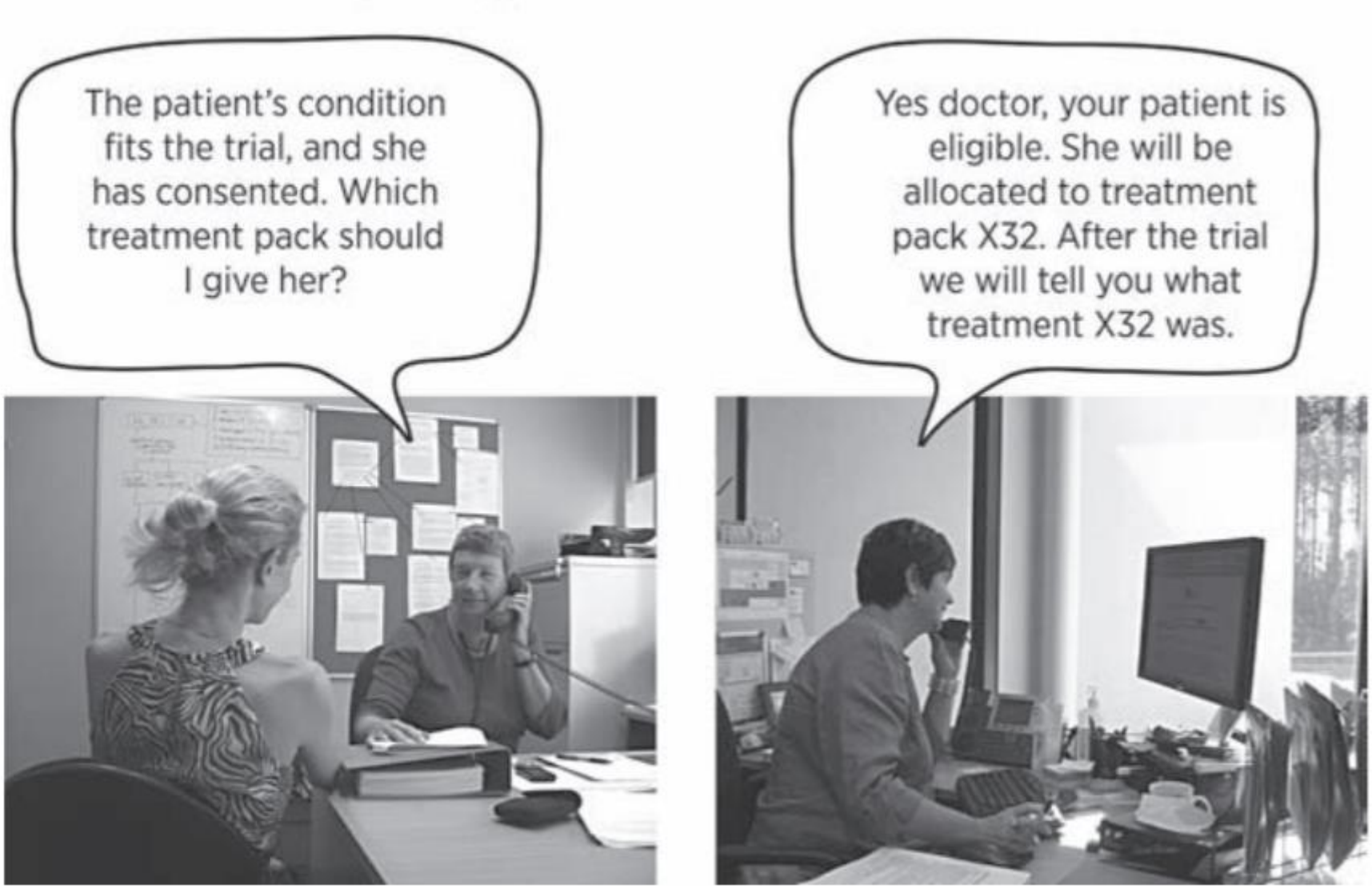
To assemble a control series, the interviewers also attempted to question all other patients who were under the care of the same physician in the same hospital at the time of an interview with a patient with pancreatic cancer.

Allocation bias

- Systematic difference in how participants are assigned to treatment and comparison groups in a clinical trial.

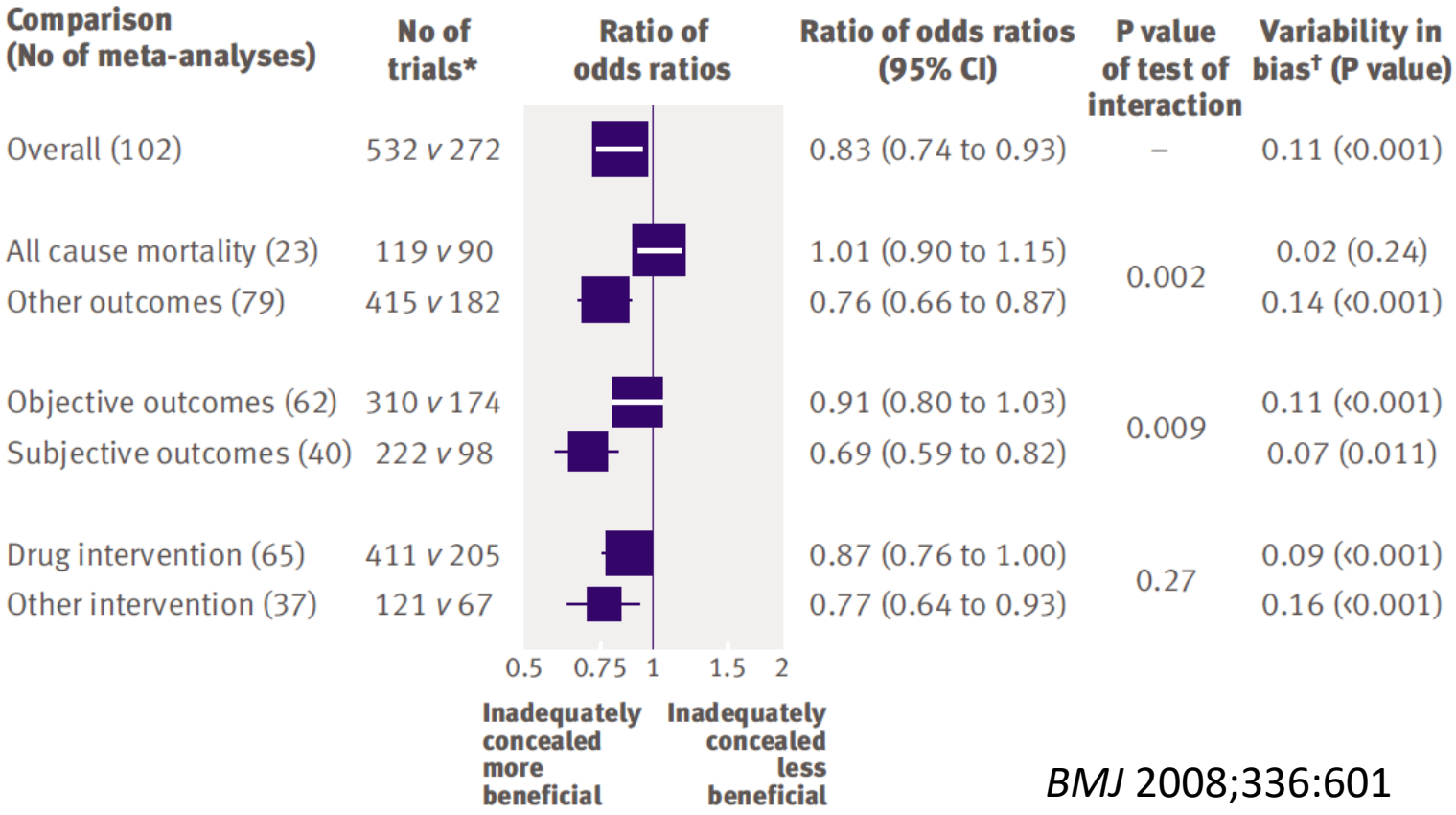
Randomisation of participants in intervention studies

Adequate allocation concealment



Source: http://en.testingtreatments.org/wp-content/uploads/sites/3/2015/12/6.3.3-Unbiased-prospective-allocationp73-74x.pdf

The inadequate or unclear allocation concealment and biased estimates of intervention effects



BMJ 2008;336:601

Doing studies that are poorly designed 2

	Attrition (drop out) bias	
Alloction bias	Detection bias	Reporting bias
Selection bias	Performance bias	Publication bias
Recruitment/Allocation	Implementation	**Analysis/Publication**

Research Misconduct

Attrition bias

Abstract

Objective To assess the reporting, extent, and handling of loss to follow-up and its potential impact on the estimates of the effect of treatment in randomised controlled trials.

Design Systematic review. We calculated the percentage of trials for which the relative risk would no longer be significant under a number of assumptions about the outcomes of participants lost to follow-up.

Data sources Medline search of five top general medical journals, 2005-07.

BMJ 201:344:e2809

Eligibility criteria Randomised controlled trials that reported a significant binary primary patient important outcome.

Results Of the 235 eligible reports identified, 31 (13%) did not report whether or not loss to follow-up occurred. In reports that did give the relevant information, the median percentage of participants lost to follow-up was 6% (interquartile range 2-14%). The method by which loss to follow-up was handled was unclear in 37 studies (19%); the most commonly used method was survival analysis (66, 35%). When we varied assumptions about loss to follow-up, results of 19% of trials were no longer significant if we assumed no participants lost to follow-up had the event of interest, 17% if we assumed that all participants lost to follow-up had the event, and 58% if we assumed a worst case scenario (all participants lost to follow-up in the treatment group and none of those in the control group had the event). Under more plausible assumptions, in which the incidence of events in those lost to follow-up relative to those followed-up is higher in the intervention than control group, results of 0% to 33% trials were no longer significant.

Conclusion Plausible assumptions regarding outcomes of patients lost to follow-up could change the interpretation of results of randomised controlled trials published in top medical journals.

Detection bias

American Journal of Epidemiology
Vol. 185, No. 8
DOI: 10.1093/aje/kww242
Advance Access publication: March 1, 2017

Practice of Epidemiology

Evidence for Detection Bias by Medication Use in a Cohort Study of Breast Cancer Survivors

Heidi S. Wirtz, Gregory S. Calip, Diana S. M. Buist, Julie R. Gralow, William E. Barlow, Shelly Gray, and Denise M. Boudreau*

* Correspondence to Dr. Denise M. Boudreau, Group Health Research Institute, 1730 Minor Avenue, Suite 1600, Seattle, WA 98101 (e-mail: boudreau.d@ghc.org).

Initially submitted June 10, 2015; accepted for publication May 6, 2016.

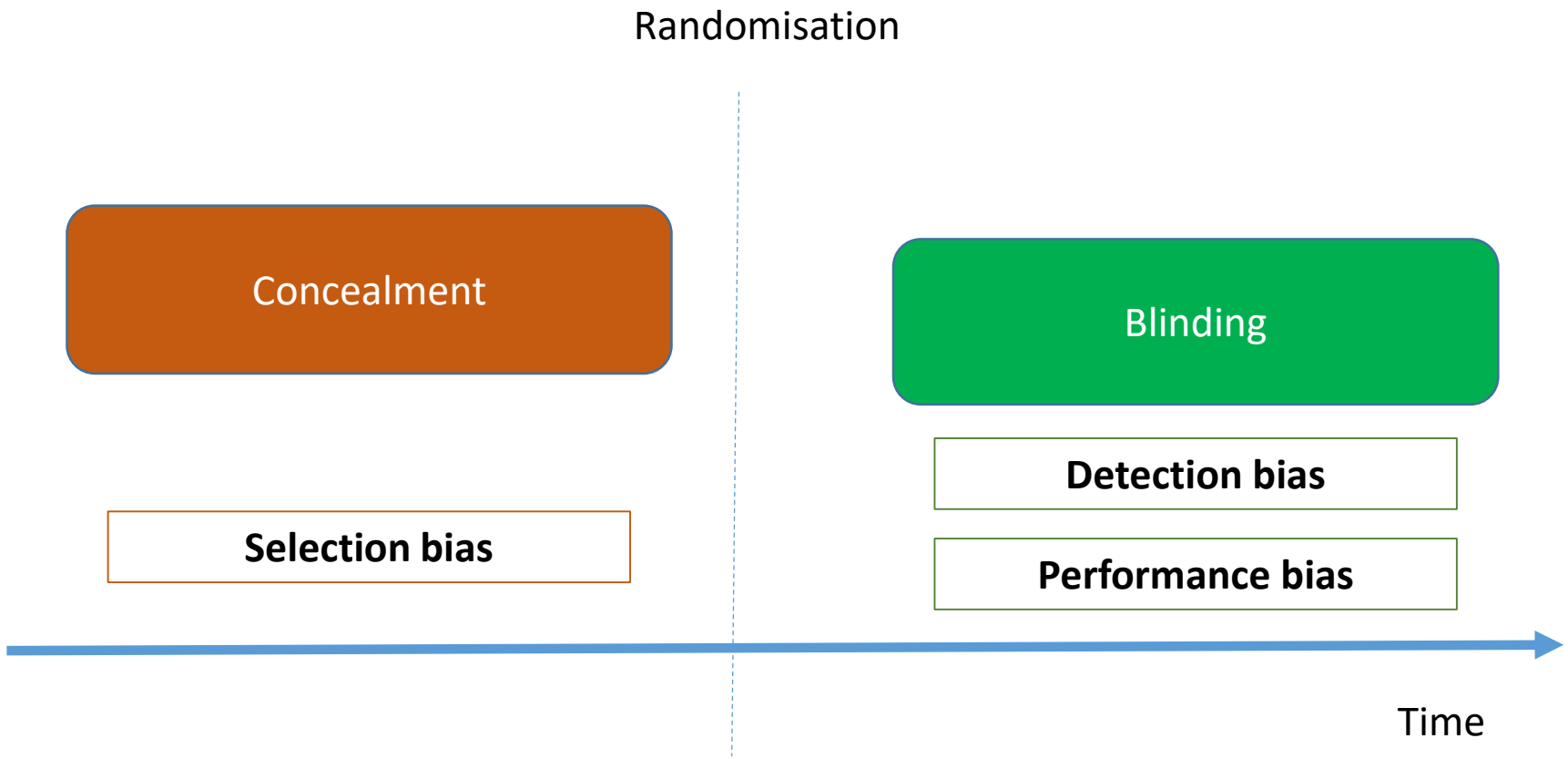
In previous studies, we found modestly decreased and increased risks of second breast cancer events with the use of statins and antibiotics, respectively, after adjustment for surveillance mammography. We evaluated detection bias by comparing receipt of surveillance mammography among users of these 2 disparate classes of medication. Adult women diagnosed with early-stage breast cancer in an integrated health-care plan (Group Health Cooperative; Washington Commonly Used Medications and Breast Cancer Outcomes) were included infrequent (1–3 dispensings/12 months) and frequent antibiotic use; statin use included less adherent (1 dispensing/6 months) and adherent. We examined associations between medication use and surveillance mammography using logistic regression equations and evaluated the impact of adjusting for surveillance within Cox proportional hazard models. Frequent antibiotic users were less likely to receive surveillance mammography (odds ratio (OR) = 0.90, 95% confidence interval (CI): 0.82, 0.99) than were nonusers; no association was found among infrequent users (OR = 0.96, 95% CI: 0.90, 1.03). Adherent statin use was associated with more surveillance compared with nonuse (OR = 1.11, 95% CI: 1.01, 1.25), but less adherent statin use was not (OR = 1.03, 95% CI: 0.81, 1.31). No difference in associations between medications of interest and second breast cancer events was observed when surveillance was removed from otherwise adjusted models. The influence of detection bias by medication use warrants further exploration.

breast cancer; cancer survivorship; detection bias; epidemiologic methods

Abbreviations: CCI, Charlson Comorbidity Index; CI, confidence interval; COMBO, Commonly Used Medications and Breast Cancer Outcomes; GHC, Group Health Cooperative; HR, hazard ratio; OR, odds ratio; SBCE, second breast cancer event; SEER, Surveillance, Epidemiology, and End Results.

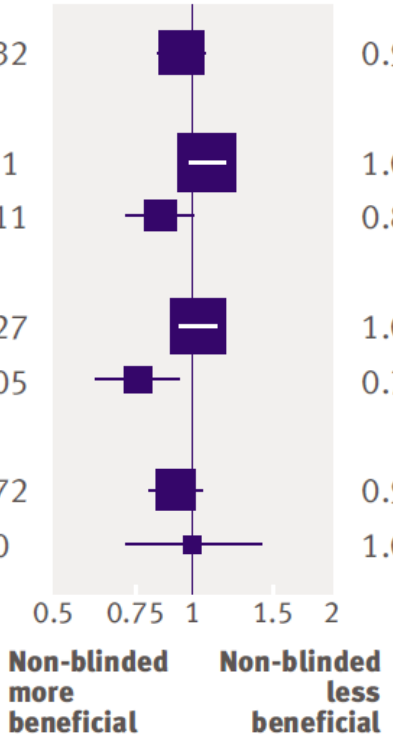
Performance bias

Systematic differences between groups in the care that is provided, or in exposure to factors other than the interventions of interest.


Randomisation
Concealment
Blinding
Detection bias
Selection bias
Performance bias
Time

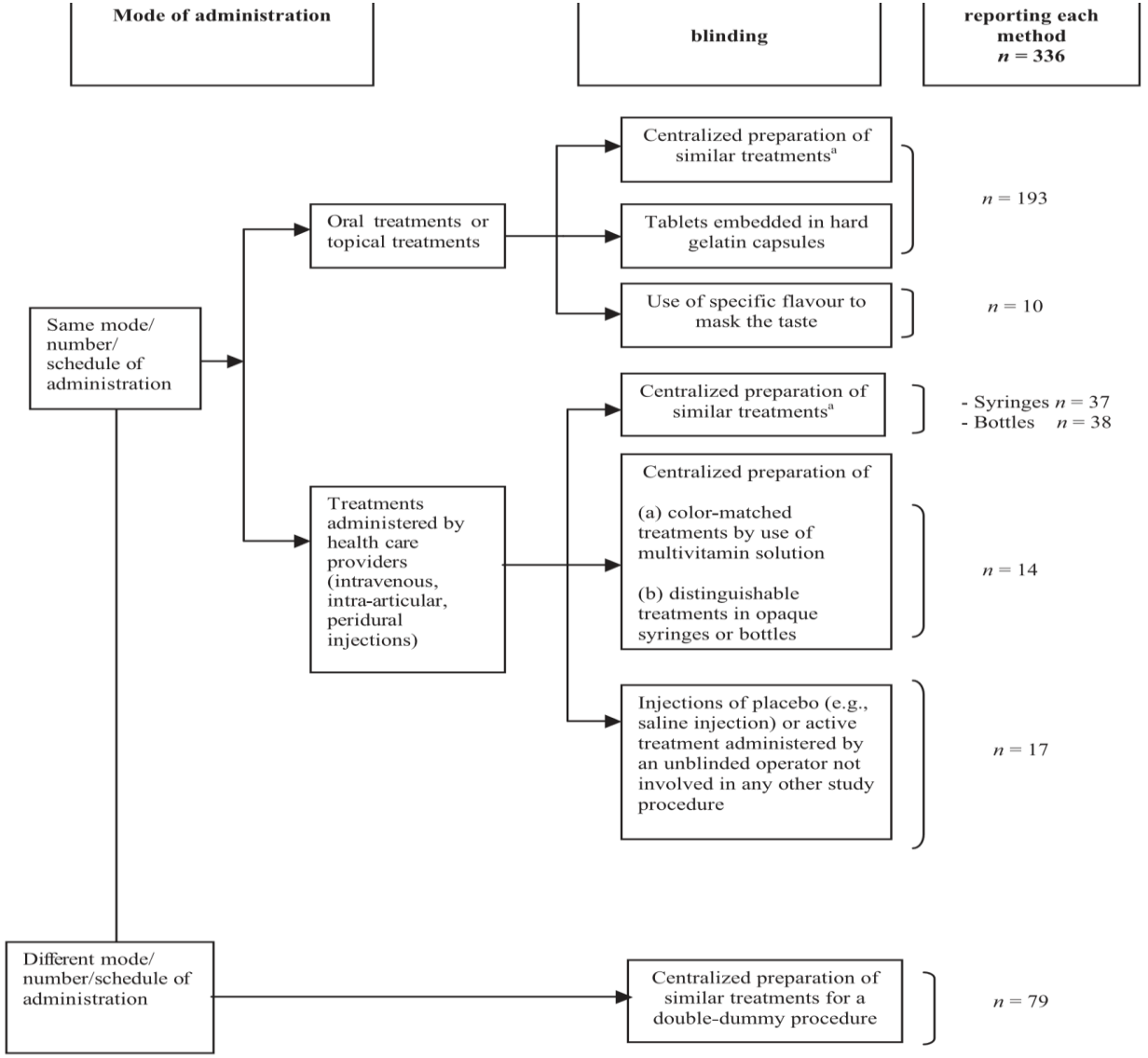
The lack of blinding and biased intervention effects

Comparison (No of meta-analyses)	No of trials*	Ratio of odds ratios	Ratio of odds ratios (95% CI)	P value of test of interaction	Variability in bias† (P value)
Overall (76)	314 *v* 432		0.93 (0.83 to 1.04)	–	0.11 (<0.001)
All cause mortality (18)	79 *v* 121		1.04 (0.95 to 1.14)	0.011	0.01 (0.27)
Other outcomes (58)	235 *v* 311		0.83 (0.70 to 0.98)		0.18 (<0.001)
Objective outcomes (44)	210 *v* 227		1.01 (0.92 to 1.10)	0.01	0.08 (<0.001)
Subjective outcomes (32)	104 *v* 205		0.75 (0.61 to 0.82)		0.14 (0.001)
Drug intervention (57)	250 *v* 372		0.92 (0.81 to 1.05)	0.66	0.10 (<0.001)
Other intervention (19)	64 *v* 60		1.00 (0.71 to 1.39)		0.22 (0.003)



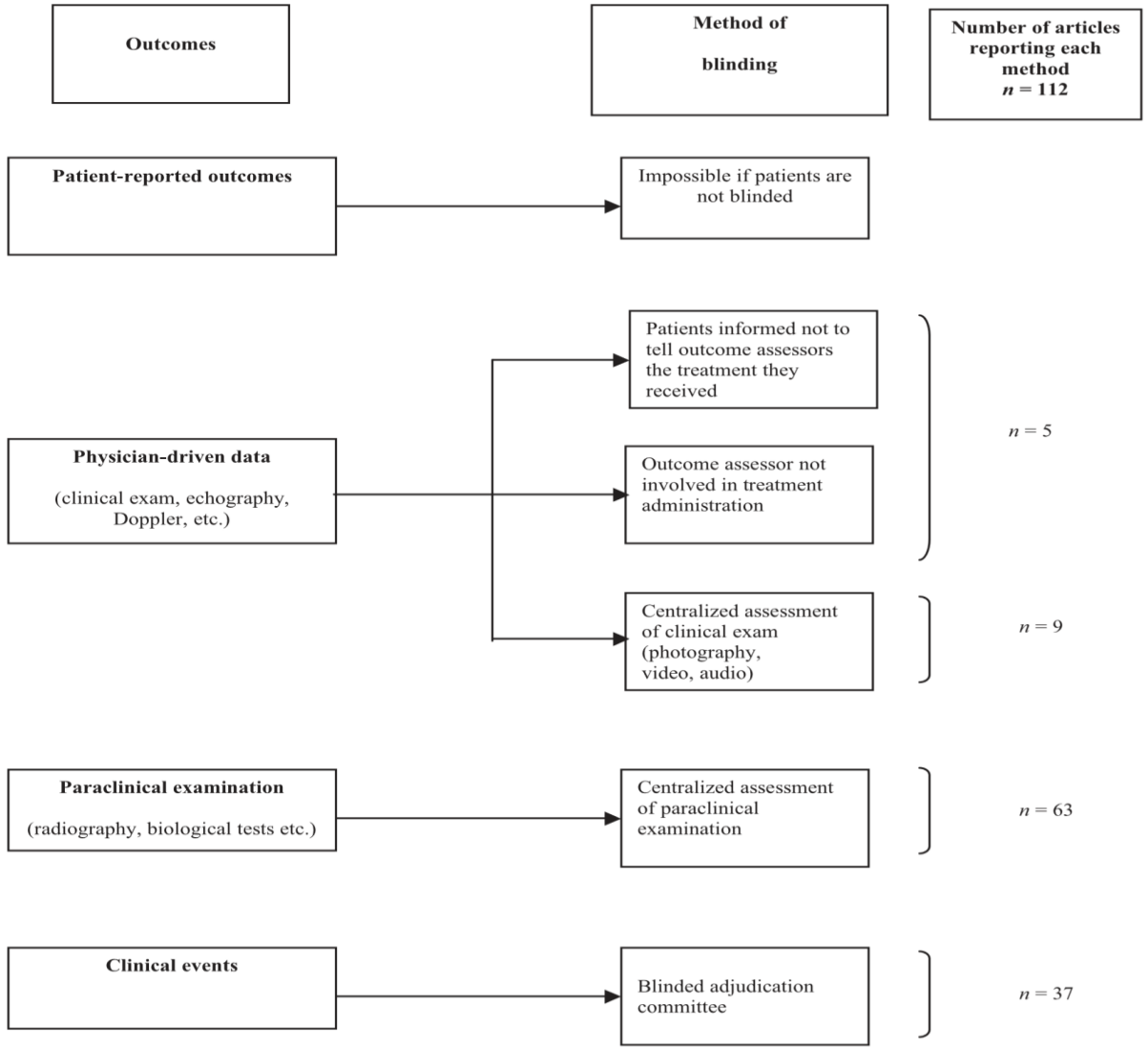
BMJ 2008;336:601

Methods to Establish Blinding in RCTs



PLOS Medicine 3(10): e425. https://doi.org/10.1371/journal.pmed.0030425

Methods of Blinded Outcome Assessment



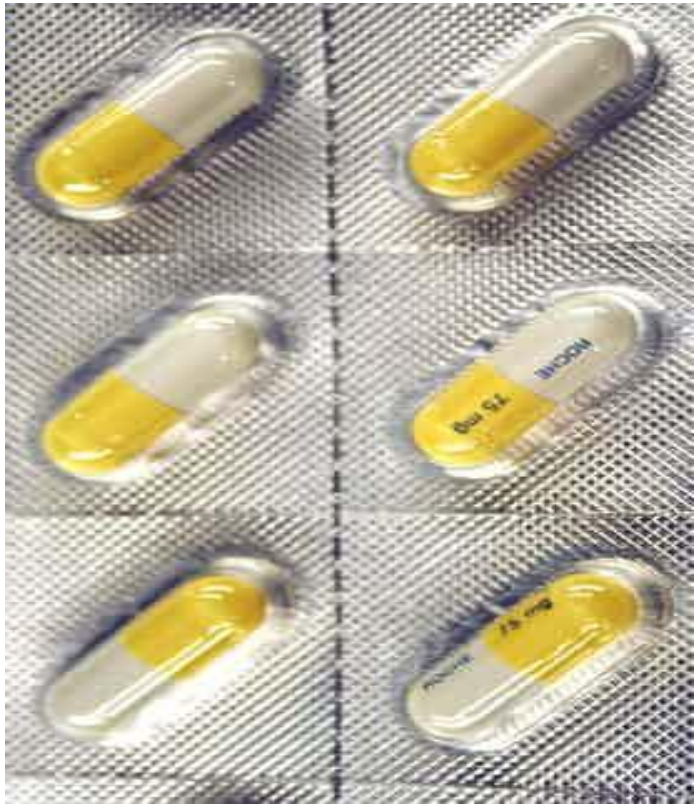
PLOS Medicine 3(10): e425. https://doi.org/10.1371/journal.pmed.0030425

Failure to publish
Biased or unusable reports

Allocation bias	Attrition (drop out) bias	
Selection bias	Detection bias	Reporting bias
Recruitment/Allocation	Performance bias	Publication bias
	Implementation	**Analysis/Publication**

Research Misconduct

Publication Bias and selective reporting: the Tamiflu Experience



Source: Tamiflu capsules. Photograph: Per Lindgren/REX via The Guardian

Tom Jefferson

Abstract

Objectives To update a 2005 Cochrane review that assessed the effects of neuraminidase inhibitors in preventing or ameliorating the symptoms of influenza, the transmission of influenza, and complications from influenza in healthy adults, and to estimate the frequency of adverse effects.

Search strategy An updated search of the Cochrane central register of controlled trials (*Cochrane Library* 2009, issue 2), which contains the Acute Respiratory Infections Group's specialised register, Medline (1950-Aug 2009), Embase (1980-Aug 2009), and post-marketing pharmacovigilance data and comparative safety cohorts.

Selection criteria Randomised placebo controlled studies of neuraminidase inhibitors in otherwise healthy adults exposed to naturally occurring influenza.

Main outcome measures Duration and incidence of symptoms; incidence of lower respiratory tract infections, or their proxies; and adverse events.

Data extraction Two reviewers applied inclusion criteria, assessed trial quality, and extracted data.

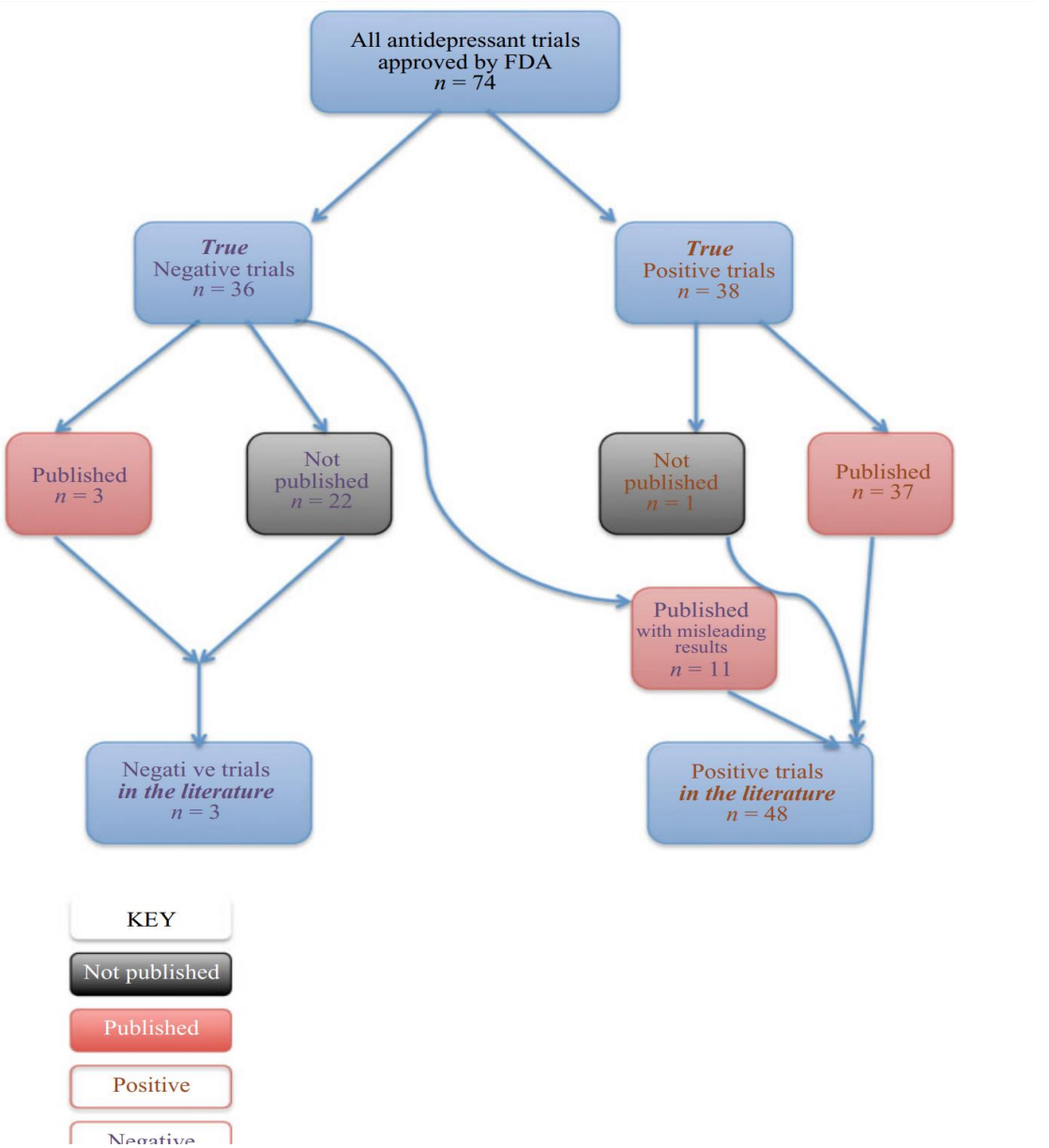
Data analysis Comparisons were structured into prophylaxis, treatment, and adverse events, with further subdivision by outcome and dose.

Results 20 trials were included: four on prophylaxis, 12 on treatment, and four on postexposure prophylaxis. For prophylaxis, neuraminidase inhibitors had no effect against influenza-like illness or asymptomatic influenza. The efficacy of oral oseltamivir against symptomatic laboratory confirmed influenza was 61% (risk ratio 0.39, 95% confidence interval 0.18 to 0.85) at 75 mg daily and 73% (0.27, 0.11 to 0.67) at 150 mg daily. Inhaled zanamivir 10 mg daily was 62% efficacious (0.38, 0.17 to 0.85). Oseltamivir for postexposure prophylaxis had an efficacy of 58% (95% confidence interval 15% to 79%) and 84% (49% to 95%) in two trials of households. Zanamivir performed similarly. The hazard ratios for time to alleviation of influenza-like illness symptoms were in favour of treatment: 1.20 (95% confidence interval 1.06 to 1.35) for oseltamivir and 1.24 (1.13 to 1.36) for zanamivir. Eight unpublished studies on complications were ineligible and therefore excluded. The remaining evidence suggests oseltamivir did not reduce influenza related lower respiratory tract complications (risk ratio 0.55, 95% confidence interval 0.22 to 1.35). From trial evidence, oseltamivir induced nausea (odds ratio 1.79, 95% confidence interval 1.10 to 2.93). Evidence of rarer adverse events from pharmacovigilance was of poor

Main results

We obtained 107 clinical study reports from the European Medicines Agency (EMA), GlaxoSmithKline and Roche. We accessed comments by the US Food and Drug Administration (FDA), EMA and Japanese regulator. We included 53 trials in Stage 1 (a judgement of appropriate study design) and 46 in Stage 2 (formal analysis), including 20 oseltamivir (9623 participants) and 26 zanamivir trials (14,628 participants). Inadequate reporting put most of the zanamivir studies and half of the oseltamivir studies at a high risk of selection bias. There were inadequate measures in place to protect 11 studies of oseltamivir from performance bias due to non-identical presentation of placebo. Attrition bias was high across the oseltamivir studies and there was also evidence of selective reporting for both the zanamivir and oseltamivir studies. The placebo interventions in both sets of trials may have contained active substances.

Publication Bias



Journal of Evaluation in Clinical Practice
Volume 20, Issue 6, pages 908-914, 12 MAY 2014 DOI: 10.1111/jep.12147

Reporting bias

BMJ Open **Feasibility study to examine discrepancy rates in prespecified and reported outcomes in articles submitted to *The BMJ***

Results: In the study period, *The BMJ* received 311 trial manuscripts, 21 of which were subsequently published by the journal. In trials published by *The BMJ*, 27% (89/333) of the prespecified outcomes in the protocol were not reported in the submitted paper and 11% (31/275) of reported outcomes were not prespecified. In the sample

Publication bias and Selective outcome reporting

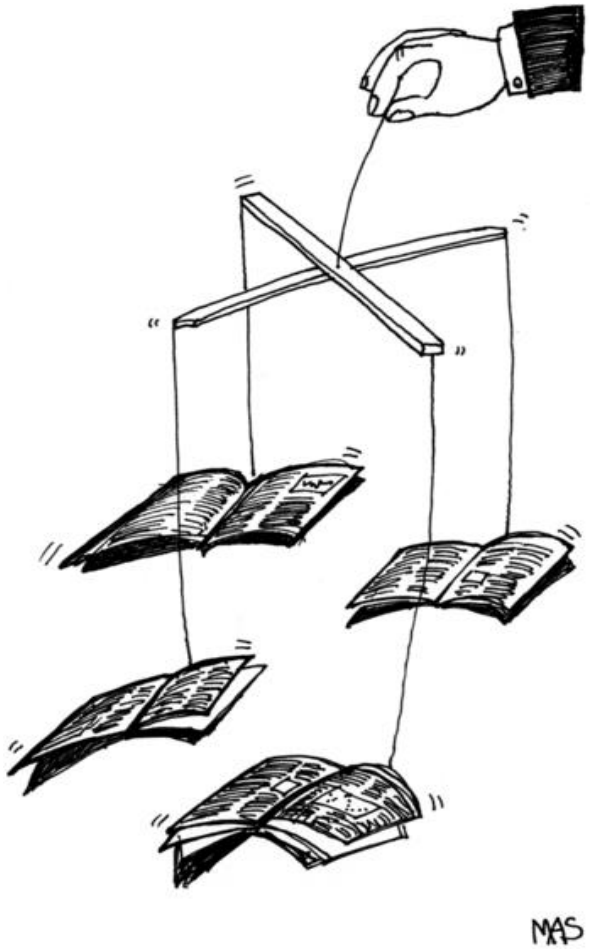
Systematic Review of the Empirical Evidence of Study Publication Bias and Outcome Reporting Bias — An Updated Review

Kerry Dwan*, Carrol Gamble, Paula R. Williamson, Jamie J. Kirkham, for the Reporting Bias Group¶

Department of Biostatistics, University of Liverpool, Liverpool, England

Methodology/Principal Findings: In this update, we review and summarise the evidence from cohort studies that have assessed study publication bias or outcome reporting bias in randomised controlled trials. Twenty studies were eligible of which four were newly identified in this update. Only two followed the cohort all the way through from protocol approval to information regarding publication of outcomes. Fifteen of the studies investigated study publication bias and five investigated outcome reporting bias. Three studies have found that statistically significant outcomes had a higher odds of being fully reported compared to non-significant outcomes (range of odds ratios: 2.2 to 4.7). In comparing trial publications to protocols, we found that 40–62% of studies had at least one primary outcome that was changed, introduced, or omitted. We decided not to undertake meta-analysis due to the differences between studies.

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



PLOS Medicine 2(5): e138. https://doi.org/10.1371/journal.pmed.0020138

(Illustration: Margaret Shear, Public Library of Science)

DEMO

ClinicalTrials

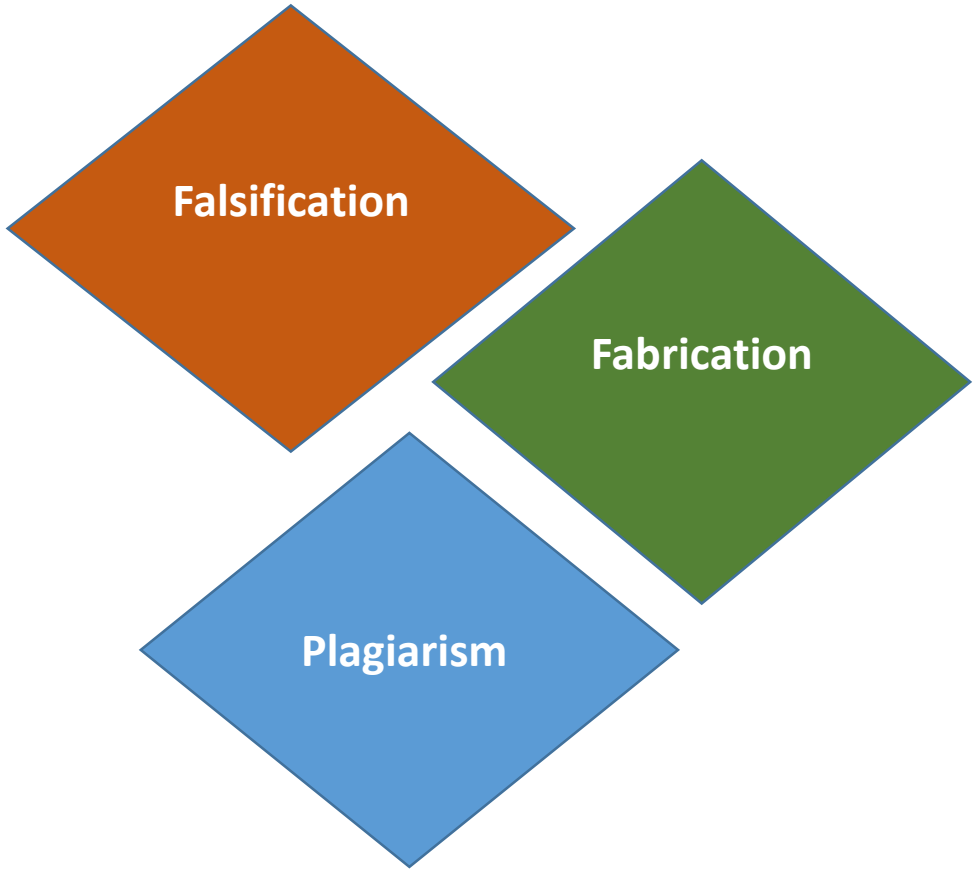
WHO ICTP

Allocation bias	Attrition (drop out) bias	Reporting bias
Selection bias	Detection bias	Reporting bias
Recruitment/Allocation	Performance bias	Publication bias
	Implementation	**Analysis/Publication**

Research Misconduct

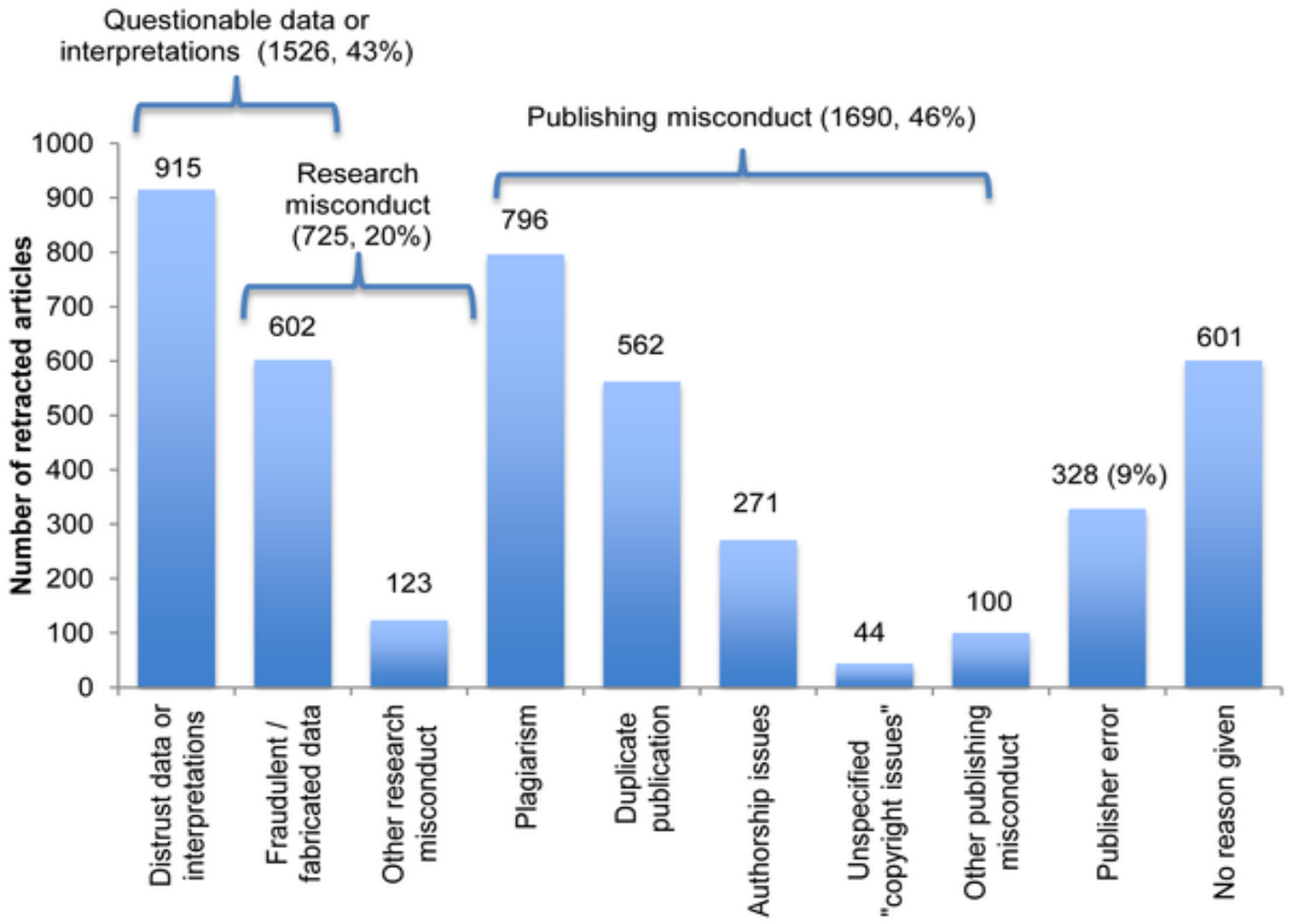
Research Misconduct

THE OFFICE OF RESEARCH INTEGRITY®



Source: https://ori.hhs.gov/definition-misconduct

Retraction

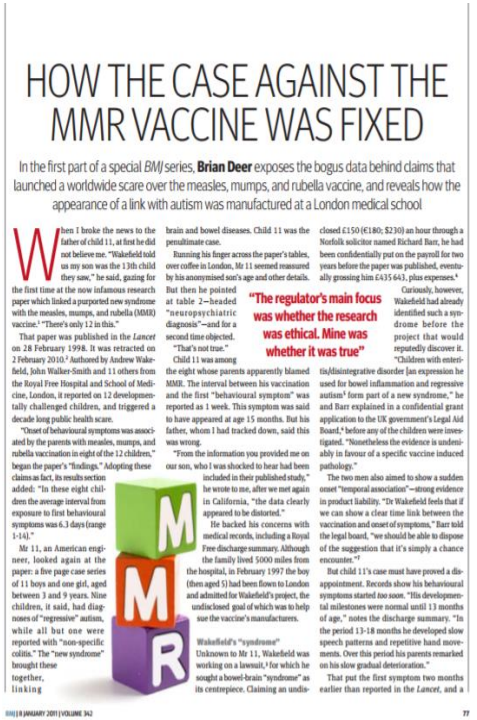


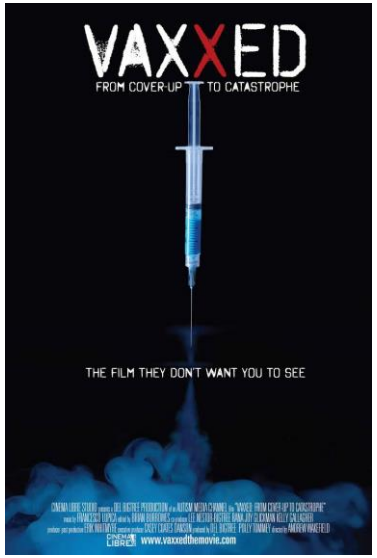
Justifications for retraction (n= 4,232)

PLOS ONE 7(10): e44118. https://doi.org/10.1371/journal.pone.0044118
http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0044118

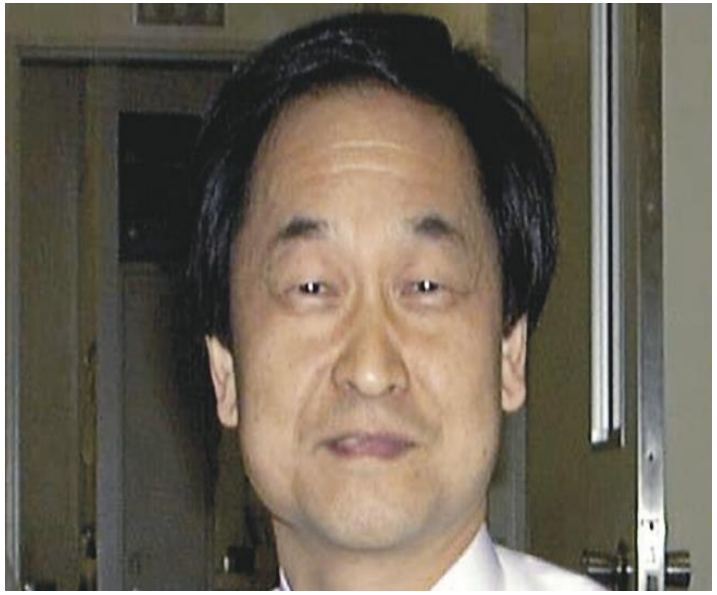
Research Misconduct

Andrew Wakefield





Research Misconduct



Yoshitaka Fujii

The Results of Investigation into Dr.Yoshitaka Fujii's papers

Toho University Faculty of Medicine announced on March 8, 2012 that 8 manuscripts of Dr.Yoshitaka Fujii had been retracted because of execution of these clinical studies without proper ethical approval. In addition, an article [Appendix 1] entitled "The analysis of 169 randomised controlled trials to test data integrity." was published on-line as a Special Article in Anaesthesia, the Journal of the Association of Anaesthetists of Great Britain and Ireland, on March 8, 2012. Three Editorials

B : Fabricated

Papers which have any discrepancy in numbers of subjects, medication, capability of the methohd :

171 papers (included 125 papers in RCT, double- blind mammer) [Appendix 5]

154 papers out of 193 papers [Appendix 3]

C : Others

Papers with no evidence to prove them fabricated or not fabricated :

38 papers

(No.1,2,3,4,5,6,7,8,13,15,17,18,23,24,25,26,32,33,34,44,45,46,68,70,71,75,92,93,94,96,97,113,122,123,139,141,152 [Appendix 5])

Research Misconduct

Joachim Boldt

KliLu
Wir leben Medizin.

Boldt: the great pretender

The withdrawal of almost 90 fraudulent studies by a German anaesthetist is one of the biggest medical research scandals of recent time. **Jacqui Wise** examines what happened and what lessons have been learnt

Jacqui Wise *freelance journalist*

BMJ

BMJ 2013;346:f1738 doi: 10.1136/bmj.f1738 (Published 19 March 2013)

Editors-in-Chief Statement Regarding
IRB Approval of Clinical Trials by Joachim Boldt

February 4, 2011

To our readers:

Landesärztekammer Rheinland-Pfalz ("LÄK-RLP"), the State Medical Association of Rheinland-Pfalz, Germany, today announced the first results of a review of the papers published by Prof Joachim Boldt. The ethics committee of LÄK-RLP serves as the Institutional Review Board (IRB) for clinical research at Klinikum Ludwigshafen, where Professor Boldt's recent research was conducted.

Based on today's announcement, LÄK-RLP has reviewed 74 scientific articles describing clinical trials subject to the requirements of the German Medicinal Act. This includes the article by Professor Boldt recently retracted by *Anesthesia & Analgesia* and an article submitted by Professor Boldt to *Anaesthesia* but not published. By law these studies required IRB approval. Although the articles typically stated that IRB approval had been obtained, LÄK-RLP could not find evidence of approval for 68 of these articles.

LÄK-RLP also identified 30 published articles that describe research that did not fall under the jurisdiction of the German Medicinal Act but physicians performing such human research must conform to the Code of Deontology, which includes a requirement for IRB review. Some articles

On behalf of our respective journals,

Lars S. Rasmussen
Editor-in-Chief, ***Acta Anaesthesiologica Scandinavica***

Steven M. Yentis
Editor-in-Chief, ***Anaesthesia***

Jürgen Schüttler
Editor-in-Chief, ***Anästhesiologie und Intensivmedizin***

Hugo Van Aken
On behalf of the Editorial Board, ***Anästhesiologie Intensivmedizin Notfallmedizin Schmerztherapie***

Steven L. Shafer
Editor-in-Chief, ***Anesthesia & Analgesia***

James C. Eisenach
Editor-in-Chief, ***Anesthesiology***

Charles S. Reilly
Editor-in-Chief, ***British Journal of Anaesthesia***

Donald R. Miller
Editor-in-Chief, ***Canadian Journal of Anesthesia/Journal canadien d'anesthésie***

Bernd Zwissler
On behalf of the Editorial Board, ***Der Anästhesist***

Martin R. Tramèr
Editor-in-Chief, ***European Journal of Anaesthesiology***

Massimo Antonelli
Editor-in-Chief, ***Intensive Care Medicine***

Research Misconduct

Anil Potti

Duke UNIVERSITY

THE LANCET Oncology

The NEW ENGLAND JOURNAL of MEDICINE

CHEST JOURNAL

OFFICIAL PUBLICATION OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS

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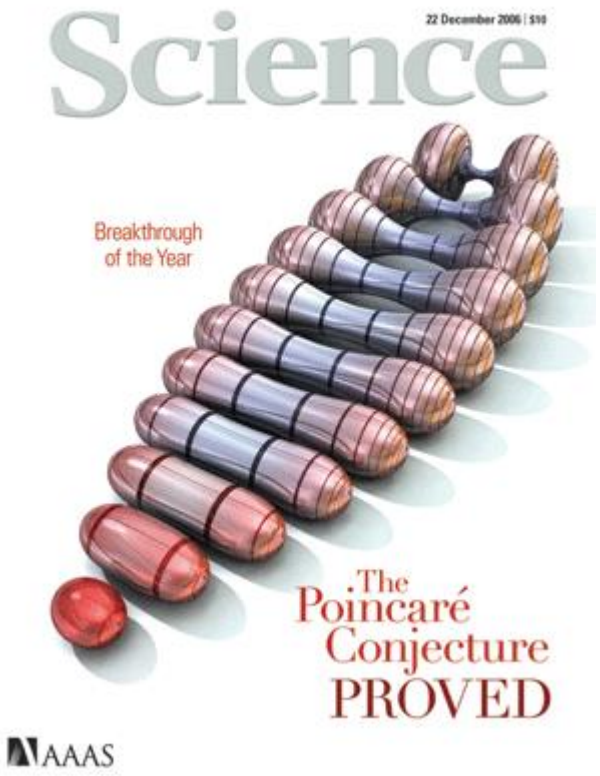
Research Misconduct



Grigori Perelman

ASIAN J. MATH.
Vol. 10, No. 2, pp. 165–492, June 2006

A COMPLETE PROOF OF THE POINCARÉ AND GEOMETRIZATION CONJECTURES – APPLICATION OF THE HAMILTON-PERELMAN THEORY OF THE RICCI FLOW*

HUAI-DONG CAO† AND XI-PING ZHU‡

ASIAN J. MATH.
Vol. 10, No. 4, pp. 663–664, December 2006

ERRATUM TO "A COMPLETE PROOF OF THE POINCARÉ AND GEOMETRIZATION CONJECTURES – APPLICATION OF THE HAMILTON-PERELMAN THEORY OF THE RICCI FLOW", ASIAN J. MATH., VOL. 10, NO. 2, 165–492, 2006*

HUAI-DONG CAO† AND XI-PING ZHU‡

We would like to thank Bruce Kleiner and John Lott for bringing to our attention the fact that the argument concerning Claim 2 in the proof of Perelman's singularity structure theorem (i.e., the Step 2 in the proof of Theorem 7.1.1 in our paper, p. 400–402) essentially appeared in the initial version of their notes on Perelman's first paper posted on the website

http://www.math.lsa.umich.edu/research/ricciflow/perelman.html

Hamilton-Perelman's Proof of the Poincaré Conjecture and the Geometrization Conjecture*

Huai-Dong Cao and Xi-Ping Zhu

ABSTRACT. In this paper, we provide an essentially self-contained and detailed account of the fundamental works of Hamilton and the recent breakthrough of Perelman on the Ricci flow and their application to the geometrization of three-manifolds. In particular, we give a detailed exposition of a complete proof of the Poincaré conjecture due to Hamilton and Perelman.

Self-regulation?

AMA Journal of Ethics®
February 2017, Volume 19, Number 2: 199-206

MEDICINE AND SOCIETY

The Case of Dr. Oz: Ethics, Evidence, and Does Professional Self-Regulation Work?

Jon C. Tilburt, MD, MPH, Megan Allyse, PhD, and Frederic W. Hafferty, PhD

Editor's Note: This article was published on February 1, 2017, and updated on February 13, 2017.

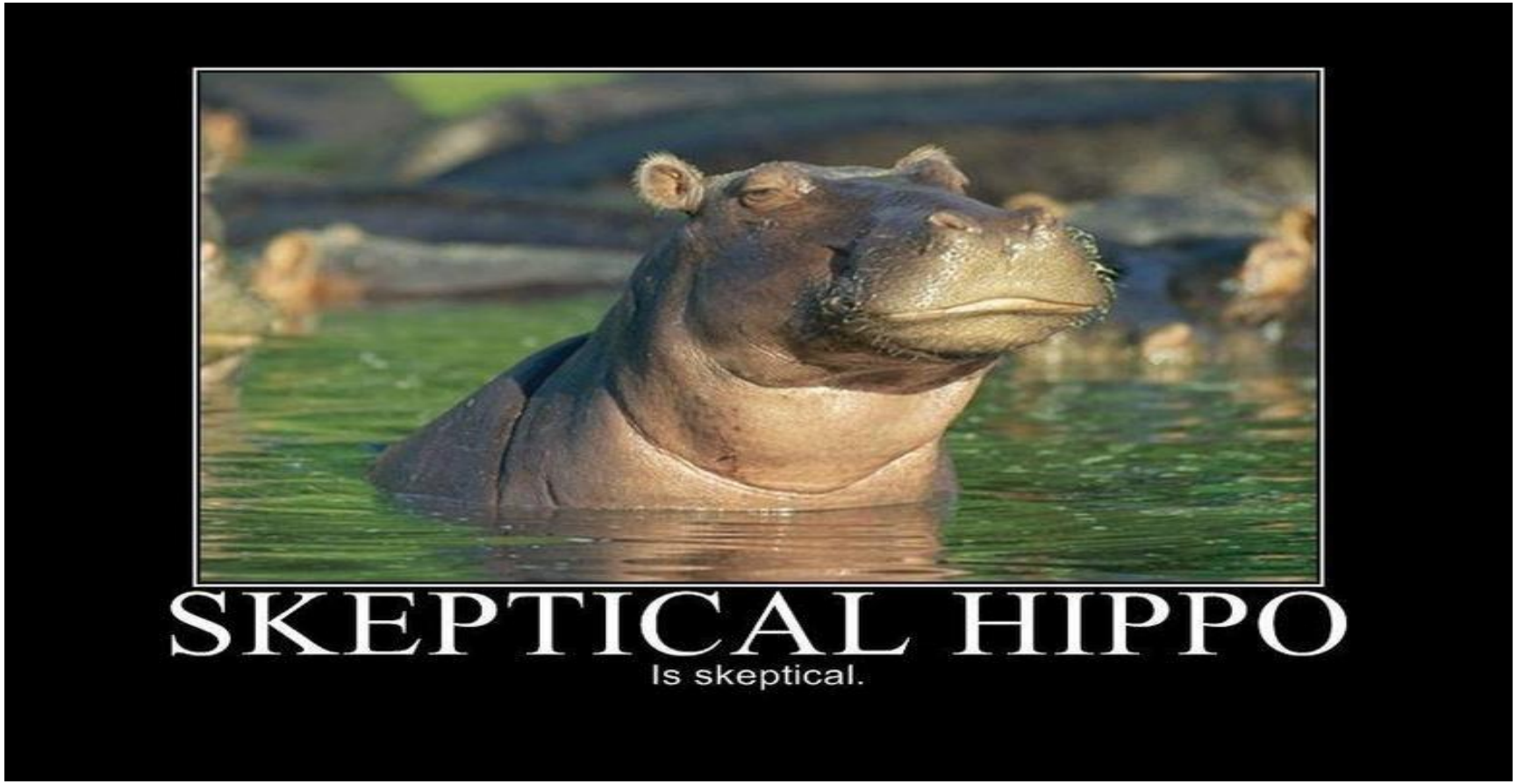
Abstract

Dr. Mehmet Oz is widely known not just as a successful media personality donning the title "America's Doctor®," but, we suggest, also as a physician visibly out of step with his profession. A recent, unsuccessful attempt to censure Dr. Oz raises the issue of whether the medical profession can effectively self-regulate at all. It also raises concern that the medical profession's self-regulation might be selectively activated, perhaps only when the subject of professional censure has achieved a level of public visibility. We argue here that the medical profession must look at itself with a healthy dose of self-doubt about whether it has sufficient knowledge of or handle on the less visible Dr. "Ozes" quietly operating under the profession's presumptive endorsement.

Introduction

Dr. Mehmet Oz's surgical credentials including expertise in minimally invasive, heart transplant, and heart valve surgery are impeccable [1]. But when Dr. Oz walks onto the stage of *The Dr. Oz Show*, he's not just a well-trained heart surgeon, he becomes

البحث العلمي المنشور بين الجيد والرديء



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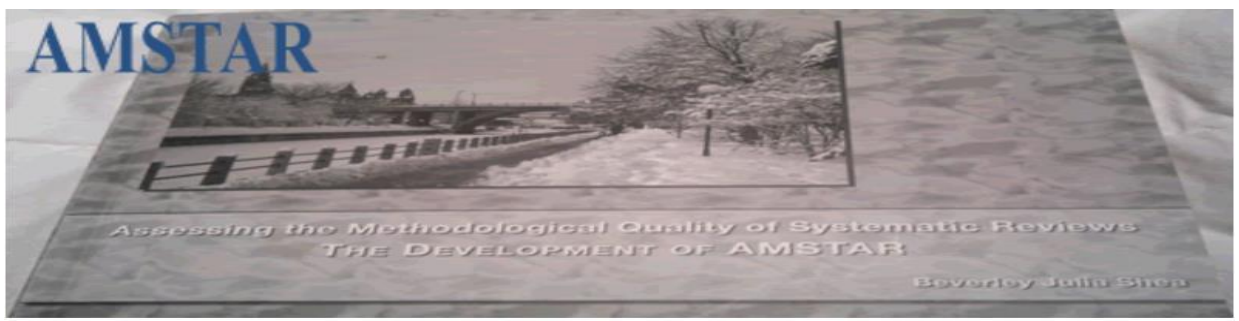
Review of Animal Data from Experimental Studies

SIGN



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Reporting guidelines for main study types

Randomised trials	CONSORT	Extensions	Other
Observational studies	STROBE	Extensions	Other
Systematic reviews	PRISMA	Extensions	Other
Case reports	CARE	Extensions	Other
Qualitative research	SRQR	COREQ	Other
Diagnostic / prognostic studies	STARD	TRIPOD	Other
Quality improvement studies	SQUIRE		Other
Economic evaluations	CHEERS		Other
Animal pre-clinical studies	ARRIVE		Other
Study protocols	SPIRIT	PRISMA-P	Other
Clinical practice guidelines	AGREE	RIGHT	Other

Visit our new browse reporting guidelines by specialty page

DEMO

Equator Network Guidelines

Journal of Multidisciplinary Healthcare

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REVIEW

Does the medical literature remain inadequately described despite having reporting guidelines for 21 years? – A systematic review of reviews: an update

This article was published in the following Dove Press journal:
Journal of Multidisciplinary Healthcare

Yanling Jin,[1,*] Nitika Sanger,[2,*] Ieta Shams,[3,*] Candice Luo,[4,*] Hamnah Shahid,[5,*] Guowei Li,[1,*] Meha Bhatt,[1] Laura Zielinski,[6] Bianca Bantoto,[7] Mei Wang,[1] Luciana PF Abbade,[8] Ikunna Nwosu,[4] Alvin Leenus,[1] Lawrence Mbuagbaw,[1] Muhammad Maaz,[1] Yaping Chang,[1] Guangwen Sun,[1] Mitchell AH Levine,[1,9] Jonathan D Adachi[1,9] Lehana Thabane,[1,9] Zainab Samaan[1,10]

[1]Department of Health Research Methods, Evidence and Impact, McMaster University, Hamilton, ON, Canada; [2]Department of Medical Science, Medical Sciences Graduate Program, McMaster University, Hamilton, ON, Canada; [3]Department of Psychology, Neuroscience and Behaviour, McMaster University, Hamilton, ON, Canada; [4]Faculty of Health Sciences, Bachelors of Health Sciences, McMaster University, Hamilton, ON, Canada; [5]Department of Arts and Science, McMaster University, Hamilton, ON, Canada; [6]Department of Neuroscience, McMaster Integrative Neuroscience Discovery and Study, McMaster University, Hamilton, ON, Canada; [7]Department of Science, Honours Integrated Sciences Program, McMaster University, Hamilton, ON, Canada; [8]Department of Dermatology and Radiotherapy, Botucatu Medical School, Universidade Estadual Paulista, UNESP, São Paulo, Brazil; [9]St. Joseph's Healthcare Hamilton, Hamilton, ON, Canada; [10]Department of Psychiatry and Behavioural Neurosciences, McMaster University, Hamilton, ON, Canada

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Purpose: Reporting guidelines (eg, Consolidated Standards of Reporting Trials [CONSORT] statement) are intended to improve reporting standards and enhance the transparency and reproducibility of research findings. Despite accessibility of such guidelines, researchers are not required to adhere to them. Our goal was to determine the current status of reporting quality in the medical literature and examine whether adherence of reporting guidelines has improved since the inception of reporting guidelines.

Materials and methods: Eight reporting guidelines, such as CONSORT, Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), STrengthening the Reporting of OBservational studies in Epidemiology (STROBE), Quality of Reporting of Meta-analysis (QUOROM), STAndards for Reporting of Diagnostic accuracy (STARD), Animal Research: Reporting In Vivo Experiments (ARRIVE), Consolidated Health Economic Evaluation Reporting Standards (CHEERS), and Meta-analysis of Observational Studies in Epidemiology (MOOSE) were examined. Our inclusion criteria included reviews published between January 1996 to September 2016 which investigated the adherence to reporting guidelines in the literature that addressed clinical trials, systematic reviews, observational studies, meta-analysis, diagnostic accuracy, economic evaluations, and preclinical animal studies that were in English. All reviews were found on Web of Science, Excerpta Medical Database (EMBASE), MEDLINE, and Cumulative Index to Nursing and Allied Health Literature (CINAHL).

Results: Among the general searching of 26,819 studies by using the designed searching method, 124 studies were included post screening. We found that 87.9% of the included studies reported suboptimal adherence to reporting guidelines. Factors associated with poor adherence included non-pharmacological interventions, year of publication, and trials concluding with significant results. Improved adherence was associated with better study designs such as allocation concealment, random sequence, large sample sizes, adequately powered studies, multiple authorships, and being published in journals endorsing guidelines.

Conclusion: We conclude that the level of adherence to reporting guidelines remains suboptimal. Endorsement of reporting guidelines by journals is important and recommended.

Keywords: guidelines, adherence, review, CONSORT

Introduction

Medical science is an evolving and dynamic field of research that impacts health care, disease outcomes, and health care systems in general. The evidence generated from millions of medical publications is meant to inform these dynamic changes

SYSTEMATIC REVIEWS

RESEARCH Open Access

Does use of the CONSORT Statement impact the completeness of reporting of randomised controlled trials published in medical journals? A Cochrane review[a]

Lucy Turner[1], Larissa Shamseer[1], Douglas G Altman[2], Kenneth F Schulz[3] and David Moher[1,4*]

Abstract

Background: The Consolidated Standards of Reporting Trials (CONSORT) Statement is intended to facilitate better reporting of randomised clinical trials (RCTs). A systematic review recently published in the Cochrane Library assesses whether journal endorsement of CONSORT impacts the completeness of reporting of RCTs; those findings are summarised here.

Methods: Evaluations assessing the completeness of reporting of RCTs based on any of 27 outcomes formulated based on the 1996 or 2001 CONSORT checklists were included; two primary comparisons were evaluated. The 27 outcomes were: the 22 items of the 2001 CONSORT checklist, four sub-items describing blinding and a 'total summary score' of aggregate items, as reported. Relative risks (RR) and 99% confidence intervals were calculated to determine effect estimates for each outcome across evaluations.

Results: Fifty-three reports describing 50 evaluations of 16,604 RCTs were assessed for adherence to at least one of 27 outcomes. Sixty-nine of 81 meta-analyses show relative benefit from CONSORT endorsement on completeness of reporting. Between endorsing and non-endorsing journals, 25 outcomes are improved with CONSORT endorsement, five of these significantly ($\alpha = 0.01$). The number of evaluations per meta-analysis was often low with substantial heterogeneity; validity was assessed as low or unclear for many evaluations.

Conclusions: The results of this review suggest that journal endorsement of CONSORT may benefit the completeness of reporting of RCTs they publish. No evidence suggests that endorsement hinders the completeness of RCT reporting. However, despite relative improvements when CONSORT is endorsed by journals, the completeness of reporting of trials remains sub-optimal. Journals are not sending a clear message about endorsement to authors submitting manuscripts for publication. As such, fidelity of endorsement as an 'intervention' has been weak to date. Journals need to take further action regarding their endorsement and implementation of CONSORT to facilitate accurate, transparent and complete reporting of trials.

Keywords: CONSORT, Endorsement, Reporting guideline, Completeness of reporting

PLOS ONE

RESEARCH ARTICLE

A checklist is associated with increased quality of reporting preclinical biomedical research: A systematic review

SeungHye Han[1¤*], Tolani F. Olonisakin[1], John P. Pribis[2], Jill Zupetic[1], Joo Heung Yoon[1], Kyle M. Holleran[3], Kwonho Jeong[3], Nader Shaikh[4,5], Doris M. Rubio[3,5,6], Janet S. Lee[1,5,7]

1 Division of Pulmonary, Allergy, and Critical Care Medicine, Department of Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania, United States of America, **2** Integrative Molecular and Biomedical Sciences Graduate Program, Baylor College of Medicine, Houston, Texas, United States of America, **3** Center for Research on Health Care Data Center, University of Pittsburgh, Pittsburgh, Pennsylvania, United States of America, **4** Department of Pediatrics, Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania, United States of America, **5** Institute for Clinical Research Education, University of Pittsburgh, Pittsburgh, Pennsylvania, United States of America, **6** Division of General Internal Medicine, Department of Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania, United States of America, **7** Pittsburgh Heart, Lung, Blood and Vascular Medicine Institute, University of Pittsburgh, Pittsburgh, Pennsylvania, United States of America

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OPEN ACCESS

Citation: Han S, Olonisakin TF, Pribis JP, Zupetic J, Yoon JH, Holleran KM, et al. (2017) A checklist is associated with increased quality of reporting preclinical biomedical research: A systematic review. PLoS ONE 12(9): e0183591. https://doi.org/10.1371/journal.pone.0183591

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Data Availability Statement: All relevant data are within the paper and its Supporting Information files.

Funding: The project described was supported by the National Institutes of Health through Grant Numbers UL1TR001857 (University of Pittsburgh CTSI), HL086884 (JSL), AI119042 (JSL), American Heart Association Award 15POST25700096 (SH), Breathe Pennsylvania Lung Health Research Grant (SH), and Howard Hughes Medical Institute Research Fellow Award (TFO). The funders had no

Abstract

Irreproducibility of preclinical biomedical research has gained recent attention. It is suggested that requiring authors to complete a checklist at the time of manuscript submission would improve the quality and transparency of scientific reporting, and ultimately enhance reproducibility. Whether a checklist enhances quality and transparency in reporting preclinical animal studies, however, has not been empirically studied. Here we searched two highly cited life science journals, one that requires a checklist at submission (*Nature*) and one that does not (*Cell*), to identify *in vivo* animal studies. After screening 943 articles, a total of 80 articles were identified in 2013 (pre-checklist) and 2015 (post-checklist), and included for the detailed evaluation of reporting methodological and analytical information. We compared the quality of reporting preclinical animal studies between the two journals, accounting for differences between journals and changes over time in reporting. We find that reporting of randomization, blinding, and sample-size estimation significantly improved when comparing *Nature* to *Cell* from 2013 to 2015, likely due to implementation of a checklist. Specifically, improvement in reporting of the three methodological information was at least three times greater when a mandatory checklist was implemented than when it was not. Reporting the sex of animals and the number of independent experiments performed also improved from 2013 to 2015, likely from factors not related to a checklist. Our study demonstrates that completing a checklist at manuscript submission is associated with improved reporting of key methodological information in preclinical animal studies.

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