

BIAS

Underreporting of Conflicts of Interest Among Trialists: A Cross-sectional Study

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Objective To determine the prevalence of conflicts of interest (COI) among non-industry-employed Danish physicians who are authors of clinical trials and to determine the number of undisclosed conflicts of interest in trial publications.

Design We searched EMBASE for papers with at least 1 Danish author. Two assessors included the 100 most recent papers of drug trials published in international journals that adhere to the ICMJE's manuscript guidelines. For each paper, 2 assessors independently extracted data on trial characteristics and author COI. We calculated the prevalence of disclosed COI among non-industry-employed Danish physician authors and described the type of COI. We compared the COI reported in the papers to those reported on the publicly available Danish Health and Medicines Authority's disclosure list to identify undisclosed COI.

Results Preliminary analysis of the first 50 included papers found 27 papers with industry sponsorship, 14 with mixed sponsorship, and 9 with nonindustry sponsorship. Of a total of 563 authors, 171 (30%) were non-industry-employed Danish physicians. Forty-four (26%) of these authors disclosed 1 or more COI in the journal. Among the 171 authors, 19 (11%) had undisclosed COI related to the trial sponsor or manufacturer of the drug being studied, and 45 (26%) had undisclosed COI related to competing companies manufacturing drugs for the same indication as the trial drug. Full analysis of all 100 trials and further exploration of data will be presented at the conference.

Conclusions Our preliminary results suggest that there is substantial underreporting of COI in clinical trials. Publicly available disclosure lists may assist journal editors in ensuring that all relevant COI are disclosed.

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Outcome Reporting Bias in Trials (ORBIT II): An Assessment of Harm Outcomes

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Objective The prevalence and impact of outcome reporting bias (ORB), whereby outcomes are selected for publication on the basis of the result, have previously been quantified for benefit outcomes in randomized controlled trials (RCTs) on a cohort of systematic reviews. Important harm outcomes may also be subject to ORB where trialists prefer to focus on the positive benefits of an intervention. The objectives of this study were (1) estimate the prevalence of selective outcome reporting of harm outcomes in a cohort of both Cochrane reviews and non-Cochrane reviews, and (2) understand the mechanisms that may lead to incomplete reporting of harms data.

Design A classification system for detecting ORB for harm outcomes in RCTs and nonrandomized studies was developed and applied to both a cohort of Cochrane systematic reviews and non-Cochrane reviews that considered the synthesis of specific harms data as their main objective. An e-mail survey of trialists from the included trials in the cohort of reviews was also undertaken to examine how harms data are collected and reported in clinical studies.

Results A total of 234 reviews were identified for the non-Cochrane review cohort and 244 new reviews for the Cochrane review cohort. In 77% (180/234) of the non-Cochrane reviews, there was suspicion of ORB in at least 1 trial. Forty-nine percent (89/180) could not be fully assessed for ORB due to shortcomings in the review reporting standards. In the Cochrane review cohort, many reviews also were not assessable as harm outcomes were poorly specified. Study findings from the reviews in which a full assessment for ORB could be carried out for both the cohorts will be presented. Responses from the trialist survey and an example of how ORB can influence the benefit-harm ratio will also be presented.

Conclusions Trade-off between benefits and harms is very important. Making informed decisions that consider both benefits and harms of an intervention in an unbiased way is essential to make reliable benefit-harm predictions.

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Systematic Review of Evidence for Selective Reporting of Analyses

Kerry Dwan,¹ Paula R. Williamson,¹ Carrol Gamble,¹ Julian P. T. Higgins,² Jonathan A. C. Sterne,² Douglas G. Altman,³ Mike Clarke,⁴ Jamie J. Kirkham¹

Objective Selective reporting of information or discrepancies in trials may occur for many aspects of a trial. Examples include the selective reporting of outcomes and the selective reporting of analyses (eg, subgroup analyses or per protocol rather than intention-to-treat analyses). Selective reporting bias occurs when the inclusion of analyses in the report is based on the results of those analyses. Discrepancies occur when there are changes between protocol and publication. The objectives of this study were (1) review and summarize the evidence from studies that have assessed discrepancies or the selective reporting of analyses in randomized controlled trials and (2) compare current reporting guidelines to identify where improvement is needed.

Design Systematic review of studies that have assessed discrepancies or the selective reporting of analyses in randomized controlled trials. The Cochrane methodology register, MEDLINE, and PsycInfo were searched in May 2013. Cohorts containing randomized controlled trials (RCTs) were eligible. This review provides a descriptive summary of the included empirical studies. Along with the collaboration with experts in this area, current guidelines, such as Consolidated Standards of Reporting Trials (CONSORT) and International Conference on

Harmonisation (ICH), have been compared to identify the specific points that address the appropriate reporting of a clinical trial with respect to outcomes, outcome measures, subgroups, and analyses and to assess whether improvements are needed.

Results Eighteen studies have been included in this review. Ten compare details within published reports, 4 compare protocols to publications, and 4 compare company documents or documents submitted to regulatory agencies with publications. The studies consider discrepancies in statistical analyses (7); subgroup analyses (9); and composite outcomes (2). No studies considered selective reporting. There were discrepancies in statistical analyses in 22% to 88% of RCTs, in unadjusted vs adjusted analyses (46% to 82%), and in subgroup analyses (31% to 100%). Composite outcomes were inadequately reported.

Conclusion This work highlights the evidence of selective reporting and discrepancies and demonstrates the importance of prespecifying analysis and reporting strategies during the planning and design of a clinical trial, for the purposes of minimizing bias when the findings are reported.

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Conflict of Interest Disclosures Kerry Dwan is a coauthor of the Outcome Reporting Bias In Trials (ORBIT) study. Paula Williamson is a coauthor of one of the included studies in the review and coauthor of the Outcome Reporting Bias In Trials (ORBIT) study. Carrol Gamble is a coauthor of the Outcome Reporting Bias In Trials (ORBIT) study. Douglas G. Altman is a coauthor of one of the included studies in the review, coauthor of the Outcome Reporting Bias In Trials (ORBIT) study, and a coauthor of the CONSORT statement. Jamie Kirkham is a coauthor of the Outcome Reporting Bias In Trials (ORBIT) study. Julian Higgins, Jonathan Sterne, and Mike Clarke report no conflicts of interest.

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Impact of Spin in the Abstract on the Interpretation of Randomized Controlled Trials in the Field of Cancer: A Randomized Controlled Trial

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Objective Spin is defined as a specific way of reporting to convince readers that the beneficial effect of the experimental treatment is greater than is shown by the results. The aim of this study is to assess the impact of spin in abstracts of randomized controlled trials (RCTs) with non-statistically significant results in the field of cancer on readers' interpretation.

Design A 2-arm parallel-group RCT comparing the interpretation of results in abstracts with or without spin. We selected from a collection of articles identified in previous work a sample of reports describing negative (ie, statistically nonsignificant primary outcome) RCTs with 2 parallel arms evaluating treatments in the field of cancer and having spin in the abstract conclusion. Selected abstracts were rewritten by 2 researchers according to specific guidelines to remove spin. All abstracts were presented in the same format without the identifying authors or journal name. The names of treatments were masked by using generic terms (eg, experimental treatment A). Corresponding authors (n=300) of clinical trials indexed in PubMed and blinded to the objectives of our study will be randomized using a centralized computer-generated randomization

to evaluate 1 abstract with spin or 1 abstract without spin. The primary endpoint is the interpretation of abstract results by the participants. After reading each abstract participants will answer the following question: "Based on this abstract, do you think treatment A would be beneficial to patients?" (answer: numerical scale from 0-10)

Results Three hundred participants were randomized; 150 assessed an abstract with spin and 150 an abstract with no spin. From abstracts with spin, the experimental treatment was rated as being more beneficial (scale 0-10, mean [SD] = 3.6 [2.5] vs 2.9 [2.6]; $P=.02$), the trial was rated as less rigorous (scale 0-10, mean [SD] = 4.5 [2.4] vs 5.1 [2.5]; $P=.04$) and participants were more interested in reading the full-text article (scale 0-10, mean [SD] = 5.1 [3.2] vs 4.3 [3.0]; $P=.0311$). There was no statistically significant difference for the importance of the study (scale 0-10, mean [SD] = 4.6 [2.4] vs 4.9 [2.4]; $P=.17$) and the need to run another trial (scale 0-10, mean [SD] = 4.8 [2.9] vs 4.2 [2.9]; $P=.06$).

Conclusion Spin in abstracts of RCTs in the field of cancer may have an impact on the interpretation of these trials.

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PUBLICATION BIAS

Authors' Reasons for Unpublished Research Presented at Biomedical Conferences: A Systematic Review

Roberta W. Scherer, Cesar Ugarte-Gil

Objective Only about half of studies presented in conference abstracts are subsequently published in full. Reasons for not publishing abstract results in full are often attributed to the expectation of journal rejection. We aimed to systematically review studies that asked abstract authors for reasons for failing to publish abstract results in full.

Design We searched MEDLINE, EMBASE, the Cochrane Library, Web of Science, and references cited in eligible studies in November 2012 for studies examining full publication of results at least 2 years after presentation at a conference. We included studies if investigators contacted abstract authors for reasons for nonpublication. We independently extracted information on methods used to contact abstract authors, study design, and reasons for nonpublication. We calculated a weighted mean average of the proportion of type of reason, weighted by total number of responses by study.

Results We identified 27 (of 367) studies published between 1992 and 2011 that were eligible for this study. The mean full publication rate was 56% (95% CI, 55 to 57%; n = 24); 7 studies reported on abstracts describing clinical trials. Investigators typi-

Table 8. Proportion of Reasons for Nonpublication by Total Number of Reasons Reported

Reason	All Reasons		Most Important Reason		Reasons Reported by Authors of Clinical Trial Abstracts	
	WMA (95% CI)	No.	WMA (95% CI)	No.	WMA (95% CI)	No.
Lack of time	31.5 (29.1 to 33.9)	14	45.4 (0.40 to 0.51)	5	31.9 (26.0 to 37.8)	4
Lack of resources	22.2 (17.2 to 27.3)	5			47.0 (34.5 to 59.5)	3
Publication not an aim	19.2 (17.0 to 21.4)	6	9.7 (6.5 to 12.9)	3		
Low priority	17.8 (15.5 to 20.1)	12	10.2 (4.5 to 16.3)	1	23.1 (13.3 to 32.9)	2
Incomplete study	17.7 (15.8 to 19.7)	15	10.0 (6.3 to 13.8)	4	15.7 (10.9 to 20.4)	5
Trouble with coauthors	12.6 (11.0 to 14.3)	15	11.6 (8.5 to 14.7)	5	17.8 (13.0 to 22.7)	3
Lack of interest	12.0 (10.0 to 13.9)	7	6.7 (3.9 to 9.4)	3	21.5 (15.2 to 27.8)	2
Expect journal rejection	11.2 (9.3 to 13.2)	9	3.7 (0.8 to 6.6)	3	13.2 (5.6 to 20.7)	1
Lost support	11.1 (5.5 to 16.7)	4	1.8 (-0.7 to 4.2)	1	66.7 (13.3 to 1.20)	1
No reason given	11.0 (4.9 to 17.1)	3	6.7 (1.0 to 12.5)	1	17.1 (4.7 to 3.0)	1
Results not important enough	7.8 (5.6 to 10.0)	8	3.6 (-0.1 to 7.4)	2	17.6 (6.6 to 28.6)	2
Publication not permitted by sponsor	7.5 (3.6 to 11.3)	4	...		8.5 (4.2 to 12.7)	2
Limitations in methodology	6.9 (5.3 to 8.4)	12	5.3 (2.8 to 7.9)	5	10.1 (3.2 to 17.1)	2
External problems	5.2 (2.9 to 7.4)	2	6.8 (3.4 to 10.3)	2	...	
Published in other version	5.0 (3.5 to 6.6)	5	4.1 (-0.4 to 8.5)	1	5.4 (0.8 to 10.0)	1
Other papers with similar findings	4.3 (1.9 to 6.7)	5	3.4 (-0.5 to 7.4)	2	16.7 (10.6 to 22.7)	1
Moved to other projects	4.1 (1.8 to 6.5)	2	5.5 (2.5 to 8.5)	2	...	
Negative results	4.0 (2.6 to 5.4)	5	3.1 (-0.3 to 6.5)	1	11.8 (4.6 to 19.1)	1
Would not reach appropriate audience	0.9 (-0.4 to 2.3)	2	
Does not remember	3.4 (1.2 to 5.2)	1	1.4 (-1.3 to 4.0)	2	1.1 (-1.0 to 3.2)	1
Other	16.1 (14.0 to 18.1)	12	8.9 (4.7 to 13.0)	3	11.3 (6.1 to 16.5)	4

Columns include studies reporting multiple reasons, the most important reason, or the reasons reported by authors of clinical trial abstracts. WMA indicates weighted mean average.

cally sent a closed-ended questionnaire with free text options to the lead and then successive authors until receiving a response. Of 24 studies that itemized reported reasons, 6 collected information on the most important reason. Lack of time comprised 31.5% of reasons in studies that had included this as a reason and 45.4% of the most important reason (**Table 8**). Other commonly stated reasons were lack of resources, publication not an aim, low priority, incomplete study, and trouble with coauthors. Limitations of these results include heterogeneity across studies and self-report of reasons by authors.

Conclusion Across medical specialties, the main reasons for not subsequently publishing an abstract in full lies with factors related to the abstract author rather than with a journal.

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Role of Editorial and Peer Review Processes in Publication Bias: Analysis of Drug Trials Submitted to 8 Medical Journals

Marlies van Lent,¹ John Overbeke,² Henk Jan Out¹

Objective Positive publication bias has been widely addressed. It has mainly been ascribed to authors and sponsors failing to submit negative studies, but may also result from lack of interest from editors. In this study, we evaluated whether submitted

manuscripts with negative outcomes were less likely to be published than studies with positive outcomes.

Design A retrospective study of manuscripts reporting results of randomized controlled trials (RCTs) submitted to 8 medical journals between January 1, 2010, and April 30, 2012, was done. We included 1 general medical journal (*BMJ*) and 7 specialty journals (*Annals of the Rheumatic Diseases, British Journal of Ophthalmology, Diabetologia, Gut, Heart, Journal of Hepatology, and Thorax*). We selected journals indexed with the highest Impact Factors within subject categories, according to Institute for Scientific Information Journal Citation Report 2011, and that had published a substantial number of drug RCTs in 2010-2011. Original research manuscripts were screened and those reporting results of RCTs were included, if at least 1 study arm assessed the efficacy or safety of a drug intervention and a statistical test was used to evaluate treatment effects. Manuscripts were either outright rejected, rejected after external peer review, or accepted for publication. Trials were classified as nonindustry, industry-supported, or industry-sponsored, and outcomes as positive or negative, based on predefined criteria.

Results Of 15,972 manuscripts submitted, we identified 472 drug RCTs (3.0%), of which 98 (20.8%) were accepted for publication. Among submitted drug RCTs, 287 (60.8%) had positive and 185 (39.2%) negative results. Of these, 135 (47.0%) and 86 (46.5%), respectively, were rejected immediately and 91 (31.7%) and 61 (33.0%) after peer review. In total, compared to the number of submitted manuscripts, 60 (20.9%) positive studies were published compared to 38 (20.5%) negative studies. One positive study was withdrawn by authors before editorial decisions were made. Nonindustry trials (n=213) had positive

outcomes in 138 manuscripts (64.8%), compared to 78 (70.9%) in industry-sponsored studies (n=110). Industry-supported trials (n=149) were positive in 71 manuscripts (47.7%) and negative in 78 manuscripts (52.3%).

Conclusion Submitted manuscripts on drug RCTs with negative outcomes are not less likely to be published than those with positive outcomes.

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Accessing Internal Company Documents for Research: Where Are They?

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Objective Internal pharmaceutical company data have attracted interest because they have been shown to sometimes differ from what is publicly reported, and because they often make unpublished data available to researchers. However, internal company documents are not readily available, and researchers have obtained data through litigation and requests to regulatory authorities. In contrast, repositories of internal tobacco industry documents, created through massive litigation, have supported diverse and informative research. Our objective was to describe sources of internal corporate documents that had been used in health research, so that we document where these important data, that could be useful to researchers, are located.

Design Although our main interest was pharmaceutical industry documents, our initial search strategy was designed to identify research articles that used internal company documents from any industry. We searched PubMed and EMBASE, and 2 authors independently reviewed retrieved records for eligibility. We checked our findings against the Tobacco Documents Bibliography (<http://www.library.ucsf.edu/tobacco/docsbiblio>), citations to included articles, and lists from colleagues. When we discovered that we had missed many articles, informationists redesigned and ran an additional search to identify articles using pharmaceutical documents.

Results Our initial electronic searches retrieved 9,305 records, of which 357 were eligible for our study. Ninety-one percent (325/357) used tobacco, 5% (17/357) pharmaceutical, and 4% (15/357) other industry documents. Most articles (325/357) posed research questions about the strategic behavior of the company. Despite extensive testing, our search did not retrieve all known studies: we missed 41% of articles listed in the Tobacco Documents Bibliography and reference lists led to

4 additional eligible pharmaceutical studies. Our redesigned search yielded 26,605 citations not identified by the initial search, which we decided was an impractical number to screen.

Conclusions Searching for articles using internal company documents is difficult and resource-intensive. We suggest that indexed and curated repositories of internal company documents relevant to health research would facilitate locating and using these important documents.

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TRIAL REGISTRATION

Publication Agreements or “Gag Orders”? Compliance of Publication Agreements With Good Publication Practice 2 for Trials on ClinicalTrials.gov

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Objective Good Publication Practice 2 (GPP2) recognizes the shared responsibility of authors and industry sponsors to publish clinical trial data and confirms authors' freedom to publish. We quantified the extent and type of publication agreements between industry sponsors and investigators for phase 2-4 interventional clinical trials on ClinicalTrials.gov and determined whether these agreements were GPP2 compliant.

Design Trial record data were electronically imported on October 7, 2012, and trials were screened for eligibility (phase 2-4, interventional, recruitment closed, results available, first received after November 10, 2009, any sponsor type, investigators not sponsor employees). Publication agreement information was manually imported from the Certain Agreements field. Two authors independently categorized agreement information for GPP2 compliance, resolving discrepancies by consensus. An independent academic statistician conducted all analyses.

Results Of the 484 trials retrieved, 388 were eligible for inclusion and 96 were excluded (12 trials that were still active and 84 trials with investigators who were sponsor employees). Of the eligible trials, 81% (313/388) reported publication agreement information in the Certain Agreements field. Significantly more publication agreements reported on ClinicalTrials.gov were GPP2 compliant than noncompliant (74% [232/313] vs 26% [81/313], χ^2 $P < .001$). Reasons for GPP2 noncompliance were insufficient, unclear, or ambiguous information reported (48%, 39/81), sponsor-required approval for publication (36%, 29/81), sponsor-required text changes (9%, 7/81), and sponsor bans on publication (7%, 6/81). Drug trials (180/255) were significantly less likely to have GPP2-compliant agreements than other trials (52/58; relative risk 0.79, 95% CI 0.70-0.89, $P = .003$). Publication agreement compliance varied among affiliates of the same sponsor. Follow-up of agreements with insufficient information and a contact e-mail (response rate, 12.5% [4/32]) revealed 2 additional agreements banning publication, 1 requiring approval, and 1 GPP2-compliant agreement.

Conclusions This study investigated publication agreements using the largest, international, public-access database of publication agreements. Most, but not all, publication agreements

for clinical trials were consistent with GPP2. Although “gag orders” forbidding publication were infrequent, any such ban is unacceptable. Sponsors and their affiliates must ensure that publication agreements confirm authors’ freedom to publish data. Sponsors should also audit agreement information reported on ClinicalTrials.gov for compliance with GPP2 and for consistency with other publication agreement information.

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Reporting of Results in ClinicalTrials.gov and Published Articles: A Cross-sectional Study

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Objective In 2007, the US Federal Drug Administration (FDA) Amendments Act expanded requirements for ClinicalTrials.gov, a public clinical trial registry maintained by the US National Library of Medicine, mandating results reporting within 12 months of trial completion for all FDA-regulated drugs. We compared clinical trial results reported on ClinicalTrials.gov with corresponding published articles.

Design We conducted a cross-sectional analysis of clinical trials published from July 1, 2010, through June 30, 2011, in high-impact journals (Impact Factor ≥ 10) that were registered and reported results on ClinicalTrials.gov. We compared trial results reported on ClinicalTrials.gov and within published articles for the following: cohort characteristics, trial intervention, primary and secondary efficacy endpoint definition(s) and results, and adverse events.

Results Of 95 included clinical trials registered and reporting results on ClinicalTrials.gov, there were 96 corresponding publications, among which 95 (99%) had at least 1 discrepancy in reporting of trial details, efficacy results, or adverse events between the 2 sources. When comparing reporting of primary endpoints, 132 (85%) were described in both sources, 14 (9%) only on ClinicalTrials.gov, and 10 (6%) only within articles. Results for 30 of 132 (23%) primary endpoints could not be compared because of reporting differences between the 2 sources (eg, tabular vs graphics); among the remaining 102 endpoints, reported results were discordant for 21 (21%), altering interpretations for 6 (6%). When comparing reporting of secondary endpoints, 619 (30%) were described in both sources, 421 (20%) only on ClinicalTrials.gov, and 1,049 (50%) only within articles. Results for 228 of 619 (37%) secondary endpoints could not be compared; among the remaining 391, reported results were discordant for 53 (14%).

Conclusion Among published clinical trials that were registered and reported results on ClinicalTrials.gov, nearly all had at least 1 discrepancy in reported results, questioning the accuracy of both sources and raising concerns about the usefulness of results reporting to inform clinical practice and future research efforts.

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Beyond Feasibility: Assessing the ClinicalTrials.gov Results Database

Deborah A. Zarin, Tony Tse, Heather D. Dobbins

Objective Prompted in part by ongoing evidence of selective publication and outcome reporting, the US Congress mandated the first public government-operated results database for the disclosure of clinical trial results, whether published or not. Following implementation of the ClinicalTrials.gov results database in September 2008, the European Medicines Agency (EMA) began developing a similar system. This de facto standard will affect results database reporting for thousands of trials around the world annually. Thus, it is imperative to engage in evaluation and continuous improvement of the 1 system that is already operational—ClinicalTrials.gov—both to allow for improvements and to inform ongoing and future efforts elsewhere. We describe a framework for guiding the evaluation of the results database.

Design A 3-domain conceptual framework was adapted from the Fryback/Thornbury Hierarchical Model of Efficacy of diagnostic tests, based on our experience in designing and operating the database: (1) feasibility, (2) usability and utility, and (3) potential impact. Each domain consists of operationally defined questions for assessing the degree to which the results database is able to meet its intended purposes.

Results Operationally defined questions have been identified for each of the 3 domains, and we provide supporting data and case studies based on our experience over the past 5 years, or point out areas that require further research, and provide some explanatory comments. The following have been identified as needing research: Do data providers enter accurate data? Do data tables provide necessary and sufficient information? How are submissions for individual studies used? Are the aggregated data useful? What is the relationship to scientific abstracts, press releases, and other gray literature? And, What is the relationship to individual participant-level data?

Conclusions This framework can guide evaluative work by the research community with the goal of improving current and future trial disclosure efforts. The areas identified as needing research should be considered high priority, especially before large additional sums of money and human capital are expended internationally to replicate or modify the current system.

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DATA/CONTENT SHARING, AVAILABILITY, AND ACCESS

How Does the Availability of Research Data Change With Time Since Publication?

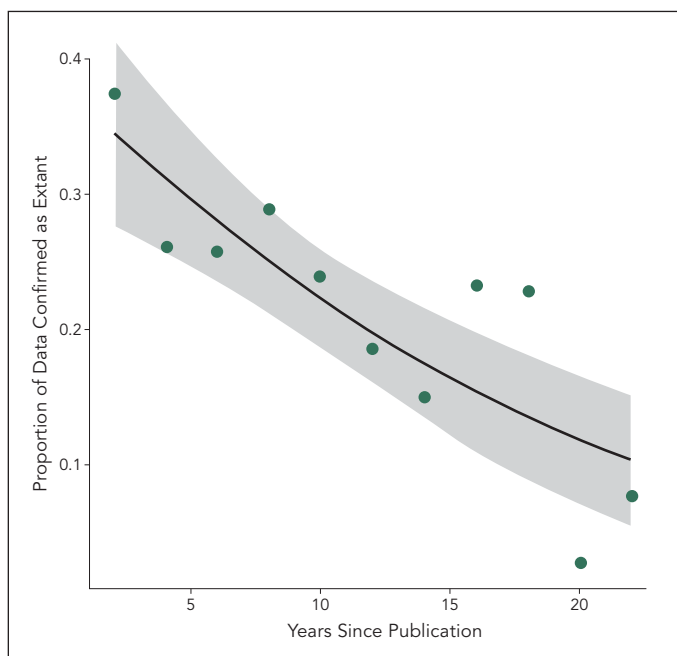
Timothy H. Vines,^{1,2} Arianne Y. K. Albert,³ Rose L. Andrew,¹ Florence Débarre,¹ Dan G. Bock,¹ Michelle T. Franklin,^{1,4} Kimberly J. Gilbert,¹ Jean-Sébastien Moore,^{1,5} Sébastien Renaut,¹ Diana J. Rennison¹

Objective To quantify how fast the availability of research data decreases with time since publication and to identify the main causes.

Design As part of a parallel study on how the reproducibility of data sets changes through time, we identified 516 papers that conducted a discriminant function analysis (DFA) on morphological data from plants, animals, or other organisms. These papers were published in the odd years between 2011 and 1991. We obtained e-mail addresses for the first, last, and corresponding authors of the papers and by searching online. We then requested the morphological data used in the DFA by e-mail. For papers where the data were not available, we also asked the authors to give a reason, such as “the data are stored on inaccessible hardware” or “the data are currently in use.”

Results We received 101 data sets, and another 20 were reported extant but could not be shared. We found that 37% of the data from papers published in 2011 still existed, but this fell to 18% for 2001 and 7% for 1991 (Figure 5). The odds of receiving the data decreased by about 7% per year. The proportion of papers with no functioning e-mails fell from 12 of 80 papers (15%) in 2011 to 10 of 26 (38%) in 1991. Furthermore, for papers where we heard about the status of the data, the proportion of authors reporting it lost or on inaccessible hardware rose gradually from 0 of 30 in 2011 to 2 of 9 (22%) in 1997, and then increased to 7 of 8 in 1993 (87%) and 4 of 6 (66%) in 1991. Other variables like the proportion of nonresponders or the proportion of datasets that could be shared showed no relationship with time.

Figure 5. Proportion of Papers With Data Available, 1991-2011



Conclusions Researchers should be able to obtain published data from the authors long after the study is complete, but we found that almost all research data was lost 10 to 15 years after publication. The main causes of data loss appeared to be a lack of working e-mails for the authors and the data being stored on outdated hardware.

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Reproducible Research: Biomedical Researchers' Willingness to Share Information to Enable Others to Reproduce Their Results

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Objective “Reproducible research” is a model for communicating research that promotes transparency of methods used to collect, analyze, and present data. It allows independent scientists to reproduce results using the original investigators' same procedures and data. Reproducible research requires a level of transparency seldom sought or achieved in biomedical research. Since 2008, *Annals of Internal Medicine* requires authors of research articles accepted for publication to state whether and under what conditions they would make available to others their protocol, statistical code, and data. The published article includes this information. This report describes trends and patterns in the willingness of biomedical researchers to share their study materials with others over the period 2008-2012.

Design We collected data for original research articles published in our journal 2008-2012 on authors' reported willingness to share study materials and examine willingness to share by study characteristics and over time.

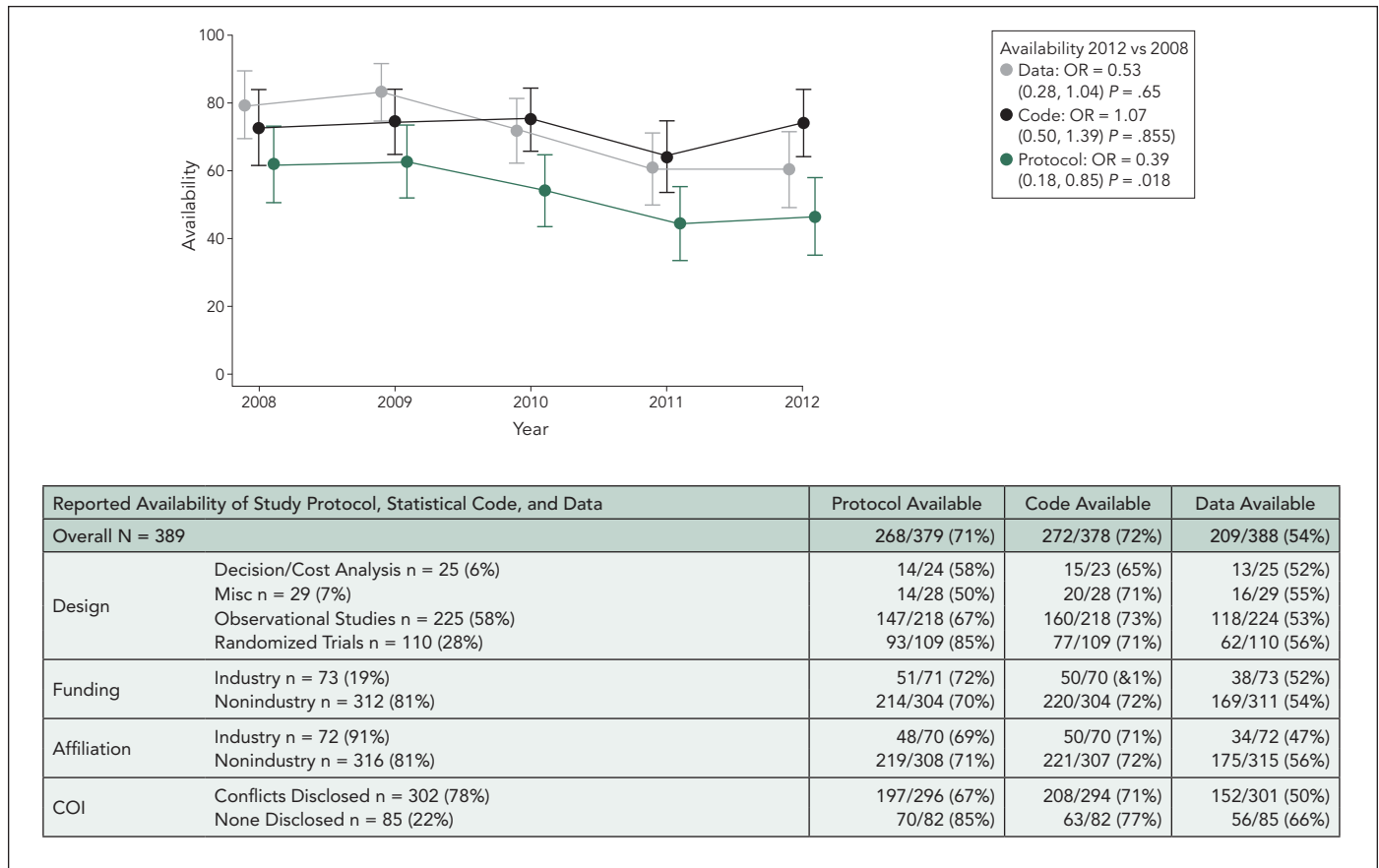
Results Of 389 articles, 17% stated that protocol was available without conditions, 54% with conditions, and 29% not available. Statistical code was available without conditions for 6%, with conditions for 66%, and unavailable for 28%. Data were available without condition for 7%, with conditions for 47%, and unavailable for 46%. Most authors who said materials were available required interested parties to contact them first, and many stated specific conditions for sharing these materials. Willingness to share varied little by the study characteristics examined (Figure 6). Over the years since the onset of this policy, there has been a decrease in authors' willingness to share protocol and data.

Conclusions While the majority of authors stated that they would make study materials available to others, most would do so only if others contacted them and attached requirements to the sharing of this information. Researchers were most willing to fully share their protocols and least willing to share data.

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Figure 6. Trends in Reported Availability Over Time



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Clinical Research Data Repositories and the Public Disclosure of Trial Data

Karmela Krleža-Jerić,^{1,2} Lee-Anne Ufholz³

Objective To explore essential features and practices of repositories that accept clinical trial data, including individual participant data (IPD), and facilitate their sharing and public disclosure.

Design This is an environmental scan. Inclusion criteria: repositories that harvest clinical trial raw data with a goal of enabling sharing and public disclosure. A list of headings was developed to capture features of selected repositories. We reviewed the literature and initiatives in this area and searched catalogues of data repositories, such as Databib (<http://databib.org/>) and interviewed repository managers.

Results Key word search of 588 repositories of Databib identified 60 repositories (38 human science, 14 clinical research, and 3 clinical trials). We identified 3 more repositories by personal contacts. After exclusion of duplicates and repositories that did not meet our criteria, we selected 4 repositories that accept and enable sharing and public disclosure of raw clinical trial data: Figshare (<http://figshare.com/>), Dryad, (<http://datadryad.org>), Inter-university Consortium for Political and Social Research (ICPSR) (www.icpsr.umich.edu), and Edinburgh DataShare (<http://datashare.is.ed.ac.uk/>). We also identified 2 large initiatives: P3G (<http://p3g.org/>) and Global Alliance (<http://www.sanger.ac.uk/about/press/assets/130605-white-paper.pdf>).

The methods and features of these repositories and initiations will be further explored in interviews with repository managers. These include unique and persistent identification systems for datasets; licenses; sustainability (business) models; information on how repositories define and describe raw data; data formats and standards; methodology of data preparation; standards of quality control; policies of data inclusion and access to data for reuse; system architecture; features that encourage data sharing across geographical and domain boundaries (such as flexibility, type of access, curation); and collaborations with other constituencies including journals and publishers.

Conclusions These results will inform the development of methodologies of public data disclosure, as well as standards and guidelines for data repositories involved in the public disclosure of participant-level datasets of clinical trials. This may further encourage collaboration and methodological consensus between repositories. The results have the potential to foster collaboration between researchers, journals, publishers, and data repositories to help enhance the reliability and connectedness of the scientific literature.

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The Democratization of Knowledge: A Supplement to Open Access

Hans Petter Fosseng, Hege Underdal, Magne Nylenna

Objective Traditionally, only university hospitals and academic institutions have access to a wide range of journals and databases. In Norway, the majority of hospitals used to have limited library services, and primary care hardly any resources at all. We have established a publicly funded and freely available digital health library and describe our experiences.

Design The Norwegian Electronic Health Library (NEHL) was established in 2006 based on 3 concepts: equality, quality, and efficiency. NEHL provides anyone with a Norwegian IP address free access to point-of-care tools, guidelines, systematic reviews, scientific journals, and a wide range of other full-text sources (eg, BMJ Best Practice, UpToDate, Cochrane Library, *BMJ*, *New England Journal of Medicine*, *Lancet*, and *JAMA*). Relevant sources freely available to the public such as open-access journals and health websites are also included. In addition, selected databases and almost 3,000 journals are available to health care personnel and students.

Results Statistics from Google Analytics available from 2008 to 2012 show an increase in visits and page views of 114% and 89%, respectively. The NEHL website had 1.6 million visits and 4.3 million page views in 2012. Major journals can be accessed directly, and their usage is not included in these figures. More than 1.5 million journal articles were downloaded and approximately 3 million searches in bibliographic databases done. The peak usage is from workplace networks on weekdays, indicating that a majority of users are professionals as intended. From 2008 to 2012 there has been an increase in traffic from search engines (from 20% to 58%). The number of first-time visitors, and the usage of patient information, indicates that the public represents an increasing proportion of the users.

Conclusions We suggest that making medical knowledge sources nationally available is an important supplement to open access. By providing both the public and professionals access to the same quality content, we believe that the basis for making health decisions becomes more transparent and verifiable. Providing free access to scientific literature by public funding can be perceived as a means for the democratization of knowledge.

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Whither Peer Review Research? Analysis of Study Design, Publication Output, and Funding of Research Presented at Peer Review Congresses

Mario Malički,¹ Erik von Elm,² Ana Marušić¹

Objective As the history of peer review research in biomedicine is the history of Peer Review Congresses, we analyzed study designs, publication outputs, and sources of funding of research presented at 6 previous Congresses (1989-2009).

Design Retrospective cohort study. We classified study design of all abstracts presented, searched MEDLINE, Web of Science,

and the Peer Review Congress website for corresponding full articles, and collected data on authorship, time to publication, article availability, and declared funding sources.

Results Research presented (n=504) was mostly observational (Table 9). Over time, the number of discussion papers decreased (χ^2_1 for trend=47.422, $P<.001$) and of cohort studies increased ($\chi^2_1=10.744$, $P=.001$). A total of 305 (60.5%) presentations were later published in journals (in 10 instances, 2 abstracts were later published as a single paper). Many articles from the first 4 Congresses were published in *JAMA* special issues (120, 39.3 %); most (63.4%) are currently freely available. The median time to publication in journals other than *JAMA* was 14.0 months (95% CI, 12.0-16.0). Funding was analyzed in 292 publications available in full text: 54.8% did not mention funding, 8.6% declared no funding, 16.1% had governmental funding, 7.2% private funding, 3.8% university funding, 3.1% publishers' funding, 3.8% declared their salary sources, 0.7% pharmaceutical funding, and 2.0% other sources. The proportion of funded studies increased over time from 20.6% in 1989 to 43.9% in 2009, with a peak of 55.9% in 2005 ($\chi^2_1=15.490$, $P<.001$). The mean number of authors increased from 2.1 (95% CI, 1.3-2.2) in 1989 to 3.9 (95% CI, 3.5-4.4) in 2009 ($P<.001$, ANOVA). There were no changes to the byline of authors between the abstract and published articles for 165 (56.5%) of papers, 82 (28.1%) had changes in the number of authors, and 45 (15.4%) had changes in the byline order.

Conclusions Underreporting is common in research conducted by a community aware of research underreporting; the causes for not publishing are not clear. There is a need for better and more systematic funding of peer review research.

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Table 9. Distribution of Study Designs and Publication Rate of Abstracts Presented at Peer Review Congresses, 1989-2009

Study Design	Congress Abstracts, No. (%)	With Subsequent Publications, No. (%)
Total	504 (100)	305 (60.5)
Observational studies	383 (76.0)	239 (62.4)
Surveys (of documents or subjects)	238 (47.2)	149 (62.6)
Cohort studies	25 (5.0)	13 (52.0)
Case-control studies	5 (1.0)	2 (40.0)
Time series studies	19 (3.8)	14 (73.7)
Systematic reviews	17 (3.4)	13 (76.5)
Qualitative studies	10 (2.0)	5 (50.0)
Other observational studies (including noncomparative studies)	69 (13.7)	43 (62.3)
Interventional studies	81 (16.0)	47 (58.0)
Randomized trials	27 (5.3)	22 (81.5)
Nonrandomized studies (eg, before-after studies)	25 (5.0)	11 (44.0)
Feasibility/pilot studies	29 (5.7)	14 (48.3)
Discussion papers	40 (8.0)	19 (47.5)