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Bibliometric Analysis of the Research Community in the Field of Publication Bias

UNCOVER project deliverable D3.1 Part B

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Deliverable D3.1 (Part B) of the UNCOVER FP7-funded project under contract number 282574: Bibliometric analysis of the research community in the field of publication bias.

This report provides information about members of the research community in the field of publication bias. It uses a quantitative approach based on bibliometric data obtained from the relevant literature stored in the Web of Science databases. Science Mapping from relational bibliometrics was applied to visualize and identify scientists, research organizations, research issues and leading publications. Maps were calculated with the software BIBTECHMON™.
This report has one attachment: Uncover_WP31b_Tab.xlsx with tables on key opinion leaders, leading institutions and published research papers in the field of 'publication bias'.

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Content

1 Executive Summary

Task 3.1 (Part B) was aimed at the identification of members of the research community, as well as key opinion leaders, in the field of publication bias through a quantitative bibliometric approach.

To this end, bibliometric data (e.g., title, authors, institution, country, abstract, keywords, and references) of the relevant literature using the search phrases “publication bias”, “citation bias”, “language bias”, “location bias”, “reference bias”, and “reporting bias” was obtained from the ISI Web of Knowledge (Thomas Reuters). The Web of Knowledge is a comprehensively indexed and searchable database of structured information for bibliometric data analysis.

Based on several thousands of publications over a twenty-year timespan, bibliometric analysis was conducted on co-authorships, networks of affiliated institutions, co-citation analysis and bibliographic coupling. Relationships between authors and between institutions were mapped and analysed with a mapping software. Research issues where identified by applying bibliographic coupling and co-citation analysis.

Four network graphs, i.e. relational maps, were constructed and analysed bibliometrically with the software BIBTECHMON™:

- *Network of Authors*: Published documents linked by co-authorship;
- *Network of Institutions*: Published documents linked by co-authorship of affiliated authors;
- *Science Map of Research Fronts:* Published documents linked by common references (bibliographic coupling);
- *Science Map of Knowledge Bases:* References linked by common citing documents (co-citation).

Key opinion leaders were assessed by bibliometric indicators such as the number of publications, times cited and co-occurrence analysis. Main tables provide overall information on the bibliometric analysis of the research community and its key opinion leaders:

1. Tables of key opinion leaders (extracted from the map of authors);
2. Tables of key institutions (extracted from the map of institutions);
3. Tables of published documents (extracted from the map of research fronts and map of knowledge bases).
4. Tables of theses and discussions in scientific literature about publication bias and researchers and institutions for interviews and workshops.

Firstly, the interactive networks and science maps were created. The software BIBTECH-MON™ provided a 'hands-on' tool for the identification of stakeholders for interviews and workshops in the UNCOVER project.

Secondly, the networks and science maps from research on "publication bias" provide insights into the overall structure of the network, the communities of authors, their research topics, organisations and countries.

Thirdly, persons were nominated as stakeholders for interviews and workshops in WP 5. Criteria for nominations were: type of organization (international organizations, agencies, national organizations, industry, and sponsors), research issues and bibliometric indicators.

The analysis showed a high dominance of publications about methods from evidence-based medicine like systematic reviews and meta-analysis performed for different medical topics. Most publications use and cite previous research, findings and methods about how to deal with publication bias. They can be classified as experienced "users and applicants" in terms of stakeholder groups.

A second dominant group of publications is related to research on publication bias concerning various aspects: publications and data for systematic reviews, adequacy of databases, publication of negative results, registration of clinical trials, outcome reporting, protocols of clinical trials, sponsorship bias, role of editors, ethic committees, guidelines for systematic reviews, and regulation of clinical trials. Stakeholders were selected on the basis of research issues and affiliated organizations.

2 Introduction

2.1 Background

The UNCOVER project is a direct contribution to overcome non-publication of clinical studies that have been designed and executed as randomized controlled trials (RCTs).

UNCOVER's aim is three-fold:

- to apply established and develop novel, solid, and useful methods for fact-finding and interventions into the socio-economic system defined by causes and sources of the publication bias;
- to engage with stakeholders and identify strategies, barriers, and facilitating factors associated with the publication bias and its consequences; and
- to synthesize lessons learned and recommend feasible measures to deal with the publication bias.

RCTs are currently best practice to avoid or minimize both systematic and random errors in clinical studies. They provide the best utility as input to systematic medicinal reviews, one cornerstone of evidence-based medicine (EbM) for improved safety and efficacy / effectiveness of patient outcomes, and their end-users.

That is guaranteed when RCTs are both correctly registered and published at least once. Because non-publication, as well as publication with time delay of RCTs, may decisively reduce the advantage of such systematic reviews of drugs, medical devices or procedures, it affects the knowledge base. Therefore, in a perspective way, this project contributes pro better allocation of funds to sponsor studies and patient value, and contra duplication of work and patients risk.

The issues of the publication bias are treated with quantitative, qualitative and participatory means in an interdisciplinary approach in areas with little or no lines of evidence as to how they perform in practice:

1. Framing the publication bias in terms of EbM and system's theory (including stakeholder mapping) to both acknowledge and reduce the complexity of the problem and focus on the main players in publishing studies as well as their strategies.
2. Objective, systematic and balanced identification of key opinion leaders, as well as measures (law, regulations, policies, practices, guidelines, methods, and tools) to overcome bias, from documents and sites by bibliometric means and comprehensive site searches on the world-wide web.

3. Systematic review of current measures substantiated by own experience ("inside-out") as well as inclusion of experts and external knowledge of international methods groups ("outside-in") in the field of systematic reviews and meta-analyses.
4. Design of interviews (telephone, or face-to-face) with editors and other stakeholders based on stakeholder mapping/analysis to reflect measures in terms of experiences, own strategies and existing conflict of interests.
5. Development of needed software solutions for the demonstration and treatment of unpublished studies on statistical meta-analyses.
6. Recommendations for the implementation of feasible measures and milestones, as well as open gaps addressed by new research, to overcome non-publication.

UNCOVER will thus both provide viable solutions for encountering publication bias.

2.2 Objectives of WP3

The objectives of Work package 3 (Identification of stakeholders and measures, barriers and facilitating factors to overcome the publication bias) are:

- Identification of existing measures to counter publication bias in clinical RCTs (policies/instruments and implementation/practices, their goals and expected impact); identification of key opinion leaders
- Identification of stakeholders and groups inside and outside the scientific community who deal with publication bias or lead initiatives against publication bias and summary of current initiatives to reduce and prevent publication bias
- Systematic assessment of the effectiveness of different initiatives to reduce publication bias in the published and unpublished literature
- Exploring motivations and barriers of journals to adopt or reject a policy that requires trial registration as a prerequisite for publication.
- Building a framework of adoption and implementation of measures, validated by expert consultation

2.2.1 Aim of Task 3.1 Part B

This task uses text-based searches for the systematic and objective identification of key opinion leaders active in the field of publication bias. To this end, this task

- collects relevant literature "abstract information" (e.g. title, author, affiliation);
- uses bibliometric analyses to cluster and visualize publications and references;

- identifies research communities working on similar themes/issues from network analysis; and
- ranks key opinion leaders by bibliometric indicators like, times cited, number of publications and central position in their thematic cluster.
- suggests persons and organizations for interviews and workshops combined with theses about publication bias related issues.

2.3 Organization of this Report

This report is structured as follows. After the Introduction (Chapter 2), Chapter 3 describes the Methods. We explain the search strategy and how the data was acquired, outline the steps of the bibliometric analysis and describe how it was performed. Chapter 4 presents the Results. It provides tables of the processed data, numerically generated network graphs, explains their meanings and interpretation, and points out central results. Finally, the report provides Conclusions in Chapter 5.

This report has one attachment (Uncover_WP31b_Tab.xlsx) with three tables:

- Excel sheet N°.1: Key opinion leaders (WP3.1b_Tab.1);
- Excel sheet N°.2: Key institutions (WP3.1b_Tab.2);
- Excel sheet N°.3: Published research papers (WP3.1b_Tab.3);

3 Methods

To gather and store information about authors and their affiliated organizations, and discussed topics of relevance (TORs) of published documents, bibliometric analysis was conducted on publicly available literature on publication bias.

The term bibliometrics comprises a quantitative form of analysis of scientific literature. Bibliometrics relies on large-scale datasets of structured bibliographic data and suitable indicators and tools for processing bibliographic data on a measurable scale. In this report, the focus is on the following bibliographic data:

- authors and co-authorships,
- citations and co-citations,
- publications and bibliographic coupling,
- content information (e.g., titles, abstracts, keywords).

Data and indicators were used to determine key opinion leaders (KOLs) and key institutions, as well as pertinent content information, to support the identification of stakeholders in the project UNCOVER.

All analyses that involve relational data structures were computed and analysed by using the software BibTechMon™, a bibliometric monitoring system to generate, illustrate and study the interrelations of authors, co-citations or content similarity. In addition to BibTechMon™, we used built-in functions of MS Access and MS Excel to analyse the data. BibTechMon™ provides relational mapping techniques with deterministic model networks (a set of nodes with edges between nodes) of authors, institutions, and other objects. The software allows to simultaneously capture all significant, occurring relations, their position in a two-dimensional space as well as the overall structure including their development over time.

Features of the software are: text analysis, calculating interrelations, network indicators, simulations and visualizations or focusing on particular nodes (e.g. authors) or subgroups of a collection of nodes, so called communities (not outside connected part of a network) and components (agglomerations of a network). A network can be analysed with regard to the overall structure or in deeper scale and detail. Original publication data can be assessed by a graphical selection of objects. Information derived from several networks can be combined. For example, a combination of co-author and keyword networks can be used to determine the TORs (topics of relevance) for a group of authors distanced sufficiently close in an author network by locating their keywords in the keyword network.

A dataset under consideration for bibliometric analysis is compiled by using a search strategy to query the online database, ISI Web of Knowledge, offering citation and reference information on scientific publications. The search strategy used for this Deliverable is given in Section 3.1.

After pre-processing of the data, the software generates network graphs. At this step of data analysis, it is important to standardize differently used terms (determine and harmonize variant forms of spelling or synonyms) and clean data (e.g. exclude unwanted terms) manually.

Any network graph consists of nodes (e.g. authors, institutions, keywords, etc.) and edges between nodes. For instance, an author network connects two authors when they co-publish a paper. Graphically, the size of nodes symbolizes the scaled number of publications for each author. In addition, colour-coding can be used to categorize different nodes. The thickness of an edge signifies how often two authors share a co-authorship. The closer two authors are in the network, the more papers they have co-authored.

3.1 Search Strategy

The search was performed by a Boolean disjunction of the following search terms (mathematical operations were performed through the OR function):

- “publication bias”
- “citation bias”
- “language bias”
- “location bias”
- “reference bias”
- “reporting bias”.

The search terms cover publication bias in general as well as a range of specific bias categories.

We used the ISI Web of Knowledge database, an academic citation indexing and search service provided by Thomson Reuters. The Web of Knowledge provides structured bibliographic information with standardized citations. The search option topic includes the title, the abstract and all keywords by the author as well as by the automated tagging of the Web of Knowledge. The search was performed on 8 June 2012 with a time-span between 1990 and May 2012. A total of 3,891 relevant publications were downloaded.

3.2 Data Synthesis

The following fields were used for our analysis:

- TI – Title
- AB – Abstract
- AU – Authors
- C1 – Author address (affiliated institution(s))
- CR – Cited references
- DE – Author keywords
- ID – Keywords plus® (automated tagging by Web of Knowledge)
- TC – Times cited
- PY – Year published.

Appendix 7.1 gives the full list of data fields.

The raw data were used for the construction of relational networks in terms of

- Nodes: Authors; Edges: Co-Authorship
- Nodes: Institutions, Edges: Co-Authorship
- Nodes: Publications: Edges: based on references
- Nodes: References; Edges: based on publications

and visualized in network and density graphs with the software BibTechMon™.

Names of organizations from the C1 "author address" field were standardized on the highest organizational level (e.g. the term "Vienna Univ Technol, Dept Stat & Probabil Theory" was standardized to the term "Vienna Univ Technol").

Besides the authors and institutions, references are suitable to determine subgroups of publications by bibliographic coupling. References of publications were analysed in two ways:

1. As a publication network (henceforth called ***research fronts network***) with publications as nodes and an edge between two publications when they list the same reference, this is called bibliographic coupling.
2. As a reference network (henceforth called ***knowledge bases network***) with references as nodes and an edge between two references when they occur in the same publication, this is called co-citation.

In either case the subgroups are indicated by a concentration of nodes within the network graph due to a comparatively stronger connection between them. In research fronts networks, a subgroup clusters publications. Hence a publication can only be part of one (1) subgroup that determines the main TORs of the corresponding set of publications. In knowledge bases networks, references are grouped. As references from a single publica-

tion can belong to more than one (1 or >1) subgroup the knowledge bases network shows all subtopics. Research fronts and knowledge bases networks complement each other. They focus on single publications according to their main research topic or subtopics, or determine all subgroups and their topic within the search field (publication bias) and how they interact. The results of the analyses of standardized raw data and advanced data structures (graphs) are summarized in formats of tables and lists in MS Excel.

For the data analysis we used the data field categories AU, TI, DE, ID, C1, CR, PY and TC (for field tag description see Appendix 7.1). Each of the 3,891 publications was complete in AU, TI, PY and TC; in the other categories they were incomplete. The corresponding levels are as follows:

AU	authors	3,891 entries	(100%)
TI	titles	3,891	(100%)
PY	publ. year	3,891	(100%)
TC	times cited	3,891	(100%)
CR	cited references	3,814	(98%)
C1	author names and affiliations	3,674	(94%)
ID	keyword	3,595	(92%)
DE	authors keywords	2,235	(57%)

4 Results

4.1 Introduction

Section 4.2 presents results from the bibliometric analysis. Subsection 4.2.1 shows descriptive statistics to overview the data drawn from the Web of Knowledge. The next subsection (Network Graphs) shows network and density graphs generated and comparisons with data obtained in Task 3.2 of Work-package 3. The remaining subsections (4.2.4 - 4.2.6) show results derived from joint analysis of networks and pertinent bibliographic information. They are formatted in form of tables. Suggestions for thematic issues, persons and organizations are part of chapter 4.3

4.2 Data Analysis

4.2.1 General Bibliometric Data

This subsection consists of different descriptive statistics about titles of sources (journals, proceedings, etc.) time series, countries with regard to the number of publications. It gives information about scientific publication and communication media, timeliness and geographic engagement. A histogram of used keywords offers some terminology.

Table 4.1 lists the top 21 journals as a percentage of all journals of the 3,891 publications. The first 21 Journals sum up nineteen percent of all publications.

Table 4.1: **List of the top 21 journals (source titles) sorted by descendant publications per journal.**
Percentages (right column) of all 3,891. Data source: Statistics provided by Web of Knowledge (downloaded on 8 June 2012).

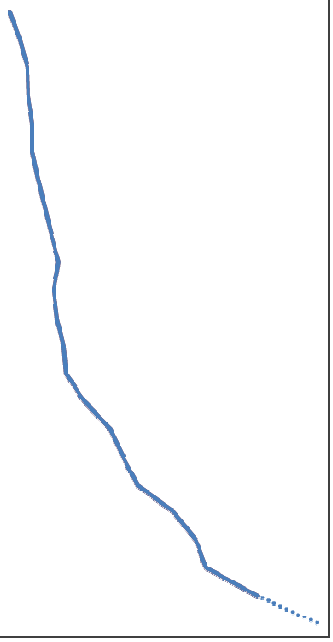
	Source Titles (Journals)	Number of Publ.	% of 3,891
1.	COCHRANE DATABASE OF SYSTEMATIC REVIEWS	101	2.60
2.	BRITISH MEDICAL JOURNAL	83	2.13
3.	JOURNAL OF CLINICAL EPIDEMIOLOGY	78	2.01
4.	JAMA JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION	57	1.47
5.	ANNALS OF INTERNAL MEDICINE	53	1.36
6.	AMERICAN JOURNAL OF EPIDEMIOLOGY	41	1.05
7.	LANCET	36	0.93
8.	STATISTICS IN MEDICINE	35	0.90
9.	PLOS ONE	34	0.87
10.	INTERNATIONAL JOURNAL OF EPIDEMIOLOGY	24	0.62
11.	EPIDEMIOLOGY	23	0.59
12.	AMERICAN JOURNAL OF CLINICAL NUTRITION	20	0.51
13.	PLOS MEDICINE	20	0.51
14.	STROKE	20	0.51

	Source Titles (Journals)	Number of Publ.	% of 3,891
15.	AMERICAN JOURNAL OF GASTROENTEROLOGY	19	0.49
16.	MOLECULAR BIOLOGY REPORTS	19	0.49
17.	ARCHIVES OF INTERNAL MEDICINE	17	0.44
18.	CANADIAN MEDICAL ASSOCIATION JOURNAL	17	0.44
19.	CURRENT MEDICAL RESEARCH AND OPINION	17	0.44
20.	EUROPEAN JOURNAL OF CANCER	16	0.41
21.	JOURNAL OF CLINICAL ONCOLOGY	16	0.41

In general, publications in the Cochrane Database of Systematic Reviews are dominating. The British Medical Journals is the second most important source for publications relevant to publication bias. Other important journals are the Journal of Clinical Epidemiology, JAMA Journal of the American Medical Association and Annals of International Medicine just to cite media with more than 50 publications. All sources are from the medical discipline. As the ISI Web of Knowledge database covers all scientific disciplines it can be concluded, that publication bias is primarily a research topic in medical research.

A small number of publications about 'publication bias' in the Web of Knowledge dates back almost two decades, to the year 1990 – the starting point of our analysis (cf. Table 4.2). Yet it took more than one decade (about 14 years) to attain a remarkable increase in the number of publications in this field.

Table 4.2: **Number of publications related to publication bias per year**.
Publication years range from 1990 to May 2012. Right column shows a trend line where 2012 was projected onto the full year. Data source: Statistics provided by Web of Knowledge (downloaded on 8 June 2012).

Publication Year	Number of Publ.	% of 3,891	Trend
1990	4	0.10	
1991	26	0.67	
1992	42	1.08	
1993	43	1.11	
1994	52	1.34	
1995	52	1.34	
1996	65	1.67	
1997	78	2.01	
1998	93	2.39	
1999	108	2.78	
2000	98	2.52	
2001	105	2.70	
2002	119	3.06	
2003	124	3.19	
2004	163	4.19	
2005	218	5.60	
2006	244	6.27	
2007	276	7.09	
2008	353	9.07	
2009	400	10.28	
2010	422	10.85	
2011	531	13.65	
2012 (January-May)	275	7.07	

Since then, the number of publications has been increasing with an approximately constant growth rate. In the last two years there are indications for further acceleration of the

growth rate (and the numbers for 2012 tend to rise further). Table 4.2 plots the trend line in the last column. The growth per year is indicative of the increasing research on publication bias from different perspectives like outcome reporting, registration of trials, ethic issues, role of editors, guidelines for performing clinical trials reporting and the increase of the number of systematic reviews on different medical topics. It reflects the growing research activities in evidence based medicine, awareness and methods for meta-analysis and systematic reviews.

Table 4.3: **List of countries/territories (with more than 3 publications) sorted descendant by number of publications**. Percentages (right column) are proportional to all 3,891 publications obtained by the search. Data source: Statistics provided by Web of Knowledge (downloaded on 8 June 2012).

	Countries/Territories	Number of Publ.	% of 3,891
1.	USA	1,480	38.04
2.	ENGLAND	760	19.53
3.	CANADA	373	9.59
4.	PEOPLES R CHINA	346	8.89
5.	GERMANY	272	6.99
6.	NETHERLANDS	225	5.78
7.	AUSTRALIA	223	5.73
8.	ITALY	186	4.78
9.	FRANCE	163	4.19
10.	SPAIN	115	2.96
11.	GREECE	113	2.90
12.	SCOTLAND	89	2.29
13.	JAPAN	87	2.24
14.	SWITZERLAND	85	2.19
15.	DENMARK	82	2.11
16.	BELGIUM	71	1.83
17.	SWEDEN	67	1.72
18.	BRAZIL	54	1.39
19.	NORWAY	51	1.31
20.	FINLAND	44	1.13
21.	AUSTRIA	39	1.00
22.	NEW ZEALAND	38	0.98
23.	SOUTH KOREA	37	0.95
24.	ISRAEL	33	0.85
25.	INDIA	32	0.82
26.	WALES	29	0.75
27.	IRELAND	20	0.51
28.	THAILAND	20	0.51
29.	IRAN	17	0.44
30.	NORTH IRELAND	16	0.41
31.	TAIWAN	15	0.39
32.	ARGENTINA	13	0.33
33.	POLAND	13	0.33
34.	SINGAPORE	13	0.33
35.	HUNGARY	11	0.28
36.	CZECH REPUBLIC	10	0.26
37.	SOUTH AFRICA	10	0.26
38.	TURKEY	8	0.21
39.	MEXICO	7	0.18
40.	RUSSIA	7	0.18
41.	SLOVENIA	7	0.18
42.	COLOMBIA	6	0.15
43.	MALAYSIA	6	0.15
44.	PORTUGAL	6	0.15
45.	CHILE	5	0.13
46.	EGYPT	5	0.13
47.	PAKISTAN	4	0.10
48.	VIETNAM	4	0.10

The field is headed by North America and dominated by the United States (with 1,480 publications), where we have the highest publication activity. A large number of European countries are listed as the address of authors and their affiliated institutions in the field of publication bias, see Table 4.3. England (with 760 publications) is leading the statistics of European countries. Positioned on the fourth place (with 346 publications), China plays a key role, too, but is not so dominating as it does in many engineering domains.

Table 4.4: **List of top keywords sorted descendant by number of publications**.
Keywords were extracted from the publication title (TI), the author keywords (DE) and the Web of Knowledge keywords (ID). DE and ID keywords are separated by semicolon; TI gets segmented into word sequences by eliminating so called stop words (common words such as 'and', 'or', 'the', and so on). Synonyms and variant forms of spelling are not standardized.

	Keyword	Number of Publ.
1	publication bias	1,594
2	meta-analysis	1,355
3	a meta-analysis	629
4	Metaanalysis	540
5	clinical-trials	452
6	Risk	384
7	Association	347
8	a systematic review	309
9	Quality	289
10	systematic review	285
11	systematic reviews	239
12	Bias	232
13	Efficacy	194
14	double-blind	185
15	Mortality	174
16	Epidemiology	167
17	Trials	161
18	Children	160
19	risk-factors	159
20	Disease	153
21	randomized controlled-trial	147

	Keyword	Number of Publ.
22	randomized controlled trials	146
23	Prevention	144
24	follow-up	142
25	randomized controlled-trials	141
26	Population	137
27	united-states	133
28	Therapy	129
29	Women	128
30	Evidence	121
31	Management	121
32	Prevalence	115
33	meta-analyses	114
34	reporting bias	106
35	Heterogeneity	105
36	Impact	105
37	Polymorphism	104
38	placebo-controlled trial	100
39	randomized-trials	100
40	myocardial-infarction	97
41	Treatment	97

Keywords were derived from three record fields: the publication title (TI); the author keywords (DE); and the Web of Knowledge keywords (ID). They are used to identify subtopics in the Research Fronts Network and Knowledge Bases Network.

Table **4.4** lists keywords pertinent to publications. Publication bias is strongly connected to meta-analysis systematic and clinical trials and not to other areas of science disciplines. Further explanations about thematic foci are given in Section 4.2.2 were keywords where used to identify stakeholders and thematic research activities.

Note: As standardization of synonyms or variant forms of spelling was estimated to be too time consuming and not needed for further analysis.

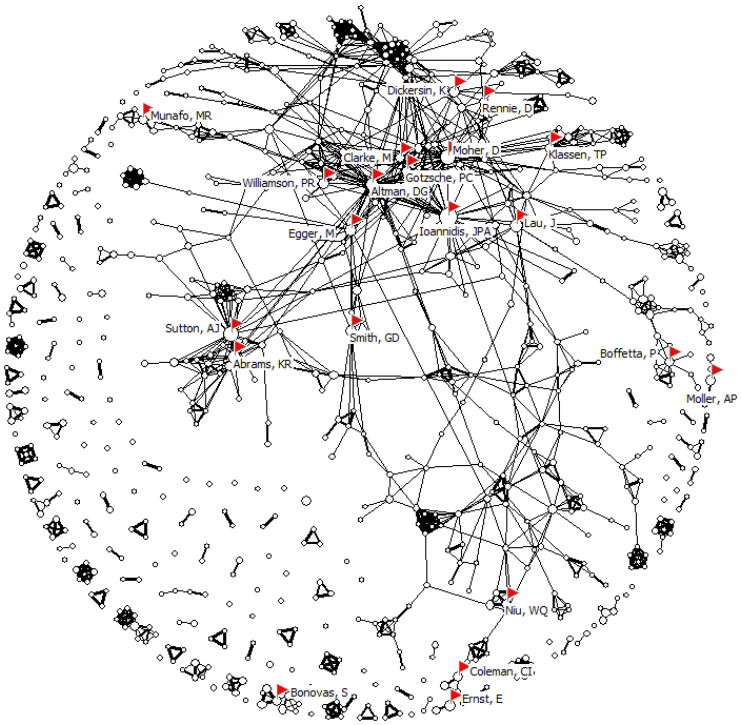
4.2.2 Network Graphs

4.2.2.1 Network of Authors

The author network consists of authors (nodes) and co-authorships (edges). Figure 4.1 shows the author network with more than 3 publications per author. The top 21 authors (ranked by the number of publications) are marked. The majority of authors of the group of "top 21" co-published.

The whole graph is dominated by a "giant" sub-network, which consists of a highly inter-linked core, including many of the "top 21" authors and with connections to various working groups via authors in a network role as brokers (central position in a sub-network) or bridges (connecting one or more sub-networks). Almost 60% of authors mapped in the graph belong to this dominant network component.

In addition, the graph shows a number of smaller components with a size of in-between 2 to 5 authors with more than 2 publications.



Author	# Pub
Ioannidis, JPA	47
Moher, D	33
Sutton, AJ	33
Altman, DG	26
Abrams, KR	22
Lau, J	22
Egger, M	19
Dickersin, K	18
Clarke, M	15
Ernst, E	15
Smith, GD	15
Boffetta, P	14
Bonovas, S	14
Coleman, CI	14
Gotzsche, PC	14
Klassen, TP	14
Moller, AP	14
Munafo, MR	14
Niu, WQ	14
Rennie, D	14
Williamson, PR	14

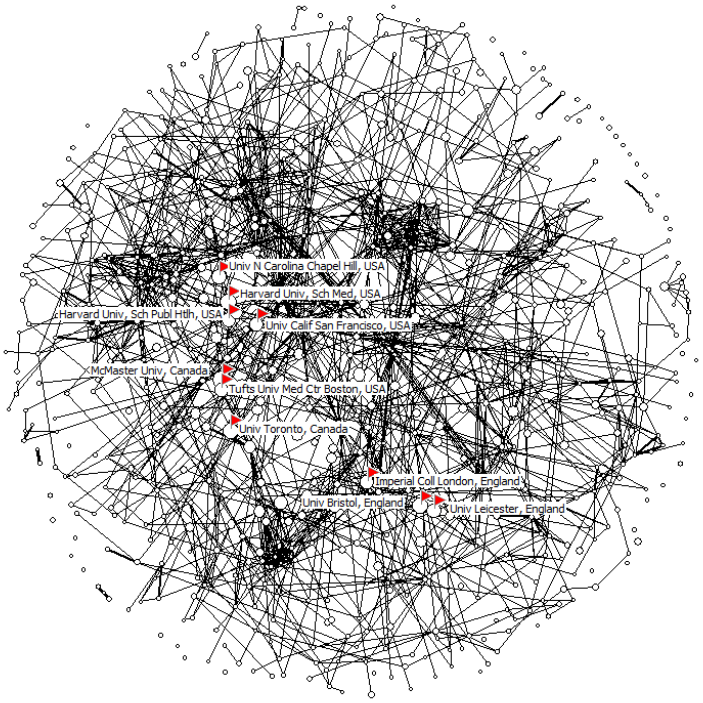
Figure 4.1: **Map of authors (co-publications).**
The top 21 authors (ranked by number of publications) are marked with flags and listed on the right-hand side. Grouping of authors on their common appearance in publications; Circle: author, the size corresponds to the number of publications; Edges: Jaccard index of co-frequencies; Timespan of analysis: 1990 to 2012; Date of research: 06 2012; Total number of publications: 3,891; each author published at least 3 publications; Number of nodes: 754; Number of edges: 1,505.

The structure of the author network is nothing out of the ordinary compared to other research fields. Although it is unusual that so many of the top 21 authors are linked instead of having their own work groups connected indirectly via brokers and bridges. Tables 4.5 and 4.6 list the top authors and related information, such as the position in the corresponding author sub-network.

Sub-networks are defined as a group of authors which are only connected to each other. As shown in Figure 4.1 there is one sub-network containing of 442 authors. To make further analysis possible this sub-network – with the representative Ioannidis, JPA – was subdivided into frequently co-operating working groups. This was achieved by hiding weak links which yields in several separated groups of strongly connected authors. Authors of such a group are co-operating frequently and form a working group.

4.2.2.2 Network of Institutions

Author-affiliated institutions were mapped by standardizing variant forms of spelling. Choosing the highest level of standardization (see Section 3) resulted in a highly interlinked graph (cf. Figure 4.2).



Institution	# Pub
McMaster Univ, Canada	75
Harvard Univ, Sch Med, USA	69
Univ Bristol, England	65
Univ Toronto, Canada	64
Univ N Carolina Chapel Hill, USA	59
Tufts Univ Med Ctr Boston, USA	53
Harvard Univ, Sch Publ Htlh, USA	52
Univ Leicester, England	52
Univ Calif San Francisco, USA	48
Imperial Coll London, England	47

Figure 4.2: **Map of institutions (co-publications).**
The top 10 institutions (ranked by number of publications) are marked with flags and are listed on the right-hand side. Grouping of organizations on their common appearance in publications; Circle: organization, the size corresponds to the number of publications; Edges: Jaccard index of co-frequencies; Timespan of analysis: 1990 to 2012; Date of research: 06 2012; Total number of publications: 3,891; each organization occurs at least in 3 publications; variant forms of spelling are standardized; Number of nodes: 675; Number of edges: 1,570 (4,700 in total).

The top 10 institutions comprise exclusively universities from English speaking countries such as USA, Canada or England. Due to the high degree of connectivity, no sub-network was identified. Tables 4.7 and 4.8 list pertinent information on the top institutions.

Figure 4.3 shows institutions according to their country of origin. The top 14 countries (ranked by number of institutions) are colour-coded. The field is dominated by the United States as well as England, Germany, Canada and China. While there are traces of international co-operation (e.g. between USA, Canada and England as well as between Australia and England), a large proportion of the connections are national. Three international working groups were identified in the graph: Spain and the United States; Germany and the United States; and one multinational group.

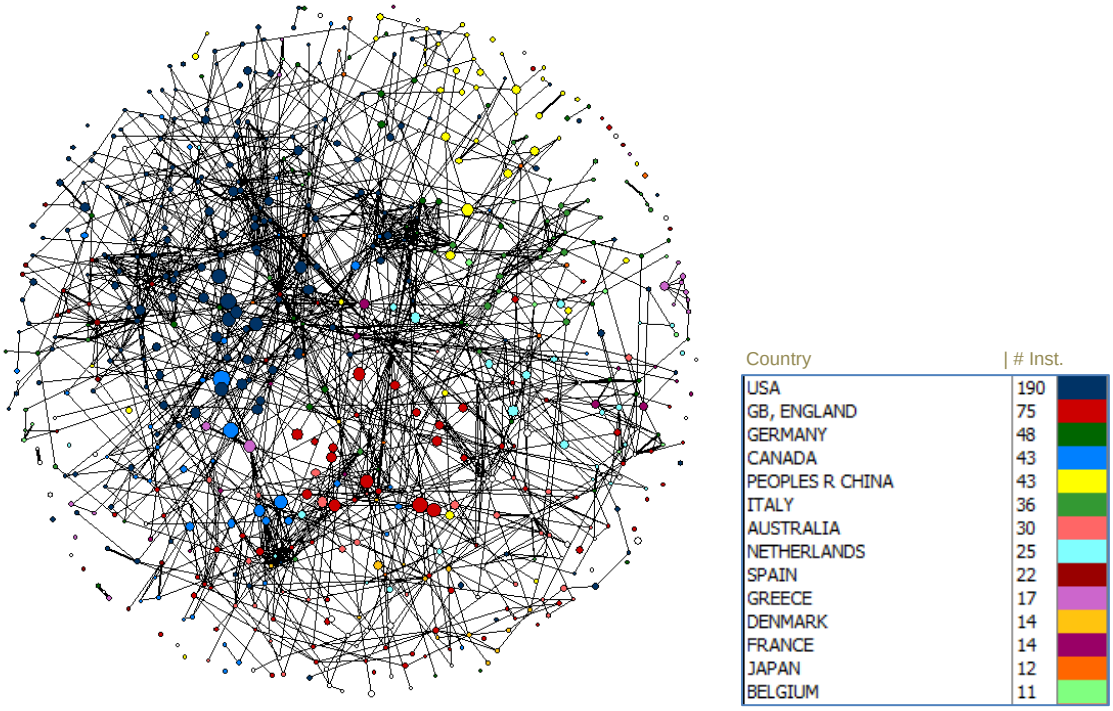


Figure 4.3: **Map of institutions (co-publications) colour-coded by countries.**
The top 14 countries (ranked by number of institutions) are listed on the right-hand side with colour codes.

The *organisation types* of the institutions are based on the categorization of stakeholders from Work package 1. The assignment of a type was done in two steps. As a first step the institution name was analysed automatically looking for keywords such as 'univ' for university, 'hosp' for hospital or 'inc' for a company. This keyword list was established by the AIT over time based on experience. Afterwards each assignment was checked manually by comparing the name of the institution and the type assigned.

As a second step faulty assigned or missing types (including uncertain assignments) were researched manually on the internet by exploring the website of the institution or wiki/encyclopaedia entries. The following organization types were mainly researched to

assure correct results: regulator, publisher, UN organization, NGO/NPO, company and governmental.

Figure 4.4 shows the eight different types of institutions identified in this study:

1. Research institute or University
2. Hospital or Medical centre
3. Governmental institution
4. Company
5. NGO or NPO
6. UN organization
7. Publishing agency
8. Regulatory agency

The majority of institutions belong to type 1 (Research institute, University) or type 2 (Hospital, Medical centre). There is practically no clustering by type, i.e. institutions of different types co-publish.

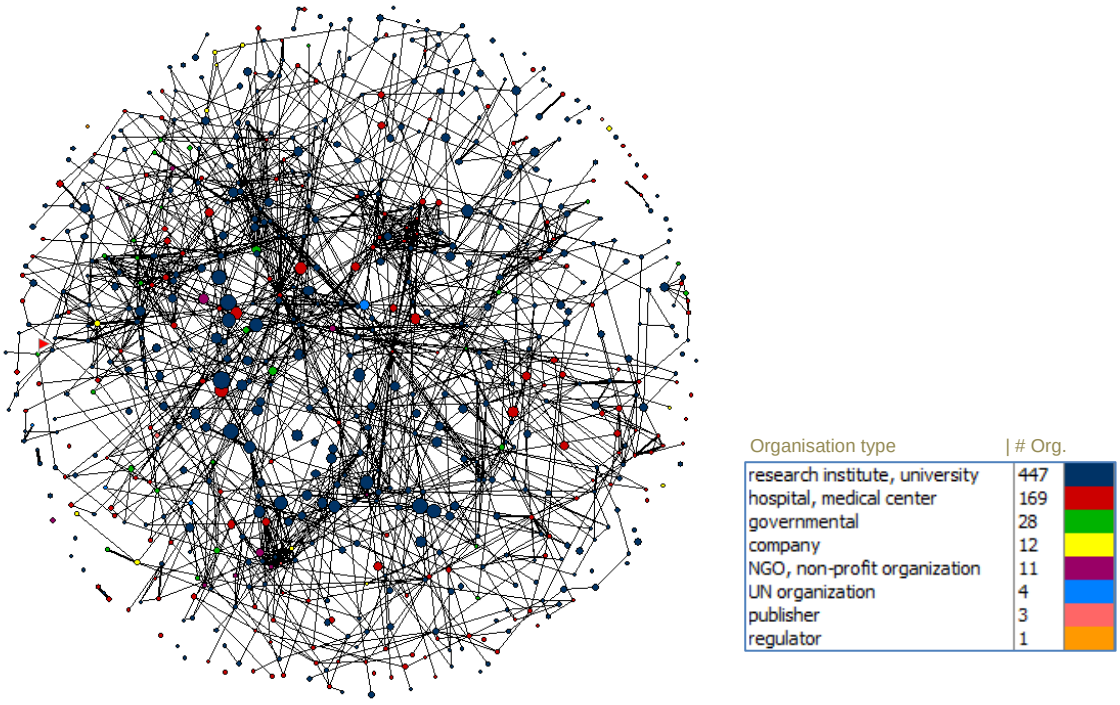


Figure 4.4: **Map of institutions (co-publications) colour-coded by organization type.**
Types (ranked by number of institutions) are listed on the right with colour codes.

4.2.2.3 Research Fronts: topics in research on publication bias

The research fronts network is formed by publications (nodes) and links between two publications if they share at least one reference. This kind of linkage is called bibliographic coupling. The underlying assumption is that the more references two publications share, the more similar is their research issue – and they are positioned closer in the network graph.

Consequently, one can use the concentrations of nodes in a research fronts network to identify subtopics of publication bias. Potential subtopics are identified by selecting an agglomeration of publications and listing keywords from the publications. The list of keywords is ranked by the higher probability of occurrence in the selected agglomeration. The index used is the 'term frequency–inverse document frequency' (TF-IDF) measure. The TF-IDF weights how often a keyword occurs in a chosen subgroup of the agglomeration relative to the overall occurrence. It causes that very common and thus unspecific terms like "publication bias" have a low rank and specific keywords like "clinical trial" have a high rank.

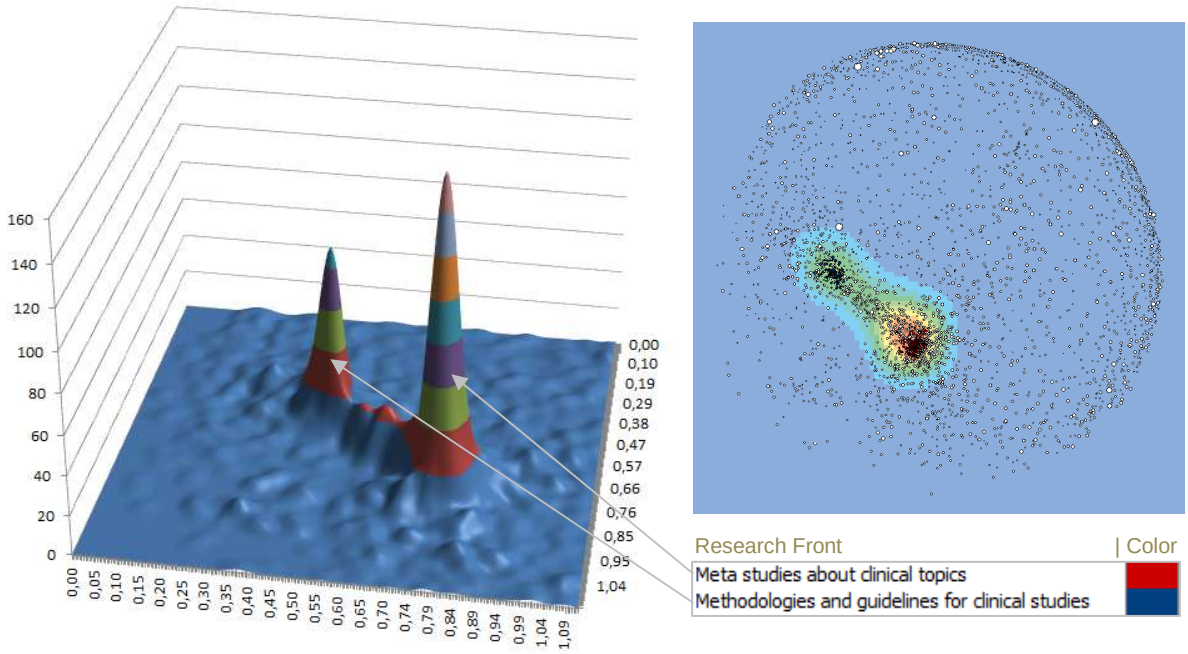


Figure 4.5: **Research fronts 3D surface map [left] and research fronts network [right].**
Grouping of publications on their common references; dot: publication; Time span of analysis: 1990 to 2012; Date of research: 06-2012; Total number of publications: 3,891; Number of nodes: 3,814; Number of edges: 1,177,507.

Figure 4.5 shows two representations of bibliographically coupled publications. The right graph represents the local agglomeration of publications with similar content. Dots are publications and the coloured contours elucidate the density of the local number of publi-

cations weighted by links that contribute to the research front. The 3D map facilitates the visibility of local concentrations and is just another representation of the same data.

The bibliographic coupling reveals two dominating agglomerations of research activities. The bigger one is formed by publications about performed systematic reviews and meta-analyses on different medical subjects such as myocardial infarction, blood pressure or diabetes mellitus. We call it **"meta-studies about clinical topics"**. It includes systematic reviews and meta-analyses.

The second peak represents publications on research about publication bias. Topics of publications include guidelines for clinical trials, mathematic and statistical methods for meta-analysis, registration of studies, as well as reporting and research about different issues related to publication bias. The assigned name is: "methodologies and guidelines for clinical studies". Table 4.9 and Table 4.100 list the top publications of each research front (ranked by times cited per year) with the information from both research fronts and knowledge bases network.

4.2.2.4 Knowledge bases: cited literature

Knowledge Bases allow us a view on the intellectual background and previous performed research of published scientific work.

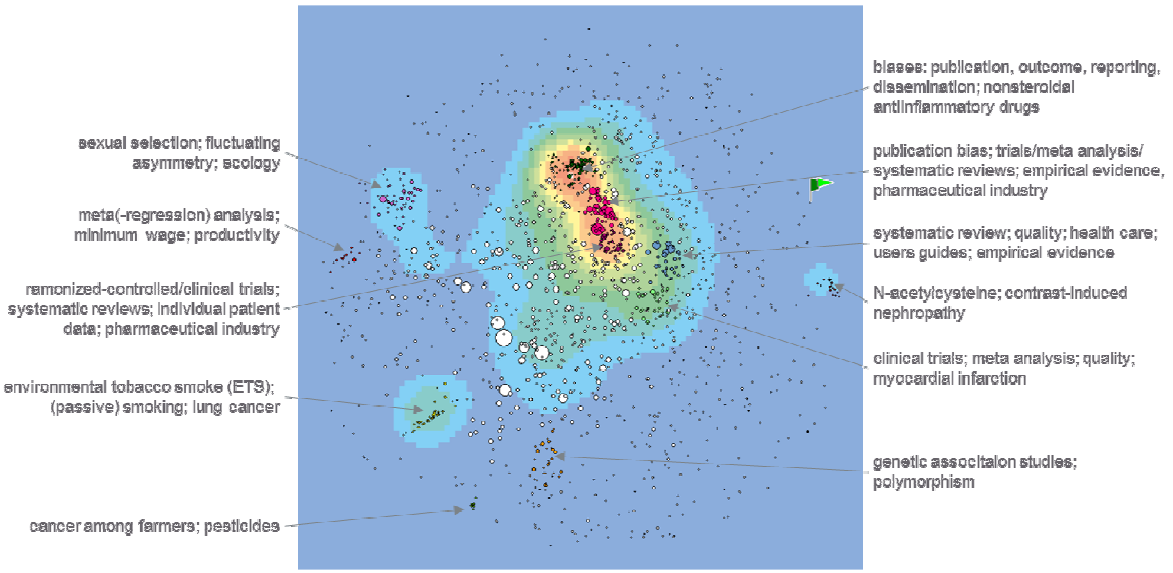


Figure 4.6: Knowledge bases network (co-references) coloured by topics.
Grouping of references on their common appearance in publications; Dots: references; Time span of analysis: 1990 to 2012; Date of research: 06-2012; Total number of citing publications: 3,891 (not as dots in the graph); contour: density map of bibliographically coupled references; Number of nodes: 1,566; Number of edges: 168,390.

The knowledge bases network is formed by references (nodes) and links between two references. References have strong links if they are often listed in the bibliographic section in publications. Similar to research fronts networks, subgroups are identified by concentrations (agglomeration) of nodes in a knowledge bases network.

Figure 4.6 shows 11 subtopics identified in the knowledge bases network. The following list assembles the subjects by the number of citing documents and the number of references

Knowledge bases	No of citing publications	No of references
publication bias; trials/meta analysis/systematic reviews; empirical evidence, pharmaceutical industry	2879	45
systematic review; quality; health care; users guides; empirical evidence	1295	41
biases: publication, outcome, reporting, dissemination; nonsteroidal antiinflammatory drugs	1104	87
sexual selection; fluctuating asymmetry; ecology	794	48
randomized-controlled/clinical trials; systematic reviews; individual patient data; pharmaceutical industry	787	38
clinical trials; meta analysis; quality; myocardial infarction	596	33
genetic association studies; polymorphism	425	35
environmental tobacco smoke (ETS); (passive) smoking; lung cancer	348	43
N-acetylcysteine; contrast-induced nephropathy	200	27
meta(-regression) analysis; minimum wage; productivity	130	13
cancer among farmers; pesticides	106	15

The huge knowledge base represents research about publication bias, systematic reviews, meta-analysis, randomized clinical trials, outcome reporting, and users' guides. Smaller knowledge bases are: studies about cancer, nephropathy, environmental tobacco smoke, polymorphism, sexual selection, etc.

To summarize, we identified research communities on publication bias and how to overcome it: improvement of performing clinical trials and reporting their outcome; and statistical improvement of available results by meta-studies and systematic reviews. This information was used to identify scientists, and organizations as stakeholders.

4.2.3 Comparison with Publications of Systematic Review of Task 3.2

This section compares the Tasks 3.2 and 3.1b of work-package 3. Task 3.2 systematically reviews the effectiveness of interventions to detect, prevent and reduce publication bias, specifically with respect to measures based on prospective study registration and clinical trial reporting. In addition, the systematic review seeks to identify barriers and facilitators of the implementation of such measures, with a focus on social, organizational and managerial factors.

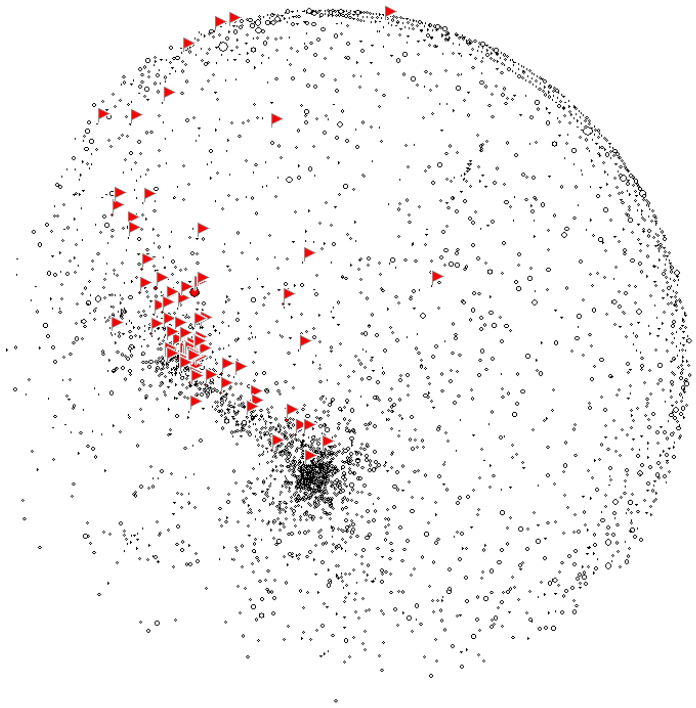


Figure 4.7: Research fronts network (co-references) compared with publications from systematic review.
78 of 234 publications included in the systematic review matched with publications from our search, 76 found in the network are marked with flags.

The systematic review carried out in Task 3.2 follows a standardized process. First, a systematic literature search of several databases (AMED, CINAHL, Cochrane Methodology Register Database [CMRD], EMBASE, Medline via Ovid, and PsycINFO) was performed. Second, a dual abstract and full-text review against predefined eligibility criteria was conducted.

Of the 234 foreseen publications for full-text review for the systematic review under Task 3.2, 78 (33%) publications matched with data obtained in this task, 2 of 78 did not have any reference listed; 76 of 78 could be identified in the research fronts network with publications in Web of Science database

Figure 4.7 shows 76 matched and identified publications. A larger proportion of these publications concentrates in the smaller agglomeration (**"methodologies and guidelines for clinical studies")** and its offshoots. It indicates that most of the selected publications for the systematic review represent research on how to overcome publication bias. The second cluster **"meta-studies about clinical topics"** about systematic reviews on medical issues that cite research work about publication bias where not selected. However, this cluster is important, because it shows that a "user group" of researchers who apply guidelines and methodologies to perform systematic reviews and meta-analysis and additionally cite the relevant literature has to be taken into account for selecting stakeholders from this part.

4.2.4 Key Opinion Leaders extracted from the Map of Authors

The network of authors does not reflect the two clusters that were identified as research fronts. Generally spoken we have a sequence of links between authors who work on publication bias and authors who work on meta-analysis and systematic review for clinical subjects.

The task to identify stakeholders requires a two-fold interpretation of the author network based on the two identified clusters. For each cluster authors were analysed by using the following indicators: the number of publications, and the number of citations of recent publications. In addition to linear indicators, we studied relational information based on co-authorships, which reveals networks of research groups. Tables 4.5 and 4.6 represent the results of the analysis of the author network. They list the top 10 authors (ranked by the number of published papers) and include information on the author network, and sub-networks. Additionally, we include the paper that is highest cited. The column “Task 3.2: Systematic review” lists if an author has published a paper which was included in the systematic review of Task 3.2.

The full table and additional information is provided in Excel sheet 1: Key opinion leaders (Uncover_WP31b_Tab.1). By using this table in the further work in this project, authors can be ranked by the number of publications and other criteria, depending on the search goal. For instance, sorting authors by the number of publications per year does not necessarily order authors as sorting by “times cited” per publication.

Table 4.5: Cluster "Meta studies about clinical topics": Top 10 authors sorted by the number of papers, including author network information and title of the highest cited paper in this cluster.

All information is according to the author. Due to co-publications, authors can have the same TOP paper. Times cited as from June 2012.

Index	Author	Author network		Author sub-networks			Task 3.2 Systematic review	Research Fronts (Number of papers in research front)		
		Times cited (diameter)	No. of papers	Rank	Sub-network	size sub-network		Top Paper in Research Front A (Title)	Meta studies about clinical topics	Methodologies and guidelines for clinical studies
1	Bagos, PG	11	12	2	Bonovas, S	8	no	Association between the plasminogen activator inhibitor-I 4G/5G polymorphism and venous thrombosis - A meta-analysis	10	
2	Nikolopoulos, GK	14	9	5	Bonovas, S	8	no	Association between the plasminogen activator inhibitor-I 4G/5G polymorphism and venous thrombosis - A meta-analysis	8	
3	Qin, LQ	6	9	1	Qin, LQ	5	no	Milk consumption is a risk factor for prostate cancer in Western countries: evidence from cohort studies	8	
4	Wang, J	10	12	23	Ioannidis, JPA	442	no	UCHL1 is a Parkinson's disease susceptibility gene	7	
5	Sutton, AJ	48	33	2	Ioannidis, JPA	442	YES	Empirical assessment of effect of publication bias on meta-analyses	7	1
6	Dong, JY	1	7	2	Qin, LQ	5	no	Erectile Dysfunction and Risk of Cardiovascular Disease Meta-Analysis of Prospective Cohort Studies	7	
7	Xu, MQ	5	7	54	Ioannidis, JPA	442	no	Quantitative assessment of the effect of angiotensinogen gene Polymorphisms on the risk of coronary heart disease	6	
8	Mengoli, C	38	5	1	Cruciani, M	2	no	Use of PCR for diagnosis of invasive aspergillosis: systematic review and meta-analysis	5	
9	Cruciani, M	38	5	1	Cruciani, M	2	no	Use of PCR for diagnosis of invasive aspergillosis: systematic review and meta-analysis	5	
10	Abrams, KR	46	22	5	Ioannidis, JPA	442	YES	A systematic review of molecular and biological tumor markers in neuroblastoma	5	

Table 4.6: Cluster: "Methodologies and guidelines for clinical studies": Top 10 authors sorted by the number of papers in the research, including author network information and title of the highest cited paper in this cluster.

All information is according to the author. Due to co-publications, authors can have the same TOP paper. Times cited as from June 2012.

Index	Author	Author network		Author sub-networks			Task 3.2 Systematic review	Research Fronts (Number of papers in research front)		
		Times cited (diameter)	No. of papers	Rank	Sub-network	size sub-network		Top Paper in Research Front B (Title)	A. Meta studies about clinical topics	B. Methodologies and guidelines for clinical studies
1	Moher, D	128	33	2	Ioannidis, JPA	442	YES	Does the inclusion of grey literature influence estimates of intervention effectiveness reported in meta-analyses?		9
2	Dickersin, K	178	18	8	Ioannidis, JPA	442	YES	Systematic reviews - identifying relevant studies for systematic reviews		8
3	Decullier, E	44	5	96	Ioannidis, JPA	442	no	Systematic Review of the Empirical Evidence of Study Publication Bias and Outcome Reporting Bias		5
4	Tannock, IF	30	8	1	Tannock, IF	2	no	Factors associated with failure to publish large randomized trials presented at an oncology meeting		5
5	Ioannidis, JPA	78	47	1	Ioannidis, JPA	442	YES	Systematic Review of the Empirical Evidence of Study Publication Bias and Outcome Reporting Bias	3	5
6	Rennie, D	217	14	11	Ioannidis, JPA	442	YES	Publication bias in editorial decision making		4
7	Smith, GD	451	15	9	Ioannidis, JPA	442	YES	Sifting the evidence - what's wrong with significance tests?		4
8	Egger, M	344	19	7	Ioannidis, JPA	442	YES	Uses and abuses of meta-analysis		4
9	Cook, DJ	361	9	35	Ioannidis, JPA	442	no	Users guides to the medical literature .6. how to use an overview		4
10	Bero, LA	133	8	43	Ioannidis, JPA	442	YES	Pharmaceutical industry sponsorship and research outcome and quality: systematic review		4

4.2.5 Key Institutions extracted from the Map of Institutions

The network of institutions, similar to the author network, does not reflect the two clusters that were identified as research fronts. Again, we have a sequence of links between institutions whose researchers work on publication bias and researcher who work on meta-analysis and systematic review for clinical subjects.

The task to identify stakeholder institutions requires, analogue to the authors, a two-fold interpretation of the network based on the two clusters.

Table 4.7 and Table 4.8 list the top 30 institutions ranked by the number of publications, including the corresponding categories. The full table and additional information is provided in Excel sheet 2: Key institutions (WP3.1b_Tab.2).

Table 4.7: Cluster "Meta studies about clinical topics": Top 20 Institutions sorted by number of papers

Index	Institutions	Institutional network			Research Fronts (Number of papers in research front)	
		Nr. Papers	Country	Organization Type	Meta studies about clinical topics	Methodologies and guidelines for clinical studies
1	Harvard Univ, Sch Publ Htlh, USA	52	USA	research institute, university	21	
2	Brigham & Womens Hosp Boston, USA	42	USA	hospital, medical center	18	
3	Harvard Univ, Sch Med, USA	69	USA	research institute, university	17	1
4	Univ Athens, Greece	25	GREECE	research institute, university	10	1
5	Univ N Carolina Chapel Hill, USA	59	USA	research institute, university	9	7
6	Univ Leicester, England	52	GB, ENGLAND	research institute, university	9	1
7	Shanghai Jiao Tong Univ, Peoples R China	43	PEOPLES R CHINA	research institute, university	9	1
8	Univ Warwick, England	29	GB, ENGLAND	research institute, university	9	1
9	Nanjing Med Univ, Peoples R China	24	PEOPLES R CHINA	research institute, university	9	
10	Sichuan Univ Chengdu, Peoples R China	25	PEOPLES R CHINA	research institute, university	8	
11	Soochow Univ Suzhou, Peoples R China	9	PEOPLES R CHINA	research institute, university	8	
12	Massachusetts Gen Hosp Boston, USA	40	USA	hospital, medical center	7	
13	Univ Toronto, Canada	64	CANADA	research institute, university	6	6
14	Fudan Univ Shanghai, Peoples R China	24	PEOPLES R CHINA	research institute, university	6	
15	Univ Padua, Italy	14	ITALY	research institute, university	6	
16	Shandong Univ Jinan, Peoples R China	13	PEOPLES R CHINA	research institute, university	6	
17	Uniformed Serv Univ Hlth Sci Bethesda, USA	12	USA	research institute, university	6	
18	Hellen Ctr Dis Control & Prevent, Greece	8	GREECE	governmental	6	
19	Univ Cent Greece Lamia, Greece	8	GREECE	research institute, university	6	
20	Wenzhou Med Coll, Peoples R China	7	PEOPLES R CHINA	research institute, university	6	

Table 4.8: Cluster "Methodologies and guidelines for clinical studies": Top 20 Institutions sorted by number of papers

Index	Institutions	Institutional network			Research Fronts (Number of papers in research front)	
		Nr. Papers	Country	Organization Type	A. Meta studies about clinical topics	B. Methodologies and guidelines for clinical studies
1	Univ Calif San Francisco, USA	48	USA	research institute, university	1	15
2	Univ Bristol, England	65	GB, ENGLAND	research institute, university	1	8
3	Univ Ottawa, Canada	46	CANADA	research institute, university		8
4	McMaster Univ, Canada	75	CANADA	research institute, university	2	7
5	Univ N Carolina Chapel Hill, USA	59	USA	research institute, university	9	7
6	Childrens Hosp Eastern Ontario Ottawa, Canada	20	CANADA	hospital, medical center		7
7	Univ Toronto, Canada	64	CANADA	research institute, university	6	6
8	Univ Washington Seattle, USA	31	USA	research institute, university	3	6
9	Yale Univ, Sch Med New Haven, USA	28	USA	research institute, university	1	5
10	Univ Bern, Switzerland	20	SWITZERLAND	research institute, university		5
11	Hosp Civils Lyon, France	7	FRANCE	hospital, medical center		5
12	Univ Ioannina, Sch Med, Greece	40	GREECE	research institute, university	3	4
13	Univ Liverpool, England	28	GB, ENGLAND	research institute, university	2	4
14	UK Cochrane Ctr Oxford, England	18	GB, ENGLAND	NGO, non-profit organization		4
15	MRC London, England	7	GB, ENGLAND	governmental	1	4
16	Princess Margaret Hosp Toronto, Canada	7	CANADA	hospital, medical center		4
17	Tufts Univ Boston, USA	32	USA	research institute, university	2	3
18	Yale Univ New Haven, USA	26	USA	research institute, university	2	3
19	NIH Natl Inst Hlth Bethesda, USA	21	USA	governmental	1	3
20	Univ Freiburg, Germany	14	GERMANY	research institute, university	2	3

4.2.6 Published Research Papers extracted from Maps of Research Fronts and Knowledge Bases

Tables 4.9 and 4.10 list the top 10 publications (ranked by times cited per year) of the publication analysis based on both research fronts and knowledge bases networks. The full table and additional information is provided in Excel sheet 3: Published research papers (WP3.1b_Tab.3).

The two columns under the header “Knowledge Bases Network” state the primary subtopic of a publication, including description and keywords (ranked by the TF-IDF scheme). Because of the landscape properties of knowledge bases networks not every publication got assigned a subtopic (cf. discussion under Section 3.2). Interestingly, several publications (e.g. several thousand citations) are listed with markedly large citation numbers, independent of normalization by the number of years.

Table 4.9: Cluster "Meta studies about clinical topics": Top 10 publications on Publication Bias sorted by" times cited" per year

All information is according to the publication. Times cited as from June 2012. 3 publications have been replaced for publications better fitted for the topic.

Index	Paper Title	Journal	Authors	Pub. Year	Times Cited	Times Cited per Year	Research Front Topic	Task 3.2: Systematic review	Knowledge Bases Network	
									Characteristic Subtopics	Keywords (based on TF-IDF)
1	Prediction of clinical cardiovascular events with carotid intima-media thickness - A systematic review and meta-analysis	Circulation	Lorenz, MW; Markus, HS; Bots, ML; Rosvall, M; Sitzer, M	2007	583	97,2	Meta studies about clinical topics	no		
2	Genetic associations in large versus small studies: an empirical assessment	Lancet	Ioannidis, JPA; Trikalinos, TA; Ntzani, EE; Contopoulos-Ioannidis, DG	2003	383	38,3	Meta studies about clinical topics	no	genetic association studies; polymorphism	genetic association studies; population stratification; association; meta-analysis; polymorphism; susceptibility; genetics; allelic association; genetic association; complex diseases
3	Explaining heterogeneity in meta-analysis: A comparison of methods	Stat. Med.	Thompson, SG; Sharp, SJ	1999	470	33,6	Meta studies about clinical topics	no		
4	The benefits of statins in people without established cardiovascular disease but with cardiovascular risk factors: meta-analysis of randomised controlled trials	Br. Med. J.	Brugts, JJ; Yetgin, T; Hoeks, SE; Gotto, AM; Shepherd, J; Westendorp, RGJ; de Craen, AJM; Knopp, RH; Nakamura, H; Ridker, P; van Domburg, R; Deckers, JW	2009	129	32,3	Meta studies about clinical topics	no	systematic review; quality; health care; users guides; empirical evidence	quality; systematic reviews; clinical-trials; publication bias; randomized controlled trials; METAANALYSIS; meta-analysis; randomized controlled-trials; healthcare; empirical-evidence
5	Meta-analysis of probiotics for the prevention of antibiotic associated diarrhoea and the treatment of Clostridium difficile disease	Am. J. Gastroenterol.	McFarland, LV	2006	204	29,1	Meta studies about clinical topics	no		
6	Salt intake, stroke, and cardiovascular disease: meta-analysis of prospective studies	Br. Med. J.	Strazzullo, P; D'Elia, L; Kandala, NB; Cappuccio, FP	2009	107	26,8	Meta studies about clinical topics	no		
7	Acute and chronic graft-versus-host disease after allogeneic peripheral-blood stem-cell and bone marrow transplantation: A meta-	J. Clin. Oncol.	Cutler, C; Giri, S; Jeyapalan, S; Paniagua, D; Viswanathan, A; Antin, JH	2001	231	19,3	Meta studies about clinical topics	no		

Index	Paper Title	Journal	Authors	Pub. Year	Times Cited	Times Cited per Year	Research Front Topic	Task 3.2: Systematic review	Knowledge Bases Network	
									Characteristic Subtopics	Keywords (based on TF-IDF)
	analysis									
8	Efficacy of probiotics in prevention of acute diarrhoea: a meta-analysis of masked, randomised, placebo-controlled trials	Lancet Infect. Dis.	Sazawal, S; Hiremath, G; Dhingra, U; Malik, P; Deb, S; Black, RE	2006	132	18,9	Meta studies about clinical topics	no	randomized-controlled/clinical trials; systematic reviews; individual patient data; pharmaceutical industry	clinical-trials; randomized controlled-trials; publication bias; systematic reviews; duplicate publication; reporting systematic reviews; elaboration; Explanation; PRISMA statement; outcome selection bias
9	The prevalence of co-morbid depression in adults with Type 2 diabetes: a systematic review and meta-analysis	Diabetic Med.	Ali, S; Stone, MA; Peters, JL; Davies, MJ; Khunti, K	2006	119	17,0	Meta studies about clinical topics	no		
10	Meat consumption and risk of colorectal cancer: A meta-analysis of prospective studies	Int. J. Cancer	Larsson, SC; Wolk, A	2006	117	16,7	Meta studies about clinical topics	no	publication bias; trials/meta analysis/systematic reviews; empirical evidence, pharmaceutical industry	publication bias; clinical-trials; systematic reviews; metaanalysis; quality; randomized controlled-trials; randomized-trials; Outcome reporting bias; meta-analysis; empirical-evidence

Table 4.10: Cluster "Methodologies and guidelines for clinical studies": Top 10 publications on Publication Bias sorted by times cited per year

Index	Paper Title	Journal	Authors	Pub. Year	Times Cited	Times Cited per Year	Research Front Topic	Task 3.2: Systematic review	Knowledge Bases Network Characteristic Subtopics	Knowledge Bases Network Keywords (based on TF-IDF)
1	Pharmaceutical industry sponsorship and research outcome and quality: systematic review	Br. Med. J.	Lexchin, J; Bero, LA; Djulbegovic, B; Clark, O	2003	646	64,6	Methodologies and guidelines for clinical studies	YES	biases: publication, outcome, reporting, dissemination; nonsteroidal anti-inflammatory drugs	publication bias; outcome reporting bias; randomized controlled-trials; publication; nonsteroidal anti-inflammatory drugs; abstracts; clinical-trials; research findings; acute myocardial-infarction; randomized-trials
2	SYSTEMATIC REVIEWS - IDENTIFYING RELEVANT STUDIES FOR SYSTEMATIC REVIEWS	Br. Med. J.	DICKERSIN, K; SCHERER, R; LEFEBVRE, C	1994	941	49,5	Methodologies and guidelines for clinical studies	no	clinical trials; meta analysis; quality; myocardial infarction	clinical-trials; metaanalysis; publication bias; design affects outcomes; systematic reviews; meta-analysis; randomized clinical-trials; randomized controlled trials; quality; myocardial-infarction
3	Systematic Review of the Empirical Evidence of Study Publication Bias and Outcome Reporting Bias	PLoS One	Dwan, K; Altman, DG; Arnaiz, JA; Bloom, J; Chan, AW; Cronin, E; Decullier, E; Easterbrook, PJ; Von Elm, E; Gamble, C; Ghersi, D; Ioannidis, JPA; Simes, J; Williamson, PR	2008	165	33,0	Methodologies and guidelines for clinical studies	no	biases: publication, outcome, reporting, dissemination; nonsteroidal anti-inflammatory drugs	publication bias; outcome reporting bias; randomized controlled-trials; publication; nonsteroidal anti-inflammatory drugs; abstracts; clinical-trials; research findings; acute myocardial-infarction; randomized-trials
4	Sifting the evidence - what's wrong with significance tests?	Br. Med. J.	Sterne, JAC; Smith, GD	2001	373	31,1	Methodologies and guidelines for clinical studies	no	publication bias; trials/meta analysis/systematic reviews; empirical evidence, pharmaceutical industry	publication bias; clinical-trials; systematic reviews; metaanalysis; quality; randomized controlled-trials; randomized-trials; outcome reporting bias; meta-analysis; empirical-evidence
5	USERS GUIDES TO THE MEDI-	JAMA-J. Am.	OXMAN, AD; COOK, DJ; GUY-	1994	511	26,9	Methodolo-	no	clinical trials;	clinical-trials; metaanalysis;

Index	Paper Title	Journal	Authors	Pub. Year	Times Cited	Times Cited per Year	Research Front Topic	Task 3.2: Systematic review	Knowledge Bases Network	
									Characteristic Subtopics	Keywords (based on TF-IDF)
	CAL LITERATURE .6. HOW TO USE AN OVERVIEW	Med. Assoc.	ATT, GH				gies and guidelines for clinical studies		meta analysis; quality; myocardial infarction	publication bias; design affects outcomes; systematic reviews; meta-analysis; randomized clinical-trials; randomized controlled trials; quality; myocardial-infarction
6	Publication bias in clinical trials due to statistical significance or direction of trial results	Cochrane Database Syst Rev.	Hopewell, S; Loudon, K; Clarke, MJ; Oxman, AD; Dickersin, K	2009	99	24,8	Methodologies and guidelines for clinical studies	YES	biases: publication, outcome, reporting, dissemination; nonsteroidal anti-inflammatory drugs	publication bias; outcome reporting bias; randomized controlled-trials; publication; nonsteroidal anti-inflammatory drugs; abstracts; clinical-trials; research findings; acute myocardial-infarction; randomized-trials
7	Epidemiology and reporting characteristics of systematic reviews	PLos Med.	Moher, D; Tetzlaff, J; Tricco, AC; Sampson, M; Altman, DG	2007	134	22,3	Methodologies and guidelines for clinical studies	no	clinical trials; meta analysis; quality; myocardial infarction	clinical-trials; metaanalysis; publication bias; design affects outcomes; systematic reviews; meta-analysis; randomized clinical-trials; randomized controlled trials; quality; myocardial-infarction
8	FACTORS INFLUENCING PUBLICATION OF RESEARCH RESULTS - FOLLOW-UP OF APPLICATIONS SUBMITTED TO 2 INSTITUTIONAL REVIEW BOARDS	JAMA-J. Am. Med. Assoc.	DICKERSIN, K; MIN, YI; MEINERT, CL	1992	425	20,2	Methodologies and guidelines for clinical studies	no	publication bias; trials/meta analysis/systematic reviews; empirical evidence, pharmaceutical industry	publication bias; clinical-trials; systematic reviews; metaanalysis; quality; randomized controlled-trials; randomized-trials; outcome reporting bias; meta-analysis; empirical-evidence
9	Publication bias: evidence of delayed publication in a cohort study of clinical research projects	Br. Med. J.	Stern, JM; Simes, RJ	1997	320	20,0	Methodologies and guidelines for clinical studies	no	publication bias; trials/meta analysis/systematic reviews; empirical evi-	publication bias; clinical-trials; systematic reviews; metaanalysis; quality; randomized controlled-trials; randomized-trials; outcome reporting bias; meta-

Index	Paper Title	Journal	Authors	Pub. Year	Times Cited	Times Cited per Year	Research Front Topic	Task 3.2: Systematic review	Knowledge Bases Network Characteristic Subtopics	 Keywords (based on TF-IDF)
									dence, pharmaceutical industry	analysis; empirical-evidence
10	Does the inclusion of grey literature influence estimates of intervention effectiveness reported in meta-analyses?	Lancet	McAuley, L; Pham, B; Tugwell, P; Moher, D	2000	197	15,2	Methodologies and guidelines for clinical studies	no	biases: publication, outcome, reporting, dissemination; nonsteroidal anti-inflammatory drugs	publication bias; outcome reporting bias; randomized controlled-trials; publication; nonsteroidal anti-inflammatory drugs; abstracts; clinical-trials; research findings; acute myocardial-infarction; randomized-trials

4.3 Research Topics and Stakeholders suggested for the Workshops

Stakeholders related to publication bias have to be envisaged from several perspectives: actors involved in a social system such as trialists, members of ethic committees, editors, funders, members of an association or international organization, etc. and scientists engaged in clinical research, meta studies or systematic reviews but also scientists involved in research about publication bias and related issues.

Methods from Science Mapping were used to structure publications by their content, identify and visualize networks of authors and affiliations. The query for the pre-selection of publications aims to provide a broader set of relevant publications because publications with similar content are separated by bibliographic coupling. As we have shown, publications of two main research fields were relevant: research about "publications bias" and methods and suggestions to avoid it and "users" who are researchers performing meta-analyses and systematic reviews, and who apply guidelines to overcome publication bias. The bibliometric analysis aimed at the selection of a list of stakeholders for interviews and participation in workshops.

The following two lists indicates persons and their affiliations from the two identified clusters.

Table 4.11: Selection of stakeholders concerned with "Meta studies about clinical topics" the so called "user group".

Author	Organisation
Bagos, PG	Univ Cent Greece, Dept Comp Sci & Biomed Informat, Lamia 35100, Greece
Nikolopoulos, GK	Univ Cent Greece, Dept Comp Sci & Biomed Informat, Lamia 35100, Greece
Qin, LQ	Soochow Univ, Dept Nutr & Food Hyg, Sch Publ Hlth, Suzhou 215123, Peoples R China
Wang, J	Anhui Med Univ, Sch Publ Hlth, Dept Epidemiol & Biostat, Hefei 230032, Anhui, Peoples R China
Sutton, AJ	Univ Leicester, Dept Hlth Sci, Leicester LE1 7RH, Leics, England;
Dong, JY	Soochow Univ, Sch Radiat Med & Publ Hlth, Dept Food Hyg & Nutr, Suzhou 215123, Peoples R China;
Xu, MQ	Sichuan Univ, W China Hosp, Dept Liver & Vasc Surg, Chengdu 610041, Sichuan Prov, Peoples R China
Mengoli, C	Univ Padua, Dept Histol Microbiol & Med Biotechnol, Padua, Italy;
Cruciani, M	HIV Outpatient Clin, Ctr Prevent Med, Verona, Italy;
Abrams, KR	Univ Leicester, Dept Hlth Sci, Leicester LE1 7RH, Leics, England;

Table 4.12: Selection of stakeholders concerned with "Methodologies and guidelines for clinical studies".

Author	Organisation
Moher, D	Univ Ottawa, Fac Med, Dept Epidemiol & Community Med, Ottawa, ON, Canada
Dickersin, K	Johns Hopkins Bloomberg Sch Publ Hlth, Dept Epidemiol, Baltimore, MD 21205 USA;
Decullier, E	Univ Lyon, Lab Sante Individu Soc EA SIS, Lyon, France;

Author	Organisation
Tannock, IF	Princess Margaret Hosp, Toronto, ON M5G 2M9, Canada;
Ioannidis, JPA	Stanford Univ, Stanford Prevent Res Ctr, Sch Med, Stanford, CA 94305 USA
Rennie, D	JAMA, Chicago, IL USA
Smith, GD	Univ Bristol, Dept Social Med, Bristol BS8 2PR, Avon, England
Egger, M	Univ Bristol, Dept Social Med, MRC, Hlth Serv Res Collaborat, Bristol BS8 2PR, Avon, England
Cook, DJ	MCMASTER UNIV,DEPT MED,HAMILTON,ON,CANADA
Bero, LA	Department of Clinical Pharmacy and Institute for Health Policy Studies, University of California at San Francisco, San Francisco, CA 94118, USA

In a second part different approaches are used to identify actors who contribute to the avoidance of publication bias from different perspectives. Firstly, all international organizations and associations where identified by the affiliations of the authors. Secondly, all publications with the keyword ethic were read. All publications with an affiliation containing “Cochrane” where also manually selected. All publications were grouped by their content in the sense of a contribution to avoid publication bias. Results are presented in the following tables structured by:

- Outcome reporting
- Study registration
- Sponsorship bias
- Editorial Bias

The persons are listed with their affiliation, main theses and outcomes of their research, title and abstract of the publication.

Table 4.13: Persons and theses of selected papers about *outcome reporting* for stakeholder involvement.

Source: Selected publications from the bibliometric analysis, times cited as from June 2012.

Index	Theses	Affiliations	Title of publication	Publ. Year	WOS ID	Abstract
1	A prospective public health interventions study registry is necessary to aid the identification of unreported or incompletely reported outcomes.	[**Pearson, Mark**; Peters, Jaime] Univ Exeter, Peninsula Technol Assessment Grp PenTAG, Peninsula Med Sch, Exeter EX2 4SG, Devon, England	Outcome reporting bias in evaluations of public health interventions: evidence of impact and the potential role of a study register	2012	WOS:000301045100002	Background Systematic reviews of the effectiveness of interventions are increasingly used to inform recommendations for public health policy and practice, but outcome reporting bias is rarely assessed. Methods Studies excluded at full-text stage screening for a systematic review of a public health intervention were assessed for evidence of study exclusion resulting from non-reporting of relevant outcomes. Studies included in the review were assessed for evidence of outcome reporting bias and the impact that this had on the evidence synthesised using a formal tool (Outcome Reporting Bias in Trials (ORBIT)). Results None of the reports excluded at full-text stage were excluded because of non-reporting of relevant outcomes. Of the 26 included papers, six were identified as having evidence of missing or incompletely reported outcomes, with 64% of unreported or incompletely reported outcomes identified as to leading to a high risk of bias according to the ORBIT tool. Where there was evidence of the effectiveness of interventions before an assessment of outcome reporting bias was undertaken, identifying possible instances of outcome reporting bias generally led to a reduction in the strength of evidence for the effectiveness of the interventions. Conclusion The findings from this single evaluation provide empirical data to support the call for a prospective public health interventions study registry to aid the identification of unreported or incompletely reported outcomes. Critical appraisal tools can also be used to identify incompletely reported outcomes, but a tool such as ORBIT requires development to be suitable for public health intervention evaluations.
2	Approximately two-thirds of methodological research studies presented at Cochrane Colloquia remain unpublished as full papers at least 5 years later. This highlights the importance of searching conference abstracts if one wishes to find as comprehensive and complete a sample of methodological research as possible.	[**Chapman, Sarah**; Eisinga, Anne; Hopewell, Sally] UK Cochrane Ctr, Natl Inst Hlth Res, Oxford OX2 7LG, England; [Clarke, Mike] Queens Univ Belfast, Inst Clin Sci, Royal Victoria Hosp, Ctr Publ Hlth, Belfast BT12 6BA, Antrim, North Ireland	Two-thirds of methodological research remained unpublished after presentation at Cochrane Colloquia: an empirical analysis	2012	WOS:000302447500006	Objectives: To determine the extent to which abstracts of methodology research, initially presented at annual meetings of The Cochrane Collaboration, have been published as full reports and over what period of time. A secondary aim was to explore whether full publication varied in different methodological subject areas. Study Design and Setting: The Cochrane Methodology Register (CMR) was searched for all abstracts reporting methodology research, presented at the 11 Cochrane Colloquia from 1997 to 2007. EMBASE, PubMed, and CMR were searched for full publications of the same research. Results: We identified 908 eligible conference abstracts and found full publications for 312 (34.4%) of these, almost half of which (47.1%) had appeared by the end of the first year after the relevant Colloquium. The proportion of abstracts that had not been published by 3 years was 69.7%, falling to 66.2% at 5 years. Publication varied considerably between different methodological areas. Conclusion: Approximately two-thirds of methodological research studies presented at Cochrane Colloquia remain unpublished as full papers at least 5 years later. This highlights the importance of searching conference abstracts if one wishes to find as comprehensive and complete a sample of methodological research as possible. (c) 2012 Elsevier Inc. All rights reserved.

Index	Theses	Affiliations	Title of publication	Publ. Year	WOS ID	Abstract
3	Outcome reporting bias is opting to publish only a subset of the original variables recorded for a study, such that the inclusion of the variables in the published work is selectively based on the results. The ongoing development and expansion of publicly accessible databases that contain transparent information about clinical trials and their results is necessary.	[**Howland RH.**] Univ Pittsburgh, Sch Med, Western Psychiat Inst & Clin, Pittsburgh, PA 15213 USA	What You See Depends on Where You're Looking and How You Look at It Publication Bias and Outcome Reporting Bias	2011	WOS:000295282900007	Study publication bias is the decision to publish or not publish a study based on its results. Compared to unpublished work, published studies are more likely to have positive or statistically significant findings. Outcome reporting bias is opting to publish only a subset of the original variables recorded for a study, such that the inclusion of the variables in the published work is selectively based on the results. Statistically significant results have a higher likelihood of being fully reported compared to nonsignificant results, and a significant proportion of published articles describe outcome variables or data analyses that differ from the pre-specified trial protocol as originally conceived. Recognition that publication bias and outcome reporting bias contribute to a distorted perception of drug effects-inflated estimates of efficacy and underreporting of adverse events-has led to the development and expansion of publicly accessible databases that contain transparent information about clinical trials and their results.
4	The prevalence of incomplete outcome reporting is high. Trialists seemed generally unaware of the implications for the evidence base of not reporting all outcomes and protocol changes. A general lack of consensus regarding the choice of outcomes in particular clinical settings was evident and affects trial design, conduct, analysis, and reporting.	[**Smyth, R. M. D.**; Kirkham, J. J.; Gamble, C.; Williamson, P. R.] Univ Liverpool, Ctr Med Stat & Hlth Evaluat, Liverpool L69 3BX, Merseyside, England; [Smyth, R. M. D.; Jacoby, A.] Univ Liverpool, Div Publ Hlth, Liverpool L69 3BX, Merseyside, England; [Altman, D. G.] Univ Oxford, Ctr Stat Med, Oxford, England	Frequency and reasons for outcome reporting bias in clinical trials: interviews with trialists	2011	WOS:000286143000002	Objectives To provide information on the frequency and reasons for outcome reporting bias in clinical trials. Design Trial protocols were compared with subsequent publication(s) to identify any discrepancies in the outcomes reported, and telephone interviews were conducted with the respective trialists to investigate more extensively the reporting of the research and the issue of unreported outcomes. Participants Chief investigators, or lead or co-authors of trials, were identified from two sources: trials published since 2002 covered in Cochrane systematic reviews where at least one trial analysed was suspected of being at risk of outcome reporting bias (issue 4, 2006; issue 1, 2007, and issue 2, 2007 of the Cochrane library); and a random sample of trial reports indexed on PubMed between August 2007 and July 2008. Setting Australia, Canada, Germany, the Netherlands, New Zealand, the United Kingdom, and the United States. Main outcome measures Frequency of incomplete outcome reporting-signified by outcomes that were specified in a trial's protocol but not fully reported in subsequent publications-and trialists' reasons for incomplete reporting of outcomes. Results 268 trials were identified for inclusion (183 from the cohort of Cochrane systematic reviews and 85 from PubMed). Initially, 161 respective investigators responded to our requests for interview, 130 (81%) of whom agreed to be interviewed. However, failure to achieve subsequent contact, obtain a copy of the study protocol, or both meant that final interviews were conducted with 59 (37%) of the 161 trialists. Sixteen trial investigators failed to report analysed outcomes at the time of the primary publication, 17 trialists collected outcome data that were subsequently not analysed, and five trialists did not measure a prespecified outcome over the course of the trial. In almost all trials in which prespecified outcomes had been analysed but not reported (15/16, 94%), this underreporting resulted in bias. In nearly a quarter of trials in which prespecified outcomes had been measured but not analysed (4/17, 24%), the "direction" of the main findings influenced the investigators' decision not to analyse the remaining data collected. In 14 (67%) of the 21 randomly selected PubMed trials, there was at least one unreported efficacy or harm outcome. More than a quarter

In-dex	Theses	Affiliations	Title of publication	Publ. Year	WOS ID	Abstract
						(6/21, 29%) of these trials were found to have displayed outcome reporting bias. Conclusion The prevalence of incomplete outcome reporting is high. Trialists seemed generally unaware of the implications for the evidence base of not reporting all outcomes and protocol changes. A general lack of consensus regarding the choice of outcomes in particular clinical settings was evident and affects trial design, conduct, analysis, and reporting.
5	Future research should focus on increasing the uptake of knowledge synthesis, how best to update reviews, the comparability between different types of reviews (eg, rapid vs. comprehensive reviews), and how to prioritize knowledge synthesis topics.	[Tricco, Andrea C.; Tetzlaff, Jennifer; **Moher, David**] Ottawa Hosp, Res Inst, Ottawa, ON, Canada; [Tetzlaff, Jennifer; Moher, David] Univ Ottawa, Fac Med, Dept Epidemiol & Community Med, Ottawa, ON, Canada	The art and science of knowledge synthesis	2011	WOS:000286153600004	Objectives: To review methods for completing knowledge synthesis. Study Design and Setting: We discuss how to complete a broad range of knowledge syntheses. Our article is intended as an introductory guide. Results: Many groups worldwide conduct knowledge syntheses, and some methods are applicable to most reviews. However, variations of these methods are apparent for different types of reviews, such as realist reviews and mixed-model reviews. Review validity is dependent on the validity of the included primary studies and the review process itself. Steps should be taken to avoid bias in the conduct of-knowledge synthesis. Transparency in reporting will help readers assess review validity and applicability, increasing its-utility. Conclusion: Given the magnitude of the literature, the increasing demands on knowledge syntheses teams, and the diversity of approaches, continuing efforts will be important to increase the efficiency, validity, and applicability of systematic reviews. Future research should focus on increasing the uptake of knowledge synthesis, how best to update reviews, the comparability between different types of reviews (eg, rapid vs. comprehensive reviews), and how to prioritize knowledge synthesis topics. (C) 2011 Elsevier Inc. All rights reserved.
6	Evidence-based medicine requires integrating the best available 'benchmark' literature with patient preferences and values (bedside) and is an evaluation process involving both patient and clinician, with a systematic assessment of the rated evidence from state-of-the-art medical literature.	[**Terracciano, Luigi**] Melloni Hosp, Dept Paediat, I-20129 Milan, Italy; [Brozek, Jan; Schunemann, Holger] McMaster Univ, Hlth Sci Ctr, Dept Clin Epidemiol & Biostat, Hamilton, ON, Canada; [Compalati, Enrico] Univ Genoa, Dept Internal Med, Allergy & Resp Dis Clin, I-16126 Genoa, Italy	GRADE system: new paradigm	2010	WOS:000279655500018	Purpose of review An exposition of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to recommendations. Recent findings In this review, we outline the process whereby the strength of evidence from the literature undergoes a systematic reappraisal. The GRADE system allows four grades of evidence (high quality, moderate, low, and very low) and strength of recommendation is qualified as strong, weak, or conditional to an intervention (pro or con) and defined as the level of confidence that desirable effects predominate over untoward ones with a certain intervention. We provide research and clinical reviews in various settings in which this approach has been used. Summary Evidence-based medicine requires integrating the best available 'benchmark' literature with patient preferences and values (bedside) and is an evaluation process involving both patient and clinician, with a systematic assessment of the rated evidence from state-of-the-art medical literature. The GRADE methodology was developed as an application of evidence-based medicine to the field of recommendations and their formulation. The GRADE working group brings together clinical researchers and methodologists who developed a rating system to assess the quality of evidence for the purpose of making clinical practice recommendations.

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7	Dissemination of research findings is likely to be a biased process. The prospective registration of clinical trials and the endorsement of reporting guidelines may reduce research dissemination bias in clinical research. In systematic reviews, measures can be taken to minimise the impact of dissemination bias by systematically searching for and including relevant studies that are difficult to access. Statistical methods can be useful for sensitivity analyses. Further research is needed to develop methods for qualitatively assessing the risk of publication bias in systematic reviews, and to evaluate the effect of prospective registration of studies, open access policy and improved publication guidelines.	[**Song, F.**; Parekh, S.; Hooper, L.; Loke, Y. K.; Ryder, J.; Kwok, C. S.; Pang, C.; Harvey, I.] Univ E Anglia, Sch Med Hlth Policy & Practice, Norwich NR4 7TJ, Norfolk, England; [Song, F.; Parekh, S.] Univ E Anglia, Sch Allied Hlth Profess, Norwich NR4 7TJ, Norfolk, England; [Sutton, A. J.] Univ Leicester, Dept Hlth Sci, Leicester LE1 7RH, Leics, England; [Hing, C.] Watford Dist Gen Hosp, Watford, Herts, England	Dissemination and publication of research findings: an updated review of related biases	2010	WOS:000275522300001	Objectives: To identify and appraise empirical studies on publication and related biases published since 1998; to assess methods to deal with publication and related biases; and to examine, in a random sample of published systematic reviews, measures taken to prevent, reduce and detect dissemination bias. Data sources: The main literature search, in August 2008, covered the Cochrane Methodology Register Database, MEDLINE, EMBASE,AMED and CINAHL. In May 2009, PubMed, PsycINFO and OpenSIGLE were also searched. Reference lists of retrieved studies were also examined. Review methods: In Part 1, studies were classified as evidence or method studies and data were extracted according to types of dissemination bias or methods for dealing with it. Evidence from empirical studies was summarised narratively. In Part II, 300 systematic reviews were randomly selected from MEDLINE and the methods used to deal with publication and related biases were assessed. Results: Studies with significant or positive results were more likely to be published than those with non-significant or negative results, thereby confirming findings from a previous HTA report. There was convincing evidence that outcome reporting bias exists and has an impact on the pooled summary in systematic reviews. Studies with significant results tended to be published earlier than studies with non-significant results, and empirical evidence suggests that published studies tended to report a greater treatment effect than those from the grey literature. Exclusion of non-English-language studies appeared to result in a high risk of bias in some areas of research such as complementary and alternative medicine. In a few cases, publication and related biases had a potentially detrimental impact on patients or resource use. Publication bias can be prevented before a literature review (e.g. by prospective registration of trials), or detected during a literature review (e.g. by locating unpublished studies, funnel plot and related tests, sensitivity analysis modelling), or its impact can be minimised after a literature review (e.g. by confirmatory large-scale trials, updating the systematic review). The interpretation of funnel plot and related statistical tests, often used to assess publication bias, was often too simplistic and likely misleading. More sophisticated modelling methods have not been widely used. Compared with systematic reviews published in 1996, recent reviews of health-care interventions were more likely to locate and include non-English-language studies and grey literature or unpublished studies, and to test for publication bias. Conclusions: Dissemination of research findings is likely to be a biased process, although the actual impact of such bias depends on specific circumstances. The prospective registration of clinical trials and the endorsement of reporting guidelines may reduce research dissemination bias in clinical research. In systematic reviews, measures can be taken to minimise the impact of dissemination bias by systematically searching for and including relevant studies that are difficult to access. Statistical methods can be useful for sensitivity analyses. Further research is needed to develop methods for qualitatively assessing the risk of publication bias in systematic reviews, and to evaluate the effect of prospective registration of studies, open access policy and improved publication guidelines.

Index	Theses	Affiliations	Title of publication	Publ. Year	WOS ID	Abstract
8	Outcome reporting bias is an under-recognised problem that affects the conclusions in a substantial proportion of Cochrane reviews. Individuals conducting systematic reviews need to address explicitly the issue of missing outcome data for their review to be considered a reliable source of evidence. Extra care is required during data extraction, reviewers should identify when a trial reports that an outcome was measured but no results were reported or events observed, and contact with trialists should be encouraged.	[**Kirkham, Jamie J**.; Dwan, Kerry M.; Gamble, Carrol; Dodd, Susanna; Williamson, Paula R.] Univ Liverpool, Ctr Med Stat & Hlth Evaluat, Liverpool L69 3GS, Merseyside, England; [Altman, Douglas G.] Univ Oxford, Ctr Stat Med, Oxford OX2 6UD, England; [Smyth, Rebecca] Univ Liverpool, Liverpool L69 3GB, Merseyside, England	The impact of outcome reporting bias in randomised controlled trials on a cohort of systematic reviews	2010	WOS:000274738600003	Objective To examine the prevalence of outcome reporting bias-the selection for publication of a subset of the original recorded outcome variables on the basis of the results-and its impact on Cochrane reviews. Design A nine point classification system for missing outcome data in randomised trials was developed and applied to the trials assessed in a large, unselected cohort of Cochrane systematic reviews. Researchers who conducted the trials were contacted and the reason sought for the non-reporting of data. A sensitivity analysis was undertaken to assess the impact of outcome reporting bias on reviews that included a single meta-analysis of the review primary outcome. Results More than half (157/283 (55%)) the reviews did not include full data for the review primary outcome of interest from all eligible trials. The median amount of review outcome data missing for any reason was 10%, whereas 50% or more of the potential data were missing in 70 (25%) reviews. It was clear from the publications for 155 (6%) of the 2486 assessable trials that the researchers had measured and analysed the review primary outcome but did not report or only partially reported the results. For reports that did not mention the review primary outcome, our classification regarding the presence of outcome reporting bias was shown to have a sensitivity of 88% (95% CI 65% to 100%) and specificity of 80% (95% CI 69% to 90%) on the basis of responses from 62 trialists. A third of Cochrane reviews (96/283 (34%)) contained at least one trial with high suspicion of outcome reporting bias for the review primary outcome. In a sensitivity analysis undertaken for 81 reviews with a single meta-analysis of the primary outcome of interest, the treatment effect estimate was reduced by 20% or more in 19 (23%). Of the 42 meta-analyses with a statistically significant result only, eight (19%) became nonsignificant after adjustment for outcome reporting bias and 11 (26%) would have overestimated the treatment effect by 20% or more. Conclusions Outcome reporting bias is an under-recognised problem that affects the conclusions in a substantial proportion of Cochrane reviews. Individuals conducting systematic reviews need to address explicitly the issue of missing outcome data for their review to be considered a reliable source of evidence. Extra care is required during data extraction, reviewers should identify when a trial reports that an outcome was measured but no results were reported or events observed, and contact with trialists should be encouraged.
9	The CONSORT 2010 Statement, this revised explanatory and elaboration document, and the associated website (www.consort-statement.org) should be helpful resources to improve reporting of randomised trials.	[Moher, David] Ottawa Gen Hosp, Ottawa Hosp Res Inst, Clin Epidemiol Program, Ottawa Methods Ctr, Ottawa, ON K1H 8L6, Canada; [Hopewell, Sally; Altman, Douglas G.] Univ Oxford, Ctr Stat Med, Wolfson Coll, Oxford OX1 2JD, England; [Schulz, Kenneth F.] Family Hlth Int, Res Triangle Pk, NC 27709	CONSORT 2010 Explanation and Elaboration: updated guidelines for reporting parallel group randomised trials	2010	WOS:000276157600007	Overwhelming evidence shows the quality of reporting of randomised controlled trials (RCTs) is not optimal. Without transparent reporting, readers cannot judge the reliability and validity of trial findings nor extract information for systematic reviews. Recent methodological analyses indicate that inadequate reporting and design are associated with biased estimates of treatment effects. Such systematic error is seriously damaging to RCTs, which are considered the gold standard for evaluating interventions because of their ability to minimise or avoid bias. A group of scientists and editors developed the CONSORT (Consolidated Standards of Reporting Trials) statement to improve the quality of reporting of RCTs. It was first published in 1996 and updated in 2001. The statement consists of a checklist and flow diagram that authors can use for reporting an RCT. Many leading medical journals and major international editorial groups have endorsed the CONSORT statement. The statement facilitates critical appraisal and interpretation of RCTs. During the 2001 CONSORT revision, it became clear that explanation and elaboration of the principles underlying the CONSORT statement would help investigators and others to write or appraise trial reports. A CONSORT explanation and elaboration article was published in 2001 alongside the 2001 version of the CONSORT

Index	Theses	Affiliations	Title of publication	Publ. Year	WOS ID	Abstract
		USA; [Montori, Victor] Mayo Clin, UK Knowledge & Encounter Res Unit, Rochester, MN USA; [**Gotzsche, Peter C.**] Rigshosp, Nord Cochrane Ctr, DK-2100 Copenhagen, Denmark; [Devereaux, P. J.] McMaster Univ, Hlth Sci Ctr, Hamilton, ON, Canada; [Elbourne, Diana] London Sch Hyg & Trop Med, Med Stat Unit, London, England; [**Egger, Matthias**] Univ Bern, ISPM, CH-3012 Bern, Switzerland				statement. After an expert meeting in January 2007, the CONSORT statement has been further revised and is published as the CONSORT 2010 Statement. This update improves the wording and clarity of the previous checklist and incorporates recommendations related to topics that have only recently received recognition, such as selective outcome reporting bias. This explanatory and elaboration document-intended to enhance the use, understanding, and dissemination of the CONSORT statement-has also been extensively revised. It presents the meaning and rationale for each new and updated checklist item providing examples of good reporting and, where possible, references to relevant empirical studies. Several examples of flow diagrams are included. The CONSORT 2010 Statement, this revised explanatory and elaboration document, and the associated website (www.consort-statement.org) should be helpful resources to improve reporting of randomised trials.
10	CONSORT 2010 is even clearer than before and includes some new items with a particular emphasis on selective reporting of outcomes. The challenge is for everyone to use it.	[**Hywel CW**] Univ Nottingham, Ctr Evidence Based Dermatol, Nottingham NG7 2UH, England	Cars, CONSORT 2010, and Clinical Practice	2010	WOS:000277427700002	Just like you would not buy a car without key information such as service history, you would not "buy" a clinical trial report without key information such as concealment of allocation. Implementation of the updated CONSORT 2010 statement enables the reader to see exactly what was done in a trial, to whom and when. A fully "CONSORTed" trial report does not necessarily mean the trial is a good one, but at least the reader can make a judgement. Clear reporting is a pre-requisite for judgement of study quality. The CONSORT statement evolves as empirical research moves on. CONSORT 2010 is even clearer than before and includes some new items with a particular emphasis on selective reporting of outcomes. The challenge is for everyone to use it.
11	Outcome reporting bias (ORB) occurs when variables are selected for publication based on their results. A review should not exclude studies if they have not reported the outcomes of interest and should consider the potential for outcome reporting bias in all included studies.	[**Dwan, Kerry**; Gamble, Carrol; Kolamunnage-Dona, Ruwanthi; Williamson, Paula R.] Univ Liverpool, Ctr Med Stat & Hlth Evaluat, Liverpool L69 3BX, Merseyside, England; [Mohammed, Shabana] Univ Sheffield, Med Care Res Unit, Sheffield S10 2TN, S Yorkshire, England; [Powell, Colin] Cardiff Univ, Childrens Hosp Wales, Univ Dept	Assessing the potential for outcome reporting bias in a review: a tutorial	2010	WOS:000279545900002	Background: Outcome reporting bias (ORB) occurs when variables are selected for publication based on their results. This can impact upon the results of a meta-analysis, biasing the pooled treatment effect estimate. The aim of this paper is to show how to assess a systematic review and corresponding trial reports for ORB using an example review of intravenous and nebulised magnesium in the treatment of asthma. Methods: The review was assessed for ORB by 1) checking the reasons, when available, for excluding studies to ensure that no studies were excluded because they did not report the outcomes of interest in the review; 2) assessing the eligible studies as to whether the review outcomes of interest were reported. Each study was classified using a system developed in the ORBIT (Outcome Reporting Bias In Trials) project to indicate whether ORB was suspected and a reason for the suspicion. Authors of trials that did not report the outcomes of interest were contacted for information. A sensitivity analysis was performed to assess the robustness of the conclusions of the review to this potential source of bias. Results: Twenty-four studies were included in the review; two studies had been excluded for not reporting either of the two outcomes of interest. Six included studies did not report hospital admission and two did not report pulmonary function. There was high suspicion of outcome reporting bias in four studies. Results from the sensitivity analysis indicate that

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		Paediat, Sch Med, Cardiff, S Glam, Wales				review conclusions were not overturned. Conclusion: This paper demonstrates, with the example of the magnesium review, how to assess a review for outcome reporting bias. A review should not exclude studies if they have not reported the outcomes of interest and should consider the potential for outcome reporting bias in all included studies.
12	Reporting bias represents a major problem in the assessment of health care interventions. Reporting bias is a widespread phenomenon in the medical literature. Mandatory prospective registration of trials and public access to study data via results databases need to be introduced on a worldwide scale. This will allow for an independent review of research data, help fulfil ethical obligations towards patients, and ensure a basis for fully-informed decision making in the health care system.	[McGauran, Natalie; **Wieseler, Beate**; Kreis, Julia; Schueler, Yvonne-Beatrice; Koelsch, Heike; **Kaiser, Thomas**] Inst Qual & Efficiency Hlth Care, D-51105 Cologne, Germany	Reporting bias in medical research - a narrative review	2010	WOS:000278333100001	Reporting bias represents a major problem in the assessment of health care interventions. Several prominent cases have been described in the literature, for example, in the reporting of trials of antidepressants, Class I anti-arrhythmic drugs, and selective COX-2 inhibitors. The aim of this narrative review is to gain an overview of reporting bias in the medical literature, focussing on publication bias and selective outcome reporting. We explore whether these types of bias have been shown in areas beyond the well-known cases noted above, in order to gain an impression of how widespread the problem is. For this purpose, we screened relevant articles on reporting bias that had previously been obtained by the German Institute for Quality and Efficiency in Health Care in the context of its health technology assessment reports and other research work, together with the reference lists of these articles. We identified reporting bias in 40 indications comprising around 50 different pharmacological, surgical (e. g. vacuum-assisted closure therapy), diagnostic (e. g. ultrasound), and preventive (e. g. cancer vaccines) interventions. Regarding pharmacological interventions, cases of reporting bias were, for example, identified in the treatment of the following conditions: depression, bipolar disorder, schizophrenia, anxiety disorder, attention-deficit hyperactivity disorder, Alzheimer's disease, pain, migraine, cardiovascular disease, gastric ulcers, irritable bowel syndrome, urinary incontinence, atopic dermatitis, diabetes mellitus type 2, hypercholesterolaemia, thyroid disorders, menopausal symptoms, various types of cancer (e. g. ovarian cancer and melanoma), various types of infections (e. g. HIV, influenza and Hepatitis B), and acute trauma. Many cases involved the withholding of study data by manufacturers and regulatory agencies or the active attempt by manufacturers to suppress publication. The ascertained effects of reporting bias included the overestimation of efficacy and the underestimation of safety risks of interventions. In conclusion, reporting bias is a widespread phenomenon in the medical literature. Mandatory prospective registration of trials and public access to study data via results databases need to be introduced on a worldwide scale. This will allow for an independent review of research data, help fulfil ethical obligations towards patients, and ensure a basis for fully-informed decision making in the health care system.

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13	THE PRISMA statement (preferred reporting items for systematic reviews and meta-analyses) as an evolution of the original QUOROM guideline for systematic reviews and meta-analyses of evaluations of health care interventions is helpful to improve reporting of systematic reviews and meta-analyses.	**[Liberati, Alessandro]** Univ Modena & Reggio Emilia, Modena, Italy; [Liberati, Alessandro] Ist Ric Farmacol Mario Negri, Ctr Cochrane Italiano, Milan, Italy; [Altman, Douglas G.] Univ Oxford, Ctr Stat Med, Oxford OX1 2JD, England…	The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration	2009	WOS:000268351400023	Systematic reviews and meta-analyses are essential to summarise evidence relating to efficacy and safety of healthcare interventions accurately and reliably. The clarity and transparency of these reports, however, are not optimal. Poor reporting of systematic reviews diminishes their value to clinicians, policy makers, and other users. Since the development of the QUOROM (quality of reporting of meta-analysis) statement-a reporting guideline published in 1999-there have been several conceptual, methodological, and practical advances regarding the conduct and reporting of systematic reviews and meta-analyses. Also, reviews of published systematic reviews have found that key information about these studies is often poorly reported. Realising these issues, an international group that included experienced authors and methodologists developed PRISMA (preferred reporting items for systematic reviews and meta-analyses) as an evolution of the original QUOROM guideline for systematic reviews and meta-analyses of evaluations of health care interventions. The PRISMA statement consists of a 27-item checklist and a four-phase flow diagram. The checklist includes items deemed essential for transparent reporting of a systematic review. In this explanation and elaboration document, we explain the meaning and rationale for each checklist item. For each item, we include an example of good reporting and, where possible, references to relevant empirical studies and methodological literature. The PRISMA statement, this document, and the associated website (www.prisma-statement.org/) should be helpful resources to improve reporting of systematic reviews and meta-analyses.
14	Investigators of systematic reviews and meta-analysis should be aware of potential biases such as poor quality of included studies, heterogeneity between studies, and the presence of publication and outcome reporting bias	[**Noordzij, Marlies; Jager, Kitty J.**] Univ Amsterdam, Acad Med Ctr, ERA EDTA Registry, Dept Med Informat, NL-1100 DE Amsterdam, Netherlands; [Hooft, Lotty] Univ Amsterdam, Acad Med Ctr, Dutch Cochrane Ctr, NL-1105 AZ Amsterdam, Netherlands…	Systematic reviews and meta-analyses: when they are useful and when to be careful	2009	WOS:000271815900004	Systematic reviews and meta-analyses are increasingly popular study designs in clinical research. A systematic review is a summary of the medical literature that uses explicit and reproducible methods for searching the literature and critical appraisal of individual studies; in contrast, a meta-analysis is a mathematical synthesis of the results of these individual studies. These study designs can be useful tools for summarizing the increasing amount of knowledge that is gained from scientific papers on a certain topic. In addition, combining individual studies in a meta-analysis increases statistical power, resulting in more precise effect estimates. Although the specific methodology of systematic reviews includes steps to minimize bias in all stages of the process, investigators should be aware of potential biases such as poor quality of included studies, heterogeneity between studies, and the presence of publication and outcome reporting bias. This paper explains how systematic reviews and meta-analyses should be performed and how to interpret and implement their results. In addition, we discuss when meta-analyses are useful and when they are not. Kidney International (2009) 76, 1130-1136; doi:10.1038/ki.2009.339; published online 2 September 2009
15	Dissemination of research findings is likely to be a biased process. Publication bias appears to occur early, mainly before the presentation of findings at conferences or submission of manuscripts to journals.	[**Song, Fujian;** Hooper, Lee; Loke, Yoon K.; Ryder, Jon J.; Harvey, Ian] Univ E Anglia, Sch Med Hlth Policy & Practice, Norwich NR4 7TJ, Norfolk, England; [Song, Fujian; Parekh-Bhurke, Sheetal] Univ E Anglia, Sch Allied Hlth	Extent of publication bias in different categories of research cohorts: a meta-analysis of empirical studies	2009	WOS:000272410100001	Background: The validity of research synthesis is threatened if published studies comprise a biased selection of all studies that have been conducted. We conducted a meta-analysis to ascertain the strength and consistency of the association between study results and formal publication. Methods: The Cochrane Methodology Register Database, MEDLINE and other electronic bibliographic databases were searched (to May 2009) to identify empirical studies that tracked a cohort of studies and reported the odds of formal publication by study results. Reference lists of retrieved articles were also examined for relevant studies. Odds ratios were used to measure the association between formal publication and significant or positive results. Included studies were separated into subgroups according to starting time of follow-up, and results from individual cohort studies within the subgroups were quantitatively pooled. Results: We identified 12 cohort studies that followed up re-

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		Profess, Norwich NR4 7TJ, Norfolk, England; [Sutton, Alex J.] Univ Leicester, Dept Hlth Sci, Leicester LE1 7RH, Leics, England; [Hing, Caroline B.] Watford Dist Gen Hosp, Watford WD18 0HB, Herts, England				search from inception, four that included trials submitted to a regulatory authority, 28 that assessed the fate of studies presented as conference abstracts, and four cohort studies that followed manuscripts submitted to journals. The pooled odds ratio of publication of studies with positive results, compared to those without positive results (publication bias) was 2.78 (95% CI: 2.10 to 3.69) in cohorts that followed from inception, 5.00 (95% CI: 2.01 to 12.45) in trials submitted to regulatory authority, 1.70 (95% CI: 1.44 to 2.02) in abstract cohorts, and 1.06 (95% CI: 0.80 to 1.39) in cohorts of manuscripts. Conclusion: Dissemination of research findings is likely to be a biased process. Publication bias appears to occur early, mainly before the presentation of findings at conferences or submission of manuscripts to journals.
16	As of 2005, the International Committee of Medical Journal Editors required investigators to register their trials prior to participant enrolment as a precondition for publishing the trial's findings in member journals. Comparison of the primary outcomes of RCTs registered with their subsequent publication indicated that selective outcome reporting is prevalent.	[**Mathieu, Sylvain**; Boutron, Isabelle; Ravaud, Philippe] Hop Bichat Claude Bernard, AP HP, Dept Epidemiol Biostat & Rech Clin, F-75877 Paris 18, France; [Mathieu, Sylvain; Boutron, Isabelle; Ravaud, Philippe] INSERM, U738, Paris, France; [Mathieu, Sylvain; Boutron, Isabelle; Ravaud, Philippe] Univ Paris Diderot, Fac Med, Paris, France…	Comparison of Registered and Published Primary Outcomes in Randomized Controlled Trials	2009	WOS:000269444900023	Context As of 2005, the International Committee of Medical Journal Editors required investigators to register their trials prior to participant enrolment as a precondition for publishing the trial's findings in member journals. Objective To assess the proportion of registered trials with results recently published in journals with high impact factors; to compare the primary outcomes specified in trial registries with those reported in the published articles; and to determine whether primary outcome reporting bias favored significant outcomes. Data Sources and Study Selection MEDLINE via PubMed was searched for reports of randomized controlled trials (RCTs) in 3 medical areas (cardiology, rheumatology, and gastroenterology) indexed in 2008 in the 10 general medical journals and specialty journals with the highest impact factors. Data Extraction For each included article, we obtained the trial registration information using a standardized data extraction form. Results Of the 323 included trials, 147 (45.5%) were adequately registered (ie, registered before the end of the trial, with the primary outcome clearly specified). Trial registration was lacking for 89 published reports (27.6%), 45 trials (13.9%) were registered after the completion of the study, 35 (10.8%) were registered with no or an unclear description of the primary outcome, 39 (12%) were registered with no or an unclear description of the primary outcome, and 3 (0.9%) were registered after the completion of the study and had an unclear description of the primary outcome. Among articles with trials adequately registered, 31% (6 of 147) showed some evidence of discrepancies between the outcomes registered and the outcomes published. The influence of these discrepancies could be assessed in only half of them and in these statistically significant results were favored in 82.6% (19 of 23). Conclusion Comparison of the primary outcomes of RCTs registered with their subsequent publication indicated that selective outcome reporting is prevalent. JAMA. 2009;302(9):977-984 www.jama.com

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17	The merit of GRADE is not that it eliminates judgments or disagreements about evidence and recommendations, but rather that it makes them transparent.	[**Guyatt, G. H.**; Schuenemann, H. J.] McMaster Univ, Hlth Sci Ctr, Dept Clin Epidemiol & Biostat, Hamilton, ON L8N 3Z5, Canada; [Brozek, J. L.] Italian Natl Canc Inst Regina Elena, Dept Epidemiol, Rome, Italy…	Grading quality of evidence and strength of recommendations in clinical practice guidelines	2009	WOS:000264823200001	The GRADE (Grades of Recommendation, Assessment, Development, and Evaluation) approach provides guidance to grading the quality of underlying evidence and the strength of recommendations in health care. The GRADE system's conceptual underpinnings allow for a detailed stepwise process that defines what role the quality of the available evidence plays in the development of health care recommendations. The merit of GRADE is not that it eliminates judgments or disagreements about evidence and recommendations, but rather that it makes them transparent. This first article in a three-part series describes the GRADE framework in relation to grading the quality of evidence about interventions based on examples from the field of allergy and asthma. In the GRADE system, the quality of evidence reflects the extent to which a guideline panel's confidence in an estimate of the effect is adequate to support a particular recommendation. The system classifies quality of evidence as high, moderate, low, or very low according to factors that include the study methodology, consistency and precision of the results, and directness of the evidence.
18	Novel contour enhanced funnel plots and a regression based adjustment method worked convincingly and might have an important part to play in combating publication biases.	[**Moreno, Santiago G.**; Sutton, Alex J.; Abrams, Keith R.] Univ Leicester, Dept Hlth Sci, Leicester LE1 7RH, Leics, England; [Turner, Erick H.] Oregon Hlth & Sci Univ, Dept Psychiat, Portland Vet Affairs Med Ctr, Portland, OR 97201 USA…	Novel methods to deal with publication biases: secondary analysis of antidepressant trials in the FDA trial registry database and related journal publications	2009	WOS:000268808200002	Objective To assess the performance of novel contour enhanced funnel plots and a regression based adjustment method to detect and adjust for publication biases. Design Secondary analysis of a published systematic literature review. Data sources Placebo controlled trials of antidepressants previously submitted to the US Food and Drug Administration (FDA) and matching journal publications. Methods Publication biases were identified using novel contour enhanced funnel plots, a regression based adjustment method, Egger's test, and the trim and fill method. Results were compared with a meta-analysis of the gold standard data submitted to the FDA. Results Severe asymmetry was observed in the contour enhanced funnel plot that appeared to be heavily influenced by the statistical significance of results, suggesting publication biases as the cause of the asymmetry. Applying the regression based adjustment method to the journal data produced a similar pooled effect to that observed by a meta-analysis of the FDA data. Contrasting journal and FDA results suggested that, in addition to other deviations from study protocol, switching from an intention to treat analysis to a per protocol one would contribute to the observed discrepancies between the journal and FDA results. Conclusion Novel contour enhanced funnel plots and a regression based adjustment method worked convincingly and might have an important part to play in combating publication biases.
19	Most discovered true associations are inflated	[**Ioannidis, John P. A.**] Univ Ioannina, Sch Med, Dept Hyg & Epidemiol, GR-45110 Ioannina, Greece; [Ioannidis, John P. A.] Tufts Univ, Sch Med, Dept Med, Boston, MA 02111 USA	Why most discovered true associations are inflated	2008	WOS:000258712000001	Newly discovered true (non-null) associations often have inflated effects compared with the true effect sizes. I discuss here the main reasons for this inflation. First, theoretical considerations prove that when true discovery is claimed based oil crossing a threshold of statistical significance and the discovery Study is Underpowered, the observed effects are expected to be inflated. This has been demonstrated in various fields ranging from early stopped clinical trials to genome-wide associations. Second, flexible analyses coupled with selective reporting may inflate the published discovered effects. The vibration ratio (the ratio of the largest vs. smallest effect on the same association approached with different analytic choices) can be very large. Third, effects may be inflated at the stage of interpretation due to diverse conflicts of interest. Discovered effects are not always inflated, and under some circumstances may be deflated-for example, in file setting of late discovery of associations in sequentially accumulated overpowered evidence, in some types of misclassification from measurement error, and in conflicts causing reverse biases. Finally, I discuss potential approaches to this problem. These include being cautious about newly discovered effect sizes, considering some rational down-adjustment, using analytical methods that correct for the anticipated inflation, ignor-

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						ing the magnitude of file effect (if not necessary), Conducting large Studies in the discovery phase, using strict protocols for analyses, pursuing complete and transparent reporting of all results, placing emphasis oil replication, and being fair with interpretation of results.
20	A review or research funders' guidelines indicates that there is a need to provide more detailed guidance for those conducting and reporting clinical trials to help prevent the selective reporting of results. Statements found in the guidelines generally refer to publication bias rather than outcome reporting bias. Current guidelines need to be updated and include the statement that all primary and secondary outcomes prespecified in the protocol should be fully reported and should not be selected for inclusion in the final report based on their results.	[**Dwan, Kerry;** Gamble, Carrol; Williamson, Paula R.] Univ Liverpool, Ctr Med Stat & Hlth Evaluat, Liverpool L69 3BX, Merseyside, England; [Altman, Douglas G.] Univ Oxford, Ctr Stat Med, Oxford, England	Reporting of clinical trials: a review of research funders' guidelines	2008	WOS:000263837300001	Background: Randomised controlled trials (RCTs) represent the gold standard methodological design to evaluate the effectiveness of an intervention in humans but they are subject to bias, including study publication bias and outcome reporting bias. National and international organisations and charities give recommendations for good research practice in relation to RCTs but to date no review of these guidelines has been undertaken with respect to reporting bias. Methods: National and international organisations and UK based charities listed on the Association for Medical Research Charities website were contacted in 2007; they were considered eligible for this review if they funded RCTs. Guidelines were obtained and assessed in relation to what was written about trial registration, protocol adherence and trial publication. It was also noted whether any monitoring against these guidelines was undertaken. This information was necessary to discover how much guidance researchers are given on the publication of results, in order to prevent study publication bias and outcome reporting bias. Results: Seventeen organisations and 56 charities were eligible of 140 surveyed for this review, although there was no response from 12. Trial registration, protocol adherence, trial publication and monitoring against the guidelines were often explicitly discussed or implicitly referred too. However, only eleven of these organisations or charities mentioned the publication of negative as well as positive outcomes and just three of the organisations specifically stated that the statistical analysis plan should be strictly adhered to and all changes should be reported. Conclusion: Our review indicates that there is a need to provide more detailed guidance for those conducting and reporting clinical trials to help prevent the selective reporting of results. Statements found in the guidelines generally refer to publication bias rather than outcome reporting bias. Current guidelines need to be updated and include the statement that all primary and secondary outcomes prespecified in the protocol should be fully reported and should not be selected for inclusion in the final report based on their results.

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21	Recent work provides direct empirical evidence for the existence of study publication bias and outcome reporting bias. There is strong evidence of an association between significant results and publication; studies that report positive or significant results are more likely to be published and outcomes that are statistically significant have higher odds of being fully reported. Publications have been found to be inconsistent with their protocols. Researchers need to be aware of the problems of both types of bias and efforts should be concentrated on improving the reporting of trials.	[**Dwan, Kerry;** Gamble, Carrol; Williamson, Paula R.] Univ Liverpool, Ctr Med Stat & Hlth Evaluat, Liverpool L69 3BX, Merseyside, England; [Altman, Douglas G.] Univ Oxford, Ctr Stat Med, Oxford OX1 2JD, England;…	Systematic Review of the Empirical Evidence of Study Publication Bias and Outcome Reporting Bias	2008	WOS:000264796600003	Background: The increased use of meta-analysis in systematic reviews of healthcare interventions has highlighted several types of bias that can arise during the completion of a randomised controlled trial. Study publication bias has been recognised as a potential threat to the validity of meta-analysis and can make the readily available evidence unreliable for decision making. Until recently, outcome reporting bias has received less attention. Methodology/Principal Findings: We review and summarise the evidence from a series of cohort studies that have assessed study publication bias and outcome reporting bias in randomised controlled trials. Sixteen studies were eligible of which only two followed the cohort all the way through from protocol approval to information regarding publication of outcomes. Eleven 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 nonsignificant 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. Conclusions: Recent work provides direct empirical evidence for the existence of study publication bias and outcome reporting bias. There is strong evidence of an association between significant results and publication; studies that report positive or significant results are more likely to be published and outcomes that are statistically significant have higher odds of being fully reported. Publications have been found to be inconsistent with their protocols. Researchers need to be aware of the problems of both types of bias and efforts should be concentrated on improving the reporting of trials.
22	CONSORT for Abstracts aims to improve reporting of abstracts of RCTs published in journal articles and conference proceedings. It will help authors of abstracts of these trials provide the detail and clarity needed by readers wishing to assess a trial's validity and the applicability of its results.	[**Hopewell, Sally;** Clarke, Mike] UK Cochrane Ctr, Oxford, England; [Hopewell, Sally; Altman, Douglas G.] Univ Oxford, Wolfson Coll, Ctr Stat Med, Oxford, England; [Clarke, Mike] Trinity Coll Dublin, Sch Nursing & Midwifery, Dublin, Ireland; [Moher, David] Childrens Hosp Eastern Ontario Res Inst,	CONSORT for reporting randomized controlled trials in journal and conference abstracts: Explanation and elaboration	2008	WOS:000254928700013	Background Clear, transparent, and sufficiently detailed abstracts of conferences and journal articles related to randomized controlled trials (RCTs) are important, because readers often base their assessment of a trial solely on information in the abstract. Here, we extend the CONSORT (Consolidated Standards of Reporting Trials) Statement to develop a minimum list of essential items, which authors should consider when reporting the results of a RCT in any journal or conference abstract. Methods and Findings We generated a list of items from existing quality assessment tools and empirical evidence. A three-round, modified-Delphi process was used to select items. In all, 109 participants were invited to participate in an electronic survey; the response rate was 61%. Survey results were presented at a meeting of the CONSORT Group in Montebello, Canada, January 2007, involving 26 participants, including clinical trialists, statisticians, epidemiologists, and biomedical editors. Checklist items were discussed for eligibility into the final checklist. The checklist was then revised to ensure that it reflected discussions held during and subsequent to the meeting. CONSORT for Abstracts recommends that abstracts relating to RCTs have a structured format. Items should include details of trial objectives; trial design (e. g., method of allocation, blinding/masking); trial partici-

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		Chalmers Res Grp, Ottawa, ON, Canada; [Moher, David…				pants (i. e., description, numbers randomized, and number analysed); interventions intended for each randomized group and their impact on primary efficacy outcomes and harms; trial conclusions; trial registration name and number; and source of funding. We recommend the checklist be used in conjunction with this explanatory document, which includes examples of good reporting, rationale, and evidence, when available, for the inclusion of each item. Conclusions CONSORT for Abstracts aims to improve reporting of abstracts of RCTs published in journal articles and conference proceedings. It will help authors of abstracts of these trials provide the detail and clarity needed by readers wishing to assess a trial's validity and the applicability of its results.
23	There is little evidence from SRs to support commonly practiced methods for conducting SRs. No SRs summarized studies with prospective designs and most had moderate or minimal risk of bias. Future research should examine bias that can occur during the selection of studies for inclusion and the synthesis of studies, as well as systematically review the existing empirical evidence.	[**Tricco, Andrea C.;** Tetzlaff, Jennifer; Sampson, Margaret; Cogo, Elise; Moher, David] Childrens Hosp Eastern Ontario, Res Inst, Chalmers Res Grp, Ottawa, ON K1N 6N5, Canada; [Tricco, Andrea C.; Cogo, Elise] Univ Ottawa, Inst Populat Hlth, Ottawa, ON, Canada…	Few systematic reviews exist documenting the extent of bias: a systematic review	2008	WOS:000254978200003	Objective: To summarize the evidence concerning bias and confounding in conducting systematic reviews (SRs). Study Design and Setting: Literature was identified through searching the Cochrane Library, MEDLINE, PsycINFO until November 2006, and the authors' files. Studies were included if they were SRs of bias that can occur while conducting a SR. Risk of bias in the SRs was appraised using the Oxman and Guyatt index. Results: Ten SRs were included. All examined biases related to searching for evidence (e.g., publication bias). One also reported bias associated with obtaining data from included studies (e.g., outcome reporting bias). To minimize bias, data suggest including unpublished material, hand searching for additional material, searching multiple databases, assessing for publication bias, and periodically updating SRs. No SRs were found examining biases related to choosing studies for inclusion or combining studies. Conclusions: There is little evidence from SRs to support commonly practiced methods for conducting SRs. No SRs summarized studies with prospective designs and most had moderate or minimal risk of bias. Future research should examine bias that can occur during the selection of studies for inclusion and the synthesis of studies, as well as systematically review the existing empirical evidence. (c) 2008 Elsevier Inc. All rights reserved.

Table 4.14: Persons and theses of selected papers about *study registration* for stakeholder involvement.

Source: Selected publications from the bibliometric analysis, times cited as from June 2012.

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1	Empirical data and normative arguments outweigh their counterarguments and present a clear case in favor of an even more restrictive obligation to register trials. Institutional review boards and better-educated stakeholders might play a crucial role in facilitating unbiased registration and publication of clinical research. For evaluation purposes, the field needs better standards for study protocols.	Hannover Med Sch, CELLS Ctr Eth & Law Life Sci, Inst Hist Eth & Philosophy Med, D-30625 Hannover, Germany	Normative arguments and new solutions for the unbiased registration and publication of clinical trials	2012	WOS:000299754800009	Objective: To present a structured account of ethical problems and possible solutions related to selective publication and incomplete trial registration. Study Design and Setting: The presentation of ethical problems and possible solutions is structured using the tools of conceptual normative analysis. Results: Selective publication runs contrary to (1) principles of ethical research, such as social value and respect for participants, (2) sound medical decision making and clinical guideline development, (3) appropriate patient information, (4) public trust in clinical research, and (5) just allocation of public resources for clinical research. Reasons against the obligation of complete registration and publication of trials can be divided into (1) protection of private data and (2) commercial interests. Empirical findings indicate that selective publication and incomplete trial registration (1) are frequent, (2) extensively distort patient-relevant outcomes, and (3) affect a large number of patients. Conclusion: Empirical data and normative arguments outweigh their counterarguments and present a clear case in favor of an even more restrictive obligation to register trials. Institutional review boards and better-educated stakeholders might play a crucial role in facilitating unbiased registration and publication of clinical research. For evaluation purposes, the field needs better standards for study protocols. (C) 2012 Elsevier Inc. All rights reserved.
2	This study shows that trial registration rates are still low in LAC (Latin America and the Caribbean's)and the quality of reporting needs to be improved.	[**Reveiz, Ludovic**] Pan Amer Hlth Org, Hlth Syst Based Primary Hlth Care, Publ Policies & Res, Washington, DC USA; [Bonfill, Xavier] Univ Autonoma Barcelona, CIBERESP, IIB St Pau, Iberoamer Cochrane Ctr, Barcelona, Spain...	Trial registration in Latin America and the Caribbean's: study of randomized trials published in 2010	2012	WOS:000302447500004	Objective: To determine the prevalence of trial registration in randomized controlled trials (RCTs) published in 2010 (PUBMED/LILACS) from Latin America and the Caribbean's (LAC) and to compare methodological characteristics between registered and nonregistered RCTs. Study Design and Setting: A search for detecting RCTs in which at least the first/contact author had a LAC's affiliation was made. We determined if RCTs were registered in the International Clinical Trial Registry Platform (ICTRP). Data were independently extracted by two authors. The risk of bias (RoB) was assessed in all registered RCTs (n = 89) and in a sample of nonregistered RCTs (n = 237). Results: The search identified 1,695 references; 526 RCTs from 19 countries were included. 16.9% (89/526) of RCTs were registered in the ICTRP; however, only 21 (4.0%) were prospectively registered. A significant difference was found in the overall assessment of the RoB between registered and nonregistered RCTs. Overall, registered RCTs were multinational, had larger sample size and longer follow-up, and reported more frequently information on funding, conflict of interests, and ethic issues. No significant differences were found when analysing prospectively registered RCTs. Conclusion: This study shows that trial registration rates are still low in LAC and the quality of reporting needs to be improved. (c) 2012 Elsevier Inc. All rights reserved.

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3	Prospective clinical trial registration (PCTR) is the public documentation of trial protocols-today primarily on the Internet-before data analysis (and ideally before trial commencement).	[**Fredrickson, Michael J.**] Univ Auckland, Dept Anaesthesiol, Fac Med & Hlth Sci, Auckland 1, New Zealand; [Ilfeld, Brian M.] Univ Calif San Diego, Med Ctr, Dept Anesthesiol, San Diego, CA 92103 USA	Prospective Trial Registration for Clinical Research What Is It, What Is It Good for, and Why Do I Care?	2011	WOS:000296532100016	Optimizing evidence-based medicine-and therefore the care of our patients-requires a public record of both the benefits and the risks of various medical interventions. Unfortunately, available evidence is often skewed because some clinical trials are withheld from publication; only selected data are reported, and statistical techniques are often inappropriately determined following data analysis. Prospective clinical trial registration (PCTR) is the public documentation of trial protocols-today primarily on the Internet-before data analysis (and ideally before trial commencement). The primary goals of PCTR are to reduce selective reporting and improve data analysis transparency, but it may also promote trial awareness for the public and other investigators. Prospective clinical trial registration is certainly not without problems, but many have been resolved, and the remainder is relatively minor in nature and easily overcome. Multiple organizations endorse (in some cases mandate) PCTR, including prominent committees of medical editors, the World Health Organization, the World Medical Association (responsible for the Helsinki Declaration), and, more recently, the US Food and Drug Administration. Although Regional Anesthesia and Pain Medicine does not currently require registration for published articles, PCTR in this and other anesthesiology and pain journals may become mandatory within the next few years. Potential authors/investigators will therefore benefit from becoming familiar with PCTR before mandatory registration implementation, and familiarity among readers may improve interpretation and understanding of clinical research results.
4	Registration of orthopaedic trauma trials does not consistently result in publication. When trials are registered, many do not cite NCT ID in the publication. Furthermore, changes that are not reflected in the registry of the trial are frequently made to the final publication.	[**Gandhi, Rajiv;** Jan, Meryam; Smith, Holly N.; Mahomed, Nizar N.] Toronto Western Hosp, Toronto, ON M5T 2S8, Canada; [Bhandari, Mohit] Hamilton Gen Hosp, Hamilton, ON L8L 2X2, Canada	Comparison of published orthopaedic trauma trials following registration in Clinicaltrials.gov	2011	WOS:000300174800001	Background: After the **Food and Drug Administration Modernization Act of 1997**, the registration of all clinical trials became mandatory prior to publication. Our primary objective was to determine publication rates for orthopaedic trauma trials registered with ClinicalTrials.gov. We further evaluated methodological consistency between registration and publication. Methods: We searched ClinicalTrials.gov for all trials related to orthopaedic trauma. We excluded active trials and trials not completed by July 2009, and performed a systematic search for publications resulting from registered closed trials. Information regarding primary and secondary outcomes, intervention, study sponsors, and sample size were extracted from registrations and publications. Results: Of 130 closed trials, 37 eligible trials resulted in 16 publications (43.2%). We found no significant differences in publication rates between funding sources for industry sponsored studies and nongovernment/nonindustry sponsored studies ($p > 0.05$). About half the trials (45%) did not include the NCT ID in the publication. Two (10%) publications had major changes to the primary outcome measure and ten (52.6%) to sample size. Conclusions: Registration of orthopaedic trauma trials does not consistently result in publication. When trials are registered, many do not cite NCT ID in the publication. Furthermore, changes that are not reflected in the registry of the trial are frequently made to the final publication.

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5	The results of the Delphi exercise have established a dataset of 22 required items for the prospective registration of systematic reviews, and 18 optional items. The dataset captures the key attributes of review design as well as the administrative details necessary for registration.	[**Booth, Alison**; Stewart, Lesley] Univ York, Ctr Reviews & Dissemin at, York YO10 5DD, N Yorkshire, England; [Clarke, Mike] Queens Univ Belfast, Ctr Publ Hlth, Belfast, Antrim, North Ireland; [Ghersi, Davina] WHO, Int Clin Trials Registry Platform, CH-1211 Geneva, Switzerland; [Moher, David] Ottawa Hosp Res Inst, Clin Epidemiol Program, Ottawa, ON, Canada; …	Establishing a Minimum Dataset for Prospective Registration of Systematic Reviews: An International Consultation	2011	WOS:000297555400033	Background: In response to growing recognition of the value of prospective registration of systematic review protocols, we planned to develop a web-based open access international register. In order for the register to fulfil its aims of reducing unplanned duplication, reducing publication bias, and providing greater transparency, it was important to ensure the appropriate data were collected. We therefore undertook a consultation process with experts in the field to identify a minimum dataset for registration. Methods and Findings: A two-round electronic modified Delphi survey design was used. The international panel surveyed included experts from **areas relevant to systematic review including commissioners, clinical and academic researchers, methodologists, statisticians, information specialists, journal editors and users of systematic reviews**. Direct invitations to participate were sent out to 315 people in the first round and 322 in the second round. Responses to an open invitation to participate were collected separately. There were 194 (143 invited and 51 open) respondents with a 100% completion rate in the first round and 209 (169 invited and 40 open) respondents with a 91% completion rate in the second round. In the second round, 113 (54%) of the participants reported having previously taken part in the first round. Participants were asked to indicate whether a series of potential items should be designated as optional or required registration items, or should not be included in the register. After the second round, a 70% or greater agreement was reached on the designation of 30 of 36 items. Conclusions: The results of the Delphi exercise have established a dataset of 22 required items for the prospective registration of systematic reviews, and 18 optional items. The dataset captures the key attributes of review design as well as the administrative details necessary for registration.
7	ICMJE journals published RCTs with proper registration but the registration data were often not adequate, underwent substantial changes in the registry over time and differed in registered and published data. **Editors need to establish quality control procedures in the journals** so that they continue to contribute to the increased transparency of clinical trials.	[**Huic, Mirjana**] Agcy Qual & Accreditat Hlth Care, Zagreb, Croatia; [Marusic, Matko; Marusic, Ana] Univ Split, Sch Med, Dept Res Biomed & Hlth, Split, Croatia; [Marusic, Ana] Univ Split, Sch Med, Croatian Ctr Global Hlth, Split, Croatia	Completeness and Changes in Registered Data and Reporting Bias of Randomized Controlled Trials in ICMJE Journals after Trial Registration Policy	2011	WOS:000295262100045	Objective: We assessed the adequacy of randomized controlled trial (RCT) registration, changes to registration data and reporting completeness for articles in ICMJE journals during 2.5 years after registration requirement policy. Methods: For a set of 149 reports of 152 RCTs with ClinicalTrials.gov registration number, published from September 2005 to April 2008, we evaluated the completeness of 9 items from WHO 20-item Minimum Data Set relevant for assessing trial quality. We also assessed changes to the registration elements at the Archive site of ClinicalTrials.gov and compared published and registry data. Results: RCTs were mostly registered before 13 September 2005 deadline (n = 101, 66.4%); 118 (77.6%) started recruitment before and 31 (20.4%) after registration. At the time of registration, 152 RCTs had a total of 224 missing registry fields, most commonly 'Key secondary outcomes' (44.1% RCTs) and 'Primary outcome' (38.8%). More RCTs with post-registration recruitment had missing Minimum Data Set items than RCTs with pre-registration recruitment: 57/118 (48.3%) vs. 24/31 (77.4%) (chi(2)(1) = 7.255, P = 0.007). Major changes in the data entries were found for 31 (25.2%) RCTs. The number of RCTs with differences between registered and published data ranged from 21 (13.8%) for Study type to 118 (77.6%) for Target sample size. Conclusions: ICMJE journals published RCTs with proper registration but the registration data were often not adequate, underwent substantial changes in the registry over time and differed in registered and published data. Editors need to establish quality control procedures in the journals so that they continue to contribute to the increased transparency of clinical trials.

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8	Registries of trials are the internationally favored strategy to compensate for this publication bias. However, it is an open question when and to what extent the registration of trials will become an established and regulated obligation for clinical trials conducted in Germany	Med Hsch Hannover MHH, Inst Geschichte Eth & **Philosophie** Med, D-30625 Hannover, Germany	The ethics of a restrictive regulation of trial registration	2011	WOS:000293635600002	Background For many years now, studies have shown that the results of clinical trials are often published selectively, with a statistically significant bias towards positive results, which becomes very significant at the clinical level. This publication bias produces a systematic misdirection of various medical decisions and the harm-benefit analyses underlying these decisions. It has to be assumed that such misdirection negatively affects the quality of patient care, patients' right to informed choice, the protection of research participants, and medical education and, thus, has diverse ethically unacceptable consequences. Registries of trials are the internationally favored strategy to compensate for this publication bias. However, it is an open question when and to what extent the registration of trials will become an established and regulated obligation for clinical trials conducted in Germany. Analysis This article describes the theoretical and empirical background of both selective publication and study registries with reference to the central international literature. The ethical problems of selective publishing are presented systematically. Building on this, the article argues for the necessity of a restrictive regulation of trials registration on the part of the self-governing bodies of the German health and research system as well as of the Federal Ministry of Health in order to significantly reduce selective publication. Conclusion The article demonstrates the extent to which German self-governing bodies and politics in medicine and research can be ascribed a prospective and retrospective responsibility for the effective regulation of study registries (or for the lack thereof).
9	In spite of numerous regional and country initiatives, clinical trials taking place in non-English-speaking parts of the Americas are underregistered	[**Krleza-Jeric, Karmela**] Inst Rech Sante Canada, Canadian Inst Hlth Res, Ottawa, ON, Canada; [Lemmens, Trudo] Univ Toronto, Fac Law, Toronto, ON M5S 1A1, Canada…	Prospective registration and results disclosure of clinical trials in the Americas: a roadmap toward transparency	2011	WOS:000299524000013	The objective of this article is to propose a roadmap toward transparency of clinical trials in the Americas by their prospective registration and results disclosure. This will broaden access to more complete and accurate data and facilitate evidence-informed decision-making and participation in research. Consequently, it should have a positive impact on people's health and should promote trust in health research. Existing initiatives were identified, registration of trials was analysed following the World Health Organization (WHO) standards on trial registration, and a roadmap is proposed to address the gaps in advancing transparency. The analysis shows that, in spite of numerous regional and country initiatives, clinical trials taking place in non-English-speaking parts of the Americas are underregistered. A roadmap is proposed to enhance research governance and good research practice by improving the transparency of clinical trials. The proposed roadmap includes strategies for implementing WHO international standards for trial registration, for developing international standards of public disclosure of trial results, and for a potential role of the Pan American Health Organization.
10	Clinical trials registration has the potential to contribute substantially to improving clinical trial transparency and reducing publication bias and selective reporting. These potential benefits are currently un-	[**Viergever, Roderik F.**; Ghersi, Davina] WHO, ICTRP, Dept Res Policy & Cooperat, CH-1211 Geneva, Switzerland	The Quality of Registration of Clinical Trials	2011	WOS:000287761700001	Background: Lack of transparency in clinical trial conduct, publication bias and selective reporting bias are still important problems in medical research. Through clinical trials registration, it should be possible to take steps towards resolving some of these problems. However, previous evaluations of registered records of clinical trials have shown that registered information is often incomplete and non-meaningful. If these studies are accurate, this negates the possible benefits of registration of clinical trials. Methods and Findings: A 5% sample of records of clinical trials that were registered between 17 June 2008 and 17 June 2009 was taken from the International Clinical Trials Registry Platform (ICTRP) database and assessed for the presence of contact information, the presence of intervention specifics in drug trials and the quality of primary and secondary outcome reporting. 731 records were included. More than half of the records were registered after recruitment of the first

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	dermined by deficiencies in the provision of information in key areas of registered records.					participant. The name of a contact person was available in 94.4% of records from non-industry funded trials and 53.7% of records from industry funded trials. Either an email address or a phone number was present in 76.5% of non-industry funded trial records and in 56.5% of industry funded trial records. Although a drug name or company serial number was almost always provided, other drug intervention specifics were often omitted from registration. Of 3643 reported outcomes, 34.9% were specific measures with a meaningful time frame. Conclusions: Clinical trials registration has the potential to contribute substantially to improving clinical trial transparency and reducing publication bias and selective reporting. These potential benefits are currently undermined by deficiencies in the provision of information in key areas of registered records.
11	To improve the comprehensiveness and completeness of registered clinical research data, it is necessary to communicate and raise awareness of the need to register clinical trials, as well as to establish national policies on clinical trial registration.	Korea Ctr Dis Control & Prevent, Natl Inst Hlth, Div Cadiovasc & Rare Dis, Cheongwon, South Korea	Primary registry of the WHO International Clinical Trial Registry Platform: Clinical Research Information Service (CRIS)	2011	WOS:000286491300013	Publication bias has a negative impact on the ability of healthcare providers and consumers to make unbiased healthcare decisions. The demand for greater transparency of clinical trials has increased and a prospective registry has been suggested by the International Committee of Medical Journal Editors. By 2008, prospective registration was considered as an ethical requirement within the Declaration of Helsinki. In Korea, the clinical research registry named 'Clinical Research Information Service (CRIS)' was recently established and became a data provider as a primary registry to the World Health Organization (WHO) International Clinical Trial Registry Platform search portal. This means that CRIS conforms to the WHO registry criteria and that registering trials with the CRIS satisfies the trial registration policies of many medical journals. To improve the comprehensiveness and completeness of registered clinical research data, it is necessary to communicate and raise awareness of the need to register clinical trials, as well as to establish national policies on clinical trial registration.
12	Discrepancies between protocols or trial registry entries and trial reports were common. Full transparency will be possible only when protocols are made publicly available or the quality and extent of information included in trial registries is improved, and trialists explain substantial changes in their reports.	[**Dwan, Kerry**] Univ Liverpool, Alder Hey Childrens NHS Fdn Trust, Inst Child Hlth, Liverpool L12 2AP, Merseyside, England; [**Altman, Douglas G**.] Wolfson Coll Annexe, Ctr Stat Med, Oxford, England; [Cresswell, Lynne; Blundell, Michaela; Gamble, Carrol L.; Williamson, Paula R.] Univ Liverpool, Ctr Med Stat & Hlth Evaluat, Liverpool L69 3BX, Merseyside, England	Comparison of protocols and registry entries to published reports for randomised controlled trials	2011	WOS:000286393200038	Background Publication of complete trial results is essential if people are to be able to make well-informed decisions about health care. Selective reporting of randomised controlled trials (RCTs) is a common problem. Objectives To systematically review studies of cohorts of RCTs to compare the content of trial reports with the information contained in their protocols, or entries in a trial registry. Search strategy We conducted electronic searches in Ovid MEDLINE (1950 to August 2010); Ovid EMBASE (1980 to August 2010); ISI Web of Science (1900 to August 2010) and the Cochrane Methodology Register (Issue 3, 2010), checked reference lists, and asked authors of eligible studies to identify further studies. Studies were not excluded based on language of publication or our assessment of their quality. Selection criteria Published or unpublished cohort studies comparing the content of protocols or trial registry entries with published trial reports. Data collection and analysis Data were extracted by two authors independently. Risk of bias in the cohort studies was assessed in relation to follow up and selective reporting of outcomes. Results are presented separately for the comparison of published reports to protocols and trial registry entries. Main results We included 16 studies assessing a median of 54 RCTs (range: 2 to 362). Twelve studies compared protocols to published reports and four compared trial registry entries to published reports. In two studies, eligibility criteria differed between the protocol and publication in 19% and 100% RCTs. In one study, 16% (9/58) of the reports included the same sample size calculation as the protocol. In one study, 6% (4/63) of protocol-report pairs gave conflicting information regarding the method of allocation concealment, and 67% (49/73) of blinded studies reported discrepant information on who was blinded.

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						In one study unacknowledged discrepancies were found for methods of handling protocol deviations (44%; 19/43), missing data (80%; 39/49), primary outcome analyses (60%; 25/42) and adjusted analyses (82%; 23/28). One study found that of 13 protocols specifying subgroup analyses, 12 of these 13 trials reported only some, or none, of these. Two studies found that statistically significant outcomes had a higher odds of being fully reported compared to nonsignificant outcomes (range of odds ratios: 2.4 to 4.7). Across the studies, at least one primary outcome was changed, introduced, or omitted in 4-50% of trial reports. Authors' conclusions Discrepancies between protocols or trial registry entries and trial reports were common, although reasons for these were not discussed in the reports. Full transparency will be possible only when protocols are made publicly available or the quality and extent of information included in trial registries is improved, and trialists explain substantial changes in their reports.
13	Although still suboptimal, the situation is improving over time, with both trial registration and declaration of registration details more likely in later years.	[**McGee, Richard G.**; Higgins, Gail Y.; Craig, Jonathan C.; Webster, Angela C.] Childrens Hosp Westmead, Ctr Kidney Res, Westmead, NSW, Australia; [McGee, Richard G.; Higgins, Gail Y.; Craig, Jonathan C.; Webster, Angela C.] Childrens Hosp Westmead, Cochrane Renal Grp, Westmead, NSW, Australia; …	Trial Registration and Declaration of Registration by Authors of Randomized Controlled Trials	2011	WOS:000296798100011	Background. Trial registration was introduced to reduce research bias by promoting trial transparency and accountability. We aimed to evaluate the frequency of, and factors associated with, trial registration and declaration of trial registration. Methods. We selected all randomized controlled trials in kidney transplantation published between October 2005 and December 2010 and determined whether a trial was registered and whether a trial declared their registration in subsequent trial reports. Results. Of 307 eligible trials identified, 24% (74/307) were registered, and of those, 59% (44/74) contained trial registration details within at least one trial report. Trial registration was more likely for trials published more than once, in later years or reported in journals that followed the International Committee of Medical Journal Editors guidelines. Trial registration was less likely for trials that did not declare their funding sources. Registered trials were more likely to declare registration details in related reports if published in later years or in a journal that followed International Committee of Medical Journal Editors guidelines. Trials that did not declare their funding sources were less likely to declare registration details. Conclusions. Although still suboptimal, the situation is improving over time, with both trial registration and declaration of registration details more likely in later years.
14	Public confidence in clinical trials has been eroded by data suppression, misrepresentation and manipulation. We propose that a global network be established. This could be accomplished in two steps. The first step is to legislate about trial registration and data transparency, such as USA's FDAAA Act 2007; and the second step to	[**Bian, Zhao-Xiang**] Hong Kong Baptist Univ, Sch Chinese Med, Hong Kong, Hong Kong, Peoples R China; [Wu, Tai-Xiang] Sichuan Univ, W China Hosp, Chinese Evidence Based Med Ctr, Dept Clin Epidemiol, Chengdu 610041, Sichuan Prov, Peoples R China	Legislation for trial registration and data transparency	2010	WOS:000279549200002	Public confidence in clinical trials has been eroded by data suppression, misrepresentation and manipulation. Although various attempts have been made to achieve universal trial registration-e. g., Declaration of Helsinki, WHO clinical Trial Registry Platform (WHO ICTRP), the International Committee of Medical Journal Editors requirement-they have not succeeded, probably because they lack the enough power of enforcement. Legislation appears to be the most efficient and effective means to ensure that all researchers register their trials and disseminate their data accurately and in a timely manner. We propose that a global network be established. This could be accomplished in two steps. The first step is to legislate about trial registration and data transparency, such as USA's FDAAA Act 2007; and the second step to establish a global network to ensure uniform, international consistency in policy and enforcement of trial registration and data transparency.

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	establish a global network to ensure uniform, international consistency in policy and enforcement of trial registration and data transparency.					
15	As sponsors struggle to meet the legal clinical trial disclosure requirements while attempting to get manuscripts published, it is not clear at this time what the final impact will be on sponsors, journals, investigators, health care providers, the media, and the ultimate customer, the patient.	**Eli Lilly** & Co, Lilly Corp Ctr, Indianapolis, IN 46285 USA	Can Clinical Trial Results Databases and Manuscripts Coexist?	2010	WOS:000277585300009	Recent changes in US legal obligations to disclose clinical,trial results have created confounding challenges for sponsors of clinical trials and for editors of medical and scientific journals with policies prohibiting prepublication of clinical trial data. For nearly two centuries, peer-reviewed manuscripts have served as the primary means of scientific communication. In recent years, however, criticisms of the delay in publishing clinical trial data and publication bias have increased. Prominent journal editors have strongly suggested that online clinical trial registration prior to study conduct would mitigate these concerns. With the recent addition of legally mandated clinical trial results disclosure within specified time limits on ClinicalTrials.gov, the very registries and results databases once used in part to address publication bias may now actually jeopardize the ability to publish the results in peer-reviewed medical journals. Both types of disclosure (ie, posting in results databases and publishing traditional manuscripts) play important roles in the dissemination of clinical trial results, but current requirements now test the medical journals' policies, which effectively reserve the right of the journal to be the primary source for clinical trial data. As sponsors struggle to meet the legal clinical trial disclosure requirements while attempting to get manuscripts published, it is not clear at this time what the final impact will be on sponsors, journals, investigators, health care providers, the media, and the ultimate customer, the patient.
16	Reporting of optional data elements varied and publication rates among completed trials registered within ClinicalTrials.gov were low. Without greater attention to reporting of all data elements, the potential for ClinicalTrials.gov to address selective publication of clinical trials will be limited.	[**Ross, Joseph S**.] Mt Sinai Sch Med, Dept Geriatr & Adult Dev, New York, NY 10029 USA; [Ross, Joseph S.] James J Peters VA Med Ctr, HSR&D Res Enhancement Award Program, Bronx, NY USA; [Ross, Joseph S.] James J Peters VA Med Ctr, Geriatr Res Educ & Clin Ctr, Bronx, NY USA; [Mulvey, Gregory K.; Krumholz, Harlan M.] Yale New Haven Med Ctr, Ctr Outcomes Res & Evaluat, New Haven,	Trial Publication after Registration in ClinicalTrials.Gov: A Cross-Sectional Analysis	2009	WOS:000270818100008	Background: ClinicalTrials.gov is a publicly accessible, Internet-based registry of clinical trials managed by the US National Library of Medicine that has the potential to address selective trial publication. Our objectives were to examine completeness of registration within ClinicalTrials.gov and to determine the extent and correlates of selective publication. Methods and Findings: We examined reporting of registration information among a cross-section of trials that had been registered at ClinicalTrials.gov after December 31, 1999 and updated as having been completed by June 8, 2007, excluding phase I trials. We then determined publication status among a random 10% subsample by searching MEDLINE using a systematic protocol, after excluding trials completed after December 31, 2005 to allow at least 2 y for publication following completion. Among the full sample of completed trials (n= 7,515), nearly 100% reported all data elements mandated by ClinicalTrials.gov, such as intervention and sponsorship. Optional data element reporting varied, with 53% reporting trial end date, 66% reporting primary outcome, and 87% reporting trial start date. Among the 10% subsample, less than half (311 of 677, 46%) of trials were published, among which 96 (31%) provided a citation within ClinicalTrials.gov of a publication describing trial results. Trials primarily sponsored by industry (40%, 144 of 357) were less likely to be published when compared with nonindustry/nongovernment sponsored trials (56%, 110 of 198; $p < 0.001$), but there was no significant difference when compared with government sponsored trials (47%, 57 of 122; $p = 0.22$). Among trials that reported an end date, 75 of 123 (61%) completed prior to 2004, 50 of 96 (52%) completed dur-

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		CT 06504 USA…				ing 2004, and 62 of 149 (42%) completed during 2005 were published (p = 0.006). Conclusions: Reporting of optional data elements varied and publication rates among completed trials registered within ClinicalTrials.gov were low. Without greater attention to reporting of all data elements, the potential for ClinicalTrials.gov to address selective publication of clinical trials will be limited.
19	Trial registration alone, without a requirement for full reporting of research results, does not appear to reduce a bias toward results and conclusions favoring new drugs in the clinical trials literature. Our findings support the inclusion of full results reporting in trial registers, as well as protocols to allow assessment of whether results have been completely reported	[**Rasmussen, Nicolas**] Univ New S Wales, Sydney, NSW 2052, Australia; [Lee, Kirby; Bero, Lisa] Univ Calif San Francisco, Dept Clin Pharm, San Francisco, CA 94118 USA	Association of trial registration with the results and conclusions of published trials of new oncology drugs	2009	WOS:000274190100001	Background: Registration of clinical trials has been introduced largely to reduce bias toward statistically significant results in the trial literature. Doubts remain about whether advance registration alone is an adequate measure to reduce selective publication, selective outcome reporting, and biased design. One of the first areas of medicine in which registration was widely adopted was oncology, although the bulk of registered oncology trials remain unpublished. The net influence of registration on the literature remains untested. This study compares the prevalence of favorable results and conclusions among published reports of registered and unregistered randomized controlled trials of new oncology drugs. Methods: We conducted a cross-sectional study of published original research articles reporting clinical trials evaluating the efficacy of drugs newly approved for antimalignancy indications by the United States Food and Drug Administration (FDA) from 2000 through 2005. Drugs receiving first-time approval for indications in oncology were identified using the FDA web site and Thomson Centerwatch. Relevant trial reports were identified using PubMed and the Cochrane Library. Evidence of advance trial registration was obtained by a search of clinicaltrials. gov, WHO, ISRCTN, NCI-PDQ trial databases and corporate trial registries, as well as articles themselves. Data on blinding, results for primary outcomes, and author conclusions were extracted independently by two coders. Univariate and multivariate logistic regression identified associations between favorable results and conclusions and independent variables including advance registration, study design characteristics, and industry sponsorship. Results: Of 137 original research reports from 115 distinct randomized trials assessing 25 newly approved drugs for treating cancer, the 54 publications describing data from trials registered prior to publication were as likely to report statistically significant efficacy results and reach conclusions favoring the test drug (for results, OR = 1.77; 95% CI = 0.87 to 3.61) as reports of trials not registered in advance. In multivariate analysis, reports of prior registered trials were again as likely to favor the test drug (OR = 1.29; 95% CI = 0.54 to 3.08); large sample sizes and surrogate outcome measures were statistically significant predictors of favorable efficacy results at $p < 0.05$. Subgroup analysis of the main reports from each trial (n = 115) similarly indicated that registered trials were as likely to report results favoring the test drug as trials not registered in advance (OR = 1.11; 95% CI = 0.44 to 2.80), and also that large trials and trials with nonstringent blinding were significantly more likely to report results favoring the test drug. Conclusions: Trial registration alone, without a requirement for full reporting of research results, does not appear to reduce a bias toward results and conclusions favoring new drugs in the clinical trials literature. Our findings support the inclusion of full results reporting in trial registers, as well as protocols to allow assessment of whether results have been completely reported.

Table 4.15: Persons and theses of selected papers about *sponsoring bias* for stakeholder involvement.

Source: Selected publications from the bibliometric analysis, times cited as from June 2012.

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1	Industry has used seeding trials, publication planning, messaging, ghostwriting, and selective publication and reporting of trial outcomes to distort the medical literature and undermine clinical trial research by obscuring information relevant to patients and physicians.	[**Ross, Joseph S**.; Gross, Cary P.] Yale Univ, Sch Med, Gen Internal Med Sect, New Haven, CT 06520 USA; [Ross, Joseph S.; Krumholz, Harlan M.] Yale New Haven Med Ctr, Ctr Outcomes Res & Evaluat, New Haven, CT 06504 USA; …	Promoting Transparency in Pharmaceutical Industry-Sponsored Research	2012	WOS:000298449400017	Strong, evidence-based practice requires that objective, unbiased research be available to inform individual clinical decisions, systematic reviews, meta-analyses, and expert guideline recommendations. Industry has used seeding trials, publication planning, messaging, ghostwriting, and selective publication and reporting of trial outcomes to distort the medical literature and undermine clinical trial research by obscuring information relevant to patients and physicians. Policies that promote transparency in the clinical trial research process, through improved and expanded disclosure of investigator contributions and funding, comprehensive publicly available trial registration, and independent analysis of clinical trial data analysis may address these subversive practices by improving accountability among industry and investigators. Minimizing marketing's impact on clinical trial research and strengthening the science will protect medical literature's integrity and the public's health. (Am J Public Health. 2012:72-80. doi :10.2105/AJPH.2011.300187)
2	Since the web-based registry ClinicalTrials.gov was launched on 29 February 2000, the pharmaceutical industry has made available an increasing amount of information about the clinical trials that it sponsors.	[**O'Kelly, Michael**] **Quintiles** Ireland Ltd, Dublin 3, Ireland; [Julious, Steven A.] Univ Sheffield, Med Stat Grp, ScHARR, Sheffield, S Yorkshire, England; [**Pyke, Stephen**] **Pfizer** Ltd, Sandwich CT13 9NJ, Kent, England; [**Day, Simon**] **Roche** Prod Ltd, Welwyn Garden City AL7 3AY, Herts, England; [Todd, Sue] Univ Reading, Reading, Berks, England; [**Seldrup, Jorgen**] **Quintiles,** Illkirch Graffenstaden, France; [**Matcham, James**] **Amgen** Ltd, Cambridge, England	Making available information from studies sponsored by the pharmaceutical industry: some current practices	2011	WOS:000287065400011	Since the web-based registry ClinicalTrials.gov was launched on 29 February 2000, the pharmaceutical industry has made available an increasing amount of information about the clinical trials that it sponsors. The process has been spurred on by a number of factors including a wish by the industry to provide greater transparency regarding clinical trial data; and has been both aided and complicated by the number of institutions that have a legitimate interest in guiding and defining what should be made available. This article reviews the history of this process of making information about clinical trials publicly available. It provides a reader's guide to the study registries and the databases of results; and looks at some indicators of consistency in the posting of study information. Copyright (C) 2010 John Wiley & Sons, Ltd.

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3	Web site posting increases public availability rate of clinical trial results from 61% to 78%. Cancellation of projects is the single factor negatively influencing publication and public availability rates.	[**Dal-Re, Rafael; Garcia-Losa, Manuel; Lahuerta, Juan; Ortega, Rafael**] **GlaxoSmithKline** SA, Dept Med, Madrid, Spain; [**Pedromingo, Alejandro**] **GlaxoSmithKline** SA, Dept Biometry, Madrid, Spain	Are results from pharmaceutical-company-sponsored studies available to the public?	2010	WOS:000283253200002	Only 53% and 63% of studies and clinical trials results presented at congresses are published. Company-sponsored trial results are being posted on publicly accessible Web sites. We analysed the public availability (publication or posting on a Web site) rate, time to publication, and factors predicting public availability of results of studies sponsored by a pharmaceutical company. This was a retrospective cohort study analyzing all studies conducted by GlaxoSmithKline in Spain between 2001 and 2006. Initiation and completion were defined as first participant/first visit and last participant/last visit (or their equivalents). Papers published up to 31 March 2009 were considered. Logistic regression models were used to identify factors predicting public availability of results. The cohort comprised 143 studies (94 clinical trials; of these, 87 were included in international products clinical development plans). Public availability rate was 80% (114/143) for all studies and 78% (73/94) for clinical trials; publication rates were 68% and 61%, respectively. The median time to publication for all studies and trials was 27.3 and 28.4 months, respectively. Study associated to a cancelled project was the only significant factor associated with lower publication rate for all studies [odds ratio (OR) 0.069; 95% confidence interval (CI) 0.02-024; $p < 0.001$) and trials (OR 0.075; 95% CI 0.016-0.343; $p = 0.001$) and a lower public availability rate (OR 0.052; 95% CI 0.007-0.382; $p = 0.004$) for trial results. Therapy area, sample size, positive trial results, duration of experimental phase, and being a clinical trial did not predict publication or public availability. Eighty percent of studies included in this analysis are publicly available. Web site posting increases public availability rate of clinical trial results from 61% to 78%. Cancellation of projects is the single factor negatively influencing publication and public availability rates.
5	Three recent systematic reviews have shown that pharmaceutical industry funding of clinical trials is strongly associated with pro-industry results.	[**Sismondo S.**] Queens Univ, Kingston, ON, Canada	How pharmaceutical industry funding affects trial outcomes: Causal structures and responses	2008	WOS:000255580400005	Three recent systematic reviews have shown that pharmaceutical industry funding of clinical trials is strongly associated with pro-industry results. This article builds on those analyses, situating funding's effects in the context of the ghost-management of research and publication by pharmaceutical companies, and the creation of social ties between those companies and researchers. There are multiple demonstrated causes of the association of funding and results, ranging from trial design bias to publication bias; these are all rooted in close contact between pharmaceutical companies and much clinical research. Given these points, most proposed measures to respond to this bias are too piecemeal to be adequate. (c) 2008 Elsevier Ltd. All rights reserved.
6	Ethical issues arising from commercial sponsorship and from relationships with the pharmaceutical industry	[**Steiner TJ.**] Univ London Imperial Coll Sci Technol & Med, Div Neurosci & Mental Hlth, IHS Eth Subcomm, London W6 8RP, England	Ethical issues arising from commercial sponsorship and from relationships with the pharmaceutical industry - Report and recommendations of the ethics subcommittee of the international headache society	2008	WOS:000257717100001	

Index	Theses	Affiliations	Title	Publ. Year	WOS ID	Abstract
7	The policies normally proposed for dealing with sponsorship bias are unable to eliminate it. Only completely separating public clinical research from pharmaceutical industry funding can eliminate sponsorship bias.	[**Doucet, M.**] Queens Univ, Dept Philosophy, Kingston, ON K7L 3N6, Canada	Evaluating solutions to sponsorship bias	2008	WOS:000258060200014	More than 40 primary studies, and three recent systematic reviews and meta-analyses, have shown a clear association between pharmaceutical industry funding of clinical trials and pro-industry results. Industry sponsorship biases published scientific research in favour of the sponsors, a result of the strong interest commercial sponsors have in obtaining favourable results. Three proposed remedies to this problem are widely agreed upon among those concerned with the level of sponsorship bias: financial disclosure, reporting standards and trial registries. This paper argues that all of these remedies either fail to address the mechanisms by which pharmaceutical companies' sponsorship leads to biased results-design bias, multiple trials with predictable outcomes, fraud, rhetorical effects and publication bias or else only inadequately address those mechanisms. As a result, the policies normally proposed for dealing with sponsorship bias are unable to eliminate it. Only completely separating public clinical research from pharmaceutical industry funding can eliminate sponsorship bias.
8	Financial conflicts of interest are exceedingly common in biomedical research. Investigators with conflicts of interest are more likely to arrive at positive conclusions, perhaps as a result of biased study design, industry suppression of negative results, preferential funding by industry of projects that are likely to succeed, or biased interpretation of results on the part of investigators.	[**Okike, Kanu**] Harvard Univ, Massachusetts Gen Hosp, Sch Med, Dept Orthopaed Surg, Boston, MA 02114 USA; [Kocher, Mininder S.] Harvard Univ, Sch Med, Dept Orthopaed Surg, Childrens Hosp, Boston, MA 02114 USA; [Mehlman, Charles T.] Univ Cincinnati, Coll Med, Cincinnati Childrens Hosp Med Ctr, Div Pediat Orthopaed Surg, Cincinnati, OH USA; [Bhandari, Mohit] McMaster Univ, Dept Orthopaed Surg, Hamilton Gen Hosp, Hamilton, ON L8S 4L8, Canada	Industry-sponsored research	2008	WOS:000257530700008	Financial conflicts of interest are exceedingly common in biomedical research. Investigators with conflicts of interest are more likely to arrive at positive conclusions, perhaps as a result of biased study design, industry suppression of negative results, preferential funding by industry of projects that are likely to succeed, or biased interpretation of results on the part of investigators. Government and professional organisations have proposed guidelines for managing conflicts of interest, but in practice it is the policies of universities and medical journals that direct the actions of investigators. Academic researchers and the media have expressed concern about the influence of industry sponsorship on biomedical research, white industry is increasingly turning to private entities (such as contract research organisations) to conduct clinical trials. Research participants appear less concerned with conflicts of interest in biomedical research, perhaps due to a faith that such conflicts are being appropriately managed by institutions. After reviewing the literature, we provide recommendations for the ethical conduct of biomedical research in the presence of financial conflicts of interest. (C) 2008 Elsevier Ltd. All rights reserved.

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9	Commercially funded studies submitted for review were not more likely to conclude with a positive outcome than were nonfunded studies, and studies with a positive outcome were no more likely to be published than were studies with a negative outcome.	[**Lynch JR,** Cunningham MR, Warme WJ, Schaad DC, Wolf FM, Leopold SS.] Univ Washington, Med Ctr, Dept Orthopaed & Sports Med, Seattle, WA 98195 USA	Commercially funded and United States-based research is more likely to be published; Good-quality studies with negative outcomes are not	2007	WOS:000246377400013	Background: Prior studies implying associations between receipt of commercial funding and positive (significant and/or pro-industry) research outcomes have analysed only published papers, which is an insufficiently robust approach for assessing publication bias. In this study, we tested the following hypotheses regarding orthopaedic manuscripts submitted for review: (1) nonscientific variables, including receipt of commercial funding, affect the likelihood that a peer-reviewed submission will conclude with a report of a positive study outcome, and (2) positive outcomes and other, nonscientific variables are associated with acceptance for publication. Methods: All manuscripts about hip or knee arthroplasty that were submitted to The Journal of Bone and Joint Surgery, American Volume, over seventeen months were evaluated to determine the study design, quality, and outcome. Analyses were carried out to identify associations between scientific factors (sample size, study quality, and level of evidence) and study outcome as well as between non-scientific factors (funding source and country of origin) and study outcome. Analyses were also performed to determine whether outcome, scientific factors, or nonscientific variables were associated with acceptance for publication. Results: Two hundred and nine manuscripts were reviewed. Commercial funding was not found to be associated with a positive study outcome ($p = 0.668$). Studies with a positive outcome were no more likely to be published than were those with a negative outcome ($p = 0.410$). Studies with a negative outcome were of higher quality ($p = 0.003$) and included larger sample sizes ($p = 0.05$). Commercially funded ($p = 0.027$) and United States-based ($p = 0.020$) studies were more likely to be published, even though those studies were not associated with higher quality, larger sample sizes, or lower levels of evidence ($p = 0.24$ to 0.79). Conclusions: Commercially funded studies submitted for review were not more likely to conclude with a positive outcome than were nonfunded studies, and studies with a positive outcome were no more likely to be published than were studies with a negative outcome. These findings contradict those of most previous analyses of published (rather than submitted) research. Commercial funding and the country of origin predict publication following peer review beyond what would be expected on the basis of study quality. Studies with a negative outcome, although seemingly superior in quality, fared no better than studies with a positive outcome in the peer-review process; this may result in inflation of apparent treatment effects when the published literature is subjected to meta-analysis.

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11	In the pulmonary and allergy literature, as in other fields, there is a publication bias towards positive results in pharmaceutical company-sponsored research.	[**Liss H.**] Rokach Ctr Prevent Lund Dis, Clalit Hlth Serv, IL-94390 Jerusalem, Israel; TB Treatment & Prevent Unit, Jerusalem, Israel	Publication bias in the pulmonary/allergy literature: Effect of pharmaceutical company sponsorship	2006	WOS:000239193100001	Background: A publication bias exists towards positive results in studies funded by pharmaceutical companies. Objectives: To determine whether drug studies in the pulmonary/allergy literature also demonstrate a publication bias towards more favorable results when a pharmaceutical company funds the study. Methods: We reviewed all original articles published in seven pulmonary and allergy journals between October 2002 and September 2003. Included in the review were studies of inhaled corticosteroids (oral or nasal), long- or short-acting bronchodilators, or leukotriene receptor antagonists. Articles with funding from a pharmaceutical company and/or one or more authors employed by a pharmaceutical company were considered pharmaceutical company-sponsored studies. The remaining studies were considered not sponsored by a pharmaceutical company. Results were compared to ascertain whether positive results were obtained more frequently in the company-sponsored studies. Results: Of the 100 articles included in this review 63 were considered pharmaceutical company-sponsored research. Results favorable for the drugs studies were significantly more common in those funded by a pharmaceutical company (98% vs. 32%). Conclusions: In the pulmonary and allergy literature, as in other fields, there is a publication bias towards positive results in pharmaceutical company-sponsored research.

Table 4.16: Persons and theses of selected papers about *editorial bias* for stakeholder involvement.

Source: Selected publications from the bibliometric analysis, times cited as from June 2012.

Index	Theses	Persons and Affiliations	Title	Publi. Year	WOS ID	Abstract
1	Editorial biases include publication bias; which refers to those situations where the results influence the editor's decision, and editorial bias refers to those situations where factors related with authors or their environment influence the decision. Editorial biases exists. Authors, when submitting their manuscript, should analyse different journals and decide where their article will receive adequate treatment.	[**Matias-Guiu, J.;** Garcia-Ramos, R.] Univ Complutense Madrid, Hosp Clin San Carlos, Inst Neurosci, Serv Neurol, Madrid, Spain	Editorial bias in scientific publications	2011	WOS:000288842900001	Introduction: Many authors believe that there are biases in scientific publications. Editorial biases include publication bias; which refers to those situations where the results influence the editor's decision, and editorial bias refers to those situations where factors related with authors or their environment influence the decision. Development: This paper includes an analysis of the situation of editorial biases. One bias is where mainly articles with positive results are accepted, as opposed to those with negative results. Another is latent bias, where positive results are published before those with negative results. In order to examine editorial bias, this paper analyses the influence of where the article originated; the country or continent, academic centre of origin, belonging to cooperative groups, and the maternal language of the authors. The article analyses biases in the editorial process in the publication of funded clinical trials. Conclusions: Editorial biases exists. Authors, when submitting their manuscript, should analyse different journals and decide where their article will receive adequate treatment. (C) 2010 Sociedad Espanola de Neurologia. Published by Elsevier Espana, S.L. All rights reserved.

Index	Theses	Persons and Affiliations	Title	Publi. Year	WOS ID	Abstract
2	Authors, editors, and peer reviewers all participate in this favoritism toward over publication of positive results.	[**Greenland, Philip**] Northwestern Univ, Feinberg Sch Med, Dept Prevent Med, Chicago, IL 60611 USA	Editorial Policies and Publication Bias The Importance of Negative Studies	2009	WOS:000266772500003	Publication bias is the tendency for certain kinds of studies, typically those showing a significant positive result in a clinical trial or an observational study, to receive more favorable publication decisions than equally well-conducted studies that report a negative or null result. Authors, editors, and peer reviewers all participate in this favoritism toward publication of positive results. An obvious outcome of the bias toward overpublication of positive results is that many treatments or exposures are overrated in the published literature. Some critics have gone so far as to claim that publication bias results in “most published research findings” being “false.” Although most researchers, reviewers, and editors would probably believe that such a claim is far too harsh, an unquestioned result of the overwhelming bias to publish mostly positive studies is that subsequent meta-analyses are distorted and result in promoting existing scientific biases. The Cochrane Collaboration admits the existence of this bias in the systematic reviews it publishes and suggests attenuating strategies such as probability models and funnel plot techniques.
3	There was a significant excess of publications from medical journals' own editorial boards, although it is not possible to determine whether this is due to bias in the peer review process or selective submission by editors.	[**Luty, J.**] S Essex Partnership NHS Trust, Taylor Ctr, Southend On Sea SS1 2RB, Essex, England; [Arokiadass, S. M. R.; Anapreddy, J. R.] S Essex Partnership NHS Trust, Runwell Hosp, Wickford, Essex, England	Preferential publication of editorial board members in medical specialty journals	2009	WOS:000263722500013	A Background: Publication bias and discrimination are increasingly recognised in medicine. A survey was conducted to determine if medical journals were more likely to publish research reports from members of their own than a rival journal's editorial board. Methods: A retrospective review was conducted of all research reports published in 2006 in the four competing medical journals within five medical specialties. Only three journals were willing to divulge the authorship of reports that had been rejected. Results: Overall, 4460 research reports were published in 2006 by the 20 journals from five subspecialties (mean 223 (SD=164) reports per journal; median 176; interquartile range 108-238). On average, 17.2 (7.7%) reports were from a journal's own editorial board (SD=10.7; median 15; interquartile range 10-23; n=20), and 6.3 (2.8%) reports were from a member of the editorial board of one of the three rival journals within the specialty (SD=7.3; median 3.5; interquartile range 1-8; n=60). There was a statistically significant excess of publications from the journal's own editorial board in 14 of the 20 journals ($p < 0.05$). Journals were almost three times more likely to publish reports from their own editorial board than from one of the three rivals within their subspecialty ($p < 0.0001$; median difference 11; Mann Whitney U test; power for 5% significance >99.99%). Conclusions: There was a significant excess of publications from medical journals' own editorial boards, although it is not possible to determine whether this is due to bias in the peer review process or selective submission by editors.
4	Editors must guard against basing the decision to publish on the significance of a study's results. Rather, they should prioritize manuscripts on the basis of the clinical question addressed, the quality of the research methods, and	[**Liesegang, Thomas J.**] Mayo Clin, Jacksonville, FL 32224 USA	Not for Your Eyes: Information Concealed through Publication Bias	2008	WOS:000260624000003	In summary, institutional review board-approved studies should not be buried when the results are indecisive or negative, because all resulting information is important if the study has been carried out properly. Editors must guard against basing the decision to publish on the significance of a study's results. Rather, they should prioritize manuscripts on the basis of the clinical question addressed, the quality of the research methods, and findings that will impact subsequent treatment. In fact, the inconclusive or negative studies provide prospective and balance against the seductive power of positive data in the literature. These steps will assure both editors and readers that the aggregate information presented is accurate and reliable and will enable journals to reflect the real world of research.

Index	Theses	Persons and Affiliations	Title	Publi. Year	WOS ID	Abstract
	findings that will impact subsequent treatment.					
5	Authors still believe in the existence of publication bias. They estimate its role to be comparable with the role of the quality of study performance and reporting. Our study also proves the presence of developing country bias, from the authors' perspective.	[**Shakiba, Behnam**] Univ Tehran Med Sci, Fac Med, Students Sci Res Ctr, Tehran 141556537, Iran	Factors influencing editors' decision on acceptance or rejection of manuscripts: The authors' perspective	2008	WOS:000258783500003	Background: There are few reports in the scientific literature on the factors taken into account by editors in deciding to accept or reject a scientific paper. The purpose of the present study was to investigate the effects of different factors on the journal editors' decisions on whether to accept or reject the manuscripts submitted to their journals. Methods: We randomly selected the participants from the authors of original articles and case reports published in six medical journals, and sent them a questionnaire by e-mail. We analysed the scores they gave to each of the 17 items of the questionnaire. Results: One hundred and nineteen of the authors responded to our survey. The scores given by the respondents were analysed comparing authors of developing and developed countries. Also, the results from authors of high- impact journals were compared with those with a low-impact factor. Multidimensional scaling was used to categorize the items based on their average scores. Highest scores were given to items addressing the quality of study performance, those addressing manuscript writing, and to the role of statistical significance of the results in the probability of studies getting published. Conclusion: Authors still believe in the existence of publication bias. They estimate its role to be comparable with the role of the quality of study performance and reporting. Our study also proves the presence of developing country bias, from the authors' perspective.
6	Editors value an original, rigorously designed manuscript with valid methodology and appropriate conclusions. Adherence to the philosophy and aims of the journal and the journal's target audience will further improve the likelihood of successful publication for the submitting authors.	[**Caulfield, R. H.;** Pleat, J. M.; Tyler, M. P. H.] Stoke Mandeville Hosp, Stoke Mandeville Burns & Reconstruct Surg Trust, Aylesbury HP21 8AL, Bucks, England; [Caulfield, R. H.; Maleki-Tabrizi, A.] Broomfield Hosp, St Andreas Ctr Burns & Plast Surg, Chelmsford CM1 7ET, Essex, England; [Pleat, J. M.; Tyler, M. P. H.] Stoke Mandeville Hosp, Dept Plast Surg, Aylesbury HP21 8AL, Bucks, England	The factors considered by editors of plastic surgery journals in evaluating submitted manuscripts	2008	WOS:000253680200026	The publication of clinical- or laboratory-based research in peer-reviewed journals is seen as the final end point rewarding many months of detailed work. For both trainees and established consultants alike, having a submitted manuscript rejected is both frustrating and disheartening. All journals publish details regarding manuscript structure and preparation. However these "in-house" guidelines tell little about what editors are looking for in their journals, and indeed what can be done to ensure acceptance of any work that researchers submit. The authors surveyed the editors of 40 peer-reviewed plastic surgery and related subspeciality journals regarding factors that influence their decision to accept or reject a manuscript. The aim was to establish factors that influence editors' decisions regarding submitted papers, which then would enable aspects to be highlighted that authors could address to expedite publication and produce relevant guidelines to facilitate this process. The results demonstrate that editors value an original, rigorously designed manuscript with valid methodology and appropriate conclusions. Adherence to the philosophy and aims of the journal and the journal's target audience will further improve the likelihood of successful publication for the submitting authors.

5 Conclusions

The aim of Task 3.1 (Part B) was to identify key opinion leaders and affiliated institutions. The task was also aimed at mapping the published research activities in the field of publication bias, including thematic clustering. The selected and implemented search strategy retrieved almost four-thousand publications, i.e. a sample of the relevant literature on publication bias with an average rate of about 170 publications per year.

In a first step, the obtained bibliometric data was examined by means of descriptive statistics. In a second step, four networks (or relational maps) were drawn. Maps for authors, institutions, research topics and knowledge bases (based on references) were constructed. The results of the network analyses and pertinent bibliographic information were comprised in three searchable data tables, suggestions for stakeholder selections and main theses from literature how to overcome publication bias

A small number of publications about 'publication bias' in the Web of Knowledge dates back almost two decades, to the year 1990 – the starting point of our analysis. Yet it took more than one decade (about 14 years) to attain a remarkable increase in the number of publications in this field.

Since then, the number of publications is increasing with an approximately constant growth rate. In the last two years there are indications for further acceleration of the growth rate. The growth per year is indicative of the increasing research on publication bias from different perspectives like outcome reporting, registration of trials, ethic issues, role of editors, guidelines for performing clinical trials reporting and the increase of the number of systematic reviews on different medical topics. It reflects the growing research activities in evidence based medicine, awareness and methods for meta-analysis and systematic reviews.

The field is headed by North America and dominated by the United States (with 1,480 publications), where we have the highest publication activity. A large number of European countries are listed as the address of authors and their affiliated institutions in the field of publication bias. England (with 760 publications) is leading the statistics of European countries. Positioned on the fourth place (with 346 publications), China plays a key role, too, but is not dominating like it does in many engineering domains.

The author network showed a high level of co-publishing in the field of publication bias. Ranking authors by the number of publications, rank numbers 1–21 (the top 21) formed a large predominant cluster (or sub-network). Interestingly, this large cluster displayed the network type of "brokers", i.e. authors *within* groups through a single or few links *between* groups. Given the accommodating information about authors (e.g. institution, country, or

topic), network positions and function can be used to optimize the selection of stakeholders for interviews and workshops.

Due to the properties of the author network, the institution network was highly interlinked as expected. The top institutions were typically universities or research institutes. As expected, hospitals and medical centres were as well markedly visible, while all other types of institutions assumed a minor role. The field is clearly dominated by native English speaking countries (e.g., USA, England, or Canada); Germany is the leading European country, followed by China. Most links of the institutional network pointed to a national level or between native English speaking countries.

The research fronts network showed publications as thematically categorized in two categories: The bigger one is formed by publications about performed systematic reviews and meta-analysis about different medical subjects like “myocardial infarction”, “blood pressure” or diabetes mellitus”. We refer to it as “*meta-studies about clinical topics*”. It includes systematic reviews and meta-analyses.

The second peak represents publications on research about publication bias. Publications are about guidelines for clinical trials, mathematic and statistical methods for meta-analysis, registration of studies, reporting and research about different issues related to publication bias. The assigned name is: *“methodologies and guidelines for clinical studies”*.

The table of key opinion leaders (WP3.1b_Tab.1) was constructed by exploiting the relational map of authors. It provides relevant author information present in the network. Note that searching and sorting authors by different criteria (e.g., the number of publications, the number of publications per year, or times cited per publication) can result in differently sorted lists of authors.

We identified research communities and persons as stakeholders for publication bias and how to overcome it: improvement of performing clinical trials and reporting their outcome; study registration; sponsorship bias; editorial bias as well statistical improvement of available trial results by meta-studies as well as systematic reviews.