Transparencia y sesgos en la diseminación de los resultados de la investigación

Dr. Gerard Urrútia
(Centro Cochrane Iberoamericano)

11 de Septiembre de 2025

XXI Reunión Anual de la Red Cochrane Iberoamericana – República Dominicana: Congreso de Políticas Públicas Basadas en Evidencias

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El problema

La publicación de los estudios depende de la **naturaleza** y **dirección** de sus resultados → los estudios con resultados 'negativos' o desfavorables tienen mayor probabilidad de no publicarse o de hacerlo solo parcialmente

- **Sesgo de publicación**
  - *Publication bias*
  - *Reporting bias*
- **Sesgo de diseminación**
  - ***Dissemination bias***
    - *Selective reporting bias*
    - *Time-lag bias*
    - *Location bias*
    - *Language bias*
    - *Citation bias*
    - …

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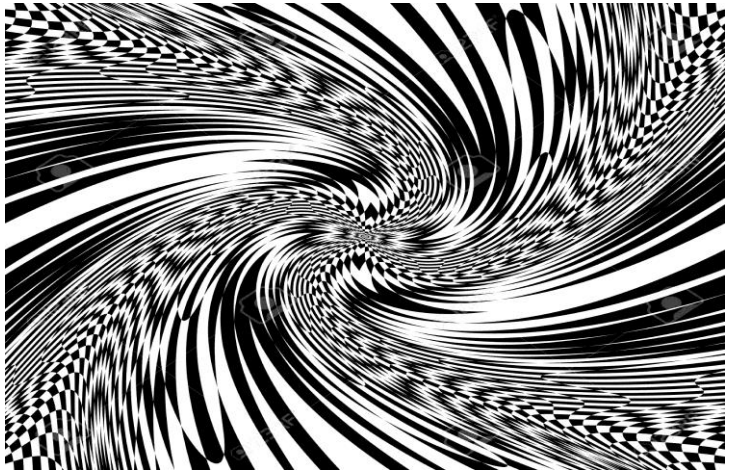
Un problema con consecuencias graves

- Percepción **distorsionada** sobre los potenciales beneficios y riesgos de las intervenciones en salud:
  - Sobrestimación de la eficacia
  - Infraestimación de los riesgos

Revisiones sistemáticas & GPC

- Decisiones en salud **mal fundamentadas** (daño a los pacientes, mal uso de los recursos [toxicidad financiera])
- **Investigación redundante** - evitable



Mala praxis científica – implicaciones éticas

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Una preocupación de antiguo

Sterling TD (1959)

Publication decisions and their possible effects on inferences drawn from tests of significance – or vice versa. Journal of the American Statistical Association 54:30-34.

Key passage(s)

PUBLICATION DECISIONS AND THEIR POSSIBLE EFFECTS ON INFERENCES DRAWN FROM TESTS OF SIGNIFICANCE —OR VICE VERSA*

THEODORE D. STERLING
University of Cincinnati

There is some evidence that in fields where statistical tests of significance are commonly used, research which yields nonsignificant results is not published. Such research being unknown to other investigators may be repeated independently until eventually by chance a significant result occurs—an "error of the first kind"—and is published. Significant results published in these fields are seldom verified by independent replication. The possibility thus arises that the literature of such a field consists in substantial part of false conclusions resulting from errors of the first kind in statistical tests of significance.

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J Clin Oncol. 1986 Oct;4(10):1529-41.

Publication bias: the case for an international registry of clinical trials.

Simes RJ.

Abstract

A problem in evaluating different therapies from a review of clinical trials is that the published clinical trial literature may be biased in favor of positive or promising results. In this report, a model is proposed for reviewing clinical trial results which is free from publication bias based on the selection of trials registered in advance in a registry. The value of a registry is illustrated by comparing a review of published clinical trials located by a literature search with a review of registered trials contained in a cancer trials registry. Two therapeutic questions are examined: the survival impact of initial alkylating agent (AA) v combination chemotherapy (CC) in advanced ovarian cancer, and the survival impact of AA/prednisone v CC in multiple myeloma. In advanced ovarian cancer, a pooled analysis of published clinical trials demonstrates a significant survival advantage for combination chemotherapy (median survival ratio of CC to AA, 1.16; P = .02). However, no significant difference in survival is demonstrated based on a pooled analysis of registered trials (median survival ratio, 1.05; P = .25). For multiple myeloma, a pooled analysis of published trials also demonstrates a significant survival advantage for CC (median survival ratio, 1.26; P = 04), especially for poor risk patients (ratio, 1.66; P = .002). A pooled analysis of registered trials also shows a survival benefit for patients receiving combination chemotherapy (all patients, P = .06; poor risk, P = .03), but the estimated magnitude of the benefit is reduced (all patients: ratio, 1.11; poor risk: ratio, 1.22). These examples illustrate an approach to reviewing the clinical trial literature, which is free from publication bias, and demonstrate the value and importance of an international registry of all clinical trials.

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Control Clin Trials. 1987 Dec;8(4):343-53. doi: 10.1016/0197-2456(87)90155-3.

Publication bias and clinical trials

K Dickersin [1], S Chan, T C Chalmers, H S Sacks, H Smith Jr

Affiliations + expand

PMID: 3442991 DOI: 10.1016/0197-2456(87)90155-3

Abstract

A study was performed to evaluate the extent to which the medical literature may be misleading as a result of selective publication of randomized clinical trials (RCTs) with results showing a statistically significant treatment effect. Three hundred eighteen authors of published trials were asked whether they had participated in any unpublished RCTs. The 156 respondents reported 271 unpublished and 1041 published trials. Of the 178 completed unpublished RCTs with a trend specified, 26 (14%) favored the new therapy compared to 423 of 767 (55%) published reports (p less than 0.001). For trials that were completed but not published, the major reasons for nonpublication were "negative" results and lack of interest. From the data provided, it appears that nonpublication was primarily a result of failure to write up and submit the trial results rather than rejection of submitted manuscripts. The results of this study imply the existence of a publication bias of importance both to meta-analysis and the interpretation of statistically significant positive trials.

JAMA

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Article

Factors Influencing Publication of Research Results

Follow-up of Applications Submitted to Two Institutional Review Boards

Kay Dickersin, PhD; Yuan-I Min, MPH, MHS; Curtis L Meinert, PhD

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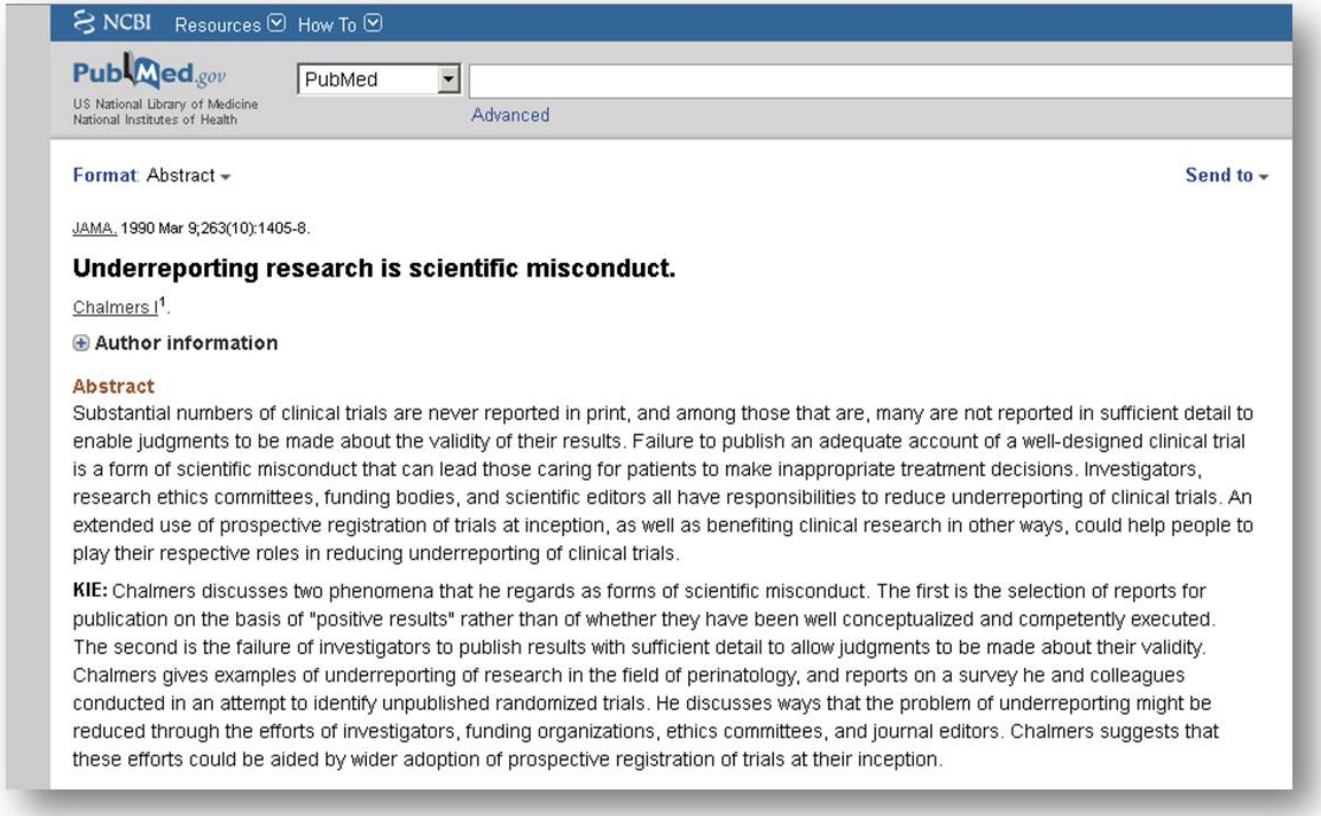

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JAMA. 1990 Mar 9;263(10):1405-8.

Underreporting research is scientific misconduct.

Chalmers I[1].

Author information

Abstract

Substantial numbers of clinical trials are never reported in print, and among those that are, many are not reported in sufficient detail to enable judgments to be made about the validity of their results. Failure to publish an adequate account of a well-designed clinical trial is a form of scientific misconduct that can lead those caring for patients to make inappropriate treatment decisions. Investigators, research ethics committees, funding bodies, and scientific editors all have responsibilities to reduce underreporting of clinical trials. An extended use of prospective registration of trials at inception, as well as benefiting clinical research in other ways, could help people to play their respective roles in reducing underreporting of clinical trials.

KIE: Chalmers discusses two phenomena that he regards as forms of scientific misconduct. The first is the selection of reports for publication on the basis of "positive results" rather than of whether they have been well conceptualized and competently executed. The second is the failure of investigators to publish results with sufficient detail to allow judgments to be made about their validity. Chalmers gives examples of underreporting of research in the field of perinatology, and reports on a survey he and colleagues conducted in an attempt to identify unpublished randomized trials. He discusses ways that the problem of underreporting might be reduced through the efforts of investigators, funding organizations, ethics committees, and journal editors. Chalmers suggests that these efforts could be aided by wider adoption of prospective registration of trials at their inception.

Mala praxis científica

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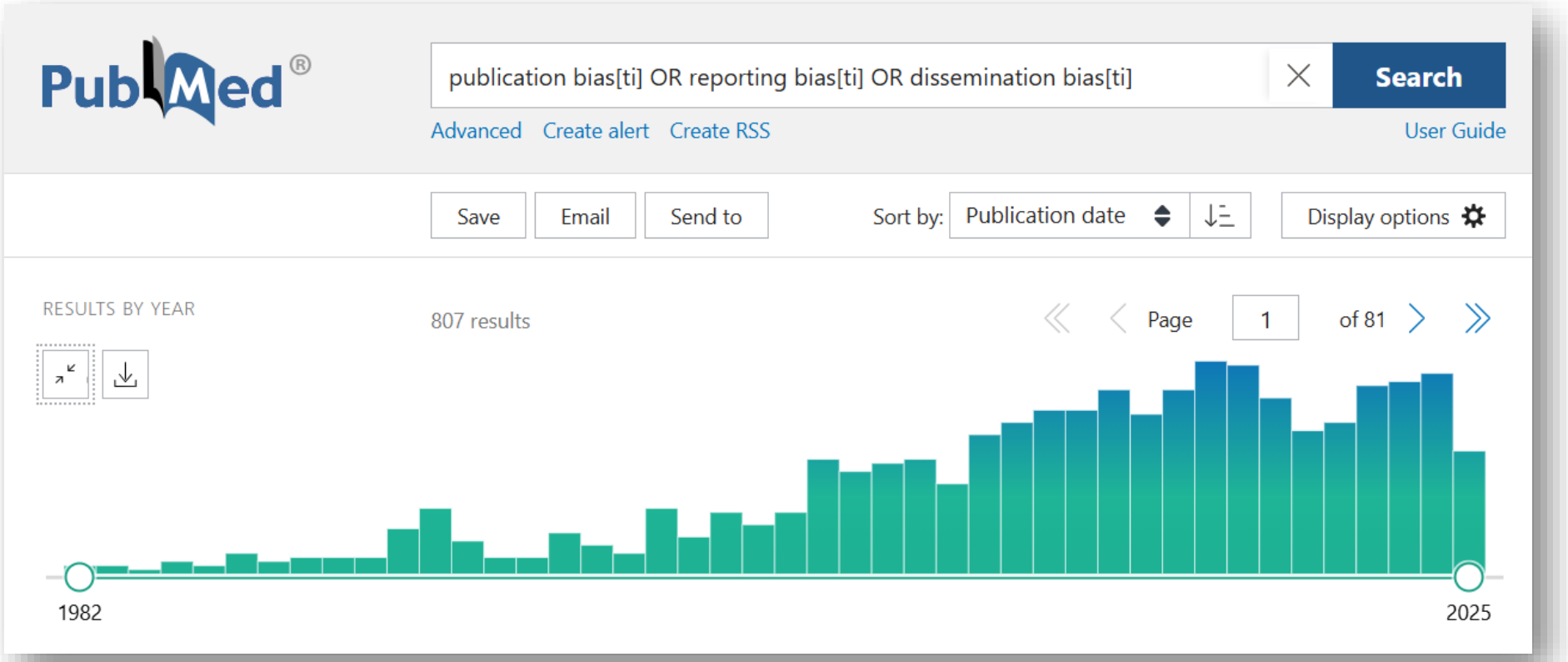
Una preocupación creciente



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Un problema complejo y multifactorial

- Registro del protocolo (repositorio de acceso público)
- Interrupción prematura del estudio
- Cierre y limpieza de la base de datos
- Análisis estadístico
- Informe final (interno)
- Presentación de resultados a congreso (preliminar)
- Redacción del manuscrito
- Informe de cierre a la agencia reguladora
- Publicación en revista científica

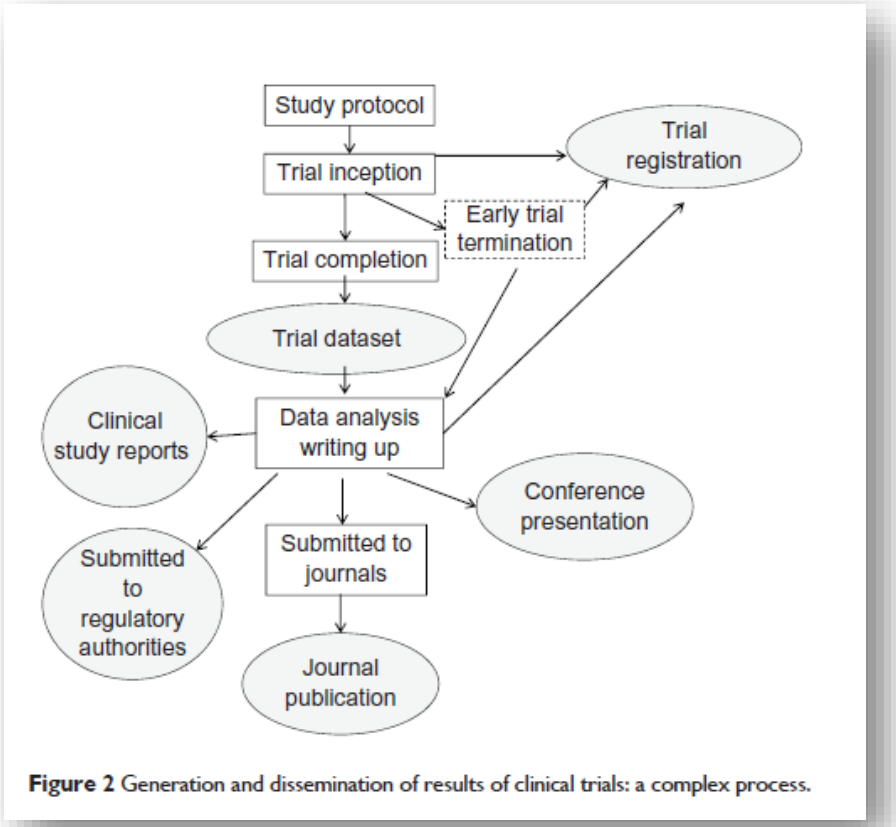

Figure 2 Generation and dissemination of results of clinical trials: a complex process.

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Proyecto OPEN

RESEARCH ARTICLE

Extent of Non-Publication in Cohorts of Studies Approved by Research Ethics Committees or Included in Trial Registries

Christine Schmucker[1], Lisa K. Schell[1], Susan Portalupi[1], Patrick Oeller[1], Laura Cabrera[1], Dirk Bassler[3], Guido Schwarzer[2], Roberta W. Scherer[5], Gerd Antes[1], Erik von Elm[4], Joerg J. Meerpohl[1]* on behalf of the OPEN consortium[¶]

Schmucker et al. PLoS One. 2014 Dec 23;9(12):e114023

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Revisión sistemática

Dos cohortes de estudios

- Comités de Ética (n=17)
- Registros de ensayos clínicos (n=22)

Resultados

- Tasa de estudios publicados
- Tiempo hasta la publicación (*full*)
- Asociación entre características del estudio y la publicación (*full*)

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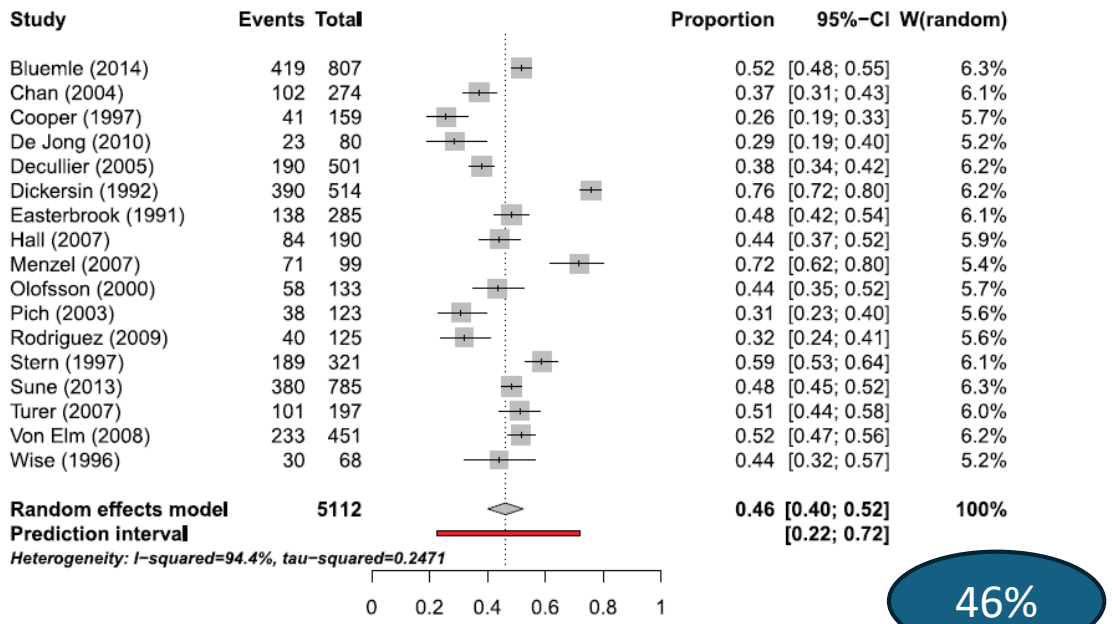
Revisión sistemática

Tasa de publicación – Comités de Ética



Study	Events	Total	Proportion	95%−CI	W(random)
Bluemle (2014)	419	807	0.52	[0.48; 0.55]	6.3%
Chan (2004)	102	274	0.37	[0.31; 0.43]	6.1%
Cooper (1997)	41	159	0.26	[0.19; 0.33]	5.7%
De Jong (2010)	23	80	0.29	[0.19; 0.40]	5.2%
Decullier (2005)	190	501	0.38	[0.34; 0.42]	6.2%
Dickersin (1992)	390	514	0.76	[0.72; 0.80]	6.2%
Easterbrook (1991)	138	285	0.48	[0.42; 0.54]	6.1%
Hall (2007)	84	190	0.44	[0.37; 0.52]	5.9%
Menzel (2007)	71	99	0.72	[0.62; 0.80]	5.4%
Olofsson (2000)	58	133	0.44	[0.35; 0.52]	5.7%
Pich (2003)	38	123	0.31	[0.23; 0.40]	5.6%
Rodriguez (2009)	40	125	0.32	[0.24; 0.41]	5.6%
Stern (1997)	189	321	0.59	[0.53; 0.64]	6.1%
Sune (2013)	380	785	0.48	[0.45; 0.52]	6.3%
Turer (2007)	101	197	0.51	[0.44; 0.58]	6.0%
Von Elm (2008)	233	451	0.52	[0.47; 0.56]	6.2%
Wise (1996)	30	68	0.44	[0.32; 0.57]	5.2%
Random effects model		**5112**	**0.46**	**[0.40; 0.52]**	**100%**
Prediction interval				**[0.22; 0.72]**	

Heterogeneity: I−squared=94.4%, tau−squared=0.2471

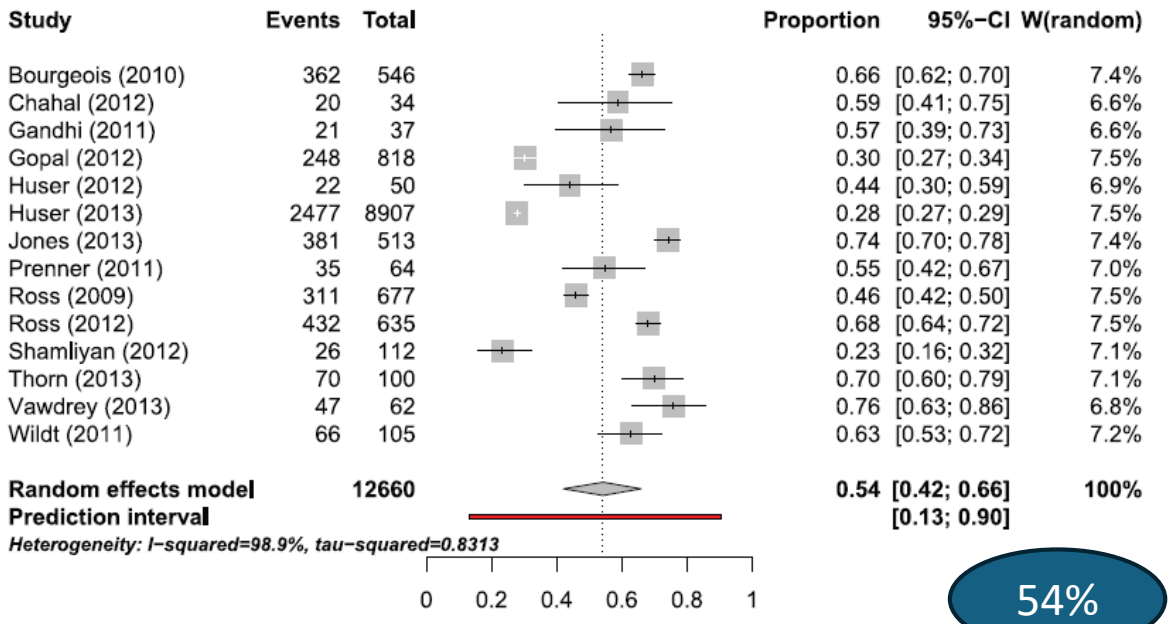
0 0.2 0.4 0.6 0.8 1

46%

Fig. 2. Weighted proportion of published studies for 17 MRPs following studies after REC approval.

doi:10.1371/journal.pone.0114023.g002

Tasa de publicación – Registros



Study	Events	Total	Proportion	95%−CI	W(random)
Bourgeois (2010)	362	546	0.66	[0.62; 0.70]	7.4%
Chahal (2012)	20	34	0.59	[0.41; 0.75]	6.6%
Gandhi (2011)	21	37	0.57	[0.39; 0.73]	6.6%
Gopal (2012)	248	818	0.30	[0.27; 0.34]	7.5%
Huser (2012)	22	50	0.44	[0.30; 0.59]	6.9%
Huser (2013)	2477	8907	0.28	[0.27; 0.29]	7.5%
Jones (2013)	381	513	0.74	[0.70; 0.78]	7.4%
Prenner (2011)	35	64	0.55	[0.42; 0.67]	7.0%
Ross (2009)	311	677	0.46	[0.42; 0.50]	7.5%
Ross (2012)	432	635	0.68	[0.64; 0.72]	7.5%
Shamliyan (2012)	26	112	0.23	[0.16; 0.32]	7.1%
Thorn (2013)	70	100	0.70	[0.60; 0.79]	7.1%
Vawdrey (2013)	47	62	0.76	[0.63; 0.86]	6.8%
Wildt (2011)	66	105	0.63	[0.53; 0.72]	7.2%
Random effects model		**12660**	**0.54**	**[0.42; 0.66]**	**100%**
Prediction interval				**[0.13; 0.90]**	

Heterogeneity: I−squared=98.9%, tau−squared=0.8313

0 0.2 0.4 0.6 0.8 1

54%

Fig. 3. Weighted proportion of published studies for 14 MRPs following studies after trial registration.

doi:10.1371/journal.pone.0114023.g003

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Revisión sistemática

Tiempo (mediana) hasta la publicación (*full results*):

- Desde la autorización: resultados favorables **62,4** meses vs resultados no concluyentes **78** meses vs resultados negativos **82,2** meses
- Desde la finalización: resultados positivos **25** meses vs resultados negativos **38,5** meses

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Implicaciones

- La literatura científica representa una muestra **incompleta** de todos los hallazgos de la investigación
- La no publicación no es un proceso que ocurra por azar sino que la probabilidad de publicación en una revista está muy asociada con la **dirección de los resultados del estudio**
- Los usuarios (decisores y pacientes) no pueden basar sus decisiones en el **conjunto completo** de la evidencia disponible, lo que podría implicar:
  - **El uso de intervenciones no efectivas o perjudiciales**
  - **El mal uso de los recursos en salud**
- **Investigación redundante**
- **Implicaciones éticas**

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Iniciativas

- Decisión del ICMJE (2004) sobre el registro prospectivo
- Posicionamiento de la OMS (2015)
  - WHO Statement on Public Disclosure of Clinical Trial Results
- Campaña ALL Trials
- Iniciativa TranspariMED
- Directiva europea de Ensayos Clínicos (2015)
  - Registro prospectivo de los EC prospectivo – registro accesible
- Acceso a las bases de datos (crudos) de los estudios
  - Reanálisis por terceros independientes
- Penalización de los incumplimientos (ej., registro de los resultados)

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Una responsabilidad compartida de todos

- Promotores * – Cumplir las normativas
- Investigadores – ¡Exigir sus derechos! (acceso a los datos, participación en la redacción de las publicaciones y derecho a discrepar) (→ no ser meros reclutadores)
- Centros – Políticas y educación en integridad de la investigación (BPC)
- Comités de Ética – Revisión cláusulas de los contratos (propiedad de los datos, compromiso de registro del estudio y difusión de los resultados)
- Agencias financiadoras – Penalización de “incumplidores”
- Agencias reguladoras – Exigir registro prospectivo de protocolo y de los resultados (agregados)
- Revistas científicas – Exigir registro prospectivo, verificar publicación selectiva y retractaciones, adherencia a las guías de reporte
- Síntesis de evidencia – Nuevos métodos para detectar sesgos de diseminación y ‘penalizar’ la certeza de la evidencia
- Medios de comunicación – Sensibilización y denuncia pública

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Muchas gracias por su atención

Es responsabilidad de todos comprometernos seriamente con la integridad de la investigación (transparencia) para restaurar la **confianza pública** en el sistema de investigación

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