Clinical trials publication rate in Spain: how far have we come?

Authors: Gerard Urrútia[1,2,3*], Xavier Bonfill[1,2,3], Javier Zamora[3,4], Juan Erviti[5]

1. Institut d'Investigació Biomèdica Sant Pau (IIB Sant Pau), Barcelona, Spain.
2. Centro Cochrane Iberoamericano (CCIb), Barcelona, Spain.
3. CIBER Epidemiología y Salud Pública (CIBERESP), ISCIII, Madrid, Spain.
4. Hospital Universitario Ramon y Cajal, Clinical Biostatistics Unit, IRYCIS, Madrid, Spain - Cochrane Madrid.
5. Sección de Innovación y Organización, Servicio Navarro de Salud – Osasunbidea, Pamplona, Spain – Cochrane Navarra.

Introduction: Publication bias is a highly complex and common problem in the area of clinical research[1]. Its adverse consequences range from the waste of resources to the unnecessary duplication of studies and the distortion of the public perception about the benefits and harms of treatments/interventions which can ultimately lead to wrong clinical and health care decisions (usually overtreatment and inappropriate use of low-value interventions). Data suggest the mean rate of publication of randomized controlled trials (RCTs) is around 50%[2], although there has been a trend towards improvement in recent years[3].

A previous study conducted by our group on a sample of 303 clinical trials in the area of cancer authorized by the Spanish Agency of Medicines and Medical Devices (AEMPS) between 1999 and 2003, with a mean follow-up of 12 years, found a publication rate of 55.4%[4].

Objectives: To assess the publication rate of RCTs in the area of cancer authorized by the AEMPS ten years after a previous survey.

Methods: We performed an observational study consisting in a cohort of RCT records with a 9-year follow-up period. We identified all the RCTs authorized by the AEMPS in 2013 corresponding to the therapeutic area of cancer from the Spanish Registry of Clinical Studies (REec). We identified the corresponding publications from the same registry, clinicaltrials.gov, through specific searches in Pubmed and, ultimately, through the Google meta-search engine.

Results: A total of 215 RCTs were identified. Of these, 129 (60.0%) had been published and 86 (40.0%) had not. A vast majority (87.9%) had been also registered in clinicaltrials.gov. Of these, in 143 (75.7%) the final results and/or the bibliographic reference of the publication(s) corresponding to the study were also available on the web. Surprisingly, in only 119 cases, the final results were also available on the REec.

Median study size was 181 (IQR 82 to 450) (Table 1). International multicentre (86.5%), phase II (39.5%) or phase III (38.1%) studies, with a commercial sponsor (84.7%) predominated.

The most frequent tumor sites were breast cancer (14%), oncohematologic cancers (11.2%), lung cancer (10.7%), lymphoma (7.4%), prostate cancer (4.7%) and melanoma (5.6%).

The main outcome most studied was progression-free survival (27.0%), followed by the response rate (18.1%) and overall survival (14.4%).

Regarding the origin of the sponsor, 78 (36.3%) of the RCTs were from Spain, followed by the USA (n=65), Switzerland (n=16), Germany (n=15) and Belgium (n=14).

Table 1. Study size

Category	N	%
0-100	67	31,2
101-200	49	22,8
201-500	57	26,5
501-1000	28	13,0
> 1000	14	6,5

The international multicentric nature of the study was positively associated with the publication of the study (int.: 65.1% vs nat.: 27.6%) (*p* 0.001), as was the size of the study (published: median 300 [IQR 119–525] vs non-published 115 [60–266]) ($p < 0.014$). Type of sponsor was not associated with the publication rate (commercial: 62.1% vs non-commercial: 48.5%) (*p* 0.177).

Conclusion: There has been an increase in the publication rate of RCTs in the area of cancer authorized in Spain in the last 10 years. Considering also the aggregated results reported on the clinicaltrials.gov registry website, the reporting rate reaches 75.7%, almost 20% (absolute) higher than 10 years ago. A common cause for non-publication was premature discontinuation of the study, usually due to lack of recruitment.

Although the trend is favorable, there is still much room for improvement. It is mandatory that all actors involved be more proactive in order to ensure compliance with current legislation and ethical codes that require full publication and transparent dissemination of results.

[1] Song F, et al. Open Access Journal of Clinical Trials 2013;5:71–81
[2] Schmucker et al. PLoS One. 2014 Dec 23;9(12):e114023
[3] Speich B, et al. PLoS Med. 2022 Apr 27;19(4):e1003980
[4] Urrútia G, et al. J Clin Epidemiol. 2016 Sept;77:84-90