ALLIANCE *FOR* TRANSPARENCY *IN* HEALTH RESEARCH

Position paper by the „Alliance for Transparency in Health Research“

Unpublished study findings endanger evidence-based health care

Summary:

» It has been estimated that around one-third of all clinical trials conducted by German university hospitals remain unpublished. As a result, the evidence base is distorted and this can ultimately result in poorer treatment.

» The non-publication of study results undermines the trust of study participants who want to contribute to medical progress.

» Research funds for studies that are not published are wasted (research waste).

» For clinical research on medicinal products and medical devices, the legal publication obligation has already solved the problem of non-publication to some extent. However, for clinical studies with other interventions (such as surgery, dentistry or psychotherapy), the non-compliance with publication remains an issue.

» Contrary to popular belief , the publication of (summary) study results within a year after completion (as suggested by the WHO) does not interfere with a later regular peer reviewed publication in a scientific journal.

» To ensure efficient monitoring, a centralised database is necessary to collate all clinical trials reviewed by ethics committees. It is important to monitor and if necessary enforce the publication of study results.

» **We therefore call for the creation of appropriate framework conditions for the complete registration of studies and publication of results in Germany.**

Cochrane Deutschland · EbM Netzwerk · HTA.de · BIH QUEST Center for Responsible Research

as of 14 May 2024

1. What is the problem?

The research conducted into new diagnostic and therapeutic procedures in clinical trials provides the foundation for the development of patient-oriented, effective and efficient medicine based on scientific evidence. However, it is worth noting that a significant number of clinical trials do not result in published results. For instance, approximately one-third of clinical trials conducted at German university hospitals between 2014 and 2017 remained unpublished even five years after the trial's conclusion [1].

In order to provide evidence-based healthcare, it is essential to have an up-to-date understanding of the current state of research. This can only be achieved if the results of clinical studies are published in a timely and comprehensive manner, and are made generally accessible.

The absence of study results impairs the ability of researchers to gain a comprehensive understanding of the evidence base. A distorted evidence base can lead to incorrect decisions and, ultimately, cause a negative impact on patients.Furthermore, the non-publication of results erodes the trust of study participants who want to contribute to the generation of new knowledge, with a view to advancing the field of medicine [2]. In their efforts to do so, they accept the time commitment, additional burdens such as blood sampling and possible risks from the interventions being investigated.

It is a waste of resources and patients time to fund studies that are not published. One of the reasons given by researchers for not publishing results is a lack of interest from scientific journals in „negative" results [3]. However, there are alternative publication avenues (see box). It is crucial to be aware of negative results, as well as to have information on discontinued or prematurely terminated studies in order to be able to better plan future studies, for example.

2. What is the situation in Germany?

In Germany, ethics committees and authorities assess more than 1,000 interventional clinical trials per year, based on data from the trial register. The registration of studies and the publication of their results has already made significant progress, in part due to political and media pressure [4]. However, there are still numerous completed studies whose results have not been made publicly accessible.

The scale of the problem is huge: in the example cited above [1], more than 21,000 patients participated in 188 studies, and the results were still not published five years after completion. The estimated cost of these studies was in the hundreds of millions.

Possible publication formats

The argument that the publication of results within 12 months is unrealistic, as this time is not sufficient for a peer-reviewed journal publication, can be refuted by referring to other publication formats. A summary can be submitted to the study register **(Summary Results)**. This is already a legally mandated requirement for drug and medical device studies, so this process is already familiar to many researchers. This is in line with the subsequent publication of the results in the form of a **peer-reviewed article** in a scientific journal [6]. In addition, pre-publication as a so-called **preprint** is also possible in most cases, in accordance with the recommendations of the International Committee of Medical Journal Editors (ICMJE) [6].

The solution to the problem is the **registration of clinical trials in public trial registers before they begin (prospective) and the prompt and complete disclosure of all trial results**. The Declaration of Helsinki, the ethical code of conduct for research involving humans, explicitly requires both.

Furthermore, doctors in Germany are also bound to this via their professional codes of conduct. Since 2017, the World Health Organization (WHO) has been urging governments worldwide to implement both into national law [5].

The EU has already established a legal basis for the prospective registration and publication of summaries of study results for clinical trials on medicinal products (EU Regulation 536/2014) and certain medical devices such as stents or pacemakers (EU Regulation 745/2017). However, studies on interventions that are not yet sufficiently regulated, for example, those used in surgery, dentistry or psychotherapy, are not covered by the aforementioned legislation.

3. What are the necessary steps?

It is recommended that all prospective, interventional clinical studies be **registered in a WHO-accredited study registry** and that **results be published within 12 months** of the end of the study. This would align with Articles 35 and 36 of the Declaration of Helsinki and the WHO guidelines. The Health Data Utilisation Act (GDNG) requires that research involving the use of patient data from healthcare be registered and published. These requirements apply equally to clinical studies in accordance with the Declaration of Helsinki. However, there is currently no legal requirement for the registration and publication of results for all clinical trials conducted in Germany. This could be achieved through the Medical Research Act (MFG), which is currently in draft form.

To resolve the issue, minimal additional resources would be required to implement the necessary steps as listed below:

1. **Registration and central overview of studies:** It is recommended that ethics committees work towards the early and complete registration of all clinical studies in a suitable study register (e.g. DRKS, CT.gov) and also make data available for central consolidation (ideally automated).

2. **Monitoring of the registry entry and publication:** It is recommended that study organisers be reminded regularly (ideally automatically) of their obligation to update the study registry entry and to publish the study results on time.

3. **Review of incentives and sanctions:** It is recommended that research funders, universities and/or ethics committees consider implementing specific incentives and means of exerting pressure, such as taking previous publication behaviour into account when reviewing funding or ethics applications. This could be in the form of performance-oriented allocation of funds (LOM) or paying out a residual amount of funding only when summaries of study results are published.

We request that the Federal Ministry of Health and the Federal Ministry of Education and Research establish an appropriate framework for complete study registration and publication of results in Germany, and propose a legal regulation. The Alliance for Transparency in Health Research is available to provide advice on the development of solutions.

Who we are

This position paper was written by the Alliance for Transparency in Health Research. Cochrane Germany, the German Network for Evidence-based Medicine, HTA.de and the BIH Quest Centre are members of the Alliance. The authors are Till Bruckner, Valérie Labonté (Cochrane Germany), Jörg Meerpohl (Cochrane Germany), Stephanie Müller-Ohlraun (BIH QUEST Centre), Matthias Perleth (HTA.de), Georg Rüschemeyer (Cochrane Germany), Stefan Sauerland (EbM Network), Susanne Schorr (BIH QUEST Centre) and Daniel Strech (BIH QUEST Centre).

This position paper is supported by

Contact

Contact for the press and further inquiries:

Valérie Labonté, Cochrane Germany

Tel.: +49 (0)761-270-85324

E-Mail: labonte@cochrane.de

Sources

[1] Riedel N et al. Results dissemination from completed clinical trials conducted at German university medical centers remained delayed and incomplete. J Clin Epidemiol. 2022 Apr;144:1-7.

[2] Hamilton DG et al. Attitudes of people living with cancer towards trial non-publication and research participation. BMJ Evid Based Med. 2024 Jan 19;29(1):64-66.

[3] Scherer RW et al. Authors report lack of time as main reason for unpublished research presented at biomedical conferences: a systematic review. J Clin Epidemiol. 2015 Jul;68(7):803-10.

[4] Franzen D et al. Institutional dashboards on clinical trial transparency for University Medical Centers: A case study. PLoS Med. 2023. Mar 21;20(3):e1004175.

[5] WHO 2017: Joint statement on public disclosure of results from clinical trials; https://www.who.int/news/item/18-05-2017-joint-statement-on-registration

[6] ICMJE: https://www.icmje.org/recommendations/browse/publishing-and-editorial-issues/overlapping-publications.html