Tidsskriftet Tidsskrift for Den norske legeforening

Register first, report later

ARE BREAN

are.brean@tidsskriftet.no
Are Brean, Editor-in-Chief of the Journal of the Norwegian Medical Association. He is a PhD and specialist in neurology.

The number of clinical trials conducted in Norway is set to double by 2025. This matters little unless the results are reported.

Photo: Einar Nilsen

Clinical research helps provide better and safer treatment, gives patients access to new diagnostics and methods of treatment, helps rationalise the health services and increases value creation in the Norwegian healthcare industry. The health trusts have a statutory responsibility for clinical research. Many of them have taken this task too lightly. Of the 2 500 agenda items that the health trusts dealt with in 2019, only 23 focused on research as their main topic (1). The university hospitals did not do much better: in the same year, research was the main topic in only 3 out of 586 agenda items in board meetings (1). Moreover, attention and resource use appear to go hand in hand: most of the health trusts spent less than one per cent of their operating costs on research in that year (1).

In January 2021, the National Action Plan for Clinical Trials was launched (2). Hereafter, clinical research shall be 'an integral component of all clinical practice and patient treatment'. The goal is to double the number of clinical trials, and to ensure that 5 per cent of all patients in the specialist health service participate in clinical trials by 2025 (2).

If this research is to benefit patients, however, research alone will not be sufficient; the results also need to be published and reported. Because research which is not published is meaningless. Many health trusts and other public funding agencies for research appear to have forgotten this fact. While it has been made mandatory to register a project before a clinical trial starts, no overview exists at all of whether the results have been published – or of whether the studies have been completed in the first place.

However, according to common European regulations, clinical research on drugs is meant to be an exception. Since 2004, all clinical drug trials and their results have been subject to mandatory registration in the European EudraCT database (3). The TranspariMED initiative has recently reviewed the registration in EudraCT in a number of European countries, in Norway's case in collaboration with the Dam Foundation (4). The results are disheartening. In Norway, results from clinical trials were reported far less frequently than in any other country. Thirteen Norwegian sponsors of trials have registered a total of 204 clinical trials since 2004. Results are available in the register for only 6 of these 204. Norwegian university hospitals are the worst offenders. Oslo University Hospital is lowest on the list, having failed to report the results of 44 studies they have initiated (4).

> ***«In Norway, results from clinical trials were reported far less frequently than in any other country»***

The consequences can be dire. Published results can always be retrieved through searches in PubMed or other research databases. However, when a registered clinical trial cannot be found by these means, it is impossible to determine whether it has been completed, but not published, whether it is still ongoing or whether it has been terminated prematurely.

This increases the risk of bias both in systematic reviews and in other documentation on drugs. There is good evidence that drug trials sponsored by the industry tend to report more beneficial results than trials that have a non-commercial sponsor (5). This is problematic, given that the results of 68 per

cent of European clinical trials that were sponsored by pharmaceutical companies were also reported, while this was the case for only 11 per cent of the trials that had a non-commercial sponsor (6). This is not only a Norwegian or European problem. In the United States, only 41 per cent of clinical trial results were registered according to the regulations in ClinicalTrials.gov, and there too, far more frequently when the trial was sponsored by the pharmaceutical industry than by a non-commercial sponsor (7). Whether the deficient registration of Norwegian results serves to increase the bias in our overall knowledge about the efficacy and adverse effects of drugs is impossible to determine. After all, we do not know which of the 204 Norwegian trials without any registered results have been published – or if not, why not.

If we are to achieve the goal of including 5 per cent of patients in clinical trials by 2025, the patients and their doctors must be able to find out what clinical trials are open for inclusion. They should be able to do so at Helsenorge.no (8). However, a review of 100 trials that according to the ClinicalTrials.gov international research database were open for recruitment in Norway as of January 2021 showed that only half of them were registered in Helsenorge.no (1). This voluntary service can therefore in no way replace the need for health trusts and universities to follow up their obligation to report the results of trials where they should be reported. Only then can we be certain that the results become 'an integrated component of clinical practice' (2). 'Ask first, investigate later', I wrote in an editorial nearly ten years ago (9). And I ought to have added: 'and report when you are done'.

LITERATURE

1. Riksrevisjonens undersøkelse av kliniske behandlingsstudier i helseforetakene. Riksrevisjonens dokument 3:9 (2020–2021). https://www.riksrevisjonen.no/rapporter-mappe/no-2020-2021/undersokelse-av-kliniske-behandlingsstudier-i-helseforetakene/ Accessed 16.6.2021.

2. Nasjonal handlingsplan for kliniske studier 2021–2025. Oslo: Helse- og omsorgsdepartementet, 2021. https://www.regjeringen.no/contentassets/59ffc7b38a4f46fbb062aecae50e272d/207035_kliniske_studier_k6_b.pdf Accessed 16.6.2021.

3. Eudra CT. https://eudract.ema.europa.eu/ Accessed 16.6.2021.

4. Bruckner T. Clinical trial transparency in Norway. Mapping unreported drug trials. Oslo/Bristol: TranspariMED, 2021. https://dam.no/content/uploads/2021/06/Clinical-Trial-Transparency-In-Norway-2021.pdf Accessed 16.6.2021.

5. Lundh A, Lexchin J, Mintzes B et al. Industry sponsorship and research outcome. Cochrane Database Syst Rev 2017; 2: MR000033. [PubMed]

6. Goldacre B, DeVito NJ, Heneghan C et al. Compliance with requirement to report results on the EU Clinical Trials Register: cohort study and web resource. BMJ 2018; 362: k3218. [PubMed][CrossRef]

7. DeVito NJ, Bacon S, Goldacre B. Compliance with legal requirement to report clinical trial results on ClinicalTrials.gov: a cohort study. Lancet 2020; 395: 361–9. [PubMed][CrossRef]

8. Helse Norge. Kliniske studier. Forskning på effekten og bivirkningene av nye legemidler og behandlingsmetoder. https://www.helsenorge.no/kliniske-studier/ Accessed 16.6.2021.

9. Brean A. Spør først, forsk siden. Tidsskr Nor Legeforen 2012; 132: 1425. [PubMed][CrossRef]

Publisert: 28 June 2021. Tidsskr Nor Legeforen. DOI: 10.4045/tidsskr.21.0502