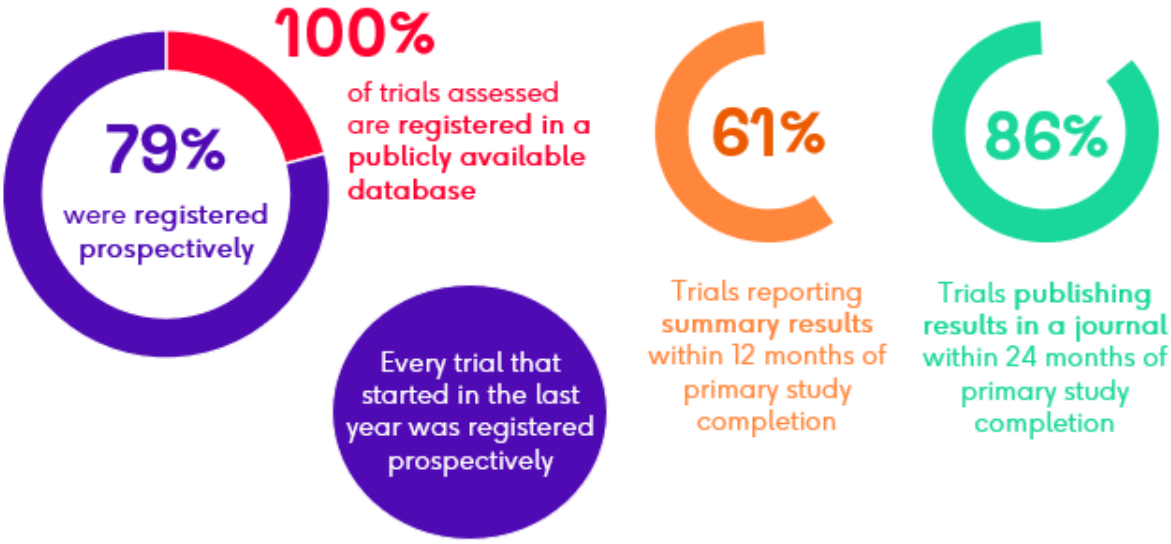
April 2024

2024 review of transparency practices for clinical trials funded by the British Heart Foundation

Clinical trials provide crucial evidence about whether new treatments, tests or pathways of care are safe and effective. Whether the results are positive or negative, these studies help to answer important questions - both for people living with a health condition and the clinicians providing their care. But for clinical trials to lead to improvements in care, it's important that information about how they are carried out and their results are made publicly available. Carrying out clinical research openly and transparently helps with interpretation and implementation of any findings, while also playing a key role in reducing research waste (for example, by helping to minimise duplication of research efforts).

British Heart Foundation (BHF) policies for researchers conducting clinical trials therefore require that key information about BHF-funded clinical trials, and their results, is made publicly available in a timely manner (see Appendix I for details). In 2023, we published our first formal review of compliance with BHF's trial registration and reporting policies and committed to regular reviews moving forward, to continue to gain insight into areas for improvement and help assess whether changes we have made (see Appendix II) are having a positive impact.

Key findings



How we carried out the review

This review includes clinical trials supported by BHF's Clinical Study Grant and Special Project Grant schemes between the 2010/2011 and 2023/2024 financial years. Data for this analysis was collected by manually checking the relevant clinical trial registry records. BHF has funded 51 clinical trials[1], with a combined grant value of £57.6m, via these schemes during this period.

[1] This figure excludes trials funded through a previous annual joint call for Clinical Study Grants with the Stroke Association.

Prior to 2017, such studies were assessed and governed by BHF's Chairs & Programme Grants Committee (CPGC). In 2017, a new Clinical Studies Committee (CSC) was set up to help encourage high quality clinical study applications and to monitor the performance and governance of ongoing studies. The CSC membership includes individuals with specific expertise in the design and conduct of multicentre clinical trials, and representatives of a Patient Advisory Group. At the time of the CSC being established, our policies for researchers conducting clinical trials were also formalised on our website.

Trials were excluded from the below analyses if:

- The BHF grant was to support the UK arm of an international trial (i.e., the recipient of the BHF funding is not the principal investigator for the overall trial) – 7 trials excluded.
- The BHF grant was supporting extending follow-up of an existing trial, where BHF was not the original funder – 2 trials excluded.

What we found

Trial registration

Of 39 clinical trials that have completed or have started recruiting participants as of 31/03/2024:

- 100% are publicly registered in a clinical trials registry.
- 79% (28/39) were registered before the start of recruitment *(1% increase since 2023).*
- The rate of prospective registration has improved over time. 100% (3/3) of trials that began recruiting since the previous review were registered prior to the start of recruitment. Overall, 92% (12/13) of trials awarded funding since 2017 have been registered prospectively, compared to 73% (19/26) of trials funded prior to the CSC being established.

Keeping the registry up to date

To monitor whether registry entries are being kept up to date in accordance with our guidance, we checked whether:

- Entries for completed or prematurely terminated trials included the final number of participants enrolled. 84% (21/25) had the final enrolment number available *(3% increase since 2023).*
- Entries for prematurely terminated trials had been updated to reflect premature closure and included the date of termination. This was the case for 60% (3/5) of these trials.
- The full protocol was available on the registry. Access to a sufficiently detailed study protocol is necessary to be able to interpret results, so BHF requires that the full protocol is made available within 12 months of primary study completion. 88% (16/18) of trials that completed or terminated at least 12 months prior to 31/03/2024 had the full protocol uploaded to or linked on the registry *(3% increase since 2023).*

Disclosing summary results

BHF expects that summary results are publicly reported within 12 months of primary study completion. For this analysis, summary results were considered reported if they were presented at a scientific conference, or posted to the trial's registry record or website.

Of 18 trials that have completed at least 12 months prior to 31/03/2024:

- 61% (11/18) reported summary results within 12 months of study completion *(no change since last review)*
- 33% (6/18) reported summary results >12 months after study completion (5 of these within 24 months). Of note, 2 of these trials experienced delays in obtaining participant outcome data from NHS England.
- 1 trial has not yet reported summary results, and completed >24 months ago.

After the last review, a new requirement was added to our policies for summary results to be made available *on the trial registry* within 12 months of primary study completion. The rationale for this was that this may enable results to be made public more quickly, help to avoid any barriers associated with publishing neutral results, and doing so does not prevent the results from being subsequently published in a journal. Results can be made available on the registry in two main ways – basic results (including 'raw' data on participant flow, baseline characteristics, outcome measures and adverse events) can be submitted by the investigators to the registry, or publications can be linked on or automatically indexed to the registry record.

Of 17 trials that have disclosed results:

- 88% (15/17) have results available on the registry. 35% (6/17) had results added within 12 months of primary study completion.
  - 18% (3/17) had raw results posted to the registry.
  - 88% (12/17) had the primary results publication linked on or indexed to the registry.
  - 12% (2/17) had both raw results posted and the primary results publication available on the registry.
- 12% (2/17) did not have results available on the registry. However, in both of these cases the results had been submitted to the registry by the investigators, but had not yet passed the registry's quality control review (Figure 1).

Figure 1. Example of delayed timeline for quality control review of results submitted to ClinicalTrials.gov. Note that their guidelines for submitting results state review process takes up to 30 days.

Submission Cycle	Results Submitted to ClinicalTrials.gov	Results Returned after Quality Control Review
1	August 2, 2023	March 8, 2024
2	March 18, 2024	

Publishing results

BHF expects that the primary results of a clinical trial are published in a peer-reviewed journal or platform within 24 months of primary study completion. All publications should also be linked on the registry record and include the unique trial ID number.

Of 16 trials that completed at least 24 months prior to 31/03/2024:

- 94% (15/16) had results published in a peer-reviewed journal *(decrease since 2023, was 100%)*.

- 86% (13/15) of studies which had published did so within 24 months of study completion *(no change since 2023)*. 13% (2/15) published primary results >24 months after study completion.
- 93% (14/15) had the primary results publication linked on the registry *(no change since 2023)*.
- 100% had the trial ID included in the primary results publication *(no change since 2023)*. 93% (14/15) had the trial ID number included in all publications. One trial had the trial ID missing from 3 out of 16 publications.

Summary and next steps

This review provides some evidence that registration practices for BHF-funded clinical trials are continuing to improve, but highlights that further improvement is needed regarding the timely reporting of results. This is particularly important in the context of upcoming changes to UK clinical trial legislation, which will include a requirement for summary clinical results to be disclosed within 12 months of study completion.

100% of BHF-funded trials are registered in a publicly available database and a growing percentage of these are registered before the trial starts recruiting. While only a small number of trials (3) began recruiting since the past review, it is encouraging that each of these trials was prospectively registered. Moving forward, we are continuing to remind Clinical Study Grant holders to register their clinical trial at the point of grant activation.

Registry records are also largely being kept up to date, but we will continue to remind grant holders of the importance of doing so at relevant points in the grant lifecycle. Investigators who hold a BHF Clinical Study Grant are asked to complete regular progress reports (every 6-12 months), plus a final report due 3 months after the grant end date, which include prompts about keeping the registry record up to date. Occasionally, where the trial is not progressing as expected, our Clinical Studies Committee may recommend that the trial and BHF funding for it is terminated. In this review, we found that the registry records for prematurely terminated have not always been updated to reflect this, and will follow up with individual trial teams to ensure this is done.

BHF offers many other types of grant in addition to Clinical Study Grants, some of which can be used as a mechanism to support smaller-scale clinical trials. Since February 2024, the final report for other types of BHF grant now also includes questions about clinical trial registration and reporting. While BHF's high-value clinical trials portfolio will continue to be the focus of these reviews, in the future the responses to these questions will be useful to assess whether our policies on clinical trials are being adhered to across the wider BHF research portfolio.

After the last review, we amended our policy on the disclosure of clinical trial results to require that results are posted *on the trial registry* within 12 months of primary study completion. However, we found that this requirement was met for only 35% of trials assessed. A major reason for this was that, in most instances, results were made available on the registry by linking to or automatic indexing of the primary results publication. This means that, in practice, results are being added to the registry in line with our requirements for the publication of results (within 24 months of primary study completion) rather than the 12-month results disclosure timeline. An alternative way of making results available on

the registry is submitting a basic results summary (see example structures for ISRCTN and ClinicalTrials.gov), but currently few investigators are doing this. Notably, the two trials assessed which did not have results available on the registry had submitted results, but these had not passed quality control review. In these two cases, there appears to be a substantial delay between submitting results to ClinicalTrials.gov and quality control review, while the process for submitting results to ISRCRN appears to be much faster. Moving forward, we will continue to encourage trial teams to register with ISRCTN (BHF's preferred registry) which may help to mitigate this.

Another barrier to results being disclosed in a timely manner for some more recently completing trials has been delays in obtaining participant outcome data from NHS England. In recent years, many BHF-funded trials have been using this service to follow up their participants (in England) using routinely collected healthcare data, which can be more cost effective than other follow up mechanisms. However, several trial teams have reported issues with applying for and delays receiving data from NHS England, and there have been cases where this has led to results not being disclosed within 12 months of primary study completion. BHF's senior leadership plans to engage with NHS England regarding this issue, which in some instances has also had financial implications for BHF (due to grant timelines needing to be extended to allow for these delays).

Finally, we will be following up with individual trial teams where this review has identified studies that are not currently compliant with our policies, and to better understand any barriers to submitting summary results to the registry. In addition, we will continue to share lay summaries of the findings of BHF-funded trials on our website as results become available. The next full review will be in April 2026.

Appendix I. Transparency requirements assessed in this review

- BHF-funded clinical trials must be prospectively registered (before the first participant is recruited) in a publicly available database.
- The registry records must kept up to date.
- Summary clinical trial results must be made publicly available within 12 months of primary study completion (defined as the last data collection time point for the last subject for the primary outcome measure). This should include *adding results to the trial registry record*.
- The main findings must be published in a peer-reviewed journal or platform within 24 months of primary study completion.
- The trial identification number (from the registry) must be included in all publications.

Appendix II. Changes made since the 2023 transparency review

- **Registration:** Clinical Study Grant holders are now reminded of the need to prospectively register their clinical trial at the point of grant activation. For other grant types, the final report now asks whether the research included a clinical trial (as defined by the WHO), and if so, for information on where it is registered/a justification for why it is not registered.

- **Keeping the registry up to date:** All BHF grant holders must submit a final report 3 months after the grant end date. For Clinical Study Grants, and as appropriate for other grant types, final reports now ask for confirmation that a plan is in place to maintain updates to the registry until the clinical trial is fully completed (including posting results to the registry).
- **Disclosing results:** The requirement for summary results to be posted *on the trial registry* within 12 months of primary study completion (in line with WHO guidelines) was added after the last review. The rationale is that posting trial results to the registry is typically much faster than publishing in an academic journal, which may help to avoid any barriers associated with publishing neutral results, and doing so does not prevent the results from being subsequently published in a journal.