12 June 2025

STEPCARE: SOP for Substudies

Content

Categories of substudies

1. STEPCARE substudies are studies designed prior to the analysis of the primary data.
    a. Studies based on data already collected in the study case report forms.
    b. Studies requiring additional data collection.
    c. Biobank substudies: Suggestions for studies based on the Biobank may be submitted, and the international steering committee will process these requests prior to locking of the database.
2. STEPCARE post-hoc analyses are studies designed after the analysis of primary data.
    a. Studies based on data that have already been collected.
    b. Studies requiring additional data collection.

Instructions for substudy proposals

All substudies proposals must be submitted in English. We encourage submissions of substudies in category 1 to be made as early as possible, allowing sufficient time for review and consideration of logistics. All substudy proposals should ideally be developed by the substudy Principal Investigator in collaboration with their National Investigator(s) or members of their National Investigator's team. The National Investigator will have a coordinating role for substudies from their region and liaise with the STEPCARE Trial Management Group.

The STEPCARE Trial Management Group will review all proposals and has an open and inclusive policy towards substudies, provided that two key criteria are met:

- The substudy will not have an adverse effect on the main trial.
- The research question and methodology are scientifically sound.

To prevent potential bias in the substudy results due to missing data, all reasonable attempts must be made to include all potential participants at a participating site during the recruitment period. The STEPCARE Trial Management Group encourages the development of comprehensive protocols and statistical analysis plans that provide detailed, predefined descriptions of the methodology. Additionally, they advocate for the publication and registration of these

documents. A synopsis of the substudy should be provided in a 2-page document, including key references to support the substudy.

Study synopsis (2-page document)

1. Title
2. Rationale for study with a clear statement of the hypothesis(es)
3. PICO
4. Data requirements from study CRF
5. Additional data required*
6. Sample size/power estimations
7. Statistical analysis plan
8. Lead Investigators
    a. Co-Investigators
    b. Participating sites
9. Funding
10. References

* Including logistics regarding additional data collection. The inclusion of additional items in the eCRF or linkage to a separate online platform (e.g. REDCap) may be possible. However, this will depend on the proposed data and timing, and associated costs may exist.
If you wish to include new items in the eCRF, please note that some lead time is required. An Excel template must be completed before Spiral can provide a quote for integrating the new data points. Additional time should be expected for the actual implementation of the changes in the eCRF.

Please submit all substudy synopses to Caroline Kamp from the Copenhagen Trial Unit (CTU) at caroline.kamp@ctu.dk

Approval process

The CTU will facilitate the contact between Principal Investigators and the STEPCARE Trial

Management Group. The CTU will bring substudy proposals for approval at weekly meetings with the STEPCARE Trial Management Group. The CTU will inform Principal Investigators after approval and upload information on approved substudies at STEPCARE.org/substudies.

Publication

Manuscripts based on substudies should not be submitted for publication before the primary outcome results of STEPCARE are published.

Additional notes on substudies

We anticipate that many approved substudies will follow, as with our previously conducted studies. The Principal Investigator of each substudy is responsible for funding, data-sharing agreements, and obtaining ethical approval (depending on country and jurisdictional requirements), which should be carefully obtained to ensure no adverse impact on the main STEPCARE trials.