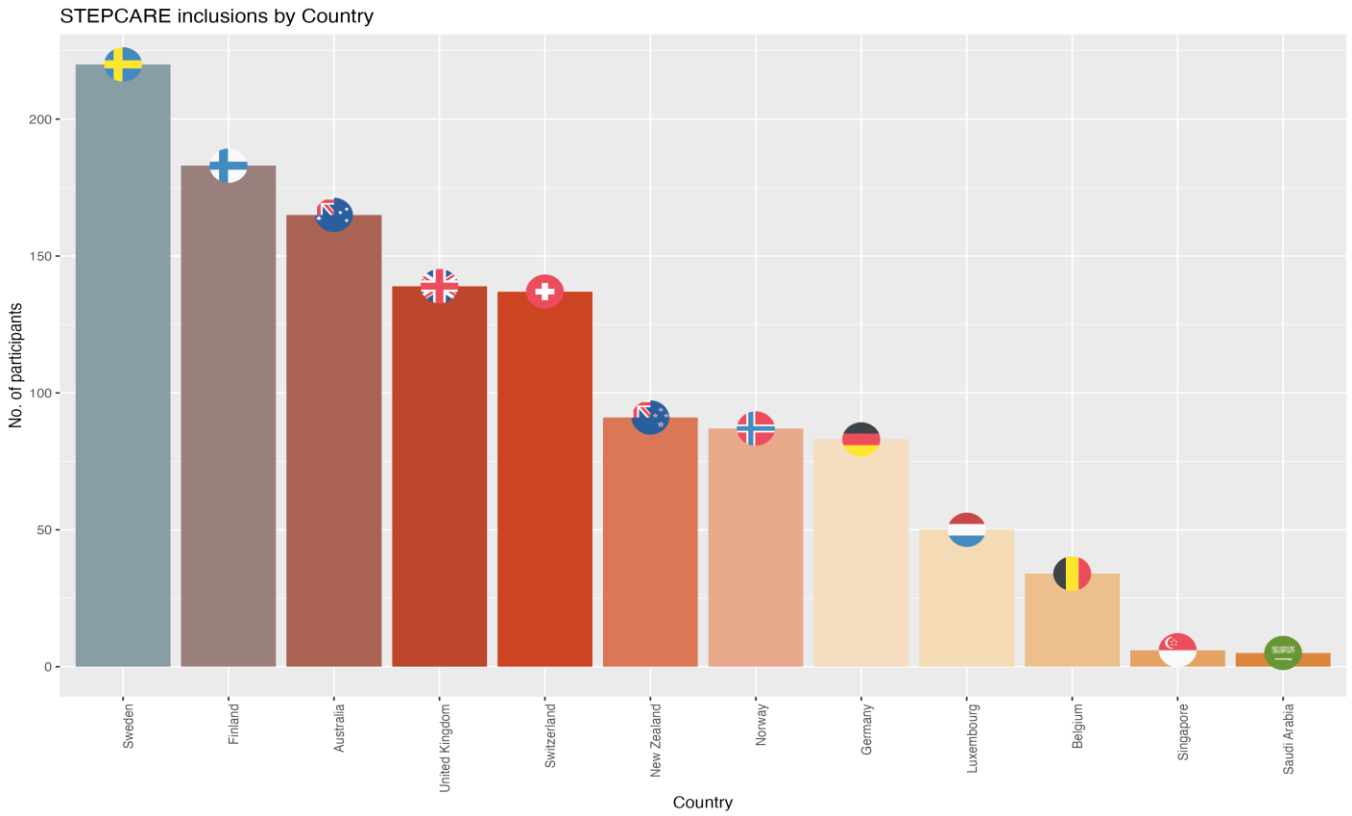
Dear all,

Four weeks into 2025 STEPCARE have continued forward. We are recruiting with around 4 participants a day and we have passed 1200 included mark! This is a great achievement for our truly international trial group. Congratulations! And still, we have a few more countries and sites ready to start, so we look at the future with confidence.

At 1250 participants recruited the clock starts ticking for our next interim analysis. This will likely be in the first week of February 2025, which means that 30-day follow-up (the primary outcome for the interim analyses) will be early March 2025. We will give all sites 30-days to complete all data in the eCRF. Data will need to be ready for the interim analysis by early April 2025. Please enter as much data as possible into the eCRF. We can expect a second report from the data safety monitoring committee well before the investigator meeting in June in Helsinki (see below).

We have realized the exclusion criterion no.2 of the STEPCARE Protocol 1.2: "suspected or confirmed intracranial hemorrhage" in the lay out of the eCRF screening/randomization module could be interpreted to be related to the cause of arrest. This is not according to the intention of the protocol. All suspected or confirmed intracranial hemorrhages should lead to non-eligibility. We will amend the ICH box in the lay-out of the eCRF, to clarify and harmonize with the protocol. In the meantime, treat the question in the screening/randomization module as per the protocol. This eCRF update will be available at the end of February 2025. We have analyzed the data entry so far and our interpretation is that this has not had any practical meaning, which is reassuring.

RECRUITMENT BY COUNTRY



IMPORTANT UPDATES

MAP INTERVENTION INFORMATION: Some patients need high doses to achieve the higher MAP of greater than 85 mmHg. Some clinicians feel uneasy about this especially in the setting of a decreased cardiac function. This is a valid point, and we simply do not have the science to be sure on what to do in these situations. What we do know from the evidence is that a higher MAP target appears to be safe. In addition, we know that most patients die of brain injury and not from cardiac complications after an out-of-hospital cardiac arrest. There is also a discrepancy in Guidelines where ERC/ESICM recommend MAP>65 mmHg and the AHA and Neurocritical Care Society a MAP >80 mmHg in the absence of invasive brain monitoring. Nonetheless if the MAP target of >85 mmHg can not be achieved, consider lowering the target in increments of 5 mmHg rather than lowering the target to 65 mmHg right away. This is according to the protocol. Have the ambition to raise the target again as soon as the clinical situation has stabilized. What is also clear from previous studies is that the vasopressor need is likely to be reduced greatly after the first 24 hours. After the MAP CARE results are available, we hopefully will know much more about what MAP to target after OHCA.

NEUROPROGNOSTICATION: We have received questions on how to perform neuroprognostication if lingering effects of sedation cannot be excluded as per guideline recommendations and recommend the following: Sites should always aim to evaluate patients level of consciousness without sedation. There may be few exceptions where this is not feasible such as ventilator related complications. If these patients fulfill several sedation-independent criteria for poor prognosis, we suggest making clinical decisions based on the multimodal approach. In borderline cases or if there is uncertainty about sedation having a role in a highly malignant EEG-pattern, we strongly recommend to achieve a sedation break or consider changing to a sedative agent with short half-life (e.g remifentanil or dexmedetomidine). It is very important that prognostication and WLST for neurological reasons should be performed after 72 h, even in patients who show several criteria of very poor neurological prognosis earlier than at 72 hours. For more information, please visit FAQs at the website.

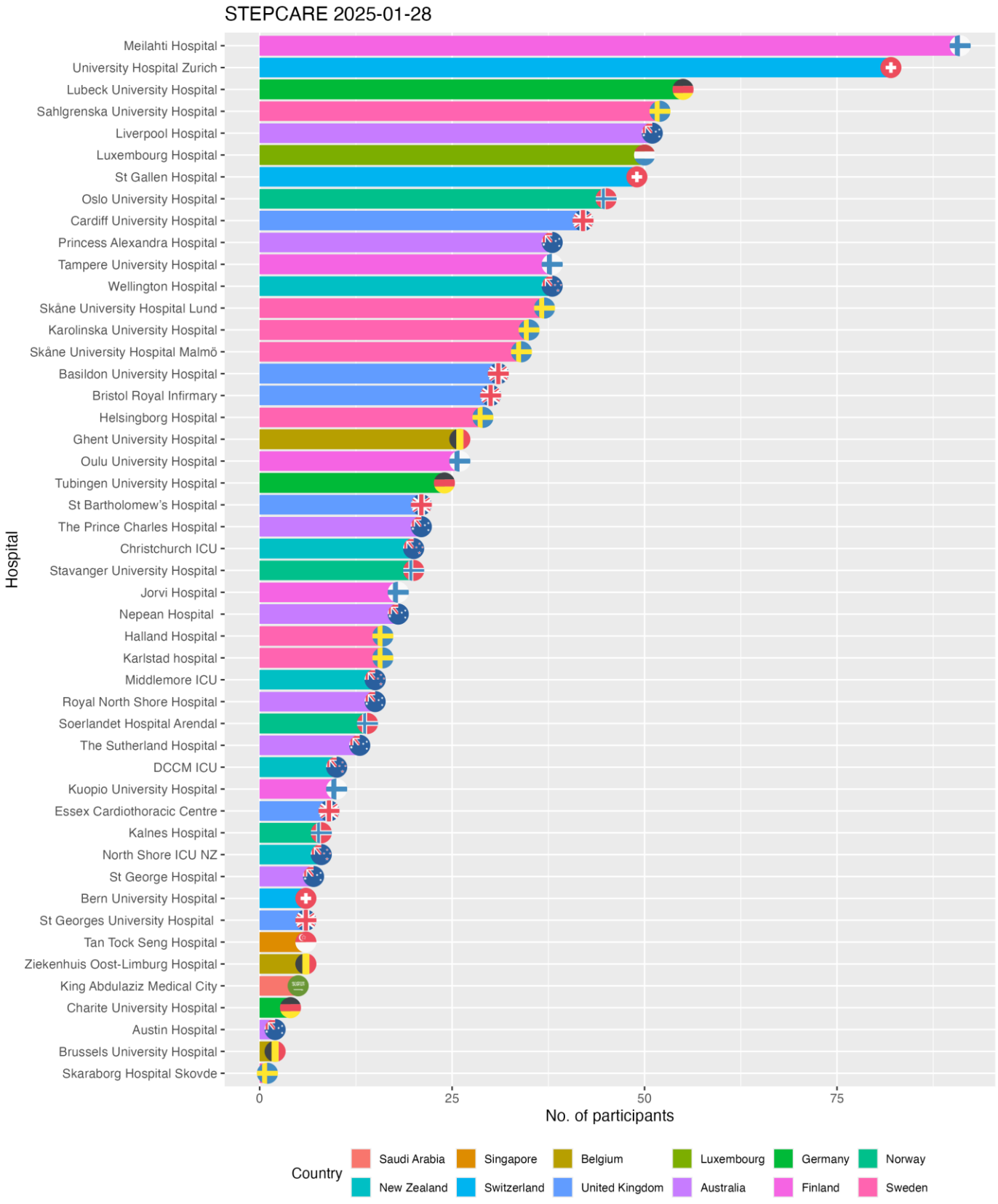
SITE NEWS: Welcome new sites:

- Brussels University Hospital, Belgium
- North Estonia Medical Centre, Tallinn, Estonia
- University Hospital of Umea, Sweden

Congratulations to top recruiting sites:

- Essex Cardiothoracic Centre, United Kingdom
- Bristol Royal Infirmary, United Kingdom
- Liverpool Hospital, Australia
- Lubeck University Hospital, Germany
- Meilahti Hospital, Finland
- Oslo University Hospital, Norway
- Zurich University Hospital, Switzerland

RECRUITMENT BY SITE



SITE FEEDBACK SESSIONS: Site feedback sessions are being scheduled with each site to go through the screening logs, recruitment, intervention performance and have time for questions and discussion. Please look out for invitations. If you have had site feedback sessions, we hope this was valuable.

STEPCARE INVESTIGATOR MEETING 2025 - HELSINKI, FINLAND:

Preparations for the meeting in Helsinki is well underway! The meeting will take place on June 16th – 17th 2025 right in the center of Helsinki at the Grand Marina Hotel and conference center. There will be two days of presentations and discussions about the STEPCARE trial. In addition to the current trial we will also have time to discuss a possible STEPCARE 2 trial. What should we study? What interventions? The registration portal will be live soon and posted on www.stepcare.org. In the interim if you have questions regarding hotel and accommodation, please contact Jenny at: jenny@mkon.se subject heading "STEPCARE Helsinki".

CRF UPDATE

We continue to work on improving the eCRF. The main updates to the eCRF since the last newsletter in December 2024 are:

- Sites that are not participating in the extended follow-up sub-study the 12-months form will not appear in the vital status form and only information for 30 -days and 6-months will appear
- Recruitment graph on the home page has been updated
- Hourly observation form: wording at the top of the page was confusing those collecting data, hence the wording has been changed to "Enter the data for each time, or where data are not available, enter data from the closest time where they were available"
- Intervention Form: the wording in the heading of "Renal Outcomes" has been modified and "during ICU stay" has been removed
- More options for reports are now able to be downloaded from "Report' tab for all sites
- A number of bugs have been fixed throughout the eCRF

There will be another sprint release to the eCRF in February 2025 and this will include the eligibility update for ICH, follow-up assessor reminder emails and the 12-month extend sub-study follow up form will be live.

As always, we would like to take the opportunity to thank all sites for their hard work and dedication towards STEPCARE trial. Keep up the amazing work!

The STEPCARE trial management committee.

For more information and updates visit: stepcare.org