

**Minutes for**

**All Stakeholders Meeting**

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**Date:** April 26, 2019

**Invited:** CRIC Steering Committee members and other stakeholders of CRIC’s programs

**Participants:** Anders Perner (AP), Morten Hylander Møller (MHM), Maj-Brit Nørregaard Kjær (MNK), Jørn Wetterslev (JW), Bodil Steen Rasmussen (BSR), Robert Winding (RW), Morten Bestle (MB), Lone Musaeus Poulsen (LMP), Ole Mathiesen (OM), Jakob Kjellberg (JK), Camilla Bekker Mortensen (CBM), Nina Christine Andersen-Ranbjerg (NCAR), Olav Schjørring (OS), Thomas Lass Klitgaard (TLK), Marija Barbateskovic (MB), Gitte Kingo Vesterlund (GKV), Anders Granholm (AG), Pernille Thornberg (PT) and Carl Johan Steensen Hjortsø (CJSH).

Agenda

1. Welcome (by Anders Perner)
2. Presentation (all, short)
3. Scientific challenges in CRIC programs presented by partners
   1. SUP-ICU (Rigshospitalet)
   2. AID-ICU (Køge)
   3. HOT-ICU (Aalborg)
   4. CLASSIC (Rigshospitalet)
   5. Reviews (CTU)
   6. Statistics (Bio KU)
   7. Socio-economics (VIVE)
4. Administrative challenges in CRIC office (by Maj-Brit Nørregaard Kjær)
5. Network and lunch/sandwich

Minutes

By 3)

1. SUP-ICU (by MHM), the results of SUP-ICU trial were published in NEJM 2018. Sub group analyses are planned to be conducted on the sickest trial population. Søren Marker is conducting a systematic review concerning all trials with prophylactic pantropazole treatment.

* To inform participants about the results of SUP-ICU trial, Danish participants receive a letter in their e-box with contact details and a link to the homepage where the results are presented for the patients [www.cric.nu/patient-sup-icu](http://www.cric.nu/patient-sup-icu)

This procedure of informing patients will be reviewed and made as a model for further trials.

1. AID-ICU (by NCAR), has enrolled 20%. There are 12 active sites and 8 pending. The optimal inclusion rate would be 55 patient/month. Hope to soon welcome Aarhus, Esbjerg, Italy and France. Expect Norway, UK and Spain to take part as well.

Initiatives to increase enrollment are to invite more sites, new invitations to participation to sites that haven’t rejected to take part. Discuss how to handle delirium interrelated between nurses and doctors. Encourage to systematically screen for AID-ICU patients.

High dropout due to withdrawn consent from relatives. One reason is that it’s a medical agency trial.

Discussion: maybe remove the box (an open option) where relatives are asked if they only want to give consent to the use of data. Expected interim analysis March 2020 (500 patients with 90 days follow-up). Encourage more information about delirium, and to downplay that is an anti-psychotic medical trial. Also, Haloperidol is not used by all sites, which may be one reason for not involving in the trial. Applies for a grant to conduct “After AID”, a developed 1-year follow-up study.

1. HOT-ICU (by OS), has 19 active sites in Denmark and sites in Schwitzerland, Norway, Finland and Netherlands. Hope to soon welcome UK and Iceland.

The inclusion rate has been rather low, and it is expected to be delayed approximately 1 year.

BSR has received a grant from Novo Nordisk Fonden for Long HOT-ICU 1-year follow-up with assessment of lung function, RBANS and EQ-5D-5L. This will be conducted on Zealand in cooperation with Køge (AID-ICU team).

Thomas Lass Klitgaard takes over the position as Coordinating Investigator for HOT-ICU from May 1st.

1. CLASSIC (by AP), started November 2018 and with 7 sites recruiting. Sweden is the first abroad and Norway is ready. Hopefully Schwitzerland and Czech will soon be ready as well. Spain, Italy, France, Finland, The Netherlands, and UK are expected to start as well, at a time.

National institution for Health Reseach (NIHR) in UK rejected CLASSIC for portfolio ressources (where if, the UK site receives money per research participant). The rejection is due to an upcoming competing UK trial. It has been suggested by the UK CLASSIC investigators to UK Critical Care Research Group (UKCCRG) that CLASSIC could be running in UK while waiting for the other trial to start.

Post meeting note: This has been accepted by UKCCRG.

1. CTU (by MB). AID-ICU; An overview of reviews and meta analyses of pharmacological interventions for delirium in ICU patients has been published. The overview showed one true systematic review (SR) and no reviews concerning haloperidol against delirium. We are conducting a SR of RCTs using haloperidol which will be updated after AID-ICU.

SUP-ICU; the SR concerning RCTs with stress ulcer prophylaxis in ICU patients supports the results of SUP-ICU. Pending is an SR in hospitalized patients receiving stress ulcer prophylaxis vs. placebo or none.

HOT-ICU; SR submitted to Cochrane indicating that high oxygen target is associated with worse outcome. This SR is going to be updated after HOT-ICU. Furthermore, we are working on a SR with the broader scope of including all trials in critically ill patients (not only ICU-trials) using high vs low targets of oxygen .

Finally, we are developing and validating a score of clinical heterogeneity in meta-analysis to be used for individual SRs and for investigating possible agreement between statistical heterogeneity and clinical heterogeneity.

1. Biostatistics, not presented for the meeting.
2. VIVE (by JK); the plan is to do health economic analyses on SUP-ICU though National Health Service (Sundhedsstyrelsen) has closed for the possibility of withdrawing data from the cost data – database. It may be necessary to find other covariates that are associated with cost data.

By 4) Instead of challenges the homepage for patients is presented (by MNK). MNK and BSR has designed [www.cric.nu/patient](http://www.cric.nu/patient) - that is intended for patients and relatives who seek further information or contact details concerning one or more trials. In SUP-ICU the way of informing participants about the results of the trial – is to give them an electronic letter with a link to the homepage ([www.cric.nu/patient-sup-icu](http://www.cric.nu/patient-sup-icu)).

MNK are welcoming all comments/ideas for the homepage. It is also discussed to involve patients and relatives to comment on the homepage.

Open discussion.

GCP; how to make the monitoring easier and the collaboration with GCP. BSR suggest settling a meeting with GCP to discuss the charge of monitoring, due to almost all money for monitoring budgeted to HOT-ICU is used half way. And, to discuss the criteria’s for accepting CRIC homepage as a common file now that everything is logged – so that we don’t have to print all documents. MNK are exploring this.

Drop out; it is discussed whether drop out due to withdrawn consent is a problem for the trial. It might be (JW), but could also be a strength that we accept withdrawals. Should be discussed as a limitation in the reports/publications of results (MHM).

Consent; could be a good idea to collect all experience of obtaining consent and conduct a manual for this.