

“Invitation to CRIC Scientific Steering Committee Meeting”  
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Dear Scientific Steering Committee Member,  
The next CRIC Scientific Steering Committee Meeting is to be held

**Date:** November 01, 2019

**Meeting time:** 10am-12am

**Place:** Rigshospitalet, Dept. of ICU 4131, Blegdamsvej 9, 2100 Copenhagen Ø

**Participating members:** Bodil Steen Rasmussen (BSR), Thorbjørn Grøfte (TG), Ingrid Egerod (IE), Jakob Kjellberg (JK), Jan Bonde (JB), Christian Gluud (CG), Morten H Bestle (MHB), Hans-Henrik Bülow (HHB), Robert Winding (RW), Theis Lange (TL), Morten H. Møller (MHM), Lone Musaeus Poulsen (LMP), Jørn Wetterslev (WET), Anders Perner (AP).

**Invited non-members:** Morten Freundlich (MF), Maj-Brit Nørregaard Kjær, CRIC project manager (MNK)

Agenda

1. Welcome (BSR) and presentation (all)
2. News from CRIC programs presented by partners (short):
   1. AID-ICU (Køge)
   2. HOT-ICU (Aalborg)
   3. CLASSIC (Rigshospitalet)
   4. Reviews (CTU)
   5. Statistics (Bio KU)
   6. Socio-economics (VIVE)
3. CRIC version 2 (AP, MHM, LMP and JB)
4. CRIC Office – budgets and accounts (MNK)
5. Next meeting
6. Other issues?

Minutes

1. Welcome to the last SSC meeting in CRIC.
   1. **AID-ICU:** there are 11 active sites in Denmark and Slagelse and Odense is pending. There are active sites in Finland, Italy is close, but haven’t randomised yet. France, Spain, and UK are pending. There are legal challenges regarding the agreement with UK.

The finishing of AID-ICU will likely be delayed with 1-year. The interim analysis is after 500 randomised patients (357 has been randomised in the moment) is expected in the spring. The Protocol has been published in Acta. There will be 1-year follow-up and as a new study also functional outcomes will be assessed as a part of Lone Museaus-Poulsens Phd. There is a high drop-out on 20%, low inclusion rate, and high mortality. AID-ICU is covering relevant knowledge though the mind-USA and two new SR has been conducted. The CRIC SR on this will supplement these and show the need for the AID-ICU trial.

Economy; the team still needs to obtain DKK 1,4 mio for the estimated budget, though it is expected to be less.

* 1. **HOT-ICU:** the last pending sites is from UK. Cardiff started this summer and recruits well. HOT-ICU is hopefully finished within a year and will be delayed by 1-year.

GCP-monitoring: the level of monitoring has been downgraded three times since the start of HOT-ICU due to an under-estimation of hours spent. The monitoring has been downgraded to the 20th patient. More Danish patients than the estimated 1500 patients have been recruited and with a new estimate being 2000 Danish patients a negotiation was needed. The new proposal defined a cost for GCP monitoring on DKK 1.408.800 compared to DKK 758.800 negotiated prior to the first inclusion of patients in June 2017. Considering that 25% more Danish patients will be recruited it ends with an additional fee on DKK 388.000 – not be negotiated.

The fund ’Regionernes Medicinpulje’ has been applied. Looking forward the solution may be to downgrade to only level 2 monitoring, which means only checking consents obtained. BSR will work on a fixed frame agreement. It is discussed if this is a political issue and maybe involve the Danish Regions.

The interim-analysis has been done and the trial continues. The Australasian ICU-ROX showed no difference in the primary outcome ‘days without ventilation’ (n=1000). LONG-ICU is funded by NNF and is ongoing measuring lung function and cognitive function after 1-year.

* 1. **CLASSIC:** There are 16 sites recruiting. Italy and Czech just started. Belgium, Spain soon ready to start.

1st interim-analysis is approved and showed clear separation between the groups. 2nd interim-analysis is expected in December. The 1-year follow-up will be performed by MNK, who is becoming part time PhD. student and part time project manager for CRIC from 1st of January 2020.

* 1. **CTU:** planned reviews have been published or submitted. JW retires by the end of the year. He therefore retires from the SCs of AID and HOT. CTU will find a replacement for JW in those SCs.
  2. **BIOSTAT KU:** The expected projects from biostatistics are nearly finished. Postdoc Aksel has taken up another position. TL has covered these projects. The remaining money from Aksels’ salary may be reclassified. TL informs that Biostatistical Dept. Focuses increasingly on RCTs and meta-analyses So, there is interest of continuing the collaboration with CRIC.
  3. **VIVI:** JK has had a meeting with the health data board and there they are close to give access to data extraction for CRIC projects. These data are needed to build a model for cost calculation when the health economic analyses are going to be conducted. The PhD student Christine Halling is back from leave and will continue the health economic analyses.

1. **CRIC v. 2**:

The Regions has been asked for support to CRIC 2, but this was not possible.

The head of departments in Denmark has been asked if there were any interest in paying a fee for CRIC 2 to exist, but this had no interest.

The last described possibility was to keep a base with methodical, administrative and financial core performance. This seems possible. AP has been granted from the Novo Nordic Foundation which could cover a CRIC v. 2 for 5-years including a full-time data manager and project manager, and a part time post doc and medical student.

It was suggested to change the ’Centre’ to ’Collaboration’ in the CRIC abbreviation.

It was discussed if we should collaborate with the medico industry – e.g. looking at have many resources used for handling a new device. A SWAT analysis to secure low risk of bias would be need if we involve with the industry.

It was agreed that collaboration should come from the agenda that we conduct independent clinical trial at the highest quality and transparency. If this is possible with the industry – then it could be possible.

It was suggested to decentralize the application for grants because the responsibility of obtaining grants shouldn’t always be centralized.

It was agreed that it will be nice if all agrees on a model making sense for all at the strategic meeting that continues to contribute science at the highest level.

JW opens a discussion of which interventions are most important for patients and therefore for CRIC to investigate and prioritise how to take the next step further and maybe up. CRIC has been ground breaking with studies thoroughly exploring interventions to come up with the best trial.

JB discuss that collaboration among many interests may challenge the process/structure of

BSR issues that we need to consider when a trial can be a ‘CRIC’ trial.

Also discussed how CRIC should be organised:

The project manager takes minutes of the meetings. The minutes could be the stamp of rules and which projects are qualified to be a CRIC project.

It was also discussed what would be the likelihood for raising a grant big enough to continue CRIC.

1. **CRIC office**. If the estimated budgets for HOT and AID holds, we will end up with a deficit -2,7mio. BUT, our experience with SUP-ICU tells us that not all case money will be collected, and some of the records on the budget is over-estimated. So maybe it doesn’t look that bad. And there are some unused funds at BIOSTAT and the ICU, RH
2. **Next meeting** depends on the strategic meeting. (At the strategic meeting it was decided to have a network meeting May 13th, 2020 before the SIM2020 symposium and that the present SC appoints a new SC before that)