### CORRESPONDENCE

# Research Collaboration Critical Care in the Netherlands: RCCCNet

#### The RCCCNet executive committee

### Correspondence

A. Slooter - a.slooter-3@umcutrecht.nl

Keywords - ICU, research, collaboration, organisation, funding

Several breakthroughs in medicine, such as the discovery of penicillin, [1] have been the merit of a single individual. Those days are over and will not return, as current medical research is more than ever a team effort. Multiple disciplines are involved due to the complexity of the studied topics and the need to use advanced research methodology that comes with very specific expertise. This holds particularly true for intensive care medicine, with heterogeneous patient populations, time-dependent determinants and outcomes, and numerous confounders. As patient-centred outcomes in intensive care medicine usually have a multifactorial aetiology, clinical studies in this field must be large enough to demonstrate meaningful effects. Large multicentre investigations are therefore needed, both for inclusion of a sufficient number of patients and for high-level scientific input.

To achieve this, collaboration is essential. However, multicentre studies are costly, to a large extent due to legal regulations that have become more and more complex. Obviously, this poses a challenge on how to optimise resources for medical research. This does not imply it is time to cut down on research efforts in our field. On the contrary, it calls for organisation of our efforts to improve the quality of intensive care medicine and to be able to compete with other medical specialties for the limited research funding.

Intensive care is at the heart of modern medicine. Without intensive care units (ICUs), high-risk therapies such as cardiac surgery or trauma surgery would take their death toll. The increase in demand for ICU facilities further underlines that modern intensive care is indispensable in modern medicine. However, fundamental issues in intensive care medicine are currently unresolved. For many routine treatments, it is currently unclear whether these are effective. New tools for diagnosis and management raise new questions, and emerging therapies need to be tested. Other medical disciplines and intensive care medicine abroad have shown how much can be gained with collaboration. [2-6]

## Examples of successful research collaborations from other disciplines in the Netherlands and from intensive care medicine abroad

Several medical disciplines have been very successful in establishing research consortia in the Netherlands, such as the Dutch Pancreatitis Study Group and the Dutch-Belgian Hemato-Oncology Cooperative Group (HOVON). [2,3] The resulting synergy of research-based patient care and clinical research have led to impressive breakthroughs. These have boosted quality of care and research, and have also given rise to opportunities to acquire new research funding.

Examples can also be found in intensive care medicine, as shown by the Australian and New Zealand Intensive Care Society (ANZICS), Canadian Critical Care Trials Group (CCCTG) and the Scandinavian Critical Care Trials Group (SCCTG). [4-6] In the Netherlands, several important investigator-initiated multicentre studies have been performed in intensive care medicine. [7-9] However, these efforts were isolated and lacked long-term organisation and structural funding.

## Aims of a collaborative research network

To improve research opportunities in the Netherlands, the Research Collaboration Critical Care in the Netherlands (RCCCNet) has recently been founded. The overall aim of RCCCNet is to improve opportunities for research in the field of intensive care medicine in the Netherlands. The first objective is to facilitate collaboration between participating ICUs in our country. We aim to create a network of ICUs from both academic and non-academic hospitals, as well as researchers active in intensive care medicine, related fields and/or research methodology. Infrastructure and expertise that has grown locally can thus be shared within the network to facilitate future collaborative efforts. This not only refers to research methodology, but also to knowhow regarding complex regulations, and the process of obtaining research funding.

The second aim is to increase the financial means to execute

these investigations. We realise that it is challenging to get a 'bigger part of the cake' as current research budgets are under pressure. Compared with many other fields of medical research (such as oncology, cardiovascular medicine and dementia) intensive care medicine has significantly less resources for research. There are no funds solely dedicated to intensive care medicine and intensivists are usually not in key positions in general funding agencies where scientists from all disciplines compete for a limited number of grants.

To increase resources, we need to bring together organisations that are relevant for research in intensive care medicine. These include the Dutch Society of Intensive Care (NVIC), public parties (The Netherlands Organisation for Health Research and Development, ZonMW; Netherlands Organisation for Scientific Research, NWO) and industry (pharmaceutical companies and manufacturers of devices used in the ICU). Public and private parties are part of society, and at present society may not be sufficiently aware of what intensive care medicine entails, nor what its relevance is in modern medicine. We therefore need to reach out to the public to improve awareness of intensive care medicine. Important in this regard is that intensive care medicine is very expensive and that cost-effectiveness has great societal impact. As fundamental issues in intensive care medicine are currently unresolved, research should not, however, be limited to health economic studies alone.

We envision that in the near future, two or three large-scale, non-commercial multicentre studies could be running simultaneously, with participation of a large number of Dutch ICUs. These studies could be interventional randomised clinical trials, but also observational investigations. In selected centres, sub-studies could be performed on separate outcomes. In addition, we wish to enhance collaboration in critical care translational research. We envision that the already high standard of translational research can be further improved by exchanging ideas and collaborative investment in expensive, highly-specialised laboratories, equipment and personnel.

Our aims to facilitate collaboration and to increase financial means are closely connected. A research network with a high-level infrastructure, expertise and knowhow will be extremely helpful in obtaining new funding for future investigations. An active research network will further mature Dutch intensive care medicine, and improve visibility towards fundraisers and society. On the other hand, any increase in financial means for research will strongly stimulate collaboration and ultimately clinical care.

### **Organisational structure**

To achieve these goals, an executive committee has been established. To be effective and decisive, the executive committee will have a limited number of members to lead RCCCNet and to coordinate the efforts of the steering committee.

The steering committee will consist of representatives from participating ICUs from academic and non-academic hospitals, scientists from related fields such as intensive care epidemiology or sepsis biology, as well as representatives of former patients such as Family and Patient Centred Intensive Care (FCIC). All RCCCNet members will have the opportunity to contribute to the research agenda, as described below. In addition, steering committee members will be able to give input to new study proposals and become principle investigators, trial coordinators, members of a Data Safety Monitoring Board, or contributing investigators by enrolling patients for a certain study. Membership of the steering committee provides the opportunity to be involved in large and relevant trials and to publish in top-ranked journals. Importantly, credits such as authorship of resulting publications, will be shared among everyone who has made a substantial contribution.

RCCCNet has been endorsed by the NVIC board and will regularly report to the NVIC members. A formal statement will be put in the statutes to ensure scientific independence of RCCCNet. NVIC will provide administrative support.

### The research agenda

A broadly supported research agenda may help to keep the focus on the topics that are considered most urgent by the research community. In contrast to other medical disciplines, there is currently no research agenda on intensive care medicine in the Netherlands. This is unfortunate, as important funding agencies such as ZonMW may have a preference for research proposals of topics that are listed on the research agenda of the involved medical discipline.

We envision that all RCCCNet members will have the opportunity to contribute to the development of a research agenda for intensive care medicine. We propose that members choose a subfield of their interest and make a short list of topics with a high priority for investigation. It is encouraged to focus new grant proposals on one of these topics. When a grant proposal is finalised, it will be distributed among all steering group members for input and feedback to improve the chances of a successful competitive bid to a funding agency. If the proposal is granted, representatives of each centre can decide whether or not to participate in this specific investigation.

Importantly, it is envisioned that the consortium is not meant to act as a 'trial bureau,' only to facilitate the conduct of randomised clinical trials. RCCCNet aims to facilitate interaction between investigators, to provide a platform for new and clinically relevant research ideas, and eventually to improve the chances of successful applications to funding agencies. In addition, RCCCNet aims to facilitate the conduct of studies. Commitment, investment of time and financial resources will be needed.

#### Kick-off

On the 21 September 2018, a meeting will be organised to which all intensive care physicians and researchers interested in this collaboration effort are invited. An invitation will also be sent by email, with the exact location. We hope to be able to welcome you all in order to start mapping relevant research topics. Now is the time to improve research collaboration in critical care in the Netherlands.

## L. Heunks<sup>1</sup>, N.P. Juffermans<sup>2</sup>, P. Pickkers<sup>3</sup>, A. J.C. Slooter<sup>4</sup>

<sup>1</sup>Department of Intensive Care Medicine, Amsterdam UMC location Vumc, Amsterdam, the Netherlands

<sup>2</sup>Department of Intensive Care Medicine, Amsterdam UMC location AMC, Amsterdam, the Netherlands

<sup>3</sup>Department of Intensive Care Medicine, Radboud University Medical Center, Nijmegen, the Netherlands

<sup>4</sup>Department of Intensive Care Medicine and Brain Center Rudolf Magnus, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands

#### References

- Shama G, La Moisissure et la Bactérie: Deconstructing the fable of the discovery of penicillin by Ernest Duchesne. Endeavour. 2016;40:188-200.
- Besselink MG, van Santvoort HC, Buskens E, et al. Probiotic prophylaxis in predicted severe acute pancreatitis: a randomised, double-blind, placebocontrolled trial. Lancet. 2008;371:651-9.
- Löwenberg B, van Putten W, Theobald M, et al. Effect of priming with granulocyte colony-stimulating factor on the outcome of chemotherapy for acute myeloid leukemia. N Engl J Med. 2003;349:743-52.
- Bellomo R, Chapman M, Finfer S, et al. Low-dose dopamine in patients with early renal dysfunction: a placebo-controlled randomised trial. Australian and New Zealand Intensive Care Society (ANZICS) Clinical Trials Group. Lancet. 2000:356:2139-43.
- Cameron JI, Chu LM, Matte A, et al. One-Year Outcomes in Caregivers of Critically III Patients. N Engl J Med. 2016;374:1831-41.
- Perner A, Haase N, Guttormsen AB, et al. Hydroxyethyl starch 130/0.42 versus Ringer's acetate in severe sepsis. N Engl J Med. 2012;367:124-34.
- de Smet AM, Kluytmans JA, Cooper BS, et al. Decontamination of the digestive tract and oropharynx in ICU patients. N Engl J Med. 2009;360:20-31.
- van Vught LA, Klein Klouwenberg PM, Spitoni C, et al. Incidence, Risk Factors, and Attributable Mortality of Secondary Infections in the Intensive Care Unit After Admission for Sepsis. JAMA. 2016;315:1469-79.
- van den Boogaard M, Slooter AJC, Brüggemann RJM, et al. Effect of Haloperidol on Survival Among Critically III Adults With a High Risk of Delirium: The REDUCE Randomized Clinical Trial. JAMA. 2018;319:680-9

