

Mission Control  
(NCRN)

## Curing Coma Campaign: 2019-2020 Update

• Claude J Hemphill

The Curing Coma Campaign (CCC) was formally announced at the 17th NCS Annual Meeting in October 2019 with a vision to create a world where patients in coma are treated early and recover. The mission of this campaign is to promote recovery of consciousness through early intervention and long-term support.

• Daiwai Olson

The strategic plan of the CCC involves several key approaches with separate action plan, milestones and metrics for each objective. The key aspects of CCC include:

• Jose Suarez

(i) Identification of the existing barriers in advancing coma science related to acute and long term care

• Leonard Polizzotto

(ii) Understanding the existing capabilities in coma management including personnel, platform, technology and therapeutics

• Keri Kim

(iii) Determination of the scope of research and appropriate restructuring/repurposing of available resources to advance coma science

• Shraddha Mainali

(iv) Defining the gaps of existing and new methods/therapeutics and development of mitigation plans to address such gaps

(v) Development of new strategies to break down barriers in coma care through research, education, collaboration and advocacy

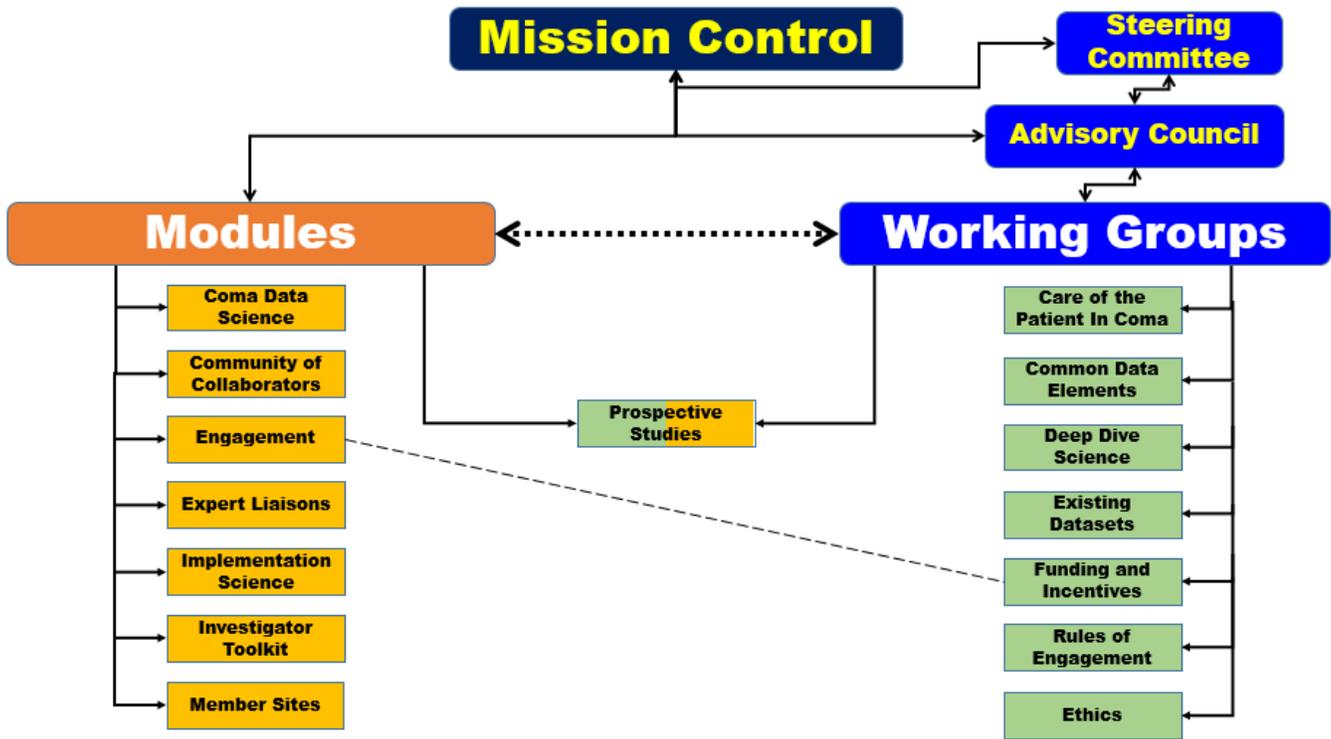
(vi) Development of resources for effective communication strategies and engagement of patients and families affected by disorders of consciousness (DoC)

(vii) Advocacy for standardized coma care worldwide

(viii) Global promotion of coma awareness and research sponsorship through outreach and marketing.

The goal of the campaign is to work in a collaborative fashion with synergistic efforts from various modules and scientific workgroups. The operational framework (fig. 1) of the CCC includes a wide network of teams with diverse members representing multifaceted aspect of coma care. The proceedings from the first scientific advisory council (SAC) meeting has been published in the NCC journal<sup>1</sup> and other reports on CCC are available on the NCS CURRENTS webpage<sup>2-4</sup>.

Figure 1. Organizational Structure of the Curing Coma Campaign



### CCC Scientific Steering Committee

The Scientific Steering Committee (SSC) of the CCC consists of 14 NCS members including the NCRC and the NCRN co-chairs. The role of the SSC is to guide the overall scientific agenda of the CCC.

### **The Executive Committee: Mission Control**

The NCRN Executive Committee (EC) comprises six members (including the two NCRN co-chairs) whose responsibility is to oversee and coordinate the operations of the CCC. This group meets twice monthly in order to assess the status of various NCRN modules, guide module leaders on activities and deliverables specific to each modules, and ensure that modules are working in synergy, especially in regards to action items with overlapping aims. The NCRN EC also serves as the primary liaison with SAC to ensure that modules and other NCRN resources (including financial and personnel) align with the scientific vision for the CCC. The NCRN EC is responsible for measuring and reporting progress on the various milestones to the NCRC and NCS BOD.

### **Scientific Advisory Council**

The CCC SAC is responsible for advising on the overall strategic plan and priorities for the scientific agenda for the CCC. This group currently includes 27 members from diverse scientific backgrounds related to coma and DoC. Many are from outside the NCS membership and thereby broaden the scientific perspective. The SAC works in conjunction with the SSC for strategic planning and helps establish collaborations with relevant clinical and basic science researchers from outside and within NCS in order to achieve the scientific goals of the Curing Coma Campaign. The SAC also works with the NCRN EC and NCRC co-chairs regarding acquisition and utilization of funding for the CCC, including internal NCS funds, philanthropic support, and grants. Various working groups deriving from the SAC have been established to focus on the 3 initial scientific pillars:

1. **Classification/Endotyping:** Endotyping is an approach that could help (i) increase diagnostic precision (ii) help build accurate prognostic models (iii) help predict response to therapy; (iv) help guide the development of proof of concept clinical trials and (v) understand pathobiological mechanisms related to disorders of consciousness. The SAC aims to achieve these tasks through establishment of workgroups focused on (i) determination of appropriate data sources, biomarkers, statistical and mathematical modeling etc to define endotypes; (ii) validation of endotypes across different populations and practice variability; and (iii) implementation of endotypes into diagnostic, prognostic and treatment workflows.
2. **Identification of relevant Biomarkers:** Action items related to this task include (i) determination of precise physiological indicators of coma for specific endotypes; and (ii) identification and/or development of pragmatic biomarkers using existing (eg, physiological or behavioural signals, imaging findings, electrophysiological data etc.) and/or novel tools (eg novel biomarkers, high resolution imaging technology that can be used in the acute clinical setting, high-dimensional datasets, mathematical and statistical models, integration of AI/machine learning technology etc) to accurately assess functional and structural integrity of neural pathways related to consciousness.
3. **Development of proof of concept clinical trials:** With appropriate endotyping and biomarker identification, the goal of CCC is to develop proof of concept clinical trials related to diagnosis, treatment and prognostication of coma.

## NCS Executive Office

The NCS Executive Office supports the NCRN and the CCC regarding activities that require administrative services. Specific NCS Executive Office resources will be needed for various aspects of the program which may include hiring of personnel for database and data science research, writing of grants for philanthropic and research funding, and administrative assistance in scheduling meetings and developing branding and other informational materials. The NCRN executive office works directly with the NCRN EC to ensure that requests for administrative resources are appropriate, tracked and reported, and align with the Curing Coma Campaign scientific and engagement priorities. Quarterly reporting of financial status with the NCRN EC is desired.

The following working groups and operational modules have been activated with successful achievement of established milestones despite the pandemic.

### Scientific Working Groups:

- 1. Deep Dive Science:** The goal of this 21 member working group (WG) is to establish the scientific foundation for effective treatment of patients with disorders of consciousness. This WG aims to (i) define the unmet science; (ii) develop tools to address the gaps and (iii) Create a blueprint for coma science. Five domains have been created to accomplish this scientific goal that include: i) Classification and Endotypes; ii) Mechanisms; iii) Prediction and Trajectory Analysis; iv) Therapies and v) Precision medicine.
- 2. Common Data Elements (The Coma and DOC CDE Project):** The goal of this WG is to develop a NIH approved comprehensive list of variables (existing + new) and measures that will be used in coma research. Eight different subgroups with 10 members (lead by designated WG chairs) from diverse background have been formed to develop and finalize CDEs related to 5 major categories: i) hospital course; ii) imaging; iii) electrophysiology; iv) biospecimen; v) physiologic data; vi) therapeutic interventions; vii) outcomes; and viii) pediatrics. The NCS will partner with NINDS to help execute this initiative. Final CDEs will be published on the NINDS website.
- 3. Funding and Incentives:** The initiative is led by NCRC co-chairs and NCRN representative. The primary aim of this WG is to raise money for coma science research. This includes all forms of funding including government, private industry, foundations and professional organizations. As an initiative of this workgroup, a virtual NIH symposium was held on September 9<sup>th</sup> 2020 to discuss the gaps and potential research avenues related to coma science. Follow-up in-person symposium is planned to take place on May 3<sup>rd</sup> 2020 in Bethesda, MD
- 4. Care of the patients in coma:** This 5 member WG will be charged to focus on a consciousness that are not aimed as curative therapy to resolve the DOC. Patient care is

defined as the continuum of care from the first moment of DOC through full recovery. This includes acute care (emergency and critical care); transition of care (intra-hospital, hospital-to-rehabilitation, hospital-to-facility, and hospital-to-home); and long term care (e.g. skilled nursing facility). This WG plans to accomplish its goals by working in 6 different subgroups focused on (i) religion and culture ii) timing the intervention iii) assessment and monitoring iv) expertise and experience v) technology and vi) external and regulatory issues.

- 5. Rules of engagement:** The goal of this 4 member WG is to establish policy statements that describes the stated principles of the CCC such that the work done collaboratively be available for open use by CCC participants, be recognized as collective work of the CCC, and that CCC participants receive appropriate credit for their work and participation. It is anticipated that aspects may potentially arise in several different domains including research data, publications, educational or other outreach product development, and intellectual property from inventions. Each CCC member (Member) is expected to abide by the principles in this policy as allowable based on restrictions from their primary employer (most often a university). This policy document, while not legally binding, is intended to set the tone of the relationship between all those involved with the CCC. Additionally, as the needs of the CCC evolve, so will this policies document. Additionally, this WG has developed a participation agreement that delineates how issues such as copyright, trademarks, patentable inventions, funding, and conflicts of interest are to be addressed. The intent of this document is to clearly establish the ground rules of CCC participation up front in order to avoid potential disputes in the future.
- 6. Existing datasets:** This WG comprised of 5 members is focused on identifying existing databases and research studies relevant to coma science. Identification and collation of existing scientific data will guide the development of proof of concept clinical trials/research studies.
- 7. Ethics:** This new WG of the CCC is formed with the intent to maintain and foster highest standards of professional and ethical conduct within the CCC community while working together to achieve the common goal of advancing coma science. This WG will oversee the ethical aspects and moral principles of scientific research pertaining to CCC.
- 8. Prospective studies:** The aims of this 15 member team falls both within the umbrella of scientific WG as well as CCC modules. The overarching goal of this team is to develop a platform for prospective studies for DOC and recovery from coma. The main objectives of this WG are to (i) provide an overview of the existing practices related to management of DOC across the world; (ii) work on understanding of mechanisms of DOC and recovery from coma; (iii) establish prediction models for recovery of coma (short-/long-term trajectory) and (iv) identify interventions for comatose patients amendable to treatment. The WG members have designed and conducted a survey on global practices related to coma, the results of which will be presented during the World Coma Day on March 22<sup>nd</sup> 2021.

### **Active Operational Modules:**

**Engagement Module:** The goal of the engagement module is to promote CCC and encourage engagement and participation from global partners/collaborators through outreach, branding (log/tagline) and development of online platform for engagement (<https://www.curingcoma.org/home>; Twitter: @CuringComa). This module continues to work on identifying cost-effective strategies to execute the mission while engaging the ‘coma community’ of patients, families, scientists, clinicians, healthcare allies and other interested parties/individuals.

**Community of Collaborators:** The goal of this module is to create and maintain a strong set of collaborators across various domains including science, education, implementation and advocacy. This module has 3 main domains (i) Family engagement: through assembly of teams of diverse volunteers focused on advocacy and family engagement for patients with acute brain injuries & disorders of consciousness with the goal of identifying available family engagement resources and linking them to the Curing Coma Campaign webpage; (ii) Webinars: through launch of the Curing Coma campaign focused webinar series (iii) Social Media Campaign: In close collaboration with the Engagement module to amplify the social media presence of the Curing coma campaign on Twitter (@curingcoma).

**Coma Data Science:** The purpose of the coma data science module is to provide a central platform for aggregation and analysis of large-scale data in neurocritical care. This 9 member team developed and completed an internal ‘survey of needs’ to understand and prioritize data needed for research related to coma and disorders of consciousness. This internal survey guided the identification of candidate database architecture scheme along with the appropriate vendors, institutions, and partners and the module members are actively working on finalizing a central platform.

**Member Sites:** The scope of the member sites module is to provide a central conduit to facilitate collaboration and research participation across organizations, countries and geographic regions. This 4 member module has actively worked on identifying global collaborators and regional leaders from Europe, Oceania, US, Canada, South America, East Africa and Sub Saharan African. The module members have also reached out to various organizations including ACCP, ANZICS and CCCTG and continue to build relations and cross collaborations across the globe.

**Prospective studies:** This WG was transformed into an operational module when the plan was developed for the COME TOGETHER research survey study. They are overseeing the acquisition of data for COME TOGETHER, its analysis, and reporting. Next studies are in the planning stage.

## **Communication platform**

MS Office 365 (Microsoft Teams) will be used as the central platform for all Curing Coma documents, communication, and collaboration. Members in respective working groups and modules will be invited to join their respective teams (at no cost to the members).

## **Upcoming Events:**

1. **World Coma Day:** March 22, 2021. Planned as a 24 hour virtual event across the globe with the goal of promoting coma awareness. Presentations and discussions will be based on 4 main categories: (i) coma science (ii) education (iii) patient and family, and (iv) celebration. Here is a link to the Facebook Event Page <https://www.facebook.com/events/210304904050469>
2. **NIH symposium;** May 3<sup>rd</sup> 2021. Bethesda, MD. Details to be determined.
3. **2021 Annual Meeting:** October 26-29, 2021. Chicago, IL.

## **References:**

1. Provencio JJ, Hemphill JC, Claassen J, et al. The Curing Coma Campaign: Framing Initial Scientific Challenges-Proceedings of the First Curing Coma Campaign Scientific Advisory Council Meeting. *Neurocrit Care* 2020;33:1-12.
2. Hocker S, Mainali S, Naidech A. The Future of Neurocritical Care Research: Looking for a Blue Ocean. *CURRENTS*. Jan 2019; <https://currents.neurocriticalcare.org/currents/blogs/currents-editor/2019/01/17/the-future-of-neurocritical-care-research>
3. Shraddha M, Chou SH-Y, McNett M, Kim J. The Curing Coma Campaign. *CURRENTS*. Jan 2020; <https://currents.neurocriticalcare.org/currents/blogs/currents-editor/2020/01/16/the-curing-coma-campaign>
4. Shraddha M, Paul V. Paving the Path to the Future: Curing Coma. *CURRENTS*, April 2019; <https://currents.neurocriticalcare.org/currents/blogs/currents-editor/2019/04/04/paving-the-path-to-the-future-curing-coma>