Identifying priority health research questions for critical care in Asia and Africa; a research prioritisation exercise in partnership with the JLA

Background:

For healthcare improvement collaborations, funders and academics, identifying unanswered research questions to promote survival and improvements in critical care is a key element in determining the agenda for healthcare research commissioning. Recent reports from global funders have highlighted the gap that remains in priority setting between funders and collaborative research groups seeking to distribute public money and prioritise research agendas within low- and middle-income countries (LMICs) and those on the front line delivering healthcare.[1] Objectives of funding calls are evolving, but remain driven by international policy, which too often focuses on addressing gaps in availability of structures and resources, which may fail to address healthcare providers or patients' priorities across the continuum of the care pathway.[2,3] For example, stakeholder research undertaken by Patient-Centred Outcomes Research Institute (PCORI) collaborators in the African continent with survivors of breast cancer, revealed patients and family members prioritised early detection, minimisation of side effects (consequences of care) including financial hardship, over new or novel treatments options and shared decision making.[1,4]

Whilst funders increasingly request funded research projects be led by LMIC based researchers, patient and multidisciplinary healthcare provider representation, at the design stage of funding calls LMIC input remains limited.[5] Increasingly recognised as an essential adjunct in the pathways of treatment and recovery for patients from a variety of specialities including oncology, surgery, infectious disease and respiratory medicine, critical care is a rapidly growing speciality internationally. In the wake of the COVID-19 global pandemic, governments, policy makers and healthcare providers invested significantly in critical care resources internationally. This global research mobilisation revealed significant gaps in infrastructure and resources for critical care, however it also revealed wide heterogeneity in adoption of evidence, management of critical illness, and in factors affecting decision making; cost, cultural preferences, access to home care and rehabilitation.[6]

In 2013/2014, the UK Intensive Care Society, with the support of the James Lind Alliance (JLA), conducted a research priority setting partnership exercise that produced a list of uncertainties around treatment decisions for critically ill patients.[7] Anaesthesia and perioperative care, clinical specialities whom often share both patient populations, and health services with critical care, have undertaken similar complementary exercises. However similar priority setting exercises in Asia and Africa remain limited.

Collaboration for Research, Implementation and Training in Critical Care in Asia and Africa (CCAA) is a Wellcome UKRI funded network of 17 countries established in 2019, and now

funded to 2025, whose co-investigator community is well placed to undertake this research. The network functions as an LMIC-led distributed community of practice which has to date established a 260+ hospital critical care registry network. The network works to generate high value data on critical care service provision, case mix and clinical outcomes, operationalise LMIC investigator-led adaptive platform trials, and provide near real time service data to inform hospital, regional service delivery and as in the case of the recent COVID-19 pandemic, public health and notifiable disease data. In conducting its activities, CCAA has established effective and productive working partnerships with patients, clinicians and clinical academic societies, academic research and health policy institutions internationally, and global funders, including; Wellcome, NIHR, UKRI-MRC, CRC.

Research question:

What are the high-value, population-specific unanswered research questions regarding management of critically ill patients cared for in Asia and Africa?

Methods:

Scope

Critical care is complex and heterogeneous in nature affecting all populations, indiscriminate of age, sex, or socio-economic profile. Critically ill patients can often be found and cared for in all areas of the hospital setting. Furthermore, recognition and management of critical illness requires coordination of care delivered by a multi disciplinary team, including but not limited to medicine, emergency care and surgery. To aid stakeholders in the identification of high value research questions regarding critically ill patients relevant to lower resourced healthcare systems, this PSP will define according to the Intensive Care Society definition of critical care ' those patients requiring Level 2 or Level 3 care ' and is described in Appendix 1 below. The PSP participants will be asked to focus on the adult population defined as 17 years and older. In addition stakeholders will be asked to draw on experiences of critical illness within the hospital setting within the Asia -Africa continents.

Study design and conduct

Design

This research prioritisation exercise (RPE) will utilise the methods outlined by the James Lind Alliance (JLA) priority setting projects,[8] including two survey rounds, each followed by a steering group meeting and a final priority setting workshop in partnership with the JLA. These steps are detailed below and summarised in figure 1. The RPE will be led by a steering committee appointed by CCAA national leads. The RPE will generate 10 priority research questions, and further subsets of unranked questions for specified domains identified in the pre-project planning.

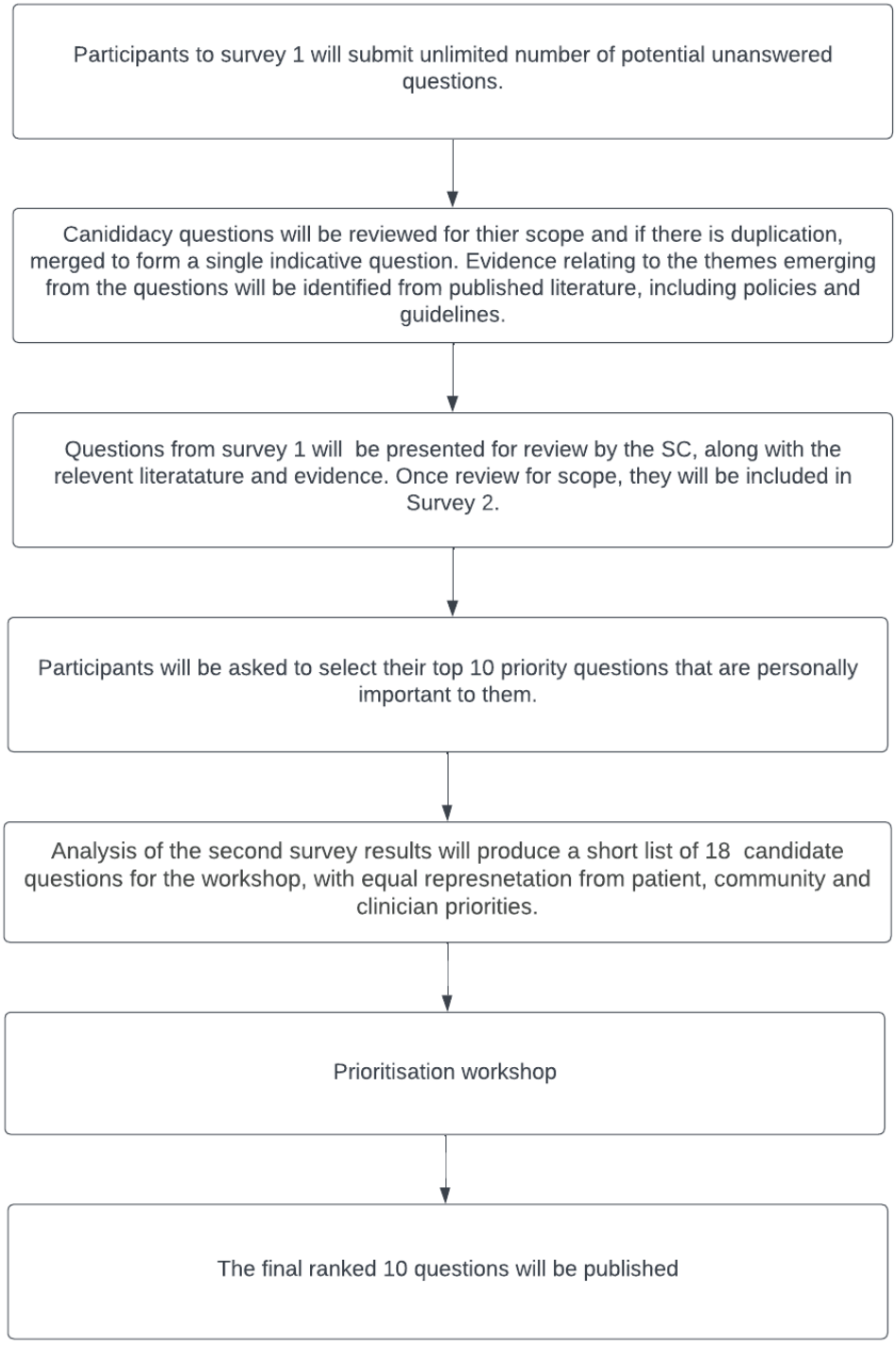

Figure 1. Overview of the process being used for the RPE.

1. *Pre-project planning*

A pre-project planning meeting was conducted on 17th September 2022 in Bangkok Thailand as part of the CCAA investigator meeting. Attendees (n=78) included representatives

(healthcare workers, researchers and funders) from the 17 collaborating CCAA countries. Representatives from critical care service provision in Australia, Canada, Japan, Netherlands and the UK were also present. The objectives of the pre-project meeting were:

1. To introduce the JLA research priority setting methods to network members
2. To discuss and refine potential domains and aims for research relevance and priority ranking categories reflective of the need to improve critical care service delivery
3. To agree on the roles and responsibilities of the steering committee

The pre-project planning meeting invited attendees to join facilitated small group discussions to identify research domains of critical care practice.

Roles and responsibilities of steering committee

The steering committee will be responsible for design and delivery of the study, in accordance with the study protocol, recruitment of participants to the RPE, and dissemination of the findings of the RPE both within the CCAA and more widely to international collaboratives and funding bodies. To achieve this, the steering committee will meet at key milestones of the project (at least once per each five key processes of the project), with flexibility for additional meetings. Any conflicts of interest from the steering committee members will be disclosed on any outputs.

The steering committee will consist of the following members (Figure 2):

1. **RPE coordinators:** Two coordinators will be appointed to organise steering group meetings and the prioritisation workshop; coordinate the write up of the manuscript, oversee the delivery of the RPE processes; liaise with the JLA advisor to prepare a website and ensure all required documentation are complete.
2. **JLA advisor:** The JLA advisor (appointed by JLA) supports and guides the RPE as a neutral facilitator, ensuring that the process is fair and transparent, with equal input from the perspectives of patients, carers and clinicians.
3. **Information specialists:** Three information specialists will be appointed. They will be responsible for the development of the surveys, the subsequent meeting, and the data analysis. These information specialist roles will be developmental, providing opportunity for those new to research, or early researchers who are seeking to develop domain and or methodological expertise. The information specialists will be supported by senior research members of CCAA.
4. **Stakeholder representatives:** 12 stakeholder representatives will include 3 patients, 3 carers (i.e. informal carers such as family members) and 6 healthcare professionals (2 physicians, 2 nurses and 2 allied healthcare professionals). Their responsibilities will include communicating with national leads within CCAA, and in connecting with wider stakeholder groups outside of CCAA (including but not limited to policy makers, healthcare funders, clinicians and patient and public representatives). The stakeholder representatives will be responsible for representing the views and opinions of their

communities, to guide the methods and development of each key RPE step. Communication and dissemination is described in Appendix 2.

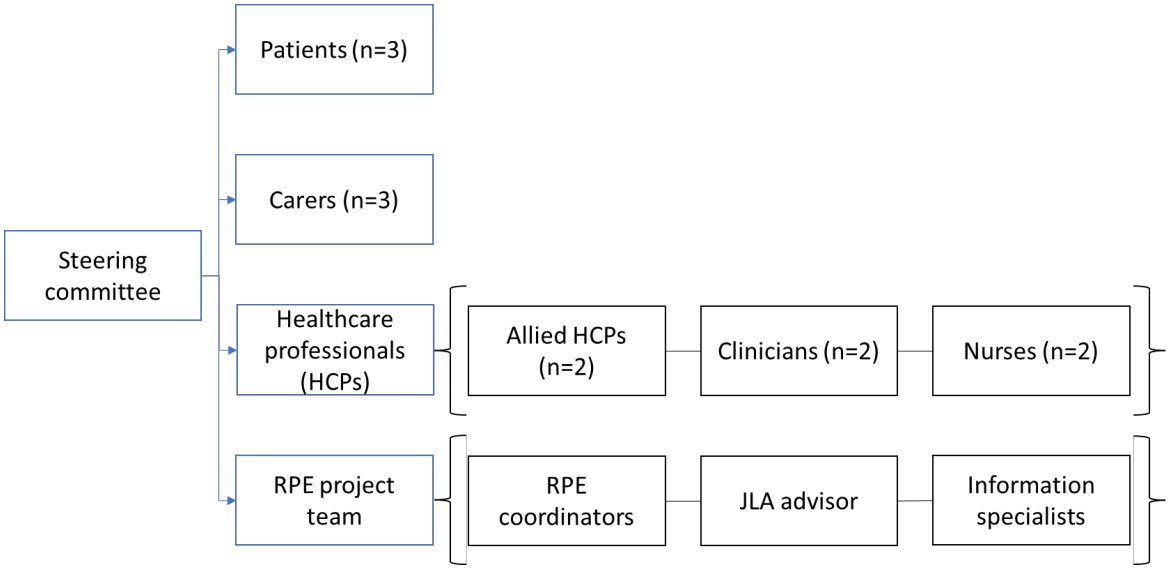

Figure 2. Steering committee formation

2. *Survey 1*

Survey 1 will comprise an online survey with an open-ended question and instructions on the scope to elicit stakeholders' (patients, carers and healthcare professionals') views on unanswered care and management uncertainties. The first survey will use a purposefully open-ended question to enable participants to consider what questions are important to them based on their experiences, expertise and prior exposure to critical care. Participants will not be limited in the number of questions they can pose. For each question the participant proposes, they will be asked to tell the condition(s) or disease relevant to their question, the population (and individuals) they feel are most affected, the departments within the hospital involved, and the setting (region, country, continent) of interest. Participants will also be asked to provide their location of clinical practice, and their professional role to understand the range of responses across Asian and African countries. The survey will be collected using an email identifier but the data will be de-identified prior to analysis.

There is no minimum sample size; however, similar JLA projects have received 100s to 1000s of respondents. This is a qualitative survey aimed at generating questions and themes; therefore, a high number of respondents may not necessarily result in more or better uncertainties and the range of themes needed may come from smaller numbers of responses. As the JLA advises, we will aim for quality not quantity, whilst ensuring that there has been reasonable representation from patients, informal carers and healthcare professionals. The steering committee will work together in deciding when enough responses have been reached based on saturation of the themes identified.

The information specialists will develop the survey with input from the steering committee using Survey Monkey.[9] A pilot of the survey will take place scoping 5-10 individuals representing different stakeholder groups. Feedback will be sought on the question construct, survey design and usability of the survey (i.e. navigation, readability, font, colours, etc). The survey will be conducted in English, with translation of the survey materials available on request of the national leads from each of the CCAA collaborating countries. Any translations will be back translated and checked for consistency with the source document.

Once the survey is launched, it will be advertised by the JLA, all members of the steering committee and the wider CCAA network. We will use a snowballing approach, reaching out to participants through existing communication networks including national committees, professional healthcare bodies, critical care societies, existing patient and public engagement groups, social media accounts, texts/WhatsApp, email and word-of-mouth. The survey will be live for 6 weeks.

Following completion of the survey the responses will be sorted according to their scope (domains) of critical care research and practice. The domains suggested below have been identified a priori based on existing priority setting work internationally and will be used as a starting point to provide structure to the final 10 priority research questions; however, survey data may indicate additional domains or themes:

A. Identification of new critical care therapies or repurposing existing critical care therapies (early phase/discovery research/investigative medical products)
B. Effective recognition of the critically ill patient in the in-hospital setting
C. Management of organ dysfunction related to critical illness
D. Prevention of complications associated with management of critical illness
E. Recognition of patient and family physical and mental comfort during critical illness in-hospital and during recovery beyond the hospital setting
F. Organisation and delivery of care from ICU admission to discharge to recovery support

Questions out of scope of this RPE will be retained for transparency but excluded from the RPE analysis conducted by the information specialists. Duplicate questions or questions that are similar will be grouped together and reviewed from the steering committee. Identical or questions substantially the same will be quantified to give some notion of relative importance in later analysis. Incomplete responses will be included in the analysis. Candidacy research questions that do not fit within one of the proposed domains listed above, will be taken forward to the steering committee and either reclassified under an existing domain or the need for an additional domain will be proposed.

In parallel to survey 1, a literature search will be conducted by the information specialists for each of the six domains, to scope the literature identifying existing research priorities, known gaps in research, and the existing published evidence. Medline via Ovid and PubMed will be searched without any limitation on date or language. In addition, ongoing or impending research registered with ClinicalTrials.gov and systematic reviews via platforms PROSPERO and Cochrane relevant to the domains will be identified.

The results of these searches will be compiled alongside the candidacy list for each domain. Where evidence exists to answer the research question (defined as the question having one or more high quality (using the GRADE approach) study either published in a peer-reviewed journal, having a systematic review or meta-analysis published in a peer-reviewed journal, or having internationally recognised and published guidelines), it will be considered answered and removed from the candidacy list.

The RPE coordinator will organise a steering committee meeting for the information specialists to provide an overview of the results (example this) including proposed exclusions. The steering committee will be asked to review the candidacy questions for each domain, consider the findings of the literature search, and make recommendations to refine the candidacy list of questions; removing those that are already answered, or part of current or ongoing research. The final list of research questions will be included in survey 2.

3. *Survey 2*

The information specialists will draft the survey, and the survey will be conducted and advertised using the same methods as survey 1. All participants who participated in survey 1 will be invited to complete survey 2. Participants will be asked to select 10 questions that are personally important to them. The survey results will be analysed by the information specialists. The frequency of which each question was chosen will be summed separately for patients/carers and healthcare professionals. We will endeavour to have equal inclusion of research questions selected by patients and carers, and of questions elected by healthcare professionals will be taken to the prioritisation workshop; total questions taking forward will not exceed 18.The RPE coordinator will organise a steering committee meeting for the information specialists to provide an overview of the results (using a table such as this) and for the ranking to be reviewed and ratified.

4. *Prioritisation workshop*

A virtual workshop will take place with an equal representation of patients, carers and healthcare professionals to discuss the findings of the surveys and prioritise the top 10 research questions. Attendance will include, as a minimum, 12 healthcare professionals, 6 patients and 6 members of the public or public body representatives. For patients, public and public body representatives participating, they will have the opportunity to join a local hub (healthcare or research facility) to facilitate online participation. The steering committee will have the option to attend the workshop as observers only; workshop participants will be a new set of stakeholders. We anticipate the worship will have approx 4 groups of 6-8 participants.

The final priority setting stage is generally a one-day (or two half days) workshop facilitated by the JLA. This can also be done online, using a platform such as Zoom for example. The workshop is designed to deliver consensus through conversation. The event involves consecutive rounds of discussion and ranking, to determine the top 10 questions for research. The Steering Group will advise on any adaptations needed to ensure that the process is inclusive and accessible.

5. *Dissemination*

The RPE coordinators will lead the writing of the JLA report and manuscript for publication on the JLA website and a peer-reviewed journal, respectively. Authorship will be inclusive and according to the CReDiT taxonomy. All participants in the RPE will be acknowledged in the publication.

Participant selection

A key element of the JLA approach is the encouragement and participation of patients and family members with personal experience of the disease area in question. This is particularly challenging for highly technical and acute areas of healthcare such as emergency medicine, intensive care and anaesthesia, especially as the patient may not have any memories of the acute events or disease from which they were suffering following their recovery. Thus, the contribution of informal carers such as family members will be an essential component of this research.

As described above critical care is allied to many specialities. Therefore, this RPE will seek to have representation from both the ICU multidisciplinary team and from allied specialties including, emergency and respiratory medicine, surgery, microbiology, haematology and infectious diseases.

Through this RPE, we aim to build local capacity in Africa and Asia in conducting stakeholder-led consensus and prioritisation research. During the five stages of the RPE, emerging researchers based in Africa and Asia will lead this project, and individuals will have the opportunity to develop skills in literature review, research coordination, mixed methods analysis and manuscript writing.[10] The roles of the participants are described above and summarised in figures 2.

Survey participants will consist of any patient, carer, member of public or healthcare professional with experience with critical care/illness, or acute care including surgery, emergency medicine, obstetrics, living or working in Africa or Asia.

Project timeline

SC meeting May 2023

Survey 1 May- June 2023

Survey 2 June- August 2023

Prioritisation Workshop October 2023

Dissemination January 2024

Ethical and regulatory considerations

Approvals

This is a minimal risk study including voluntary participants. Ethical approval in the UK and countries where the survey will be advertised will be sought where necessary.

Participant confidentiality

Participants in either survey who wish to be contacted again to take part in further stages of the PSP, or who would like to continue to receive information about the project, will be able to provide their contact information (email only); this information will be stored securely on a designated shared drive storage space used by the CCAA network, which will only be accessible by study staff and authorised personnel. For participants that wish not to be contacted again, no personal or identifiable information will be collected. The study will comply with the General Data Protection Regulations [11] and country specific data protection regulations.

Compensation

Participation is voluntary and there is no financial remuneration for involvement. All meetings will be conducted online. No travel is anticipated.

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Appendix 1.

Levels of Adult Critical Care

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6. Redefining the levels of adult critical care to reflect modern delivery and changing demands

Ward Care

- Patients whose needs can be met through normal ward care in an acute hospital.
- Patients who have recently been relocated from a higher level of care, but their needs can be met on an acute ward with additional advice and support from the critical care outreach team.
- Patients who can be managed on a ward but remain at risk of clinical deterioration.

Level 1 – Enhanced Care

- Patients requiring more detailed observations or interventions, including basic support for a single organ system and those 'stepping down' from higher levels of care.
- Patients requiring interventions to prevent further deterioration or rehabilitation needs which cannot be met on a normal ward.
- Patients who require on going interventions (other than routine follow up) from critical care outreach teams to intervene in deterioration or to support escalation of care.
- Patients needing a greater degree of observation and monitoring that cannot be safely provided on a ward, judged on the basis of clinical circumstances and ward resources.
- Patients who would benefit from Enhanced Perioperative Care.[3]

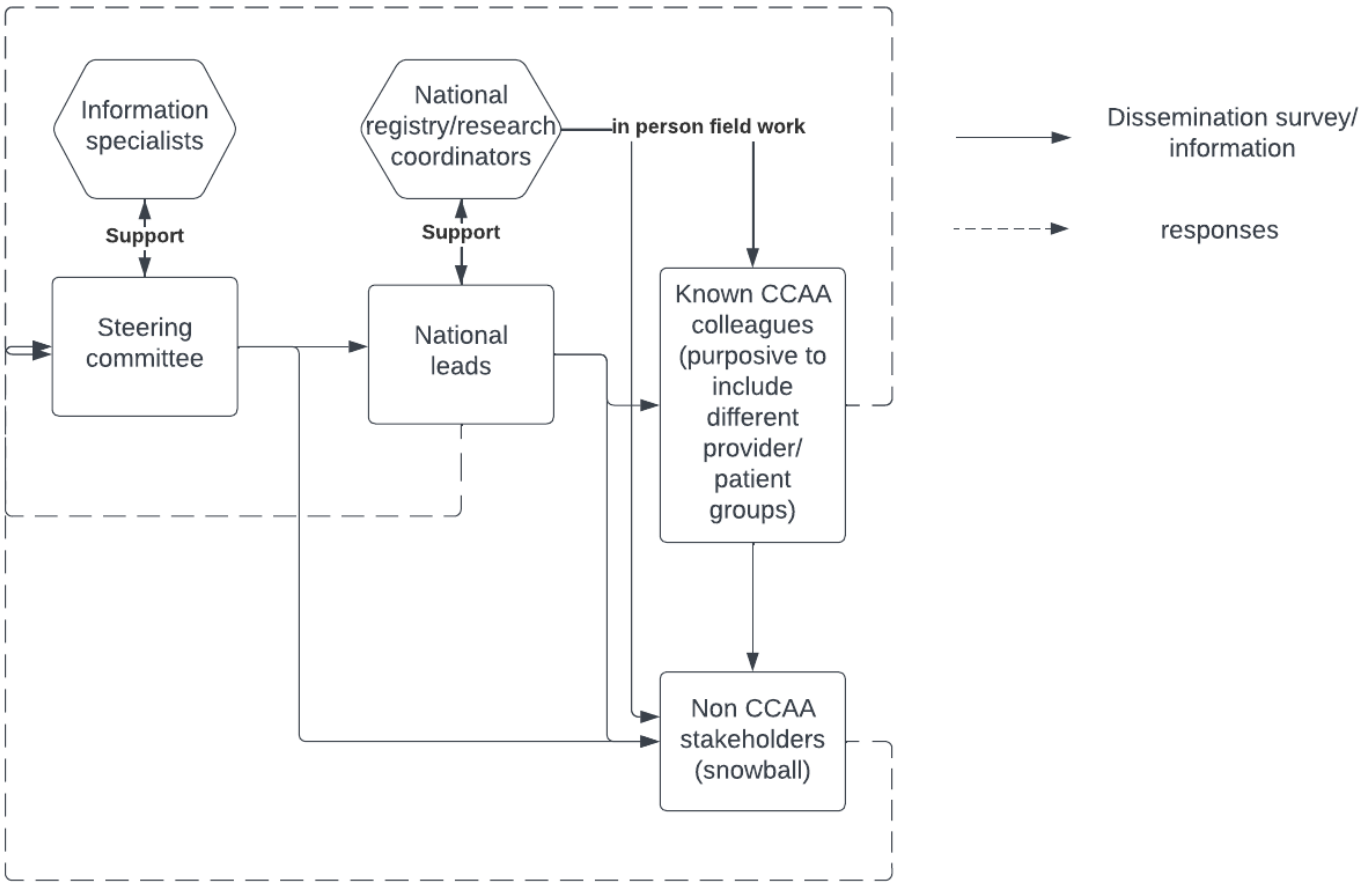
Level 2 – Critical Care

- Patients requiring increased levels of observations or interventions (beyond level 1) including basic support for two or more organ systems and those 'stepping down' from higher levels of care.
- Patients requiring interventions to prevent further deterioration or rehabilitation needs, beyond that of level 1.
- Patients needing two or more basic organ system monitoring and support.
- Patients needing one organ systems monitored and supported at an advanced level (other than advanced respiratory support).
- Patients needing long term advanced respiratory support.
- Patients who require Level 1 care for organ support but who require enhanced nursing for other reasons, in particular maintaining their safety if severely agitated.
- Patients needing extended post-operative care, outside that which can be provided in enhanced care units: extended postoperative observation is required either because of the nature of the procedure and/or the patient's condition and co-morbidities.
- Patients with major uncorrected physiological abnormalities, whose care needs cannot be met elsewhere.
- Patients requiring nursing and therapies input more frequently than available in level 1 areas.

Level 3 – Critical Care

- Patients needing advanced respiratory monitoring and support alone.
- Patients requiring monitoring and support for two or more organ systems at an advanced level.
- Patients with chronic impairment of one or more organ systems sufficient to restrict daily activities (co-morbidity) and who require support for an acute reversible failure of another organ system.
- Patients who experience delirium and agitation in addition to requiring level 2 care.
- Complex patients requiring support for multiple organ failures, this may not necessarily include advanced respiratory support.

Appendix 2.



PSP communication and dissemination