Research in anaesthesia update

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The Australian and New Zealand College of Anaesthetists has two research networks embedded into its organisation; the Clinical Trials Network (CTN) and the more recently conceived Professional Practice Research Network (PPRN). The ANZCA CTN is a world leading clinical trials network in anaesthesia, pain and perioperative medicine delivering high quality multicentre clinical trial research to improve patient safety and outcomes around the world. The ANZCA PPRN promotes and fosters research in the domains of communicator, collaborator, leader and manager, scholar, health advocate and professional and is aligned with the social sciences and qualitative or mixed-methods research. Both the CTN and PPRN build networks of clinical researchers and aim to foster excellent research.

Large randomised clinical trials remain the gold standard for determining the effectiveness of an intervention. However, traditional multicentre clinical trials are expensive, slow, difficult to conduct, and highly dependent on funding and research infrastructure. Evidence from trials may take years (or decades) to be adopted into clinical practice. Traditional clinical trials are also able to answer only one clinical question at a time, in a specific population of patients which may not be generalisable to different countries, regions or institutions. The trial protocol is fixed, and the scope of evaluation is limited to the interventions selected at the beginning of protocol development, which can become problematic if external scientific discovery or changes to clinical practice outpace trial delivery.

Adaptive platform trials (APTs) have been used in Intensive Care research in the last decade and has the potential to mitigate some of the problems with traditional perioperative clinical trials. APTs are perpetual learning platforms focused on a single clinical condition. Multiple interventions across different domains (treatments with a common mechanism) are evaluated simultaneously, and new treatments can be added to the platform over time. Data are analysed frequently in repeated interim analyses, and treatments discontinued if predetermined thresholds for harm, futility or efficacy are met. The adaptive nature of the platform implies that key features of the trial design are modified during the trial in response to accumulating data, which maximises statistical efficiency. For example, response-adaptive randomisation allows randomisation ratios to be altered to increase allocation to the treatment groups demonstrating efficacy, which accelerates trial conclusions and benefits trial participants. The sample size is not fixed and recruitment to a treatment arm continues until conclusions are reached. The control group is shared amongst the treatment arms, which increases trial efficiency. There is a common master protocol which specifies the study population, enrolment features, outcome measures and standardises procedures.

For example, REMAP-CAP (Randomised, Embedded, Multifactorial, Adaptive Platform trial for Community Acquired Pneumonia) was established by an international group of intensivists and trialists after the 2009-2010 H1N1 influenza pandemic, in response to the lack of research and evidence during the pandemic. Community acquired pneumonia was chosen as an important condition with significant burden of disease and unresolved therapeutic questions. A pandemic arm was written into the original REMAP-CAP protocol and remained dormant until it was activated by the COVID-19 pandemic in February 2020. Recruitment into the COVID-19 population commenced a month later, and within the year, evidence had emerged for hydrocortisone, tocilizumab, and therapeutic heparin, demonstrating the power and efficiency of APTs within a highly organised global network. Although APTs are more cost and time-efficient compared to running multiple individual clinical trials over time, they are operationally challenging and require substantial funding for the initial set up and ongoing maintenance. Very few national health research agencies have the ability to fund APTs. APTs are also statistically complex, and extensive statistical simulations are required during study development. The methods to control for bias due to time (non-concurrent control group), region and multiple treatment interactions are debated.

What are the important unanswered questions in perioperative research? There is increasing emphasis on consumer engagement to determine priorities in clinical research. In Australia, researchers are required to demonstrate rigorous consumer engagement to apply for health research funding through the National Health Medical Research Council. The James Lind Alliance (UK) funded by the National Institute of Health and Care Research (NIHR) was established to bring patients, carers, and clinicians together in Priority Setting Partnerships to identify top priorities for future health research in a variety of areas, including Anaesthesia and Perioperative Care. Funders are encouraged to direct funding towards identified areas of importance. The top 10 questions for Anaesthesia and Perioperative Care from 2019 are listed below:

1. Which factors before, during, and after receiving anaesthesia for surgery are most important to **improve patient outcomes and satisfaction**?
2. What are the impacts of involving patients in **shared decision making** about anaesthesia and care options before, during, and after surgery?
3. What **data** should be collected from patients about anaesthesia care before, during, and after surgery to better understand their outcomes and experiences?
4. How can **errors and patient injuries** in anaesthesia care be prevented?
5. How can outcomes in **frail and/or elderly** patients be improved after receiving anaesthesia for surgery?
6. What is the impact of **reducing opioids** (a type of medication that reduces pain, like morphine) during anaesthesia on patient outcomes and opioid dependence after surgery?
7. What **preparation**, treatment, or assessment before receiving anaesthesia for surgery improves patient outcomes?
8. How can **patients' feedback** about their experiences before, during and after surgery be used to improve anaesthesia care?
9. How can anaesthesiologists improve **pain control** after surgery?
10. What are the common **long-term side effects** of anaesthesia after surgery?

These are not specific research questions, but broadly cover most of perioperative care, and highlight the importance of many types of research methodology in perioperative research (clinical trials, qualitative studies, registry-based studies). There are many strengths of perioperative research in Aotearoa – including our world class national registries, centralised ethics process, strong public health system and our unique position to lead on perioperative health equity.

Resources

1. https://www.anzca.edu.au/research/anzca-clinical-trials-network
2. https://www.anzca.edu.au/research/anzca-professional-practice-research-network
3. Marcucci M, Painter TW, Conen D, et al. Hypotension-Avoidance Versus Hypertension-Avoidance Strategies in Noncardiac Surgery : An International Randomized Controlled Trial. *Ann Intern Med* 2023; 176: 605-614. 2023/04/24. DOI: 10.7326/M22-3157.
4. Devereaux PJ, Marcucci M, Painter TW, et al. Tranexamic Acid in Patients Undergoing Noncardiac Surgery. *N Engl J Med* 2022; 386: 1986-1997. 2022/04/02. DOI: 10.1056/NEJMoa2201171.
5. Myles PS, Yeung J, Beattie WS, et al. Platform trials for anaesthesia and perioperative medicine: a narrative review. *Br J Anaesth* 2023; 130: 677-686. 2022/12/02. DOI: 10.1016/j.bja.2022.10.030.
6. https://www.remapcap.org/covid19publications
7. https://www.jla.nihr.ac.uk/top-10-priorities/