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**Pilot testing of a neonatal nurse led model of analgesia to manage pain in the surgical neonate.**

## [PAINS: Pain and Analgesia Improvement in Neonates with Surgical conditions.]

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**LAY DESCRIPTION OF THE PROJECT**

A model of neonatal nurse controlled analgesia (NNCA) to manage neonatal surgical pain has been developed in phase 2 of this program of research. This model was informed through the literature, the results of a systematic review, a survey of current Australasian neonatal pain practices and an expert panel of neonatal clinicians/researchers with knowledge/expertise of pain assessment and management practice across Australia and New Zealand. The final model of this NNCA will be pilot tested in the Cardiac/surgical neonatal intensive care unit (C/S:NCCU) of the Mater Mothers’ Hospital South Brisbane.

This study will be conducted to comply with:

* Any requirements as defined by the Australian Health Practitioner Regulation Agency];
* Catholic Health Australia (2001). Code of Ethical Standards for Catholic Health and Aged Care Services in Australia;
* Current best practices in neonatology;
* Current best practice in ethics including abiding by the *National Statement* and all other relevant NHMRC standards;
* Relevant State and Commonwealth Acts and legislations; and
* Relevant Institutional policies and procedures (available on Mater Document Center).

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# GLOSSARY OF ABBREVIATIONS

|  |  |
| --- | --- |
| NCCU: | Neonatal Critical Care Unit |
| P/NCA: | Parent/Nurse Controlled Analgesia |
| NHMRC: | National Health and Medical Research Council |
| NICU: | Neonatal Intensive Care Unit |
| IWS: | Iatrogenic Withdrawal Syndrome |
| ACNN: | Australian College of Neonatal Nursing |
| AZNN: | Australian and New Zealand Neonatal Network |
| NNP | Neonatal Nurse Practitioner |
| MO | Medical Officer |
| CNC | Clinical Nurse Consultant |
| MFM | Maternal Fetal Medicine |
| NNCA | Neonatal Nurse Controlled Analgesia |
| C/S | Cardiac Surgical unit |

## 

## INTRODUCTION

Advances in neonatal surgery over the past 20 years have improved the short-term management and survivability of neonates, with both congenital anomalies or acquired neonatal illness requiring surgical intervention.1 Though surgical management has become a critical component of care in the Neonatal Intensive Care Unit (NICU), the sequelae of under treated or poorly managed pain in the surgical neonate can lead to immediate physiological effects and re-modeling of the central nervous system, resulting in permanent alterations in pain processing and the ongoing neurodevelopment of the neonatal brain. 2 Considering this, accurate assessment and a prompt consistent approach to the management of pain is warranted. A method of responsive analgesia administration delivered in alignment with a pre-determined algorithm, may provide the bedside nurse with a consistent and agreed approach to managing surgical pain by minimizing the need for continual escalation and review for the instigation, titration and weaning of opioids.

This proposed pilot study aims to test the effectiveness of a newly developed model of Neonatal Nurse-Controlled Analgesia (NNCA) analgesia compared to the current standard management of neonatal post-operative management. This pilot will inform the study methods for a larger RCT including; training, recruitment, randomisation, data collection tools, processes and neonatal outcomes. The model of NNCA (to be tested in this pilot study) was developed with data generated from a program of research conducted by this research team including from the results a systematic review (Safety and effectiveness of parent or nurse-controlled of analgesia in neonates: a systematic review) 3as well as from a survey of pain practices of all 15 neonatal surgical units across Australia and New Zealand and a Delphi study with a panel of neonatal specialists. The Delphi panellists were invited clinical experts working within surgical neonatal intensive care units across Australasia and/or recognised for clinical research in this specialty both nationally and internationally. This panel of experts were involved in several rounds of feedback on the proposed model of NNCA until final consensus of all aspects of the model was reached in November 2022.

## BACKGROUND

Neonatal pain treatment and prevention should be a priority of care for the neonatal team, and health care professionals have an obligation to ensure that patients are pain free.4 As direct care clinicians, neonatal nurses are best placed to assess and manage analgesia. Therefore, the provision of effective pain management is integral to the role of the neonatal nurse. Despite this, the neonate remains at risk of suboptimal pain management due to several factors such as the inability of the neonate to effectively communicate pain; insufficient prescription of analgesia by physicians; delays in medical reviews to titrate analgesia; and inconsistencies in pain practices amongst the treating neonatal team.5

Literature and research in the area of neonatal pain offers no gold standard for how to manage neonatal pain in a comprehensive and consistent manner that avoids excessive use of analgesics. Despite the development of over 40 neonatal pain tools to optimise pain assessment,6 neonatal pain remains undertreated with subsequent physical and neurological effects on the immature and critically unwell neonate.7 Repeated and prolonged pain exposure has also been associated with alterations in long term pain processing ability and brain development due to remodelling of the nociceptive pain pathways of the central nervous system.8  Researchers have postulated that white matter injury from untreated pain in this critical period of brain development, may be in part responsible for the increase in

pain sensitivity and behavioural disorders witnessed in children and adolescents.6,9-12 Alternatively, the increased use of opioid analgesia to ameliorate the complications associated with untreated or poorly managed pain has been associated with many other complications including over sedation, prolonged mechanical ventilation, increased length of stays and the subsequent development of iatrogenic withdrawal syndrome (IWS), a syndrome of tolerance and dependence that has deleterious physiological effects on the vulnerable newborn.13,14,

Surgical emergencies are an integral part of neonatal admissions in tertiary NICU’s globally, accounting for 5-10 % of all newborns admitted. 15,16 With such a large cohort of neonates undergoing invasive surgical management, optimal pain assessment and analgesic therapy is a critical component of their care. The assessment and management of pain remains a challenge for members of the neonatal multi-disciplinary team and consequently families of neonates being cared for in a surgical neonatal intensive care. Effectively assessing and scoring neonatal pain using validated tools is integral to this process, but responsive individualised pain management is also vital if prompt alleviation of pain is to occur with minimisation of excessive use of opioid therapy. Considering the aforementioned complications and adverse outcomes associated with managing neonatal pain, particularly with emerging new evidence that the surgical newborn is at greater risk of poorer neurodevelopmental outcomes than those newborns who have not had surgery, 17 accurate assessment and a prompt consistent approach to the management of pain must be a priority for clinicians in the NICU.

The introduction of a nurse-led model and/or algorithm may improve pain practices in the neonatal intensive care for the postoperative neonate based on the results of studies implementing these tools in other populations.18,19

NCA is a method of pain management that provides nursing staff with the autonomous ability to titrate analgesia according to patient need.20 This modality of analgesia, allows opportunities for the nurse to administer bolus dosing on top of a continuous background infusion rate and titrate analgesia within defined boundaries. This form of analgesic management, not only allows the patient to receive analgesia promptly for episodes of breakthrough pain, but prior to any anticipated painful event or procedure.21

Researchers have found that algorithm based sedation protocols with targeted comfort scoring in children, were not only safe and feasible, but decreased the use of sedatives and improved overall comfort assessments in these patients.22,23 A study by Falange et al, also reported that using a pain assessment tool in conjunction with a nurse led analgesic algorithm in post-operative paediatric patients, reduced the incidence of moderate to severe pain from 46% to 4% in the early postoperative period.24 Similar results have been seen in the neonatal population. A recent systematic review completed by Muirhead and colleagues 3analysing 14 studies on nurse -controlled analgesia in the neonatal population concluded that the use of nurse-controlled has shown some effect in reducing the amount of opioid analgesia required without compromising pain relief or increasing the risk of any adverse events.

This Neonatal Nurse Controlled model has been developed to minimise the need for continual escalation and review for the instigation, titration and weaning of opioids and other pharmacological measures ensuring a consistent and individualised approach to managing neonatal pain.

## AIM OF STUDY

To conduct a pilot RCT comparing the use of a model of neonatal nurse controlled analgesia (NNCA) to standard care (medically managed post -operative analgesia) for infants equal to or greater than 35 weeks’ gestation. This pilot will inform the study methods for a larger RCT: including training, recruitment, randomisation, data collection tools, procedures and neonatal outcomes.

**STUDY DESIGN**

A parallel two-arm, unblinded pilot randomised controlled trial.

**STUDY SETTING**

The Cardiac/Surgical intensive care (C/S), Neonatal Critical Care Unit (NCCU), Mater Mothers’ Hospital (MMH), South Brisbane, QLD.

## STUDY POPULATION

Participants will be babies admitted to the NCCU who require surgical intervention.

Inclusion Criteria

* Infants admitted to the Neonatal Critical Care Unit (NCCU) for neonatal surgery
* Infants ≥35 PMA
* Opioid naïve infants or infants commenced on opioids for the first time within the previous 48hrs
* Haemodynamically stable as determined by treating medical team
* Able to be cared for in a 1:1 nurse allocation (for at least the first 24hrs post-operatively) by a nursing clinician with a minimum of 2-3years neonatal surgical experience
* Parent present that is able to provide informed consent

Exclusion Criteria

* Infants < 35weeks gestation (PMA)
* Infants with any Illness complicated by physical instability (e.g. Persistent Pulmonary Hypertension of the Newborn ) in which additional sedation/muscle relaxation is required to manage clinical condition.
* Infants with complex surgical conditions (as determined by treating neonatologist)
* Infants with impaired hepatic or kidney function/Unconjugated hyperbilirubinaemia

**STUDY OUTCOMES**

Primary Outcomes

The outcomes for this pilot RCT are focussed on determining feasibility of the study methods. Feasibility outcomes will be measured via an audit of recruitment processes, NNCA pathway, Babies on Board (BOB) database as well as the neonatal Fluid Quota Flow Record and Prescription form-neonatal and Paediatric Medication chart.

Primary (feasibility) outcomes are listed below:

* Number of infants meeting the inclusion criteria within the study period.
* Number of infants recruited.
* Proportion of potentially eligible infants not recruited.
* Reasons infants were not recruited.
* Compliance with the trial intervention (Adherence to model of NNCA).
* Reasons for non-compliance.
* Completeness of data collection for main trial outcomes.
* Proportion of participants who were withdrawn from the study or are lost to follow-up and reasons.
* Number of parent surveys completed.

Secondary (neonatal) Outcomes are listed below:

* Intensity of pain scores
* Overall opioid consumption
* Time to cessation of all analgesics
* Time on invasive ventilation
* Time to full enteral feeds
* Number of adverse events
* Parental satisfaction score
* Incidence of Iatrogenic Withdrawal Syndrome (IWS)
* Length of Stay

**STUDY PROCEDURES**

Recruitment and Consent

As part of their CNC clinical role at the Mater Mothers’ Hospital, the lead researcher of this pilot trial is involved in orientating families to the NCCU and providing information on clinical management to families with an antenatal diagnosis of a surgical condition (case managed through the Maternal Fetal Medicine department (MFM). Families generally visit the NCCU for this orientation and familiarisation between 25- 39weeks gestation. Information provided to families include:

* Anticipated clinical care requirements for illness and recovery period
* Equipment and monitoring
* Pain management strategies utilised to provide comfort and alleviate pain
* Family centred care interventions they can participate in while an inpatient in the NCCU

At this orientation and information sharing session, parents are provided with an information pack. Standards documents currently provided to families include a NCCU orientation booklet and brochures/handouts on:

* General neonatal pain management practices in the NCCU
* Various tests/procedures that a baby may undergo as part of their admission to the NCCU
* NCCU visiting policy
* Hand hygiene and infection control
* Expressing and breast feeding for a baby in the NCCU
* Surgical condition specific information
* QR link to online resources
* Approved parent information brochure that outlines the NCCU’s commitment to improving the family experience by conducting various research projects focused on family centered developmental care.

A separate parent information sheet will be added to this standard orientation pack for parents so that they have early information on current unit pain interventions/care requirements that their baby may experience following an operation. (refer to managing post-operative pain in the NCCU document)

Participants will be actively recruited after birth. Identification of infants admitted to the NCCU and diagnosed either antenatally or post-natally with a surgical diagnosis requiring surgical intervention will be done by the lead researcher using the inpatient electronic system “Babies on Board (BOB).” This is the admission database accessible to all neonatal clinicians working within the NCCU. Once the infants have been identified, parent/s of potential participants meeting the study inclusion criteria will be seen at the cot-side prior to the infant’s operation, invited to partake in the study and provided with a Participant Information and Consent Form(PICF) detailing the purpose, aims and design of the trial, what participation involves and the voluntary nature of the trial. Parents will not be approached if the infant’s operation is imminent (within 30 mins). Parent’s will be informed that participation in this pilot trial is not a requirement of care in the C/S unit at the MMH and that there will be no consequences to themselves or impact on the care their baby receives if they choose not to participate. Following this, parent/s who decide to participate will be asked to complete a consent form. Consent forms will be securely stored separately from the data. The lead researcher will conduct in-services sessions about the study for staff across the NCCU.

Withdrawal

If parents decide to consent for their infant to take part in the pilot trial and later change their mind, they are free to withdraw their infant from the trial at any time without giving any reason. Post-operative analgesic management will revert to standard medical management. A ‘Withdrawal of Consent’ form will be provided for the parent/s to complete. The withdrawal of consent form will offer the option to allow the investigators to continue to use (or not) any data already collected. They will be advised that the treatment of their infant will not be impacted by their decision to participate, or not, in the study.

Investigators may withdraw the infant from the study at any time for administrative or safety reasons. This will be communicated to the infant’s parents or guardians and their clinical team.

Reasons infant’s may be withdrawn from the study early include:

* Parental request
* The decision of the investigator
* The attending Neonatologist has concerns about the haemostability of the infant
* Clinical deterioration of the infant

Randomisation

A batch of 26 opaque, sequentially numbered envelopes will be prepared by a research assistant, independent of the research team. Following identification of a potential participant, one envelope will be selected in sequential order and brought to the site of the potential participant. This will be opened outside the parent/ participant’s room by the lead researcher once consent has been verified. This envelope will direct the lead researcher to assign the participant to either the control or intervention group and care will be followed accordingly. The envelopes will be kept in a locked drawer within the office of the Clinical Nurse Consultant in the NCCU. This is an open label study as both parents and clinicians will be aware of and utilising a different process to manage post-operative pain.

Measurement tools

Data for the primary and secondary outcomes will be collected by the lead researcher from the infant’s medical CAR, electronic database (Babies on Board/BOB) standard Mater Health clinical forms used in care of the post-operative infant and newly developed data collection tools:

1. Neonatal Observation Clinical Record
2. Neonatal Fluid Quota Flow Record and Prescription Form-Neonatal
3. Pain Assessment Tool(PAT) -Neonatal -07CFM
4. Neonatal Long Stay Medication Chart-Clinical Form-07
5. Acute Cardio/Respiratory Events-Neonatal
6. Ventilation Flow Record –Neonatal
7. WAT-1 Clinical Record-Neonatal

Other tools used to collect data will include:

1. Three clinical audit tools developed for this pilot study
2. Neonatal Nurse Controlled Analgesia Model
3. Parent attitudes about infant nociception (PAIN) tool: *reproduced with permission from author*
4. Comforting your baby after surgery parental information sheet
5. PICF
6. Parent information on post-operative pain management in the NCCU

|  |  |
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| Primary Outcome | Data Collection Tools |
| Number of infants meeting the inclusion criteria within the study period. | BOB database |
| Number of infants recruited | Daily study checklist, Site Randomisation Log, PICF. |
| Number of infants recruited from families with an antenatal awareness of study compared to number of infants recruited where families had no knowledge of study antenatally. | BOB database. |
| Proportion of potentially eligible infants not recruited. | BOB database. |
| Reasons infants were not recruited. | CAR, BOB database. |
| Compliance with the trial intervention (Adherence to model of NNCA). | Daily participant data audit form, Neonatal Observation Clinical Record, Fluid Quota Flow Record and Prescription Form-Neonatal, Neonatal Long Stay Medication Chart-Clinical Form-07 CMF, Pain Assessment Tool(PAT) -Neonatal -07CFM, Neonatal Nurse Controlled Analgesia Clinical Pathway. |
| Reasons for non-compliance. | Daily participant data audit form, BOB database, Neonatal Observation Clinical Record, CAR. |
| Completeness of data collection for main trial outcomes. | Daily participant data audit form, Neonatal Observation Clinical Record, Fluid Quota Flow Record and Prescription Form-Neonatal, Neonatal Long Stay Medication Chart-Clinical Form-07 CMF, Daily study checklist, Participant enrolment data form, BOB database, Pain Assessment Tool(PAT) -Neonatal -07CFM, Acute Cardio/Respiratory Events-Neonatal, Ventilation Flow Record –Neonatal, Parent attitudes about infant nociception (PAIN) tool, WAT-1 Clinical Form-Neonatal, Neonatal Nurse Controlled Analgesia Clinical Pathway. |
| Proportion of participants who were withdrawn from the study or are lost to follow-up and reasons. | Form for Withdrawal of Participation -Parent/Guardian. |
| Number of parent surveys completed | Parent attitudes about infant nociception (PAIN) tool completed surveys |

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| **Secondary Outcomes** | **Data Collection Tools** |
| Intensity of pain scores | Pain Assessment Tool(PAT) -Neonatal -07CFM, Neonatal Fluid Quota Flow Record and Prescription Form-Neonatal. |
| Opioid consumption | Neonatal Long Stay Medication Chart-Clinical Form-07, Fluid Quota Flow Record and Prescription Form-Neonatal, BOB Database. |
| Time to cessation of all analgesics | BOB Database, Neonatal Fluid Quota Flow Record and Prescription Form-Neonatal, Neonatal Long Stay Medication Chart-Clinical Form-07. |
| Time on invasive ventilation | BOB database, Ventilation Flow Record –Neonatal. |
| Time to full enteral feeds | BOB database, Neonatal Fluid Quota Flow Record and Prescription Form-Neonatal. |
| Number of adverse events | Acute Cardio/Respiratory Events-Neonatal, CAR. |
| Parental satisfaction score | Parent attitudes about infant nociception (PAIN) tool. |
| Incidence of IWS | WAT-1 Clinical Form-Neonatal. |
| Length of stay | BOB database. |

Overview of intervention and control group procedure

Post-operative care will remain the same for infants in both control and treatment groups apart from the Neonatal Nurse Controlled Analgesic model of care.

**Control group:**

Infants allocated to the control group will receive current standard medical management of post-operative pain. There is no current guideline or standardisation for neonatal post-operative pain relief and clinical management of analgesia is dependent on Neonatologist/treating medical team on service. Titration and weaning of analgesia is completed following review/discussion with MO/NNP. Pain scores, using the MPAT tool may be used to help guide the decision to titrate analgesia weaning

Interventions may include:

* Commencement of an opioid at a rate determined by treating team (either morphine/fentanyl). Usual commencement rate may be between 10-20micrograms/kg/hr
* Maximal morphine rate may be prescribed up to 40micrograms/kg/hr
* A loading dose may be given at commencement of infusion though no instructions on when this should be utilised.
* Prescribed PRN bolus medication may be given via nursing clinicians if there is predetermined criteria or if there is escalation for the need for a review to obtain further administration of opioid administration
* Other sedatives may be prescribed to be administered concurrently.
* Review of management occurs on the daily ward round. There is no other mandatory review times.
* Possible commencement of IV paracetamol in the first 72hrs post-operative.
* Possible use of nominated non-pharmacological measures (repositioning, swaddling, containment, decreasing external stimuli, soothing voice, nappy change, non-nutritive sucking, kangaroo care and breastfeed)
* Use of pain tool to measure pain intensity (current protocol is hrly for 24hrs then 2-4hrly while an inpatient in the NCCU)
* Parents may be encouraged to provide some non-pharmacological measures, though specific education to families is not currently given
* Commencement of dexmedetomidine for additional adjunctive analgesia if required.
* Use of an Iatrogenic withdrawal scoring tool that is commenced on day 5 to facilitate detection of Iatrogenic withdrawal. No current guideline or recommendations for ongoing management once Iatrogenic withdrawal has been identified is available in the NCCU

**Treatment group:**

* Commencement, titration and weaning of analgesia will be via the developed model of NNCA, including more detailed information on the use of non-pharmacological measures and education on supportive interventions families may utilise to manage post-operative pain.
* The intervention education to both clinical staff and families will be provided by the lead researcher. Ongoing support will be provided to families by the primary care nurse.

**Control and treatment groups: Parental Views**

Data on parental views related to parental experience in respect to pain and pain management for their infant in the NICU will be sought from both the control and treatment group participant parent/s. This will be done via the Parent attitudes about infant nociception (PAIN) tool. This is a 51 question self -reported questionnaire that aims to measure parents’ attitudes about their infant’s pain including their expectations (beliefs about future events), involvement (knowledge and participation in care), and satisfaction (personal evaluation of health services and health providers). In previous studies, this instrument has showed good internal consistency reliability for the expectations and satisfaction dimensions.26,27  This survey will be conducted via either an electronic format using the Checkbox™ platform or a paper version if required.

Data management

1. All data will be entered onto an excel database and stored on a secure computer owned by Mater Health with password-controlled access. Only the primary research team will have access to the data. The de-identified data set and identified data set will be stored in separate folders on the L drive on the Mater server. The data will be retained for a five-year period following the date of final publication. Data will be stored in line with State and Federal Privacy Legislation, Good Clinical Practice and the NHMRC guidelines. Bimonthly reports will be generated to look for missing data, outliers, and inconsistencies. Inconsistencies will be checked against original data forms and corrections made as needed.

## Safety considerations /patient safety

Infants will have continuous pulse oximetry and cardiopulmonary monitoring as per standard neonatal intensive care practice. Standard post-operative neonatal blood pressure is routinely attended 4-6th hourly for non-invasive monitoring and continuously for invasive blood pressure monitoring. The treatment arm of this study will have blood pressure monitoring completed 2nd hourly at a minimum as an additional safety measure. Pain scores are routinely attended hourly post operatively for 24hrs then 2nd hourly until off all analgesics. This will continue for both arms of the trial though the treatment arm may have more frequent assessment if required as per the NCCA pathway. All infants in the NCCU have access to emergency resuscitation equipment and the availability of skilled staff with the ability to provide advanced respiratory support if required 24 hours per day.

For infants not receiving invasive respiratory support in the treatment arm of the trial, the maximal morphine rate able to be administered is 15micrograms/kg/hr as per the NNCA. If an infant is requiring a greater amount than this, a medical/Neonatal Nurse Practitioner review is required for further management decisions as per the NNCA.

The NNCA will be prescribed using defined parameters as outlined in the model. These parameters were agreed upon by an expert multi-disciplinary Delphi panel of neonatal medical/nursing clinicians and pharmacists to ensure pharmacological agents, dosages, and escalation process was appropriate, relevant, and within accepted thresholds for safety. For any infant receiving the treatment arm of the pilot study, a Medical/NNP review can be requested at any stage of the NNCA but a mandatory review is required after two (2) cycles through each pathway to assess current clinical condition of infant prior to any further escalation in management.

All rate changes and administration of bolus medications as per NNCA, will be independently double checked by two (2) registered nurses/midwives/medical officers. Hourly assessment and documentation of IV administration site for patency. This is standard process for all intravenous medications and fluids in the neonatal intensive care. This includeshourly documentation of dose infused for previous hour. Any non-pharmacological/pharmacological interventions must be clearly documented on infant’s standard observation/fluid administration/pain assessment tool or clinical form as per standard clinical care.

Any enrolled infant who requires the commencement of other pharmacological agents to maintain haemostability, will be withdrawn from the study and will revert to clinical management as per the treating medical team.

Serious Adverse Events (SAEs) are not expected in this study. If any SAEs do occur in either the control or treatment arm, they will be documented and reported as per standard Mater incident reporting processes (ERIC). They will also be recorded, categorised, assessed and reported to the clinical monitor, who will be a clinician not directly associated with this study. A SAE is an adverse event that occurs after enrolment in the study and causes any of the following outcomes:

* Death or
* Is life threatening, or
* Requires prolongation hospitalisation, or
* Results on a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions.

All staff in the Cardiac/Surgical intensive care who have a minimum of two years neonatal surgical experience will receive formalised education on the model of NNCA prior to the commencement of the pilot study. All medical/NNP staff will also receive education on the model of NNCA.

## Sample size and statistical power

General guidelines for pilot studies recommend using 10% of the sample required for a full study, however this may be inadequate to provide statistical estimates for a larger study.25 Samples ranging in size from 10 to 40 per group are generally considered adequate for a pilot study. 25

To estimate the sample size for this study three areas were considered. Firstly, the estimated timeframe to complete the study, secondly, this pilot is being conducted to assess feasibility of study design primarily, and finally the number of surgical infants admitted to the NCCU over one year (there are 200 surgical infants on average admitted per year, though not all infants require surgical intervention). Allowing for this, attrition rate and inability of lead researcher to be available 24hrs per day to obtain consent, it was expected that a sample size of 26 participants in total, 13 in each arm, would be required for this pilot study.

## DATA ANALYSIS

This is a pilot study and as such we acknowledge that the study is underpowered but the sample size is sufficient to obtain estimates of the size of the effects for use in sample size calculation for a larger trial and to assess the feasibility and acceptability of the mode of NNCA. All data will be transferred to a SPSS dataset and analysed using SPSS Statistics Version 27 (IBM Corporation, Armonk, NY, USA). Categorical data will be described using frequencies and percentages and continuous data using, mean and standard deviation for normally distributed data and median and interquartile range for non-normally distributed data. The comparison of interest is between NNCA and standard care. Categorical variables will be examined using Pearson’s Chi-squared test or Fisher’s exact test where more than 20% of the expected values are less than 5. Continuous variables will be examined using Student t-test or Mann Whitney U test if data is not normally distributed. *P* values <0.05 will be considered statistically significant. The decision as to whether we present p-value in a manuscript is not known at present, but the above hypothesis testing will be completed. The statistical methods used are robust to small sample size although a non-significant p-values are expected. Their use is primarily assisting the researcher with observing trends and interpretation.

Further acceptability of the NNCA model will be determined by a researcher developed survey using a 5-point Likert scale where 1=strongly agree to 5 =strongly disagree. Questions will focus on use of the tool, impact on practice, perceived benefit, promotion of nurse autonomy and strengths and limitations. A decision to proceed to a larger scale evaluation will be based on recruitment, retention, outcome data generated, intervention acceptability and feasibility and fidelity of delivery.

Staff acceptability survey

1. The NCCA model pathways are logical and able to be followed without difficulty
2. Guidelines for use of the NNCA model are comprehensive and contain relevant and appropriate information for holistic management of Infant’s pain
3. It is beneficial to have a formalised escalation pathway for post-operative pain management
4. Management of post-operative pain is simplified by having a formalised titration and weaning pathway
5. The pathways give me greater autonomy in managing infant’s comfort and pain
6. The pathways improve overall analgesic management in the post-operative period
7. Would you like to provide any additional feedback on the NNCA model?

**STUDY DURATION**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Milestone | 2022 | 2023 | | | | | | | | | | | | 2024 | |
| [Year Quarter or months in this row ->] | Dec | Jan | Feb | March | April | May | June | July | Aug | Sep | Oct | Nov | Dec | Jan | Feb |
| Ethics application |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Governance (Site Specific Application or SSA) and contract Agreements |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Study Planning |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Participant recruitment |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Data analysis |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Write up of results |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Progress report to Ethics and Governance |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Final report to Ethics and Governance |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Presentation and/or Publication of findings |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

## ETHICAL CONSIDERATIONS

All procedures in this study will conform to the NHMRC National Statement on Ethical Conduct in Human Research (2007, updated 2018) and will be conducted according to protocol approved by the Human Research Ethics Committee, Mater Misericordiae Limited, South Brisbane, Queensland. Following approval form Mater HREC and Mater Governance, the protocol and any documents relating to approval will be forwarded to Human Research Ethics Committee, The University of Queensland for administrative review.

Vulnerable Subject group

Testing a model of NNCA is important to determine the effectiveness of NNCA in providing a more individualised and responsive analgesic approach that may reduce the excessive use of opioid therapy and its subsequent complications while ensuring optimal pain relief. To be able to answer this question, a small pilot study to test the study methodology is necessary on this post-operative cohort of infants. Consequently, extreme care will be taken to ensure that this research project is not contrary to the infant’s interest. The inclusion and exclusion criteria clearly outline the suitability for recruitment into this study and the infant will not be randomised unless there is Neonatologist approval. Every effort will be made not to burden the parents and consent will be free and informed and refusal will not in any way compromise the care of the infant. Clinical care of the infant will always take priority over the study and the clinical team caring for the infant can request cessation of the study at any time if it is deemed to be in the infant’s best interest. The medications and dosages utilised in the treatment arm of this pilot RCT are currently utilised in the post-operative care of the surgical infant at the NCCU, MMH.

#### DISSEMINATION OF RESULTS AND PUBLICATIONS

The results from this study will be disseminated via internal and external reports; publications in peer-reviewed journals; abstracts presented at peer-reviewed meetings on both national and international platforms. If parents would like to be informed of the final results at study completion, they may contact the principal investigator via the details outlined in the PICF for further information.

**BUDGET**

|  |  |  |  |
| --- | --- | --- | --- |
| Item/s | BUDGET for Site | In-Kind | Cash |
| FUNDING | | | |
| Grant | Betty McGrath Seeding grant |  | $50,000 |
| Sponsor [Individual / organisation or group taking in responsibility to initiate, manage or finance the study] | Mater Research |  |  |
|  | | | |
| Personnel |  |  |  |
| Principal Investigator | Funding for 28 hours per fortnight has been achieved to support this research. This allows for back fill of current CNC appointment at 0.35 fte over a 12month period. |  |  |
| Associate Investigator/s |  | Time required to assist and support principal investigator. |  |
| TOTAL Expenses |  |  | $50,000 |

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