**Title Page**

**Title:**

Early Nutrition Support in Neurosurgical Patients

-Prospective Cohort Study Based on Post-operative Gastrointestinal Recovery Scores

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**Abbreviated title:**

Early Nutrition Support in Neurosurgical Patients

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**Disclosure Statement:**

Authors have no significant financial or non-financial disclosures to make

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| --- | --- | --- | --- | --- |
| Version Number | Date | Changes | Author | |
| 1.1 | 1/10/2018 | Initial document version in line with  best s scientific and research principles | Dr Ana Licina | |
| 1.2 | 9/10/2018 | Additional Sample Size calculations | Dr Ana Licina | |
| 1.3 | 24/10/2018 | Review and Change of Primary Outcome  Review and Change of Sample Size  Additonal Sample Size Calculation | Dr Ana Licina  Dr Andrew Silvers | |
| 1.4 | 26/10/2018 | Editing of Primary Outcome | Dr Andrew Silvers  Dr Ana Licina | |
| 1.5 | 12/11/2018 | Review and Change of Study Methodology | | Dr Ana Licina  Dr Andrew Silvers |
| 1.6 | 25/11/2018 | Review of Statistical Methods and Project Update | | Dr Ana Licina  Dr Andrew Silvers |

**PROJECT TITLE:**

Early Nutritional Support for Elective Neurosurgical Patients

-Prospective Cohort Study

**Version Number: 1.8 and Date: 26/11/2018**

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**1. Glossary and abbreviation of terms**

Early recovery after surgery (ERAS), Enteral Nutrition (EN), Patient Reported Outcome Measures ( PROM’s)

**2. Study Sites**

**2.1 Study location**

St Vincents Private Hospital Fitzroy, Melbourne

**3. Relevant Background Information and Literature Review**

**3.1 Lay Summary**

With the modern developments in surgery and perioperative patient care, there has been a focus on early patient recovery after surgery. Enhanced recovery processes in neurosurgical patients have not been well established in evidence based medicine or quality assurance programmes. It has been shown that enhanced recovery processes can have marked improvement on recovery following surgical procedures. Patient perioperative experience has been shown to be improved through comprehensive multimodal care. Part of this multimodal care involves decreasing the post-operative fasting periods through utilising objective measures of gut function. We plan to measure the oral intake as guided by more objective measures of bowel function recovery. We will use this opportunity to survey the attitudes of health professionals towards early nutrition in the post-operative period in neurosurgical patients.

**3.2 Introduction**

Early recovery after surgery (ERAS) has been well established in different surgical sub-specialties, facilitating patient recovery and improving the patient outcomes. Colorectal Surgical subspecialty has led the way in terms of the pre-operative, intra-operative and post-operative evidence based quality improvements in order to positively impact patient care. ERAS in Neurosurgical patient care, is increasingly recognized as essential to peri-operative management of this group of patients. Essential part of the early recovery after surgery protocols is post-operative nutritional management. Currently in our institution patients are often fasted on empirical basis until the subjective return of post-operative bowel function. This is not a well-defined process.

**3.3Background informationand literature review**

Through the nature of the complex patient care required, there can be challenges in establishing and setting up an Early Neurosurgical Recovery Program in patients having major spinal surgery. In particular there are cognitive biases reflected in prolonged peri-operative fasting of neurosurgical patients, which may have an effect on the patient recovery, surgical and anaesthetic complications as well as patient satisfaction measures. A number of international centers are leading the way in establishing Neurosurgical Early Recovery Programs in major spinal surgery.

St Vincent’s Private Hospital has been a leader in Australasian patient focused on quality improvement programs combined with evidence based practice improvements. This project aims to facilitate improved outcomes in patient having spinal neurosurgical procedures through minimization of the fasting periods and preventing peri-operative deconditioning in the post-operative period. Patients are often fasted for prolonged periods in the post-operative period due to concerns with regards to the management of analgesia, post-operative nausea and vomiting and patient tolerance of nutrition. In addition, historical beliefs from the multidisciplinary care team may impact upon this process.

In patients having colorectal surgery there have been multiple benefits shown from earlier institution of nutrition in evidence based studies. Studies have consistently demonstrated that early enteral nutrition (EN) is safe and well tolerated, showing a reduction in wound morbidity and healing, fewer septic complications and improved protein kinetics in patients administered early EN.

Minimally invasive surgery where possible, multimodal analgesia, early mobilization and early enteral nutrition have been considered key elements of enhanced recovery protocols in spinal surgery ( Elsarrag). Many of the studies report on early mobilization in conjunction with dietary libertization, therefore making it difficult to distinguish the clinical benefit of either intervention.

Prolonged fasting and inconsistent fasting practices have been identified as a clinician dis-satisfaction measure in the peri-operative neurosurgical population at our institution. In the colorectal patient population, studies have shown an independent association of poor post-operative nutrition with lower five-year survival.

There can often be difficulties in the assessment of suitability of patients for instituting the post procedural feeding in neurosurgical patients. In this multi-stage project, we aim to address the post-operative fasting through an implementation of post-op evidence based nutritional protocols as guided by the I-FEED score in the neurosurgical patients having spinal surgery.

Through the qualitative aspect of the study, we plan to survey the attitudes of our Nursing Cohort. In addition, we plan to survey the attitudes of Neurosurgeons and Anaesthetists towards post-operative feeding and nutrition.

The quantitative aspect of the study is structured as a prospective cohort study. The first cohort will receive the current standard of care with regards to post-operative nutrition. The second cohort will receive the newly implemented standard of care using the I-FEED score as a measure of post-operative gastro-intestinal function. I-FEED score will therefore guide the post-operative fasting period and time to nutrition.

I-FEED score is an increasingly used measure of the gastrointestinal system function used to guide nutritional and clinical support in peri-operative gastrointestinal patient care. It is a measurement tool, which is gaining construct validity due to its applicability.

We aim to address the prolonged the peri-operative fasting through a post-operative nutritional program as guided by the I-FEED score, whilst using a modified protocol suitable for neurosurgical spinal patients.

We plan to measure the practice improvement outcome, by comparing the period of time fasted after the institution of the protocol, with the current post-operative fasting times. In addition, we plan to measure a number of anaesthetic and surgical clinical outcomes as well as selected Patient Reported Outcome Measures (PROM). Patient Reported Outcome Measures (PROM) of health status are elicited directly from the patient. PROM’s are increasingly gaining recognition as valid and reliable measures of patient experience used to guide the quality improvement in enhanced recovery programs.

Anticipated benefits of this project include:

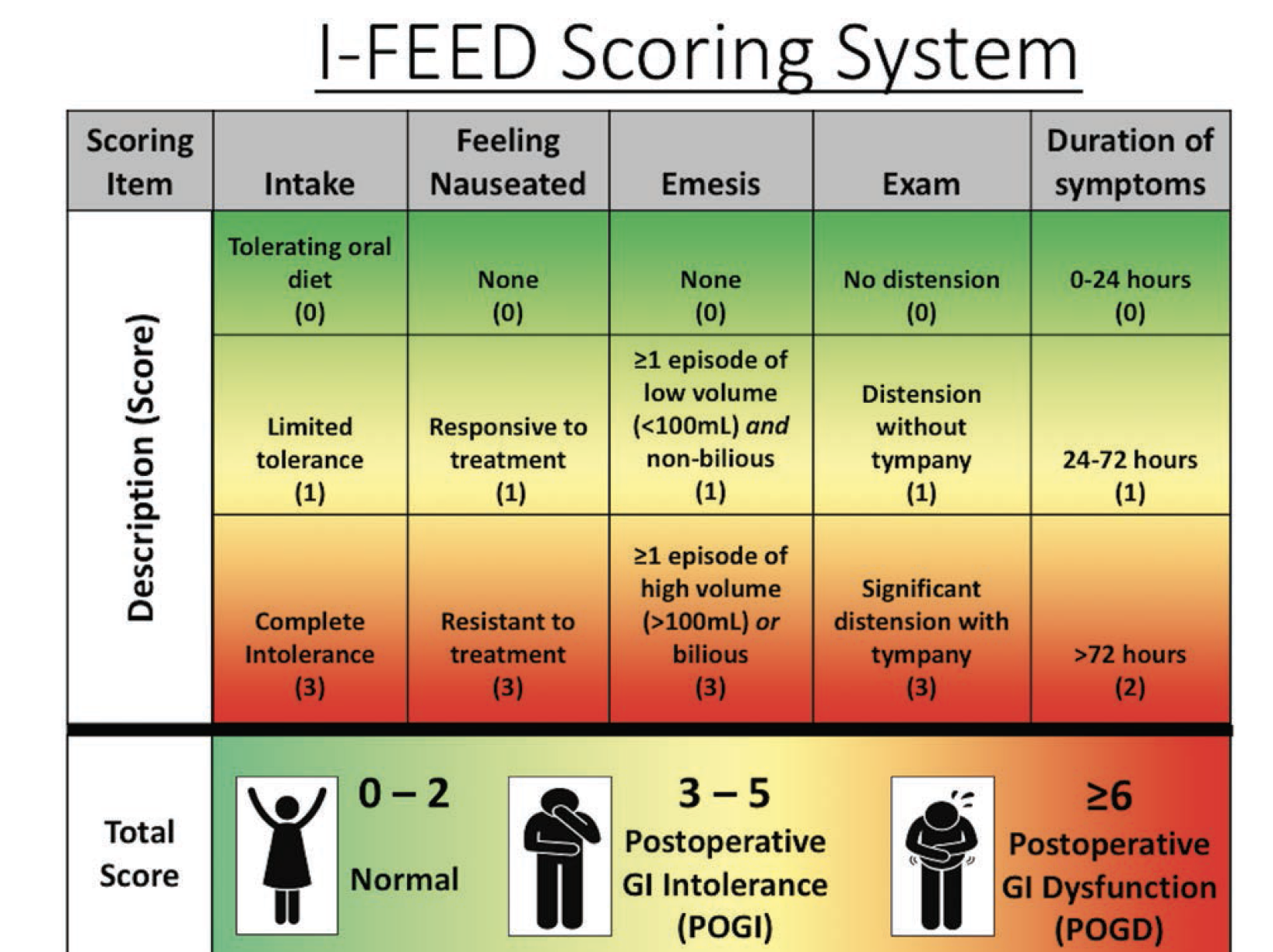
1. Improve the nutritional post-operative management of patients having major spinal at St Vincent’s Private Hospital Melbourne.

2. Increase awareness among the nursing staff of more optimal post-operative nutritional management in neurosurgical patients.

3. Introduce a more objective measure of post-operative gastrointestinal function in neurosurgical patients having spinal surgery.

4. Allow a model of accelerated post-operative care which may be applicable to other surgical groups within St Vincent’s Healthcare Australia.

*Figure 1* Illustrative I-FEED Scoring System



*Table 1* Postoperative nutritional management according to the I-FEED Score

|  |  |
| --- | --- |
| *I-FEED score classification* | *Nutritional Management* |
| 0-2 Normal Gastrointestinal Function | In recovery area offer free fluids  On the ward, offer dietary libertization |
| 3-5 Postoperative GI Intolerance (POGI) | Offer free fluids as tolerated  Offer anti-emetic therapy  Initiate medical review as per standard institutional criteria |
| Greater than 6 Postoperative GI Dysfunction (POGD) | Offer anti-emetic therapy  Continue intravenous fluids as charted  Initiate medical review as per standard institutional criteria |

**4. Study Objectives**

**4.1 Hypothesis**

Our null hypothesis states that there will be no difference in the fasting times between the two cohorts observed (first control cohort with current fasting practices, second cohort following the agreed change in practice with regards to post-operative status).

**4.2 Study Aims**

The primary aim of the project is to compare the current period of post-operative fasting in neurosurgical spinal surgery patients with the period of fasting following the implementation of an early nutritional programme guided by the I-FEED scores.

Secondary aims including the comparison in the two cohorts of length of stay outcomes, relevant post-operative complications and selected Patient Reported Outcome Measures (PROM’s).

**4.3. Overview and Outcome Measures**

**The first stage** of this multidisciplinary quality improvement outcome will consist of a Survey of Nursing and Neurosurgical and Anaesthetic attitudes to post-operative feeding. We plan to assess and evaluate underlying attitudes of the main stake holders as well as potential barriers to change management. As a measure of the level of clinician satisfaction and quality improvement, we plan to survey the same clinical group following the institution of the Early Nutritional Program.

**The second stage** will consist of undertaking a prospective **cohort study**, analysis of the current post-operative fasting related outcomes and comparison to the relevant outcomes following the implementation of the intervention. The primary objective of this stage of the project will consist of generating benchmark data measuring accurately the post-operative fasting outcomes relating and potentially relating to fasting and nutrition.

|  |  |
| --- | --- |
| *Outcome classification* | *Specific outcome* |
| Primary clinically measured outcome | 1.1 Time elapsed from wake up to solid oral intake. |
| Secondary clinically measured outcomes | 1.2 Time elapsed to first clear fluid intake. |
|  | 1.3 Surgical and anaesthetic complications including:  1.3.1 Rates of Post-operative Infection.  1.3.2 Gastrointestinal Complications  Measured two days post-operatively. |
|  | 1.4. Surgical and anaesthetic complications including:  1.4.1 Rates of post-operative infection,  1.4.2 Gastrointestinal complications  Measured seven days post-operatively. |
|  | 1.5Time from admission to discharge home. |
|  | 1.6 Hospital Re-admission rates within a month of the surgical intervention. |
|  | 1.7 Patient Reported Outcome Measures (PROM) as  reflected in the QoR15 score (Quality of Recovery Score) measured at 24 and 48 hours. |

**5. Study Design**

**5.1 Study Type, Design and Schedule**

This project is low-cost prospective cohort study with one cohort having the current standard care. Following an agreed protocol change in post-operative nutrition, the second cohort of patients will be observed.

We also intend to conduct a qualitative study aspect of this project through a pre-and post initiation of change attitudes of nursing and medical staff.

As the nursing staff will be the primary participants in this practice change, it will be vital to ascertain any barriers to practice change.

**5.2 Standard Care and Additional to Standard Care Procedures**

All usual peri-operative high standard care will be delivered as per surgeons and anaesthetists preferences.

**5.3 Subject Allocation**

Initially subjects will be enrolled on continuous basis in order to assess the the primary and secondary outcomes including PROM’s (Patient Reported Outcome Measures), with the current model of care. This will consist of baseline data collection and will be supported wholly by the investigators.

Following the institutional change of the Early Feeding Initiative utilising the I-FEED score, subjects will be allocated on continuous basis until the quota of patients in the study group has been exhausted.

**5.4 Study methodology**

This is a prospective cohort study consisting of the control group and post- intervention group. We will collect the outcome data on the control group as projected. Following the intervention implementation, we will recruit patients on continuous basis for the interventional group. Each patient will undergo as consent process in line with appropriate research governance.

Investigators will facilitate ongoing project implementation, trouble shoot any ongoing queries, assist with the ward management as needed. We will also ensure timely compliant data collection of all outcomes. Compliance with instituted changes is a well-known established issue in ERAS programmes. We plan to manage this issue by supporting the institutional change both in the wards and through nursing management.

Heterogeneity due to underlying patients, anaesthesia and surgical factors is a well-known aspect of ERAS programmes. We plan to collect the data on the relevant peri-procedural factors and deal with the underlying heterogeneity in the analysis stages of the project.

**6. Study Population**

**6.1. Recruitment Procedure**

The allocated time for this study is 12 months in order to meet the demands for the clinical review of 140 patients. We plan to inform the anaesthesia and neurosurgical care providers of the study where the initial patient contact is made. Most of the data collection will occur in the post-operative period.

**6.2 Inclusion Criteria:**

1. All patients having Spinal Neurosurgical procedures.

**6.3 Exclusion Criteria:**

2.1. All patients where the Primary Care Provider (the Neurosurgeon in charge of the patient care) does not consider the agreed change of protocol implementation appropriate.

2.2 All patients who have a known intolerance to CHO supplements.

2.3 All patients who are unable to sign their own consent form.

2.4 All patients who need interpreting services.

**6.4 Illustrative Diagram of Patient Flow**

**Illustrative Patient Flow Diagram:**

PATIENT FLOW

Collect baseline data measures including

Patient and non-patient outcome variable

demographics

OPERATION

PRIOR TO PACU DISCHARGE

I-FEED SCORE

0-2

Give CHO drink according to I-FEED score

2 HOURS

I- FEED SCORE

0-2

Give solid normal diet according to I-FEED score

4 HOURS

I-FEED SCORE

8 HOURS

I-FEED SCORE

DAY 1

I-FEED SCORE

Patient and non-patient outcome variables

Discharge characteristics

**6.5 Timing and Duration of Study**

As per estimated sample size calculation, we plan obtain the underlying benchmark data on

70 patients in order to demonstrate a difference of 2 hours in the time to first solid oral intake Total of 140 patients will be included in the pre- and post- analysis to allow for lower than anticipated compliance, loss to follow up and data loss.

**6.6. Consent**

This project will comply with the NHMRC (Australia) best research practice guidelines.  Consent will be sought from patients as we will be collecting additional study data from patients. Data accessed for this project will be used for a purpose related to that of its original collection (ascertaining quality of care) and will be collected by clinicians and/or researchers/quality monitors who would normally have access to that data.

All potential participants will be provided with the Quality of Recovery Score 15 in the post-operative period both prior to and following the institution of the agreed change in protocol initiative through the use of the I-FEED score.

Patients will need to be autonomous, able to sign their own consent and informed under comfortable circumstances without undue influence to participate in the study.

**7. Participant Safety and Withdrawal**

**7.1 Risk Management and Safety**

This project is an observational cohort study, collecting descriptive data on the procedures performed routinely. There is minimal to no physical harm or discomfort involved. We will be collecting QoR15 data (Quality of Recovery Scores) for the patients involved in the study, which may cause minimal administrative burden on patients completing it the following day after surgery. However, ability to express their views on the quality of care received, may enhance patient satisfaction.

There will be an agreed change in post-operative nutrition protocols, with the use of the I-FEED scores post-operatively to guide the initiation of enteral feeding. This simple objective scoring system is unlikely to inconvenience the patients. It may however provide a greater administrative burden on the nursing staff during their regular duties. This however will be offset through increased training and professional improvement.

The nursing staff will be continually supported on the ward sin their assessments by the principal investigators. This will allow for a supportive environment minimizing the inter-disciplinary administrative burden. In addition, we will conduct our research in line with the best principles of research governance as outlined by NHMRC.

In particular, we will ensure the project meets the required research standards, our data is accurately collected and study is appropriately supervised by the relevant HREC.

**7.2 Handling of Withdrawals**

If patient choose to withdraw from being observed, a patient withdrawal form will be completed. Data will be analysed on an intention to treat basis.

**8. Data Security and Handling**

The Principal Investigator will be responsible for the secure storage of the data collected in this project. The case report forms will be stored securely in a locked office St Vincent’s Private Hospital, level 5. Electronic datasets will be stored securely within the St Vincent’s Private Hospital server as a password protected excel file.

A data re-identification key file will be stored as an encrypted file separate to the file containing the data. This will be a password protected file stored on a hospital server computer. Paper Case Report Forms will also be stored separately to any paper master identifier lists, which will maintain the security of the information.

All data will be kept for a minimum of 24 months from completion of the project. All Datasets will be kept for a period of five years from publication or for 5 years from subsequent decision not to publish. The data will then be destroyed in a secure confidential manner in accordance with local policies.

A permanent databank/database will not be established. The dataset is only intended to be used for this project only. It will be kept for the required timeframe as outlined in this section. Patients however will be consented for any other research projects resulting from this data.

**8.1 Data Collection and Identification:**

The information will be collected in a re-identifiable format. All the data collected will be entered onto the project case report form and issued with its own unique project identification number. A master identifier list with the patient UR and the corresponding project identification number dataset will be kept separately in a password protected file accessible only to the research personnel involved with the project.

**9. Statistical analysis**

**9.1 Sample Size and Justification**

Our sample size calculation was based on the primary outcome and the significant difference of 2 hours between the pre- and post-intervention cohort.

The data collected will be analysed through the STATA 13 statistical program.

**Continuous summary outcome**

Mean and standard deviation

**The outcome**

**Post-Operative number of hours normal oral diet resumed.**

**The values assumed for outcomes in each group**

Mean number of hours until oral intake for Control Group **8**

Mean number of hours until oral intake for Study Group **6**

**Standard Deviation 4**

**The statistical test**

Test comparing two independent means of continuous outcomes

**Alpha error**

Two tailed P value **<0.05**

**Power**

**0.8**

**The calculated sample size per group, both assuming no loss of data**

64 per group.

Due to the potential for decreased compliance, loss to follow up and missing data, we plan to enrol additional 12 patients to a total of 140 inclusive of both groups.

**9.2 Statistical Methods-Outcomes**

The intervention arm will be compared against the control for all primary analysis.

Descriptive statistics (mean (SD) or median (IQR)) will be used for continuous variables. Normality will be confirmed using the Kolmogorov-Smirnov test.

After confirming a parametric data distribution through a histogram validation, we plan to use the student’s T-test to compare the means of different groups for the continuous outcome of number of hours to first meal. Quantitative variables (continuous outcomes) will be compared using the Student’s t-test or Mann-Whitney U-test to compare independent means. When indicated, a one-way repeated measures ANOVA will be performed. Categorical variables will be presented as absolute frequencies and percentage and compared between the two groups using the X2  or Fisher exact test.

**For subgroup analysis**, we will use regression methods with appropriate interaction terms. Multivariable regression will be based on logistic regression for binary outcomes and linear regression for continuous outcomes. The odds ratio(OR) will be calculated with its 95% confidence interval. A Bonferroni correction will be applied for multiple comparisons. We will use the Bonferroni method to appropriately adjust the overall significance for multiple primary and secondary outcomes. We will examine the residual to assess model assumptions and goodness of fit. For timed end-points such as mortality we will use the Kaplan-Meier survival analysis followed by multi-variable Cox proportional hazards model for adjusting the baselined variables.

P values will be reported to four decimal places with p-values less than 0.001 reported as p<0.001. STATA 13 will be used for statistical analysis. For all tests, we will use 2-sided p-values with alpha<0.05 level of significance.

**Statistical Methods-Additional Analysis** We plan to conduct subgroup analysis both with strong biological rationale and possible interaction effects.

**The subgroup analysis** will consist of assessing the primary outcome based on the

-anatomical site of the surgery.

-patient post-operative opioid intake in the first 24 hours.

-major versus minor spinal surgery.

**Potential confounders** with biological basis in this study will be considered as following:

1.Age 2.Weight/BMI 3.Gender 4.Underlying chronic pain conditions. 5.Underlying chronic analgesic consumption 6.underlying opioid consumption 7. Intra-operative opioid consumption (excluding remifentanil) 8. Intraoperative Technique, Volatile or Total Intravenous Anaesthesia.

**Univariate analysis** will be conducted and parameters which have a trend toward association with the primary outcome will be entered into the multivariable logistic model.Univariate analysis will be conducted on the significance of the following parameters: 1.Age 2.Weight/BMI 3.Gender 4.Underlying chronic pain conditions. 5.Underlying chronic analgesic consumption 6.underlying opioid consumption 7. Intra-operative opioid consumption (excluding remifentanil) 8. Intraoperative Technique, Volatile or Total Intravenous Anaesthesia With any of the above parameters demonstrating a two-tailed p value of less than <0.1, they would be entered in a multi-variable logistic regression model. This strategy would be employed in order to assess any significant contribution of these factors on the primary and secondary outcomes of interest.

|  |  |  |  |
| --- | --- | --- | --- |
| Variable/  outcome | hypothesis | outcome  measure | methods of  analysis |
| Primary  - total time to fasting as measured in oral diet | Improvement with I-FEED Scores in time to fasting | Number of hours  Fasted prior to oral diet intake | Comparison between 2 groups  T-test |
|  |  |  |  |
| Secondary  - total time to fasting as measured in clear fluids | Improvement | Number of hours fasted prior to clear fluid intake | Comparison between 2 groups  T-test |
|  |  |  |  |
| -time to discharge | Improvement | Number of hour spent in hospital prior to discharge | Comparison between 2 groups  T-test |
|  |  |  |  |
| -complication rates | Improvement | Number of individual complications per patients | Odds ratio comparison between two groups |
|  |  |  |  |
| -improvement in QOR15 scores at 24 hrs | Improvement | Continous QOR score | Comparison between 2 groups  T-test |
|  |  |  |  |
| Subgroup analysis |  |  | Regression Methods with appropriate interaction terms |

**9.3 Statistical Methods-Analysis Population and Missing Data**

Data collected from all randomised participants regardless of protocol adherence will assessed on an intention to treat and analyse accordingly. Therefore, any patients who have withdrawn or been lost to follow up will be managed on an intention to treat basis. Analysis of harms will be limited to participants who received the intervention.

Imputation Procedure for Missing Data Should any patients withdraw, we will report reasons for doing so and compare the reasons qualitatively. The effect that missing data might have on results will be assessed via sensitivity analysis of augmented data sets. Dropouts will be included in the analysis by modern imputation methods for data analysis. Treatment effect will be estimated through the method for multiple imputations.

**10. Dissemination of results**

Results will be presented at peer group education sessions, within departmental reports and potentially published in peer-reviewed journals and at conferences. Only non-identifiable pooled results will be presented with regards to both survey results and cohort study outcomes.

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**12. Appendices**

**Appendix A** Survey of Nursing Attitudes to Post-operative Fasting.

**Appendix B** Survey of Neurosurgical Attitudes to Post-operative Fasting.

**Appendix C** Data Collection Form for Prospective Cohort Study.

**Appendix D** Patient Reported Outcome Measure -Quality of Recovery 15 (QOR 15).

**Appendix E** I-FEED Illustration Form