Abbreviated Study Protocol

Australasian **MARS**: Australasian **M**ulticentre **A**spiration **R**isk **S**tudy

A pragmatic, multicentre observational cohort study comparing the incidence of pulmonary aspiration in hospitals with liberal (Sip Til Send) versus restrictive (usual care) preoperative fluid fasting

Lead investigators: **Dr Phuong Markman**, Staff specialist anaesthetist

Dr Ruth Blank, Staff specialist anaesthetist

Department of Anaesthesia and Perioperative Medicine
Cairns Hospital, Cairns, Queensland, AUSTRALIA

Associate investigator: **Dr Alec Beresford**, Specialist Anaesthetist,
Health NZ Waitaha Canterbury – Christchurch hospital,
New Zealand.

Supervisor: **Professor David Story**
Head, Department of Critical Care, The University of Melbourne.
President, ANZCA.

WHY SHOULD I CONTRIBUTE TO AUSTRALASIAN MARS?

- To ensure that anaesthetists have access to definitive evidence supporting the safety of perioperative fasting recommendations
- Completion of ANZCA CPD requirement for Practice Evaluation: Clinical Audit
- Principal investigator for each participating hospital or health network will be listed in resulting publications
- Data collection can be delegated to trainees as a scholar role activity

WHAT IS INVOLVED IN PARTICIPATING?

- Seek local governance approval for your hospital to participate, supported by our nationally recognised, multicentre ethics approval
- Submit de-identified data from operating theatre records regarding the number of anaesthetics undertaken in your hospital during the data collection period and their basic characteristics (typically provided by a theatre data manager in bulk, **does not** require manual data collection).
- Collect more detailed information about individual aspiration events as they occur (with an estimated aspiration rate of approximately 1/5000 this is likely a small number of cases)
- *There is no requirement to alter your hospital's current fasting policy, no need to recruit participants and there will be no impact on routine patient care.*
- Should you choose to take part, we will assist you throughout the process to ensure it is as efficient and streamlined as possible

BACKGROUND

Preoperative fasting is essential to minimise the risk of aspiration and 2 hours of fluid fasting in adults and 1 hour in children has been the standard recommendation [1]. However, with unpredictable theatre schedules, patients commonly end up fluid fasting for 7 to 13 hours [2]. Prolonged fluid deprivation can lead to thirst, nausea, anxiety, difficult IV access, hypotension during anaesthesia, and hypoglycaemia. Since 2022, a new program called "Sip Til Send" (STS) has been implemented across Australasia and in centres around the world, allowing patients to sip clear fluid until they are transported to theatre. The introduction of STS has successfully reduced fluid fasting times to 2 hours [3].

Although STS is gaining traction, its acceptance is still based on limited safety evidence from underpowered studies. Conducting adequately powered prospective randomised trials poses challenges due to the rarity of pulmonary aspiration, making it logistically difficult and expensive. There is consensus amongst the Australasian Sip Til Send Network that the best evidence for safety will be derived from pooling aspiration data into an Australasian multicentre study.

RESEARCH QUESTIONS

1. Is the incidence of pulmonary aspiration in hospitals practicing STS non-inferior compared to that in hospitals practicing restrictive fluid fasting?
2. What are the characteristics of the reported cases of aspiration?

METHODS

Study design
Multicentre observational cohort study of pulmonary aspiration during anaesthesia.

Hypothesis
The incidence of pulmonary aspiration in hospitals practicing Sip Til Send is non-inferior to that in hospitals practicing restrictive fluid fasting, whereby the non-inferiority limit for the incidence of aspiration in the Sip Til Send group is defined as double that in the restrictive fluid fasting group.

Setting
Participating hospitals across Australia and New Zealand, with central study co-ordinators located in Cairns Hospital, QLD.

Exposure
Patients of all ages will be included. Participating hospitals will continue their current fasting practices and report this accordingly. There is no requirement for a hospital to change their fasting program for the purpose of the study.

Outcomes
The primary outcome is the incidence of verified pulmonary aspiration. Secondary outcomes include the need for escalation of care due to aspiration events.

We will also conduct an exploratory analysis looking at variation in the incidence of aspiration between different hospitals according to reported fasting times and other known risk factors such as surgical specialty and patient demographics.

Data collection
The principal investigator from each participating hospital will provide reports to the central study co-ordinator based at Cairns Hospital. Each participating site submits reports at 1, 3, 6, 9 and 12 months after it starts data collection. The study will terminate once the total number of anaesthetics delivered reaches the pre-determined required sample size to power the study.

The reports will include:

- Number of verified pulmonary aspiration cases (numerator), with detailed information collected regarding each of these events (see below)

- Number of procedures under anaesthesia (denominator) and their characteristics (see below)
- Fluid fasting duration, obtained from hospital electronic records where available, or alternatively from random sampling of a subset of patients.

For each case of pulmonary aspiration, the report will contain the following data:

- Age
- Urgency of procedure (elective, emergency)
- ASA classification
- Surgical Subspecialty
- Phase of anaesthesia when aspiration occurred (induction, maintenance or emergence)
- Airway in situ at onset of aspiration
- Mode of anaesthesia - (general anaesthesia, unconscious sedation, conscious sedation, awake)
- Which diagnostic criteria for aspiration were met?
    - New dependency on supplemental oxygen that persists after recovery unit stay
    - Liquid or solid gastric content observed in or suctioned from the trachea
    - New chest radiographic imaging suggestive of aspiration
- Did the aspiration lead to an escalation of care? (Unplanned intubation or re-intubation, increased stay in recovery unit, unplanned over-night hospital admission, unplanned stay in high-dependency or intensive care unit, ventilator therapy, hypoxic brain damage, death)
- What fasting policy was active in the cohort to which the patient belonged? (6-2, 6-0, 6-4-2, 6-4-1, 6-4-0, 4-3-1, 4-3-0, other)
- When did the patient drink before induction? How much, and which fluid?
- When did the patient eat solid food before induction? What food and how much?
- (For paediatric cases) When did the child eat/drink milk-based food or breast milk? How much?
- Presence of risk factors for aspiration (BMI, diabetes, gastro-oesophageal reflux, GLP-1 receptor agonist therapy, previous bariatric surgery, Parkinson's disease, sepsis, gastrointestinal obstruction).

For all anaesthetic cases completed during the study period (denominator), the report will contain the following data:

- ASA classification
- Age
- Fasting duration
- Urgency of procedure (elective, emergency)
- Surgical subspecialty
- Procedure name
- Anaesthetic type
- Whether pulmonary aspiration was reported for the patient

A data collection template is used to facilitate standardised and accurate data entry.

Definition of a verified pulmonary aspiration

Clinical suspicion of aspiration of gastric contents on the basis of coughing, bucking, regurgitation or vomiting during the induction, maintenance or emergence phases of anaesthesia, in conjunction with at least one of:

- New oxygen requirement persisting beyond the recovery unit.
- Presence of gastric contents in the sub-glottic airways, as determined by bronchoscopy or endotracheal suctioning.
- New radiographic findings suggestive of aspiration.

Sample size and data analysis

In patients managed according to restrictive fluid fasting protocols, the reported rates of aspiration under anaesthesia range from 1 in 10,000 elective procedures in healthy populations, to 12 in 10,000 emergency procedures. We have therefore performed separate sample size calculations for each situation. *We consider a doubling of the baseline rate of aspiration to be a clinically significant increase.*

Assuming the baseline incidence of aspiration in the restrictive fluid fasting group is 2 in 10,000, to detect a doubling of aspiration rate, testing at the 5% significance level, with power 0.8, requires 112,689 elective procedures and 22,517 emergency procedures per comparison group (STS & restrictive fluid fasting). Therefore, assuming 1:1 ratio of group size the total sample size will be 270,412 anaesthesia cases.

On an intention-to-treat basis, anaesthesia cases count as Sip Til Send cases if they have an anaesthetic in a hospital with an active STS program and belong to a group of patients in whom the hospital has decided to allow STS. These patients will be counted towards the STS group whether or not they were individually eligible for STS or actually participated in STS.

In addition to reporting on the primary outcome, we will aim to conduct additional exploratory analysis considering:

- The impact of fluid fasting duration on aspiration rates
- Exploration of variability in reported rates between different hospitals
- Assessment of risk factors identified in patients who have aspiration events
- Conducting interim analyses to ensure that enough data is collected to have adequate statistical power, and flag unexpectedly high or dangerous aspiration rates if these are observed

Hospital recruitment

Participating sites will be required to meet prerequisites before data collection can commence, including local governance approval and the presence of a robust audit system for identifying cases of aspiration. When any hospital has met these prerequisites, data collection can commence for that site. We anticipate staggered start dates as each hospital will progress at their own rate. Recruitment will end once the data accrued meets the pre-determined sample size requirement.

ETHICS AND GOVERNANCE

Multicentre ethics approval has been granted by respective authorities in Australia and New Zealand, which include a waiver of the requirement for direct informed consent.

IMPACT

The safe fasting of patients before surgery and prevention of aspiration under anaesthesia are fundamental goals in daily practice for anaesthetists, surgeons and theatre teams. STS is a simple and pragmatic solution to prolonged preoperative fasting, but robust aspiration safety data do not yet exist. The Australasian MARS is expected to be world-first in providing a high quality and sufficiently large dataset for aspiration events for Sip Til Send hospitals. The outcome of Australasian MARS is likely to be of worldwide interest and widely generalisable to most patient groups.

REFERENCES

1. The Australian and New Zealand College of Anaesthetists. *PG07 Guideline on pre-anaesthesia consultation and patient preparation.* 2024.
2. Markman P, Grimmett W, Ramsay D, Sartain J, Stoeter D, Jaramillo C, et al. *SipTilSend: Commentary from a national perspective*. ANZCA Bulletin Summer 2023;32(4):31–2.
3. Markman P, Nolan T. Sip Til Send Nation - Insights from the Australasian Sip Til Send Implementation Survey. ANZCA Bulletin Summer 2024:31-33.