Optimising Nutrition Delivery in Acute and Chronic Diseases using a Smart Tube: A Pilot Healthy Volunteer Study

INVESTIGATORS

Professor John Windsor
Surgical and Translational Research Centre
Faculty of Medical and Health Sciences
The University of Auckland
j.windsor@auckland.ac.nz

Professor Anthony Phillips
Applied Surgery and Metabolism Laboratory
Surgical and Translational Research Centre
School of Biological Sciences
The University of Auckland
a.phillips@auckland.ac.nz

Professor Gregory O'Grady
Department of Surgery
Faculty of Medical and Health Sciences
The University of Auckland
greg.ogrady@auckland.ac.nz

STUDY COORDINATOR

Dr. Sakina H Bharmal
Surgical Trials Unit
Surgical and Translational Research Centre
Faculty of Medical and Health Sciences
The University of Auckland
s.bharmal@auckland.ac.nz

STUDY RATIONALE

Inadequate food intake and malnutrition is a global concern, both in the community and hospitals[1]. In developed nations, more than a third of hospitalised patients are malnourished[2] which increases morbidity, mortality, hospital stay and costs[3–7]. Artificial nutritional support is required when patients cannot voluntarily meet their nutritional requirements by eating. Enteral tube feeding (ETF) is a preferred method for artificial nutrition support[8–11]. It is part of the treatment for many different acute and chronic diseases, including sepsis, burns, trauma, transplantation, pancreatitis, major surgery and cancer[12–19].

Enteral tube feeding is a common treatment around the world, with approximately 10% of hospitalised patients receiving ETF at any time[20]. Based on 1.2 million case weighted discharges per annum in New Zealand[21], it is estimated that at least 120,000 patients will receive ETF each year in public hospitals. Although ETF is widely used for nutrition support, it is often associated with gastrointestinal dysfunction[22–26]. Gastrointestinal dysfunction could be a short-term, self-limiting condition causing abdominal distension, impaired gut motility, feeding intolerance, and/or ileus (in the milder form), or increase the risk of non-occlusive mesenteric ischaemia (NOMI), intestinal infarction, perforation and/or peritonitis (in the severe form)[27,28]. These complications lead to prolonged hospital stays and morbidity, thus having a significant impact on the healthcare industry and increasing the economic burden.

Given the increasing clinical burden of ETF-associated gastrointestinal dysfunction, it is critical to detect the early onset of feeding intolerance to prevent symptoms progression. We hypothesised that in critically ill or post-surgical patients, the loss of small intestine peristaltic contractions and resulting abdominal distension could lead to an increase in the gut luminal pressure. The gut pressure could be further elevated by infusion of enteral feed. Therefore, measuring intraluminal pressure in patients on ETF might help in the detection of feeding intolerance before it became clinically evident. This would prevent patients from getting sub-optimal nutrition by allowing modification to the ETF rate and/or pattern, minimising the risks associated with gastrointestinal dysfunction.

The overall objective of this translational project is to test, improve and implement an innovative ETF system that uses pressure biofeedback from the gut to optimise the safe delivery of ETF, in turn reducing the risks of feeding intolerance and ischaemia. As part of

this project preliminary studies from our group have confirmed that gut intraluminal pressure can be measured from back-propagated pressure through the fluid feed column in the nasogastric tube. However, the back-propagated pressure measurement has not been validated against a direct measurement of pressure in the lumen of the stomach. To do so, we have designed a dual pressure sensing nasogastric feeding tube (see technical details below) which allows simultaneous measurements of back-propagated gastric pressure and direct gastric pressure (Figure 1).

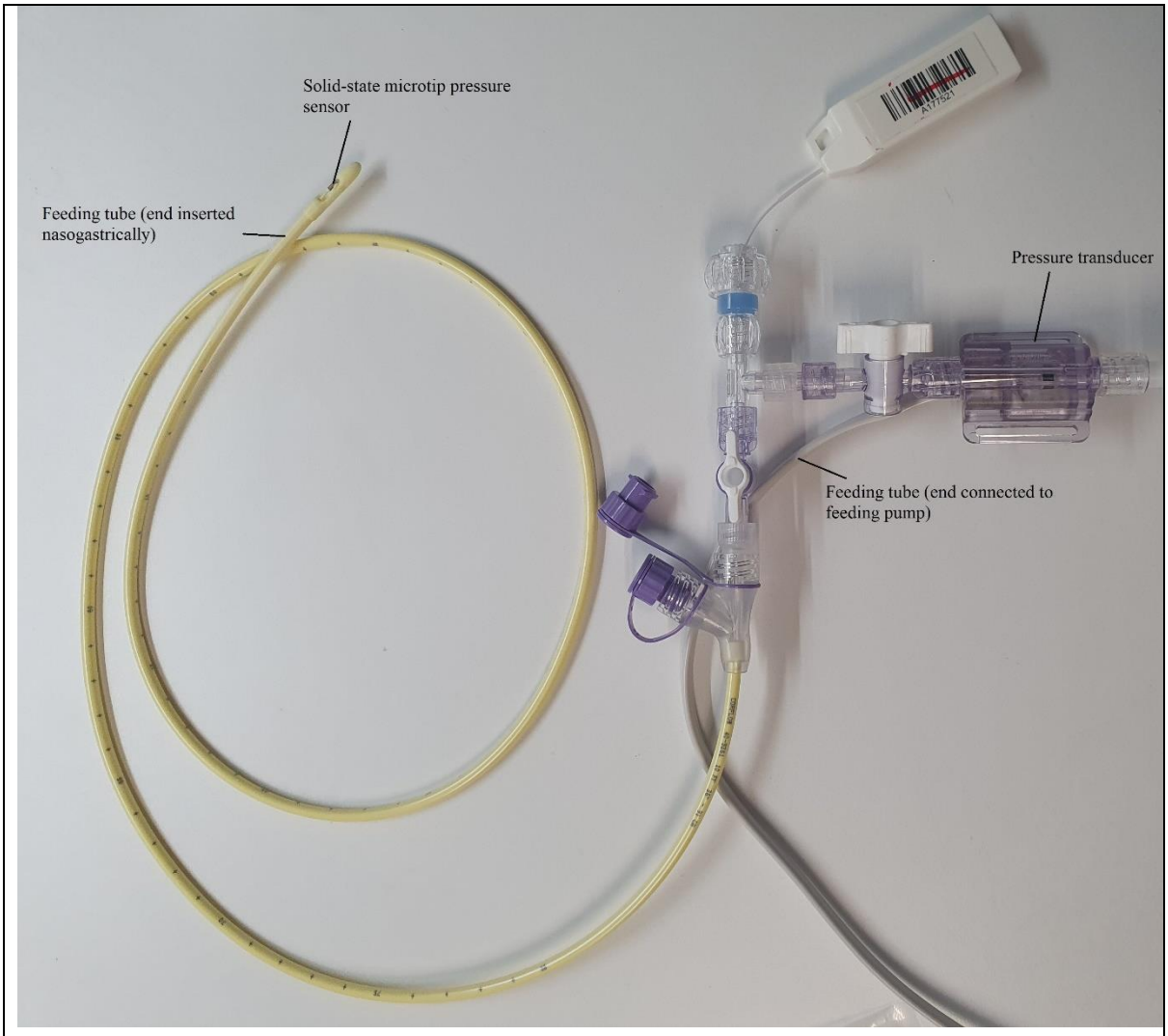


Figure 1. Dual intraluminal pressure measurement setup

The complex back-propagated pressure trace signal is noisy because of respiratory, cardiac, and movement artifacts, and requires signal processing to extract meaningful metrics. Hence, this approach of dual measurement will confirm the reliability and accuracy of back-propagated pressure measurement and help with the interpretation of the back-propagated pressure signals.

STUDY AIM

The aim of this study is to validate the performance of the back-propagated pressure measurement method using a custom-designed dual pressure sensing nasogastric feeding tube in healthy volunteers. The other aim is to further aid interpretation of the pressure signals by comparing the pressure measurements with other technologies used for assessing the status of the stomach and intestine, used in approved patient studies (AHREC 1130), including body surface gastric mapping (Alimetry®, Auckland) and bowel sounds

METHODS

Recruitment

Healthy volunteers (n=10) will be identified by word-of-mouth. Those interested in participating will be screened for eligibility and recruited. Exclusions include those with any functional gastrointestinal disorders (diabetic/ idiopathic and post-surgical gastroparesis, chronic motility disorders), pregnancy or postpartum, and those under 18 years of age. Information sheet will be provided, and informed consent will be obtained from all participants.

Booking

Clinic visit date will be scheduled with the participant and an email sent to Clinical Research Centre (Lower ground, Building 507, School of Medicine, University of Auckland) to confirm room booking.

Protocol

1. Participants will visit the clinic in a **fasted state** (>8 hours).
2. The study procedure will be explained including an explanation of potential discomfort e.g., gagging during procedure. **Written consent** will be obtained and questions answered.
3. **Anthropometrics** (height, weight, and waist circumference) will be measured.

4. Prior to inserting the feeding tube in volunteers, the **Millar pressure sensor** will be incorporated into the nasogastric tube. It will be 2cm less than full insertion, so that the sensor unit is fully within the tube and not exposed in the hole at the end of the tube, to avoid the risk of it being snagged during insertion. The solid-state pressure sensing unit will be advanced once the feeding tube is in place which provides the opportunity to determine whether the presence of the solid-state sensor and wire in the lumen of the tube alters the measurement of back-propagated pressure.
5. The **nasogastric feeding tube** will then be inserted via the nose into the stomach (nasogastric tube (NG)) as per the Auckland City Hospital clinical guidelines for enteral tube management. Briefly, participants will sit in an upright position with the head kept straight. The length of the tube will be measured and marked from the tip of the nose to ear lobe and then down to the xiphoid process. The end of the tube will be lubricated with a gel, and the tube inserted from the nose until the marked length is reached. The participant will be offered a glass of water to assist passage of tube through the oro-pharynx. The tube will be strapped and secured at the top of the nose using a plaster.
6. **Correct positioning of the feeding tube** will be confirmed by testing the pH of the gastric aspirate. A 60mL enteral tipped syringe will be used to aspirate 5-10 mL of gastric fluid and tested with pH indicator sticks (Baker® pHix). A pH reading of ≤5 would confirm the tube's position in the stomach.
7. The Millar sensing unit will be advanced the final 2cm, to allow the sensor to be exposed within the terminal hole of the tube without extending into the stomach lumen.
8. Following the feeding tube insertion**, three standard ECG dots** will be applied to the participants chest and abdomen. The ECG dots will be connected to a signal processing unit (ProtoCentral Electronics, Bengaluru) and a data acquisition unit to interpret the cardiac and respiration rate measurements.
9. Next, a **body surface gastric mapping** (BSGM) electrode adhesive array (total area approximately 20cm x 30cm, Alimetry®, Auckland) will be placed over the skin on the stomach region (as per Alimetry's protocol). Briefly, the participants will be asked to lie in the supine position. Using an algorithm on the Alimetry® app a 64-electrode array placement area on the abdomen will be identified and marked. The abdominal skin area where the electrode array needs to be placed will be prepared with approved hospital-grade bioelectrode skin preparation gel (NuPrep skin gel). Any excess hair

may be removed by shaving. In women, if the bra wire interferes with the array placement, then they will be requested to remove it for the study. The electrode array will then be applied to the prepped abdomen area. A recording device to measure electrophysiological signals will be attached to the array. Care will be taken to avoid overlapping the electrode array with the positioning of the ECG electrodes used for cardiac and respiratory rate measurements (Figure 2).

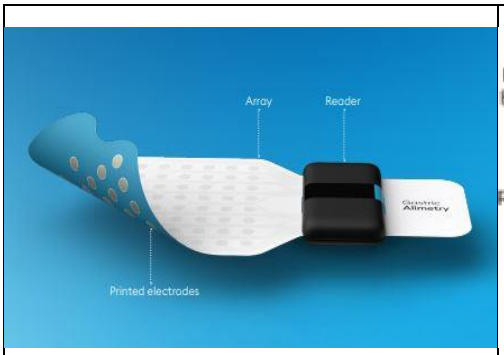


Figure 2(A). Gastric mapping 66 electrode array with the recording device

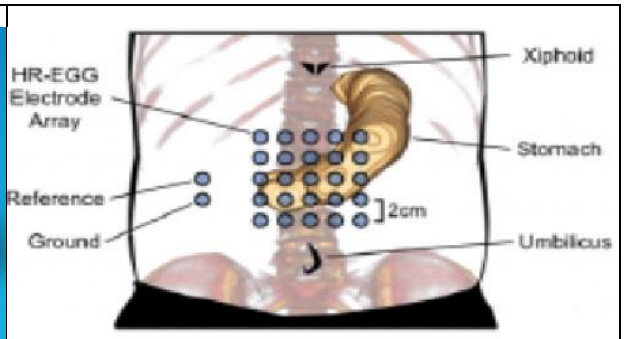


Figure 2(B). Schematic representation of the electrode array placement

10. Following the BSGM electrode array placement, two **digital stethoscopes** (Thinklabs Medical LLC®, Colorado) will be placed on the participants' abdomen area for recording bowel sounds. Stethoscopes will be placed one on each side of the median plane, positioned in the mid-clavicular line, and at least one centimetre below the lower edge of the BSGM electrode array. The stethoscopes will be connected to a digital recorder for dual bowel sounds recording from the left and right abdominal quadrants (Figure 3).

Figure 3(A). Bowel sounds recording digital stethoscope with recorder

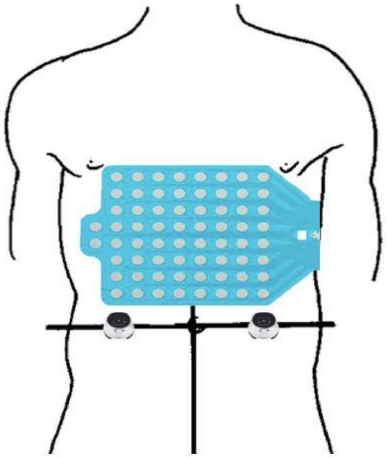


Figure 3(B). Digital stethoscopes and BSGM electrode array placement

Measurements

Measurements will be done at eight timepoints over approximately 75-90 minutes. The measurements will include intraluminal pressure (via the prototype NG tube), gastric mapping (by BSGM), heart rate and respiratory rate (by three lead electrocardiogram (ECG)), and bowel sounds (via a digital stethoscope).

For timepoints 1-3, participants will lie in the supine position to measure the **effects of feeding**.

- **Timepoint 1**: Once the participant lies on the bed, all the recording devices will be turned on. After a devices 'warm-up' period of 15 minutes, fasting baseline measurements will be taken for 10 minutes.
- **Timepoint 2**: The feeding tube will then be adjusted (advanced 5cm and withdrawn 2cm) and measurements repeated for 5 minutes.
- **Timepoint 3**: An enteral feed (Nutricia® Nutrison Energy (feed) pack) will be given at a rate of 400 mL/hour for 15 minutes (total energy content 150 kcal). After 15 minutes, the feeding pump will be turned off. Measurements will be recorded for 10 minutes.

The recordings for timepoints 4-8 will measure the **effects of body movement**. The feeding pump will be off for the following measurements.

- **Timepoint 4**: Participants will be asked to turn to their side (right side down) from supine position and 5 minutes of measurements recorded.
- **Timepoint 5**: Participants will be sat up (60 - 90 degrees from horizontal) and 5 minutes of measurements recorded.
- **Timepoint 6**: Participants will be asked to cough for 15 seconds, and measurements continued through this period.
- **Timepoint 7**: Participants will be asked to perform Valsalva's manoeuvre for 30 seconds and measurements continued through this period.
- **Timepoint 8**: Participants will resume supine position (as in Time point 1) and a further 10 minutes of measurements will be taken.

After completion of this protocol the feeding tube, BSGM electrode array, and stethoscope attachments will be carefully removed.

Analysis of results

The suite of measurements will be analysed for the following

1. Comparison of pressure measurements obtained from two methods: back-propagated pressure and direct solid-state pressure measurements.
2. Determine the effect of feeding on pressure, electrophysiology, and bowel sounds.
3. Determine the effect of catheter position, body position, coughing and raised abdominal pressure on the intraluminal pressure measurements, electrophysiology, and bowel sounds.
4. Analysing the pressure trace to optimise the pressure signal analysis, particularly to filter out the effects of feeding, body movement, cardiac and respiratory rate/movement.

Statistical analyses

Descriptive and comparative statistical analyses will be conducted by a contract biostatistician.

- **Pressure** data (mmHg) will be presented as mean ± SD.
- **Heart rate** (BPM) and **respiration rate** (BPM) will be presented as mean ± SD, and these parameters will be used to optimise intraluminal pressure signal interpretation.
- **Bowel sounds** will be correlated with pressure measurements to determine its accuracy as a predictor of feeding intolerance symptoms.
- **Body surface gastric mapping** will provide additional information on electrophysiological changes underlying gastric pressure measurements.

This is a pilot study to investigate changes in intraluminal pressure in healthy volunteers using a custom-designed dual pressure sensing nasogastric feeding tube hence there is insufficient data for sample size power calculation.

CUSTOM-DESIGNED DUAL PRESSURE SENSING NASOGASTRIC FEEDING TUBE

Two pressure sensors will be used to measure and validate the measurement of intraluminal gastric pressure. Firstly, a commercially available pressure transducer (TruWave PX600, Edwards Lifesciences, California, USA) typically used for invasive arterial pressure monitoring. The sensor is placed in-line between the feed pump giving set and feeding tube (Corflo 40-9361, Avanos (Halyard), Georgia, USA) to measure the intraluminal pressure via back-propagation through the fluid (feed) filling the feeding tube's lumen. This setup has been utilised previously. Secondly, a catheter (SPR-524, Millar, Texas, USA) with a solid-state pressure sensor at its tip, will be passed through the feeding tube’s lumen to directly measure the intraluminal pressure at the distal end of the feeding tube where feed exits. The solid-state pressure sensor (Millar®) does not change the dimension of the feeding tube because the pressure sensing unit which sits within the exit hole of the feeding tube (Figure 4).

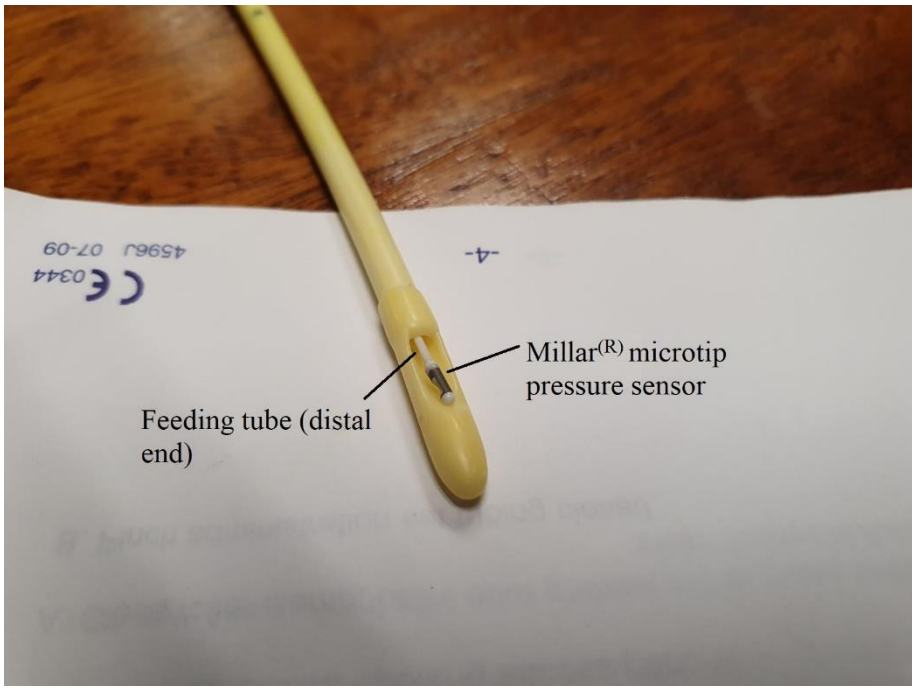


Figure 4. Millar® microtip solid-state pressure sensor inserted in a feeding tube

The pressure catheter will be introduced via a haemostatic valve (Tuohy Borst Adapter 80330, Qosina, New York, USA) connected to one of the two feeding tube ports. The pressure catheter body diameter is 2.3 French (0.8mm) with a 3.5 French (1.2mm) tip. This will have minimal effect on feed flow through the feeding tube as the pressure catheter body occupies 11 percent of the 2.3 mm diameter in lumen's cross-sectional area. Correct placement of the pressure catheter, Figure 4, will ensure the wider tip has little to no impact on flow.

Cardiac rate and respriation rate measurement

Cardiac and respiration rate will be determined from measurements taken with a three-lead ECG. Three standard ECG dots will be applied to the participants chest and abdomen. A cable will connect the ECG dots to a signal processing unit (PC-4116, ProtoCentral Electronics, Bengaluru, India) and custom battery powered data acquisition unit as described below. The PC-4116 system uses a signal processing circuit (ADS1292R, Texas Instruments, Texas, USA) to interpret heart rate and respiration rate from ECG signals.

Signal processing, data acquisition, and control systems

Signal data from both pressure transducers and the three-lead ECG will be recorded to memory card by a custom recording device this group previously developed for such applications. This device is battery powered and is charged via the same connector used by the pressure transducer. Therefore, the pressure transducers must be disconnected before charging, thus eliminating electrical safety risks. This device has been approved for use at Auckland City Hospital by their clinical engineers.

Data from the recording devices will be extracted as measurement files into a password protected e-Data Grabber software. This data will be retrospectively filtered and analysed in MATLAB. A filtering algorithm will be used to strip the signal of biological noise (heart rate, movement, and respiration artefacts) to give clean pressure measurements over time.

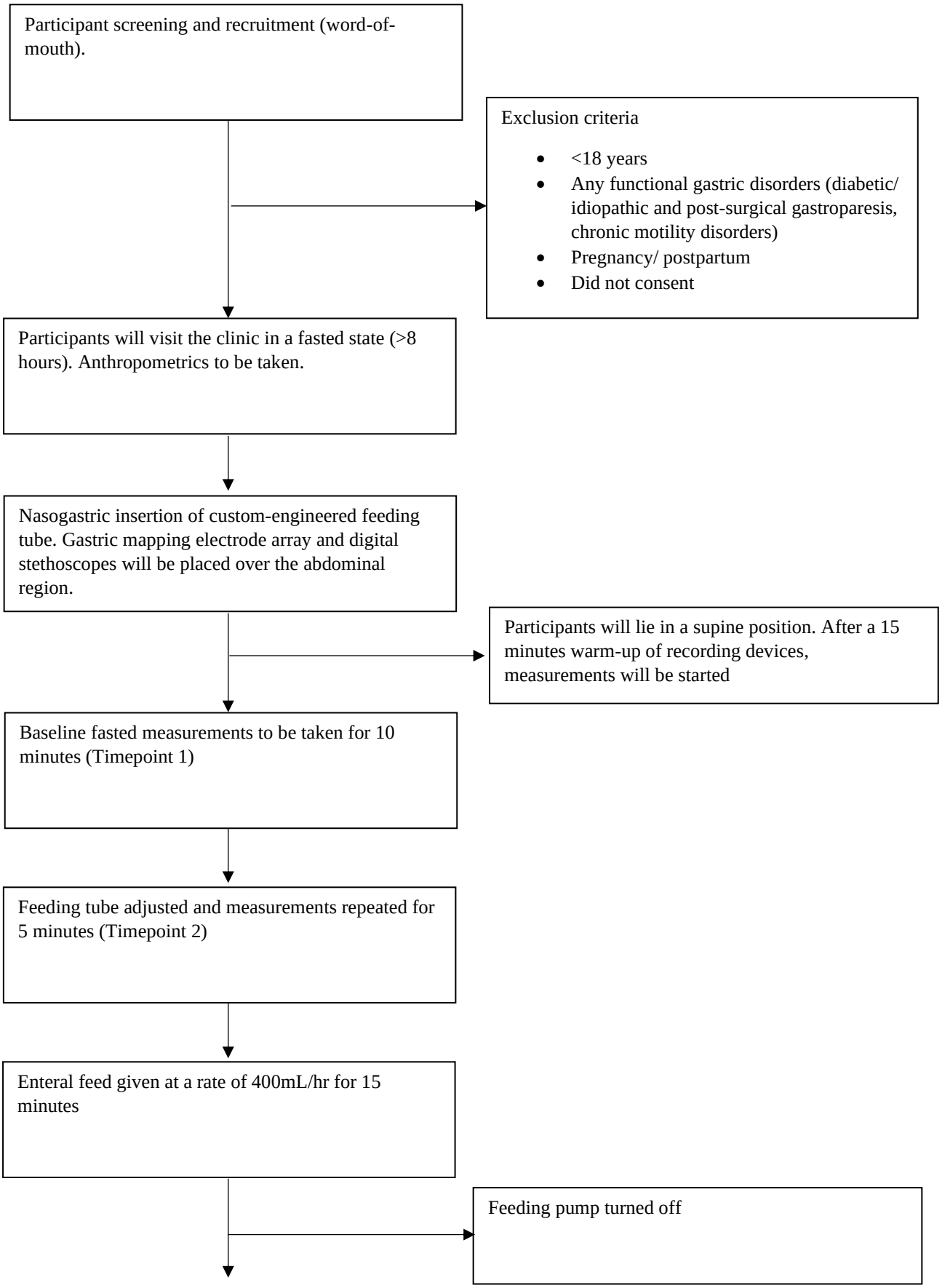
REFERENCES

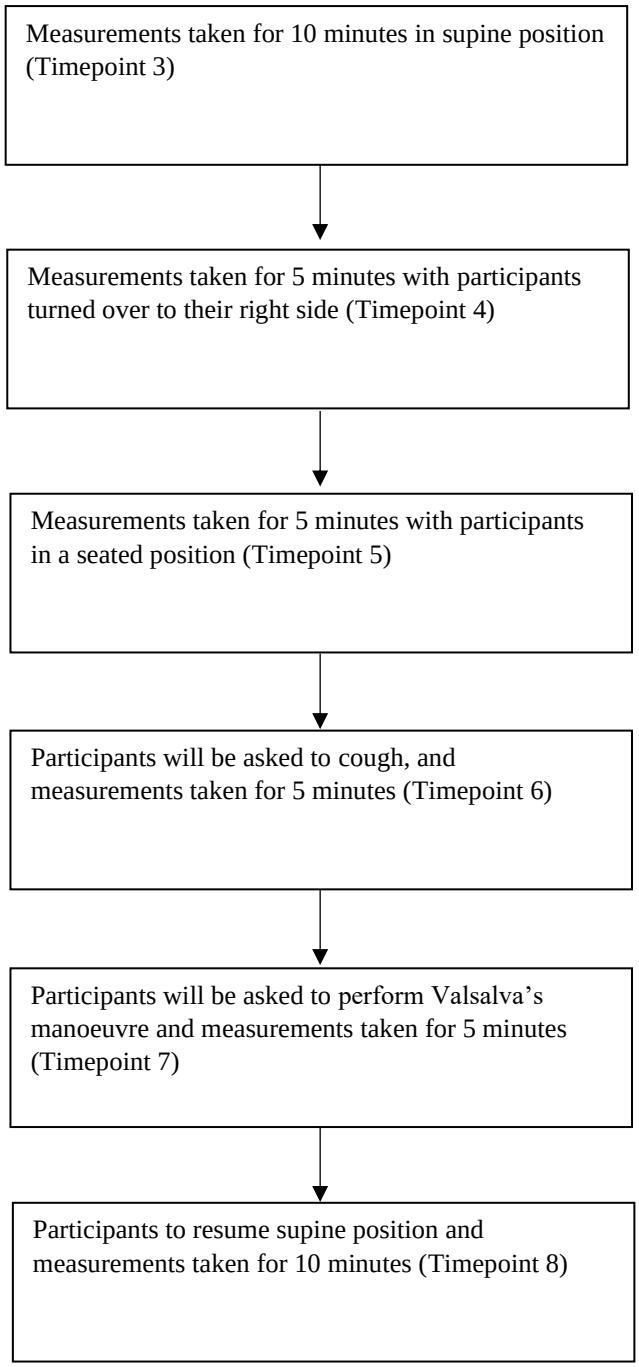
1. May L, Delston JB. United Nations Universal Declaration of Human Rights. In: *Applied Ethics*. Routledge; 2017:54-57.
2. McWhirter JP, Pennington CR. Incidence and recognition of malnutrition in hospital. *BMJ*. 1994;308(6934):945-948. doi:10.1136/bmj.308.6934.945
3. Windsor JA, Hill GL. Weight loss with physiologic impairment. A basic indicator of surgical risk. *Ann Surg*. 1988;207(3):290-296. doi:10.1097/00000658-198803000-00011
4. Griffiths RD, Bongers T. Nutrition support for patients in the intensive care unit. *Postgrad Med J*. 2005;81(960):629-636. doi:10.1136/pgmj.2005.033399
5. Martin CM, Doig GS, Heyland DK, Morrison T, Sibbald WJ, Southwestern Ontario Critical Care Research Network. Multicentre, cluster-randomized clinical trial of algorithms for critical-care enteral and parenteral therapy (ACCEPT). *CMAJ*. 2004;170(2):197-204.
6. Villet S, Chiolero RL, Bollmann MD, et al. Negative impact of hypocaloric feeding and energy balance on clinical outcome in ICU patients. *Clin Nutr*. 2005;24(4):502-509. doi:10.1016/j.clnu.2005.03.006
7. Wischmeyer PE. Tailoring nutrition therapy to illness and recovery. *Crit Care*. 2017;21(Suppl 3):316. doi:10.1186/s13054-017-1906-8
8. Dissanaike S, Pham T, Shalhub S, et al. Effect of immediate enteral feeding on trauma patients with an open abdomen: protection from nosocomial infections. *J Am Coll Surg*. 2008;207(5):690-697. doi:10.1016/j.jamcollsurg.2008.06.332
9. Flint R, Windsor J, Bonham M. Trends in the management of severe acute pancreatitis: interventions and outcome. *ANZ J Surg*. 2004;74(5):335-342. doi:10.1111/j.1445-1433.2004.02940.x
10. Koretz RL, Avenell A, Lipman TO, Braunschweig CL, Milne AC. Does enteral nutrition affect clinical outcome? A systematic review of the randomized trials. *Am J Gastroenterol*. 2007;102(2):412-429; quiz 468. doi:10.1111/j.1572-0241.2006.01024.x
11. Neumayer LA, Smout RJ, Horn HG, Horn SD. Early and sufficient feeding reduces length of stay and charges in surgical patients. *J Surg Res*. 2001;95(1):73-77. doi:10.1006/jsre.2000.6047
12. Gianotti L, Besselink MG, Sandini M, et al. Nutritional support and therapy in pancreatic surgery: A position paper of the International Study Group on Pancreatic Surgery (ISGPS). *Surgery*. 2018;164(5):1035-1048. doi:10.1016/j.surg.2018.05.040

13. Marik PE, Zaloga GP. Early enteral nutrition in acutely ill patients: a systematic review. *Crit Care Med*. 2001;29(12):2264-2270. doi:10.1097/00003246-200112000-00005
14. Thibault R, Pichard C. Nutrition and clinical outcome in intensive care patients. *Curr Opin Clin Nutr Metab Care*. 2010;13(2):177-183. doi:10.1097/MCO.0b013e32833574b9
15. Weimann A, Braga M, Carli F, et al. ESPEN practical guideline: Clinical nutrition in surgery. *Clin Nutr*. 2021;40(7):4745-4761. doi:10.1016/j.clnu.2021.03.031
16. Heyland DK, Schroter-Noppe D, Drover JW, et al. Nutrition support in the critical care setting: current practice in canadian ICUs--opportunities for improvement? *JPEN J Parenter Enteral Nutr*. 2003;27(1):74-83. doi:10.1177/014860710302700174
17. Petrov MS, van Santvoort HC, Besselink MGH, van der Heijden GJMG, Windsor JA, Gooszen HG. Enteral nutrition and the risk of mortality and infectious complications in patients with severe acute pancreatitis: a meta-analysis of randomized trials. *Arch Surg*. 2008;143(11):1111-1117. doi:10.1001/archsurg.143.11.1111
18. Grammatikopoulou MG, Theodoridis X, Gkiouras K, et al. AGREEing on Guidelines for Nutrition Management of Adult Severe Burn Patients. *JPEN J Parenter Enteral Nutr*. 2019;43(4):490-496. doi:10.1002/jpen.1452
19. Deane AM, Lamontagne F, Dukes GE, et al. Nutrition Adequacy Therapeutic Enhancement in the Critically Ill: A Randomized Double-Blind, Placebo-Controlled Trial of the Motilin Receptor Agonist Camicinal (GSK962040): The NUTRIATE Study. *JPEN J Parenter Enteral Nutr*. 2018;42(5):949-959. doi:10.1002/jpen.1038
20. Wang K, McIlroy K, Plank LD, Petrov MS, Windsor JA. Prevalence, Outcomes, and Management of Enteral Tube Feeding Intolerance: A Retrospective Cohort Study in a Tertiary Center. *JPEN J Parenter Enteral Nutr*. 2017;41(6):959-967. doi:10.1177/0148607115627142
21. Publicly funded hospital discharges – 1 July 2018 to 30 June 2019. Ministry of Health NZ. Accessed January 25, 2023. https://www.health.govt.nz/publication/publicly-funded-hospital-discharges-1-july-2018-30-june-2019
22. Reintam Blaser A, Jakob SM, Starkopf J. Gastrointestinal failure in the ICU. *Curr Opin Crit Care*. 2016;22(2):128-141. doi:10.1097/MCC.0000000000000286
23. Reintam A, Parm P, Redlich U, et al. Gastrointestinal failure in intensive care: a retrospective clinical study in three different intensive care units in Germany and Estonia. *BMC Gastroenterol*. 2006;6:19. doi:10.1186/1471-230X-6-19
24. Mutlu GM, Mutlu EA, Factor P. GI complications in patients receiving mechanical ventilation. *Chest*. 2001;119(4):1222-1241. doi:10.1378/chest.119.4.1222

25. Montejo JC. Enteral nutrition-related gastrointestinal complications in critically ill patients: a multicenter study. The Nutritional and Metabolic Working Group of the Spanish Society of Intensive Care Medicine and Coronary Units. *Crit Care Med*. 1999;27(8):1447-1453. doi:10.1097/00003246-199908000-00006
26. Mentec H, Dupont H, Bocchetti M, Cani P, Ponche F, Bleichner G. Upper digestive intolerance during enteral nutrition in critically ill patients: frequency, risk factors, and complications. *Crit Care Med*. 2001;29(10):1955-1961. doi:10.1097/00003246-200110000-00018
27. Hong J, Gilder E, Blenkiron C, et al. Nonocclusive mesenteric infarction after cardiac surgery: potential biomarkers. *J Surg Res*. 2017;211:21-29. doi:10.1016/j.jss.2016.12.001
28. Li H, Zhang D, Wang Y, Zhao S. Association between acute gastrointestinal injury grading system and disease severity and prognosis in critically ill patients: A multicenter, prospective, observational study in China. *J Crit Care*. 2016;36:24-28. doi:10.1016/j.jcrc.2016.05.001

CLINIC VIST FLOWCHART




Measurements taken for 10 minutes in supine position (Timepoint 3)
Measurements taken for 5 minutes with participants turned over to their right side (Timepoint 4)
Measurements taken for 5 minutes with participants in a seated position (Timepoint 5)
Participants will be asked to cough, and measurements taken for 5 minutes (Timepoint 6)
Participants will be asked to perform Valsalva's manoeuvre and measurements taken for 5 minutes (Timepoint 7)
Participants to resume supine position and measurements taken for 10 minutes (Timepoint 8)