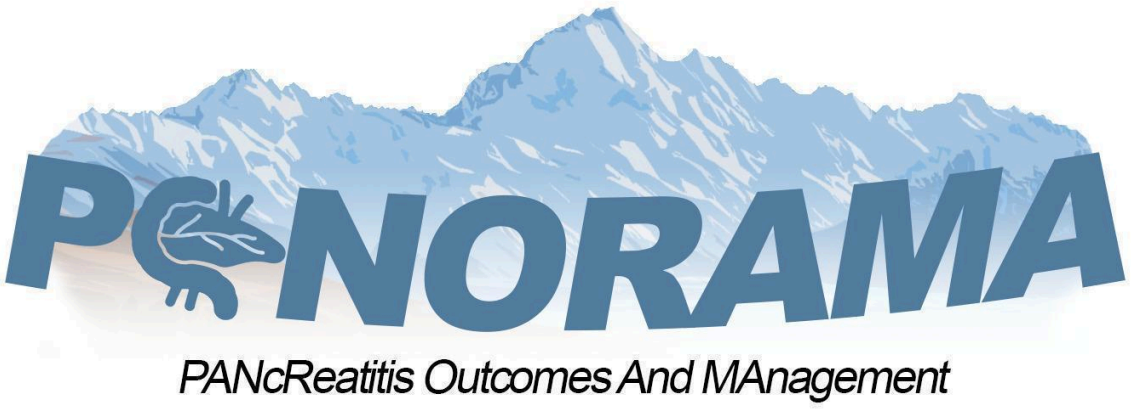

An Aotearoa-New Zealand multi-centre study of acute pancreatitis management and outcomes

Study protocol version 1.1.0
24th April 2024

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Steering Committee

Name	Training stage	X
Nejo Joseph	PGY1 Doctor, Palmerston North, NZ	@joseph_nejo
Matthew McGuinness	GSET3 Trainee, Northshore Hospital, NZ	@DrMattMcG
William Xu	PGY2 Doctor, Auckland, NZ	@william_xu98
Brodie Elliot	GSET2 Trainee, Whangarei Hospital, NZ	
Chris Varghese	PGY2 Doctor, Auckland, NZ	@chrisvarghese98
Cameron Wells	GSET1 Trainee, Hawkes Bay, NZ	@drcamwells
Luke Paterson	PGY4 Doctor, Auckland, NZ	
Melissa Edwards	Consultant general surgeon, Wellington, NZ	

Scientific Advisory Group

Name	Position	X
John Windsor	Professor of surgery, Auckland, NZ	@jwindsor3
Saxon Connor	Consultant HPB surgeon, Christchurch, NZ	
Sanjay Pandanaboyana	Consultant HPB and transplant surgeon, Newcastle Upon Tyne, UK	@sanjay_HPB
Christopher Harmston	Consultant general and colorectal surgeon, Whangarei, NZ	
Jonathan Koea	Consultant HPB surgeon, Auckland, NZ	
Joy Panoho	Maori health directorate, Whangarei, NZ	
Deborah Wright	Consultant general and colorectal surgeon, Dunedin, NZ	@Scalpel_Deborah

Primary Contacts

Dr Nejo Joseph
Email: njos821@aucklanduni.ac.nz
Phone: +64 21 058 3207

Professor John Windsor
Email: j.windsor@auckland.ac.nz
Phone:

Collaborative Partners

STRATA is an Aotearoa New Zealand (AoNZ) based trainee-led collaborative network. STRATA, the first AoNZ trainee-led collaborative research network, was created in 2018 following the success of medical students and trainees in Aotearoa in contributing to international collaborative studies.

Twitter: @STRATA_collab Email: info@stratacollaboration.com

The New Zealand Association of General Surgeons supports STRATA in its objective to establish a AoNZ based trainee-led collaborative network of future surgeons designing and undertaking meaningful research.

Aotearoa Clinical Trials Trust (ACTT) is a world class clinical trial site management organisation. ACTT is an independent charitable trust that administers both commercial and grant funded research on behalf of Te Whatu Ora. ACTT runs clinical trials from phase I to phase IV across multiple therapeutic areas. Their aim is to make a lasting difference to the health of all New Zealanders through innovative medicines and therapies. ACTT has partnered with STRATA to deliver PANORAMA across AoNZ.

Study Timeline

Dates	Description
10 February 2024	● Preliminary protocol drafted ● Quality performance indicators finalised
March 21 2024	● HDEC submission (expedited pathway) in ● Tupu grant application in
March 27 2024	● Data collection form finalised/ redcap form created
April (first week) 2024	● Second general meeting of investigators and protocol finalised ● Slide made for NZAGS conference and presented ● REDCap users generated and sent to investigators
April - June 2024	Centres recruited and locality ethics applications in ● Prepare for data collection
01 July 2024	Data upload window opens
30 September 2024	Data upload window ends - REDCap locked for new entries
31 October 2024	30-day follow up from day of admission
Novemebr/December 2024-January 2025	Data analysis and manuscript writing

Study Summary

Study title	An Aotearoa-New Zealand (AoNZ) multi-centre, prospective cohort study of acute pancreatitis management and outcomes.
Internal ref. no./ short title	PANORAMA Study
Study design	Multicentre prospective observational cohort study.
Study population	Adult patients diagnosed with acute pancreatitis admitted to any public hospital in AoNZ.
Eligible centres	All public hospitals in AoNZ.
Planned cohort	Enrolment for 3 months.
Objective	To measure adherence to quality performance indicators of the early (<72 hours) management of acute pancreatitis (AP) in AoNZ.
Primary outcomes of interest	• Proportion of patients that were managed in compliance with quality performance indicators overall
Secondary outcomes of interest	• Variation in compliance with QPIs between hospitals for each of the management domains • Requirement for mechanical ventilation (invasive and non-invasive) • Requirement for renal replacement therapy • Requirement for inotropic or vasopressor support • Intervention for complication of AP • Alive and discharged at 30-days
Follow-up	30-days after admission.
Data collection period	1 July 2024 - 30 September 2024

1. Background and rationale

Acute pancreatitis (AP) is one of the most common gastrointestinal conditions resulting in hospital admission. It has an estimated annual incidence of 58 per 100,000 in Aotearoa-New Zealand (AoNZ) adults (1–3). AP is characterised by a local and systemic inflammatory response with variable clinical progression, from mild to severe as defined by the degree of organ dysfunction (4).The majority of patients with AP suffer only mild disease that is self-resolving. However, 20% develop moderate or severe AP, which involves pancreatic or peripancreatic necrosis, organ failure, or both. Severe pancreatitis is a serious condition with a risk of mortality between 20-40% (5–8). Despite substantial disease burden, there are no effective therapies that alter the course of disease and management remains largely supportive.

In the last decade, a number of landmark clinical trials have provided substantial guidance on the management of the AP, particularly with regards to antibiotic use, endoscopic retrograde cholangiopancreatography (ERCP)(9), and management of necrosis (10,11). Furthermore, multiple scientific bodies have developed and disseminated evidence-based guidelines for managing AP. However, their adoption into clinical practice remains suboptimal. An international cohort study that assessed the compliance rate with current guidelines in the treatment of patients with acute biliary pancreatitis showed a wide variability of practice (12). While it is commonly believed that noncompliance with published guidelines indicates areas in which recommendations are based on insufficient evidence, previous studies have shown a lack of compliance even in areas where randomised controlled trials (RCTs) have already resolved controversial issues during the last 10 years (12,13).

A multicentre national observational study will enable the assessment of compliance to quality performance indicators (QPIs) for the early management of AP in the AoNZ context. Furthermore, it will demonstrate any potential excess morbidity associated with noncompliance to best evidence driven clinical practice. Currently there is no such data for AoNZ. This data can be used to standardise and optimise care nationally to create more equitable outcomes for all patients.

2. Aims

Primary Aim:
To measure adherence with quality performance indicators (QPIs) for the management of AP during the first 72 hours after admission in AoNZ.

Secondary Aims:
- To measure the variation in compliance with QPIs between each hospital in AoNZ for each management domain for the management of AP during the first 72 hours after admission.
- To correlate compliance (overall and for each management domain) with QPIs and defined clinical outcomes stratified by AP severity.
- To compare clinical outcomes between compliant and non-compliant management of patients stratified by AP severity.

3. Quality Performance Indicators

Multiple practice guidelines have been published for the management of AP (14–19). The recommendations in these guidelines are usually based on a systematic review of the relevant literature and the evidence on which is based on the available evidence, which is usually graded. Quality performance indicators will be drawn from these evidence-based recommendations for each of the nominated management domains that are relevant to the management of patients within the first 72 hours from admission to hospital. Any differences in the recommendations between the source guidelines will be resolved by discussion amongst the Scientific Advisory Group and consensus established for the QPIs.

The QPIs were developed for the following management domains: (Appendix D: Table 1 with guidelines)

Table 1. Quality Performance Indicators

	Domain	QPI	Ref*	Metrics
1	**Diagnosis**	All patients diagnosed within 12 hours of admission	IAP	RAC criteria for diagnosis: enzymes 3xUL, typical pain ± CT scan
2	**Aetiology**	All patients had tests for aetiology determined within 24 hours of admission	IAP	U/S for gallstones ETOH history with intake (units per week, timing of binge to pain) If both negative then lipids, IgG4, drugs
3	**Severity (predicted)**	All patients had prediction of severity on admission	IAP	N / Y, if yes method (drop-down of all options and other) Further drop-down bar will the give options for severity (mild, moderate, and severe)

4	**Severity (actual)**	All patients had actual severity determined at 48 hours	-	N / Y, if yes method (drop-down RAC, DBC and other) Further drop-down bar will the give options for severity (mild, moderate, and severe)
5	**CT scan**	Initial CT assessment performed after 72-96 hours if poor response to initial management or clinical deterioration, unless there is diagnostic uncertainty. Not required for severity prediction.	IAP	N / Y, if yes indication (drop-down with other)
6	**Transfer**	All patients with predicted or actual severe AP in the first 72 hours are discussed with specialist pancreas service.	Nice	N / Y Indication for transfer (drop-down)
7	**Analgesia**	All patients given narcotic analgesia within one hour of admission	-	Step-up or step-down approach? IV analgesia given on admission N / Y NSAIDS given to mild AP Analgesics prescribed
8	**Fluids**	1. All patients commenced on IV Hartmann's solution within one hour of admission to the emergency department by a clinician and at an initial rate of 5-10 ml /kg in response to hypovolemia until resuscitation goals reached. 2. Then a rate of 1-2 ml/kg/hour for patients not tolerating PO in the first 48 hours.	IAP	IV fluids N / Y Time commenced from admission What initial fluid was given? Initial prescribed rate Initial received rate Average rate 2nd 24 hours Average rate 3rd 24 hours Fluid bolus given (# times and and timing) Volume / 24 hours over 72 hours?
9	**Anticoagulation**	All patients with predicted severe AP considered for or started on anticoagulation within 24 hours of admission	-	Anticoagulation N / Y Medication prescribed When started (hours from admission)
10	**Antibiotics**	Antibiotic prophylaxis not recommended for the prevention of infectious complications in AP	IAP	Antibiotic N / Y Antibiotic indication

11	**Nutrition**	1. No patients made 'nil-by-mouth' and no food withheld unless there was a clear reason. 2. Offer EN to anyone with MSAP or SAP starting within 72 hrs. 3. PN avoided unless EN fails or is contraindicated	NICE	Initial NBM N / Y From admission given trial of light diet. N / Y Initial NG or NJ? EN started within 72 hours if needed N / Y EN prescribed rate PN started if EN was not tolerated or contraindicated.
12	**ERCP/ES**	ERCP is indicated in patients with biliary pancreatitis and acute cholangitis within 48 hours of admission.	IAP	ERCP N / Y Indication: cholangitis or cholestasis When done? (hours)

** Reference of guideline from which the QPI is primarily taken from*

4. Outcomes

4.1. Primary outcomes

- Proportion of patients that were managed in compliance with quality performance indicators overall

4.2. Secondary outcomes

- Variation in compliance with QPIs between hospitals for each of the management domains
- Requirement for mechanical ventilation (invasive and non-invasive)
- Requirement for renal replacement therapy
- Requirement for inotropic or vasopressor support
- Intervention for a complication of AP
- Alive and discharged at 30-days

5. Methods

5.1 Study Setting

PANORAMA welcomes the participation of any publicly funded secondary or tertiary hospital in AoNZ under the Te Whatu Ora Health NZ directorate. All centres intending to take part in the study must register in accordance with local regulations and proof of registration must be provided to ACTT before initiating the data collection process.

5.2. Study Design

This study will use the trainee-led collaborative research model successfully used in NZ and internationally. Each hospital will have a 'mini team' of collaborators which will include a supervising consultant, a hospital lead and data collectors (explained in Figure 1 below). These collaborators will include medical students, junior doctors, trainees, registrars, and supervising consultants (Figure 1). It is compulsory to have a consultant supervisor in each mini team who is able to provide guidance and advice around how the study may be registered at a hospital and the approvals that will be required.

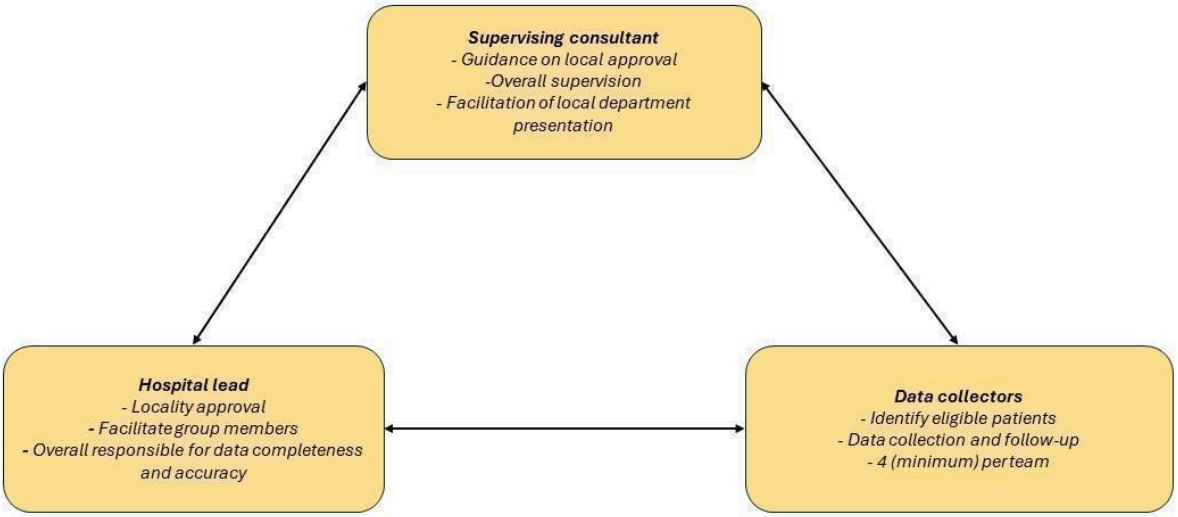

Figure 1. Mini-team structure and responsibilities

5.3. Data Collection

An investigator at each contributing hospital will be appointed to be responsible for data collection of all appropriate patients. Patients for AP may be admitted under multiple teams, it is the hospital lead's responsibility to capture all patients with AP that occur during the study inclusion period.

Data will be collected and stored using the web application REDCap. This web application is encrypted with HIPAA-Security, compliant with guidelines in the United States, and is widely used by academic institutions.

REDCap is a secure, web-based software platform designed to support data capture for research studies. It provides: 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources.

Clinical data at each participating hospital will only be accessed by medical students and resident medical officers who already have access to the clinical data being collected. Individuals working at other centres, and those without access to patient clinical data, will not be involved in data collection. Locality approval will be sought and obtained at all centres prior to study commencement. An excel spreadsheet will be kept alongside the REDCap database at each hospital. This will be stored on a password protected hospital computer at each hospital. A unique RedCap number will be created for each patient. This number will allow re-identification of patients by the local hospital lead if required. After data has been uploaded into REDCap the local hospital copy of the data will be destroyed to protect patient privacy. An excel spreadsheet containing the REDCap key and the relevant patients NHI will be kept. This excel spreadsheet will allow future patient re-identification if required. During REDCap data upload there will be no data fields where identifiable data can be uploaded; for example, names or NHI's. Local excel files will be stored at each hospital for 10 years and destroyed following this. The central de-identified data set will be stored for 10 years using REDCap electronic data capture tools.

If further studies using this data set are to be performed a subsequent ethics application will be required before its use.

All hospital leads will also be required to complete a hospital-survey which assess hospital-related variables (*Appendix C*).

Data collection will occur at two timepoints. The first time point will be within or at 48 hours of admission to hospital and secondly at 30-days follow-up following admission to the emergency department .

5.4. Patient eligibility

Inclusion Criteria

- All patients ≥16 years old who present with AP, as defined by the revised Atlanta criteria (*Appendix B*)
- Presenting to a public hospital that manages acute patients in AoNZ.

Exclusion Criteria

- Age less than 16
- Chronic pancreatitis (*Appendix B*)
- Patients with suspected respiratory distress (SpO2/FiO2 ≤ 315) who did not have an arterial blood gas test done to confirm respiratory failure.
- Postoperative pancreatitis following upper gastrointestinal surgery (not including endoscopic retrograde cholangiopancreatography [ERCP])

5.5. Required data

Demographic details	
Age	Year of birth
Sex	Male/ Female/ Other
Ethnicity	European/ Pasifika/ Maori/ Asian/ Middle-Eastern/ Latin American/ African (MELAA)/ other ethnicity
Postcode	
Weight	kg
Height	cm
Smoking history	Current smoker /previous smoker /never smoker e-cigarette /cigarette
Admission details	
Date of first review by doctor/prescriber	Date (dd/mm/yyyy) *From ED admission note
Time of first review by doctor/prescriber – as per admission note	24 hour clock time
Pancreatic enzymes at admission	Lipase/ Amylase/ *Pancreatic amylase* (tick one or more and give admission level and indicate what 3x upper limit is
Lipase/ amylase/ pancreatic amylase level	U/L
Epigastric pain confirmed on admission note	Yes/Non-epigastric abdominal pain/ No abdominal pain
Confirmation of AP diagnosis with imaging as per radiological report	MRI/ CT/ Abdominal USS
Charlson Comorbidity Index (*Appendix E*)	Score out of 37
Aetiology	
Significant ETOH history investigated in first 72 hours	Yes - from medical history, Yes - ETOH blood test, No

Hypertriglyceridemia investigated in first 72 hours	Yes/No
Acute pancreatitis severity	
Predicted severity on admission as ***documented*** in clinical notes (72 hours)	Mild/ moderately severe/ severe
Method used to predict severity	Modified Glasgow/ Ransons'/ BISAP/ APACHE II/ SIRS/ CRP (>150)/ Other (please specify)/ Clinical judgement (no prediction tool)/ No prediction made.
Imaging	
CT assessment performed in the first 72 hours of presentation	Yes/ No
Indication for CT prior to 72 hours	Diagnostic uncertainty/ confirmation of severity based on clinical predictors of severe AP/ Failure to respond to conservative treatment or in the setting of clinical deterioration/ other (please specify)
Imaging of the gallbladder during admission	USS/ CT (gallstones seen on CT)/ MRI/ EUS/ prior imaging confirming gallstones/ previous cholecystectomy/ no imaging
Antibiotics	
Antibiotics administered in first 72 hours of presentation	Yes/ No
Indication for antibiotics	Cholangitis concomitant extrapancreatic infection/ prophylactic/ other – please state
Analgesia	
Simple analgesia (paracetamol/ NSAIDs) prescribed	Paracetamol/ NSAIDs/ Not charted
Simple analgesia frequency	regular/ PRN
Date simple analgesia first administered	Date (dd/mm/yyyy)
Type of opioid prescribed (if any)	Codeine/ Morphine/ Fentanyl/ Tramadol/ Oxycodone/ Other (please specify)/ no opioids prescribed
Date opioid analgesia first administered	Date (dd/mm/yyyy)
Time opioid medication is administered to patient	24 hour clock
Route	PO/ IV
(If regular) daily dose	mg
(If PRN) total dose in first 72 hours	mg

(*If yes*) Date opioids first administered	Date (dd/mm/yyyy)
(*If yes)* Time opioid medication first administered as per drug chart?	24 hour clock
Further analgesic modalities	PCA/ ketamine/ local nerve blocks/ other (please specify)
Transfer to different hospital	
Patients with predicted severe disease discussed with specialised pancreas service (*Appendix B)* in first 72 hours from admission	Yes/ No/ not applicable
Patient transferred to a different hospital in the first 72 hours?	Yes/No
(*If yes*) Date of transfer	Yes/No
(*If yes*) Location transferred to	List of hospitals
(*If yes*) Reason for transfer to different hospital?	Severe disease/ requires ERCP/ requires interventional management of local complication/ other (free text)
ERCP	
Cholangitis in first 72 hours (*Appendix F*)	Yes/ No
Cholestasis in first 72 hours (radiological + deranged LFTs)	Yes/ No
ERCP performed in the first 72 hours	Yes/ No
Fluid management*	
Baseline variables	
Bag 1	
Date of administration	Date (dd/mm/yyyy)
Time of administration	Time (24-hour)
Volume administered	Volume (ml)
How long does fluid run for?	Time (hours)
Type of fluid	0.9% Normal saline/ Hartmann's/ plasmalyte/ colloid/ 0.45 saline + dextrose/ 0.18 saline + dextrose/ other (please specify)
Further administration of intravenous fluid (IVF) in the first 3 days of admission? (*Appendix B*)	Yes/no
Bag 2	
Date of administration	Date (dd/mm/yyyy)
Time of administration	Time (24-hour)

Volume administered	Volume (ml)
Time fluid is administered	Time (hours)
Type of fluid	0.9% Normal saline/ Hartmann's/ plasmalyte/ colloid/ other (please specify)
Further administration of intravenous fluid (IVF) in the first 2 days of admission?	Yes/no
Documented fluid review after 12 hours (± 4 hours)	Yes/no
Documented fluid review after 24 hours (± 4 hours)	Yes/no
Documented fluid review after 48 hours (± 4 hours)	Yes/no
Documented fluid review after 72 hours (± 4 hours)	Yes/no
Early Nutritional support	
On admission patient kept nil by mouth (NBM)	Yes/no
Indication for NBM	for ultrasound scan/ for surgery/ for ERCP/ unknown reason/ other (please specify)
Patient tolerating PO oral intake (clear fluids) by 24 hours	Yes/no
Patient tolerating PO oral intake (clear fluids) by 48 hours	Yes/no
Patient tolerating PO oral intake (clear fluids) by 72 hours	Yes/no
Enteral feeding started in the first 72 hours?	Yes/no
Tolerating enteral feed	Yes/no
Type of Enteral feeding	NJ/NG
Rate of enteral feed	ml/hr
PN in the first 72 hours?	Yes/no
Rate of PN	ml/hr
Anticoagulation	
On regular anticoagulation therapy prior to admission	Warfarin/ dabigatran/ rivaroxaban/ other (please specify)/ Not on regular anticoagulation therapy
Regular anticoagulation continued on admission	Yes/No
(If yes) type of anticoagulation drug	warfarin/ dabigatran/ rivaroxaban/ other
Regular anticoagulation commenced on	Yes - at 24 hours/ Yes - at 48 hours/ No

admission	
Anticoagulation commenced on admission	Prophylactic-dose clexane/ treatment-dose clexane/ anticoagulation not started/ other (please specify)
Local complications in the days prior to the 30-day follow-up	
Necrotising pancreatitis (*Appendix B*)	Yes/no
Acute necrotic collections (ANC)	Yes/no
Infected ANC	Yes/no
(If yes) intervention	Endoscopic/ percutaneous/ open necrosectomy
(if yes) date of intervention	Date (dd/mm/yyyy)
Acute pancreatic fluid collection (APFC)	Yes/no
Infected APFC	Yes/no
(if yes) intervention	Endoscopic/ percutaneous/ open necrosectomy
(if yes) date of intervention	Date (dd/mm/yyyy)
Portal/ splenic vein thrombosis	Yes/no
Other local complications	Pleuro-peritoneal fistula/ pleural effusion/ enteric fistula/ gastrointestinal bleeding/ pancreatic ascites/ arterial pseudoaneurysm/ other (free text)
Organ failure and other outcomes during the last 30-days follow-up	
Final aetiology	Alcoholic/ gallstone/ hypertriglyceridaemia/ others
Acute renal failure (as per RIFLE criteria - *Appendix A*)	Yes/no
Acute renal failure > 48 hours	Yes/no
ICU admission	Yes/no
(If yes) duration of ICU admission	day(s)
New renal dialysis required	Yes/no
(If yes) duration of dialysis	day(s)
New high-flow oxygen/ AIRVO requirement	Yes/no
Duration of high-flow/ AIRVO	days
Noninvasive ventilation required	Yes/no
(If yes) duration of noninvasive ventilation	days
Mechanical ventilation required	Yes/no

(If yes) duration of mechanical ventilation	day(s)
Inotropes required	Yes/no
(If yes) duration of inotropic support	day(s)
Date of mortality (within 30 days of first admission)	Date (dd/mm/yyyy)/ not dead
Date of discharge	Date (dd/mm/yyyy)/ not discharged

***** *Fluid therapy data collection guide: If collaborators respond, 'yes' to the question 'further administration of IVF in first 72 hours of admission?' a further set of questions will arise for 'bag 2', 'bag 3' etc.*

5.6. Follow-up

All patients will be followed for the initial 72 hours following admission into ED by a clinician and then again chart reviewed at 30 days from initial admission.

6. Ethical and regulatory considerations

6.1 Ethical considerations

This study will take the form of a prospective cohort study. There will be no change to the management of patients, no advice or guidelines given to the data collectors/clinical team. The aim will be to collect information on the routine practice of different hospitals around AoNZ. There is no foreseen impact on standard patient care and therefore no risk to patients involved in this study. There will be no contact with patients and follow-up data will be collected from routine clinical notes; No phone calls will be made.

6.2 Ethical approval

HDEC approval will be applied for considering the prospective design of the study. Each participating centre will be required to apply for locality ethical or audit approval as appropriate to their centre.

6.3 Data handling and storage

Data will be collected and stored using the web application Research Electronic Data Capture (REDCap). It is encrypted with HIPAA-Security and compliant with guidelines in the United States and is widely used by academic institutions. Each collaborator will be given secure REDCap server login details, allowing secure data storage on the REDCap system. Collaborators will be unable to upload identifiable information to the REDCap database. All anonymous data will be held for a total of ten years, after which it will be permanently removed from the server space.

When creating an entry for a patient in REDCap a unique REDCap ID for each patient is created. Each collaborator will be asked to keep a spreadsheet on a password protected hospital computer to store NHI and the corresponding REDCap ID. This will give investigators the opportunity to use the data in the future if required. Data will only be stored for a period of 10-years after which it will be permanently deleted.

All centres will be required to have locality approval prior to starting data collection.

6.4 Transfers

In the event of patient transfer to another participating site, data collectors are required to inform the hospital lead at the transferring hospital. The hospital lead will then liaise with the hospital lead at the receiving site to ensure continuity of data collection. Each individual will only have one entry for a given episode of AP.

6.5. Maori Health Directorate

The Whangārei Hospital Māori Health Directorate and Professor Jonathan Koea offered guidance and advice in the conceptualisation stages of this project. Previous research has shown that Māori have significantly higher rates of AP and diabetes mellitus following ap than non-Māori. In a study of Northland hospitals, a retrospective study found no significant differences in severe AP, mortality or intensive care admission between Māori and non-Māori (20). However, its retrospective design and modest sample size limits the validity of the conclusions, warranting further investigation of this phenomenon.

Ethnicity data will be collected and its impact on the outcomes investigated. If a disparity in outcomes is found it will be imperative that this is reported with the aim of improving outcomes for our Māori patients. Findings (including any preliminary findings) of the study will be discussed early with local research offices who will have systems in place for dissemination to those relevant stakeholders for discussion and action.

7. Funding

Application for funding will be made to the Auckland Medical Research foundation.

8. Statistical analysis

The study will be reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement (21). The primary analyses will be descriptive assessments of adherence to unambiguous recommendation in the selected domains of early AP management. Descriptive analysis will be performed where normal continuous variables will be compared via student's t test, and non-normal continuous variables will be compared via Mann-Whitney U test; if >2 categories a one-way ANOVA or Kruskal-Wallis test will be used for normal and non-normal variables respectively, Chi-square tests will be used to detect differences between categorical variables. All analyses will be conducted under a two-tailed hypothesis. Multiple imputation may be used in the case of missing data.

Secondary analyses will evaluate the differences in results according to the hospital. Risk-adjusted funnel plots will be produced to test the performance of individual, anonymised centres for normal rates of primary and selected secondary outcomes. Funnels plots' Y-axes will demonstrate QPI of a management domain and X-axis will show the number of patients admitted in each hospital. Furthermore, differences in clinical outcomes between patients that are managed according to best available evidence (QPI) and those that were not will be explored through mixed effects multivariable logistic models. These models will use the patient at the fixed effect level 1 and the hospital as the random effect level 2 (using the R lmer package) will be performed. A one level, fixed effect binary logistic regression model using a pooled dataset from 5 multiply imputed datasets will also be used in the event of substantial missing data.

Variable selection will be based on statistically significant univariable analysis and those variables deemed clinically significant. Fixed, forced entry will be used to adjust the main outcome measure, The effect of interaction, and sequential removal of non-significant variables will be assessed using changes in Akaike information criteria for multilevel models, and p-values for multiple imputed fixed models.

9. Collaborator roles

1. Supervising consultant
Provide guidance for approval processes, provide advice as to registration of the study at the hospital, facilitate communication within the hospital, and mentor and facilitate medical students, junior doctors and registrars in conducting the study at their local site. They have overall responsibility for the site governance registration and should support data collection. Only one person can fulfil this role. Minimum requirements for authorship include:

- Sponsorship of local study registration, and responsibility to ensure local collaborators act in accordance with local governance guidelines.
- Successful completion of data collection at a centre which meets the criteria for inclusion within the PANORAMA dataset.

Sponsorship through the audit approval/ project registration process by a consultant does not constitute authorship, nor does inclusion of a consultants' patients alone in the audit serves as sufficient for authorship.

2. Hospital lead:
This role will ideally be fulfilled by GSET/SET registrar but can be fulfilled by a medical student, junior doctor, trainee, or the consultant supervisor. They will be the single lead point of contact for data collection at each site. They must be responsive to communication from the management team and governance bodies. The hospital lead is the primary person responsible in obtaining local approvals for conduct of the PANORAMA Study. Successful completion of data collection at a centre which meets the criteria for inclusion within the dataset.

3. Local collaborators:
A team of up to 8 data collectors per hospital. Minimum requirements for authorship on PANORAMA publications include:

- Compliance with local audit approval processes and data governance policies.
- Active involvement in data collection at a centre which meets the criteria for inclusion.
- Collaboration with the hospital leads to ensure that the audit results are reported *back to the audit office/ clinical teams.*

4. Writing and analysis group:
A group of medical students, junior doctors, and external advisory board members responsible for the overall scientific content, data analysis, and preparation of individual research manuscripts.

5. Study management group:
This group will manage the running of this study and have overall responsibility for project coordination and data handling.

6. Expert advisory group:
A panel of experts who are able to ensure contextual and scientific relevance of the protocol design, data fields, and data interpretation.

10. Study completion

10.1. Completion

The study will be deemed complete after 4 months (3 months of recruitment and 1 month of follow up) of prospective data collection. The data will then be pooled and analysed by the chief investigator.

10.2. Publication and authorship

The manuscript will be prepared by a writing committee. Prior to publication all hospital leads will be invited to be involved in reviewing drafts of the manuscripts, abstracts, press releases and any other publications arising from the study. All investigators and collaborators in mini-teams including supervising consultant(s) will be acknowledged as PubMed-citable co-authors using a corporate authorship model. Collaborators will have the responsibility of registering this study at their locality, acquiring appropriate approvals, identifying patients, collecting data and completing 30-day follow-up. Where hospital leads fail to submit complete data, or if a hospital's data is removed, collaborators at that hospital will be excluded from the authorship list; if substantially incomplete data is submitted, the writing committee may decide to exclude that unit from further analysis. Authors will acknowledge the study funding sources and other contributors.

References

1. Sellers ZM, MacIsaac D, Yu H, Dehghan M, Zhang KY, Bensen R, et al. Nationwide Trends in Acute and Chronic Pancreatitis Among Privately Insured Children and Non-Elderly Adults in the United States, 2007-2014. Gastroenterology. 2018 Aug;155(2):469–78.e1.

2. Garg SK, Sarvepalli S, Campbell JP, Obaitan I, Singh D, Bazerbachi F, et al. Incidence, Admission Rates, and Predictors, and Economic Burden of Adult Emergency Visits for Acute Pancreatitis: Data From the National Emergency Department Sample, 2006 to 2012. J Clin Gastroenterol. 2019 Mar;53(3):220–5.

3. Pendharkar SA, Mathew J, Zhao J, Windsor JA, Exeter DJ, Petrov MS. Ethnic and geographic variations in the incidence of pancreatitis and post-pancreatitis diabetes mellitus in New Zealand: a nationwide population-based study. N Z Med J. 2017 Feb 17;130(1450):55–68.

4. Mederos MA, Reber HA, Girgis MD. Acute Pancreatitis: A Review. JAMA. 2021 Jan 26;325(4):382–90.

5. Schepers NJ, Bakker OJ, Besselink MG, Ahmed Ali U, Bollen TL, Gooszen HG, et al. Impact of characteristics of organ failure and infected necrosis on mortality in necrotising pancreatitis. Gut. 2019 Jun;68(6):1044–51.

6. van Santvoort HC, Bakker OJ, Bollen TL, Besselink MG, Ahmed Ali U, Schrijver AM, et al. A conservative and minimally invasive approach to necrotizing pancreatitis improves outcome. Gastroenterology. 2011 Oct;141(4):1254–63.

7. Gurusamy KS, Belgaumkar AP, Haswell A, Pereira SP, Davidson BR. Interventions for necrotising pancreatitis. Cochrane Database Syst Rev. 2016 Apr 16;4(4):CD011383.

8. Bang JY, Wilcox CM, Arnoletti JP, Varadarajulu S. Superiority of endoscopic interventions over minimally invasive surgery for infected necrotizing pancreatitis: meta-analysis of randomized trials. Dig Endosc. 2020 Mar;32(3):298–308.

9. Schepers NJ, Hallensleben NDL, Besselink MG, Anten MPGF, Bollen TL, da Costa DW, et al. Urgent endoscopic retrograde cholangiopancreatography with sphincterotomy versus conservative treatment in predicted severe acute gallstone pancreatitis (APEC): a multicentre randomised controlled trial. Lancet. 2020 Jul 18;396(10245):167–76.

10. Boxhoorn L, van Dijk SM, van Grinsven J, Verdonk RC, Boermeester MA, Bollen TL, et al. Immediate versus Postponed Intervention for Infected Necrotizing Pancreatitis. N Engl J Med. 2021 Oct 7;385(15):1372–81.

11. van Brunschot S, van Grinsven J, van Santvoort HC, Bakker OJ, Besselink MG, Boermeester MA, et al. Endoscopic or surgical step-up approach for infected necrotising pancreatitis: a multicentre randomised trial. Lancet. 2018 Jan 6;391(10115):51–8.

12. Podda M, Pacella D, Pellino G, Coccolini F, Giordano A, Di Saverio S, et al. coMpliAnce with evideNce-based cliniCal guidelines in the managemenT of acute biliaRy pancreAtitis): The MANCTRA-1 international audit. Pancreatology. 2022 Nov;22(7):902–16.

13. Talukdar R, Tsuji Y, Jagtap N, Pradeep R, Rao GV, Reddy DN. Non-compliance to practice guidelines still exist in the early management of acute pancreatitis: Time for reappraisal? Pancreatology. 2021 Sep 1;21(6):1152–60.

14. Tenner S, Baillie J, DeWitt J, Vege SS, American College of Gastroenterology. American College of Gastroenterology guideline: management of acute pancreatitis. Am J Gastroenterol. 2013 Sep;108(9):1400–15; 1416.

15. Yokoe M, Takada T, Mayumi T, Yoshida M, Isaji S, Wada K, et al. Japanese guidelines for the management of acute pancreatitis: Japanese Guidelines 2015. J Hepatobiliary Pancreat Sci. 2015 Jun;22(6):405–32.

16. Working Group IAP/APA Acute Pancreatitis Guidelines. IAP/APA evidence-based guidelines for the management of acute pancreatitis. Pancreatology. 2013 Jul-Aug;13(4 Suppl 2):e1–15.

17. NICE. National Institute for Health Care Excellence. 2020 [cited 2024 Feb 24]. Pancreatitis. Available from: https://www.nice.org.uk/guidance/ng104

18. Leppäniemi A, Tolonen M, Tarasconi A, Segovia-Lohse H, Gamberini E, Kirkpatrick AW, et al. 2019 WSES guidelines for the management of severe acute pancreatitis. World J Emerg Surg. 2019 Jun 13;14:27.

19. Podda M, Di Martino M, Ielpo B, Catena F, Coccolini F, Pata F, et al. The 2023 MANCTRA Acute Biliary Pancreatitis Care Bundle: A Joint Effort Between Human Knowledge and Artificial Intelligence (ChatGPT) to Optimize the Care of Patients With Acute Biliary Pancreatitis in Western Countries. Ann Surg. 2024 Feb 1;279(2):203–12.

20. Birrell L, McGuinness M, Elliott B, Harmston C. Effect of rurality and ethnicity in severity and outcomes in patients with acute pancreatitis. ANZ J Surg. 2021 Jul;91(7-8):1558–62.

21. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol. 2008 Apr;61(4):344–9.

22. Wick KD, Matthay MA, Ware LB. Pulse oximetry for the diagnosis and management of acute respiratory distress syndrome. Lancet Respir Med. 2022 Nov;10(11):1086–98.

23. Ostermann M, Joannidis M. Acute kidney injury 2016: diagnosis and diagnostic workup. Crit Care [Internet]. 2016 [cited 2024 Mar 5];20. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5037640/

24. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. Gut. 2013 Jan 1;62(1):102–11.

25. Löhr JM, Dominguez-Munoz E, Rosendahl J, Besselink M, Mayerle J, Lerch MM, et al. United European Gastroenterology evidence-based guidelines for the diagnosis and therapy of chronic pancreatitis (HaPanEU). United European Gastroenterol J. 2017 Mar;5(2):153–99.

26. Cowan KB, Cassaro S. Enterocutaneous Fistula. StatPearls Publishing; 2023.

27. Gapp J, Hoilat GJ, Chandra S. Pancreatic Ascites. StatPearls Publishing; 2022.

Appendix A (i) - Revised Atlanta Classification of AP severity

Severity	Definition
Mild acute pancreatitis	Absence of organ failure Absence of local complications
Moderately severe acute pancreatitis	1. Local complications AND/OR 2. Transient organ failure (<48 hours)
Severe acute pancreatitis	1. Persistent organ failure (>48 hours)

Appendix A (ii) - RIFLE criteria for acute kidney injury/ failure

Class	Glomerular filtration rate criteria	Urine output criteria
Risk	Serum creatinine x 1.5	< 0.5 ml/kg/hour x 6 hours
Injury	Serum creatinine x 2	< 0.5 ml/kg/hour x 12 hours
Failure	Serum creatinine x 3, or serum creatinine ≥ 4 mg/dL with an acute rise >0.5 mg/dL	< 0.3 ml/kg/hour 24 hours, or anuria x 12 hours
Loss	Persistent acute renal failure = complete loss of kidney function > 4 weeks	
End-stage kidney disease	End-stage kidney disease > 3 months	

Appendix B - Definitions

Local complication	Definition
Acute pancreatitis (AP)	The diagnosis of acute pancreatitis requires two of the following three features: ● Abdominal pain consistent with acute pancreatitis (acute onset of a persistent, severe, epigastric pain often radiating to the back) ● Serum lipase activity (or amylase activity) at least three times greater than the upper limit of normal ● Characteristic findings of acute pancreatitis on contrast-enhanced computed tomography (CECT) and less commonly magnetic resonance imaging (MRI) or transabdominal ultrasonography (24).
Chronic pancreatitis (CP)	Identification of the following signs via high quality imaging modalities (computed tomography, magnetic resonance imaging): ● Increased density of the parenchyma ● Atrophy of the gland ● Calcification ● Pseudocysts and irregularities of the main pancreatic duct and its side branches. Diagnosis should be based on imaging performed in symptomatic patients presenting with indicators suggestive of pancreatic disease (25).
Specialised pancreas service	Performs elective pancreatic resections
Gallstone (biliary) AP	Confirmation of gallstones using radiological imaging (including abdominal or endoscopic ultrasonography, CT and magnetic resonance cholangiopancreatography)(14,16)
Alcohol induced AP	History of alcohol consumption (>10g) prior to the diagnosis of acute pancreatitis. 10g alcohol is approximately: ● 300ml beer ● 100ml wine ● 30ml spirits (14,16)
Hypertriglyceridaemia induced AP	● Biliary and alcohol-induced pancreatitis ruled out ● Serum triglyceride >1,000 mg/dl ((14).
Necrotising AP	Inflammation associated with pancreatic parenchymal necrosis and/or peripancreatic necrosis, CECT criteria: ● Lack of pancreatic parenchymal enhancement by intravenous contrast agent and/or ● Presence of findings of peripancreatic necrosis (see below—ANC and WON)(24)
Interstitial oedematous AP	Acute inflammation of the pancreatic parenchyma and peripancreatic tissues, but without recognisable tissue necrosis contrast enhanced CT (CECT) criteria ● Pancreatic parenchyma enhancement by intravenous contrast agent ● No findings of peripancreatic necrosis (see above) (24)

Acute necrotic collection (ANC)	● Associated with necrotising pancreatitis (defined above) ● Collection containing variables amounts of both fluid and necrosis ● Necrosis can involve the pancreatic parenchyma and/or peripancreatic tissues (24).
Infected necrosis	● Pyrexia (>38.0 degrees celsius) ● Radiological evidence of infection (presence of gas within the collection seen on CECT) (24).
Acute pancreatic fluid collection (APFC)	● Associated with interstitial oedematous pancreatitis with no associated peripancreatic necrosis. ● Areas of peripancreatic fluid seen within the first 4 weeks after onset of interstitial oedematous pancreatitis and without the features of a pseudocyst (24).
Enteric fistula	Fistulous tract (abnormal connection between two epithelialized surfaces) proven on high quality imaging modalities (CT/MRI), or endoscopic visualisation or intraoperatively (26)
Pancreatic ascites	This results from persistent leakage of pancreatic secretions in the peritoneum from pancreatic duct injury. Confirmed with diagnostic paracentesis ● Amylase level over 1000 IU/L ● Protein level greater than 3 g/dL ● The calculated serum-ascites albumin gradient (SAAG) is normally less than 1.1 g/dL. This distinguishes from ascites secondary to portal hypertension where amylase levels of ascitic fluid are not elevated, and fluid albumin levels are normally below 1.5 g/dL with a SAAG greater than 1.1 g/dL (27)

Appendix C - Hospital Survey

Questions	***Options***
How many beds does your hospital have?	
How many ICU beds does your hospital have?	
Does your hospital have a high dependency unit (HDU)?	Yes/no
(If yes) how many beds does your HDU have	value
Do you have an interventional radiology service at your hospital?	Yes/no
Do you have an endoscopy service at your hospital?	Yes/no
Is ERCP routinely offered to patients in your hospital?	Yes/no
Is EUS routinely offered to patients in your hospital?	Yes/no

Appendix E - Charlson Comorbidity Index

Comorbidity	**Scoring**
Age	0 points (<50 years) 1 point (50 - 59 years) 2 points (60 - 69 years) 3 points (70 - 79 years) 4 points (≥ 80 years)
Previous myocardial infarction (MI)	1 point
Congestive heart failure (CHF)	1 point
Peripheral vascular disease	1 point
Previous cerebrovascular accident (CVA) or transient ischaemic attack (TIA)	1 point
Dementia	1 point
COPD	1 point
Connective tissue disease	1 point
Peptic ulcer disease	1 point
Liver disease	1 point (mild) 3 points (moderate to severe)
Diabetes mellitus	0 point (none or diet-controlled) 1 point (uncomplicated) 2 points (end-organ damage)
Hemiplegia	2 points
Moderate to severe chronic kidney disease *(Moderate = creatinine > 3mg/dL (0.27 mmol/L), Severe = on dialysis, status post kidney transplant, uraemia)*	2 points
Solid tumour	0 point (none) 3 points (localised) 6 points (metastatic)
Leukaemia	2 points
Lymphoma	2 points
Acquired immunodeficiency syndrome (AIDS)	6 points
Total Charlson Comorbidity Index (maximum score = 37)	

Appendix F - Tokyo guidelines diagnostic criteria for cholangitis

Class	***Criteria***
A. Systemic inflammation	1. Pyrexia (>38 degrees Celsius) 2. White blood cells <4 or >10 ×1,000/μL and/or CRP ≥1
B. Cholestasis	1. Jaundice: T-Bil ≥2 (mg/dL) 2. Deranged liver function tests (>1.5 × STD)
C. Imaging	1. Biliary dilation 2. Evidence of aetiology on imaging