

# A randomised controlled trial of a procalcitonin-based algorithm to guide antibiotic use in acute pancreatitis

<b>Submission date</b> 20/12/2017	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 07/02/2018	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 22/07/2022	<b>Condition category</b> Digestive System	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

The pancreas is an organ in the upper abdomen sitting below the stomach. Its function is to produce enzymes to digest food, as well as producing hormones to control blood sugars. When the pancreas becomes inflamed it can cause pain and sickness, as well as affecting other vital organs. This condition is termed acute pancreatitis. The severity of acute pancreatitis can range from being mild to very severe where some patients spend a long time in hospital. Acute pancreatitis is treated mainly by rehydration, as well as giving pain relief and anti-sickness medications. The inflammation usually settles on its own. However, for the small minority of patients who are unfortunate to develop a severe form of acute pancreatitis, bacterial infection around the pancreas can be a problem, and this may require additional treatment such as antibiotics. Telling the difference between inflammation and bacterial infection in acute pancreatitis can be difficult. Both conditions can cause a fever and a fast heart rate. Antibiotics are often prescribed where there is no bacterial infection, so there will be no benefit to patients, but can cause harmful side-effects such as severe diarrhea and inflammation of the bowel. There is also a risk of developing bacteria that are resistant to common antibiotics, limiting the choice of antibiotics if they are needed in the future. It is therefore important to only give antibiotics to those patients who have a bacterial infection. There are blood tests, such as Procalcitonin, that can help to distinguish between inflammation and infection. The aim of this study is to see how effective Procalcitonin is at guiding doctors in using antibiotics in acute pancreatitis. Procalcitonin is produced by the cells in our body in response to infection. This can be measured in blood samples. At the moment, it can be used to guide antibiotic treatment in common conditions such as chest infections. Its role for patients with acute pancreatitis who are suspected of having infection, however, is not yet clear.

### Who can participate?

Patients aged over 18 with acute pancreatitis

### What does the study involve?

Participants are randomly allocated to receive antibiotics either in response to a procalcitonin algorithm or by standard decision making. All other aspects of the care of patients are the same.

The study assesses whether the use of procalcitonin measurement allows for a reduction in the use of antibiotics without compromising patient outcome.

What are the possible benefits and risks of participating?

There is evidence from other studies that the use of procalcitonin measurement to guide antibiotic use results in more appropriate use of antibiotics. There are not likely to be any risks from participation.

Where is the study run from?

Manchester Royal Infirmary (UK)

When is the study starting and how long is it expected to run for?

January 2017 to December 2020

The study opened to recruitment on the 26th July 2018 and will recruit for two years

Who is funding the study?

Manchester University NHS Foundation Trust (UK)

Who is the main contact?

Prof. Ajith Siriwardena

## Contact information

### Type(s)

Scientific

### Contact name

Prof Ajith Siriwardena

### Contact details

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## Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

Version 1.0

# Study information

## Scientific Title

PROCalcitonin-based algorithm for antibiotic use in Acute Pancreatitis: a randomised controlled trial

## Acronym

PROCAP

## Study objectives

This study tests the hypothesis that a procalcitonin-based algorithm to guide initiation, continuation and discontinuation of antibiotics will lead to reduced antibiotic use in patients with acute pancreatitis without an adverse effect on outcome.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Approved 27/04/2018, North West - Haydock Research Ethics Committee (3rd Floor - Barlow House, 4 Minshull Street, Manchester, M1 3DZ; Tel: +44 (0)207 104 8012; Email: nrescommittee.northwest-haydock@nhs.net), REC ref: 18/NW/0255

## Study design

Single-centre randomised controlled single-blind two-arm phase III pragmatic clinical and cost-effectiveness trial

## Primary study design

Interventional

## Secondary study design

Randomised controlled trial

## Study setting(s)

Hospital

## Study type(s)

Diagnostic

## Participant information sheet

Not available in web format, please use the contact details to request a patient information sheet

## Health condition(s) or problem(s) studied

Acute pancreatitis

## Interventions

Method of randomisation:

Web-based randomisation will be provided by the Clinical Trials Unit of the University of Edinburgh (<https://www.ed.ac.uk/usher/edinburgh-clinical-trials>). Allocation will be in a ratio of 1:1 to routine or algorithm-guided care. Randomization will be stratified by severity (mild or

moderately severe/severe) and admission pathway (whether or not the patient has their index (first) admission with acute pancreatitis to the Manchester Royal Infirmary [direct] or is transferred from another hospital [tertiary transfer]). A random block size of 4, 6 or 8 will be applied to each stratum.

Patients will be randomly allocated to receive antibiotics either in response to a procalcitonin algorithm or by standard decision making. All other aspects of the care of patients will be the same. The main endpoint is whether the use of procalcitonin measurement allows for a reduction in use of antibiotics without compromising outcome.

#### Summary methodology for intervention arm:

The intervention is the use of a procalcitonin-based algorithm to guide antibiotic use. The algorithm is a simplified, bi-modal guide: consider antibiotic use if PCT >1 ng/mL, do not use if PCT below this point. Patients will undergo baseline and follow-up sampling of PCT. In addition, PCT should be measured if there is a clinical suspicion of infection or if antibiotic use is being considered. Where possible, antibiotic use should be commenced with appropriate support from the PCT algorithm and discontinued in compliance with repeat PCT measurement. All care of patients with acute pancreatitis in the intervention arm will be standard with the sole exception of antibiotic use which will be guided by the PCT algorithm.

#### Summary methodology in the control arm:

All care of patients with acute pancreatitis in the control arm will be standard.

#### Duration of treatment:

Patients will remain within the study for 90 days or until discharge from hospital (if later).

#### Follow-up:

Patients will be followed for 90 days or until discharge from hospital (if later).

### Intervention Type

Other

### Primary outcome measure

Current primary outcome measure as of 25/03/2020:

Whether antibiotic use is initiated during the index stay. Trial antibiotic use will exclude mandated routine antibiotic use, specifically prophylaxis before procedures such as laparoscopic cholecystectomy or ERCP.

Antibiotics prescribed before the index admission (from the referring hospital or community) will be recorded at admission but not included in the primary endpoint.

#### Previous primary outcome measure:

Days of antibiotic use, defined as any day (24 hour period) when antibiotics were prescribed on the patient's drug prescription chart and administered. This will be recorded as days of antibiotic use until the 90th day or until discharge from hospital (if later).

### Secondary outcome measures

All secondary outcomes measured as occurring up to the 90th day or until discharge from hospital (if later):

1. Clinical infections as defined according to the centers for disease control
2. New isolates of multi-resistant bacteria (Clostridium difficile, vancomycin resistant enterococcus [VRE], methicillin resistant staphylococcus aureus [MRSA], carbapenemase

producing enterobacteriaceae [CPE])

3. Incidence of multi-resistant organism bacteraemia

4. Infection of pancreatic necrosis, defined either as a result of fine needle aspiration (FNA), radiological evidence of gas in a peri-pancreatic collection or positive microbiological cultures from surgical or post-mortem specimens

5. Use of radiological, endoscopic or surgical intervention

6. Length of inpatient stay (by level of care: critical care levels II/III, ward-based care)

7. Re-admission to hospital within 6 weeks of onset of index episode

8. Episode-related mortality and cause

9. Quality of life, assessed by the EQ-5D-5L questionnaire

10. Cost analysis from an NHS perspective, including inpatient resource use

**Overall study start date**

03/01/2017

**Completion date**

31/12/2020

## **Eligibility**

**Key inclusion criteria**

Adult patients presenting with acute pancreatitis admitted or referred to the service. Inclusion criteria include:

1. Patients over the age of 18 years of age

2. Ability to provide informed consent

3. The diagnosis of acute pancreatitis requires two of the following three features:

3.1. Abdominal pain consistent with acute pancreatitis (acute onset of a persistent, severe, epigastric pain often radiating to the back)

3.2. Serum lipase activity (or amylase activity) at least three times greater than the upper limit of normal

3.3. Characteristic findings of acute pancreatitis on contrast-enhanced computed tomography (CECT) and less commonly magnetic resonance imaging (MRI) or transabdominal ultrasonography

**Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

260

**Total final enrolment**

260

**Key exclusion criteria**

1. Patients under the age of 18 years of age
2. Patients who are unable to give informed consent (criterion removed 14/06/2019)
3. Infectious conditions requiring prolonged antibiotic therapy – such as infective endocarditis
4. Severely immunocompromised patients – such as those with human immunodeficiency virus and with a CD4 count of less than 200 cells/mm<sup>3</sup>; neutropenic patients (<500 neutrophils/mm<sup>3</sup>)
5. Patients on immunosuppressive therapy
6. Previous thyroid surgery

**Date of first enrolment**

26/07/2018

**Date of final enrolment**

31/12/2020

**Locations****Countries of recruitment**

England

United Kingdom

**Study participating centre**

**Manchester Royal Infirmary**

Oxford Road

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**Sponsor information****Organisation**

Manchester University NHS Foundation Trust

**Sponsor details**

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**Sponsor type**

Hospital/treatment centre

ROR

<https://ror.org/00he80998>

## Funder(s)

### Funder type

Hospital/treatment centre

### Funder Name

Manchester University NHS Foundation Trust

## Results and Publications

### Publication and dissemination plan

It is the trialists' intention to publish the protocol in a peer-reviewed journal. It has not currently been submitted. Clinical and economic analysis will be conducted to a prospective analysis plan made available to journal referees. The results will be presented at appropriate national and international meetings. The results will be published regardless of the final results of the trial.

### Intention to publish date

05/10/2021

### Individual participant data (IPD) sharing plan

The participant-level data that will be recorded for this study are highly specific to the PROCAP analysis and should not be used for unspecified secondary analyses. Therefore the trialists do not plan to make these data available. The primary data will be stored as paper-based case report forms in a locked office in the Manchester Royal Infirmary.

### IPD sharing plan summary

Not expected to be made available

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol article</a>	protocol	29/07/2019	31/07/2019	Yes	No
<a href="#">Protocol file</a>	version v3.0	24/03/2020	26/03/2020	No	No
<a href="#">Results article</a>		18/07/2022	22/07/2022	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No