DIVERTICULITIS MANAGEMENT: A SNAPSHOT COLLABORATIVE AUDIT STUDY

DAMASCUS

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Abbreviations

ACPGBI	Association of Coloproctology of Great Britain and Ireland
ASA	American Society of Anaesthesiologists
ASCRS	American Society of Colon and Rectal Surgeons
BiSTC	Birmingham Surgical Trials Consortium
BMI	Body Mass Index
CI	Chief Investigator
CSSANZ	Colorectal Surgical Society of Australia and New Zealand
CT	Computed Tomography
DD	Diverticular Disease
DM	Diabetes Mellitus
ESCP	European Society of Coloproctology
GCP	Good Clinical Practice
IRAS	Integrated Research Application System
IRB	Institutional Review Board
i.v	Intravenous
NELA	National Emergency Laparotomy Audit
PI	Principle Investigator
PIS	Patient Information Sheet
p.o	Per oral
SMG	Study Management Group

1. Signature Page

We the undersigned hereby approved the clinical audit protocol version……

Signature_____Date_____

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2. Study Summary

Full Study Title	International, prospective snapshot collaborative audit of acute diverticulitis
Short Title	Diverticulitis Management: A Snapshot Collaborative Audit
Study Design	Multicentre, prospective audit
Study Duration	Approx. one year
Study Objectives	**Primary Objective** 1. Prospectively audit the national and international variability in the presentation and index management of acute diverticulitis; **Secondary Objectives** 2. What are the national and international variations in operating strategies employed for those patients undergoing surgery? 3. What are the international variations in 30-day mortality rates?
Study Outcomes	1. The short term clinical outcomes at 30-days (from index admission); 2. Readmission and/or re-intervention rates at 6-months (from index admission); 3. Clinical outcomes post radiological and/or surgical intervention; 4. If any patient- or disease-specific covariates affect treatment strategy or short term clinical outcomes; 5. Clinician equipoise for the recruitment of patients to future randomised controlled trials.
Coordinating Centre	Birmingham Surgical Trials Consortium
Collaborating Institutions	Association of Coloproctology of Great Britain and Ireland European Society of Coloproctology American Society of Colon and Rectal Surgeons Colorectal Surgical Society of Australia and New Zealand
Number of subjects	Approx. 4000

Eligibility Criteria	• Patients presenting with acute diverticulitis (newly incident within the audit period) • Adults (age 16 years and above) • Acute diverticulitis diagnosed either: - via multiplanar CT OR - during emergency surgery
Duration of data collection	6 months from the start of recruitment

3. Introduction

Diverticular disease is a common problem affecting up to 65% of people aged over 80 [1]. Complications may affect 10-25% of these patients [2], and although some such as bleeding and inflammation can usually be managed conservatively, others such as perforation are more serious. Perforation may present as peritonitis requiring urgent surgery but can also occur in a more indolent fashion becoming sealed off, resulting in abscess formation.

The incidence of acute diverticulitis and hospital admissions for its complications are steadily increasing, not least due to a population cohort that exhibits the main risk factors for complicated diverticular disease (age and obesity). UK admission rates for acute diverticulitis increased from 0.56 to 1.20/1000/year between 1996 and 2006 along with a 2.28-fold increase in admissions for perforated disease, equating to approximately 12,000 emergency bowel resections/year [3].

Perforated disease has an associated short (8.2%) [4] and long-term mortality rate (14.5%) [4,5], and these rates are particularly high in the UK. The exact cost to the NHS of this disease is unknown, but European and US studies have suggested direct and indirect costs range from £63 million to over £1 billion/year, respectively [6,7].

The broad initial management strategies for acute diverticulitis can vary from conservative strategies such as antibiotics and drainage procedures, through to more invasive surgical procedures such as laparoscopic lavage and bowel resection. Although there are a number of prospective studies advocating optimal treatment strategies, little is known about true clinical practice. Retrospective analysis of administrative dataset has suggested that there exists significant international variability in the index management of acute diverticulitis, and that such differences may contribute to the observed differences in mortality rates [4].

There are however very little prospective data regarding this perceived international variation, and furthermore there are specific subgroups of patients with acute diverticulitis such as diverticular abscess in which very little is known about the optimal management.

This study will audit the different types of management employed in patients presenting with acute diverticulitis. The aim is to explore whether an international variation in practice exists and if there is association between index management and short and medium term clinical outcomes only. From

this dataset, the variations in the index management and corresponding outcomes of patients with acute diverticulitis will be assessed.

This study will not investigate any patient reported outcomes, but it is hoped that the findings of this study will inform the design of future studies of acute diverticulitis which will collect patient level data.

4. Study Aims

4.1 Overall aims and design rationale

Little is known of the natural history and variation in strategies applied to managing acute diverticulitis. Furthermore, the feasibility of developing large scale, prospective interventional studies is also unclear due to the lack of baseline data regarding the incidence, initial management and outcomes of acute diverticulitis. The aim of this study is therefore to determine the international variability in disease management at index admission and to collect data that may inform the design of future studies. The large, global scale of this initial study will only allow the collection of short and medium term clinical data.

4.2 Primary Objective

1. To prospectively audit the national and international variability in the presentation and index management of acute diverticulitis;

4.3 Secondary Objectives

2. What are the national and international variations in operating strategies employed for those patients undergoingsurgery?
3. What are the international variations in 30-day (post index admission) mortality rates?

4.4 Outcomes

1. The short term clinical outcomes at 30-days (from index admission);
2. Readmission and/or re-intervention rates at 6-months (from index admission);
3. Clinical outcomes post radiological and/or surgical intervention;
4. If any patient- or disease-specific covariates affect treatment strategy or short term clinical outcomes;
5. Clinician equipoise for the recruitment of patients to future randomised controlled trials.

5. Study Design

5.1 Overview

DAMASCUS is an international, multi-centre, prospective audit aiming to collect short term 30-day and 6-month clinical outcome data on the national and international variabaility in the presentation and management of acute diverticulitis.

Routine patient and clinical data will be recorded electronically (via the REDCap system) on bespoke CRFs.

5.2 Setting

At least 80 acute general or university teaching hospitals, the study will be conducted across the Tripartite regions; UK, America, Australasia and Europe.

5.3 Target population

Adults attending hospital acutely with acute diverticulitis (CT proven or diagnosed during surgery for acute peritonitis) who undergo conservative, radiological or surgical treatment for their disease.

5.4 Eligibility criteria

5.4.1 Inclusion criteria

- Patients presenting with acute diverticulitis (newly incident within the audit period)
- Adults (age 16 years and above)
- Acute diverticulitis diagnosed either:
  - via multiplanar CT

    OR
  - during emergency surgery

NOTE:

- Patients who are admitted and require urgent surgery where the diagnosis is made either intra- or post operatively should be included in the audit
- Patients who have been admitted previously with acute diverticulits should be included in the audit.

5.4.2 Exclusion criteria:

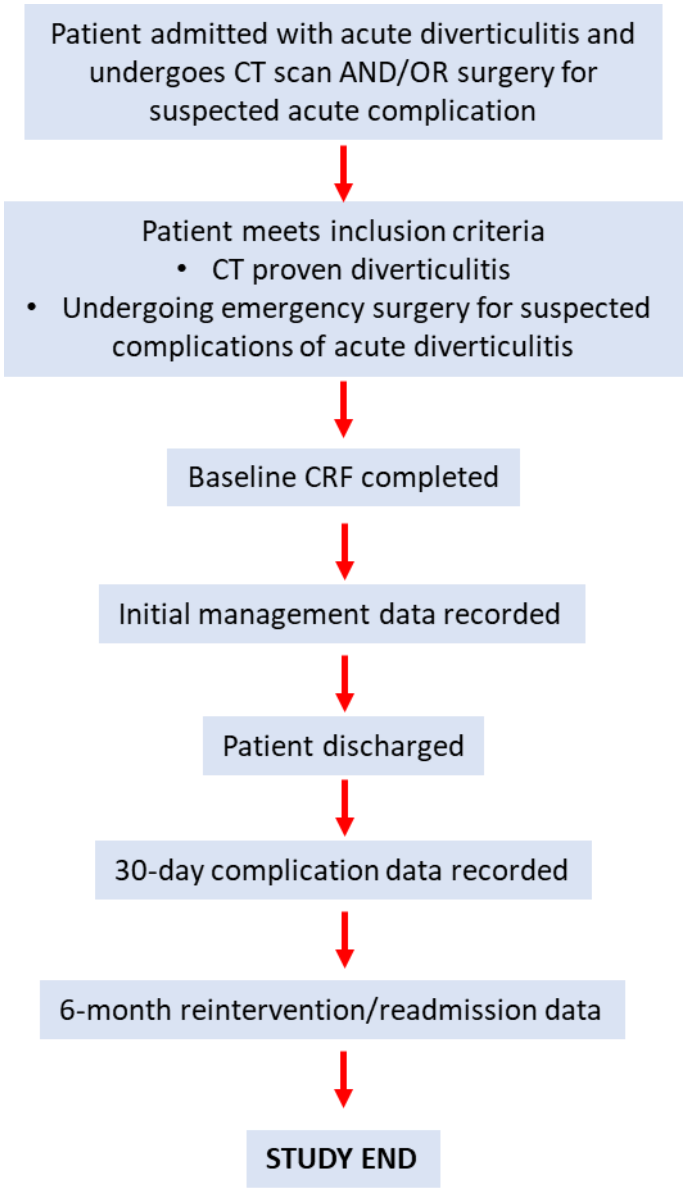
- Diagnoses other than diverticulitis

5.5 Interventions

The study is observational and low risk. There are no interventions and only routinely collected data will be used.

5.6 Patient Pathway and Identification

Within routine care, following confirmation of the diagnosis and eligibility, patient data can be included in the audit. Patients may present with a range of severeties from relatively mild diverticultis through to localised abscess formation or peritonitis. Consequently treatment may range from i.v antibiotics, percutaneous drainage or surgery and these treatments may occur in single, combined or sequential regimens. Each treatment regimen will be recorded and if patients are readmitted within 6 months, data regarding any treatment or interventions will also be recorded. Patients who are admitted acutely with peritonitis and undergo emergency surgery without any form of imaging and are subsequently found to have acute diverticulitis should be included following surgery and/or pathological diagnosis



6. Data Collection

6.1: Baseline data

Baseline data will be recorded at the index admission following confirmation of eligbility. Data will be collected by consultant surgeons, research fellows, surgical trainees, research nurses or a study co-ordinator. Electronic case report forms (incorporating baseline, 30-day outcome data and 6-monthly outcomes) [Appendix 1] will be used by the clinical care team to capture data on (a) the patient (fitness, frailty and main risk factors for disease recurrence [previous admissions, NSAID use[8] and obesity[9]; (b) the disease (including sepsis markers and CT findings); (c) the index management and any operative findings and strategy; (d) 30-day outcome (routine perioperative

measures) and; (e) 6-month readmission/re-intervention rates. This CRF has been minimalised to facilitate rapid completion based on the principles embodied by other large scale studies in the emergency setting e.g. NELA[10]. **Only routine data will be collected, no additional information will be sought as this is an audit of practice only**.

6.2 Clinical outcomes

Data collected by clinical team at index admission, 30-day and 6- month follow up:

1. Main disease state and trait characteristics
2. Initial management at index admission
3. Length of stay
4. Post-intervention complication rates
5. 30-day recurrent admission rate (as a surrogate marker of all health utilisation)
6. 30-day recurrent admission rate for diverticulitis and complications (as a surrogate of disease specific health utilisation)
7. 30-day recurrent intervention rate
8. 6-month readmission and/or re-intervention rate

6.3 Assessment of Clinician Equipoise

Future studies assessing the management of acute diverticulitis may need to be conducted as randomised trials, however it is known that such randomisation can be difficult due to lack of both clinician and patient equipoise. In order to assess this further within this audit, clinicians will be asked, as part of the index management CRF, whether they would in theory be prepared to recruit their patient to a study that may randomise treatment between conservative or surgical strategies.

6.4 Recruitment Projection

Emergency admissions for acute diverticulitis are increasing in the UK and are suspected to continue increasing year on year. Accurate figures for individual hospitals are difficult but in 2005/6 there were just under 24,000 in-patient admissions for acute diverticulitis [3]. It is anticipated that units will expect to admit on average 10 patients/month with acute diverticulitis, in practice the actual figure may be much lower or higher than this. Based on this estimation, with a recruitment base of 80 units globally, it is anticipated that up to 4,000 patients may be recruited over a 6 month period.

Estimated milestones are:

Pilot sites: October 2019

First patient recruited: December 2019

Last patient recruited: May 2020

Last follow up data collected: December 2020

7. Data Handling and Record Keeping

7.1 Data Management

Data will be collected at the following times:

- During the index hospital admission
- At 30 days after index admission or emergency surgery for complications of acute diverticulitis
- At six months after index admission or emergency surgery for complications of acute diverticulitis.

Data will be entered directly onto the secure electronic DAMASCUS REDCap [11, 12] database by study collaborators at participating hospitals sites. REDCap is a secure, web-based software platform designed to support data capture of single and multi-site studies.

Site study collaborators will be provided with a paper copy of the eCRF to facilitate data collection. If this is used, they should then transfer data from the paper CRF to the online DAMASCUS database (https://www.bistc.redcap.bham.ac.uk). DAMASCUS data management staff will check all incoming data CRFs for completeness, data consistency and compliance with the protocol. If discrepancies or missing data are identified, the DAMASCUS data management staff will raise queries with the research team at the participating hospital.

7.2 Data Security and Data Protection

The security of the study database system is governed by the policies of the University of Birmingham. The DAMASCUS study database will be hosted on the REDCap system managed and maintained by the BiSTC.

Data management and data security within the BiSTC will abide by the requirements of the General Data Protection Regulations (GDPR) and any subsequent amendments. The study will be conducted at collaborating sites in accordance with the country-specific data proection requirments. Data will

be acquired and stored on the REDCap platform. Access to data will be restricted, each individual collaborator entering data for DAMASCUS will have their own username and password. Each participant will be allocated a unique study number at entry. All communication will use this as the identifier. All data will be analysed and reported in summary format. No individual will be identifiable.

7.3 Confidentiality

Patient identifiable information will not be collected in this study. All participant data held at the University of Birmingham will be anonymised.

All data collected about participants will be identified using only a unique DAMASCUS study number (REDCap ID). This number will be automatically allocated via REDCap once a new patient record is created in the DAMASCUS database.

Any correspondence between the DAMASCUS study office and hospital sites will use the DAMASCUS study number only.

The linkage between REDCap study ID and participants will be maintained in strict confidence at participating sites. This data will not be submitted to the DAMASCUS study office and will not be sent outside of the participating site.

Confidentiality of all particpants' data will be maintained and there will be no disclosure of information by which participants may be identified to any third party other than those directly involved in the treatment of the participant. The participants will not by identifiable with regards to any future publications relating to this study.

Patient identifiable information will only be held at participating sites. This data will be kept confidential and managed in accordance with the Data Protection Act, NHS Caldicott Principles.

8. Ethical Approval

In the UK, this study is categorised as an audit, not research (see appendix VI for the HRA decision tool outcome). Therefore, sites may participate once local clinical audit approval is in place.

Non-UK centres should seek advice from their local regulatory bodies (e.g. ethical committees) and apply for the required approvals, according to local, state or national policy, prior to study start. For centres in the US, surgeons must obtain Institute Review Board (IRB) approval prior to enrolling patients.

9. Study Administration

The study has been developed by an international study management team which will have at least two members from each Tripartite continent. This study management group will be chaired by the CI and further members from other countries will be added as appropriate.

The project will be under the auspices of the Chief Investigators and the Birmingham Surgical Trials Consortium. The project will be overseen by a Study Management Group (SMG).

9.1 Local study teams

Each participating centre will be responsible for identifying a PI, trainees or research fellows may also act as associate PIs. Where feasible the use of trainee collaboratives will be encouraged to aid in the delivery of this study. The role of PI is to:

- Promote the study at site and facilitate delivery at site
- Liaise with the SMG
- Ensure that mechanisms for upload of data relating to eligible participants is in place
- Ensure appropriate local staff resources are maintained (cover provided for absence) to deliver the study

9.2 Patient and Public Development

The protocol has been developed in conjunction with patients and public, and the SMG includes a lay member.

9.3 Publication Policy

The Chief Investigator will co-ordinate dissemination of data from this study. All publications using data from this study to undertake original analyses will be submitted to the SMG for review before release. The success of the study depends on a large number of clinicians. For this reason, credit for the results will not be given to the committees or central organisers, but to all who have collaborated and participated in the study. Acknowledgement will include all local co-ordinators and collaborators, members of the study committees, the SMG and administrative staff. Authorship at the head of the primary results paper will be cited as a collaborative group to avoid giving undue prominence to any individual. All contributors to the trial will be listed at the end of the report, with their contribution to the study identified. Those responsible for other publications reporting specific aspects of the study may wish to utilise a different authorship model, such as "[name], [name] and [name] on behalf of the collaborative Group". Decisions about authorship of additional papers will be discussed and agreed by the study investigators and the SMG.

9.4 Dissemination of Research Findings

The results of this study will be submitted for publication in peer reviewed scientific journal, given the international nature of this study it is anticipated that this will be reflected in the selected journal. Results of the study will also be presented at meeting both national and international, according to the contributing nations. The findings of this study may be used to inform the design of further studies into diverticular disease.

9.5 Finance and Funding

This study has been funded by the Bowel Disease Research Foundation in the United Kingdom. The study will be coordinated via Birmingham Surgical Trials Consortium and thus the burden of the cost will lie within the UK. Participating centres will not bear any costs for being part of this audit. Similarly, no financial reimbursement will be made to units or investigators for their involvement.

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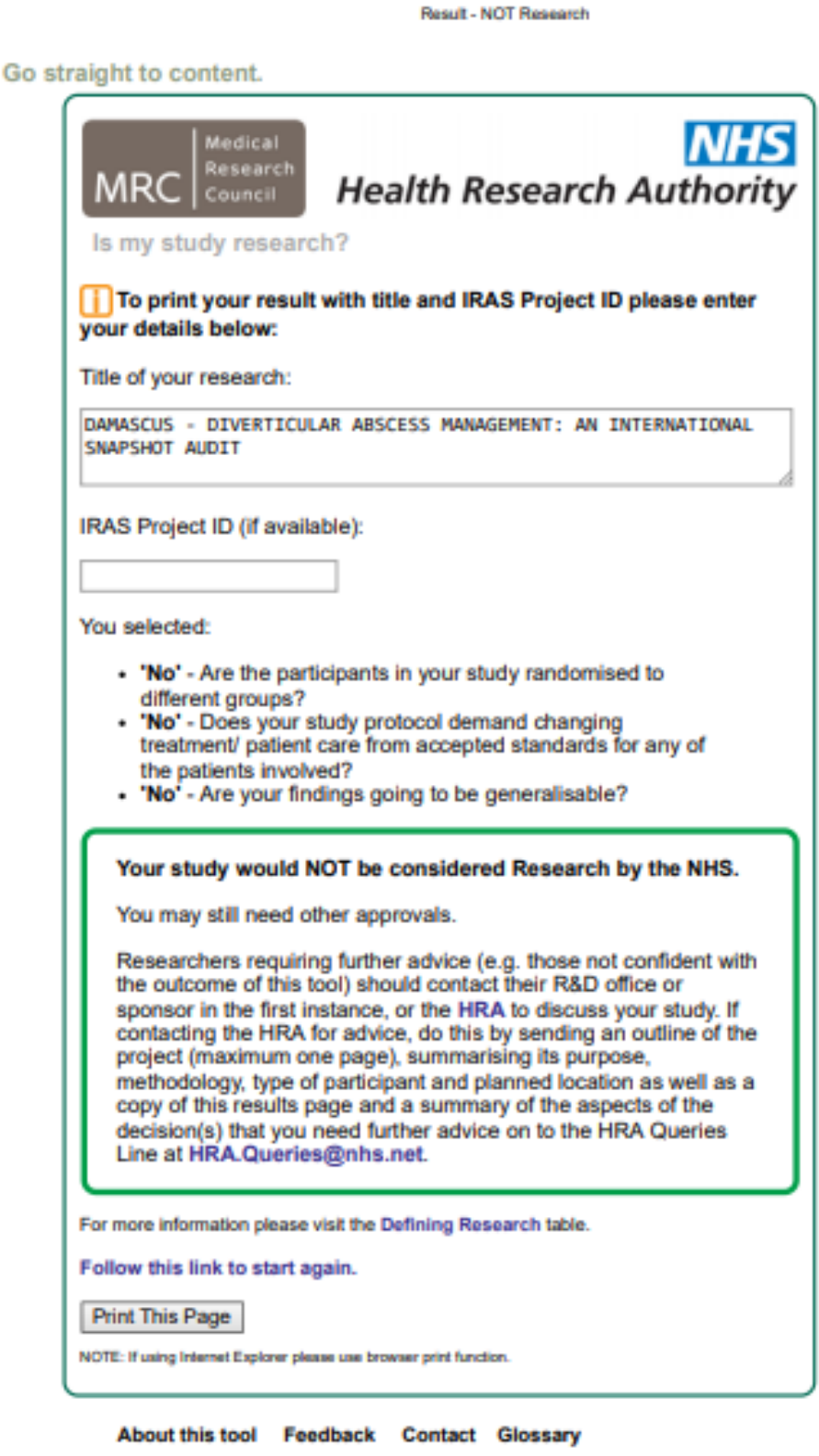
11. APPENDIX

HRA decision tool



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Is my study research?

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DAMASCUS - DIVERTICULAR ABSCESS MANAGEMENT: AN INTERNATIONAL SNAPSHOT AUDIT

IRAS Project ID (if available):

You selected:

- **'No'** - Are the participants in your study randomised to different groups?
- **'No'** - Does your study protocol demand changing treatment/ patient care from accepted standards for any of the patients involved?
- **'No'** - Are your findings going to be generalisable?

Your study would NOT be considered Research by the NHS.

You may still need other approvals.

Researchers requiring further advice (e.g. those not confident with the outcome of this tool) should contact their R&D office or sponsor in the first instance, or the HRA to discuss your study. If contacting the HRA for advice, do this by sending an outline of the project (maximum one page), summarising its purpose, methodology, type of participant and planned location as well as a copy of this results page and a summary of the aspects of the decision(s) that you need further advice on to the HRA Queries Line at HRA.Queries@nhs.net.

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