FULL/LONG TITLE OF THE STUDY

Full Study title:

Comparative Study on the Diagnostic Validity of Alvarado Score, Appendicitis Inflammatory Response (AIR) and Adult Appendicitis Score (AAS) in Acute Appendicitis in East Lancashire Hospitals NHS Trust

Study Acronym: DV-AAA ELHT

Protocol Version number and date: Version 1.0 - 15/07/2025

Version 2.0 - 19/11/2025

IRAS ID Number: 360349

SPONSORS Number: DEV123

FUNDERS Number: N/A

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, **East Lancashire Hospitals NHS Trust** SOPs, and other regulatory requirement.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor.

I also confirm that I will make the findings of the study publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

For and on behalf of **East Lancashire Hospitals NHS Trust**

Signature:

JinRen Date: 8 Sept 2025

Name (please print): JinRen Lau

Position: Foundation Year 2 Doctor

Chief Investigator:

Signature:

M.Butt Date: 8 Sept 2025

Name: (please print): Mr Muhammad Adeel Butt

Position: General Surgery Consultant

LIST of CONTENTS

GENERAL INFORMATION	**Page No.**
HRA PROTOCOL COMPLIANCE DECLARATION	i
TITLE PAGE	ii
RESEARCH REFERENCE NUMBERS	ii
SIGNATURE PAGE	iii
LIST OF CONTENTS	iv
KEY STUDY CONTACTS	v
STUDY SUMMARY	v
FUNDING	vi
ROLE OF SPONSOR AND FUNDER	vi
ROLES & RESPONSIBILITIES OF STUDY STEERING GROUPS AND INDIVIDUALS	vi
STUDY FLOW CHART	vii
SECTION	
1. BACKGROUND	
2. RATIONALE	
3. THEORETICAL FRAMEWORK	
4. RESEARCH QUESTION/AIM(S)	
5. STUDY DESIGN/METHODS	
6. STUDY SETTING	
7. SAMPLE AND RECRUITMENT	
8. ETHICAL AND REGULATORY COMPLIANCE	
9. DISSEMINATION POLICY	
10. REFERENCES	
11. APPENDICES	

KEY STUDY CONTACTS

Chief Investigator	Mr Muhammad Adeel Butt, General Surgery Consultant M: 07828798748 Email: muhammad.butt@elht.nhs.uk Royal Blackburn Teaching Hospital Haslingden Road, Blackburn, Lancashire, BB2 3HH
Principal Investigator	Dr Jin Ren Lau, Foundation Year 2 Doctor M: 07920795416 Email: jinren.lau@elht.nhs.uk / laujinren2001@gmail.com Royal Blackburn Teaching Hospital Haslingden Road, Blackburn, Lancashire, BB2 3HH
Study Co-ordinator	Dr Ker Yin Tee, Foundation Year 2 Doctor M: 07920746398 Email: keryin.tee@elht.nhs.uk / keryin16@gmail.com Royal Blackburn Teaching Hospital Haslingden Road, Blackburn, Lancashire, BB2 3HH
Sponsor	**Michelle Stephens** **(Main contact on behalf of the sponsor for all correspondence relating to applications for this project)** Head of Research and Innovation M: 07976 152397 Email: research.sponsorship@elht.nhs.uk Directorate of Education, Research & Innovation |Learning and Development Centre | Park View Offices, Royal

	Blackburn Teaching Hospital | Haslingden Road | Blackburn | Lancashire | BB2 3HH **Aleksandra (Ola) Metryka** Research and Innovation Operations Manager East Lancashire Hospitals NHS Trust - A University Teaching Trust Tel: 01254 733984 (Ext. 83984) Mobile: 07977267956 Email: research.sponsorship@elht.nhs.uk Directorate of Education, Research & Innovation |Learning and Development Centre | Park View Offices, Royal Blackburn Teaching Hospital | Haslingden Road | Blackburn | Lancashire | BB2 3HH
Key Protocol Contributors	Dr Jin Ren Lau (Foundation Year 2 Doctor) Dr Ker Yin Tee (Foundation Year 2 Doctor) Mr Karim Heiba (General Surgery Senior Clinical Fellow) Mr Muhammad Adeel Butt (General Surgery Consultant)
Committees	-

STUDY SUMMARY

Study Title	Comparative Study on the Diagnostic Validity of Alvarado Score, Appendicitis Inflammatory Response (AIR) and Adult Appendicitis Score (AAS) in Acute Appendicitis in East Lancashire Hospitals NHS Trust
Internal ref. no. (or short title)	DV-AAA ELHT
Study Design	Retrospective Observational Study
Study Participants	All adult emergency patients (aged 16 years and above) of any gender admitted between June 2023 and June 2024 with clinical suspicion of acute appendicitis and who underwent appendicectomy (via laparoscopy, open, or laparotomy)
Planned Size of Sample (if applicable)	Approx 300 patients
Follow up duration (if applicable)	-
Planned Study Period	25 August 2025 – 30 June 2026
Research Question/Aim(s)	Which scoring system -- Alvarado Score, Appendicitis Inflammatory Response (AIR) Score or Adult Appendicitis Score (AAS) has the highest diagnostic accuracy for predicting histologically confirmed appendicitis among patients undergoing emergency appendicectomy?

FUNDING AND SUPPORT IN KIND

FUNDER(S) (Names and contact details of ALL organisations providing funding and/or support in kind for this study)	**FINANCIAL AND NON FINANCIALSUPPORT GIVEN**

http://www.invo.org.uk/find-out-more/information-for-researchers/

List of Abbreviations

AIR	Appendicitis Inflammatory Response
AAS	Adult Appendicitis Score
PPV	Positive Predictive Value
NPV	Negative Predictive Value
WCC	White blood cell counts
CRP	C-reactive protein
ELHT	East Lancashire Hospitals NHS Trust

PROTOCOL CONTRIBUTORS

This protocol was developed collaboratively by the following contributors:

Dr Jin Ren Lau – responsible for protocol design, research approval applications, data extraction, data analysis, and manuscript writing.

Dr Ker Yin Tee – assisting in protocol design, data extraction and validation, data analysis, and manuscript writing.

Supervisors: Mr Muhammad Adeel Butt (General Surgery Consultant) and Mr Karim Heiba (General Surgery Senior Clinical Fellow) – responsible for overseeing the clinical governance, supervising data analysis, and providing clinical insights into interpretation and dissemination of findings.

KEY WORDS: Acute appendicitis, Alvarado score
Appendicitis Inflammatory Response (AIR) score
Adult Appendicitis Score (AAS), Diagnostic accuracy

STUDY FLOW CHART

Presentation to Emergency Department (ED)/ Surgical Ambulatory Emergency Care Unit (SAECU) with suspected appendicitis (June 2023 – June 2024)

▼

Underwent appendicectomy (via laparoscopy, open, or laparotomy)

▼

Case identified via electronic patient record (Cerner)

▼

Data extraction (clinical signs and symptoms, laboratory results, histopathology reports)

▼

Retrospective calculation of Alvarado, AIR, and AAS scores

▼

Comparison of scores against histology (reference standard)

▼

Statistical analysis – sensitivity, specificity, PPV, NPV, Receiver Operating Characteristic (ROC) analysis and Area Under the Curve (AUC)

▼

Interpretation and dissemination of results

STUDY PROTOCOL

Comparative Study on the Diagnostic Validity of Alvarado, Appendicitis Inflammatory Response (AIR) and Adult Appendicitis Score (AAS) in Acute Appendicitis in East Lancashire Hospitals NHS Trust

1 BACKGROUND

Acute appendicitis (AA) is one of the most common surgical emergencies worldwide, with a lifetime risk of 7–8%. It predominantly affects adolescents and young adults but can occur across all age groups. Despite its prevalence, the clinical presentation can vary significantly, particularly in children, females, and the elderly, leading to diagnostic uncertainty and high rates of negative appendicectomy.

To improve diagnostic accuracy and reduce unnecessary surgical interventions, several clinical scoring systems have been developed. These include the Alvarado Score, the Appendicitis Inflammatory Response (AIR) Score, and the Adult Appendicitis Score (AAS). These tools utilize combinations of symptoms, clinical signs, and laboratory markers (such as white cell count and C-Reactive Protein) to stratify patients into low, intermediate, or high-risk categories for appendicitis to guide clinical decision-making regarding imaging, admission and surgical intervention. However, none of these is widely accepted and general consensus on any of these scores is still lacking (Tanrikulu et al., 2015).

The Alvarado Score, developed in 1986, has been widely adopted due to its simplicity and ease of use. However, it has limited specificity, particularly in certain subgroups like women and children (Alvarado A., 1986). In contrast, the AIR Score, developed more recently, includes inflammatory markers like C-reactive protein (CRP) and has demonstrated improved diagnostic accuracy in both uncomplicated and complicated appendicitis (Yeşiltaş M. et al., 2018). For example, a randomized controlled trial involving over 900 patients reported that the AIR Score had an area under the ROC curve (AUC) of 0.96, significantly higher than the Alvarado Score's 0.82, with notably better performance in difficult-to-diagnose subgroups (Andersson et al., 2012; de Castro SM et al., 2012).

Similarly, another comparative study found that although the Alvarado Score categorized more patients as high-risk, the AIR Score demonstrated significantly higher specificity (97% vs. 76%) and positive predictive value (PPV) (88% vs. 65%), suggesting that it may be more effective in reducing unnecessary imaging and surgery (Andersson et al., 2015).

The Adult Appendicitis Score (AAS) is a more recent tool that incorporates additional demographic and clinical factors and has shown promising diagnostic validity. However, its comparative performance in real-world UK NHS settings remains under-explored. (Ghali MS et al., 2023, Sammalkorpi et al., 2014)

Clinical scoring systems remain vital in the surgical triage of suspected AA. High clinical scores may support proceeding directly to surgery without imaging, while intermediate scores can guide selective use of diagnostic tools like ultrasound, or CT. Low scores may support conservative management or

further evaluation for alternative diagnoses as recommended by the World Journal of Emergency Surgery. Risk stratification through clinical scoring has the potential to reduce unnecessary admissions, optimize diagnostic imaging utilization, and prevent negative surgical explorations such as diagnostic laparoscopy.

Indeed, clinical scores alone seem sufficiently sensitive to identify low-risk patients and reduce the need for imaging and negative surgical interventions in suspected appendicitis cases (Andersson et al., 2017).

This retrospective observational study at East Lancashire Hospitals NHS Trust (ELHT) aims to evaluate and compare the diagnostic performance of the Alvarado Score, AIR Score, and AAS over a one-year period in all emergency cases of suspected appendicitis that resulted in appendicectomy. Using histopathology as the reference standard, we will assess the sensitivity, specificity, PPV, and NPV of each scoring system in our local setting.

Our patient population reflects a wide demographic range, including children, which adds further value to the comparative analysis. Findings from this study may support the evidence-based standardisation of scoring systems across the Trust, guide imaging protocols, and ultimately reduce negative appendicectomy rates and unnecessary investigations.

2 RATIONALE

Accurate and timely pre-operative diagnosis of acute appendicitis is essential to minimise the incidence of negative appendicectomies while avoiding unnecessary diagnostic investigations. In clinical practice, this often requires careful balancing of the potential benefits of further imaging against the associated risks and resource implications. Although several scoring systems have been developed to aid diagnostic accuracy, their application remains inconsistent. Some clinicians incorporate these tools into routine assessment, whereas others rely primarily on clinical judgement.

Comparing the diagnostic validity of existing scoring systems within our local population may help identify the most effective tool for implementation. This is particularly pertinent in East Lancashire, a region characterised by its diverse demographic profile and variability in clinical resource utilisation. Enhancing risk stratification protocols could optimise clinical decision-making, minimise unnecessary delays in care, reduce the burden of avoidable investigations, and promote more consistent, evidence-based management across emergency settings.

3 THEORETICAL FRAMEWORK

This study is based on the principles of diagnostic test evaluation, which involve assessing how accurately a clinical scoring system can predict the presence or absence of acute appendicitis. (Di Saverio et al., 2020).

The Alvarado Score, AIR Score, and AAS are all clinical decision tools that combine a patient's symptoms, signs, and blood test results to help estimate the likelihood of appendicitis.

In this study, we will retrospectively calculate these scores for each patient and compare them against the final histopathology result, which serves as the gold standard for diagnosis.

This comparison will allow us to assess the diagnostic accuracy of each scoring system using commonly accepted measures:

Sensitivity - how well the score identifies patients who do have appendicitis.

Specificity - how well it identifies those who do not.

Positive predictive value (PPV) - The positive predictive value refers to the likelihood that a patient with a positive result from the scoring system truly has acute appendicitis. It reflects the proportion of true positives among all patients who test positive according to the score.

Negative Predictive value (NPV) - The negative predictive value indicates the likelihood that a patient with a negative result from the scoring system does not have acute appendicitis. It represents the proportion of true negatives among all patients who test negative based on the score.

Receiver Operating Characteristic (ROC) analysis and Area Under the Curve (AUC) - Assess overall discriminative performance

By using this framework, we can evaluate how reliable each scoring system is in our local patient population and determine which one performs best overall. This can help guide more consistent clinical decision-making and reduce the need for unnecessary imaging or surgery in low-risk cases.

4 RESEARCH QUESTION/AIM(S)

Which scoring system -- Alvarado Score, Appendicitis Inflammatory Response (AIR) Score or Adult Appendicitis Score (AAS) has the highest diagnostic accuracy for predicting histologically confirmed appendicitis among patients undergoing emergency appendicectomy?

4.1 Objectives

To compare the diagnostic accuracy of the Appendicitis Inflammatory Response (AIR) Score, Adult Appendicitis Score (AAS), and Alvarado Score in adult patients with suspected acute appendicitis at East Lancashire Hospital NHS Trust.

To evaluate and compare the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of each scoring system in predicting histologically confirmed appendicitis.

To determine the most effective scoring system for risk stratification in the local adult population, considering the demographic diversity and clinical practice patterns at East Lancashire Hospital NHS Trust.

To provide recommendations for the standardisation of appendicitis risk assessment tools in emergency surgical practice within the trust.

4.2 Outcome

Identification of the most diagnostically effective scoring system.

Recommendations for local pathway integration to improve surgical triage and reduce negative appendicectomy rates.

5 STUDY DESIGN and METHODS of DATA COLLECTION AND DATA ANALYIS

Study Design: Retrospective observational study

Data Source: Cerner (clinical presentation), ICE (blood results, histopathology report)

Period: June 2023 – June 2024

Data collected in Excel template by research team

Data points include:

Demographics: Age, sex

Symptoms: Vomiting, Anorexia, Right lower quadrant pain, Migration of pain

Signs: Right lower quadrant tenderness, Right iliac fossa tenderness, Rebound tenderness, or guarding, Fever

Labs: White blood cell counts (WCC), neutrophils, C-reactive proteins (CRP)

Surgical and histopathology outcomes

Analysis:

Scoring systems retrospectively applied

Histology = diagnostic gold standard

Sensitivity, specificity, PPV, and NPV calculated

Receiver Operating Characteristic (ROC) analysis and Area Under the Curve (AUC) to assess overall discriminative performance

Analysis performed using SPSS or Excel - to compare diagnostic accuracies

6 STUDY SETTING

Data will be collected within East Lancashire Hospitals NHS Trust, across the Emergency Department and Surgical Assessment & Emergency Care Unit. This data study setting is appropriate as it captures emergency patients from admission pathway.

7 SAMPLE AND RECRUITMENT

7.1 Eligibility Criteria

7.1.1 Inclusion criteria

- Patients of any gender
- Patients aged 16 and above
- Admitted as an emergency with suspected appendicitis
- Must have undergone appendicectomy (laparoscopic, open, or laparotomy) from June 2023 to June 2024 at East Lancashire Hospitals NHS Trust

7.1.2 Exclusion criteria

- Patients who have undergone elective, interval, or incidental appendicectomies.

- Patients younger than 16

7.2 Sampling

7.2.1 Size of sample

Based on a retrospective review and power calculation, approximately 300 patients are expected to be included in the study. According to the 2020 WSES Jerusalem guidelines, the AIR score demonstrates a sensitivity of 92%, while the AAS shows a specificity of 93% in high-probability patient groups (Di Saverio et al., 2020). To detect a meaningful difference in diagnostic accuracy between these scoring systems, a sample size calculation using McNemar's test indicates that approximately 275 patients are needed (α = 0.05, power = 80%). Given that we anticipate enrolling around 300 patients over the study period, this sample size is sufficient to meet the study objectives. In our analysis, we will calculate the sensitivity and specificity of the AIR and AAS scores specifically within the ELHT patient population, allowing for local validation and comparison with published data.

7.2.2 Sampling technique

Purposive sampling of all eligible cases within the specified time frame.

7.3 Recruitment

Patients will be identified retrospectively through a search of Cerner electronic health records. The study will include all emergency patients of any gender and aged 16 and above who were admitted between June 2023 and June 2024 with a clinical suspicion of acute appendicitis and who subsequently underwent an appendicectomy (via laparoscopy, open surgery, or laparotomy). Only patients meeting these criteria will be included. Identification and screening of eligible cases will be conducted by members of the approved research team.

7.3.1 Sample identification

The sample will be identified through a retrospective review of electronic patient records (Cerner) at East Lancashire Hospitals NHS Trust. Members of the approved research team, who are also part of the clinical team, will perform a structured search to identify adult patients admitted to the Emergency Department (ED) or Surgical Assessment & Emergency Care Unit (SAECU) between June 2023 and June 2024 with a clinical suspicion of acute appendicitis who underwent emergency appendicectomy (laparoscopic, open, or via laparotomy).

Identification will be based on hospital coding data, operative logs, and discharge summaries to ensure patients meet the inclusion criteria. During this screening stage, identifiable information (e.g., name, date of birth, gender, hospital number, and relevant clinical information) will be accessed by members of the clinical research team to determine eligibility.

Once eligible patients are identified, data required for the study will be extracted and pseudonymised using unique study IDs. Identifiable information will be removed from the working dataset. No direct patient contact will occur. The final dataset used for statistical analysis and any subsequent publication will be fully anonymised.

The dataset is stored on a restricted-access Trust network drive (L Drive), accessible only to the research team involved in the project. A separate backup copy is stored in an encrypted folder on the

same secure drive to prevent accidental loss or deletion. No data is stored on personal devices. Data analysis will be performed using Excel and SPSS statistical software. The data will not be transferred outside of the Trust.

7.3.2 Consent

There will be no recruitment of participants, no patient contact, and no collection of new or prospective data. Therefore, written or verbal informed consent is not required.

This is a retrospective study and as the dataset on both the outcome measures (i.e. histological diagnosis of appendicitis) and clinical assessment parameters (used to calculate Alvarado, AIR, and AAS scores) is already available to the research team as members of the direct care team, there is no plan for consent to be obtained (see also section 8 below).

8 ETHICAL AND REGULATORY CONSIDERATIONS

8.1 Assessment and management of risk

The data to be analysed will be collected by members of the research team who are also part of the patients' direct care team. While patients may not be individually informed that their data will be used for purposes beyond their direct care, all data handling will strictly comply with relevant data protection legislation and NHS information governance standards. During data extraction, identifiable information will be accessed by the research team to determine eligibility.

In accordance with National Data Opt-Out (NDOO) policy, patients who have opted out of their data being used for research purposes will be excluded from the study. The research team will ensure that appropriate checks against the NDOO register are completed before including any patient data.

Once eligible patients have been identified and cross-checked against the opt-out list, required data will be extracted and pseudonymised using unique study identifiers, with direct identifiers removed from the working dataset. No identifiable data will be used in analysis or shared beyond the immediate research team.

The research team understands that any future use of the dataset by individuals outside the approved study team would require appropriate ethical review, and access would only be permitted to fully anonymised data or following further approval.

By including all eligible patients (excluding those who have opted out), and not relying on individual consent, the study aims to minimise respondent bias. Although the study is not expected to directly impact patient care, the findings will help evaluate the effectiveness of current clinical assessment tools and contribute to optimising care pathways and resource use in future service delivery.

NHS Research Ethics Committee (REC) advice and approval will be sought. All extracted data will be stored securely in an Excel spreadsheet, with access restricted to authorised members of the research team only. Patient identifiers will not be included in the working dataset. All data will be handled and archived in line with the Data Protection Act 2018, ELHT information governance policies, and ethical approval. Any data security breaches will be reported to the sponsor without delay.

research.sponsorship@elht.nhs.uk
Tel: 01254 733984 (Ext. 83984)

8.2 Research Ethics Committee (REC) and other Regulatory review & reports

The Chief Investigator has obtained approval from the Research Ethics Committee and Health Research Authority (HRA). The study will be submitted to each proposed research site for Confirmation of Capacity and Capability. The study will be conducted in accordance with the recommendations for physicians involved in research on human subjects adopted by the 18th World Medical Assembly, Helsinki 1964 and later revisions.

Regulatory Review & Compliance

Before any site can begin data collection or participate in the study, the Chief Investigator and their delegate will ensure that all required approvals from participating organisations are in place. In this study, as it is a single-site, retrospective observational project, only East Lancashire Hospitals NHS Trust is involved, and no new patient recruitment or intervention is planned.

Amendments

- Accidental protocol deviations can happen at any time. They must be adequately documented on the relevant forms and reported to the Chief Investigator and Sponsor immediately.

  Deviations from the protocol which are found to frequently recur are not acceptable, will require immediate action and could potentially be classified as a serious breach.

8.3 Peer review

Given the retrospective nature of this study, which involves the analysis of clinical data that will be pseudonymised following initial identification and extraction, there has been no direct involvement of patients, service users, carers, or members of the public in the design or conduct of the research at this stage.

8.4 Patient & Public Involvement

Given the retrospective nature of this study, which involves analysis of clinical data that will be pseudonymised following initial identification and extraction, there has been no direct involvement of patients, service users, carers, or members of the public in the design or conduct of the research to date.

As there is no patient contact, intervention, or prospective data collection, involvement in aspects such as recruitment, acceptability, or management was not applicable in this current study.

However, we intend to seek patient and public involvement (PPI) in the next phase of the research, particularly in shaping future research questions and priorities based on the findings of this initial analysis.

8.5 Protocol compliance

Accidental protocol deviations can happen at any time. They must be adequately documented on the relevant forms and reported to the Chief Investigator and Sponsor immediately.

Deviations from the protocol which are found to frequently recur are not acceptable, will require immediate action and could potentially be classified as a serious breach.

The study may be subjected to risk-adaptive monitoring, inspection and audit by the East Lancashire Hospitals NHS Trust RD&I under their remit as Sponsor and other regulatory bodies to ensure adherence to GCP and the UK Policy Framework for Health and Social Care Research, 2017.

8.6 Data protection and patient confidentiality

As a research Sponsor, East Lancashire Hospitals Trust acts as the “Data Controller”. The Data Controller determines the purpose and means of processing personal data. It is the Sponsor who determines what data is collected for the research study through the protocol, case report form and/or structured data fields in a database.

The Chief Investigator will preserve the confidentiality of participants taking part in the study and will abide by the Data Protection Act 2018 and the UK GDPR as amended from time to time and any successor legislation in the UK and any other directly applicable regulation *relating to data protection and privacy*

Only members of the approved research team (Dr Jin Ren Lau, Dr Ker Yin Tee, Mr Muhammad Butt and Mr Karim Heiba) will have access to the clinical records for the purpose of data extraction.

Patient data will be pseudonymised at the point of extraction. This means that identifiable information (such as name, NHS number, date of birth, and hospital number) will be removed from the working dataset and replaced with unique study identifiers. A separate, securely stored linkage file will be maintained only if necessary and accessible only to authorised research team members.

The pseudonymised dataset will be stored in an Excel file with access restricted to authorised research team members. No identifiable data will be shared, stored externally, or transferred outside of the Trust.

All analyses will be conducted using the pseudonymised dataset. The final dataset used for statistical analysis and dissemination (e.g. in reports, publications, or presentations) will be fully anonymised, with all identifiers permanently removed.

Data access and management procedures will be reviewed regularly to ensure compliance with information governance standards and Sponsor requirements. The research team will ensure that all data are stored, accessed, and archived securely in accordance with ELHT’s information governance policies.

8.7 Indemnity

The East Lancashire Hospitals NHS Trust will provide NHS Indemnity Cover as the Sponsor of this study**.** NHS bodies are legally liable for the negligent acts and omissions of their employees. If study participants are harmed whilst taking part in the study as a result of negligence on the part of a member of the study team this liability cover would apply.

Non-negligent harm is not covered by the NHS indemnity scheme. East Lancashire Hospitals NHS Trust, therefore, cannot agree in advance to pay compensation in these circumstances.

8.8 End of Study

The study will be declared as ended on completion of data collection and the analysis.

End of study declaration form will be completed and submitted to the sponsor and regulatory bodies within 90 days of study closure and 15 days for early termination.

Any retained data for possible future evaluation after the end of study has been declared should be with the appropriate REC approval.

Any change to the end of study definition after approval has been given for the research should be notified as an amendment to the appropriate review bodies.

8.9. Archiving

Data and all appropriate research documentation should be stored for a minimum of 5 year after the completion of the study, unless otherwise directed by the sponsor/regulatory bodies.

ELHT as Sponsor will be responsible for Archiving the Trial Master File.

9 DISSEMINIATION POLICY

9.1 Dissemination policy

The data arising from this study will be legally owned by East Lancashire Hospitals NHS Trust (ELHT) as the Sponsor and Data Controller. The research team will act as data custodians, responsible for the secure collection, storage, and analysis of the data in accordance with ethical approval, information governance policies, and data protection regulations.

Upon completion of the study, data will be analysed and results will be tabulated. A Final Study Report will be prepared and submitted to the Trust's Research & Development (R&D) Department. In line with regulatory requirements, the results will be published on ClinicalTrials.gov and submitted to the Research Ethics Committee (REC) within 12 months of study completion.

The findings may also be submitted for presentation at academic or surgical meetings and for publication in peer-reviewed medical journals. There are currently no restrictions or time limits on the academic publication of study results. All participating investigators listed in this protocol will have the right to publish or present findings, in accordance with standard authorship and publication agreements.

Although individual participants will not be contacted due to the retrospective nature of the study, results will be disseminated through academic channels. If findings lead to changes in local clinical practice or service delivery, these may be communicated through departmental meetings or Trust-wide quality improvement platforms.

At present, there are no plans to release the anonymised participant-level dataset or statistical code for public access. However, data may be made available upon reasonable request to the Chief Investigator, subject to appropriate ethical and governance approvals and in line with ELHT information governance and data protection standards.

9.2 Authorship eligibility guidelines and any intended use of professional writers

Authorship for any publications resulting from this study will follow the criteria established by the International Committee of Medical Journal Editors (ICMJE), which requires substantial contributions to the conception or design of the work, or the acquisition, analysis, or interpretation of data; drafting or critically revising the manuscript; final approval of the version to be published; and agreement to be accountable for all aspects of the work.

Dr Jin Ren Lau and Dr Ker Yin Tee will be recognised as joint first authors for their contributions to protocol development, data collection, and analysis. Mr Karim Heiba and Mr Muhammad Butt will also be listed as an author for their role as clinical supervisors, study design advisors, and contributors to interpretation and review of findings.

This study is conducted at East Lancashire Hospitals NHS Trust (ELHT), which also acts as the study sponsor. Appropriate acknowledgement will be given to ELHT in all presentations and publications arising from this work.

10 REFERENCES

1. Andersson M, Kolodziej B, Andersson RE. Randomized clinical trial of Appendicitis Inflammatory Response score-based management of patients with suspected appendicitis. Br J Surg. 2017;104(11):1451–61. doi:10.1002/bjs.10563

2. Sammalkorpi HE, Mentula P, Leppäniemi A. A new adult appendicitis score improves diagnostic accuracy of acute appendicitis: a prospective study. BMC Gastroenterol. 2014;14:114. doi:10.1186/1471-230X-14-114

3. Kollar D, McCartan DP, Bourke M, Cross KS, Dowdall J. Predicting acute appendicitis? A comparison of the Alvarado score, the Appendicitis Inflammatory Response score and clinical assessment. World J Surg. 2015;39(1):104–9. doi:10.1007/s00268-014-2765-8

4. de Castro SM, Unlu C, Steller EP, van Wagensveld BA, Vrouenraets BC. Evaluation of the Appendicitis Inflammatory Response Score for Patients with Acute Appendicitis. World J Surg. 2012;36(7):1540–5. doi:10.1007/s00268-012-1529-6

5. Andersson RE. Meta-analysis of the clinical and laboratory diagnosis of appendicitis. Br J Surg. 2004;91(1):28–37. doi:10.1002/bjs.4464

6. Lahaye MJ, Lambregts DMJ, Mutsaers E, et al. Mandatory imaging cuts negative appendectomy rate in half in community hospital. J Am Coll Surg. 2015;220(6):976–83. doi:10.1016/j.jamcollsurg.2014.12.045

7. Doria AS, Moineddin R, Kellenberger CJ, et al. US or CT for diagnosis of appendicitis in children and adults? A meta-analysis. Radiology. 2006;241(1):83–94. doi:10.1148/radiol.2411050913

8. Mostbeck GH, Adam EJ, Nielsen MB, et al. How to diagnose acute appendicitis: ultrasound first. Insights Imaging. 2016;7(2):255–63. doi:10.1007/s13244-016-0469-6

9. Bhangu A, Søreide K, Di Saverio S, Assarsson JH, Drake FT. Acute appendicitis: modern understanding of pathogenesis, diagnosis, and management. Lancet. 2015;386(10000):1278–87. doi:10.1016/S0140-6736(15)00275-5

10. Clinical scores (Alvarado and AIR scores) versus imaging (ultrasound and CT scan) in the diagnosis of equivocal cases of acute appendicitis: a randomized controlled study. Cureus. 2023;15(4):e37125. doi:10.7759/cureus.37125

11. Tanrıkulu, C. Ş., Karamercan, M. A., Tanrıkulu, Y., Öztürk, M., Yüzbaşıoğlu, Y., & Coşkun, F. (2015). The predictive value of Alvarado score, inflammatory parameters and ultrasound imaging in the diagnosis of acute appendicitis. *Ulus Cerrahi Derg*, *32*(2), 115–121. doi: 10.5152/UCD.2015.3103

12. Alvarado, A. (1986). A practical score for the early diagnosis of acute appendicitis. *Annals of Emergency Medicine*, *15*(5), 557–564. doi: 10.1016/s0196-0644(86)80993-3

13. Yeşiltaş, M., Karakaş, D. Ö., Gökçek, B., Hot, S., & Eğin, S. (2018). Can Alvarado and Appendicitis Inflammatory Response scores evaluate the severity of acute appendicitis? *Ulus Travma Acil Cerrahi Derg*, *24*(6), 557–562. doi: 10.5505/tjtes.2018.72318

14. Ghali, M. S., Hasan, S., Al-Yahri, O., et al. (2023). Adult Appendicitis Score versus Alvarado score: a comparative study in the diagnosis of acute appendicitis. *Surgery Open Science, 14, 96-102.* doi: 10.1016/j.sopen.2023.07.007.

15. Di Saverio, S., Podda, M., De Simone, B. et al. Diagnosis and treatment of acute appendicitis: 2020 update of the WSES Jerusalem guidelines. *World J Emerg Surg 15, 27 (2020).* https://doi.org/10.1186/s13017-020-00306-3

11. APPENDICIES

11.1 Appendix 1- Required documentation

Research Proposal Form

Research CV

HRA Decision Tool outcome summary

Good Clinical Practice (GCP) certificate

11.2 Appendix 2 – Schedule of Procedures (Example)

Procedures	Week 1	Week 2	Week 3
Identification of eligible cases	x		
Data extraction (from Cerner)	x		
Anonymisation of data	x		
Calculation of clinical scores		x	
Statistical analysis		x	
Interpretation of results			x
Writing of final report			x

13.3 Appendix 3 – Amendment History

Amendment No.	Protocol version no.	Date issued	Author(s) of changes	Details of changes made
1.	2	19/11/25	JinRen Lau KerYin Tee	Highlighted above in yellow - Study period updated to August 2025 - June 2026 - Clarified the main contact on behalf of the sponsor for all correspondence: Michelle Stephens - Updated information on dataset security

List details of all protocol amendments here whenever a new version of the protocol is produced.

Protocol amendments must be submitted to the Sponsor for approval prior to submission to the REC.