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Study Protocol

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Presentations and outcomes of people with unexplained symptoms in acute general surgery: protocol for a mixed-methods study

Daniel Romeu[1,2,*], Anna K. Taylor[1], Elspeth Guthrie[1], Adam Peckham-Cooper[3], Max Henderson[1] and Giles Toogood[3]

[1]Leeds Institute of Health Sciences, School of Medicine, University of Leeds, Leeds, UK
[2]Department of Liaison Psychiatry, Leeds and York Partnership NHS Foundation Trust, Leeds, UK
[3]Leeds Institute of Emergency General Surgery, Leeds Teaching Hospitals NHS Trust, Leeds, UK

*Correspondence address. Leeds Institute of Health Sciences, School of Medicine, University of Leeds, Leeds LS2 9LH, UK.
Tel: +44-07837292094; E-mail: hs18djr@leeds.ac.uk

Abstract

Introduction: Unexplained symptoms are common across healthcare settings and are associated with increased mental and physical morbidity and healthcare expenditure. Improving the identification, explanation and management of unexplained symptoms will be helpful to patientsand healthcare systems. Limited data exists exploring unexplained acute abdominal pain in the surgical setting.
Objectives: This protocol describes three interlinked studies. Study one will determine the prevalence of anxiety and depression in patients presenting with explained and unexplained abdominal pain in an acute surgical setting. Study two will explore how the explanation and management of unexplained symptoms is conveyed to patients. Study three will explore how patients with unexplained symptoms understand these explanations.
Methods and analysis: Patients aged ≥18 years who present to a surgical same day emergency care unit with acute abdominal pain will be eligible. In study one, participants will be asked to complete a questionnaire, including validated self-report measures, at the time of presentation and six months later. They will be divided into explained and unexplained symptom groups based on clinical presentation and investigation outcomes. The proportion in each group meeting diagnostic thresholds for anxiety and depression will be compared and baseline predictors of pain and quality of life six months later will be determined. In study two, recordings of consultations between patients and surgeons involving the explanation and management of unexplained abdominal pain will be analysed. In study three, participants will be interviewed to explore their experiences and understanding of their symptoms.

INTRODUCTION

Many people present to healthcare services with symptoms that cannot be explained by currently understood pathological mechanisms, referred to as 'unexplained' symptoms. Presentations include a range of symptom syndromes such as irritable bowel syndrome (IBS) and fibromyalgia [1]. Symptoms vary in nature and severity, from minor and infrequent to severe and persistent resulting in significant morbidity [2]. Many people with unexplained symptoms suffer from common mental disorders that exacerbate or partly underlie symptoms [3]. The more persistent and severe the symptoms, the greater the likelihood that psychological factors contribute to symptoms and associated disability [4]. Unexplained symptoms therefore represent a heterogeneous and diagnostically challenging entity.

Unexplained symptoms are common, representing 22% of primary care consultations [5] and 52% of referrals to secondary care outpatient services [6]. Individuals may be referred for repeated assessments and investigations, resulting in higher healthcare costs and potential iatrogenic harm [7]. Unexplained symptoms account for ∼10% of the total National Health Service (NHS) expenditure for working-age adults in England [8]. Improved identification of unexplained symptoms with consistent explanation and holistic management could be clinically and economically beneficial by reducing morbidity and healthcare costs.

Unexplained gastrointestinal symptoms, such as IBS, are considered to be a result of disorders of gut–brain interaction [9]. These disorders are thought to arise from gut motility disturbances, visceral hypersensitivity, altered mucosal and immune function, gut microbiota and/or central nervous system processing [10]. Most research exploring unexplained gastrointestinal disorders has been undertaken by gastroenterologists or primary care specialists, focusing on patients with chronic or subacute symptoms. Creed found that among those who underwent an appendicectomy after presenting with acute abdominal pain, patients with a normal appendix (unexplained symptoms) were more likely to report adverse life events than those with an inflamed appendix (confirmed pathology) [11]. Since this study over 30 years ago, to our knowledge, there have been no other additions to the literature focusing on patients presenting to surgical services with unexplained acute abdominal pain.

Providing an explanation for patients' unexplained symptoms represents a unique challenge for clinicians. Medical and surgical clinicians commonly describe the experience of diagnosing,

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communicating and managing unexplained symptoms as 'difficult' [12]. They report little to no formal training in the management of patients who present this way; they use highly variable explanations to communicate these concepts [13], highlighting the need for a more informed and evidence-based approach. A further challenge is to identify underlying psychosocial issues that may contribute to the clinical picture. Reasons for presentation to healthcare services are diverse, including to seek emotional support, explanation and reassurance and somatic intervention [14]. Evidence suggests that patients often present clinicians with opportunities to explore the emotional aspects of their, but, for a number of patient- and clinician-related reasons, such discussions rarely occur [15]. Clinicians could therefore avoid unnecessary investigations and surgical interventions by noticing and addressing cues within the clinician–patient relationship.

To improve care for people who present with unexplained acute abdominal pain to surgical settings, there is a need to understand which factors are associated with poorer outcomes and to understand how explanations of unexplained pain are conveyed to and received by patients.

METHODS AND ANALYSIS

Study one

Aims

To compare the prevalence of anxiety and depression in patients with explained and unexplained abdominal pain on presentation to a surgical same day emergency care unit (SDEC) and to determine which baseline factors independently predict pain and quality of life 6 months later.

Study design

Single-site prospective longitudinal observational cohort study.

Participants

Patients aged ≥18 years who present to a surgical SDEC in Leeds Teaching Hospitals NHS Trust with acute abdominal pain will be eligible. Those lacking capacity to adhere to study requirements will be excluded; we will record the number of patients excluded. Potential participants will be identified by consecutive sampling and approached by clinical staff who are part of the direct clinical care team. After completed clinical assessment, participants will be divided into two categories: those with explained pain, such as appendicitis, and those with unexplained pain, where examination findings and investigation results are inconsistent with, or offer insufficient explanations of, organic pathology.

Assuming that 10% of participants with explained symptoms score ≥10 on the PHQ-9 (consistent with general population sampling [16]) and 25% of participants with unexplained pain score ≥10 (conservative estimate of prevalence of depression in populations with acute pain [17]), the study will require a minimum sample size of 133 for each group to achieve a power of 90% for detecting a difference in proportions of 0.15 between the groups (test-reference group) at a two-sided *P*-value of 0.05. Approximately 20% of patients who attend the SDEC are expected to have unexplained abdominal pain, based on preliminary evidence collected by surgical staff. As participants will be allocated to study groups retrospectively, after completing the baseline questionnaires, more participants with explained pain will be recruited to the study than those with unexplained pain. Approximately 665 patients will be recruited to reach the required sample size of 133 participants with unexplained pain.

Data collection

Participants will complete a self-report questionnaire via Research Electronic Data Capture (REDCap [18, 19]), a secure, browser-based web application widely used for survey data collection. They will be asked to provide online consent using the e-consent feature before proceeding.

The questionnaire includes demographic questions and eight validated self-report measures: Gastrointestinal Quality of Life Index (GI-QLI [20]), EuroQol-5D-5L (EQ-5D-5L [21], measures generic health status), Patient Health Questionnaire-15 (PHQ-15 [22], assesses somatic symptoms), 36-Item Short Form Survey (SF-36 [23], somatic subscale only to assess pain), Patient Health Questionnaire-9 (PHQ-9 [24], assesses depressive symptoms), Generalized Anxiety Disorder-7 (GAD-7 [25], assesses symptoms of anxiety), List of Threatening Experiences (LTE-Q [26], assesses the presence of recent threatening personal experiences) and Lubben Social Network Scale-6 (LSNS-6 [27], gauges social isolation). This questionnaire has been piloted to confirm acceptability and can be viewed in Supplementary file 1.

At the end of the baseline questionnaire, participants will be asked whether they would be willing to participate in a follow-up questionnaire. All participants who agree will be invited to complete the same questionnaire 6 months later. The primary outcome measures are quality of life and presence of pain 6 months following initial presentation, as measured by theEQ-5D-5L and the pain subscale of SF-36, respectively.

Analysis

For all demographic variables, questionnaire scores and hospital admission data, numbers and percentages for categorical variables and mean scores with standard deviation (SD) for continuous variables will be presented. Explained and unexplained symptoms groups will be compared using independent sample *t*-tests for continuous data, with mean and SD. Categorical variables will be compared using Chi squared tests.

A cumulative link model will determine the impact of covariates, including age, sex, presence of major comorbidities, depression and anxiety measures, other baseline measures and whether baseline pain was explained or unexplained, on the primary outcome measures of pain and quality of life 6 months after initial presentation. Lasso regularization will be used to avoid overfitting of the model, with regularization strength chosen via 10-fold cross-validation. Model performance will be assessed using accuracy, the C-index and Spearman correlation plots. Model fit will be assessed using calibration plots and checking distribution of residuals. These metrics will be tested for robustness using bootstrapping. In addition to the main predictor analysis, we will repeat the analysis for those with explained and unexplained pain separately.

All analyses will be carried out using SPSS 26.0 [28]. Results will be reported in accordance with the STROBE checklist [29]. An expert statistician has reviewed the protocol whose advice and suggestions have been incorporated into the analysis plan.

Study two

Aims

To understand how the explanation and management of unexplained acute abdominal pain is conveyed to patients by surgeons.

Study design

Observational qualitative study of consultations between patients and surgeons involving the explanation and management of unexplained acute abdominal pain.

Participants

Study One participants will have a consultation with a surgeon as part of their usual care pathway. These participants will be invited to participate in Study Two. It will be explained that consultations are being recorded regardless of diagnosis and that participation is voluntary and will not change their clinical care. Data saturation will determine sample size [30]; however, it is anticipated that this may be up to 40–50 consultations.

Data collection

All clinical consultations will be audio-recorded and take place in a private clinical room. Consultations will be recorded regardless of diagnosis; diagnosis will not be known to the study team at the time of recording. Following the consultation, participants whose pain can be explained by known pathology will be identified and recordings deleted. Similar methodology has been used previously [31, 32].

Analysis

Recordings will be transcribed verbatim. The concept of normalization will be used as a starting point for analysis. Normalization will be defined as statements indicating the probable absence of serious disease and therefore not requiring healthcare intervention [33]. This typology will be used to divide instances according to: normalization without explanation; normalization with ineffective explanation and normalization with effective explanation. The degree to which these different types of reassurance are delivered will be recorded.

Attention will be paid to cues that patients present to surgeons to address emotional problems or their need for explanation, previously noted primary care settings [31]. Data will be analysed inductively and thematically [34]. Transcripts will be coded independently by at least two members of the research team. Codes will be discussed collaboratively with the team to identify and agree key themes. Deviant cases will be identified and discussed. As consultations continue, analysis will be refined using the principles of constant comparison [35–37] and reported in accordance with COREQ criteria [38].

Study three

Aims

To explore how unexplained acute abdominal pain is experienced and understood by patients.

Study design

Qualitative interview study.

Participants

Participants of Studies One and Two will be purposively sampled to gain a wide range of experiences [39]. Attention will be paid to include underserved groups such as minority ethnic populations who are more likely to experience somatic symptoms related to psychological distress [40]. Potential participants will be approached via postal mail with an invitation letter. Approximately 30 participants will be recruited to ensure feasibility and variation across psychological morbidity and demographic variables, but this will be determined by data saturation [30].

Data collection

Semi-structured interviews will be conducted with participants via a remote conferencing tool. Telephone and online consultations have been implemented successfully in research on sensitive topics [41]. Interviews will take place 2–3 weeks after the participant's visit to the surgical SDEC and are expected to last 40–60 minutes. A topic guide will be developed with a patient advisory group to explore participant's experiences of seeking care, the progression of their symptoms and their understanding of their aetiology.

Analysis

Interviews will be audio-recorded and transcribed verbatim. Transcripts will be coded line-by-line and analysed independently by at least two members of the research team using inductive thematic analysis [34]. Codes will be discussed collaboratively in the team and key themes will be agreed, with particular attention to deviant cases. Analysis will then be integrated with consultation records from Study Two to explore how the explanation of symptoms was communicated to the participant and how they understood this. Data will be continually refined using the principles of constant comparison [35–37] and reported in accordance with COREQ criteria [38].

ETHICS AND DISSEMINATION

Research ethics approval

Ethical approval for this study has been granted by the NHS Health Research Authority (REC Wales; reference 22/LO/0734). Procedures will be followed in accordance with the ethical standards of the Helsinki Declaration.

Data storage

Completed questionnaires, consent forms and audio recordings will be encrypted, password-protected and stored on a secure server behind the NHS firewall. Password-protected files will link participants' unique study numbers and sensitive data.

Dissemination

Findings will be shared with clinicians through presentations at conferences and publications in open-access peer-reviewed journals. They will be shared with patients and the public through established patient groups such as The IBS Network. The dissemination plan will be continually updated and co-developed with a patient advisory group.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *Journal of Surgical Protocols and Research Methodologies* online.

CONFLICT OF INTEREST STATEMENT

None declared.

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DATA AVAILABILITY

Data availability is not applicable to this protocol as no new data has yet been created.

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