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Predicting pain and function outcomes in people consulting with shoulder pain: the PANDA-S clinical cohort and qualitative study protocol

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ABSTRACT

Introduction People presenting with shoulder pain considered to be of musculoskeletal origin is common in primary care but diagnosing the cause of the pain is contentious, leading to uncertainty in management. To inform optimal primary care for patients with shoulder pain, the study aims to (1) to investigate the short-term and long-term outcomes (overall prognosis) of shoulder pain, (2) estimate costs of care, (3) develop a prognostic model for predicting individuals' level and risk of pain and disability at 6 months and (4) investigate experiences and opinions of patients and healthcare professionals regarding diagnosis, prognosis and management of shoulder pain.

Methods and analysis The Prognostic And Diagnostic Assessment of the Shoulder (PANDA-S) study is a longitudinal clinical cohort with linked qualitative study. At least 400 people presenting to general practice and physiotherapy services in the UK will be recruited. Participants will complete questionnaires at baseline, 3, 6, 12, 24 and 36 months. Short-term data will be collected weekly between baseline and 12 weeks via Short Message Serevice (SMS) text or software application. Participants will be offered clinical (physiotherapist) and ultrasound (sonographer) assessments at baseline. Qualitative interviews with ≈15 dyads of patients and their healthcare professional (general practitioner or physiotherapist).

Short-term and long-term trajectories of Shoulder Pain and Disability Index (using SPADI) will be described, using latent class growth analysis. Health economic analysis will estimate direct costs of care and indirect costs related to work absence and productivity losses. Multivariable regression analysis will be used to develop a prognostic model predicting future levels of pain and disability at 6 months using penalisation methods to adjust for overfitting. The added predictive value of prespecified physical examination tests and ultrasound findings will be examined. For the qualitative interviews an inductive, exploratory framework will be adopted using thematic analysis to investigate decision making, perspectives of patients and clinicians on the importance of diagnostic and prognostic information when negotiating treatment and referral options.

Ethics and dissemination The PANDA-S study has ethical approval from Yorkshire and The Humber-Sheffield Research Ethics Committee, UK (18/YH/0346, IRAS Number: 242750). Results will be disseminated through peer-reviewed publications, social and mainstream media, professional conferences, and the patient and public involvement and engagement group supporting this study, and through newsletters, leaflets and posters in participating sites.

Trial registration number ISRCTN46948079.

Strengths and limitations of this study

- ► Follow-up uniquely includes weekly data collection of the impact of shoulder pain on everyday activity, mood and work during the first 3 months after presentation as well as long-term pain and function outcomes.
- ► The use of 'dyad' interviews allows for a rich understanding of the views and experiences of clinicians and patients towards shoulder pain management.
- ► The COVID-19 pandemic has impacted on recruitment and data collection resulting in a smaller proportion of participants than planned able to attend face-to-face research clinics.
- ► This means the study can only investigate the added predictive value of a limited number of physical examination tests and ultrasound scan findings, based on a priori defined hypotheses.
- ► This study will include an exploration of influence of related (lockdown) measures and restrictions on the experience and management of shoulder pain.

BACKGROUND AND RATIONALE

Shoulder pain considered to be of musculoskeletal origin is common, with the 1-month population prevalence estimated to be between 7% and 26%,[1] and an annual

incidence in primary care of 29.3 per 1000 person-years.[2] Annually, approximately 3% of adults in the UK will consult their general practitioner (GP) for shoulder pain.[3] The prognosis of shoulder pain is variable with 40%–50% of patients reporting persistent pain 6–12 months after first consulting their GP or physiotherapist,[4 5] generating high costs to both healthcare and society.[6–8] Systematic reviews and trials have highlighted modest short-term effects of commonly used treatments such as corticosteroid injection, therapeutic exercise and manual therapy, but limited evidence for long-term benefits.[9–13]

Diagnostic uncertainty

Achieving a definitive diagnosis for the underlying cause of the shoulder pain remains contentious, resulting in uncertainty regarding optimal management. Systematic reviews of shoulder physical examination tests have highlighted variety in performance and interpretation of these tests, resulting in low diagnostic accuracy. There is a lack of evidence pertaining to combinations of signs and symptoms that most accurately predict patient outcome and response to treatment.[14–17] Qualitative research has illustrated that GPs experience uncertainty in the diagnostic workup of shoulder pain and apply different strategies to deal with uncertainties.[18] There is limited evidence regarding the usefulness of diagnostic imaging, partly due to observations of structural changes that frequently do not correlate with symptom severity.[19 20] The use of diagnostic ultrasound scans (US) has rapidly increased in the assessment of shoulder pain in primary care, as it does not involve radiation and is less expensive than MRI. However, evidence for their role in the diagnostic pathway, and in particular, their added value for estimating prognosis and utility for clinical decision making, is still unclear.

Prognostic uncertainty

Despite evidence for the prognostic value for a range of factors, it is not clear which combination of prognostic factors optimally discriminates between patients at high risk versus low risk of poor outcome, with limited evidence for predictive performance of existing prognostic models[21–24] and for their usefulness in routine clinical practice.[25] Short-term symptom change has rarely been investigated but may be highly predictive of long-term outcome, and incorporating monitoring of this early response in the prognostic assessment of individuals with shoulder pain can potentially provide better guidance regarding decisions for further treatment.[26 27] Furthermore, little is known about the pathways that explain favourable or poor outcome in patients with shoulder pain, and generating evidence regarding the role of prognostic factors along these pathways may allow the identification of new targets for treatment.

In summary, given the high impact of shoulder pain, diagnostic uncertainty, variable prognosis and limited evidence for long-term treatment outcomes, there is a clear need for research investigating short-term and long-term outcomes of shoulder pain with the aim of improving the primary care management of shoulder pain in future.

Aims and objectives

The overall aim of this study is to enhance the primary care management of patients with shoulder pain, by investigating the short and long-term outcomes of shoulder pain and developing a prediction model using diagnostic and prognostic information that will provide reliable individualised risk prediction for 6-month outcomes of shoulder pain and disability. Specific objectives are to:

1. Describe the short term (≤6 months) and long term (up to 3 years) overall prognosis in people presenting with shoulder pain, in terms of pain and function trajectories and impact on sleep, mood, work and health-related quality of life.
2. Describe healthcare resource use and estimate the costs associated with care for shoulder pain; and describe and estimate time off work and loss of productivity associated with shoulder pain in the short term (6 months) and long term (up to 3 years).
3. Develop a prognostic model for predicting individuals' level and risk of pain and disability at 6 months after presentation, based on self-reported candidate prognostic factors, and estimate and internally validate the model's predictive performance and clinical utility.
4. Estimate the added prognostic value of physical examination tests and US findings in the prediction of future pain and disability.
5. Explore candidate predictors of response to commonly used treatments in a real-life, observational setting.
6. Explore perspectives, influences and uncertainty of patients and clinicians regarding the importance of diagnostic and prognostic information when negotiating treatment and referral options, and making decisions about the management of shoulder pain.

METHODS

Study design

Multicentre observational cohort study, including patients presenting with shoulder pain in general practices, and National Health Service (NHS) physiotherapy services (including self-referrers to physiotherapy), with a linked qualitative study. Figure 1 details the recruitment methods and participant flow through the study.

Patient and public involvement

Study questions and design were informed by patient contributors during four dedicated meetings. They highlighted the importance of clear information about the possible cause and prognosis of pain, as this is important to people with shoulder pain when planning their everyday life and considering treatment options. They stressed concern regarding the commonly used approach of 'watchful waiting'. Postponing treatment/referral decisions was considered frustrating and unhelpful, prolonging the condition and potentially increasing

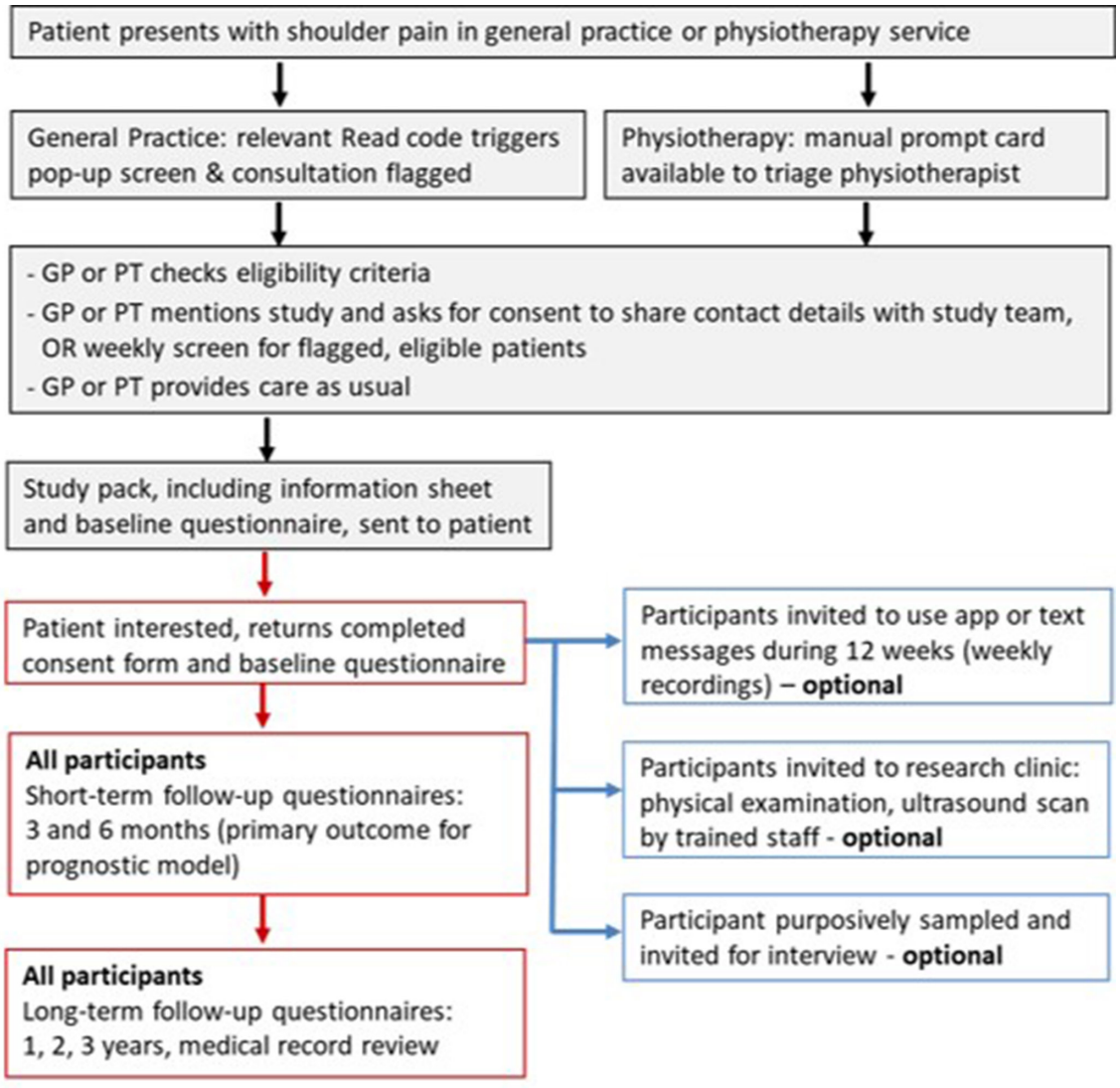

Figure 1 Patient flow chart. GP, general practitioner.

healthcare and personal costs. They expressed the need for a thorough assessment of shoulder pain, along with an early discussion of the possible benefits and drawbacks of diagnostic procedures (eg, US) and treatment options. The group contributed to the design of the study by advising on recruitment processes, the content of data collection and how to explain the role of clinical assessment and US to study participants. Annual Patient and Public Involvement and Engagement (PPIE) meetings are planned to ensure ongoing involvement and engagement during data collection, analysis, interpretation and dissemination of findings.

Study population

Potential participants will be identified when they consult with an episode of shoulder pain at general practices, or NHS physiotherapy service (including self-referrers to physiotherapy) in five regions in the UK: Staffordshire, Cheshire, Oxfordshire, Birmingham and Gloucestershire. Recruitment of participants started in February 2019, with baseline data collection planned to be completed in September in 2021. Follow-up data collection is planned to be completed in September 2024.

Eligibility criteria

Potential participants must be registered at participating general practices or referred to NHS physiotherapy (including self-referrers), aged 18 years or over and presenting with a new episode of shoulder pain. Previous studies of shoulder pain in primary care indicate that many people consult quite late in the trajectory of their shoulder pain episode, with the median/mean duration of symptoms at presentation varying between 12 weeks and 1 year.[4 5 21 22] Based on discussion with our clinical advisory group, a new care episode will be defined as no shoulder pain related consultation, no injection, surgery or physiotherapy-led exercise for shoulder pain, in the last 6 months, reflecting a point in time when primary care clinicians make (new) decisions regarding advice, treatment or referral.

Potential participants will be excluded on the basis of the following criteria:

- Present to their GP or physiotherapist with symptoms or signs indicative of serious pathology (eg, fractures, infection).
- Have shoulder pain caused by stroke-related subluxation.
- Have a diagnosis of inflammatory arthritis (eg, rheumatoid arthritis or polymyalgia rheumatic).
- Have shoulder pain caused by cervical pathology.
- Are considered by the GP or physiotherapist to be vulnerable (eg, severe physical and/or mental health problems, dementia).

Recruitment

Potential participants consulting with shoulder pain will be identified through one of three methods:

i. Identification using an automated medical record template (pop-up) in GP sites, activated when a Read/Systematised Nomenclature of Medicine (SNOMED) code for shoulder pain is entered into the medical record because of a patient consultation.
ii. Identification using an Egton Medical Information Systemts (EMIS) embedded 'referral' form which will autopopulate for eligible patients when triggered by the clinician in physiotherapy sites.
iii. Identification of patients from waiting lists for physiotherapy. Referrals received from GPs, other healthcare professionals or self-referrals will be centrally triaged by senior physiotherapists using the PANDA-S eligibility checklist.

Potential participants will be asked for consent to share their contact details with the Keele Clinical Trials Unit who will send them a study pack, or a study pack will be sent directly from the GP or physiotherapy practices, depending on site preference. The study pack will contain: an invitation letter; a participant information leaflet; baseline questionnaire with consent form and eligibility screening questions; prepaid reply envelope.

Patients interested to take part in the study will be asked to complete the consent form and answer eligibility questions relating to whether they have received treatment (eg, supervised exercise, injection, surgery) for their shoulder pain in the 6 months prior to consultation. Those who have not yet received treatment are eligible and invited to complete and return the baseline questionnaire. As this is an observational study, all participants will continue to receive care as usual for their shoulder pain.

Data collection

Data collection will be carried out by postal questionnaire at baseline, 3, 6, 12, 24 and 36 months. Since June 2020, in response to the COVID-19 pandemic, follow-up questionnaires have also been made available as online surveys. Short-term data will be collected weekly through a specifically designed smartphone/tablet Shoulder Pain application (App) or text messages over 12 weeks. Clinical data will be collected during a clinical assessment comprising a shoulder examination by a physiotherapist and an US. In response to the pandemic, face-to-face clinical assessments will be carried out (or paused) in accordance with national and local restrictions. Table 1 provides an overview of the content and timing of data collection for this study.

Primary outcome measure

The primary outcome measure for investigating course, prognosis and treatment response is the SPADI.[28] The SPADI is scored using a 0–10 Numerical Rating Scale (NRS) for each question from 'no pain' to 'worst imaginable pain' (for the pain scale) and from 'no difficulty' to 'so difficult that help is required' (for the disability scale). Numerical scores are summated and divided by the maximum score possible for all relevant questions and then multiplied by 100 to generate a score from 0 to 100 with higher scores indicating worse shoulder pain and/or disability.

Secondary outcomes

Pain intensity will be measured on an NRS from 0 to 10 asking the participant to report their worst pain in the past week. Sleep will be measured using the Jenkins Sleep Questionnaire.[29] Global perceived change in shoulder pain since the baseline questionnaire will be asked in all follow-up questionnaires with one question providing participants with six possible response options from 'completely recovered' to 'much worse'. Work absence will be assessed through two methods:

- Employed participants will be asked if they are currently absent from work due to their shoulder pain, and, if so, for how long they have been absent.
- Fit note data for shoulder pain will be collected from the medical record (where participants have provided consent) allowing data on the number of days and number of episodes of clinician certified work absence to be collected.

Participants will also be asked to indicate how their shoulder pain has impacted on their work performance using the question 'On average, to what extent has pain affected your performance at work in the past x months'[30] and are asked about attitudes and beliefs regarding health and work, measured using a new developed set of 11 items.

Healthcare utilisation will be estimated based on self-report (follow-up) questionnaires, and include primary care consultations (GPs and practice nurses), secondary care consultations (eg, hospital consultants, physiotherapists), prescriptions, hospital based procedures (diagnostic tests, injections and investigations) nature and length of inpatient stays, and surgery. Patients will be asked to distinguish between UK NHS and private provision. Finally, the EQ-5D-5L[31] will be used to measure participants' health-related quality of life.[32]

Candidate prognostic factors and moderators

Questionnaires will measure self-report candidate prognostic factors and predictors of treatment outcome

Table 1 Data collection schedule (Self-Report Questionnaires)

Description	Measure (no of items, response options, score range)	Baseline (shortly after consultation)	3 months	6 months	12 months	24 months	36 months
Primary outcome measure							
Severity of pain	SPADI total score (5 pain, 8 disability items, 0–10 NRS, 0–100)	✓	✓	✓	✓	✓	✓
Severity of disability		✓	✓	✓	✓	✓	✓
Secondary outcome measures							
Sleep	Jenkins sleep questionnaire (4 items, 3 options each, 0–8)	✓	✓	✓	✓	✓	✓
Work absence	How many days off work have you had in the past month (days/weeks)	✓	✓	✓	✓	✓	✓
Work performance	Single item question (0–10)	✓	✓	✓	✓	✓	✓
Global perceived change	Single item question (6 options)	✗	✓	✓	✓	✓	✓
Health-related quality of life	EQ-5D-5L (5 items, 5 options each)	✓	✓	✓	✓	✓	✓
Sociodemographics							
Age	Date of birth	✓	✗	✗	✗	✗	✗
Gender	Male/female/prefer not to say	✓	✗	✗	✗	✗	✗
Education	Highest qualification (single item, 5 options)	✓	✗	✗	✗	✗	✗
Health literacy	Single item question (5 options)	✓	✗	✗	✗	✗	✗
Work status	3 items	✓	✗	✗	✓	✓	✓
Shoulder pain characteristics							
Side involved	Left/right/both	✓	✗	✓	✓	✓	✓
History	No of episodes in both shoulders (2 items, 4 options)	✓	✗	✗	✗	✗	✗
Onset	Acute versus gradual (2 options)	✓	✗	✗	✗	✗	✗
Duration	Single item question (6 options)	✓	✗	✗	✗	✗	✗
Which is your dominant arm	Left/right	✓	✗	✗	✓	✓	✓
Continued shoulder pain at follow-up	Two single item questions	✗	✗	✗	✓	✓	✓
Pain elsewhere	Full body manikin	✓	✗	✗	✗	✗	✗
Previous imaging for shoulder pain	Predefined list (4 options)						
Previous shoulder pain treatments	Predefined list (6 options)	✓	✗	✗	✗	✗	✗
Analgesic use (over the counter and GP prescribed)	predefined list (10 options)	✓	✓	✓	✓	✓	✓

Continued

Table 1 Continued

Description	Measure (no of items, response options, score range)	Baseline (shortly after consultation)	3 months	6 months	12 months	24 months	36 months
Comorbidities and lifestyle							
Comorbidity	Diabetes, insulin-dependent or not (3 options)	✓	✗	✗	✓	✓	✓
Height and weight (BMI)	Self-reported	✓	✗	✗	✓	✓	✓
Smoking and vaping (frequency)	Two single item questions (4 options each)	✓	✗	✗	✓	✓	✓
Alcohol consumption (frequency)	Single item question (6 options)	✓	✗	✗	✓	✓	✓
Physical activity (frequency)	Single item question (7 options)	✓	✗	✗	✓	✓	✓
Work-related factors							
Most recent paid job title	Single item question	✓	✗	✗	✓	✓	✓
Current work situation	Single item question	✓	✗	✓	✓	✓	✓
Psychosocial work environment	Single component of the Work Organisation Assessment Questionnaire (4 items, 5 options, 0–16)	✓	✗	✓	✓	✓	✓
Attitudes and beliefs towards work	Newly developed questionnaire, 11 items, 7 options, 0–66)	✓	✗	✓	✓	✓	✓
Psychosocial and behavioural factors							
Anxiety and depression	Hospital Anxiety and Depression Scale (14 items, 4 options each, 0–42)	✓	✓	✓	✓	✓	✓
Fear of moving the arm	Single item question (0–10 NRS)	✓	✓	✓	✓	✓	✓
Pain self-efficacy	Pain Self Efficacy Questionnaire (10 items, 7 options each, 0–60)	✓	✓	✓	✓	✓	✓
Consultation-based reassurance	Consultation-based reassurance questionnaire, 12 items, 7 options, 4 subscales 0–28)	✓	✓	✓	✗	✗	✗
Worry about shoulder pain	Single item question (0–10 NRS)	✓	✓	✓	✓	✓	✓
Treatment expectations (confidence)	List of potential treatment options (seven items, 0–10 NRS)	✓	✗	✓	✓	✓	✓
Health economic measures							
Healthcare utilisation for shoulder pain (prescriptions, GP consultations, investigations referrals)	Self-reported (follow-up questionnaires; four items) and medical record review	✓	✗	✓	✓	✓	✓

BMI, body mass index; EQ-5D-5L, European Quality of Life five Dimension ; GP, general practitioner; NRS, Numerical Rating Scale; SPADI, Shoulder Pain and Disability Index.

(objectives 1, 3 and/or 5) which have been selected based on previous systematic reviews and cohort studies:

- Sociodemographic variables: age, gender, level of education, health literacy.[33]
- Shoulder pain characteristics: history, duration, onset and baseline severity of shoulder pain/disability; pain elsewhere (full body manikin).[34]
- Comorbidities and lifestyle: diabetes and other relevant long-term conditions, height and weight to calculate body mass index, smoking and vaping, alcohol consumption and physical activity.
- Work-related factors: current work status.
- Psychosocial and behavioural factors:
  - Symptoms of anxiety and depression (Hospital Anxiety and Depression Scale).[35]
  - Fear-avoidance beliefs, derived from the Fear-Avoidance and Beliefs Questionnaire,[36] and worry about shoulder pain measured using single item questions.
  - Pain self-efficacy (Pain Self Efficacy Questionnaire).[37]
  - Cognitive and affective reassurance (Consultation-based Reassurance Questionnaire).[38 39]
  - Treatment expectations: questions asking participants how confident they are that specified treatments will help their shoulder pain.

During the COVID-19 pandemic it is anticipated that participants' responses to some questions may be influenced by the pandemic or related restrictions, particularly questions relating to current work status, ability to participate in usual activities, shoulder pain treatments, self-management of shoulder pain, anxiety and depression. To capture this, participants will be given the opportunity to comment on any conditions or circumstances that may have affected their responses in the follow-up questionnaires (open-ended question).

Medical record review

Participants will also be asked for consent to access and export aspects of their medical records, to provide information on healthcare resource use including information on fit notes; prescriptions; consultation frequency; referrals for further treatment and procedures (eg, imaging, surgery); non-shoulder-related musculoskeletal consultations and other relevant comorbidity (coronary heart disease, diabetes, thyroid disease, cancer).

Follow-up data collection

Participants will be sent follow-up questionnaires at 3, 6, 12, 24 and 36 months after the return of their baseline questionnaire; these follow-up questionnaires will be sent by post or a link to an online questionnaire will be sent by email. Non-responders to follow-up questionnaires will receive a reminder questionnaire after 2 weeks, 4 weeks and a telephone call a further 2 weeks later if no response has been received, with the option of completing a short (Minimum Data Collection) questionnaire by telephone, and if no telephone contact can be made, by post.

Short-term data collection

On return of the baseline questionnaire participants will be offered the option of completing the shoulder pain App or text messages reporting their pain and function (0–10 NRS) weekly for 12 weeks. The App also collects weekly data across eight further domains using single item questions: self-efficacy, work absence, mood, sleep, medication use, fear of movement, worry, treatment and recovery expectations.

Clinical assessment

Those participants who have returned a completed questionnaire will be offered the option to attend a clinical assessment by an experienced and trained physiotherapist, guided by a detailed manual and using a standardised case report form for data collection. Participants will be notified that all information collected at the clinic will be collected for research purposes, and that no recommendations will be given regarding diagnosis, treatment or referral. Findings from the clinical assessment will only be discussed with their GP if the assessor feels there is a need for immediate clinical attention. In response to restrictions imposed during the coronavirus pandemic, ethical approval was requested (as an amendment to the original approval) to share a brief report from the US with the participants' GPs. This may avoid the need for a separate referral for ultrasonography for clinical purposes in a context where there is a need to reduce physical contact and travel for non-essential purposes.

Physical examination

The assessment will include a standardised history based on questions regarding duration, severity, impact and (self) management of shoulder pain. The physical examination will include an examination of the neck using repeated movements through flexion, extension and side flexion to assess whether the patient's shoulder pain is related to a neck problem. Shoulder range of movement will be visually assessed (in degrees) during active abduction (in degrees) and external rotation, compared with the contralateral side. Additional tests designed to distinguish between different shoulder conditions have variable reliability and diagnostic test accuracy, but their selection was informed by systematic reviews:[14 16 17]

- Painful arc, Neer sign and Hawkins-Kennedy tests.
- External rotation lag sign.
- Glenohumeral external rotation (50% reduction compared with the less/non-painful side).
- Scapular assistance test.
- Empty Can and Full Can test.
- Scarf test and Bear Hug test
- Step-standing elevation.
- Muscle performance tests aiming to identify weakness and pain.

Anthropometric measurements will include height (in centimetres) and weight (in kilograms) and waist-hip circumference (in cm). To assess balance, strength, and mobility, we will include a brief standardised protocol,

consisting of grip strength, lower limb strength (sit-to-stand) and a balance test.

Following the assessment, the research physiotherapist will record their opinion regarding the pathoanatomical classification of the shoulder problem (rotator cuff disorder, frozen shoulder, glenohumeral osteoarthritis, acromioclavicular joint pain, instability, neck-related dysfunction), and rate their confidence in this classification using a 0–10 NRS. The physiotherapist will also estimate the participant's prognosis, through answering the question 'Do you think this participant will have interfering shoulder pain in 6 months' time? Yes/No/Don't know'.

Ultrasound assessment

The US will be performed by experienced ultrasonographers/radiologists using high-resolution ultrasound systems and transducers[40] according to a standardised scanning protocol.[41] The structures scanned will include long head of biceps tendon, rotator cuff (subscapularis, supraspinatus, infraspinatus and teres minor tendons and muscles), posterior glenohumeral joint, subacromial/deltoid bursa and acromioclavicular joint. A standardised structured report based on[42] will include information regarding tendon and bursal pathology including structural appearances, site and size of tendon tears, observed glenohumeral or acromioclavicular fluid, synovitis or cortical bone changes and muscle atrophy. Dynamic scanning of some shoulder movements will be performed to assess for restriction or instability. Colour Doppler will be used to assess the presence of neovascularisation in any areas of tendon, sheath or bursal abnormality. Both shoulders will be scanned to enable later analysis of abnormalities in affected versus pain-free shoulders.

Qualitative interview study

Recruitment of patient-clinician dyads

Patient-participants: Questionnaires will be screened to enable a purposive sampling frame to be applied. A range of participant characteristics will be sampled for, including age, sex, reported pain intensity, pain duration, shoulder diagnoses, socioeconomic status, health literacy and Fit Note status (ie, absent from work or not). Participants who are selected for interview will be sent an invitation letter, reply slip and participant information leaflet about the interview. Those who return a reply slip indicating a willingness to be interviewed will be telephoned to arrange the interview.

Clinician participants: As part of the patient-participant consent process, the participant will be asked the name of the clinician with whom they consulted for their shoulder pain (GP or physiotherapist) and for permission to contact the clinician to arrange a separate individual interview in which the consultation will be discussed. If a participant declines consent to contact their clinician, then the participant's interview will be used alone.

Data collection

Topic guides will be used in interviews, which will be informed by the study objectives and the future aim of designing an optimal (stratified) model of care for shoulder pain, and by previous research on participant-clinician communication, effective reassurance and diagnostic and prognostic uncertainty in musculoskeletal pain.[38 43 44] Separate topic guides are developed for participant and clinician interviews. Clinicians will be asked about their views and experiences of treating shoulder pain, particularly in relation to the given consultation (online supplemental file 1). Topic guides will be iteratively revised throughout the data-collection process in light of emergent findings.

Topics will include (but not be limited to):

- Participants' experiences of managing their shoulder pain condition and its impact on their lives.
- Participants' understanding of possible causes of shoulder pain, including the 'label' attached to explanations and identified issues associated with this.
- The value participants and clinicians attribute to diagnostic tests, including physical examination and imaging.
- Consideration of explanations, concerns and uncertainty regarding prognosis.
- Views on decisions and advice given about self-management, work and other activities.
- Clinician–patient communication regarding diagnosis, prognosis and treatment options.
- Participants' and clinicians' views and experiences regarding the impact of the coronavirus pandemic on management of shoulder pain and on treatment and referral decisions.

Semistructured interviews will be carried out with approximately 15 participant–clinician dyads (ie, approximately 30 interviews in total). The final number of interviews will be guided by data saturation, defined in terms of 'informational redundancy'[45]—the point at which additional data no longer offers new insights.

Analysis cohort study (objectives 1–5)

A detailed analysis plan will be written for each of the study objectives; a summary is given here. Most analyses will be conducted using Stata software v16.

Objective 1

Investigate pain and function trajectories (overall prognosis): Descriptive statistics (estimates and measures of dispersion) will be used to report baseline characteristics of the study population, and the course of symptoms over time, for the primary outcome (SPADI) and secondary outcome measures. For each follow-up time point (0, 3, 6, 12, 24, 36 months), we will report means (SD) for continuous outcomes, and proportions (n, %) for binary outcomes, based on longitudinal models that account for correlated responses over time. Attrition (n,%) will be described for each follow-up time point. Baseline characteristics among those lost during follow-up

(whose outcomes are hence not fully observed) will be summarised and compared with characteristics of those remaining in the study to assess for risk of attrition bias.

Latent class growth analysis or other latent trajectory analysis will be used to identify distinct groups of participants with similar short-term trajectories of shoulder pain and function scores (0–10 NRS) using weekly measurements of outcome data at up to 12 time points over the first 3 months. For inclusion in the analysis, participants will be required to have available data in week 1 and at ≥2 further time points. The optimal number of trajectories will be selected using a combination of statistical, parsimony and interpretability criteria.[46]

Appropriate polynomial functional form for each trajectory will be chosen, based on the significance of the estimated parameters related to each polynomial component. Participants will be assigned to trajectories according to maximum probability assignment principle. The number of trajectories will be increased, and model fit assessed using Bayesian information criterion (BIC) and sample size adjusted BIC. The Lo, Mendell and Rubin adjusted likelihood ratio test (LRT),[47] and the bootstrap LRT were used to assess whether there was a significant improvement in model fit between k-1 and k trajectory models. The following criteria will also be used for model selection: (1) delineation of trajectories assessed by higher entropy, (2) average posterior probability of trajectory membership >0.7, (3) trajectory membership ≥4% and (4) clinical relevance and interpretation of the identified trajectories. Mplus software is planned to be used for analysis of pain and function trajectories.[48]

Baseline characteristics of subgroups showing distinct trajectories will be described, including any treatment received for shoulder pain during the first 3 months. Similar methods will be used to describe long-term trajectories, using outcome data at 6, 12, 24 and 36 months. Based on previous studies investigating trajectories in other conditions (n=350–700)[49 50] we expect to identify between three and five classes, for which a sample size between 400 and 500 participants should be sufficient. The GRoLTS checklist for reporting latent trajectory studies will be followed.[51]

Objective 2

Describe healthcare resource use and productivity losses: Healthcare costs will be estimated by combining resource use data with unit costs, obtained from standard sources including the British National Formulary for drugs,[52] NHS Reference costs[53] and Unit Costs of Health and Social Care.[54] Productivity costs will be estimated using the human capital approach with salary costs based on respondent job-specific average wage estimates identified from annual earnings data and UK Standard Occupational Classification coding.[55] Responses to the EQ-5D-5L at each time point will be converted to utility values obtained using the cross-walk value set, in line with current National Institute for Health and Care Excellence recommendations.[56] Utility values will also be converted into quality-adjusted life-years (QALYs) using the area under the curve approach linking utility scores at various time points. A descriptive analysis of resource use, healthcare costs, time off work, productivity costs, EQ-5D-5L utility values and total QALYs will be conducted, with presentation of means and confidence intervals obtained by non-parametric bootstrapping.

Objective 3

Develop a prognostic model for predicting individuals' level and risk of pain and disability: We will develop and validate a multivariable prediction model for reliably estimating expected levels of pain and disability (using SPADI total score as a continuous outcome) over 6 months follow-up. Development of prognostic prediction model will be guided by the PROGRESS framework[57–59] and reported using Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis reporting guidelines. The number of variables (candidate predictors) for potential inclusion will be restricted to meet sample size requirements (see below), based on existing or emerging evidence regarding the prognostic value of variables, combined with clinical and patient expertise, and consider sociodemographic variables, lifestyle factors, shoulder pain characteristics, comorbidity and psychosocial factors. Candidate predictors will be based on participant self-report to allow wide App of the prognostic model, with data extracted from the baseline questionnaire. Multivariable linear regression using the elastic net penalty (to penalise for potential overfitting and to allow variable selection). Continuous prognostic variables will not be categorised during the process of developing the models, with splines or fractional polynomials used to examine non-linear associations with outcome. Prognostic subgroups will be defined based on predicted SPADI values at 6 months, using a priori defined thresholds for SPADI for recovery (eg, SPADI score <20) or persistent high levels of pain and disability (eg, SPADI score ≥50). We will additionally describe predictive performance of the model to accurately predict the probability of individuals with shoulder pain to experience recovery and risk persistent high SPADI scores. Internal validation will be undertaken using bootstrapping of the entire development dataset, and optimism-adjusted estimates of predictive performance produced for calibration (eg, R^2, calibration-in-the-large, calibration slope) and discrimination (eg, C-statistic, area under the curve) for predicted risks.

We have estimated minimum sample size using the approach proposed by Riley *et al*,[60 61] and using the Stata pmsampsize command, aiming to reduce overfitting of the prediction model. Based on previous studies, we expect R^2 to be 0.5 when including baseline level of the primary outcome (SPADI total score) in the model as planned. Based on an expected mean change of 25 points and SD of 23[5] and a model including 20 candidate predictors, the required minimum sample size is 254 participants. Accounting for loss to follow-up of 25% we need to

recruit at least 339 participants to the cohort. When using a binary outcome, a minimum sample size of 377 participants with follow-up (503 at baseline) would be needed.

Objective 4

Explore the added prognostic value of physical examination tests and US findings: Due to lockdown measures during the COVID-19 pandemic, a much smaller number of participants than originally planned can be invited for a clinical assessment. Given the expected small sample size, the statistical analysis of data from the clinical assessment will focus on testing a priori defined hypotheses, informed by previous literature and clinical expertise, and explore the value of adding specific physical examination tests or US findings for predicting outcome (higher SPADI scores over 6 months follow-up), over and above prognostic information included in the prediction model using self-report data only. Assuming R^2 from the prediction model will be 0.5 using 20 predictors (as described above), to have 80% power to detect one additional predictor adding 0.05 to the R^2 to the model, we would need 74 participants without drop-out, and 99 participants assuming 25% will drop-out.[62]

Objective 5

Explore candidate predictors of response to commonly used treatments in a real-life, observational setting: Developmental work (systematic review, workshops with clinicians and international choice-based conjoint-survey of clinicians)[63] has generated a shortlist of candidate treatment moderators that may modify the response to commonly used treatments for shoulder pain in primary care (advice and pain relief only, corticosteroid injection, exercise/mobilisation), as recorded by participants in the three and 6 months follow-up questionnaires. These candidate moderators will include: symptom duration; presumed cause of shoulder pain (injury or other); coexisting neck pain; psychosocial complexity (fear-avoidance, catastrophising, anxiety, depression); positive expectations or preferences regarding treatment and comorbidity (in particular diabetes). Linear (random effects) regression analysis will be used to estimate the outcomes of treatment received (eg, corticosteroid injection compared with advice/analgesics only), using SPADI score over 6 months follow-up as the primary outcome. Propensity score methodology (using matching, stratification or inverse probability of treatment weighting approach) will be used to adjust for confounding by indication due to observed covariates. Sensitivity analysis will be performed to assess the robustness of findings to potential unmeasured confounding, using the E value approach.[64] The effects of moderator*treatment interactions will be explored, and overall treatment outcomes as well as outcomes for relevant subgroups (where relevant moderator*treatment interactions will be identified) described. Based on previous primary care studies[7] and our GP survey[65] we expect that 20%–40% of patients receive an injection and 25%–50% of patients see a physiotherapist following GP consultation. Depending on the distribution of candidate predictors, this will give subgroups of ≥100 to explore the role of candidate moderators. These are exploratory analyses, given that predictors of treatment effect need to be confirmed using data from randomised trials, but will offer insight into their value in the broader population of people with shoulder pain presented in routine primary care.

Missing data

For all quantitative analyses patterns of missing data will be described. Under a 'missing-at-random' assumption, individuals with partially missing outcome data (eg, at some time points) will be included in analyses (without imputation) using a longitudinal data (hierarchical) modelling framework. If there is a considerable amount of missing baseline data for candidate predictors or covariates of interest this will be handled using multiple imputation, and Rubin's rules used to combine results across imputed datasets. The imputation will be conditional on observed outcomes and candidate predictors, and auxiliary variables, to help ensure a 'missing-at-random' assumption is appropriate.

Analysis qualitative study (objective 6)

All interviews will be audiorecorded, fully transcribed and then cleaned and anonymised. An inductive, exploratory framework will be adopted using thematic analysis and influenced by grounded theory.[66] The constant comparison method[67] will be used in the analysis, looking for connections within and across interviews, and across codes, highlighting data consistencies and variation.

The participant–clinician dyad will be the unit of analysis. Exploring dual perspectives on the consultation can provide a rich data source which can strengthen trustworthiness of data.[68] Comparisons will be made between the matched participant and clinician interviews, looking for similarities and differences in the separate accounts given. Analysis will, therefore, draw comparisons both between clinician and participant perceptions of specific consultations as well as between different clinician–participant dyads across the sample.

DISCUSSION

This study protocol describes a prospective cohort study investigating the course and prognosis of shoulder pain in primary care, as well as healthcare costs and productivity losses associated with an episode of shoulder pain. The study includes a linked qualitative study, interviewing dyads of patients and their clinicians about the influences on decision making and their perspectives on the importance of diagnostic and prognostic information in the management of the shoulder problem. Recruitment is expected to be completed in July 2021.

The cohort study is part of a programme of work aiming to improve patient outcomes and healthcare resource use by early, more effective targeting of patients

to treatments from which they are likely to benefit most. The cohort study will provide insight into the content and outcomes of current primary care for patients presenting with shoulder pain, describe overall prognosis and use self-report information from participants to develop a prognostic model for predicting future levels of pain and disability in individuals with shoulder pain, allowing early identification of those who can be reassured and self-manage their shoulder condition, as well as those who are at risk of persistent pain and disability and would benefit from further treatment. The PANDA-S research programme also includes an individual participant data (IPD) meta-analysis of randomised trials to test candidate predictors of the effect of commonly used treatments for shoulder pain.[69] The data from the cohort study, linked qualitative study, and IPD meta-analysis will then be used to co-design, together with clinicians and patients, a prognostic screening and treatment decision tool to inform improved decision making for people presenting with shoulder pain. The use of the tool will subsequently be evaluated in a multicentre, pragmatic randomised trial.

The coronavirus pandemic, including restrictions required to reduce the risk of infection, has impacted significantly on recruitment and data collection for the cohort study. Recruitment to the PANDA-S cohort study had to be paused between March and August 2020. Recruitment gradually restarted in GP practices after this lockdown period but was significantly impacted by further restrictions implemented in November 2020 and again in January 2021, resulting in fewer patients accessing health services for shoulder pain. Recruitment was additionally affected by increasing pressures on GP services, including illness of staff and patients, dealing with the consequences of limited access to care, and contribution to the vaccination programme. Recruitment through physiotherapy waiting lists was therefore initiated in February 2021. All changes to protocol and recruitment targets were discussed with our Programme Steering Committee. Postal questionnaires were converted to online surveys, and reminder processes were amended from paper versions to telephone and online reminders. Additionally, questionnaires were amended to include a comments section allowing participants to record any circumstances that may have affected their responses, as we expected that COVID-19-related restrictions would impact on their access to care, ability to work and exercise, and on their mental health and well-being.

Face-to-face research clinics could only be resumed in April 2021, limiting the number of patients that can be offered a physical examination and US within the time frame of the study. We initially planned to incorporate data from the clinical assessment (physical examination test results and US findings) in the development of the prediction model, requiring a minimum sample size of more than 250 attending research clinics (see analysis plan for objective 3). Given the expected smaller number of participants attending clinic, the statistical analysis of physical examination tests and US findings will, therefore, focus on testing specific hypotheses regarding the prognostic value of a limited number of these diagnostic tests over and above a prediction model based on self-report findings. The results will inform the development of recommendations regarding relevant tests to perform during a clinical assessment, and regarding the value of US findings in making decisions regarding treatment and referral. The prognostic model will be based on self-report information only, which will allow the future screening tool to be used during remote as well as face-to-face consultations with healthcare professionals.

Ethics and dissemination

The PANDA-S study has ethical approval from Yorkshire and The Humber-Sheffield Research Ethics Committee (18/YH/0346, IRAS Number: 242750). Results will be disseminated through peer-reviewed publications, social and mainstream media, professional conferences and the patient and public involvement and engagement group supporting this study and through newsletters, leaflets and posters in participating sites.

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