The LISTEN study.

Listening: involving SLE patients To Empower and Negotiate recognition

Phase 1- small group peer support

Phase 2 – Large-scale patient and physician questionnaires and interviews

Exploring the acceptability, feasibility and impact of peer support email groups and involvement in research in patients with systemic autoimmune rheumatic diseases

Investigating key factors in effects of the disease and patient-physician interactions on patient behaviour, mental health/ wellbeing and disease acceptance

STUDY PROTOCOL
Version number: Draft
Version date: 2 Nov 2019

ETHICS SUBMISSION – APPENDIX 1

Table of Contents

		Page
1.	Protocol version control	3
2.	Study Contacts	3
3.	Abbreviations	4
4.	Study synopsis	5
5.	Study background and rationale	7
6.	The LISTEN study	9
6.1	Study Objectives	9
6.2	Inclusion criteria	10
6.3	Participant recruitment	10
6.4	Consent	10
6.5	Participant withdrawal	10
6.6	Participant Follow Ups	11
6.7	Analysis	11
7.	Study management and Governance arrangements	11
7.1	Research Team	11
7.2	Study funding	12
7.3	Records	12
7.4	Insurance/indemnity	12
7.5	Adverse incidence reporting	12
7.6	Ethical approval	13
7.7	PPI involvement	13
7.8	Dissemination of research results	13
7.9	Proposed study timetable	13
8.	References	14

1 Protocol version control

Version number	Version Date	Protocol approvals and dates (e.g. REC etc)	Supersedes approved version number/date
DRAFT	02.11.19	For ethical approval	Not applicable

2 Study Contacts

Funder:

Lupus UK
St James' House
Eastern Road
Romford
Essex

Chief Investigator:

Professor Stephen Sutton
Professor of Behavioural Science
Behavioural Sciences Group
Institute of Public Health
University of Cambridge
Forvie Site, Robinson Way
Cambridge, CB2 0SR
Email: srs34@medschl.cam.ac.uk
Tel: 01223 330594

Co-investigators/ collaborators:

Lead researcher and protocol author:
Melanie Sloan
Behavioural Science Group
Institute of Public Health
University of Cambridge
Forvie Site, Robinson Way
Cambridge, CB2 0SR
Email: mas229@medschl.cam.ac.uk
Mobile: 07975799052

Professor Caroline Gordon
Professor of Rheumatology
University of Birmingham
Email: P.C.Gordon@bham.ac.uk

University of Cambridge Collaborators:
Dr Mark Pilling

External Collaborators:
Professor David D'Cruz, Louise Cootes lupus unit
Dr Felix Naughton, UEA
Dr Chris Wincup, UCLH
Dr Elliott Lever, UCLH
Paul Howard, LUPUS UK
Chanpreet Walia, LUPUS UK

Patient Collaborators:
Michael Bosley, Lynn Holloway, Rupert Harwood, Moira Blane, Collette Barrere

3 Abbreviations

ACR – American college of rheumatology

BSG – Behavioural Sciences Group

COREQ – Consolidated criteria for reporting qualitative research

HCP – Health Care Professional

MCTD – Mixed connective tissue disease

PPI – Patient and Public Involvement

RA – Rheumatoid arthritis

SLE Systemic Lupus Erythematosus

SLICC – Systemic Lupus International Collaborating Clinics

UCTD – Undifferentiated connective tissue disease

4 Study Synopsis

Study title	The LISTEN study Listening: Involving SLE patients To Empower and Negotiate recognition
Short title	The LISTEN study
Chief Investigator	Professor Stephen Sutton
Chief Investigator's employing Institution	University of Cambridge
Funder	LUPUS UK
Study Duration	Phase 1 – small support email groups – duration 4 months, followed by questionnaire at 12 months after randomisation Phase 2A – Updated questionnaires to physicians, all LUPUS UK members, healthy control group and available online to RA and fibromyalgia patients. Response collection and analysis – 6 months Phase 2B – Interviews with physicians and patients – 6 months Total study duration (phases will overlap) – approx. 16 months
Participants	Phase 1 - Patients with SLE, UCTD, discoid/cutaneous lupus, Sjögren's syndrome or MCTD/Overlap disease responding to an invitation to complete online questionnaire introduced by online forums and support groups moderators. Phase 2A – All LUPUS UK members. RA questionnaire – ppts with self-verified RA. Fibromyalgia – ppts with self-verified fibromyalgia (available online on HealthUnlocked) Healthy friends – nominated friends of LUPUS UK members. Randomly selected physicians to receive physician questionnaire. Phase 2B – Purposively selected physicians and patients for interviews
Sample size	Phase 1 – Email support groups (180) 60 in each of three groups Phase 2A – Questionnaire to all LUPUS UK members (5500), made available online on RA and fibromyalgia forums (expected 200 responses per disease category), link given by lupus forum members to healthy friends (expected 300 responses). Physician questionnaires (260) Phase 2B – Interviews until theoretical saturation reached. Estimated 15-25.
Objectives	1. To explore the acceptability and feasibility of peer support by small group email. 2. To measure the impact of peer support and research involvement on the mental health, wellbeing, self-esteem and disease acceptance of patients with systemic autoimmune rheumatic diseases 3. To empower patients and improve research quality and relevance by actively involving them in research into their own disease; generating

	research questions and research materials that are relevant to their priorities, needs and experiences. 4. To investigate key factors in effects of the disease and patient-physician interactions pre and post diagnosis on patient behaviour, mental health/ wellbeing and disease acceptance 5. To compare lupus and related disease patients' wellbeing, mental health and perception of medical care with patients with RA, fibromyalgia and healthy friend controls
Eligibility criteria	• Participants aged 18 years or over • UK residents • Participants with self- verified SLE, UCTD, discoid/cutaneous lupus, Sjögren's syndrome or MCTD/ Overlap disease. • Phase 2 – Also includes Ppts with RA, fibromyalgia and healthy controls ('healthy controls' excluded if any significant chronic or acute severe illness) • Physician questionnaires and interviews eligibility: A consultant or GP currently practising in the UK
Description of intervention	1. Phase 1 questionnaire will be made available through the online platform Qualtrics on LUPUS UK forum, lupus UK sufferers Facebook page and other online health forums if recruitment insufficient. This questionnaire contains questions on the impact of the disease and support on their wellbeing and mental health. 2. Questionnaire respondents will be randomly allocated into one of 3 groups: Gps A and B will be divided into email support groups of 5-6 Ppts with the aim to provide peer support. In addition, Gp A will be given research tasks to discuss, including the pilot questionnaire to redesign in order to distribute to all LUPUS UK members. Gp C will be the control group. 3. The email support groups will communicate for 4 months, after which time all 3 Gps will receive another questionnaire to ascertain any changes to their mental health, wellbeing, support perceptions and acceptance. They will also be asked to evaluate the positive and negative aspects of the group support. Another questionnaire will be sent 12 months after baseline questionnaire 4. The patient-adapted questionnaire will be made available online and by post to LUPUS UK members and online groups, including the RA and fibromyalgia forums and an adapted questionnaire link given to healthy friends by forum members. The physician questionnaire will be sent to a random sample of consultants and GPs. These questionnaires will contain questions on perceptions of support, wellbeing, mental health, medical relationships and patient behaviour. 5. In-depth interviews will be carried out with purposively selected participants from questionnaire responses.
Analysis	Qualitative - Thematic analysis including using Nvivo software

	Quantitative – Descriptive statistics, ANOVA and correlations/ regressions.

5 Study background and rationale

Background

Previous studies and our current work with SLE and related autoimmune diseases patients have identified a clear and urgent need for patient-focused research further exploring the psychological impact and changes in patient behaviour from the often lengthy diagnostic delays, misdiagnoses and perceptions of level of support. The exploratory phase involved an online pilot questionnaire, in-depth interviews with purposively selected patients and an analysis of the forum. This found a majority of participants reporting significant – and often ongoing- psychological distress from their medical encounters, predominately during the diagnostic journey but also post diagnosis. The widespread loss of trust in the medical profession from the diagnostic journey has serious implications as trust is widely reported to be associated with adherence to treatment, improved quality of life, satisfaction with care and better health outcomes.

A US study of over 3000 SLE patients found that over 50% were initially told there was nothing wrong or symptoms were psychological. [1] 70% of participants in our phase 1 survey stated that a psychological misdiagnosis felt worse than being misdiagnosed with another disease with 84% reporting it reduced their trust in doctors in the future and 87% reporting it changed their behaviour in seeking medical help in the future. An earlier (2014) survey of over 2500 Lupus UK members found the mean time to diagnosis from initial symptoms was 6.4 years with approximately half reporting they were initially misdiagnosed.[2] This study and our pilot study highlights the urgent necessity of an agenda for patient focused research. These studies will assist with highlighting to HCPs (Health care professionals) the often extremely damaging impact of the diagnostic uncertainly period and the influence physician behaviour has on patient mental health and behaviour pre and post diagnosis. More support prior to diagnosis is essential to improve the current situation for all undiagnosed rare disease patients on their often long and complicated medical journeys[3]

Delays in SLE diagnosis and therefore treatment are associated with a worse physical prognosis as morbidity and mortality are improved by early use of hydroxychloroquine and an immunosuppressive regime.[4,5,6] The perception of poor care on the diagnostic journey, especially for the many who report feeling their symptoms were disbelieved, can have a continued influence on a patient's mental health and behaviour, thus also potentially damaging their physical health, long after the correct diagnosis. Insecurity, fear of rejection and physician's disbelief were widely reported by these patients in phase 1 to be always present even in subsequent positive medical relationships. This was also found in a study of parents of children with autoinflammatory disease where they reported becoming increasingly fearful, confused, lost self-confidence and began doubting their own judgement in the face of medical criticism and disbelief. Participants reported this generated a persisting distrust of the medical establishment even after diagnosis.[7] Studies of other diseases with lengthy diagnostic journeys have demonstrated the perceptions of stress, isolation and exclusion that worsens with the chaotic journey through numerous referrals, investigations and disease evolutions.[8]

With no definitive test for SLE and related systemic autoimmune rheumatic diseases, a diversity of manifestations and often non-specific presenting symptoms[9], patients are reliant on expert opinion in diagnosing the disease. Studies report that teaching in medical schools is inadequate, medical students lack confidence in diagnosing musculoskeletal disorders[10], there is a lack of rheumatological experience in GP training[11] and teaching does not reflect the impact of rheumatological conditions.[12] Other studies have also highlighted the need for increased emphasis on musculoskeletal disorders in medical teaching to increase accurate rheumatology referrals[13] and more awareness of SLE amongst all HCPs to aid faster diagnosis.[14] Analysing and publishing the patient perspectives is key to improving understanding and educating both clinicians and patients.

SLE and related autoimmune diseases are often reputed to be an 'invisible' disease with both social and medical diagnoses seemingly reliant upon the ability to see illness, with an often prolonged period of time before symptoms are validated by a diagnosis.[15] Validation is a key theme identified in both the existing literature and our recent research. Santiago et al found that invalidation occurred in all

rheumatic diseases with psychological factors, loneliness and pain intensity associated with invalidation and deserving of dedicated intervention.[16] Our initial research is in agreement with previous research that the reliance amongst many HCPs on often inconclusive test results rather than considering subjective symptoms can leave many patients feeling disbelieved and dismissed.[17,18,19] Price and Walker found that for some the SLE diagnostic journey often has no satisfying conclusion and can be an iatrogenic experience with the journey to diagnosis mirroring the disease in terms of ambiguity and chaos.[20] The ambiguous complexity of SLE and other related autoimmune diseases causes difficulty with the desire for clarity and certainty [21] with insecurity and uncertainty identified in both physicians and patients.[22]

Without a mutually trusting relationship, patients are more likely to not adhere to medication regimes and not inform their physician of changes to medication and symptoms. Only 53% of those who stopped/altered their medication in the phase 1 survey reported that they always informed their rheumatologist. Previous studies show non-adherence for reasons including lack of understanding, fear of adverse effects and perception that the medications are not effective, sometimes leading to discontinuation without physician advice or approval.[23, 24, 25] Our questionnaire results also demonstrate that the cognitive impairment common in SLE patients leads to frequent non-intentional non -adherence as a significant proportion of patients reported memory difficulties and forgetting medications at times. Poor adherence is difficult to evaluate with reported rates in SLE varying from 3%-85% between studies[26 27,28,29,30] so quantifying non-adherence in this large study and exploring this from the perspective of both the patients and clinicians will provide valuable insight into methods of improving adherence, such as good communication[31,32], patient involvement in medication decisions[33,34] memory aids and trust in the medical profession[34].

Under-reporting has also been frequently raised in phase I in terms of general SLE symptoms, seemingly related to patients' frequently expressed fear of being viewed as a '*hypochondriac'* due partly to the diversity, changeability and quantity of symptoms but predominantly due to previous non-organic or psychosomatic misdiagnoses. This avoidance of reporting symptoms has been discussed by patients as particularly likely for any mental health issues arising amongst those whose SLE was originally misdiagnosed as mental health problems, such as depression or anxiety and requires further investigation. Approximately 1/5 to 1/2 of rheumatological patients have psychosocial problems due to their disease and these are frequently not reported or detected by their physician[35]. In the 2011 (US) National burden of lupus survey, 52% of lupus patients reported they minimise symptoms when reporting to physicians yet 72% of physicians were unaware of this tendency to underreport[36]. Quantifying this under-reporting from the large-scale questionnaire proposed for phase 2, comparing with the proposed physician's questionnaire and correlating with variables such as length of diagnostic journey and reported level of trust in physicians will allow a much deeper understanding to help design targeted interventions for the most vulnerable.

Relationships between HCPs and patients have altered in recent years with decreasing automatic trust among patients in the advice of doctors. Patients value communication, information and use of evidence to support decisions[37] with encouragement of questioning and obtaining information about their condition.[38] Empathetic listening and belief in the patient's subjective reporting of symptoms was highlighted as the top patient priority – yet often felt to be unsatisfactory - in this phase 1 study and other studies of rheumatic diseases.[19] Patients in phase 1 have reported that there is often a disparity in priorities between wanting to discuss with physicians their quality of life (with the most frequent and debilitating concerns being fatigue, cognitive difficulties and pain) whilst some physicians are reported to be more focused on check lists of symptoms and discussing medications. Gordon et al found a substantial burden of disease in SLE patients, with most (82.5%) reporting fatigue, which was associated with a significantly reduced quality of life. This study highlighted that further work is needed to educate HCPs on the consequences of reduced quality of life.[39]

Lazare et al highlight the three inter-linked functions of medical encounters: to gather information, develop and maintain a therapeutic relationship and communicate information. The quality of the relationship is the major influence on patient and physician satisfaction. It also largely determines the quality and quantity of information elicited and comprehended as a patient who is anxious from previous poor interactions may not comprehend information clearly and a patient who feels distrust or dislike for the physician/ physicians may not disclose information or comply with recommendations.[40] Patients in phase 1 regularly report both high anxiety during medical encounters and reduced trust in physicians.

As rheumatic diseases are chronic, patient- physician relationships need to be established and maintained for the patient's lifetime with the phase 1 study reporting increased trust from continuity of care and often great attachment to the physician who diagnosed and first '*believed*' them. Those with long standing chronic rheumatological diseases desire to work with physicians from a position of mutual respect and trust with a qualitative study of rheumatoid arthritis patients finding that they felt it was important in building a trusting relationship that the physicians acknowledged the patient's expert knowledge and admitted openly to areas where they themselves lacked knowledge. [19] This has also been highlighted as a key point from the phase 1 forum analysis, questionnaires and interviews where participants regularly identified the difficulties of negotiating the doctor-patient relationship where they have significant knowledge of their own disease. This research will allow a deeper understanding of patient and physician views of methods of developing positive medical relationship where the patient can feel trust and security leading to improved physician and self-management with associated improved outcomes in physical and mental health. '*Insecurity*' was the key over-riding theme found in all methodology from our preliminary studies, both in terms of uncertainty of the disease course and in medical relationships.

Despite the WHO action plan for chronic disease management encouraging governments to provide education, incentives and tools for self-management and care,[41] many patients with lupus report there is limited assistance with self-management education from medical sources, thus often relying on peers in online forums and Facebook groups for knowledge transfer and emotional support. Peer support from those who experience the same challenges of living with the same chronic health condition[42] is increasingly being researched in terms of measuring health outcomes, improved adherence to treatment, empowerment, psychological outcomes and improved quality of life.

Studies have shown varied success from peer support initiatives across multiple disease types with a recent systematic review finding 4 out of 6 RCTs reporting no statistically significant differences in measured outcomes in heart disease patients comparing usual care with peer support.[43] Another study found no significant difference in wellbeing scores in diabetes patients provided with peer support in addition to usual care.[44] However, improvements have been reported from other studies including improved adherence from peer support interventions in HIV patients.[45] Studies have also demonstrated that peer education can be as effective as professional training in diabetes patients.[46]

The WHO is also increasingly recognising the importance of mental wellbeing as an important component of health.[47] This study will measure the impact of small group peer support on mental wellbeing and the large-scale questionnaire will determine the current state of mental wellbeing and perceptions of support, in a significant proportion of patients with systemic autoimmune rheumatic diseases in the UK.

6. The 'LISTEN' study

6.1 Study objectives

The main aims of the study are:

1. To explore the acceptability and feasibility of peer support by small group email.

2. To measure the impact of peer support and research involvement on the mental health, wellbeing, self-esteem and disease acceptance of patients with systemic autoimmune rheumatic diseases.

3. To empower patients and improve research quality and relevance by actively involving them in research into their own disease; generating research questions and research materials that are relevant to their priorities, needs and experiences.

4. To investigate key factors in effects of the disease and patient-physician interactions pre and post diagnosis on patient behaviour, mental health/ wellbeing and disease acceptance.

5. To compare lupus and related disease patients' wellbeing, mental health and perception of medical care with patients with RA, fibromyalgia and healthy controls.

6.2 Inclusion Criteria

Patients can be included in the study if they meet all of the inclusion criteria below:

- Participants with a self-verified diagnosis of SLE, UCTD, Sjögren's syndrome, discoid/cutaneous lupus or MCTD/overlap disease.
- Resident in the UK.
- Participants aged 18 or over.
- Additional Ppts for phase 2 includes those with self-verified RA or fibromyalgia, resident in UK and aged 18 or over. Healthy controls must be resident in UK, aged 18 or over and have no significant chronic or acute illness.
- Physician participants must be Consultants or General Practitioners currently practising in the UK.

6.3 Participant recruitment

Following ethical approval, patients will be approached by joint message on the LUPUS UK HealthUnlocked forum by LUPUS UK and research staff, with the study information detailed and the participant information sheet attached. A minimum of 24 hours will be left before the consent form and questionnaire are made available on the site. Consent will be returned with the questionnaire. We require 180 participants. If recruitment numbers are not satisfactory, prospective ppts will be approached through lupus UK support groups, other health forums and LUPUS UK Facebook page.

Phase 2 questionnaires and/or the online link will be sent to all LUPUS UK members by email and/or post with information sheets and made available online. The adapted versions for RA and fibromyalgia Ppts will be made available on the RA and fibromyalgia HealthUnlocked forum with an information sheet. Healthy friend controls will be recruited by Ppts with lupus/ related disease giving a friend the online link to their information sheet and questionnaire.

Physicians will be randomly selected, stratified by UK location. They will be approached by email, with contact details of the study team, a participant information sheet and online link to a questionnaire.

Purposive sampling will be used to select participants for interview from those who have given consent for this on their questionnaire response.

6.4 Consent

The process for obtaining participant informed consent will be in accordance with ethical guidelines and Good Clinical Practice. Potential participants will be asked whether they wish to consider taking part, emphasising that participation is entirely voluntary. The participant information sheet, questionnaire and consent form will be made available online, on the forums and by post/email in phase 2. Participants may take as long as they wish to decide whether to participate in the study and will be given the opportunity to ask questions. Consent to be contacted to potentially participate in the interview study will be requested at the end of the questionnaires. Consent for the interview and to be audio-recorded will be verbally retaken at the start of the interview with the consent statements audio recorded.

6.5 Participant withdrawal

Participants may be withdrawn from the email groups and/or the whole study either at their own request or at the discretion of the investigator. Participants will be made aware from the information sheet and in the allocation of group letter of how to withdraw and that it will not affect their medical care. Participants will be given the contact details of research staff and informed of how to report unacceptable or unkind emails within their groups in their group allocation letters. Participants who send unacceptable emails within their groups will be withdrawn from the group by study staff.

6.6 Participant Follow Ups

Participants in phase 1 will be sent up to 3 reminders for non-response to the 4 and 12-month questionnaires. Physicians will be emailed up to two reminders for non-response to initial questionnaire request. If non-response, another random selection will be carried out from the same UK area.

6.7 Analysis

Qualitative – Interviews and qualitative responses to the questionnaires will be coded and entered onto NVivo software with double coding to ensure reliability and repeatability. Analysis will be thematic.[48] The consolidated criteria for reporting qualitative research (COREQ)[49] will be followed.

Quantitative - SPSS will be used for entry and initial descriptive summary of quantitative data, stratified by characteristics and group. Data will also be presented graphically to ensure the results are easily accessible to patients, clinicians and policy makers.

Multiple regression analysis will be used to test variability between groups.
For phase 1, the primary outcome to be tested is mental wellbeing as measured by the validated Warwick Edinburgh Mental Wellbeing scale, between groups B to C, using the within-person change from baseline to month 4 and the primary endpoint (difference of differences), with illness outcome as a secondary outcome. Similarly, the comparison between groups A to C, and A to B will be examined as secondary tests, with a significance threshold of 5%/2 due to the reuse of groups. The primary hypothesis for phase 2 is illness impact. There will also be secondary tests for phase 1 and 2 using different endpoints such as 'the length of delay in diagnosis has a negative correlation with medication adherence'.
Following receipt of Group A's draft phase 2 questionnaires and suggested changes/additions, principal component analysis will be carried out to reduce questions and redesign the phase 2 questionnaire for distribution.
Correlations between two variables from groups and between the clinician/patient groups will be measured by Pearson correlation coefficient (if linearly related) or Spearman's correlation if not. Spearman's rank correlation will used for ordinal variables. Chi Squared testing will be used where appropriate.

Mixed methods analysis will be used at every stage. Validated tools for measuring QoL, Self-esteem, wellbeing and trust in physician will be used.

7. Study Management and Governance Arrangements

7.1 Research Team

Chief Investigator:	Professor Stephen Sutton	University of Cambridge
Lead researcher	Melanie Sloan	University of Cambridge
Co- investigators/ collaborators: (Academic and clinical)	Dr Mark Pilling	University of Cambridge
	Professor Caroline Gordon	University of Birmingham
	Professor David D'Cruz	Louise Cootes lupus unit
	Dr Felix Naughton	University of East Anglia
	Dr Chris Wincup	UCLH
	Dr Elliott Lever	UCLH

Collaborators(patient): Michael Bosley, Lynn Holloway, Rupert Harwood, Moira Blane, Collette Barrere
Collaborators (charity): Paul Howard (deputy CEO LUPUS UK) Chanpreet Walia (LUPUS UK)

The study will be conducted by Melanie Sloan, supervised by Professor Stephen Sutton and Professor Caroline Gordon, with input, support and advice from additional academic, clinical, charity and patient collaborators. It will be based at the Primary Care Unit, Department of Public Health & Primary Care, Institute of Public Health, University Forvie Site, Cambridge. The team will hold regular meetings to review ongoing progress of the study and any amendments required.

The Chief Investigator has overall responsibility for the study and shall oversee all study management.

7.2 Study Funding

The research costs for the study are funded by Lupus UK

7.3 Records

Questionnaires will all be filled in electronically and will be captured on the Qualtrics online survey platform, under licence through the University of Cambridge. Data is transferred and held on the Qualtrics servers securely, within a specific location in the EU (https://www.qualtrics.com/privacy-statement/) Questionnaire data will be entered anonymously – identified only by the unique participant ID – into SPSS for data analysis.

Electronic data from Qualtrics and returned questionnaires by email will be transferred and stored on a Secure Data Hosting Service (SDHS) located on a firewall protected network (LAN), certified to ISO29001 security. At the close of the recruitment, all data study on the Qualtrics online will be deleted. Once uploaded to the SDHS, the questionnaire data will be accessible only by the research team using a two-factor authentication (password and security fob). Questionnaire data will be anonymised – identified by the participant ID – and transferred to SPSS for data analysis.

A document linking participant ID numbers and contact details will be stored on the SDHS, accessible only by the research team.

Anonymised data will be stored for five years post publication as required by APA Ethical Guidelines.

Each participant will be assigned a study identity code number for use on study documents and the database. All potentially identifying material will be removed. The investigator will make a separate confidential record on the secure data hosting service of the participants' names, addresses, contact details and identifying code to permit identification of all participants enrolled in the study. Study staff will adhere to GDPR 2018.

Interviews will be audio recorded and transcribed verbatim. All potentially identifying material will be removed from transcripts and Ppts will be assigned a number.

Study staff will adhere to the Data Protection Act 1998 and GDPR 2018.

7.4 Insurance/Indemnity

The University of Cambridge as research sponsor indemnifies its staff, research participants and research protocols with public liability insurance and clinical trials insurance.

7.5 Adverse Incident reporting

As this study is not a 'clinical trial of an investigational medicinal product (CTIMP)' it does not fall under The Medicines for Human Use (Clinical Trials) Regulations 2004 (as amended).

The research team will not collect data on adverse events (AEs), serious adverse events (SAEs) or suspected unexpected serious adverse reactions (SUSARs) as defined by these regulations. However, even in non-pharmaceutical research, such as this study, adverse incidents may still happen, for example;

- breach of confidentiality
- patient complains about any aspect of study

- deviation from study protocol (eg. recruiting before consent)
- equipment failure
- aggressive/ unacceptable behaviour of a participant towards the support group, researcher, staff or others.
- Responses highlights serious concern of risk to a patient

Concerns of risk to a participant will be immediately reported to the relevant authorities and the Chief Investigator. Unacceptable behaviour within support groups will result in expulsion of that participant from the group. Adverse incidents relating to the conduct of this research must be reported to the Chief Investigator within 5 working days of the researcher becoming aware of the incident

7.6 Ethical approval

Ethical approval will be sought from the Cambridge Psychology Research Ethics Committee

7.7 PPI Involvement

Individuals and focus groups of SLE/ related systemic autoimmune disease patients, approached through online forums and LUPUS UK support groups, have assisted with the development of the study.

Ongoing discussions with patients, LUPUS UK, rheumatologists and experts in the field will inform the further development of follow up studies. Five participants have been invited to represent patients' interest on this study. They have provided recommendations on the design of materials, such as information sheets and draft questions. They will review the final manuscript. LUPUS UK have been involved in the design of materials and will review the final manuscripts. Two consultant rheumatologists and two rheumatology registrars have been involved in the development of the study and materials and will assist in the study and review the manuscripts

7.8 Dissemination of research results

Results of the research will be published in peer-reviewed journals and findings presented to a wide audience. A lay summary will be provided for the LUPUS UK magazine

All participants in the study will have the option to request receipt of the final report.

7.9 Proposed study timetable

	2019			**2020**				**2021**
	Oct-Nov 2019	Dec 2019	Dec 19/Jan 2020	Jan-Apr 2020	May 2020	May - Jul 2020	Aug-Dec 2020	Jan-Mar 2021
Produce draft protocol	X							
Finalise participant information sheets and consent forms based on finalised protocol. Finalise pilot questionnaire	X							
Submit ethical proposal	X							
Study introduced and questionnaire made available online			X					
Patients randomly allocated to groups			X					

4 months of Group communication				X				
4 and 12 month Follow up questionnaire to all Ppts					X		Jan X	
Patient-altered questionnaire to all LUPUS UK members, fibromyalgia and RA forum members and physicians					X			
Data collection					X	X		
Interviews with patients and physicians						X		
Analysis						X	X	
Write up							X	X
Dissemination/ Publication								X

8. References

1. Lupus diagnosis: Process and patient experience. Daly R et al. *Arthritis rheumatol*, 2017; 69 (suppl 10)
2. Individuals living with lupus: findings from the lupus UK members survey 2014. Morgan C, Bland A, Maker C et al. *Lupus* (2018) 0, 1-7
3. Diagnostic odyssey for rare diseases: exploration of potential indicators. Black N, Martineau F, Manacorda T. London: Policy Innovation Research Unit, LSHTM (2015)
4. Clinical efficacy and side effects of antimalarials in systemic lupus erythematosus; a systematic review. Ruiz- Irastorza et al. *Annals of the rheumatic diseases.* Nov 2009,69(1): 20-8.
5. The importance of early diagnosis in SLE. Sebastiani G, Prevete I, Juliano A. *Iss med Assoc J.* 2016 Mar-Apr 18 (3-4) 212-5
6. The benefit of early treatment with immunosuppressive drugs in lupus nephritis. Esdaile J, Joseph L, MacKenzie T et al. *J rheumatol.* 1995, Jun 22 (6):
7. The patient journey to diagnosis and treatment of autoinflammatory diseases. Hausmann J, Lomax K, Shapiro A et al. Orphanet journal of rare diseases (2018) 13:156
8. International Joint Recommendations to address specific needs of undiagnosed rare diseases patients. October 2016.
9. Unmet medical needs in systemic lupus erythematosus. Lateef A and Petri M. *Arthritis Research and Therapy.* 2012 14 (suppl 4)
10. Musculoskeletal medicine: an assessment of the attitudes and knowledge of medical students at Harvard medical school. Day C, Yeh A, Franco O et al. *Acad med* 2007, May, 82 (5) 452-7
11. Early clinical features in Systemic Lupus Erythematosus: Can they be used to achieve earlier diagnosis? A risk prediction model. Rees F, Doherty M, Lanyon P et al. Arthritis Care and Research, 2016, vol 69, issue 6
12. Improved education in musculoskeletal conditions is necessary for all doctors. Akesson K et al.*Bulletin of the World Health Organisation*, 2003, 81 (9) 677-683
13. Referral and diagnosis of common rheumatic diseases by primary care physicians. Gamez-Nava J, Gonzalez-Lopez L, Davis P et al. Br J Rheumatol. 1998 Nov; 37(11): 1215-9
14. Burden of illness in Systemic Lupus Erythematosus: results from a UK patient and carer online survey. Kent T, Davidson A, D'Cruz D et al. Lupus (2017) 26, 1095-1100
15. Living with invisible illness: social support experiences of individuals with SLE. Brennan K, Creaves A. *Quality of life research*, May 2016, vol 25, issue 5, pp 1227-1235

16. Invalidation in patients with rheumatic diseases: clinical and psychological framework. Santiago M, Marques A, Kool M et al. The Journal of Rheumatology. April 2017, 44 (4) 512-518
17. Experience and perspectives of Adults living with SLE: Thematic analysis of qualitative studies. Sutanto B, Singh-Grewal D, McNeil H. *Arthritis care and research,* Nov 13, vol 65, iss 11, pg 1752-1765
18. Diagnosis: A liminal state for women living with lupus. Mendelson C. *Health care for Women International*. Vol 30, 2009, issue 5
19. How do patients with rheumatic disease experience their relationship with their doctors? Haugli L, Strand E, Finset A. A qualitative study of stress and support in the doctor-patient relationship. Patient education and counselling. 52 (2004) 169-174
20. Diagnostic vertigo: The journey to diagnosis in systemic lupus erythematosus. Price E and Walker E. Health, 2014 vol 18 (3) 223-239
21. The Body multiple: Ontology in medical Practice. Mol A. Durham, NC and London: Duke University Press. 2002
22. Complex syndromes, ambivalent diagnosis and existential uncertainty: The case of Systemic Lupus Erthematosus (SLE). Stockl A. Social Science & Medicine. 2007, 65: 1549-1559
23. Why do patients with SLE take or fail to take their prescribed medications? A qualitative study in a UK cohort. Chambers S, Raine R, Rahman A. *Rheumatology* (Oxford) 2009, Mar 48 (3) 266-71
24. Determinants of treatment adherence in ethnically diverse, economically disadvantaged patients with rheumatic disease. Popa-Lisseanu M, Grieinger A, Richardson M et al. J Rheumatol. 2005; 32 (50: 913-919)
25. Drug survival and reasons for discontinuation of intramuscular methotrexate: a study of 212 consecutive patients switching from oral methotrexate. Linde L, Hetland M, Astergaard M. Scand J Rheumatol, 2006; 35 (2): 102-106
26. Adherence to treatment in SLE patients. Costedoat- Chalumeau N, Pouchot J, Guettrot G et al. *Clinical rheumatology.* June 2013, vol 27, issue 3, pg 329-340
27. Why do patients with systemic lupus erythematosus take or fail to take their prescribed medications? A qualitative study in a UK cohort. Chambers S, Raine R, Rahman a, Isenberg D. Rheumatology. 2009; 48 (3): 266-271
28. Depression, medication adherence, and service utilization in systemic lupus erythematosus. Julian L, Yelin E, Yazdany J et al. Arthritis Rheum. 2009; 61 (2): 240-246
29. Adherence to medication in systemic lupus erythematosus. Koneru S, Kocharla L, Higgins G et al. J Clin Rheumatol. 2008: 14 (4): 195-201
30. Effectively measuring adherence to medications for systemic lupus erythematosus in a clinical setting. Koneru S, Shisov M, Ware A et al. artritis Rheum. 2007; 57 (6): 1000-1006
31. Concerns of patients with SLE and adherence to therapy- a qualitative study. Farinha F, Freitas F, Agueda A et al. *Patient prefer and adherence.* 2017; 11: 1213-1219
32. Physician communication and patient adherence to treatment: a meta-analysis. Zolnierek K, Dimatteo M. Med care 2009; 47 (8): 826-834
33. 'Compliance' is futile but is 'concordance' between rheumatology patients and health professionals attainable? Treharne G, Lyons A, Hale E et al. rheumatology, 2006: 45 (1): 1-5
34. Patient decision making related to antirheumatic drugs in rheumatoid arthritis: The importance of patient trust of physician. Martin R, Head A, Rene J. J Rheumatol 2008: 35 (4): 618-624.
35. Doctor-patient communication in rheumatological disorders. Daltroy L. Bailliere Clin Rheumatol 1993; 7: 221-39
36. Data from 2011 National (US) Burden of Lupus Survey, GSK
37. Trust relations in health care- the new agenda. Rowe R, Calnan M. European journal of public health, vol 16, issue 1, Feb 2006, 4-6
38. Effective physician- patient communication and health outcomes: a review. Stewart M. Can Med assoc J, 1995; 15:140-92
39. The substantial burden of systemic lupus erythematosus on the productivity and careers of patients: a European patient- driven online survey. Gordon C, Isenberg D, Lerstrom K et al. Rheumatology. 2013; 52: 2292-2301

40. The Medical Interview: Clinical Care, Education, and Research. Lipkin M, Putnam s, Lazare A, editors, New York, NY, Springer- Verlag 1995 pp 3-19 and 134-44
41. World Health Organisation. 2008-2013 Action plan for the global strategy for the prevention and control of noncommunicable diseases. WHO, 2008
42. Peer support within a health care context: a conceptual analysis. Dennis CL. Int J Nurs Stud. 2003 Mar: 40(3): 321-332
43. Peer support intervention trials for individuals with heart disease: a systematic review. Peery M, Watt-Watson J. Eur J cardiovasc Nurs. 2010 Mar;9(1): 57-67
44. Peer support for patients with type 2 diabetes: cluster randomised trial. Smith SM, Paul G, Kelly A, Whitford D, O'Shea E, O'Dowd T. BMJ
45. Feasability, acceptability and preliminary efficacy of an online peer-to-peer social support ART adherence intervention. Horvath KL, Oakes JM, Rosser BR, Danilenko G, Vezina H, Amico KR et al. AIDs Behav. 2013 Jul:17(6): 2031-44.20.
46. Type 2 diabetes patients educated by other diabetes patients perform at least as well as patients trained by professionals. Gagliardino JJ, Arrechea V, Assad D, Gagliardino GG, Gonzalez L, Lucero S, et al. Diabetes Metab Res Rev. 2013 Feb; 29(2): 152-60
47. Promoting Mental Health: Concepts, Emerging Evidence, Practice. World Health Organisation Geneva, 2004
48. Using thematic analysis in psychology. Braun V and Clarke V. *Qualitative Research in psychology.* 2006; 3 77-101.
49. Consolidated criteria for reporting Qualitative research (COREQ), a 32 item checklist for interviews and focus groups. Tong A, Sainsbury P, Craig J. *International journal for quality in Health care.* 2007, vol 19, 6, 349-357