UNIVERSITY OF CAMBRIDGE

ADAPT: Adapting, Disease self-management and Acknowledgement by Psychosocial Targeted interventions

Phase 1 – feasibility trial of remote psychosocial interventions (text message support, Listening support, physical activity)

Phase 2 – Randomised controlled trial of psychosocial interventions

Exploring the acceptability, feasibility (Phase 1) and effectiveness (Phase 2) of remote psychosocial interventions for patients with systemic autoimmune rheumatic diseases.

STUDY PROTOCOL
Version number: V1
Version date: 17/02/23

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1 Protocol version control

Version number	Version Date	Protocol approvals and dates (e.g. REC etc)	Supersedes approved version number/date
V1	17/02/23	Approved: PRE.2023.026	Draft for ethics approval – amended to V1 following ethics committee suggestions

2 Study Contacts

Funders: LUPUS UK and The Lupus Trust

Co-Principal Investigators:

Prof Stephen Morris and Melanie Sloan

Department of Public Health and Primary Care
University of Cambridge
Forvie Site, Robinson Way
Cambridge, CB2 0SR
Emails: sm2428@medschl.cam.ac.uk and mas@medschl.cam.ac.uk
Tel: 07975799052

Study team, advisors and collaborators:
James Brimicombe, Department of Public Health, Cambridge University
Michael Bosley, Patient Partner
Professor David D'Cruz, SLE specialist, Louise Cootes lupus unit and Kings College London
Wendy Diment, Patient Partner
Dr Elliott Lever, Rheumatology consultant, Royal Free Hospital
Prof Felix Naughton, health psychologist, School of Health Sciences, University of East Anglia
Dr Farhana Mann, Psychiatrist, University College London
Efhalia Massou, Department of Public Health, Cambridge
Kate Middleton, Patient Partner and CEO of The Wren Project
Dr Thomas Pollak, Neuropsychiatrist, Kings College London and South London and Maudsley NHS Foundation Trust
Dr Chris Wincup, Rheumatology consultant, Kings College London

Advisory Group:
Professor Caroline Gordon, Birmingham (lupus specialist)
Lynn Holloway – Patient member
Professor David Jayne, Addenbrookes (Vasculitis and nephritis consultant)
Ali Seamer- Patient member

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

SARD – Systemic Autoimmune Rheumatic Disease

SLE Systemic Lupus Erythematosus

SLICC – Systemic Lupus International Collaborating Clinics

UCTD – Undifferentiated connective tissue disease

4 Study Synopsis

Study title	The ADAPT study (**A**dapting, **D**isease self-management and **A**cknowledgement through **P**sychosocial **T**argeted interventions)
Short title	The ADAPT study
Principal Investigators	Prof Stephen Morris and Melanie Sloan
Chief Investigators' employing Institution	University of Cambridge
Study sponsor	University of Cambridge
Funder	LUPUS UK and The Lupus Trust
Study Duration	3 years (over 2 phases)
Participants	
Sample size	**Phase 1** N=120 (n=30 in each of the 3 intervention groups of text messaging intervention, listening support (The Wren Project) and the online physical activity course (Flexifit Pilates) and n=30 in control. **Phase 2** N=800 (approximately) Numbers dependent on which interventions progress to phase 2, and sample size calculations informed by phase 1. Provisional estimates of N=100 for online physical activity, N=100 for The Wren support, N= 300 for text messaging support and N=300 control. Process and acceptability evaluation interviews with phase 1 participants will take place until theoretical saturation (the point at which no new concepts are generated) is reached. Estimated 15 for each intervention group.
Objectives	**Aim** To assess the acceptability, feasibility and effectiveness of methods of remote psychosocial support for SARDs patients. For the interventions trialled (if effective and acceptable) to be incorporated as an adjunct to usual care. **Objectives** • To trial multiple quality of life and mental health measures to determine the most appropriate primary and secondary outcomes for phase 2. • To test processes to inform phase 2 effectiveness trial. • To develop and trial our own ADAPT instrument to more accurately

	reflect, measure and monitor SARD patient personal, social and medical satisfaction. • To assess the acceptability (phase 1) and effectiveness (phase 2) of remote psychosocial interventions on the mental health, wellbeing, self-esteem, resilience, loneliness and disease acceptance of patients with systemic autoimmune rheumatic diseases.
Eligibility criteria	Both phases - Aged 18 years and over Phase 1: Any INSPIRE (Ethics reference: PRE2022.027) study participant reporting a diagnosis of SLE and requesting on the INSPIRE survey (completed Jul-Sep 23) to be considered for the ADAPT trial. Phase 2: Reporting a diagnosis of any SARD
Recruitment and group allocation	For both phases, patients expressing an interest in participating in ADAPT at the end of INSPIRE survey will be emailed to confirm continued interest in participating. They will be randomly selected (until trial numbers filled) and then, once consent is given, randomly allocated (block allocation by the study statistician) into one of the intervention or control groups. If INSPIRE study participant responses do not generate sufficient ADAPT participant numbers, additional recruitment will be through online advertising via patient charities and support groups.
Description of intervention	**Individual Interventions** 1. **Text messages**. The text message intervention will be over 8 weeks for each phase and consist of regular (initially twice daily then tapering off gradually as the intervention progresses to 3 x texts a week in the final week) texts. Messages will be a mixture of informative and supportive, and include patient behavioural change techniques. Each automated text will be from named sources (rheumatologist, patient, psychologist and neuropsychiatrist). Participants will be sent the source details at the start, including photos and a link to a recorded video where the sources introduce themselves. The text message intervention will be adapted and improved from patient feedback in the pilot trial. Example texts from the planned programme include: 'Hi [patient name], o*ther people don't always understand how bad the fatigue we get can be. Never feel bad for saying no to doing things when you need to rest!'* – Wendy (fellow patient) *'Please tell your rheumatologist or GP if you're having any mental health problems. Many people with lupus get them, it's nothing to be embarrassed about and your doctors can only help if you tell them'* – Dr Tom (neuropsychiatrist) *The sun can cause a flare in many lupus patients. Please use factor 50 sunscreen, cover up and avoid the sun as much as possible* Prof D'Cruz (rheumatologist) *Hello [name], remembering to take lots of medications can be hard for anyone. If you're struggling, try using a Dossett box, setting alarms or have the tablets next to where you get breakfast so it becomes a routine'* Felix (psychologist).

	Some text messages will also contain links to support or educational sources, or to short videos from each source giving additional advice and support. Text topics have been informed by the INSPIRE study results on the impact of the disease on patient lives and the most common (and/or most distressing) neuropsychiatric symptoms experienced in this patient group, and from the study team's respective experiences. Text intervention group participants (if willing) will also be joined into WhatsApp groups with 3-5 other text intervention participants with guidance provided on providing mutual understanding and support. A researcher will set up each group, provide introductions and initial suggestions for discussion and then leave the group. Groups will also be requested to discuss the intervention and their opinions, and make suggestions for improvements at follow-ups. This will help reduce participants feeling abandoned at the end of the intervention as they may continue with the WhatsApp groups for as long as they wish (outside of the study). **2. Listening support.** This will be provided by The Wren Project, in line with their standard programme of offering listening support (via Zoom) by a trained 'listener' (as opposed to counsellor) to patients with an autoimmune disease. Each Ppt will have fortnightly 50 minute one to one 'talking' sessions over 12 weeks. The focus will be talking about the impact of the disease and coping. **3. Physical activity course** This will be provided by a trained Pilates instructor (Flexifit Pilates) via Zoom. Participants will receive the intervention in groups of 15, twice a week, in 50-minute sessions over 8 weeks via Zoom. Exercises will be tailored to Ppts with chronic diseases with the emphasis on participation, social interaction and enjoyment. **4. Post-study support** Follow-up support will also be available to The Wren intervention Ppts in line with The Wren projects usual follow-up procedures. This consists of joining a group of 'graduate Wrens' with regular contact (if desired) with the organisation and each other. Similarly, Ppts in the physical activity intervention will be offered attendance (at small cost) in weekly sessions outside of the study for people with chronic conditions. This will be following their courses (intervention period) finishing.
Data collection	Baseline survey: On entry into the ADAPT trial prior to being randomised to an intervention or the control group. Follow-up 1: Baseline + 12 weeks. Follow-up 2: Baseline + 6 months to more accurately ascertain potential longer-term effects. In-depth interviews will be carried out with purposively selected participants from questionnaire responses. Interviews will also be carried out during the interventions (in phase 1 only) to assess views of different intervention components, in order to refine the interventions and processes for phase 2.

Analysis	Qualitative - Thematic analysis including using Nvivo 12 software Quantitative – Descriptive and inferential statistics, including multiple regression analysis.

5 Study background and rationale

Systemic autoimmune rheumatic diseases (SARDs) have significant and lifelong negative impacts on patients' physical and mental health, and quality of life. SLE in particular has been found to increase the risk of mental health symptoms (1, 2) which have a major impact on QoL(3). The prevalence of depression in SLE is estimated at 30–50% (1, 2), and one study found that 20–50% of rheumatology patients have psychosocial problems attributable to their disease, which were frequently not discussed with their physician (4). MH problems, ongoing trauma and post-traumatic stress disorder (PTSD) in response to misdiagnoses and/or the impact of chronic illness have been reported in other studies (5, 6).

Although approximately 50% of rheumatology patients in our earlier studies (7, 8) reported either good or excellent support for their disease overall and from their rheumatologist, there were common gaps in care identified. There was a clearly expressed need for more support for patients in coming to terms with a life-changing chronic disease and more consideration of psychosocial needs and quality of life. In addition, a recent study found that the majority of respondents with rheumatic diseases struggled to cope with their condition, yet only 16% had been offered psychological support from the UK National Health Service (9). Time constraints in clinic mean that discussion of MH, QoL and coping/ adaptation strategies can often not be a priority for physicians who are understandably focused on preventing organ damage, and patients are thus required to seek support elsewhere. Rheumatology clinicians in our exploratory work stated they felt psychosocial support and MH was an unmet need that they could not feasibly address within the NHS time constraints.

With the ongoing impact of changes to care from Covid-19 having reduced the frequency of rheumatology appointments for many patients, large back-logs and less contact with clinicians, there has been a widespread sense of abandonment expressed by this patient group (10). There is thus an even greater urgency to ensure (and provide evidence for NHS funding) adequate psychosocial support and patient-education through other means especially as these can be the first casualty of increased physician time constraints (11). Many of this patient group were in the clinically extremely vulnerable classification for Covid-19 risk (12). With Covid-19 becoming endemic, a degree of risk is highly likely to continue long into the future and many of these patients remain very cautious about face-to-face contact. Trialling remote interventions is therefore of key importance and will ensure those who are most fearful and/or vulnerable from infection will not be excluded. In addition to infection risks of face-face interventions, remote interventions may also be preferable to some of the lupus population where high levels of debilitating fatigue are prevalent.

Chang et al carried out a recent systematic review of remote and in-person psychosocial interventions in SLE patients (13). This included a range of interventions, such as different exercise-based activities (14, 15), and counselling (16), of which many demonstrated significant improvements in outcome measures. Outcome measures in previous SARD psychosocial studies have been largely QoL measures, such as SF36, depression and/or anxiety, and disease activity measures. A minority of studies have focused on psychological distress (17) or coping strategies (18). Our current INSPIRE study (unpublished) results suggests that loneliness has a major negative impact on SARD patient QoL. Although this has been explored in other conditions, and Mann et al reported an association between loneliness and onset of depression (19), as far as we know it has not been studied in SLE. Resilience is an important aspect of adapting to living with chronic diseases, yet few studies (20) have assessed resilience in SLE, or the wider SARD population. Therefore, we will be trialling measures of loneliness and resilience in addition to the more commonly assessed QoL, depression and anxiety.

The three interventions to be trialled are:1) An online exercise course, 2) The Wren Project listening support, and 3) a text messaging support programme. The interventions have been selected based

on patient surveys eliciting their priorities for methods of support, and to attempt to fill some of the multiple gaps in the literature identified.

Remote exercise course

Increasing physical activity has been supported in the recent review to inform the 2021 EULAR recommendations for lifestyle improvements in rheumatology patients (21). Significantly improved fatigue scores were found in an aerobic exercise group compared to a control group (22), and another recent study found exercise led to improvements in various outcomes including QoL (23). Importantly, exercise was also found by Kao et al to not exacerbate disease activity in SLE (24). We will be trialling an online (Zoom), combined Pilates and yoga instructor-led course, adapted for patients with SARDs with the focus on MH health and participation. This type of more gentle exercise has been trialled in both SLE (25) and other SARDs (26) with positive findings on physical measures. Our intervention and assessment measures will be focusing more on the Impact on mental and psychosocial health, which are currently very under-researched areas.

Listening therapy

Several studies have assessed effectiveness of formal counselling and cognitive behavioural therapy (27) and mindfulness (28) in SLE. Outside of trials, these types of therapy are often prohibitively expensive to either the NHS or to the individual, making them unlikely to be cost-effective to include as part of SLE care, however effective and acceptable. One of our interventions will therefore be a charity run project, The Wren Project, that provides free listening support to patients with autoimmune diseases, and potentially represents a more sustainable cost-effective method of support. The listening support is provided by trained volunteers with the focus on a safe space for patients to talk about their disease and impact on their lives. Although patients report a high level of satisfaction with the listening support provided by the Wren Project, acceptability and the impact in improving people's lives including in reducing loneliness and increasing resilience has yet to be formally evaluated.

Text message programme

Research indicates mobile health technology in lupus is of increasing interest (29) and Ra et al reported a ''desire [for] increased diversity in the methods of delivering digital SLE information'' (30), yet currently available tools were felt to be of poor quality (29). As far as we are aware, no studies have trialled text messaging support and education in SLE. Evidence of potentially high acceptability of a text programme was found in our Covid and shielding study (31) demonstrating a high acceptability and perception of 'care' and support from Government generic texts to the clinically extremely vulnerable.

We have found a large disparity in patient satisfaction with rheumatology medical care, particularly apparent amongst those living in the devolved nations (7). Educational text messages from the most eminent UK specialists will allow their knowledge to be disseminated to any UK patient, regardless of location, leading to a reduction in inequalities of care. Patient self-management and knowledge will be improved leading to potential improvements in physical outcomes, and the effect on patient MH and feeling supported will likely be enhanced by regular text messages from peers, psychologists and clinicians. The Behavioural Science group at Cambridge has carried out many successful text messaging interventions in a variety of patient groups (32, 33) and will utilise that expertise to develop a programme tailored to the needs of this patient group. Text messaging programmes are extremely cost-effective and once the programme has been designed can be easily incorporated into usual care if the trial is found to be effective.

6. The 'ADAPT' study

6.1 Study aims, objectives and progression

Aim

To assess the acceptability, feasibility and effectiveness of methods of remote psychosocial support for SARDs patients. For the interventions trialled (if effective and acceptable) to be incorporated as an adjunct to usual care.

Objectives

- To trial multiple quality of life and mental health measures to determine the most appropriate primary and secondary outcomes for phase 2.
- To test processes to inform phase 2 effectiveness trial.
- To develop and trial our own ADAPT instrument to more accurately reflect, measure and monitor SARD patient personal, social and medical satisfaction.
- To assess the acceptability (phase 1) and effectiveness (phase 2) of remote psychosocial interventions on the mental health, wellbeing, self-esteem, resilience, loneliness and disease acceptance of patients with systemic autoimmune rheumatic diseases.

Progression of interventions to phase two.

In phase one, we will be evaluating various potential outcome measures for phase two whilst also ascertaining acceptability and feasibility of the three interventions to progress to phase 2. Phase two will be assessing the effectiveness of any interventions that progress to phase 2. Further selection criteria are explained below.

Interventions will only progress to phase two (effectiveness trial) if there is a high degree of acceptability and feasibility demonstrated in phase 1, Thresholds for progression to phase two are:

1. Green: Progress to phase 2 if >75% of phase 1 participants are satisfied/ very satisfied with the support and engaged with the support.
2. Amber: Consider progression to phase 2 with study team, charity, and patient group discussion, and if intervention acceptability and engagement can be feasibly improved, if between 50-75% of participants are satisfied and engaged with the support.
3. Red: Do not progress any intervention where <50% of participants are satisfied and engaged.

In addition, interventions that are found to not be feasible for the providers or the research team to progress to larger numbers in phase 2 will be excluded. Interventions may be trialled together for comparison or may be separate trials with separate control groups for phase two depending on phase one findings.

6.2 Inclusion Criteria

Both phases - Aged 18 years and over

Phase 1: Any INSPIRE (Ethics reference: PRE2021.27) study participant reporting a diagnosis of SLE and requesting on the INSPIRE survey (completed Jul-Sep 23) to be considered for the ADAPT trial.

Phase 2: Reporting a diagnosis of any SARD.

6.3 Participant recruitment

For both the phases, patients who expressed an interest in participating in ADAPT at the end of the INSPIRE survey will be emailed with an ADAPT information sheet to confirm continued interest in participating in ADAPT. They will be randomly selected (until trial numbers filled) and then randomly allocated by the study statistician using block randomisation into one of the intervention or control groups. If INSPIRE study participant responses do not generate sufficient ADAPT participant numbers, additional recruitment will be through online advertising via patient charities and support groups and then randomly allocated to intervention groups. If numbers interested in phase 1 exceed study capacity, those participants will be emailed to be informed they were not randomly selected to

participate in phase 1 but will be invited to apply again for phase 2 if interested. Exact sample sizes for phase 2 will be calculated from phase 1 effectiveness result indications. Phase 1 participants will not be eligible for phase 2 participation.

6.4 Consent

The process for obtaining participant informed consent will be in accordance with ethical guidelines and Good Clinical Practice. Potential participants from the INSPIRE study 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 sent by email to interested INSPIRE study Ppts, and made available online if INSPIRE Ppts do not generate sufficient numbers. There will be an opportunity to ask questions. Consent for both phases of the psychosocial trials (including to potentially be interviewed) will be requested electronically at the start of the baseline questionnaires. Consent for the interview and to be audio-recorded will also be verbally taken at the start of the interview with the consent statements audio recorded.

6.5 Participant withdrawal

Participants may be withdrawn from the intervention groups and/or the whole study either at their own request, at the request of the intervention provider 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 behaviour within their intervention group. Participants whose behaviour is not acceptable or unkind will be initially warned for more minor issues and/or withdrawn from the group by study staff.

6.6 Data collection and participant follow-ups

Data collection will be both quantitative through surveys, and qualitative through open-ended survey responses and in-depth interviews with purposively selected Ppts following each intervention. In addition to the instruments listed below, questions will elicit sociodemographic data and acceptability of the instruments and the interventions. Interviews will explore intervention experiences and acceptability views in depth.

For phase 1 we will be trialling multiple potential outcome measures for phase 2. This includes:

- The UCLA 6 item loneliness scale (RULS-6)
- The Connor Davidson resilience scale
- GAD-7
- PHQ-8
- Our own ADAPT instrument (Appendix 1)
- FACIT-F
- EQ-5D-5L (https://euroqol.org/eq-5d-instruments/eq-5d-5l-about/)

In addition, for phase 2 we will be evaluating health and social care use, and costs borne by patients, measured using a retrospective resource use questionnaire, an adapted version of the Client Receipt Service Inventory (https://www.pssru.ac.uk/csri/what-is-the-csri/). Phase 1 assessment of costs will be qualitative to determine the appropriate categories for phase 2 costings.

Economic analysis

An economic analysis is warranted given the potential economic implications of the interventions, both in terms of the costs they will incur to deliver, and their impact on subsequent health service use. We will estimate costs and outcomes during 'within-trial' period only. Costs will be assessed from the perspective of the NHS and personal social services (PSS), and also from a wider societal perspective, which includes productivity loss and out of pocket costs incurred by participants and their families. We will undertake a cost consequences analysis, which is used to assess a wide range of costs and consequences (effects) and reports them separately (https://www.gov.uk/guidance/cost-consequence-analysis-health-economic-studies).

The economic analysis outcome measures will be EQ-5D-5L scores, quality-adjusted life years (QALYs) and the measures listed above (QALYs will be calculated based on the reported EQ-5D-5L scores using an 'area under the curve' approach). We will undertake a detailed micro-costing of each of the interventions during Phases 1 and 2. To measure other NHS, PSS and broader societal costs in Phase 1 we will undertake qualitative research to identify what cost components to include; these will then be measured retrospectively at each follow-up point in Phase 2. These are likely to include the following NHS contacts:

- GP contacts at the surgery, home or by telephone or videoconferencing
- Practice nurse contacts at the surgery, home or by telephone or videoconferencing
- Emergency Department visits
- Outpatient visits with the Rheumatologist
- Admitted patient stays
- Medications

We will also ask participants about their use of PSS and, in terms of broader societal costs, travel costs for families going to and from NHS visits, days taken off work, and any other out-of-pocket costs incurred (e.g., for medications or home adaptations).

Unit costs will be obtained from published sources and inflated where appropriate, before being applied to the volume of resource use data to calculate costs.

We will also be obtaining the level and impact of fatigue, pain, cognitive dysfunction on their lives and obtaining a self-assessment of level of disease activity.

An additional measure for the physical activity component will be a short physical ability test as measured by the flexifit instructor to include: strength, mobility and stamina.

Follow-ups

Follow-up 1 - Baseline+ 12 weeks

Follow-up 2 - Baseline + 6 months

Participants will be sent up to 3 email reminders for non-response to the follow-up questionnaires.

6.7 Selection of outcome measures for phase 2

Phase 2 primary and secondary outcome measures will be selected from the analysis of phase 1 quantitative and qualitative results. Following phase 1 analysis, the multidisciplinary ADAPT study team will meet to decide which intervention(s) will proceed to phase 2 and which outcome measures to select for phase 2. The selection criteria will include (with most weight given to patient views on importance):

1. Acceptability and perceived importance and relevance of each measure to patients. These will be assessed quantitively by questions on the survey about each instrument, and qualitatively during interviews. Any measures that are rated as unacceptable or irrelevant by >25% of participants will be excluded. Participants will be asked to rank the measures in terms of importance to them and a mean score calculated. The top 3 scoring outcome measures will be discussed, taking into account additional patient views from interviews, team views and sensitivity as detailed below to select one measure for the primary outcome measure. Other measures will be considered for inclusion as secondary outcomes, by considering the ordering of patient scores, and patient willingness to complete different lengths of follow-up surveys. A minimum of one phase 1 outcome measure will be excluded for phase 2.

2. Sensitivity of each measure to change by psychosocial interventions. Short-term effectiveness of each intervention will be measured by using the within-person change from baseline to follow-up one, for each phase 1 instrument.

We will be trialling The ADAPT instrument (Appendix 1), a new disease adapting tool which includes 21 items incorporating: disease acceptance, coping, control, empowerment, knowledge, participation in life and satisfaction with life and medical care. Its validity and reliability will also be tested in this study. The factorial structure of this tool will be investigated using exploratory and confirmatory factor analysis, while its reliability will be tested using the Cronbach's alpha coefficient. For the validation of this tool, we will also calculate its correlation with other previously validated tools (The Connor Davidson resilience scale and the PHQ depression scale), using the Pearson correlation coefficient. If acceptable and considered to be relevant to patients, ADAPT (personal and social domains) will be considered as a primary or secondary outcome. EQ-5D-5L will be a secondary outcome regardless of phase 1 results due to the importance to the NHS. FACIT-F (unless unacceptable to >25% of respondents) will be a (primary or secondary) outcome measure for the stage two physical activity trial as fatigue is a key target of this aspect of the trial to improve.

6.7 Analysis and outcome measures

Qualitative – The qualitative data will be analysed using thematic analysis and NVivo12 for managing and coding data and follow the criteria for reporting qualitative research (COREQ) . Briefly, the stages of analysis involved in our qualitative research involves an inductive-deductive process, including: (i) immersion in the data where transcripts and subsequent coded sections are repeatedly read and discussed by multiple team members to improve reliability, and ensure multiple perspectives and possible interpretations are represented; (ii) a coding (classification) scheme is developed, trialled, discussed and refined, and each line of qualitative data is coded; and (iii) participant extracts for each code are combined. The key themes emerge directly from the data and team discussions, including with multiple patients and clinicians.

Consideration of deviant cases, member checking, triangulation of quantitative and qualitative results and multiple perspectives will be conducted to improve validity.

Quantitative - Transferral of online data from Qualtrics online survey platform and manual data entry, data cleaning, recoding and generation of new variables onto SPSS V26.

Descriptive statistics (means, medians, Interquartile range (IQR), modes and range for continuous data and percentages for categorical data) will be used to describe the demographic, survey and trial data. Contingency tables will be used to describe the multivariate frequency distribution of categorical variables. Bar charts, histograms and boxplots will be used additionally to the above-mentioned statistics and in order to ensure the results are easily accessible to patients, clinicians and policy makers. We will assess the association between variables of interest using Pearson correlation coefficient, T-tests, Wilcoxon-Mann Whitney tests, Chi-Square tests and Kruskal Wallis tests. Regression models will be used to assess the effect of multiple variables on specific outcomes. The within-person change from the baseline to follow-ups and the primary endpoint will also be investigated for each outcome measure. Multiple regression analysis will be used to test differences between groups on multiple measures.

We will also assess the association between pre-defined pairs of variables of interest) using Pearson correlation coefficient with Chi- Square test. T-tests, Wilcoxon-Mann Whitney tests, Chi-Square tests, Kruskal Wallis tests and one-way/factorial ANOVA will be used appropriately to compare the mean scores, frequencies and impact between groups of patients. Regression models will be used to assess the effect of multiple variables on specific outcomes. As this is a very unexplored area, some additional exploratory analysis will occur in addition to pre-specified measures in order to identify priorities for future research.

Prior to the main analysis, we will conduct data cleaning. Percentages of invalid values, outliers and missing data will be reported. We will also investigate any patterns of missing data. Where appropriate, theoretical and/or clinical criteria will be used to identify invalid values or outliers. Depending on their type and prevalence we will decide on the most appropriate way of addressing. Our options include data exclusion from the rest of the analysis, data replacement with mean or mode values, or data inclusion as separate category (in case of missing data). Our primary option is to conduct "complete-case" analyses. We will not use multiple imputation for missing data. In case of highly prevalent missing data (more than 10% of the sample), sensitivities analyses based on the other option of missing data addressing will be used to assess the robustness of our findings.

7. Study Management and Governance Arrangements

7.1 Research Team

Co-Principal Investigators:

Prof Stephen Morris and Melanie Sloan

Department of Public Health and Primary Care
University of Cambridge
Forvie Site, Robinson Way
Cambridge, CB2 0SR
Emails: sm2428@medschl.cam.ac.uk and mas@medschl.cam.ac.uk
Tel: 07975799052

Study team, advisors and collaborators:
James Brimicombe, Department of Public Health, Cambridge University
Michael Bosley, Patient Partner
Professor David D'Cruz, SLE specialist, Louise Cootes lupus unit and Kings College London
Wendy Diment, Patient Partner
Dr Elliott Lever, Rheumatology consultant, Royal Free Hospital
Prof Felix Naughton, health psychologist, School of Health Sciences, University of East Anglia
Dr Farhana Mann, Psychiatrist, University College London
Efhalia Massou, Department of Public Health, Cambridge
Kate Middleton, Patient Partner and CEO of The Wren Project
Dr Thomas Pollak, Neuropsychiatrist, Kings College London and South London and Maudsley NHS Foundation Trust
Dr Chris Wincup, Rheumatology consultant, Kings College London

Advisory Group:
Professor Caroline Gordon, Birmingham (lupus specialist)
Lynn Holloway – Patient member
Professor David Jayne, Addenbrookes (Vasculitis and nephritis consultant)
Ali Seamer- Patient member

The study 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 monthly meetings to review ongoing progress of the study and any amendments required. The team will include patient and clinician advisors. An advisory board led by Professor David Jayne (Addenbrookes) and containing two patient representatives will meet with the study team a minimum of 3 times including: prior to the interventions commencing, during the intervention period, and on deciding which interventions to proceed to phase 2. They will meet on additional occasions should any difficulties arise at any stage.

The Principal Investigators have 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 and The Lupus Trust.

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 captured anonymously – identified only by the unique participant ID – and converted to 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) within a firewall protected network (LAN), certified to ISO-27001 security. At the close of recruitment, all data on the Qualtrics online version will be deleted. Once uploaded to the SDHS, any personal information will be accessible only by the data manager using a two-factor authentication (password and security fob). Questionnaire data will be pseudo-anonymised – identified by the participant ID – and transferred outside of the SDHS for data analysis in SPSS.

A document linking participant ID numbers and contact details will be stored on the SDHS, accessible only by the data manager (JB), and principal investigators (MS and SM). This will be stored until six months after publication and then securely wiped. Each participant will be assigned a unique study identity code for use on study documents and analysis sets. All potentially identifying material will be removed. The data manager (JB) 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.

Interviews will be audio recorded and transcribed verbatim. All potentially identifying material will be removed from transcripts and Ppts will be assigned a study identity code. Once transcripts are complete and checked, the original recordings will be wiped within six months of the end of the study.

All data will be kept and processed in accordance with the General Data Protection Regulation (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 (e.g. recruiting before consent)
- equipment failure
- aggressive/ unacceptable behaviour of a participant towards the support group, researcher, staff or others.
- Responses highlight 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 any team member becoming aware of the incident.

7.6 Ethical approval

Ethical review has been obtained from the Cambridge Psychology Research Ethics Committee.

7.7 PPI Involvement

Individuals and focus groups of systemic autoimmune rheumatic disease patients, approached through online forums and support groups, have heavily assisted with the development of the study.

Ongoing discussions with patients, rheumatologists and experts in the field will inform the further development of follow up studies. Five patients with autoimmune rheumatic diseases 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 are equal members of the research team and will be involved throughout the studies. Charity leaders have advised on the surveys and interventions and will be consulted throughout.

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 relevant rheumatology charities.

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

7.9 Proposed study timetable and proposed outputs

	2023			**2024**				**2025**
	Jan 2023	April 23	May-Dec 23	Jan-Mar 24	Apr-Jul 24	Aug-Oct 24	Nov - Dec 24	2025
Produce draft protocol	X							
Finalise participant information sheets and surveys	X							
Submit ethics proposal	X							
Trial surveys	X							
INSPIRE Ppts who expressed interest in ADAPT contacted and randomised if consenting to participate		X						
Interventions commence. Text messages and controls: All commence in /May 23 The Wren project: 5 ppts commence intervention per month Online exercise: First group of 15 ppts commences in Apr, second group in Sep 23			X					
Interviews with selected participants		X	X	X				

Follow-ups at individual ppts F-up 1 and 2 points			X					
Final follow-up 2s for later intervention ppts (initially controls)				X				
Initial analysis and assessment of adaptions to interventions required for phase 2, and development of stage 2 interventions				X	X			
Phase 2 commences						X		
Phase 2 follow-ups							X	X
Quantitative and overall analysis (separate analysis for each phase and combined final analysis) and draft papers					X	X	X	X
Qualitative analysis (ongoing throughout interventions and post-intervention in-depth interviews		X	X	X	X	X	X	X
Publications						X		X

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APPENDIX 1:

Adapt survey (our own ADAPT tool)

Please move the sliders to where best fits how you feel (please consider how you have felt over the past month on average)

Personal

1. **Adapting**. How well do you feel you have adapted to the changes in your life from having a chronic disease: 0= Not adapted at all to 100= Fully adapted

2. **Coping**. How well do you feel you cope mentally with the challenges from your disease: 0= Not coping at all to 100 = Fully coping

3. **Control.** How in control of your life do you feel: 0= No control over my life to 100 = Full control

4. **Knowledge.** How much knowledge do you feel you have about your disease: 0= No knowledge to 100 = Full knowledge of my disease

5. **Confidence in self-managing**. How confident do you feel in self-managing your disease symptoms where appropriate: 0= No confidence to 100 = Fully confident to self-manage my symptoms where appropriate

6. **Self-esteem.** How do you feel your self-esteem is (confident in your own worth): 0=I feel completely worthless to 100=I am fully confident in my own worth

7. **Satisfaction** with life. H**ow do you feel OVERALL** in terms of being satisfied with your life: 0= completely unsatisfied to 100 = Fully satisfied

Social

8. **Participation** in everyday life – activities, socialising etc. How much do you feel you participate in everyday life: 0= No participation at all to 100= fully participate

9. **Satisfaction with level of participation in life** - How satisfied you are with your current level of participation in everyday life: 0= Not satisfied at all to 100= Fully satisfied

10. **Loneliness.** How lonely do you feel: 0= not at lonely to 100= completely lonely

11. **Community**. How much do you feel a part of a supportive community. 0=not a part of a community at all to 100 = fully a part of a supportive community

12. **Social support.** How certain are you that you would get practical and/or emotional support from friend/family/neighbours if you need it. 0=certain you would not get any support if needed to 100=certain you would get support if needed.

Medical support

13. **Medical security**. How medically secure (whether they will be there when you need them and help you) do you feel with your clinicians: 0=completely abandoned to 100 = completely medically secure

14. **Trust- own clinicians.** How much do you trust your OWN clinicians: 0=complete distrust to 100=complete trust

15. **Trust- general.** How much do you trust clinicians in GENERAL: 0=complete distrust to 100=complete trust

16. **Listening.** How well do you feel your clinicians listen to your symptoms. 0=Don't listen at all to 100= Fully listen

17. **Belief.** How much do you feel your clinicians believe the symptoms you report to them. 0=Don't feel believed at all to 100=Feel completely believed.

18. **Knowledge.** How much knowledge you feel your clinicians have about your disease. 0= No knowledge to 100= full knowledge

19. **Confidence in medical relationships.** How confident do you feel in saying your symptoms and expressing your needs to your doctors: 0=No confidence at all to 100= Fully confident

20. **Teamwork.** How well do you feel your clinicians view you as a valuable and knowledgeable part of the team in deciding on your care, plans and treatment together: 0= No teamwork to 100=full teamwork

21. **Teamwork.** How well do you feel your clinicians work with other clinicians in your care. 0=no teamwork at all to 100=full teamwork

22. **Satisfaction with care.** How do you feel OVERALL in terms of being satisfied with your medical care: 0=completely unsatisfied to 100=completely satisfied