

Pilot study of feasibility and acceptability of PREVAIL

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Principal Investigator: Louise M Thoma, PT DPT PhD

Sponsor: University of North Carolina at Chapel Hill

Grant Title: Helping Adults with RA PREVAIL: Developing a model to Preserve Valued Activities in Life

Grant Number: 1 K23 AR079037

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Version Number: 5.0

Summary of Changes from Previous Version:

Affected Section(s)	Summary of Revisions Made	Rationale
1.2 Schema	Visit 4 extended from “Day 15” to “Day 42”.	We will continue to target reaching participants within 2 weeks of their routine visit to schedule their call, but extending this window allows for reasons people may not be able to complete their call within 2 weeks (Ex. traveling for summer vacation).

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STATEMENT OF COMPLIANCE

The trial will be carried out in accordance with International Council on Harmonisation Good Clinical Practice (ICH GCP) and the following:

- United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 312, and/or 21 CFR Part 812).

National Institutes of Health (NIH)-funded investigators and clinical trial site staff who are responsible for the conduct, management, or oversight of NIH-funded clinical trials have completed Human Subjects Protection and ICH GCP Training.

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the Institutional Review Board (IRB) for review and approval. Approval of both the protocol and the consent form(s) must be obtained before any participant is consented. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form(s) will be IRB approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

INVESTIGATOR'S SIGNATURE

The signature below constitutes the approval of this protocol and provides the necessary assurances that this study will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable US federal regulations and ICH guidelines.

Principal Investigator or Clinical Site Investigator:

Signed: _____ Date: _____
Name: Louise Thoma, PT DPT PhD

Title: Assistant Professor

Investigator Contact Information

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1.1 SYNOPSIS

Title: Pilot study of feasibility and acceptability of PREVAIL
Grant Number: 1 K23 AR079037
Study Description: The overall objective of this pilot study is to determine the feasibility and acceptability of the PREVAIL model of care among at least 50 adults with rheumatoid arthritis (RA). The PREVAIL model of care seeks to systematically integrate exercise guidance and rehabilitation referral into routine rheumatology care for adults with RA. Participants will be screened and classified into disability categories to triage levels of care related to physical therapy and exercise guidance. Assessments will be conducted at baseline and 3 months to determine feasibility and acceptability, refine the model of care, and inform the design of a larger trial.

Objectives*: Aim 1: Determine feasibility of the PREVAIL model of care for adults with RA.
Aim 2: Assess patient acceptability of the PREVAIL model of care for adults with RA.

Endpoints*: Primary Endpoint:

- % of participants who receive the PREVAIL model of care essential components (Feasible if $\geq 70\%$ of participants receive the essential components)
- % of participants who access the exercise resource at least one time (Feasible if $\geq 70\%$ of participants access website)
- Average score on the Feasibility of Intervention Measure (Feasible if FIM ≥ 4 out of 5)
- Average score on the Acceptability of Intervention Measure (Acceptable if AIM ≥ 4 out of 5)

Secondary Endpoints:

- % of recruitment pool who enroll in the study (Feasible if $\geq 15\%$)
- % of participants that complete follow-up assessments (Feasible if $\geq 90\%$)

Exploratory Endpoints: Exploratory outcomes include the Intervention Appropriateness Measure (IAM), Short Valued Life Activities (SVLA) Questionnaire, Clinical Disease Activity Index (CDAI) Patient Global Assessment (PGA), Routine Assessment of Patient Index Data (RAPID3), PROMIS Pain Interference, Fatigue, Physical Function, and Ability to Participate in Social Roles and Activities Short Forms, Stopping Elderly Accidents, Deaths, and Injuries (STEADI) Fall Risk Questions, Life Space Questionnaire (LSQ), Self-Efficacy for Exercise (SEE) scale, Tampa Scale for Kinesiophobia (TSK), Expectation for Treatment Scale (ETS), and questions on physical activity and exercise participation, functional status, rehabilitation experience, and intervention utilization.

Study Population: $N \geq 50$ participants with RA scheduled to receive routine treatment from a UNC Rheumatology clinician who are not currently or recently utilizing physical therapy services.

Phase* or Stage: Single-Group feasibility pilot trial

Description of Sites Enrolling Participants: We will recruit patients from the UNC Rheumatology Clinic.

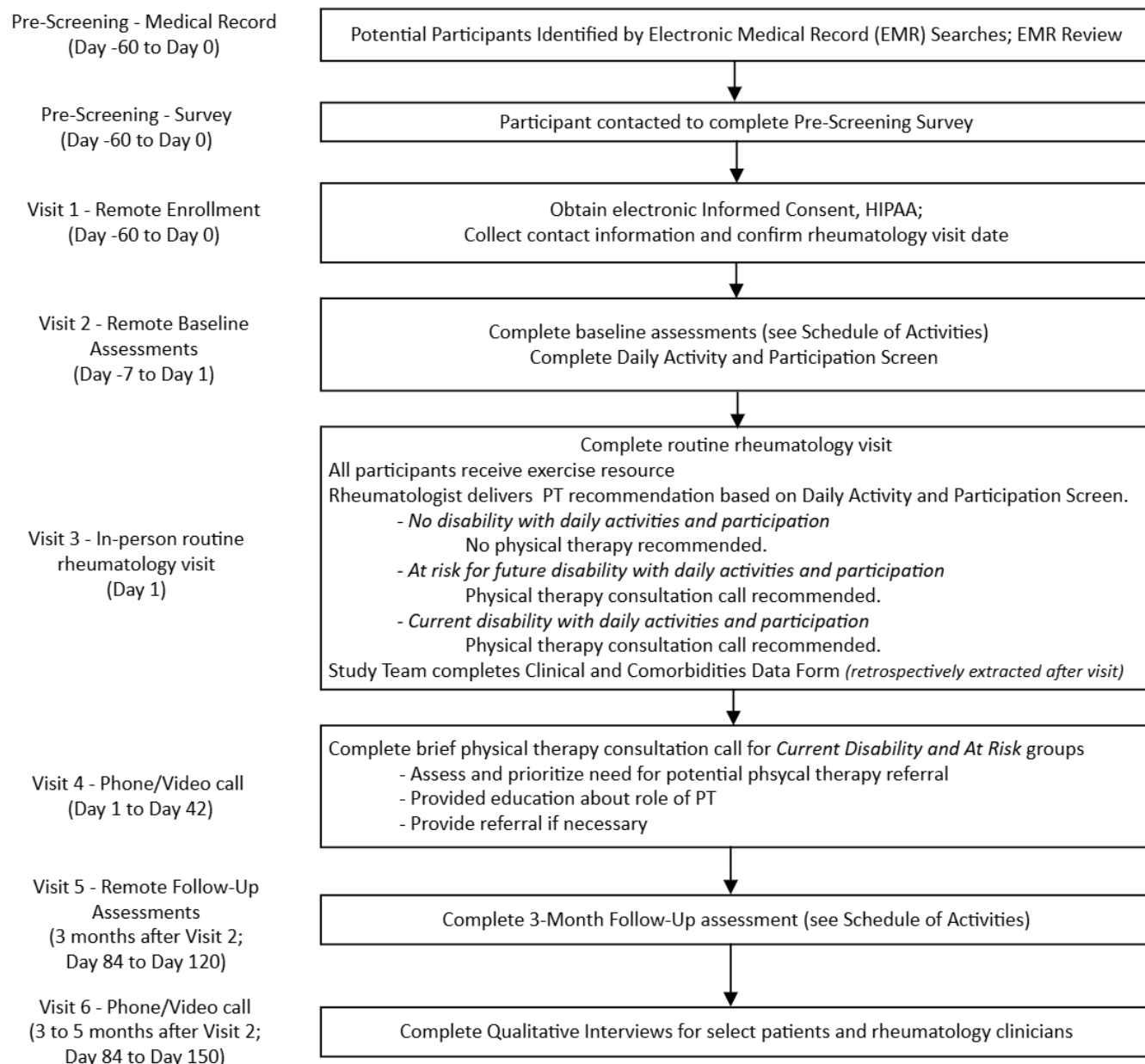
Description of Study Intervention: The PREVAIL model of care includes (1) a screening tool, the “Daily Activity and Participation Screen” (DAPS), completed one week prior to a routine rheumatology visit, (2) a recommendation to a participating rheumatology clinician based on the screening tool results to provide an exercise resource and/or recommend a PT consultation call at the participants routine rheumatology visit, (3) an exercise resource (PREVAIL Website) provided by the rheumatology clinician to all participants, (4) if recommended for it, a brief consultation call with a PT who is a member of the study team to gather information to determine level of priority for PT referral, and (5) if necessary, a referral for physical therapy. Components 1, 2, and 3 are essential components of the PREVAIL model of care.

Study Duration*: 1 year

Participant Duration: 4-6 months

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1.2 SCHEMA

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1.3 SCHEDULE OF ACTIVITIES

	Pre-Screening	Visit 1 Remote enrollment	Visit 2 Remote baseline assessment	Visit 3 In-person routine rheumatology visit	Visit 4 Phone/video call	Visit 5 Remote follow-up assessment	Visit 6 Phone/video call
EMR Review Eligibility	X						
Pre-screening Survey	X						
Informed Consent & HIPAA		X					
Demographic Questionnaire			X				
Comorbidities and Medication EMR Extraction				X			
Clinical Questionnaire			X			X	
Assessments							
Rehabilitation experience questions			X				
Routine Assessment of Patient Index Data 3 (RAPID3)			X			X	
Clinical Disease Activity Index (CDAI) Patient Global Assessment (CDAI-PGA)			X			X	
Short Valued Life Activities (SVLA)			X			X	
PROMIS Pain Interference Short Form (PROMIS PI6b)			X			X	
PROMIS Fatigue Short Form (PROMIS F7a)			X			X	
PROMIS Physical Function Short Form (PROMIS PF10a)			X			X	
Stopping Elderly Accidents, Deaths, and Injuries (STEADI) Fall Risk Questions			X			X	
PROMIS Ability to Participate in Social Roles and Activities Short Form (PROMIS APSRA8a)			X			X	
Life Space Questionnaire (LSQ)			X			X	
Physical activity, exercise, and sleep questions			X			X	
Self-Efficacy for Exercise (SEE) Scale			X			X	
Tampa Scale for Kinesiophobia (TSK)			X			X	
Functional status questions			X			X	
Expectation for Treatment Scale (ETS)			X			X	
Feasibility of Intervention Measure (FIM)						X	
Acceptability of Intervention Measure (AIM)						X	
Intervention Appropriateness Measure (IAM)						X	
Intervention utilization questions						X	
Qualitative Interview							X
Intervention (PREVAIL Model of Care Components)							
Daily Activity and Participation Screen (DAPS) – Uses items from SVLA			X				
Recommendation for Exercise Resource Website				X			
Recommendation for PT consultation call				X			
PT Consultation Call					X		
Safety monitoring							
Adverse Event Reporting			X	X	X	X	X

2.1 STUDY RATIONALE AND BACKGROUND

2.1.1 CLINICAL SIGNIFICANCE

Disability prevalence in adults with rheumatoid arthritis (RA) is higher than the general population^{1,2}. Early after RA diagnosis, function typically improves due to drugs that reduce joint inflammation and destruction. However, initial improvement is usually followed by progressive functional decline³, leading to disability, unemployment, and poor quality of life^{4,5}. The proportion of patients affected by disability depends on the impacted activities. Adults with RA have disability with *obligatory* activities, or those required for survival and self-sufficiency^{6,7}, at twice the rate as adults without RA². Disability prevalence and costs rise when those with RA demonstrate difficulty with *committed* activities, or those required for productive social roles^{6,7} like caregiving and employment. Just two years after symptom onset, 20% of adults with RA are unemployed due to the disease⁸, and RA-related functional limitations, work disability, and quality of life deterioration cost over \$20 billion/year⁹. Lost household productivity costs 7x more than lost work productivity¹⁰. Furthermore, nearly all adults with RA (92%¹¹) report difficulty with *discretionary* activities (leisure activities; e.g. socializing, exercise, and community engagement^{6,7}). While loss with *obligatory* activities limits independence, losing participation in *committed* and *discretionary* activities is detrimental to quality of life and comorbidity^{12,13}. Reducing disability among adults with RA will preserve quality of life and reduce costs from RA.

Disability persists despite pharmacologic innovations 20 years ago that improved disease control. RA disease management was revolutionized in the early 2000s with innovations in drug regimens and the advent of biologic therapies¹⁴. These advances resulted in more patients with low disease activity or remission^{4,5,15-18}. However, these improvements in disease control, which slowed joint erosion and inflammation^{4,16,17,19,20}, did not translate to comparable improvements in disability and function^{4,16}. Pain persists in 58% of patients after 3 months on a disease modifying anti-rheumatic drug, including 29% of those who responded well²¹. Unlike disease activity markers, pain, weakness, and fatigue are primary contributors to function and disability, and are not well addressed with pharmaceuticals^{11,18,22}. Even in those with low disease activity, functional limitation and disability present at higher rates than the general population²³⁻²⁷, gradually worsen over time^{5,28,29}, and often lead to premature job loss³⁰. In summary, pharmacological strategies alone are inadequate to treat adults with RA.

2.1.2 SCIENTIFIC RATIONALE

Physical therapy (PT) and exercise interventions reduce disability³¹ by improving pain, weakness, and fatigue^{32,33}. Despite continued high prevalence of functional limitations, often related to pain, weakness, and/or fatigue, PT and exercise are underutilized for adults with RA in the US³⁴⁻³⁶. These low utilization rates do not align with the high disability rate (up to 92%¹¹). Rheumatologists are without clear guidance regarding when to refer for PT^{37,38}, which may contribute to low utilization.

Physical activity and exercise are unequivocally beneficial for adults with RA^{32,39-41}, yet recommendations from providers are often limited, generic, or vague⁴²⁻⁴⁵. Adults with RA have lower physical activity levels⁴⁶ than the general population, including those with low disease activity⁴⁷. Patients want information from a trusted expert who understands RA⁴⁴. Further, receiving a provider recommendation for exercise is strongly associated with engagement⁴⁵. Systematically integrating exercise recommendations, tailored to RA, in routine RA care is needed to increase exercise and delay disability.

We developed a model of care to PREserve Valued Activities in Life (PREVAIL) and facilitate the integration of PT for adults with RA who need it. The preliminary version of the PREVAIL model of care was developed

based on current literature, which consistently identified a need for non-pharmacological treatment strategies for RA^{15,48-50}, and had three primary components: (1) Disability Screening (now referred to as Daily Activity and Participation Screening). Participants completed the S-VLA and were categorized into a disability group based on the results. This component was critical because there are currently no systematic methods to guide intervention in RA care in the US. (2) Recommendation for Referral to PT. The rheumatology clinician received a recommendation to refer to PT for patients with or at risk for disability. This component was critical because PT interventions improve RA impairments associated with disability. (3). Exercise Guidance. All participants received evidence-based, RA-specific exercise guidance via web-based videos and links to self-directed and community resources that were developed and curated by previous research. This component was critical because exercise preserves function in adults with RA, and these patients want exercise guidance from trusted sources that acknowledge their RA.

2.1.3 PRIOR STUDIES AND RATIONALE FOR DEVELOPMENT

This study builds on preparatory survey and interview studies to help refine the PREVAIL model of care before testing in this pilot clinical trial. Key findings resulting in changes to the PREVAIL model of care and study design for the pilot clinical trial are summarized below:

Key findings from the survey study. In the survey study, patients with RA (n=310) completed the proposed screening tool, which was intended to categorize patients into disability categories to help direct rehabilitation referral and exercise guidance. Based on prior work⁵¹, we expected the distribution of the adults with established RA into disability categories to be 48% current disability, 16% at risk for disability, and 36% with no disability. Since the survey study could also include patients with early RA, we expected that the proportions may shift towards less disability. In contrast, the distribution of our survey sample was 81% current disability, 10% at risk for disability, and 9% no disability. The survey sample was recruited from the same potential patient pool as the planned pilot clinical trial, which suggested that nearly all participants (91%) of the sample would receive a referral to physical therapy. This was much higher than expected.

Changes to the pilot trial in response to the survey study. We made changes to the PREVAIL model of care for the pilot clinical trial to enable us to gather more information and further refine the screening tool to prioritize referrals for judicious use of health services. Briefly, we are adding an interim physical therapy consultation call as the initial referral from rheumatology. In the physical therapy consultation call, a physical therapist will have a brief (10-15 minutes) conversation with the participant to determine the priority level (high, moderate, low) for physical therapy referral using clinical judgement. The calls will be recorded to code what content was addressed when informing priority level. This will give us a clinical standard, against which we can validate and refine the screening tool. We will also collect several complementary and alternative outcome measures in the baseline assessment that may replace or add to the current screening tool with the goal the future models of care do not require a resource-intensive physical therapy consultation call.

Key findings from the interview study. We interviewed 24 adults with RA, 6 rheumatology clinicians and 6 physical therapists to learn about the initial feasibility and acceptability of the PREVAIL model of care, with the goal of refining the model of care for this pilot clinical trial. Patients and clinicians had predominantly positive reactions to the PREVAIL model of care. Patients particularly expressed enthusiasm for integrating rehabilitation early into routine care. For patients without prior experience with PT, a lack of knowledge of rehabilitation contributed to some uncertainty. For those with rehabilitation experience unrelated to RA, their perspectives of rehabilitation were often limited to their experiences. Most patients trusted their clinicians' recommendations. Rheumatology clinicians perceived rehabilitation in rheumatology care as a way to treat non-inflammatory musculoskeletal concerns. Some clinicians expressed hesitation but curiosity regarding the value of rehabilitation early after RA diagnosis. Physical therapists expressed confidence in addressing functional limitations in adults with RA; those with less experience with RA desired brief educational resources. Patients and clinicians discussed time constraints, costs, and travel as potential barriers to rehabilitation. Time

constraints included the time necessary before appointments to complete the survey materials. Overall, the PREVAIL model of care was perceived as a feasible and acceptable approach to addressing the current barriers to rehabilitation in routine RA care.

Changes to the pilot trial in response to the interview study. Using the interview results, we refined the model of care and pilot study design. We will deploy the survey one week before the rheumatology visit to relieve the stress of not having the time to thoroughly complete all survey materials. We also added an interim physical therapy consultation call in the pilot trial. The call will enable us to learn more about patients' educational needs and guide the prioritization for immediate physical therapy referral to further refine the model of care.

2.2 RISK/BENEFIT ASSESSMENT

2.2.1 KNOWN POTENTIAL RISKS

Emotional distress: It is unlikely that the types of questions participants will be asked in this study will result in emotional distress, but we understand that participants may be uncomfortable with answering questions about some aspect of their health or other things about them. To minimize this risk, we will let participants know they may choose not to answer any study questions and can still be involved in the study.

Breach of confidentiality: We will be collecting some elements of personal health information necessary for the study. To minimize breaches of confidentiality, all data will be stored on a secure UNC server or a UNC IRB approved platform for sharing protected health information (PHI). Any paper information will be stored in locked filing cabinets in a locked office. Only approved study personnel will have access to this data. Personal health information (e.g. patient name and contact information only) will only be shared with approved study team members. Any information shared among approved UNC study team members will be done verbally, by phone, by encrypted email or by another UNC IRB approved platform for sharing PHI.

Risks of Exercise: Participants will be provided with exercise resources. The resource will be tailored to individuals with RA and each participant can choose how to use the resource. However, exercise may be associated with risk of injury, muscle soreness, and temporary joint pain. In general, the risk of these events with moderate physical activity is very low.

2.2.2 KNOWN POTENTIAL BENEFITS

Participants may experience improvements in pain, physical function or other symptoms related to RA from following through with exercise and/or physical therapy recommendations. It is possible that this study may not benefit participants directly, but participation in this study may lead to information that can benefit other patients with RA, as well as their health care clinicians.

2.2.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

This is a minimal risk study with physical risks comparable to those that would be encountered with general exercise advice. We do not anticipate any significant psychological, social, financial, or legal risks to be associated with participation in this study. Given the low rate of rehabilitation utilization for adults with RA and consistent desire for more tailored exercise recommendations, we believe the value of the information to be gained outweighs the risks of participation in the study.

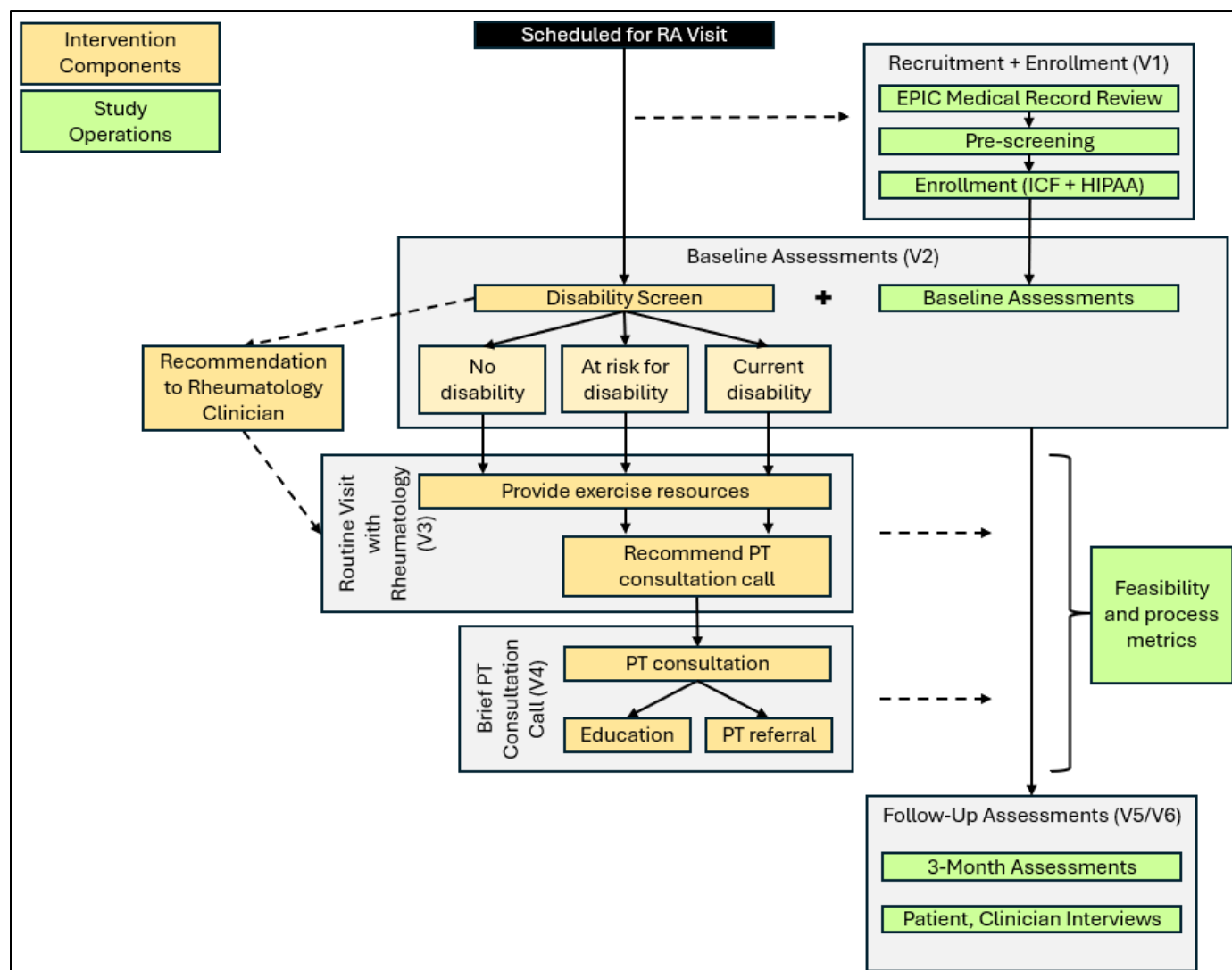
3 STUDY OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS
Primary		
Determine feasibility of the PREVAIL model of care for adults with RA.	• % of participants who receive the PREVAIL model of care essential components (Feasible if $\geq 70\%$ of participants receive the essential components) • % of participants who access the exercise resource at least one time (Feasible if $\geq 70\%$ of participants access website) • Average score on the Feasibility of Intervention Measure (Feasible if FIM ≥ 4 out of 5)	These metrics are essential for assessing the feasibility of the PREVAIL model of care from the patient perspective.
Assess patient acceptability of the PREVAIL model of care for adults with RA.	• Average score on the Acceptability of Intervention Measure (Acceptable if AIM ≥ 4 out of 5)	These metrics are essential for assessing the acceptability of the PREVAIL model of care from the patient perspective.
Secondary		
Determine feasibility of testing the PREVAIL model of care in future studies.	• % of recruitment pool who enroll in the study (Feasible if $\geq 15\%$) • % of participants that complete follow-up assessments (Feasible if $\geq 90\%$)	These metrics are essential for assessing the feasibility of conducting a larger scale trial of the PREVAIL model of care.
Tertiary / Exploratory		
Obtain patient-reported outcome data to refine the PREVAIL model of care.	Exploratory outcomes include the Intervention Appropriateness Measure (IAM), Short Valued Life Activities (SVLA) Questionnaire, Clinical Disease Activity Index (CDAI) Patient Global Assessment (PGA), Routine Assessment of Patient Index Data (RAPID3), PROMIS Pain Interference, Fatigue, Physical Function, and Ability to Participate in Social Roles and Activities Short Forms, Stopping Elderly Accidents, Deaths, and Injuries (STEADI) Fall Risk Questions, Life Space Questionnaire (LSQ), Self-Efficacy for Exercise (SEE) scale, Tampa Scale for Kinesiophobia (TSK), Expectation for Treatment Scale (ETS), and questions on physical activity and exercise participation, functional status, rehabilitation experience, and intervention utilization.	The exploratory patient-reported outcomes quantify RA disease activity, functional limitation, disease symptoms, physical activity levels, and psychosocial factors associated with exercise and movement. They are important for helping us refine the PREVAIL model of care, including the DAPS tool, for model improvement and planning for future trials.

4.1 OVERALL DESIGN

The overall aim of this study is to conduct a pilot trial of the PREVAIL model of care to determine feasibility and acceptability among adults with RA. This will be a single group feasibility pilot study with at least 50 patients with RA. Assessments will occur at baseline and 3-month follow-up.

Figure 1. PREVAIL Model of Care Invention and Study Procedures. This diagram depicts study visits (grey boxes), the intervention components of the PREVAIL model (yellow boxes), and the study operations (green boxes) that will enable us to examine the feasibility of the model and study processes.



4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

This study design will provide the research team with information regarding the feasibility and acceptability of the current PREVAIL model of care, as well as sufficient data to optimize and refine the PREVAIL model of care and study design and processes for future effectiveness and implementation trials.

4.3 JUSTIFICATION FOR INTERVENTION

Rehabilitation referrals are low among rheumatologists. This research addresses a clear clinical need to facilitate the integration of rehabilitation into rheumatology care by helping rheumatology clinicians identify individuals who will benefit most from rehabilitation. A model that effectively integrates rehabilitation and therapeutic exercise into routine RA care is required to enable patients to preserve existing function and delay disability.

4.4 END-OF-STUDY DEFINITION

A participant is considered to have completed the study if they complete the 3-month follow-up assessment. Some participants will be selected for a qualitative interview after completing the follow-up assessments, but participation is not required for the study to be considered complete. The study will stop enrolling participants when at least 50 patients have enrolled AND at least 10 participants receive a referral to physical therapy after the consultation call. Both criteria must be met in order to develop model of care pathway estimates for future trials.

5 STUDY POPULATION

5.1 INCLUSION CRITERIA

Participants for this trial will be patients over the age of 18 with a clinician diagnosis of RA who are receiving routine care from a UNC Rheumatology clinician and have not attended any physical therapy in the last 6 months. We will identify our patient pool for recruitment as patients with an International Classification of Diseases 10 (ICD 10) code for RA and upcoming scheduled visit with a UNC Rheumatology clinician for a routine follow up.

5.2 EXCLUSION CRITERIA

Exclusion Criteria and Sources of Information		
	Data source	
Criterion	Medical record review	Pre-screening survey
No documented diagnosis of RA	X	
Under the age of 18	X	
Significant cognitive impairment	X	
Condition that restricts ability to complete surveys and patient reported outcomes	X	
Severe hearing or visual impairment	X	
Serious/terminal illness as indicated by referral to hospice or palliative care	X	
Current participation in other study related to RA	X	X
Current or recent (within the last 6 months) participation in physical therapy	X	X
Unable to speak or read English	X	X
Recent (within the last 6 months) major surgery requiring overnight hospital admission and/or resulting in functional loss, requiring rehabilitation".	X	X
Upcoming (within the next 6 months) major surgery requiring overnight hospital admission and/or resulting in functional loss, requiring rehabilitation".	X	X

5.3 LIFESTYLE CONSIDERATIONS

N/A

5.4 SCREEN FAILURES

Screen failures include any patients included in electronic medical record (EMR) chart review that do not enroll in the study. This includes individuals who do not pass chart review, do not complete the pre-screen survey, do not pass the pre-screen survey, or pass the survey and decline to participate. If this is due to not meeting inclusion criteria, or having or developing exclusion criteria, patients will not be re-screened.

5.5 STRATEGIES FOR RECRUITMENT AND RETENTION

Recruitment Plan

We will recruit active patients at UNC Rheumatology who are scheduled for an upcoming routine rheumatology visit with a participating clinician in the next 4-8 weeks. We will receive a list of patients from the Carolina Data Warehouse (CDWH) who are scheduled for an upcoming visit at UNC Rheumatology and have RA (as defined by ICD-10 code). We may also review clinician schedules to identify individuals meeting the same criteria. For each method, we will further review the medical record for inclusion and exclusion criteria. Once a potential participant is identified, they will be contacted utilizing a tiered approach as outlined below:

- If they have a physical address listed, we will send a letter detailing the study and a method for accessing the pre-screening survey.
- If they have an activated MyChart, we will send a secure message through MyChart with a short description of the study and a link to the pre-screening survey.
 - If they have an email address but no MyChart account or were not responsive to the MyChart message in one week, we will email them a short description of the study and a link to the pre-screening survey.
 - If they do not respond in one week, we will send them a follow-up email.
 - If they have a phone number listed and have not responded to any prior method of communication, we will call them one week after the follow-up email to invite them to complete the pre-screening survey. We will call them no earlier than one week after the letter was mailed. We will call three times over three weeks, on different days of the week and at different times.

Participants are considered “unable to be reached” if they do not respond to any of the previously listed recruitment methods.

Retention Plan

The components of the intervention occur within days -7 to 15 of the study through the baseline assessments, routine visit with rheumatology, and the PT consultation call if applicable. Because the intervention components occur at the beginning of the study, we do not expect difficulty with participant retention. For those who do not fully complete the baseline assessment, a study team member will call the participant to complete the assessment over the phone prior to the rheumatology visit.

After the rheumatology visit and PT consultation call, there is a follow-up assessment that is scheduled 3 months after the baseline assessments are completed. The completion rate of the follow-up assessment is part of the study outcomes in this feasibility trial, thus there are no additional retention efforts. We will collect preferred and alternative contact information and methods to maximize opportunities to capture the follow-up visit. To help with retention, participants will be given a \$25 gift card for baseline and follow-up assessments

(\$50 total) and \$50 for completing the qualitative interview. All participant payments will be made using TANGO gift cards.

Participants who discontinue or are withdrawn prior to the routine rheumatology visit will be replaced. If a participant does not complete the essential baseline assessment before their routine rheumatology visit, they will be discontinued from the study. If they miss their scheduled routine visit and can reschedule within the data collection window, they will continue in the study and the baseline assessment will be resent within one week of their new appointment date. If they reschedule their appointment outside of the data collection window, they will be discontinued from the study.

6 STUDY INTERVENTIONS

6.1 STUDY INTERVENTION ADMINISTRATION

PREVAIL Model of Care Intervention.

Overview.

The PREVAIL model of care includes (1) a screening tool, the “Daily Activity and Participation Screen” (DAPS), previously referred to as the disability screening tool, completed at baseline to categorize participants current level of limitation with valued life activities, (2) a recommendation to a participating rheumatology clinician based on the screening tool results to provide an exercise resource and/or recommend a PT consultation call at the participants routine rheumatology visit, (3) an exercise resource (PREVAIL Website) provided by the rheumatology clinician to all participants, (4) a brief consultation call with a PT who is a member of the study team to gather information to determine level of priority for PT referral, and (5) a referral for physical therapy. Components 1, 2, and 3 are essential components of the PREVAIL model of care. Each component of the model of care intervention is described below.

PREVAIL Model of Care Components.

1. *Screening tool.* The purpose of the screening tool is to help rheumatology clinicians prioritize patients for a rehabilitation referral based on their current ability to participate in activities of daily life. We adapted a previously validated patient-reported outcome for adults with RA (Short Valued Life Activities Questionnaire [SVLA]) to create a “Daily Activity and Participation Screen”. The screening tool utilizes the items from the SVLA and categorizes patients (Figure 1). In brief, the criteria uses the responses to the screening tool to categorize adults with current disability, at risk for disability, and no disability with daily activities and participation. These categories will direct the recommended action for the rheumatology clinician (Figure 1). The screening tool will be sent to the participants for completion one week prior to their scheduled rheumatology visit, and will be completed at the same time as the baseline assessment.
2. *Recommendation from rheumatology clinician at routine visit guided by screening results.* All participants will receive a rehabilitation and exercise recommendation from their rheumatology clinician (i.e. rheumatologist or rheumatology advanced practice provider) at their routine rheumatology visit. The rheumatology clinician will be provided with the results of the screening tool and respective recommendations based on the results. In brief, the recommendations are as follows:
 - a. *Screening tool indicates no disability with daily activities and participation*
 - i. *Recommendation to rheumatology clinician:* Encourage consistent participation in exercise and physical activity, and share the exercise resource to facilitate participation. Share with your patient that based on the results, rehabilitation is not currently needed related to their RA.
 - b. *Screening tool indicates at risk for future disability with daily activities and participation*
 - i. *Recommendation to rheumatology clinician:* Encourage consistent participation in exercise and physical activity, and share the exercise resource to facilitate participation. Share with your patient that based on the results of the screening tool, rehabilitation may

help them participate in daily activities that are becoming challenging. To learn more about their current needs and tailor recommendations, a brief consultation call with a physical therapist is recommended.

- c. *Screening tool indicates current disability with daily activities and participation*
 - i. Recommendation to rheumatology clinician: Encourage consistent participation in exercise and physical activity, and share the exercise resource to facilitate participation. Share with your patient that based on the results of the screening tool, rehabilitation may help them participate in daily activities that are challenging. To learn more about their current needs and tailor recommendations, a brief consultation call with a physical therapist is recommended.
3. *Exercise resource.* The purpose of the exercise resource is to facilitate the distribution of useful exercise recommendations that are targeted for adults with RA. For this study, the exercise resource is a website with evidence-based information on exercise and physical activity recommendations for adults with RA, as well as a curated collection of videos, websites, documents, and local support organized by focus area (e.g. UNC Walk with Ease, low-impact exercise programs, hand exercise video series). Website use will be quantified through the duration of the study through Google Analytics.
4. *Brief physical therapy consultation call (if appropriate per screening results).* The purpose of the brief physical therapy consultation call is to use expert clinical judgement to prioritize need for physical therapy and educate the patient on the role of physical therapy for RA. This consultation call is an interim component of the PREVAIL model of care that was added for this pilot trial. We aim to gather additional needed information to help refine the screening tool and design education resources for future trials. The consultation call will be conducted by a licensed physical therapist who will use their clinical expertise to determine if physical therapy is indicated and the level of priority. The physical therapist is also responsible for briefly educating the patient on the role of physical therapy in their personal treatment plan. The calls will be recorded for later review.
5. *Referral for physical therapy (if appropriate per consultation call).* As determined by the physical therapy consultation call, participants may receive a referral for physical therapy. The delivery of physical therapy is not dictated by the study. Rather, their use of physical therapy after referral will be observed and recorded as a study outcome.

6.2 FIDELITY

Interventionist Training

Rheumatology clinician. Participating rheumatology clinicians will work with the study team to develop tools and resources to efficiently deliver the referral recommendations and exercise guidance at a routine rheumatology visit. The study team will train the rheumatology clinicians on the intervention components to deliver in the routine clinical visit. Prior to the scheduled visit, the study team will provide the rheumatology clinician with the participant-specific recommendation (i.e. Option 2a, 2b, or 2c detailed in section 6.1) and any associated tools to deliver the intervention (e.g. template language or dot phrases in the electronic medical record, links to the exercise resource for the after-visit summary).

Physical therapy consultation calls. All consultation calls will be conducted by a licensed physical therapist(s) who is trained by the study team on the goals of the consultation call. Guidance for the physical therapy consultation calls is provided in the MOP Appendix, and will be available as a resource to the physical therapist. Calls will be recorded and reviewed by two additional licensed physical therapists after they are completed.

Fidelity Monitoring

Monitoring of delivery participant-specific exercise and rehabilitation recommendations. We will monitor delivery of the exercise education resource and the rehabilitation recommendations by reviewing the visit documentation in the medical record after the visit. Missed interventions will be monitored and followed-up to

learn why the intervention was not delivered as intended. This information will be collected to evaluate feasibility.

Monitoring of physical therapy consultation calls. All consultation calls will be recorded to monitor and assess content. Dr. Thoma or another experienced study team member will monitor the call content to ensure that it is consistent with the guidance as the study proceeds.

6.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

This study design does not require any randomization and blinding.

6.4 STUDY INTERVENTION ADHERENCE

The study database Research Electronic Data Capture (REDCap) will be used to track participants' completion of all assessment visits, as well as all contacts with the Research Coordinators/Assistants. The Principal Investigator will also maintain close communication with the Research Coordinators/Assistants regarding facilitation of all activities within the PREVAIL model of care. For each participant, the Research Coordinators/Assistants will maintain a checklist of intervention activities, target dates, dates of completion, and comments.

6.5 CONCOMITANT THERAPY

Participants will be permitted to continue any other RA treatment during the course of the study except ongoing PT which is a component of the exclusion criteria.

7 STUDY INTERVENTION/ DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 DISCONTINUATION OF STUDY INTERVENTION

When a participant discontinues the intervention or does not pursue PT consultation, they will be asked if they are willing to continue with other remaining activities (e.g., follow-up assessments). If a clinically significant finding is identified after enrollment (e.g. health-related changes that may change the safety level of participation), the investigator or qualified designee will determine if any change in participant management is needed. Any new clinically relevant finding will be reported as an adverse event (AE). The data to be collected at the time of study intervention discontinuation will include the reason(s) for discontinuing the participant from the intervention, and methods for determining the need to discontinue.

7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

Participants are free to withdraw from participation in the study at any time upon request.

An investigator may discontinue a participant from the study for the following reasons:

- Lost-to-follow up; unable to contact subject
- Any event or medical condition or situation occurs such that continued collection of follow-up study data would not be in the best interest of the participant or might require an additional treatment that would confound the interpretation of the study
- The participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation

The reason for participant discontinuation or withdrawal from the study will be recorded in the study database.

Participants who discontinue or are withdrawn prior to the routine rheumatology visit will be replaced. If a participant does not complete the essential baseline assessment before their routine rheumatology visit, they will be discontinued from the study. If they miss their scheduled routine visit and can be rescheduled within the

data collection window, they will continue in the study and the baseline assessment will be resent within two weeks of their new appointment date. If they reschedule their appointment outside of the data collection window, they will be discontinued from the study.

7.3 LOSS TO FOLLOW-UP

A participant will only be considered lost to follow-up if he or she cannot be contacted for a missed 3-month follow-up, as missing baseline assessments and missing RA routine visits would result in removal from the study. The study team must attempt to contact a participant at least 3 times, on different days of the week, different times of day, and across at least 2 weeks, before they are considered to have missed a visit / assessment or be lost to follow-up. These contact attempts will be documented in the study database.

8 STUDY ASSESSMENTS AND PROCEDURES

8.1 ENDPOINT AND OTHER NON-SAFETY ASSESSMENTS

Feasibility Metrics. Feasibility metrics will include assessments of the PREVAIL model and other aspects of study processes important for informing a larger trial in routine RA care. The primary endpoints for feasibility include:

- The percentage of participants who receive the PREVAIL model of care essential components (*DAPS, recommendation, and exercise resource*)
 - Feasible if $\geq 70\%$
 - Completion of the DAPS will be recorded in REDCap as part of the baseline assessments (Visit 2). Clinician notes will be reviewed after the participant's routine rheumatology visit (Visit 3) to confirm delivery of the recommendation and exercise resource.
- The percentage of participants who access the exercise resource at least once
 - Feasible if $\geq 70\%$
 - Participants will self-report their website usage in the intervention utilization questions on REDCap during follow-up (Visit 5).
- The average score of the FIM
 - Feasible if ≥ 4 out of 5
 - *Feasibility of Intervention Measure*⁵² (*FIM*): The FIM is a method for determining if a treatment or intervention can be carried out in a particular setting. It is a valid and reliable 4-item outcome measure scored on a 5-point Likert scale (completely disagree = 1, completely agree = 5). The FIM will be completed on REDCap during Visit 5.

Secondary endpoints address the feasibility of testing the PREVAIL model of care in future studies. They include the percentage of the recruitment pool who enrolls in the study (feasible if $\geq 15\%$) and the percentage of participants who complete the follow-up assessments (feasible if $\geq 90\%$), measured after Visit 1 and Visit 5, respectively.

Acceptability of RA PREVAIL

*Acceptability of Intervention Measure*⁵² (*AIM*): The AIM is a valid and reliable 4-item outcome measure to test whether the intervention is agreeable and appealing to individuals. It is also scored on a 5-point Likert scale, with higher answers indicating higher acceptability.

The primary endpoint for acceptability is the average score of the AIM (feasible if ≥ 4 out of 5). The AIM will be completed on REDCap during Visit 5.

Most measures will be collected remotely at baseline (Visit 2) and 3-month follow-up (Visit 5) via REDcap. If any assessment components are missed, either as individual items or full survey instruments, the study team will contact the participant and provide the opportunity to complete the missed portions over the phone.

Intervention Appropriateness Measure⁵² (IAM): The IAM is a four-item questionnaire given in tandem with the AIM and FIM to gauge perceived fit of an intervention. This valid and reliable survey will be collected remotely only during visit 5. It will also be scored on a 5-point Likert scale and its scores are only for exploratory purposes.

Short Valued Life Activities (SVLA) Questionnaire⁵³: The SVLA Questionnaire is a measure of 14 activity domains to assess RA burden and disability. All items are rated on a Likert scale of 0 (no difficulty) to 3 (unable to perform). The SVLA is a validated tool to assess RA-related disability and is well-suited for screening due to its brevity and ability to identify those at risk for disability. At baseline, the SVLA questions will be used as the essential screening tool (DAPS) to categorize participants based on disability.

Clinical Disease Activity Index⁵⁴ (CDAI) Patient Global Assessment (PGA): The CDAI-PGA is a question from the CDAI focused on a patient's self-assessment of RA disease activity for the current day. It asks participants to consider their symptoms as well as how RA impacts their quality of life and daily activities and rate how they feel on a sliding scale. The PGA is scored from 1-10, with 1 being 'very well' and 10 being 'very poorly'.

Routine Assessment of Patient Index Data 3⁸² (RAPID3): The RAPID3 is a validated patient-reported outcome measure for RA disease activity that evaluates a patients' physical function, pain, and global health estimate. RAPID3 weighted scores range from 0-10, with 0 – 1.0 as near remission, 1.3 – 2 as low severity, 2.3 – 4 as moderate severity, and 4.3 – 10 as high severity.

PROMIS short-form for physical function⁸⁶ (PROMIS PF10a): The PROMIS PF10a is a reliable and valid 10-item questionnaire to assess current self-reported physical function in patients with chronic disease, such as rheumatoid arthritis. Raw scores range from 10 to 50 and can be transformed to T-scores. Higher T-scores represent better physical function.

PROMIS short-form for pain interference⁸⁵ (PROMIS PI6b): The PROMIS PI6b is a validated, self-reported measurement of consequences of pain on relevant aspects of a patient's life and may include the extent to which pain hinders engagement in social, cognitive, emotional, physical and recreational activities. PROMIS PI6b consists of 6 items scored from 6-30, producing a raw score. Raw scores are converted to T-scores for interpretation. Higher T-scores represent more of the concept being measured, meaning consequences of pain are relevant to many aspects of the patient's life.

PROMIS short-form for fatigue⁸³ (PROMIS F7a): The PROMIS F7a is a reliable, valid tool to measure both the experience of fatigue and the interference of fatigue on daily activities over the past week. PROMIS F7a consists of 7 items scored on a 5-point Likert scale, with scores ranging from 7 to 35. Higher scores indicate greater fatigue.

Stopping Elderly Accidents, Deaths, and Injuries⁵⁵ (STEADI) fall risk questions: These four questions from the STEADI Stay Independent Fall Risk Self-Assessment have been used in prior literature to identify fall risk. If participants answer 'yes' to any of the three key questions, 'have you fallen in the past year', 'do you feel unsteady when standing or walking', or 'do you worry about falling', they are considered at risk. If a participant answers 'yes' to 'have you fallen in the last year', they will be prompted to answer, 'how many times' and 'were you injured' as well. The fourth main question addresses whether an individual uses their hands when getting up from a chair.

*PROMIS short-form for ability to participate in social roles and activities*⁵⁶ (*PROMIS APSRA8a*): The PROMIS APSRA8a is a reliable, valid tool to assess one's perceived ability to perform usual social roles and activities. PROMIS APSRA8a is an 8-question tool scored on a 5-point Likert Scale, with raw scores ranging from 8 to 40. Raw scores can be transformed into standardized T-scores. Higher T-scores represent fewer limitations.

Life Space Questionnaire^{57,58} (*LSQ*): The LSQ is a validated measure to collect information on how much time an individual spends out and about, or the extent of their mobility. Questions are asked in yes/no format in relation to the last three days, with 0 being yes and 1 being no. The higher the LSQ score, the less time an individual spends engaging in activities outside of their 'bubble' (e.g. bedroom).

*Self-Efficacy for Exercise*⁹¹ (*SEE*) *Scale*: The SEE is a valid and reliable 9-item instrument that focuses on self-efficacy expectations related to the ability to continue exercising in the face of barriers to exercise. Total score is calculated by summing the responses to each question. Scores range from 0 to 90, with higher scores indicating higher self-efficacy for exercise.

*Tampa Scale for Kinesiophobia*⁵⁹ (*TSK*): The TSK is a reliable self-reported measurement of fear of physical movement or (re)injury in patients with chronic conditions. The version we will use is adapted for use in participants with chronic conditions by replacing 'pain' with 'symptoms' in certain questions. The TSK presents 17 questions on a 4-point Likert scale. Scores range from 17-68, with higher values (>37) linked to higher degrees of kinesiophobia and poorer health outcomes.

*Expectation for Treatment Scale*⁶⁰ (*ETS*): The ETS is a reliable, validated self-report instrument to assess patients' expectations for treatment outcomes. It consists of 5 items on a 4-point scale addressing coping, vitality, physical health, and reduction of complaints. We have adapted the survey by replacing 'treatment' with 'physical therapy' and 'exercise', so participants will complete two version of the survey, each with a maximum of 20 points. Higher scores indicate higher expectations for treatment.

*Functional status questions*⁵⁶: The functional status questions address fatigue, pain, and the ability to carry out daily activities. These questions were used while testing various PROMIS measures for individuals with RA to assess global ratings of change in outcomes. Questions are asked in reference to one year ago as well as three months ago. They are scored on a 5 point scale ranging from "got a lot better" to "got a lot worse", with lower values (1,2) considered "better" and higher values (3-5) considered "worse."

We will be asking questions about sleep⁶¹, exercise participation and type of activity (i.e. muscle strengthening, flexibility⁶²), to assess activity level^{63,64}. The rehabilitation experience questions capture prior use of physical therapy or occupational therapy, and belief about the role of physical therapy for individuals with RA.

During the 3-month follow-up (Visit 5), participants will be asked questions regarding their utilization of the components of the PREVAIL model of care. We will also conduct follow-up interviews with select clinicians and patients who participated in the pilot study to assess acceptability and gather comprehensive feedback on the model of care.

8.2 SAFETY ASSESSMENTS

Safety will be assessed from commencement of the intervention until the last visit is complete or the participant withdraws from the study. All safety events will be documented as described below.

8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

8.3.1 DEFINITION OF ADVERSE EVENTS

This protocol uses the definition of adverse event (AE) from Department of Health and Human Services (DHHS) Office for Human Research Protections (OHRP): Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research (modified from the definition of adverse events in the 1996 International Conference on Harmonization E-6 Guidelines for Good Clinical Practice). Any medical or psychiatric condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. However, if the study participant's condition deteriorates at any time during the study, it will be recorded as an AE.

8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS

This protocol uses the definition of serious adverse event (SAE) from DHHS OHRP: Any adverse event temporally associated with the subject's participation in research that meets any of the following criteria: results in death; is life-threatening (places the subject at immediate risk of death from the event as it occurred); requires inpatient hospitalization or prolongation of existing hospitalization; results in a persistent or significant disability/incapacity; results in a congenital anomaly/birth defect; or any other adverse event that, based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

8.3.3 CLASSIFICATION OF AN ADVERSE EVENT

8.3.3.1 SEVERITY OF EVENT

All AEs will be assessed by the PI or co-investigators, if the PI is not available. The following guidelines will be used to describe severity:

- **Mild** – Events require minimal or no treatment and do not interfere with the participant's daily activities.
- **Moderate** – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
- **Severe** – Events interrupt a participant's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating. Of note, the term "severe" does not necessarily equate to "serious".

8.3.3.2 RELATIONSHIP TO STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

All AEs will have their relationship to study procedures, including the intervention, assessed by the PI or co-investigators based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below.

- **Definitely Related** – There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out. The clinical event, including an abnormal laboratory test result, occurs in a plausible time relationship to study intervention administration and cannot be explained by concurrent disease or other drugs or chemicals. The response to withdrawal of the study intervention (dechallenge) should be clinically plausible. The event must be pharmacologically or phenomenologically definitive, with use of a satisfactory rechallenge procedure if necessary.
- **Probably Related** – There is evidence to suggest a causal relationship, and the influence of other factors is unlikely. The clinical event, including an abnormal laboratory test result, occurs within a

reasonable time after administration of the study intervention, is unlikely to be attributed to concurrent disease or other drugs or chemicals, and follows a clinically reasonable response on withdrawal (dechallenge). Rechallenge information is not required to fulfill this definition.

- Not Related – The AE is completely independent of study intervention administration, and/or evidence exists that the event is definitely related to another etiology. There must be an alternative, definitive etiology documented by the clinician.

8.3.3.3 EXPECTEDNESS

The PI will be responsible for determining whether an AE is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study procedures.

8.3.4 TIME PERIOD AND FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

The occurrence of an AE or SAE may come to the attention of study team members during study visits or in following up for missed study visits. All AEs, not otherwise precluded per the protocol, will be captured on the Adverse Event Form linked in the MOP Appendix. Information to be collected includes event description, AE Onset Date, AE Stop Date, PI or co-investigator's assessment of severity, relationship to study procedures (assessed only by those with the training and authority to make a diagnosis), action taken with study intervention due to AE, Outcome, Expectedness, Serious (y/n), Unanticipated Problem (y/n), and Initials. All AEs occurring while on study will be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. Documentation of onset and duration of each episode will be maintained for AEs characterized as intermittent.

The Project Coordinator will record events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation. Events will be followed for outcome information until resolution or stabilization.

8.3.5 ADVERSE EVENT REPORTING

Once the PI (or a co-investigator) is contacted about an AE, they will make a determination about the reporting requirements in accordance with UNC IRB guidelines. AEs that suggest new or increased risk to participants or others is considered an unanticipated problem (UP) and the PI or co-investigator will follow UP reporting procedures detailed in Section 8.4.2 of the protocol. For AEs that are not related to participation in the research and do not suggest new or increased risks to the participant, these will be reported to the IRB and The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) on the quarterly safety report submitted to the safety officer (SO).

8.3.6 SERIOUS ADVERSE EVENT REPORTING

Once the PI (or a co-investigator) is contacted about a SAE, they will make a determination about the reporting requirements in accordance with UNC IRB guidelines. This will include notification of the UNC IRB within 24-hours if a study-related death and within 48 hours if another SAE.

All SAEs will be reported to the NIAMS (through the NIAMS Executive Secretary) within 48 hours of the investigator becoming aware of the event. The SAE Report Form will be completed and the SO's review of the SAE report will be shared with the NIAMS once received.

8.3.7 REPORTING EVENTS TO PARTICIPANTS

N/A

8.3.8 EVENTS OF SPECIAL INTEREST

N/A

8.3.9 REPORTING OF PREGNANCY

N/A

8.4. UNANTICIPATED PROBLEMS

8.4.1 DEFINITION OF UNANTICIPATED PROBLEMS

This protocol uses the definition of Unanticipated Problems (UPs) as defined by the Office for Human Research Protections (OHRP). OHRP considers unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets all of the following criteria:

- (1) Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied
- (2) Related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research)
- (3) Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized

Only a small subset of AEs occurring in human subjects participating in research will meet these three criteria for an unanticipated problem. Furthermore, there are other types of incidents, experiences, and outcomes that occur during the conduct of human subjects research that represent UPs but are not considered AEs. For example, some UPs involve social or economic harm instead of the physical or psychological harm associated with adverse events. In other cases, unanticipated problems place participants or others at increased risk of harm, but no harm occurs.

8.4.2 UNANTICIPATED PROBLEMS REPORTING

All UPs will be reported to UNC IRB within 48 hours of the PI becoming aware of the event. All UPs will be reported to the NIAMS and the SO (through the NIAMS Executive Secretary) within 48 hours of the PI becoming aware of the event.

8.4.3 REPORTING UNANTICIPATED PROBLEMS TO PARTICIPANTS

Participants will be given any new information gained during the study that might affect their willingness to continue participation in the study.

9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL HYPOTHESES

The aim of this study is to conduct a single-group feasibility trial of the PREVAIL model of care with at least 50 patients with RA who are receiving routine care from a rheumatology clinician.

The aims and associated targets are as follows.

Aim 1. Determine feasibility of the PREVAIL model for adults with RA.

There are no specific hypotheses associated with this aim. Analyses will be descriptive in nature. We have *a priori* targets to indicate the model of care is feasible. The primary endpoints are:

- % of participants who receive the PREVAIL model of care essential components (Feasible if $\geq 70\%$ of participants receive the essential components)
- % of participants who access the exercise resource at least one time (Feasible if $\geq 70\%$ of participants access website)
- Average score on the Feasibility of Intervention Measure (Feasible if FIM ≥ 4 out of 5)

Aim 2. Assess patient acceptability of the PREVAIL model of adults with RA.

There are no specific hypotheses associated with this aim. Analyses will be descriptive in nature. We have an *a priori* target to indicate the model of care is acceptable. The primary endpoint is:

- Average score on the Acceptability of Intervention Measure (Acceptable if AIM ≥ 4 out of 5)

9.2 SAMPLE SIZE DETERMINATION

Due to the exploratory nature of this trial, the objective is to inform estimates for a larger randomized controlled trial (RCT). In particular, we aim to inform the estimate of the proportion of the sample that follows each path in the model of care and acts upon recommendations. Thus, we will enroll at least 50 participants and continue enrolling until at least 10 participants receive a referral for physical therapy, so we can estimate utilization proportion after referral.

9.3 POPULATIONS FOR ANALYSES

The primary analyses will be conducted using an intent-to-treat approach. Supportive exploratory analyses may be conducted to consider samples with greater completion of study intervention visits. Since this is an exploratory trial, the nature of these supportive analyses will be based on observed patterns of intervention contacts.

9.4 STATISTICAL ANALYSES PLAN

Primary outcomes: Analyses will be descriptive in nature (e.g. frequency, proportion, mean, median, 95% confidence intervals). We have *a priori* targets to indicate the model of care is feasible and acceptable.

The primary endpoints are:

- % of participants who receive the PREVAIL model of care essential components (Feasible if $\geq 70\%$ of participants receive the essential components)
- % of participants who access the exercise resource at least one time (Feasible if $\geq 70\%$ of participants access website)
- Average score on the Feasibility of Intervention Measure (Feasible if FIM ≥ 4 out of 5)
- Average score on the Acceptability of Intervention Measure (Acceptable if AIM ≥ 4 out of 5)

Secondary outcomes: Analyses will be descriptive in nature (e.g. frequency, proportion). We have *a priori* targets to indicate the study design and study processes are feasible.

The secondary endpoints are:

- % of recruitment pool who enroll in the study (Feasible if $\geq 15\%$)
- % of participants that complete follow-up assessments (Feasible if $\geq 90\%$)

Tertiary/exploratory outcomes: The exploratory outcomes will be used to describe the overall sample and the subsamples of participants that follow each pathway of the model of care to comprehensively characterize clinical utility. Analyses will be descriptive in nature (e.g. frequency, proportion, mean, median, 95% confidence intervals). The exploratory patient-reported outcomes quantify RA disease activity, functional limitation, disease symptoms, physical activity levels, and psychosocial factors associated with exercise and movement. These are candidate primary outcomes for a larger scale trial. These outcomes measures also include candidate questions for refining the DAPS tool.

Qualitative data: The post-intervention interviews will be analyzed with thematic approaches to learn comprehensively about feasibility and acceptability of the model, and suggestions for modifications.

We will also evaluate the agreement of the physical therapists in prioritizing need for physical therapy, and learn from the contents from the call how to refine the DAPS to predict the prioritizations.

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

10.1.1 INFORMED CONSENT PROCESS

10.1.1.1 CONSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

Consent forms describing in detail the study intervention, study procedures, and risks will be given to the participant and electronic documentation of informed consent will be completed prior to starting the study procedures. The Informed Consent Form will be linked in the Manual of Procedures (MOP).

10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

Once a potential participant meets the medical record and REDCap screening criteria for eligibility, and is interested in participating, they will be asked to complete the Informed Consent Form and HIPAA Authorization waiver via online survey. No other study activities will occur until this process is completed.

We will use a UNC IRB approved consent form with included language that satisfies the HIPAA requirements and outlines the protection of health information utilized in the study. Informed consent will be obtained via REDCap. During this phase of the consent process, it will be stressed that the participant is not obligated to participate in the study, that participation is completely voluntary, and that he/she may withdraw from the study at any time without penalty. Potential risks from participating in the study will be outlined in the consent form, as are the measures taken to protect against study specific risks. Once the information in the consent form is fully reviewed and understood by the individual, he/she will be asked a series of questions to indicate assess their comprehension. Once an individual answers all questions correctly, or has spoken with a study team member to confirm their understanding of the material, he/she will then be asked to decide at that time if they would like to voluntarily participate in the research study. Participants will be allowed to request a phone call from the study team if they have questions about their participation. If the individual does choose to participate in the study, they will complete a HIPAA authorization waiver. The study team will confirm

completion of the informed consent process and HIPAA authorization waiver and may follow up with the participant if necessary. Once enrolled, they will complete the disability screening and other baseline assessments via REDCap.

Participants will only be included if they have capacity to give legally effective consent. Additionally, this study will only recruit participants whom are English speakers.

10.1.2 STUDY DISCONTINUATION AND CLOSURE

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to study participants, investigator, funding agency, and regulatory authorities. If the study is prematurely terminated or suspended, the PI will promptly inform study participants, the IRB, and sponsor/funding agency and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable
- Determination of futility

The study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the funding agency, sponsor, IRB or other relevant regulatory or oversight bodies (OHRP, SO).

10.1.3 CONFIDENTIALITY AND PRIVACY

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, the safety and oversight monitor(s), and the sponsor(s) and funding agency. This confidentiality is extended to the data being collected as part of this study. Data that could be used to identify a specific study participant will be held in strict confidence within the research team. No personally identifiable information from the study will be released to any unauthorized third party. All research activities will be conducted in as private a setting as possible.

The study monitor, other authorized representatives of the sponsor or funding agency, representatives of the IRB, or regulatory agencies, may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the participants in this study.

The study participant's contact information will be securely stored in REDCap for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for at least 6 years

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be stored on a secure UNC server. The study data entry and study management systems used by research staff will be secured and password protected. At the end of the study, all study databases will be de-identified and archived on a secure UNC server.

Measures Taken to Ensure Confidentiality of Data Shared per the NIH Data Sharing Policies. It is NIH policy that the results and accomplishments of the activities that it funds should be made available to the public (see <https://grants.nih.gov/policy/sharing.htm>). The PI will ensure all mechanisms used to share data will include proper plans and safeguards for the protection of privacy, confidentiality, and security for data dissemination and reuse (e.g., all data will be thoroughly de-identified and will not be traceable to a specific

study participant). Plans for archiving and long-term preservation of the data will be implemented, as appropriate.

Certificate of Confidentiality. To further protect the privacy of study participants the Secretary (Health and Human Services [HHS]), has issued a Certificate of Confidentiality (CoC) to all researchers engaged in biomedical, behavioral, clinical or other human subjects research funded wholly or in part by the federal government. Recipients of NIH funding for human subjects research are required to protect identifiable research information from forced disclosure per the terms of the NIH Policy (see <https://humansubjects.nih.gov/coc/index>). As set forth in 45 CFR Part 75.303(a) and NIHGPS Chapter 8.3, recipients conducting NIH-supported research covered by this Policy are required to establish and maintain effective internal controls (e.g., policies and procedures) that provide reasonable assurance that the award is managed in compliance with Federal statutes, regulations, and the terms and conditions of award. It is the NIH policy that investigators and others who have access to research records will not disclose identifying information except when the participant consents or in certain instances when federal, state, or local law or regulation requires disclosure. NIH expects investigators to inform research participants of the protections and the limits to protections provided by a Certificate issued by this Policy.

10.1.4 FUTURE USE OF STORED DATA

Data collected for this study will be analyzed and stored on a secure UNC server. After the study is completed, the de-identified data will be made available to other researchers, available by request to the PI. Investigators requesting study data must adhere to regulatory requirements for data use (e.g., IRB approvals, data use agreements). No biological samples are collected for this study.

10.1.5 KEY ROLES AND STUDY GOVERNANCE

Principal Investigator	Independent Safety Monitor
Louise M. Thoma, DPT, PhD	John M. Baratta, MD, MBA
University of North Carolina at Chapel Hill	University of North Carolina at Chapel Hill
3041 Bondurant Hall CB #7135 Chapel Hill, NC 27599-7280	321 S Columbia St Chapel Hill, NC 27599
919-843-7317	984-974-9747
Louise_Thoma@med.unc.edu	John_Baratta@med.unc.edu

10.1.6 SAFETY OVERSIGHT

Safety oversight will be under the direction of the Safety Officer (SO). The SO will be independent from the study conduct and free of conflict of interest. The SO's role is to advise the PI (and not the NIAMS) regarding participant safety, scientific integrity and ethical conduct of the study. On a quarterly basis or as requested, the PI will provide to the SO a study summary, a report of all AEs, and any problems or issues that have been identified.

10.1.7 CLINICAL MONITORING

Since this is a single site study there will not be site visits conducted by the PI or co-investigators. However, we will monitor the fidelity of intervention delivery as described above. The Executive Secretary may conduct a site

visit on behalf of the NIAMS, however, the Executive Secretary will not have the responsibility of the overall clinical monitoring for this study.

10.1.8 QUALITY ASSURANCE AND QUALITY CONTROL

Quality control (QC) procedures will be implemented as follows:

- **Informed consent** --- Since the informed consent process will be completed remotely, we added questions to be answered to ensure comprehension and fully informed consent. Potential participants may also request a phone call with a member of the study team to review the informed consent document and answer any remaining questions.
- **Electronic data** --- Data from patient reported electronic questionnaires will be entered directly into the study database (REDCap); all other data from study measures will be entered directly into the study database.
- **Protocol Deviations** --- The study team will review protocol deviations on an ongoing basis and will implement corrective actions when the quantity or nature of deviations are deemed to be at a level of concern.

Should independent monitoring become necessary, the PI will provide direct access to all source data/documents, and reports for the purpose of monitoring and auditing by the sponsor/funding agency, and inspection by local and regulatory authorities.

10.1.9 DATA HANDLING AND RECORD KEEPING

10.1.9.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

Study data will be stored on a secure UNC server in a folder accessible only to IRB-approved study team members. We will use REDCap to store all patient information and dispositions, responses to screenings, and outcome assessments. REDCap is a secure web application supported at UNC that can be used to build and manage case report forms, surveys, and other data capture mechanisms. Paper copies will be rare and if necessary will be kept to a minimum. Any paper copies will be stored in the participant's individual study folder, which will be kept in a locked file cabinet of a study team member.

10.1.9.2 STUDY RECORDS RETENTION

Research study records will be maintained for no less than 6 years following the completion of the study, after which time personal identifying information will be removed. Research information in a subject's medical record will be kept indefinitely. No records will be destroyed without the written consent of the sponsor/funding agency, if applicable. It is the responsibility of the sponsor/funding agency to inform the investigator when these documents no longer need to be retained.

10.1.10 PROTOCOL DEVIATIONS

This protocol defines a protocol deviation any unplanned excursion from the protocol that is not intended as a systematic change. Examples of protocol deviations include enrollment of an ineligible participant, failure to obtain and document informed consent, unreported or improperly reported AEs, SAEs, and UPs, multiple visits outside of study windows.

Protocol deviations potentially impacting participant safety (i.e. serious noncompliance) or show a pattern of noncompliance (i.e. continuing noncompliance) will be reported to the UNC IRB within 48 hours of the PI becoming aware of the event so that a real time assessment can be conducted, and the outcome shared in a

timely manner. If the UNC IRB determines the protocol deviations to be serious or continuing noncompliance and/or requires suspension or termination of IRB approval, SO and NIAMS (through the NIAMS Executive Secretary) will be notified within 3 business days.

All other events (i.e. minor protocol deviations that are sporadic and do not impact participant safety) will be recorded in the Protocol Deviation Log with a corrective and preventative action plan, as appropriate. The Protocol Deviation Log is subject to review upon request by the UNC IRB and will be reported at the time of the routine report to the SO.

10.1.11 PUBLICATION AND DATA SHARING POLICY

This study will be conducted in accordance with the following publication and data sharing policies and regulations:

- National Institutes of Health (NIH) Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.

This study will comply with the NIH Data Sharing Policy and Policy on the Dissemination of NIH-Funded Clinical Trial Information and the Clinical Trials Registration and Results Information Submission rule. As such, this trial will be registered at ClinicalTrials.gov, and results information from this trial will be submitted to ClinicalTrials.gov. In addition, every attempt will be made to publish results in peer-reviewed journals. Data from this study may be requested from other researchers after the completion of the primary endpoint by contacting the study PI. Considerations for ensuring confidentiality of these shared data are described in Section 10.1.3

10.1.12 CONFLICT OF INTEREST POLICY

The independence of this study from any actual or perceived influence is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this trial. The University of North Carolina at Chapel Hill requires all investigators to disclose all conflicts of interest and has a mechanism for the management of all reported dualities of interest.

10.2 ADDITIONAL CONSIDERATIONS

N/A

10.3 ABBREVIATIONS

AE	Adverse Event
AIM	Acceptability of Intervention Measure
CDAI-PGA	Clinical Disease Activity Index- Patient Global Assessment
CDWH	Carolina Data Warehouse
CFR	Code of Federal Regulations
CoC	Certificate of Confidentiality
DAPS	Daily Activity and Participation Screen
DHHS	Department of Health and Human Services
EMR	Electronic Medical Record
ETS	Expectation for Treatment Scale
FIM	Feasibility of Intervention Measure
GCP	Good Clinical Practice
HHS	Health and Human Services
HIPAA	Health Insurance Portability and Accountability Act of 1996
IAM	Intervention Appropriateness Measure
ICD	International Classification of Diseases
ICH	International Council on Harmonisation
IRB	Institutional Review Board
LSQ	Life Space Questionnaire
MOP	Manual of Procedures
NIAMS	National Institute of Arthritis and Musculoskeletal and Skin Diseases
NIH	National Institutes of Health
OHRP	Office for Human Research Protections
PA	Physical Activity
PHI	Protected Health Information
PI	Principal Investigator
PREVAIL	PREserve Valued Activities In Life
PROMIS APSRA8a	Patient-Reported Outcome Measurement Information System Ability to Participate in Social Roles and Activities-Short Form
PROMIS F7a	Patient-Reported Outcome Measurement Information System Fatigue-Short Form
PROMIS PF10a	Patient-Reported Outcome Measurement Information System Physical Function-Short Form
PROMIS PI6b	Patient-Reported Outcome Measurement Information System Pain Interference-Short Form
PT	Physical Therapy
QC	Quality Control
RA	Rheumatoid Arthritis
RAPA	Rapid Assessment of Physical Activity
RAPID 3	Routine Assessment of Patient Index 3
RCT	Randomized Controlled Trial
REDCap	Remote Electronic Data Capture
SAE	Serious Adverse Event
SEE	Self-Efficacy for Exercise Scale
SNAP	Speedy Nutrition and Physical Activity Assessment
SO	Safety Officer
STEADI	Stopping Elderly Accidents, Deaths, and Injuries
SVLA	Short-Valued Life Activities questionnaire
TSK	Tampa Scale for Kinesiophobia
UNC	University of North Carolina
UP	Unanticipated Problem
US	United States

10.4 PROTOCOL AMENDMENT HISTORY

Version	Date	Description of Change	Brief Rationale
2.0	03/05/2025	1.1 Synopsis Exploratory Outcomes: Refined questions related to physical activity, exercise, and sleep, removed SNAP and RAPA, added the ETS, and built out questions for functional status, rehabilitation experience, and intervention utilization.	The list of assessments was modified to better capture RA disease activity, functional limitation, disease symptoms, physical activity levels, and psychosocial factors associated with exercise and movement. This is important for refining the PREVAIL model of care.
2.0	03/05/2025	1.2 Schema Edited to include “Provide referral if necessary”	This was updated to reflect current PT consult call processes.
2.0	03/05/2025	1.3 Schedule of Activities Rehabilitation Experience Questions added for Visit 2. RAPA removed from Visits 2 and 5. Physical Activity and Exercise Participation Questions, Functional Status Questions, and Expectation for Treatment Scale added to Visits 2 and 5. Intervention utilization questions added to Visit 5.	See rationale for 1.1 Synopsis.
2.0	03/05/2025	2.1.2 Scientific Rationale “(1) <u>Disability Screening (now referred to as Daily Activity and Participation Screen).</u> ”	The screening tool has been renamed for participant acceptability.
2.0	03/05/2025	3 Study Objectives and Endpoints See edits to 1.1. Synopsis	See rationale for 1.1 Synopsis.
2.0	03/05/2025	5.5 Strategies for Recruitment and Retention Included that we will review clinician schedules as part of recruitment, and that there will be up to three phone calls during the recruitment process.	Clinician schedules will be reviewed to identify eligible participants that were not captured in the CDWH list, if any. Phone call processes were updated to match previously approved recruitment follow-up procedures.
2.0	03/05/2025	6.1 Study Intervention and Administration “the “Daily Activity and Participation Screen” (DAPS), previously referred to as the disability screening tool”.	See rationale for 2.1.2 Scientific rationale. Google Analytics will be used to quantify website use without collecting individual participant data. This will be used to refine the exercise resource for future studies.

		Using Google Analytics to quantify website use.	
2.0	03/05/2025	6.2 Fidelity Removed Dr. Johnathan Gerald's name from PT consult call training section.	Dr. Gerald's will no longer be the only trained study physical therapist.
2.0	03/05/2025	8.1 Endpoint and Other Non-Safety Assessments Updated attainment of feasibility metrics to include reviewing clinician notes and collecting intervention utilization questions specific to model of care components. Removed descriptions of RAPA and SNAP, included descriptions of ETS and functional status questions, and added physical activity and exercise participation questions as measured endpoints.	Reviewing clinician notes after the participant's routine visit allows the study team to track delivery of two of the essential components (recommendation and exercise resource). Intervention utilization questions capture website use and other key information for refining the PREVAIL model of care.
2.0	03/05/2025	10.3 Abbreviations ETS was added to the abbreviations list.	List was updated to reflect all abbreviations used in the protocol.
3.0	04/11/2025	5.2 Exclusion Criteria Updated recent/upcoming surgery to "Major surgery requiring overnight hospital admission and/or resulting in functional loss, requiring rehabilitation".	We wanted to minimize screening individuals out for minor procedures or surgeries that didn't impact rehabilitation utilization.
3.0	04/11/2025	5.5 Strategies for Recruitment and Retention Removed second MyChart message from recruitment methods.	MyChart functionality is different than we expected, and it is not useful to have a second message.
3.0	04/11/2025	10.1.1.2 Consent Procedures and Documentation Included that study team will be following up to aid in completion of remote enrollment if necessary.	Clarified additional contacts that may be needed to follow up with potential participants who begin the remote enrollment process but do not complete for some reason. We will contact them to assist with completion or ask if they are no longer interested.
1.2 Schema	05/06/2025	Baseline assessment visit extended from ending Day 0 to ending Day 1	This is to account for people that enroll closer to their visit date or are having technical difficulties but are able to complete the screening tool before their visit.

		Clinical and comorbidities moved from Visit 2 to after Visit 3.	See rationale for 1.3 Schedule of Activities
1.3 Schedule of Activities	05/06/2025	Clinical and comorbidities moved from Visit 2 to after Visit 3.	Ensuring that this information is up to date as of the date of their rheumatology visit (Ex. current medications).
1.2 Schema	05/20/2025	Visit 4 extended from “Day 15” to “Day 42”.	We will continue to target reaching participants within 2 weeks of their routine visit to schedule their call, but extending this window allows for reasons people may not be able to complete their call within 2 weeks (Ex. traveling for summer vacation).

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