A.COVER PAGE:

1. Identifying Information

Program Title:	**Improving RA Flare Management: Developing and testing an intervention using a toolkit informed by patients and providers**	
Grant ID Number:	15330785	
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	Eric Ruderman, MD	Academic rheumatologist; T2T expert
	Jeffrey Curtis, MD, MS, MPH	Outcomes researcher with expertise in direct to patient interventions
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2. Abstract

The goal of rheumatoid arthritis (RA) treatment is to minimize disease activity. To achieve this goal, rheumatologists and their RA patients need to actively monitor and manage disease flares and respond to persistently elevated levels of disease activity. However, our past work has demonstrated that only 1 in 5 RA patients seek medical attention for disease flares and less than 50% of biologic naïve patients on a nonbiologic disease modifying anti-rheumatic drug (DMARD) had their dose increased or were prescribed another DMARD (nonbiologic or biologic) in the setting of flare or sustained moderate/high disease activity. In the context of understanding how best to optimize management of RA flares and inadequate disease control, we propose to leverage an ongoing Treat-to-Target (T2T) clinical trial and conduct in-depth interviews with patients and rheumatologists randomized to the T2T arm, which required DMARD therapy acceleration and monthly clinical visits in patients with active disease. Interviews will be conducted in both those adherent and nonadherent to the intervention treatment protocol. Based on these results, we will adapt an available chronic condition toolkit to the RA patient population targeting RA flare management. This toolkit will provide action-oriented guidance for patients, rheumatologists and their office staff to better manage RA disease flares. The toolkit will be tested as part of a cluster randomized clinical trial to assess whether an intervention that introduces the toolkit into routine clinical care reduces the frequency and duration of RA flares and improves clinical outcomes including disease activity, pain, and function.

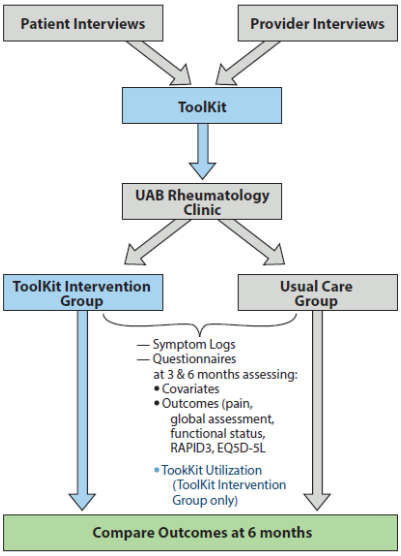
C. MAIN SECTION OF PROPOSAL

C.1 Overall Goals and Objectives. The overall goal is to develop and test an intervention that introduces a rheumatoid arthritis (RA) toolkit (an action-oriented compilation of RA related information, resources and tools with a focus on optimizing care) into routine clinical care engaging patients, rheumatologists and their office staff, and designed to improve flare management. We will accomplish this goal by achieving the following objectives:

1. In partnership with the Corrona Research Foundation, we will leverage a soon-to-be completed Treat to Target (T2T) clinical trial and learn from participating patients and rheumatology practices that were randomized to the T2T arm, which mandated treatment accelerated and monthly visits in those with RA flares and persistently elevated disease activity. We will conduct in-depth interviews with these participating patients, rheumatologists and office staff to understand the facilitators of, and barriers to, reducing disease activity and more aggressive recommendation-based intervention with a focus on flare management in everyday clinical practice.
2. We will adapt a currently available chronic illness toolkit developed by the Institute for Healthcare Improvement (IHI) for the RA patient population based on the in-depth interviews. The toolkit will be designed for patients, rheumatologists and their office staff. Sample tools include symptoms logs for patients to use, RA action plans for patients to complete with their provider outlining flare symptoms and treatment strategies, and flowcharts for office staff to guide triaging of patient phone calls.
3. We will conduct a cluster randomized controlled trial (RCT), comparing the patients who received the toolkit to those who did not in terms of flare frequency and days in flare over 6 months. We will also examine differences between groups in disease activity, patient pain, and functional status over the study period.

C.1.a Study Overview. The outline for the study is displayed in Figure 1. Working with the Corrona Research Foundation, we will identify the patients and providers (rheumatologists and their office staff) who were randomized to the T2T arm in the Corrona T2T trial. From that group, we will recruit both patients and rheumatology practices who were adherent to the treatment protocol (meaning accelerated treatment and more frequent visits when required based upon the occurrence of RA flare or sustained moderate or high disease activity) and those who did not for in-depth interviews. Based on the interviews we will identify the facilitators of, and barriers to, reducing disease activity with a focus on flare management. The "lessons learned" by the participants, including their attitudes towards aggressive treatment based on disease activity levels and strategies they used to be adherent to the protocol, will inform the adaptation of the IHI patient and clinician toolkits on chronic disease management for

Figure 1. Study outline



the RA patient population. We propose to create 1 toolkit to be used by all stakeholders, and it will include both physician practice and patient components. The toolkit will be a collection of text documents including flowcharts, patient education and self-management materials, treatment algorithms and scientific publications. It will be made available both in paper and electronic format. We will include RA action plan templates for patients to complete with their rheumatologist. Together the patient and provider will document on the form what symptoms are suggestive of flare and how to respond, in terms of calling the office or initiating or dose escalating medication therapy. This allows each RA action plan to be tailored to the unique characteristics of the patient. Additionally there will be flowcharts for office staff to follow to provide guidance on how to triage patient phone calls for urgent symptoms. The toolkit will be tested through use of a cluster RCT comparing those who receive the toolkit (intervention group) as compared to those receiving usual care to assess the impact on flare frequency, days in flare and clinical outcomes including disease activity using the Routine Assessment of Patient Index Data (RAPID3), patient pain, patient global assessment of disease activity, and function. As the RFP states, there is no commonly accepted understanding of the constituents of a flare in RA and no well-validated measure for evaluating flares in RA. We anticipate using the Outcome Measures in Rheumatology Clinical Trials (OMERACT) provisional definition of flare but will work closely with our expert panel (below), which includes an international expert in flare (Dr. Clifton Bingham III), on how best to define and quantify flares. [1, 2] Throughout the conduct of the study, we will seek input and feedback from our expert panel which includes rheumatologists Drs. Joel Kremer, Clifton Bingham III, Eric Ruderman and Jeffrey Curtis as well as the research director of an arthritis patient advocacy organization, Dr. W. Benjamin Nowell (**see Section D**).

C.2 Technical Approach

C.2.a Current Assessment of Need. The current goal of RA management is to reduce disease activity to achieve remission, or when not possible, low disease activity. [3, 4] This requires active monitoring for and management of disease flares in RA patients. RA flares can impact a patient's quality of life, his/her ability to perform usual tasks and put him/her at higher risk for irreversible joint damage. Thus systematic monitoring for flares with appropriate self-management and titrating of medications in response to symptoms are important. Additionally, for those patients with persistently active disease, titrating medication therapy until low disease activity or remission is achieved (e.g., the T2T approach) is recommended. However, this frequently does not occur in clinical practice.

Flares of RA are exceedingly common with reports of 50 to 60% of patients experiencing flares in the prior 6 months. Of concern is that 1 in 4 patients reported no pharmacologic or nonpharmacologic treatment for their flares. [5] Additionally, using Corrona patient survey data to evaluate RA flare-related needs we found that ***only 1 in 5 patients sought medical attention from their rheumatology provider (doctor, physician assistant, nurse practitioner or nurse) to treat the flare*** *(unpublished data)***.** The low proportion of patients seeking immediate care from their rheumatology provider raises the importance of 1) the need to better connect patients to their clinicians, 2) educating patients on the consequences of sustained active inflammation, and 3) promoting patient self-tracking and self-management behaviors. A similar trend is seen at routine encounters with rheumatologists with substantial numbers of patients with active

disease not receiving the recommended care. [6] Specifically, within Corrona we identified that ***less than 50% of eligible biologic naïve RA patients on a nonbiologic disease modifying anti-rheumatic drug [nbDMARD] had treatment acceleration,*** defined as: 1) a dose increase in their nbDMARD; 2) adding or switching to another nbDMARD, or 3) initiation of a biologic, when presenting for routine care when in a flare or persistent moderate or high disease activity. [7]

To improve flare management, better methods for patient education, teaching of self-management strategies and facilitation of patient-provider communication are needed. Toolkits have been shown in other medical conditions have been well received by patients and providers and shown to improve clinical outcomes. [8, 9] Overall, patients have been receptive to toolkits, reporting that they meet a genuine need and patients have implemented the recommendations contained within the toolkits. Clinicians have also reported a high satisfaction rate, noting benefits associated with use of the toolkit including improved patient dialogue and better explanation of treatment side effects than what can be typically discussed during routine clinical encounters. Toolkits have also been shown to increase the proportion of patients who receive recommended care and reduce adverse events. [8, 9] ***Thus we propose to develop and iteratively refine a toolkit for the RA patient population and evaluate its effectiveness via a cluster RCT.***

C.2.a.i Data Sources and Methods. A noteworthy strength of this proposal is that it leverages the fully-enrolled T2T trial being conducted by Corrona, LLC (Dr. Kremer, a member of the expert panel is PI of the T2T trial). The trial is a cluster-randomized behavioral intervention to assess the feasibility and effectiveness of the T2T approach within the Corrona network, and Dr. Harrold (PI of this application) is a co-investigator. Specifically the T2T clinical trial was designed to evaluate whether T2T improved RA outcomes when compared to a control group treated with "usual care" (UC) enrolling 536 patients across 28 practices. Those practices randomized to the T2T arm (40 rheumatologists) were required to escalate therapy and see patients (249 patients) monthly until they achieved low disease activity or remission. The trigger for this treatment escalation was either an RA flare or more sustained moderate or high disease activity, as measured by the Clinical Disease Activity Index (CDAI). The trial will end July 31, 2014, creating an ideal opportunity to the follow-up study proposed in this application. Learning from the patients and rheumatology practices participating in the T2T arm will be invaluable as they will know firsthand both the challenges and the successful strategies (e.g., adding more urgent visits to providers' schedules) needed to overcome barriers to more frequent disease monitoring and titration of medications in response to disease activity.

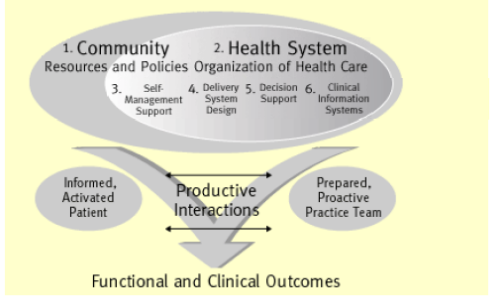
The team will conduct in-depth interviews with the T2T patients and rheumatology practices, which will be analyzed using qualitative methods and guided by Dr. Kathleen Mazor, who is a psychometrician with extensive experience in using both quantitative and qualitative methods to understand patients' and providers' views on complex health topics, including medication decision making, and has more than 20 peer reviewed publications reporting on results from in-depth interviews and focus groups. Drs. Harrold and Mazor with Ms. Lemay (project manager) have previously received funding from the National Institutes of Health and Agency for Healthcare Research to conduct in-depth interviews with subsequent toolkit creation. [10, 11]

C.2.a.ii Primary Audience and Expected Beneficiaries of Intervention. The RA toolkit will be evaluated at the University of Alabama at Birmingham (UAB), in a diverse and busy rheumatology clinic with 17 clinical providers caring for over 20,000 patients. ***Additionally, the toolkit will be disseminated more broadly to RA patients and rheumatologists through the arthritis patient organization, CreakyJoints, and the Corrona network of >600 rheumatologists across 40 states in the US*** (see Section C.2.c.i.14 on Dissemination).

C.2.b Project Design and Methods

C.2.b.i Theoretical Framework. The Chronic Care Model summarizes the basic elements for improving chronic illness care and will therefore serve as the theoretical framework for the planned intervention (See **Figure 2** below). [12] The Chronic Care Model states optimal chronic care is achieved when a "prepared, proactive team interacts with an informed, activated patient." This suggests a patient-professional partnership that consists of 2 components: collaborative care and self-management education. Collaborative care assumes professionals are experts about diseases and patients are experts about their own lives and that both parties share responsibility for solving problems and achieving optimal outcomes. This is critically important in RA, a disease that flares and abates and thus active engagement of patients is essential. Self-management education builds upon traditional patient education as it teaches problem-solving skills. **The toolkit will be designed to improve flare management as it will address many of the critical elements of the Chronic Care Model including 1) self-management support, 2) delivery system design so that patients with flare can be seen urgently by providers as needed, and 3) decision support with action plans developed collaboratively with patients and providers specific for RA flare management, modeled after the Asthma Action Plan developed by the National Heart Lung and Blood Institute.**

Figure 2. Chronic Care Model



C.2.b.ii Objective 1: Patient & Provider Interviews--Understanding Facilitators of, and Barriers to, Flare Management.

C.2.b.ii.1 Overview. The patient, provider and system factors that facilitate as well as impede medical therapy to suppress disease activity have not been previously explored. Thus we propose to conduct in-depth interviews with patients and rheumatology practices randomized to the T2T intervention arm in an ongoing T2T trial (16 practices, 40 rheumatologists and 249 patients), as their experiences in this trial—aggressive management of flare or persistent disease activity – will give them unique insights into how to manage care coordination, interactions outside of regularly scheduled appointments, and altering therapy in response to disease activity. Specifically patient and rheumatology practice participants in the trial can tell us about the hurdles they faced and the strategies they tried when patients had worsening of their CDAI of ≥6 units (equivalent to a 28 joint Disease Activity Score [DAS28] increase of ≥1.2), which required escalating frequency of office visits and medication therapy. Patient interviews are designed to examine patients' understanding of RA and the need for disease control, their

perceptions of the barriers to, and facilitators of, effective disease self-management focusing on what to do when flares occur and what clinicians need to do in order to help patients (**Table 1**). The purpose of the interviews with rheumatologists is to describe providers' perceptions regarding appropriate flare management and gather information from their perspective on the most effective strategies for improving patients' ability to manage their flares. The interviews with the rheumatology practice staff will focus on how to triage patients when they call with flare symptoms and how to rearrange schedules to accommodate more urgent health care visits (**Table 1**).

Table 1. Domains and sample questions for the interviews.

Domain	Sample questions to identify facilitators of, and barriers to, optimal management
Rheumatology practices (rheumatologists and their office staff)	
System-level	What system-level barriers did you face? For example, did patients decline enrollment into the T2T study due to high co-pays for office visits or concerns about medication costs? Did patients' pharmacy benefits limit your ability to follow the T2T protocol? What, if any, system-level factors hindered and which factors helped you effectively follow the T2T protocol?
Practice-level	Was it difficult for your practice to follow the T2T protocol? For example, was it challenging for your office to accommodate the more frequent office visits? Do you have team based care with patients following up with mid-levels or fellows? If patients called with urgent symptoms, how often and how quickly were they typically seen in the office? What practice strategies facilitated the T2T approach?
Patient-level	Were patients receptive to the T2T approach? Was it difficult to communicate and implement the T2T approach with patients during routine visits? What materials or resources did you use to explain the T2T concept with patients? What are your concerns if patients do not achieve good disease control? What approaches were helpful to encourage patients to follow the T2T protocol?
Patients	
System-level	Did you ever skip medications or office visits because of high out of pocket health insurance or pharmacy costs? Do you have access to a rheumatologist who is close to where you live?
Practice-level	Were you able to see a provider when you needed to? Have you ever talked with your rheumatologist about what to do if your symptoms worsen? Does your rheumatologist provide a written summary of your visit? Has he or she ever given you a written summary of how to manage a flare? What has your doctor done that has been helpful (or not helpful) in terms of communicating treatment goals or therapeutic options?
Patient-level	What is your understanding of rheumatoid arthritis? What is your goal for treatment? How well is your arthritis controlled? What do you do to manage symptoms flares? Do you feel well equipped to manage your arthritis symptoms? What would be helpful for you to better control your arthritis?

C.2.b.ii.2 Patient and Rheumatology Practice Sample. In-depth interviews will be conducted with patients and rheumatology practices that were approached for the T2T trial, which mandated in the intervention arm visits as frequently as monthly in patients with flare (increase of CDAI ≥ 6 units) or sustained elevated disease activity. We will specifically target patients in the following categories: 1) those who declined participating in the T2T study, 2) those who enrolled in the T2T intervention arm of the study but were not adherent to the protocol, and 3) those in the T2T intervention arm who were adherent. For each of the 3 categories, we anticipate completing 8 to 10 interviews with patients, for a total of 24-30 patient interviews, or until we reach content saturation. For rheumatology practices, we will include those who participated in the T2T intervention arm and thus had to accommodate the increased visit frequency among patients with inadequately controlled disease and accelerate care.

Specifically, we will target 5 to 6 rheumatologists and 5 to 6 office staff personnel (triage nurses, patient schedulers and office managers) that were successful in implementing T2T. In addition, we will target those practices that were unsuccessful in following the T2T protocol, with the goal of performing interviews with 5 to 6 rheumatologists and 5 to 6 office staff personnel. Thus in total we anticipate conducting interviews with 10-12 rheumatologists and 10-12 office staff members. Based on prior experience, we anticipate these sample sizes will be more than adequate for achieving saturation, but we are prepared to conduct additional interviews if needed. [10]

C.2.b.ii.3 Patient interviews.

Content: The interviews with patients will focus on their knowledge and beliefs regarding the consequences of persistent active disease, their strategies for management of flares, barriers to treatment acceleration, and their approaches to self-monitoring and self-management (**Table 1**). The patient interviews will provide information on patient experiences of particularly effective or ineffective patient-provider communication regarding education around flare management and health system barriers. Therefore, this phase of the proposed study will consist of a series of non-directive, in-depth telephone interviews with a sample of **24-30** patients with active RA.

Recruitment: We will identify potential participants using the eligibility criteria described above. We will stratify recruitment based on patient age (50% < 65 and 50% ≥ 65) and DMARD therapy (50% on monotherapy and 50% on combination therapy when in flare) to ensure we interview a broad range of patients. A letter describing the purpose of the interviews will be sent to potential interviewees, with a telephone number to allow patients to request additional information, or to schedule an interview time. Participants who agree to the interviews will be contacted via the telephone by a trained interviewer. Interviews will begin with open-ended questions to elicit the maximum amount of information with minimal bias. Probes will be used as needed to ensure that all key domains are addressed. Participants will be offered $25 gift cards for their time and trouble; interviews will take no more than 1 hour and will be audiotaped; audiotapes will be transcribed to facilitate analysis. Informed consent will be obtained. Given these patients already consented to the T2T trial and our prior experiences conducting in-depth interviews, we do not anticipate challenges recruiting patients for these interviews. [10]

C.2.b.ii.4 Rheumatology practice interviews.

Content: Rheumatologists will be interviewed to gain insights into the barriers to, and facilitators of, effective RA flare management and will parallel the patient interviews (**Table 1**). Provider interviews will focus on their treatment approaches (both to flare management and in response to persistent active disease), patient training in self-monitoring and self-management, and communication strategies with patients in between visits. We will also question providers on how they instruct their patients to manage flare symptoms. In addition, we will solicit providers' views on what information points are most essential for patients to fully understand disease management around the time of a flare, and what strategies are most effective in conveying those points. Interviews with the rheumatology office staff will focus on the strategies they used for the T2T trial which required more frequent visits, such as changing

their scheduling system to accommodate more acute visits as compared to routine visits, and use of mid-level providers.

Recruitment: Potential rheumatology practice participants (rheumatologists and office staff) will be selected from the list of rheumatologists randomized to the T2T intervention arm and who meet eligibility criteria as outlined above. Dr. Harrold will be the interviewer for the clinician interviews as she has previously used this methodology with physicians and rheumatologists are more likely to respond to an invitation from a colleague. She will contact clinicians via email, fax or telephone to invite participation and to schedule a time for the telephone interview. We anticipate conducting **10-12** interviews, each lasting approximately 30-45 minutes given the challenges engaging physicians. A $200 gift card will be provided to rheumatologists for their time and trouble. A similar procedure will be performed with the rheumatology office staff with a goal of conducting **10-12** interviews total, including rheumatology practice triage nurses, schedulers and office managers and each lasting 30-45 minutes. These professionals will receive a $50 gift card for their time and trouble. Informed consent will be obtained. Interviews will be audiotaped and transcribed.

C.2.b.ii.5 Data Analysis. Analyses of both the patient and rheumatology practice transcripts will inform the development of the toolkit as they will identify the critical elements needed for optimal flare management and titrating medication in response to elevated disease activity. Specifically, we will use the interview guides as an organizing framework. Written transcripts for each taped interview will be reviewed and themes identified. Drs. Harrold and Mazor with Ms. Lemay will review transcripts and identify themes. This process will be performed separately for patient and rheumatology practice interviews. Overall, the analysis of the patient transcripts will focus on identification of barriers to, and facilitators of, effective flare management and patients' views of effective RA self-management, and the consequences of poorly controlled disease activity. Review of the rheumatology practice transcripts will identify successful strategies for physicians to work with patients to address flare symptoms. Lastly, analyses of both the patient and rheumatology practice transcripts will seek to identify commonalities in the most effective strategies for patient education and self-management training, skills that are necessary for controlling RA disease activity and flares. **These results will be used to inform the development of the toolkit to be used by RA patients, rheumatologists, and office staff.**

C.2.b.iii Objective 2: Development of Educational and Quality Improvement Tools to Improve RA Flare Management

C.2.b.iii.1 Overview. Guided by the in-depth interviews, we will produce a toolkit containing tailored products targeting: (a) RA patients; (b) rheumatologists and their clinical staff (nurse practitioners, physician assistants, and nurses); and (c) office support staff (office administrator, and office scheduler). To facilitate this being used by multiple members of busy clinical sites, we will create binders with the text documents but also make the materials available online. The creation of the toolkit will be an iterative process with input from our expert panel and cognitive interviews with potential users of the toolkit.

C.2.b.iii.2 Developing the Toolkit and Supplemental Materials. We will adapt the IHI toolkits designed to instruct clinicians on partnering with their chronic disease patients, including facilitating patient self-monitoring and self-management for those involved in patient care: (a) RA patients; (b) rheumatologists/clinical staff; and (c) office staff. The IHI toolkits for clinicians (http://www.innovations.ahrq.gov/disclaimer.aspx?redirect=http://www.ihi.org/resources/Pages/Tools/SelfManagementToolkitforClinicians.aspx) and for patients (http://www.ihi.org/resources/Pages/Tools/SelfManagementToolkitforPatientsFamilies.aspx) are available online. The IHI toolkits focus on promoting collaborative care (patients and providers being a team working together), building relationships, gathering clinical and patient experience data, team care (mid-levels, nurse and medical assistant) coaching and support, providing ongoing follow-up and sustaining self-management support. This will be adapted for RA patients and rheumatology practices based on the in-depth interviews. Additionally we will perform a literature review to identify summaries of evidence-based treatment recommendations, international consensus statements on flare and T2T, and consequences of inadequately controlled disease. We will also include patient educational materials, patient tools for self-monitoring, and RA action plan templates. ***Using the Asthma Action Plan developed by the National Heart Lung and Blood Institute as a model, we envision the RA action plan template to be completed by patients and providers together at the time of clinical encounters so that patients will know the symptoms of flare and what do to when the symptoms occur.*** We will also provide "tips from the field" based on interviews conducted as part of Objective 1 with a focus on successful approaches by patients and providers to overcome barriers to optimal flare and disease management.

The toolkit will include documents adapted for multiple audiences. For example, information on the consequence of poorly controlled disease activity will result in 2 adaptions—one for patients using lay language and another for providers. When patients receive the toolkit, they will be directed to their section. However, they will have access to all sections to share with all involved providers such as primary care providers and specialists, in addition to rheumatologists. Likewise, the rheumatologist will have access to the materials the patients are receiving. Potential products to be included in the toolkit are outlined below in **Table 2**. To develop the products, we will use an iterative process. The research team will draft the toolkit based on the IHI toolkits which are available publically. The tools will be revised based on the in-depth interviews in Objective 1 and the literature review. Following this, the revised version of the toolkit will be reviewed by our expert panel of rheumatologists (Drs. Kremer, Bingham, Ruderman, and Curtis) and a representative from a patient advocacy organization (Dr. W. Benjamin Nowell from CreakyJoints). Working with the research team, the expert panel will be evaluating the toolkit's thoroughness in identifying and addressing barriers, meeting the needs of the different constituents, and ensuring the developed tools are patient-centered. We will also recruit 3-5 members of each intended audience (patients, providers [rheumatologists, nurse practitioners, physician assistants, nurses] and office staff), who have not participated in the in-depth interviews, to review draft materials. We will perform cognitive interviews using the "think aloud" procedure and probes to ensure understandability and fidelity to the tool intent. During this pre-testing, participants will provide feedback on perceived relevance, salience, comprehensibility, and acceptability of the adaptation and supplemental materials. The interviewer will also solicit feedback on both the content and the

format of the adaptations, and methods of delivering the information so as to maximize impact. After each review, the RA toolkit will be revised again until the expert panel and the investigator team concur that the adaptation is appropriately targeted, and the intended audience finds the information relevant to flare management.

Table 2. Potential tools to be created for toolkit and the relevant stakeholders.

Stakeholder Group	Rationale (justification of target)	Potential Product
Patient	Responsible for communicating changes in health status	Proposed Adaptation: The IHI Patient toolkit sections on shared decision-making, self-monitoring and chronic disease management resources will be adapted for flare management. Proposed Use: Patients will receive 1 page fact sheets on RA, the consequences of inadequately controlled disease, the current state of the art regarding the definition and impact of RA flare, and the T2T treatment paradigm. They will receive self-monitoring tips, action plans to fill out with providers for when symptoms are flaring, and patient educational tools/brochures about the benefits and risks of biologic and nonbiologic DMARDs and anti-inflammatory medications.
Rheumatol-ogists and their clinical staff	Providers need to introduce team members and explain their roles	Proposed Adaptation: The IHI Clinician toolkit sections on team care, providing follow-up and sustaining self-management will be adapted for chronic RA disease management. This will include flow diagrams and a variety of successful strategies demonstrated by the sites adherent to the T2T protocol. Proposed Use: Providers and their clinical staff will receive diagrams and care plans they can use in daily practice outlining successful team-based strategies for flare and RA management.
Office staff	Office staff is responsible for booking appointments and sending messages to clinicians	Proposed Adaption: Adapt the IHI Clinician toolkit team care section. Proposed Use: The office team will have flow diagrams displaying algorithms on how to triage patient phone calls for symptoms consistent with RA disease flares including scheduling of these patients for urgent appointments.

C.2.b.iii.3 The Toolkit. When the adapted components of the IHI toolkits have been thoroughly reviewed and finalized, they will be assembled into a toolkit for dissemination. The toolkit will provide an introduction to the materials and rationale for use, supporting materials to facilitate implementation, and forms for tracking implementation at the physician's office.

C.2.c Evaluation Design

C.2.c.i Objective 3: To Conduct a Cluster RCT to Evaluate the Impact of an Intervention Centered on a Toolkit to Improve RA Disease Management.

C.2.c.i.1 Overview. We have designed a cluster RCT at the level of the provider with the unit of analysis being the patient to evaluate the impact of an intervention centered on an RA toolkit to reduce flare and improve patient outcomes over a 6-month period. The population for this RCT will be RA patients with moderate-high disease activity, since they have the most frequent disease flares. Within the UAB rheumatology clinic, we will randomize 8 providers to enroll 132 eligible patients to receive the toolkit (toolkit intervention "TI" group) and 8 to enroll 132 patients in the usual care group ("UC") (**see letter of support from Dr. Louis Bridges**). Of note, the toolkit will include an RA action plan template in which providers and patients together

document the RA symptoms signifying flare and the therapeutic steps to address these symptoms when they occur. Because of this, we were concerned that rheumatologists would be unable to treat their patients in the TI group differently than their patients in the UC group. Thus we randomized based on the providers. The providers and patients randomized to the TI group will receive training on the content of the toolkit. Both the TI and UC patients will be asked to complete flare tracking logs recording flare incidence (based upon the provisional OMERACT RA flare definition), symptoms (e.g., pain, stiffness, swelling, etc) and their actions around the time of flare including medication changes, nonpharmacologic therapy and contacting their provider for more urgent evaluation. All patients will receive biweekly reminders to complete the flare tracking logs at the time of flare. In addition, patients will complete self-administered mailed or emailed questionnaires at baseline, 3 months and 6 months to evaluate changes in outcome measures. At study completion, we will compare TI and UC patients in terms of changes in flare frequency and days in flare based on the flare tracking logs as well as disease activity using the RAPID3, and patient reported outcomes including pain, global assessment of disease activity, and functional status using the Multidimensional Health Assessment Questionnaire (MD-HAQ). In addition, we will compare utilization of self-management behaviors between the two groups over the study period.

Table 3. Schedule for cluster RCT

	TI group	UC group
Patient and Rheumatologist toolkit orientation	X	
Symptom logs	X	X
Baseline assessment	X	X
3-month assessment	X	X
6-month assessment	X	X

C.2.c.i.2 Study Setting and Population. The intervention will be performed within the UAB rheumatology clinics, which includes 17 clinical providers and 20,000 patients. The demographics of the UAB RA clinic reflect the geographic area including 22% Whites, 73% Black/African American, and 4% Latino. The median annual household income is $31,500 with 29% of the population below the poverty level.

C.2.c.i.3 Eligibility Criteria and Screening. Eligibility criteria include: 1) patient has a diagnosis of RA based on the 2010 revised ACR/EULAR diagnosis criteria; 2) able to understand and participate in the protocol; 3) patient speaks English; and 4) able to understand and provide informed consent (for persons with low literacy we will require that a representative of the patient also understands and signs the consent on behalf of the patient). Exclusion criteria include: 1) low disease activity or remission at the time of enrollment based on the RAPID3; 2) inability or unwillingness to be contacted (mailings, emails, telephone calls, or SMS messaging) from research staff; 3) inability or unwillingness to complete the self-administered questionnaires at baseline, 3 months and 6 months; 3) inability or unwillingness to keep flare tracking logs and 4) inability or unwillingness to provide informed consent.

C.2.c.i.4 Recruitment. Patients with a diagnosis of RA who receive care at the UAB rheumatology clinic will be approached by a study coordinator at UAB for enrollment into the study. Specifically, the study coordinator will identify all potentially eligible RA patients based

on reviewing charts to confirm the patient's RA diagnosis. Then at the time of the clinic appointment, a study coordinator will approach patients to describe the study and quickly screen the patient including administering the RAPID3 to exclude patients in remission or low disease activity (score 0-2 on a 0-10 scale). This assessment is greatly facilitated by the fact that RA patents at UAB routinely have RA flare (using the draft OMERACT specifications) and the RAPID3 (and other disease activity measures such as the CDAI) collected at each routine office visit. The study coordinator will follow an interview script during his/her conversations with potential participants and the script will include questions related to the eligibility and exclusion criteria (described above). The study coordinator will obtain written informed consent for study participation in those patients who are willing to participate. If there are questions the study coordinator is unable to answer, Dr. Harrold will be contacted to follow up with the patient as appropriate. Following study consent, the study coordinator will provide the Research Assistant working with Dr. Harrold at the University of Massachusetts Medical School (UMMS) the patient contact information. The team at UMMS is skilled in patient engagement and retention using the approach outlined here. In a large observational registry at UMMS enrolling a national sample of >20,000 patients undergoing joint replacement, we have successfully enrolled >90% of eligible patients over the phone from busy orthopedic offices with >90% complete surveys over a 6 month follow-up without any patient financial incentives.

C.2.c.i.5 Study Orientation for Patients. For both TI and UC patients, the Research Assistant will review the study objectives and expectations with them over the phone or via a webinar, depending on the patient's preference. This includes reviewing the importance of filling out the flare tracking logs and completing the baseline, 3-month and 6-month assessments. These questionnaires will be administered via email or mailed based on the patient's preference. For those randomized to the TI group, the Researcher Assistant will conduct the training on the toolkit. This will be done based on the patient's preference including via a webinar or over the phone with hardcopies of the materials provided to the patient prior to the training.

C.2.c.i.6 Study Orientation for the Rheumatologists. The rheumatologists randomized to the TI group will be oriented to the study and the toolkits by Dr. Harrold. This includes reviewing the different sections of the toolkit, as well as brainstorming how to effectively and efficiently develop RA action plans with patients during busy office visits. We anticipate this orientation will only take 45 minutes and providers would be compensated for their time and thus the burden on the physicians for this one-time training is minimal.

C.2.c.i.7 Data collection. At all three time points (baseline, 3 months, and 6 months), both the TI and UC groups will be sent self-administered questionnaires assessing the following: 1) RA treatments; 2) comorbidities; and 3) outcomes including the patient pain, patient global assessment of disease activity, functional status using the MD-HAQ, and disease activity using the RAPID3. In the TI group, at the 3 and 6 month time points there will be an assessment of the utilization of the toolkits in terms of which sections were reviewed, how often were they used, whether the RA action plan was completed with a physician and whether they followed the RA action plan. Those who do not return the questionnaires in the subsequent 2 weeks will be contacted with up to three contacts from the Research Assistant to encourage data

collection. This may include secure emails (through the UAB Patient Portal, for those who use it), phone calls (expected for the majority of patients), SMS text messaging or reminder postcards. Both the TI and UC groups will be asked to complete flare tracking logs with patients being asked if they had a flare of their RA over the past 2 weeks based on the provisional OMERACT flare definition. Those patients in flare will be asked to provide information on a weekly basis until the flare resolves, including the number of days in flare. Patients will be asked to record flare symptoms (e.g., pain, swelling, redness, fatigue, etc), location, severity and flare management behaviors. Flare management behaviors includes increasing the dosages of current medications (e.g., narcotic, nonsteroidal anti-inflammatory drug [NSAID], prednisone, nbDMARD and biologics) or initiation of a new medication (e.g., narcotic, NSAID, prednisone, nbDMARD and biologics), steroid injections, nonpharmacologic therapy (e.g., resting, applying heat or ice, physical therapy, and splinting/bracing) and contacting the physician for an urgent evaluation. These biweekly reminders to complete the flare tracking logs will be sent using the patient's preferred method of communication.

Participant compensation. Patients in both arms will receive $100 at the completion of the study.

C.2.c.i.8 Outcome Measures. In order to assess the impact of the toolkit on flare management, the following outcome measures have been chosen:

1. Flare frequency and days in flare. This information will be gathered from the flare tracking logs. Patients will be asked to provide information on the occurrence of flare and the number of days in flare using the provisional OMERACT definition.
2. Disease activity using the RAPID3 (0-10 range). The RAPID3 is a brief self-administered questionnaire that is a summation of the function scale from the MD-HAQ, pain Visual Analog Scale (VAS) and patient global assessment of disease activity VAS.
3. Patient pain (0-100 VAS). Patients report pain using a continuous 100mm scale anchored by 2 verbal descriptions (no pain and pain as bad as it could be). [13]
4. Patient global assessment of disease activity (0-100 VAS). Patients report their assessment using a continuous 100mm scale.[14, 15] The wording of the question is "Considering all of the ways your arthritis has affected you, how do you feel your arthritis is today?" with the two anchors being very well and very poor.
5. Functional status using the MD-HAQ (0-3 range) - The MD-HAQ includes 10 items asking about daily living over the prior week with higher scores representing worse function.[16]
6. Flare management behaviors. Patients will be asked on the actions they have undertaken to address flare symptoms, including medication changes, steroid injections, nonpharmacologic therapy (e.g., resting, applying heat or ice, physical therapy, and splinting/bracing) and contacting the physician for an urgent evaluation.

C.2.c.i.9 Moderating variables

For the purpose of this study, we will identify moderating variables including how the participants use the toolkit. This includes which sections were reviewed and how frequently as well as whether the patient developed an RA action plan with their treating rheumatologist as these factors may have led to a differential response to the intervention. Demographic

information including age and gender, RA disease characteristics (disease duration, and severity) and burden of comorbidity will also be explored as potential moderating factors.

C.2.c.i.10 Co-Primary Outcomes

Examine the impact of the toolkit to reduce flare frequency and days in flare. Using the flare tracking logs, patients in both the TI and UC groups will record when they have a flare and the duration of the flare. Using that information, we will perform an intent-to-treat analysis. Our statistical analysis will account for the clustering of flares within patients (patients can have more than 1 flare) and patients within physician. We will assess whether the mean number of flares and mean number of days in flare over the 6 months differs in the IT group as compared to the UC group using a random effects Poisson regression approach. We will also evaluate for trends in these measures, meaning mean number of flares/month or mean number of days in flare/month over the study period, to assess whether there are decreases or increases over the study period. If despite randomization there are differences between the two groups such as patient demographics, RA disease characteristics, and comorbid conditions (including chronic pain syndromes) we will control for these.

Examine the impact of the toolkit to improve disease activity at 6 months. Similar to the analysis plan above, we will compare the mean change in RAPID over the 6 months in the IT group versus the UC groups. The modeling framework will be a random effects linear regression model. The unit of analysis will be the patient with the patient clustered within physician. We will also examine whether type and frequency of toolkit utilization (e.g., ever use and frequency of implementation of the RA action plan and self-management materials) influenced results.

C.2.c.i.11 Secondary outcomes

Examine the impact of the toolkit to improve components of the RAPID3 (patient pain, patient global assessment of disease activity and function based on the MDHAQ) at 6 months. We will examine the components of the RAPID3 (patient pain, patient global assessment of disease activity and function) and whether the mean change in each of these scores over the 6 month period is different in TI as compared to UC patients.

Examine the impact of the toolkit to increase flare management behaviors over 6 months. Using the flare tracking logs, patients will capture at the time of each flare whether they initiative a flare management behavior and if so the type (pharmacologic, nonpharmacologic and contacting the physician). We propose to look at the proportion of flares managed and whether that differs in the TI group as compared to the UC group. Our analytic approach will adjust for clustering of flares within patients, and clustering of patients by physician. We hypothesize that the toolkit will improve patient self-management behavior. We will develop random effects logistic regression models evaluating use vs. nonuse of flare management behaviors, as well as random effects multinomial regression models to evaluate differences in flare management behaviors between groups. We will also investigate whether there is a difference over time between the two groups.

C.2.c.i.12 Power analysis
We evaluated power comparing change in RAPID3 over 6 months between the two randomized groups (TI versus UC) given there is no validated measure of flare currently. The study is a cluster RCT with the physician as the unit of randomization and the patient the unit of analysis. Power is influenced by effect size, sample size and intraclass correlation (ICC), which reflects the similarity of patient responses within physician. Using existing data from Corrona, we estimated and identified the estimated standard deviation was 1.75 and ICC was 0.008. Using these estimates, with our proposed 8 physicians per arm and 15 patients per physician (N=120/arm), there is 88% power for detecting a difference of 0.8 in change in RAPID3 between groups. There is 80% power for a difference of 0.71. This translates to a small to moderate effect size. Assuming a 10% loss to follow-up, we will aim to enroll 132 patients/arm.

C.2.c.i.13 Innovation: This study is innovative as it leverages an ongoing T2T clinical trial and thus we can target patients and providers who were adherent and nonadherent to the increased visit frequency and treatment acceleration as outlined in the study protocol for the in-depth interviews. We also propose to create the first ever RA toolkit designed to address the needs of patients, providers and office staff in order to overcome barriers to optimal care and disease management. Lastly, we propose a rigorous evaluation of the toolkit though use of a cluster RCT.

C.2.c.i.14 Dissemination
We will make available the toolkit for use by patients and providers. Specifically, the toolkit will be posted on the CreakyJoints website as well as their Facebook page and advertised to their Facebook followers. The ***Creaky Joints' Facebook page has been viewed by 10 million people, and they average a few hundred thousand conversations a day with arthritis patients, thus enabling direct dissemination to*** thousands of RA patients. CreakyJoints will develop a log-in page and track the types of users (e.g., patients, providers etc) who download the material and feedback they receive (see Dr. Nowell's letter of support), which they will share with the research team. In addition, we will distribute the toolkits to the >600 rheumatologists who participate within the Corrona network across 40 states in the US (see Dr. Kremer's letter of support). Each participating physician will receive a personal email with an electronic version of the toolkit and an offer for training of the material. Because the toolkit will include previously vetted scientific consensus statements, templates for patients to develop with their provider and general self-management strategies based on the IHI framework, we anticipate the contents of the toolkit will be of interest to patients and rheumatologists even if the TI group does not have a statistically significant decrease in disease activity as compared to the UC group. As an incentive, physicians who review the educational materials in the toolkit can receive ***up to 1.5 Continuing Medical Education (CME) Credits*** (administered by the UAB CME Division, an ACCME accredited CME provider- see letter of support from Dr. Monika Safford). In addition, any feedback we receive from these dissemination activities to patients and providers will be used to further refine and improve the toolkit. The findings of our study will also be presented at national and international rheumatology conferences. We propose to develop 3 manuscripts for publication after study completion focused on the following: 1) patient and provider views on the barriers to, and facilitators of, optimal flare management; 2) a methods

manuscript focused on toolkit development; 3) results of the cluster RCT comparing outcomes in the TI versus UC group.

C.2.c.i.15 Strengths and Limitations

The strength of this application is that the assembled team has prior experience in performing in-depth interviews, creation of toolkits, performing direct-to-patient research and conducting cluster RCTs ensuring successful performance of this grant. There are however, some limitations. We realize that the T2T patient population from Objective 1 may not be generalizable to the national RA patient population. However, to be enrolled in the T2T study patients were required to have moderate to high disease activity based on the CDAI which includes a physician global assessment of disease activity and physician derived swollen joint count, thus the target population for better disease control. Another limitation is that this is a pilot study. However, we anticipate this work will be the basis for additional investigations of the toolkit, including a multisite cluster RCT evaluating a greater number of clinical outcomes including the DAS28 RA flare criteria.[17]

C3. Detailed Workplan and Deliverable Schedule

The workplan overview is as follows. The **first year** will be focused on the conduct of the in-depth interviews. This will entail the Corrona Research Foundation identifying and contacting the patients and providers for interviews. Dr. Harrold working with Dr. Mazor will develop the interview scripts. Dr. Harrold will conduct the physician interviews and Ms. Lemay will perform the patient and office staff interviews. The resulting transcripts will be analyzed by Dr. Harrold, Dr. Mazor and Ms. Lemay. In the **second year** of the study, the toolkit will be adapted for RA patients to optimize flare management and the cluster RCT will be initiated at UAB. Dr. Harrold working with Dr. Mazor and Ms. Lemay will develop the toolkit based on their prior federally funded work adapting a toolkit for medication use in nursing home patients. The toolkit will be refined based on feedback from the expert panel and cognitive interviews with potential users of the toolkit. Then the cluster RCT will be implemented at UAB with patient completing the assessments. The **third year** of the study (last 6 months of the 30-month study period) will focus on gathering the remaining data from the RCT participants, finishing the analyses initiated in year 2, dissemination of the toolkit (through CreakyJoints and Corrona) and drafting the study final report. Dr. Harrold will supervise data collection, data analyses and summary of results. **Table 4** outlines the project deliverables and their due dates. The detailed schedule of tasks based on study objectives and the associated deliverable is provided in **Table 5**.

Table 4. Project Deliverables and Due Dates (assuming an October 1, 2014 start)

Deliverables	Expected date of completion	Suggested distribution
Study kickoff (Secure IRB approval and create patient and rheumatologist interview guide)	December 31, 2014	$84,500
Create a summary of lessons learned from in-depth interview	September 30, 2015	$84,939
Final RA toolkit	March 31, 2016	$161,500
Finalized cluster RCT protocol and finalize IRB approval for cluster RCT	September 30, 2016	$53,787
Create the final report of the study findings	March 31, 2017	$108,248

C3. Detailed Workplan and Deliverables Schedule

Table 5. Detailed Outline of Tasks for Each Objective with Deliverables.

	Year 1				Year 2				Year 3	
	1-3	4-6	7-9	10-12	13-15	16-18	19-21	22-24	25-27	28-30
Meetings with expert panel	■		■		■	■				■
Objective 1- Interviews										
Deliverable: IRB approval	■									
Identify and contact potential interviewees	■									
Deliverable: Patient and rheumatologist interview guides	■									
Conduct interviews		■								
Review and analyze transcripts			■							
Deliverable: Summary of lessons learned from the in-depth interviews				■						
Develop manuscript				■	■					
Objective 2—RA Toolkit										
Identify elements to keep and to change from IHI toolkits			■							
Literature review to identify materials for the RA toolkit (e.g., consensus statements and evidence-based RA flare management and treatment recommendations)			■							
Adapt IHI toolkits for RA				■	■					
Revise IHI toolkits based on in-depth interviews				■	■					
Perform cognitive interviews with potential toolkit users (patients, clinicians, office staff)					■					
Revise RA toolkit based on feedback					■					

Deliverable: Finalized RA toolkit										
Develop manuscript										
Objective 3—Cluster RCT										
Deliverable: Finalized cluster RCT protocol										
Deliverable: IRB approval for cluster RCT										
Train study coordinator										
Orient providers randomized to receive the toolkit										
Enroll patients in the trial										
Orient all patients (intervention and usual care) to the study protocol										
Orient those patients randomized to the intervention arm on the toolkit										
Send reminders for symptom logs										
Baseline patient questionnaire										
3-month patient questionnaire										
6 month patient questionnaire										
Analyze outcomes										
Deliverable: Toolkit disseminated to patients through CreakyJoints										
Deliverable: Toolkit disseminated to rheumatologists participating in Corrona										
Deliverable: Final report of study findings										
Develop manuscript										

C4. References

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D. ORGANIZATIONAL DETAIL

D.1 Leadership and Organizational Capacity

D.1.a Investigative team. This work will be a collaboration of the University of Massachusetts Medical School (UMMS), Corrona Research Foundation, the University of Alabama at Birmingham (UAB), Johns Hopkins University and Northwestern University Feinberg School of Medicine. Leadership of the proposal includes **Leslie R. Harrold, MD, MPH** (Principal Investigator), a rheumatologist-epidemiologist, and funded NIAMS researcher at UMMS. She holds a contract with Corrona for Epidemiologic and Biostatistical Services with funding for 4 full-time analysts, whom she directs. She is also a co-investigator of the Corrona T2T trial which is the basis for Objective 1. Her work in RA has focused on patient safety, comparative effectiveness and quality of care. [7, 18-26] Dr. Harrold has previously conducted qualitative research and thus will supervise the conduct and analysis of the in-depth interviews as well as perform the interviews with the rheumatologists as outlined. She has previously adapted a toolkit, skills that will be applicable for this application. Lastly, she has many years of experience leading multi-sites studies through her participation in the HMO Research Network Center for Education and Research on Therapeutics (CERT). [27-32] **Kathleen Mazor, EdD** (Section 4.7) is a psychometrician at UMMS with extensive experience in using both quantitative and qualitative methods to understand patients' and providers' views on complex health topics, including medication decision making, and has more than 20 peer reviewed publications reporting on results from in-depth interviews and focus groups. She also brings expertise in physician-patient communications, patient education and health literacy. Dr. Mazor will lend her expertise in developing interview guides, training and providing feedback to the interviewers, participating in the qualitative analyses, and interpreting interview findings. Additionally she has prior experience adapting toolkits so will provide her expertis as we develop an RA toolkit.

Representing the Corrona Research Foundation is **Joel Kremer, MD**. Dr. Kremer is the President of the Corrona Research Foundation and PI of the Corrona T2T trial which is the foundation for Objective 1. He will facilitate the recruitment of patients and rheumatology practices that participated in the T2T trial into this follow-up study. Additionally, he will facilitate the dissemination of the RA toolkit to the >600 rheumatologists participating within Corrona (see letter of support). **Jeffrey Curtis, MD, MS MPH**, an outcomes researcher at UAB and a coauthor of the 2008 and 2012 ACR recommendations for the management of RA. He and Dr. Harrold have worked collaboratively on many projects resulting in over 10 joint publications. In addition to providing his research expertise, he will facilitate implementation of the cluster RCT at the UAB site. **Clifton Bingham III, MD**, is a rheumatologist from Johns Hopkins University and a recognized expert in RA flare, serving on the Executive Committee for the international OMERACT group and subcommittee evaluating optimal ways to identify flares. He will provide expertise in developing the materials for the toolkit as well as evaluating flare in the cluster RCT. **Eric Ruderman, MD** is a Professor of Medicine and practice director for the rheumatology clinical practice at Northwestern University Feinberg School of Medicine. Dr. Ruderman is a participating rheumatologist in the Corrona T2T trial and has published on the challenges in implementing the T2T approach in everyday clinical practice. Thus he can provide unique insights as we develop the interview guides for the in-depth interviews as well as the

material for the toolkit. **W. Benjamin Nowell, PhD** is Director of Patient-Centered Research for the Global Healthy Living Foundation and is currently serving as co-PI in the development of a patient-powered research registry for patients with inflammatory arthritis, funded by the Patient Centered Outcomes Research Institute (PCORI). His input will be critical to ensure the developed toolkit will truly serve the needs of patients including improving patient care, disease management and quality of life. This expert panel will participate in 6 scheduled meetings over the study time period. The topics for each study meeting are listed in **Table 6** below.

Table 6. **Meeting schedule and topics for the expert panel.**

Study month	Topic for discussion
0	Orientation to the study with goals, expectations and timelines
3	Discussion of draft interview scripts for patients and providers
9	Discussion of study results from patient and provider in-depth interviews
15	Review and feedback on the draft RA toolkit
17	Review training materials and protocol for the RA toolkit intervention
29	Review study results, anticipated next steps and deployment of the toolkit

D.1.b Organizational capacity

Corrona Research Foundation. The Corrona Research Foundation was formed as a not for profit 501(c) 3 private foundation in the fall of 2013. The mission of the Corrona Research Foundation is to further quality of patient care and enhance clinical research by connecting qualified academic researchers with the Corrona registry of longitudinal clinical data in rheumatoid arthritis. The Corrona registry was founded by Dr. Joel Kremer in 2000. Corrona has developed a registry of > 40,000 patients with RA who are enrolled by participating rheumatologists in both academic and private practice sites. Data are collected from both patients and their treating rheumatologists, who gather information on disease duration, prognosis, disease severity and activity, medical comorbidities, surgeries, hospitalizations, use of medications including nonbiologic and biologic DMARDs and corticosteroids, and adverse events.

UAB. The Rheumatology Clinic at UAB facilitates urgent clinic appointments for approximately 20,000 patients each year with suspected or established rheumatologic diseases. RADAR, UAB's *Rheumatology Database and Repository*, has been established to optimize patient care, to enhance education of rheumatology trainees, and to create a database and repository of samples (DNA, serum, plasma, RNA, synovial fluid). The purpose of collecting these data and biological samples is to facilitate patient-oriented and comparative effectiveness research in rheumatology and to share data with investigators at UAB and other institutions. RADAR seeks to provide rheumatologists with the resources to better understand not only the pathogenesis of rheumatologic disease, but also the mechanisms of treatment response, for the advancement of the personalized medicine model and "treat to target" recommendations.

RADAR was co-founded by Drs. Lou Bridges and Jeff Curtis in 2008, and currently, the UAB physicians who see the majority of RA patients at UAB contribute patient data to RADAR. At each visit, patients are first evaluated by study coordinators, who perform chart reviews and patient interviews to collect medication histories and historical RA disease activity information to satisfy 1987 and/or 2010 ACR criteria for RA. Standardized assessments by RADAR clinicians

include 28 joint counts and collection of physician and patient-reported outcomes including the CDAI, physician global, MDHAQ, and the RAPID3. These data are captured on tablet computers (iPads) and longitudinal data is available across visits. Inflammatory markers including ESR and CRP are collected by protocol. Biospecimens for RADAR patients are collected at baseline (i.e. enrollment) and at subsequent visits. Thus UAB has the infrastructure to enable successful enrollment of patients for the cluster randomized trial. **Dr. Bridges, who is director of the UAB rheumatology clinic, is supportive of this application and supplied a letter of commitment.**

CreakyJoints. For more than 10 years, Creaky Joints, a component of the Global Health Living Foundation, has provided in-person education, advocacy and grassroots patient mobilization though community programs, partnerships with provider networks, and professional societies. Additionally, Global Healthy Living Foundation was recently awarded a Patient-Powered Research Network grant focused on inflammatory arthritis from the Patient Centered Outcomes Research Institute (PCORI). Of note, the ***Creaky Joints' Facebook page has been viewed by 10 million people as of January 2014, and they average a few hundred thousand conversations a day with arthritis patients***. They are committed to partnering with us for dissemination (see Dr. Nowell's letter of support). They will post online via their webpage and their Facebook page the RA toolkit. Additionally they monitor the types of individuals who download the materials (e.g., patients, providers etc) and forward to the team any feedback they receive on the toolkit for future revisions. Capitalizing on digital and social media will be an efficient and effective approach to disseminate to literally thousands of arthritis patients.

Administration of Continuous Medical Education Credits. Monika Safford, MD is the Assistant Dean of the Division of CME at UAB. She has had long-standing collaborative ties with Dr. Curtis and Corrona. She will ensure that participating physicians who review the educational materials receive up to 1.5 Continuing Medical Education (CME) Credits (administered by the University of Alabama at Birmingham CME Division, an ACCME accredited CME provider).

D.2 Staff Capacity

Ms. Lemay has been a project manager on numerous federally and foundation funded studies. She has performed >100 in-depth interviews or focus groups with patients over the last 10 years. She had previously worked with Drs. Harrold and Mazur on a project funded by the Agency for Healthcare Quality and Research that involved identical methodology, specifically using in-depth interviews to inform the adaptation of a toolkit to improve clinical care. She will be performing the in-depth interviews with the patients and the office staff. In addition, she will work with Dr. Harrold to adapt the toolkit to the RA patient population. Also with Dr. Harrold, she will supervise the activities of the Research Assistant, who will be hired for this study. The **Research Assistant** will handle administrative tasks including scheduling the in-depth interviews, coordinating meetings, developing research materials and performing data entry. The Research Assistant will also develop relationships with the participants in the cluster RCT intervention study, contacting them for the collection of the study materials as well as providing the reminder contacts to ensure the participants follow the study protocol. The **Biostatistician** would develop the study database and conduct the analyses to compare outcomes in the TI vs. UC patients.

G. Letter(s) of Commitment:

1. William Benjamin Nowell, Consultant, Global Health Living Foundation
2. Joel M. Kremer, Consultant, Corrona Research Foundation
3. Clifton O. Bingham III, Consultant, John Hopkins University
4. Eric M. Ruderman, Consultant, Northwestern University Feinberg School of Medicine
5. Jeffrey R. Curtis, Consultant, University of Alabama at Birmingham
6. Monika M. Safford, CME, University of Alabama at Birmingham
7. S. Louis Bridges, Jr., University of Alabama at Birmingham

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July 3, 2014

Leslie R. Harrold, MD, MPH
Associate Professor of Orthopedics and Medicine
University of Massachusetts Medical School
55 Lake Avenue North Worcester, MA 01655

Dear Leslie,

I am writing to express my strong support of your grant application, "Development and Testing of a Toolkit to Improve RA Flare Management." in response to a Request for Proposals on *Management of Flares in Rheumatoid Arthritis Patients.* I believe in the mission of the grant application, specifically, to improve flare management in rheumatoid arthritis. I applaud you for gathering information directly from patients and using it to develop a patient-centered toolkit.

As the Director of Patient-Centered Research at the Global Health Living Foundation, I am excited to be involved with a research effort that puts the patient perspective front and center. Understanding the perceptions and experiences of people living with rheumatoid arthritis regarding effective disease self-management is crucial to the development of educational tools and interventions that improve patient care, disease management, and quality of life. I also currently serve as Co-Principal Investigator in the creation of a patient-powered research registry for inflammatory arthritis, funded by the Patient Centered Outcomes Research Institute (PCORI). The registry aims to involve patients in meaningful comparative effectiveness research, utilizing active and passive data collection. My unique expertise in patient advocacy and patient-centered research dovetails perfectly with the aims of your proposed project.

I am writing to confirm my willingness to participate in the six planned meetings over the course of the study period to do the following: (1) review progress toward study aims; (2) inform the development of the interview guides and toolkit; (3) plan and assist with dissemination activities; and (4) ensure that the developed tools are patient-centered. The finalized tools will be made available on the *CreakyJoints* website and Facebook page. I understand that in recognition for my participation I will be compensated during each of the years of the project.

I believe this grant will be viewed favorably during the review process and I look forward to collaborating with you on this important study.

Sincerely,

W. Benjamin Nowell, Ph.D.,
Director, Patient-Centered Research

CORRONA
research foundation

July 7, 2014

Leslie R. Harrold, MD, MPH
Associate Professor of Orthopedics and Medicine
University of Massachusetts Medical School

Dear Leslie,

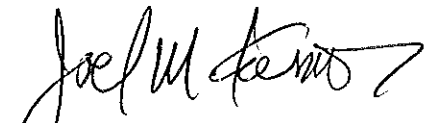
It is with great enthusiasm that I write this letter in strong support of your proposal entitled "Development and Testing of a Toolkit to Improve RA Flare Management." As PI of the Corrona Treat to Target (T2T) trial, I am excited and supportive of leveraging this trial to identify the barrier to, and facilitators of titrating rheumatoid arthritis treatments based on disease activity. There are many lessons we can learn from patients and providers who have participated in the trial and thus truly experienced the T2T treatment paradigm.

I endorse your strategy to identify participants of the Corrona T2T trial for your in-depth interviews and will work with you to roll out the toolkits to be developed as part of the grant to the rheumatologists participating in Corrona. As you know, Corrona is a unique resource in that it is the only large, multi-center, longitudinal cohort in North America that captures clinical data (e.g. tender/swollen joint counts) and outcomes reported by both patients and physicians. Currently, we have >600 rheumatologists participating in the registry. We are committed to academic pursuits with over 50 manuscripts published to date in top tier rheumatology journals. Your project will nicely complement our vision for research that improves patient care.

As President of the Corrona Research Foundation, I will facilitate the working relationship between Corrona and the scientific team you have assembled. In addition, I will participate as part of the expert panel over the course of the study period. I agree to provide input on study design, review research materials and preliminary results, and contribute to the development and adaptation of the educational tools included in the toolkit.

Our ongoing relationship with you over the past several years has been very productive. Your existing relationship with Corrona will ensure successful execution of this proposal. I have high hopes that the review panel will recognize the importance of this application.

Sincerely,



Joel M. Kremer, MD
Pfaff Family Professor of Medicine,
Albany Medical College,
President, Corrona Research Foundation

Clifton O. Bingham III, MD
Associate Professor of Medicine
Director, Johns Hopkins Arthritis Center
Deputy Director for Research

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July 1, 2014

Leslie R. Harrold, MD, MPH
Associate Professor of Orthopedics and Medicine
University of Massachusetts Medical School
55 Lake Avenue North Worcester, MA 01655

Dear Leslie,

It is with great enthusiasm that I write this letter in support of your grant proposal entitled “Development and Testing of a Toolkit to Improve RA Flare Management" and express my willingness to participate on your expert panel. Your goal of improving flare management for patients with rheumatoid arthritis (RA) aligns with my clinical and research interests.

As you know, I Chair the RA Flare Definition Working Group for the international Outcome Measures in Rheumatology Clinical Trials (OMERACT) group. Specifically I have been involved in several publications examining how to define and evaluate RA disease flares, thus I have much to contribute to this proposed project. My clinical interests and prior work in patient reported outcomes as well as educational interventions for both patients and health care providers will provide important insights as you conduct the objectives of this grant.

I look forward to participating in and contributing to routine expert panel meetings as a Consultant during the proposed grant timeline. I understand that my involvement will include reviewing the progress made regarding the aims of the grant, informing the development of the educational tools needed for providers and patients, and planning the dissemination activities. In return for my contribution to this proposed project I will be compensated for each year of the project.

In summary, I am very excited about this proposal. I believe this work is greatly needed to improve RA flare management.

Sincerely,

Clifton O. Bingham III, MD
Associate Professor of Medicine
Johns Hopkins University
Divisions of Rheumatology and Allergy and Clinical Immunology
Director, Johns Hopkins Arthritis Center
Deputy Director for Research
Co-Director, Rheumatic Diseases Research Core Center

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July 1, 2014

Leslie R. Harrold, MD, MPH
Associate Professor of Orthopedics and Medicine
University of Massachusetts Medical School
55 Lake Avenue North Worcester, MA 01655

Dear Leslie,

I enthusiastically support your research proposal entitled "Development and Testing of a Toolkit to Improve RA Flare Management." Having participated in the Corrona, LLC Treat to Target {T2T) trial, I think there are definitely lessons to be learned from the experiences of the participating patients and providers. Performing in-depth interviews with patients and providers who were adherence and nonadherent to the T2T treatment protocol will provide important insights, which will lead to the development of educational and quality improvement tools to facilitate optimal flare management in patients with rheumatoid arthritis (RA).

As you are aware, I have firsthand knowledge of the benefits and challenges of controlling RA disease activity both as a clinician and as a researcher. In order to achieve sustained low disease activity or remission in rheumatoid arthritis patients, I believe that more information is needed to guide patients and providers to overcome the inherent barriers. Your proposed project will address that need.

I understand that I will be a Consultant participating in 6 meetings over the course of the grant. This will involve providing feedback on the draft study materials and tools, reviewing results, and ensuring that the developed tools address the challenges encountered by providers and providers. I understand that in recognition for my participation that I will be compensated for my involvement.

I look forward to working with you and other members of the team on this important and worthwhile project.

All my best,

Eric M. Ruderman, M.D.
Professor of Medicine, Division of Rheumatology
Northwestern University Feinberg School of Medicine

UAB SCHOOL OF MEDICINE

Division of Clinical Immunology and Rheumatology

July 3, 2014

Leslie R. Harrold, MD, MPH
Associate Professor of Orthopedics and Medicine University of
Massachusetts Medical School
55 Lake Avenue North Worcester, MA
01655

Dear Leslie,

I am writing this letter in support of your grant proposal entitled “Development and Testing of a Toolkit to Improve RA Flare Management.” I am very excited about your proposed approach to improving clinical outcomes as our work together has demonstrated that substantial numbers of patients are not getting the recommended care. Additionally, I agree with you that engaging patients as well as rheumatologists will be critical to improve flare management and reduction of disease activity.

As you know, the University of Alabama at Birmingham (UAB) program is an ideal location to evaluate the impact of the toolkit to improve clinical outcomes in patients with rheumatoid arthritis (RA). Specifically the UAB Division of Clinical Immunology and Rheumatology has been listed as one of the best clinical rheumatology programs in the country by *US News & World Report* and is internationally recognized for its dedication to pursuing new knowledge and translating research findings into more effective diagnosis and treatment of patients with rheumatic diseases. As one of the largest academic rheumatology units in the nation, the division's clinical program employs 17 rheumatology clinicians and is responsible for the care of more than 20,000 RA patients.

I look forward to working with you to implement and evaluate the new educational materials developed for providers and patients as part of this study. I pledge to take part in meetings of the expert panel, and contribute to the creation of the toolkit. In addition, I will be an "on the ground" resource for you as you work to implement the randomized control trial at UAB evaluating the impact of the toolkit to improve outcomes.

I look forward to collaborating with you on this proposed project. I enthusiastically provide my support for this application.

Thank you,

Jeffrey Curtis, MD MS MPH
William J. Koopman Endowed Professor in Rheumatology and Immunology Director UAB
Arthritis Clinical Intervention Program Co-Director
UABCenter for Education and Research on Therapeutics (CERTS) Co-Director UAB
PharmacoEpidemiology and Economic Research (PEER) Group

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Monika M. Safford, MD
Endowed Professor of Medicine
Assistant Dean, Continuing Medical Education
Department of Medicine, Division of Preventive Medicine
University of Alabama School of Medicine
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July 1, 2014

Leslie R. Harrold, MD, MPH
Associate Professor of Orthopedics and Physical Rehabilitation
University of Massachusetts Medical School
55 Lake Avenue North Worcester, MA 01655

Dear Leslie,
I am pleased to write this letter confirming my willingness to work with you and the team to ensure that participating physicians who review the educational materials receive up to 1.5 Continuing Medical Education (CME) Credits (administered by the University of Alabama at Birmingham CME Division, an ACCME accredited CME provider). As you know I am both an Assistant Dean of the Division of CME and a physician-investigator, so ideally positioned to work with you. I have had long-standing collaborative ties with the research team, so am enthusiastic about working with you.

Sincerely,

Monika M. Safford, MD

UAB SCHOOL OF MEDICINE

Division of Clinical Immunology and Rheumatology

July 15, 2014

Leslie R. Harrold, MD, MPH
Associate Professor of Medicine
University of Massachusetts Medical School
Worcester, MA 06155

Dear Leslie,

I am delighted to write this letter of support for your Pfizer grant application related to rheumatoid arthritis (RA) flare. This topic is very important to help optimize the care that we provide our patients, especially when they have suboptimal disease control, both chronically and with acute worsening. Your investigative team, including Drs. Curtis, Bingham, Kremer, and Ruderman, brings together well-recognized experts in this domain and will ensure that your project yields valuable results to improve RA care.

As you know, our rheumatology clinic at UAB provides care for approximately 20,000 patients each year, distributed across the practices of 17 clinicians, and includes around 2,000 RA patients. The resources of our UAB RA Database and Respository (RADAR), including the availability of a study coordinator in part supported by the grant, will be instrumental in recruiting the necessary patients for Aim 3 of the project. I look forward to UAB's involvement in this endeavor and wish you the best of success as the application goes forward.

Sincerely,

S. Louis Bridges, Jr., MD, PhD
Anna Lois Waters Professor of Medicine
Director, Division of Clinical Immunology and Rheumatology
Director, Comprehensive Arthritis, Musculoskeletal, and Autoimmunity Center

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