

**Capturing Patient Reported Outcomes in RA
To Improve Quality of Care & Outcomes
in Real-World Settings**

Grant ID 10183257

Key Personnel:

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Abstract: We will develop a national, highly-generalizable software platform to electronically capture patient reported outcome (PRO) data for RA patients. This tool will be used by clinicians to improve process of care and outcomes in the management of RA. Our proposed work builds on past and ongoing research and electronic clinical tool development at the University of Alabama (UAB) in rheumatoid arthritis (RA), provider-patient activation in the context of evidence implementation trials, health information technology (HIT), and our current relationship with CreakyJoints, the largest arthritis patient community in the world. Seeking to effect tangible improvement in RA patients' outcomes and better quality of care consistent with national guidelines, many of which we have developed in partnership with the American College of Rheumatology (ACR), we will build on existing relationships collaborations to bring together researchers with expertise in rheumatology, epidemiology, bioinformatics, statistics, risk communication and medical decision-making. We will leverage our past work at UAB building electronic PRO data capture tools. This system is complementary to but not redundant with an electronic health record (EHR) and can be used with paper-based medical records systems. The main objectives of this project are to implement and rigorously test the deployment of practical, real-world tools in routine clinical practice to measure Patient Reported Outcomes (PROs) and RA disease activity.

B. Table of Contents

	Page #
Cover Page	1
Abstract	1
Table of Contents	2
Goals and Objectives	3
Technical Approach	3
Workplan and Deliverables	9
Organizational Detail	11
Bibliography	14
Budget	15
Budget Justification	17
UAB F&A Terms and Agreement	20
UAB Institutional Letter of Commitment	27
Biosketches of Key Personnel	28
Appendices	N/A

C.1 Goals and Objectives: To implement practical, real-world tools in routine clinical practice to measure Patient Reported Outcomes (PROs) and RA disease activity. We will accomplish this goal by achieving the following objectives:

1. In partnership with Creakyjoints (CJ), one of the largest arthritis patient networks in the world with more than 50,000 members, to a) determine barriers to PRO data capture in routine clinical practice and at home; and b) examine patient perspectives regarding using PROs to resolve discordance in patient-provider assessments as it relates to decision-making in achieving RA treat-to-target (T2T) goals
2. Demonstrate the feasibility and usefulness of electronically capturing patient reported outcome (PRO) data at patients' homes and in rheumatology clinics
3. Using Internet and mobile (e.g. Smartphone) technology, quantify the effect of this PRO data collection on patients-provider communication, RA treatment changes, and attainment of improved PROs and better RA disease activity states (low disease activity or remission). These outcomes are consistent with the American College of Rheumatology (ACR) 2012 RA guidelines (developed at UAB).

Summary: We will develop a national, highly-generalizable software platform to electronically capture patient reported outcome (PRO) data for RA patients. This tool will be used by clinicians to improve process of care and outcomes in the management of RA. Our proposed work builds on past and ongoing research and electronic clinical tool development at the University of Alabama (UAB) in rheumatoid arthritis (RA), provider-patient activation in the context of evidence implementation trials, health information technology (HIT), and our current relationship with CreakyJoints, the largest arthritis patient community in the world. Seeking to effect tangible improvement in RA patients' outcomes and better quality of care consistent with national guidelines, many of which we have developed in partnership with the American College of Rheumatology (ACR), we will build on existing relationships collaborations to bring together researchers with expertise in rheumatology, epidemiology, bioinformatics, statistics, risk communication and medical decision-making. We will leverage our past work at UAB building electronic PRO data capture tools. This system is complementary to but not redundant with an electronic health record (EHR) and can be used with paper-based medical records systems.

C.2.1. Needs Assessment: As described in the RFP, there are several validated measures and instruments to measure PROs in RA, but few are used in real-world clinical settings. Paper-based tools suffer from limitations as they must be scored by hand, and missing data makes calculations problematic. Longitudinal PRO data must be available at the point of care so as to enable real-world decision-making. A small group of electronic tools exist, but most are impractical and require appreciable time from clinicians to collect, record, longitudinally track, and be useful to make decisions in real time. Single centers, practices, or health systems may have such tools, but these are not easily exportable outside of those contexts to a national audience. We will address these barriers in the proposed project to demonstrate the feasibility and usefulness of collecting PROs using validated instruments in a highly generalizable way that improves outcomes for RA patients in diverse health care settings across the country.

Based upon 2006-9 data focused on RA disease activity related to quality of care, we found that few U.S. practices collect RA disease activity using any tool (1). The data supporting this national need and under-capture of RA disease activity was derived from national U.S. Medicare data collected at a person-level. Using national data from the CORRONA RA registry, we found that the publication of the ACR guidelines recommending measurement of RA disease activity and PROs, with the goal of achieving low disease activity or remission, had a negligible impact on treatment (2). This finding underscores the need for more practical tools deployed via evidence implementation programs like ours. Finally, to support our needs assessment, a national survey of U.S. rheumatologists conducted by Jack Cush (presented at the ACR 2008 meeting) found that at most, only about one-third of U.S. rheumatologists collected any quantitative disease activity measures. With Dr. Cush, we are currently updating this national survey to reassess this, with results available within the next 6 months.

Despite the relative dearth of information and tools to capture PROs in diverse practice settings described above, patients themselves have even fewer options to capture PRO data and use it in a meaningful way. Given ever-increasing time pressures on physician office visits, maximizing the efficiency of clinical encounters with rheumatologists is imperative, and determining methods that engage patients in capturing their own PROs offers considerable efficiencies. For that reason, the primary audience for this project is RA patients. This project will empower patients by providing them with a set of flexible electronic tools to capture existing, validated PROs and then facilitating their sharing of this information with their doctor. Our proposed assessments in this project will include not only field-testing of the approach and patient interface but also assessment of the impact of deployment of these tools on both process and outcome measures.

C2.2. Summary: First, we will deploy and evaluate novel methods for systematic data collection using direct, patient-provided data using healthcare information technology that collects PROs via a patient-facing, smartphone/Internet-based system (RheumPRO) coupled with a companion in-office iPad-based system (READY2). Either system can be used independently, but they are anticipated to be most effective when used together. Moreover, this platform has high potential for downstream integration to EHR data. We will enable use of these tools based upon input from multiple stakeholders collected as part of this project. Beta versions of these tools already have been developed through R01 funding from the Agency for Health Research and Quality (PI: Curtis), the National Institutes of Health (1P60AR064172-01, Project 2; PI: Curtis) and UAB institutional funds. These leveraged resources have enabled initial development of these electronic PRO capture tools. However, they have not yet been subjected to large scale evaluation or deployment from patients providing PRO data at home, as we now propose.

Following this formative work to refine the PRO data collection approach (Aim 1), these methodologic advances will be applied to evaluating the feasibility and usability of the enhanced electronic tools (Aim 2). Finally, this innovation will be tested in a randomized controlled evidence implementation study that will rigorously evaluate the impact on quality of RA care and associated outcomes (Aim 3). Overall, we will evaluate an approach that enables longitudinal PRO data captured in real-time to facilitate shared decision-making and personalized approaches consistent with patients' values and goals; provides real-time decision

support to encourage treatment changes without being prescriptive; is able to provide a better context for specific PROs in light of symptoms (e.g. pain) and concomitant comorbidities (e.g. depression, fibromyalgia) that may impact the interpretation of RA disease activity; and is feasible at home and in busy rheumatology clinic settings. This platform of tools can be widely adopted at the point-of-care by a diverse group of arthritis patients and their treating clinicians, including those not ordinarily able to support complex computational infrastructures (e.g. community physicians, with or without an EHR). To our knowledge, there is no other system that exists that can provide these capabilities that can scale easily to a national rheumatology audience. Our research findings will have immediate direct impact on RA quality of care and also will be a significant incremental improvement in PRO methodology in RA.

C.2.3 Technical Approach

Program Design & Methods:

Aim 1: we will convene two sets of RA patient focus groups, both in-person and online for two key domains. The first domain covered by the focus groups is patients' interest, needs, and barriers/facilitators around PRO data collection. The second domain that will be discussed in the focus groups will be patients' perceptions of the need, goals, and concerns regarding applying PRO data to RA treatment decisions in light of T2T disease activity targets. There will be 4 patient focus groups: 2 online and 2 in-person, one set for each of the two domains. The focus groups will consist of Creakyjoints members with RA (for the online groups) and RA patients at the UAB RA clinic (for the in-person focus groups). A fifth focus group will be conducted online and consist of rheumatologists who treat RA patients to assess their perspectives on PRO data as it relates to RA treatment decisions and T2T goals (Domain 2).

Each focus group will be 10-12 people each. The two sets of focus groups will be run by Dr. James Willig, who has extensive experience in PRO data collection in diverse settings and in conducting qualitative research. By way of example, Dr. Willig initially led a similar effort at UAB with HIV+ patients and subsequently has extended this type of interaction to patients with other chronic diseases and conditions (e.g. geriatric patients, those receiving hospice). The groups will be presented key questions for the 2 relevant domains, and dialogue can "piggy-back" on the comments of other group members and can enrich the discussion in ways that could not be achieved through one-on-one interviews. Our expectation is that two focus groups for each of these two topics will be sufficient to achieve saturation for key major themes. In the event that the group moderator feels that saturation has not been achieved, we will conduct additional focus groups as necessary.

Examples of the themes to be discussed as part of these focus groups for Domain 1 include motivation, barriers and concerns (e.g. privacy, security) to collection and adoption of PROs at home and in clinician office settings. We also will explore how the impact of comorbidities and patients' own health goals relate to which specific PROs are most important to patients to capture and share with their physician. Following completion of the Domain 1 topics, a second round of focus groups for Domain 2 will be conducted and will explore barriers/facilitators, motivations, and concerns regarding how to best visually present PROs to patients and clinicians to facilitate shared decision-making to achieve the RA disease activity targets recommended in national guidelines.

As the third and final task for Aim 1, we will use the themes obtained from the focus groups to develop and deploy a national survey. We will assess the prevalence and generalizability of the various motivations, barriers, and concerns around PRO data capture that emerged from the focus groups to better understand these issues on a broader scale. Major themes will be abstracted using standard commercial software available for this purpose (e.g. NVivo, which allows for qualitative and mixed-methods research; it supports data collected from focus groups as well as large social media-based discussions (which we will use for this aim). The survey will be deployed online to the Creakyjoints membership and in person (using iPad tablets deployed in the waiting room of the UAB RA Clinic) to collect the same data from the pool of 2,000+ RA patients who are not part of the Creakyjoints online membership. The incorporation both of an online RA patient community as well as in-person at the UAB RA clinic will ensure that the results from Aim 1 are highly generalizable to all RA patients, not only those who are part of an online arthritis community. From within the UAB population, we will oversample RA patients who are non-Caucasian, those with low socioeconomic status, and lower education.

As the second component of this sub-aim, we will use the survey to ask patients to rank various existing, validated PRO instruments chosen by patients in the focus groups with respect to their importance, feasibility, and relevance to RA. We will include RA-specific measures derived solely from patients (e.g. RAPID3, RAPID4, SF-12, pain visual analog scale, Multidimensional Health Assessment Questionnaire, fatigue) and those that incorporate some physician data (e.g. Clinical Disease Activity Index [CDAI](3)). We will also present our patient partners with options to rank several of the instruments relevant to RA that are part of the NIH Patient Reported Outcomes Measurement Information System (PROMIS). PROMIS consists of precise, customizable instruments to capture domains that are likely very important to patients. While not disease specific, these are often impacted by RA. Examples of relevant PROMIS domains include depression, psychosocial impact, anxiety, pain intensity, sleep dysfunction, social roles, and peer relationships.

Aim 2: In this aim, we will demonstrate the feasibility and usefulness of electronically capturing the PROs that were most highly prioritized as a result of the Aim 1 findings. The UAB Mobile Application lab will work with the rest of the project team, including reknown RA patient advocates Seth Ginsberg, Amye Leong, and other arthritis patients that are part of Creakyjoints or the UAB RA clinic to evaluate electronic representation of PRO data that will be incorporated into the RheumPRO mobile application that has been developed at UAB. We will obtain patients' feedback on use of the tool deployed both for at-home data collection, as well as collected in the waiting rooms at rheumatology clinics. The Questionnaire for User Interaction Satisfaction (QUIS) (4) will be used for this purpose.

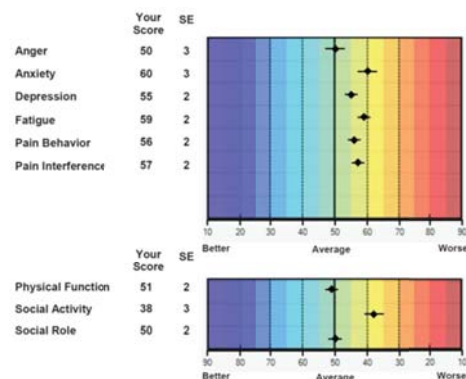


Figure 1: Heat Map representation of PROs across multiple domains

As part of this Aim, we will test different ways of displaying quantitative information around PROs and obtain patients' perceptions of the understandability, importance, and usefulness of the presentation of the results of the PRO instruments that were most highly ranked by participants in Aim 1. For example, the NIH PROMIS measures typically display the results of the PRO instruments as a number ranging from 0 to 100, normalized to a mean of 50. We will test alternative representations, such as with a 'heat map' (Figure 1). Variations on this display would include allowing patients to 1) pick which PROs they feel are most relevant to them, and most helpful to talk about with their doctor; 2) compare themselves with the other RA patients ('benchmarking'), using data collected by the tool; 3) prioritize which of the various PROs they want to discuss with their physician at the next clinic visit; and 4) decide on an intervention threshold, meaning the level of the PRO at which they feel that they would want to do something different with respect to their RA treatment approach. This will help stimulate patients to consider their interest and readiness to make treatment changes, using an instrument such as the Stages of Change questionnaire derived from Prochaska.

Although the focus of the evaluation is on PROs, the benefits of RA treatment and their impact on PROs must be considered in light of potential risks. For that reason, we will also examine patients understanding and perception of safety risks and associated presentation of information (e.g. risk of serious infection, displayed as a pictograph [Figure 2]. Presentation of this information will be tailored in light of patients' graphical and numeric literacy, which will also be captured as part of this aim using existing instruments.

At the conclusion of this Aim, we will have a field-tested electronic PRO data capture tool. It will allow patients to pick the PRO instruments of highest relevance to them, yet maintain a 'core set' of PRO instruments (e.g. RAPID3) commonly used in RA. Thus, for analysis purposes, there will always be a standard, stable core foundation of PRO instruments collected by all patients, yet customization will let patients additionally choose from a set of existing, validated instruments to capture the PRO domains of highest relevance to them.

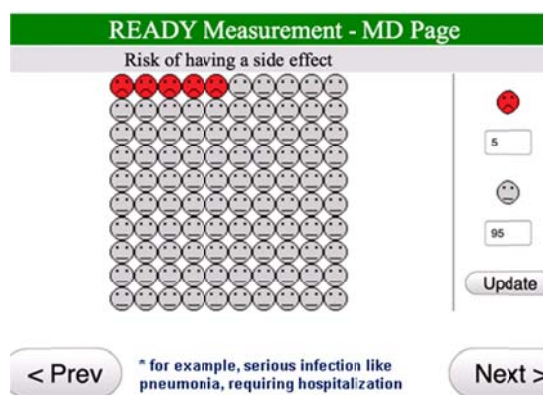


Figure 2: Icon Array showing Safety Risks for Serious Infections (5/100 patient-years)

Aim 3:

Following Aims 1 and 2, we will scale RheumPRO to be available for distribution within the Apple App store (for Apple-based devices, like the iPhone and iPad), Google Play (for Android-based devices), and via the Internet (through a browser). We will enable connectivity to READY2 so that the PRO data can be integrated between the two systems. We then will engage twelve rheumatology clinics in both university and private practice settings to enable their RA patients who have either at-home Internet access, and/or own Smartphones, to collect PROs. To select sites, we will leverage our ongoing relationships with many rheumatologists with interest in this topic including the extensive site network of CORRONA (more than 80 sites), the 42 sites participating in the TEAR trial (PI: Curtis), and the 12 site VARA registry (which UAB

investigators are part of). Preliminary discussions with a number of these sites indicate that many have high interest in participating in such a program. We will evaluate effectiveness and efficiency of the tool platform in these real world settings at 6 months after deployment at each site.

Of note, we have found that although many clinical sites report that they are already adopting T2T treatment strategies, there is wide variability as to what this actually means. Typically, many clinical sites collect a RAPID3 or MDHAQ on paper, with no specified use of the data, nor any means to know whether the PROs or other quantitative information (e.g. CDAI) is being used in treatment decision making. This type of site will be eligible to be selected for our project. Moreover, we will help each site understand that this project is not enforcing and evaluating a rigid T2T treatment strategy but rather seeks to collect and incorporate patient-derived PRO data into real-world encounters and RA treatment decisions.

C.2.4 Design of Outcomes Evaluation: The main outcomes to be assessed as part of Aim 3 are whether the PROs data is discussed at the clinic visit, and whether changes in RA therapies were made. These outcomes will be assessed over the 6 month study period. A secondary outcome is the proportion of RA patients in each physician's practice who achieve low disease activity or remission at 1 year, measured using validated instruments based on their established cutpoints (e.g. CDAI < 10 [0-76 scale], RAPID3 < 6 [0-30 scale]).

As part of this latter evaluation, we will cross-classify (i.e. stratify) achieving the recommended disease activity targets by CDAI against other PROs (e.g. pain, fatigue, sleep, function measured by MDHAQ) to examine the impact on improvement or worsening on those scales. This addresses a concern whereby RA patients may be improving in certain ways (e.g. fatigue) that traditional measures of RA disease activity (e.g. CDAI) fail to capture, or conversely, fail to improve in domains that patients care about the most, despite improving in RA disease activity measures (5). Through capture of key patient and clinician-reported comorbidities (derived from the formative work in Aim 1), we will assess PRO data in light of symptoms or problems that may not be related directly to RA-associated inflammation yet impact PROs and perceptions of RA treatment benefits.

We will evaluate the two main outcomes of the study: 1) time (in minutes) that the patient and clinician spend discussing PRO data at clinic visits; and 2) RA treatment changes. We will assess these outcomes upon data collected via both RheumPRO and READY2. We will collect the amount of time that was spent discussing PROs based upon patients' perspectives, and their medications and medication changes. For the outcome of time spent with the clinician discussing PROs, we will test the hypothesis that the time spent is significantly different from zero (i.e. H_0 : PROs were not discussed, i.e. 0 minutes). We will also use RheumPRO and READY2 to assess whether patients' RA medications were changed (either non-biologic DMARDs, and/or biologics) during the 6 month study period compared to the 6 months prior to the intervention start, a within-person, pre-post comparison, testing the hypothesis that RA medications were more likely to be changed during the study period than immediately prior to it. As part of this analysis, we will examine discussion of PROs as a mediating factor that increased the likelihood of medication change.

The third study outcome (a secondary endpoint), will examine changes in RA disease activity using both the RAPID3 and the CDAI (for sites who collect CDAI), testing the hypothesis

that the within-person change in these measures is significantly different than 0. Finally, the amount of engagement with PRO data collection will be quantified both as how much the tool is used by patients (quantified by their frequency of PRO data input), and within physician practices at each of the 12 sites. Finally, we will qualitatively obtain feedback and satisfaction with electronic PRO data capture from clinicians, staff & patients following the conclusion of Aim 3 of the project based upon the Agency for Healthcare Research and Quality Health Information Technology Evaluation Toolkit.

The number of sites was chosen based upon the goal of having at least 80-90% power to show significant differences in the two main outcomes described above. The assumptions made in these calculations assume that there are 50 RA patients/site who are willing and able to use the RheumPRO tool (based upon having at-home Internet access, and/or a Smartphone), and $\alpha = 0.05$. For RA medication treatment changes during the 6 month study period, we have assumed a 20% 'background' rate of DMARD/biologic changes, based upon our past work and using CORRONA data (6). These calculations also allow for sufficient power even assuming the presence of within-site clustering using an intra-class correlation of 0.05. For the dichotomous outcomes of RA medication changes and proportion achieving remission/LDA, we have used a 10% improvement over baseline (i.e. pre-intervention) to represent a clinically significant change, and we have based our hypothesis testing on these assumptions.

C.3 Workplan and Deliverables

Each Period (P) represents 6 month periods beginning 1/2014 (P1) and extending through 7/2016 (P5)

Description of Task & Deliverables	P1	P2	P3	P4	P5
Obtain IRB approval	X				
Aim 1: Patient focus groups for Domain 1 (barriers, preferences, concerns for PRO data collection)	X	X			
Aim 1: Patient focus groups for Domain 2 (barriers, preferences, goals, concerns for achieving T2T goals, informed by PRO data)		X	X		
Aim 1 Deliverable: Results from patient focus groups and patient surveys			X		
Aim 2: Enhancement of mobile application PRO platform, informed by Aim 1, with assessment of usability and user interface		X	X	X	
Aim 2 Deliverable: Results from beta-tested version of patient-facing mobile application, evaluated by the Creakyjoints membership and UAB RA Clinic patients				X	
Aim 3: Deployment and evaluation of PRO application to 12 clinic sites and their RA patients				X	X
Aim 3 Deliverable: Results from evaluation of PRO data collection on process measures (discussion around PRO data; RA treatment changes) and outcome measures (RA disease activity)					X

C.4. Dissemination: We will publish our results in the peer reviewed literature based upon the Deliverables described above, under the leadership of Dr. Curtis. Also, we will include hands-on demonstration of the electronic PRO data collection at an ACR workshop at the ACR annual meeting (based upon interest on the part of the ACR meeting planning committee and Registry committee, of which Dr. Curtis is a member) and through other rheumatology regional and national meetings. The tools also will be available in the iTunes App store and Google Play, facilitating easy of acquisition by RA patients across the U.S. Seth Ginsberg, the president and founder of Creakyjoints, will also facilitate dissemination of the study results and PRO tools as part to the Creakyjoints member community via Facebook, Twitter, the Creakyjoints arthritis community website, and bi-weekly newsletters.

C.5. Limitations and Alternative Approaches

Engagement of Creakyjoints and online arthritis patient communities. Our Creakyjoints RA patient partners represent a convenient, highly-accessible, motivated, and willing set of patient participants to help with the formative work described in Aim 1, and the electronic PRO data capture assessment for Aim 2. However, this group is by no means the only large group of patients with RA. Indeed, Dr. Curtis has established relationships with other large RA patient groups (e.g. RA Warrior, at www.rawarrior.com; recent joint presentation at the ACR, and Rheumatoid Awareness Day Twitter chat, sponsored by the Rheumatoid Patient Foundation). Irrespective of an RA patients' membership in an online RA patient community, based upon results from the most recent Pew Internet survey, over 50% of Americans currently have access to smartphone technology. Nevertheless, we recognize that some RA patients are not currently members of any such community, nor do they have Internet access or smartphone technology (e.g. iPhone). Our intent is that the PRO data collection tools will be generalizable to a national audience, at a minimum through in-office PRO data collection through READY2 or a similar system. For that reason, the formative work and technology evaluation described in Aims 1 and 2 also will engage UAB RA Clinic patients (numbering more than 2,000 overall) to ensure that patients' views and comfort with PRO data collection represent not only those with Internet access but also include RA patients contributing PRO data in rheumatologists' offices. While in this project, in-office PRO data capture will be accomplished via the READY2 iPad tool, we will maximize generalizability by clearly delineating our results related to PRO data capture through any means (electronic or paper) as distinct from the operational aspects of electronic PRO data capture we will use for this project (Aim 2). Thus, our results regarding barriers/facilitators, concerns, and use of PRO data will generalize to data capture deployed via other electronic tools or even on paper (e.g. MDHAQ, RAPID3, or NIH PROMIS paper-based short forms).

Interface between RheumPRO (at-home PRO data collection), READY2 (in-office data collection), and Electronic Health Record (EHR) Systems.

As part of Aim 3, we will evaluate PROs collected at home via Internet and Smartphone technology (RheumPRO), coupled with in-office data collection via READY2. This set of tools will be provided to 12 rheumatology clinics and all of their RA patients. The two tools are most efficient when used together, because they allow at-home PRO data collection to flow to the physician 'automatically' to enable point-of-care use of PRO data, facilitate real-time clinical

decision support for T2T targets, and facilitate providers' RA-related data collection (e.g. Swollen Joint Count, CDAI) to flow back to patients to address discordance between patient and provider perceptions of RA disease activity (7).

However, outside of the context of this project, we recognize that not all physicians will use the READY2 tool. For that reason, we will enable the RheumPRO application to allow patients to capture their PROs and provide the information to their doctors (even if they do not use READY2) to discuss their PRO measures through a 'PRO summary sheet' that can be printed at home and brought to the office visit, or shown to the physician in the office setting (for mobile devices brought to the encounter).

Finally, although both these tools can be used as standalone systems or work together, they need to and will often be used in the context of an existing EHR. For that reason, these tools will not replace or be redundant with information that clinicians will already be inputting into their EHR. Rather, the PRO scores (e.g. RAPID3, MDHAQ, CDAI) will be easily available to simply input the resulting scores into a template EHR-note, saving the clinician time. [This is how we most efficiently use READY2 with the UAB EHR]. In the future, this system is expected to be able to interface with the ACR's Rheumatology Information System for Effectiveness (RISE) registry, enabling EHR and PROs data to be used in an integrated fashion.

Link between PRO Data Capture and Attainment of the T2T Targets of Remission/Low Disease Activity.

Despite our high expectation that longitudinal capture of PROs will facilitate discussions between patients and their clinicians and promote shared decision-making, it is possible that this interaction may not lead to a higher likelihood of RA medication changes nor attainment of T2T disease activity goals. While this possibility exists, this end result may be warranted for RA patients who have other concerns besides minimizing RA disease activity. Moreover, patients may have comorbidities (e.g. malignancy, cardiovascular disease, osteoporotic fractures, fibromyalgia) that reflect adversely on PRO measurement independent of RA disease activity. While this possibility exists, the data capture that is part of this project will enable efficient characterization of the phenotype of patients who do desire to improve and provide tools to help patients communicate with their physician about their own RA treatment goals.

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**Pfizer, Inc. Use of PROs in RA
BUDGET JUSTIFICATION SUMMARY**

Personnel

Jeffrey R. Curtis, MD, MS, MPH, Principal Investigator, 5% effort, is Associate Professor of Medicine in the Division of Clinical Immunology and Rheumatology and Co-Director of the Deep South Musculoskeletal (DSM) Center for Education and Research on Therapeutics (CERTs), at the University of Alabama at Birmingham. As Director of the UAB Arthritis Clinical Intervention Program, he leads the clinical trials unit for the rheumatology division at UAB, with focus on rheumatoid arthritis (RA). He is a co-author on the ACR 2008 and 2012 Recommendations for the use of DMARDs and Biologics in RA. He currently is the Deputy Director for the collaborative project between the FDA and the Agency for Healthcare Research and Quality (AHRQ) studying the safety of biologic agents using multiple, pooled national data sources. He and Dr. Elizabeth Delzell lead the UAB Large Database Workgroup, which houses substantial Medicare and Medicaid data. He has extensive experience linking cohorts such as Study of Osteoporotic Fractures (SOF), Reasons for Geographic and Racial Differences in Stroke (REGARDS) to Medicare data. Dr. Curtis has a prior background in the computer science and informatics field and was a full time computer systems analyst prior to his career in medicine, and will provide his expertise in outcomes research, clinical trials, evidence implementation and comparative effectiveness research.

Seth Ginsberg, BS, Consultant, is arthritis patient, President of the Board of the Global Healthy Living Foundation and Co-founder and President of CreakyJoints, an arthritis advocacy organization with more than 55,000 registered users. GHLF actively advocates on the State and Federal Level for improved access-to-care, moves beyond online social networking with events such as free Healthy Living Forums and A-Games (Arthritis Games) and other patient mobilization efforts held in local communities throughout the U.S. and Europe, and provides support, education, advice and up-to-date information for people living with chronic illnesses such as arthritis. 40 hrs x \$100/hr

Ragib Hasan, PhD, MS Co-investigator, 5% effort, is Assistant Professor in the Department of Computer and Information Sciences at the University of Alabama at Birmingham, will work with Mr. Owen to ensure proper security measures are taken to protect the confidentiality, integrity, and privacy of patient data, and will work with the researchers to provide provable and strong security guarantees. In addition, he will leverage his research and development experience with Amazon AWS and other cloud platforms to ensure compliance with HIPAA and other data protection regulations, and provide training and briefings to researchers about data security best practices and techniques for protecting personally identifiable information and other sensitive data.

Amye Leong, MBA, Consultant, is a nationally recognized motivational speaker, is president of the health education and advocacy consulting firm Healthy Motivation. She currently travels the world as spokesperson for the UN-endorsed Bone and Joint Decade 2000-2010. One of 'America's Fifty Heroes,' as named by The Arthritis Foundation (AF), she also serves on the AF Board of the Santa Barbara branch of the Pacific Region, the AF RA Alliance National Leadership Group. She carried the torch for the 1996 Summer Olympic Games. She was appointed advisor to the U.S. National Institute of Arthritis, Musculoskeletal, and Skin Diseases, and chaired the

Surgeon General's National Council on Self-Help and Public Health. Leong, who founded the nation's first and largest network of young adults with arthritis education programs, continues to provide extensive peer counseling to those affected by arthritis and other rheumatic diseases and their families. Ms. Leong will serve in a key role as a patient pilot tester for the mobile app technologies and participant in the focus group leadership. (28 hr x \$150/hr).

Sheila Moore, BS Consultant. As former head of the UAB IRB (now retired), Ms. Moore will serve as Research Advisor as an expert with patient privacy, security and consent. She will participate in 1-2 hr phone calls quarterly, and review draft consent language as needed. 40 hrs x \$100/hr.

Larry Owen, Senior Systems Analyst, 25% effort, directs the UAB Mobile App Developer Lab. He has extensive experience with developing and testing cross-platform, interoperable Internet and mobile applications. He will be responsible for the execution of the activities that develop the new technologies to collect Patient Reported Outcome and other patient data.

Kenneth G. Saag, MD, MSc, Co-Investigator, 1% effort, is *Jane Knight Lowe* Professor of Medicine in the Division of Clinical Immunology and Rheumatology, at the University of Alabama at Birmingham (UAB), and Professor of Epidemiology, at the UAB School of Public Health. He is the founding Director of the Deep South Musculoskeletal (DSM) Center for Education and Research on Therapeutics (CERTs) and Director of three AHRQ-supported training grants (a T32 in Health Services Research, a T32 and K12 in Comparative Effectiveness Research). Dr. Saag is also Director of the UAB Center for Outcomes and Effectiveness Research (COERE), a university-wide supported interdisciplinary research center and Associate Director of the Multidisciplinary Clinical Research Center (NIAMS P60). He is a practicing rheumatologist and outcomes researcher with a focus on bone health evidence implementation and pharmacoepidemiology, and has also led sentinel clinical trials in osteoporosis. Dr. Saag will participate in scientific aspects of the project and participate on regularly scheduled study meetings.

James Willig, MD, MSPH Co-Investigator, 5% effort, is Assistant Professor in the UAB Division of Infectious Diseases and has served as Medical Director of Informatics at the 1917 HIV/AIDS Clinic (1917 Clinic) since 2006. He is an Associate Scientist in the UAB Center for AIDS Research (CFAR), and the Center for Outcomes and Effectiveness Research and Education (COERE). Dr. Willig will be involved in the design of the web-app to capture patient data, integrate into existing databases, and investigate methods to present these data back to patients and practitioners to allow for future utilization in clinical care and research. Dr. Willig will have responsibility for the feasibility and barrier assessment aspect of the project especially for Aim 1.

Other Personnel

Lang Chen, PhD, Statistician, 6% effort, will serve as a lead staff statistician. Dr. Chen has considerable experience with common data models, large databases, complex multivariable modeling as well as with hierarchical modeling, data linkages, and statistical software. His activities will include data acquisition and manipulation for analytical purposes, quality control, security, linkage and confidentiality of data for the project. He has substantial experience in working with national Medicare and Medicaid data and registry/cohort data that will be used for this project. He will re-use common data formats that have been developed for previous

projects and oversee the mapping to the OMOP common data model (Section 6). He will also allow us to evaluate the generalizability of our patient network and has substantial experience working with multiple national cohorts, U.S. Census, and health plan data.

TBN, Graduate Student Assistant, 40% effort, will be responsible for research and development of the mobile application and cloud services as architected by Mr. Owen.

TBN, Undergraduate Student, 20% effort, will be responsible for development and implementation of the mobile application and cloud services as architected by Mr. Owen.

Travel

Funds are requested for travel of PI and investigators to attend national or international meetings or conferences to discuss research design and implementation or present experimental results and outcomes (\$2,200).

Facilities and Administrative Cost Reimbursement and Offsets

Facilities and Administrative (“F&A”, formerly “Indirect”) costs are real costs incurred by the Schools/Centers and institution for common or joint objectives in support of sponsored research and activities but cannot be directly identified with a specific grant or contract. The costs result from shared services such as libraries, physical plant operation and maintenance, utility costs, general, departmental, units/school and sponsored projects’ administrative expenses, and depreciation for buildings and equipment. These are real costs built into the University budget.

The F&A costs recovered on grants allow the institution to build, maintain and operate research facilities (as opposed to teaching facilities). It is the obligation of all researchers who use institutional facilities to bring in grant funding along with the attendant F&A costs. The F&A dollars received are not extra dollars, but are part of the budget and are fully used to make the system work. Without them, research laboratories and facilities cannot be built and maintained.

UAB’s F&A cost reimbursement is driven by its [Colleges and Universities Rate Agreement](#) (Rate Agreement) negotiated with and mutually executed with its cognizant audit agency, the Department of Health and Human Services (DHHS).

UAB’s Rate Agreement is applicable to and covers all sponsored research, other sponsored activities and sponsored instruction per the federal OMB Circular A-21 guidelines and UAB policy. UAB has three policy exceptions to its Rate Agreement, the [Clinical Trials F&A Rate](#), the [Continuing Professional Education Agreements Reviewed by OSP \(CPE\)](#) and the [Industry Sponsored Training Awards Submitted to the Office of Sponsored Programs \(OSP\)](#). These three exceptions are (1) effective by execution and implementation of the Vice President for Research and Economic Development, (2) only applicable relative to the appropriate study type, and (3) only when all criteria of the applicable guidelines are met.

The link to UAB’s [Indirect Cost Reimbursement Policy](#) (December 21, 1999) is provided for your convenience and among other important information it states the following –

1. All externally funded projects conducted by UAB shall seek reimbursement of indirect costs at the federally approved rates.
2. When the sponsor is a *legally constituted federal, state, or local government entity or not-for-profit entity* such as a foundation or health agency and has a *published and uniformly applied policy* regarding the payment of indirect costs, UAB will abide by that sponsor's policy. Written evidence of such an agency's indirect cost payment policy must accompany any proposal bearing less than the rates referred to in item 1.

Note the requirement is a *published and uniformly applied policy*.

Note that for-profit entities are not eligible for an alteration of the payment of indirect costs. Therefore, the expectation is that UAB will fully recover all F&A on any project funded by such an external agency.

Note all sponsored projects, other sponsored activities and sponsored instruction projects are subject to federal and other audit. Account setup, billing and other post-award financial activities are managed by UAB's Grants and Contracts Accounting (GCA) department.

Pfizer, Inc. Use of PRO in RACurtis, Jeffrey R., MD, MS, MPH**ORIGINAL****COLLEGES AND UNIVERSITIES RATE AGREEMENT**

EIN: 1636005396A6

DATE:10/17/2013

ORGANIZATION:

FILING REF.: The preceding
agreement was dated
06/20/2012University of Alabama at Birmingham
921 Administration Building
701 20th Street South
Birmingham, AL 35294-0109

The rates approved in this agreement are for use on grants, contracts and other agreements with the Federal Government, subject to the conditions in Section III.

SECTION I: INDIRECT COST RATES

RATE TYPES: FIXED FINAL PROV. (PROVISIONAL) PRED. (PREDETERMINED)

EFFECTIVE PERIOD

<u>TYPE</u>	<u>FROM</u>	<u>TO</u>	<u>RATE (%)</u>	<u>LOCATION</u>	<u>APPLICABLE TO</u>
PRED.	10/01/2011	09/30/2013	46.50	On-Campus	Organized Research
PRED.	10/01/2013	09/30/2015	47.00	On-Campus	Organized Research
PRED.	10/01/2011	09/30/2015	27.50	Off-Campus (1)	Organized Research
PRED.	10/01/2011	09/30/2015	26.00	Off-Campus (2)	Organized Research
PRED.	10/01/2011	09/30/2012	43.50	On-Campus	Instruction
PRED.	10/01/2012	09/30/2015	45.00	On-Campus	Instruction
PRED.	10/01/2011	09/30/2015	26.00	Off-Campus	Instruction
PRED.	10/01/2011	09/30/2012	31.00	On-Campus	Other Spons Activity
PRED.	10/01/2012	09/30/2015	36.00	On-Campus	Other Spons Activity
PRED.	10/01/2011	09/30/2015	26.00	Off-Campus	Other Spons Activity

Pfizer, Inc. Use of PRO in RACurtis, Jeffrey R., MD, MS, MPH

ORGANIZATION: University of Alabama at Birmingham

AGREEMENT DATE: 10/17/2013

<u>TYPE</u>	<u>FROM</u>	<u>TO</u>	<u>RATE (%)</u>	<u>LOCATION</u>	<u>APPLICABLE TO</u>
PROV.	10/01/2015	Until Amended			Use same rates and conditions as those cited for fiscal year ending September 30, 2015.

*BASE

Modified total direct costs, consisting of all salaries and wages, fringe benefits, materials, supplies, services, travel and subgrants and subcontracts up to the first \$25,000 of each subgrant or subcontract (regardless of the period covered by the subgrant or subcontract). Modified total direct costs shall exclude equipment, capital expenditures, charges for patient care, student tuition remission, rental costs of off site facilities, scholarships, and fellowships as well as the portion of each subgrant and subcontract in excess of \$25,000.

(1) Off-Campus, Adjacent: Locations within the 45 mile radius-commuting distance of the University.

(2) Off-Campus, Remote: Locations outside the commuting distance of the University.

Pfizer, Inc. Use of PRO in RACurtis, Jeffrey R., MD, MS, MPH

ORGANIZATION: University of Alabama at Birmingham

AGREEMENT DATE: 10/17/2013

SECTION I: FRINGE BENEFIT RATES**

<u>TYPE</u>	<u>FROM</u>	<u>TO</u>	<u>RATE (%)</u>	<u>LOCATION</u>	<u>APPLICABLE TO</u>
FIXED	10/1/2013	9/30/2014	28.60	University	Faculty
FIXED	10/1/2013	9/30/2014	8.80	University	Part Time, Temp, Irregular
FIXED	10/1/2013	9/30/2014	34.70	University	All Others
FIXED	10/1/2013	9/30/2014	9.00	Hospital	Part Time, Temp, Irregular
FIXED	10/1/2013	9/30/2014	22.30	Hospital	Residents, Post Docs, Fellows
FIXED	10/1/2013	9/30/2014	34.20	Hospital	All Others
PROV.	10/1/2014	Until amended			Use same rates and conditions as those cited for fiscal year ending September 30, 2014.

**** DESCRIPTION OF FRINGE BENEFITS RATE BASE:**

Salaries and Wages.

Part-Time Temporary/Irregular are not being combined with Students. The University has elected to waive any recovery for the Students.

Pfizer, Inc. Use of PRO in RA

Curtis, Jeffrey R., MD, MS, MPH

ORGANIZATION: University of Alabama at Birmingham

AGREEMENT DATE: 10/17/2013

SECTION II: SPECIAL REMARKS

TREATMENT OF FRINGE BENEFITS:

The fringe benefits are charged using the rate(s) listed in the Fringe Benefits Section of this Agreement. The fringe benefits included in the rate(s) are listed below.

TREATMENT OF PAID ABSENCES

Vacation, holiday, sick leave pay and other paid absences are included in salaries and wages and are claimed on grants, contracts and other agreements as part of the normal cost for salaries and wages. Separate claims are not made for the cost of these paid absences.

OFF-CAMPUS DEFINITION: For all activities performed in facilities not owned by the institution and to which rent is directly allocated to the project(s) the off-campus rate will apply. Grants or contracts will not be subject to more than one F&A cost rate. If more than 50% of a project is performed off-campus, the off-campus rate will apply to the entire project.

Fringe Benefits include: FICA, Health & Life Insurance, Workers' Compensation, Salary Continuation, State Unemployment, Disability Insurance, Educational Assistance, Employee Training, EAP, Terminal Vacation Pay, Teacher's Retirement and TIAA/CREF.

Equipment means an article of nonexpendable tangible personal property having a useful life of more than one year, and an acquisition cost of \$5,000 or more per unit.

This agreement updates the Fringe Benefits Rates section only.

Pfizer, Inc. Use of PRO in RA

Curtis, Jeffrey R., MD, MS, MPH

ORGANIZATION: University of Alabama at Birmingham

AGREEMENT DATE: 10/17/2013

SECTION III: GENERAL

A. LIMITATIONS:

The rates in this Agreement are subject to any statutory or administrative limitations and apply to a given grant, contract or other agreement only to the extent that funds are available. Acceptance of the rates is subject to the following conditions: (1) Only costs incurred by the organization were included in its facilities and administrative cost pools as finally accepted; such costs are legal obligations of the organization and are allowable under the governing cost principles; (2) The same costs that have been treated as facilities and administrative costs are not claimed as direct costs; (3) Similar types of costs have been accorded consistent accounting treatment; and (4) The information provided by the organization which was used to establish the rates is not later found to be materially incomplete or inaccurate by the Federal Government. In such situations the rate(s) would be subject to renegotiation at the discretion of the Federal Government.

D. ACCOUNTING CHANGES:

This Agreement is based on the accounting system purported by the organization to be in effect during the Agreement period. Changes to the method of accounting for costs which affect the amount of reimbursement resulting from the use of this Agreement require prior approval of the authorized representative of the cognizant agency. Such changes include, but are not limited to, changes in the charging of a particular type of cost from facilities and administrative to direct. Failure to obtain approval may result in cost disallowances.

C. FIXED RATES:

If a fixed rate is in this Agreement, it is based on an estimate of the costs for the period covered by the rate. When the actual costs for this period are determined, an adjustment will be made to a rate of a future year(s) to compensate for the difference between the costs used to establish the fixed rate and actual costs.

D. USE BY OTHER FEDERAL AGENCIES:

The rates in this Agreement were approved in accordance with the authority in Office of Management and Budget Circular A-21, and should be applied to grants, contracts and other agreements covered by this Circular, subject to any limitations in A above. The organization may provide copies of the Agreement to other Federal Agencies to give them early notification of the Agreement.

E. OTHER:

If any Federal contract, grant or other agreement is reimbursing facilities and administrative costs by a means other than the approved rate(s) in this Agreement, the organization should (1) credit such costs to the affected programs, and (2) apply the approved rate(s) to the appropriate base to identify the proper amount of facilities and administrative costs allocable to these programs.

BY THE INSTITUTION:

University of Alabama at Birmingham

(INSTITUTION)

Richard L. Margison

(SIGNATURE)

Richard L. Margison

(NAME)

Vice President for Financial Affairs & Administration

(TITLE)

October 24, 2013

(DATE)

ON BEHALF OF THE FEDERAL GOVERNMENT:

DEPARTMENT OF HEALTH AND HUMAN SERVICES

(AGENCY)

Darryl W. Mayes

(SIGNATURE)

Darryl W. Mayes

(NAME)

Deputy Director, Division of Cost Allocation

(TITLE)

10/17/2013

(DATE) 0297

HHS REPRESENTATIVE: Steven Zuraf

Telephone: (301) 492-4855