



## Program Narrative

The Arthritis Internet Registry (AIR) is an online, longitudinal arthritis patient cohort that combines the patient-direct infrastructure of the National Data Bank for Rheumatic Diseases (NDB), the nation-wide availability of Quest Diagnostics blood collection sites, and the patient outreach infrastructure of various patient advocacy groups. Created by Drs. Kaleb Michaud, Robert Plenge, John Hardin, and Stanley Naides, AIR tested the feasibility of developing a large RA research registry with biospecimen collection. Developed in 2009-2010, AIR started to recruit patients in July 2010.

*The ultimate goal of AIR is to enroll at least 20,000 RA and other rheumatic disease patients, including adults with osteoarthritis or juvenile idiopathic arthritis, with detailed longitudinal clinical and treatment data as well as biospecimens to foster research and understanding in RA and improve the status of arthritis patients throughout the US.*

AIR is unique as one of the only nationwide arthritis research cohorts that is almost completely powered by patients. Patients choose to report on their well-being and medical status. They choose to donate blood samples by travelling to laboratories. They provide AIR access to their institution's medical records, and they are involved in the design, review, and implementation of future studies including those involving new technologies for collecting data (e.g., smartphones, pedometers) and ways of collecting biosamples (e.g., mouth swabs, finger-prick blood mailed from home). Because of this, AIR is able to offer a great value to the arthritis research community by providing large amounts of quality observational data from patients at a cost greatly reduced from usual methods at academic institutions.

**Enrollment.** As of November 2016, AIR has grown to 6,554 enrolled patients with 4,975 with active study status, and 1,385 total lab samples received (874 RA, 313 OA, and 198 other diagnoses). We have received 6-month questionnaires from 4,122 patients.

**Website.** In order to improve enrollment and participant retention, we launched features on the web-based questionnaires. These included: reporting laboratory results of ACPA, RF, and CRP that the patient could print and take to their rheumatologist; a simplified medication reporting page that includes a summary for the patient to keep for their records; and a 50% shorter version of the questionnaire available online.

## Details on AIR:

**1. Recruitment.** *The primary method for recruiting patients to use AIR is through advertising on various organization websites.* AIR first started recruiting with the Arthritis Foundation, which dedicated a small portion of their online ad space that was linked to a longer page describing the AIR study. From here, the reader was invited to enroll in AIR by clicking the "Enroll in the Arthritis Internet Registry" link that took them to the online Consent to Participate webpage housed on the NDB webserver. AIR currently is being advertised via various other patient groups, along with the NDB website, and Google ads.

**2. Use of controls.** Participation bias is an expected issue with online recruitment. This bias is due to certain individuals being more likely to seek out, enroll, and participate in studies as compared to those who choose not to enroll. By not specifically advertising to RA patients, but rather advertising to all arthritis patients, we had hoped to reach osteoarthritis (OA) and other rheumatic disease patients so that we would accomplish the following: a) appeal to the greatest number of visitors on the website, b) receive data from other inflammatory arthritis patients for future studies, and c) obtain controls in the form of non-inflammatory OA. The OA controls are crucial for future comparison analyses with RA patients because they greatly alleviate participation bias, which affects both OA and RA diagnosis groups.

**3. Confirmation of diagnosis.** The first question AIR participants answer after consenting to enroll is, "What is your primary rheumatic disease diagnosis?" If one indicates RA, then they are asked four subsequent screening questions. After enrollment and with the patient's consent, a brief letter is sent to the patient's physician requesting confirmation and/or clarification of the actual diagnosis. Of the 2,538 physicians contacted, 1,925 have responded (76%). Diagnoses are also confirmed via medical records, if obtained to validate questionnaire data. The distribution of reported diagnosis is: 67% reporting RA, 23% OA, and 10% were other rheumatic diseases (e.g., 5% psoriatic arthritis, 2% lupus, 3% fibromyalgia, etc).

**4. Patient-reported data.** At enrollment, AIR patients provide their demographic information, medical history, treatment history, and current arthritis clinical status. Participants were primarily female (89%), Caucasian (87%), married (60%), college educated (86%), never smoked (59%), and their mean age was 55 years. Overall mean pain, fatigue and clinical measures including the RA disease activity as measured by PAS-II were moderate. AIR patients are encouraged to complete comprehensive semiannual questionnaires every January and July the same as their NDB participant counterparts. In terms of patient data collection and health event validation, AIR participants are treated the same as those in the NDB, though they have been under much less cumulative observation time.

**5. Biospecimen collection.** After physician confirmation of diagnosis, AIR participants are asked if they would consent to having blood and serum samples collected. Because of the sensitive nature of the request and length of the consent form, only 72% of patients provided consent. Coded kits with eight test tubes are shipped to the consenting patients. Either on their own using the Quest Diagnostics website or with the help of NDB staff, the patients schedule an appointment with a local Quest Diagnostics Patient Service Center (PSC). While the patient must confirm their identity at the PSC, no identifiable information is sent with the biospecimens as they are shipped overnight to the Quest Diagnostics Nichols Institute San Juan Capistrano storage and analysis facility. The NDB site retains identifying information of the coded biosample kits, allowing de-identified samples to be linked to diagnostic and clinical information held by the NDB that does not contain personally identifiable information. An aliquot of serum is sent for CRP, RF, and CCP analysis; specific details on this analysis are provided in the appendix. Of the remaining sample, serum, EDTA plasma, peripheral blood cells, DNA, and RNA aliquots are prepared; half of each sample aliquot is stored for future use by AIR researchers, and the other half is kept for use by Quest Diagnostics for test development and clinical validation. There is an average 4 to 8 month delay from AIR enrollment to receipt of biosamples. *Currently, biospecimens have been collected for 1,385 AIR patients and 874 were RA patients, of which 53% were CCP+ and 53% RF+; of the 511 non-RA patients, 5% were CCP+ and 12% RF+.*

**If you are interested in finding out more about AIR, please contact:  
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