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The Osteoarthritis Initiative: A NIH Public–Private Partnership

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Introduction

Osteoarthritis affects over 27 million individuals in the USA [1]. The National Institutes of Health (NIH) has long supported research to improve outcomes for patients with this debilitating disease. Knee osteoarthritis is associated with significant pain and development of disability over time. People who are severely compromised have few effective treatment options other than joint replacement. Differences exist in the prevalence, incidence, and severity of osteoarthritis between men and women. Furthermore, the course of disease is frequently associated with significant morbidity and disability. Currently no disease-modifying agents exist for the treatment of osteoarthritis, although new treatments are currently under development. The discovery of osteoarthritis biomarkers, including structural characteristics that can be observed with MRI, could lead to identification of new treatment targets and mechanisms for shorter, more efficient trials of disease-modifying agents.

The Osteoarthritis Initiative (OAI) is a multicenter, longitudinal, and prospective observational study of knee osteoarthritis, which was launched by NIH in 2002. The overall aim of the OAI is to develop a public domain research resource to facilitate the scientific evaluation of biomarkers for osteoarthritis as potential surrogate endpoints for disease onset and progression. The goals of the OAI were to enroll approximately 5,000 subjects with risk factors for or evidence of early knee osteoarthritis and to collect clinical and imaging data and biological specimens from these participants for originally four and now 8 years of follow-up.

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OAI Materials and Methods

Overviews of the study start up, protocol development, and recruitment and enrollment are available on the web site of the National Institute for Arthritis and Musculoskeletal and Skin Diseases (NIAMS): (http://www.niams.nih.gov/Funding/Funded_Research/Osteoarthritis_Initiative/default.asp); technical details are available on the OAI website: (www.oai.ucsf.edu/datarelease/StudyOverview.asp).

Funding for the OAI has been contributed by both NIH and private sector participants. The private sector funding was initially provided from Pfizer, Merck, GlaxoSmithKline, and Novartis. The Foundation for the National Institutes of Health has coordinated private sector participation. Funding from the NIH institutes and centers initially included NIAMS and the National Institute on Aging (NIA), the National Center for Complementary and Alternative Medicine (NCCAM), the National Center on Minority Health and Health Disparities (NCMHD), the National Institute of Dental and Craniofacial Research, the NIH Office of Research on Women's Health (ORWH), and the National Institute for Biomedical Imaging and Bioengineering (NIBIB). Financial support for the extension of the follow-up for the OAI cohort (with an additional four contacts with study subjects from 2010 through 2014) has been provided by Pfizer and Novartis from the private sector and NIAMS, NIA, NCCAM, NCMHD, ORWH, and NIBIB.

The OAI research team consists of the following centers and their principal investigators: University of Maryland School of Medicine, Baltimore: Marc Hochberg, M.D., M.P.H.; The Ohio State University, Columbus: Rebecca Jackson, M.D.; University of Pittsburgh: C. Kent Kwoh, M.D.; Memorial Hospital of Rhode Island, Pawtucket: Charles Eaton, M.D.; and University of California, San Francisco (data coordinating center): Michael Nevitt, Ph.D. A steering committee, comprised of representatives from

these centers, the NIH, and the pharmaceutical partners, advises on the scientific aspects of the study. The US Food and Drug Administration provide a representative to serve as a liaison to the steering committee in an advisory manner.

The OAI cohort of 4,796 subjects is 58% female and ranged in age from 45 to 79 at the time of their recruitment. As of early 2011, the entire OAI cohort had completed their baseline, 12-, 24-, 36-, and 48-month visits. The 60-month visit is by telephone and is approximately 95% complete. The 72-month visits are in-clinic and well underway at all sites (48% of the cohort has completed this follow-up). Eight 4-month telephone and mail visits have begun in two of the clinics and will begin in the other two in the next several months. Planning is underway for the 96-month in-clinic visits to begin in 2012. A subset of participants in the progression cohort was also seen at 18 months (n=288) or 30 months (n=494) for knee MRI, blood collection, exam, and collection of questionnaire data to allow for analysis of change over shorter intervals; these data are already posted on the OAI website. Retention remains high, although some participants (~7%) from the original cohort did not continue for the additional 4 years of follow-up. The rate of no contact has stabilized in the 15% to 18% range.

Seventy-three percent of study participants have at least one knee X-ray and 70% have one knee MRI for all five time points. Any bias regarding those who do not have an MRI can be addressed in analysis. The OAI is supporting some analyses of the MRI and X-ray data, which are being annotated with the source and posted to the website. Since the preferred method for reading the MRIs is unclear, no efforts are planned to read the MRIs for the entire cohort at this time. Selected readings are posted to allow researchers to test their own hypothesis for what components and methods of reading provide the best diagnostic variable for predicting progression. It is proposed that funds from the American Revitalization and Recovery Act (ARRA) will be used to read the OAI X-rays. Other OAI investigators are requesting supplemental funding from the ARRA to support ancillary studies.

Four separately NIH-funded (R01 and R21 mechanisms) ancillary studies to the OAI are well underway. One of the most recent addresses the effects of physical activity on disability progression. Physical activity is measured using an accelerometer to measure whether participants who meet the recommended activity guidelines can slow disability progression compared to those who cannot. In 2010, NIAMS also funded three contracts for analysis of OAI data to: Dr. Charles Eaton at Memorial Hospital of Rhode Island for "Osteoarthritis Patient-centered Outcomes and Complementary and Alternative Therapy (CAM)" (http://www.niams.nih.gov/Funding/Funded_Research/Osteoarthritis_Initiative/patient_outcomes_cam.asp); Dr. C. Kent Kwoh at University of Pittsburgh for "Pivotal Osteoarthritis Initiative Magnetic Resonance Imaging Analyses" (http://www.niams.nih.gov/Funding/Funded_Research/Osteoarthritis_Initiative/pivotal_mri.asp); and Dr. Michael Nevitt at University of California San Francisco for "Hip Morphology and Limb-specific Risk Factors for Radiographic Hip Osteoarthritis" (http://www.niams.nih.gov/Funding/Funded_Research/Osteoarthritis_Initiative/hip_morphology.asp).

Summary

Data are released on a regular basis to OAI online. As of April 2011, 1,911 users had registered for OAI Online from 83 countries, with over 7,975 datasets downloaded and 321 image sets distributed. Data are currently being released in a single bolus for the entire visit. Recent releases have included the 36-month questionnaire and exam data and images for the full cohort, as well as the 30-month questionnaire and exam data and images for a subset of the progression cohort. Clinical data and images from the 48-month visits should also have been released by the time this article is published. An increasing number of abstracts and papers are being produced based on the use of the OAI data and images (see www.oai.ucsf.edu/datarelease/Publications.asp).

This groundbreaking study is expected to advance our understanding of how modifiable and non-modifiable risk factors are linked to the development and progression of knee osteoarthritis. These findings may in turn lead to improved strategies for disease prevention, identification of novel treatment targets, and ways to prevent disability in later life.

Disclosure The author certifies that he or she has no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted article.

The author certifies that his or her institution has approved the reporting of these cases, that all investigations were conducted in conformity with ethical principles of research, and that if necessary, an informed consent for participating in the study was obtained.

Reference

1. Dillon CF, Rasch EK, Gu Q, Hirsch R. Prevalence of knee osteoarthritis in the United States: arthritis data from the Third National Health and Nutrition Examination Survey 1991–94. J Rheumatol. 2006 Nov;33(11):2271–9.