AMERICAN COLLEGE OF RHEUMATOLOGY
POSITION STATEMENT

SUBJECT: Comparative Effectiveness Research

PRESENTED BY: Committee on Rheumatologic Care

FOR DISTRIBUTION TO: Members of the American College of Rheumatology
Agency for Healthcare Research and Quality
National Institutes of Health
Medical Societies
Arthritis Foundation

POSITION:

1. We applaud the goals of national comparative effectiveness research (CER) initiatives and encourage the active involvement of ACR members with unique expertise in clinical research, basic science, statistics, healthcare policy and community-based research as they relate to rheumatologic diseases. They must be involved to ensure these studies are well designed, well executed and provide meaningful results.

2. High-quality CER and cost effectiveness analyses (CEA) can and should inform individual provider and patient decisions about the relative value of diagnostic and therapeutic options. Indeed, CER has the potential to enhance understanding of the pros and cons of different treatments, as well as *highlight the need for multiple treatment options to address heterogeneous groups of patients*. However, CER and CEA results must not be misconstrued or inappropriately applied to individual patients via inflexible insurer policies designed to control costs, thereby overriding medically appropriate, individualized decision making by providers and patients.

3. CER should be applied to common problems that impact rheumatology patients and providers. The ACR advocates that federal funders of CER research (such as the Patient-Centered Outcomes Research Institute (PCORI), the Agency for Healthcare Research and Quality (AHRQ), the National Institutes of Health, etc.) should target RA and other musculoskeletal disorders with requests for applications from rheumatology researchers.

4. The ACR supports the collection of anonymized patient data in registries such as RISE (rheumatology informatics system for effectiveness), which can serve as powerful databases for CER if they are robustly populated with sufficient patient data.

5. The ACR supports ongoing funding of CER initiatives to follow up the initial $1.1 billion investment made in 2009 through the American Recovery and Reinvestment Act (ARRA), understanding that groups such as PCORI and AHQR are subject to ongoing funding allocation and perennially at risk of underfunding.

6. The ACR supports ongoing transparency regarding oversight of the distribution of CER funds and communication of results.

BACKGROUND:

Comparative effectiveness research (CER) compares two active forms of treatment or usual care in comparison to an additional intervention and is fundamentally distinct from research that compares new treatments to placebo. Comparative effectiveness research was central to a $1.1 billion initiative funded by the American Recovery and Reinvestment Act (ARRA) of 2009 to promote evaluation of the benefits and risks of medical treatments or services *relative to other treatments* for the same condition.

In the broadest sense, CER has extended and legitimized newer methods of evaluation of healthcare interventions. The US Food and Drug Administration ushered in changes of similar magnitude in the past, with laws in 1938 and 1962 that required, respectively, pre-marketing safety analysis and a demonstration of the efficacy of new drugs. With the second change, placebo-controlled clinical trials became the standard by which the effectiveness of new drugs was assessed. Often, these trials are not designed to compare new treatments to existing therapies. As a result of the placebo-control standard, we now have a legacy of interventions with proven efficacy, but with unmeasured *comparative* efficacy (1,2).

In addition to an emphasis on comparative analysis, the CER initiative has focused on high- impact clinical problems that were ranked with scientific rigor by the Institute of Medicine. In recognition of the limits of clinical trials that examine highly selected, homogeneous groups of patients, CER emphasizes research on real-world populations in real-world settings and promotes analysis of heterogeneous populations to prevent "one-size-fits-all" answers. The need for CER is especially apparent in light of the realization that there are profound regional differences in the management of many diseases and that these regional variations are associated with high costs of care (3). It is also important to establish a framework for conducting CER, particularly for interventions where there are no strong regulatory requirements that must be met, prior to introduction into usual care.

Opportunities abound for comparative research in rheumatoid arthritis (RA) which affects 3.6 out of 100 women and 1.7 of 100 men in their lifetimes in the US (4). Biologic treatments now cost upwards of $70,000/year and in spite of an increasing number of treatment options, CER and biomarkers to guide treatment decisions are, for the most part, lacking.

It must be acknowledged that payers' interest in CER data is rooted in a desire to reduce utilization of expensive diagnostic and therapeutic modalities. In this context, it is worth noting that the Patient-Centered Outcomes Research Institute (PCORI), an organization established by Congress that underwrites CER, is prohibited from funding studies that evaluate costs or cost effectiveness of interventions or from focusing on insurance coverage or reimbursement decisions. Other organizations are not so constrained and CER efforts are incorporated into cost effectiveness analyses (CEA) (https://icer-review.org/). Under ideal circumstances, CER and CEA data may eventually help to establish which treatment options provide the best value. However, a major concern is that payer restrictions may not be based on robust, high-quality, CER or CEA analyses that are relevant to the *individual patient* (adjusting for the unique blend of co- morbidities and tolerances inherent in the care of an individual patient.) On the other hand, if CER becomes the new standard, payer restrictions not supported by relevant CER data could be identified and confronted and financially-driven "rationing" decisions might become less frequent. Of course, it will be challenging to effectively apply cost effectiveness analyses, at least in the commercial insurance market, so long as true drug costs are veiled behind opaque rebate structures between payers and pharmacy benefit managers.

To aid these CER efforts, in 2014 ACR launched the rheumatology informatics system for effectiveness (RISE) that allows rheumatologists throughout the country to seamlessly and effortlessly transfer anonymous patient outcome data to a national registry. Thus far, RISE has collected more than 25 million patient encounters, positioning RISE to become the premier source for real-world CER data in rheumatology. The greater the participation of rheumatology providers in RISE and other similar registers, the more powerful CER analyses comparing therapeutics in real life circumstances can become.

Individuals with unique expertise in clinical research, basic science, statistics, healthcare policy and community-based research as they relate to rheumatologic diseases, are abundantly represented in the membership of the ACR. They must be involved in CER to ensure these studies are well designed, well executed and provide meaningful results. Avoiding potential waste will require active, personal involvement by experts in a range of disciplines.

The impressive $1.1 billion allotment from ARRA in 2009 was an essential commitment which should be followed by appropriation of significant ongoing resources towards CER so that the original CER initiative can achieve its goals. Knowing that a *one-time* funding cycle, without continued funding to support these studies, might be short-sited, we were gratified that in 2010 Congress authorized the independent, non-profit, non- governmental PCORI, whose goal is to identify critical research questions and fund patient- centered comparative clinical effectiveness research (5). The ACR also supports continued funding for AHRQ which is chronically under-funded and perennially on the verge of being defunded in spite of their critical mission to disseminate and implement CER findings generated by PCORI.

Finally, oversight of the distribution of CER funds and communication of results must be carefully and transparently coordinated. A Federal Coordinating Council (FCC-CER) is charged with providing oversight for all research efforts, avoiding duplication of effort, and making recommendations to Congress regarding further resources and infrastructure. In addition, coordination with like-minded organizations, such as the PCORI, will be integral to the success of the CER initiative.

References:

1.Conway- PH, Clancy C. Comparative-effectiveness research-implications of the Federal Coordinating Council's report. N Engl J Med 2012; 361:328-330.

2.Blackstone EA, Fuhr JP Jr., Ziernicki D. Will comparative effectiveness research finally succeed? Biotechnol Health. 2012; 9: 22-26.

3.Clement FM, Harris A, Li JJ, et al. Using effectiveness and cost-effectiveness to make drug coverage decisions: a comparison of Britain, Australia, and Canada. JAMA 2012; 302: 1437-1443.

4.Crowson CS, Matteson EL, Myasoedova E, et al. The lifetime risk of adult-onset rheumatoid arthritis and other inflammatory autoimmune rheumatic diseases. Arthritis Rheum 2011; 63(3):633-639.

5.Selby JV, Beal AC, Frank L. The Patient-Centered Outcomes Research Institute (PCORI) national priorities for research and initial research agenda. JAMA 2012; 307:1583-1584.

Approved by Board of Directors: 08/17 8/21