

Too Little Too Late: Effect of Poor Access to Biologics for Patients with Rheumatoid Arthritis



Biologic disease-modifying antirheumatic drugs (bDMARD), in particular anti-tumor necrosis factor (anti-TNF) medications, which were developed in the 1990s, have improved the radiographic and functional status of patients with rheumatoid arthritis (RA)¹. It has been thought as a corollary that rates of joint replacement in patients with RA would decrease. Results in various national databases since the advent of biologic medications have been discrepant; for example, in a US cohort there was a decrease in arthroplasty in juvenile idiopathic arthritis, but not RA from 1991 to 2005², whereas in Ireland the arthroplasty rate was halved from 1995 to 2010³. In Japan there was no change in the rate up to 2008, while in Sweden the hip arthroplasty rate decreased, but the knee rate did not⁴. Overall, however, the trend seems to be toward lower rates of arthroplasty in patients with RA.

An article in this issue of *The Journal*, by Stamp, *et al*⁵, provides an interesting analysis of the rates of joint replacement in New Zealand from 1999 to 2015 in both OA and RA since the advent of biologic medications. The results show that according to a New Zealand Joint Registry (1999–2015), while OA joint replacement rates for total knee replacement (TKR) and hip replacement (THR) increased, for patients with RA there was no decrease in the rate of TKR and THR.

How should one interpret these data of no decrease in the RA TKR and THR rates? One should look through the lens of the current situation in New Zealand regarding access to the biologics. Per the authors, biologics were not available in New Zealand until 2006, and even then only 1 was available. Contrast this to the situation of the United States, where there was biologic access nearly a decade earlier.

Further, the authors cite draconian eligibility criteria for biologics in New Zealand: patients need to not only fail triple therapy, but also have erosions on their radiographs. As a stark example, the rate of biologic use in this RA cohort undergoing arthroplasty was < 10%; in a similar US-based cohort the rate was over 50%^{6,7}. Clearly the government

policy has affected biologic access for patients with RA in New Zealand.

To demonstrate a contrast, other countries have far less stringent access criteria. These countries have shown better outcomes regarding decreased rates of arthroplasty. In Sweden, although failure of 2 traditional DMARD is recommended, rheumatologists are given discretion to use biological therapy⁸. In the United States, patients with RA typically must first fail methotrexate, but rheumatologists can use bDMARD as a first-line therapy in early and aggressive disease or in those with contraindications to use of traditional DMARD. In Japan, patients can also be prescribed bDMARD at the discretion of a rheumatologist if they fail traditional DMARD, a policy also far less stringent than the New Zealand criteria. England and Wales have criteria more similar to New Zealand regarding the prescription of biological agents — the patient must fail 2 traditional DMARD, and a state of severe disease is also required (28-joint Disease Activity Score > 5.1), but even these countries do not require erosions prior to biologic initiation⁸.

This article raises a salient question on the international platform: what should inform a government's policy for access to biologics for patients with RA? Costs are invariably part and parcel of any discussion of access to biologics. A population-based analysis of indirect and direct costs attributable to RA in Sweden showed the total national burden of illness of 600 million euros in 2010⁹ (US\$708 million), and in the United States, it has been estimated at up to US\$19.2 billion¹⁰. A 2009 study by the National Audit Office in England estimated that RA costs the UK National Health Service £560 million annually, and puts the additional costs from absence from work and aspects of work-related disability at £1.8 billion a year¹¹.

These tremendous costs of RA should not be surprising for rheumatologists, but the additional burden of joint replacements for patients with RA who have poor disease control can significantly compound these costs. Biologic

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agents, despite their costs, can lower the disease burden for society. This was shown in an analysis of the Swedish Rheumatology Registers, which demonstrated that TNF-inhibitor treatment was associated with an increase in quality-adjusted life years and an incremental cost compared to no biological treatment¹².

According to the Global Burden of Disease 2010 study, RA was ranked as the 42nd-highest contributor to global disability, representing a modest global disability, but with severe consequences for the individuals affected¹³. The European League Against Rheumatism (EULAR) and American College of Rheumatology (ACR) recommend starting bDMARD immediately after diagnosis or after traditional DMARD failure. However, because of the high cost of biology therapies, many national guidelines remain far removed from the goals-based approach recommended by EULAR and ACR. Government policies and national guidelines should consider adopting the societal perspective on reimbursement, as in Sweden, which suggests that the availability of biologic agents may award longterm benefits to both patients with RA and to healthcare systems.

The advent of biosimilars opens a brave new world of opportunity to reduce the cost of access to biological DMARD¹⁴. It is our hope that the data from the article by Stamp, *et al* will open the eyes not just in New Zealand of those who determine access rules for biologics, but also in countries around the world. It is clear from this article that access to biologics for patients with RA after the presence of erosions is too little too late.

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