The price of escalating drug dose to treat rheumatoid arthritis

Rheumatoid arthritis (RA) with its characteristic joint swelling, inflammation, pain and stiffness, may be treated with biologic disease-modifying drugs. One class of drug belonging to this group inhibits tumor necrosis factor (TNF), which plays an important role in RA development. Drugs that inhibit TNF include adalimumab, etanercept, infliximab, certolizumab and golimumab.

Although TNF inhibitors are effective, some people do not adequately respond or they may lose response over time. The development of antibodies against adalimumab or infliximab has been linked to a reduction in drug concentration and reduced response. In contrast, antibodies to etanercept do not appear to have an effect on its clinical activity.

To compensate for an inadequate or reduced response to TNF inhibitors, drug dose may be escalated by increasing the dose or by reducing the dosing interval. A recent systematic review (Moots et al, 2015) showed that escalating the dose of TNF inhibitors is common in patients with RA to improve or achieve an adequate response. The weighted proportion of dose escalators was 15% for adalimumab, 5% for etanercept, and 42% for infliximab. This was associated with an increase in TNF inhibitor- and RA-related treatment costs, resulting in an increase in total health care costs, yet the clinical benefit of such an approach is still not confirmed.

Although costs have been worked out at the patient level, population costs have not been calculated, therefore our study aimed to determine the cost of such dose escalation across five countries in Europe: Germany, France, UK, Spain and Italy.

The proportion of people who escalate their dose of TNF inhibitor, and the average percentage increase in TNF inhibitor cost associated with escalators versus non-escalators was calculated from previously published estimates, weighted by the sample size for each study. The number of people with RA treated with a TNF inhibitor, and the corresponding total drug sales for Germany, France, UK, Spain and Italy were estimated using the ‘Decision Resources’ Pharmacor Market Forecast’. This Forecast factors in price estimates per treated day, number of treated days, and how well people adhere to therapy.

Two methods were used to estimate the cost of dose escalation: the first assumed that the TNF inhibitor cost per day was based on the average person, whether a dose escalator or not; the second assumed that the drug cost per day represented the average cost for non-escalators.

The weighted average percentage increase in TNF inhibitor cost for escalators versus non-escalators was 38% for adalimumab, 13% for etanercept, and 42% for infliximab. This translated to an estimated cost increase across the countries for these three drugs of €51.5–54.4 million, €5.8–5.9 million, and €44.8–52.8, respectively.

Marginal cost was estimated by multiplying the difference in cost between escalators and non-escalators by the number of escalators. The estimated marginal cost across the five countries per 1000 treated patients was 0.8 million for adalimumab, 0.1 million for etanercept, and 2.1–2.5 million for infliximab (Fig. 1).

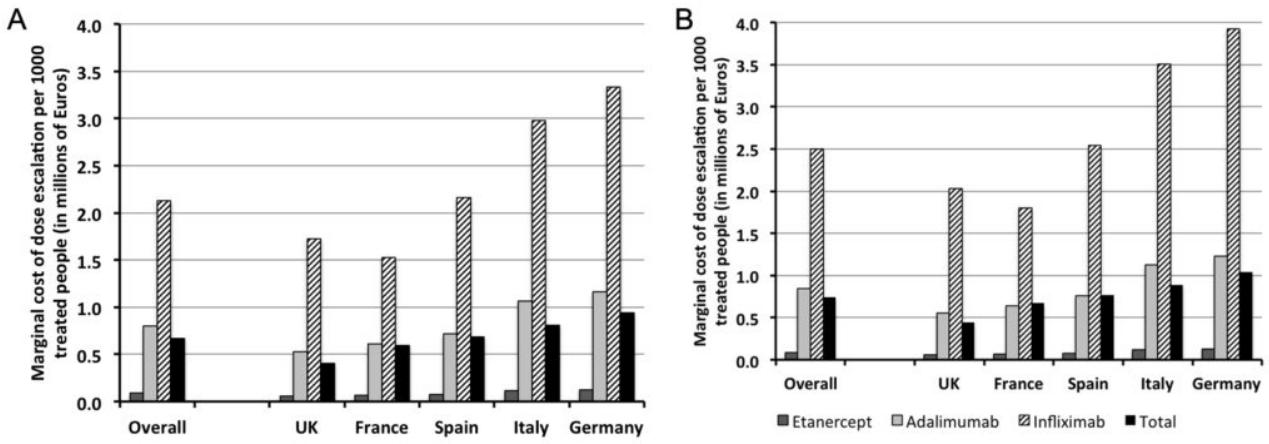

Fig. 1. A. Method 1: Marginal cost of dose escalation per 1000 treated people. B. Method 2: Marginal cost of dose escalation per 1000 treated people

Reasons for the lower dose escalation rates seen with etanercept versus adalimumab and infliximab, may include etanercept antibodies not having an effect on clinical efficacy, and product labeling for etanercept not encouraging flexible dosing.

Our study has shown that dose escalation of the TNF inhibitors adalimumab, etanercept and infliximab in people with RA resulted in an estimated increase in costs of between €102.2 and 113.1 million across five European countries. This highlights the need to consider other strategies when response is inadequate or reduced, because despite this cost escalating the dose may not improve clinical response.

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inhibitors across Europe.
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