Payers' views on treating-to-target in rheumatoid arthritis: an English perspective

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ABSTRACT

Objective. *Delivering treat-to-target strategies in rheumatoid arthritis (RA) involves commitments from both providers and payers for healthcare. We have summarised the perspectives of payers from England, where the National Health Service (NHS) provides universal care that is without cost for patients.*

Methods. *We reviewed the literature – including that from the NHS and National Institute for Health and Clinical Excellence (NICE) – concerning payers views on the clinical effectiveness and cost-effectiveness of treat-to-target strategies for RA.*

Results. *Commissioners pay for government-funded English healthcare and providers (divided between General Practitioners (GPs) and Hospital Consultants) and deliver it according to NICE guidance. Treat-to-target using intensive disease-modifying drug (DMARD) combinations with glucocorticoids are recommended for early active RA. Treatment tapering is recommended when disease control is achieved. Some aspects of treat-to-target are recommended in established RA, including the early management of flares and the use of biologics in persistently active RA that is non-responsive to DMARDs. However, treat-to-target is not widely recommended in established RA, mainly because the evidence base is incomplete. English healthcare is moving towards quality care becoming the main driver and is adopting "integrated care" involving both GPs and consultants for most long-term disorders; RA is likely to be included within these approaches, which are unlikely to focus specifically on treat-to-target.*

Conclusion. *Payers strongly support treat-to-target in early RA. In established disease there is limited enthusiasm; without stronger evidence for efficacy and cost-effectiveness this is unlikely to change.*

Introduction

Individuals who wish to pay for their healthcare can invariably do so provided they are able to pay (1). Even in England, where healthcare is paid for by the Government, private medical services are available for patients with rheumatoid arthritis (RA). However, most people cannot afford to pay directly. Consequently healthcare costs are usually met by insurance schemes or by governments. Many countries mix these two approaches. England lies at one end of the spectrum with most health care funded by the Government through taxation. It is delivered without cost to patients at the point of care by the National Health Service (NHS) (2). This article explores how this arrangement affects treat-to-target strategies in RA.

How England pays for healthcare

The NHS has two arms. Commissioners pay for health care with government money. Providers deliver health care. Clinical services including rheumatology are usually funded by local commissioners. Some rare or complex disorders are funded by national commissioners. Government reforms may change different arrangements (3).Rising health care costs and increasing demands for treatment combined with fixed government funding mean that commissioners continually try to deliver cost effective health care. They want the best possible patient care at the least possible cost.

The National Institute for Health and Clinical Excellence (NICE)

Commissioners and providers need rules for their interactions (4). NICE play a pivotal role based on general principles. Firstly, health care decisions should be evidence-based. Secondly, patients must receive the best possible quality care. Finally, interventions should be both clinically and cost-effective. These general principles are universally ac-

ceptable but challenging in their interpretation and application.

Primary and secondary care

The NHS (5) provides all English residents with general practitioners (GPs) responsible for their care; this comprises primary care. Consultants, who usually are hospital-based, advise GPs on specialist aspects of care; this comprises secondary care. Commissioners effectively pre-pay GPs to care for their patients. Consequently only investigations, treatments and hospital attendances incur added costs.

This arrangement creates complexities in long-term disorders like RA. When patients develop RA, commissioners invariably agree they should see a rheumatologist, who usually initiates treatment. Most RA patients continue under specialist follow up but their overall treatment, including managing co-morbidities, is their GP's responsibility. Long-term disease-modifying anti-rheumatic drug (DMARD) prescribing and monitoring is usually organised by GPs; specialists have "watching briefs".

Some extra activity by GPs attracts limited additional funding; for example DMARD monitoring can lead to small extra payments. However specialist care, which is usually entirely undertaken in outpatient clinics and only rarely involves hospital admissions, incurs substantial additional expenditure for commissioners. Consequently, payers want to minimise hospital follow-up for RA patients, whilst continuing to provide high quality care.

NICE as referee

NICE has created rules for RA care as an impartial referee. It does not reach conclusions itself. Instead NICE advice is developed by independent experts spanning specialists, GPs and other clinicians, patients, care givers and health economists. NICE gives all interested parties the opportunity to comment on its guidance. An appeal process can be used if there substantial disagreements with NICE recommendations arise.

NICE Health Technology Appraisals which evaluate individual interventions are mandatory (6). They assess mainly high cost treatments. Healthcare providers and commissioners are mandated to provide funding for treatments approved in Health Technology Appraisals within 3 months of their publication. In occasional patients, this mandatory guidance cannot be followed, and high cost treatments may be used outside recommendations of NICE Health Technology Appraisals, provided payers agree their use represents "exceptional circumstances".

NICE Guidelines are more advisory (7, 8). Clinicians are expected to follow them in general, especially as they are used to define quality standards for clinical care. However, it is clinically inappropriate and sometimes impractical to meet all aspects of NICE guidelines at all times. They are therefore not intended to be mandatory.

NICE technology appraisals and guidelines are not static. They are continually updated. This is inevitable as evidence-based recommendations require change as the evidence is updated.

NICE has its proponents and opponents who provide well argued support and cogent criticism (9, 10). Without NICE providing national recommendations, the pressure on healthcare budgets are likely to result in many RA patients who meet the current NICE criteria not receiving high cost biologics. This is because funders would find it very challenging to meet the substantial costs involved. Thus, whilst its overall impact is beneficial, there will never be universal agreement about its recommendations.

NICE and treat-to-target

Three sets of NICE recommendations influence treat-to-target policies in RA (11). In early RA, advice is clear-cut. NICE recommends that patients with suspected RA should be referred urgently for specialist assessment. Patients diagnosed with RA should be offered a combination of DMARDs, including methotrexate, together with short-term glucocorticoids. Treatment should be initiated urgently and ideally within 3 months of persistent symptoms (12). Disease activity assessed using composite scores like disease activity score for 28 joints (DAS28) and C-reactive protein (CRP) levels, should be measured monthly until disease control is achieved. In the many patients in whom CRP and erythrocyte sedimentation rate (ESR) are normal this focus on laboratory assessments will be of limited benefit (13). When satisfactory levels of disease control are achieved, drug doses should be cautiously reduced to levels that maintain control. This guidance, which encapsulates a treat-to-target in early RA, is illustrated in Figure 1.

In established RA, NICE guidance is less clear-cut. NICE recommends DAS28 and CRP are measured regularly to inform decision-making about increasing treatment to control disease. Firstly, there is a specific recommendation that RA patients have annual reviews, which include disease activity assessments. Secondly, RA patients with flares need early specialist assessment and interventions to reduce disease activity. Thirdly, patients with persistently active RA who have failed two DMARDs can receive biologics, provided they have DAS28 scores consistently over 5.1. These recommendations are summarised in Figure 2. Finally patients who fail one biologic and have active RA can receive alternative biologics.

NICE specifically do not recommend initially treating active RA with biologics. They have not expressed views concerning three crucial areas for treat-to-target strategies. These concern the role of combination DMARDs and steroids in established RA, intensive treatment including biologics in established RA patients not currently experiencing disease flares, and whether the optimal treatment target should be remission, low disease activity or overcoming active disease. The main reason NICE have not considered these issues is the relative dearth of clinical evidence.

Evidence for efficacy of intensive DMARDs and glucocorticoids in early RA

Commissioners want to be certain treatment is effective, particularly expensive treatments. Treat-to-target using combination DMARDs with steroids is initially more expensive than DMARD monotherapy in early RA, but there is

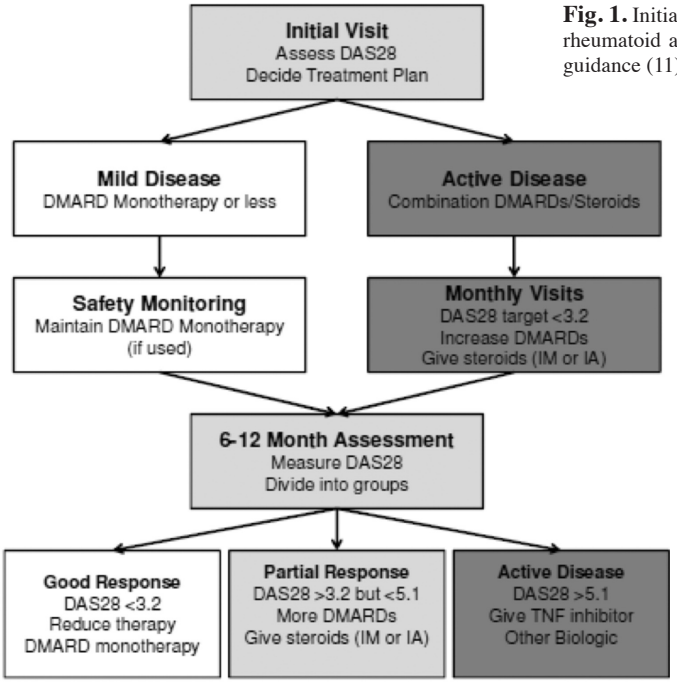

Fig. 1. Initial treatment pathway for rheumatoid arthritis based on NICE guidance (11).

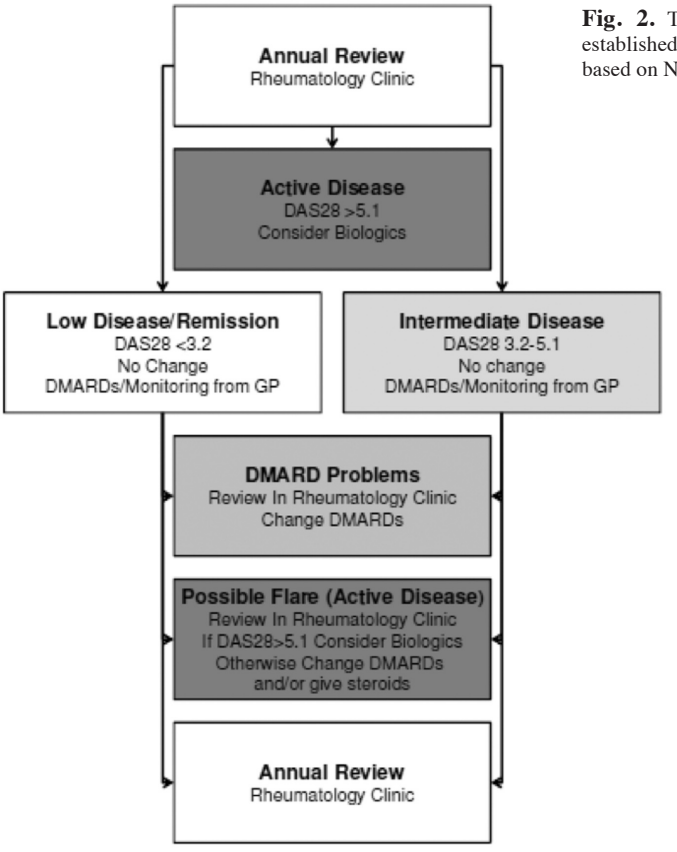

Fig. 2. Treatment pathway for established rheumatoid arthritis based on NICE guidance (11).

strong evidence that it is effective. Ma *et al*. (14) have systematically reviewed all the relevant trials following NICE RA Guidance. They identified 15 trials of intensive treatments over and above methotrexate monotherapy; these trials enrolled 4,200 patients. They found intensive combination therapies using DMARDs were equally effective as TNF inhibitors combined with methotrexate (Fig. 3). The only specific benefit of biologic combinations was that they did not give excessive withdrawals for toxicity.

Most trials reviewed by Ma *et al*. did not involve "head to head" comparisons of combination DMARDs against TNF inhibitors given with methotrexate. Instead they relied on indirect comparisons. Two trials directly compare these strategies – the BeSt (14) and Swefot (16) trials. Both showed treatment with DMARD combinations had similar impacts on RA to giving TNF inhibitors with methotrexate; Figure 4 illustrates one comparison for ACR70 responses.

None of this means combination DMARDs are preferable to early biologics from patients' perspectives. A systematic review of biologics and employment shows several benefits for patients, which have not been reported with intensive DMARDs (17); this most likely reflects the benefits of biologics on factors such as fatigue and mental health. However, NICE and payers currently do not directly assess the impact of treatments on productivity. This arrangement may change with the introduction of a new system of "Value-Based Pricing" in the near future. From the perspective of NICE and commissioners using biologics as initial treatment for early RA has not been judged to achieve sufficient benefits to make it an appropriate approach based on an assessment of their relative clinical and cost effectiveness.

Cost-effective treatment strategies in early RA

In addition to evidence that treatments are clinically effective commissioners also want them to be cost-effective. There is strong evidence that treatment using early biologics is too expensive for widespread use, and is associated with an increased risk of adverse events. Schoels *et al*. (18) systematically reviewed cost-effectiveness studies in RA and found that most studies assessing early biologics reported cost effective ratios over $50,000, which is broadly equivalent to what UK payers consider reasonable (Fig. 5). However, it is important to realise that there is no hard threshold and many factors in addition to cost effective ratios may be taken into account in assessing the overall

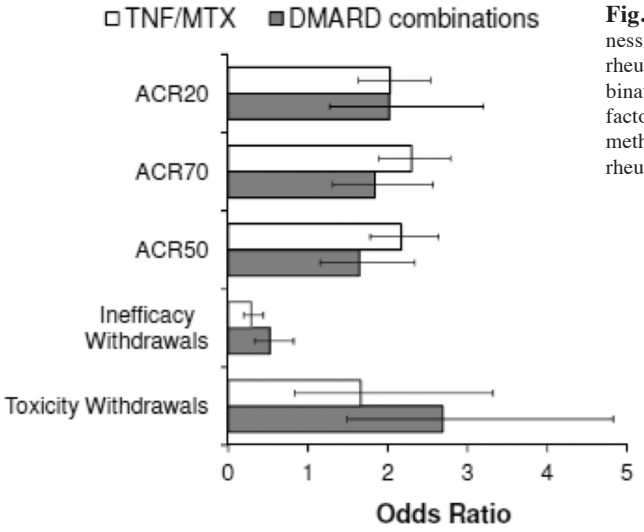

Fig. 3. Comparative effectiveness of disease- modifying antirheumatic drug (DMARD) combinations and tumour necrosis factor (TNF) inhibitors with methotrexate (MTX) in early rheumatoid arthritis (13).

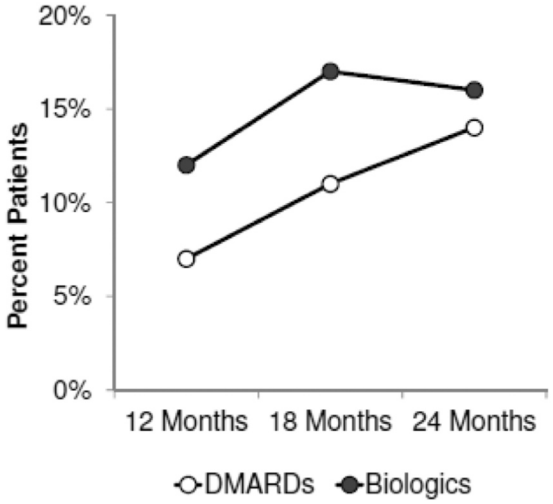

Fig. 4. American College Of Rheumatology 70 percent (ACR70) responders with combination disease-modifying antirheumatic drugs and tumour necrosis factor (TNF) inhibitors (Biologics) in early rheumatoid arthritis trial (15).

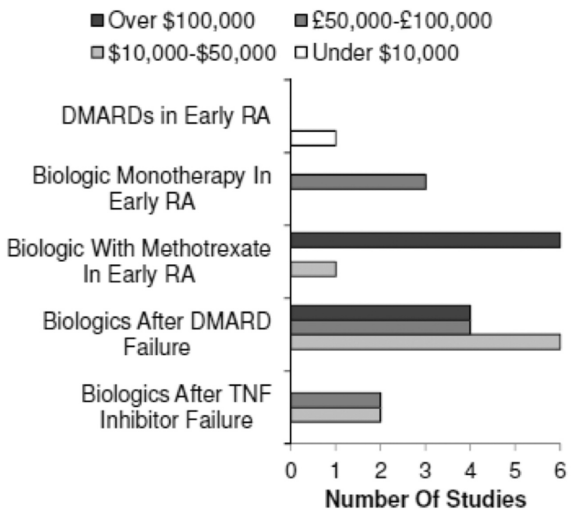

Fig. 5. Cost-effectiveness of different treatment strategies in early and established rheumatoid arthritis (17).

benefits of treatment. By contrast early DMARDs were strongly cost-effective. Schoels and her colleagues did not examine intensive DMARDs.

The cost-effectiveness of different initial DMARD and steroid strategies in early RA has been evaluated by Tosh *et al*. (19). They analysed data from randomised controlled trials, which compared DMARD monotherapies with DMARD combinations, with or without steroids. They estimated the relative effectiveness of different strategies using mixed treatment comparison methods. They also developed a mathematical model, which compared long-term costs and benefits of different strategies, examining costs from a health sector viewpoint and benefits as quality-adjusted life-years (QALY). If payers used thresholds of £20,000 (US$29,000) per QALY, they found the most cost-effective strategies were DMARD combination therapy with downward titration and intensive, triple DMARD combination therapy. Their results were robust when examined in a range of scenario sensitivity analyses. Their key findings are shown in Figure 6. This evidence for the cost-effectiveness of intensive DMARD combinations strongly supports NICE RA guidance. However, there remains one crucial area of uncertainty – the impact of adverse events on the assessment of the effectiveness and cost-effectiveness of intensive DMARD combinations; some experts consider the relative lack of adverse effects with methotrexate monotherapy gives specific advantages for this approach as initial therapy (20).

Reducing treatments

"Treat-to-target" involves increasing DMARDs, steroids and biologics until patients achieve low disease activity states or remission. There is limited evidence about which target is preferable; the benefits of remission are handicapped by the difficulty in achieving it in many patients. NICE guidelines side-step this problem by focussing on "satisfactory control", which is a general as opposed to specific term. However, they provide specific advice by suggesting that treatment should be reduced when satisfactory control has been achieved, with a target of sustaining control on DMARD monotherapy.

A systematic review produced during the development of the NICE guidance showed that stopping DMARDs entirely increases the risk of RA flares (21). NICE guidance therefore did not recommend discontinuing all DMARDs.

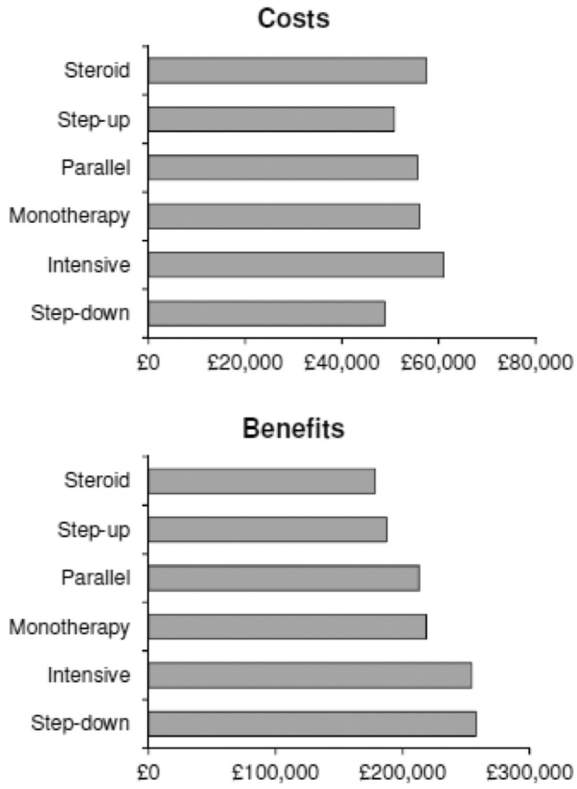

Fig. 6. Costs and benefits of different treatment strategies using combination disease modifying drugs (DMARDs) and steroids in early rheumatoid arthritis (18).

At present, the evidence-base for tapering DMARDs and biologics to monotherapy is incomplete (22, 23), although there is probably sufficient evidence to justify it provided patients are closely followed.

Quality standards and integrated care

Instead of concentrating on the details of how best to manage established RA and deal directly with "treat-to-target" strategies, the NHS and its commissioners plan to focus on two related areas in the immediate future. The first is developing quality standards for RA. This is part of a general drive in England to ensure that patients receive high quality care. The standards will concentrate on clinical effectiveness, patient safety and the patient experience. Quality standards are somewhat different from guidance, and it is difficult to judge their impact prospectively. However, they are likely to incorporate some consideration of treat-to-target strategies in established RA.

The second area is integrated care. Although this has several potential meanings, within England there is a growing emphasis on developing care pathways that transcend primary and secondary care (24-27). It is widely believed such integrated care has the potential to be both clinically effective and cost-effective. Although the evidence supporting its introduction is incomplete, there is enthusiasm to embrace it for the care of patients with long-term conditions, such as RA. The extent to which "treat-to-target" will form an essential part of such care pathways for patients with established RA is open to debate. Many rheumatologists may believe it is of crucial importance. However, such positive views are unlikely to be universal. As integrated care involves GPs, many different allied healthcare professionals and pharmacists, and will also take into account patients' views, there may not be strong support to pursue a treat-to-target strategy.

Many aspects of the management of established RA are crucial to achieve good outcomes, ranging from ensuring patients exercise regularly to providing timely orthopaedic interventions, and these other issues may crowd out treat-to-target and thus stop it becoming a priority. It is likely many other approaches will be considered equally helpful compared to treat-to-target strategies; many of these are supported by clinical evidence.

Conclusions

Everyone wants patients with RA to have the best possible treatment at the least possible cost. However, English health care commissioners views, which will almost certainly aim to be be logical and evidence based, may differ from those of rheumatologists on the extent to which they should pay for treat-to-target strategies. If rheumatologists wish to make this treatment approach universally accepted in established RA they will need to act together and provide stronger evidence for its benefits.

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