A Survey of Barriers to Treatment Access in Rheumatoid Arthritis

Country Annex Report: UK

October 2009

1 Interviews

In the UK, five rheumatologists and one patient representative were interviewed. The interviewees came from Nottingham, Glasgow, Birmingham, Newcastle upon Tyne and West Hertfordshire, which are regions with a lower density of specialists.

2 Environment

The UK has a total population of 61 million with an adult population of 49 million (80%) [1]. All of the population is insured under the UK NHS, which is tax funded, and 11–13% of the population has additional private health insurance [2].

The Medicines and Healthcare Products Regulatory Agency (MHRA) is the national body responsible for issuing marketing authorizations. The MHRA draws on its own staff, on advisory committees of independent experts and on an agency board to make its regulatory decisions, which are decisions of the Secretary of State for Health, who is responsible to Parliament. The MHRA's decisions can be characterised as benefit-risk decisions on whether a drug may be sold in the UK.

In the UK, HTA is an important post-regulatory hurdle to market access. The relevant national authority for England is NICE, which differs from the MHRA in that it makes benefit-cost as opposed to benefit-risk decisions to determine whether drugs should be purchased by the NHS. Outside of England, the counterparts of NICE are the Scottish Medicines Consortium (SMC) and the All-Wales Medicines Strategy Group (AWMSG). Manufacturers of all new drugs are obliged to submit clinical and economic evidence to the SMC and AWMSG within a few months of launch, whereas the NICE technology assessment remit is limited to specific topics identified by the Department of Health where the impact of a technology on the NHS is likely to be significant.

NICE also may conduct Single Technology Assessments based on manufacturers' submissions. In practice, these differences between NICE and the SMC has given the latter a level of influence out of proportion to the size of the population it serves. Manufacturers may regard negotiations around an SMC submission as a useful test case for the reception likely to be granted by NICE to a future submission. There are no special conditions attaching to RA treatments submitted to these authorities, other than the expectation that clinical and economic evidence should conform to accepted standards.

3 Features specific to RA

There are several national and regional registries

- The British Society for Rheumatology Biologics Register (BSRBR) [2,3] is a national registry that tracks the progress of patients with severe RA and other rheumatic conditions who are taking anti-TNF therapy. The BSRBR is the largest prospective register of rheumatology patients receiving anti-TNFs in the world and currently has over 15,500 registered patients. Both patients and rheumatology health professionals complete BSRBR questionnaires on a 6-monthly basis. The BSRBR is a collaboration between the University of Manchester, the British Society for Rheumatology and the pharmaceutical industry and is supported by a team of 15 staff at the Arthritis Research Campaign Epidemiology Unit at the University of Manchester. All consultant rheumatologists in the UK who have prescribed anti-TNFs participate in the register, supported by allied health professionals.
- The Early Rheumatoid Arthritis Study (ERAS) [4] is a national cohort started in 1986 by nine rheumatologists in different regions of England. Since then, all patients from nine hospitals with early RA prior to treatment have been included, and standardised assessments which have been made yearly by trained health professionals. Over 1,000 patients are now part of this study, which has allowed analysis of less common outcomes, according to different stages of RA and varying treatment patterns. Because the ERAS centres cover quite different regions of England, including rural, urban and inner city communities, it has been possible to investigate differences in socio-economic effects and resource use on the outcome of RA.
- There is also the Early Rheumatoid Arthritis Network (ERAN) [5,6], a national network of British rheumatology departments who collect and monitor clinical details on all early RA patients in a standard way in order to assess long-term outcomes.
- The Norfolk Arthritis Register (NOAR) [7] is a regional register started in 1989 that has recruited over 3,500 incidence cases of inflammatory polyarthritis. Descriptive and analytical studies have been undertaken on risk factors for onset but the main focus is on outcomes and their prediction. Current work focuses on comorbidities (in particular cardiovascular comorbidity), predictors of treatment response and gene-environment interactions for inflammatory arthritis onset and outcome.

4 Guidelines

There are several guidelines in the UK, both national and regional.

- The National Collaborating Centre for Chronic Conditions and the Royal College of Physicians published a guidance document on RA in early 2009 after appraisals of several biologics (rituximab, abatacept, adalimumab, etanercept and infliximab) by NICE [8]. The guidance includes recommendations for referral to specialists, use of DMARDs and work with a multidisciplinary team.
- Guidance on individual biologics is found in their respective NICE appraisals.
  - NICE guidance on adalimumab, etanercept and infliximab [11] is that these are recommended as options for the treatment of adults who have active RA with a DAS28 above 5.1 for at least a month who have already used two DMARDs including MTX for at least 6 months with 2 months at standard dosing (unless contraindication or toxicity has limited their use)
  - NICE guidance on rituximab in RA [9] is that rituximab is recommended in combination with MTX in patients with severe active RA who have had an inadequate response to or intolerance of other DMARDs, including treatment with at least one anti-TNF.
  - NICE guidance on abatacept in RA does not recommend its use within its marketing authorization [10].
- The British Society for Rheumatology (BSR) and British Health Care Professionals in Rheumatology (BHPR) group have published several guidance documents in the field (see www.rheumatology.org.uk/resources/guidelines/bsr_guidelines.aspx [accessed October 2009]), including guidelines for the management of RA during the first 2 years; guidelines for management after the first 2 years; guidelines for DMARD therapy; guidelines for the prescription of anti-TNFs in adults; and guidelines on standards of care for people with RA.
- Other sources include the Scottish Intercollegiate Guidelines Network (SIGN) guidelines on the management of early RA, and the Arthritis and Musculoskeletal Alliance (ARMA) document on standards of care for people with inflammatory arthritis (see Section 9.5)

5 Provision of care

Access to specialists is through GPs who act as gatekeepers. Special training for rheumatologists takes 4 years after the initial medical degree. The work of rheumatologists tends to be outpatient based, and they generally work as part of a

multidisciplinary team that includes specialist nurses, physiotherapists, occupational therapists, chiropodists, podiatrists and orthopaedic surgeons. Rheumatologists may also find themselves working in the growing number of day assessment and treatment centres.

Many patients with inflammatory arthritis are managed in a 'shared care' arrangement with GPs. Common procedures for rheumatologists include soft tissue and joint injections. Some specialists perform various spinal injections for relief of back pain, biopsy procedures such as synovial or muscle biopsies, and musculoskeletal ultrasound.

There are associated sub-specialty interests, i.e. paediatric rheumatology, metabolic bone disease, neurophysiology and sports medicine. The responsibility of rheumatologists in 'shared care' arrangements is to initiate treatment until the patient is clinically stable, while GPs monitor patients and continue prescriptions [12]. Patients are required to co-pay for treatment at £7.10 per prescribed item, with exemptions based on criteria such as age and income.

The total number of consultant rheumatologists is 584, and there are an additional 105 GPs with a special interest in the field. If both groups are taken together then there is one specialist per 85,000 members of the population or one per 65,000 adults. If we estimate the total patient population in RA to be 472,000, this translates into one per 685 patients; considering only certified rheumatologists the ratio is one per 800 patients and one per 77,000 members of the adult population. There are 3.2 MRI scanners per 1,000,000 population, which is 50% of what is available in France.

A recent survey by Harrison *et al.* [13] concludes that provision of rheumatology services has continued to expand over the past decade; however, inequalities persist at the national and local levels. There is evidence of improvement in regions with the lowest provision, but there are indications of increased perceived job threat in areas with traditionally higher provision and where CAT (Clinical Assessment and Treatment) centres have been introduced. Levels of optimal provision exceed 70% in England and Wales, and 50% in Scotland and Northern Ireland. Levels of provision remain substantially higher in London than anywhere else.

6 Diagnosis

Diagnosis is mainly established by the rheumatologist (80–100%), but GPs also diagnose patients (up to 20% of cases). Patients consult with a GP typically 6 months after first symptoms and are then referred to a rheumatologist within another month, i.e. 7 months from first symptoms to diagnosis. However, estimates from respondents on time from symptoms to diagnosis range from 3–4 months to 9 months and the main reasons for exceeding the target of 6 months are late presentation of the patient and long waiting lists.

Diagnosis is supported by a range of procedures supported by the EULAR recommendations, i.e. physical examination, blood tests (ESR, CRP, RF, anti-CCP), rarely MRI and ultrasound and X-ray if indicated. Whilst ESR and CRP tests are fully funded within the NHS, there are reimbursement restrictions for the anti-CCP test. MRI is not used routinely due to funding restrictions and insufficient facilities. Lack of training for ultrasound was also mentioned as one reason for lower use of imaging tests.

Half the respondents in our study segment patients into 'poor prognosis' and 'other patients' using the following criteria: early onset, high disease activity, high titre of RF, high markers of inflammation (anti-CCP) and erosions (X-ray, ultrasound).

7 DMARDs

Treatment is initiated by rheumatologists immediately after confirmed diagnosis. If the diagnosis was established by a GP the patient is referred to a rheumatologist for initiation of treatment. Time from symptoms to DMARD prescription is thus typically 240 days.

For 75% to 90% of patients the first treatment choice is MTX as recommended by the national guidelines. MTX is mostly used as a monotherapy (> 75%). Typical co-medication includes analgesics, NSAIDs, COX2-inhibitors and PPIs. Other first-line treatments include leflunomide, cyclosporine, cyclophosphamide and Sulphasalazine, which are used in mild forms of RA (sulphasalazine) or according to special individual cases (leflunomide, cyclosporine, cyclophosphamide). Steroids are recommended as symptomatic treatment and are used as a bridging therapy (30–50%). Once DMARD treatment is initiated steroids are withdrawn. NICE recommends a combination of DMARDs (including MTX and at least one other DMARD, plus short-term glucocorticoids) as first-line treatment to be initiated within 3 months of the onset of persistent symptoms.

Treatment is changed immediately for severe side effects, but patients are typically treated for 3 to 6 months until efficacy is assessed. If there is insufficient effect the dose may be increased or patients may be switched to another DMARD. Tolerability issues also motivate treatment switches.

8 Biologics

Biologics are considered third-line treatment for most patients (fourth-line by the office-based rheumatologist in this study) and are used mainly due to their better efficacy. Biologics are used in around 10–20% of patients, which is lower than suggested by the guidelines. The sequence of treatment is consistent with the guideline recommendation,

which asks that small molecules – MTX in particular – are used in first-line therapy and that another DMARD should be tried before switching the patient to biologics.

Anti-TNFs are the first treatment option after small molecule DMARDs. Typically, biologics are used in patients with severe RA or in those who fail to sufficiently respond to DMARDs after 6 months. Efficacy considerations drive the choice of drug, with priority given to drugs with fewer side effects and longer clinical experience. Drugs that are not recommended by NICE can only be used on a named patient basis and are thus rarely used (e.g. Orencia).

- First line: Adalimumab (Humira), etanercept (Enbrel) and infliximab (Remicade) are the most frequently used biologics. Efficacy and long-term experience are the main reasons given by interviewees for their use.
- Second line: another anti-TNF or rituximab (MabThera) are used next options, motivated by better efficacy and safety.
- Further options depend on the treatment history of the patient, i.e. using a another anti-TNF or a different mechanism of action, such as rituximab (MabThera), abatacept (on a named patient basis) or anakinra (Kineret).

Most respondents do not report capacity issues with current infusion facilities. However, in some regions there is insufficient capacity (Northern Ireland) and waiting time can be up to 18 months. Some respondents felt that treatment strategies are shaped by the capacity and that there would be issues if more infliximab were prescribed. Shortage of nurses due to lack of funding was also mentioned as an issue that hinders the use of available infusion chairs.

9 Treatment consistency with EULAR recommendations

The consistency with which the diagnosis and treatment of RA in the UK follows key EULAR recommendations is shown below (Table 1) for information gathered from desk research and from the interview panel.

Table 1. Consistency of UK RA practice with EULAR recommendations

		National practice consistent with EULAR recommendations		
	EULAR recommendation	**Desk research**	**Interviews**	**Comments**
Diagnosis	Patient presenting with arthritis is referred to and seen by a rheumatologist ideally within 6 weeks of symptomatic onset	No	60% No 40% Yes	Guidance does not specify a time BSR/ERAN report 7 months. Kumar *et al.* 2007 report 23 weeks [14]
	Clinical examination for detecting arthritis includes ultrasound, power Doppler and MRI	No	No	Other than radiographs, no imaging modalities mentioned Limited facilities MRI and ultrasound are rarely used, mostly X-ray if any
	Diagnosis requires at least the following laboratory tests: complete blood cell count, urinary analysis, transaminases, and antinuclear antibodies	No	No	Guidance does not specify any baseline laboratory tests Anti-nuclear antibodies not used
	Measurement of the following factors for patients presenting with early arthritis: number of swollen and tender joints, ESR or CRP, level of RF and anti-CCP antibodies, and radiographic erosions bodies	No	No	Anti-CCP and radiographic erosion bodies restricted
Treatment	Patients developing persistent/erosive arthritis should initiate DMARDs as early as possible	Yes	Yes	Guideline specifies 3 months, but delays are reported of 120 days (interviewees report delays up to 240 days) [15,16]. Delays are due to waiting time for consultations
	Use of patient information and education programmes about coping with pain and disability and maintaining work	Yes	Yes	Provided by patients' organizations
	NSAIDs are considered in symptomatic patients	Yes	Yes	NRAS survey 2005 [17]
	Among DMARDs, MTX is considered the anchor drug and should be used first in patients at risk of developing persistent disease	Yes	Yes	Jobanputra *et al.* 2003 [18], Edwards *et al.* 2005 [19]

	National practice consistent with EULAR recommendations			
	EULAR recommendation	**Desk research**	**Interviews**	**Comments**
	Systematic glucocorticoids to reduce pain and swelling are considered as a (mainly temporary) adjunct to DMARD treatment	Yes	Yes	NRAS survey 2005 [17]
	The main goal of DMARD treatment is to achieve remission. Regular monitoring of disease activity and adverse events guide decisions on the choice or change of DMARDs and/or biologics used	Yes	Yes	NRAS survey 2005 [17]
	Non-pharmaceutical interventions, such as dynamic exercises, occupational therapy and hydrotherapy, are applied as treatment adjuncts	Yes	Yes	NICE guideline is that these interventions 'should not replace conventional treatment' [20]
Monitoring	Disease monitoring includes tender and swollen joint counts, ESR and CRP assessment at 1 to 3 months	No	60% Yes 40% No	Monitoring intervals longer, i.e. 6–12 months
	Structural damage is assessed by X-ray every 6 to 12 months. Functional assessment is used to complement disease activity and structural damage	No	No	NICE guideline is for monthly monitoring until disease is controlled; annual review [20]. Not routinely done

Note: The specific wording of the recommendations has been shortened in some instances for editorial reasons

11 Sources

In addition to the references listed in the text the following sources were used in compiling UK details in this monograph.

Registries

- BSRBR = British Society for Rheumatology Biologics Register http://www.medicine.manchester.ac.uk/epidemiology/research/arc/inflammatorymusculoskeletal/pharmacoepidemiology/bsrbr/
- NOAR = Norfolk Arthritis Register http://www.medicine.manchester.ac.uk/epidemiology/research/arc/inflammatorymusculoskeletal/outcomestudies/noar/
- ERAS = Early Rheumatoid Arthritis Study http://www.rheumatoid.org.uk/article.php?article_id=42

Delivery of care

- Harrison *et al. Rheumatology (Oxford)* 2008; **47:**1065–1069
- Census of Consultant Physicians in the UK, 2007 http://www.rcplondon.ac.uk/pubs/contents/a36405ec-c792-4ac2-af00-7bddc28914a8.pdf
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- Speciality Training Curriculum for Rheumatology http://www.pmetb.org.uk/fileadmin/user/QA/Curricula/Approved_curricula/RHEUMATOLOGY/Rheumatology_3_Jul_07_v.Curr_0030.pdf
- http://www.nhs.uk/aboutnhs/Pages/About.aspx
- http://www.euro.who.int/document/Obs/Private_Medical_Insurance_UK.pdf
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Guidelines

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Medical Treatment

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4. Early Rheumatoid Arthritis Study (ERAS). http://www.rheumatoid.org.uk/article.php?article_id=42. (Accessed 02 Oct 2009).

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