Inequality of access to advanced therapies for patients with inflammatory arthritis: a postcode lottery?

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Abstract

Objectives. Advanced therapies (AT) including biologics, biosimilars and JAK inhibitors have dramatically improved the quality of life of patients with Rheumatoid arthritis (RA), Psoriatic Arthritis (PsA) and Axial spondyloarthritis (axSpA). Evidence-based criteria for prescribing these drugs in England and Wales is formulated by the National Institute for Health and Care Excellence (NICE) through Health Technology Appraisals (HTAs) and guidelines with the aim of providing equitable access to AT for patients with severe or resistant disease.

Similar bodies exist in some, but not all European countries with disparities in AT access between countries in AT access for RA. We examined whether this disparity was mirrored in England for RA, PsA and axSpA despite the NHS in England and Wales being legally obliged to provide funding for AT recommended by NICE’s HTA board, through commissioning bodies, Clinical Commissioning Groups (CCGs).

Methods. We requested AT pathways from CCGs in England. Where these were not available, individual hospital Trusts were contacted using Freedom of Information (FOI) requests.

Results. We found marked variability in the way that CCGs in England interpret NICE guidance. We found 41, 29 and 25 different pathways for RA, PsA and axSpA respectively. Similar disparities existed with sequential prescribing where one AT did not work, with limits on numbers of sequential AT in 54%, 59% and 59% of CCGs for RA, PsA and axSpA respectively, with these limits being different for the same condition between CCGs.

Conclusion. While patients at identical stages of their disease course should have access to the same NICE approved AT, we found this is not the case for large parts of England. Inequality of access was found between regions mirroring the variability which occurs between countries throughout Europe. Harmonisation of access needs to be addressed by policymakers, ensuring fairness in the way that clinicians and patients can access AT.
Keywords: advanced therapies, access, inequality, rheumatoid arthritis, psoriatic arthritis, axial spondyloarthritis

Key Messages

- NICE guidance for inflammatory arthritis should provide equal access to advanced therapies (AT).
- NICE guidance is implemented in England by clinical commissioning groups (CCGs); we demonstrate pathway variations by geographical region.
- This postcode lottery in AT access restricts optimal management based on cost and geography.

Introduction

Advanced therapies (AT, biologics, biosimilars and JAK inhibitors), have revolutionised the management of Rheumatoid arthritis (RA), Psoriatic Arthritis (PsA) and Axial spondyloarthritis (axSpA). AT have a significant financial impact on healthcare. In 2020, global sales of Humira exceeded US$19 billion\(^1\)

Locally based NHS decisions previously led to inequitable funding in England and Wales. This situation led to the development of harmonised evidence-based standards by the National Institute for Health and Care Excellence (NICE) through Health Technology Appraisals (HTAs) and guidelines, permitting equitable access to AT on meeting criteria. The NHS in England and Wales is legally obliged to fund therapies recommended by NICE's HTA board. Similar AT approval bodies exist in Europe, for example, The Institute for Quality and Efficiency in Health Care in Germany but AT funding processes vary between countries for RA\(^2\).

Responsibility for funding AT in England is delegated to clinical commissioning groups (CCGs). We examined whether pathway variability between CCGs promotes inequality of access to AT within England, by examining pathway concordance with the NICE guidance principles of equitable access.
**Methods**

All 135 CCGs in England, (post CCG merger from April 1st, 2020) were sent Freedom of Information (FOI) requests for their AT pathways for RA, PsA and axSpA. We estimate data covered most of the >392000 RA patients in England, 100,000 PsA patients and similar numbers with axSpA. We requested information on pathways for, and the maximum number of, AT commissioned for these conditions before an individual funding request (IFR) was required. IFRs allow consideration of funding for healthcare interventions outside the treatments which CCGs have agreed to fund.

Some CCGs directed us to contact acute Trusts for information. Responses were recorded under the CCG for that Trust. All CCG pathways were current as of May 2020 and were compared to the relevant NICE guidance.

AT pathways were given a unique number so that common CCG pathways were identifiable. Some CCGs’ responses were unclear, no information was sent, or a review of pathways was underway.

AT numbers commissioned were recorded. CCG ‘local pathways’ were analysed to see if AT numbers commissioned were stated. If not or the CCG did not publish local pathways, we used FOI request responses which requested clarification on whether there was a local AT pathway for RA, PsA and AS and maximum ATs the CCG would commission. Through this method we did not get any situations in which FOI and local pathway information differed. Email confirmation was sought when no pathway existed. Where a clear answer was not provided, ‘N/A’ (Not Available) was recorded and where the CCG responded that there was no limit, restrictions, or hierarchy regarding the number of biologics a patient could attempt, ‘No Cap’ was recorded. No ethical approval was required for this study.

**Results**

CCG responses were obtained from 123/135 CCGs for RA, 122/135 for PsA and 119/135 for axSpA (See Table 1 and Fig 1). Overall, we found 41 distinct pathways for RA, 29 for PsA and 25 for axSpA demonstrating regional variation and variable interpretation of NICE guidance. All pathways allowed anti-TNF alpha as first line therapy. There was no specified pathway in...
44/123 (35%) responses for RA, 59/120 responses for PsA (49%), 62/119 responses for axSpA (52%). Where there was no specified pathway, responses confirmed by the CCGs or Trusts, was that they had no specific order of AT, allowing clinicians to prescribe any AT in any order without any hierarchy provided NICE guidance was followed.

Where distinct pathways existed, the rationale in directing the choice of AT for the formulation of the pathway was sought (See Supplementary Figure S1, available at Rheumatology Advances in Practice online, for RA). The commonest rationale for distinct pathways was cost (8/41, 19%) with the commonest combination reason being cost, clinical factors, and patient choice (17/41, 41%). In 3/41 (7%), no rationale was provided (Supplementary Figure S1, available at Rheumatology Advances in Practice online).

Where pathway information was recorded, we determined limits (Cap) on the number of and/or the lines of NICE approved AT which could be prescribed before an IFR was needed. Surprisingly, for NICE approved AT supposedly all legally available to prescribe, limits varied by region including for specific drugs. Some pathways specified Etanercept biosimilar first line, followed by other anti-TNF alpha second/third line while other pathways approved different Mode of Action (MoA) as second/third line.

Where data was interpretable, (113, 113 and 111 CCGs for RA, PsA and axSpA respectively), we found 46%, 41% and 41% of CCGs did not specify a cap on the number of AT’s which could be prescribed for RA, PsA and axSpA respectively. However, this meant limits were placed in 54%, 59% and 59% of the interpretable CCG pathways for the respective conditions. Limits varied between CCGs, some permitting two lines of RA therapy, others more despite five different NICE approved AT MoA. Anomalies existed where four lines of AT were permitted for axSpA despite only two NICE approved MoA (anti-TNF-alpha and Secukinumab) because three different anti-TNF-alpha were approved in series followed by Secukinumab.

Discussion
We found inconsistency in the interpretation of AT NICE guidance for RA, PsA and axSpA in England by CCGs. Identical patients could be subject to different prescribing arrangements
depending on location. NICE was designed to ensure equal access to therapies regardless of geography. AT access variations for RA also exist in comparable European bodies despite similar stated aims\textsuperscript{2}.

The number of CCGs with specified pathways was highest for RA where several AT MoA are available. This suggests greater AT choice is counterbalanced by more restrictive pathways. NICE Multiple Technology Appraisal (MTA) covering several MoA states the cheapest drug should be used but not sequential biologic order (an exception, Rituximab for RA is only allowed second line, unless anti-TNF alpha are contra-indicated). We found many CCG pathways mandated sequential AT, specified first line and the order of subsequent AT. After first line, usually anti-TNF alpha, second line agents varied by region for the same indication. Of concern, some pathways did not permit return to previously used MoA, irrespective of secondary rather than primary failure.

CCGs took cost as the commonest arbiter of AT choice, explicitly stated in some pathways. However, phrasing of NICE guidance encourages disparity. NICE state that “If more than one treatment is suitable the least expensive (taking into account administration costs and patient access schemes) should be chosen”. However, “If more than one treatment is suitable” could mean a similar MoA (e.g., different anti-TNF-alpha therapies) or different MoA (e.g., anti-IL-6, JAK Inhibitors). Thus, while anti-TNF-alpha drugs may be equally efficacious for RA (similar MoA), Etanercept biosimilar is cheaper than Golimumab bio-originator. Patients, for reasons of travel or convenience, may prefer four-weekly Golimumab to weekly Etanercept. We found this kind of variation was not permitted in some pathways despite NICE guidance in some HTA stating “consider patient choice”.

Commissioning arrangements cause inequality in other rheumatic conditions. Between 2015-2017, NHS England commissioning for Bosentan and Digital Ulcers in Scleroderma were introduced, with no similar arrangements in Wales. Consequently, Bosentan prescriptions in England increased 47%, but were stable in Wales, where IFR’s were needed\textsuperscript{15}.
While all devolved UK nations use NICE guidance to direct AT eligibility, access varies by nation (see Acknowledgements). The Scottish Medicines Consortium (SMC) approves AT for local health boards if clinicians wish to prescribe although NICE TA have no formal status. (Murphy, E and Macdonald A, Personal Communication). Wales follows NICE guidance through four Health Boards. If NICE criteria are fulfilled, no AT hierarchy exists. In Northern Ireland, the five healthcare trusts follow NICE guidance. A Managed Entry programme mandates biosimilars as first line, but subsequent AT can be prescribed in any order if NICE approved. These arrangements may change in future due to cost with more pathway orientated prescribing similar to England (Lennon, R, personal communication). When a clinician requests an AT which falls outside the CCGs sequencing, an Individual Funding Request (IFR) is needed despite AT being legally permitted on fulfilment of NICE criteria in England. IFR processes in our experience, are time-consuming and opaque and can be approved for one patient but not another in identical circumstances. IFR’s in Northern Ireland are reserved for AT which are licenced but not NICE approved rather than those which are, as in England.

Wide disparities in access arrangements for RA AT despite similar pledges by public funding bodies occur in European countries. From a survey of 46 European countries\(^1\), 10 did not reimburse any AT, requirements for RA disease duration varied in 34% of countries while 64% had no requirement. Required disease activity scores varied with 56% having DAS28 $\geq 3.2$ as a cut-off, but many such as Switzerland, Ireland and Luxembourg had no requirement. Using a population model and EULAR recommendations, Kalo et al\(^16\) estimated that 32% of the RA population in Europe were eligible for AT, but only 18% were prescribed AT. As a result, 700,000 RA patients would be excluded from AT treatment, because national eligibility and reimbursement criteria are discordant to EULAR recommended eligibility criteria.

Variations in healthcare systems are likely to contribute to inter-European disparities. Article 32 of the Italian constitution protects health as a fundamental right of the individual. The Italian Medicines Agency (AIFA) grants “guaranteed access to medicines and their safe and appropriate use as a health protection instrument”. However, Italy’s public health system has 21 autonomous areas with each region having distinct AT access arrangements.
with consequent lack of consistency. As with England, cost is frequently a primary
determinant in providing access to AT rather than patient or clinician choice (Galeazzi, M,
personal communication).

In Germany, through the Institute for Quality and Efficiency in Health Care, AT access is free
for all patients with RA, axSpA or PsA. Physicians initiate or switch AT provided the reason is
documented. Biosimilars are preferred to bio-originators, while quotas (different for each
region) for the proportion of biosimilars used need to be fulfilled (Baraliakos, X, personal
communication). In Belgium, clinicians have freedom to prescribe whichever biologic MoA
they feel is best for the patient at any stage of treatment with no hierarchy (Lories, R,
personal Communication).

Access variations are not only caused by commissioning arrangements. In Canada, females,
patients in urban areas and younger patients, had their first AT sooner despite identical
healthcare coverage. Healthcare professionals practice variations may determine these
access variations\(^\text{17}\). Across Europe, deprivation, geography, clinical practice, demand and
finance all affect access to healthcare while Guidelines may standardise practice and reduce
variations\(^\text{18}\). Levesque et al\(^\text{19}\) suggested five domains affecting accessibility to interventions:
Approachability (when patients recognise there is a service available), Acceptability
(acceptance of the cultural and social implications of therapy), Availability (healthcare
interventions can be reached in a timely manner), Affordability (people or services having
the economic capacity to provide or engage with the intervention) and Appropriateness (the
fit between intervention, service and patient’s needs). Any or all of these factors may be
relevant to AT access.

The strengths of our study include comprehensive responses from the majority of CCGs
covering most of the RA, PsA and axSpA patients in England. This is the first study as far as
we know to show variable AT access in conditions other than RA and demonstrate access
problems are generic across conditions. The weaknesses of the study include data collection
from one country only. Larger studies to collect similar data across Europe may show
broader geographical access variations, to complement known disparities across Europe\(^2\).
Data collection from less wealthy nations may confirm AT access is related to socioeconomic wealth\textsuperscript{2} a factor which affects numerous healthcare interventions\textsuperscript{18}.

In May 2020, NHS England’s Regional Medicines Optimisation Committee stated commissioning policies which limit patients’ access to appropriate treatments based on prior treatment numbers go against the NHS Constitution. Clinical assessment of treatment appropriateness should override policy implementation for cost saving.\textsuperscript{20}

This interpretation of NICE guidance harmonises treatment access in the way NICE intended. We suggest clear guidance from regulatory authorities on AT prescribing is essential to uphold this principle. Work is needed to realise these principles within the UK and Europe where equality is embedded in constitutional arrangements. Clinical, political and financial discussions are needed to ensure reimbursement criteria for AT are translated into access equity for patients with RA, PsA and axSpA.

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18. FOCUS on HEALTH Geographic Variations in Health Care, OECD, September 2014


Figure 1. Variation in sequential prescribing limits in rheumatoid arthritis (A), psoriatic arthritis (B) and axial spondyloarthritis (C). N/A = data not available
Table 1. Clinical commissioning group advanced therapies prescribing pathway details for each indication

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**Sequential Prescribing Limits**

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<td>6 AT</td>
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Sequential prescribing limits for interpretable responses only. These included similar or different modes of action as first and subsequent lines. CCGs could also have “No Specified Pathway” with either “No Cap” or a variable Caps.

CCG: clinical commissioning group; AT: advanced therapies
Figure 1. Variation in sequential prescribing limits in Rheumatoid Arthritis (A), Psoriatic Arthritis (B) and axial SpA (C). N/A = data not available

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