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The Burden of Rheumatoid Arthritis across Europe: a Socioeconomic Survey (BRASS)

Summary Report

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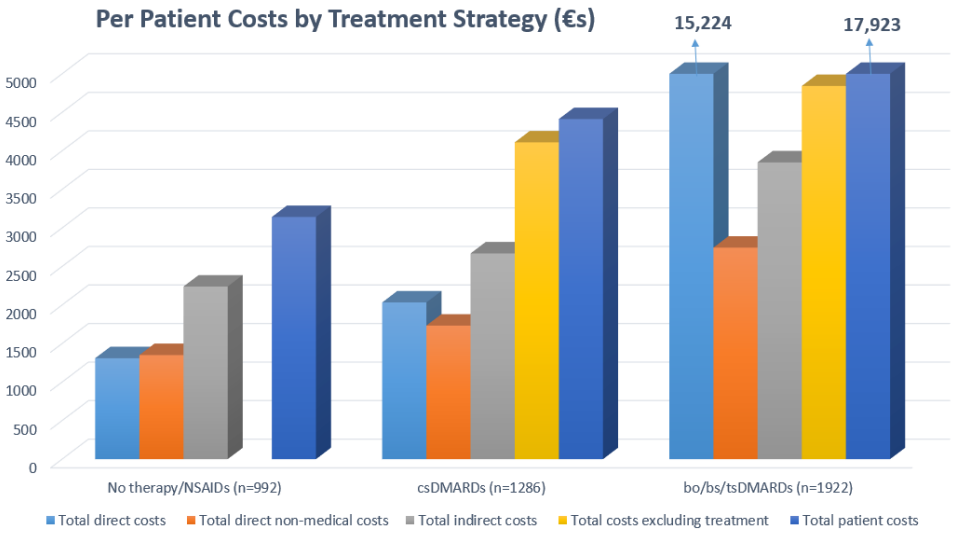
Contents

Key Findings

- People living with RA have an annual cost of €3-5000 depending on RA severity (excluding prescription costs), accrued from direct medical, direct non-medical and indirect costs
- Indirect cost is the individual element with greatest financial impact across each treatment strategy, with and annual cost of €2-4000
- The true impact of RA on individuals, caregivers, health services and to society can only be understood when considering a comprehensive burden study as represented by BRASS
- Along with financial implications, the humanistic burden must also be considered



Treatment groups: No therapy or NSAIDs only (+/- steroids), Conventional synthetic DMARD(s) (+/- steroids), Biologic, biosimilar or targeted synthetic DMARD (+/- steroids, csDMARDs, NSAIDs)

Prescription costs for No therapy / NSAIDs not collected

Abstract

Background:

This study presents a bottom-up comparative approach to quantify the burden of disease for persons living with rheumatoid arthritis (RA) across the following European countries: Denmark, France, Germany, Hungary, Italy Poland, Romania, Spain, Sweden and UK. The objective was to quantify annual direct and indirect costs of three treatment groups, NSAIDs/no therapy, Conventional synthetic DMARD(s) +/- NSAIDs: no biologics, referred to throughout as csDMARD(s), and Biologic, biosimilar or targeted synthetic drug, referred to as bo/bs/tsDMARD. Group definitions did not consider corticosteroids. Our retrospective cross-sectional sample captured resource use for a 12-month period and health-related quality-of-life.

Methods:

Rheumatologists, RA specialising internists and general practitioners were recruited and surveyed during the period April-June 2016. These practitioners were then tasked with providing a non-random cohort of RA patients meeting the study inclusion/exclusion criteria. Our total target sample size was 4,000 patients, based on achieving a representative sample of RA patients within each country. The study was governed by an independent Expert Reference Group consisting of charity representatives, university representatives, medics and health economists. This study was approved by the University of Chester Research Ethics Committee and conducted in accordance with relevant European guidelines. We developed an online survey, in collaboration with patients (in particular with the National Rheumatoid Arthritis Society, NRAS, in the UK) and clinicians. This enabled our specialist sample to provide demographic and clinical information and 12-month ambulatory and secondary care activity for between 4 to 10 consulting patients. In turn, those patients were invited to provide direct and indirect non-medical cost information via a paper-based patient self-completed (PSC) questionnaire, covering work loss and out-of-pocket expenses, as well as information on quality of life and therapy adherence. A corresponding cost database was developed for each participating country, with a comprehensive cost profile for each patient.

Results:

A total of 476 physicians participated in the study from across 10 countries, capturing information on 4,200 patients. Within this sample the defined treatment groups comprised 992 NSAIDs/no therapy, 1,286 csDMARD(s) and 1,922 bo/bs/tsDMARD. The mean age and standard deviation for each treatment group was estimated at 54 (15.4), 55.9 (13.4) and 54.4 (14) years respectively. Females comprised the majority within each group ranging from 66 – 71%. Overall mean disease duration ranged between 10.7 (12.6) -12.3 (12.3) years. A total of 2,087 patients completed corresponding PSC questionnaires. Mean annual total non-drug cost for the NSAIDs/no therapy group was €3,142, for the csDMARDs group €4,111, and the bo/bs/tsDMARD group €4,842.

Conclusions:

BRASS has enabled the production of a granular database from which the research team will aim to achieve their objectives of producing a comprehensive burden of disease study on a scale larger than previous studies. This evidence base will help the community understand per patient costs and wider societal burden associated with living with RA.

Background and therapeutic landscape

Rheumatoid arthritis (RA) is a progressive autoimmune disease that, often over a course of more than 20 years, causes increasing levels of disability and pain to patients.[1,2] It is a degenerative disease, and thus the management and treatment of RA aims to achieve remission or a low disease activity state, by suppressing inflammation, slowing the progress of the disease, alleviating symptoms and preventing disability. RA is the most common inflammatory systemic autoimmune disease worldwide; however, insidious onset of symptoms and inconsistencies in diagnostic criteria create varying estimates of prevalence. As a result, the annual incidence of RA is estimated to be anywhere between 20 and 50 cases per 100,000 population in European countries.[3] Recent studies have suggested that more than 2.3 million individuals are diagnosed with RA in Europe, generating annual direct and indirect costs of management of over €45billion.[4]

In some cases, RA exhibits only mild to moderate symptoms, and can be reasonably well controlled. By contrast RA can involve chronic disabling pain, inflammation, stiffness, extreme fatigue, reduced joint function, impaired mobility and other systemic complications. RA is diagnosed in adults of all ages but is most common in persons over the age of 40; women are nearly three times more likely to suffer from RA than men.[5] Severe or untreated RA can shorten life expectancy by between six and ten years, equivalent to the impact of diabetes, stroke or coronary heart disease.[6] Globally, in 2010 RA was responsible for 4.8 million disability-adjusted life years lost (DALYs) [7]

Cardiovascular conditions (CV) are commonplace amongst the RA population. The risk of CV events for persons with established RA is comparable to that observed in patients with type 2 diabetes.[8] In addition, approximately one third of people stop work because of the disease within 2 years of onset, and after 10 years, 30% of patients are severely disabled.[4,5]

There is no single diagnostic test for RA; rather, diagnosis is made by studying the patient's history and symptoms, and conducting joint exams, blood tests, and diagnostic imaging. However, gradual onset of clinical symptoms is common in RA, and often contributes to a delay in referral and diagnosis.[9] RA is diagnosed and managed by a specialist in rheumatology; in a number of countries, a timely diagnosis also relies on an efficient referral system via primary care. Given the low incidence of RA, primary practitioners may have few opportunities to develop their skills in identifying the disease in regular practice.

Whilst clinical consensus favours a multidisciplinary approach to the management of RA, a number of European countries have yet to publish formal management guidelines.[5] This has led to disparities in the way treatment is approached, and differing eligibility requirements for certain drug therapies. Timely use of pharmacological treatment can improve long-term outcomes for people with RA; European clinical guidelines recommend that pharmacological treatment of RA commences immediately following diagnosis.[5] There are three main groups of drugs used for the management of RA: painkillers including non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids and disease-modifying anti-rheumatic drugs (DMARDs). Historically drug treatment aimed to reduce symptoms, for example NSAIDs, help to temporarily alleviate joint-related symptoms of RA. More modern treatment regimens aim to achieve remission by prescribing DMARDs early in treatment. Initiating treatment with DMARDs as soon as possible after diagnosis produces significant clinical and functional benefit and appears to retard the rate of radiographic progression of erosions.[10]

Conventional systemic DMARDS (csDMARDs) are the front line of RA treatment, and are commonly characterised by their capacity to reduce or reverse signs and symptoms, disability, impairment of quality of life, inability to work, and progression of joint damage and thus to interfere with the entire disease process.[11] In the majority of cases DMARD treatment is initiated with csDMARD(s). Biologic originators, biosimilars and targeted synthetic DMARDs (Bo/bs/tsDMARDs) are relatively costly and are therefore reserved for those in whom csDMARD(s) treatment fails. To illustrate this, methotrexate, a csDMARD, is recommended by NICE in England, as the first-line treatment for RA. This medication has very modest drug costs (£75 per year, per patient); however, only 55 % of patients remain on this therapy 2 years post diagnosis. Patients whose treatment by methotrexate and at least one other csDMARD has failed to give an adequate response become eligible for the more expensive bo/bs/tsDMARD treatments (costing approximately £8–10,000 per patient, per year). [12,13]

Access to bo/bs/tsDMARD treatment varies by geography, and depends on local reimbursement systems and healthcare rationing policies. A number of countries (e.g. Germany, UK)[5][12] specify that a minimum number of csDMARDs be trialled before a biologic originator is prescribed and / or reimbursed. This has resulted in low rates of use of biologic originator in some European countries: approximately 8% of patients in Germany receive an anti-TNF, the most common form of biologic originator used in RA; 10% of patients in the UK, and 13% of patients in France receive anti-TNFs.[5]

Many of the biologic originators used in RA are reaching patent expiration. As a result, other manufacturers are now permitted to produce biologically similar versions of the agents, known as biosimilars. Critically biosimilars are not absolutely identical to the original agent, as they are manufactured by biological means from living organisms, and cannot therefore be regarded as a generic drug. For this reason clinicians and patient organisations have voiced safety concerns regarding the switching of patients from a biologic originator to a biosimilar for the purposes of cost saving. However, this market development is likely to incentivise payers to adopt a cost minimisation approach in the commissioning of this class of drug treatment. Biosimilar pricing has to be considered on a market by market basis, ranging from 15% price reduction when compared to the reference product in the USA, to 72% in Norway.[14,15] In the EU, the median price retail reduction as a result of biosimilar competition from 2006 to 2013 was 35%.[16]

Robust data on the 'real-life' burden and true costs of rheumatoid arthritis is needed to quantify the wider impact of the condition and enable a full understanding of the potential impact of both treatments and treat to target strategy. However, the commissioning and funding of upcoming, potentially life-changing treatments is not straightforward. Conventional market access methodology relies on health technology assessment (HTA) / cost-effectiveness analysis which currently focuses almost exclusively on direct costs. This may underestimate the true impact of access to effective treatment on individuals and on caregivers' ability to work, and on the health services themselves.

HTA processes are now becoming more sophisticated, aiming to ensure that a full analysis of social costs and benefits features in the decision-making process. To facilitate this, decision-makers, as well as other stakeholders, need greater access to quantitative evidence detailing the wider impact of rheumatoid arthritis at national level.

Given this context, the National Rheumatoid Arthritis Society (NRAS) identified the need for a comprehensive burden of illness study.

Study Aims

The primary objective of this study was to provide a comprehensive 'bottom up' burden of illness study in 10 European economies; Denmark, France, Germany, Hungary, Italy, Poland, Romania, Spain, Sweden and the UK to capture the annual economic and human burden of living with rheumatoid arthritis. The burden will be characterised from a societal perspective using a range of relevant measures of burden. These include patient-reported outcomes, national health services' resource use, and personal medical and non-medical costs. This provides the foundation for a comprehensive evidence portfolio from which the burden of rheumatoid arthritis can be properly identified and quantified and the existing provision of services to individuals living with rheumatoid arthritis can be identified and landscaped at a regional, national and pan-European level.

This summary report provides a high-level overview of the pan-European average annual patient costs associated with rheumatoid arthritis across the study treatment groups.

Study approach

The research is based on a stratified sample of RA patients in 10 European economies; Denmark, France, Germany, Hungary, Italy, Poland, Romania, Spain, Sweden and the UK. This required recruitment of physicians (n=476) from across Europe, who reported the direct resource utilisation from a specified number of consulting patients, and corresponding patient forms which collated information on indirect medical and non-medical costs incurred by the patient, plus included patient-reported outcome measures.

The UoC is able to access centres and physicians through medical fieldwork agencies which allow participating physicians and patients to remain anonymous to study investigators. Through physicians who actively care for RA patients, the UoC is able to collect a range of information: from qualitative data on the perceptions and attitudes and workload information of the average treating physician, to quantitative physician- and patient-reported data on quality of life and productivity loss, as well as caregiver involvement.

Study design

The study incorporates a mixture of demographic, clinical, and economic information about each patient The inclusion and exclusion criteria were not exhaustive or overly restrictive, so as to avoid inhibiting the breadth of the study or impacting on sample size (**Figure 1, Treatment stratified group definitions Table 1)**.

Figure 1
Overview of study design

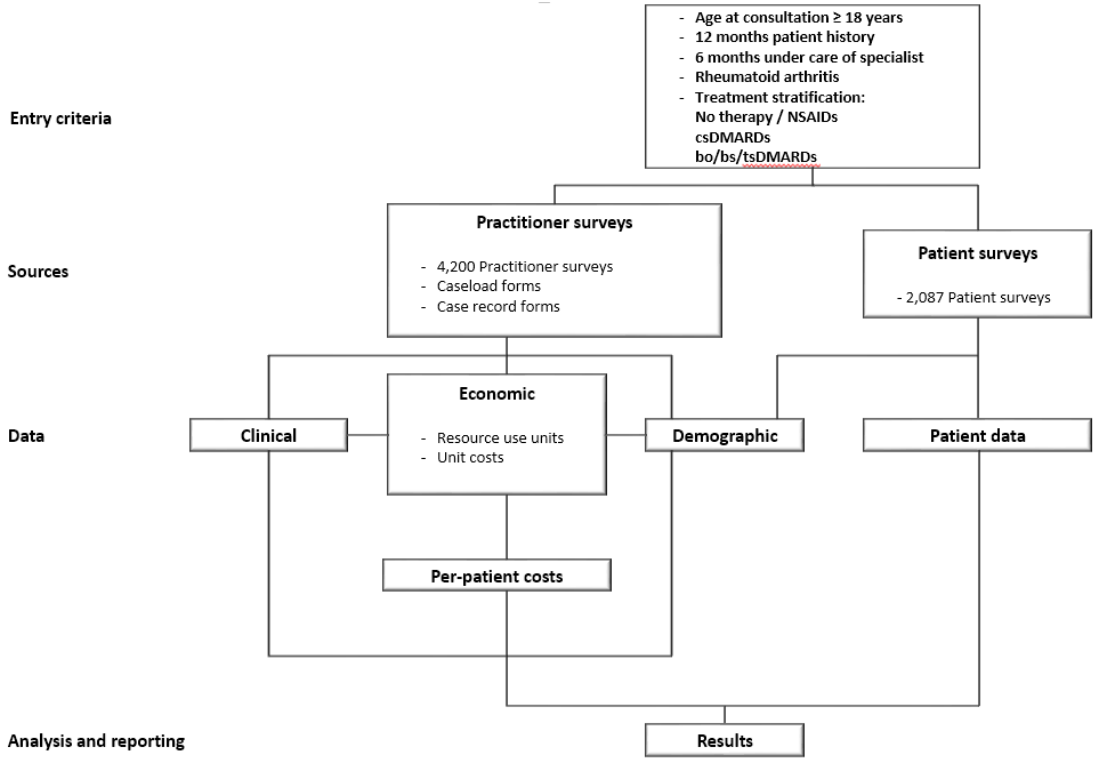


Table 1 Treatment group strata definitions

Name assigned within this report	No therapy / NSAIDs group	csDMARD(s) group	Bo/bs/tsDMARD group
Contains at least one of:	No therapy or NSAIDs only (+/- steroids)	Conventional synthetic DMARD(s) (+/- steroids)	Biologic, biosimilar or targeted synthetic DMARD (+/- steroids, csDMARDs, NSAIDs)
Description	Includes patients receiving either no therapy or NSAIDs. *Steroid use was captured within the study but not considered for the treatment definition*	Includes patients receiving a csDMARD alone or in combination with another csDMARD (combination therapy) and/or use of NSAIDs. *Steroid use was captured within the study but not considered for the treatment definition*	Includes patients receiving a bo/bsDMARD, or tsDMARD alone or in combination with a csDMARD (combination therapy) and/or use of NSAIDs. *Steroid use was captured within the study but not considered for the treatment definition*

Ethical approval

This research project was approved by the Research Ethics Sub Committee of the Faculty of Health and Social Care within the University of Chester. The approval stipulated that the study was to be carried out in accordance with regional and relevant guidelines.

Costing sources

The cost burden of any disease can be categorised broadly as either direct or indirect expenditures (**Table 2**). Therapy and management costs (i.e. drugs and devices, including home aids, and non-medical therapies such as alternative medicine and exercise) are examples of direct costs; as are primary and secondary care costs (consultations, admissions, surgeries, etc.). Indirect costs are those that are less tangible in their relation to the disease of interest, but are nonetheless quantifiable, such as the loss of wages and productivity due to absenteeism – either for the patient or a caregiver – or the loss of health-related quality of life due to illness.

Table 2

BRASS cost components [17]

Cost type	Category	Element
Direct medical	Hospitalisations	Day case
		Outpatient (e.g. for planned treatments)
		Inpatient – and lengths of stay
	Surgical procedures	Number and type of surgeries
		Length of stay
		Time spent in intensive care
	Consultant visits	Rheumatologist
		Other HCPs
	Tests and examinations	Blood tests (rheumatoid factor, CT etc.)
		Other tests and examinations (diagnostic imaging, etc.)
	csDMARD, tsDMARD and bo/bs/tsDMARD	Brand where applicable (current)
	Self-medication and alternative therapies	Over-the-counter (OTC) medications
		Holistic therapies
		Exercise, physiotherapy etc.
	Professional caregiver	Hourly wage
		Hours per week
Direct non-medical	Travel costs	Car
		Public transport
	Requirement for aids / equipment	Walking aids
		Home adjustments
	Informal Care	
Indirect	Work productivity impact	Short term sick leave
		Medium to long term sick leave (including early retirement)

Results

Demographics and average annual patient costs

Figure 2: Demographics and average annual patient costs

Demographic	Pan European Sample (n=4200)
Age, mean (SD)	55 (14)
% female	68%
Disease duration (SD)	12 (12)
BMI, mean (SD)	25 (4)

Cost Component	No therapy / NSAIDs (n=992) (SD)	csDMARDs (n=1286) (SD)	Bo/bs/tsDMARDs (n=1922) (SD)
Total direct medical costs (per-patient)	1310 (3096)	2034 (3493)	15224 (6553)
Total direct non-medical costs (per-patient)	1351 (4511)	1733 (4917)	2745 (6167)
Total indirect costs (per-patient)	2240 (6441)	2670 (6960)	3851 (8667)
Total patient costs (ex. Rx. Treatment)	-	4111 (9182)	4842 (9604)
Total patient costs	3142 (8184)	4413 (9197)	17923 (10773)

SD, standard deviation

Concluding Comments

The BRASS study aimed to provide comprehensive and accurate insight into the cost landscape for adult RA patients across the stratified patient groups and by sample countries. This top level summary report aimed to provide total costs at the pan-European level stratified by treatment groups.

Results across all countries showed total average annual per-patient direct and indirect costs increasing as treatment becomes more aggressive. Total direct and indirect costs excluding prescription treatment stand at €3,142 in the No therapy/NSAIDs group, €4,111 in the csDMARD(s) group, and €4,842 in the bo/bs/tsDMARD group. When prescription costs are considered, the incremental cost amongst the bo/bs/tsDMARD group is notable, rising to an overall average annual cost of €17,923. CsDMARD(s) group increases to €4,413.

Indirect costs account for the better part of overall costs amongst the two less aggressive treatment groups, No therapy/NSAIDs and csDMARD(s), with direct medical costs accounting for the bulk of costs amongst the bo/bs/tsDMARD group (due to prescription treatment cost). Indirect costs are attributed to medium-long term sick leave including early retirement. Granularity on sick leave and early retirement with respective financial and humanistic burden requires further investigation.

Acknowledgements

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