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Authors: Magdalena Strach, Alen Brkic, Marcin Kaczor, Rafał Wójcik , Piotr Kuszmiersz, Tone Birkenes, Marcin Krzanowski, Roman Topór-Mądry, Glenn Haugeberg, Mariusz Korkosz

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Direct medical costs in inflammatory arthritis: a single center real-world analysis of cost drivers and impact of a national drug reimbursement program

Magdalena Strach[1,2], Alen Brkic[3], Marcin Kaczor [4,5], Rafał Wójcik [4], Piotr Kuszmiersz[1,2], Tone Birkenes[6], Marcin Krzanowski[2,7], Roman Topór-Mądry[8], Glenn Haugeberg[9], Mariusz Korkosz[1,2]

[1] Department of Rheumatology, Immunology and Internal Medicine, University Hospital in Krakow, Kraków, Poland

[2] Department of Rheumatology and Immunology, Jagiellonian University Medical College, Kraków, Poland

[3] Division of Rheumatology, Department of Internal Medicine, Sørlandet Hospital, Kristiansand, Norway

[4] Aestimo s.c., Kraków, Poland

[5] Jagiellonian University Medical College, Kraków, Poland

[6] DiagraphIT, Kristiansand, Norway

[7] Department of Nephrology and Transplantology, Jagiellonian University Medical College, Kraków, Poland

[8] Department of Epidemiology and Population Studies, Institute of Public Health, Jagiellonian University Medical College, Kraków, Poland

[9] Department of Neuromedicine and Movement Science, Faculty of Medicine and Health Sciences, NTNU, Norwegian University of Science and Technology, Trondheim, Norway

Correspondence to: Magdalena Strach MD, PhD, Department of Rheumatology, Immunology and Internal Medicine, University Hospital in Krakow, Poland, Department of Rheumatology

and Immunology, Jagiellonian University Medical College, Kraków, Poland, ul. Jakubowskiego 2, Kraków 30-688, phone Poland +48 124003100, email: magdalena.strach@uj.edu.pl

What's new?

This is the first health-technology-assessment–oriented real-world analysis in Poland evaluating direct medical costs in rheumatoid arthritis, psoriatic arthritis, and axial spondyloarthritis within the national drug program. Our work integrates clinical data and real reimbursement expenditures, providing a unique, data-driven assessment of cost structures and the specific contribution of drugs used in rheumatic diseases. The analysis can provide system-level solutions for optimalization of treatment costs. Summary: The highest medical costs in the management of inflammatory arthritis are associated with the high share of b/tsDMARDs and low use of biosimilars, indicating potential savings through increased biosimilar uptake.

Abstract

Introduction: The introduction of biological and targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs) has improved healthcare and health outcomes in patients with rheumatic inflammatory diseases but their cost is substantial.

Objective: Explore direct treatment costs of patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and axial spondyloarthritis (axSpA) using real-world data from a tertiary single-center.

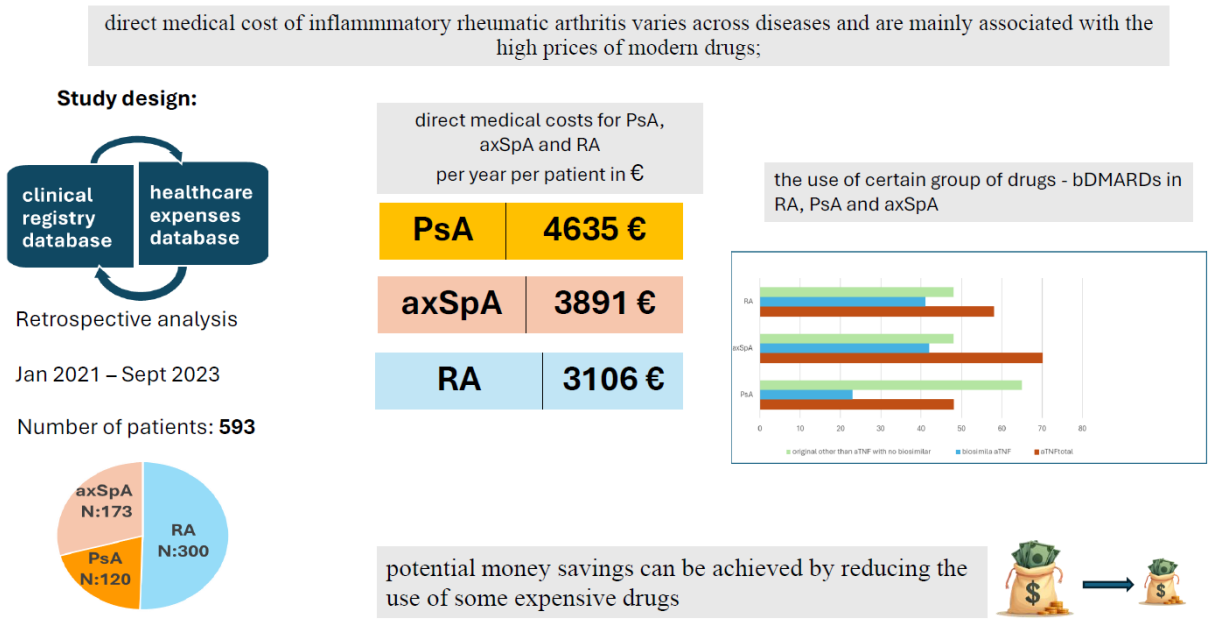
Methods: A retrospective study integrating data from two databases: a clinical registry and a healthcare expenses database covering the period from January 2021 to September 2023 was performed. Direct medical costs were calculated from the public payer and the patient perspectives, encompassing fully reimbursed services and out-of-pocket expenses.

Results: The study comprised 593 patients with RA (50.6%), PsA (20.3%), and axSpA (29.1%). The annual average per patient direct medical costs were €4635 for PsA, €3891 for axSpA, and €3106 for RA. The highest healthcare costs were driven by b/tsDMARDs, which accounted for 94.7% of total costs in PsA, 91.8% in axSpA, and 90.9% in RA. Anti-TNF use was highest in axSpA with 61.3% (37.6% biosimilars), 58.3% with RA (41.7% biosimilars), and 34.2% with PsA (17.5% biosimilars). Anti-IL-17/IL-23 agents were used in 42.5% of PsA and 36.9% of axSpA patients, while anti-IL-6 in 48.7% of RA patients.

Conclusions: The direct cost of b/tsDMARDs varies across diseases. Expenditures on PsA management were the highest and were mainly associated with the high prices of the drugs used and the lowest share of biosimilar anti-TNFs. Potential savings can be achieved by reducing the use of expensive agents.

Key words

direct medical cost; health technology assessment; inflammatory arthritis



Graphical abstract

Introduction

Most prevalent chronic inflammatory rheumatic diseases, such as rheumatoid arthritis (RA), psoriatic arthritis (PsA), and axial spondyloarthritis (axSpA), are lifelong conditions causing pain, disability, and diminishing the quality of life. These diseases impose a substantial financial burden on the healthcare system and patients, encompassing both direct medical and indirect costs [1, 2, 3]. Over the past two decades, the management of those disorders has been transformed by early intervention and the introduction of innovative biological and targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs). These therapies, including TNF, IL-6, IL-17, IL-23, and Janus kinase (JAK) inhibitors, have significantly improved disease activity control, functional outcomes, and work productivity [4,5,6]. However, b/tsDMARDs are 10–40 times more costly than conventional synthetic DMARDs [7, 8, 9,10]. The use of b/tsDMARDs has therefore reshaped cost structures and driven a several-fold increase in direct medical costs, but this was partly offset by reductions in hospital admissions and work disability costs [2, 11, 12]. In effect, total RA-related costs increased during the b/tsDMARDs era, albeit with a shift from indirect to direct costs as hospital stays and sick leave declined among those achieving better disease control [13].

Access to b/tsDMARDs is still a critical issue. In many healthcare systems, high drug costs led to restrictions on who should receive b/tsDMARDs reimbursed [14]. Poland's healthcare system addresses this via a nationally financed drug reimbursement program for expensive therapies. In Poland, all b/tsDMARD treatments for rheumatic diseases are fully reimbursed through dedicated government "drug programs," implemented in specialized rheumatology centers that meet strict administrative and organizational criteria. This program ensures that approved patients receive b/tsDMARDs at no personal cost, but historically, only a small percentage of patients could access these treatments [15]. For example, in 2009, fewer than 1% of RA patients

in Poland were treated with biologics, compared to much higher rates in Western Europe (up to 10% or more) [16,17]. Recent nation-level data indicate that access has improved — by 2022, approximately 3.2% of RA, 8.7% of PsA, and 3.5% of axSpA patients in Poland were receiving b/tsDMARDs [15] — yet these proportions remain low relative to disease prevalence and unmet need. By contrast, in some higher-income countries, 30–50% of patients with moderate-severe RA receive b/tsDMARDs therapy [14,17,18,19]. This gap highlights the impact of economic constraints and policy decisions on treatment availability.

Biosimilar drugs have been a game-changer in reducing treatment costs and expanding access. The introduction of biosimilars for TNF inhibitors and other biologics has led to substantial price reductions globally, enabling more patients to be treated within the same budget. Norway, for instance, leveraged a national tender system to drive biosimilar uptake, resulting in a 47% reduction in average biologic treatment cost per patient between 2010 and 2019 [11]. In Poland, the availability of biosimilars since 2014 has similarly cut the per-patient annual biologic cost by about 60% (from €7300 to €2886), and the number of treated patients increased several-fold (e.g., a 4.3-fold increase in RA patients on bDMARDs from 2013 to 2022) [1]). Nonetheless, the uptake of biosimilars in practice can vary by drug and disease, and certain expensive agents without biosimilar alternatives still strain the national budget.

In this context, health technology assessment (HTA) and real-world cost analyses are crucial for guiding policy and rheumatology practice. Understanding the drivers of direct medical costs under the national reimbursement program can identify opportunities for cost optimization. Real-world data reflect current and real prescribing patterns, healthcare utilization and reimbursement costs in clinical practice. Such analyses allow an appropriate response from the payer, adjustment of treatment standards with consideration of both drug prices and their effectiveness [20].

The study aimed to provide a comprehensive real-world analysis of direct medical costs associated with inflammatory arthritis in a single tertiary center in Poland. The main cost drivers for each disease were identified. The impact of expensive original and biosimilar b/tsDMARDs and of costs from comorbidities, hospitalizations, and prescribed drugs was examined. Additionally, systemic solutions, such as expanding biosimilar use and treatment optimization strategies to reduce costs while maintaining the quality of care, were proposed. We aimed to inform both the rheumatology community and healthcare decision-makers in Poland about the real-world economic burden of inflammatory arthritis and steps to improve cost-effectiveness.

Patients and methods

Study design and data sources

A retrospective observational study integrating data from two complementary databases at a single tertiary care center was conducted. Clinical data were obtained from a structured medical record system (GoTreatIT Rheuma, DiagraphIT, Norway) implemented in Poland as part of the PolNorRHEUMA project [31]. This database provided longitudinal patient-level information, including demographics, diagnoses, disease duration, disease activity scores, patient-reported outcomes, and medication use for all RA, PsA, and axSpA patients managed at the Department of Rheumatology, Immunology, and Internal Diseases at the University Hospital in Krakow. Cost data were retrieved from the hospital's internal billing database, which records all healthcare services and prescriptions billed to the National Health Fund (Narodowy Fundusz Zdrowia, NFZ) as well as patient co-payments. These two datasets were linked using unique patient identifiers.

Cohort and timeframe

We identified patients aged 18 years or older with RA, PsA, or axSpA who had regular follow-up and were enrolled in the GoTreatIT registry between January 2021 and January 2024. Patients with these diagnoses were selected because they represent the major inflammatory arthritis and our clinical data base was primary designed for those selected conditions. Corresponding healthcare utilization and cost records were obtained for the period from January 2021 to September 2023, with costs annualized as described below. Patients were classified by primary rheumatic diagnosis (RA, PsA, or axSpA) as recorded by their treating rheumatologist. The median observation period for cost data was 730 days (range 365–1296 days), i.e., one to three years of follow-up per patient.

Cost calculation

The public payer and patient perspectives were adopted to assess direct medical costs. Costs were tallied in 2023 Euros (€) and include: (1) costs that are covered by the public payer (NFZ) for inpatient hospitalizations, outpatient visits (specialist consultations, day-case infusions), diagnostic tests, imaging, and medications (including those provided through the national drug program); and (2) out-of-pocket costs paid by patients (full or co-payment for outpatient prescriptions not covered entirely by NFZ). Currency conversion from Polish złoty to Euro was performed at the average exchange rate for the period. For each patient, we calculated the total annualized direct medical cost, representing the cost observed during their follow-up, normalized to a 1-year period to account for varying follow-up lengths. Costs were further broken down into two subcategories: (1) "drug program" costs – i.e. costs of b/tsDMARD medications covered through the national drug reimbursement program plus any associated day-hospital infusion charges or monitoring mandated by the program; (2) "non-drug-program" medical costs – including hospitalizations (unrelated to b/tsDMARDs administration), routine

outpatient visits, and conventional medications (e.g. conventional synthetic DMARDs (csDMARD), non-steroid anti-inflammatory drugs (NSAIDs), glucocorticoids covered through full or partial payer reimbursement; and patient out-of-pocket partial or complete expenses.

Two subgroups for each disease were defined: "Drug program patients" (those on at least one b/tsDMARDs under the program during ≥1 year of follow-up) and "Non-program patients" (those managed without b/tsDMARDs). This allowed comparison of cost profiles between these subgroups. For patients in the drug program, we also captured the specific b/ts DMARDs molecules used and whether they were biosimilar or original brands. We also distinguished between patients who received b/tsDMARD therapy via the national drug program during the study and those who did not. Eligibility for the drug program follows national guidelines (e.g., active disease meeting criteria/failure of conventional therapy) and requires NFZ approval.

Statistical Analysis

Descriptive statistics were used to summarize baseline characteristics and costs. Continuous variables were reported as medians with interquartile ranges [Q1–Q3], alongside means and standard deviations (SD) for broader comparability. Categorical variables were reported as counts and percentages. Group comparisons (RA vs. PsA vs. axSpA) were performed using ANOVA or Kruskal-Wallis tests, followed by unadjusted pairwise Wilcoxon rank-sum tests as post-hoc analyses when overall differences were significant. Chi-square tests were used for proportions. A significance threshold was set at $p < 0.05$. All analyses were performed in Python and R. Given the descriptive and exploratory nature of the study, no multiple-testing adjustments were made.

Ethical approval was obtained for the analysis of de-identified registry data (approval N 118.6120.07.2023, 2021 from the Jagiellonian University Bioethics Committee, with a waiver

of informed consent for the retrospective use of anonymized data). The study was conducted in accordance with the Declaration of Helsinki.

Results

Patient Characteristics

A total of 593 patients (300 RA, 120 PsA, 173 axSpA) were included. Key demographic and clinical characteristics are summarized in Table 1. At baseline, the limited subset of patients was in low disease activity or remission, and RA patients had the highest disability on average (mean Health Assessment Questionnaire Disability Index, HAQ-DI was 1.0), axSpA patients had relatively preserved function (78.6% had HAQ-DI in the range 0–1, vs 58.2% in RA). The comorbidity burden was substantial across diseases (Table 1); 84.7% of patients had at least one comorbid condition. RA patients were slightly more likely to have comorbidities (86.3% with ≥1 comorbidity) than axSpA patients (81.5%). RA patients, being older and predominantly female, carried more age-related and cardiometabolic risks.

Among those on b/tsDMARDs, patterns differed: in RA, 48.7% of patients were on an IL-6 inhibitor (tocilizumab) and 58.3% on anti-TNF (some sequentially), whereas in PsA and axSpA, the dominant biologics were anti-TNF and anti-IL-17. Biosimilar anti-TNFs uptake was highest in axSpA. JAK inhibitors were primarily used by RA patients, as they were not yet widely approved for axSpA during the study period. 76.4% of patients with RA and 58% with PsA not enrolled into the drug program were on csDMARDs; 56% of axSpA patients were on NSAIDs.

Direct Medical Costs – Overall and by Disease Category

Over the study period, the annual direct medical cost per patient (payer and patient expenses) averaged €3,106 for RA, €4,635 for PsA, and €3,891 for axSpA. PsA incurred the highest yearly

costs, 19% higher than axSpA and 33% higher than RA on average (Figure 1, column A). The vast majority of costs were attributable to b/tsDMARD therapy provided through the national drug program in all three diseases. Specifically, b/tsDMARD accounted for 94.7% of total direct costs in PsA, 91.8% in axSpA, and 90.9% in RA.

We also stratified costs by whether patients were on the drug program (biologic/JAK therapy) or not. Among the 355 patients who received ≥1 year of b/tsDMARDs, the average annual cost was much higher, given the medication expenses: €5,301 in RA, €7,294 in PsA, and €4,817 in axSpA (Figure 1, column B; Table 2 for details). By contrast, in the 210 patients managed without b/tsDMARDs, annual costs were low: €633 in RA, €569 in PsA, and €349 in axSpA (Figure 1, column C and Table 3). Our RA patients who were not on the drug program incurred somewhat higher costs than their PsA or axSpA counterparts, due to more frequent hospitalizations, comorbidities, and higher conventional medication use in RA.

Costs in the drug program patients

Focusing on those receiving b/tsDMARDs within the drug program, PsA patients had the highest medication costs. The mean annual drug cost for a PsA patient on biologic therapy was €6,736, compared to €4,455 in RA and €4,320 in axSpA (Table 2). These figures correspond solely to drug costs (excluding related services). When adding the program-related service costs (day-case infusions, required monitoring) of roughly €200–€400 per patient, the total "in-program" cost was €7,294 in PsA versus €5,307 in RA, and axSpA program costs were €4,688.

The higher biologic cost in PsA is explained by the specific therapies used: a large number of PsA patients were on secukinumab (an original anti-IL-17 agent dedicated for the treatment of PsA and axSpA but not for RA), which, during the study period, had no biosimilar and was one of the most expensive agents. Secukinumab alone contributed on average €3,903 per PsA

patient-year, accounting for 53% of total PsA costs. In axSpA, secukinumab was also a major contributor (mean €2,361 per patient, 49% of axSpA total costs), but many axSpA patients were on TNF inhibitors (often on biosimilars, which cost less).

In RA, the most costly drug was tocilizumab; slightly less than half of RA b/ts program patients used it. Its average cost impact was €1,855, accounting for 41.6% of RA costs. Anti-TNFs were the most frequently used category (58.3% of RA biologic patients), contributing to €1,463 per patient (32.8% of RA costs). Many RA patients were on biosimilar adalimumab or etanercept, which cost roughly €100–€300 per patient-year in our cohort (very low due to tender pricing and partial-year use). In contrast, golimumab had a higher cost (€863 per RA patient on biologics, used in 16% of RA patients). Table 2 shows the detailed costs of each b/ts DMARDs.

In PsA, golimumab was used in 20% of PsA patients included in the drug program and accounted for €1,330 per patient (72% of all anti-TNF agent costs in PsA and nearly 20% of total PsA drug costs). In axSpA, golimumab and certolizumab pegol (another original TNF inhibitor) each contributed roughly €700–€800 per patient.

Table 2 shows that in PsA, secukinumab was by far the largest cost driver (used by 58% of PsA patients on biologics, contributing to €3,903 per patient-year). The IL-17/IL-23 inhibitor category (secukinumab, ixekizumab, risankizumab) accounted for €4,632 (68.8%) of PsA drug program costs. In axSpA, secukinumab was also the single biggest contributor (€2,361, 54.7% of costs). In PsA, golimumab accounted for 20% of treated patients and 19.7% of total PsA drug costs; in axSpA, golimumab was used in 12.3% of patients and contributed to 15% of costs. This reflects golimumab's high price relative to other anti-TNFs. Figure 2 shows the direct cost of medications within total drug program expenditures.

Another angle is the service costs associated with the drug program. RA patients incurred the highest program-related service cost (€428 per year) compared to PsA (€346) and axSpA (€368) (Table 2). Those patients who were on intravenous drugs (e.g., tocilizumab or rituximab) required hospital day-unit infusions (extra cost) and monitoring visits. RA patients had the highest "non-drug-program" medical cost, even among those on b/ts – on average, an extra €424 in costs outside of the drug program, versus only €212 in PsA and €129 in axSpA. This non-program cost for RA included higher hospitalization rates (€116 per RA patient on b/ts vs €28 in PsA or €35 in axSpA), as well as more outpatient visits and non-biologic prescriptions. RA patients, even on b/tsDMARDs therapy, utilized more healthcare resources outside of their b/ts treatment, likely due to managing comorbidities and complications.

Costs in the non-program patients

Two hundred ten patients were treated without b/tsDMARDs during the study (Table 3). These costs are much lower. RA patients were the most costly, averaging €633 per year, followed by PsA (€569) and axSpA (€349). Hospitalization and specialist visits constituted a significant portion of these costs. Drug costs in this group mostly come from csDMARDs and NSAIDs prescription costs. PsA, non-program patients had higher prescription costs (€341, including €96 out-of-pocket), largely due to higher use of csDMARDs and perhaps topical and/or conventional psoriasis treatments. AxSpA non-program patients had the lowest prescription costs (€87, mostly NSAIDs). Notably, RA patients outside the program had more hospitalizations: 18% had hospitalizations, compared with 5% among PsA patients. This aligns with RA's higher comorbidity burden and propensity for flares requiring inpatient care in moderate-to-severe cases. Across all diseases, patients not receiving biologics still incurred regular outpatient costs (€210 per year in visits each for RA and €200 for PsA, €227 for axSpA; Table 3).

It was instructive to compare prescription costs between those on vs off the program: for instance, RA patients on b/ts drugs still had some conventional prescription costs (€180 per year outside the program, often for folate, osteoporosis prophylaxis/treatment, or comorbidity meds), but RA patients off b/ts drugs had €307 in prescriptions. Similar trends held true for PsA (€125 vs. €341) and axSpA (€52 vs. €87) – those not receiving b/tsDMARDs actually spent more on conventional medications (particularly csDMARDs and NSAIDs).

Discussion

We found that direct costs are substantially driven by b/tsDMARDs, but the magnitude and composition of these costs vary by disease. PsA had the highest costs due to reliance on expensive original biologics (especially an IL-17 inhibitor secukinumab), whereas RA had lower costs, aided by higher biosimilar uptake and lower attendance in the dedicated drug program. AxSpA costs were intermediate, largely reflecting the extensive biologic use (often anti-TNFs, a substantial percentage on biosimilars) and tempered by fewer ancillary healthcare needs.

A key cross-disease observation was the budget impact of golimumab, an original anti-TNF. In our cohort, golimumab was a top contributor to costs in PsA, RA, and axSpA alike, illustrating how even a minority usage of a high-cost drug can raise overall expenditures. Despite being one of several anti-TNF options, golimumab's convenience (monthly dosing), satisfactory safety, and effectiveness made it a frequently chosen therapy, but its cost remained high. According to a meta-analysis of treatment options in PsA, golimumab was not superior to other drugs, and the highest efficacy and safety were observed with adalimumab and secukinumab [2]. Our finding suggests that encouraging the use of lower-cost alternative drugs could yield savings. If more PsA patients were managed with biosimilars, the cost difference over a year would be substantial (in our data, adalimumab biosimilar cost €100 per PsA patient vs

golimumab at €1,330). This is a clear target for policy intervention – whether through formulary incentives, prescriber education, or updated guidelines emphasizing cost-effectiveness.

Our results also highlight the consequences of limited biosimilar availability for certain mechanisms. The IL-17 inhibitors (secukinumab, ixekizumab) do not have biosimilars during the study. These agents fill an important clinical position (especially for PsA patients with significant skin psoriasis/obesity or axSpA who fail anti-TNF) [2], but their cost can strain budgets. In PsA, secukinumab plus golimumab accounted for over 70% of total costs. One approach to mitigating this is national-level, central price negotiation and tendering – the national payer could negotiate for better pricing given its high volume use. Another approach is to ensure that patients truly need these higher-cost agents – i.e., by optimizing the use of cheaper anti-TNFs first. Patients may have been moved to secukinumab while a more affordable option was still available (skin disease severity or obesity plays a role). From an HTA perspective, it would be valuable to analyze the cost-effectiveness of secukinumab in PsA, given current pricing – something the national agency could review to adjust guidelines if needed.

By contrast, biosimilar anti-TNFs have clearly provided cost relief [11,12]. In RA and axSpA, roughly 38–42% of patients on anti-TNFs were using biosimilars. This contributed to the relatively lower costs for those diseases. The introduction of biosimilars caused the market share of anti-TNFs to shift from 87% original down to 46%, and the average biologic cost per patient fell approximately 60% [15]. Our findings reinforce this positive impact. In RA patients, biosimilar usage (adalimumab, etanercept) represented only 30% of the RA anti-TNFs (€443 of €1,463) segment but covered a similar number of patients as the remaining 70% on anti-TNFs. This demonstrates how each percentage-point increase in biosimilar uptake translates into concrete savings. Poland's national program should continue to aggressively promote

biosimilars, mandating that new initiations use the most cost-effective agents unless contraindicated. Some European countries have successfully implemented switching programs for stable patients to biosimilars without clinical worsening, yielding huge savings for society [10,11,12].

From the perspective of a public payer our findings point to several possible cost-optimization strategies. These include broader uptake of biosimilar therapies, sequencing step by step b/tsDMARDs, use of lower-cost alternatives when available, national price negotiations for high-cost originator drugs without biosimilar equivalents. Such strategies may improve the efficiency of care without reducing treatment quality. At the same time, cost optimization should not be understood as simple restriction of access to expensive therapies, but rather as a rational arrangement of treatment choice, clinical need, and reimbursement policy [16].

Another point is the burden of non-drug costs, especially in RA. While >90% of costs in drug-programs patients were drug-related, RA patients still had notable costs from hospitalizations, comorbidities, and conventional care. Our RA patients had more cardiovascular and metabolic diseases, which resulted in higher inpatient and outpatient resource use. This is in line with the literature showing that RA can lead to comorbid conditions (e.g., cardiovascular disease, lung disease, metabolic diseases, osteoporosis, infections) and higher healthcare utilization [23, 25]. Even in patients without classic cardiovascular risk factors and with well-controlled disease, RA may exacerbate the detrimental effects of elevated total cholesterol and low-density lipoprotein on endothelial function. Patients with RA and unfavorable lipid profile may be at higher cardiovascular risk compared with those without RA and require lipid level monitoring, which may increase overall costs of RA [26]. Also, our RA patients not on b/tsDMARDs had more hospital admissions than PsA and axSpA, suggesting that poorly controlled RA or its complications demand more intense care [27]. In another Polish study hospitalizations of RA

patients in intensive care units were analyzed over 10-year period. Most admissions were urgent, the median length of stay was 14 days and mortality rate was 39.1%. Cardiovascular and respiratory diseases were the most common primary diagnoses. These findings support the view that comorbidities and their complications in RA increase healthcare resource utilization and contribute to non-drug costs [28].

Achieving tight disease control in RA may reduce long-term costs. Effective RA treatment can prevent disability and comorbid complications, potentially lowering costs. Studies from Sweden proved that despite increased drug costs, the fraction of costs due to hospitalization and disability in RA declined from 75% to 58% over two decades [29, 30]. Thus, one could argue that judicious spending on effective therapies might save costs in other areas ("pay now to save later"). This reflects that when biologics are not used, patients rely on csDMARDs to manage disease activity, which, while cheaper than biologics, can accumulate in cost and potentially still not control disease accurately. Decision-makers should consider the holistic cost of disease, not just drug line-items. In RA, for instance, supporting comprehensive care programs (including comorbidities, infection, osteoporosis, and physical therapy) could reduce non-drug costs.

The patient profiles that emerge from our data are illustrative of personalized care approaches: one-size-fits-all cost-cutting (like restricting all patients to only one cheapest drug) may go wrong clinically, whereas targeted strategies (e.g., switching stable patients to biosimilars, managing comorbidities in RA) are more likely to preserve outcomes and save money.

Our study provides a template for ongoing local cost audits. Poland's NFZ and scientific societies should continuously monitor real-world data on utilization and costs [16]. Such data

can identify whether one region is overutilizing an expensive drug when a cheaper one would suffice, allowing corrective measures. HTA can use these data to update cost-effectiveness analyses and adjust reimbursement criteria accordingly. For instance, if the cost of secukinumab remains very high and usage extends, they might negotiate a risk-sharing scheme with the producer or restrict it to certain patient subgroups where its value is highest.

One must also consider that our high-cost center data reflect patients who received the best possible treatment according to internationally endorsed management recommendations followed by our team, but for many patients, access to modern therapies is still limited. The solution to that is not to deny or block therapy to those centers like ours, but to lower drug prices enough so that more patients can be treated nationwide, and by facilitating more rheumatology centers to provide b/tsDMARDs treatment. It seems paramount to expand the use of biosimilars and possibly leverage regional tenders or centralized pressure to secure better prices for the most costly drugs.

As more expensive therapies (such as novel IL-23 inhibitors or JAK inhibitors) emerge, understanding where to allocate resources most effectively is crucial. For example, JAK inhibitors were increasingly used in our PsA and RA patients, and their costs are currently comparable to those of biologics [16]. In the future, market competition might reduce their price and potentially make them a cost-favorable option.

Limitation of the study

It is a single-center analysis, and prescribing patterns or tender results at our hospital may not exactly illustrate all of Poland (though national patterns seem directionally similar). Single-center studies are common in rheumatology, however they are well-known limitations due to

restricted generalization [32,33]. Our center likely dealt with more severe cases that are referred from the clinics without the possibility to provide b/tsDMARD treatment. However, since we annualized costs and included those not on b/tsDMARDs, the comparative findings across diseases remain valid. Patients with RA, PsA, and axSpA were included in study because complete clinical and cost data were available only for these conditions. We must be aware that other condition like systemic vasculitis, lupus which are also treated with expensive biologic therapies may also generate substantial costs however their incidence is lower compared with inflammatory arthritis.

Stratification according to PsA patients with or without skin changes was not performed due to the study limitation

Another limitation is that we did not often calculate indirect costs, which are often even higher than direct costs. Also, our follow-up was about 2 years on average – a longer-term study could see how costs evolve as patients age or switch therapies. Our cost estimates are based on current drug prices in Poland; these may change with new biosimilars or policy changes (indeed, by 2025, some prices may have further decreased). Despite these limitations, our analysis provides a real-world snapshot of the cost drivers not only for Poland but also for any healthcare system balancing b/tsDMARDs costs with patient outcomes.

Conclusions

Direct medical costs in RA, PsA, and axSpA differ and are largely driven by the cost of biologic and targeted therapies, with PsA and axSpA currently incurring high costs due to the high cost of the original IL-17 inhibitor and low uptake of biosimilar anti-TNFs. RA, while having lower b/tsDMARDs costs on average, still imposes a considerable burden through comorbidities and associated healthcare services. Enhancing biosimilar uptake, prioritizing cost-effective first-line biologics, and implementing treatment-optimization strategies (such as dose tapering in

sustained remission/low disease activity) could substantially reduce expenditures. At the same time, a comprehensive approach to patient care – managing comorbid conditions and preventing disease complications – is essential to reduce non-drug costs, especially in RA.

Our first real-world HTA analysis in Poland based on a very well characterized group of patients underscores these points and provides evidence to inform policy decisions. By identifying specific cost drivers (e.g., originator tocilizumab, golimumab, and secukinumab), we highlight opportunities for cost savings without compromising care. Ultimately, reinvesting those savings into treating more patients or into newer, more efficacious therapies could improve outcomes at the population level. Our study exemplifies how detailed local data can guide more intelligent global resource allocation in the management of inflammatory arthritis, ensuring that patients receive effective care while the system remains financially sustainable.

Contribution statement Concept and design: MS and MK; methodology and statistical analysis: MKa, RW, TB, writing- draft preparation: MS, writing- draft revision: AB, supervision: GH, MKrz, RTM, MK, data collection: PK, MS.

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Table 1. Characteristic of the study population (RA, PsA, axSpA).

	RA (n=300)	**PsA (n=120)**	**axSpA (n=173)**	**Total (N=593)**	***p*-value (RA vs PsA vs axSpA)**
Characteristic features					
Female sex, %	80.7	49.2	41.6	62.9	<0.001
Age years median [Q1;Q3]	55.0 [45 ; 66]	43.0 [38.0 ; 55.8]	38 [31.0 ; 47.5]	47.0 [37.0 ; 60.0]	<0.001 (RA > PsA > axSpA)
Disease duration (years) median [Q1; Q3]	10.0 [3.0 ; 14.7]	5.0 [1.0 ; 11.1]	4.5 [1.0 ; 9.5]	6.5 [2.0 ; 13.0]	<0.001 (RA longer)
Body mass index (kg/m²) median [Q1;Q3]	25.1 [11.2 ; 29.0]	27.1 [24.1 ; 30.5]	25.2 [23.2 ; 27.8]	25.5 [23.0 ; 29.0]	0.002 (PsA > RA, axSpA)
Clinical Measure					
DAS28-CRP median [Q1;Q3]	3.9 [2.8 ; 5.1]	3.1 [2.1 ; 4.2]	-	not directly comparable[#]	
ASDAS-CRP median [Q1;Q3]	-	-	2.2 [1.4 ; 3.0]	not directly comparable[#]	
BASDAI median [Q1;Q3]	-	-	3.4 [1.9 ; 5.5]	not directly comparable[#]	
DAPSA, median [Q1;Q3]	-	14.7 [6.9 ; 26.1]	-	not directly comparable[#]	

Remission at baseline, %	19 (DAS28-CRP)	35.6 (DAS28-CRP) 17 (DAPSA)	18.5 (ASDAS-CRP)		not directly comparable[#]
Low disease activity, %	14.6 (RA DAS28-CRP)	16.1 (DAS28); 31.3% (DAPSA)	57.2 (BASDAI); 28.3 (ASDAS-CRP)		not directly comparable[#]
HAQ-DI (0–3); median [Q1;Q3]	0.9 [0.3 ; 1.5]	0.8 [0.1 ; 1.4]	0.5 [0.1 ; 1.0]		<0.001 (axSpA < PsA < RA)
Patients with HAQ-DI ≤ 1; %	58.2	63.5	78.6		0.003
Comorbidity category					
≥1 comorbid condition N; (%)	259; (86.3)	102; (85.0)	141; (81.5)	502; (84.7)	0.4
Cardiovascular disease* N; (%)	134; (44.7)	43; (35.8)	49; (28.3)	226; (38.1)	0.002 (RA > axSpA)
Metabolic/endocrine disorder** N; (%)	152; (50.7)	53; (44.2)	49; (28.3)	254; (42.8)	0.005 (axSpA lowest)
Treatment status					
b/tsDMARDs; total users N; (%)	179; (59.7)	83; (69.2)	151; (87.3)		<0.001 (axSpA highest)
anti-TNF; % [##]	58.3	47.8	69.2		<0.001(PsA lowest)

biosimilar anti-TNF; % of anti-TNF	41.7	23.2	43.8	0.002 (PsA lowest)
non-biosimilar anti-TNF % of anti-TNF	21.8	27.5	29.2	RA lowest
anti-IL-17/IL-23 biologic %	0.6	65.2	48.5	PsA, axSpA only
anti-IL-6 %	48.7	-	-	RA only
JAK inhibitor %	32.1	13	5.4	0.01 (axSpA lowest)
csDMARDs %	95.0	90.8	14	<0.001 (axSpA lowest)
systemic steroids %	52.0	20.8	12.1	<0.001 (RA >> others)

Values are median [Q1; Q3] or N or (%); anti-IL-17/IL-23: anti-interleukin17/anti-interleukin-23; anti-TNF: anti-Tumor Necrosis Factor; ASDAS-CRP: Ankylosing Spondylitis Activity Score-C-reactive protein; axSpA: axial spondyloarthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; b/tsDMARDs: biological and targeted synthetic disease-modifying antirheumatic drugs; csDMARDs: conventional synthetic disease-modifying antirheumatic drugs; *CVD: ischemic heart disease, heart failure, cerebrovascular disease, or peripheral vascular disease; DAPSA: Disease Activity index for Psoriatic Arthritis; DAS28-CRP: Disease Activity Score in 28 joints - C reactive protein; HAQ-DI: Health Assessment Questionnaire Disability Index; JAK inhibitor: Janus kinase inhibitor; **Metabolic/endocrine: diabetes type II, obesity, dyslipidemia, thyroid disorders. PsA: psoriatic arthritis; RA: rheumatoid arthritis;

[#] Comparison not applicable due to the use of distinct clinical scoring systems tailored to each specific diagnosis. [##] percentages for individual b/tsDMARDs category refer to the subgroup of patients receiving biologic/targeted therapy.

Table 2. Detailed annual costs (€) of biologic/targeted therapies in patients receiving drug-program treatment (≥1 year) for RA, PsA, and axSpA.

	RA (n=156)	**PsA (n=69)**	**axSpA (n=130)**
Total direct cost (in-program)	€5.301	€7.294	€4.817
Drug cost (b/tsDMARDs)	€4.455	€6.736	€4.320
Program-related service cost	€428	€346	€368
TNF inhibitors			
TNF inhibitors (users: N; %)	€1.463 (91; 58.3)	€1.838 (33; 47.8)	€1.903 (9; 69.2)
Adalimumab (users: N; %)	€106 (36; 23.1)	€102 (11; 15.9)	€235 (46; 35.4)
Etanercept (users: N; %)	€336 (30; 19.2)	€82 (4; 5.8)	€109 (11; 8.5)
Infliximab (users: N; %)	-	€28 (2; 2.9)	€33 (4; 3.1)
Golimumab (users: N; %)	€863 (25; 16.0)	€1.330 (14; 20.3)	€734 (16; 12.3)
Certolizumab pegol (users: N; %)	€157 (9; 5.8)	€296 (6; 8.7)	€792 (23; 17.7)
Others: anti IL-17/IL-23, anti IL-6, anti-CD20			
IL-17/IL-23 inhibitors (users: N; %)	€19 (1; 0.6)	€4.632 (41; 59.4)	€2.361 (63; 48.5)
Secukinumab (IL-17A) (users: N; %)	€19 (1; 0.6)	€3.903 (41; 59.4)	€2.361 (63; 48.5)
Ixekizumab (IL-17A) (users: N; %)	-	€676 (8; 11.6)	-
Risankizumab (IL-23) (users: N; %)	-	€53 (3; 4.3)	-

Tocilizumab (IL-6) (users: N; %)	€1.855 (76; 48.7)	-	-
Rituximab (CD20) (users: N; %)	€151 (9; 5.8)	-	-
JAK inhibitors			
JAK inhibitors (users: N; %)	€966 (50; 32.1)	€266 (9; 13.0)	€55 (7; 5.4)
Tofacitinib (JAK) (users: N; %)	€438 (22; 14.1)	€117 (2; 2.9)	-
Baricitinib (JAK) (users: N; %)	€151 (5; 3.2)	-	-
Upadacitinib (JAK) (users: N; %)	€378 (33; 21.2)	€149 (7; 10.1)	€55 (7; 5.4)

Costs are the mean per patient (including those not on that particular drug). Numbers in parentheses indicate the number of patients on that drug during the year and % of the drug-program subgroup.

Table 3. Annual direct costs (mean € per patient) for patients managed without biologic/JAK therapy (non-drug program, n=210 with ≥1 year follow-up)

Cost category	RA (n=136)	PsA (n=44)	axSpA (n=30)
Total annual cost	**€633**	**€569**	**€349**
Hospitalizations (total)	€116	€28	€35
• Rheumatology-related	€64	-	€17
• Other causes	€52	€28	€18
Outpatient visits	€210	€200	€227
Prescription drug costs	€307	€341	€87
• Paid by NFZ (reimbursed)	€234	€245	€12
• Paid out-of-pocket	€73	€96	€75

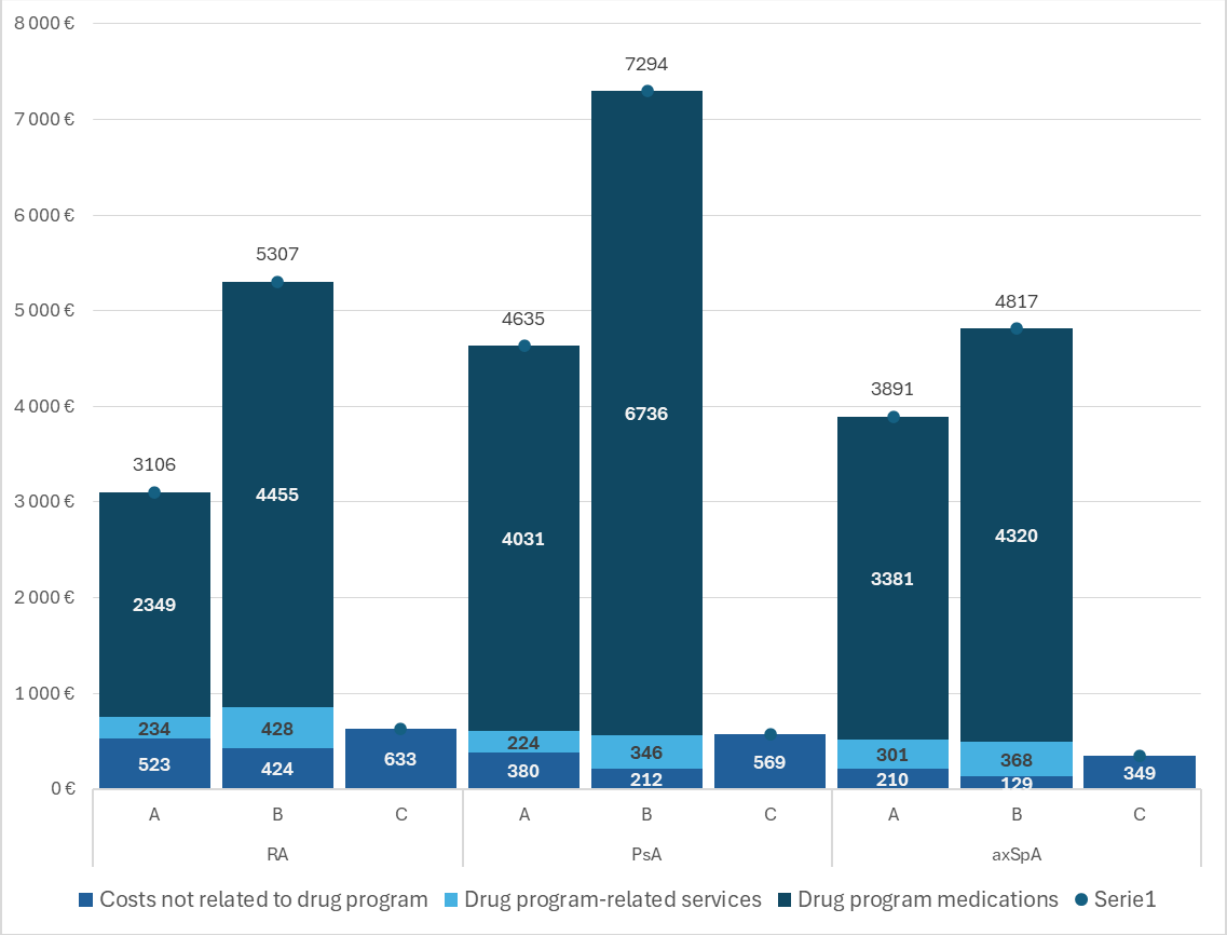

Figure 1. Annual mean direct medical costs (€) in rheumatoid arthritis (RA), psoriatic arthritis (PsA), and axial spondyloarthritis (axSpA).

Column A – total cohort (all patients with at least 1 year follow-up, N=593); Column B – costs for patients on the biologic/targeted synthetic drug program (n=355); Column C – costs for patients managed outside the drug program (n=210).

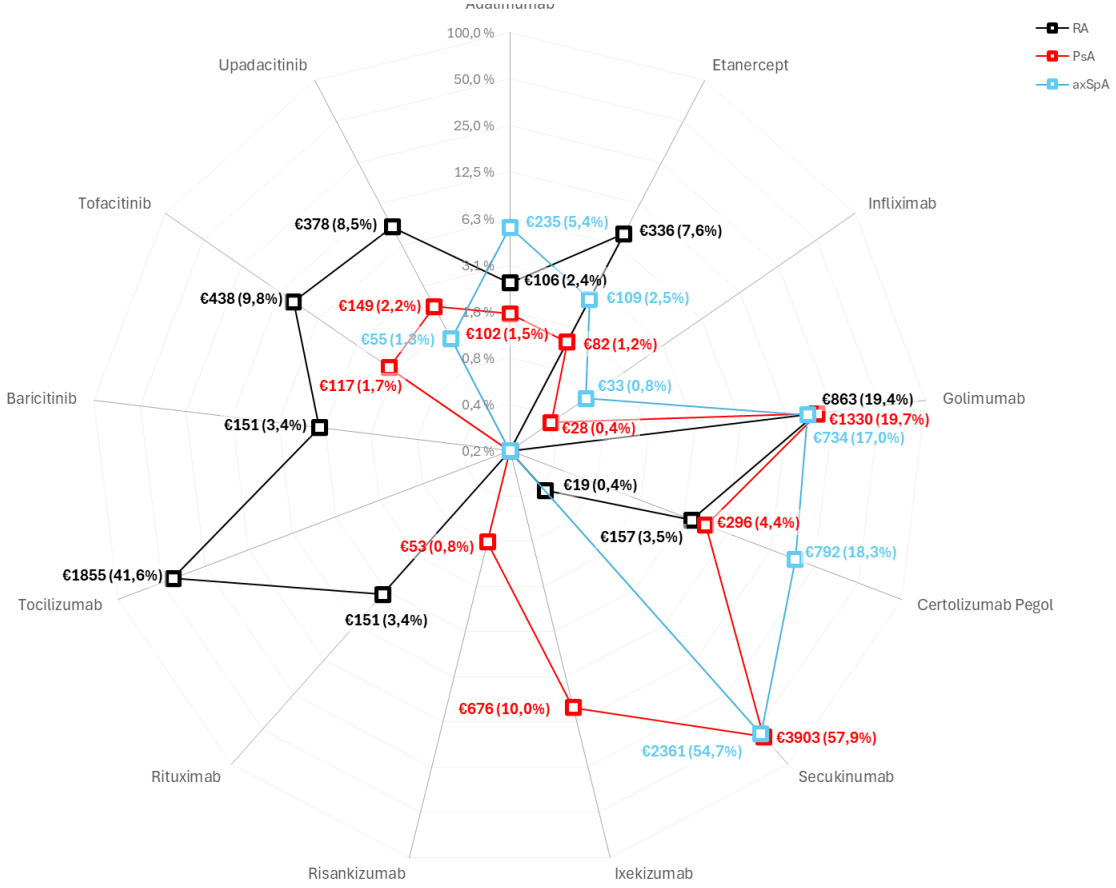

Figure 2. The percentages and direct cost of medications within total drug program medications expenditures (on a logarithmic scale) among subjects with rheumatoid arthritis (RA, N=156), psoriatic arthritis (PsA, N=69), and axial spondyloarthritis (axSpA, N=130). This analysis includes patients with at least one year of cost observation while undergoing drug program treatment (N = 355).

Short title: Direct Medical Costs in Inflammatory Arthritis