Clinical impact analysis and treatment availability with biosimilar TNF inhibitors in rheumatic diseases in Poland: real-world evidence using a nationwide database

Marcin Stajszczyk, I Obarska, S Jeka, et al.

ABSTRACT

Objectives: Although several years have passed since biologic disease-modifying antirheumatic drugs were introduced to the market, considerable disparities in access still remain. Tumour necrosis factor inhibitors (TNFi) have proven to be highly effective and safe for treating patients with rheumatic musculoskeletal diseases (RMDs). The emergence of biosimilars is promising for cost reduction and more equitable, widespread access.

Methods: A retrospective budget impact analysis based on final drug prices was conducted using 12 687 treatment courses for infliximab, etanercept and adalimumab. Estimated and real-life savings for public payer were calculated from an 8-year perspective of TNFi use. Data on the treatment cost and on the evolution in the number of patients treated was provided.

Results: From a public payer perspective, the estimated total savings amount to over €243 million for TNFi, with over €166 million attributed to treatment cost reduction in RMDs. Real-life savings were calculated as €133 million and €107 million, respectively. The rheumatology sector generated between 68% and 92% of total savings across models, depending on the adopted scenario. The overall decrease in mean annual cost of treatment ranged between 75% and 89% in access still remain. Tumour necrosis factor inhibitors (TNFi) have proven to be highly effective and safe for treating patients with rheumatic musculoskeletal diseases (RMDs). The emergence of biosimilars is promising for cost reduction and more equitable, widespread access.

Methods: A retrospective budget impact analysis based on final drug prices was conducted using 12 687 treatment courses for infliximab, etanercept and adalimumab. Estimated and real-life savings for public payer were calculated from an 8-year perspective of TNFi use. Data on the treatment cost and on the evolution in the number of patients treated was provided.

Results: From a public payer perspective, the estimated total savings amount to over €243 million for TNFi, with over €166 million attributed to treatment cost reduction in RMDs. Real-life savings were calculated as €133 million and €107 million, respectively. The rheumatology sector generated between 68% and 92% of total savings across models, depending on the adopted scenario. The overall decrease in mean annual cost of treatment ranged between 75% and 89% in

Conclusions: This is the first nation-level analysis that shows estimated and real-life direct cost-savings for TNFi biosimilars. Transparent criteria for reinvesting savings should be developed on both a local and an international level.

INTRODUCTION

Biological disease modifying antirheumatic drugs (bDMARDs), including tumour necrosis factor alpha inhibitors (TNFi), are well-established treatment modality that has been shown to improve disease-related outcomes in several rheumatic musculoskeletal diseases (RMDs).

Although the efficacy and safety of a given DMARD remains crucial in treatment choice, current recommendations also raise the issue of drug cost.

In many low-income and middle-income (LAMI) countries (eg, Romania, Poland, Hungary and Bulgaria), high drug prices limit the availability of innovative therapies, including TNFi.

In this setting, biosimilar availability is viewed as a favourable factor that generates savings due to on-market competition and renegotiation of biologic drug prices.

Both disease activity and bDMARD use are associated with socioeconomic factors, drug affordability and reimbursement stringency. Across Europe, considerable disparities in bDMARD access and eligibility are prevalent. An analysis conducted in 2014 showed that the annual price...
of treatment exceeded gross domestic product per capita in 26 countries. It was also observed that even after adjusting for sociodemographic and clinical characteristics, bDMARD usage remains variable across nations. Other studies have shown that in low-income nations, a greater rate of patients with moderate-to-high disease activity do not receive bDMARDs. These findings are consistent with those of other studies.

Infliximab (INF), etanercept (ETN) and adalimumab (ADA) biosimilars have been approved for use in indications equivalent to their reference drugs. Studies have shown that biosimilars may provide substantial financial savings by reducing drug cost expenditures. Compared with the time prior to biosimilar market introduction, the average price (based on list price) per treatment in the entire group of TNFi (both reference drugs and biosimilars) decreased by approximately 13% in the European Union in 2017. The development of biosimilar TNFi that share the efficacy and safety of the primary agents has led to a more realistic promise of decreased costs and widespread access. However, this optimistic outlook is still limited by several barriers, including doubts over equivalent effectiveness and tolerability and a lack of patient or provider awareness in some healthcare systems or biosimilar naïve countries.

The recent introduction of novel, conveniently administered oral agents is also relevant as a market competitor and therapeutic choice. Updated recommendations regarding Janus kinase inhibitors might re-establish the key role of TNFis in clinical practice. Compared with individuals in higher welfare nations, patients in Poland face additional barriers to biologic treatment. Restrictive eligibility criteria inconsistent with European Alliance of Associations for Rheumatology (EULAR) recommendations have been partially attenuated within recent years. However, other administrative constraints, such as access to therapy only in centres that sign specific National Health Fund (NHF) contracts, remain relevant. This leads to a limited number of rheumatologists who can treat with biologics, which is compounded by an upper funding limit set by the NHF. Other personal factors, such as travel difficulties, need to be considered. These restrictions persist after the reimbursement of biosimilars, which makes it difficult to increase the number of biologic treated patients. On the other hand, the Polish reimbursement system stimulates competition through local tenders, leading to biosimilar price reductions and reference drug repricing.

This study aimed to assess the impact of the TNFi biosimilars on the public payer budget and examine the availability of TNFis following their market introduction.

METHODS

Study design and patient population
A retrospective budget impact analysis (BIA) was performed to evaluate the introduction of TNFi biosimilars on the Polish market. INF, ETN and ADA data regarding drug prices, the annual drug budget and the number of patients treated were extracted from the NHF. The total value was calculated for all patients for whom TNFi are reimbursed, including patients with RMDs, rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, non-radiographic axial spondylarthropathy, juvenile idiopathic arthritis, inflammatory bowel diseases (IBDs), Crohn’s disease, ulcerative colitis and psoriasis. Additionally, the share of rheumatology in the total savings of the public payer was determined. The first biosimilar for INF was available in Poland from 1 January 2014, from 1 July 2016 for ETN and from 1 January 2019 for ADA. This is relevant to the timeframe of drug-specific analyses for which reference costs are calculated at the level of the preceding year. Analyses were performed as recommended by Health Technology Assessment Guidelines, which are consistent with recommendations provided by the International Society for Pharmacoeconomics and Outcomes Research.

The study was based on data calculated annually for a total of 12,687 patients (2,438 on INF, 3,613 on ETN and 6,636 on ADA) throughout the study timeframe. Two models for the assessment of savings were considered—estimated savings, which are a measure of potential savings based on ‘prebiosimilar’ prices and ‘postbiosimilar’ volume—and real-life savings, which show real drug budgets in the prebiosimilar and postbiosimilar era (online supplemental figure 1).

Data on the annual price of one drug unit and annual cost of treatment for one patient are not based on list prices, which are most commonly used in other relevant studies, but include the final price of drugs for hospitals resulting from the tender procedures, thereby representing the real cost for the payer. The data cover the entire period of market presence of TNFi biosimilars in Poland.

Estimated savings of the public payer
Estimated savings associated with INF, ETN and ADA treatment were calculated for actual drug utilisation and for the drug price maintained at the level of the reference drug from the year preceding the coverage of the first biosimilar drug. The presented data cover all clinical indications (table 1) and RMDs separately (table 2). In the alternative scenario of estimated savings, fixed drug cost and constant drug utilisation were both considered at the level of the year preceding access to biosimilar drugs (not shown in detail).

Real-life savings of the public payer
Real-life savings are the NHF savings based on the real-life payer’s expenses for the treatment of patients with INF, ETN and ADA after introducing biosimilars. The real-life savings of the public payer for ETN and ADA were calculated for the entire period of biosimilars availability. The real-life savings of the public payer for INF were calculated for 2019–2021 in relation to 2018, in which the expenditure reached its highest level (significantly higher than in the year preceding the reimbursement of the first biosimilar when the numbers of people treated were very small). The presented data cover all clinical indications (table 3) and RMDs separately (table 4). An alternative scenario for INF in a real-life model includes the entire period of biosimilars availability, that is, the reference year for INF 2013 (not shown in detail).

Treatment costs
The average annual costs for each drug and its year-by-year reduction were calculated. To rule out hypothetical inconsistency of data published in the public payer’s reports, sensitivity analyses were performed. The annual costs were determined using two independent analytical methods based on public payer data gathered from different sources (see data source section): 1. Average annual cost of one drug unit (per milligram per year). 2. Average annual cost of treatment for one patient (per patient per year).

Data on treatment costs are presented jointly with the number of biosimilars reimbursed in each year, which reflects the degree of market competition (table 5).

Access to treatment
Treatment availability is defined both directly as the number of patients treated and indirectly as a measure of drug exposure
expressed as the defined daily dose (DDD) per 1000 inhabitants per year according to WHO. The use of a year instead of a day was due to the unit scale (tables 6 and 7).

Based on the number of patients treated, ETN and ADA growth in patients with RMDs during the biosimilars competition era (ETN, 2016–2021; ADA, 2019–2021) was compared with growth in the corresponding period of market exclusivity of reference drugs (ETN, 2010–2015; ADA, 2016–2018) (figure 1). Data for INF would not be reliable due to the very small numbers of patients treated prior to 2014 and patients with RMDs in general.

The potential additional total number of patients treated per year if all real-life savings in 2019–2021 were spent on reimbursement of additional INF, ETN and ADA is shown in table 7. This was calculated based on real-life savings in each year and the average annual treatment cost per patient in the corresponding year. The market share of the reference biologic compared with biosimilars was also calculated using reimbursement data (figure 2).

**Data source**

Data on the annual public payer expenses related to reimbursement of INF, ETN and ADA, the number of patients treated and...
The total real-life public payer savings were calculated as €133.447 million (details provided in Table 3), of which €107.175 million were generated by rheumatic patients (see Table 4). The alternative scenario, which uses as reference value INF budget at the year prior to biosimilar coverage instead of 2018, yielded considerably different results. A net positive for INF was observed only for 2015, 2020 and 2021, while in the remaining years, an increase in expenses related to the number of patients treated was observed. Consequently, instead of savings for INF, we obtain an increase in the payer’s expenses of €5.915 million. The total savings in this scenario are then reduced to €103.619 million. Similarly, in the RMD population, the NHF recorded an increase in expenditures related to INF reimbursement of €1.036 million, and the total savings decreased to €103.619 million. The rheumatology sector accounts for over 80% and 92% of savings, depending on the scenario.

### Treatment

#### Table 3  Real-life public payer savings resulting from the reimbursement of tumour necrosis factor inhibitor biosimilars in rheumatology, gastroenterology, and dermatology for 2013–2021 in Poland

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<td>N/A</td>
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<td>N/A</td>
<td>Reference</td>
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<td>Savings versus reference value</td>
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<td>N/A</td>
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<td>N/A</td>
<td>N/A</td>
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<td>26.127</td>
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<td>8.054</td>
<td>32.595</td>
<td>42.567</td>
<td>43.922</td>
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</table>

Savings are calculated as the difference of the reimbursement value in the reference year and that of subsequent years. The single unit value is €1 million. N/A, not applicable.

The number of drug units were sourced from different published NHF data sets: the NHF Council resolutions, the Department of Drug Management announcements and the NHF Statistics Portal.20–22 Population size estimates were based on the average for the analysed period. Currency conversion was based on average euro (€) exchange rates in the last 5 years (1 Polish Zloty = €4.124).

## RESULTS

### Estimated savings of the public payer

Total savings were estimated at €243.083 million (Table 1), of which €166.711 million were generated within the rheumatology sector (Table 2). In the case of an alternative scenario that assumed no increase in the number of patients treated during the biosimilar reimbursement period, total and RMDs savings were reduced by 54% and 38%, respectively (total estimate of €111.683 million, €103.816 million for RMDs). The treatment of rheumatic diseases accounts for over 68% of total savings in the basic scenario and up to 92% in the alternative scenario.

### Real-life savings of the public payer

The total real-life public payer savings were estimated at €243.083 million (Table 1), of which €166.711 million were generated within the rheumatology sector (Table 2). In the case of an alternative scenario that assumed no increase in the number of patients treated during the biosimilar reimbursement period, total and RMDs savings were reduced by 54% and 38%, respectively (total estimate of €111.683 million, €103.816 million for RMDs). The treatment of rheumatic diseases accounts for over 68% of total savings in the basic scenario and up to 92% in the alternative scenario.

## Table 4  Real-life savings for the public payer due to tumour necrosis factor inhibitor biosimilar reimbursement in rheumatic musculoskeletal diseases (rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, non-radiographic axial spondylarthropathy) for 2013–2021 in Poland

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<td>0.543</td>
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<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>Reference</td>
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<td>0.948</td>
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<td>N/A</td>
<td>Reference</td>
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<tr>
<td>Savings versus reference value</td>
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<td>N/A</td>
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<td>N/A</td>
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<td>Reference</td>
<td>19.623</td>
<td>25.129</td>
<td>26.127</td>
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<tr>
<td>Total savings</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>1.357</td>
<td>4.952</td>
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<td>32.595</td>
<td>42.567</td>
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Savings are calculated as the difference of the reimbursement value in the reference year and that of subsequent years. The single unit value is €1 million. N/A, not applicable.
lowest annual cost of therapy applies to ADA, which represents approximately 64% and 38% of the cost of INF and ETN treatment, respectively.

Access to treatment

Overall, access to TNFi treatment slightly increased after the introduction of biosimilars and was most pronounced for INF, and these observations were consistent across both outcome measures: DDD per 1000 inhabitants per year and number of patients (for details, see tables 6 and 7).

In the case of RMDs, compared with the number of patients treated in the last year of market exclusivity, we observe an increase in INF (8 years on the market) by approximately 200% (absolute value +216 pts) and approximately 36% (+955 pts) and 38% (+1 576 pts) in the case of ETN (6 years on the market) and ADA (3 years on the market), respectively. However, when comparing the growth of the number of ETN-treated and ADA-treated patients during the biosimilar reimbursement period to the corresponding period of market exclusivity of the reference drug, we find that the observed percentage change is negative. Moreover, the absolute growth is lower for ETN (−552 pts) and almost equal for ADA (+1 pt) (figure 1).

If all budget real-life savings were spent on reimbursement of additional INF, ETN and ADA treatments, approximately 1.5–3.3-fold, 2.1–2.6-fold and 2.7–6.3-fold more total patients per year by drug in the indicated years in all indications. Given the contribution of rheumatology to the total NHF savings, the hypothetical increase in the number of patients with RMDs treated with INF, ETN and ADA is equal to 198–921, 3751–5787 and 7959–28 407 in 2019–2021 per year, respectively (table 7).

The market share analysis indicates a yearly increase and ultimately dominant market share for biosimilars. In 2021, the use of reference drugs accounted for close to 0% for INF, 5% for ADA and 29% for ETN. The number of patients with rheumatic diseases treated with TNFi biosimilars could be much greater if we consider the decrease in drugs prices and the savings achieved (figure 2).

DISCUSSION

This is the first complex, retrospective, nation-level BIA covering all available TNFi biosimilars that provide an exact analysis of public payer savings associated with their market introduction. We provide detailed data on both estimated and real savings generated by biosimilar presence on the market in an 8-year timeframe from a public payer perspective. By reporting both the number of patients treated and drug utilisation data, potential extrapolation of projected and real-life savings can be performed despite cross-country differences. It is important to emphasise that on a healthcare system level, the majority of savings are generated by TNFi biosimilar use in rheumatic conditions.
of biologic drugs takes place at the hospital level and is neither reimbursed under one DP. Tendering related to the purchase and various drugs with different mechanisms of action can be costs covered by NHF. DPs are dedicated to several RMDs, drug programme (DP), which enables hospitals to have their of all conditions facilitates patient enrolment in a dedicated ability criteria published by the Ministry of Health. Fulfilment among biosimilar users.

diseases, which reflects the predominance of patients with RMDs among biosimilar users.

In Poland, biologic reimbursement is based on a set of eligibility criteria published by the Ministry of Health. Fulfilment of all conditions facilitates patient enrolment in a dedicated drug programme (DP), which enables hospitals to have their costs covered by NHF. DPs are dedicated to several RMDs, and various drugs with different mechanisms of action can be reimbursed under one DP. Tendering related to the purchase of biologic drugs takes place at the hospital level and is neither regional nor central. If more than one medical product with the same active substance is reimbursed, the active substance product is mandated to undergo a tender procedure. Switching to the drug selected in a tender is mandatory but not automatic at the pharmacy level (eg, reference to biosimilar, biosimilar to reference, biosimilar to biosimilar). Each hospital has the right to provide patients with a specific product if a return to the original is requested due to suspicion of intolerance or lower effectiveness. Physicians are obliged to inform patients if the drug is switched and provide additional information regarding

### Table 6 Utilisation of infliximab-containing, etanercept-containing and adalimumab-containing products expressed as DDD per 1000 inhabitants per year, along with the degree of exposure increase in rheumatology, gastroenterology and dermatology for 2013–2021 in Poland

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<td>Milligrams of the drug</td>
<td>958 714</td>
<td>1 422 089</td>
<td>1 519 884</td>
<td>1 833 183</td>
<td>2 976 943</td>
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<td>3 805 104</td>
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<tr>
<td>Number of DDD</td>
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<td>379 224</td>
<td>405 302</td>
<td>488 843</td>
<td>793 851</td>
<td>1 068 464</td>
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<td>DDD per 1000 inhabitants per year</td>
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<td>9.98</td>
<td>10.66</td>
<td>12.86</td>
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<td>28.12</td>
<td>29.64</td>
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<td>% of the reference prescription</td>
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<td>158%</td>
<td>191%</td>
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<td>418%</td>
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<td>396%</td>
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<td>4 379 420</td>
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### Table 7 The potential additional number of patients per year if all real-life savings were spent on reimbursement of additional infliximab, etanercept and adalimumab treatment for 2013–2021 in Poland

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These data include the number of patients treated in all clinical indications (all) and separately the number of patients with rheumatic musculoskeletal diseases (rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, non-radiographic axial spondylarthritids) (REUMA). The potential additional number of patients has been calculated based on real-life savings in each year and the average annual treatment cost per patient in the corresponding year.

N/A, not applicable; pts, patients.
equivalence with the reference drug. All patients are also informed about the possibility of undergoing a reverse switch (in case of related concerns). Therefore, to be used in practice, the reference drug must be selected in a tender, which also stimulates price reduction.

We observed a high degree of integration for biosimilars in the treatment of rheumatic diseases in Poland, which, as described above, is based on observations regarding new prescriptions and non-medical switching from a reference product. In part, this reflects mutual agreement on a strategy supported by the public payer and experts from Polish Society for Rheumatology (PTR) and effective transition and acceptance by the specialist provider. The PTR has promoted educational programmes for rheumatologists and patients in line with EULAR recommendations\(^{23}\) and The PTR has promoted educational programmes for rheumatologists and patients in line with EULAR recommendations\(^{23}\) and maintained a generally favourable image of biosimilars in media communications. As part of the biosimilar adoption programme, the PTR and NHF have cooperated on the final shape of incentives to use INF, ETN and ADA (biosimilar or original) over other innovative therapies, which includes other TNFi. If the expected benefit and safety of different therapeutic options is comparable, treating patients with the afore-mentioned drugs provides hospitals with higher remuneration for healthcare services. A fixed upper limit for the final drug prices of INF, ETN and ADA (based on nationwide average prices) is an additional condition that guarantees benefits related to the provision of services. It also stimulates the repricing of reference drugs.

Together, these efforts culminate in significant savings. In rheumatology alone, it can be estimated that potential savings of the public payer range from €104 to €167 million, depending on the adopted scenario. These projections include different drug consumption levels but savings estimations assuming actual drug utilisation (ie, year-on-year growth with a trend not exceeding that noted prior to biosimilar reimbursement) credibly reflects the payer’s savings.

Estimated savings are derived from the number of treated patients and drug cost reduction. However, the calculation of estimated savings does not mean that the payer has obtained a net benefit (ie, lower annual expenses related to reimbursement of a given drug compared with the prior year). The increase in the number of treated patients may be high enough that the payer’s expenses may remain at a similar level as that prior to the price drop. Ideally, this is the most desirable scenario as it reflects a full reinvestment of savings for the treatment of a greater number of patients. The payer’s real savings appear when the decrease in treatment costs is not used to treat a correspondingly larger number of patients. By financing treatment at an equivalent accessibility level (ie, as prior to the biosimilar era), the public payer achieves significant savings, but this strategy does not facilitate potential improvement in disease control and associated socioeconomic burden on a population level. Indirect costs associated with the progression of disease-related disability can constitute the majority of expenses in rheumatic disease.\(^{24}\) Enabling access to biosimilars earlier in the disease course and an increased number of patients is likely to improve the state of RMD control population-wise, especially since biologic availability in Poland is low. Our analysis provides evidence that savings generated due to the price drop of TNFi were mainly used by the public payer to reduce expenses by over €100 million among patients with RMDs rather than to increase drug access.

The current analysis is difficult to compare with other reports. Few data are available regarding biosimilar market presence and budget impacts.\(^ {25}\) Prior projections are based on fixed degrees of market penetration and expected price reductions estimated at a time point when biosimilars were being introduced to the market, often covered only a single drug or clinical indication.\(^ {15} 26–29\) We identified only one study that included a savings analysis based on real drug prices over the long term.\(^ {30}\) Although conducted on a national level, the study (corresponding to our estimated savings model) has several limitations, including no reporting of patients treated or drug unit utilisation and no calculation of real-life savings, which precludes a direct comparison. In the case of Poland, the presented data indicate that estimated savings were achieved primarily due to the reduced cost of therapy. For other countries, a smaller reduction in the price of biologic drugs can yield economic gains given a larger sample of treated patients.

We observed that following their market introduction, INF and ADA biosimilars practically replaced their reference drugs in the third year of availability. Only the market share for the reference ETN remained significant due to successful competition in hospital-level tenders. Access to biosimilars has also resulted in downward repricing of reference drugs in Poland. This applies with the greatest extent to ETN, and less to INF and ADA (data not presented in detail). However, this scenario is not replicated on a similar level in other countries and likely depends on a variety of factors (eg, local economic policy, healthcare system construction). Notably, despite having the shortest presence on the market, the greatest savings are generated by ADA, which is likely the least expensive TNFi treatment. The market penetration of biosimilars in Poland reflects a similar trend to that observed in the Nordic countries, along with the effective

**Figure 1** The rise of etanercept (ETN) and adalimumab (ADA) use in patients with rheumatic musculoskeletal diseases (rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, non-radiographic axial spondyloarthritides) in Poland during the biosimilar competition era (ETN, 2016–2021; ADA, 2019–2021) and in the corresponding period of market exclusivity of reference drugs (ETN, 2010–2015; ADA, 2016–2018).

We noted the greatest increase in drug availability for INF, with biosimilar medicines (cost; percentage treatment cost reduction due to the reimbursement of reimbursement value data (stacked clustered chart). Additionally, the share of the reference biologic (REF) and biosimilars (BIOSIM) is based on epidemiological data35 37 38 with a total population of patients with inflammatory arthritis in Poland estimated at approximately 550,000—yields an estimate of 14%–20% of eligible patients that might be treated with TNFi instead of the current 3%–4%. This is predicated on full reinvestment of savings into biologic reimbursement. Although biologic eligibility does not equate to TNFi eligibility, if we assume a conservative rate of 20%, the estimated number of treated patients could be achieved in practice.

The current biologic reimbursement regulations in Poland do not enable enhanced drug access. The observed increase in the number of treated patients is still mainly derived from very low rates of initial drug availability. For the most cost-effective subcutaneous therapies (eg, ETN or ADA) to become widely available, extension of prescription mandate to all retail pharmacies and access for all rheumatologists (rather than limitation to selective inpatient care) appears necessary. Transparent criteria for reinvesting savings due to benefit-sharing programmes should be developed; otherwise, patients who have been promised accessible and affordable therapy will suffer.39 A study by Jensen et al from Denmark has shown that cost reduction is still achievable, even when maximising treatment access is prioritised.34 On a population-level, developing similar policies may facilitate the expected effects of biosimilar market presence for the Polish market competition of the reference ETN in Norway, winning the central tender in 2020.31

From a healthcare perspective, savings generation requires a high amount of biologic users. We observed that the uptake of biosimilars within the Polish market is very high. In contrast, market share for INF were only 2% after 5 years in the UK, Germany, France, Spain and Italy.32 The Polish actual scenario is most similar to Norway, although with no central tendering.33 We noted the greatest increase in drug availability for INF, with patients’ access to treatment improving over four-fold between 2014 and 2018. INF market penetration mainly covers patients with IBD (almost 90% of the INF market in Poland), as the setting of INF use in RMDs is quite specific. According to the current reimbursement criteria, a patient may be treated with up to two (ineffectiveness) or three (intolerance) TNFis; hence, physicians tend to favour less immunogenic drugs, which results in an expectedly low penetration of INF in patients with RMDs.

Less pronounced figures are noted for the availability of ETN and ADA. For both drugs, the increase in the number of patients does not exceed 40% and should be interpreted in context of a small set of users prior to the biosimilar era. Based on data published by Jensen et al,34 we estimated that the increase in ADA consumption in Denmark (12 months prior to and after biosimilar reimbursement) was close to 30%, as compared with 21% in the corresponding period for Poland. In line with our findings, the authors showed considerable real-life savings of about 80% when compared with the prior (annual) payer budget. Similarly, access to treatment in Norway has considerably improved for ADA (>200% for 2018–2021) and ETN (~50% for 2016–2021).31 When comparing the Polish scenario with both studies,31 34 the rate of improvement in biologic accessibility is partially comparable. However, the absolute number of initial therapy users leads to different implication on both an economic and patient level. To illustrate this, we quantified the number of 40 mg ADA pens (from the Jensen study) into DDD per 1000 inhabitants (per country, per year). We observed that the initial drug utilisation was close to 28 times greater than in Poland. This is a remarkable disparity, which impacts savings calculation that could infer for, for example, treatment-related improvements in work ability of the RMD population. It also illustrates the real-life setting of LAMI countries.

If all budget savings were spent on reimbursement of additional TNFis, a total of over 46,000 additional patients could benefit from treatment. For the rheumatology sector, this represents over 35,000 additional biologic users, giving a total of almost 45,000 biologic patients treated annually. Adopting two conservative thresholds of 40% and 60% for the rate of biologic eligible patients with RMDs—defined as not achieving at least low disease activity under conventional treatment35 36 and based on epidemiological data35 37 38 with a total population of patients with inflammatory arthritis in Poland estimated at approximately 550,000—yields an estimate of 14%–20% of eligible patients that might be treated with TNFi instead of the current 3%–4%. This is predicated on full reinvestment of savings into biologic reimbursement. Although biologic eligibility does not equal to TNFi eligibility, if we assume a conservative rate of 20%, the estimated number of treated patients could be achieved in practice.

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setting, with improvement of healthcare outcomes, as has been reported in other countries.

Strengths
The major advantage of this analysis is an exact calculation based on the public payer’s data, which includes final (not list) drug prices derived from all treatments on the population level. Since the vast majority of healthcare in Poland is financed by NHF, such sourcing of data represents a reliable approach to describe the nation-level effect of biosimilar market introduction. Determination of the rheumatology sector contribution to the total results is an added advantage.

Limitations
The current analysis may be limited by the hypothetical inconsistency of data published by the public payer. To evaluate the discrepancies across different NHF records, treatment costs and availability were calculated in two different approaches using various NHF sources. We did not observe relevant differences in the obtained calculations. It should be noted that the share of rheumatology in total savings for individual countries will vary depending on the number of patients treated in each clinical indication.

CONCLUSIONS
This study demonstrates that biosimilar-related reduction in TNFi prices mainly led to reduced expenditure within the RMDs sector of Polish healthcare. No relevant increase in treatment availability was observed due to limited savings reinvestment into additional TNFi treatments. If no systemic changes towards a patient-centric healthcare model are undertaken, we can expect only a modest yearly increase in biologic drug access, for which the observed rate of change is still likely driven by low starting drug availability. Our findings illustrate the extent of real-life (in contrast to the expected) patient-level benefits in an LAMI country, and demonstrate how a reductive fiscal policy (with stringent reimbursement and restrictive prescription) constrains biologic accessibility.

Acknowledgements
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Contributors
MS: study concept and design, data acquisition, analysis and interpretation, writing the article. ID: data analysis. SJ: data interpretation. BB: data interpretation, writing the article. All authors contributed to the critical revision of the manuscript. It should be noted that the share of rheumatology in total savings for individual countries will vary depending on the number of patients treated in each clinical indication.

Data availability statement
Data are available in a public, open-access repository. The source raw data are available through published NHF data sets: the NHF Council resolutions, the Department of Drug Management announcements and NHF Statistics Portal.

Supplemental material
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REFERENCES
31 Kvien TK, Patel K, Strand V. The cost savings of Biosimilars can help increase patient access and lift the financial burden of health care systems. Semin Arthritis Rheum 2022;52:151939.
Supplemental figure 1

Budget impact analysis – retrospective models for assessing the benefits of biosimilars reimbursement. Both models are based on real drug utilization and the final drug price for hospitals, reflecting the true cost of the public payer.

Estimated savings

- **data more accessible**
  - current drug utilization
  - final price of drugs for hospitals resulting from the tender procedures
  - retrospective analysis

- current vs estimated value of reimbursement based on current vs reference drug price – difference between the estimated and current value (reference price – price of reference drug from the year preceding the coverage of the first biosimilar)

- the more patients treated, the greater savings always present if cost of the therapy is lower

- does not provide information on the potential use of the treatment costs reduction to treat more patients, i.e. increasing access

Real-life savings

- **more difficult to access**
  - current value of reimbursement vs value in the reference year – difference between the reference year and the analyzed year (reference year – generally the year preceding the coverage of the first biosimilar)

- the more patients treated, the less savings may not occur if savings are fully reinvested in the treatment of a correspondingly larger number of patients

- allows to determine whether the reduction of the cost of therapy is related to the increased availability, i.e. to what extent it is reinvested in the reimbursement of the analyzed drugs