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Indirect costs of the Rheumatoid arthritis in Poland

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Abstract

It is estimated that about 400,000 people in Poland suffer from rheumatoid arthritis (RA). Only a few epidemiological studies documenting the incidence of musculoskeletal disorders in the Polish population have been conducted. The medical literature mainly states that rheumatoid arthritis affects approximately 1% of the population and occurs 2-4 times more often in women than in men. RA is a disease that can develop at any age. In this group of diseases, indirect costs significantly exceed direct costs. Easier and more efficient access to rheumatology outpatient clinics would contribute to a quicker diagnosis of patients and, consequently, to reducing indirect costs of RA, and access to modern therapies would translate into a reduction of indirect costs related to rheumatoid arthritis. Results of studies conducted by other authors available in literature demonstrate that these diseases cause both an increased absence at work, i.e. missing days at work, and presenteeism, i.e. an increased ineffective presence at work due to ill-being. Indirect costs increase with increased disease activity. These costs can be significantly reduced through early diagnosis and introduction of effective treatment.

Key words: Indirect costs; Rheumatoid arthritis

Rheumatic diseases are chronic and usually cause irreversible damage to the musculoskeletal system, which leads to progressive disability of the patient. They are not fatal, but they lead to shortening of life and deterioration of its quality[1].

Rheumatic diseases can be divided into inflammatory, e.g. rheumatoid arthritis, and non-inflammatory. Inflammatory joint diseases, among others RA, are very dangerous for patients' health. In the case of RA, doctors have twelve weeks from the first symptoms to diagnose the disease and to undertake effective treatment. According to the only data available for Poland, the mean time from the onset of the first symptoms to the visit to a rheumatologist is 35 weeks[2].

- Rheumatoid arthritis - definition, etiopathogenesis

Rheumatoid arthritis (RA; *Latin: arthritis rheumatoidea*, ICD-10-> M05, M06) is an inflammatory, chronic rheumatic disease of connective tissue with an immunological basis. A characteristic feature of RA is non-specific inflammation of mostly symmetrical joints - mainly minor joints of the hands and feet. Pain and swelling in the joints are accompanied by morning stiffness caused by the accumulation of edema fluid in inflamed tissues during sleep. In addition, systemic changes are observed (slightly elevated temperature, muscle pain, fatigue, lack of appetite, weight loss). There are often systemic complications that lead to disability and premature death[3].

The cause of the disease is not known yet. It is thought that the influence of many factors, i.e. environmental factors such as microvascular and bacterial viral infections, genetic factors and immunological disorders, plays an important role in its etiopathogenesis. In the course of

[1] E. Suresh, "Diagnosis of early rheumatoid arthritis: what the non-specialist needs to know", J R Soc Med, no. 97, pp. 421-424, 2004.

[2] "Wczesna diagnostyka chorób reumatycznych- ocena obecnej sytuacji i rekomendacje zmian" [Early diagnosis of rheumatic diseases - assessment of the current situation and recommendations for changes], Brygida Kwiatkowska, Warsaw, 2014, p. 44

[3] "Postępy reumatologii klinicznej" [Advances in clinical rheumatology], Irena Zimmermann-Górska, Warsaw, 2014, p. 43

RA, internal organs (kidneys, heart, lungs) may be damaged. The disease can also lead to pathological changes in the eye[4].

The main feature of pathological changes in rheumatoid arthritis is an inflamed synovium. Histopathological examination shows increased angiogenesis, cell hyperplasia, inflow of inflammatory leukocytes and changes in the expression of adhesion proteins associated with the cell membrane[5]. A characteristic feature of RA is the formation of invasive tissue, which is involved in the destruction of cartilage and the formation of articular erosions[6].

Access to epidemiological data on rheumatic diseases for Poland is very limited - this applies to both primary and secondary sources. Information about the number of issued medical certificates is easily available, as you can easily find them on the ZUS (Social Insurance Company) website. You can also easily find data on the Social Insurance Fund expenses for disability pensions. However, there is no data on the number of days of absence due to caring for a child and another family member, broken down into ICD-10 classification units. It is not available on the ZUS statistical portal. Also, there is no ZUS data on the number of disability pensioners and new disability pensions awarded broken down into individual ICD-10 classification units. Data on presenteeism is limited because available research is based on subjective questionnaires. There is no objective methods available to measure presenteeism. In the world, most scientific publications on this subject are based on various types of medical records.

The medical literature mainly states that rheumatoid arthritis affects approximately 1% of the population and is 2-4 times more common in women than in men. It can develop at any age, but usually starts between 25 and 50 years of age[7]. RA is one of the most common inflammatory rheumatic diseases. The incidence ranges from 31 to 50 people per 100,000 people[8].

In Poland approximately 400,000 people suffer from RA, and between 8,000 and 16,000 people are diagnosed annually. The incidence of RA falls between 4 and 5 decade of life, and patients with this disease live about 7 years shorter on average[9].

Patients with rheumatoid arthritis are twice as likely to die compared to people who do not suffer from RA in the same age group. Population studies show that after 20 years of suffering from RA, 19% of patients are completely disabled and 35% die[10]. Rheumatoid arthritis leads to losing their jobs by the majority of patients in the first 10 years of the disease[11].

[4] "Wczesna diagnostyka chorób reumatycznych- ocena obecnej sytuacji i rekomendacje zmian" [Early diagnosis of rheumatic diseases - assessment of the current situation and recommendations for changes], Brygida Kwiatkowska, Warsaw, 2014, p. 17

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[10] Humphreys JH, Warner A, Chipping J, et al. Mortality trends in patients with early rheumatoid arthritis over 20 years: Results from the Norfolk Arthritis Register. Arthritis Care Res 2014

[11] Wiland P, Świerkot J, Maśliński W. Certolizumab pegol w leczeniu reumatoidalnego zapalenia stawów [Certolizumab pegol in the treatment of rheumatoid arthritis]. Reumatologia 2011; 49: 253-263.

RA with high inflammatory activity can lead to irreversible damage and joint deformities. Often, they become stiff, which prevents patients from functioning properly[12]. Rheumatoid arthritis can affect every joint, joints of the feet and hands are most often deformed, and muscles of the hands disappear, which causes the patient to lose precision in the grip and use of the hands. In rheumatoid arthritis, compared to the general population, there is a 3-fold greater risk of lower limb venous thrombosis and a 2-fold greater risk of pulmonary embolism. Between 11 and 30% of patients die within 30 days from the diagnosis of these complications[13].

Rheumatic diseases, especially inflammatory diseases, cause many negative health consequences. In addition to limiting movements, they cause depression and lead to deterioration of patients' mental health. They also lead to losses incurred by the state, and more specifically, they generate indirect, direct and social costs for the health care system[14].

Due to the fact that most rheumatic diseases are incurable and lead to permanent damage to health, they generate high direct costs associated with the need to provide patients with, inter alia, orthopedic devices that are needed by them for the rest of their lives as well as high indirect costs associated with the loss of patients' productivity.

Material and methods

Indirect costs presented in the pharmacoeconomic analysis are estimated using the human capital approach (HCA). The use of this approach is supported by its grounding in the economic theory and the relative ease of application in practice. Indirect costs include: absenteeism - loss of production, resulting from the absence of the patient at work; presenteeism - reduction of productivity related to the malaise or sickness of a person present at work; loss of production caused by permanent inability to work; loss of production, which is caused by death and costs of informal care.

In this paper, we presented estimates of indirect costs of seropositive RA (M05) and other RA (M06).

Rheumatoid arthritis (RA) is a chronic, autoimmune disease of connective tissue that causes symmetrical articular and extra-articular ailments. It is characterized by non-specific inflammation leading to the destruction of joint cartilage and erosions of bones[15]. Causes of RA are unknown. It is important to quickly diagnose and treat the disease because the sooner the therapy is undertaken, the more likely the patient is to have mobility and normal life.

The calculations were based on data from the ZUS statistical portal, Eurostat and Statistics Poland. In the absence of data, reasonable assumptions were made or the values derived from empirical studies were used.

Data for the calculation of individual components of indirect costs is very limited for RA, therefore I was unable to calculate all indirect costs.

Results

1) Absenteeism

Absenteeism M05

In order to estimate the extent of lost production as a result of absenteeism, data from the ZUS statistical portal on the absence of employees due to their sickness in 2016 was used.

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[14] P. Scutellari and C. Orzincolo, "Rheumatoid arthritis: sequences," Eur J Radiol, no. 27 (1), pp. 3138, 1998.

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The total number of medical certificates issued due to seropositive rheumatoid arthritis (M05) was 24,535, which corresponded to 397,053 working days of absence (calculated in 1,575 working years - assuming that we have 252 working days a year).
As a measure of productivity, GDP per employee was assumed, which in 2016 amounted to PLN 121,046.95. Then, by multiplying the number of lost years of work by the value of GDP per employee, the total loss of production as a result of absenteeism was obtained and it was PLN 190,648,946.25. In order to obtain the final result, a correction factor of 0.65 was applied. In the end, the indirect cost resulting from sick leave as a result of the incidence of seropositive RA was 123,921,881.1 PLN.

Absenteeism M06

In order to estimate the extent of lost production as a result of absenteeism, data from the ZUS statistical portal on the absence of employees due to their sickness was used in 2016. The total number of medical certificates issued due to other rheumatoid arthritis (M06) was 14,686, which corresponded to 211,991 working days of absence (calculated in 841 working years - assuming that we have 252 working days a year).
As a measure of productivity, GDP per employee was assumed, which in 2016 amounted to PLN 121,046.95. Then, by multiplying the number of lost years of work by the value of GDP per employee, the total loss of production as a result of absenteeism was obtained and it was PLN 101,800,106.5. In order to obtain the final result, a correction factor of 0.65 was applied. In the end, the indirect cost resulting from sick leave as a result of the incidence of other RA was PLN 66,170,069.2.

2) Presenteeism

Presenteeism is an ineffective presence at work. It is a situation in which an employee comes to work despite their sickness, but because of their sickness and malaise is not fully productive. This phenomenon is considered in many aspects - health, social and work efficiency.

Presenteeism is difficult to estimate and using it to calculate indirect costs causes a lot of controversy, as there are no objective methods to measure it. Most of the available tools are questionnaire surveys. The research procedure consists in asking questions to respondents about their work and how their sickness affects their work. The phenomenon of presenteeism is also not well described in scientific literature, especially when it comes to rheumatic diseases.

Rheumatic diseases constitute a significant problem causing an ineffective presence at work. They also generate high socio-economic costs. They lead to gradual reduction of efficiency and, as a result, increasing difficulties in everyday functioning and coping with basic activities.

It is estimated that in the case of RA presenteeism generates a loss of 3.2 days per every 20 business days. For comparison: losses due to absenteeism are determined as 0.2 days[16].

Although there is a relatively large number of tools used to assess the loss of productivity (here we talk about numerous questionnaire studies, such as Endicott Work Productivity Scale (EWPS), Health and Labor Questionnaire (HLQ), Health and Work Questionnaire (HWQ), Health and Work Performance Questionnaire, Work Limitations Questionnaire (WLQ) and Work Productivity and Activity Impairment Questionnaire (WPAI), so far none of them has become a common standard[17].

[16] Escorpizo R, Bombardier C, Boonen A, et al. Worker productivity outcome measures in arthritis. J Rheumatol 2007; 34: 13721380.

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The analysis of the loss of productivity is used not only to assess the impact of the disease on the situation of a given person or to count the costs associated with it, but also to determine the effectiveness of treatment. This also applies to rheumatic diseases.

According to available studies conducted among patients who assessed the degree of negative impact of RA on their professional life themselves, 33% of patients assessed that they were less productive at work. In Poland, the problem of rheumatoid arthritis affects 400,000 people, 228,000 of whom are professionally active.

According to calculations presented in the section on absenteeism, in total people with RA took 24,535 days of sick leave in the case of M05 and 14,686 days of sick leave in the case of M06.

In order to estimate the total number of days during which they felt worse, but nevertheless were at work, the total number of days of sick leave was deducted from the total number of days of lost productivity, resulting in 705,065 (M05) and 714,914 (M06). The loss of productivity was 33%. This estimation was multiplied by the number of days during which the sick were at work despite a worse condition, consecutively resulting in 232,671.45 days (M05), and 235,921.62 days (M06). Assuming that there are 250 working days a year, we received 11,494,343.14 years of lost work. In order to obtain the final result, a correction factor of 0.65 and the value of GDP per employee were applied. As a result, the indirect cost resulting from the presenteeism of patients suffering from rheumatoid arthritis was PLN 73,226,840.37 for M05, and PLN 74,249,740.6 for M06.

3) Informal care

Informal care M05

Data on the number of days of absence due to care for a child and another family member, broken down into ICD-10 classification units, is currently not available on the ZUS statistical portal.

The estimated cost of lost production due to informal care was based on the total number of medical certificates for care and the assumption that the share of the total length of sick leave due to care in the case of seropositive rheumatoid arthritis (M05) in all medical certificates due to care is the same as the corresponding share in the case of medical certificates due to employees' diseases.

The total number of sick leave days due to all diseases in 2016 was 238,659,822 days, of which the certificates for seropositive RA accounted for approx. 0.17 percent. In turn, the total number of sick leave days due to care was 397,053 days. Thus, the number of working days spent on informal care due to the incidence of seropositive RA was - based on the above assumptions – 1,667.6 which corresponded to 7 years of lost work. By multiplying the number of lost years of work by the value of GDP per employee and a correction factor of 0.65, the final indirect cost resulting from informal care due to seropositive RA amounted to PLN 550,763.7.

Informal care M06

Data on the number of days of absence due to care for a child and another family member, broken down into ICD-10 classification units, is currently not available on the ZUS statistical portal.

The estimated cost of lost production due to informal care was based on the total number of medical certificates for care and the assumption that the share of the total length of sick leave due to care in the case of seropositive rheumatoid arthritis (M05) in all medical certificates due to care is the same as the corresponding share in the case of medical certificates due to employees' diseases.

The total number of sick leave days due to all diseases in 2016 was 238,659,822 days, of which the certificates for other RA accounted for approx. 0.09 percent. In turn, the total number of sick leave days due to care was 211,991 days. Thus, the number of working days spent on informal care due to the incidence of other RA was - based on the above assumptions – 882.8 which corresponded to 3.5 years of lost work. By multiplying the number of lost years of work by the value of GDP per employee and a correction factor of 0.65, the final indirect cost resulting from informal care due to other RA amounted to PLN 275,381.8.

4) Permanent or temporary incapacity to work

Due to the lack of ZUS data on the number of pensioners and newly-granted disability pensions divided into individual ICD-10 classification units, the consequences of permanent and temporary incapacity to work due to rheumatoid arthritis (M05, M06) were estimated on the basis of data on Social Insurance Fund expenses for disability pensions. Then, the assumptions regarding the structure of pensions with regard to partial and total incapacity to work as well as temporarily and indefinitely granted disability pensions were adopted.

Additionally, on the basis of ZUS data, the average time of incapacity to work was determined in the case of a temporary pension for 15 to 17 months (respectively for total and partial incapacity). It was also assumed that a person with partial incapacity to work is able to work for 0.25 working time, which is consistent with the amount of the benefit, which in principle amounts to 75% of the total disability pension.

The value of disability pensions due to osteoarticular, muscular and connective tissue diseases (M00 - M99) in 2016 amounted to PLN 4,943,984.4 (the most recent available data) and accounted for 14.1% of total disability pensions paid out from Social Insurance Fund. It was assumed that the same proportion of cases caused by RA can also be attributed to the number of newly-granted disability pensions in each age group. In the absence of more accurate data regarding rheumatoid arthritis, it was assumed that the share of the four groups isolated in this manner in the population of people who are incapable to work due to RA is the same as in the case of general population of new pensioners in 2016.

Table 1. Expenses for disability pensions due to incapacity to work in 2016 according to incapacity to work and disease groups that cause incapacity

Disease group	Total contribution amount	Total incapacity to work and exist independently	Total incapacity to work	Partial incapacity to work
osteoarticular, muscular and connective tissue diseases (M00 - M99)	PLN 2,101,475.5 (14.0 %)	PLN 118,347.4 (6.6 %)	PLN 409,467.3 (9.8 %)	PLN 1,573,660.8 (17.4 %)

Source: based on data from ZUS

The total number of medical opinions determining the degree of incapacity to work, including incapacity to exist independently, total incapacity to work and partial incapacity to work is 364. According to data from Statistics Poland, in 2016 there were 38,433,000 people living in Poland. Based on data presented at the beginning of my paper, we know that in Poland about 400,000 people suffer from RA. In the study of economic activity of the population (BAEL), it was established that the professional activity rate in 2016 was 56.2%. The number of professionally active people suffering from RA is 224,800. The average time

of incapacity to work in the case of a temporary disability pension for 15 to 17 months has been determined. The average time of incapacity to work was determined in the case of a temporary disability pension of 15 months, i.e. 456.55 days multiplied by the number of professionally active people and by the number of medical opinions issued regarding partial incapacity to work, which resulted in the number of 32,329,218,600 (for M05) and 10,673,773,760 (for M06). The same was done in the case of total incapacity to work, which resulted in 5,699,484,784 (for M05) and 1,512,108,208 (for M06). In order to obtain the final result, a correction factor of 0.65 was applied. As a result, the indirect cost is PLN 24,718,657,199.6 (M05) and 7,920,823,279.2 (M06).

5) Deaths

The assessment of indirect costs also covers the issue of the loss of the average number of years of work caused by premature death.

Table 2 shows the total number of deaths in 2001-2010. In the Eurostat database only data until 2010 is available for this category. Analyzing the number of deaths, it can be noted that from 2008 according to ICD-10 for Rheumatoid arthritis and arthrosis (M05-M06, M15-M19) the number of deaths falls from 284 in 2008 to 262 in 2010. It is not a big drop - only by 22.

Table 2. The total number of deaths due to rheumatoid arthritis and arthrosis (M05-M06,M15-M19)

GEO/ TIME	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
Poland	312	286	336	305	298	287	278	284	279	262

Source: Eurostat database

Table 3 presents a standardized mortality rate by place of residence due to rheumatoid arthritis and arthrosis (M05-M06,M15-M19) between 2011-2015. Data comes from the Eurostat statistical portal.

Analyzing, it can be noted that from 2013, the mortality rate was decreasing from 1.01 in 2013 to 0.87 in 2015.

Table 3. Standardized mortality by place of residence

GEO/TIME	2011	2012	2013	2014	2015
Poland	0.98	1.04	1.01	0.96	0.87

Source: Eurostat database

The available data at the beginning of the study indicate that 35% of people with RA die. In total, 400,000 people are struggling with this disease, so it results in 140,000 patients who do not survive the disease. After applying a correction factor of 0.65, the final indirect cost of deaths in the amount of PLN 91,000 was received.

Discussion

The indirect costs generated by RA patients have been analyzed by scientists around the world. The results of the analysis carried out in Germany by Huscher et al. [18] showed that in the group of RA patients at working age (18-64) indirect costs of sick leave and permanent incapacity to work constitute a significant part of the patient's annual cost from a social perspective. The costs of sick leaves (per person) in 10 years decreased from EUR 1,707 in 2002 to EUR 1,525 in 2011. Permanent incapacity to work constitutes the main component of indirect costs.

Calculated using the FCA approach, the costs related to permanent incapacity to work decreased from EUR 1,680 in 2002 to EUR 1,552 in 2011. Using the HCA approach, these costs amounted to EUR 8,902 and EUR 8,229, respectively. The total indirect costs decreased in the analyzed period. Depending on the approach used, the difference was 310 EUR (FCA) and 855 EUR (HCA)[19].

The results of the analysis carried out in Austria by Radner et al. in the group of 356 patients with RA showed a statistically significant relationship between disease activity and indirect costs: an increase in disease activity entails an increase in the costs related to incapacity to work ($p < 0.01$). A similar relationship was observed for the annual costs of sick leave. In the group of patients with low disease activity it amounted to 1,874 EUR, while in the group of patients with high disease activity it amounted to 3,291.9 EUR[20].

The results of a study conducted in Norway by Kvamme's team in a group of 1,152 patients with RA showed that during a two-year observation period, the indirect cost in the group treated with classic disease-modifying anti-rheumatic medications measured using the HCA approach amounted to EUR 66,975, and measured using the FCA approach it amounted to EUR 20,420 . The two-year biological therapy period, as measured using the HCA approach, generated a cost of 122,233 EUR, while measured using the FCA approach it amounted to 57,910 EUR. The authors calculated the cost of productivity loss in the group. In the group of patients treated with classic disease-modifying anti-rheumatic medications, it amounted to EUR 57,564 (HCA) and 13,881 (FCA), while in the group of patients undergoing biological therapy it was 82,754 EUR (HCA) and 18,807 EUR (FCA)[21].

In the United States, indirect costs related to the deterioration of the quality of life and lost income due to RA are estimated at USD 3,000-9,000 per patient per year and depend mainly on the degree of disease activity[22].

After calculating RA costs in individual countries, the following results are obtained as a percentage of GDP in these countries: for Germany 1.01×1^{-17} % using the FCA approach and 2.8×10^{-17} % using the HCA approach; for Austria with low disease activity 5.4×10^{-7} %, and for high disease activity 9.6×10^{-7} %; for Norway 2.05×10^{-5} % using the HCA approach and 6.2×10^{-6} using the FCA approach; for Poland the total for M05 and M06 is 0.59& (with GDP of: Germany - 3,478 sextillion USD, Austria - 390.8 billion USD, Norway - 371.1 billion USD, USA - 18.62 sextillion USD, Poland - 471.4 billion USD)[23]. They are also divergent, because there is no relationship between the country's GDP and the costs related to the

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disease. In countries with high GDP and a low GDP, the costs associated with the disease are high, but they depend mainly on the severity of the disease.

Poland has relatively high indirect costs of RA compared to other countries. Among the inflammatory rheumatic diseases, the total costs of therapy in rheumatoid arthritis are particularly high. They include medical expenses and costs associated with the loss of productivity. The strategy of dealing with inflammatory joint diseases, including RA, must be based primarily on early diagnosis. This is the most important element that would improve patients' situation. Unfortunately, most patients disregard the first key symptoms. Research shows that within three months of the onset of symptoms, about 10% of RA patients have erosions, and thus irreversible structural changes. The problem also concerns the lack of settlement procedures supporting the functioning of quick rheumatic diagnostics centers. The average waiting time to have an appointment in a rheumatology outpatient clinic is about six months. This results in a longer diagnostics for the patient. The time from the onset of symptoms to the diagnosis of RA is consequently long, contributing to irreversible changes and ultimately to the deterioration of patients' life and productivity levels. Increasing expenditures for modern, effective therapies will also translate into reduction of indirect costs caused by RA.

The combined effect of indirect costs (absenteeism, presenteeism, informal care, permanent or temporary incapacity to work and deaths) for Poland in 2016 for rheumatoid arthritis is PLN 24,916,447,618.77 (M05) and PLN 8,061,609,470.8 (M06).

It should be taken into account that - due to some data limitation - the above calculations were made with the adoption of certain simplifying assumptions. As a result, the values presented constitute only an approximation of the actual indirect costs generated by rheumatoid arthritis.

To improve the availability of data, it would be a good idea to keep accurate records in terms of the number of patients suffering from a given disease, in particular rare diseases, regarding which access to information is particularly limited.

The creation of a database in which people who are interested could quickly find information necessary to calculate indirect costs of diseases with the use of appropriate search filters would significantly simplify the work and validate the results. The combination of facts and data collected from various sources constitutes a significant obstacle, all the more so when the materials available are limited to individual countries. Then, the need for estimations arises, which simultaneously generates certain errors and as a result the values are rounded up, approximated.

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