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Economic Evaluations in Systemic Lupus Erythematosus

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1. Introduction

Systemic lupus erythematosus (SLE) is a prototype of autoimmune diseases with a wide range of clinical and laboratory features that involves almost every organ system. The prevalence is 52 x 100000 inhabitants in U.S, 21 x 100000 in Canada and 25-91 x 100000 in European countries (1). There is an early-onset SLE disease in young women after teenager years and a late-onset before the beginning of fifth decade. Women are affected 9 times more frequently than men.

SLE is a complex disease characterized by recurrent relapses and remissions subsequent. Nowadays, there is no cure for SLE and this disease can be threatening when major organs are affected.

Unfortunately, SLE can be considered as a disease with a high implication in terms of morbi-mortality and also, the patients undergoing a great impairment of quality of life, considering their potential systemic compromise and/or organ-specific. The patients show decline on physical activity as a result of arthritis, undesirable changes in appearance or damage produced by long-term use of steroids (often used therapy to treat patients with SLE) such as osteoporosis, cataracts, or angina, making it one of diseases with major implications at the individual, family, social and economic levels. It affects public health in relation to the increase of resources health consumption.

A better awareness among physicians and patients about this disease, the advent of more effective therapies but also more expensive and longer survival of patients with SLE, it has led toward an important and better perception of the disease in recent years. The socioeconomic data are important as well, since patient survival improves, the accumulation of disease and complications treatment-related are crucial in order to appraisal the financial burden on both individuals and society. In countries where chronic diseases are prevalent, with a growing population and limited economic resources, it is critical a suitable decision-making on resources to health care. Our current knowledge about the economic impact of SLE is very limited and there are only few cost studies conducted by North America and Europe, unfortunately.

This chapter shows a historical description of approaches to economic evaluation in SLE, both at national and international framework and highlighting the main elements that must be considered in clinical practice and decisions to avoid increasing the economic burden of health care. A non-systematic review of all published literature in English, French and Spanish from 1990 to April 2011 was performed using Medline, Pubmed, Cochrane, Lilacs and Scielo in peer-reviewed articles, including the Mesh-terms of systemic lupus erythematosus, direct costs, indirect and intangible cost, economic impact, disease burden, Cost-of-illness (COI) studies, pharmacoeconomics analysis, cost-effectiveness and cost-utility. It will have three types of approaches: the economic impact of the disease, COI studies and finally, a complete pharmacoeconomic assessment.

2. Overview

As previously mentioned, the economic evaluations on autoimmune diseases are lack and most of them have been carried out on Rheumatoid Arthritis (RA). In the case of SLE has virtually been restricted to studies of disease burden and cost-of-illness (COI). The COI studies measures the monetary burden that disease entails on society caused by morbidity and premature mortality in terms of consumption of health resources and lost of productivity.

In 1967, Rice was the first to outline a methodological framework for calculating single-year cost of illness, disability, and death by major category of illness (2). In 1982, Hodgson and Meiners created the first guide to study COI (3). The studies' results are crucial to provide informative data to emphasize the extent of the disease problem and highlight the profile of patients with SLE. They also have the potential to serve as the basis to a major component in economic evaluations such as COI. A valuable COI study included direct, indirect, and intangible cost associated with the disease.

Direct costs represent the opportunity costs of all kind of resources used to treat a disease (3). They usually include direct medical costs and direct non-medical costs. The first refer to the costs involved to provide treatment, including costs associated with the diagnosis, treatment, monitoring, emergency and rehabilitation, while non-medical costs refer to those which patients and their families spend on disease but are not medical in nature, including transportation costs, cost for household expenditures, and informal care.

Indirect costs represent lost productivity associated with morbidity, which may be related to work or non-work activities. Indirect costs usually represent a large proportion of total costs in most of the COI. Indirect costs are usually measured by two methods: Human Capital Approach (HCA) and Friction Cost Method (FCT). The results obtained with one and another are not comparable and the first estimates tend to be lower than the second. The HCA estimates the indirect costs associated with illness and premature death in terms of lost productivity (lost wages), thus excluding the costs of pain and suffering, leisure time and work on a voluntary. The FCT, which considers the amount people would pay to reduce their risk of injury, illness or death, this is subjective and can be difficult to use in children and the elderly, due to the complexity of the questions (4).

Intangible costs refer to patients' psychological pain of, discomfort, anxiety, depression, and stress related to disease or its treatment (5). These are difficult to quantify in monetary terms, therefore, they are usually omitted in COI studies or presented as quality of life.

3. Economic impact of disease

The first assessment about economic impact of SLE was published in 1994 and it was undertaken to assess both the cyclophosphamide (CYC) in intravenous cycles and prednisone PO impact for the treatment of severe lupus nephritis (6). The authors conducted a hypothetical cohort of patients considering the incidence of severe lupus nephritis for U.S. in 1988 (1130 patients). They calculated and compared the costs of prednisone as monotherapy vs. prednisone with intravenous CYC, the rate of renal failure with each comparative option was also considered, as well as age, gender, and economic value of working years gained. The results found that although the costs of combination therapy are greater, the analysis shows an overall savings due to reduced need for dialysis or kidney transplantation, and the economic value of work capacity won. The savings attributable to the costs of patient care were $ 50.8 million and $ 42.3 million earned by working capacity. Finally, they conclude that for a period of 10 years, about $ 93.1 million to year-cohort is saved with the use of combination therapy for treatment of severe lupus nephritis.

Clarke et al (7) presented a study to compare the costs of health care and health status of patients with SLE in three countries (Canada, U.S. and UK), which have different health systems and financing. 708 patients with SLE were involved in 2 centers for each country (Canada 229, UK 268 and U.S. 211), they were evaluated about activity and damage of the disease and information on physical and psychological well-being, satisfaction, social support, and utilization of health resource. All of the costs were calculated using Canadian dollars for 1997. After adjusting for covariate representatives, the Canadian patients, compared with the British and Americans, reported a significantly higher health status in 3 of 8 sub-scales of the SF-36. In general, the annual use of health resources was not significantly different, with an average annual cost per patient of CAD $ 4,853, $ 5,285 and $ 4,760 for Canada, USA and UK, respectively. However, it was found some differences within each resource category. Canadians visited more specialists than British, British visited more general physician. Canadians and Americans used more emergency services, Canadians had higher hospital costs than Americans, and Americans required more paraclinical tests and imaging services.

Zink et al, in 2004, in a comparative study of the disease burden in SLE and rheumatoid arthritis (RA), analyzed retrospectively data of 1,248 patients with SLE and 10,068 patients with RA, who were seen by rheumatologists in 2001. Significant differences were observed in patients who were treated by the rheumatologist; patients with SLE were treated mainly with antimalarials (37%), azathioprine (29%), 61% of patients received at least one immunosuppressive medication plus steroids. In AR, Methotrexate was the drug most used in 63% of patients. A matched analysis showed that SLE patients with a short duration of the disease had pain, functional limitations and general deterioration of health, as well as patients with RA; however, in patients with disease duration of more than ten years, deterioration in health status, was greater in patients with RA. The authors report that in the early stages of both diseases, related costs of health care and burden of disease are similar, but in chronic disease, RA significantly increased costs in relation to pain, poor overall health state and disease activity, as well as greater severity classified by the specialist, suggesting a better long-term prognosis in SLE in the areas observed. Regarding the current treatment, showed an impact when the two diseases are treated by rheumatologists since onset-disease (8).

The same author Clarke et al in 2004, published an interesting study which sought to determine whether the consumption of health resources are correlated with outcome in the health status of SLE patients in three developed countries: USA, UK and Canada. 715 patients were surveyed semi-annually (Canada 231, U.S. 269, and UK 215) to determine the utilization of health resources and outcomes in health status. In 2002, the average cumulative costs per patient over 4 years were CAD $ 15,845, $ 20,244 and $ 17,647 for Canada, USA, and UK respectively, they experimented similar outcomes in health. After adjusting differences in input data, on average, Canadian and British patients utilized 20% and 13% less resources than American patients, respectively. The authors comment that despite incurring higher health expenditure, American patients did not experiment great results in health (9).

Grootscholten C et al in 2007 (10) developed a prospective randomized controlled study to measure the effect of treatment with CYC pulses or azathioprine (AZA) plus methylprednisolone (MP) for a period of 24 months, evaluating health-related quality of life (HRQOL) of patients with Proliferative Lupus Nephritis (PLN). This study measured HRQOL and disease activity at the beginning and after at 12 and 24 months. It was applied the Visual Analog Scale (VAS), SF-36, and a questionnaire to measure activity disease (SLEDAI). The impact of treatment was measured 24 months later and disease activity was measured with the SLEDAI and physician's VAS. They included 87 patients, and only 47 of them completed the questionnaires. HRQOL improved significantly with treatment, particularly during the first year; however, there were no significant differences between the group treated with CYC and AZA/MP; on the other hand, there was a strong favorability in the group treated with AZA/MP when SF-36 was applied. The average reported in the impact on treatment within 24 months was significantly higher in the group treated with CYC. HRQOL was not correlated neither with the SLEDAI nor the physician's VAD. This study concluded that treatment of PLN patients with immunosuppressive drugs and corticosteroid improve QOL, particularly in the first year and this effect was sustained in the second year of treatment. But because such a small sample and lack of differences in HRQOL between CYC and AZA/MP groups, these results should be interpreted with caution. The CYC-treated group showed a high impact on the budget. Data from this study do not support the use of AZA/MP as first line treatment for PLN, but this could be an alternative for women who wish to become pregnant. They propose future studies with Mycophenolate Mofetil and low-dose CYC as therapeutic alternatives in these patients.

An interesting evaluation performed by Campbell et al (11), involved the impact of SLE on working capacity. This study evaluated the status of work (such as job loss, changes in the amount worked) and predictors of job-loss in patients with SLE. The patients with onset-disease recently diagnosed were included, followed-up at least two years and matched by sex and age. Patients were followed-up for an average of 4 years from diagnosis. Work history was obtained through a personal interview during the recruitment and through telephone interviews to follow-up. The authors highlight an important difference for working withdrawals during follow-up between SLE patients and controls (26 vs. 9%, $p < 0.0001$). 92 of SLE patients showed that the cause of abandonment was related to their health status. Patients with SLE who had arthritis were three times more likely to quit their jobs due to changes in health compared with those who did not have arthritis (adjusted OR 3.3 IC95% 1.1 to 8.8). Finally, an association with the presence of pleuritis was founded (adjusted OR 2.3 95% 1.1 to 4.6).

4. Cost-of-illness studies in SLE

Until the last century the most studies in SLE tended to ignore the evaluations that included both loss of productivity in work activities and diary live activities and they focus only on direct costs such as number of hospitalizations and health status measures.

In 1993, Clarke et al (12) published the first assessment which identified the direct and indirect costs of 164 patients with SLE who entered to the Lupus register of Montreal General Hospital between January 1977 and January 1990; they compared the costs with the general population of Quebec and also determined the predictors of costs. The estimated cost was $ 13,094 CAD in 1990, of which 54% represent indirect costs ($ 7,071). In average, SLE hospitalizations were 4 times more frequent than general population of Quebec (matched by gender and age), and the number of outpatient visits were twice than which represented by the general population. The best predictors of direct costs were high levels of creatinine and poor level of physical performance. A poor level of well-being, a combination of education level and employment status, and poor social support were the best predictors for indirect costs.

Clarke et al, in 2000, carried out an indirect costs analysis and it was calculated as a result of decreased productivity in women with SLE. Indirect costs incurred by women with SLE were calculated obtaining the costs from labour and non-labour activities decreased. Six hundred forty-eight women with SLE reported their employment status and time lost for themselves and their employers as well as non-labour activities over a period of 6 months. The average annual indirect costs ranged from $ 1,424 to $ 22,604 CAD to 1997, and they depended on the value assigned to the labour market and non-labour activities (13).

Sutcliffe et al, in 2001, determined the direct costs, indirect costs and predictors in patients with SLE. 105 patients with SLE completed the questionnaires about using of health services and employment history. A multiple regression analysis determined predictors of costs. Direct, indirect and total costs were the depending variables, and demographic data, health status, disease activity, target organ damage, social support and satisfaction with care were used as predictors. The average total annual cost per patient was £7,913. Direct costs were a third of the total costs and indirect costs represented 2/3 of total cost. A good level of education, greater disease activity and reduced physical function were associated with increased direct, indirect and total costs. The major direct costs are also associated with greater impairment and younger age of onset-disease. The authors conclude that SLE has a considerable impact on the health system and society. Improving disease activity and physical health, as well as the prevention of organ damage can significantly reduce costs in SLE (14).

In 2001, Clarke et al compared the direct and indirect costs of care for SLE patients in Canada, USA and UK. In general, the cost of care of patients with SLE is cheaper in UK, because of fewer resources used and number of hospitalizations reduced; however, a significant statistical difference were not found. Additionally, indirect costs of SLE increased dramatically the cost of the disease was another finding. When indirect costs included only job loss, the cost per patient was $ 10,000 a year and if it is considered household task, the cost increased to $ 22,000 (4 times the annual direct costs) (15).

A comparative assessment of costs of rheumatic diseases was made in Germany. In this study, Li et al, in 2006 (16) estimated and compared direct and indirect costs of illness in Rheumatoid Arthritis (RA), Ankylosing Spondylitis (AS), Psoriatic Artritits (PA) and SLE; they evaluated the gender, disease duration and functional status effect on various costs

domains. Data were extracted from the German national data set from 1993. The costs were calculated for each patient for the last twelve months prior to recruitment date. The direct costs were € 4,737 per year in RA, € 3,676 in EA, € 3,156 in PA and € 3,191 SLE. Costs increased with duration of disease and they were heavily dependent on functional status. Compared with RA, drug costs in SLE were less than half; patients with AS and PA had less treatment costs in hospitalized patients for acute complications than those with RA and SLE. Calculating the indirect costs were higher in SLE (€ 11.220), followed by AR (€ 10,901).

Panopalis et al in 2007 compared cumulative indirect costs over 4 years in the care of patients with SLE in the U.S., Canada and UK. They surveyed a total of 715 patients with SLE (269 U.S., 231 in Canada and 215 in UK) at baseline and semi-annually, during four years (May 1999-October 2001). Participants completed questionnaires about the use of health resources, employment status, lost work days and lost time spent by caregivers on administrative procedures to access health services and / or daily household tasks. Annually, the patients reported surveys about quality of life, social support, and satisfaction with care. This study is a cross-national comparison of indirect costs in SLE, this is valuable information due to the difficulty of measuring indirect costs and the importance they represent because they contribute to a high percentage of total costs in SLE. The authors found that indirect costs accounted for 74% of total costs, being significantly higher in American patients, and this increase corresponded to the additional labour hours that patients would have worked, if they had not been ill. The authors concluded that indirect costs represent a significant proportion of total costs in the care of patients with SLE and they suggest that among SLE economic evaluations should include indirect costs attributed to productivity lost (17).

Clarke et al in 2008 compared the costs and quality of life among patients with SLE with and without kidney damage; the authors evaluated 715 patients through a semi-annualized interview during four years, in order to determine the use of medical services, loss of productivity and annually the quality of life. The accumulated direct and indirect costs and quality of life (analyzed through the SF-36) were compared between SLE patients with and without renal damage, through of Damage Index for SLE from System Lupus International Collaborating Clinics/ACR. On this scale was considered 0, one patient without renal impairment; 1, with a glomerular filtration rate or creatinine clearance less than 50%; 2, proteinuria greater than 3.5 g; or 3, end-stage kidney disease. Each criterion should be present in at least six months to be considered as kidney damage. Cumulative average direct costs per patient in 2006 were CAD $ 20,337, $ 27,869, $ 51,191 and $ 99,544 for stages 0-3 respectively. For every increased unit on renal damage, it was associated with an increase on average of 24% on direct costs through regression analysis. In addition, patients with end-stage renal disease incurred 103 % more than those without kidney damage. Cumulative indirect costs, lost productivity and the annual change in SF-36 did not show difference between patients (18).

Panopolis et al estimated health care costs and costs associated with changes in labour productivity among people with SLE in the U.S. The data were derived from the University of California. Participants provided information on the use of health resources and employment. Estimations about costs were derived for both of health care costs and costs related to changes in labour productivity. Direct health care costs included hospitalization costs, emergency service use, doctor visits, ambulatory surgery, dialysis and drugs. Productivity costs were calculated by measuring the decrease of productive working hours

since onset SLE disease, although these estimates were also compared with general data from U.S. population. For all participants, the average annual direct costs were $ 12,643 (2004, U.S. dollars). The average annual costs of the productivity in working-age people (> or = 18 and <65 years) were $ 8,659. The average total annual costs for working-age were $ 20,924. The increase of disease activity, a longer duration of illness, and mental and physical health impairment were significant predictors of increase in direct costs, because to changes in labour productivity. The authors concluded that the direct costs and costs associated with changes in labour productivity are important and they represent an important contribution to the total costs associated with SLE (19).

Carls et al in 2009 estimated the medical costs related to the productivity of SLE and Lupus Nephritis (LN) in a population of employees between 2000 and 2004. These costs were compared with other chronic diseases costs. The average annual medical expenses and the short-term costs given by disabilities for patients with SLE were US (2005) $ 12,238 and $ 1,184 respectively, in comparison to control diseases. The average medical expenses in LN patients were $ 46,862 higher than the controls. Compared with other chronic health conditions that occurred in this group of employees, SLE / LN was the most expensive condition. The authors conclude that SLE, particularly with LN, is associated with significant costs. The treatment that lead to manage earlier and effective to the patients with SLE, it can result in an important decrease of costs, if they are started on time in order to reduce complications that generate more costs of care (20).

In another study, Zhu T, et al in 2009 determined the direct and indirect costs for patients with SLE in a rheumatology center in Hong Kong. They determined the relationship between Neuropsychiatric SLE (NP-SLE) and costs of the disease through a retrospective cross-sectional, non-randomized study. All participants completed questionnaires on demographic data, employment status and personal expenses. The consumption of health resources was registered in a file.

The onset of NP-SLE since the beginning of SLE was determined using the 1999 ACR criteria. Costs of the disease among patients with and without NP-SLE were compared by the Mann-Whitney test and the predictors of costs were obtained by a multiple linear regression analysis. 306 Chinese patients were recruited with an average age of 41 years and the disease duration of 9.6 years. There were a total of 108 events of NP-SLE in 83 patients. The most common manifestations were seizures and cardiovascular disease. The total annual costs were US $ 13,307 per patient. Direct costs dominated total costs, and hospital care costs accounted for 52% of direct costs. Patients with NP-SLE incurred in direct and indirect costs significantly higher when they were compared to those without NP-SLE. The number of events NP-SLE was an independent variable associated with direct and indirect costs. So, the implementation of an intervention in the prevention of organ damage, especially in neuropsychiatric manifestations may reduce the costs of patients with SLE (21).

In another study, in 2009, Li et al estimated the direct medical costs to long-term of SLE patients and a subgroup of patients with SLE and LN. Active SLE patients of a large database and during this monitoring period, 2298 patients and a control group between 1999 and 2005 were included. The average annual medical costs for patients with SLE were higher than in the control group in the first year (US $ 16,089 vs. $ 6,831, respectively). Costs decreased slightly in the second year but increased 16% annually for five years to $ 23,860. LN patients (n = 489) were USD $ 13,228 - $ 34,907 higher than the control patients and the hospitalization rate in the subgroup with LN was 0.6 to one per capita, which was double

compared with SLE patients without LN, and 3 to 4 times higher than the control group. This study concluded that SLE is an expensive condition, and medical expenses increased steadily over time, particularly for patients with LN SLE (22).

Zhu T et al in 2009 (23) assessed the direct and indirect costs of flare SLE patients and non-flare SLE patients from a social perspective in order to investigate the severity impact and the direct and indirect costs from flare clinical manifestations. The authors defined as activity 3 points or more in SELENA – SLEDAI, and 4 points or more in the BILAG, being this between 0 and 105 (maximum activity). Mild or moderate relapse was defined as one or more of the following:

1. Change in SELENA - SLEDAI of three points.
2. Worsening discoid lesions or new lesions, photosensitivity, cutaneous vasculitis, nasopharyngeal ulcers, pleuritis, pericarditis, arthritis or fever.
3. Increase of prednisolone dose without exceeding 0.5 mg / kg / day.
4. Necessity of adding or increasing NSAID or hydroxychloroquine.

While severe relapse was defined as:

1. Change in SELENA-SLEDAI twelve-points.
2. New or worsening vasculitis, nephritis, myositis, thrombocytopenia less than 60,000 or anemia with Hb less than 7, requiring increase prednisolone dose to 0.5 mg / kg / day
3. Use of new immunosuppressive agents.
4. Hospitalization for SLE.

A validated physical index consists of 41 items in 12 organs frequently used to measure the accumulated damage was used to measure damage (Systemic Damage Index -SDI). Damage was defined as any irreversible change occurred since the onset-disease of SLE which is observed for at least 6 months. The total SDI scores ranging from 0 to 49. They also defined each of the activities according to the organ involved.

This was a retrospective study of the disease costs; 306 Chinese patients between 18 and 65 with SLE were included and recruited between January 2006 and August 2007. Participants completed questionnaires on demographic data, employment status, and out-of-pocket expenses. The consumption of health resources was recorded in a questionnaire that patients self-reported. Total number of flares and the organs affected in the last 12 months were recorded. The authors found that patients with flare were younger with a shorter duration of illness and a higher disease activity at the evaluation time. The overall incidence of lupus flares was 0.24 episodes per patient-year. Patients with flares used more frequently health resources and increased significantly the direct and indirect annual costs.

The total average costs per patient-year were two times higher for patients with flare (USD 2006 $ 22,580 versus $ 10,870, $p < 0.0005$). A multiple regression analysis showed that the number of relapse was an independent variable that leads to increase direct costs. Patients with renal / neuropsychiatric flare had higher direct costs compared with those with single-organ flare. The main conclusion of this study was that patients with flare incurred higher direct and indirect costs compared with those without crisis. The main organs affected by flares were renal and neuropsychiatric whose patients incurred higher costs for the disease than flares of other organs. The treatments that control effectively the disease activity and prevent relapses, especially the flare in vital organs, may reduce the high costs associated with relapse in SLE.

In Colombia, Quintana et al (24) conducted a study to determine the direct costs of health care for the first year of treatment for LN, based on the classification system of the

International Society of Nephrology / renal Pathology Society (ISN / RPS) (25); it is the first assessment that discriminates on type of renal histopathologic injury, finding a cost of $ 1,160 (USD, 2009) for LN type I and II; the type III and V share the same costs of $ 3,498 using the EUROLUPUS scheme in induction and maintenance with azathioprine (AZA). In case of use of mycophenolate (MMF), the costs increased to $ 13,646 for type III LN and $ 14,161 for the LN type V. In type IV the cost was $ 3,499 using the EUROLUPUS scheme and maintenance with AZA. The costs amount to $ 14,163 if is used MMF for induction and maintenance.

5. Complete pharmacoeconomic evaluations

Wilson et al in 2007 conducted a study that sought to determine whether the results of LN treatment with MMF, represented a positive impact on quality of life (QoL) and a better use of resources. The authors created a simulation model to estimate the costs of quality-adjusted life year (QALY) of a LN patient treated with intravenous Cyclophosphamide (CYC) or with MMF for an adjusted period of six months. The efficiency, quality of life, resource uses and cost data were obtained from literature and standard databases and where necessary, data were supplemented by expert opinion. The model predicts that the use of MMF improved the quality of life compared with intravenous CYC. In addition, MMF is less expensive than CYC, at a cost of £ 1.600 (€ 2,400, $ 3,100), a lower cost based on 2005 prices the National Health System. The additional price in the application of intravenous of CYC was the main determinant of this variation. The sensitivity analysis shows a 81% probability that the use of MMF is more cost effective compared with intravenous CYC, with a willingness to pay £ 30,000 (€ 44,700, $ 58,500) per QALY gained. The authors of this study concluded that the use of MMF represented an improvement in the quality of life, and is less expensive than intravenous CYC as induction therapy for LN (26).

6. Conclusions

SLE costs are primarily determined by factors related to disease state such as: duration, disease activity, damage, and also the state of physical and mental health of patients which are influenced by the disease progression and the accumulated damage. The compromise of major organs such as nephritis and neuropsychiatric lupus, and relapses are also known factors associated with increased direct and indirect costs, independent of demographic factors. It is well-known that interventions that lead to the control of disease activity, prevent relapses, and delay the progression of the disease, can potentially save large amounts of costs attributable to the damage and the compromise of target-organ.

In the studies reviewed in this chapter were found large discrepancies in both direct and indirect costs, a situation that cannot simply be explained by demographic and clinical differences, across different populations. These discrepancies can be attributed to the absence of defined guidelines for cost-effectiveness analysis. It should be noted that there are great differences in the context of the costs, methods of costing, the health system, and practice patterns through studies. It should also be considered, the studies reviewed are derived from several different types of studies from different countries over a period of at least 16 years. Changes in the state of knowledge about disease, medical technology and practice patterns can have substantial influence on the estimate of the costs. It is important

to set out more studies to highlight the magnitude of the problem of SLE to society and people in different countries, and these studies should have innovative designs that will be able to resolve methodological lack found in some studies.
Nowadays, there are new therapies specifically routed to the immune system (Belimumab); these therapies can control the activity of the disease and prevent exacerbations of target organ in SLE. Their costs are probably much higher than conventional therapies. Given the substantial costs associated with SLE, it is expected that the potential benefits of these therapies offset their costs and new economic evaluations will give more information about the properties.

7. Key point section

1. SLE costs are related to health statement which is influenced by the disease progression and the accumulated damage.
2. Direct and indirect costs are influenced mainly by major organs compromise such as nephritis and neuropsychiatric lupus and flares.
3. Save large amounts of costs can achieve through the control of disease activity, prevent relapses, and delay the progression of the disease.
4. There are discrepancies in the results of both direct and indirect cost studies which can be attributed to the absence of defined guidelines for cost-effectiveness analysis
5. New studies are necessaries to innovate designs in order to resolve methodological lack found in before studies, including the new therapies like Belimumab.

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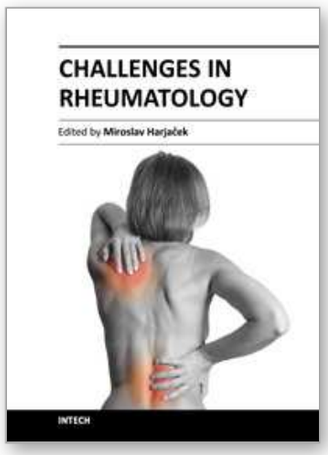
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Rheumatology is a subspecialty of medicine that focuses on the biology, cause, diagnosis and the treatment of a variety of musculoskeletal and other systemic diseases. The field of rheumatology is expanding rapidly and several very exciting developments have occurred during the recent years. Firstly, there has been a new dramatic understanding of the nature of inflammation and the possibility of specifically regulating the aberrant immune inflammatory response. Secondly, an understanding of pathogenesis has lead to the development of new, more targeted therapies. Challenges in Rheumatology has assembled an impressive group of international experts who have studied specific aspects of certain rheumatic diseases and have extensive experience either in pathophysiology, or with the in-depth diagnosis and/or management of rheumatic patients. They communicate their knowledge and experience to the reader in chapters that are conveniently organized as pathophysiology, clinical manifestations and diagnosis of selected rheumatic diseases, medical and perioperative orthopedic management, and the economic impact of rheumatic diseases. We hope that this book will help trainees become better physicians and scientists, and that it will help practicing rheumatologists to provide better care, and ultimately, improve the quality of life of our patients.

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