

Improving rheumatoid arthritis management within the Spanish National Health System: a social return on investment study

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Abstract

Objective

To define a set of proposals that would improve the current management of patients with rheumatoid arthritis (RA) within the Spanish National Health System (SNHS), and to estimate the impact of their implementation from a social perspective.

Methods

A one-year forecast-type Social Return on Investment (SROI) analysis was performed on the basis of information collected from a scientific literature review, official data, and multiple stakeholders regarding RA. A sub-analysis was performed within the areas of diagnosis, early RA (<2 years from diagnosis), and established RA (≥2 years from diagnosis).

Results

Stakeholders agreed on a set of 22 proposals, which included incorporating specialised nursing, addressing adherence issues, providing psychological support, or promoting the role of patient associations, among others. Their implementation would require an investment of 289 million euros and yield a social return of 913 million euros, i.e. a social return of 3.16 euros per euro invested (2.92 euros in the worst-case scenario and 3.40 euros in the best-case scenario). The greatest social return relative to investment and the greatest attributed to intangible aspects were observed within the area of early RA.

Conclusion

Evidence-based recommendations for the management of RA are aspirational. Nevertheless, the present study estimated that the implementation of the set of proposals would result in a positive impact relative to the investment needed to implement them. The results may guide management decisions to reduce the burden associated with RA, and help bridge the gap between evidence-based recommendations and routine clinical practice.

Key words

rheumatoid arthritis, practice guidelines, disease management, economic evaluation

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Introduction

Rheumatoid arthritis (RA) is a chronic, autoimmune, systemic, inflammatory disease (1, 2). Without proper management, the disease may progress toward joint destruction, disability, and reduced health-related quality of life (HRQoL) (2). The prevalence of RA in Spain is 0.9% (95% CI, 0.7–1.3) in adults on or over 20 years of age (3) and contributes greatly to the overall burden of disease (0.25%) with a rate of 63.81 disability-adjusted life years (DALYs) per 100,000 inhabitants according to the 2017 Global Burden of Disease study (4). This has been attributed primarily to the years lived with disability (YLDs) rather than the years of life lost (YLLs) (86.8% and 13.2% respectively) (4). While the latter have steadied over time, the YLDs and hence the rate of age-standardised DALYs per 100,000 inhabitants have shown a tendency to increase over time given the increase in life expectancy (2, 4, 5). Consequently, the future poses a great challenge on health care systems as more people will be living more years with RA (2, 5).

Alongside, the management of RA has changed substantially over the past few years with improved diagnostic and treatment strategies (2, 6-8). Largely, a treat-to-target (T2T) strategy has been recommended for the management of RA to achieve sustained remission or low disease activity. Moreover, classification criteria for RA have been modified to allow for an earlier diagnosis and to identify patients with undifferentiated arthritis with a high risk of developing persistent and/or erosive arthritis which should be treated with disease-modifying anti-rheumatic drugs (DMARDs) (1, 6). The early treatment with DMARDs, within the T2T strategy, may prevent, halt, or minimise joint destruction (7, 8), and significantly reduce early hospitalisation (9). Ultimately, the implementation of the T2T strategy aims to maximise HRQoL of patients with RA, further normalising function, activities, and participation within the patient's personal and environmental context (7, 10).

Despite significant progress in the clinical management of RA and the

availability of evidence-based clinical guidelines (2, 6-8), RA continues to present a considerable burden on patients and society (11). A large proportion of patients with RA and ongoing treatment are still being inadequately controlled (no remission or moderate-to-high disease activity) (12-14). These patients present higher levels of pain and depression, are more likely to experience flares, and have a greater work and activity impairment compared to those who are adequately controlled, resulting in significantly worse HRQoL and greater costs (11, 13). This may be attributed in part to recent observations of a large gap between evidence-based clinical guidelines and routine clinical practice (15-17).

In Spain, over 50% of patients with RA do not achieve sustained remission and rheumatology units barely implement evidence-based treatment strategies mainly due to lack of time to use disease activity indexes and difficulty performing frequent follow-up appointments (14, 17). Moreover, patients inform of the negative impact of the disease on their personal relationships and a general lack of understanding by others of the physical and emotional impact of the disease on the activities of the daily living; contrasting with the less impactful physician reports on the matter. Notably, while 32% of patients indicated having dropped their jobs due to RA, physicians reported this was the case in only 10% of patients (18, 19). This apparent lack of communication between patients and physicians highlights the need to comply with the overarching principles on the current RA management guidelines (8). In order to provide an optimal management of RA within the Spanish National Health System (SNHS), current barriers to the implementation of evidence-based clinical recommendations and patients' unmet needs must be identified and addressed, while comprehensively assessing their impact.

The Social Return on Investment (SROI) method provides a framework for a comprehensive evaluation of the social, environmental, and economic impact of interventions relative to the investment required to implement

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them (20-22). This method has been widely used to guide decision-making in health care areas such as oncology (23, 24), cardiology (25, 26), nephrology (27), neurology (28-30), dermatology (31), ageing (32, 33), or maternity (34, 35), among others (36, 37). To our knowledge, no other study to date has used the SROI method to assess the impact of interventions in rheumatology. Thus, the aims of the present study were: 1) to define a set of proposals that would improve the current management of patients with RA within the SNHS; and 2) to estimate the net impact of their implementation in the SNHS using the SROI method.

Materials and methods

The SROI framework comprises six sequential stages: 1) establishing the scope and identifying key stakeholders; 2) mapping outcomes; 3) evidencing outcomes and giving them a value; 4) establishing impact; 5) calculating the SROI; and 6) reporting, using, and embedding (20). The first four stages of this analysis were based on the collection of relevant quantitative and qualitative information from the scientific literature, official data, and expert consultation.

Expert consultation was carried out in-person through two separate meetings. In the first meeting, a Project Advisory Committee (PAC) defined the current management of patients with RA within the SNHS and identified key areas of analysis for the subsequent meeting: diagnosis, early RA (<2 years from diagnosis), and established RA (≥ 2 years from diagnosis). In the second meeting, a Multidisciplinary Working Group (MWG) defined a set of proposals to improve the current management of patients with RA within the key areas of analysis (Table I). To that end, the MWG was divided into three balanced subgroups to represent three distinct perspectives: physicians, other healthcare professionals, and patients. Each group defined a series of proposals which were subsequently discussed with the rest of the groups. Thereafter, MWG members individually rated each proposal according to their relevance for improving the current management of

Table I. Main stakeholders in rheumatoid arthritis management.

Multidisciplinary Working Group

Project Advisory Committee

Physician at rheumatology service
Head of rheumatology service
Head of ConArthritis*

Expert Committee

Primary care physician and coordinator of the *Grupo Nacional de Enfermedades Reumatológicas de la semFYC*[†] (semFYC National Group of Rheumatic Diseases)
Head of hospital pharmacy service
RA nurse specialist
Psychologist specialised in RA
Three health management professionals
Patient with RA
Informal caregiver of a patient with RA

*National patient association which represents patients with rheumatoid arthritis (RA), psoriatic arthritis, idiopathic juvenile arthritis, and spondyloarthritis. [†]semFYC (*Sociedad Española de Medicina de Familia y Comunitaria*, Spanish Society of Family and Community Medicine).

RA on a scale from 0 (“not important”) to 10 (“very important”) and scores were averaged. Finally, the proposals with the highest average score were selected for the SROI analysis. These proposals were individually scored by each member of the MWG regarding their impact on the patients’ different life domains from 0 (no positive impact) to 10 (large positive impact) to help outline the outcomes. Finally, proposals were discussed through three additional committees representing three regions of Spain. Each committee included rheumatology and health management professionals which assessed each proposal based on the current situation, and the feasibility, difficulties, and challenges regarding their implementation. To determine the impact associated with the implementation of the selected proposals in relation to the investment needed to implement them, a forecast-type SROI analysis with a one-year timeframe was performed.

First, to determine the required investment for the implementation of each proposal, the resources needed (medical or non-medical, and material or human) were identified and multiplied by their unit prices. The number and cost of these resources were obtained through the scientific literature, official data, public prices of health services of the Spanish autonomous communities, and market prices. Following the current convention on SROI methodology, no financial value was assigned to

the time patients and caregivers spend on interventions, as they are the main beneficiaries. Thereafter, the outcomes associated with the implementation of each proposal (positive or negative, and tangible or intangible) were identified and quantified through information provided by the MWG, the scientific literature, official data, public prices of health services of the Spanish autonomous communities, and market prices. Financial proxies were used to quantify intangible returns, namely, those without a market price. Moreover, returns were adjusted by deducting deadweight (percentage of return that would have likewise been obtained without the proposal), attribution (percentage of the return resulting from other activities independent from the proposal), and displacement (percentage of the return that would have displaced another return). Total investment and net social return were estimated for each area of analysis, and for the complete set of proposals. Finally, in the fifth stage of the SROI analysis, SROI ratios for the implementation of the complete set of proposals and within areas of analysis were calculated (Fig. 1). A SROI ratio greater than 1 was considered positive, meaning that the total impact was greater than the investment required for the implementation of a set of proposals. All prices were updated to 2017 euros according to the corresponding Consumer Price Index. Assumptions were used for missing data required for the

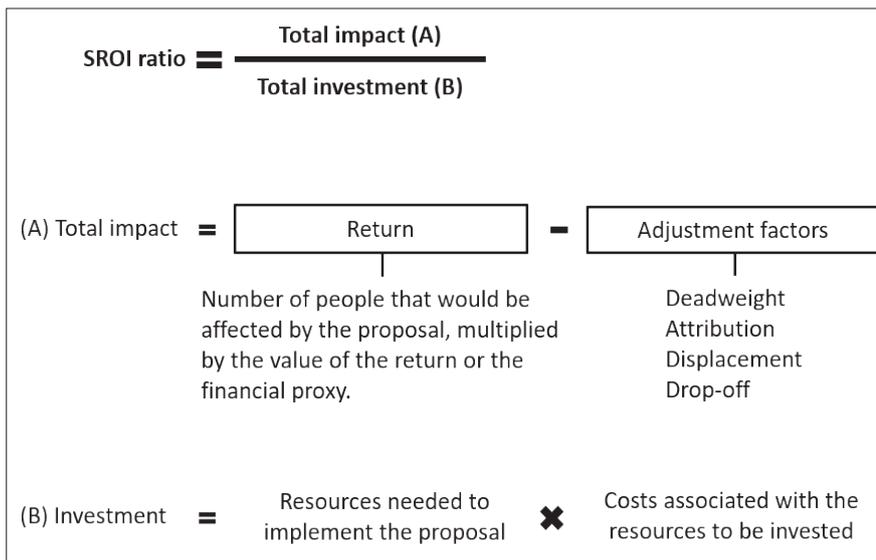


Fig. 1. Breakdown of the Social Return on Investment ratio.

estimation of investment or return, which were later included in a sensitivity analysis to determine the impact of their variation (best-case scenario and worst-case scenario) on results. Due to the nature of this project (SROI analysis based on information from the scientific literature, official data and expert consultation), it has not received institutional review board or other ethical review board approval. Study procedures were in accordance with the Helsinki Declaration of 1975/83.

Results

The MWG agreed on a total of 22 proposals, five of which were relative to the area of diagnosis, seven to early RA, and ten to established RA (Table II). Proposal number 6 has been used as an example of how outcomes were mapped and evaluated, and the impact was established according to the previously outlined stages of the SROI analysis. For a detailed analysis of each proposal refer to the Online Appendix. The aim of proposal 6 was to implement the T2T strategy, perform a tight control over patients with early RA, and expedite the treatment with DMARDs in order to control disease activity and improve prognosis. This would require investing on working hours of rheumatology professionals and nursing professionals with advanced skills in rheumatology (Appendix: Table 6). Furthermore, the implementation of pro-

posal 6 would reduce healthcare costs associated with remission, yielding a positive return which was estimated from the number of patients with early RA who would achieve remission with the implementation of the T2T strategy and the difference in cost between a patient with low disease activity and a patient in remission. The control over the disease would improve and physical function would be preserved, yielding a positive return which was estimated from the number of patients with early RA who would be well controlled with the implementation of the T2T strategy and the willingness to pay for a 50% improvement in physical function. However, negative returns were also associated with the implementation of proposal 6 which contemplated a reduction of patients' work productivity and an increase of caregivers' burden due to the time spent on additional medical visits, monetised through the average gain per normal working hour for the patient and through cost per hour of non-professional care for the caregivers. Finally, no adjustments were needed to establish the impact (Appendix: Table 28).

Taken together, the implementation of the 22 proposals in the SNHS would require an investment of 289 million euros (M€), most of which would be spent on the area of established RA (93.6%), followed by diagnosis (4.7%) and early RA (1.7%). Moreover, the implementation of these proposals would

yield a social return of 913 M€, most of which would be obtained from the area of established RA (95.2%), followed by early RA (3.3%) and diagnosis (1.6%) (Table III). The implementation of this set of proposals would result in a positive SROI ratio of 3.16 euros, whereby most of the social return would be attributed to intangible aspects (79%). In the areas of early and established RA, most of the social return would be intangible (*e.g.* reduced stress and anxiety, increased patient satisfaction with their treatment, improved personal/sexual relationships, or reduced caregiver burden, among others). Regarding the area of diagnosis, negative tangible returns would be compensated by intangible returns, yielding a positive SROI ratio.

The greatest SROI ratio was obtained in the area of early RA (Fig. 2). Within this area, the proposals with the highest impact were proposal number 6 on the implementation of the T2T strategy, tight control, and early treatment with DMARDs following diagnosis; proposal number 7 on the consideration of the patient regarding treatment plan decisions; and proposal number 12 on the comprehensive approach to care regarding other intangible aspects. Furthermore, within the area of established RA, the proposals with the highest impact were proposal number 20 on the use of a comprehensive, multidisciplinary, and individual approach to RA, ensuring access to other healthcare professionals; and proposal 13 on the implementation of the T2T strategy and tight control. Within the area of diagnosis, the proposal with the highest impact was proposal number 1 on the implementation of education and social awareness programs. This resulted in the largest intangible social return, associated with the improvement of the patients' emotional status as they would feel better understood by society.

The sensitivity analysis showed that the overall SROI ratio could vary between 2.92 euros in the worst-case scenario and 3.40 euros in the best-case scenario. Moreover, the greatest difference with respect to the reference case was observed in the area of established RA where the SROI ratio could vary between 2.96 in the worst-case sce-

Table II. Set of proposals by area of analysis.

Area of analysis	Proposal
Diagnosis	1 Education and social awareness programmes.
	2 Diagnostic training for Primary Care and Emergency Departments.
	3 Fast track access from Primary Care to Rheumatology.
	4 Fast track access from Specialised Care to Rheumatology.
	5 Psychological support following diagnosis.
Early RA	6 T2T strategies and tight control.
	7 Early treatment with DMARDs following diagnosis.
	8 Reach an agreement with the patient on the therapeutic plan to follow (pharmacological and non-pharmacological).
	9 Access to the rheumatologist without an appointment in case of out-breaks or decompensations.
	10 Nursing practice in rheumatology for early RA.
	11 Training on adherence and drug use in early RA.
	12 Training and adherence regarding non-pharmacological aspects associated with the disease for patients with early RA.
Established RA	13 Comprehensive approach to care regarding other intangible aspects.
	14 T2T strategies and tight control.
	15 Coordination between Primary Care and Specialised Care for the treatment and follow-up of the patient.
	16 Equity in access to all available marketed drugs.
	17 Nursing practice in rheumatology for established RA.
	18 Training on adherence and drug use in established RA.
	19 Training and adherence regarding non-pharmacological aspects associated with the disease for patients with established RA.
	20 Extension of Specialised Care working hours.
	21 Comprehensive, multidisciplinary, and individual approach, ensuring access to other healthcare professionals.
	22 Encourage the role of associations as a complementary element to the benefits of the National Health System.
23 Disability awareness: coordination of health and social care, and general social support.	

DMARDs: disease-modifying anti-rheumatic drugs; RA: rheumatoid arthritis; T2T: treat-to-target.

Table III. Investment and social return by areas of analysis.

Area of Analysis	Investment (M€)	Social Return (M€)
Diagnosis	13.67	14.29
Early RA	4.80	29.78
Established RA	270.44	869.21
Total	288.92	913.28

M€: million euros; RA: rheumatoid arthritis.

nario and 3.47 in the best-case scenario (Table IV).

Discussion

The present study established a set of 22 proposals to improve the current management of RA within the SNHS. The vast majority of these proposals, including those with the greatest social impact, are consistent with previously reported evidence-based recommendations on patterns of practice (2, 6-8). This suggests that current evidence-based recommendations are not being implemented within the SNHS. However, the present study has defined spe-

cific actions within each proposal that may close the gap between evidence-based recommendations and routine clinical practice.

Overall, the set of proposals within the area of established RA accounted for most of the total investment and the associated social return. While the area of established RA included the greatest number of proposals, social returns within this area may be the reflection of improvements within the area of diagnosis and early RA. Actions in these areas would be more likely to redirect the long-term course of the disease. In fact, a recent study showed that a higher de-

gree of adherence to quality-of-care indicators for early RA, specially to early treatment with DMARDs, significantly reduced the risk of early hospitalisation, a measure of failure for the RA care pathway (9). Moreover, basing pharmacological and non-pharmacological treatment strategies on joint decisions between the patient, the rheumatologist, and other healthcare professionals, generated the greatest social impact relative to investment. This proposal is an over-reaching principle for the treatment of RA and is of special relevance as it may improve adherence and acknowledges the patients' needs within their context (2, 6-8). Accordingly, specific actions have been recommended to successfully implement this proposal in the SNHS. Nevertheless, the optimal management of RA would require the implementation of the complete set of proposals. For example, including the patient in developing treatment strategies would not improve the management of the disease without the successful implementation of the T2T strategy and tight control of the disease. In fact, a recent study has observed that recommendations for the implementation of the T2T strategy are currently not being met within rheumatology departments in Spain (17), a strategy that the present study estimates would result in a positive social impact.

The hypothetical implementation of the set of proposals was estimated to yield a positive social return of 3.16 euros per euro invested, mostly attributed to intangible aspects (79%). This ratio is difficult to compare within the scientific literature since this is the first study to use the SROI method to assess the impact of interventions in rheumatology, with previous studies focusing mostly on the economic burden of the disease (11). Previous studies have shown a positive economic impact of treatment strategies in line with current evidence-based recommendations (38-40) or other type of interventions such as fall prevention programs (41). Accordingly, the implementation of a continuing medical education initiative to educate primary care physicians about the benefits of early diagnosis and treatment of RA resulted in a significant increase in early

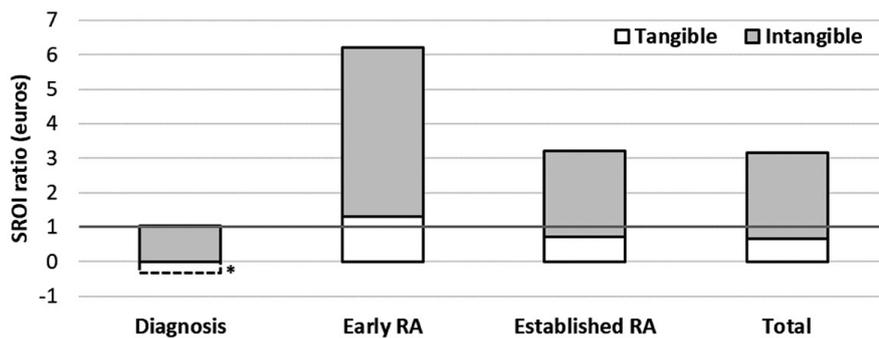


Fig. 2. Social Return on Investment Ratio (SROI) by areas of analysis and return typology. *Negative tangible SROI ratio. Tangible SROI ratio has been subtracted from intangible SROI ratio to obtain the SROI ratio for the area of diagnosis. RA: rheumatoid arthritis.

Table IV. Sensitivity analysis on the Social Return on Investment ratio.

Area of analysis	Worst-case scenario (€)	Reference scenario (€)	Best-case scenario (€)
Diagnosis	0.99	1.04	1.10
Early RA	6.20	6.20	6.21
Established RA	2.96	3.21	3.47
Total	2.92	3.16	3.40

RA: rheumatoid arthritis.

diagnosis, referral, and treatment of RA leading to remission, which would limit expenses due to reduced healthcare utilisation and productivity losses (38). Moreover, tight control of disease activity through the implementation of a biomarker disease activity test generated savings associated with improved patient health status, and increased labor force participation and work productivity (40). Similarly, tight control of disease activity through joint inflammation monitoring would generate savings compared to a non-tight-control (41). A recent study observed that one-year of treatment with biological drugs in naïve patients with RA reduced absenteeism, presenteeism and missed household work days (42), which could further reduce direct costs if biological therapy is maintained in time (43). However, none of these studies considered the quantification of intangible aspects such as pain, fatigue, sexuality, depression and anxiety, or suboptimal HRQoL associated to different treatment strategies which further contribute to the economic burden of RA (11). Intangible aspects accounted for most of the social return in the present study.

The SROI method involves stakeholders, those people or organisations who affect or are affected by the activities

within the scope of the analysis, providing a global perspective to the SROI analysis. Using multiple stakeholders related to RA rather than an individual stakeholder to reach an agreement on the proposals may better respond to the existing gap in the current management of patients with RA. Furthermore, including patients as stakeholders allows for the introduction of their perspectives into the identification and evaluation of proposals, accounting for intangible aspects which would have probably not been considered otherwise. Accordingly, the SROI method gives value to intangible aspects such as poor HRQoL which is common among patients with RA but is rarely considered for disease management.

Several limitations associated with the SROI method should be taken into account. First of all, the present study used a forecast-type SROI analysis with a one-year timeframe, displaying only the short-term impact associated with the implementation of the proposals. Moreover, this type of analysis provides an estimate of the potential social return. In addition, there is certain subjectivity inherent to the SROI method which has been associated with the configuration of the MWG, the selection of financial proxies for intangible aspects,

or the use of assumptions, among others. Nevertheless, the sensitivity analysis in the present study showed that the total SROI ratio, and within most areas of analysis, was still positive even in the worst-case scenario. While this was not the case for the area of diagnosis, it should be noted that positive ratios in other areas may be attributed in part to improvements resulting from the implementation of proposals in the diagnosis area.

The results of the present study may provide valuable information to guide decision-making. However, it should be noted these may vary depending on the setting (*e.g.* different countries) and how the evaluation method was applied (*e.g.* different sources of information). Accordingly, the activities associated with the complete set of proposals would most likely not be implemented as a whole outside the context of the present study. Moreover, specific activities that may be applicable to other contexts, may need to be modified to adapt to the new context. More importantly, the resulting SROI ratio would most likely change from one context to another. Previous systematic reviews including SROI analyses from different countries have shown a large variability in ratios obtained from the valuation of public health interventions, which seem to decrease with greater specificity of the intervention (*e.g.* healthcare interventions, healthcare management, physical activity and sports interventions) (36, 37, 44). Accordingly, more similar SROI ratios may be obtained from the implementation of proposals within the specific context of RA management in other countries which aim to achieve common standards of practice (8).

The present study has defined a set of proposals to improve the current management of RA within the SNHS that respond to current unmet needs regarding patients, caregivers, healthcare professionals, and the SNHS. The SROI analysis estimated that their implementation would entail a positive social impact. Nevertheless, future studies should consider performing an evaluative SROI analysis based on actual outcomes of the implementation of the set of proposals defined in the present study.

References

1. ALETAHA D, NEOGIT, SILMAN AJ *et al.*: 2010 Rheumatoid Arthritis Classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Ann Rheum Dis* 2010; 69: 1580-8.
2. GRUPO GUIPCAR: *Guía de Práctica Clínica para el Manejo de Pacientes con Artritis Reumatoide*. Madrid: Sociedad Española de Reumatología; 2019. Available at: <https://www.ser.es/wp-content/uploads/2019/03/Guia-de-Practica-Clinica-para-el-Manejo-de-Pacientes-con-Artritis-Reumatoide.pdf>. Accessed March 19, 2019.
3. SEOANE-MATO D, SÁNCHEZ-PIEDRA C, DÍAZ-GONZÁLEZ F, BUSTABAD S: THU0684 Prevalence of rheumatic diseases in adult population in Spain. *Episer* 2016 study. *Ann Rheum Dis* 2018; 77: 535.
4. INSTITUTE FOR HEALTH METRICS AND EVALUATION: Global Burden of Disease Study 2017 (GBD 2017) Results. *Glob Burd Dis Results Tool* 2020. Available at: <http://ghdx.healthdata.org/gbd-results-tool>. Accessed February 18, 2020.
5. SAFIRI S, KOLAH AA, HOY D *et al.*: Global, regional and national burden of rheumatoid arthritis 1990–2017: a systematic analysis of the Global Burden of Disease study 2017. *Ann Rheum Dis* 2019; 78: 1463-71.
6. COMBE B, LANDEWE R, DAIEN CI *et al.*: 2016 update of the EULAR recommendations for the management of early arthritis. *Ann Rheum Dis* 2017; 76: 948-59.
7. SMOLEN JS, BREEDVELD FC, BURMESTER GR *et al.*: Treating rheumatoid arthritis to target: 2014 update of the recommendations of an international task force. *Ann Rheum Dis* 2016; 75: 3-15.
8. SMOLEN JS, LANDEWÉ RBM, BIILSMA JWJ *et al.*: EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. *Ann Rheum Dis* 2020; 79: 685-99.
9. ZANETTI A, SCIRÈ CA, ARGNANI L, CARRARA G, ZAMBON A: Can the adherence to quality of care indicators for early rheumatoid arthritis in clinical practice reduce risk of hospitalisation? Retrospective cohort study based on the Record Linkage of Rheumatic Disease study of the Italian Society for Rheumatology. *BMJ Open* 2020; 10: e038295.
10. STUCKI G, CIEZA A, GEYH S *et al.*: ICF Core Sets for rheumatoid arthritis. *J Rehabil Med* 2004; 36: 87-93.
11. TAYLOR PC, MOORE A, VASILESCU R, ALVIR J, TARALLO M: A structured literature review of the burden of illness and unmet needs in patients with rheumatoid arthritis: a current perspective. *Rheumatol Int* 2016; 36: 685-95.
12. YUC C, JIN S, WANG Y *et al.*: Remission rate and predictors of remission in patients with rheumatoid arthritis under treat-to-target strategy in real-world studies: a systematic review and meta-analysis. *Clin Rheumatol* 2018; 38: 727-38.
13. TAYLOR PC, ALTEN R, GOMEZ-REINO JJ *et al.*: Clinical characteristics and patient-reported outcomes in patients with inadequately controlled rheumatoid arthritis despite ongoing treatment. *RMD Open* 2018; 4.
14. ACOSTA-MÉRIDA Á, NARANJO A, RODRÍGUEZ-LOZANO C: Prognostic factors for sustained remission in a “real life” cohort of rheumatoid arthritis patients. *Reumatol Clínica* 2018; S1699258X18302316.
15. BATKO B, BATKO K, KRZANOWSKI M, ZUBER Z: Physician adherence to Treat-to-Target and practice guidelines in rheumatoid arthritis. *J Clin Med* 2019; 8: 1416.
16. TAYLOR PC, ALTEN R, GOMEZ REINO JJ *et al.*: Factors influencing use of biologic therapy and adoption of treat-to-target recommendations in current European rheumatology practice. *Patient Prefer Adherence* 2018; 12: 2007-14.
17. ANDRÉU J-L, MARTÍN MA, COROMINAS H *et al.*: Treat-to-Target strategy in patients with rheumatoid arthritis: audit of adherence from real world clinical data. *Reumatol Clínica* 2019. Available at: <https://linkinghub.elsevier.com/retrieve/pii/S1699258X19301664>. Accessed February 21, 2020.
18. ELI LILLY AND COMPANY. #RAMatters | Página de inicio. 2017. Available at: http://www.ramatters.eu/es_ES. Accessed August 17, 2018.
19. LILLY. Presentación de los resultados españoles del estudio internacional RA Matters [Nota de prensa]. https://www.lilly.es/es/noticias/notas-de-prensa-sobre-terapias-2017/np_delaalarespana.pdf. Published June 26, 2017. Accessed August 24, 2020.
20. NICHOLLS J, LAWLOR E, NEITZERT E, GOODSPEED T: *A guide to Social Return on Investment*. Second. UK: The SROI Network. Accounting for Value; 2012. Available at: <http://www.socialvalueuk.org/app/uploads/2016/03/The%20Guide%20to%20Social%20Return%20on%20Investment%202015.pdf>.
21. NICHOLLS J: Social return on investment – Development and convergence. *Eval Program Plann* 2017; 64: 127-35.
22. YATES BT, MARRA M: Social Return On Investment (SROI): Problems, solutions ... and is SROI a good investment? *Eval Program Plann* 2017; 64: 136-44.
23. CASTRO CARPEÑO J DE, FÍRVIDA PÉREZ JL, LIANES BARRAGÁN P *et al.*: Cuantificando el beneficio de la sustitución por vinorelbina oral en los pacientes susceptibles de tratamiento con vinorelbina. Estudio del retorno social de la inversión. *Rev Esp Econ Salud* 2018; 13: 336-53.
24. LAING CM, MOULES NJ: “It’s not Just Camp!”: Understanding the meaning of children’s cancer camps for children and families. *J Pediatr Oncol Nurs* 2016; 33: 33-44.
25. DURÁN PIÑEIRO G, SÁNCHEZ CARREIRA MC, PEÑA GIL C *et al.*: El retorno económico y social de la e-interconsulta de cardiología en el área de Vigo. *ICEDE Work Pap Ser ISSN 2254-7487* 2015; 11: 1-28.
26. MERINO M, JIMÉNEZ M, MANITO N *et al.*: The social return on investment of a new approach to heart failure in the Spanish National Health System. *ESC Heart Fail* 2020; 7: 130-7.
27. LOPHONGPANIT P, TONGSIRI S, THONGPRASERT N: Social return on investment for patient treated by continuous ambulatory peritoneal dialysis: a case study in Ubon Ratchathani Province, Thailand. *Clin Outcomes Res* 2019; 11: 569-78.
28. WILLIS E, SEMPLE AC, DE WAAL H: Quantifying the benefits of peer support for people with dementia: A Social Return on Investment (SROI) study. *Dementia* 2018; 17: 266-78.
29. MORAL TORRES E, FERNÁNDEZ FERNÁNDEZ Ó, CARRASCAL RUEDA P *et al.*: Social value of a set of proposals for the ideal approach of multiple sclerosis within the Spanish National Health System: a social return on investment study. *BMC Health Serv Res* 2020; 20: 84.
30. JONES C, EDWARDS RT, WINDLE G: Social return on investment analysis of an art group for people with dementia. *Lancet* 2014; 384: S43.
31. CARRETERO G, MORENO D, GONZÁLEZ DOMÍNGUEZ A *et al.*: Multidisciplinary approach to psoriasis in the Spanish National Health System: A social return on investment study. *Glob Reg Health Technol Assess* 2020; 7: 50-6.
32. JONES RB, ASHURST EJ, ATKEY J, DUFFY B: Older people going online: its value and before-after evaluation of volunteer support. *J Med Internet Res* 2015; 17: e122.
33. SCHARLACH AE: Estimating the value of volunteer-assisted community-based aging services: a case example. *Home Health Care Serv Q* 2015; 34: 46-65.
34. GOUDET S, GRIFFITHS PL, WAINAINA CW *et al.*: Social value of a nutritional counselling and support program for breastfeeding in urban poor settings, Nairobi. *BMC Public Health* 2018; 18: 424.
35. BANKE-THOMAS A, MADAJ B, KUMAR S, AMEH C, VAN DEN BROEK N: Assessing value-for-money in maternal and newborn health. *BMJ Glob Health* 2017; 2: e000310.
36. BANKE-THOMAS AO, MADAJ B, CHARLES A, VAN DEN BROEK N: Social Return on Investment (SROI) methodology to account for value for money of public health interventions: A systematic review. *BMC Public Health* 2015; 15: 582-95.
37. MASTERS R, ANWAR E, COLLINS B, COOKSON R, CAPEWELL S: Return on investment of public health interventions: a systematic review. *J Epidemiol Community Health* 2017; 71: 827-34.
38. GAZELEY D, WEINBLATT M, BENDER S: Early diagnosis and treatment of RA: clinical performance and economic outcomes from a continuing education initiative. *Arthritis Rheumatol* 2017; 69. Available at: <https://acrabstracts.org/abstract/early-diagnosis-and-treatment-of-ra-clinical-performance-and-economic-outcomes-from-a-continuing-education-initiative/>. Accessed March 4, 2020.
39. NAIR SC, WELSING PMJ, JACOBS JWG *et al.*: Economic evaluation of a tight-control treatment strategy using an imaging device (handscan) for monitoring joint inflammation in early rheumatoid arthritis. *Clin Exp Rheumatol* 2015; 33: 831-8.
40. MICHAUD K, STRAND V, SHADICK NA *et al.*: Outcomes and costs of incorporating a multibiomarker disease activity test in the management of patients with rheumatoid

- arthritis. *Rheumatology* 2015; 54: 1640-9.
41. ABDULRAZAQ S, OLDHAM J, SKELTON DA *et al.*: A prospective cohort study measuring cost-benefit analysis of the Otago Exercise Programme in community dwelling adults with rheumatoid arthritis. *BMC Health Serv Res* 2018; 18: 574.
42. MANARA M, CAPORALI R, LOMATER C *et al.*: Impact of one-year treatment with biotechnological drugs on work ability in patients with rheumatoid arthritis in Italy: a prospective real-life study. *Clin Exp Rheumatol* 2021; 39(2): 263-8.
43. MARTÍNEZ-LÓPEZ-DE-CASTRO N, ÁLVAREZ-PAYERO M, SAMARTÍN-UCHAM *et al.*: Direct costs in patients with chronic inflammatory arthropathies on biological therapy: a real-world data study. *Clin Exp Rheumatol* 2021; 39(4): 736-45.
44. GOSSELIN V, BOCCANFUSO D, LABERGE S: Social return on investment (SROI) method to evaluate physical activity and sport interventions: a systematic review. *Int J Behav Nutr Phys Act* 2020; 17: 26.