The Value of Achieving Remission in Inflammatory Rheumatic Conditions

An Evidence Glossary

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GAfPA
Global Alliance for Patient Access

About

This evidence glossary summarises current research on inflammatory arthritis and the value of remission.

This document serves as a companion to the Global Alliance for Patient Access report entitled *The Value of Achieving Remission in Inflammatory Rheumatic Conditions* (April 2024).

The Global Alliance for Patient Access partnered with OPEN Health to compile the research highlighted in this glossary.

Prevalence

Prevalence will rise substantially

Rheumatoid Arthritis

- More than **18 million people** worldwide live with rheumatoid arthritis (RA).[1,2] Prevalence is twice higher among females than males.[3]
- This number will grow to nearly **32 million by 2050—an 80% increase—**as estimated by the Global Burden of Disease Study.[2]
- Certain regions have a projected increase of over 200%:
  - Eastern, central, and western sub-Saharan Africa
  - South Asia
  - Oceania
  - Southern sub-Saharan Africa.[2]

Spondyloarthritis

- The worldwide prevalence of spondyloarthritis (SpA)* is less well known. It has been estimated to range from 0.20% in South East Asia to 1.61% in northern Arctic communities.
- This means that about:
  - **13.1 million people** live with SpA in **East Asia**
  - **4.5 million people** live with SpA in the **United States**
  - **4.0 million people** live with SpA in **Europe.**[4]

* SpA includes ankylosing spondylitis, axial SpA, enteropathic SpA, peripheral SpA, psoriatic arthritis, and reactive arthritis.

1. World Health Organization. Rheumatoid arthritis: key facts. 28 June 2023. https://www.who.int/news-room/fact-sheets/detail/rheumatoid-arthritis
2. GBD 2021 Rheumatoid Arthritis Collaborators. Global, regional, and national burden of rheumatoid arthritis, 1990–2020, and projections to 2050: a systematic analysis of the Global Burden of Disease Study 2021. *Lancet Rheumatol.* 2023;5(10):e594-e610.
3. Cross M, et al. The global burden of rheumatoid arthritis: estimates from the global burden of disease 2010 study. *Ann Rheum Dis.* 2014;73(7):1316-22.
4. Stolwijk C, et al. Global prevalence of spondyloarthritis: a systematic review and meta-regression analysis. *Arthritis Care* Res. 2016;68(9):1320-31.

Impact

Musculoskeletal diseases are **debilitating**

- Inflammatory rheumatic conditions are members of the larger family of musculoskeletal (MSK) diseases. **The burden of MSK diseases increased significantly** between 2000 and 2015, according to a systematic analysis of the World Health Organization burden of disease database, which covers 183 countries. The burden is seen in the increase from 80 million to 108 million disability-adjusted life years (DALYs) in these years.
- MSK diseases were the **second cause of years lived with disability (YLDs)** in the world in 2015, after psychiatric disorders.[1]
- In the European Union (EU):
  - MSK diseases are the **primary cause of disability.**[2]
  - Up to half of member states' working-age populations could be diagnosed with a chronic MSK disease by 2030.[2]
  - **Half of all absences** are due to MSK diseases.[3]
  - **60% of permanent work disability** is due to MSK diseases.[3]
- The rise in burden is particularly stark in high-income countries, which have a long life expectancy and a high older-to-younger people ratio. Due to the overall improvement of medical care and rapid shifts in lifestyle-associated risks, such as smoking, obesity, and reduced physical activity, however, a similar rise is expected in lower-income countries.[4]
- In the United Kingdom (UK), an example of a high-income country, the MSK conditions are part of the Major Conditions Strategy, with **early diagnosis, early intervention, and quality treatment** highlighted as main strategies.[5]
- In the UK's political debate, it is recognized that, besides the humanistic impact of illness itself, it can lead to **unemployment** and **impoverishment,** as well as substantial costs to the state in the form of social security and NHS spending. **'It is a matter of economic vitality.'**[6]

1. Sebbag E, et al. The world-wide burden of musculoskeletal diseases: a systematic analysis of the World Health Organization burden of diseases database. *Ann Rheum Dis.* 2019;78(6):844-48.
2. Cross M, et al. The global burden of rheumatoid arthritis: estimates from the global burden of disease 2010 study. *Ann Rheum Dis.* 2014;73(7):1316-22.
3. Why early management of chronic disease in the EU workforce should be a priority: a call for action for the Latvian presidency of the EU & member states.
4. Sebbag E, et al. The world-wide burden of musculoskeletal diseases: a systematic analysis of the World Health Organization Burden of Diseases Database. *Ann Rheum Dis.* 2019;78(6):844-48.
5. Department of Health & Social Care. Major conditions strategy: case for change and our strategic workforce. 21 Aug 2023. https://www.gov.uk/government/publications/major-conditions-strategy-case-for-change-and-our-strategic-framework/major-conditions-strategy-case-for-change-and-our-strategic-framework--2
6. UK Parliament. Musculoskeletal conditions and employment. 10 Jan 2024. https://hansard.parliament.uk/commons/2024-01-10/debates/0ABAEE0C-A704-4A15-8362-7FD0D6B2020B/MusculoskeletalConitionsAndEmployment

Early Action

Acting early is crucial to prevent long-term disability

- Acting early in inflammatory MSK diseases can avoid irreversible damage from disease. In 2010, it is estimated that RA caused **4.8 million DALYs** worldwide.[1]
- A study from the United States found that people with RA experience a significantly **higher risk of death, with 27% excess mortality.**[2]
- While people with RA frequently also suffer from other diseases, it has been proven that RA itself, regardless of the presence of comorbid disease, is significantly associated with mortality.[3]
- Though the disease still lessens life expectancy, **today people with RA are living longer than ever before,** mainly due to improved medication. This means that they may spend **many years facing disability.**
- Years lived with disability is the largest contributor to the 4.8 million DALYs worldwide. That's equivalent to 4,800,000 healthy life years lost.[1]
- Though early intervention is crucial, too few patients recognize this fact. In the UK, 50%-75% of people with RA delay seeking medical healthcare for 3 months or more. After that, patients visit their general practitioner on average 4 times before being referred. This accumulates to an average of **9 months from symptom onset to treatment.**[4]

1. Cross M, et al. The global burden of rheumatoid arthritis: estimates from the global burden of disease 2010 study. *Ann Rheum Dis.* 2014;73(7):1316-22.
2. Gabriel SE, et al. Survival in rheumatoid arthritis: a population-based analysis of trends over 40 years. *Arthritis Rheum.* 2003;48(1):54-58.
3. Navarro-Cano G, et al. Association of mortality with disease severity in rheumatoid arthritis, independent of comorbidity. *Arthritis Rheum.* 2003;48(9):2425-33.
4. NAO. Services for people with rheumatoid arthritis. 15 Jul 2009. https://www.nao.org.uk/reports/services-for-people-with-rheumatoid-arthritis/

Benefits of Remission

Achieving remission is a game-changer for patients and healthcare systems

Approaching inflammatory diseases *only* from a broad MSK angle is not doing right by those with inflammatory conditions. Such strategies are often geared towards lower back pain and osteoarthritis, and the accompanying physical therapy, surgery, and workplace adjustments.

People with inflammatory arthritis currently are not given optimal care:

- Treatment is frequently not initiated within the therapeutic window of 12 weeks.[1]
- Of those receiving medical treatment, 70% do not achieve remission.[2]

For inflammatory conditions, **the aim should be prevention through early diagnosis and a 'treat-to-remission' approach,** with remission being the absence of disease signs and symptoms.

Achieving remission is a game-changer for both individuals and healthcare systems and should be a goal for public health officials.

Benefits of Remission

Work Productivity

37%-75% gain[3,4,5]

Medical Care Expenditures

19%-52% savings[5]

Improved Outcomes

Better physical health, i.e., less pain and fatigue, and improved mental status[3,6,7,8,9]

1. NAO. Services for people with rheumatoid arthritis. 15 Jul 2009. https://www.nao.org.uk/reports/services-for-people-with-rheumatoid-arthritis/
2. Yu C, 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.* 2019;38(3):727-38.
3. Radner H, et al. Remission in rheumatoid arthritis: benefit over low disease activity in patient-reported outcomes and costs. *Arthritis Res Ther.* 2014;16(1):R56.
4. Miranda LC, et al. Finding Rheumatoid Arthritis Impact on Life (FRAIL Study): economic burden. *Acta Reumatol Port.* 2012;37(2):134-42.
5. Ostor AJ, et al. value of remission in patients with rheumatoid arthritis: a targeted review. *Adv Ther.* 2022;39(1):75-93.
6. Curtis JR, et al. Patient perspectives on achieving treat-to-target goals: a critical examination of patient-reported outcomes. *Arthritis Care Res (Hoboken).* 013;65(10):1707-12.
7. Ishida M, et al. Residual symptoms and disease burden among patients with rheumatoid arthritis in remission or low disease activity: a systematic literature review. *Mod Rheumatol.* 2018;28(5):789-99.
8. Kekow J, et al. Improvements in patient-reported outcomes, symptoms of depression and anxiety, and their association with clinical remission among patients with moderate-to-severe active early rheumatoid arthritis. *Rheumatology (Oxford).* 2011;50(2):401-409.
9. Son CN, et al. Sleep quality in rheumatoid arthritis, and its association with disease activity in a Korean population. *Korean J Intern Med.* 2015;30(3):384-90.

BENEFIT #1

Remission Allows People to **Work**

One of the most compelling benefits of remission is how it enables people to be **more productive in daily life.**

When people are no longer burdened by the debilitating effects of inflammatory arthritis, they can be more active in the workforce. In contrast, people who cannot achieve remission may find themselves in a cycle of disability benefits and unemployment. This not only affects their financial independence but also strains social welfare systems.

Increasing the rate of remission empowers people to lead fulfilling and economically productive lives, benefiting them as well as society as a whole. The UK's National Audit Office has stated that 'Delay in treatment (of RA) is detrimental to patients' health, their quality of life and, with three quarters of people of working age when diagnosed, the economy.'[1]

Work disability, in other words early retirement, is the main driver of productivity losses. Avoidance or delay of early retirement can therefore result in substantial cost savings.

There are several ways to look at work productivity: productivity impairment, workdays lost and work disability.

Several studies quantify the lost workdays associated with inflammatory rheumatic conditions.

- **In the UK, the cost of working days lost due to osteoarthritis and RA were estimated at £2.6 billion in 2017** according to Versus Arthritis, which forecast that **the figure will rise to £3.4 billion by 2030.**[2]
- Also in the **UK,** the National Axial Spondyloarthritis Society estimated that a patient aged 26 who has waited 8.5 years for an **axial SpA** diagnosis is likely to **lose around £187,000** in their lifetime, the majority from a **loss of productivity** due to reduced employment.[2]
- A study of people with **RA** in **Argentina** found that **indirect costs due** to workdays lost were higher by a **factor of 2.3** in those with active disease compared with those in remission, using the best score group on the Health Assessment Questionnaire as a proxy for remission / as an approximation of remission.[3]

Both an **Austrian** and a **Japanese** study that looked at levels of **RA**-related impairment in people in the workforce found that **people in remission had less productivity impairment** than those with low disease activity (LDA) or medium/high disease activity (M/HDA).

1. NAO. Services for people with rheumatoid arthritis. 15 Jul 2009. https://www.nao.org.uk/reports/services-for-people-with-rheumatoid-arthritis/
2. UK Parliament. Musculoskeletal conditions and employment. 10 Jan 2024. https://hansard.parliament.uk/commons/2024-01-10/debates/0ABAEE0C-A704-4A15-8362-7FD0D6B2020B/MusculoskeletalConitionsAndEmployment
3. Secco A, et al. Epidemiología, uso de recursos y costos de la artritis reumatoidea en Argentina. *Rev Peru Med Exp Salud Publica.* 2020;37(3):532-40.

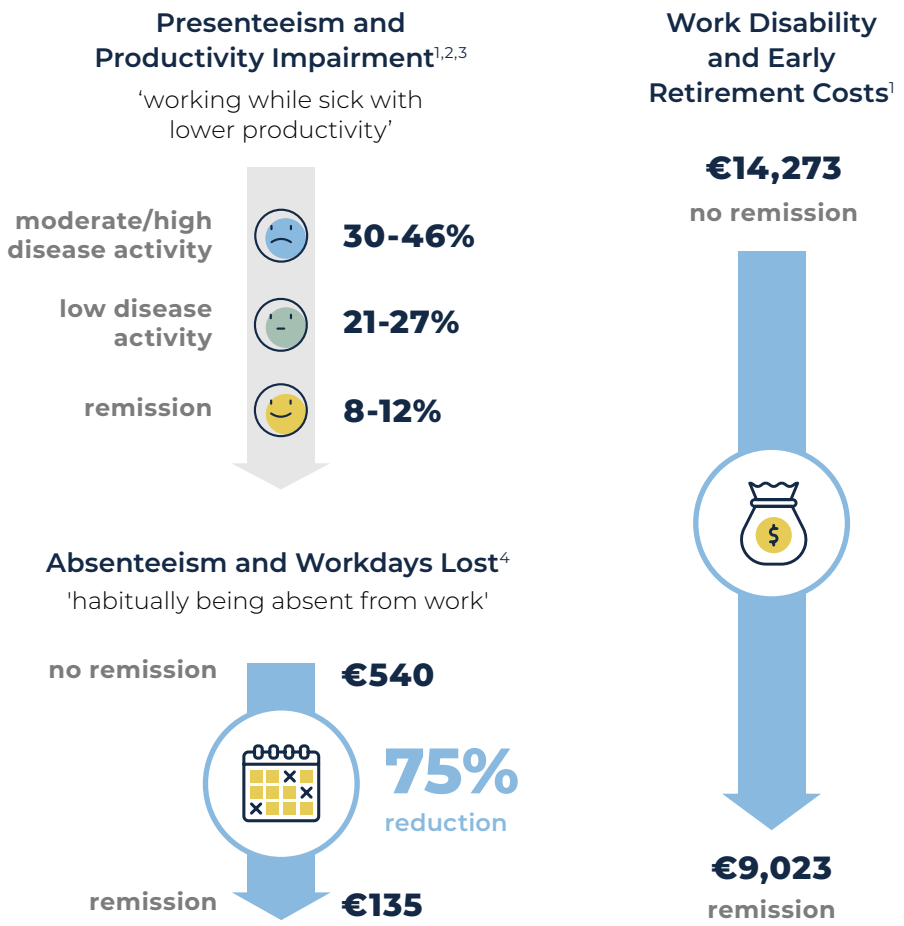
Compared with the productivity of a person without RA, someone in remission is only 8%-12% less productive; by contrast, those with LDA are 21%-27% less productive and those with M/HDA are 30%-46% less productive.[1,2,3]

- **Remission can reduce indirect costs, including losses in work productivity:**
  - In **Portugal, work productivity loss**—in terms of workdays lost, including those of family members—**was reduced by 75%** (namely, from €540 to €135) annually.[4]
  - **In Austria, remission was associated with reducing annual indirect costs** (namely, from €14,273 to €9,023). The Austrian study considered work productivity loss, including early retirement (work disability).[1] In fact, 34% of the retired study participants were in early retirement due to RA.[3]

Returning to the point made by the UK's National Audit Office, **investing in health, in prevention, in ability has a positive return on investment** by lowering welfare expenditure due to disability. While the case has been clearly made, namely that £11 million worth of investment in health would be more than compensated by welfare savings of £31 million, the cross-ministry impact has hampered action.[5]

Put crudely, from a societal perspective, high morbidity is more expensive than high mortality.

Annual Impact Per Person on Productivity



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2. Kim D, et al. Importance of obtaining remission for work productivity and activity of patients with rheumatoid arthritis. *J Rheumatol.* 2017;44(8):1112-17.
3. Radner H, et al. Remission in rheumatoid arthritis: benefit over low disease activity in patient-reported outcomes and costs. *Arthritis Res Ther.* 2014;16(1):R56.
4. Miranda LC, et al. Finding Rheumatoid Arthritis Impact on Life (FRAIL Study): economic burden. *Acta Reumatol Port.* 2012;37(2):134-42.
5. Bevan S. Reducing temporary work absence through early intervention: the case of MSDs in the EU. Fit for Work. The Work Foundation (part of Lancaster University).

BENEFIT #2

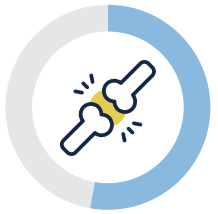
Remission **Reduces** Medical Care Expenditures

- There is a stark contrast in medical costs and healthcare resource utilisation between patients who reached remission and those who did not.
- **Patients in remission consistently had lower direct medical costs and less health care resource utilisation** compared with those without remission, according to a recent review in RA that covered 16 studies across 12 countries and 3 continents.[1]
- Remission was associated with **19%-52% savings** in direct medical costs.[1]
- Patients in remission were reported to have a median annual medical cost of €2464 (range €821 to €11,272) as compared with median costs of €4717 (range €1042 to €16,879) among those not in remission.[1]
- Cost savings associated with remission, compared with low or medium-high disease activity, were reported as €285 (20%) and €3,804 (51%), respectively.[1]
- The number of **hospitalizations was 64% lower** for people in remission compared to those with medium-high disease activity. **Joint surgeries were 53% lower and radiographs were 24% lower**.[2]

Hospitalizations

↓ **64%**
reduction

Joint Surgeries



↓ **53%**
reduction

Radiographs

↓ **24%**
reduction

1. Ostor AJ, et al. Value of remission in patients with rheumatoid arthritis: a targeted review. *Adv Ther.* 2022;39(1):75-93.
2. Boytsov N, et al. Increased healthcare resource utilization in higher disease activity levels in initiators of TNF inhibitors among US rheumatoid arthritis patients. *Curr Med Res Opin.* 2016;32(12):1959-67.

- Research in Argentina found that hospital costs among RA patients were 20 times higher among patients reporting within Health Assessment Questionnaire band 2.6-3.0 compared with those within band 0.0-0.5, where the latter band could be interpreted as a proxy for remission.[1]
- An Austrian study found annual medical costs for RA patients with low disease activity were 20% higher and with medium-high disease activity were 71% higher compared with those in remission.[2]
- A Colombian study found the direct medical costs 2.1 times greater in patients with severe RA disease activity compared with patients in remission.[3]
- A US registry analysis in psoriatic arthritis (PsA) and ankylosing spondylitis (AS)* assessed the impact of remission and found that patients without disease control were 3.0 (PsA) to 7.7 (AS) times more likely to have an inpatient visit.[4]
- Moreover, per-patient, per-year inpatient costs were found to be 3.5 times higher for patients with uncontrolled PsA versus those with controlled PsA.[4]
- Patients with AS in Central and Eastern Europe who achieved low disease activity status after 12 months had up to an 83% reduction in the number and length of hospitalizations, as well as a reduced number of healthcare provider visits.[5]

Lastly, it's worth noting that out-of-pocket expenses are substantial for people with uncontrolled inflammatory disease[6] and can consume close to 20% of the household income (US, 2009).[7] Out-of-pocket savings due to achieving remission come on top of the above-reported savings in direct medical costs.

* SpA includes ankylosing spondylitis, axial SpA, enteropathic SpA, peripheral SpA, psoriatic arthritis, and reactive arthritis.

1. Secco A, et al. Epidemiología, uso de recursos y costos de la artritis reumatoidea en Argentina. *Rev Peru Med Exp Salud Publica.* 2020;37(3):532-40.
2. Radner H, et al. Remission in rheumatoid arthritis: benefit over low disease activity in patient-reported outcomes and costs. *Arthritis Res Ther.* 2014;16(1):R56.
3. Santos-Moreno P, et al. Centers of excellence implementation for treating rheumatoid arthritis in Colombia: a cost-analysis. *Clinicoecon Outcomes Res.* 2021;13:583-91.
4. Bergman MJ, et al. Clinical and economic benefit of achieving disease control in psoriatic arthritis and ankylosing spondylitis: a retrospective analysis from the OM1 Registry. *Rheumatol Ther.* 2023;10:187–99.
5. Opris-Belinski D, et al. Impact of adalimumab on clinical outcomes, healthcare resource utilization, and sick leave in patients with ankylosing spondylitis: an observational study from five Central and Eastern European countries. *Drugs Context*. 2018;7:212556.
6. UK Parliament. Musculoskeletal conditions and employment. 10 Jan 2024. https://hansard.parliament.uk/commons/2024-01-10/debates/0ABAEE0C-A704-4A15-8362-7FD0D6B2020B/MusculoskeletalConitionsAndEmployment
7. Wolfe F, et al. Out-of-pocket expenses and their burden in patients with rheumatoid arthritis. *Arthritis Rheum.* 2009;61:1563-70.
8. Ostor AJ, et al. Value of remission in patients with rheumatoid arthritis: a targeted review. *Adv Ther.* 2022;39(1):75-93.

BENEFIT #3

Improved Outcomes

Improved outcomes and physical functioning observed in patients in remission translate to humanistic benefits, even when compared with those with low disease activity. [1,2,3]

- RA patients in remission have higher (better) scores on the EQ-5D and the 36-Item Short Form Health Survey (SF-36), both of which assess quality of life (QoL) based on different domains.[4]
- Specifically, patients in remission have better QoL in terms of physical health, as indicated by **less pain and fatigue,**[2,5,6] **improved mental status** (e.g., better sleep quality and less depression and anxiety),[5,6,7,8] and **greater work productivity or capacity**.[2,5,9]
- The ability to perform paid work in itself has been proven to positively impact QoL, as measured with the SF-36 in a **Norwegian RA** study that controlled for demographics and disease severity.[9]
- A **Turkish** study among people (N = 962) with **AS** reported significantly reduced HRQoL among patients with poor disease control, as indicated by the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI).[10] Namely, patients with a BASDAI < 4 reported a QoL of 4.6 on the AS Quality of Life Questionnaire (ASQoL)[11,12] and those with a BASDAI >= 4 of 11.2. The ASQoL ranges from 0 to 18, with a higher score indicating poorer quality of life.[13]

1. Klarenbeek NB, et al. Association with joint damage and physical functioning of nine composite indices and the 2011 ACR/EULAR remission criteria in rheumatoid arthritis. *Ann Rheum Dis.* 2011;70(10):1815-21.
2. Radner H, et al. Remission in rheumatoid arthritis: benefit over low disease activity in patient-reported outcomes and costs. *Arthritis Res Ther.* 2014;16(1):R56.
3. Van Tuyl LH, et al. Evidence for predictive validity of remission on long-term outcome in rheumatoid arthritis: a systematic review. *Arthritis Care Res (Hoboken).* 2010;62(1):108-17.
4. Ostor AJ, et al. Value of remission in patients with rheumatoid arthritis: a targeted review. *Adv Ther.* 2022;39(1):75-93.
5. Ishida M, et al. Residual symptoms and disease burden among patients with rheumatoid arthritis in remission or low disease activity: a systematic literature review. *Mod Rheumatol.* 2018;28(5):789-99.
6. Curtis JR, et al. Patient perspectives on achieving treat-to-target goals: a critical examination of patient-reported outcomes. *Arthritis Care Res (Hoboken).* 013;65(10):1707-12.
7. Kekow J, et al. Improvements in patient-reported outcomes, symptoms of depression and anxiety, and their association with clinical remission among patients with moderate-to-severe active early rheumatoid arthritis. *Rheumatology (Oxford).* 2011;50(2):401-409.
8. Son CN, et al. Sleep quality in rheumatoid arthritis, and its association with disease activity in a Korean population. *Korean J Intern Med.* 2015;30(3):384-90.
9. Grønning K, et al. Paid work is associated with improved health-related quality of life in patients with rheumatoid arthritis. *Clin Rheumatol.* 2010;29(11):1317-22.
10. Garrett S, et al. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. *J Rheumatol.* 1994;21(12):2286-91.
11. Doward LC, et al. Development of the ASQoL: a quality of life instrument specific to ankylosing spondylitis. *Ann Rheum Dis.* 2003;62:20-26.
12. van der Heijde DM, et al. Physical function, disease activity, and health-related quality-of-life outcomes after 3 years of adalimumab treatment in patients with ankylosing spondylitis. *Arthritis Res Ther.* 2009;11:R124.
13. Bodur H, et al. Quality of life and related variables in patients with ankylosing spondylitis. *Qual Life Res.* 2011;20(4):543-49.

In a multinational clinical study among people with PsA, responders with minimal disease activity were contrasted with non-responders. Compared with baseline, **minimal disease activity responders showed significantly greater improvements** versus non-responders in each SF-36 domain, the SF-36 summary score, the EQ-5D-5L, and the EQ-5D VAS.[1]

- Of interest is also that a large 20-year follow-up study[2] found that the **HAQ and other patient-reported variables were the most powerful predictors of mortality in RA**, more powerful than laboratory, radiographic, and physical examination data. These findings stress the importance of collecting patient-reported data and acting on it.

RA and its comorbidities quickly lead to disability. A study conducted in **Poland** with 1,000 participants showed that 53% of RA patients had been diagnosed with disability.[3]

- RA also leads to depression, which occurs in 17%-42% of patients, as well as anxiety: 53%-71% of patients experience either depression or anxiety or both.[4]

Patients in Remission Have Better Quality of Life

Less Pain & Fatigue

Improved Mental Status

Greater Work Productivity

1. Coates LC, et al. Achieving minimal disease activity in psoriatic arthritis predicts meaningful improvements in patients' health-related quality of life and productivity. *BMC Rheumatol.* 2018;2:24.
2. Wolfe F, et al. Out-of-pocket expenses and their burden in patients with rheumatoid arthritis. *Arthritis Rheum.* 2009;61:1563-70.
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4. Isik A, et al. Anxiety and depression in patients with rheumatoid arthritis. *Clin Rheumatol.* 2007;26(6):872-78.

Proven Solutions

Proven **Solutions**

Since 2009, the Fit for Work Europe Coalition has pushed for a sustainable approach to reduce the enormous burden associated with MSK conditions. Several cost-effective solutions have been put forth and proven in practice.

Some important strategies include:

1. Early diagnosis and intervention,

ideally within 12 weeks of symptom onset, are key to the successful treatment of inflammatory arthritis.[1,2,3] These 12 weeks constitute the so-called 'therapeutic window.'[4,5,6] The only predictive factor in achieving remission in RA is early diagnosis and initiation of effective treatment,[7] with chances of remission doubling if this happens.[8,9] Early diagnosis starts with awareness, and **public awareness** needs to improve.

- Awareness of the benefits of remission should be strengthened through improved **medical education for general practitioners.** Too often debilitation is seen as inevitable.[10]
- **National strategies** need to be developed regarding best practices and implementation of early diagnosis and intervention, including agreed-upon standards of care and quality indicators.[10]

LATIN AMERICA

In **Latin America,** a care model for early **SpA** clinics has been developed.

The model consists of three types of centers, according to the level of complexity of the specific institution. The model defines indicators of structure, processes, and results, and focuses on comprehensive, multidisciplinary, patient-centred care.[11]

1. NAO. Services for people with rheumatoid arthritis. 15 Jul 2009. https://www.nao.org.uk/reports/services-for-people-with-rheumatoid-arthritis/
2. Suresh E. Diagnosis of early rheumatoid arthritis: what the non-specialist needs to know. *J R Soc Med.* 2004;97(9):421-24.
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4. Raza K, et al. Timing the therapeutic window of opportunity in early rheumatoid arthritis: proposal for definitions of disease duration in clinical trials. *Ann Rheum Dis.* 2012;71(12):1921-23.
5. Cush JJ. Early rheumatoid arthritis—is there a window of opportunity? *J Rheumatol Suppl.* 2007;80:1-7.
6. Raza K, et al. The therapeutic window of opportunity in rheumatoid arthritis: does it ever close? *Ann Rheum Dis.* 2015;74(5):793-94.
7. Gremese E, et al. Very early rheumatoid arthritis as a predictor of remission: a multicentre real life prospective study. *Ann Rheum Dis.* 2013;72(6):858-62.
8. Akdemir G, et al. Predictive factors of radiological progression after 2 years of remission-steered treatment in early arthritis patients: a post hoc analysis of the IMPROVED study. *RMD Open.* 2016;2(1):e000172.
9. Heimans L, et al. Two-year results of disease activity score (DAS)-remission-steered treatment strategies aiming at drug-free remission in early arthritis patients (the IMPROVED-study). *Arthritis Res Ther.* 2016;18:23.
10. Global Alliance for Patient Access. The value of achieving remission in inflammatory rheumatic conditions. April 2024. https://gafpa.org/wp-content/uploads/2024/04/GAfPA-Remission-MeetingReport-April-2024.pdf
11. Santos-Moreno P, et al. Engagement process for patients with spondyloarthritis: PANLAR early SpA clinics project — centers of excellence . *Clin Rheumatol.* 2021;40: 4759–66.

POLAND

In Poland, a national programme was set up specifically for the prevention and early detection of **RA** (2016-2020).[1] Poland has the longest diagnostic delays in Europe; the time from first symptoms to treatment initiation can be as long as 35 weeks.[2] **The programme implemented education of medical staff and patients, screening tools, and validation of diagnosis by a rheumatologist in ambulatory care.**

- To save 1 day of temporary work disability, $12 had to be invested in healthcare
- Each $1 invested generated a benefit of $2

SPAIN

The most pioneering programme to date is the Early Intervention Clinic at the Hospital Clinico San Carlos in **Madrid, Spain**,[3] which focused on early intervention in MSK-related work disability, involving 13,000 patients (1998-1999). The programme accepted patients referred after 5 days of absence from work, and it included patient education programmes.

- Temporary work disability was 39% lower and permanent work disability 50% lower compared with standard care
- To save 1 day of temporary work disability, $6 had to be invested

  Patient satisfaction was high
- For every $1 of expenditure, $11 was saved on lost productivity and healthcare costs
- The programme's net benefit was in excess of $5 million (2003 USD)

If this approach were implemented across Spain, 81,000 additional people would be fit for work rather than taking sick leave.

46M
Working days lost to MSK conditions each year in Spain

↓ 39%
Reduction in temporary work disability

↓ 50%
Reduction in permanent work absence in study

81,000
Additional Spanish workers would be available for work each day in Spain

€11
Savings made in societal costs for every €1 of expenditure

1. Program polityki zdrowotnej. Nazwa programu: ogólnopolski program profilaktyki pierwotnej i wczesnego wykrywania reumatoidalnego zapalenia stawów. Okres realizacji: 2016-2020.
2. Raza K, et al. Delays in assessment of patients with rheumatoid arthritis: variations across Europe. Ann Rheumatic Dis. 2011;70(10):1822-25.
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2. Appropriate referral and patient journey standardisation[1] are required, including the provision of quick response appointments in the event of a flare-up. In addition, access to psychological services needs to be improved, as depression is common among people with inflammatory arthritis.

- Getting the appropriate medicine prescribed is crucial. Performance-based risk sharing arrangements, as for instance those implemented for RA in Argentina, may take down payer barriers.[2]
- Whereas TNF cycling may seem a good solution to contain drug costs, it likely does not lessen overall expenditure on medical costs. Switching to a treatment with a different mechanism of action may be more effective and less expensive.[3]

THE UK

In the UK, **only 20% of people with RA are seen by a rheumatologist** within the first 3 months,[4] while in Austria the proportion is 38%.[5]

There is **extra triaging of waiting lists** in the **UK** to make sure the right people are on the waiting list to see a rheumatologist.[6]

COLOMBIA

In **Colombia,** an **innovative disease management program for RA** took a multidisciplinary approach, involving rheumatology, nutrition, psychology, physical and occupational therapy, physical medicine, and rehabilitation according to the patient's RA activity status.

In a real-world comparison to standard of care, they **increased the proportion reaching remission from 21% to 59%** and reduced the proportion with HDA from 18% to 5%.[7]

Moreover, the authors estimated the efficiency of using centres of excellence and estimated **cost savings of up to $223,874 per patient per year** (USD 2017).[8]

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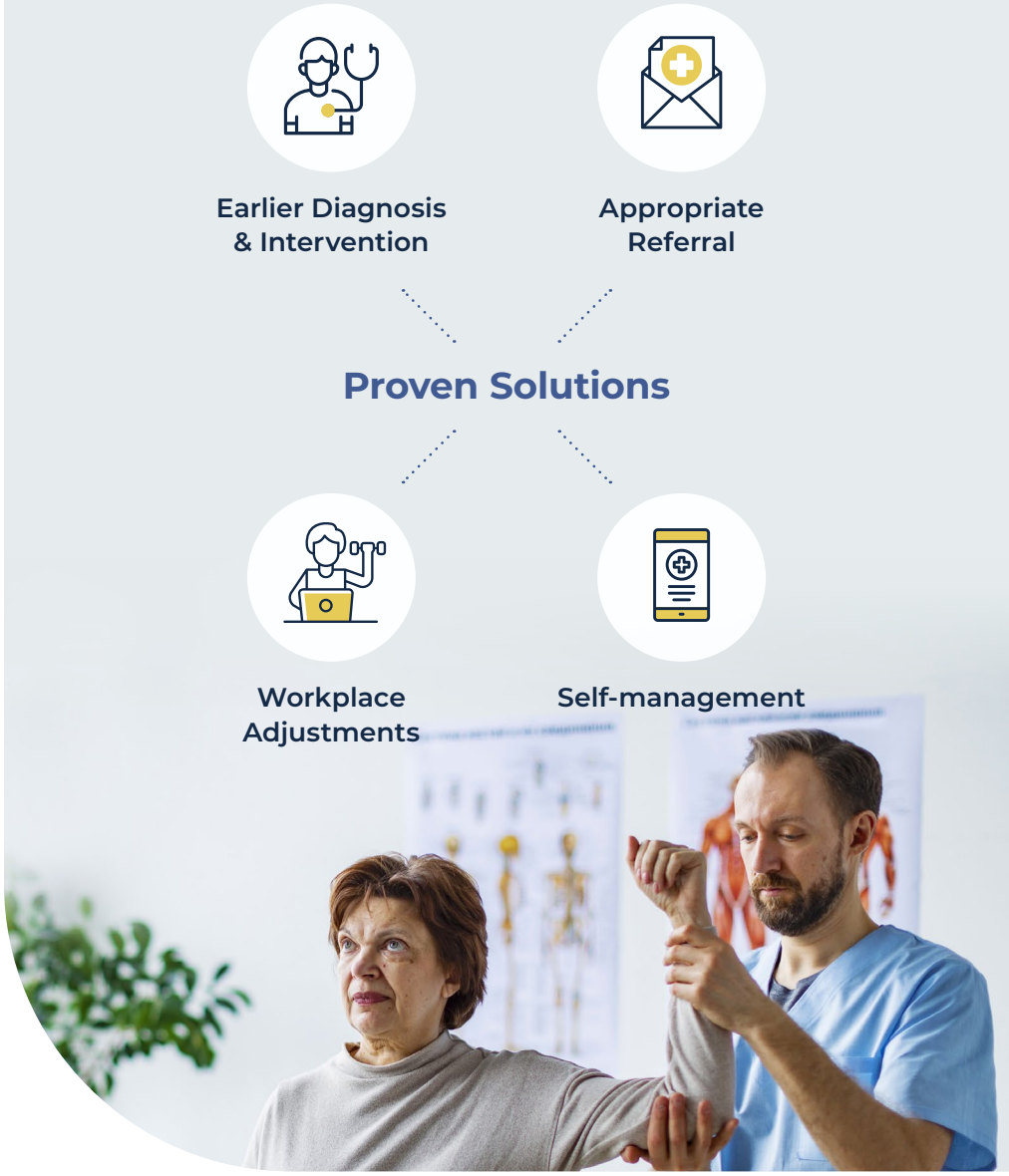
3. Workplace adjustments

Initiatives to underscore the benefits employers stand to reap from investing in a healthy workforce should be implemented. It is not only in the interest of employers to promote a healthy work environment, it is their responsibility.[1]

4. Self-management

- In some countries or communities, inflammatory arthritis is unfortunately stigmatised. To allow patients to properly self-manage their condition, the stigma should be addressed through broad citizen education.[2]
- Patient organisations should be embraced as part of the care team. In the UK, there is a pilot with rheumatologists referring patients to a patient organisation, i.e., setting up an appointment. The organisation can proactively inform and empower patients and make them understand their own role in disease management.[2]
- There is a program in Switzerland that covers physical therapist–led exercise to address the physical activity component.[2]
- Digital tools can be a great support in self-management, but in some countries, patients can be overwhelmed by the number of apps without guidance or accreditation; in other countries, no apps are available in the local language.



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Closing

What societies do not spend on health, on prevention, on ability, they will spend on disability.

Spending on ability allows people to live a fruitful life and have good quality of life.

People with inflammatory arthritis who achieve remission can experience a profound transformation in quality of life, feeling less pain, diminished fatigue, and the ability to engage in activities that bring joy. In essence, remission can empower individuals to live the life they choose.

The financial burden of uncontrolled inflammatory arthritis is not limited to hospitalisation costs alone. It encompasses a range of direct and indirect costs, including frequent doctor visits and reduced productivity due to pain, disability, and early retirement. By achieving remission, individuals can significantly reduce financial burdens both for themselves and for society.

Urgent action is to achieve remission for more patients. Joint damage cannot be reversed. It is key to stop the disease process early.

Health investments are not a drain on public resources, they are an investment.[1] It's clear that investing in remission for inflammatory arthritis is not only a matter of personal health but also a step towards a stronger and more sustainable society.

The Global Alliance for Patient Access thanks AbbVie for sponsor support of this evidence glossary.

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Abbreviations

AS: Ankylosing spondylitis

ASQoL: AS Quality of Life Questionnaire

BASDAI: Bath Ankylosing Spondylitis Disease Activity Index

COPD: Chronic obstructive pulmonary disease

DALY: Disability-adjusted life year

EU: European Union

HCRU: Healthcare resource utilisation

HAQ: Health Assessment Questionnaire

HDA: High disease activity

LDA: Low disease activity

MDA: Minimal disease activity

MSK: Musculoskeletal

PsA: Psoriatic arthritis

QoL: Quality of life

RA: Rheumatoid arthritis

SF-36: 36-Item Short Form Health Survey

SpA: Spondyloarthritis

TNF: Tumour necrosis factor

UK: United Kingdom

US: United States

YLDs: Years lived with disability

YLLs: Years of life lost due to premature death

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