# Implementation of physical activity recommendations in people with axial spondyloarthrtis

Rausch Osthoff, A.K.

# 1

# General introduction

Rheumatic and Musculoskeletal Diseases (RMDs) encompass over 200 conditions of the musculoskeletal system, including osteoarthritis and inflammatory arthritis. RMDs are characterized by pain, stiffness, loss of locomotor function and, sometimes, premature death (1). About one quarter of the European population of all ages is affected by RMDs. This results in direct and indirect healthcare costs of around EUR 240 billion per year, or some 2% of the gross domestic product of European countries (2). Physical Activity (PA) is one of the most important lifestyle factors influencing human health, along with balanced diet, cessation of smoking and/or abusive substance use, and reduction of stress. PA is considered a modifiable behaviour that can reduce the risk of developing an RMD, positively influence its course and prevent some of its consequences (3-6). This thesis will in part focus on axial spondyloarthritis, a form of inflammatory arthritis.

## Definition, consequences, and epidemiology of axial spondyloarthritis

Axial spondyloarthritis (axSpA), which includes both radiographic axSpA (r-axSpA) and non-radiographic axSpA (nr-axSpA), is a chronic, inflammatory RMD that predominately affects the sacroiliac joints and spine. Approximately 30% of people with axSpA have both axial and peripheral joint involvement (7). AxSpA can also present with associated musculoskeletal (e.g., arthritis, enthesitis, dactylitis) or extra-articular manifestations (e.g., uveitis, inflammatory bowel disease, cardiovascular diseases) (8, 9). In people with axSpA, the presence of disease characteristics based on the Assessment of Spondyloarthritis international Society (ASAS) classification varies significantly. These variations include, for example, radiographic or non-radiographic changes (10), or the presence of biomarkers such as the C-reactive protein, the human leukocyte antigen (HLA) B27 status, or the erythrocyte sedimentation rate (11). The chronic inflammation of the axial skeleton leads to back pain and progressive stiffness. The symptoms can be improved with exercise, but not through inactivity. The chronic inflammation may also result in functional and structural impairments (8), e.g., reduced flexibility (12), balance (13), muscle strength (14), or cardio-respiratory capacity (15). Comorbidities are common in people with axSpA. According to data from an international ASAS comorbidity study including 3'370 patients (66% male, mean ±SD age 43±14 years), 51% of people with axSpA suffered from at least one comorbidity and 9% from three or more comorbidities (16). This study also showed that the higher the number of comorbidities (reflected by a higher score on the Rheumatic Disease Comorbidity Index (17)), the greater the impact on physical function, work ability, and quality of life (16). In Spanish, German and Dutch cohorts, the comorbidities most commonly found were hypertension, depression and obesity (18-20). It has also been demonstrated that people with axSpA have an increased risk of cardiovascular diseases (21).

The prevalence of axSpA in the general population is about 0.1%-0.6%, according to European disease prevalence data (22, 23). The male-female prevalence ratio is equal (24).

However, there are gender differences regarding radiologic prognosis (with males more affected) and burden of disease (with females more affected) (25). Characteristically, disease onset is in early adulthood and results in considerable personal burden of disease and negative economic consequences for the individual and society (26-29). Despite efforts in clinical practice to increase awareness and improve diagnostic procedures, the diagnostic delay is still 2-11 years on average, with women waiting longer than men (30-32).

## The management of axSpA

The recommendations of the European Alliance of Associations for Rheumatology (EULAR) for the management of axSpA define the aim of primary treatment as: 'To maximise long-term health-related quality of life through control of symptoms and inflammation, prevention of progressive structural damage, preservation/normalisation of function and social participation' (8). This treat-to-target strategy (goal of remission or low disease activity) implies that the management of axSpA should be personalised, and a combination of pharmacological and non-pharmacological treatment modalities applied (8, 9, 33). The recommended first-line pharmacological treatment for people suffering from pain and stiffness is the prescription of nonsteroidal anti-inflammatory drugs (NSAIDs). For people with consistently high disease activity, additional biological therapies are available (8). Two groups of biological disease-modifying antirheumatic drugs (bDMARDs) and their biosimilars (drugs that are virtually identical to the original) have been approved as effective and safe: tumour necrosis factor inhibitors (TNFi) and interleukin17A inhibitors (IL17Ai) (34). The bDMARDs are used to achieve a threshold of remission or low disease activity and focus on physical function (35). The maximal reduction of symptoms by pharmacological treatment enhances the success of non-pharmacological treatment (36). The ASAS recommendations for non-pharmacological treatment include physiotherapy, education, smoking cessation, and the promotion of PA (8).

Regarding the reduction of disease activity in the management of axSpA, there is evidence to show that combining pharmacological and non-pharmacological treatment modalities through the combination of bDMARDs and physiotherapy is superior to medication alone (36-38). The effect on disease activity was established using the Bath Ankylosing Spondylitis Mobility Index (BASMI) and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) scores (37, 38).

In research specifically on the effectiveness of exercise programmes, routine pharmacological therapy was usually continued in both the intervention and the control groups. In the most recent Cochrane review from 2019, 14 randomized controlled trials investigating the effect of exercise programmes were examined. The exercise programmes had a mean duration of 12 weeks at a median frequency of three sessions per week and consisted mainly of land-based flexibility, breathing and strength exercises, in combination with standard-NSAIDs or

DMARDs (39). The conclusions drawn from the pooled data were that these programmes slightly improve function, potentially reduce pain and, probably, slightly reduce disease activity (moderate-to-low quality evidence) in comparison with no intervention (but standard-NSAIDs) (39). The authors were uncertain about potential adverse events due to lack of evidence and insufficient reporting in the studies (39). The effectiveness of physiotherapy interventions is difficult to demonstrate because of methodological weaknesses, such as small sample sizes, heterogeneous study populations, insufficient description of the interventions and/or flaws in the assessments (39).

The studies investigated in the Cochrane review (39) represent the traditional exercise concept for people with axSpA that is commonly employed in current clinical practice. However, it has been suggested that this traditional exercise concept is no longer state-of-the-art. Recent studies, for example from Sveaas and colleagues (40), have shown that high-intensity aerobic exercise interventions have promising effects on disease activity, inflammatory markers, and symptoms such as pain, fatigue, and stiffness. A greater focus on aerobic exercises also seems to be advisable because of the growing body of knowledge on the increased cardiovascular risk in this patient group (41, 42). Patients also appear to support such a shift in the focus of axSpA exercises and concur with the inclusion of fitness-related exercises alongside to conventional disease-specific exercises (43).

## Definition of physical activity and recommendations

*Physical Activity* (PA) is defined as 'any bodily movement produced by skeletal muscles that results in energy expenditure above resting (basal) levels' (44, 45). PA encompasses any exercise, sport or physical activities done as part of daily living, occupation, leisure and active transportation (46). *Exercise* is a subcategory of PA that is 'planned, structured, and repetitive and [that] has as a final or intermediate objective to improve or maintain one or more dimensions of physical fitness' (44). In contrast, *therapeutic exercises and exercise therapy* comprise specific exercises designed to address distinct functional health problems and are supervised by a qualified health professional, e.g., a physiotherapist.

The World Health Organisation (WHO) provides current, evidence-based public health PA recommendations on the amount (frequency, intensity, and duration) and type of regular PA necessary to offer significant health benefits and mitigate health risks. The *current PA recommendations* for adults (including elderly or people with chronic conditions) encompass four exercise dimensions: cardiorespiratory/aerobic; muscle strength; flexibility; and neuromotor exercises (3, 47). A person is advised to perform at least 150-300 minutes of moderate-intensity PA, or 75-150 minutes of vigorous-intensity aerobic PA (or combination of these) per week, plus additional muscle strengthening activities involving the major muscle groups on at least two days of the week (47). Flexibility and neuromotor exercises are additionally recommended on three or more days during the week (3, 47). Correspondingly,

sitting time should be reduced to a minimum (47).

The intensity of PA is defined through the estimation of energy demands of the metabolic system, i.e., metabolic equivalent of task (MET) (48): for example, walking at 5km/h is described by 3.2METs and classified as a moderate-intensity aerobic activity; and jogging at 9km/h is described by 8.8METs and classified as vigorous aerobic activity. The use of absolute measures may be misleading, however, because personal factors, such as weight, sex, age, and fitness level are not considered (46). For this reason, a relative *measure of intensity* (e.g., $\%MET_{max}$, $\%HR_{max}$ or perceived exertion), which measures the energy costs relative to the individual's maximal capacity, is more appropriate. Moderate exercise is defined as 64% - 76% of the maximum heart rate ($\%HR_{max}$) and vigorous exercise as 77% - 95%$HR_{max}$. Another commonly used assessment to evaluate the intensity of exercise is the Borg Rating of Perceived Exertion Scale, which measures the individual's effort and exertion, breathlessness, and fatigue during PA (49). On a numeric visual scale of 6-20, the numbers 6- 12 indicate a moderate-intensity exercise and the numbers 13-20 a vigorous-intensity exercise (49).

The dose-response relationship between daily PA and health benefits has been confirmed (50). Exceeding the minimum recommended amount of PA improves fitness, reduces the risk factors of chronic conditions, and prevents unhealthy weight gain (46). Furthermore, there is evidence that shorter vigorous-intensity exercise (e.g., 30 minutes of activity ≥ 6METs) is better than longer moderate-intensity exercise (e.g., 60 minutes of activity at 3-6METs) and is associated with a greater reduction of cardiovascular risk (51) and lower mortality rate in the general population (52).

People not meeting the minimum recommendations are considered physically inactive. The WHO stresses that, when possible, people with chronic conditions should try to meet the public health PA recommendations. It also states that exercising below the recommended levels may still be beneficial to people not able or willing to fulfil the recommended amount of PA (47). The American College of Sports Medicine (ACSM) supports this statement, providing evidence on the importance of PA in the prevention and treatment of chronic conditions. It provides examples of appropriate PA programmes and guidance for the performance of exercise (3).

## Physical activity and axSpA

Meeting the PA recommendations described above and incorporating the four exercise dimensions of aerobic, muscle strength, flexibility and neuromotor exercising is especially difficult for people with axSpA. They face barriers of pain, fatigue, or stiffness that healthy people do not have (53). Other aspects, such as the fear of flare-ups or the presence of comorbidities, may also hamper participation in certain types of exercise. Some physical

consequences of the disease, such as osteoporosis (risk of fracture), severe deformities of the spine (risk of neurological complication), or extra-articular manifestations (e.g., tendons, bowels, kidney, eyes), can make an active lifestyle even more difficult to realise (54). It is therefore not surprising that people living with axSpA have been found to be generally less physically active than healthy controls (55-57). Expert support from physicians and health professionals in rheumatology (HPRs), e.g., physiotherapists, may thus be required to identify and address the individual challenges with respect to PA behaviour.

## Exercise is medicine for people with axSpA: clear recommendations are needed

Despite the fact that exercise (and group exercise, in particular) is mentioned in the recommendations and guidelines for the management of axSpA (8, 58), it has been uncertain for some time whether the public health PA recommendations are applicable to people with axSpA. The public health PA recommendations focus on aerobic exercises at an appropriate dosage (moderate/vigorous intensity, and most days per week frequency) which contrasts with the content of most exercise programmes for people with axSpA found in the literature (39, 47). This is an important distinction.

In 2016, this highly relevant issue led to the initiation of an EULAR task force on the development of PA recommendations for people with RMDs, including axSpA (among others).

*The first part of this thesis concerns the development process of the EULAR PA recommendations for people with RMDs, while the second part describes the lessons learned from their pilot implementation specifically in people with axSpA.*

## Implementation of PA recommendations in people with axSpA

After the development of a clinical innovation, it must subsequently be translated and implemented into clinical routine. Implementation is the uptake of research findings by routine health care in the clinical, organisational and policy contexts using strategies tailored to the target population, setting, and goals for improvement (59). However, the implementation of innovations into clinical routine is a great challenge (60, 61). It needs a planned, systematic approach with clear strategies. Successful implementation must be based on an analysis of the contextual factors and the knowledge-practice gap, inclusion of stakeholders, and theory-informed systematic approach (59, 62). The Grol&Wensings' model of change (63) is a theoretical approach that is commonly applied to guide and describe an implementation process. After a comprehensive analysis of current practice

and targets of change, implementation strategies and interventions can be developed, evaluated, and continuously and cyclically adapted (63).

It is known that awareness of the public health PA recommendations and their resulting benefits does not necessarily lead to behavioural changes (64-66). PA is behaviourally complex and increasing PA as a lifestyle change remains a challenge (67, 68). A successful health behaviour change can be defined as 'the shift from risky behaviours to the initiation and maintenance of healthy behaviours and functional activities, and the self-management of chronic health conditions' (69). Several theories have been proposed to explain PA behaviour, which is determined by individual, social, environmental, and societal factors (68). Common to many theories is the central distinction of motivation, which is conceptualised (for example) in intention, stage of change, and autonomous motivation (70). Motivation determines whether an individual will change PA behaviour over the long term. Consequently, an understanding of how PA promotion interventions can influence motivation is critical. The use of behaviour change techniques (71), such as goal-setting and self-monitoring, has been shown to be associated with beneficial changes in PA behaviour (70, 72). Fenton and colleagues (73) summarised the evidence on theory-informed interventions for people with axSpA. They emphasised that motivation and theories should be used more intensively to develop interventions and learn "how things work". This would help to develop new strategies, optimise current interventions, and support the translation of the theory into practice process.

## Physical activity promotion in people with axSpA in Switzerland

In Switzerland, 76% of the adult population is considered physically active (74). The Swiss health care system is fee-for-service and regulated by law and organised at cantonal level (75, 76). The cost of only a few PA promotion intervention programmes for people with chronic conditions is partly refunded by health insurance (77). A Swiss national agency for the development of guidelines does not exist and evidence-based interventions are often not systematically applied in clinical care (78). The Swiss Association for Rheumatology did not publish its own guidelines for the management of axSpA, but referenced those published by EULAR and the American College of Rheumatology.

The Ankylosing Spondylitis Association of Switzerland (Schweizerische Vereinigung Morbus Bechterew, SVMB, www.bechterew.ch) represents approximately 4'300 members with axSpA. The SVMB is connected to the national association Swiss League Against Rheumatism and is a member of the Ankylosing Spondylitis International Federation (ASIF) and the European Alliance of Associations for Rheumatology Patient Representatives (EULAR PARE). Since the early 1980s, the SVMB offers - among other services - physiotherapist-supervised, weekly exercise group therapy in approximately 65 locations

across Switzerland. The concept of this exercise group therapy was, however, outdated since it was mainly based on flexibility and low-intensity strength exercising. Recent evidence indicates that greater attention should be paid to cardiovascular exercise (79-82), individual dosage of exercise intensity based on regular assessments (72, 83-85), encouragement to use exercise for self-management of disease and regular performance of individual exercise (86). Consequently, in line with the ambition of the EULAR task force, the SVMB aimed to translate the EULAR PA recommendations into a new exercise group concept that would meet both disease-specific exercising and general PA recommendations, and to subsequently implement it into routine clinical care.

## Outline of this thesis

Given the lack of specific PA recommendations for people with RMDs, particularly axSpA, and their deficient implementation into clinical care, the aims of this thesis were to:

1) Describe the development, definition, and evidence base of the 2018 EULAR recommendations for PA in people with inflammatory arthritis and osteoarthritis.
2) Evaluate the pilot implementation of exercising according to the EULAR PA recommendations in exercise groups for people with axSpA in Switzerland, including the analysis of the situation, determinants of PA behaviour, and the exploration of a muscle strength assessment.

The first aim is addressed in the following chapters:

- Chapter 2 describes the development and definition of the 2018 EULAR recommendations for PA in people with inflammatory arthritis and osteoarthritis.
- Chapter 3 summarises the evidence on the effects of exercise and PA promotion, according to public health recommendations, in people with rheumatoid arthritis, spondyloarthritis, and hip/knee osteoarthritis. This meta-analysis informed the EULAR task force, defining the EULAR recommendations for PA.

The second aim is addressed in the following chapters:

- Chapter 4 evaluates patients' use of physiotherapy and their perspective on it. A quantitative analysis of the current situation in the Netherlands and Switzerland.
- Chapter 5 explores the patients' beliefs related to PA. A qualitative evaluation of the current situation in Switzerland.
- Chapter 6 describes the reliability of an adapted core strength endurance test battery. This assessment is needed to tailor individual exercises. It is a relevant component of the implementation strategy described below.
- Chapter 7 elucidates the implementation strategy and lessons learned from the pilot implementation of the PA recommendations in axSpA exercise group therapy in Switzerland.
- Chapter 8 discusses the most important findings of the studies in this thesis

and their implications for clinical care. Suggestions for further research are also presented.

- Chapter 9 summarises the thesis.

# References


1. EULAR. Horizon 2020 Framwork Programme: EULAR's position and recommendations Brussels: European League against Rheumatism; 2011 [cited December 2021]. Available from: https://www.eular.org/myUploadData/files/EU_Horizon_2020_EULAR_position_paper.pdf.
2. EULAR. EULAR contribution to the EU reflection on chronic diseases. Postion stand. Kilchberg, Switzerland: European League Against Rheumatism; 2012.
3. American College of Sports Medicine. ACSM's Guidelines for exercise testing and prescription. tenth edition ed. Philadelphia: Wolters Kluwer; 2018.
4. Europe WHO. Physical activity strategy for the WHO European Region 2016-2025 Copenhagen, Denmark; 2016 [cited December 2021] Available from: https://www.euro.who.int/en/health-topics/disease-prevention/physical-activity/publications.
5. Azeez M, Clancy C, O'Dwyer T, Lahiff C, Wilson F, Cunnane G. Benefits of exercise in patients with rheumatoid arthritis: a randomized controlled trial of a patient-specific exercise programme. Clinical rheumatology. 2020;39(6):1783-92.
6. Kraus VB, Sprow K, Powell KE, Buchner D, Bloodgood B, Piercy K, et al. Effects of Physical Activity in Knee and Hip Osteoarthritis: A Systematic Umbrella Review. Medicine and science in sports and exercise. 2019;51(6):1324-39.
7. de Winter JJ, van Mens LJ, van der Heijde D, Landewe R, Baeten DL. Prevalence of peripheral and extra-articular disease in ankylosing spondylitis versus non-radiographic axial spondyloarthritis: a meta-analysis. Arthritis research & therapy. 2016;18:196.
8. van der Heijde D, Ramiro S, Landewe R, Baraliakos X, Van den Bosch F, Sepriano A, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. Annals of the rheumatic diseases. 2017;76(6):978-91.
9. Magrey MN, Danve AS, Ermann J, Walsh JA. Recognizing Axial Spondyloarthritis: A Guide for Primary Care. Mayo Clin Proc. 2020;95(11):2499-508.
10. Sieper J, Rudwaleit M, Baraliakos X, Brandt J, Braun J, Burgos-Vargas R, et al. The Assessment of SpondyloArthritis international Society (ASAS) handbook: a guide to assess spondyloarthritis. Annals of the rheumatic diseases. 2009;68:1-44.
11. Brown MA, Li Z, Cao KL. Biomarker development for axial spondyloarthritis. Nature reviews Rheumatology. 2020;16(8):448-63.
12. Dagfinrud H, Kvien TK, Hagen KB. Physiotherapy interventions for ankylosing spondylitis. The Cochrane database of systematic reviews. 2008(1):CD002822.
13. Dursun N, Sarkaya S, Ozdolap S, Dursun E, Zateri C, Altan L, et al. Risk of falls in patients with ankylosing spondylitis. J Clin Rheumatol. 2015;21(2):76-80.
14. Sahin N, Ozcan E, Baskent A, Karan A, Kasikcioglu E. Muscular kinetics and fatigue evaluation of knee using by isokinetic dynamometer in patients with ankylosing spondylitis. Acta reumatologica portuguesa. 2011;36(3):252-9.
15. Peters MJ, Visman I, Nielen MM, Van Dillen N, Verheij RA, van der Horst-Bruinsma IE, et al. Ankylosing spondylitis: a risk factor for myocardial infarction? Annals of the rheumatic diseases. 2010;69(3):579-81.
16. Nikiphorou E, Ramiro S, van der Heijde D, Norton S, Molto A, Dougados M, et al. Association of Comorbidities in Spondyloarthritis With Poor Function, Work Disability, and Quality of Life: Results From the Assessment of SpondyloArthritis International Society Comorbidities in Spondyloarthritis Study. Arthritis care & research. 2018;70(8):1257-62.
17. England BR, Sayles H, Mikuls TR, Johnson DS, Michaud K. Validation of the rheumatic disease comorbidity index. Arthritis care & research. 2015;67(6):865-72.
18. Redeker I, Callhoff J, Hoffmann F, Marschall U, Haibel H, Sieper J, et al. The prevalence and impact of comorbidities on patients with axial spondyloarthritis: results from a nationwide population-based study. Arthritis Res Ther. 2020;22(1).
19. Maas F, Arends S, van der Veer E, Wink F, Efde M, Bootsma H, et al. Obesity Is Common in Axial Spondyloarthritis and Is Associated with Poor Clinical Outcome. Journal of Rheumatology. 2016;43(2):383-7.
20. Puche-Larrubia MA, Ladehesa-Pineda L, Font-Ugalde P, Escudero-Contreras A, Molto A, Lopez-Medina C, et al. Distribution of comorbidities in spondyloarthritis with regard to the phenotype and psoriasis: data from the ASAS-COMOSPA study. Therapeutic Advances in Musculoskeletal Disease. 2021;13.
21. Mathieu S, Gossec L, Dougados M, Soubrier M. Cardiovascular profile in ankylosing spondylitis: a systematic review and meta-analysis. Arthritis care & research. 2011;63(4):557-63.
22. Bohn R, Cooney M, Deodhar A, Curtis JR, Golembesky A. Incidence and prevalence of axial spondyloarthritis: methodologic challenges and gaps in the literature. Clin Exp Rheumatol. 2018;36(2):263-74.
23. Hamilton L, Macgregor A, Toms A, Warmington V, Pinch E, Gaffney K. The prevalence of axial spondyloarthritis in the UK: a cross-sectional cohort study. BMC musculoskeletal disorders. 2015;16:392.
24. Baumberger H, Khan MA. Gradual Progressive Change to Equal Prevalence of Ankylosing Spondylitis among Males and Females in Switzerland: Data from the Swiss Ankylosing Spondylitis Society (svmb). Annals of the rheumatic diseases. 2017;76:929.
25. Rusman T, van Vollenhoven RF, van der Horst-Bruinsma IE. Gender Differences in Axial Spondyloarthritis: Women Are Not So Lucky. Curr Rheumatol Rep. 2018;20(6):35.
26. Ramonda R, Marchesoni A, Carletto A, Bianchi G, Cutolo M, Ferraccioli G, et al. Patient-reported impact of

spondyloarthritis on work disability and working life: the ATLANTIS survey. Arthritis Res Ther. 2016;18:78.
27. Strand V, Singh JA. Patient Burden of Axial Spondyloarthritis. J Clin Rheumatol. 2017;23(7):383-91.
28. White D, Lao C, Williams M, Lawrenson R, Dalbeth N. The costs associated with ankylosing spondylitis/axial spondyloarthritis in Aotearoa/New Zealand. N Z Med J. 2019;132(1505):38-47.
29. Redeker I, Callhoff J, Hoffmann F, Saam J, Haibel H, Sieper J, et al. Krankheitskosten bei axialer Spondyloarthritis für Patienten mit und ohne Tumor-Nekrose-Faktor-Inhibitor-Behandlung: Ergebnisse einer Routinedatenanalyse. Zeitschrift für Rheumatologie. 2019:1-9.
30. Korotaeva T, Dina O, Holdsworth E, Fallon L, Milligan G, Meakin S, et al. Investigating diagnosis, treatment, and burden of disease in patients with ankylosing spondylitis in Central Eastern Europe and the United States: a real-world study. Clinical Rheumatology. 2021.
31. Redeker I, Callhoff J, Hoffmann F, Haibel H, Sieper J, Zink A, et al. Determinants of diagnostic delay in axial spondyloarthritis: an analysis based on linked claims and patient-reported survey data. Rheumatology (Oxford, England). 2019;58(9):1634-8.
32. Jovani V, Blasco-Blasco M, Ruiz-Cantero MT, Pascual E. Understanding How the Diagnostic Delay of Spondyloarthritis Differs Between Women and Men: A Systematic Review and Metaanalysis. Journal of Rheumatology. 2017;44(2):174-83.
33. Smolen JS, Schols M, Braun J, Dougados M, FitzGerald O, Gladman DD, et al. Treating axial spondyloarthritis and peripheral spondyloarthritis, especially psoriatic arthritis, to target: 2017 update of recommendations by an international task force. Annals of the rheumatic diseases. 2018;77(1):3-17.
34. Mease P. Emerging Immunomodulatory Therapies and New Treatment Paradigms for Axial Spondyloarthritis. Curr Rheumatol Rep. 2019;21(7):35.
35. Braun J, Baraliakos X, Kiltz U. Treat-to-target in axial spondyloarthritis - what about physical function and activity? Nature reviews Rheumatology. 2021;17(9):565-76.
36. Noureldin B, Barkham N. The current standard of care and the unmet needs for axial spondyloarthritis. Rheumatology (Oxford, England). 2018;57(suppl_6):vi10-vi7.
37. Liang HL, W. R.; Zhang, H.; Tian, X.; Wei, W.; Wang, C. M. Concurrent Intervention With Exercises and Stabilized Tumor Necrosis Factor Inhibitor Therapy Reduced the Disease Activity in Patients With Ankylosing Spondylitis: A Meta-Analysis. Medicine. 2015;94(50):e2254.
38. Lubrano ES, A.; Amato, G.; Benucci, M.; Cavazzana, I.; Chimenti, M. S.; Ciancio, G.; D'Alessandro, G.; Angelis, R. D.; Lupoli, S.; Lurati, A. M.; Naclerio, C.; Russo, R.; Semeraro, A.; Tomietto, P.; Zuccaro, C.; De Marco, G. Tumour necrosis factor alpha inhibitor therapy and rehabilitation for the treatment of ankylosing spondylitis: a systematic review. Seminars in arthritis and rheumatism. 2015;44(5):542-50.
39. Regnaux JP, Davergne T, Palazzo C, Roren A, Rannou F, Boutron I, et al. Exercise programmes for ankylosing spondylitis. The Cochrane database of systematic reviews. 2019;10:CD011321.
40. Sveaas SH, Bilberg A, Berg IJ, Provan SA, Rollefstad S, Semb AG, et al. High intensity exercise for 3 months reduces disease activity in axial spondyloarthritis (axSpA): a multicentre randomised trial of 100 patients. British journal of sports medicine. 2020;54(5):292-+.
41. Ferraz-Amaro I, Rueda-Gotor J, Genre F, Corrales A, Blanco R, Portilla V, et al. Potential relation of cardiovascular risk factors to disease activity in patients with axial spondyloarthritis. Therapeutic advances in musculoskeletal disease. 2021;13:1759720X211033755.
42. Kim JH, Choi IA. Cardiovascular morbidity and mortality in patients with spondyloarthritis: A meta-analysis. Int J Rheum Dis. 2021;24(4):477-86.
43. Bilberg A, Sveaas SH, Dagfinrud H, Mannerkorpi K. How Do Patients With Axial Spondyloarthritis Experience High-Intensity Exercise? Acr Open Rheumatol. 2020;2(4):207-13.
44. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. Public Health Rep. 1985;100(2):126-31.
45. Keogh JWL, Grigg J, Vertullo CJ. Is Home-Based, High-Intensity Interval Training Cycling Feasible and Safe for Patients With Knee Osteoarthritis?: Study Protocol for a Randomized Pilot Study. Orthopaedic Journal of Sports Medicine. 2017;5(3).
46. Garber CE, Blissmer B, Deschenes MR, Franklin BA, Lamonte MJ, Lee IM, et al. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. Medicine and science in sports and exercise. 2011;43(7):1334-59.
47. World Health Organization. WHO Guidelines on physical activity and sedentary behaviour. Geneva: World Health Organization; 2020.
48. Jette M, Sidney K, Blumchen G. Metabolic equivalents (METS) in exercise testing, exercise prescription, and evaluation of functional capacity. Clin Cardiol. 1990;13(8):555-65.
49. Williams N. The Borg Rating of Perceived Exertion (RPE) scale. Occup Med-Oxford. 2017;67(5):404-5.
50. World Health Organization. WHO Guidelines on Physical activity and sedentary behaviour Web Annex Evidence Profiles [cited December 2021] Available from: https://apps.who.int/iris/bitstream/handle/10665/336656/9789240015128-eng.pdf2021
51. Swain DP, Franklin BA. Comparison of cardioprotective benefits of vigorous versus moderate intensity aerobic exercise.

Am J Cardiol. 2006;97(1):141-7.
52. Lee IM, Paffenbarger RS, Jr. Associations of light, moderate, and vigorous intensity physical activity with longevity. The Harvard Alumni Health Study. Am J Epidemiol. 2000;151(3):293-9.
53. Liu SH, Morais SA, Lapane KL, Kay J. Physical activity and attitudes and perceptions towards physical activity in patients with spondyloarthritis: A systematic review. Seminars in arthritis and rheumatism. 2020;50(2):289-302.
54. Iversen MD, Scanlon L, Frits M, Shadick NA, Sharby N. Perceptions of physical activity engagement among adults with rheumatoid arthritis and rheumatologists. Int J Clin Rheumtol. 2015;10(2):67-77.
55. Swinnen TW, Scheers T, Lefevre J, Dankaerts W, Westhovens R, de Vlam K. Physical activity assessment in patients with axial spondyloarthritis compared to healthy controls: a technology-based approach. PloS one. 2014;9(2):e85309.
56. O'Dwyer T, O'Shea F, Wilson F. Decreased physical activity and cardiorespiratory fitness in adults with ankylosing spondylitis: a cross-sectional controlled study. Rheumatology international. 2015;35(11):1863-72.
57. Passalent LA, Soever LJ, O'Shea FD, Inman RD. Exercise in Ankylosing Spondylitis: Discrepancies Between Recommendations and Reality. Journal of Rheumatology. 2010;37(4):835-41.
58. Ward MM, Deodhar A, Gensler LS, Dubreuil M, Yu D, Khan MA, et al. 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. Arthritis & rheumatology (Hoboken, NJ). 2019;71(10):1599-613.
59. Wensing M. Implementation science in healthcare: Introduction and perspective. Z Evid Fortbild Qual Gesundhwes. 2015;109(2):97-102.
60. Ferreira de Meneses S, Rannou F, Hunter DJ. Osteoarthritis guidelines: Barriers to implementation and solutions. Annals of physical and rehabilitation medicine. 2016;59(3):170-3.
61. Swinkels RAHM, van Peppen RPS, Wittink H, Custers JWH, Beurskens AJHM. Current use and barriers and facilitators for implementation of standardised measures in physical therapy in the Netherlands. BMC Musculoskeletal Disorders. 2011;12.
62. Coles E, Anderson J, Maxwell M, Harris FM, Gray NM, Milner G, et al. The influence of contextual factors on healthcare quality improvement initiatives: a realist review. Systematic reviews. 2020;9(1):94.
63. Grol R, Wensing M. Improving patient care. The implementation of change in health care. 2nd ed. Oxford: Wiley Blackwell; 2013.
64. McGuire WJ. Attitudes and attitude change. In: Lindzey G, Aronson E, editors. Handbook of social psychology:Vol 2 Special fields and applications (3rd ed, pp233-346). New York, NY: Random House1985.
65. Nicolson PJA, Hinman RS, French SD, Lonsdale C, Bennell KL. Improving Adherence to Exercise: Do People With Knee Osteoarthritis and Physical Therapists Agree on the Behavioral Approaches Likely to Succeed? Arthritis Care Res (Hoboken). 2018;70(3):388-97.
66. Roter DL, Hall JA, Merisca R, Nordstrom B, Cretin D, Svarstad B. Effectiveness of interventions to improve patient compliance: a meta-analysis. Med Care. 1998;36(8):1138-61.
67. Gabriel KKP, Morrow JR, Woolsey ALT. Framework for Physical Activity as a Complex and Multidimensional Behavior. Journal of physical activity & health. 2012;9:S11-S8.
68. Biddle SJH, Mutrie N. Psychology of Physical Activity. London: Routledge; 2001.
69. Nieuwenhuijsen ER, Zemper E, Miner KR, Epstein M. Health behavior change models and theories: contributions to rehabilitation. Disability and rehabilitation. 2006;28(5):245-56.
70. Knittle K, Nurmi J, Crutzen R, Hankonen N, Beattie M, Dombrowski SU. How can interventions increase motivation for physical activity? A systematic review and meta-analysis. Health Psychol Rev. 2018;12(3):211-30.
71. Michie S, Richardson M, Johnston M, Abraham C, Francis J, Hardeman W, et al. The behavior change technique taxonomy (v1) of 93 hierarchically clustered techniques: building an international consensus for the reporting of behavior change interventions. Ann Behav Med. 2013;46(1):81-95.
72. O'Dwyer T, Monaghan A, Moran J, O'Shea F, Wilson F. Behaviour change intervention increases physical activity, spinal mobility and quality of life in adults with ankylosing spondylitis: a randomised trial. Journal of physiotherapy. 2017;63(1):30-9.
73. Fenton SAM, Duda JL, Veldhuijzen van Zanten J, Metsios GS, Kitas GD. Theory-informed interventions to promote physical activity and reduce sedentary behaviour in rheumatoid arthritis: a critical review of the literature. Mediterr J Rheumatol. 2020;31(1):19-41.
74. Bundesamt für Statistik. Schweizerische Gesundheitsbefragung 2019: Körperliche Aktivität und Gesundheit. Neuchatel: Bundesamt für Statstik; 2019. [cited December 2021] Available from: https://www.swissstats.bfs.admin.ch/collection/ch.admin.bfs.swissstat.de.issue19142131708/article/issue19142131708-01
75. Bundesamt für Gesundheit. Gesetzgebung 2021 [cited December 2021] Available from: https://www.bag.admin.ch/bag/de/home/gesetze-und-bewilligungen/gesetzgebung.html.
76. Monitor THSaP. Health Systems in Transition (HiT) profile of Switzerland 2021 [cited December 2021] Available from: https://www.hspm.org/countries/switzerland25062016/livinghit.aspx?Section=3.7%20Payment%20mechanisms&Type=Section.
77. Nast I, Niedermann K, Carlander M, Mattli R, Rausch Osthoff AK, Sommer B, et al. Bewegung als Therapie. Schlussbericht im Auftrag des Bundesamt für Gesundheit Winterthur: Zürcher Hochschule für Angewandte Wissenschaften; 2021.
78. Birrenbach T, Kraehenmann S, Perrig M, Berendonk C, Huwendiek S. Physicians' attitudes toward, use of, and perceived

barriers to clinical guidelines: a survey among Swiss physicians. Adv Med Educ Pract. 2016;7:673-80.
79. Sveaas SH, Smedslund G, Hagen KB, Dagfinrud H. Effect of cardiorespiratory and strength exercises on disease activity in patients with inflammatory rheumatic diseases: a systematic review and meta-analysis. British journal of sports medicine. 2017;51(14):1065-72.
80. Bilberg A, Dagfinrud H, Sveaas SH. Supervised intensive Exercise strengthen Exercise Health Beliefs in Patients with Axial Spondyloarthritis: A Multicentre Randomized Controlled Trial. Arthritis care & research. 2021.
81. Niedermann K, Muggli C, Dagfinrud, H, Hermann M, Tamborrini, G, Ciurea A, Bischoff-Ferrari H. Effect of cardiovascular training on fitness and perceived disease activity in people with ankylosing spondylitis. Arthritis care & research. 2013;65(11):1844-52.
82. Hilberdink B, Vlieland TV, van der Giesen F, van Gaalen F, Goekoop R, Peeters A, et al. Adequately dosed aerobic physical activity in people with axial spondyloarthritis: associations with physical therapy. Rheumatology international. 2020;40(9):1519-28.
83. Millner JRB, Beinke KM, Butterworth RH, Chasle BE, Dutton LJ, Lewington MA, Lim EG, Morley TB, O'Reilly JE, Pickering KA, Winzenberg T, Zochling J. Exercise for ankylosing spondylitis: An evidence-based consensus statement. Seminars in arthritis and rheumatism. 2016;45(4):411-27.
84. Hilberdink B, van der Giesen F, Vliet Vlieland T, Nijkamp M, van Weely S. How to optimize exercise behavior in axial spondyloarthritis? Results of an intervention mapping study. Patient education and counseling. 2020;103(5):952-9.
85. Fongen C, Sveaas SH, Dagfinrud H. Barriers and Facilitators for Being Physically Active in Patients with Ankylosing Spondylitis: A Cross-sectional Comparative Study. Musculoskeletal care. 2015;13(2):76-83.
86. Zangi HA, Ndosi M, Adams J, Andersen L, Bode C, Bostrom C, et al. EULAR recommendations for patient education for people with inflammatory arthritis. Annals of the rheumatic diseases. 2015;74(6):954-62.