Optimizing physical activity and exercise in people with axial spondyloarthritis

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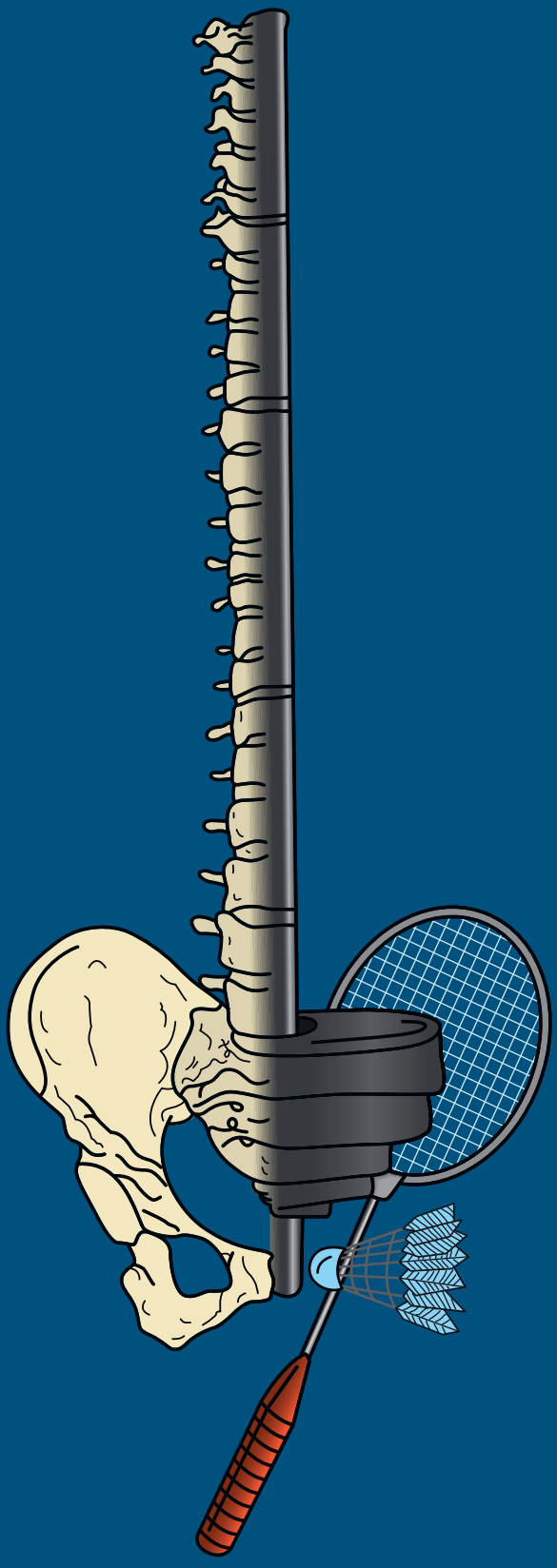

Chapter 1

General introduction

Axial spondyloarthritis and its treatment

Epidemiology, pathophysiology and clinical characteristics

Axial spondyloarthritis (axSpA) is a chronic inflammatory rheumatic disease primarily affecting the spine and sacroiliac joints (1-3). It is characterized by inflammatory back pain and stiffness (1, 2, 4). As shown in Figure 1, extraspinal articular and peri-articular characteristics of axSpA are peripheral arthritis, enthesitis and dactylitis. Extra-articular manifestations may include (among others) anterior uveitis, psoriasis and inflammatory bowel disease (2, 3, 5).

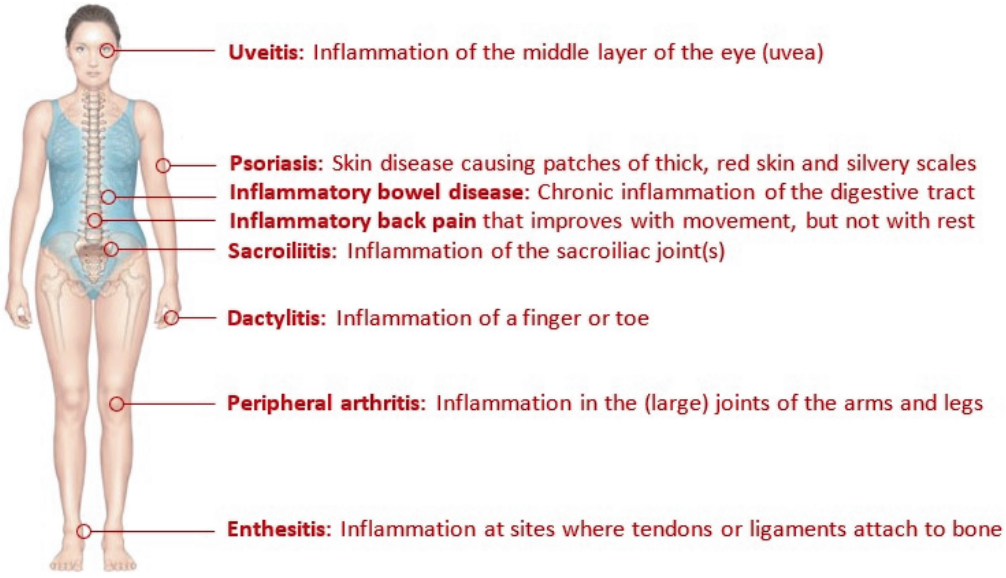

Figure 1. Common clinical features of axial spondyloarthritis

AxSpA encompasses both non-radiographic axSpA (nr-axSpA) and radiographic axSpA, also known as ankylosing spondylitis (AS). Nr-axSpA and AS are distinguished by the absence or presence of structural damage to the sacroiliac joints on radiographs (1, 2, 4). Among patients with nr-axSpA, magnetic resonance imaging (MRI) may show signs of inflammation in the spine and sacroiliac joints (6). It was found that within two years, 10-12% of the patients with nr-axSpA develop structural damage and fulfill the criteria for AS (7, 8). However, not all nr-axSpA patients will ultimately develop radiographic sacroiliitis and progress to AS (1, 2). Similarly, not in all AS patients new bone formation (syndesmophytes) will form over time in the sacroiliac joints and spine (1, 2): approximately 60-70% of AS patients develop bony growths eventually leading to vertebrae fusion (9, 10).

The onset of axSpA is typically before the age of 45 years, often in people in their twenties (5, 11). The global prevalence of axSpA among adults is between 0.2% and 1.4% (1, 11, 12). Overall, axSpA is equally prevalent in men and women (5, 13), while nr-axSpA is more prevalent in women and AS in men (7, 14). In the remainder of this thesis, the term axSpA refers to both nr-axSpA and AS.

People with axSpA have an increased risk for comorbidities, such as osteoporosis (15), depression (16, 17) or cardiovascular diseases (15, 16, 18, 19). These comorbid conditions are associated with more disease activity, reduced work productivity, decreased quality of life, lower treatment response and higher mortality (16). People with axSpA are also more likely to have common cardiovascular disease risk factors, such as decreased cardiorespiratory fitness (20-23), hypertension (16) and obesity (16, 24).

General management of axSpA

Several national and international guidelines provide comprehensive recommendations for the treatment of people with axSpA. An example of these is the '2016 Update of the ASAS-EULAR management recommendations for axial spondyloarthritis' (2), a set of recommendations from a collaboration between the Assessment of SpondyloArthritis international Society (ASAS) and the European Alliance of Associations for Rheumatology (EULAR). These recommendations state (among others) that the optimal management requires a combination of pharmacological and non-pharmacological modalities, in order to maximize health-related quality of life by controlling symptoms and inflammation, preventing progressive structural damage and preserving and normalizing function and social participation.

In this and other sets of recommendations (2, 3, 19, 25, 26), multiple treatment modalities are advocated. This thesis mainly covers non-pharmacological treatment modalities, in particular physical activity, exercise and physical therapy, as shown in Figure 2.

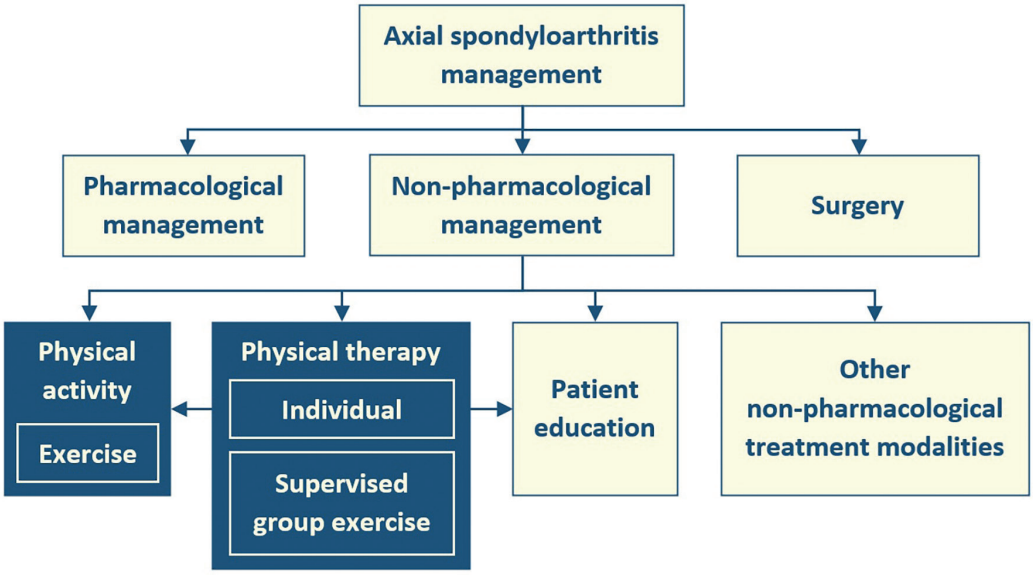

Figure 2. Recommended treatment modalities, with this thesis' focus highlighted in blue

- Pharmacological management: Non-steroidal anti-inflammatory drugs (NSAIDs) are recommended as a first-line drug treatment (2, 3, 25). Moreover, in case of persistent high disease activity, the initiation of biological disease-modifying antirheumatic drugs (bDMARDS), particularly tumor necrosis factor inhibitors (TNFi), is advocated (2, 3, 25).
- Non-pharmacological management: Sets of recommendations particularly advocate education, physical activity and physical therapy (2, 3, 19, 25-27), but patients with axSpA can also use other non-pharmacological treatment modalities, e.g. occupational therapy or vocational rehabilitation.
    - *Physical activity and exercise*: According to the 2018 EULAR recommendations for physical activity (27), exercise and physical activity according to public health recommendations are effective, feasible and safe for people with axSpA.
    - *Physical therapy*: In various guidelines, it is stated that physical therapy should be considered (2, 3) and should include exercise therapy (3, 25, 28). In some countries, including the Netherlands, exercise therapy can also be provided by certified exercise therapists (in Dutch: Oefentherapeuten Cesar and Mensendieck (29)). In this thesis, the terms physical therapy and physical therapist therefore also refer to the profession of exercise therapists.

- *Patient education*: It is recommended to educate patients on axSpA and on the benefits of a healthy lifestyle, including a healthy diet, smoking cessation and regular exercise (2, 19, 25, 28), which may have a beneficial effect on the course of the disease (30) and on the cardiovascular risk (19). Furthermore, education can cover a much wider range of topics, e.g. medication use, fall prevention, sleep, psychosocial support, coping, pain-, stress- and fatigue-management, joint protection, energy conservation, environmental modifications, assistive technologies, orthoses and available treatment possibilities: the content of the education should be individually tailored and needs-based (28, 31). Multiple health care professionals can be involved in patient education, such as the rheumatologist, clinical nurse specialist, general practitioner, physician assistant, physical therapist, certified exercise therapist, social worker, psychologist, occupational therapist, dietitian, podiatrist, dermatologist or gastroenterologist.
- *Other non-pharmacological treatment modalities*: Recommendations may also mention other non-pharmacological treatment modalities, such as occupational therapy, vocational rehabilitation, cognitive behavioural therapy, podiatry and medical nutrition therapy, which are especially common in multi-disciplinary treatment (26).

- Surgical management: Sets of recommendations particularly suggest to consider total hip arthroplasty in axSpA patients with refractory hip pain or disability and radiographic evidence of structural damage (2, 3).

This thesis focuses mainly on physical activity, exercise and physical therapy (as highlighted in Figure 2).

Physical activity, exercise and physical therapy

Definitions

Although exercise has been recommended to axSpA patients for a long time (32-34), in recent years there appears to be more focus on physical activity in general (20, 27, 35). This is probably caused by recent developments in public healthcare, including: a) definition and promotion of health enhancing physical activity recommendations for the general population (36-38); b) new insights in the increased cardiovascular risk in axSpA patients (15, 16, 18, 19); and c) new evidence on the benefits and safety of (high-intensity) aerobic physical activity in axSpA patients (27, 28, 39-42). Before elaborating further on physical activity and exercise, it is important to define the relevant concepts:

- Physical activity (PA) is defined as "any bodily movement produced by skeletal muscles that results in energy expenditure" (43).
- Exercise is a subcategory of PA that is "planned, structured and repetitive and has as a final or an intermediate objective to improve or maintain physical fitness" (43). Other categories of PA are occupational, household, transport or leisure-time activities. Exercise can be performed supervised or unsupervised, individually or in a group and land-based or aquatic. It can also be used as a therapeutic intervention: exercise therapy (28, 29, 44).
- Exercise therapy consists of practicing functional movements and performing aerobic, mobility, strength and/or neuromotor exercises in order to optimize physical functioning and participation (28, 29). This can be provided individually or in a group by a physical therapist or, in some countries, by a certified exercise therapist (29, 44). Exercise therapy is often supplemented with patient education (28, 44, 45).

Most therapeutic interventions concern combinations of supervised and unsupervised exercises and education including general PA promotion. In the literature, the terms used for these various aspects often overlap (2, 25, 28, 35, 46, 47).

Physical activity and exercise in axSpA

Sufficient engagement in both overall PA and exercise are important for people with axSpA. Exercise interventions have shown to have positive effects on cardiorespiratory function, spinal mobility, pain, stiffness, fatigue, disease activity, physical functioning and quality of life (32, 42, 47-56). However, the effects are often small (54, 55). Supervised exercise appears to be more beneficial than unsupervised exercise (57). Furthermore, maintaining an adequate PA level is important for general health and well-being, for prevention of comorbidities such as osteoporosis, depression and cardiovascular diseases and for their beneficial effects on cardiovascular risk factors such as hypertension and obesity (37, 46, 58). These preventive effects are particularly important for people with axSpA, because they have an increased risk for these comorbidities and risk factors (15-17).

In order to achieve optimal effects, a combination of aerobic, mobility and strengthening exercises according to general PA recommendations shown in Table 1 is recommended for axSpA patients (27, 28, 35, 46, 48). Some guidelines also recommend neuromotor exercise (27, 28, 46).

Recent literature suggests that in the general population vigorous-intensity aerobic exercise has superior benefits over moderate-intensity aerobic exercise (60-63). Exercise with vigorous-intensity has shown to be beneficial and safe in axSpA patients (42, 64).

Table 1. General physical activity recommendations (27, 36, 59)

	Recommended weekly dosage of PA
Aerobic physical activity	≥150 minutes with moderate-intensity, ≥75 minutes with vigorous-intensity or an equivalent combination Increased amounts have more health benefits
Mobility exercise	≥2 days
Strength exercise	2-3 days
Neuromotor exercise	≥2 days

Physical therapy in axSpA

Individual physical therapy

Based on the available scientific evidence and consensus among different stakeholders and experts (including patients, physical and exercise therapists, rheumatologists and researchers), detailed Dutch recommendations on physical therapy in people with axSpA were published in 2019 (28). In these recommendations, it is advised to provide:

- Periodic assessments, including evaluation of physical functioning, PA behavior, personal needs and potential barriers and facilitators.
- A personalized exercise program, tailored to individual needs, disease status and the periodic assessments and including aerobic, mobility, strengthening and neuromotor exercises, possibly supplemented with breathing exercises, all with the appropriate intensity, duration and frequency, according to the ACSM criteria (37). Exercise intensity should be monitored by heartrate or with a Borg Rating of Perceived Exertion Scale (65).
- Patient education on (among others) axSpA, PA, exercise, coping and lifestyle.

Supervised group exercise

After a period of individual physical therapy, patients with axSpA are encouraged to engage in supervised group exercise (SGE) if deemed necessary, in order to maintain (improvements in) physical functioning over time (28, 46).

Differences in effectiveness between SGE and supervised individual exercise are largely unknown, but SGE is found to have better effects on symptoms, cardiorespiratory fitness and physical functioning than unsupervised individual exercise in axSpA patients (32, 46, 47, 66). Therefore, axSpA-specific SGE has been

implemented in many countries since the early nineties, including the Netherlands, where it is organized by many local patient associations spread across the country.

An evaluation of SGE was done in the Netherlands in 1991, showing that it consisted of relatively long, weekly sessions, combining land-based and aquatic mobility and strengthening exercises and sports activities (e.g. badminton and volleyball), supervised by physical therapists (67, 68). However, 30 years later, the current situation with respect to the organization, usage and contents of SGE in the Netherlands is unknown. Such information is also limited for other countries: it appears that, similar to the Netherlands, SGE in Switzerland and the United Kingdom generally focuses on mobility and strength, uses land-based and often aquatic exercises, is performed once weekly and supervised by a physical therapist (40, 69, 70).

Optimizing physical activity and exercise

Although the proportion of patients with axSpA engaging in sufficient moderate-intensity aerobic PA is comparable to the general population, only a small minority seems to engage in vigorous-intensity aerobic PA (71-76). This might be caused by specific PA and exercise barriers axSpA patients experience due to their disease, e.g. pain, stiffness, fatigue, limited functioning and comorbidities. Furthermore, it appears that, apart from SGE and individual exercise therapy programs, the majority of axSpA patients does not engage in exercise activities with mobility and strength components (76, 77), let alone with an appropriate dosage according to the public health recommendations for health enhancing PA. However, the evidence on engagement in specific types of exercise is limited and does not take engagement in SGE or therapeutic exercise programs into account (78). Therefore, more research on engagement in specific exercise types, including their dosage, both in patients with and without physical therapy, seems warranted.

Findings of such research could subsequently guide interventions promoting adequately dosed PA and exercise in axSpA patients. Such interventions should also account for axSpA-specific exercise barriers. After all, engagement in the adequate types and dosage of PA requires a change in patients' behavior and behavior change is a complex process for which only providing advice is often insufficient (79-82). Exercise interventions could be provided through physical therapists and can take place on an individual basis or in a group setting.

Individual physical therapy

Individual physical therapy might be an appropriate setting for optimizing PA and exercise behavior. After all, most exercise interventions for axSpA patients are

provided by physical therapists and they play an important role in the promotion of PA (27, 28, 83). In addition, the large majority of axSpA patients have individual physical therapy treatment during the course of their disease (83).

Regarding the contents of individual physical therapy programs for axSpA patients, it was recently found that although the majority of these programs included advice on home exercise, just a minority included strength and aerobic exercises during treatment (83). Meanwhile, recent literature shows that the addition of aerobic and strength exercises to mobility exercise has extra benefits and is safe for people with axSpA (27, 41, 42, 47). Thus, although individual physical therapy might be a suitable setting for optimizing PA and exercise, there appears to be room for improvement of its contents.

Supervised group exercise

AxSpA-specific SGE appears to focus mainly on mobility exercises and in lesser extent on strengthening and aerobic exercises, let alone with appropriate dosage (35). The exercise program from three decades ago on which axSpA-specific SGE classes in the Netherlands are based, mainly focused on mobility and strength exercises and not specifically on (high-intensity) aerobic exercises (67, 68). Those exercise programs took place once weekly, without promotion of additional PA or (home) exercise (67). The current contents of SGE are however unknown, as well as the engagement of SGE participants in other exercise activities besides SGE.

Thus, it may be warranted to examine the current SGE contents and the weekly exercise engagement of SGE participants, in order to assess if there is room for improvement. If certain SGE enhancements are identified, the patient perspective towards current SGE and towards the proposed changes should be explored (84-86). This way, relevant barriers and facilitators for implementation of these potential enhancements can be identified (64). Subsequently, the proposed enhancements can be tested in a few regions using a pilot implementation, prior to a nationwide implementation. In such a pilot implementation, a hybrid study design would be ideal to evaluate both the effects and feasibility (87, 88). This study design could both speed the scientific progress and help translate the research findings into routine practice (87, 88).

Optimizing exercise in axSpA patients not using physical therapy

Not all axSpA patients use individual physical therapy or SGE. Thus, in order to optimize PA and exercise of those without physical therapy, an intervention without involvement of a physical therapist is needed. The requirement of such an intervention would be that it is context- and population-specific, targeting axSpA-specific barriers and facilitators. Regarding the developmental process for such an intervention, there are many different (theory- and evidence-based) approaches

(89) and the Intervention Mapping framework appears particularly suitable: it provides detailed guidelines to identify relevant environmental and personal factors before selecting corresponding intervention components (90). Intervention Mapping uses a stepwise approach, guiding the path from problem identification to solution development, while combining literature with stakeholders' perspectives.

Aims of this thesis

Given the potential need for improvement of PA and exercise of axSpA patients and the knowledge gaps found in the available literature, this thesis aims to:

1. Describe the current PA and exercise engagement of axSpA patients in the Netherlands and their relationship with physical therapy use.
2. Identify the need for evidence-based enhancements in axSpA-specific SGE in the Netherlands and evaluate the effectiveness and feasibility of the implementation of these enhancements.
3. Determine the components needed for an intervention to optimize PA and exercise of axSpA patients in general.

These aims are addressed in the following chapters:

- **Chapter 2** includes a study on the engagement of axSpA patients with and without physical therapy (individual and/or SGE) in aerobic PA.
- **Chapter 3** compares engagement in aerobic, mobility and strength exercise between axSpA patients using and not using SGE.
- **Chapter 4** describes the current organization and content of SGE for people with axSpA in the Netherlands and it is examined if the content meets recent scientific insights and how the quality can be further improved.
- **Chapter 5** outlines a study on the satisfaction of axSpA patients with current SGE and their perspective on potential evidence-based SGE enhancements.
- **Chapter 6** includes an evaluation of the effects and feasibility of a pilot implementation of enhancements of SGE in four regions.
- **Chapter 7** describes the intervention components needed for an intervention aiming to optimize exercise behavior of axSpA patients, using the Intervention Mapping protocol.
- **Chapter 8** provides a summary and a general discussion of the findings of this thesis.

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