Chapter 1

General introduction
Background

Physical activity provides fundamental health benefits in the general population, and appears to be even more essential in people with chronic physical disabilities. Physical inactivity, observed in a large part of the general population, is a serious risk factor for developing several health complications (e.g. cardiovascular disease, obesity, type 2 diabetes) and an important cause of mortality. Due to physical impairments, people with chronic disabilities are mostly less physically active and fit than the general population, and consequently have an even higher risk for developing these health complications.

Compared to other populations with physical disabilities, people with spinal cord injury (SCI) have among the lowest physical activity and fitness levels. An SCI is a damage to the spinal cord, caused by a trauma (e.g. falls or traffic accidents) or non-trauma (e.g. cancer or infections). As a result of the injury to the spinal cord, the communication between the brain, spinal cord and peripheral nerves is disrupted, leading to senso-motoric and autonomic dysfunction below the lesion level. Due to the motoric dysfunction, manifested by muscle paralysis, ~80% of the people with SCI become lifetime wheelchair users. As a consequence of the paralysis and wheelchair dependency, many people with SCI have a seriously inactive lifestyle, associated with deconditioning and a high incidence of secondary health complications (e.g. metabolic syndrome, chronic low-grade inflammation, visceral adiposity, osteoporosis and muscle atrophy), negatively influencing functioning, participation and quality of life.

Because of the improved medical care, life expectancy after SCI has considerably improved over the last few decades. However, an additional problem is that people aging with SCI and those with long-term SCI have even greater difficulties with staying physically active and fit, consequently leading to a greater risk for the development of secondary health complications and a further reduction of participation and quality of life. Avoiding the above-described downward spiral, that appears to worsen with age and duration of injury, is crucial for people with long-term SCI.

A rehabilitation aftercare system that covers the lifespan in people with SCI has been suggested, including preventive actions and interventions to preserve a long-term active lifestyle and physical fitness, and to decrease the frequency, duration and severity of secondary health complications. In this context, self-management and regular exercise seem to play an important role, since ‘Self-management is Power’ and ‘Exercise is
It has been demonstrated that self-management is effective in preventing several health problems and modifying behavior, especially when active learning strategies are included. Participation in regular exercise activities has also been shown to promote a range of health benefits, including improved physical fitness and prevention or reduction of several secondary complications.

Currently, there is no structured SCI-specific aftercare system operational in the Netherlands, and there is insufficient knowledge on the relations between physical activity, fitness and secondary complications, and the effectiveness of intervention strategies to improve these facets in people with long-term SCI. To get more insight in these relations and to examine different interventions, the multicenter and multidisciplinary research program ‘Active Lifestyle Rehabilitation Interventions in long-term Spinal Cord injury (ALLRISC)’ was conducted.

**Research program ALLRISC**

The research program ALLRISC was embedded in the active Dutch SCI clinical research network, financially supported by The Netherlands Organization for Health Research and Development (ZonMw). This well-organized network is a multicenter and multidisciplinary collaboration among the eight Dutch rehabilitation centers with a specialized SCI unit, academic research groups, the Dutch Flemish Spinal Cord Society (DuFSCoS) and the Dutch SCI patient organization (Dwarslaesie Organisatie Nederland (DON)). Fourteen years ago, it started as the multicenter research program ‘Restoration of Mobility in SCI Rehabilitation’ that mainly focused on the clinical rehabilitation phase and up to five years after discharge from inpatient rehabilitation. Building upon the outcomes and experience of this previous clinical research program, ALLRISC focused on the long-term impact of SCI on active lifestyle, fitness, health, participation and quality of life, and on interventions to improve these facets in the context of lifelong rehabilitation follow-up care.

ALLRISC consisted of four research projects (one cross-sectional study and three randomized controlled trials (RCTs)) focusing on the same program-wide outcome measures (i.e. physical activity, fitness, health, participation and quality of life), as well as on project-specific measures, following the International Classification of Functioning, Disability and Health (ICF; Figure 1.1). The primary aims of ALLRISC were (1) to
obtain a better understanding of the importance and requirements of regular rehabilitation aftercare in the context of long-term preservation of an active lifestyle, fitness, health, participation and quality of life in people with long-term SCI (time since injury ≥ 10 years), and (2) to develop evidence-based components and guidelines for an adequate SCI-specific rehabilitation aftercare plan in the Netherlands.

Figure 1.1 Health status in spinal cord injury, based on the International Classification of Functioning, Disability and Health (ICF).\textsuperscript{160,172}

The cross-sectional study (ALLRISC study 1)\textsuperscript{1} aimed to describe the prevalence of several secondary health complications (e.g. urinary tract and bowel problems, spasticity and pressure ulcers), and the impact of these complications on the program-wide outcome measures in a group of 300 individuals with long-term SCI. All eight Dutch rehabilitation centers with a specialized SCI unit participated in this study. Since the intervention studies were expected to be most relevant for people with low physical activity levels, study 1 participants were invited to participate in one of the three RCTs (ALLRISC studies 2–4) if they met the inclusion criterion ‘physically inactive’ (i.e. a score lower than 30 on the Physical Activity Scale for Individuals with Physical Disabilities (PASIPD))\textsuperscript{169}. 

\textsuperscript{1} \textsuperscript{169}
The three RCTs aimed to investigate the effects of a 16-week self-management (study 2),
low-intensity wheelchair exercise (study 3), and hybrid cycle exercise (study 4) intervention on the program-wide and project-specific outcome measures. The self-management intervention, performed in four of the eight Dutch rehabilitation centers with a specialized SCI unit, focused on problem-solving ability, proactive coping, education and self-efficacy. The experimental group (n = 40) received individual and group teaching and counseling sessions, while the control group (n = 40) only received oral and written information (knowledge transfer). Study 3, performed in two other rehabilitation centers, focused on the upper-body overuse paradigm. To avoid overuse of the upper-body musculoskeletal system, the intensity of exercise should not be too high in people with SCI. Therefore, a low-intensity (30% heart rate reserve) wheelchair exercise intervention group (n = 20) was evaluated and compared with a non-trained control group (n = 20). Study 4, central in the current thesis, is extensively described in the next section.

**ALLRISC study 4: hybrid cycling in spinal cord injury**

ALLRISC study 4 focused on the lower-body disuse paradigm. Due to paralysis of the lower limbs, exercise in people with long-term SCI predominantly involves activities of the non-paralyzed upper body. Manual wheelchair exercise used to be one of the most frequently used exercise modes in people with SCI. However, handrim wheelchair propulsion was found to be highly mechanically inefficient and stressing to the upper body, often leading to overuse of the upper-body musculoskeletal system (including discomfort and pain), and consequently impaired functioning. To (partly) prevent these overuse problems, a handcycle can be used as a better alternative for upper-body exercise since handcycling is more mechanically efficient and less stressing to the upper-body than manual wheelchair propulsion. Nowadays, the handcycle is a commonly used mobility device and upper-body exercise mode in the Netherlands, already introduced during clinical rehabilitation. Many Dutch people with SCI have an add-on handcycle together with their wheelchair that can be easily used for exercise and indoor and outdoor mobility (Figure 1.2).

However, several physiological factors related to SCI and upper-body exercise alone (e.g. handcycling), including the relatively small active muscle mass, inactivity of the
skeletal muscle pump of the legs and insufficient cardiovascular reflex responses, may reduce desired (aerobic) training effects. Moreover, due to the specificity principle, it is likely that upper-body training alone would not notably contribute to the prevention or improvement of several secondary complications in the lower limbs, such as osteoporosis, muscle atrophy, and vascular dysfunction.

![Image](image.jpg)

**Figure 1.2** The add-on handcycle for voluntary upper-body exercise.

Functional electrical stimulation (FES) can be used to reactivate the paralyzed lower-limb musculature and consequently reduce some of the above-mentioned problems. FES is a technique that uses computer-generated low-level electrical pulses to stimulate the contraction of targeted muscles through surface electrodes strategically placed over these muscles. Since the early 1980s, this technique became a promising aid for the rehabilitation of people with SCI. The most common system for lower-extremity FES exercise is the leg cycle ergometer, which is pedaled via FES-induced contractions of the paralyzed quadriceps, hamstrings and gluteus muscle groups. The computer of the ergometer controls the stimulation parameters, including the magnitude, frequency and sequence of the electrical stimulation in order to produce a fluid pedaling motion. The most common commercially available leg cycle ergometer in use is the ERGYS Clinical Rehabilitation System (Therapeutic Alliances Inc., Fairborn, OH, USA; Figure 1.3).

A major advantage of FES-induced leg exercise over voluntary arm exercise alone is that a large muscle mass can be activated that otherwise would be passive due to paralysis. This has the potential to improve lower-limb integrity, increase the circulation by
activating the skeletal muscle pump of the legs, and induce larger aerobic exercise responses. Various studies on FES-induced leg exercise have indeed found beneficial effects on aerobic fitness, and lower-extremity bone mineral density (BMD), muscle mass, and vascular function. Thus, these findings suggest that FES-induced leg exercise may positively influence deconditioning and secondary health complications (e.g. lower-body osteoporosis, muscle atrophy and vascular dysfunction) in people with SCI.

To further increase the active muscle mass and subsequently provide greater aerobic exercise responses, a hybrid mode of exercise can be used in which voluntary arm exercise is combined with FES-induced leg exercise. This was previously done by attaching a separate arm crank ergometer to the FES system (e.g. the ERGYS). However, more recent technological developments have introduced more user-friendly hybrid exercise devices as alternatives for in- and outdoor exercise. One of these hybrid exercise devices is the BerkelBike (BerkelBike B.V., St. Michielsgestel, the Netherlands) that combines synchronous handcycling with asynchronous FES-induced leg cycling (Figure 1.4). Despite the potentially greater benefits of hybrid exercise over arm exercise alone, this commercially available hybrid cycle is not yet as commonly used as the handcycle in Dutch SCI rehabilitation.
Figure 1.4 The hybrid cycle for combined FES-induced leg and voluntary arm exercise.

Several training studies on hybrid exercise showed positive effects on fitness and vascular function. However, limitations of these studies were the absence of a control group, the relatively small number of participants, and the fact that only one aspect of hybrid exercise (i.e. fitness or vascular function) was investigated. To date, there is insufficient knowledge of (1) the integrated effects of hybrid exercise on the ICF levels of functions and anatomical properties, activities and participation in people with long-term SCI, and (2) the potential greater benefits of hybrid exercise over upper-body exercise alone.

Therefore, the purpose of ALLRISC study 4 was to investigate the effectiveness of a 16-week hybrid cycle versus handcycle exercise program on the program-wide outcome measures (i.e. physical activity, fitness, health, participation and quality of life), as well as on project-specific measures (i.e. metabolic syndrome, inflammatory status, visceral adiposity, immune function, lower-body soft tissue composition, proximal tibia and distal femur BMD, bone turnover markers, and vascular function) in inactive people with long-term SCI. During this 16-week RCT (Figure 1.5), both the experimental (hybrid cycle) and control (handcycle) group trained twice a week for 18–30 minutes in a rehabilitation center with a specialized SCI unit (Reade Amsterdam or Sint Maartenskliniek Nijmegen). Outcome measures were obtained in the week before the training program (T1), after 8 weeks of training (T2), in the week after (T3), and 26 weeks after the training program (T4).
Aim and outline of this thesis

The main aim of the current thesis was to evaluate the effectiveness of the above-described 16-week RCT on a selection of the obtained outcome measures. In chapter 2 of this thesis, the experimental design of this RCT is extensively described. To get more insight in the metabolic and cardiorespiratory responses during hybrid cycling versus handcycling at equal subjective exercise intensity levels, a cross-sectional study was conducted parallel to the RCT, of which the results are presented in chapter 3. In chapter 4, the effects of the 16-week RCT on fitness and physical activity are evaluated. Chapter 5 describes the effectiveness of the RCT on the cardiovascular disease risk factors metabolic syndrome, inflammatory status and visceral adiposity. To be able to examine training effects on proximal tibia and distal femur BMD, we developed a new method to measure these sites using dual-energy X-ray absorptiometry. This method, as well as the reliability of it, is described in chapter 6. Chapter 7 evaluates the effects of the RCT on lower-body soft tissue composition, proximal tibia and distal femur BMD, and bone turnover markers. Finally, in chapter 8, the main findings of this thesis are summarized and discussed, and implications for clinical practice and recommendations for future research are provided.