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**Energy Expenditure and Accelerometer Cut-points for  
Sedentary Behavior and Physical Activity in Spinal Cord  
Injury – Implication for Guiding and Prevention**

Tobias Holmlund



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# Energy Expenditure and Accelerometer Cut-points for Sedentary Behavior and Physical Activity in Spinal Cord Injury – Implication for Guiding and Prevention

## THESIS FOR DOCTORAL DEGREE (Ph.D.)

By

**Tobias Holmlund**

*Principal Supervisor:*

Associate professor Kerstin Wahman  
Karolinska Institutet  
Department of Neurobiology, Care Sciences and Society  
Division of Neurogeriatrics,

*Opponent:*

Clinical Associate Professor Páll Ingvarsson  
University of Iceland and Landspítali  
University Hospital  
Department of Rehabilitation and Medical Faculty

*Co-supervisor(s):*

Associate professor Elin Ekblom-Bak  
Swedish School of Sport and Health Sciences  
Åstrand Laboratory of Work Physiology

*Examination Board:*

Professor Eva Jansson  
Karolinska Institutet  
Department of Laboratory Medicine  
Division of Clinical Physiology

Associate professor Erika Franzén  
Karolinska Institutet  
Department of Neurobiology, Care Sciences and Society  
Division of Physiotherapy

Associate professor Patrick Bergman  
Linnaeus University  
Department of Sport Science

Professor Claes Hultling  
Sophiahemmet University  
Department of Neurobiology, Care Sciences and Society  
Division of Neurogeriatrics

Assistant Professor Sonja De Groot  
University of Groningen  
Faculty of Medical Sciences  
Center of Human Movement Sciences

### AKADEMISK AVHANDLING

som för avläggande av medicine doktorsexamen vid Karolinska Institutet offentligen försvaras i Eugeniasalen/Eugeniahemmet  
Fredagen den 4:e oktober, 2019, kl 09.30



This book is dedicated to my daughter Agnes



## ABSTRACT

**Background:** A motor-complete spinal cord injury (SCI) alters the prerequisites for physical activity (PA) and subsequently energy expenditure. Persons with SCI above thoracic level six have a compromised physiological response, which further compromises energy expenditure, during exercise. Weight gain and lower levels of PA increase the risk of lifestyle-related diseases and their risk factors. Yet little is known about energy expenditure and the intensity of different activities from rest to maximal effort, nor about clinically useful cut-points for accelerometer in motor-complete SCI.

**Aim:** The aim of the work reported in this dissertation was to extend knowledge about energy expenditure, oxygen consumption and heart rate during rest, standardized activities and peak capacity in people with motor-complete SCI. A further aim was to evaluate how clinically accessible methods can be used to measure and describe activity patterns and intensity levels.

**Methods:** Participants were 64 persons with motor-complete SCI. Seventeen were women. Twenty-six had tetraplegia (C5-C8) and 38 (T7-T12) had paraplegia. Studies I and II are based on data from indirect calorimetry during rest and during standardized activities. In study III data from peak capacity ( $VO_{2peak}$ ), peak heart rate ( $HR_{peak}$ ) and Borg rating of perceived exertion (RPE) were used for categorizing standardized activities into different levels of intensity. In study IV dominant-wrist-worn accelerometer (ActiGraph GT3X+) cut-points were created by using receiver operating characteristic (ROC) curves, and the relative intensities established in Study III.

**Results:** Studies I and II showed that mean resting oxygen consumption for the whole group, no gender differences, was  $2.52 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  and the variable that best explained the variance for energy expenditure during rest (24 hours) was bodyweight  $r^2 = 0.37$  for the total cohort. During non-exercise activities (wheeling indoors/outdoors Borg RPE 10-11 and setting table), the activity energy expenditure (total energy expenditure minus resting energy expenditure) for tetraplegia increased between two and four times compared to sedentary, and between three and five times during exercise activities. Motor-complete paraplegia could increase energy expenditure between three and six times during non-exercise activities and between 6 and 14 times during exercise. In study III absolute  $VO_{2peak}$  was  $0.76 \text{ L} \cdot \text{min}^{-1}$  in tetraplegia and  $1.36 \text{ L} \cdot \text{min}^{-1}$  in paraplegia, differing significantly between men and women for both tetraplegia and paraplegia ( $p \leq 0.001$ ). The significant difference disappeared for both groups when the  $VO_2$  was related to body weight ( $p = 0.43$ ). Further, in study III all activities were categorized into sedentary, light, moderate and vigorous levels of intensity, based on percentage of  $VO_{2peak}$ , heart rate and Borg. Thus, many of the non-exercise physical activities (NEPA) were categorized as moderate or vigorous for persons with tetraplegia. Study IV showed a high correlation of 0.8-0.9 between percentage of  $VO_{2peak}$ , absolute  $VO_2$  (MET) and accelerometer vector magnitude counts (VMC). The ROC curve analysis showed an area under the curve (AUC) of 0.8, which resulted in cut-points for different intensity

levels such as, moderate-to-vigorous intensity of 4887 VMC (tetraplegia) and 9515 VMC (paraplegia).

**Conclusion:** Given the large inter-individual differences, person-specific information regarding RMR is crucial. The  $VO_{2peak}$  was lower for person with tetraplegi, affecting the relative intensity level for activities of daily living. Activity energy expenditure, especially during daily activities, may increase total daily energy expenditure since daily activities are easily accessible and can be performed for long periods. Specific accelerometer cut-points for motor-complete tetraplegia and paraplegia from ROC curve analysis may be used in rehabilitation and research to capture activity patterns objectively.



## SVENSK SAMMANFATTNING

**Bakgrund.** Efter en motorisk komplett ryggmärgsskada (RMS) förändras förutsättningarna för fysisk aktivitet och sedermera energiomsättning. Personer med en RMS ovanför bröstkota sex har en ändrad fysiologisk respons framförallt vid träning. Denna förändring gör att även energiomsättning minskar vid aktiviteter. Låg grad av fysisk aktivitet och viktuppgång ökar risken för hjärt- och kärlsjukdomar och dess riskfaktorer. Det saknas kunskap kring energiomsättning och intensitetsnivåer från vila till maximalt syreupptag. Dessutom saknas kliniskt användbara tröskelvärden (cut-points) för accelerometer registrering för personer med motorisk komplett RMS.

**Syfte.** Avhandlingen syftar till att öka kunskapen kring energiomsättning, syreupptag och hjärtfrekvens under olika aktiviteter så som vila, vardagsaktiviteter, träning samt maximalt syreupptag. Därutöver att skapa information kring att objektivt mäta fysisk aktivitet med hjälp av accelerometer eller Borg RPE skalan.

**Metod.** Sextiofyra personer med motorisk-komplett RMS varav sjutton var kvinnor. Tjugosex personer hade en tetraplegi (C5-C8) och 38 personer med paraplegi (T7-T12). Studie I och II är baserade på mätningar med hjälp av indirekt kalorimetri under vila och standardiserade aktiviteter. I Studie III kategoriseras aktiviteterna i olika intensitetsnivåer som bygger på data från maximalt syreupptag, maximal hjärtfrekvens samt Borgskalan. I Studie IV presenteras tröskelvärden utifrån relativa intensitetsnivåer för handledsburen accelerometer (ActiGraph GT3X+) som skapats utifrån receiver operating characteristic (ROC- kurvor).

**Resultat.** Studie I och II visade på en genomsnittlig syreförbrukning vid vila på  $2.52 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  för hela gruppen och det fanns inte några signifikanta könsskillnader. Kroppsvikt (kg) var den variabeln som bäst kunde förklara variansen för energiomsättningen under vila (24 timmar)  $r^2 = 0,37$ . Vid vardagsmotion ökade aktivitetsrelaterade energiomsättningen (total energiomsättning minus energiomsättning vid vila), för personer med tetraplegi, två till fyra gånger (rulla inomhus/utomhus Borg 10-11 och duka bord) jämfört med stillasittande och mellan tre till fem gånger vid träning. För personer med paraplegi ökade den aktivitetsrelaterade energiomsättningen tre till sex gånger vid vardagsmotion och 6 till 14 gånger vid träning, jämfört med stillasittande. Den maximalt syreupptag var  $0,76 \text{ L} \cdot \text{min}^{-1}$  för personer med tetraplegi och  $1,36 \text{ L} \cdot \text{min}^{-1}$  för personer med paraplegi och det var en signifikant skillnad mellan män och kvinnor för både grupperna (Studie III).

Könsskillnaderna uteblev när det maximala syreupptaget relaterades till kroppsvikt. I Studie III kategoriserades samtliga standardiserade aktiviteter som; stillasittande, lågintensiva, måttligt intensiva eller högintensiva. Aktivitetsnivåerna baserades på procent (%) av maximalt syreupptag, % av maximal hjärtfrekvens samt Borg RPE-skalan. För personer med tetraplegi kategoriserades de flesta vardagsaktiviteterna som måttlig eller högintensiva. Studie IV visade på en hög korrelation 0,8 - 0,9 mellan procent av maximala syreupptaget, absolut syreupptag (MET) och accelerometer registrering vector magnetud counts (VMC). Resultatet analyserades vidare med ROC-kurvor och visade en area under kurvan (AUC) på 0,8. Utifrån

detta skapades separata tröskelvärden (cut-points) för de olika intensitetsnivåerna såsom måttlig till högintensiv 4887 VMC (tetraplegi) och 9515 VMC (paraplegi).

**Konklusion.** Med tanke på skillnaderna i energiomsättning under vila mellan deltagarna så är det viktigt med personspecifik information för energiomsättningen. Det maximala syreupptaget var relativt lågt för personer med tetraplegi vilket gör att vardagsaktiviteter utförs i måttlig till hög intensitetsnivå. Aktivitetsenergiomsättningen vid vardagsmotion har potentialen att öka den totala energiomsättningen eftersom dessa aktiviteter är lättillgängliga och kan utföras under lång tid. Ryggmärgsskadespecifika tröskelvärden (cut-points) för handlesburen accelerometer skulle kunna användas för att objektivt mäta aktivitetsmönster både under rehabilitering och vid forskning.

## LIST OF SCIENTIFIC PAPERS

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- II. Holmlund T, Ekblom-Bak E, Franzen E, Hultling C, Wahman K. Energy expenditure after spinal cord injury in people with motor-complete tetraplegia or motor-complete paraplegia. *Spinal Cord*.2017; 56:274–283.
- III. Holmlund, T., Ekblom-Bak, E., Franzen, E., Hultling, C. & Wahman, K. Intensity of physical activity as a percentage of peak oxygen uptake, heart rate and Borg RPE in motor-complete para- and tetraplegia. Editorial accept PLOS ONE.
- IV. Holmlund, T., Ekblom-Bak, E., Franzen, E., Hultling, C. & Wahman, K. Defining accelerometer cut-points for different intensity levels in motor-complete spinal cord injury. *Spinal Cord*. 2019. doi: 10.1038/s41393-019-0308-y. [Epub ahead of print]

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## LIST OF ABBREVIATIONS

ACE	Arm-crank ergometry
ACSM	American Sports and Medicine
AEE	Activity energy expenditure
AISA	American Spinal Injury Association
AIS	ASIA Impairment Scale
BMI	Body mass index
C	Cervical
CI	Confidence interval
CVD	Cardiovascular disease
HR	Heart rate
H	Hour
IQR	Interquartile range
Kcal	Kilocalorie
Kg	Kilogram
LOA	Limits of agreement
MET	Metabolic equivalent for task
Min	Minutes
ml	milliliter
N/A	Not applicable
O <sub>2</sub>	Oxygen
PA	Physical activity
REE	Resting energy expenditure
RER	Respiratory exchange ratio
RMR	Resting metabolic rate
ROC	Receiver operating characteristics
RPE	Rating of perceived exertion
RPM	Revolutions per minute
S	Sacral
SCI	Spinal cord injury
SEE	Standard error of estimation

T	Thoracic
TV	Television
VMC	Vector magnitude count
W	Watt
WHO	World Health Organization





# 1 INTRODUCTION

As used in the present work, physical activity (PA) covers all intensities and types. It is fundamental for a healthy life as a basic element of energy expenditure and cardiovascular fitness<sup>1,2</sup>. Maintaining the level of PA, e.g. moderate-to-vigorous, positively affects health-related features such as decreasing risk factors for cardiovascular disease (CVD)<sup>1</sup>. It also affects important body functions such as sleep, the immune system, and is used in the management of certain chronic conditions<sup>1-4</sup>. There is growing interest in PA and its effects<sup>5</sup>. For example, in 2015, the World Health Organization (WHO) strategy “Physical activity for the WHO European Region 2016 – 2025”<sup>6</sup> included the goal of providing equal opportunities for PA regardless of prerequisites such as: gender, age, income, education, ethnicity or disability<sup>6</sup>. Adopting this strategy is important because a global trend indicates that people are becoming less physically active, especially in daily activities or none-exercise physical activity (NEPA), while the capital burden of disease in Europe is non-communicable diseases, such as CVD (17-33% of all deaths). In Sweden CVD causes 18% of all the deaths where the major cause is ischemic heart disease<sup>7</sup>. Further, in Sweden 28 % of women and 42 % of men (age 18-65 years) are overweight with a body mass index (BMI)  $\geq 25$  and this figure is increasing<sup>8</sup>. Therefore, PA is of utmost importance to prevent and decrease these health-related diseases<sup>1</sup>.

After a spinal cord injury (SCI) numerous cellular, muscular and regional body-system changes occur, which affects metabolic profiles<sup>9</sup>. The loss of large parts of active muscle-mass after motor-complete SCI results in lower energy expenditure both during rest and during activity<sup>10,11</sup>. Persons with an SCI are less physically active and have a higher risk of becoming overweight or obese than the general population, and this further increases the risk of CVD and its risk factors<sup>9,12-15</sup>. In the SCI population, approximately 2/3 have been reported as overweight or obese one year after the injury<sup>15-18</sup>.

The word rehabilitation is from Latin: *re = again* and *habitare = make fit*, and interpreted as measures to regain an original state. Here, a fundamental part of rehabilitation is for the person with SCI to regain control over the body and to reach an optimal level of independence. This includes activities such as: mobility, e.g. wheelchair skills, transfers (bed, sofa, car, floor), and self-care, e.g. toileting, showering, dressing, eating, drinking. Obesity can negatively affect rehabilitation and the prerequisites for living an active, optimally dependent life after SCI. Persons with SCI that are independent in mobility items, and also self-care items, correlate with a higher quality of life<sup>19</sup>. Higher BMI is associated with lower physical health and less active participation<sup>19,20</sup>. The loss of functional muscle mass and the altered cardiovascular response after motor-complete SCI limits the understanding of energy expenditure. Moreover, there is a lack of objective ways of assessing intensity, duration and frequency during independent living. Specific information based on injury level regarding energy expenditure during different activities at different intensity levels is scarce. In addition, objective ways of assessing independent living PA patterns are needed to build adapted evidence-based programs.

## **2 BACKGROUND**

### **2.1 SPINAL CORD INJURY**

The spine includes 33 vertebrae: cervical (C1-C7), thoracic (T1-T12), lumbar (L1-L5) and sacral (S1-S5), and the four bones of the coccyx. The spinal cord is divided into 31 segments. It ends at L1-L3 (medullary cone) and re-forms to a 'tail' of nerves (cauda equina) for the rest of its length. An SCI can be a serious medical event and can appear after a trauma or after a non-trauma-related event. It can result in damage in the spinal canal where the neural pathways between brain and spinal cord are located<sup>21,22</sup>. This results in total or partial loss of motor and/or sensory function in the segments below the level of injury. In addition to this loss, individuals with SCI experience several direct consequences of the injury such as bladder and bowel dysfunction, respiratory dysfunction and spasticity<sup>22</sup>. Secondary complications are also common after an SCI; for instance, neuropathic/musculoskeletal pain, edema, urinary tract infections and pressure ulcers<sup>23</sup>.

#### **2.1.1 Incidence and prevalence**

Data for Europe, North America and Australia have recently reported incidence ranging between 2.1 and 195 cases per million population<sup>24,25</sup>. The global incidence for traumatic SCI is estimated to 23 cases per million<sup>26</sup>. In the Stockholm region in Sweden the crude incidence rate is estimated to be about 19.5 cases per million<sup>27,28</sup>. Since medical care has improved for persons with SCI, life expectancy has increased, resulting in an increase in global prevalence. The global prevalence rate reportedly ranges between 250 and 960 cases per million population<sup>29</sup>. Both prevalence and incidence globally are uncertain due to methodological issues and failure to report<sup>30,31</sup>. In Sweden, the prevalence is estimated to be around 240 cases per million population<sup>32</sup>, with estimations mainly based on the Stockholm region, where roughly 1100 persons have a traumatic or systemic SCI<sup>33,34</sup>.


#### **2.1.2 Classification of level and severity of SCI**

An SCI is classified according to international standards for neurological classification of spinal cord injury<sup>35</sup>. Injuries located at segment C8, between vertebra C7-T1 and above are referred to as tetraplegia and those at T1 and below as paraplegia<sup>35</sup>.


The classification is based on an American Spinal Injury Association (ASIA) worksheet that includes assessment of the motor function of the key muscles of the upper (C5-T1) and lower extremities (L2-S5)<sup>35</sup> (Figure 1). Muscle strength grading is scored on a 0-5 scale. Further, the ASIA assesses sensory function as light touch and pin-prick, scored as 0-2 (C2-S5) (Figure 1). These two assessments provide a standardized score for motor and sensory function<sup>35</sup> (figure 1). The neurological level of the injury is determined by the most caudal

level of the spinal cord that has maintained normal neurological function. Examination results are further classified according to the ASIA impairment scale (AIS) A – E (table 1).

**Figure 1.** ASIA neurological examination sheet. The international standards booklet for neurological and functional classification of spinal cord injury <sup>21,36</sup>.



**INTERNATIONAL STANDARDS FOR NEUROLOGICAL CLASSIFICATION OF SPINAL CORD INJURY (ISNCSCI)**



Patient Name \_\_\_\_\_ Date/Time of Exam \_\_\_\_\_  
 Examiner Name \_\_\_\_\_ Signature \_\_\_\_\_

**RIGHT**

**MOTOR KEY MUSCLES**

Upper Extremity Right (UER)

Elbow flexors C5

Wrist extensors C6

Elbow extensors C7

Finger flexors C8

Finger abductors (little finger) T1

Lower Extremity Right (LER)

Hip flexors L2

Knee extensors L3

Ankle dorsiflexors L4

Long toe extensors L5

Ankle plantar flexors S1

(VAC) Voluntary anal contraction (Yes/No)

RIGHT TOTALS (MAXIMUM)

**SENSORY KEY SENSORY POINTS**

Light Touch (LT)

Pin Prick (PP)

**LEFT**

**MOTOR KEY MUSCLES**

Upper Extremity Left (UEL)

Elbow flexors C5

Wrist extensors C6

Elbow extensors C7

Finger flexors C8

Finger abductors (little finger) T1

Lower Extremity Left (LEL)

Hip flexors L2

Knee extensors L3

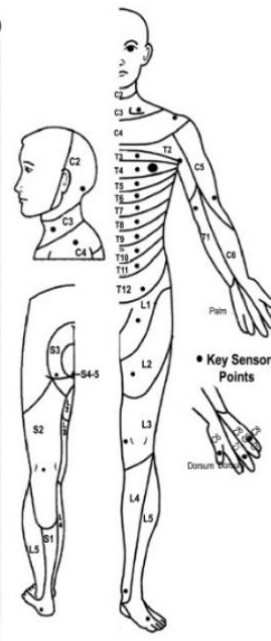
Ankle dorsiflexors L4

Long toe extensors L5

Ankle plantar flexors S1

(DAP) Deep anal pressure (Yes/No)

LEFT TOTALS (MAXIMUM)



• Key Sensory Points

**SCORING ON REVERSE SIDE**

0 = total paralysis

1 = palpable or visible contraction

2 = active movement, gravity eliminated

3 = active movement, against gravity

4 = active movement, against some resistance

5 = active movement, against full resistance

5\* = normal corrected for pain/diuse

NT = not testable

**SCORING ON REVERSE SIDE**

0 = absent

1 = altered

2 = normal

NT = not testable

**MOTOR SUBSCORES**

UER  + UEL  = UEMS TOTAL  (MAX 25)

LER  + LEL  = LEMS TOTAL  (MAX 25)

**SENSORY SUBSCORES**

RLT  + LLT  = LT TOTAL  (MAX 56)

RPP  + LPP  = PP TOTAL  (MAX 56)

**NEUROLOGICAL LEVELS**

1. SENSORY 

R	L
<input type="text"/>	<input type="text"/>

2. MOTOR 

R	L
<input type="text"/>	<input type="text"/>

3. NEUROLOGICAL LEVEL OF INJURY (NLJ)

4. COMPLETE OR INCOMPLETE?

5. ASIA IMPAIRMENT SCALE (AIS)

(In complete injuries only)  
**ZONE OF PARTIAL PRESERVATION**  
Most caudal level with any innervation

SENSORY 

R	L
<input type="text"/>	<input type="text"/>

MOTOR 

R	L
<input type="text"/>	<input type="text"/>

This form may be copied freely but should not be altered without permission from the American Spinal Injury Association. REV 02/13

**Table 1.** Classification system for injury severity according to the ASIA Impairment Scale (AIS) <sup>35,36</sup>.

<b>Neurological classification system</b>		
<b>(AIS) for SCI</b>		<b>Description</b>
<b>AIS A</b>	Motor and sensory complete	No sensory or motor function is preserved in the sacral segments S4-S5
<b>AIS B:</b>	Motor complete and sensory incomplete	Sensory but not motor function is preserved below the neurologic level and includes the sacral segments S4-S5, AND no motor function is preserved more than three levels below the motor level on either side of the body.
<b>AIS C</b>	Motor and sensory incomplete	Motor function is preserved below the neurologic level and and more than half of key muscle functions below the single neurologic level of injury have a muscle grade less than 3 (Grades 0-2).
<b>AIS D</b>	Motor and sensory incomplete	Motor function is preserved below the neurologic level and at <i>at least half</i> (half or more) of key muscle functions below the neurologic level of injury have a muscle grade of 3 or greater.
<b>AIS E</b>	Normal	If sensation and motor function as tested with the ISNCSCI are graded as normal in all segments, and the patient had prior deficits, then the AIS grade is E. Someone without a SCI does not receive an AIS grade.

### 2.1.3 Autonomic nervous system

After SCI, one of the most critical consequences for PA and exercise is the altered response of the autonomic nervous system (injury level above T6). Understanding how the autonomic nervous system affects exercise and peak capacity is of importance in motor-complete SCI. The autonomic nervous system controls vital organs to create homeostasis by responding differently depending on stimuli such as exercise, stress or food. The system is divided into three subsystems, the sympathetic nervous system, the parasympathetic nervous system and the enteric nervous system. The parasympathetic is located in the brainstem, cranial nerves and pelvic plexus (S2-S4) and it is a slowly-activating system active mostly during rest and digestion. The sympathetic system is predominantly located at the lateral horns of the spinal cord T1-L2 and prepares the body for fast physiological changes. The parasympathetic system controls the heart by lowering heart rate (HR), the lungs by slowing respiration and blood pressure by controlling blood vessels <sup>37-40</sup>. The sympathetic system interacts with the same organs in the opposite way by directing blood to the skeletal muscles (T1-5) of the upper and lower body (T6-L2), increasing HR and stroke volume, and increasing respiratory rate, oxygen uptake (T1-T5) and blood pressure <sup>37,38,41-43</sup> (Figure 2). The lack of facilitation from the sympathetic system correspondingly affects the cardiovascular system during

exercise, with reduced cardiac output, stroke volume and oxygen delivery. The result from this is a lower maximum HR, lower peak oxygen ( $O_2$ ) consumption ( $VO_{2peak}$ ) and lower peak power for individuals with a motor-complete SCI above T6. The altered function differs between individuals with motor-complete injury, individuals with an injury T1-T5 having higher maximum heart rate,  $VO_{2peak}$  and peak power than those among individuals injured between C5 and T1<sup>44,45</sup>. Individuals with a motor-complete injury below T6 have an almost normal cardiovascular response for heart rate,  $VO_{2peak}$ , blood pressure and peak power<sup>46,47</sup>.

**Figure 2.** simplified scheme of autonomic nervous system control of cardiovascular system during exercise. Red lines are the parasympathetic system and blue lines the sympathetic system.

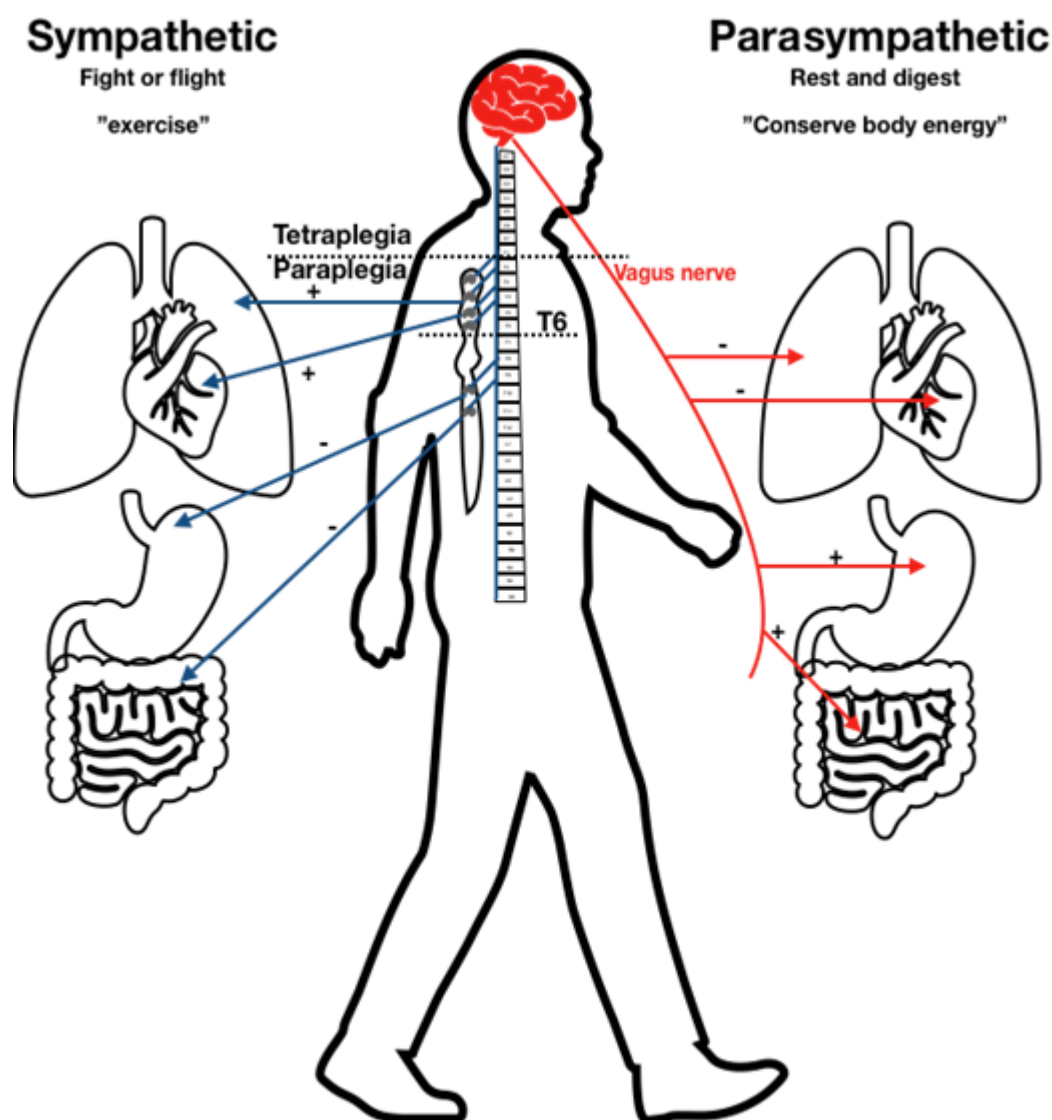


Figure by Tobias Holmlund

## 2.2 PHYSICAL ACTIVITY

Physical activity (PA) is defined as “*any bodily movement produced by skeletal muscles that results in energy expenditure*”<sup>48</sup>. Further, PA occurs while “*sleeping, at work and at leisure*” and can be categorized into different types such as, ‘*occupational, sports, conditioning, household or other activities*’<sup>48</sup>. Exercise is a subset of PA and is defined as ‘*planned, structured, and repetitive and has as a final or an intermediate objective the improvement or maintenance of physical fitness*’<sup>48</sup>. Physical fitness consist of improvement or maintenance components or attributes that are related to health, such as cardiovascular endurance or skill (coordination, balance)<sup>48</sup>.

### 2.2.1 Intensity of physical activity

Activities are performed at different intensity levels. Intensity level range from sedentary (low), to peak capacity. They have different cardiovascular- and health-related benefits. The moderate and vigorous intensity level has in previous research been shown to have most health-related benefits<sup>1</sup>, but recent research implies that also lower intensity levels may have important health benefits<sup>49-51</sup>. Higher intensity levels require higher oxygen consumption, leading to cardiovascular, respiratory and metabolic (e.g. lactate) adaptation to foster endurance<sup>52,53</sup>. The oxygen demand also depends on available muscle mass, which allows comparisons between individuals of different size during weight-bearing activities<sup>53</sup>.

#### 2.2.1.1 Absolute intensity

Absolute intensity describes the metabolic need during specific work (regardless of peak capacity), and is expressed as energy expenditure per time unit or speed and is<sup>52</sup>. Aerobic PA expressed in absolute intensity may also be described in variables related to work performed, such as watt (W), kilocalories (kcal) or speed<sup>52</sup>. In more general terms, absolute intensity is often described as multiples of basal metabolic rate (in kcal) or oxygen consumption during rest, also known as metabolic equivalents (METs)<sup>54</sup>. MET values range from low (just above 0.9 MET when sleeping up to 18 MET when running 17.4 km/h (Table 2). 1 MET is also referred to as either 1 kcal·kg<sup>-1</sup>·h<sup>-1</sup> or 3.5 ml·O<sub>2</sub>·kg<sup>-1</sup>·min<sup>-1</sup> and a compendium for the general population describes a large range of activities and their corresponding MET values<sup>54,55</sup>.

#### 2.2.1.2 Relative intensity

Relative intensity is the absolute workload related to the individual’s peak capacity, which commonly is described as percentages (%) of VO<sub>2peak</sub> or peak HR<sup>52</sup> (table 2). Relative intensity can also be expressed as % of HR reserve, (peak HR minus HR at rest), and as % of VO<sub>2</sub> reserve (VO<sub>2peak</sub> minus VO<sub>2</sub> at rest). Another and maybe the most useful way of

describing relative intensity in clinical settings is by ratings of perceived exertion using the Borg RPE using a rating scale as the Borg RPE scale <sup>56</sup> (table 2).

### 2.2.1.3 Intensity levels

**Table 2.** Intensity levels in the general population <sup>1,2</sup>.

Level of intensity	Relative and absolute intensity	Activities within the different intensity levels
<b><i>Sedentary</i></b>	<1.5 MET, <20% VO <sub>2peak</sub> , <40 HR peak or Borg RPE <8	Sitting or lying down but awake <sup>53</sup>
<b><i>Light intensity</i></b>	1.5 METs to 2.9 METs, 20-39% VO <sub>2peak</sub> , 40-59 HR peak or Borg RPE 8-11	Low/light intensity PA is often a part of daily life activities: occupation, leisure, walking (slow), talking, playing a musical instrument, shopping, computer work etc.
<b><i>Moderate intensity</i></b>	3.0 METs to 5.9 METs, 40-59 % VO <sub>2peak</sub> or 60-74 HR peak or Borg RPE 12-13	Moderate intensity PA may be a part of life activities, e.g. brisk walking (>6km/h), mowing lawn, bicycling (>16km/h), cleaning, recreational sports etc.
<b><i>Vigorous intensity</i></b>	6 METs up to 8.9 METs 60-89% VO <sub>2peak</sub> , 75-94 HR peak or Borg RPE 14-17.	Vigorous PA refers to intentional exercise; bicycling (>22km/h), running (>9 km/h), sports or carrying heavy loads

### 2.2.1.4 Physical activity for motor-complete SCI

The different prerequisites for PA and the heterogeneous nature of motor-complete SCI limit the generalizability of the health benefits (cardiovascular or cardiometabolic) from PA. Most research on its effects is based on exercise and there is limited information about the cardiometabolic effects of daily activities or non-exercise physical activities (NEPA) <sup>57-59</sup>. Moreover, the SCI-specific description of different intensity levels is mainly based on absolute intensity measurements, such as information about MET values for different activities. Research on the intensity, duration and frequency of PA for cardiovascular or

cardiometabolic health benefits shows that, e.g. six weeks of 30-45 min arm-cranking at an intensity of 60-70% of peak oxygen consumption ( $VO_{2peak}$ ) 3 times a week is associated with higher  $VO_{2peak}$ , lower BMI, waist circumference and fasting insulin<sup>59,61,62</sup>. Other reported effects are a lower HR during submaximal testing and lower lactate levels after 8 weeks of 3x20 min of moderate-intensity (70-80% of max HR-reserve) wheelchair ergometry<sup>63</sup>. For persons with motor-complete tetraplegia, circuit resistance training three times a week for 40-45 min (60% HR reserve) improves strength, aerobic capacity/fatigue resistance<sup>64</sup>.

## 2.2.1 Physical activity recommendations

WHO recommendations for PA are based on the link between level of PA and cardiovascular fitness and the reduced risk of CVD and its associated risk factors<sup>1</sup>. The current recommendation is to be physically active at moderate intensity for at least 150 min a week, or at least 75 min of vigorous aerobic activity a week<sup>65</sup>.

### 2.2.1.1 Physical activity recommendations for SCI

Currently, two different recommendations for SCI are used: one that are similar to the WHO guidelines, five times 30 minutes of moderate activity and three times 20 minutes of vigorous (instead of 75 min)<sup>66</sup>, and a recommended 30 minutes of moderate-to-vigorous aerobic exercise three times a week (90 min), for cardiometabolic health for adults with SCI<sup>67</sup>. The latter recommendation is based on a review of current evidence for cardiometabolic effects for persons with motor-complete SCI<sup>67</sup>. The WHO guidelines show that PA is lower among persons with SCI than in the general population and specifically in those with motor-complete tetraplegia<sup>68,69</sup>. In Sweden, as many as 80 % of wheelchair-dependent individuals with SCI do not reach these guidelines for PA<sup>70</sup>.

There is an ongoing debate concerning the health benefits of 150 min of moderate aerobic activity compared to 30 minutes of moderate-to-vigorous aerobic exercise three times a week (90 min), for cardiometabolic health for adults with SCI<sup>71</sup>. Both recommendations will probably affect health depending on individual fitness levels. Persons with poor fitness might find it easier to follow the low level of PA<sup>67</sup> and persons with a higher level might be able to follow the recommendation for the general population<sup>65,66</sup>. Due to the heterogeneous nature of motor-complete tetraplegia and paraplegia, the general information for level of intensity, duration and frequency needs to be customized for the different groups.

## 2.3 MONITORING PHYSICAL ACTIVITY

The time, intensity and duration of PA may be assessed with tools such as questionnaires, HR-monitors, activity bands and accelerometers. The different tools have different validity,



reliability and accessibility, where subjective tools (questionnaires) have the lowest validity and high accessibility (low cost). Objective tools (HR-monitors, activity bands and accelerometers) have higher reliability, where accelerometers having the highest reliability and validity, nonetheless least accessible (high cost) <sup>72,73</sup>.

### 2.3.1 Questionnaires

The most commonly used and accessible tool is questionnaires or surveys in many different variants <sup>74</sup>. The least extensive variants include only questions about regular PA and use predetermined answers on a 3-to-5 scale. The more extensive questionnaires ask about type, duration and intensity for a specific time period. Questions about regular PA are easiest to remember and have higher reliability, while self-reported PA has the highest correlation with health-related effects <sup>72,73,75</sup>.

#### 2.3.1.1 *The SCI-population*

In the SCI-population almost all information on patterns of PA is assessed with questionnaires, with their lower validity compared to objective assessment. This is because it is hard to accurately recall behavior i.e. the intensity of the exercise activity <sup>76</sup>. Even so, two instruments have been validated for PA; PARA-SCI <sup>77</sup> and the Swedish questionnaire <sup>70</sup>.

### 2.3.2 Accelerometers

An accelerometer is a small, light electronic device worn on the hip or wrist. It objectively captures movements by recording the subject's movement in three axes: vertical, horizontal and perpendicular. This provides the volume, intensity and frequency of activity (summarized in counts per minute). Moreover, accelerometry provides high resolution feedback regarding the time and the percentage of time spent at different intensity levels such as sedentary, NEPA and exercise <sup>78</sup>.

#### 2.3.2.1 *SCI-population*

Few studies have validated objectively measures such as. % of HR peak, % of VO<sub>2peak</sub>, activity band, HR monitors and accelerometers for persons with SCI <sup>79-83</sup>. Persons with motor-complete SCI are restricted to movements in the upper body, so placement of an activity monitor would preferably be on the upper body and desirably the wrist or upper arm <sup>84</sup>. Recent studies of accelerometer use to create SCI-specific cut-points for different intensities are scarce and show a large discrepancy for moderate-to vigorous PA cut-points <sup>81,82</sup>. This is probably due to heterogeneous sampling and choice of statistical analysis <sup>81,82</sup>.

## 2.4 METABOLIC RATE AND ENERGY EXPENDITURE

During an activity, the body consumes a higher amount of oxygen and subsequently produces a higher demand for calories than when resting or sedentary. Metabolism increases linearly with the rate of work (power output) until it reaches peak capacity during aerobic work<sup>53</sup>. The metabolic rate can be divided into three different components; basal metabolic rate, thermic effect of food, and activity-induced energy expenditure. The latter is the most modifiable through PA. *The basal metabolic rate* is often related to whole-body mass and reported as  $\text{kcal}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ . The resting metabolic rate (RMR) is thus more commonly used to replace basic metabolic rate since RMR does not require that the participant sleep over at the hospital to be measured, as the basal metabolic rate does<sup>53</sup>. RMR is in this thesis referred to as resting energy expenditure (REE) reported as  $\text{kcal}\cdot\text{kg}\cdot\text{min}^{-1}$  and kcal over 24 hours. This in turn is based on resting oxygen consumption measured in  $\text{L}\cdot\text{min}^{-1}$  or  $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ . REE can also be calculated with the Harris-Benedict formula. This uses specific models for men  $\text{REE (Men)} = 66.473 + 13.7516 (\text{weight}) + 5.0033 (\text{height}) - 6.755 (\text{age})$  and for women  $\text{REE (Women)} = 655.0955 + 9.5634 (\text{weight}) + 1.8496 (\text{height}) - 4.6756 (\text{age})$ <sup>85</sup>. *ii), the thermic effect of food*, is the energy expended, above REE, when processing food for use and storage<sup>86</sup>. *iii) The metabolic rate during different activities* in this thesis is referred to as activity energy expenditure (AEE) and this component is the easiest to alter to increase energy expenditure.

Today, indirect calorimetry is probably the most common clinical method for measuring energy expenditure during rest and/or during rapid fluctuation of intensity levels during activities<sup>78,87,88</sup>. The method relies on the respiratory gas exchange of the inhaled volume of oxygen ( $\text{VO}_2$ ) and the production of carbon dioxide which is collected through a face mask and analyzed manually (Douglas-Bag method) or with an on-line system<sup>53,87</sup>. Other methods for measuring energy expenditure are direct calorimetry and the doubly-labeled water technique<sup>89</sup>. In the latter, the subject receives a dose of two isotopes known as doubly labeled water ( $^2\text{H}_2$   $^{18}\text{O}$ ). This is an accurate way to measure total daily energy expenditure during free living conditions of 7 to 14 days duration. Direct calorimetry measures the heat produced by a subject enclosed in a sealed chamber<sup>87</sup>. This has its limitations in capturing rapid fluctuations and activities performed for a limited time.

### 2.4.1 Metabolic rate and energy expenditure during Resting conditions

The RMR is based on measurements of  $\text{VO}_2$  together with the production of carbon dioxide ( $\text{CO}_2$ ). This is further used in the Weir equation to REE. The REE is the smallest amount of energy required for basal body processes<sup>53</sup>. These involuntary processes are regulated from the autonomic nervous system and account for approximately 60 to 70% of total daily energy expenditure for a sedentary person in the general population. Three-quarters of the variation in REE is predicted from fat-free mass<sup>86,90</sup>. The REE is measured in the morning after sleep in a post-absorptive state. The distribution of the basal processes as estimated energy expenditure in percentage for the different organs has been reported in the following order;

liver 30%, brain 20%, muscles 18%, heart 10%, kidneys 7% and, 15% from breathing, cell formation, body temperature etc.<sup>91,92</sup>. The rate is based on whole-body oxygen consumption, reported as relative oxygen consumption ( $\text{ml}\cdot\text{O}_2\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ). In the general population there is a commonly used value of  $3.5\text{ O}_2\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ , 1 MET i.e. the cost of an activity as a multiples of RMR<sup>55</sup>. However, recent research has a more individualized approach, reporting RMR stratified by age and BMI<sup>93</sup>.

#### 2.4.1.1 *The SCI population*

Research on REE in the SCI population shows a large variation in measured REE when reported as 24-hour energy expenditure, ranging from 1256 to 1854 kcal<sup>11</sup>. Many studies investigating REE in SCI differ with regard to level of injury and severity AIS A-D. This may explain the large intra-individual variation within each study and the difference between the studies. RMR for persons with SCI compared to the general population with the same BMI is about 15- 22% lower<sup>93-99</sup>. The variation in REE among persons with SCI is not clear and studies that include both persons with paraplegia and those with tetraplegia show contradictory results; two studies report significant differences between the groups for kcal 24/h and for Kcal/kg<sup>100</sup>, while others report no significant difference when REE is related to bodyweight<sup>96</sup>. Nor do comparisons for gender-specific REE show significant differences when REE is related to bodyweight<sup>94,95,101,102</sup>. Moreover, there seems to be a decrease in REE (kcal 24 h) over time, the largest decrease being between 2 and 10 weeks post injury and then flattening over 10 to 26 weeks, with further reduction until 130 weeks. The mean 24 h reduction in kcal after 2.5 years was 300 kcal<sup>103</sup>.

#### 2.4.2 **Energy expenditure during activity**

Energy expenditure during activity is often described in METs. A MET =  $1\text{ kcal}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ , and the Ainsworth compendium includes MET values for over 600 specific activities<sup>54,55</sup>. Activity-related metabolism is in this thesis referred AEE, which is the energy consumed above REE, calculated by subtracting REE from total energy expenditure. AEE is the only component that a person can alter instantly by changing behavior, by increasing or decreasing activity level. Physical activities are modifiable by three different components; intensity, frequency and duration - and an increase in any of them affects energy expenditure. The AEE during activities of daily life includes NEPA, which is the predominant component of daily spontaneous PA<sup>104</sup>. Performance of NEPA can contribute to total daily energy expenditure up to  $1000\text{ kcal day}^{-1}$ , with a large day-to-day variation<sup>104</sup>. Due to the accessible and achievable nature of NEPA it is easy to engage in such activity frequently for both shorter and longer periods<sup>104,105</sup>. Moreover, a high level of NEPA can be of importance for preventing and reducing fat gain and obesity<sup>104</sup> as well as decreasing CVD risk and premature mortality<sup>106</sup>.

#### 2.4.2.1 *The SCI population*

Energy expenditure during activities has been described for sixty-three different activities, for wheelchair dependent persons, with twenty-one specifically for SCI<sup>60,96</sup>. Energy expenditure and subsequent MET values are lower than in the general population, especially during exercise<sup>60,96,107</sup>. Since there seems to be a large inter-individual difference for RMR, MET values might not be the best way of calculating energy expenditure during activity. An alternative could be to use AEE related to bodyweight and completeness such as in motor-complete tetraplegia and paraplegia. At present date (919), no studies have reported AEE<sup>94-96</sup>.

### 2.4.3 **Energy balance and bodyweight**

Energy balance is when a person's intake of energy in kcal matches the output in kcal. Intake is calculated from food and drink consumed and output from REE and AEE in kcal, over a specific time. This information is the theoretical basis for regulating the intake of kcal to achieve energy balance, which is one component used for weight management. Other important components that affect bodyweight are stress and sleep<sup>1</sup>. How and why an individual gain or loses weight during positive or negative energy balance is complex<sup>108,109</sup>. How we use (during activity) and store energy from food varies, due to individual metabolic response<sup>109-112</sup>. Moreover, low REE has been associated with both weight gain and weight loss<sup>113-116</sup>. Therefore, there is no clear evidence for how energy balance affects weight. However, exercise activity together with dietary interventions seems to be an effective weight loss intervention<sup>117</sup>.

#### 2.4.3.1 *The SCI population*

Little is known about the energy balance after SCI except that in the acute phase persons with motor-complete SCI lose weight due to loss of muscle mass and the stress on the body after an accident. During the rehabilitation phase bodyweight tends to increase and these people increase their bodyweight around 2 kg or more during the first year, this may be explained by positive energy balance<sup>118,119</sup>. Special weight-loss programs for SCI, which focus on negative energy balance and education about food, PA, planning, goal setting and stress management, show promising results for weight loss (average of 3.5 kg after 12 weeks)<sup>61,118</sup> and reduction of total fat mass. These results are consistent with a Cochrane report from 2006 focusing on the effects of PA on health benefits and body weight for overweight and obese participants<sup>117</sup>.

## 2.4.4 Maximal physical capacity

Physical capacity is the individual ability to increase oxygen consumption to the maximal limit during aerobic voluntary exertion. This is referred to as peak aerobic capacity,  $\text{VO}_2$  peak or  $\text{VO}_2$  max (in this thesis  $\text{VO}_{2\text{peak}}$ ). Whereas  $\text{VO}_2$  max is viewed as the most accurate measurement of aerobic fitness or cardiorespiratory endurance<sup>53</sup>, peak capacity is described in absolute uptake  $\text{VO}_2 \text{ L}\cdot\text{min}^{-1}$  or, more commonly, relative to bodyweight ( $\text{VO}_2 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ), since higher bodyweight increases metabolic need. In the general population, physical capacity is well documented, as is how to categorize the result of physical fitness (whole-body relative  $\text{VO}_{2\text{peak}}$ ) based on gender and age<sup>53,120,121</sup>.

### 2.4.4.1 The SCI population

Peak oxygen consumption is well documented in the SCI population both for motor-complete tetraplegia and motor-complete paraplegia<sup>122</sup>. Further, there are tables for physical fitness level specifically adjusted for persons with tetraplegia and paraplegia<sup>123</sup>. The physical fitness values for the general population differ to large extent from those for the SCI population. Thus for example, excellent physical fitness for motor-complete tetraplegia is  $\text{VO}_2 > 15 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  and  $>22.4 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  for paraplegia<sup>123</sup>, whereas the limit for very poor fitness for 60-65 years-old persons in the general population is  $\text{VO}_2 16\text{-}21 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  (women - men)<sup>121</sup>.

## 2.4.5 Assessment of physical capacity

In the general population, physical capacity is assessed with an individual ramp protocol, most commonly using leg ergometer bike or treadmill<sup>124</sup>.

### 2.4.5.1 The SCI population

For persons with motor-complete SCI the most valid assessment tool for peak physical capacity is either arm crank ergometry (ACE) or wheelchair ergometry (WCE)<sup>125</sup>. While there are a few protocols for how to perform a  $\text{VO}_{2\text{peak}}$  test<sup>122,125-127</sup>, standardized determination criteria for true  $\text{VO}_{2\text{max}}$  are still lacking<sup>125</sup>. Moreover, there is uncertainty about what these tests really assess, as other parameters could affect the result. For example, upper body balance (skill) could be a confounding variable. Hence, recent research suggests that there is no difference in  $\text{VO}_{2\text{peak}}$  between arm crank and wheeling wheelchair in persons with injury at T3 – L1 (AIS A-C)<sup>127-130</sup>. Regardless of method, these two assessments differ slightly from the traditional  $\text{VO}_{2\text{peak}}$  in the general population where aerobic capacity is limited mainly by cardiac output. Hence, persons with a motor-complete SCI are limited to a small volume of upper-body muscle mass, which is less dependent on cardiac output than on regional physical adaptations e.g. the aerobic capacity of the muscles involved<sup>125</sup>.

## **2.5 RATIONALE OF THIS THESIS**

After a motor-complete SCI, altered body composition changes the prerequisites for activities. The loss of active muscle mass, predominantly in the leg, affects energy expenditure both at rest and during activities. Additionally, persons with an injury above T6 have a compromised cardiometabolic response, which further compromises energy expenditure. Changes in body composition and cardiometabolic response negatively affect peak capacity, which further affects intensity levels. Around 80% of the motor-complete SCI population in Sweden do not reach the WHO recommendation for PA <sup>131</sup>, and over half are overweight or obese. All the above-mentioned factors lead to an increased presence and risk of lifestyle-related diseases such as CVD and its risk factors.

There is a knowledge gap concerning activities and their intensity levels, especially information based on homogeneous samples for level of injury and severity. The current SCI-specific guidelines need to be validated for effects on health and to include recommendations for activities and objective data for intensity levels. This knowledge gap has led to an unequal situation regarding health-related information, which may affect CVD prevention and overweight in people with motor-complete SCI.

For this reason, injury-specific information concerning energy expenditure, intensity levels and objective ways of assessing free living PA patterns is needed for producing adapted evidence-based programs.

### 3 AIMS

The research reported in this thesis sought to extend knowledge about energy expenditure, oxygen consumption and heart rate during rest, standardized activities and peak capacity in persons with motor-complete SCI. Additionally, it aimed at describing clinically accessible methods for measuring and describing activity patterns and intensity.

#### 3.1 SPECIFIC AIMS

**Study I:** To describe and compare REE and energy expenditure during different standardized sedentary, non-exercise and exercise activities in people with motor-complete paraplegia (Th7 to Th12.). A secondary aim was to compare men and women.

**Study II:** To describe and compare resting oxygen consumption and energy expenditure, and oxygen consumption and energy expenditure, for different, standardized, sedentary, non-exercise, and exercise activities in people with motor-complete tetraplegia (C5–C8). Further, we aim to compare REE, total energy expenditure and AEE during sedentary, non-exercise, and exercise activities between people with motor-complete tetraplegia and a reference group of people with motor-complete paraplegia.

**Study III:** In two defined cohorts of persons with tetraplegia (C5-C8) AIS A-B and paraplegia (T7-T12) AIS A-B, aimed a) To describe peak oxygen uptake ( $VO_{2peak}$ ) and explore the potential influence of anthropometrics, demographics and level of physical activity within each cohort; b) to define common, standardized activities as percentages of  $VO_{2peak}$  and categorize these as light, moderate and vigorous intensity according to present classification systems, and c) to explore/describe how clinically accessible methods such as heart-rate monitoring and rating of perceived exertion correlate, or can describe light, moderate and vigorous intensity.

**Study IV:** Aimed at defining accelerometer cut-points values for motor-complete paraplegia and motor-complete tetraplegia with wrist-worn Actigraph GT3X+ for absolute and relative intensities, based on indirect calorimetry from at resting, during activities and peak effort. Secondly, the study sought to propose accelerometer-based cut-points for light, moderate and vigorous intensity levels for person with motor-complete paraplegia and motor-complete tetraplegia.

## 4 METHODS

This thesis is based on over 700 measurements of oxygen consumption assessed during rest, standardized activities and peak exertion, using indirect calorimetry, together with measurements of HR, level of PA, Borg RPE and accelerometer data (Table 3).

**Table 3.** The four studies

Study	I	II	III	IV
<b>Aim</b>	To describe and compare REE and energy expenditure during different standardized sedentary, non-exercise and exercise activities in people with motor-complete paraplegia (Th7 to Th12.). A secondary aim was to compare men and women.	To describe and compare resting oxygen consumption and energy expenditure, and oxygen consumption and energy expenditure, for different, standardized, sedentary, non-exercise, and exercise activities in people with motor-complete tetraplegia (C5–C8). Further, we aim to compare REE, total energy expenditure and AEE during sedentary, non-exercise, and exercise activities between people with motor-complete tetraplegia and a reference group of people with motor-complete paraplegia.	In two defined cohorts of persons with tetraplegia (C5-C8) AIS A-B and paraplegia (T7-T12) AIS A-B, aimed.a) To describe peak oxygen uptake ( $VO_{2peak}$ ) and explore the potential influence of anthropometrics, demographics and level of physical activity within each cohort; b) to define common, standardized activities as percentages of $VO_{2peak}$ and categorize these as light, moderate and vigorous intensity according to present classification systems, and c) to explore/describe how clinically accessible methods such as heart-rate monitoring and rating of perceived exertion correlate, or can describe light, moderate and vigorous intensity.	Aimed at defining accelerometer cut-points values for motor-complete paraplegia and motor-complete tetraplegia with wrist-worn Actigraph GT3X+ for absolute and relative intensities, based on indirect calorimetry from at resting, during activities and peak effort. Secondly, the study sought to propose accelerometer-based cut-points for light, moderate and vigorous intensity levels for person with motor-complete paraplegia and motor-complete tetraplegia.
<b>Design</b>	Descriptive cross-sectional	Descriptive cross-sectional	Descriptive cross-sectional	Descriptive cross-sectional
<b>Participants</b>	38 participants (10 women and 28 men) T7-T12 AIS A,B	26 participants (7 women and 19 men) C5-C8 AIS A,B	64 participants (17 women and 47 men) C5-C8 AIS A,B + T7-T12 AIS A,B	64 participants (17 women and 47 men) C5-C8 AIS A,B + T7-T12 AIS A,B
<b>Methods</b>	Standardized protocol for indirect calorimetry during rest and 13 activities	Standardized protocol for indirect calorimetry during rest and 11 activities	Standardized protocol for indirect calorimetry during $VO_{2peak}$ and 11 activities	Accelerometer and indirect calorimetry measurements for 6 standardized activities, and $VO_{2peak}$
<b>Outcome Measures</b>	Rest: Absolute and relative $VO_2$ and energy expenditure. Activities: absolute and relative $VO_2$ and energy expenditure. HR, Borg RPE	Rest: Absolute and relative $VO_2$ and energy expenditure. Activities: absolute and relative $VO_2$ and energy expenditure, MET and HR, Borg RPE and level of PA.	Absolute and relative $VO_{2peak}$ and $HR_{peak}$ , Borg RPE, PA-level	Accelerometer Vector magnitude counts (VMC) related to Absolute and relative $VO_{2peak}$
<b>Analysis</b>	Independent sample <i>t</i> test (between men and women)	Independent sample <i>t</i> test (between men/ women and tetraplegia/tetraplegia)	Correlation coefficient, variance analysis and distributions	Correlation coefficient and ROC curve analysis



## 4.1 RECRUITMENT PROCEDURES

To reach as many persons as possible, we used different channels for recruitment, such as advertisements on SCI-specific websites, SCI-specific organizations, the regional SCI unit and word-of-mouth. Inclusion started when the prospective participant contacted the research group via e-mail. Next, the researcher phoned to ensure that the person was eligible to participate. During the phone call, the researcher asked about medication and level of injury, and informed about the data collection and use of equipment. If there were any uncertainties concerning the inclusion or exclusion criteria, the researcher requested permission to ask the attending doctor, or whether the participant could do this. All information so obtained was sent to all included participants (appendix 1) by e-mail or regular mail. Lastly, the participants gave their informed consent and returned it by regular mail or brought it to the first day of data collection. All participants gave their informed consent.

### 4.1.1 Inclusion and exclusion criteria

The criteria for inclusion were for motor-complete tetraplegia level of injury C5-C8, injury completeness AIS A+B, and for motor-complete paraplegia level of injury T7-T12, injury completeness AIS A+B. All participants should be at least 18 years of age and at least 1 year post-injury. Absent or minimal spasticity self-reported on the PENN spasm frequency scale (described below).

The exclusion criteria were; known coronary artery disease, angina, chronic congestive heart failure, resting hypertension, chronic obstructive pulmonary disease, shoulder pain or other problems known to limit exercise ability.

There were 64 participants included for all four studies (table 4). Twenty-six had motor-complete tetraplegia C5-C8, AIS A+B and 38 motor-complete paraplegia T7-T12 AIS A+B.

**Table 4. Characteristics of all participants included in studies I, II, III and IV.**

	Tetraplegia n=26			Paraplegia n=38		
	<i>All</i>	Mean SD		<i>All</i>	Mean SD	
		♂ ( <i>n</i> =19)	♀ ( <i>n</i> =7)		♂ ( <i>n</i> =28)	♀ ( <i>n</i> =10)
<b>Age (years)</b>	41.5±14.0	41.2±14.5	42.4±11.9	43.0±11.5	44.6±11.7	38.8±10.8
<b>Height (cm)</b>	178±0.09	181±0.08 <sup>b</sup>	1.68±0.05	177±0.10	181±0.07	165±0.05
<b>Body weight (kg)</b>	65.3±12.9*	70.1±11 <sup>b</sup>	52.3±7.41	73.7±15.1	78.7±13.8	59.7±8.50
<b>BMI</b>	20.5±3.0*	21.3±2.93 <sup>b</sup>	18.4±1.94	23.4±3.70	23.9±3.71	21.9±3.28
<b>Years since injury</b>	15.3±10.9	15.2±11.8	15.4±8.70	15.8±11.3	16.2±11.7	14.6±10.8
<b>Penn S/F</b>	0.8/1.1			0.9/1.1		

\*=Significant difference  $p < 0.05$  between motor-complete tetraplegia and motor-complete paraplegia

<sup>b</sup>=significant difference between men and women tetraplegia

BMI=body mass index. S/F=Severity/Frequency

#### 4.1.1.1 Self-reported spasticity

Spasticity was reported on the Penn spasm frequency scale, frequency 0-4 and severity 1 - 3. The participants were asked report the spasticity over the last 24 hours with Penn and 71% of the total sample reported a none or mild spasm induced by stimulation. Moreover, 20% of the participants reported a spasm frequency less than once per hour (frequency 2) and 9 % reported spasm occurring more than once per hour (frequency 3). Two participants a severity over 2, during the previous 24 hours. These participants were further assessed with a modified Ashworth scale by the investigator and included in the study. To determine if there was any relation between Penn and REE Pearson correlations was completed at  $r=-0.04$  ( $p=0.86$ ) (tetraplegia) and  $r=0.18$  ( $p=0.28$ ) (paraplegia)

## 4.2 DATA COLLECTION

Data were collected in two settings. The first was a laboratory environment where RMR and HR were assessed. The second setting was a rehabilitations facility, where oxygen consumption, metabolic rate and HR were assessed during standardized activities and maximal effort. Bodyweight was assessed using a calibrated scale, where the participant and the wheelchair were weighed and later the wheelchair by itself to able to calculate the participant's bodyweight. Height was self-reported and BMI was calculated as  $\frac{Weight (kg)}{Height (m)^2}$ . Tire pressure was checked before the testing begun.

### 4.2.1 Resting conditions

RMR was assessed in a post-absorptive state in the morning using indirect calorimetry. The participant was asked to lie supine in a thermoneutral environment and to breathe into a ventilated hood connected to a computerized metabolic analyzer (Jaeger Oxycon Pro, Hoechberg, Germany). The equipment was calibrated with built-in procedures using high-precision gas 30 minutes prior to testing. The participants arrived between 06:30 – 10:00 after overnight fasting (>8 hours). They had been asked to refrain from nicotine, coffee and vigorous exercise the evening before testing. After information about the testing procedure and familiarization with the equipment, the participants were asked to lie down and rest without falling asleep. Data for oxygen consumption and HR were collected during 30 minutes. The first 20 minutes of assessment were used to obtain steady state, and the mean values of  $VO_2$ ,  $VCO_2$  and HR during the last 10 minutes were used to calculate resting relative  $VO_2$  ( $ml \cdot kg^{-1} \cdot min^{-1}$ ), REE ( $kcal \cdot min^{-1}$ ) and HR (beats per  $min^{-1}$ ).

#### 4.2.2 Standardized activities

Thirteen standardized activities commonly performed during daily living and in rehabilitation settings were selected and performed by the participants. The activities were also selected to represent sedentary, light, moderate, and vigorous levels of intensity (Table 5). All the participants' activity data were collected on the same day.

**Table 5.** Activities selected for individuals with motor-complete paraplegia:

Activities	n (Women/Men)	
	Tetraplegia)	Paraplegia
<b>Watching television (TV)</b>	26 (7/19)	38 (10/28)
<b>Computer desk work</b>	26 (7/19)	38 (10/28)
<b>Setting a table</b>	26 (7/19)	38 (10/28)
<b>Wheeling the wheelchair indoors Borg 10-11</b>	26 (7/19)	38 (10/28)
<b>Wheeling the wheelchair outdoors Borg 10-11</b>	21 (6/15)	37 (10/27)
<b>Hand bike outdoors “walking pace”</b>	N/A	18 (3/15)
<b>Weight training</b>	25 (7/18)	37 (10/27)
<b>Arm cranking low</b>	21 (5/16)	38 (10/28)
<b>Arm cranking high</b>	20 (4/16)	38 (10/28)
<b>Ski ergometer</b>	5 (2/3)	37 (10/27)
<b>Circuit training</b>	21 (5/17)	37 (10/27)
<b>Wheeling the wheelchair outdoors Borg 13-14</b>	10 (2/8)	37 (10/27)
<b>Hand bike outdoors Borg 13-14</b>	N/A	17 (3/14)

N/A=not applicable

Prior to testing, the participants were asked to answer a questionnaire about PA level and spasticity. Body weight/height were measured and tire pressure was checked. After this, the equipment (face mask, harness, HR strap, and accelerometer) was fitted and ‘acclimatized’. A verbal instruction (appendix 2) and demonstration of each activity were completed before respective testing. During the resistance activities, the participants tested each machine to find the resistance at which they could perform 3x10 repetitions. Participants with poor hand-function used special gloves to be able to hold on to the arm bike or gym machines. An assistant helped when switching between the gym machines.

Data for the standardized activities was collected in a rehabilitation setting and assessed with indirect calorimetry with a mobile system (Jaeger Oxycon mobile system, Hoechberg, Germany). The activity-related metabolic rate was assessed using a face mask which directed the air into a ventilation turbine and a sampling tub, thence to portable housing where the oxygen and carbon dioxide content was analyzed. The breath-by-breath method was used. This measure inhaled oxygen and exhaled carbon dioxide (non-protein respiratory exchange ratio). Heart rate data was collected using Polar chest straps via telemetry (model T31)

Each activity lasted at least six minutes where the last three minutes of  $\text{VO}_2$  measurements for the activity were used to calculate absolute energy expenditure ( $\text{Kcal} \cdot \text{min}^{-1}$ ), relative energy expenditure ( $\text{Kcal} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ) and relative oxygen consumption ( $\text{VO}_2 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ), HR.



Figure 3. Jaeger Oxycon mobile system, Hoechberg, Germany

Photo by Tobias Holmlund

#### 4.2.2.1 Accelerometer

The ActiGraph GT3X+ (ActiGraph, LLC Pensacola, FL, USA) accelerometer was used. This accelerometer measures  $46 \times 33 \times 15$  mm, weighs 19 g and captures movement in three axes vertical, horizontal and perpendicular. The accelerometer can be placed at the hip, trunk or wrist and the data output is in counts per min or by time unit i.e. 15 min (epoch). A more intense activity yields higher acceleration registered by the accelerometer. The counts can be presented for each axis or for all together called vector magnitude counts (VMC).

All participants used three ActiGraph GT3X+ accelerometers. The first was positioned at the center of the right wheelchair wheel. The second, at the wrist of the dominant hand and the third was strapped over M. pectoralis. Activity counts were measured during all activities and later matched with  $\text{VO}_2$  data for the same time frame. Prior to testing the accelerometer was set to record at a sampling frequency of 30Hz. A few previous studies have used this particular accelerometer for different purposes in the SCI population<sup>81,82</sup>.



Figure 4. ActiGraph GT3X+

Photo by Tobias Holmlund

#### 4.2.2.2 *Borg RPE*

The Borg RPE is an ordinal scale ranging between 6 – 20, where 6 is light and 20 is maximum perceived exertion during an activity<sup>56</sup>. The Borg RPE subjectively measures the participant's experience of physical workload in relation to increased HR, breathing and muscle fatigue, during PA. The instrument has been used in previous studies in the SCI population<sup>83,132</sup>. In the present work, the Borg RPE scale was used during NEPA and exercise activities.

#### 4.2.2.3 *Self-reported PA*

The questionnaire, previously used in persons with SCI, targets different characteristics of PA such as frequency, duration and intensity<sup>70</sup>. The present investigation concentrated on the reported time (minutes) each participant spent in moderate and vigorous activity, both reported as regular exercise and NEPA. The result was further dichotomized according to current SCI guidelines for cardiorespiratory fitness (0 – 44 or 45 – ∞ minutes per week)<sup>133</sup>.

#### 4.2.2.4 *Validation of the Oxycon mobile system for low levels of VO<sub>2</sub>*

The Oxycon mobile equipment used for activity assessment was validated for lower levels of VO<sub>2</sub> (<0.6 L·min<sup>-1</sup>) in a method study prior to testing. Measurements were taken from ten persons, five men and five women (non-SCI), who sat quietly and breathed into a facemask. The facemask was connected by the test leader to the Oxycon mobile device and the Douglas Bag equipment (10 min each, in a random order between participants). The mean VO<sub>2</sub> data for both methods were compared using a paired sample *t* test, and a variation <3% were

accepted. The result showed a non-significant difference between the two methods with a mean error of -0.27 range 0.22-0.32 L·min<sup>-1</sup> and a mean variation of 3%.

### 4.2.3 Physical capacity

The test-protocol design for VO<sub>2peak</sub> was individualized and based on international laboratory protocols<sup>124</sup> and previous research<sup>125</sup>. The test took place in the rehabilitation setting and began after the participant positioned his or her wheelchair by the arm ergometer (Ergonomic 89E Monark, Sweden) that was placed on a height-adjustable table. All participants were asked if they wanted to use an upper-body strap or gloves (poor hand function).

This individualized ramp test protocol was based on the participant's performance during exercise arm-cranking (Borg RPE 13-14) Table 7. Testing began with a 3-minute warm-up with starting resistance (table 7). The cadence was individually chosen between 70 and 110 revolutions per minute (RPM) for persons with motor-complete paraplegia and 50 and 90 RPM for those with tetraplegia. After the warm-up, the resistance was increased every minute for at least three and up to six minutes (table 7). Further individualization during the last 1-3 minutes of testing included increasing the cadence instead of increasing the resistance.

**Table 6.** Increase in watts for the peak capacity test

<b>Resistance at arm-cranking (exercise Borg 13-14)</b>	<b>Increase during test</b>	<b>Starting resistance</b>
<b>10-15 Watt</b>	0.25 Watt	10 Watt
<b>20-25 Watt</b>	0.50 Watt	10 Watt
<b>36 Watt</b>	0.50 Watt	24 Watt
<b>42 Watt</b>	0.75 Watt	36 Watt

Continuous measurement of VO<sub>2</sub> and HR was analysed in ten-second averages and peak VO<sub>2</sub> was determined based on the highest mean VO<sub>2</sub> value during 30 seconds. Other criteria for acceptance as VO<sub>2peak</sub> were a test time of at least 6 minutes, levelling-off despite increased resistance or cadence (RPM) and Borg RPE >16 supported by respiratory exchange ratio (RER) or respiratory quotient (RQ) above 1.1.

#### 4.2.3.1 Mechanical efficiency

Mechanical efficiency is the work generated for the total energy expended; a higher work rate usually has a higher energy expenditure. Higher mechanical efficiency gives more effective exercise since more power is used by the actual work. For leg ergometer biking at 60 revolutions per minute (RPM), the gross efficiency is between 15 and 25% depending on external power and skill<sup>134</sup>, and asynchronous arm ergometry has showed a gross efficiency of 7-20%<sup>135,136</sup>. Efficiency is here reported in percentages and calculated by multiplying the work load in watts (W) by 0.0143, divided by the total energy cost. The value 0.01344 is the energy cost for the power output of 1W in kcal·min<sup>-1</sup>.

$$\text{Gross mechanical efficiency (\%)} = \frac{\text{Watt} * 0.01433}{\text{Total energy expenditure}} * 100$$

### 4.3 STATISTICAL METHODS

Statistical analysis was performed using SPSS (SPSS for Windows Version 23.0; Inc. Chicago, IL, USA). The statistical tests are summarized for each study in table 8. For descriptive statistics, normally distributed data were reported as mean with SD. Independent two tailed *t* tests ( $\alpha < 0.05$ ) were used for group comparisons. To assess whether the data was skewed, visual assessments with Q-Q plots and a Kolmogorov -Smirnov test were used. Skewed data is presented as median with interquartile range (IQR). Further, the Mann-Whitney U test was used for group comparisons for skewed data. Spearman's rho correlation coefficient was used to investigate the association between anthropometrics, demographics, questionnaires and VO<sub>2peak</sub>. The correlation coefficient was categorized as moderate 0.4 – 0.59, strong 0.6 – 0.79 and very strong 0.8 – 1.0. The variables needed a correlation coefficient of at least 0.4 and to show a significant correlation ( $p < 0.05$ ) for inclusion in regression analysis.

Regression analysis was completed following the linear multiple stepwise (forward and backward) method and used for identifying factors that could explain the variance for RMR and VO<sub>2peak</sub>. The probability for variables to be entered in the regression model was set to an F value =  $p < 0.05$ . For the opposite, i.e. removal from the regression model, the F value was set to  $> 0.10$ . To avoid multicollinearity the variance inflation factor for exclude variables were set to  $\geq 4$ . However, the present models showed a variance inflation factor between 1.0-2.0.

Categorization of the activities into different intensity levels was based on visual examination of how many persons in each activity reached the level for % of VO<sub>2peak</sub>, Borg RPE and % of HR<sub>peak</sub>. At least 2/3 of the individuals needed to be categorized correctly.

For accelerometer cut-points, ROC curve analysis was used in the present work two classes were analyzed at the same time. The ROC curve visualizes and organizes the classifiers (cut-points) by plotting the false positive rate and true negative rate for all the different classifiers

from 0.0 to 1. This is also known as sensitivity and 1-specificity, and the rule of decision is to have as high a true- positive rate (sensitivity) and as low a false-positive rate (1-specificity) as possible<sup>137,138</sup>. The Area under the curve (AUC) is the probability that a classifier will rank a randomly chosen positive observation over a negative observation<sup>137</sup>. The first analysis was based on the area under curve (AUC), where an  $AUC \leq 0.5$  indicates that the test is no better than chance, poor between 0.6-0.7, fair between 0.7-0.8, good between 0.8-0.9 and excellent 0.9-1.0<sup>139</sup>. To obtain optimal cut-points both Youden's index and accuracy and diagnostic odds-ratios were used, the latter calculated manually with sensitivity/specificity and false/true positive and negative ratios<sup>140</sup>. Further, the stratification % of  $VO_{2peak}$  and MET was done by dichotomizing each individual value below =0 and equal or above as=1 (i.e.  $\geq 50\%$  of  $VO_{2peak}$  =1 and  $< 49.99\%$  =0). In the present work, the AUC showed that the analysis performed was good-to-excellent ( $AUC > 0.8$ ) for all the cut-points. ROC curve analysis lets the user decide what cut-point has the highest precision based on their preference (sensitivity vs specificity) for separating the two classes. This is how the ROC curve differs from other statistical tools. The benefit of using ROC analysis is that it does not matter if the classes are highly unbalanced.

**Table 7.** Statistical methods for each study

<b>Study</b>	<b>I</b>	<b>II</b>	<b>II</b>	<b>IV</b>
<b>Descriptive statistics</b>				
<b>Mean (SD)</b>	•	•	•	•
<b>Median (IQR)</b>		•	•	•
<b>Percentage (%)</b>			•	•
<b>Interferential statistics</b>				
<b>Confidence intervals (95 %CI)</b>				•
<b>Independent t-test</b>	•	•		
<b>Mann-Whitney U test</b>		•	•	•
<b>Multiple linear regressions</b>			•	•
<b>Odds ratio</b>				•
<b>Receiver operating characteristic</b>				•
<b>Spearman's rho correlation coefficient</b>			•	•
<b>Youden's index</b>				•



#### **4.4 ETHICS**

The present work follows the Helsinki Declaration, which includes basic principles for all medical research involving human subjects <sup>141</sup>. To observe these principles, ethical approval was given by the Stockholm region ethics committee, reference number 2011/1989-31/1. Briefly, the participants' health and privacy were protected by the supervision of scientifically competent researchers and medically responsible persons, together with anonymization of the data. Further, costs and benefits were carefully considered before and during this research. Written and verbal information about the procedures together with testing and acclimatization of the equipment used during the data collection, were one way of reducing the risk of discomfort. Further, the participants could at any time take a break for pressure relief, or withdraw from the study without explanation. The foreseeable benefits were carefully considered by assessing cost and benefit: the benefits were considered to outweigh the costs or harm. For example, the participants got their own energy expenditure at rest and during activities, which was highly appreciated. The other benefits from the work are that the group-specific results have presented as scientific articles in peer-reviewed scientific journals and in this thesis.



## 5 RESULTS

This part summarizes and synthesizes the main findings from studies I-IV.

### 5.1 RESTING CONDITIONS

The main results for  $\text{VO}_2$ , HR and energy expenditure during rest (studies I-II) are summarized in table 8. There were significant differences for absolute values in RMR between men and women with motor-complete paraplegia, whereas relative values showed no significant differences. In addition, individual REE in kcal during 24 h was 40 % lower than predicted with the Harris-Benedict formula <sup>85</sup>. Another finding was a large inter-individual variation for relative  $\text{VO}_2$  (range 1.78-3.57  $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ) (Figure 5 b).

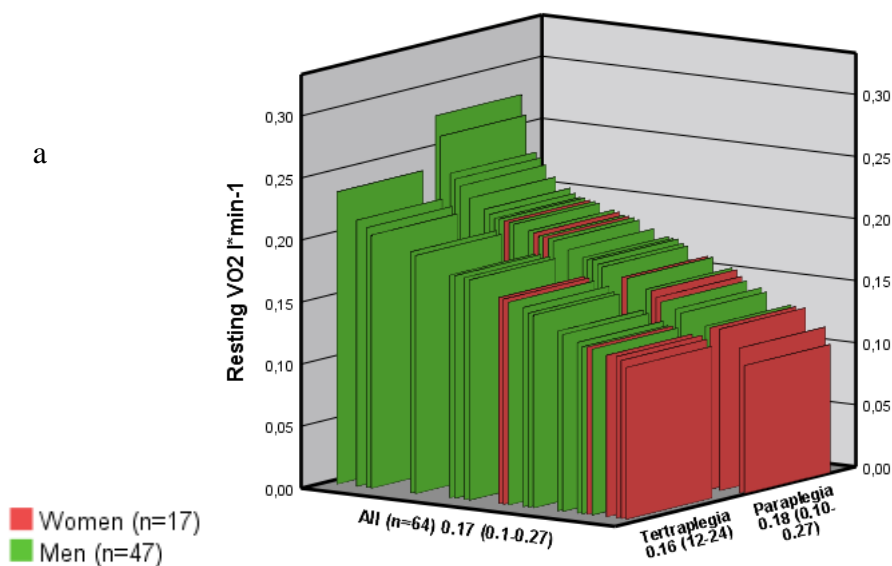
**Table 8.** Absolute and relative oxygen consumption, energy expenditure and HR during rest.

	<i>Tetraplegia</i>			<i>Paraplegia</i>		
	<i>all (n=26)</i>	<i>Mean sd.</i> <i>men (n=19)</i>	<i>women (n=7)</i>	<i>all (n=38)</i>	<i>Mean sd.</i> <i>men (n=28)</i>	<i>women (n=10)</i>
<b>REE (kcal 24 h)</b>	1132±216	1195±206 <sup>a</sup>	959±140 <sup>a</sup>	1218±244	1286±223 <sup>a</sup>	1030±206 <sup>a</sup>
<b>REE kcal·kg<sup>-1</sup></b>	17.5±2.2	17.1±2.10	18.5±2.50	16.9±3.4	16.7±3.3	17.5±3.8
<b>RMR VO<sub>2</sub> (L·min<sup>-1</sup>)</b>	0.16 ± 0.03	0.17 ±0.03 <sup>a</sup>	0.14 ±0.02 <sup>a</sup>	0.18*±0.04	0.15±0.03 <sup>a</sup>	0.19±0.03 <sup>a</sup>
<b>RMR VO<sub>2</sub> (ml kg<sup>-1</sup> min<sup>-1</sup>)</b>	2.56 ± 0.26	2.54 ± 0.22	2.60 ± 0.36	2.47±0.51	2.57±0.57	2.43±0.49
<b>HR rest</b>	47 (44-53) <sup>b</sup>	48 (45-52) <sup>b</sup>	46 (39-59) <sup>b</sup>	61 (53-69) <sup>b</sup>	56 (48-64) <sup>b</sup>	68±3

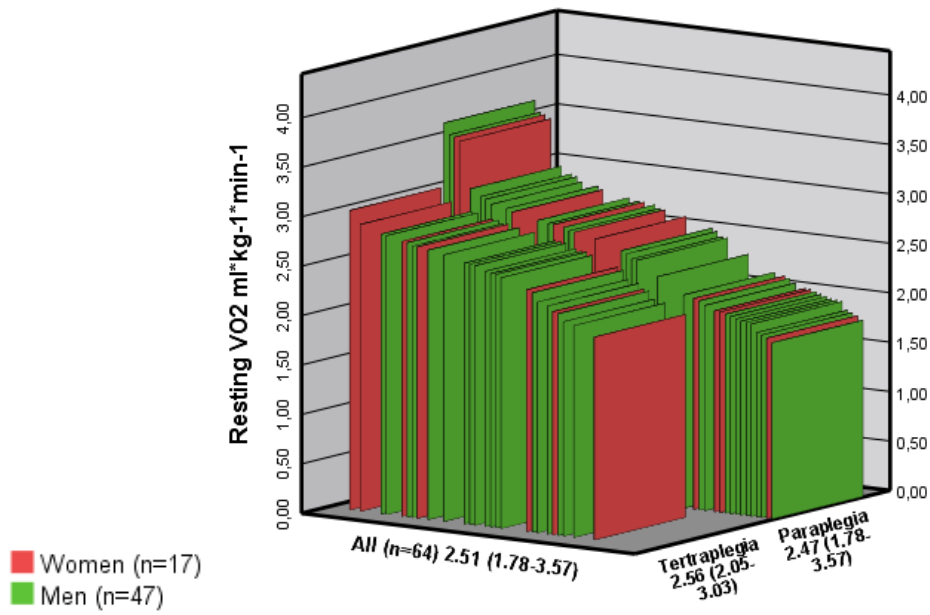
Tetraplegia= motor-complete tetraplegia, Paraplegia= motor-complete paraplegia. <sup>a</sup>Significant difference between men and women ( $p < 0.01$ ). <sup>b</sup> Median (Inter Quartile Range)

\* Significant difference between tetraplegia and paraplegia  $p < 0.05$

**Figure 5** (a, b). Individual absolute  $\text{VO}_2$  (a) and relative  $\text{VO}_2$  (b) and range, during resting conditions, for motor-complete tetraplegia and motor-complete paraplegia

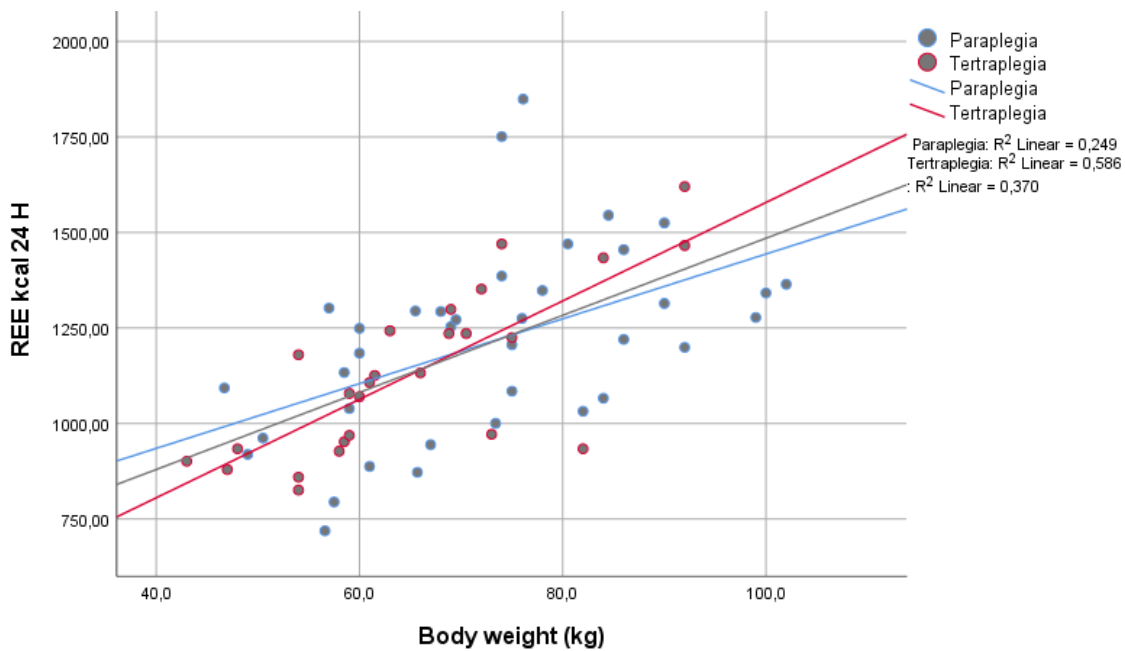


b



Further, the variable that best explained the interindividual variance for REE during rest (24 hours) was bodyweight ( $r^2 = 0.37$ ) for whole group;  $r^2 = 0.25$  for motor-complete paraplegia and  $r^2 = 0.59$  for tetraplegia (Figure 6).

**Figure 6.** Group scatter of resting energy expenditure (REE) during 24h in relation to bodyweight for motor-complete paraplegia (blue) and tetraplegia (red).



The result for the REE and bodyweight was further analyzed with regression analysis, which resulted in a standard error of estimate of 189 kcal. The standard error of estimate is the average of how far the individual data points are from the regression line. Together with the squared correlation coefficient ( $r^2$ ) they describe the precision and explained variance for the model (Table 9). This result implies that bodyweight can explain 36% of the variance of the measured REE, which is considered as low accuracy.

The equation formula for calculating kcal during 24h.:

$$\text{kcal 24h} = 476.077 + \text{bodyweight} * 10.089$$

**Table 9.** The result for the stepwise regression analysis

<b>Model Summary</b>				
Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	,609 <sup>a</sup>	,370	,360	189,17472

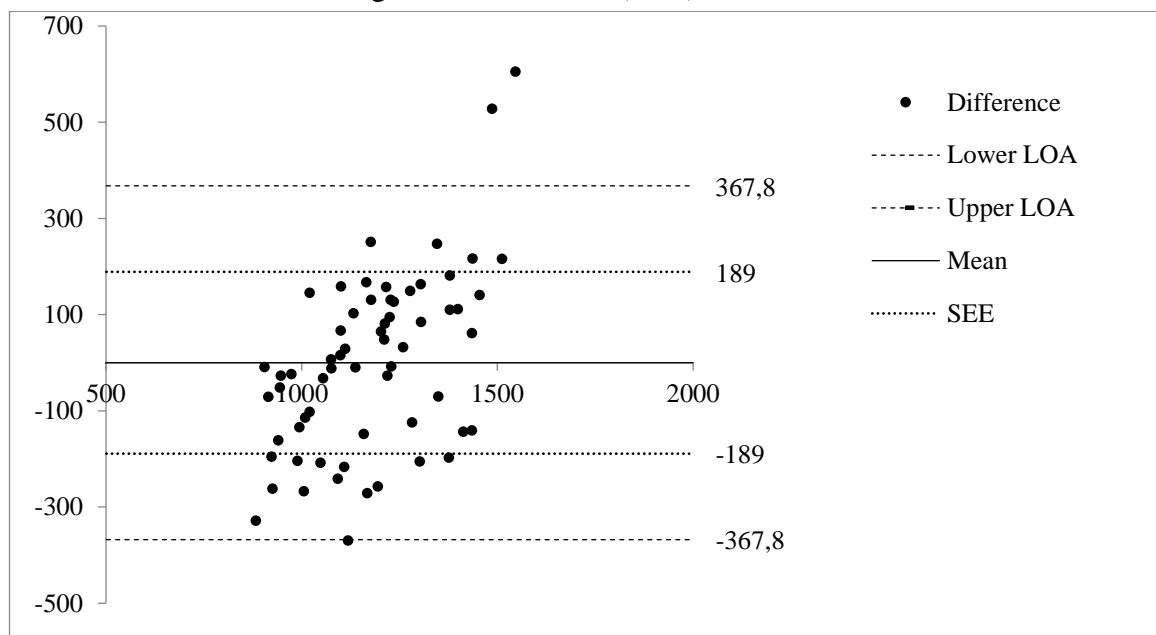
a. Predictors: (Constant), Bodyweight

<b>Coefficients<sup>a</sup></b>								
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95,0% Confidence Interval for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
1	(Constant)	476,077	119,919		3,970	,000	236,284	715,871
	Bodyweight	10,089	1,684	,609	5,991	,000	6,721	13,457

a. Dependent Variable: REE\_kcal\_24h

Further, the Bland-Altman plot for the equation formula shows that persons with high measured REE will most likely show an underestimated predicted REE, while those with low measured REE will most likely get an overestimated predicted REE. Moreover, the 95% limits of agreement (LOA) shows that five persons of 100 will have a predicted value of +/- 368 kcal from the predicted value. (Figure 7).

**Figure 7.** Bland-Altman plot showing the spread in kcal over 24h between measured and predicted REEs for all participants. The Y-axis is the mean of the measured and predicted REE (kcal 24 hours) and the X-axis is the difference between measured and predicted REE in kcal 24 hours. Limits of agreement is  $\pm 2$  SD (95%) of the mean.

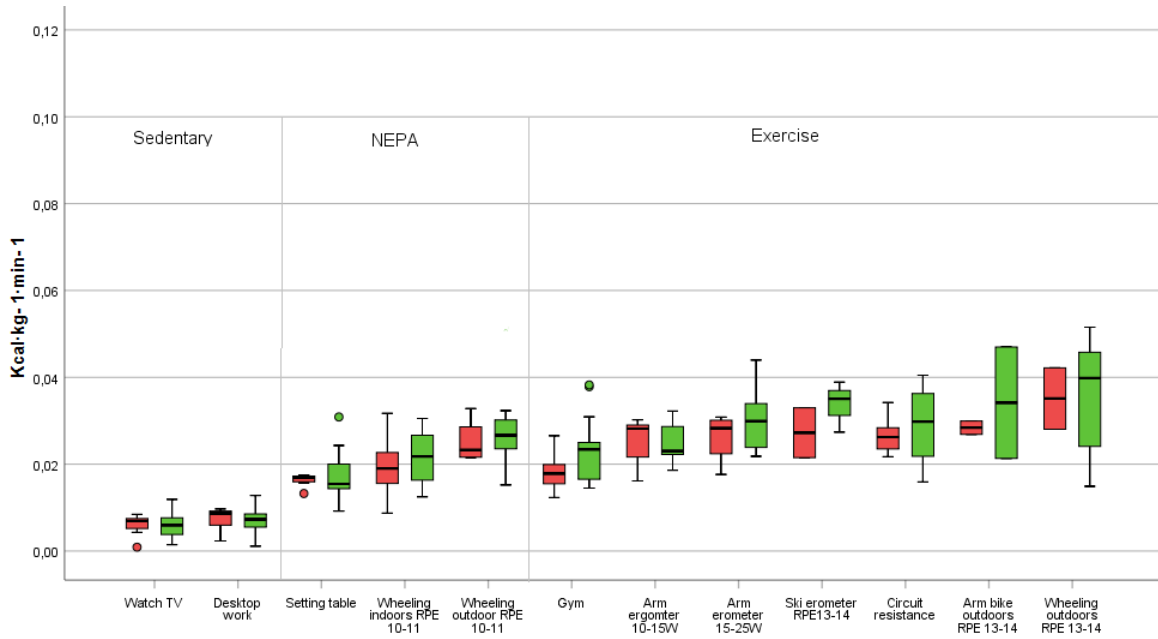


LOA= limits of agreement (95%), SEE=standard error of estimate

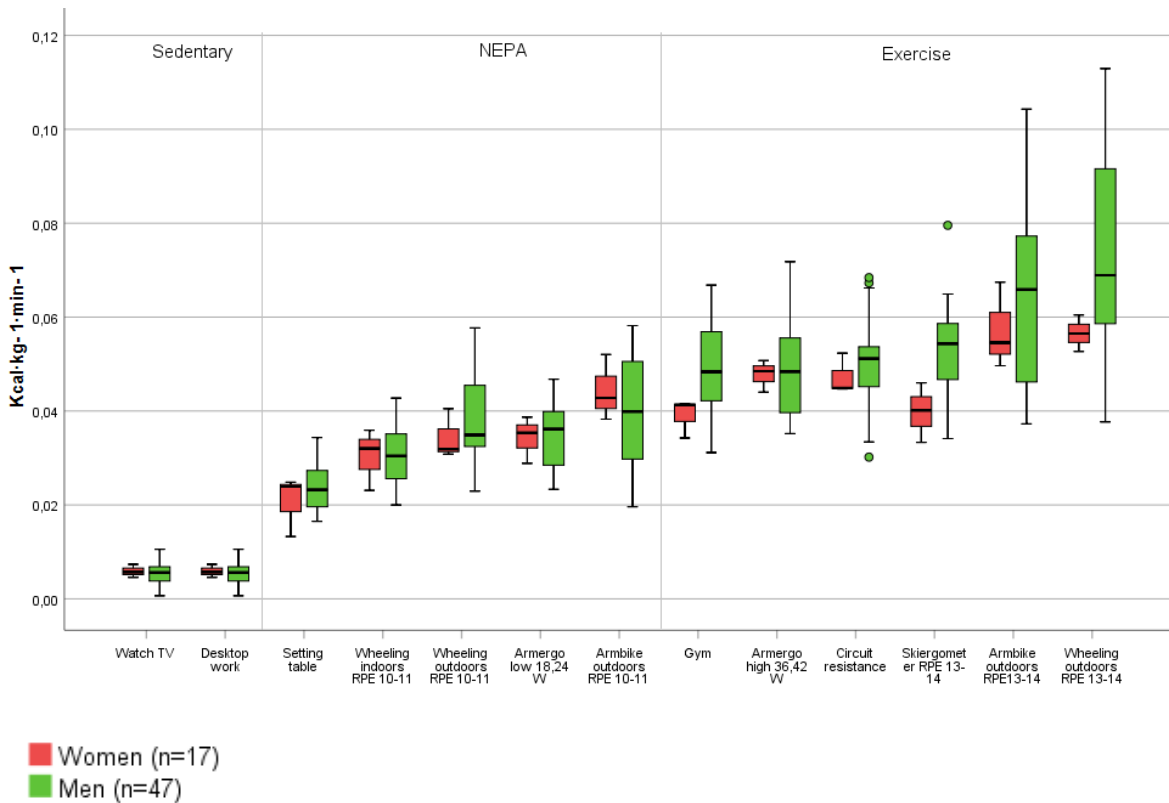
## 5.2 STANDARDIZED ACTIVITIES

The result related to the standardized activities (studies I and II) is described as total and bodyweight/speed related  $VO_2$  and EE during all the measured activities (study I and II table 2 and 3). The main findings were that persons with motor-complete tetraplegia could increase their AEE approximately 2 to 4 times during NEPA and 4 to 6 times during exercise activities compared their energy expenditure during sedentary activities. This was when using AEE  $kcal \cdot kg^{-1} \cdot min^{-1}$  for e.g. wheeling the wheelchair outdoors divided by the AEE  $kcal \cdot min^{-1}$  for watching TV  $kcal \cdot kg^{-1} \cdot min^{-1}$  (Figure 8, 9, Table 3 in study II). Persons with motor-complete paraplegia increased AEE 3 to 6 times during NEPA and between 6 and 14 times during exercise (Figure 10, Table 3 in study I). There were no gender differences for weight-bearing activities when oxygen consumption was related to bodyweight and speed of movement (km/h). Still, there was a large difference in AEE during exercise between the motor-complete tetraplegia and motor-complete paraplegia activities (Figures 8 and 9).

**Figure 8.** Box plots for activity energy expenditure separately for men (green) and women (red) with motor-complete tetraplegia. Watt (W), and Borg rating of perceived exertion (RPE) used as standardization for the some activities



**Figure 9.** Box plots for activity energy expenditure separately for men (green) and women (red) with motor-complete paraplegia. Watt (W), and Borg rating of perceived exertion (RPE) used as standardization for the some activities



Further, the results for AEE showed a large inter-individual variation for activities that included speed of motion (wheeling indoors and outdoors) (Figures 9, 10). This could be explained by the high correlation between speed (km/h) and AEE ( $R^2=0.77$  for the whole group). Additionally, there were no correlations between km/h and Borg RPE ( $R^2=0.003$ ), which indicates variance in peak capacity.

The results for the activities were further analyzed and categorized into different intensity levels; sedentary, light, moderate and vigorous. These levels were based on percentage of peak capacity, % of  $HR_{peak}$  and Borg RPE (Tables 10 and 11) published in study III. These results show the difficulty of distinguishing between moderate and vigorous levels (especially for tetraplegia), which is explained by the short span for  $VO_{2peak}$ . However, this could be compensated for by the larger span for percentage of  $HR_{peak}$ , which also strongly correlated to percentage of  $VO_{2peak}$  ( $r=0.68$ ,  $p<0.001$ ) for motor-complete tetraplegia and ( $r=0.78$ ,  $p<0.001$ ) for motor-complete paraplegia. The correlation between Borg RPE and % of  $VO_{2peak}$  showed a coefficient of  $r=0.57$  for the total group and  $r=0.38$  ( $p<0.001$ ) for tetraplegia and  $0.67$  ( $p<0.001$ ) for paraplegia.

**Table 10.** Eleven activities categorized into proposed intensity level by American College of Sports Medicine, based on the result for percentage of peak exertions ( $VO_{2peak}$ ), Borg RPE and percentage of  $HR_{peak}$

<b>TETRAPLEGIA</b>	<b>RELATIVE INTENSITY</b>	<b>ACTIVITIES</b>
<b>LEVEL OF INTENSITY</b>		
<b>SEDENTARY</b>	< 44% $VO_{2peak}$ < 64 % $HR_{peak}$ < 40 HRR% RPE <9	<ul style="list-style-type: none"> <li>▪ Watch TV</li> <li>▪ Desk work</li> </ul>
<b>LIGHT INTENSITY</b>	45–51 % $VO_{2peak}$ 65–70 % $HR_{peak}$ RPE 10–12	
<b>MODERATE INTENSITY</b>	52–67% $VO_{2peak}$ 71– 76% $HR_{peak}$ RPE 13–14	<ul style="list-style-type: none"> <li>▪ Setting table</li> <li>▪ Weight training</li> <li>▪ Wheeling indoors 2.0-6.7kmh</li> <li>▪ Arm-crank 10-15W</li> <li>▪ Wheeling outdoors “walk” 2-6 kmh</li> </ul>
<b>VIGOROUS INTENSITY</b>	68–94 % $VO_{2peak}$ 77–89% $HR_{peak}$ 70-92 HRR% RPE 15–17	<ul style="list-style-type: none"> <li>▪ Wheeling outdoors exercise (&gt;5kmh)</li> <li>▪ Circuit resistance</li> <li>▪ Ski ergo</li> <li>▪ Arm crank (20, 25W)</li> </ul>



**Table 11.** Eleven activities categorized into proposed intensity level by American College of Sports Medicine, based on the result for percentage of peak exertions ( $VO_{2peak}$ ), Borg RPE and percentage of  $HR_{peak}$ .

PARAPLEGIA LEVEL OF INTENSITY	RELATIVE INTENSITY	ACTIVITIES,
<b>SEDENTARY</b>	< 37% $VO_{2peak}$ < 50 % $HR_{peak}$ RPE <8	<ul style="list-style-type: none"> <li>▪ Watch TV</li> <li>▪ Desk work</li> </ul>
<b>LIGHT INTENSITY</b>	37–45 % $VO_{2peak}$ 51–60 % $HR_{peak}$ RPE 8-9	<ul style="list-style-type: none"> <li>▪ Setting table</li> <li>▪ Wheeling indoors (3.7-4.7 kmh)</li> <li>▪ Arm-crank 18W</li> </ul>
<b>MODERATE INTENSITY</b>	46–63 % $VO_{2peak}$ 61–72 % $HR_{peak}$ RPE 10-13	<ul style="list-style-type: none"> <li>▪ Wheeling indoors (4.8-5.8kmh)</li> <li>▪ Wheeling outdoors 4.7-6kmh “walk”</li> <li>▪ Arm-crank 24 W, 36W</li> <li>▪ Weight training</li> </ul>
<b>VIGOROUS INTENSITY</b>	64–90 % $VO_{2peak}$ 73–90 % $HR_{peak}$ RPE 14–17	<ul style="list-style-type: none"> <li>▪ Arm crank 48W</li> <li>▪ Wheeling outdoors 6.1-12kmh “exercise”</li> <li>▪ Circuit resistance</li> <li>▪ Ski-ergo</li> </ul>

### 5.3 PEAK CAPACITY

The main result regarding  $VO_{2peak}$  was that persons with motor-complete tetraplegia had median  $VO_2$  of  $11.1 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ , less than 5 MET (Table 15), while persons with motor-complete paraplegia showed a median of  $VO_{2peak}$  of  $18.5 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ , less than 8 MET. Moreover, absolute  $VO_{2peak}$  ( $\text{L}\cdot\text{min}^{-1}$ ) differed significantly between men and women both for motor-complete tetraplegia and motor-complete paraplegia ( $p\leq 0.001$ ), Table 15. The significant difference disappeared when the  $VO_{2peak}$  was related to bodyweight ( $p=0.43$ ), (Table 15). Moreover, there were no correlation between time since injury and  $VO_{2peak}$  ( $\text{L}\cdot\text{min}^{-1}$ )  $r=0.05$ ,  $p=0.70$  for the whole group or separate as tetraplegia/paraplegia. Furthermore, Spearman’s rho showed a correlation coefficient of  $r=0.44$  ( $p=0.007$ ) between being physically active over 45 min during a week and  $VO_{2peak}$  ( $\text{L}\cdot\text{min}^{-1}$ ) for persons with paraplegia. Persons with tetraplegia had a correlation coefficient of  $r=0.45$  ( $p=0.02$ ) between being active in 60 min of moderate-vigorous PA and  $VO_{2peak}$  ( $\text{L}\cdot\text{min}^{-1}$ ).

The result for peak HR revealed no significant differences between men and women within each cohort (Table 10). Another finding regarding  $VO_{2peak}$  was that persons with motor-complete paraplegia who were active at vigorous intensity more than 45 min per week had a 30 % higher ( $p=0.03$ ) absolute  $VO_{2peak}$  ( $\text{L}\cdot\text{min}^{-1}$ ), while the difference among motor-complete tetraplegias was 28% higher ( $p=0.51$ ).

**Table 12.** Result from Peak testing for absolute and relative VO<sub>2</sub>, RER and HR

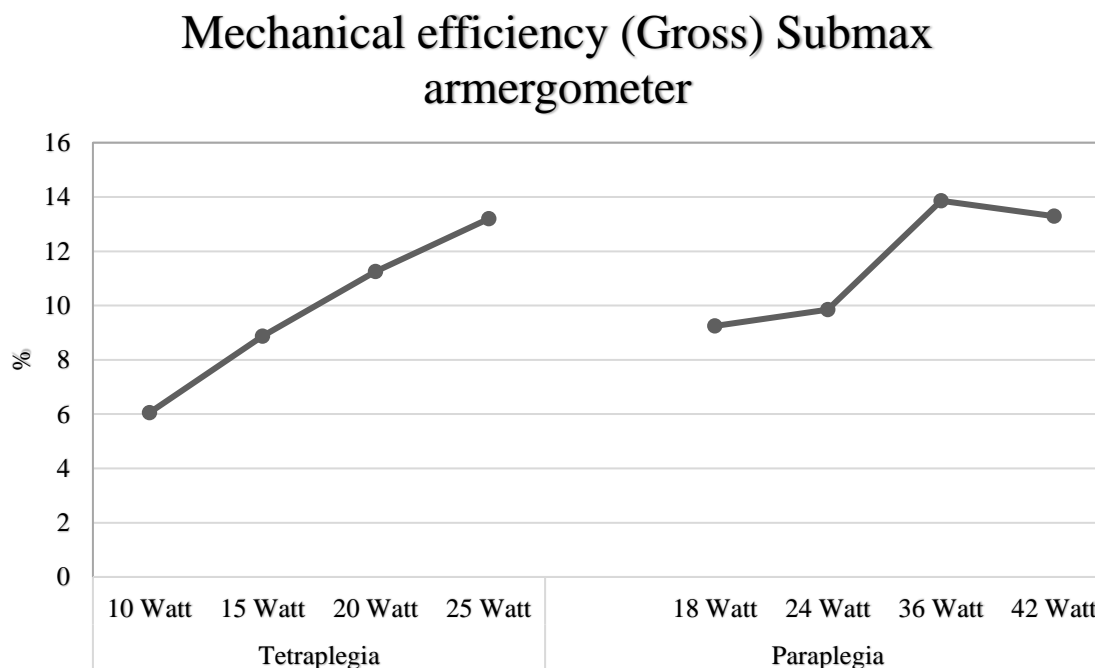
	Tetraplegia n=26			Paraplegia n=37		
	Median(IQR)					
	all (n=26)	men (n=19)	women (n=7)	all (n=38)	men (n=28)	women (n=10)
VO <sub>2peak</sub> L·min <sup>-1</sup>	0.74(0.60-0.89) <sup>a*</sup>	0.84(0.67-0.96)	0.53(0.46-0.64)	1.36(1.16-1.64) <sup>*</sup>	1.57(1.26-1.77)	1.02(0.86-1.10)
VO <sub>2peak</sub> ml·kg <sup>-1</sup> ·min <sup>-1</sup>	11.1(9.6-12.5) <sup>*</sup>	11.4(9.6-14.8)	9.9(9.4-12.0)	18.5(17.2-20.4) <sup>*</sup>	19.0(17.7-21.5)	17.7(15.4-18.3)
RER	1.15(1.10-1.18)	1.15(1.13-1.19)	1.1(1.10-1.15)	1.23(1.17-1.30)	1.26(1.16-1.32)	1.23(1.19-1.25)
HR <sub>peak</sub>	108(97-119)	107(98-122)	109(94-114)	176(164-187)	177(163-187)	174(168-189)

RER=respiratory exchange ratio. L=liter. mL=mililiter. Kg=kilogram. HR=heratrate. <sup>a</sup>Significant difference between men and women ( $p<0.01$ ). <sup>\*</sup>significant difference between taraplegia and paraplegia

### 5.3.1 Mechanical efficiency

Investigation of mechanical efficiency during submaximal arm-ergometer showed that it was lower at lower workloads, especially for persons with motor-complete tetraplegia (Figure 10). Higher workloads produced higher mechanical efficiency, which was almost equal for both motor-complete tetraplegia and motor-complete paraplegia. Moreover, mechanical efficiency had a low relation to VO<sub>2peak</sub> ( $r^2=0.11$ ).

**Figure 10.** Mechanical efficiency during arm-ergometer with different resistance in W for respective groups.



## 5.4 ACCELEROMETER CUT-POINTS

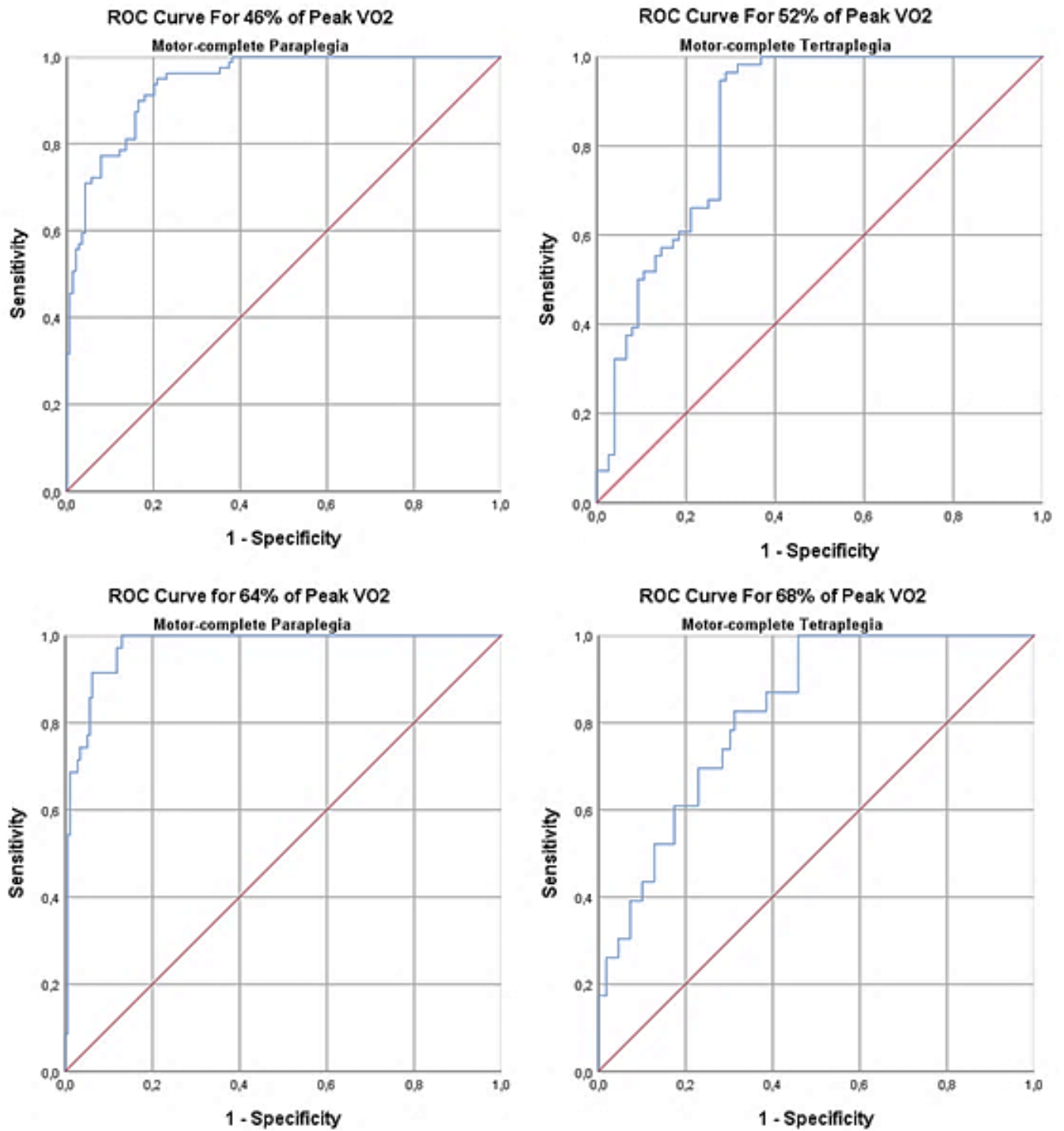
The main result for the accelerometer data was the cut-points for the different intensity levels, obtained separately for motor-complete tetraplegia and motor-complete paraplegia (Study IV). The cut-points were based on the same relative intensity as the result for the categorization of the standardized activities in study III. The accelerometer cut-points are based on physiological prerequisites for oxygen consumption for each group. There was a strong correlation between percentage of  $VO_{2peak}$  and accelerometer VMC ( $r=0.77-0.9$ ) and between MET values and VMC (0.81-0.83).

**Table 13.** Accelerometer cut-points in vector magnitude counts per min (VMC) categorized into intensity levels based on group-specific intensity levels

LEVEL OF INTENSITY	% of $VO_{2peak}$	Accelerometer vmc per minute for motor-complete	
		tetraplegia	paraplegia
SEDENTARY	N/A	<2000	<2000
(LOW LIGHT)	< 44% $VO_{2peak}$	2001-3461	2001-6865
LIGHT	45–51 % $VO_{2peak}$	3462-4886	6997-9514
MODERATE	52–67% $VO_{2peak}$	4887-9278	9515-13238
VIGOROUS	68–94 % $VO_{2peak}$	$\geq 9279$	$\geq 13239$

The AUC were over 0.8 for both absolute and relative cut-points and there was higher sensitivity/specificity for moderate and vigorous cut-points for motor-complete paraplegia than for motor-complete tetraplegia (Figure 12).

**Figure 11.** Visualization of ROC curve for moderate intensity (52–67%  $VO_{2peak}$ ) for tetraplegia and (46–63 %  $VO_{2peak}$ ) for paraplegia, and vigorous intensity (64–90 %  $VO_{2peak}$ ) for tetraplegia and (68–94 %  $VO_{2peak}$ ) for paraplegia.



## 6 DISCUSSION

### 6.1 MAIN RESULTS

This thesis provides a description of oxygen and energy consumption during rest and standardized activities ranging from sedentary to maximal effort. The results can be used as a crude estimate of energy expenditure during rest and activity. This is useful in clinical settings to exemplify the difference between a sedentary lifestyle and an active. Further, the thesis provides clinically useful tools and methods for reaching desirable intensity levels using common activities and the Borg RPE or relative HR. Finally, the studies have generated accelerometer cut-points for absolute and relative intensity activity levels that can be used to assess and describe free-living activity patterns for persons with a motor-complete tetraplegia or a motor-complete paraplegia.

#### 6.1.1 Resting conditions

Studies I and II present resting oxygen consumption and energy expenditure for persons with a motor-complete SCI. The result for bodyweight-related oxygen and energy consumption is comparable to that of other studies with similar inclusion criteria<sup>94-97,119,142</sup>. Oxygen consumption during rest ( $2.52 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ) was 38 % lower than the commonly-used value for the general population ( $3.5 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ). The group result for REE in kcal/day was 40% lower than the REE estimated with the Harris-Benedict formula: this has also been reported in a review article by Nevin et al.<sup>11</sup>. However, when the result was compared with those of persons with similar BMI and age according to the study by Byrne et al., bodyweight-related  $\text{VO}_2$  was only 11 % lower<sup>93</sup>. In addition, the non-significant gender difference reported in the general population<sup>101</sup> seems to be maintained after an SCI, at least for persons with paraplegia<sup>95,142</sup>, and most likely also for persons with tetraplegia, as shown in this thesis. Another result from the present work is the relatively large standard deviation for REE and oxygen consumption, also reported in other studies<sup>95,97,142 94,96,119</sup>.

The standard deviation or the interindividual difference for REE among persons with motor-complete SCI, together with the low correlation to bodyweight ( $r^2=36$ ) implies difficulties for creating prediction models with low estimation errors for REE. The present equation model for estimating REE showed a SEE of  $\pm 189$  kcal and LOA of  $\pm 367$  kcal, and bodyweight explained 36% of the variance for this cohort. Previous research models for estimating REE have included fat-free mass and report a lower SEE, namely 103 kcal/day<sup>142</sup>. However, when that model was used by another researcher including fat-free mass, the LOA was -410 to +441 kcal/day<sup>143</sup>. The present model shows that persons with a high measured REE will be underestimated and those with a low predicted REE will be overestimated. However, for the more homogenous sample of motor-complete tetraplegia, the explained variance for REE was 59 %: this might be related to fat free mass.

In the general population bodyweight, BMI, gender and age are often used for categorizing and estimating REE<sup>85,93</sup>. This is based on a linear relationship between bodyweight and fat-free mass where fat-free mass accounts for 70 % of the variation and is the single most important predictor of REE<sup>93,94,114,144</sup>. This is also seen in the SCI population when dual-energy x-ray is used<sup>57,82,94,103</sup>. However, there is no proxy for an individual dual-energy x-ray measure for persons with SCI with a higher correlation than bodyweight (reported in this thesis)<sup>94</sup>. Still, bodyweight here had the highest linear association with REE. This means that the best crude indicator at present, for body composition for persons with motor-complete SCI, is bodyweight. Hence, we still lack validated prediction models here. REE might be one of many factors that could affect early weight gain and catabolic conditions after SCI.

#### 6.1.1.1 *Influencing factors*

While bodyweight could explain only 36 % of the variance for REE, and none of the other variables used could significantly increase the explained variance, other variables may contribute to the understanding of REE. One of these could be a measurement error: despite standardization and exclusion criteria intended to reduce the error, there is always a risk. In previous literature other variables are suggested, for example, bone mineral density<sup>100</sup>, testosterone replacement therapy<sup>145</sup>, pressure ulcers and urinary tract infections<sup>146</sup>, and injury completeness<sup>96,147</sup>. An alternative variable correlated to REE and perhaps explaining a large part of the interindividual difference of REE is variation in mitochondrial affinity ( $p_{50\text{mito}}$ )<sup>148</sup>. Previous studies on elite athletes in the general population have shown a large difference between the individuals mitochondrial  $p_{50\text{mito}}$  and metabolic (energy) changes<sup>148</sup>. Maybe, the best solution at present is to bridge the knowledge gap by measuring REE (indirect calorimetry) after the acute phase and starting to estimate REE at least one year after the SCI, since REE seems to decrease over the first ten weeks after SCI and then reach a plateau.<sup>103</sup> This could be beneficial both for building a large stock of data for different injury characteristics at different time points post injury and, most importantly, to permit accurate information about REE in the early stages post injury that might prevent weight gain.

#### 6.1.2 **Standardized activities**

This thesis reports, for the first time, results for AEE during standardized activities. Studies such as that by Collins et al. reported total energy expenditure instead<sup>96</sup>. However, the total energy expenditure found in the present work can be compared to that in previous studies for some activities<sup>96,149</sup>. Further, the present result for AEE displays both similarities and differences within the two groups of motor-complete tetraplegia and paraplegia. One important result is that NEPA, such as wheeling indoors /outdoors with a perceived exertion of 10-11 on the Borg RPE scale, and setting table showed similar AEE for both groups. Interestingly, the AEE ( $\text{kcal}\cdot\text{kg}^{-1}\cdot\text{min}$ ) during NEPA could be increased approximately 2 - 6 times depending on speed in km/h and level of injury, which could affect total daily energy

expenditure, since such activities are easy accessible and could be performed for longer time periods. Hence, exercise activities such as wheeling the wheelchair outdoors at Borg RPE 13-14, showed a 60% higher AEE for paraplegia than for tetraplegia, even when energy expenditure was related to bodyweight and speed. This is also reflected in the MET values, which showed that wheeling wheelchair outdoors (RPE 13-14) had a mean MET value of 7 for persons with a motor-complete paraplegia and 4 for those with tetraplegia. This difference is related to alteration in cardiovascular response between motor-complete tetraplegia and paraplegia. Consequently, persons with motor-complete tetraplegia need to spend more time in exercise activity to expend the same amount of energy due to their altered response from the autonomic nervous system and less active muscle mass. Still, exercise activities for motor-complete tetraplegia are important for increasing aerobic capacity. Since a higher aerobic capacity may increase the time spent in NEPA, by decreasing the relative level for activities.

The results from studies I and II could be used to make a crude estimate of energy expended during activity (AEE kcal·kg<sup>-1</sup>·min<sup>-1</sup>). Using the mean values for the AEE data in the tables from studies I and II and multiplying by bodyweight (kg), time (min) and, when possible, speed or resistance (km/h, watt), it is possible to estimate AEE. Still, these values need to be treated with caution since they are only crude estimations due to the sometimes large interindividual variance. To illustrate the increase for kcal per day in activity an estimation has been made (Table 14) using the values from Studies I and II.

**Table 14.** Example AEE estimation, based on values published in studies I and II

<b>Tetraplegia</b>			
<b>Sedentary</b>	<b>NEPA</b>	<b>Exercise</b>	<b>Total energy expenditure</b>
14 hours Deskwork and TV	2 hours	N/A	<b>1782 kcal</b>
13 hours Deskwork and TV	2 hours	1 hour. 30 min wheeling outdoors and 30-min circuit resistance training	<b>1892 kcal</b>
<b>Paraplegia</b>			
14 hours Deskwork and TV	2 hours	N/A	<b>1795 kcal</b>
13 hours Deskwork and TV	2 hours	1 hour. 30 min wheeling outdoors and 30-min circuit resistance training	<b>2058 kcal</b>

On a daily basis, the increase for kcal seems small; yet over 5 days there is an increase of around 500-600 kcal through one hour's activity (per day) at moderate intensity for a person with motor-complete tetraplegia, compared to being sedentary (Table 14). This is comparable

to the result in a recent study for motor-complete tetraplegia<sup>94</sup>. The same estimation for motor-complete paraplegia with the same prerequisites based on Table 3 in Study I showed an increase of  $\approx 1300$  kcal for 5 days. These examples show clearly that it is possible increase energy outtake both for motor-complete tetraplegia and motor-complete paraplegia.

The present work provides methods for estimating activity-related energy expenditure during a day or week. However, even if it is possible to estimate total energy expenditure for persons with motor-complete SCI, this is not equal to caloric restriction and losing body weight, there are more factors that affects the bodyweight<sup>108,109,112</sup>. The body's metabolic processes adapt to new prerequisites and change throughout life, which makes the theoretical model for energy balance less valid since many variables interact and affect energy balance.

### 6.1.3 Physical capacity

The main result in study III for  $VO_{2peak}$  was that absolute and relative oxygen consumption was low compared to that in the general population<sup>121</sup>. This leads to a narrow span for oxygen consumption from rest to peak capacity. Further, the result for absolute and relative  $VO_{2peak}$  is comparable to those in other studies with equal groups of persons with SCI regarding PA-level<sup>122,150-153</sup>. Still, there seems to be a large variation for peak capacity as reported among wheelchair-dependent athletes with SCI<sup>154</sup>. Nevertheless, the present result is based on a group of individuals that was heterogeneous for age and level of PA, and this is reflected in the results when these are compared to athletes'<sup>154</sup>. Something that needs to be addressed is that, despite a protocol for peak testing, there is still a risk that participants might not reach their peak capacity during the test; there is also a risk of measurement error.

Based on the result from the  $VO_{2peak}$  (study III), it is possible to create a framework for relative intensity levels. This framework is based on a homogenous sample for level of injury and injury completeness, heterogeneous for age, bodyweight (BMI), gender and activity level. This is of importance for the validity of the results reported in this thesis. However, the narrow span of oxygen consumption, especially for motor-complete tetraplegia, makes it hard to categorize the standardized activities and to distinguish between different intensity levels. This is related to restrictions for peak capacity for motor-complete SCI. Previous research has reported that being physically active seem to affect the  $VO_{2peak}$ , both for tetraplegia and paraplegia<sup>155</sup>. This was also seen in this thesis, being physically active in vigorous activity (self-reported) PA was one of the variables that explained the variance  $VO_{2peak}$  ( $L \cdot min^{-1}$ ).

#### 6.1.3.1 Peak heart rate

This thesis reports values of  $HR_{peak}$  for both motor-complete tetraplegia and paraplegia comparable to other studies using asynchronous arm-crank tests<sup>156-158</sup>. Previous studies have reported a difference in  $HR_{peak}$  between athletes and non-athletes with motor-complete



tetraplegia<sup>158</sup>: non-athletes had a mean of 102 beats per minute compared to a mean of 160 bpm for the athletes<sup>158</sup>. The explanation is that elite athletes with a peak HR between 140 and 160 may have a preserved autonomic function whereas others close to 130 bpm do not. A peak HR between 120 and 140 seem to be related to regular high-level exercise. Some of the present participants reported a high dose of aerobic exercise, but none had an HR<sub>peak</sub> above 130 beats per minute. Similar results are reported elsewhere<sup>47,159,160</sup>. Thus, the present result confirms that persons with motor-complete tetraplegia participating in this thesis most likely were motor-complete due to the low HR<sub>peak</sub>. The result for motor-complete paraplegia show no difference for HR<sub>peak</sub> compared to other studies and to non-SCI, that have used asynchronous arm-crank tests<sup>47,161</sup>.

#### 6.1.4 Relative and absolute levels of intensity

Exercise at specific intensity is generally important for cardiovascular fitness and maybe even more so for wheelchair-dependent persons to maintain and enhance cardiovascular fitness. Therefore, individualized exercise prescription based on knowledge from VO<sub>2peak</sub>, HR<sub>peak</sub> and Borg RPE for motor-complete cervical and thoracic SCI is essential<sup>125</sup>.

This thesis follows the American College of Sports Medicine recommendation for describing level of intensity: low/light, light, moderate and vigorous intensity<sup>162</sup>. The main idea is that for persons with a VO<sub>2peak</sub> below 10 MET intensity levels should be categorized based on relative values<sup>162</sup>. The rationale for this is that the increase between the steps for MET values is far too large. This appears in the result from Studies III-IV where the peak absolute oxygen uptake, based on individual RMR, is  $\approx 5$  SCI MET (11.1 ml·kg<sup>-1</sup>·min<sup>-1</sup>) for motor-complete tetraplegia and  $\approx 8$  SCI MET (18.5 ml·kg<sup>-1</sup>·min<sup>-1</sup>) for motor-complete paraplegia.

Consequently, it was not impossible for persons with motor-complete tetraplegia to reach the WHO recommendation for vigorous intensity of 6 MET (21 ml·kg<sup>-1</sup>·min<sup>-1</sup>), and only a few reached moderate intensity  $\geq 3$  METs, (10.5 ml·kg<sup>-1</sup>·min<sup>-1</sup>). However, persons with motor-complete paraplegia could possibly reach moderate intensity but not all can reach vigorous<sup>162</sup>. Even if the RMR from this thesis is used as 1 MET (2.52 ml·kg<sup>-1</sup>·min<sup>-1</sup>), still 3 SCI MET (7.6 ml·kg<sup>-1</sup>·min<sup>-1</sup>) is  $\approx 68$  % of VO<sub>2peak</sub> for tetraplegia. Therefore, the best way of describing intensity levels in motor-complete SCI is to use relative measures of oxygen consumption, as also recommended by the American College of Sports Medicine<sup>162</sup>. This is that persons with a VO<sub>2peak</sub>  $\leq 10$  MET should use 37-45 % of VO<sub>2peak</sub> as light intensity, 46-63 % of VO<sub>2peak</sub> as moderate intensity and 64-91 % of VO<sub>2peak</sub> as vigorous intensity. Likewise, persons with a VO<sub>2peak</sub> equal to or below 5 MET should use 44-51 % of VO<sub>2peak</sub> as light intensity, 52-67 % of VO<sub>2peak</sub> as moderate intensity and 68-94 % of VO<sub>2peak</sub> as vigorous intensity. The percentage of VO<sub>2peak</sub>, together with relative HR levels (% of HR) and Borg RPE, constitute the framework for creating the clinical tool published in study III (Table 3), with results comparable to previous research<sup>83,132,163-165</sup>.

The major challenge for the creation of this clinical tool was the small span of oxygen consumption for persons with motor-complete tetraplegia. This limits the distinction between moderate and vigorous activities, which can partly be corrected by using speed of movement (km/h), Borg RPE and percentage of  $HR_{peak}$ . Of these, using the Borg RPE seems the most accurate way to describe different intensity levels in motor-complete tetraplegia<sup>66,132</sup>. All the NEPA were categorized as moderate-to-vigorous intensity (52-94 % of  $VO_{2peak}$ ) for motor-complete tetraplegia. These findings indicate that persons with motor-complete tetraplegia might not be able to perform daily activities or NEPA for longer periods due to the high intensity level. Another factor that adds to less time spent in daily activities and NEPA is that the lactic threshold for persons with motor-complete tetraplegia is around 60% of  $VO_{2peak}$ <sup>151</sup>. This indicates that rehabilitation might focus even more on increasing peak capacity for better endurance during daily life activities. It may also be related to the participants' failure to reach peak capacity during testing.

This unique clinical tool permits a more individualized approach to recommending activities, together with Borg RPE and % of  $HR_{peak}$ . Further, the tool could be a good support for clinicians when discussing and recommending different activities for reaching a desired level of intensity. As described earlier under Background there are two different guidelines for the SCI population. There is uncertainty as to which of these is the more suitable. Both use moderate-to-vigorous intensity levels but there is little information on how to reach these. Moreover, there is little information on what activities have the potential to reach the right level for either motor-complete tetraplegia or motor-complete paraplegia. Table 3 in Study III might bridge the knowledge gap about what activities to perform to reach a certain intensity level. Besides, there is a need for PA-forms that are easy accessible and cheap, which may bridge the barriers for PA such as lack of facilities and time<sup>166</sup>.

Based on the work on relative intensity levels and peak capacity, one may argue that a more individualized approach for PA recommendation might be a consideration for persons with motor-complete SCI. The difference in peak capacity within and between motor-complete tetraplegia and paraplegia affects the ability to spend time in daily activities and NEPA. A more individualized approach could reach persons with low and high physical capacity. One way of doing this could be by using different levels of recommendation based on individual capacity. The first step could be to increase  $VO_{2peak}$  so as to be physically active for longer periods at low-to-moderate intensity. The second step could be to use the recommendations by Ginis et al.,<sup>67</sup> and the third to follow the recommendation from Tweedy et al.<sup>66</sup>. One way of assessing physical capacity is to use a submaximal arm-ergometer test, which includes resistance in watts, and to measure HR and Borg RPE.

### **6.1.5 Accelerometer cut-points**

The main outcome for wrist-worn-accelerometer measurements is the cut-points for different PA levels for motor-complete paraplegia and motor-complete tetraplegia. The cut-points for

absolute (MET) and relative (% of  $VO_{2peak}$ ) intensity levels could be used in research as well as in clinical settings. This is the first time that ROC curve analysis has been used for creating accelerometer cut-points for motor-complete SCI. Two previous studies have presented cut-points based on mixed-model regression and linear regression analysis<sup>81,82</sup>. Their results show a large discrepancy for MVPA, which might be related to the heterogeneous cohorts (tetraplegia, paraplegia, multiple sclerosis, spina bifida and amputees)<sup>81,82</sup>. The difference between the statistical approaches is that the mixed model and linear regression may have a higher error of misclassification compared to ROC<sup>167</sup>. Moreover, ROC analysis seems to be a better statistical tool when analyzing uneven groups<sup>137</sup>.

The cut-points presented here are based on oxygen consumption from six standardized activities (2 sedentary, 3 NEPA and 1 exercise), 125 unique measurement points for motor-complete tetraplegia and 212 unique measurement points for motor-complete paraplegia. This is a reasonable number and comparable to those in studies of the general population<sup>168,169</sup>.

One may argue that the decision to use dominant wrist is a weakness since recent studies have indicated that accelerometer data should be captured from the non-dominant wrist<sup>84</sup>. However, these studies show, in the error statistics where they compare between dominant and non-dominant wrist, that there seems to be higher accuracy for computer work and mopping from the non-dominant wrist, whereas, watching TV, wheelchair wheeling at slow and fast speeds has similar or higher accuracy when using the dominant wrist<sup>84</sup>. Another argument against dominant wrist is that it will provide much “noise” during light intensity; however, this is disproved by looking at the correlation matrix (study IV) where none of the data-points for sedentary exceeds low/light intensity for motor-complete paraplegia and one data point for sedentary exceeds low/light intensity for motor-complete tetraplegia. More important is how energy is expended: this is through movement of the upper body, preferably the arms, during weight-bearing activities such as wheelchair wheeling, which was equally accurate for either wrist<sup>84</sup>. This is why other researchers found no difference for accelerometer measurements between left and right hand, for wheelchair-dependent persons<sup>76,82</sup>.

The cut-points from study IV could be used to describe activity patterns in free living or during rehabilitation or research projects. This tool could also complement the activity tool (study III) where the accelerometer can be seen as a feedback or facilitator for changes in activity pattern.

## 6.2 METHODOLOGICAL CONSIDERATIONS

### 6.2.1 External validity

External validity is based on representatives of a recruited sample and the validity of applying the conclusions outside the context of this thesis. The sample recruited for the present work was a convenience sample and part of a minor population of persons with motor-complete SCI (AIS A, B) with injury level between C5-C8 and T7-T12. Several aspects of the criteria for inclusion in this investigation could be debated. The low number of women participants affects the robustness of the gender-specific statistical calculations, which affects external validity. Another liability could be the wide spread in age, body weight/height and BMI, but this also reflects the total SCI population <sup>170</sup>.

One risk with a convenience sample is that people interested in the study theme – in this case PA and exercise – are more likely to be interested in participating in this kind of study. Nevertheless, the present sample was widely spread, from highly physical-active people to those who did no organized aerobic PA. However, 36 % of the sample reported that they were physically active according to WHO guidelines. This is comparable to other studies reporting time spent in MVPA over the WHO guidelines <sup>171-173</sup>. So, the present sample, regarding PA, is not weighted towards elite athletes; rather, it represents a group of persons that are physically active intermittently.

Further, the present work has employed a clear distinction between motor-complete tetraplegia and motor-complete paraplegia by excluding persons with a level of injury between T1-T6. The rationale for this was the different prerequisites for PA depending on the function of the autonomic nervous system <sup>46</sup>. The choice to exclude the T1-T6 group was based on the uncertain cardiovascular response, which could blur the result for HR and energy expenditure.

Moreover, variation in mechanical efficiency between the more standardized arm ergometry and the more variable wheeled mobility may have influenced the variation in relative intensity level of performance between these two different modes of activity. Unfortunately, we were not able to compare mechanical efficiency between the wheeled mobility and arm ergometry, as valid measurements of the power output for latter was not available.

A most arbitrary inclusion criterion was ‘absent or minimal’ spasticity, which does not reflect the total population, in fact only 71 % of the participants reported none or mild spasm induced by stimulation. Spasticity is common among motor-complete SCI and a recent study from Sweden reported that 35% had spasticity <sup>174</sup>. A Canadian study reported that 37% of admitted patients were prescribed anti-spasticity medication <sup>175</sup>. So far, no studies including persons with motor-complete SCI have, despite attempts to do so, showed that RMR decreases after reduction of spasticity in a group of motor-complete SCI <sup>97,176,177</sup>. One study has reported that energy expenditure and VO<sub>2</sub> decreased 4-9 % after treatment with tizanidine (6-12 mg) in non-injured persons <sup>178</sup>. Studies show that some persons with motor-complete SCI seem to gain weight after spasticity treatment <sup>176</sup>. Subsequently, there is some kind of

connection between reduction of spasticity and weight gain, and this might be related to energy expenditure. In the present work participants could use Baclofen, and spasticity was self-reported with Penn and the intention was to see whether anyone reported a high level of spasticity which potentially could influence energy expenditure during activity testing. The results from the self-report were used to make a statistical check on the potential influence of spasticity on the RMR result, which it did not have.

With the above-mentioned precautions for maximizing the external validity, the results become generalizable to groups with the same injury levels/severity, age groups and BMI limits.

### 6.2.2 Internal validity

Internal validity is based on control for potential confounding variables to minimize the likelihood that there are other explanations for the oxygen consumption, HR and energy expenditure measured in the present work. In an attempt to eliminate the effect of alternative explanations, the inclusion and exclusion criteria were tailored to minimize confounding factors such as beta blockers, and hormone replacement such as thyroid hormone. Beta blockers do not affect the measurement of oxygen; however, they do affect regulation of the HR especially during exercise. Thyroid hormone will affect oxygen uptake by increasing RMR. Other confounding variables taken into consideration were diabetes and hypertension, though neither of these affect oxygen uptake.

To reduce the threats to internal validity during the test phase, a specific protocol was used for both RMR and activity testing. The protocol for RMR included overnight fasting (8 h), avoiding vigorous exercise the evening before the test and emptying the bladder before testing. Further, the activity protocol included written standardized instructions for the activities and the Borg RPE scale to ensure that the participants did the activity under the same prerequisites. The instructions also included testing external resistance or weights most suitable if the activity was to take more than 30 minutes. Another factor that was investigated was mechanical efficiency during arm crank, which showed that a higher workload was equal to around 13-14% higher mechanical efficiency. This result is comparable to that in some studies and lower than that in others<sup>136,152,179</sup>. The arm-ergometer used in the present work was asynchronous: there seem to be different views on mechanical efficiency for synchronous or asynchronous arm-cranking<sup>135,136,157,180</sup>. However, biomechanical conditions, such as position in the wheelchair, index between upper body and arm length, coordination and skill – all these complex variables affect work efficiency. To lower mechanical loss, we used a height-adjustable arm-ergometer that was only used in the project and we provided gloves and straps for those who needed.

### 6.2.2.1 Protocol for peak oxygen consumption

An individualized ramp protocol was used that consisted of individualize starting resistance based previous testing. Further, the last two minutes of the test were without increase in watts. Instead, the cadence was either increased or kept for the final push<sup>122,125,181</sup>.

There are different methods and protocol for  $VO_{2peak}$  testing for motor-complete SCI. The two most valid are the ACE test or the wheelchair ergometry test (WCE). Here the ACE was used, the test protocol including standardized determination criteria for a true  $VO_{2peak}$ . This is comparable to previous studies<sup>125-127</sup>. However, there are still conflicting results regarding the difference between ACE and WCE, some studies reporting a higher  $VO_{2peak}$  and HR from ACE<sup>182</sup> and others the opposite for ACE<sup>130,183</sup>. Recent research suggests that there is no difference in  $VO_{2peak}$  between ACE and WCE in persons with a level of injury T3 – L1 and completeness AIS A-C<sup>127-130</sup>. More important is what ACE and WCE really assess, since motor-complete SCI is limited to a small volume of muscle mass and lack of autonomic response; thus, these tests assess, rather, regional aerobic capacity<sup>125</sup>. Other confounding factors could affect the result such as sitting balance and lactic acid. To avoid these, the protocol included a pretest (submaximal arm-ergometry), an optional upper-body strap and gloves fixed to the arm-ergometer handles. Even though the testing procedure used an individualized protocol there is no guarantee that our participants reached their potential peak capacity.

### 6.2.3 Statistical considerations

The method used in studies I and II was the independent *t* test between men and women and between tetraplegia and paraplegia. This was direct and comprehensive since all data was normally distributed. The multiple stepwise linear regression analysis for  $VO_{2peak}$  included 4 variables and 63 participants (15 per variable), a reasonable number. The linear regression model for REE was further analyzed and visualized with a Bland-Altman plot, which showed that low values were overestimated and high values were underestimated. This phenomenon could be called regression towards the mean.

ROC curve analysis illustrates the diagnostic ability and accuracy to discriminate between two different conditions for continuous values. This is effected by examining the combination of sensitivity (true positive) and specificity (true negative) for all measured data, to identify the optimal predictor value and its associated cut-point. The AUC describes the overall accuracy of the predictor, which reflects the probability that a cut-point correctly categorizes the specific level of intensity<sup>184</sup>. The advantages of using this statistical model is a lower rate of misclassification than with other models<sup>167,184</sup>.

#### **6.2.4 Generalizability**

The present results are generalizable to other SCI groups with equal levels of injury and injury severity, same range of BMI, age and level of PA. Regarding the generalizability to other wheelchair-dependent groups such as persons with multiple sclerosis, amputees and spina bifida, the result might be useful as long as these persons have equal amounts of available muscle mass.





### 6.3 CONCLUSIONS AND CLINICAL IMPLICATIONS

This thesis provides information, based on homogenous samples of injury characteristics for motor-complete tetraplegia and paraplegia on: energy expenditure, oxygen consumption, heart rate and Borg ratings of perceived exertion during rest, physical activity and peak exertion. Further, the spinal cord injury -specific accelerometer cut-points permit assessment of activity patterns during free-living conditions i.e. their daily life. These data can be used as clinical tools in rehabilitation settings in order to tailor and evaluate recommendations for physical activities, weight-management and cardio vascular disease -prevention programs.

- Resting metabolic rate and resting energy expenditure were lower in persons with motor-complete SCI than in the general population. Relative oxygen consumption showed no difference between the genders and motor-complete tetraplegia and paraplegia. Further, resting metabolic rate showed a large interindividual variance and needs to be measured (indirect calorimetry) rather than estimated.
- Activity energy expenditure, especially during non-exercise physical activities, can potentially increase energy expenditure 3-6 times compared to sedentary. This is important since these activities are easily accessible and could be performed over longer periods with little negative effect on the shoulders.
- $VO_{2peak}$  is low among persons with motor-complete SCI and affects the intensity levels at which different physical activities are performed. Persons with motor-complete tetraplegia can reach vigorous intensity (>68% of peak oxygen consumption) already during daily activities. This indicates that, when possible, rehabilitation should focus on increasing aerobic capacity.
- The categorization of physical activities into intensity levels in relation to peak oxygen consumption, Borg and percent of peak heart rate can be used as a clinical tool to guide persons with SCI to reach desirable intensity levels.
- Specific accelerometer cut-points for motor-complete tetraplegia and paraplegia derived from ROC-analysis were defined. Based on these results, it is possible to capture activity patterns objectively during free living.

## 6.4 FUTURE RESEARCH

The present results can be used as an evidence-based foundation in future research in the field of lifestyle-based CVD prevention in the SCI population.

There is still a need for scientific clarification regarding

- effects of established SCI-specific physical activity recommendations
- physical activity patterns in the free-living SCI population
- resting energy expenditure and AEE in other SCI populations
- effects of SCI-adapted lifestyle-based CVD prevention programs, including both physical activity and food and weight management components
- weight management programs for the SCI population
- resting energy expenditure and variables that can explain plausibly the interindividual difference in the SCI population.

The present investigation has shown large interindividual differences in REE among persons with motor-complete SCI. These findings suggest that future studies should focus on measuring variables that can explain interindividual differences plausibly, and so increase understanding. Further larger national and international studies are needed to investigate the effects of different intensity levels on risk factors for CVD.

Another interesting area for future research is to assess activity during free living with the use of accelerometers, for understanding how much time is spent in sedentary and different intensity levels; moreover, whether there are any differences in CVD risk factors between active and inactive free-living patterns.

Further, there is a need to evaluate the effect of SCI-specific physical activity guidelines in larger studies. Finally, researchers need to collaborate nationally and internationally, together with rehabilitation units, to be able to include cohorts that are large enough to allow valid conclusions.

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Division of Neurogeriatrics

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