# SCIRE

SPINAL CORD INJURY REHABILITATION EVIDENCE

# Aging Following Spinal Cord Injury

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## Key Points

**Life Expectancy**

- Life expectancy for males with SCI is likely lower than the general male population.

- Persons injured at a younger age will likely have a longer life expectancy than persons injured at an older age.

- Causes of death post-SCI may be similar to those of the general population.

**SCI and Premature Aging**

- SCI may represent a partial model for premature aging.

- There is strong evidence that the endocrine and musculoskeletal systems are prematurely aging, while there is limited evidence for the respiratory, skin and subcutaneous tissues, genitourinary, and gastrointestinal systems.

- There is weak and limited evidence that the immune and nervous system are prematurely aging.

**Cardiovascular**

- Greater levels of arthersclerotic burden, higher levels of C-reactive protein levels and abnormal lipid profiles compared to the able-bodied population increases the risk for the development of cardiovascular disease in persons with SCI.

- Men with complete SCI have abnormal heart rate and blood pressure responses to isometric exercise compared to able-bodied controls, which are indicative of altered autonomic control, but this may not represent premature aging.

**Endocrine**

- Impaired secretion of both testosterone and human growth hormone in men with SCI may be due to SCI, and not from advancing age per se.

- Serum IGF-I levels may be impaired compared to the able-bodied population, which may be a sign of premature aging.

- Glucose tolerance and slower plasma-free cortisol responses may be impaired in persons with SCI, which may lead to an increased risk for premature diabetes mellitus.

- Persons with SCI are at higher risk for the development of cardiovascular disease and diabetes mellitus than the able-bodied population.

**Body Mass**

- Persons with SCI may have higher levels of fat mass than the able-bodied population. Although BMI increases over time in people with SCI, an active lifestyle may help to preserve physical capacity.

- Age-related declines of lean tissue in males with SCI may occur at a significantly faster rate than the able-bodied population.

- Body mass index increases over time in persons with SCI.

### Hematological / Immunological

- Age of onset may not influence hematologic abnormalities at the acute phase post-SCI (within first week post-injury).

- Immune function after SCI at both the acute and chronic phase is compromised compared to able-bodied controls, but age may not play an important role.

### Musculoskeletal

- Premature aging may occur in the femoral and hip regions in persons with SCI. It may be that declines in bone mass occur rapidly following injury, and reach a new steady-state within 3-8 years post-injury, depending on the bone parameter and skeletal site.

- Older males and females (> 60 years) with SCI may not experience rapid declines in bone mass in certain regions when compared to able-bodied controls.

- Duration of injury may be more associated with bone loss after SCI than chronological age.

- Women with complete SCI may be at a greater risk for fracture at the knee compared to males with SCI and the able-bodied population.

- Premature aging may not occur in the lumbar spine after SCI.

- Premature aging may not occur in hand grip strength in men with complete paraplegia. Rather, continual wheelchair use may retard the aging process in relation to handgrip strength.

- Regardless of age or years post-injury, persons with SCI may have increased thoracic kyphosis than the able-bodied population.

### Pain

- Upper limb pain in males with complete paraplegia may be attributed to longer durations of injury and not to the aging process.

- The incidence of shoulder pain increases over time, and that age of onset may contribute to the development of pain. Adults with SCI (< 10 years post-injury) who were 30 years and older were more likely to report shoulder pain over time than those who were less than 30 years of age.

- Younger persons (< 30 years) may have less pain interference at one and at two years post-injury than older persons (> 60 years).

- Previous reports of pain interference after SCI, irrespective of age, may be predictive of later pain interference.

### Respiratory

- Persons with SCI may have reduced lung capacity compared to able-bodied controls, but this reduction is due to SCI and not aging.

- Sleep disordered breathing may increase or persist with the aging process in persons with SCI.

- Seated breathing patterns after tetraplegia are compromised early post-injury but recover over time.

- Adults who are older (50 years +) and ventilator dependent have a higher mortality rate and lower weaning rate than adults who are younger and who are ventilator dependent.

**Dermal**

- Males with SCI have higher levels of collagen metabolite, glu-gal Hyl, than the able-bodied population, which may be a sign of premature aging of the skin. Further work is needed to conclusively demonstrate this.

- Behavioural factors play a stronger role in the development of pressure ulcers in persons with SCI than either age or years post injury.

**Genitourinary and Gastrointestinal**

- Various bladder management techniques (indwelling catheterization versus intermittent catheterization) may not impact renal functioning in persons with SCI over time.

- Repeated episodes of vesicoureteral reflux can cause kidney damage as early as four years post-injury.

- After SCI, renal plasma flow declines until 10 years post-injury, at which time, a slight reversal occurs.

- Age of onset may play a role in minimizing renal decline; adults who are under 20 and older than 50 have comparable renal functioning to the able-bodied population, but those between 20 and 50 years of age have impaired functioning.

- Bowel incontinence increased with age in the able-bodied population but does not change in persons with SCI.

- Persons with SCI may experience an increase in constipation-related symptoms and decrease in fecal incontinence over time.

- Level of injury, and not age or years post-injury, plays a primary role in the extent of bowel dysfunction.

**Secondary Complications of Multiple Systems**

- Fatigue and the need for physical assistance may increase over time with SCI.

- The number of secondary health complications increases with more years post injury.

- The incidence and severity of UTIs decrease over time in persons with SCI but prevalence of pressure sores remains stable.

- The co-occurrence of pain and depression is common in persons who have lived with SCI for many years.

**Functional Independence**

- Functional independence decreases with more years post injury.

**Quality of Life and Community Reintegration**

- Selected domains of life satisfaction (i.e., social life and sex life) may decline as one ages with a SCI. Other domains (i.e., employment and finances) may improve as one

ages with a SCI. It may be that these changes in satisfaction of certain domains are comparable to changes in the general population.

- Changes in environmental factors over time (i.e., economics; technology) may influence QoL in persons with SCI rather than the aging process per se.

- Community participation may decline with age after SCI. However, these changes in community participation may be similar to the aging general population.

- Individuals with new SCI (i.e. ≤ 5YPI) consistently report improvements to their QoL, whereas, individuals with longer term SCI consistently report high and stable QoL over time.

- Age of SCI-onset may be an influential factor on life satisfaction.

- Previous perceptions of life satisfaction may be predictive of later perceptions of life satisfaction.

- Aging has greater influence on self-rated health in people with SCI than those without a SCI.

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## Abbreviations

| | |
|---|---|
| 25(OH)-D | hydroxyvitamin D |
| AB | able-bodied |
| AIS | ASIA Impairment Scale |
| AN | anemia |
| BCM | body cell mass |
| BEE | basal energy expenditure |
| BMC | bone mineral content |
| BMD | bone mineral density |
| BMI | body mass index |
| CAC | coronary artery calcium |
| CHD | coronary heart disease |
| CRP | C-reactive proteins |
| CTT | colorectal transit time |
| CSA | cross-sectional area |
| DBP | diastolic blood pressure |
| DPA | dual photon absorptiometry |
| DXA / DEXA | dual-energy X-ray absorptiometry |
| ECM | extra-cellular mass |
| ECW | extra-cellular water |
| FBG | fasting blood glucose |
| FEV1 | forced expiratory volume in 1 second |
| FFM | fat-free mass |
| FIM | functional independence measure |
| FM | fat mass |
| FVC | forced vital capacity |
| GITT | gastrointestinal transit time |
| HA | hypoalbuminemia |
| HDL | high density lipoprotein |
| hGH | human growth hormone |
| IGF-1 | insulin-like growth factor 1 |
| LBM | lean body mass |
| LDL | low density lipoprotein |
| LH | luteinizing hormone |
| MRI | magnetic resonance imaging |
| MSK | musculoskeletal |
| OGTT | oral glucose tolerance test |
| PH | plasma homocysteine |
| PL | plasma leptin |
| pQCT | peripheral quantitative computed tomography |
| PSA | prostate specific antigen |
| PTH | parathyroid hormone |
| REE | resting energy expenditure |
| SBP | systolic blood pressure |
| SDB | sleep disordered breathing |
| sEMG | surface electromyography |
| SHBG | sex hormone binding globulin |
| SmC | somatomedin C |
| SMR | standardized mortality ratio |
| SRP | self reported health |
| T3 | triiodothyronine |
| T4 | thyroxin |

| | |
|---|---|
| TBK | total body potassium |
| TBM | total bone mass |
| TBW | total body water |
| TC | total cholesterol |
| TG | triglycerides |
| US | ultrasound |
| UTI | urinary tract infection |
| QoL | quality of life |
| YPI | years post-injury |

# Aging Following Spinal Cord Injury

## 1.0 Introduction

Life expectancy following spinal cord injury (SCI) has increased steadily in the past few decades, and is approaching that of the able-bodied population (Geisler et al. 1983; Whiteneck et al. 1992; Hartkopp et al. 1997; McColl et al. 1997; Frankel et al. 1998; DeVivo et al. 1999; Yeo et al. 1998; Krause et al. 2004). Due to advances in emergency, acute, and rehabilitation treatments, persons with SCI are now living many decades post-injury. There are increasing numbers of persons with long-term SCI who are over 55 years of age (Adkins 2001).

Initially, SCI was considered a relatively stable condition, and persons with SCI were thought to be able to maintain the same functional level for most of their lives (Trieschmann 1987). However, this static view of aging with SCI has been replaced by one that acknowledges that aging is a multi-dimensional and complex process of physical, psychological, and social change (Aldwin & Gilmer 2004).

McColl and colleagues (2002) described five changes that persons with SCI undergo as they age: 1) the effects of living with SCI long-term (e.g. shoulder pain, chronic bladder infections); 2) secondary health conditions of the original lesion (e.g. post-traumatic syringomyelia); 3) pathological processes unrelated to the SCI (e.g. cardiovascular disease); 4) degenerative changes associated with aging (e.g. joint problems); and 5) environmental factors (e.g., societal, cultural) that may potentially complicate the experience of aging with a SCI.  All of these factors have the potential to compromise a person with SCI's ability to sustain independence and ability to participate in their communities at later stages in life.

### Chronological Age, Years Post-Injury, and Age at Injury

One problem with research on aging after SCI is that the relationship between age at injury, current chronological age, and years post-injury (YPI) are all linearly dependent. This limits the ability to assess the influence of all three factors at the same time statistically (Adkins 2001). Hence, investigators are limited to examine only three possible combinations of factors, which include: 1) current age and YPI; 2) current age and age at injury; and 3) age at injury and YPI.  Furthermore, historical changes in the treatment and rehabilitation of SCI, increases the complexity of the assessment of aging effects associated with this condition (Adkins 2004).

Despite these issues, the field continues to strive to attribute changes in health and wellbeing to these aging variables.  Thompson and Yakura (2001) comment that, "developing an understanding of the effect of advancing age versus longer durations of injury on the incidence and type of changes can help in the prediction of when people with SCI might be susceptible to changes in function" (p. 73). This information can inform the creation of better health promotion strategies to mitigate declines in health and wellbeing since even slight changes in functioning after SCI can adversely affect a person's level of independence.

### Spinal Cord Injury: A Model of Premature Aging?

SCI has been described as a model of premature aging (Bauman & Spungen 1994).  According to this theory, premature aging of certain body systems may occur because additional stresses, resulting from SCI, can exceed the capacity of those body systems to repair themselves (e.g., cardiovascular, musculoskeletal) (Charlifue & Lammertse 2002). Although the aging process occurs at varying rates and at different ages for each individual (Charlifue 1993), it is generally accepted that bodily functions reach a maximum capacity prior to or during early adulthood, and then begin a gradual decline. This decline is thought to commence at approximately 25 years of age when the developmental process plateaus and biological capacity has peaked (Capoor & Stein 2005).  A classic study published in

Science (Strehler & Mildvan 1960) used mathematical models to show that physiological function declines at a consistent rate of 0.5-1.3% per year beyond age 30. This physical peak can be measured by examining the functioning of individual organ systems. For example, we can assess cardiovascular capacity by how well the heart can pump blood. Similarly, we can assess the individual's maximum functional capacities (e.g. how much weight an individual can lift). Hence, the average person at age 70 has approximately 50% of his/her capacity remaining in each organ system, which does not necessarily impact negatively on health or functioning since all organ systems have an 'excess reserve' (i.e., more cells, structure and supportive tissue than is required to meet daily life needs; Adkins 2004).

When reserve capacity declines below 40% of original functioning, there is greater chance of becoming injured, and/or more susceptible to infection or disease (Kemp & Thompson 2002). With the occurrence of a SCI, physiological and functional changes potentially accelerate bodily declines for a period of time, after which the effect of aging is thought to proceed at a normal rate (Adkins 2004).

Age of injury may have important consequences on different aspects of health. Because there are increasing numbers of seniors incurring a SCI due to falls, a bi-modal age-of-onset distribution exists, with the prevalence of SCI peaking among individuals who are 30 and 60 years of age (Pickett et al. 2006). As a result, researchers have been able to investigate and compare age-related outcomes after SCI. For example, there are a number of studies showing that persons who incur a SCI at later ages have poorer functional outcomes than those injured at younger ages (DeVivo et al. 1990; Alander et al. 1997; Alander et al. 1994; Scivoletto et al. 2004), although in some instances, the impact of SCI may be minimized in older persons.

Within a reserve capacity model of biological aging that is disrupted by SCI, Adkins (2004) theorizes that the impact of injury "decreases the further out on the age continuum the injury occurs" (p. 5). However, if the injury occurs far enough along the continuum, then even a minimal change in rate will lower reserve capacity below 40% soon after injury since capacity is already low. Further, adults with older ages of SCI-onset may have other pre-existing or vulnerabilities to co-morbidities that affect outcomes compared to younger adults (Furlan et al. 2009).

Given the increasing mean age of SCI onset, along with increased life expectancy, it may be possible to identify changes to systems that are 1) attributed to the SCI, 2) related to chronological age and the aging process, and 3) caused as a result of their interaction. Adkins (2004), however, suggests that it may be prudent to establish age of onset exclusion criteria when studying biological aging with SCI. In addition, completeness and neurological level of SCI must also be taken into account since a person with a complete lesion may experience aging in a different manner than someone with an incomplete lesion (Charlifue 1993).

**Aging and Quality of Life**

Although some biological changes are unavoidable with aging, other aspects are more malleable. Unlike physical aging, it may be that these aspects of a person's life may actually improve, and may be more amenable to intervention to either delay, modify or eliminate their potential negative impact (Charlifue & Lammertse 2001). There are a multitude of factors that must be considered when evaluating how people age with SCI, including personality traits, economic factors, environmental barriers and facilitators, cultural issues, and social networks (intimate and remote) (Charlifue & Lammertse 2001). Given the complex interaction among these factors, it is not surprising that several studies report contradictory findings, with life satisfaction and community integration decreasing with age, but increasing with years post-injury (YPI; i.e. Eisenberg & Saltz 1991; Krause & Crewe 1991; McColl & Rosenthal 1994; Pentland et al. 1995; Westgren & Levi 1998; Dowler et al. 2001; Tonack et al. 2008). To ensure that people with SCI are not only living long, but that they are also living well, it is

important to identify factors that lead to higher levels of quality of life that would be amenable to intervention.

## Chapter Purpose

The chapter summarizes some key issues in the SCI aging literature, and evaluates the level of evidence provided by selected studies on aging with SCI.  The selected research for evaluation includes longitudinal studies (duration of at least 2 years or more), case-control and cross-sectional comparative studies that focus on analyses relevant to aging. As longitudinal studies inherently include at least a baseline and follow-up evaluation, these studies were graded with a level of evidence of 4 (at least equivalent to pre-post studies).  Prospective longitudinal studies that also included a control group (e.g., able-bodied group) were graded with a level of evidence of 2 as they are considered cohort studies where one group is exposed to a particular condition (in this case, a spinal cord injury). Longitudinal studies that included historical controls (from chart review or database) were graded with a level of evidence of 3. Comparative studies utilizing both individuals with SCI and able-bodied controls at one point in time were graded with a level of evidence of 5. Studies involving mixed populations in which < 50% of the subjects had a SCI were excluded as were articles not in English. As well, studies with small sample sizes (less than 5 SCI participants) and/or with limited age ranges (i.e., only persons in their twenties and/or early thirties, etc.) were excluded.

Although the use of longitudinal designs is preferred, comparison studies with age-matched able-bodied (AB) controls is a useful approach for studying aging after SCI because it provides some awareness of the factors associated with the typical aging process (Charlifue 1993), while helping to illuminate whether changes are due to YPI rather than current age *per se*. After sustaining a SCI, age and YPI increase at the same pace, and so using age-matched AB controls allows us to determine the effects that might have occurred without SCI and those that occurred with SCI (Adkins 2004). This approach may offer some insight on whether changes after SCI are unique and/or accelerated in persons with SCI or if they are typical of the aging process.

The issues related to aging are described as mortality and life expectancy (see Table 1), physiological aging, which includes health status and physical functioning (see Table 2), the cardiovascular and endocrine systems (see Table 3), immune system (see Table 4), musculoskeletal system (see Table 5), respiratory system (see Table 6), nervous system (see Table 7), skin and subcutaneous tissues (see Table 8), the genitourinary and gastrointestinal systems (see Table 9), secondary health complications (see Table 10 &11), functional independence (see Table 12 & 13), and quality of life and community reintegration (see Table 14 & 15).

## 2.0 Mortality and Life Expectancy

Survival rates for individuals with SCI have made steady improvements over the past five decades. Prior to World War II life expectancy for individuals with SCI was quite poor (Geisler et al. 1983). Leading causes of death were those resulting from renal failure and infection (Lammertse 2001). Since the introduction of antibiotics, improved emergency transportation, advances in long-term health interventions, and the availability of preventative care at specialized treatment centres, mortality rates have been steadily decreasing and the causes of death have begun to mirror those of the general population (Whiteneck et al. 1992; DeVivo et al. 1999). However, life expectancy is still diminished compared to the general population (Whiteneck et al. 1992; Hartkopp et al. 1997; McColl et al. 1997; Frankel et al. 1998; DeVivo et al. 1999; Yeo et al. 1998; Krause et al. 2004).

Causes of death among individuals with SCI and those in the general population appear to be similar. In 2011, the two leading causes of death in high- and middle-income countries for the general population were ischemic heart disease and stroke (WHO 2011).  Other common causes were tracheal bronchus and lung cancers, chronic obstructive pulmonary disease, lower respiratory infections, and Alzheimer's disease and other dementias (WHO 2011). Similarly, two leading causes

of death in the SCI population are respiratory complications and heart disease (Hartkopp et al.1997; Frankel et al.1998; DeVivo et al. 1999; Soden et al. 2000; Zeilig et al. 2000; Garshick et al. 2005). Additionally, the latest report from the National Spinal Cord Injury Database (NSCIDB) indicates the main causes of death in persons with SCI in the United States are pneumonia and septicemia (NSCISC 2013). The high rates of cardiovascular disease in the SCI population may be partly due to physiological and functional changes following injury (Dearwater et al. 1986; Yekutiel et al. 1989; Bauman et al. 1992a, b; Gupta 2006). Interestingly, cancer is a growing cause of death in persons with SCI (DeVivo et al. 1999; Zeilig et al. 2000; Imai et al. 2004).

In general, it appears that as individuals with SCI age, cause of death becomes similar to age matched controls (Capoor & Stein 2005). Some deaths, however, may occur prematurely (e.g., from cardiovascular disease; Yekutiel et al. 1995), and there are some notable differences in mortality patterns between the SCI and the general populations.

In this section, 5 longitudinal studies and 1 cross-sectional study (see Table 1) on mortality and life expectancy among individuals with spinal cord injury are reviewed.

## Table 1: Mortality and Life Expectancy

| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| Cao et al. 2013; USA Retrospective longitudinal N=2685 | **Population:** 2685 persons with traumatic SCI who had been discharged from 62 acute care non-federal hospitals in South Carolina between 1998 and 2009. **Methodology:** Data were collected through a comprehensive data system spanning 11 years of observation; the mortality experiences of traumatic SCI subjects were compared with the general population of South Carolina using standardized mortality ratios (SMRs) for selected causes of death, adjusting for age, race, and sex. **Outcome Measures:** Mortality, and causes of death identified by ICD-10. | 1. The crude annual mortality rate during the period was 33 per 1000 person-years. 2. Increasing number of comorbidities, admission into non-trauma centers, advancing age, type of insurance (Medicaid and commercial payers), higher injury level and completeness, and being female were positively and significantly associated with the risk of death after discharge from acute care facilities. 3. The overall mortality rate of the cohort was 3.6 times (95% CI, 3.3,3.9) higher than the general population. 4. Likelihood of death was 1.6 times (95% CI: 1.2,2.2) higher for persons with C1-4 level injuries than other levels. |
| Rabadi et al. 2013; USA Retrospective longitudinal N=147 | **Population:** 147 veterans with SCI (144M 3F); mean (SD) age: 59.6(13.5), range 26-90; mean (SD) age at injury (yrs): 37.7(14.4), range 18-82; Level of injury: 53% cervical, 33.3% thoracic, 13.6% lumbosacral; Severity: 53% complete, 47% incomplete. **Methodology:** Patients enrolled in an SCI program from 1 Jan 2000 until 31 Dec 2011 were retrospectively studied (followed every 4 months and annually until end of study); the sample was divided into 2 groups based on the survival status by Dec 31 2011. **Outcome Measures:** Mortality, life expectancy | 1. There were 3 major causes of death: **infection-related:** 46% (pneumonia [21%], urinary infection [14%], infection of pressure ulcers [11%]); **cardiovascular-relate**d: 25% (myocardio infarction [14%], stroke, [4%] congestive heart failure [4%], other cardiovascular [4%]); **cancer-related:** 16%; **other** 15%. 2. In individuals with complete SCI, deaths were mainly infection-related and occurred in the hospital (51%). 3. In individuals with incomplete SCI, deaths were mainly cardiovascular and cancer-related and occurred in the community. |

| Author Year; Country<br>Score<br>Research Design<br>Total Sample Size | Methods | Outcome |
|---|---|---|
| | | 4. Age at the time of injury was the main predictor of SCI-related mortality.<br>5. The estimated survival since time of injury for SCI patients was 39.3 (2.3) yrs. The 10- and 20- yr survival rates after injury were 87% and 78% respectively. |
| Frisbie 2010;<br>USA<br>Retrospective longitudinal<br>N=322 | **Population:** 322 subjects with SCI (318M 4F); had follow up service for SCI with scheduled annual checkups between 1998 and 2007.<br>**Methodology:** Cohort was divided into two groups: surviving and deceased through 2008.<br>**Outcome Measures:** prevalence rates of anemia, severe anemia and hypoalbuminemia. | 1. The 239 subjects who survived had an average age of 60 and 30 yrs of paralysis and the 83 subjects who died had an average age of 70 and 27 yrs of paralysis.<br>2. Prevalence rates were high for anemia and hypoalbuminemia, and higher for those deceased subjects, suggesting they are markers for inflammation and poor prognosis. |
| Pickelsimer et al. 2010;<br>USA<br>Retrospective longitudinal<br>N=988 | **Population:** 988 subjects with traumatic SCI (731M 257F); differed significantly in age at TSCI, race and type of SCI.<br>**Methodology**: Using 2 statewide datasets, prevalence and incidence of medically attended health conditions during emergency department visits, acute care hospitalizations, and outpatient hospital visits, across all ages and SCI severity over a 10 year follow-up period were reported. A time-to-event life table method was used to calculate the prevalence and incidence of health conditions and Cox proportional hazard ratio of mortality by gender controlling for age and SCI severity.<br>**Outcome Measures:** Morbidities identified by ICD-9-CM; ICDMAP-health care billing data. | 1. During 10 yr follow-up period, 49 (19.1%) women and 104 (14.2%) men died. No difference between genders for mortality after controlling for age and TSCI severity.<br>2. The reported 15.5% mortality rate is higher than other reports (7 to 9%) examining outcomes in the SCI population over a 10-yr period. |
| Savic et al. 2010;<br>UK<br>Longitudinal<br>N=282 | **Population:** 282 individuals with traumatic SCI injured prior to 1971; age at time of injury 15-55 years; mean age at enrollment 52.7; 86.7% males; 29.2% tetra ABC, 49.8% Para ABC; 21.0% Incomplete injuries.<br>**Methodology:** Full physical assessment, diagnostic procedures, detailed medical and psychosocial interview, retrospective medical records review.<br>**Outcome Measures:** Medical History and Current Status; battery of outcomes including quality of life, depression, pain, and environmental factors. | 1. Over a 16-year period, the mortality rate increased over time: 1993 (4.1%), 1996 (9.9%), 1999 (16.4%), 2002 (22.5%), 2006 (35.8%). |
| Samsa et al. 1993;<br>USA<br>Cross-sectional with Able-boided (AB) comparison<br>N SCI=6147 | **Population:** 5545 veterans with SCI; mean (SD) age at onset: 23(6) yrs; mean YPI: 24(13).<br>**Methodology:** Comparison of long-term survival of veterans with SCI to a population-based life table. Life table formed from age-matched American men from same time period.<br>**Outcome Measures:** Survival curves, extending from 3 mos to 40 yrs after injury. | 1. Mean life expectancy of veterans with traumatic SCI and surviving at least 3 months is an additional 39 yrs after injury – 85% of age-matched American males.<br>2. Older age at injury is a stronger predictor of poorer long-term survival than is complete tetraplegia. |

**Discussion**

Rabadi et al. (2013) reported a 10-year survival rate of 87% from time of injury and a mean age of injury of 39. Pickelsimer and colleagues (2010) reported a 10-year survival rate of 84.5% from time of injury with a mean age of injury of 41 and excuded those that died in the first 89 days.

Although Samsa et al. (1993) found that injury level was not a significant predictor for mortality, they noted a near significant effect (p=0.06) for complete cervical injuries compared to all other injuries. Similarly, in an 11-year longitudinal study, Cao et al. (2013) reported the likelihood of death in individuals with injuries at the C1-4 levels to be 1.6 times greater than for individuals with injuries at other levels. Several studies have found no association between impairment and mortality (e.g. Liang et al. 2001; Imai et al. 2004; Garshick et al. 2005), whereas other studies have highlighted the importance of impairment as a prognostic factor (Whiteneck et al. 1992; McColl et al. 1997; Coll et al. 1998; DeVivo et al. 1998; Soden et al. 2000; Yeo et al. 1998; Strauss et al. 2006). Samsa and colleagues (1993) found age of onset to be a significant predictor of long-term survival, which is consistent with other longitudinal studies that did not meet our inclusion criteria (Whiteneck et al. 1992; Frankel et al. 1998). Rabadi et al. (2013) reported age of onset to be the only predictor of mortality.

With regards to causes of mortality, Samsa et al. (1993) found that diseases of the genitourinary system (i.e. renal failure, septicemia) disproportionately accounted for death in their SCI sample, but the patterns of death began to approach that of the general population by 20 years post-injury. For instance, the rates of circulatory disease and neoplasms steadily increased across time points. Interestingly, the causes of death due to injury and poisoning, and external conditions were the highest at 3-months to 5 years post-SCI, and steadily decreased across time points. In a 12-year longitudinal study of 147 veterans with SCI, Rabadi et al. (2013) reported infection, cardiovascular, and cancer to be the three primary causes of death. Although not discussed, causes of death may have also included suicides. Regardless, the findings of lower levels of evidence highlighting the high rates of suicide as a cause of death (i.e. Imai et al. 2004) reinforces the need to provide psychosocial services to help minimize the occurrence of suicide in persons with SCI.

An acknowledged limitation of the study by Samsa et al. (1993) is the reliance on secondary data sources for case identification, control selection, and mortality assessment. The study was also only on male veterans and did not include women or persons who did not survive acute SCI (i.e. less than 3 months post-SCI). Causes of death were not reported by Pickelsimer et al. (2010) or by Savic et al. (2010).

**Conclusion**

*There is level 4 evidence that the 10 year survival rate post injury is 84-87% (Rabadi et al. 2013; Picklesimer et al. 2010).*

*There is Level 4 evidence (Frisbie et al. 2010) that the mortality rate post-SCI over a 10-year period may be 15.5% to 25.8%, and level 4 evidence (Cao et al. 2013) that the mortality rate is higher for individuals with SCI than the general population.*

*There is Level 4 evidence (Cao et al. 2013) that mortality may be higher for persons with SCIs at the C1-4 level than other spinal cord levels.*

*There is Level 4 (Frisbie 2010) to Level 5 evidence (Samsa et al. 1993) that the causes of death post-SCI are beginning to approximate those of the general population.*

*There is Level 5 evidence (Samsa et al. 1993; Cao et al. 2013) that life expectancy for males with SCI is lower than the general male population.*

*There is level 4 evidence (Rabadi et al. 2013) that older age at time of injury is a predictor of SCI-related mortality.*

> Life expectancy for males with SCI is likely lower than the general male population.
>
> Persons injured at a younger age will likely have a longer life expectancy than persons injured at an older age.
>
> Causes of death post-SCI may be similar to those of the general population.

## 3.0 Physiological Aging

Aging is a highly complex phenomenon that can be examined at the genetic, cellular, organ-system, and psychosocial levels (Aldwin & Gilmer 2004). Although there are some conflicting evidence on which systems decline, for the most part, persons aging with SCI exhibit decreases in health status and physical functioning over time (see Table 2), which could serve as markers of premature aging.

In this section, 1 systematic review (see Table 2) on physiological aging after SCI is reviewed.

**Table 2: Systematic Review on Physiological Aging**

| Author Year; Country<br>Date included in the review<br>Total Sample Size<br>Level of Evidence<br>Type of study<br>Score | Methods<br>Databases | Outcome |
|---|---|---|
| Hitzig et al. 2011; Canada<br><br>Reviewed published articles from 1980 to December 2009<br><br>N=74<br>(16 with longitudinal design)<br><br>**Level of Evidence:**<br>Downs & Black Modified Sackett scale<br><br>**Type of study:**<br>Longitudinal<br><br>AMSTAR: 5 | **Methods:** Literature search for English articles with non-intervention studies exploring aging of the body systems after spinal cord injury.<br>No intervention.<br>Outcome measures include effects of aging with SCI on cardiovascular, respiratory, endocrine, immune, genitourinary, gastrointestinal, nervous, skin subcutaneous tissues, and musculoskeletal systems.<br><br>**Databases:** MEDLINE/PubMed, CINAHL, EMBASE and PsycINFO**.** | 1. Premature aging in SCI was supported by level 2 evidence for the musculoskeletal system, level 5 evidence for the cardiovascular and endocrine systems and limited level 5 evidence for the immune system.<br>2. Premature aging in SCI was supported by level 4 and 5 evidence for the respiratory system.<br>3. Evidence on the genitourinary system, gastrointestinal system, and for skin and subcutaneous tissues provide level 4 and 5 evidence that premature aging may not be occurring in these systems. |

## Discussion

In this systematic review (Hitzig et al. 2011), the hypothesis that SCI represents a model for premature aging is supported by level 5 evidence for the cardiovascular and endocrine systems, level 2, 4 and 5 evidence for the musculoskeletal system, and limited level 5 evidence for the immune system. Only a few level 4 and 5 studies for the respiratory system were found. Evidence on the genitourinary system, gastrointestinal system, and for skin and subcutaneous tissues provide level 4 and 5 evidence that premature aging may not be occurring in these systems.

> SCI may represent a partial model for premature aging.
>
> There is stronger evidence that the endocrine and musculoskeletal systems are prematurely aging.
>
> There is limited evidence that the respiratory, skin and subcutaneous tissues, genitourinary, and gastrointestinal systems are prematurely aging.
>
> There is weak and limited evidence that the immune and nervous system are prematurely aging.

The following sections review each body system individually, including the cardiovascular and endocrine systems (see Table 3), immune system (see Table 4), musculoskeletal system (see Table 5), respiratory system (see Table 6), nervous system (see Table 7), skin and subcutaneous tissues (see Table 8), and the genitourinary and gastrointestinal systems (see Table 9).

## 3.1 Cardiovascular and Endocrine Systems

Similar to the general population, cardiovascular disease has become one of the leading causes of death in the SCI population (DeVivo et al. 1989; DeVivo et al. 1993; Frankel et al. 1998).  There are multiple risk factors for its premature development due to physiological and functional changes following SCI (Bauman et al. 1994; Bauman & Spungen 2001a; Bauman & Spungen, 2001b).  For instance, many age-associated disorders such as carbohydrate intolerance, insulin resistance (Duckworth et al. 1980; Duckworth et al. 1983; Bauman et al. 1992; Karlsson et al. 1999) and lipid abnormalities (LaPorte et al. 1983; Brenes et al. 1986; Bauman et al. 1992; Bauman & Spungen 2001) are known to occur prematurely in persons with SCI.  Some have hypothesized that a marked decrease in physical activity (Myers et al. 2007), along with injury-related changes in metabolic function lead to an increased risk and premature development of cardiovascular disease (Bravo et al. 2004) and diabetes mellitus (Bauman 1993).

Related to the metabolic changes noted above, there is a high prevalence of muscle weakness in persons with SCI attributed to a loss of lean body mass (Thompson & Yakura 2001) that is possibly linked to reduced activity, and abnormally low levels of endogenous anabolic hormones (i.e., human growth hormone and testosterone; Bauman et al. 1994).  In the general population, age-related declines in the endocrine systems also lead to decreases in lean muscle mass and an increase in fat (Tenover 1999).  However, these declines have been shown to be greater in persons with SCI (Bauman & Spungen 2001b).  Similarly, noted changes in insulin resistance are thought to account for the high rates of diabetes mellitus in persons with SCI (Yekutiel et al. 1989).  This in turn leads to an increased risk for cardiovascular disease since the development of diabetes impairs the circulatory system (Halter 1999).  As such, it may be that alterations in body composition, which occur early following SCI, contribute to premature development of these disorders as compared to the AB population (Bauman et al. 1994).  With some of the literature below, young adults with SCI are compared to young adults without SCI. Thus, aging effects due to SCI may be a factor when changes in the cardiovascular and endocrine systems occur in these young adults with SCI that would be typically expected to occur in older adults (e.g., characteristics associated heart disease such as poor lipid profiles, elevated glucose, high BMI).  However, it is not always possible to disentangle mechanisms involving premature aging versus direct effects on the organs from the SCI itself.

In this section, 3 longitudinal studies and 26 cross-sectional studies (see Table 3) on cardiovascular and endocrine systems after SCI are reviewed.

## Table 3: Cardiovascular and Endocrine Systems

| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| de Groot et al. 2013; The Netherlands Prospective Longitudinal N=130 | **Population:** 130 persons with SCI (91M 39F); mean (SD) age: 40.1(13.8) yrs. **Methodology:** Blood lipids and body mass index (BMI) were determined at discharge from inpatient rehabilitation and at 1 and 5 yrs after discharge; using multilevel regression models the effects of lifestyle (drinking alcohol, smoking, active lifestyle and self-care) on the lipid profiles and BMI were determined. **Outcome Measures:** Total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides (TG), BMI. | 1. After correction for lesion and personal characteristics, no changes in lipid profiles in the 5 yrs after discharge were seen, whereas BMI increased 1.8kgm$^{-2}$ between discharge and 5 years later<br>2. A high percentage was at risk of cardiovascular disease after 5 yrs due to high BMI (63-75%) or HDL (66-95%). The percentage at risk of other unfavorable lipid levels was lower (3-35%).<br>3. Age was significantly and unfavorably related to total cholesterol, low-density lipoprotein, triglycerides and BMI.<br>4. Individuals who indicated they maintained their fitness level and individuals with low BMI showed better lipid profiles.<br>5. Individuals with a more active lifestyle showed higher HDL levels, but individuals, who "often or always avoid(ed) smoking" had a 1.5kgm$^{-2}$ higher BMI. |
| Hosier et al. 2012; USA Cross-sectional N=17 | **Population:** 17 women with SCI; *Premenopausal group* (n=11): mean (SD) age in yrs: 32.4 (10); 1 tetraplegia, 11 paraplegia; AIS: AIS A n=5, AIS B n=6 *Postmenopausal group* (n=6): mean (SD) age in yrs: 56.0 (9.4); 3 tetraplegia, 3 paraplegia; AIS: AIS A n=4, AIS B n=2; Age at menopause (yrs): mean 43.8. **Methodology:** Participants were stratified into 2 groups according to menopausal status. **Outcome Measures:** Fasting serum total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), calculated low-density lipoprotein (LDL-C), fasting blood glucose (FBG), systolic blood pressure (SBP). | 1. Groups were similar on BMI (22.4 vs. 22.2), HDL-C (52.5 vs. 53 mg/dL), FBG (79.3 vs. 84.8 mg/dL), and SBP (104.6 vs. 111.8 mm Hg).<br>2. TG, TC and LDL-C were significantly higher in post-menopausal group (55.7 vs. 101.8 mg/dL; 158.3 vs. 191.6 mg/dL; 94.7 vs. 118.2 mg/dL). |
| de Groot et al. 2010; The Netherlands Longitudinal N=184 | **Population:** 184 persons with SCI (138M 46F); mean(SD) age 40.2(14.1) yrs; mean(SD) time since injury 94.8(65.8) days; 61% paraplegia, 70% complete lesion. **Methodology:** BMI was determined at the start of active rehabilitation, 3 months later, at discharge, and 1, 2, and 5 yrs after discharge. **Outcome Measures:** BMI | 1. BMI did not significantly increase during inpatient rehabilitation, but showed a significant increase the year after discharge.<br>2. BMI increased by 1 kg/m$^2$ for each 10-year increase in age. |
| Liang et al. 2007; USA Cross-sectional with AB controls | **Population:** 185 men with SCI, mean(SD) age 39(10.4) yrs; mean YPI 11.7 (range 1-40.4 yrs); age, gender, and race-matched AB controls. | 1. Group with SCI had decreased levels of all of the followings: HDL, TG, glucose, TC, and LDL.<br>2. Characteristics of metabolic |

| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| N SCI=185 N controls=185 | **Methodology:** Comparison of prevalence rates of metabolic syndrome. **Outcome Measures:** Total cholesterol (TC), HDL and LDL; Elevated glucose; Triglyceride (TG). | syndrome (a condition associated with aging) were more prevalent in young SCI individuals than controls. |
| Orazaki et al. 2007; USA Cross-sectional with AB controls N SCI=82 N controls=273 | **Population:** 82 subjects with SCI (67M 15F); mean(SD) age 49.7(12) (range 20-90 yrs), mean(SD) YPI 19.7(10); 273 age, gender, ethnicity, and risk factor-matched AB controls. **Methodology:** Comparison of the burden of atherosclerosis between SCI and control groups. **Outcome Measures:** Coronary artery calcium (CAC) scores, mean calcium scores. | 1. Prevalence of coronary artery calcium (CAC) was greater in persons with SCI than in AB controls 2. Atheroselerosis, a condition related to aging was more prevalent in SCI. |
| Wang et al. 2007; Taiwan Cross-sectional with AB controls N SCI=62 N controls=29 | **Population:** 62 males with complete SCI; mean(SD) age 28.0(9.7) yrs (range 16.2–59.1 yrs); mean(SD) YPI 11.8(7.0) (1.2–27.7 yrs); age- and gender-matched AB controls. **Methodology:** Comparison of serum levels of markers of inflammation and endothelial activation between SCI and controls. **Outcome Measures:** Body weight, BMI, serum levels of albumin, creatinine, LDL, HDL, insulin, C-reactive proteins (CRP), interleukin-6, endothelin-1, and sVCAm-1. | 1. Compared to AB controls, group with SCI had significantly lower body weight and BMI, as well as lower serum albumin and creatinine levels. 2. Group with SCI had lower levels of density lipoprotein-cholesterol (LDL), lower levels of high-density lipoprotein-cholesterol (HDL), and an increased total cholesterol/HDL cholesterol ratio, and a trend toward increased insulin levels than AB controls. 3. Group with SCI had increased serum levels of CRP, interleukin-6, endothelin-1, and sVCAm-1 than AB group. |
| LaVela et al. 2006; USA Cross-sectional with AB controls N SCI=3708 N controls=18018 | **Population:** 741 veterans (98.2% male) with SCI disorder (e.g., traumatic injury, multiple sclerosis), mean age 64.1 (range < 40 to 70+ yrs); mean YPI 23.9 yrs; 2,967 veterans with SCI/D (96.8%) and no diabetes; mean age 59.2 yrs, mean YPI 23.8 yrs; 1342 veteran AB controls (age range <40 - >70 yrs) and 16676 general population AB controls (age range <40 - >70 yrs). **Methodology:** Comparison of prevalence rates of diabetes mellitus. **Outcome Measures:** Prevalence of diabetes. | 1. Diabetes prevalence increased among veterans with SCI disorders compared to general population, but similar to other veterans. 2. For those 45 to 59 yrs of age, diabetes prevalence was increased in veterans with an SCI/D. |
| Bauman et al. 2004; USA Cross-sectional with AB controls N SCI=13 N controls=13 | **Population:** 13 men with SCI, mean(SD) age 37(8) yrs; mean(SD) YPI 15(9); AB identical twins of subjects were control. **Methodology:** Comparison of energy expenditure and fat-free mass (FFM) with monozygotic twin. **Outcome Measures:** Basal energy expenditure (BEE) and resting energy expenditure (REE) by indirect calorimetry; Fat-free mass (FFM) and fat mass (FM) assessed by dual-energy X-ray absorptiometry; Total body potassium (TBK). | 1. Twin with SCI had decreased BEE and REE compared to AB twin. 2. Fat mass was equivalent between groups, but ratios of FM to FFM and FM to TBK were decreased in twins with SCI. |

| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| Jones et al. 2004; New Zealand Cross-sectional with AB controls N SCI=20 N controls=20 | **Population:** 20 men with SCI, mean(SD) age 33(2) (range 16-52 yrs); mean(SD) YPI 10.3(1.8) yrs; 20 age, gender, height, weight, and activity level-matched AB controls. **Methodology:** Comparison of prevalence of metabolic syndrome (i.e., symptoms that increase cardiovascular risk such as high blood pressure and glucose levels). **Outcome Measures:** Lean and fat mass; Plasma glucose and insulin; Total cholesterol; HDL; Oral glucose tolerance test (OGTT). | 1. 55% of the group with SCI met the criteria for metabolic syndrome, whereas none of the controls did. |
| Jones et al. 2003; New Zealand Cross-sectional with AB controls N SCI=19 N controls=19 | **Population:** 19 men with SCI; mean(SD) age 34(8) (range 16-52 yrs); mean YPI > 1 yr; age, gender, height, and weight-matched AB controls. **Methodology:** Comparison of BMI and adiposity. **Outcome Measures:** BMI; Total body and regional lean tissue and fat mass. | 1. BMI was similar in both groups but total body lean tissue mass was decreased and total body fat mass was increased in the SCI group. 2. Body fat percentage was increased in group with SCI. |
| Petrofsky & Laymon 2002; USA Cross-sectional with AB controls N SCI=50 N controls=50 | **Population:** 50 men with complete paraplegia, divided into four age groups (20 – 30 yrs, 31 – 40 yrs, 41 – 50 yrs, 51 – 65 yrs); YPI range 3 – 10 yrs; age-, gender-, and height-matched AB controls **Methodology:** Comparison of blood pressure and heart rate during isometric exercise and at rest (leg and arms) **Outcome Measures:** Heart rate, blood pressure. | 1. Group with SCI had a larger change in blood pressures both at rest and during leg exercise. 2. Heart rate during handgrip exercise was normal for both SCI and AB groups, but was absent in the SCI group during the leg exercise. |
| Bauman et al. 2001; USA Cross-sectional with AB controls N SCI=835 N controls=14,838 | **Population:** 835 subjects with SCI (723M 122F); mean(SD) age 38(11) yrs, mean(SD) YPI 12(9). **Methodology:** Comparison of levels of plasma homocysteine to AB reference population. **Outcome Measures:** Plasma homocysteine (PH). | 1. Older group with SCI (>50 yrs) had increased mean PH than the younger age group. 2. Group with SCI had increased levels of PH compared to the control group. 3. SCI group had elevated plasma homocysteine which is associated with an increased risk of vascular disease. |
| Demirel et al. 2001; Turkey Cross-sectional with AB controls N SCI=69 N controls=52 | **Population:** 69 subjects with SCI (53M 16F); mean(SD) age 33.9(11.37) yrs (range 10–70); mean(SD) YPI 16(10) (range 1–41); age- and gender-matched AB controls. **Methodology:** Comparison of standard risk factors for coronary heart disease (CHD). **Outcome Measures:** BMI, blood pressure, diabetes mellitus, HDL, LDL, total cholesterol. | 1. Impaired fasting glucose, diabetes mellitus, hyperuricemia, high total cholesterol (TC), low density lipoprotein-cholesterol (LDL), low high-density lipoprotein-cholesterol (HDL), high TC/HDL, LDL/HDL ratios were more common in persons with SCI than in the AB group. |
| Spungen et al. 2000; USA Cross-sectional with AB controls N SCI=8 N controls=8 | **Population:** AB twins of 8 males with SCI with complete paraplegia, mean(SD) ages 40.4(10) yrs, mean(SD) YPI 16(9) yrs. **Methodology:** SCI subjects were compared with twin on total and regional lean tissue and fat mass. **Outcome Measures:** Body composition. | 1. Group with SCI had significant decrease in total body lean mass compared to AB twin group, independent of age. 2. Group with SCI had significantly increased total body fat mass compared to AB twin group. |

| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| Bauman et al. 1999; USA Cross-sectional with AB controls N SCI=320 N controls=303 | **Population:** 320 subjects with SCI (234M 86F); mean (SD) age 41(0.62) yrs (range 20-77), mean (SD) YPI 15(0.52) (range 1-57 yrs); 303 age-, gender-, ethnicity-, and activity level-matched AB controls. **Methodology:** Comparison of serum lipid profiles between SCI and controls. **Outcome Measures:** Serum levels: total cholesterol (TC), triglycerides (TG), HDL-cholesterol (HDL-c), LDL-cholesterol (LDL-c), body mass index (BMI). | 1. Group with SCI had decreased levels of TC, TG, HDL-c and LDL-c, and increased levels of TC/HDL-c ratio compared to the AB control group. 2. The AB control group had increased BMI compared to the group with SCI, but the estimated per cent body fat was increased in the group with SCI. |
| Yamamoto et al. 1999; Japan Cross-sectional with AB controls N SCI=7 N controls=7 | **Population:** 7 men with complete tetraplegia; mean(SD) age 41(10.0) (range 33–58 yrs); mean(SD) YPI 13.7(3.4) (range 9–18 yrs); age- and gender matched AB controls (n=7). **Methodology:** Comparison of blood pressure, heart rate, and hormonal changes during 2 minutes of sustained contraction. **Outcome Measures:** Heart rate, blood pressure. | 1. Group with SCI had no changes in heart rate during exercise, whereas AB controls did change. 2. Blood pressure increased in both groups. |
| Apstein & George 1998; USA Longitudinal with AB controls N SCI=100 N controls=80 | **Population:** 100 men with SCI, mean age 45; 80 age- and gender-matched AB controls. **Methodology:** Evaluate changes in serum lipids at 4, 16, 36 and 52 weeks post-injury, and compared at 52 weeks compared to AB controls. **Outcome Measures:** Serum levels of total cholesterol (TC), LDL, HDL. | 1. Total serum cholesterol (TC) levels were always decreased in males with tetraplegia compared to males with paraplegia. 2. No differences in triglycerides between SCI groups at any time. 3. At 4 weeks after injury, low-density lipoprotein-cholesterol (LDL) were decreased in males with tetraplegia compared to males with paraplegia, but were equivalent at 1 YPI. 4. Serum high-density lipoprotein cholesterol (HDL) were decreased in the group with tetraplegia compared to group with paraplegia at 4 weeks, but increased compared to AB levels at 1 YPI. 5. LDL/HDL ratio was lower at 4 weeks to 1 YPI in the group with tetraplegia compared to group with paraplegia, whose LDL/HDL was comparable to AB controls. |
| Huang et al. 1998; China Cross-sectional with AB controls N SCI=25 N controls=25 | **Population:** 25 men with SCI; mean age 35.4 (range 18-55 yrs); mean YPI 7.5 (range 1.1-15.8 yrs); age and gender matched AB controls. **Methodology:** Comparison of hypothalamus-pituitary-adrenal axis. **Outcome Measures:** Radioimmunoassay methods, corticotropin-releasing hormone levels. | 1. Cortisol response to corticotropin-releasing hormone was decreased in SCI group, but differences disappeared if correction was made for baseline values. |
| Bauman et al. 1996; USA Cross-sectional with AB controls | **Population:** 34 males with SCI, mean(SD) age 50(2) yrs, mean(SD) YPI 11(2); 48 age- and gender-matched AB controls. **Methodology:** Comparison of Body Mass | 1. Group with SCI had increased levels of PL compared to the control group. 2. No significant differences in BMI between SCI and control groups. |

| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| N SCI=34 N controls=48 | Index (BMI) and plasma leptin (PL) between SCI and control groups. **Outcome Measures:** Plasma leptin levels, BMI. | |
| Cheville & Kirshblum 1995; USA Cross-sectional with AB controls N SCI=30 N control=30 | **Population:** 30 subjects with SCI (29M 1F); mean age 59 (range 22-82 yrs); mean YPI 24 (range 2-50 yrs); age and gender-matched AB controls. **Methodology:** Comparison of thyroid function and to determine the incidence and clinical prevalence of low T3 syndrome. **Outcome Measures:** Serum levels of triiodothyronine (T3) and thyroxin (T4). | 1. Mean triiodothyronine (T3) levels and thyroxin (T4) levels were significantly decreased in the group with SCI. 2. T3 resin uptake levels (measure of serum thyroid hormone) were significantly increased in the group with SCI. 3. Altered thyroid function was found in the SCI group. |
| Tsitouras et al. 1995; USA Cross-sectional with AB controls N SCI=20 N controls=16 | **Population:** 20 men with SCI, mean(SD) age 42(2) yrs, mean(SD) YPI 15(2); 16 healthy males, mean(SD) age 39(4) yrs. **Methodology:** Comparison of serum growth hormone and testosterone between the 2 groups. **Outcome Measures:** Serum testosterone (T), human growth hormone (hGH) and insulin-like growth factor 1 (IGF-I). | 1. SCI is associated with impaired secretion of both T and hGH (not the result of aging). 2. Time since injury appears to have an adverse effect on serum T. |
| Bauman et al. 1994; USA Cross-sectional with AB controls N SCI=16 N controls=16 | **Population:** 16 men with SCI; mean(SD) age 45(3) yrs, mean(SD) YPI 19(3); 16 controls mean(SD) age 39(4) yrs. **Methodology:** Comparison of growth hormone response to intravenous infusion of arginine hydrochloride (30 g/subject over 30 minutes). **Outcome Measures:** Plasma human growth hormone (hGH) release and plasma insulin-like growth factor (IGF-I) levels; Body Mass Index (BMI). | 1. Mean hGH responses at 30 and 60 minutes were significantly decreased in the group with SCI than in the control group (3.4(0.7) vs. 10.7(2.5) ng/ml; and 5.2(1.5) vs. 12.5(2.7) ng/ml), even when controlled for age and BMI. 2. Mean plasma IGF-I levels were decreased in SCI subjects <45 years old than in AB counterparts (202(19) vs. 324(27) ng/ml). Comparison of those >45 years old revealed no differences. 3. Lower daily physical activity depresses hGH/IGF-I axis in younger individuals with SCI and may be considered a state of premature aging. |
| Bauman & Spungen 1994; USA Cross-sectional with AB controls N SCI=100 N controls=50 | **Population:** 50 men with paraplegia (mean(SD) age 51(2) yrs, mean(SD) YPI 19(2)) and 50 men with tetraplegia (mean(SD) age 47(2) yrs, mean(SD) YPI 17(2)); 50 male controls (mean(SD) age 51(2) yrs). Age- and Body Mass Index (BMI)-matched. **Methodology:** Comparison of responses from oral glucose tolerance test (OGTT). **Outcome Measures:** Mean plasma glucose and insulin values, serum lipid levels. | 1. 82% of controls had normal oral glucose tolerance vs. 38% of those with tetraplegia and 50% with paraplegia. 2. 22% of SCI group were diabetic vs. 6% of controls. 3. Those with SCI develop carbohydrate disorders at younger ages. 4. Subjects with SCI had significantly higher mean glucose and insulin values during the OGTT when compared to controls. 5. Serum lipid levels in subjects with SCI showed a decreased HDL cholesterol level (38(1) mg/dL). |

| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| Huang et al. 1993; China Cross-sectional with AB controls N SCI=30 N controls=30 | **Population:** 30 men with SCI, ages 17.4 – 43.9 yrs, mean 31.4 yrs; 30 healthy males, ages 21.0 – 38.7 yrs, mean 29.6 yrs. **Methodology:** Comparison of pituitary-testicular and pituitary-thyroid axes with age matched, sexually active control population. **Outcome Measures:** Endocrinologic studies, Radioimmunoassay methods. | 1. 4 persons with SCI had low levels of serum triiodothyronin (i.e., altered thyroid metabolism), 1 with increased serum follicle-stimulating hormone, 8 with increased serum testosterone levels, and 11 with increased serum prolactin levels. 2. Compared to AB controls, persons with SCI had increased luteinizing hormone (LH) responses (hormone from pituitary gland), with 8 having exaggerated or prolonged LH responses. |
| Leaf et al. 1993; USA Longitudinal N SCI=47 | **Population:** 22 subjects with tetraplegia (mean(SD) age 39.0(16.7), range 15-80 yrs); 25 persons with paraplegia, (mean(SD) age 42.0(18.8), range 19-82 yrs); YPI range for both groups 35-3605 days. **Methodology:** Characterize the risk of cardiac dysrhythmias via 24 hrs Holter monitoring, and to determine if significant cardiac event occurred at 2 yrs post-baseline. **Outcome Measures:** Holter monitoring. | 1. Despite the theoretical basis for increased incidence of cardiac dysrhythmias following SCI, no significant cardiac events occurred for sample at 2 yr follow-up. |
| Shetty et al. 1993; USA Cross-sectional with AB controls N SCI=41 N controls=119 | **Population:** 41 men with tetraplegia, mean age 41 yrs (range 24-66 yrs); 119 AB control, age range 30-70 yrs. **Methodology:** Comparison of growth hormone (GH) and Somatomedin C (SmC) concentrations in the two groups. **Outcome Measures:** Radioimmunoassay of SmC. | 1. SmC was decreased in the group with SCI than AB controls. Inverse relationship between SmC level and increasing age in both groups. 2. Severe inactivity or SCI may cause hyposomatomedinemia, which could contribute to decreased lean body mass and muscle atrophy, increased risk for pressure sore formation and osteoporosis post-SCI. |
| Wang et al. 1992; China Cross-sectional with AB reference population N SCI=63 | **Population:** 63 men with SCI; mean age 31.2 (range 18-44 yrs); mean YPI 6.2 (range 8 mos-20 yrs); AB reference population. **Methodology:** Comparison of hormone patterns of gonadotropin and testosterone. **Outcome Measures:** Serum levels of triiodothyronine, testosterone, serumfollicle-stimulating hormone, luteinizing hormone. | 1. 7 persons with SCI had decreased serum triiodothyronine below reference level, and 8 people had low serum testosterone. 2. 17 persons with SCI had hyperprolactinemia, and 9 cases had elevated serum testosterone level. 6 persons with SCI had elevated serumfollicle-stimulating hormone and 4 cases had elevated luteinizing hormone. |
| Zlotolow et al. 1992; USA Cross-sectional with AB controls N SCI=28 N controls=52 | **Population:** 28 men with paraplegia, mean(SD) age 48(2) yrs (range 25-65 yrs); YPI ≥1.5 yrs; 52 age- and gender-matched AB controls. **Methodology:** Comparison of diet, BMI, and serum lipid levels between SCI and AB control groups. **Outcome Measures:** Serum levels of total cholesterol, HDL, and triglycerides; total caloric and cholesterol intake from diet; BMI. | 1. No differences in BMI, total caloric or cholesterol intake between SCI and AB control groups. 2. Serum HDL cholesterol levels decreased compared to AB controls. 3. Total caloric intake decreased with age in AB controls but not SCI group. |
| Nuhlicek et al 1988; | **Population:** 37 men with SCI; 19 with | 1. Diminishing TBW, LBM, BCM, and |

| Author Year; Country<br>Score<br>Research Design<br>Total Sample Size | Methods | Outcome |
|---|---|---|
| China<br>Cross-sectional with AB controls<br>N SCI=37<br>N controls=10 | tetraplegia; 18 with paraplegia; age range 19-49 yrs; age and gender matched AB controls.<br>**Methodology:** Comparison of body composition between control and groups of different SCI injury levels.<br>**Outcome Measures:** Anthropometry; Total body water (TBW); Predicted extracellular water (ECW); Lean body mass (LBM) and body cell mass (BCM); Extracellular mass (ECM) and extracellular water (ECW). | muscle cell mass, and increasing fat mass with higher spinal lesions.<br>2. No change in total body weight, ECM or ECW. |

## Discussion

### *Cardiovascular System*

In this section, the evidence reviewed appears to support the notion that the cardiovascular system is prematurely aging. With regard to risk factors for cardiovascular disease, Bauman and colleagues (2001) found that regardless of age or sex, persons with SCI had significantly higher levels of plasma homocysteine than able bodied (AB) controls, and that older persons with SCI (>50 years) had higher levels than younger persons with SCI. Plasma homocysteine is thought to promote coagulation and to decrease the resistance of the endothelium to thrombosis (Malinow 1994), and is a clear independent marker for the prediction of vascular disease (Clarke et al. 1991; Stampfer et al. 1992). The findings regarding lipid profiles also support an increased risk for the development of cardiovascular disease. Several studies (Demirel et al. 1991; Zlotolow et al. 1992; Bauman & Spungen 1994; Bauman et al. 1995; Bauman et al. 1999; Liang et al. 2007; Wang et al. 2007) found that serum high-density lipoprotein cholesterol (HDL-c) are depressed in persons with SCI compared to AB controls, which is associated with an increased risk for developing coronary heart disease (Goldbour & Medalie 1979; Castelli 1984).

An important factor influencing these variables might be lifestyle. For instance, one longitudinal study (Shiba et al. 2010) on athletes with SCI (N = 7) found that physical capacity was maintained over a span of two decades. The results of this study, however, are limited to individuals participating in strenuous sport activities, a sample that is not representative of the general SCI population (Maki et al. 1995). Although no blood pressure changes were noted, the sample did have a significantly higher BMI from baseline to 20-year follow-up. Unfortunately, data on lipid profiles were not collected in this study. Further work on the role of diet and physical activity is needed to help clarify their impact on aging with SCI.

One study provides evidence that C-reactive protein levels were higher in men with SCI (N = 62) compared to AB controls (N = 29), which could also account for the decreases in total cholesterol, low-density lipoprotein and high-density lipoprotein. At the same time, increases in C-reactive protein levels may also partly explain why persons with SCI are nonetheless at increased risk for accelerated atherogenesis (Wang et al. 2007). A risk factor for vascular disease in both symptomatic (Budoff 2005) and asymptomatic (Raggi 2000) populations is coronary artery calcification (CAC), which is a component of atherosclerotic plaque. Orakzai and colleagues (2007) found significantly higher levels of CAC in persons with SCI (N = 82) compared to AB controls (N = 273), and that the risk was higher for males and for persons with tetraplegia.

Sustaining a SCI also affects blood pressure by altering the sympathetic activity to blood vessels. There is evidence that men with tetraplegia (Yamamoto et al. 1999) and paraplegia (Petrofsky & Laymon 2002) have increased blood pressure responses during exercise compared to AB controls.

As well, Petrofsky and Laymon (2002) found that their group with paraplegia had a larger change in blood pressure both at rest and during exercise and was more associated with aging than for the controls. Disturbingly, static exercise has been found to cause tachycardia in AB controls, but not in persons with SCI (Petrofsky & Laymon 2002; Orakzai et al. 2007) when paralyzed muscles were engaged. Several studies highlight that irregular blood pressure responses post-SCI have significant implications for cardiovascular health (Bluvshtein et al. 2011; Groothuis et al. 2010a; Groothuis et al. 2010b; LaFountaine et al. 2010; Yasar et al. 2010). Overall, these findings are indicative of altered autonomic control, but not necessarily of aging. Further work is needed to determine the long-term implications for cardiovascular health.

Decreases in physical activity may contribute to the development of cardiovascular disease, which may be reflected in body composition changes following SCI. Two longitudinal studies from the same author (de Groot et al. 2010; 2013) found that body mass index (BMI) increases over time in individuals with SCI. In the de Groot et al. (2010) study of 184 individuals, BMI was observed to significantly increase the year after discharge from in-patient rehabilitation. In the de Groot (2013) study of 130 individuals, BMI was observed to increase from discharge to a 5-year follow up. Individuals in this study, however, showed no change in their lipid profie over the 5 years of observation. Similar BMI findings have been reported by Crane and colleagues (Crane et al. 2011). However, studies comparing BMI between individuals with SCI and AB individuals have demonstrated mixed results. One study (Spungen et al. 2000) found greater BMI levels in persons with SCI compared to AB controls, whereas other studies found the opposite (Bauman et al. 1999; Bauman et al. 2004; Wang et al. 2007), or no differences at all (Zlotolow et al. 1992; Jones et al. 2003; Bauman et al. 1996).

Given these contradictory findings, BMI may not be an appropriate measure for SCI since studies that also examined lean and fat mass tissue (Bauman et al. 1996; Bauman et al. 1999; Spungen et al. 2000; Bauman et al. 2004; Jones et al. 2004) found that persons with SCI had significantly higher levels of fat mass tissue and lower levels of lean tissue than AB controls. These differences in lean and fat mass tissue appear to be attributable to YPI, and not age. For instance, Spungen et al. (2000) found lower lean mass and higher fat mass in persons with SCI who were matched with their AB monozygotic twin, which was directly related to YPI. As well, Bauman and colleagues (2004) concluded from their monozygotic SCI twin study that reductions in lean muscle tissue lead to reduced energy expenditure, which appeared to be related – albeit not significantly – to YPI. These findings are congruent with SCI-only cross-sectional studies examining body composition (Cardus & McTaggart 1985; Shizgal et al. 1986; Rossier et al. 1991).

The findings from a cross sectional study (Hosier et al. 2012) comparing cardiometabolic risk profiles in pre and post-menopausal women reported that post-menopausal women with SCI have higher triglycerides, total cholesterol, and low density lipoprotein than pre-menopausal women. No differences were observed in BMI or glycemic indices. The authors suggest that post-menopaual women with SCI have risk profiles that are similar to those observed in women without SCI, characterized by increases in triglycerides, total cholesterol, and low density lipoprotein, despite favorable BMIs and glycemic indices.

### Endocrine System

Metabolic changes after SCI may also be associated with changes in body composition, and may increase the risk of developing diabetes mellitus. Tsitouras and colleagues (1995) posited that impaired hGH secretion may be partially responsible for SCI- and aging-associated lean body and muscle mass depletion. Several identified studies (Shetty et al. 1993; Bauman et al. 1994; Tsitouras et al. 1995) provide evidence that serum IGF-I levels are lower in persons with SCI compared to age-matched controls, and that this depletion is associated with impaired hGH. Bauman et al. (1994) found that the average IGF-I was significantly lower in younger individuals with SCI than that in younger AB controls, but not in those greater than 45 years of age. As such, this pattern of IGF-I

levels in younger males with SCI appears to be similar to those of elderly AB individuals (Bauman et al. 1994).

Related to this, Bauman and Spungen (1994) found that persons with SCI had a higher mean glucose and insulin levels, and lower mean fasting plasma glucose levels than the AB control group. This intolerance was found to be present in two-thirds of their group with tetraplegia, and in half their group with paraplegia. Further, 22% of the persons with SCI met the diagnostic criteria for having diabetes mellitus, whereas only 6% of the AB controls were found to be diabtetic. Since these adverse clinical features occurred at younger ages in their SCI sample, Bauman and Spungen (1994) interpreted their findings as being a model of premature aging. The findings of Jones and colleagues (2004), and LaVela and colleagues (2006) appear to support this hypothesis as they both found higher rates of metabolic syndrome and diabetes in their SCI samples compared to the AB population. Conversely, Liang et al. (2007) found that males with SCI (N = 185) were not at higher risk for metabolic syndrome compared to AB controls (N = 185). This discrepancy may be due to some of the study's limitations (i.e. reliance on self-report height and weight to calculate BMI) and because they used a standard, rather than a modified, criteria for the syndrome which is not appropriate for persons with SCI.

The predisposition to diabetes and lipid abnormalities is thought to be largely a consequence of extreme inactivity, and the constellation of metabolic changes (i.e. human growth hormone deficiency, testosterone deficiency) appears to be occurring prematurely in persons with SCI (Bauman & Spungen 1994). As well, several studies have shown evidence of thyroid impairment after SCI compared to the AB population (Wang et al. 1992; Huang et al. 1993; Cheville et al. 1995). All of these findings suggest that persons with SCI may be frequently physiologically comprised, and more susceptible to minor pathologic insults. Along with associated changes in body composition, an increased risk for the development of cardiovascular disease, diabetes mellitus, and infection is higher following SCI (Bauman & Spungen 2001b).

**Conclusion**

*There is Level 5 evidence from one cross-sectional study (Bauman & Spungen 2001) that plasma homocysteine levels are higher in persons with SCI compared to the AB population, with the greatest discrepancy in older adults with SCI (> 50 years).*

*There is Level 5 evidence from nine cross-sectional studies (Zlotolow et al. 1992; Huang et al. 1993; Bauman & Spungen 1994; Bauman et al. 1996; Huang et al. 1998; Bauman et al. 1999; Demirel et al. 2001; Liang et al. 2007; Wang et al. 2007) that lipid profiles are altered after SCI which may contribute to the development of cardiovascular disease.*

*There is Level 4 evidence (Shiba et al. 2010) that physical capacity can be maintained long-term in male athletes with SCI.*

*There is Level 4 evidence from one longitudinal study (de Groot et al. 2013) that lipid profiles in adults with SCI remain stable during the 5 years after inpatient rehabilitation.*

*There is Level 4 evidence (Apstein & George 1998) that total cholesterol (TC), total glycerides (TG), and low-density lipoproteins (LDL) increased while LDL/high-density lipoproteins (HDL) ratios decreased for males with tetraplegia and paraplegia from the acute phase until 1 YPI. All lipid profiles were significantly depressed compared to controls.*

*There is Level 4 evidence (Apstein & George 1998) that persons with tetraplegia had low HDL and elevated LDL/HDL ratios, which places them at an increased risk for coronary artery disease.*

*There is Level 5 evidence (Wang et al. 2007) that C-reactive protein levels are higher in males with SCI, which could also account for the decreases in TC, LDL, and HDL. Elevated C-reactive protein levels may also partly explain why persons with SCI are at increased risk for accelerated atherogenesis.*

*There is Level 5 evidence (Orakzai et al. 2007) that persons with SCI have greater atherosclerotic burden compared to an AB reference population.*

*There is Level 5 evidence from two studies that men with complete paraplegia ((Petrofsky & Laymon 2002) and with complete Tetraplgia (Yamamoto et al. 1999) have an abnormal (absent) heart rate response to isometric exercise.*

*There is Level 5 evidence that men with complete tetraplegia demonstrate increased blood pressure (Yamamoto et al. 1999) response to isometric contraction.*

*There is Level 5 evidence (Wang et al. 1992: 63 men; Tsitouras et al. 1995; Shetty et al. 1993) that there is lower secretion of testosterone and human growth hormone levels in men with SCI compared to AB controls.*

*There is Level 5 evidence from two studies (Tsitouras et al. 1995; Bauman et al. 1994) that serum IGF-I levels are impaired in persons with SCI compared to the AB population, which may be a sign of premature aging.*

*There is Level 5 evidence from three studies (Bauman & Spungen 1994; Jones et al. 2004; Liang et al. 2007) that glucose tolerance is impaired after SCI, which may lead to an increased risk for premature diabetes mellitus.*

*There is Level 5 evidence (LaVela et al. 2006) that diabetes mellitus occurs prematurely in male veterans with SCI compared to AB individuals in the general population, but not veteran controls.*

*There is Level 5 evidence (Lewis et al. 2010) that men with SCI have slower plasma-free cortisol responses than AB controls.*

*There is Level 4 evidence from three longitudinal studies (de Groot et al. 2013 & 2010; Crane et al. 2011) that BMI increases significantly over time in persons with SCI.*

*Seven studies (Nuhlicek et al. 1988; Bauman et al. 1996; Bauman et al. 1999; Spungen et al. 2000; Jones et al. 2003; Jones et al. 2004; Emmons et al. 2011) provide Level 5 evidence that persons with SCI are likely to have higher levels of fat mass, and that age-related declines of lean tissue in males with SCI may occur at a significantly faster rate than the AB population.*

*There is Level 5 evidence from one monozygotic twin study (Bauman et al. 2004) that basal and resting energy expenditures are lower in males with SCI compared to their AB twin.*

*There is Level 5 evidence from one cross-sectional study (Hosier et al. 2012) that post-menopaual women with SCI have cardiometabolic risk profiles that are similar to those observed in women without SCI.*

Greater levels of arthersclerotic burden, higher levels of C-reactive protein levels and abnormal lipid profiles compared to the able-bodied population increases the risk for the development of cardiovascular disease in persons with SCI.

Men with complete SCI have abnormal heart rate and blood pressure responses to isometric exercise compared to able-bodied controls, which are indicative of altered autonomic control, but this may not represent premature aging.

Impaired secretion of both testosterone and human growth hormone in men with SCI may be due to SCI, and not from advancing age per se.

Serum IGF-I levels may be impaired compared to the able-bodied population, which may be a sign of premature aging.

Glucose tolerance and slower plasma-free cortisol responses may be impaired in persons with SCI, which may lead to an increased risk for premature diabetes mellitus.

Persons with SCI are at higher risk for the development of cardiovascular disease and diabetes mellitus than the able-bodied population.

Persons with SCI may have higher levels of fat mass than the able-bodied population. Although BMI increases over time in people with SCI, an active lifestyle may help to preserve physical capacity.

Age-related declines of lean tissue in males with SCI may occur at a significantly faster rate than the able-bodied population.

Age of onset may not influence hematologic abnormalities at the acute phase post-SCI (within first week post-injury).

## 3.2 Immune System

Although the immune system is affected by a number of factors, including nutritional status, stress, exercise, neuroendocrine change, and disease, there is consensus that immune functioning undergoes some age-related declines (Miller 1996; Burns & Leventhal 2000; Rabin 2000). There is limited evidence on the effects of SCI on the immune system with aging, but several studies (i.e., Lyons 1987; Nash 1994; Kliesch et al. 1996; Campagnolo et al. 1999; Cruse et al. 2000) suggest deficits in immune functioning. Hence, there is greater likelihood of immune impairment in the aging SCI population compared to the non-disabled population (Charlifue & Lammertse 2002).

In this section, 1 longitudinal study and 4 cross-sectional studies (see Table 4) on the immune system after SCI are reviewed.

**Table 4: Immune System**

| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| Zajarias-Fainsod et al. 2012; Mexico Cross-sectional with AB controls N SCI=12 N controls=18 | **Population:** 12 SCI subjects (8M 4F), >10 YPI; mean (SD) age in yrs: 32(5), range 22-46; mean (SD) YPI: 19.55 (8.4), range 12-37; Level of injury: 41.66% cervical, 58.34% thoracic; AIS scale: 50% A, 50% B. 18 age-matched healthy blood donors; mean (SD) age 33(6) yrs. **Methodology:** Blood samples were drawn through standard venipuncture and lymphocyte | 1. SCI patients presented a significant auto-reactive immune response as shown by T-cell proliferation against MBP compared to AB controls. 2. The authors suggest that this could indicate that immune cells are expanding tissue damage after the injury or alternatively, promoting neuroprotection and regeneration. |

| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| | proliferation and antibody titers against myelin basic protein (MBP). **Outcome Measures:** lymphocyte proliferation (colorimetric-BrdU ELISA assay), and antibody titers against MBP (ELISA Human IgG MBP-specific assay). | |
| Frisbie 2010; USA Retrospective longitudinal N=322 | **Population:** 322 SCI subjects (318M 4F); had follow up service for SCI with scheduled annual checkups between 1998 and 2007. **Methodology:** Cohort was divided into two groups: surviving and deceased through 2008. **Outcome Measures:** prevalence rates of anemia (AN), severe anemia (SAN) and hypoalbuminemia (HA) which might serve as markers for infection. | 1. 72% of surviving subjects experienced AN during survey period. 2. 99% of deceased subjects experienced AN. 3. SAN or HA also higher in deceased (54.2% vs. 28.0% and 61.4% vs. 28.5%). 4. Number of survey years positive for AN, SAN, or HA higher in deceased (82.7%, 18.0%, 22.2%) vs. survivor (33.7%, 6.0%, 6.4%). 5. SAN and HA occurred together in same survey year 78% of the times. |
| Furlan et al. 2006; Canada Cross-sectional with AB controls N SCI=21 N controls=11 | **Population:** 21 subjects with cervical SCI, ages 17-83 yrs, AIS A-D. 11 males and females with spine trauma, ages 18-75 yrs, AIS E as controls. **Methodology:** Consecutive individuals with acute C-spine trauma from 1998-2000 were reviewed. **Outcome Measures:** Blood hemoglobin concentration, leukocyte, lymphocyte and platelet count within first week of trauma. | 1. With age controlled, SCI individuals showed a significantly higher frequency for decreased hemoglobin concentration, leukocytosis, lymphopenia, and thrombocytopenia than controls within the first week post-trauma. 2. SCI had significantly higher leukocyte count and significantly lower blood lymphocyte count than controls. 3. Males with SCI had significantly lower hemoglobin concentration than male controls, but no differences detected between females. |
| Campagnolo et al. 1999; USA Cross-sectional with AB controls N SCI=18 N controls=18 | **Population:** 18 SCI subjects (11M 7F); for persons with tetraplegia, mean age 29 (19-51 yrs), mean YPI 56.6 months; for persons with paraplegia, mean age 32.6 (21-50 yrs), mean YPI 38.6 months. **Methodology:** Comparison of pituitary and adrenal function with age and gender matched AB controls. **Outcome measure:** Immunoassay methods. | 1. Plasma cortisol and dehydroepiandrosterone sulfate (DS) were higher in persons with SCI. 2. When examined within level of injury, no differences on mean plasma cortisol emerged, but persons with tetraplegia had higher levels of mean plasma dehydroepiandrosterone sulfate than AB controls which may suggest adrenal dysfunction |
| Campagnolo et al. 1994; USA Cross-sectional with AB controls N SCI=5 N controls=5 | **Population:** 5 subjects with complete tetraplegia (4M 1F); mean age 36.2 yrs, (range 20-69 yrs); mean YPI 33.8 (range 7-120 mos). **Methodology:** Comparison of an immunologic parameter, and psychological wellbeing with age and gender matched AB controls. **Outcome measure:** Lymphocyte proliferation | 1. No difference in cytometry, depression or stress. 2. Persons with SCI had significant suppression in lymphocyte balstogenic response for the three mitogens tested (pokeweed, conconavalin, |

| Author Year; Country<br>Score<br>Research Design<br>Total Sample Size | Methods | Outcome |
|---|---|---|
| | assay; Natural killer cell cytotoxicity assay; Cell counts; Ilfeld Psychiatric Symptom Index. | phytohemagglutinin). |

## Discussion

One study provides level 4 evidence (Frisbie 2010) that persons with SCI have a high prevalence of anemia and hypoalbuminemia which might serve as markers for infection. Additionally, two studies provide level 5 evidence that this system is compromised at the acute and chronic stages of SCI compared with AB controls.  Persons with acute and chronic SCI who have complete injuries (N = 5) demonstrated altered immune function compared to AB controls (Campagnolo et al. 1994).  As well, Campagnolo et al. (1999) compared persons with SCI (N = 18) to AB controls (N = 18), and found that persons with SCI have higher levels of cortisol and dehydroepiandrosterone sulfate (DS), but comparable levels of dehydroepiandrosterone, adrenocorticotropin, and prolactin.  Additionally, they found that DS and dehydroepiandrosterone were higher in persons with tetraplegia compared to controls, but no differences were found between persons with paraplegia and controls.  Campagnolo et al. (1999) concluded that immune functioning is altered after SCI, but may be mediated by level of injury.  Thus, persons with tetraplegia may have a greater degree of alteration to the immune system compared to persons with paraplegia.  Unfortunately, the sample sizes in both studies were quite small.

Further research related to the immune system is required given that older age of SCI-onset leads to poorer outcomes (Prusmack et al. 2006), and SCI of long duration results in increased infection (Whiteneck et al. 1992).  Because persons with SCI are treated with antiobiotics throughout their lives, there are a number of important questions regarding the long-term effects on the immune system (Adkins 2004).

## Conclusion

***There is Level 4 evidence that persons with SCI have a prevalence of anemia and hypoalbuminemia (Frisbie 2010), which might serve as markers for infection.***

***There is Level 5 evidence (Campagnolo et al. 1994; Campagnolo et al. 1996; Furlan et al. 2006) that the immune function of persons with acute and chronic SCI is compromised compared to the able-bodied population, but there is no influence due to aging.***

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Immune function after SCI at both the acute and chronic phase is compromised compared to able-bodied controls, but age may not play an important role.

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## 3.3 Musculoskeletal System

The musculoskeletal (MSK) changes are the most obvious external signs of aging, as most people have some wear and tear on this system as they age (Aldwin & Gilmer 2004).  Changes in the MSK system after long-term SCI may lead to upper extremity pain (Waters et al. 1993), reduced strength due to muscle atrophy (Giangregorio & McCartney 2006), and an increased risk for fractures (Lazo et al. 2001). Hence, the complications associated with a degenerating MSK system hold serious implications in terms of functionality for the person aging with SCI.

In terms of bone health, peak bone mass is achieved by the age of 30 in the general population and then declines, but the rate of decline is affected by a number of factors such as age, gender, and lifestyle (e.g., smoking). Although the risk for osteoporosis and fracture are greater among post-menopausal women over the age of 65 in the general community (Goddard & Kleerekoper 1998), there is evidence for increased risk in the SCI population (Ingram et al. 1989; Garland et al. 1992; Lazo et al. 2001).  After sustaining a SCI, there are several reports of bone loss occurring in the early months following injury (Garland et al. 1992).  These losses are regional; areas rich in trabecular bone are demineralized to the greatest degree, with the distal femur and proximal tibia bones being the most affected, followed by the pelvis and arms (Garland et al. 2001a).  However, there is some evidence that there is a continual loss of bone mass with time since injury (Demirel et al. 1998; Bauman et al. 1999), which suggests that a steady state of lower extremity bone mineral homeostasis is not reached (Craven et al. 2014).  Assuming that the rate of bone loss in the aging SCI-population is similar to that of the non-disabled population, it is likely that the degree of osteoporosis will be much more severe since they will have less skeletal mass at the onset of typical age-related declines in bone mass (Waters et al. 1993).

As a result of bone loss associated with SCI, there is an increased risk for fracture (Garland et al. 2001a; Craven et al. 2014).  After SCI, the most common areas at risk for fracture include the distal femur and proximal tibia, and are consistent with site-specific decreases in bone mineral density around the knee (Craven et al. 2014).  The majority of fragility fractures occur following transfers or activities that involve minimal or no trauma (Ragnarsson & Sell 1981). Individuals with SCI are more at risk for osteoporosis if they are older, and the time since injury is longer (Lazo et al. 2001).  However, it is BMD, and not age *per se*, that is the significant predictor for risk of fracture (Lazo et al. 2001).  Interestingly, the BMD of the spine is often maintained or actually increases (Garland et al. 2001a; Sabo et al. 2001).

Although BMD of the spine after SCI does not appear to be affected by aging, there are other age-related changes to the spine. With age the spine undergoes degeneration, which may cause deformity or nerve root compression that produces symptoms of pain radiating into the extremities, loss of sensation and/or motor function (Waters et al. 1993). Age-related degenerative changes in the spine may severely impact individuals with SCI whose functional capacities are already limited (Waters et al. 1993).  Long-term SCI is associated with scoliosis and/or Charcot spine (progressive destruction of the spine and surrounding ligament leading to major spinal instability)(Sobel et al. 1985; Park et al. 1994; Krause 2000; Vogel et al. 2002; Abel et al. 2003). Age at injury, however, may also play a role as there is some lower level evidence that the odds of developing curvature of the spine is lower in persons who are older when injured (Krause 2000).

There are a variety of musculoskeletal changes associated with aging.  In the general population, there is degeneration in the joints of the upper and lower extremities, and common sites include the shoulder, knee, and hip (Waters et al. 1993).  As well, muscle atrophy is inevitable with age, although the rate of decline varies from person to person (Loeser & Delbono 1999).  These age-related changes may lead to joint pain, stiffness, restricted range of motion, or trauma (i.e. fracture) that would not typically occur in a younger person. As a result, independence when performing daily activities may be compromised due to restricted activities of daily living, mobility. Lack of mobility may also affect temperature regulation (Aldwin & Gilmer 2004).

In addition to bone loss (see section 2.2.1), persons with SCI experience muscle atrophy (Giangregorio & McCartney 2006), especially among muscles that are denervated from complete SCI (Lam et al. 2006).  In the lower extremities, muscle degeneration typically occurs around the knee in those who are capable of ambulation but have persistent gait abnormalities, which in turn may generate pathologic forces at the knee (Waters et al. 1993). Although persons who primarily utilize wheelchairs rarely develop clinically significant degenerative problems in the lower extremities, they are more likely to have problems in the upper extremities due to overuse of muscles needed to push

their wheelchairs, to transfer, and perform weight-shift maneuvers to prevent pressure ulcers (Waters et al. 1993).

Upper extremity pain is common in persons with long-term SCI, and most frequently affects the shoulder and wrist (Sie et al. 1992; Thompson & Yakura 2001; Waters & Sie 2001), and typically increases with duration of injury (Sie et al. 1992; Ballinger et al. 2000; Waters & Sie, 2001). The prevalence of shoulder pain in SCI ranges between 30-100% (Curtis et al. 1999) and is likely a consequence of increased physical demands and overuse (Nichols et al. 1979; Pentland & Twomey 1991). It is unclear, however, if these findings are independent of treatment era effects or are related to environmental changes in mobility technology, accessibility, and rehabilitation practices (Adkins 2004).

Losses in strength and diminished joint capacity along with joint degeneration due to overuse can negatively impact functional ability, which makes maintaining high levels of independence difficult. Since persons with SCI are operating at a near-maximum capacity but have a low reserve capacity, declines in functionality may occur prematurely (Thompson & Yakura 2001).

In this section, 12 longitudinal studies, 1 mixed longitudinal/cross-sectional study and 23 cross-sectional studies (see Table 5) on the musculoskeletal system after SCI are reviewed.

**Table 5: Musculoskeletal System**

| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| Verdijk et al. 2012; The Netherlands Observational N SCI=8 N controls=16 | **Population:** 8 young males with SCI (mean(SD) age: 32(4) yrs), 8 age-matched AB young males (mean (SD) age: 31(3) yrs), 8 AB elderly males (mean(SD) age: 75(2) yrs); SCI subjects: mean (SD) DOI: 9(2) yrs; Level of injury: between C5-C6 and T9-T10. **Methodology:** Muscle biopsies were collected from all subjects to determine skeletal muscle fibre type composition, fibre size, and satellite cell content. **Outcome Measures:** Muscle tissue characteristics; muscle fibre type, size, and composition; myonuclear content; satellite cell content. | 1. Severe atrophy and a shift toward approximately 90% Type II muscle fibres were observed in muscle obtained from males with SCI. 2. Muscle fibre size was substantially smaller in both the SCI (Types I and II fibres) and elderly subjects (Type II fibres) when compared with the controls. Despite the young age, the SCI group had similar type II muscle fibre cross-sectional area as the elderly group. 3. Satellite cell content was substantially lower in the wheelchair-dependent SCI subjects in both the Types I and II muscle fibres when compared with the young controls. 4. SCI group demonstrated severe muscle atrophy beyond what was observed in the elderly group |
| Dionyssiotis et al. 2011; Greece Cross-sectional with AB controls N SCI=31 N controls=30 | **Population:** 31 men with complete paraplegia (AIS A); >1.5 YPI; 16 in Subgroup A (T4-T7, mean (SD) age 32.88(15.6) yrs) and 15 in Subgroup B (T8-T12, mean(SD) age 39.47(13.81) yrs); 30 age-height-weight-gender matched AB controls, mean(SD) age 33.9(3.81) yrs. **Methodology**: Comparison of the influence of positive (spasticity, standing-therapeutic walking), and negative factors (duration of paralysis) on bone structures between groups using pQCT measurement. | 1. All BMD parameters were significantly reduced for individuals with paraplegia compared to the control group. 2. Individuals with SCI who used standing frames or long brace orthoses had statistically higher BMD trabecular, BMD total, and cortical thickness compared to individuals with SCI who used wheelchairs. 3. Duration of SCI was significantly related to trabecular bone loss and |

| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| | **Outcome Measures:** Total, trabecular and cortical bone mineral density (BMD), cortical thickness at distal tibial epiphysis and tibial diaphysis, Stress Strain Index at 14% (SSI2) and 38% (SSI3) of tibial diaphysis. | cortical thickness in both SCI groups. |
| Akbar et al. 2010; Germany Cross-sectional with AB controls N SCI=100 N controls=100 | **Population:** 100 subjects with paraplegia (72M 28F); SCI level T2-L3; mean(SD) age 52(9) yrs, range 29-70 yrs; mean YPI 33.7, range 29-48 yrs; wheel chair dependent for minimum 30 yrs; BMI <40; no active shoulder infection; no previous upper extremity surgery; 100 age and gender matched AB controls. **Methodology:** Comparison shoulder function, pain and prevalence of rotator cuff tears between individuals with paraplegia with at least 30 years experience with using a wheelchair and an age and sex matched control group. **Outcome Measures:** MRI, shoulder function (Constant score), pain (visual analog scale). | 1. Shoulder joint pathology in paraplegic patients is caused by over-use rather than being primarily age-related. 2. Shoulder function was significantly worse in the group with paraplegia compared to the AB control group. 3. Pain scores were signifcanlty worse in the group with paraplegia. 4. The prevalence of rotator cuff tears was significantly higher in the group with paraplegia than age-match controls. |
| Dudley-Javoroski & Shields 2010; USA Mixed cross-sectional/longitudinal N SCI=15 N=10 | **Population:** 15 subjects with SCI (14M 1F); age at SCI (range 18-49 yrs); 10 age- and stature- (femur length) matched AB controls (9M 1F). **Methodology**: Comparison of BMD of the femur metaphysis (12% of length from distal end) by using pQCT imaging over two yrs. **Outcome Measures:** Bone mineral density (BMD). | 1. The BMD of individuals with SCI was 1 standard deviation below the control groups BMD at 1.5 years and 2 standard deviations below at 2 years. 2. In the first two years after SCI, individuals with SCI lost an average of 1.7% of the initial BMD per month. |
| Rittweger et al. 2010; Germany Cross-Sectional with AB controls N SCI=9 N controls=9 | **Population:** 9 men with SCI (lesions between L1 and T5, 8 motor complete, 1 motor incomplete); mean YPI 21.4 (range 9-32 yrs); mean age 21.4 yrs (range 17-35 yrs); 9 age-height-weight matched AB controls. **Methodology:** Comparison of the total mineral bone content in the tibia of SCI participants and AB controls. **Outcome Measures:** Serial tomographic scans performed sequentially in steps of 5% of the tibia length from distal to proximal. | 1. Individuals with SCI had lower total bone mineral content than their AB counterparts. 2. Differences were more pronounced at the distal and proximal regions than at the shaft regions of the tibia. |
| Frotzler et al. 2008; Switzerland Longitudinal N=39 | **Population:** 39 subjects with SCI; 28 paraplegic, 11 tetraplegic; ASIA A and B; mean(SD) age 42.0(13.4) yrs, range 21-64 yrs; mean(SD) YPI 12.0(10.8), range 0.9-34 yrs. **Methodology:** To evaluate changes in bone mineral density (BMD) of distal epiphyses and midshafts of femur, tibia. **Outcome Measures:** Bone measurements by pQCT in the radius of the non-dominant arm and the tibia and femur of the opposite leg at baseline, 15 mos, and 30 mos. | 1. No significant difference in any measurements in the femur (77.9% of scans show no change, 12.3% show decrease, and 9.7% show increase) or the tibia (69.4% show no change, 19.0% show decrease, and 11.6% show increase). 2. Changes in the radius bone were not related to changes in the tibia or the femur. 3. Neither time post-injury nor age was significant covariates for the tibial and femoral bone parameters 4. Data show that there is initially a large decrease in bone parameters post-injury but reaches a steady |

| Author Year; Country<br>Score<br>Research Design<br>Total Sample Size | Methods | Outcome |
|---|---|---|
| | | state after 3-8 yrs. |
| Kivimaki & Ahoniemi 2008;<br>Finland<br>Cross-sectional with AB controls<br>N SCI=120<br>N controls=103 | **Population:** 120 subjects with SCI at least 3 months post-injury (54 paraplegic, 66 tetraplegic, age 18-65 yrs), and 103 AB control subjects.<br>**Methodology:** Comparison of shoulders.<br>**Outcome Measures:** Ultrasonography; on the acromioclavicular joint, the supraspinatus tendon, bicipitus longus tendon and the tendon sheath, posterior glenohumeral joint space; performance-corrected Wheelchair User's Shoulder Pain Index (PC-WUSPI). | 1. Osteophytes noted in 14% of AB, 22% of paraplegic, and 26% of tetraplegic subjects; mean(SD) acromioclavicular joint space was 4.0(1.2) mm in AB and 3.7(1.3) mm in subjects with SCI.<br>2. The mean(SD) thickness of the bicipitus tendon sheath was 4.0(0.5) mm in AB and 4.5(1.4) mm in subjects with SCI.<br>3. Glenohumeral effusion was noted in 6% of subjects who use no assistive device, 27% of those using manual wheelchairs, and 25% using electric wheelchairs.<br>4. Frequency of effusion increased with age; shoulder pain was related to effusion in subjects with paraplegia. |
| Amsters & Nitz 2006;<br>Australia<br>Cross-sectional with AB controls<br>N SCI=30<br>N controls=30 | **Population:** 30 men with tetraplegia, divded into four groups (age > 50 yrs and YPI < 5 yrs; age < 40 yrs and YPI < 5yrs; age > 50 yrs and YPI > 15 yrs; age < 40 yrs and YPI > 15 yrs); age and gender matched AB controls.<br>**Methodology:** Comparison of posture.<br>**Outcome Measures:** Posture, through photography of bony landmarks. | 1. Group with SCI had higher occurrence of thoracic kyphosis than AB controls in all (age/YPI injury) groups and suggest that postural changes, such as thoracic kyphosis, might be independent of age and YPI.<br>2. Regardless of age and duration of injury, persons with SCI do not sit with greater pelvic tilt than AB controls. |
| de Bruin et al. 2005;<br>Switzerland<br>Longitudinal<br>N=10 | **Population:** 10 subjects with SCI (9M 1F); mean(SD) age 40.9(19.7) yrs, range 19-81 yrs at follow-up.<br>**Methodology:** Comparison of trabecular and compact bone mineral density (BMD) of tibia and radius at 5 wks post-injury and at approx. 3.5 YPI.<br>**Outcome Measures:** Trabecular and compact BMD. | 1. Trabecular tibia and compact bone BMD decreased within 3.5 YPI.<br>2. No changes in radius trabecular bone were observed.<br>3. Patterns suggest no steady state of bone BMD following 3 YPI. |
| Giangregorio et al. 2005;<br>Canada<br>Cross-sectional with AB controls<br>N SCI=2<br>N controls=2 | **Population:** Both females; Twin pair 1 (TP1) – mean age 32 yrs; mean YPI 7; C7 complete tetraplegia; Twin pair 2 (TP2) – mean age 47 yrs; mean YPI 20; T8 paraplegia.<br>**Methodology:** Comparison of bone mineral density (BMD), bone geometry, and muscle cross-sectional area (CSA) with monozygotic twin.<br>**Outcome Measures:** BMD, bone geometry, and muscle CSA. | 1. TP1: Twin with SCI, BMD of hip, distal femur, proximal tibia, and spine were 59.5 46.6, 53.1, and 93.3%, respectively, of AB control.<br>2. TP2: Twin with SCI, BMD of hip, distal femur, proximal tibia, and spine were 36.2 35.9, 39.2, and 62.2%, respectively, of AB twin control. |
| Jensen et al. 2005;<br>USA<br>Longitudinal<br>N=147 | **Population:** 147 subjects with SCI (110M 37F); mean(SD) age at follow-up 48.8(13.0) yrs, range 21-88 yrs; mean(SD) YPI at follow-up 16.6(10.4), range 3.2-57.4 yrs. | 1. There was increase prevalence of shoulder pain over the time period (2-6 years). |

| Author Year; Country<br>Score<br>Research Design<br>Total Sample Size | Methods | Outcome |
|---|---|---|
| | **Methodology:** Examine the change in the prevalence and intensity of pain over time.<br>**Outcome Measures:** Brief Pain Inventory Interference scale; Bodily Pain scale; SF-36; Mental Health scale (range of 2-6 yrs between assessments). | |
| Slade et al. 2005;<br>USA<br>Cross-sectional with AB controls<br>N SCI=19<br>N controls=17 | **Population:** 19 women with complete SCI; separated into pre-menopausal and post-menopausal groups.<br>Mean(SD) age of premenopausal (< 30 yrs) 23.0(2.55) yrs; mean(SD) YPI 5.6(2.33), Mean(SD) age of premenopausal (>35 yrs) 42.6(4.66) yrs; mean(SD) YPI 12.2(8.14) yrs.<br>Mean(SD) age of post-menopausal 54.5(7.7) yrs; mean(SD) YPI 14.17(11.9); 17 age and gender matched AB controls.<br>**Methodology:** Comparison of the trabecular bone of the knee.<br>**Outcome Measures:** Trabecular bone thickness, trabecular bone volume. | 1. SCI group: trabecular bone was significantly lower compared to AB controls.<br>2. SCI groups had fewer (-19 and -26% less) and thinner trabeculae (-6%) that were spaced further apart (40% and 62% more space between structures) resulting in less trabecular bone volume (-22% and -33%) compared to AB controls. |
| Eser et al. 2004;<br>Switzerland<br>Cross-sectional with AB controls<br>N SCI=89<br>N controls=21 | **Population:** 89 men with SCI; mean(SD) age 41.5(14.2) yrs, range 10-65 yrs; mean(SD) YPI 29.3(12.5), range 2 mos-50 yrs. Age and gender matched AB controls.<br>**Methodology:** Comparison of bone mineral density of distal epiphyses and midshafts of femur, tibia, and radius.<br>**Outcome Measures:** BMD of distal epiphyses and midshafts of femur, tibia, and radius. | 1. Group with SCI had lower BMD than the AB control group. |
| Garland et al. 2004;<br>USA<br>Longitudinal<br>N=6 | **Population:** 6 subjects (5M 1F) with complete paraplegia (1 with L1 incomplete paraplegia); mean(AD) age 24.4(3.9) yrs.<br>**Methodology:** Bone mineral density (BMD) measured from proximal to distal sites assessed at 33.5 and 523 days post-injury.<br>**Outcome Measures:** Dual-energy X-ray absorptiometry (DXA) and ultrasound (US). | 1. BMD of os calcis significantly decreased by 38% (as measured by DEXA) and 48% (as measured by US).<br>2. BMD of knee, distal femur, and proximal tibia significantly decreased by 24%, 27%, and 32% respectively. |
| Siddall et al. 2003;<br>Australia<br>Longitudinal<br>N=73 | **Population:** 73 subjects with SCI (60M 13F); mean age at baseline 40 yrs, range 21-81 yrs; mean time post-injury at baseline < 6 mos.<br>**Methodology:** Assessed the prevalence, onset, and severity of pain at less than 1 YPI and at 5 YPI.<br>**Outcome Measures:** Pain intensity via numeric scale; Psychological distress; Von Korff chronic pain disability to assess pain interference on daily activities; assessed at less than 1 YPI and again at 5 YPI. | 1. Mean onset for musculoskeletal pain was at 1.3(1.7) yrs, with a high prevalence at 5 yrs with an initial decline in the first 6 months post-injury. |
| Vlychou et al. 2003;<br>Greece<br>Cross-sectional with AB controls<br>N SCI=57 | **Population:** 57 subjects with paraplegia (33M 24F); mean age 37.8 yrs, range 21-66 yrs; YPI range 6 mos-27 yrs; age and gender-matched AB controls.<br>**Methodology:** Comparison of bone mineral | 1. Group with SCI had lower BMD of femoral neck, greater trochanter, and Ward's triangle.<br>2. Among males, 23.3% lower BMD in femoral neck, 22.5% lower BMD in |

| Author Year; Country<br>Score<br>Research Design<br>Total Sample Size | Methods | Outcome |
|---|---|---|
| N controls=92 | density (BMD) of the proximal and distal forearm, the femoral neck, the greater trochanter, and Ward's triangle.<br>**Outcome Measures:** BMD of the proximal and distal forearm, the femoral neck, the greater trochanter, and Ward's triangle. | greater trochanter, and 20.8% lower BMD in Ward's triangle compared to AB controls. In females, the deficiencies were 24.1%, 24.3%, and 24.2%. |
| Petrofsky & Laymon 2002;<br>USA<br>Cross-sectional with AB controls<br>N SCI=50<br>N controls=50 | **Population:** 50 AB male controls and 50 men with paraplegia (T4 complete, 3-10 YPI), age range 20-65 yrs, age-, height-, and weight-matched.<br>**Methodology:** Both groups were stratified according to age and compared.<br>**Outcome Measures:** Strength, endurance, blood pressure and heart rate responses to fatiguing isometric exercise. | 1. Handgrip strength was higher in subjects with paraplegia than controls (avg 589 N vs. 463 N); quadriceps extension strength increased in controls (avg 696 N vs. 190 N) with decreases with age in both groups.<br>2. Leg endurance was lower in the group with paraplegia but handgrip endurance was similar in both groups with endurance increases with age in both groups.<br>3. Resting BP increased with age in both groups.<br>4. Magnitude of pressor response to exercise increased with age in both groups.<br>5. HR remained constant with age in both groups in response to quadriceps contractions; decreased 50% between ages 20-60 yrs in both groups for handgrip exercise. |
| Garland et al. 2001b;<br>USA<br>Cross-sectional with AB controls<br>N SCI=31<br>N controls=17 | **Population:** 31 women with complete SCI, mean(SD) age 43.9(19.7) yrs, mean(SD) YPI 16.9(7.7). 17 AB age-matched women, mean(SD) age 44.7(2.5) yrs.<br>**Methodology:** Bone mineral density (BMD) measured from lumbar spine, hip, and knee.<br>**Outcome Measures:** Dual-energy X-ray absorptiometry (DXA). | 1. BMD of spine in women with SCI was maintained or significantly higher compared to age-matched controls.<br>2. BMD of hips and knee in women with SCI was significantly lower compared to controls.<br>3. Women with a complete SCI incur a rapid bone loss in the knee, resulting in a BMD that is approximately 40% to 45% of the AB population, and that this loss is greater than the loss found in the literature for males with comparable injuries. |
| Dauty et al. 2000;<br>France<br>Cross-sectional with AB controls<br>N SCI=31<br>N controls=31 | **Population:** 31 men with SCI; mean(SD) age 36(12.3) yrs, range 18-60 yrs; mean YPI 6, range 6 mos-19 yrs; age and gender matched AB controls.<br>**Methodology:** Comparison of supra- and sublesional bone mineral density (BMD) and bone mineral content (BMC), and of blood and urine samples that included phosphocalcic parameters with determination of urinary hydroxyproline and deoxypyridinoline.<br>**Outcome Measures:** supra- and | 1. SCI group had a lower sublesional BMD of 41% compared to AB controls. This loss of mass is increased at the distal femur (-52%) and proximal tibia (-70%).<br>2. SCI group had lower BMD at the femoral neck and at the trochanter (39%) compared to AB controls. Also had lower BMC in lower limb (48%) and pelvis (55%).<br>3. Blood phosphate level and urinary phosphate level were increased in |

| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| | sublesional BMD and BMC, blood and urinary phosphate level, and urinary levels of calcium, hydroxyproline and deoxypyridinoline. | the group with SCI compared to AB controls. Urinary levels of calcium, hydroxyproline, and deoxypiridoline are increased in the group with SCI compared to AB controls. |
| de Bruin et al. 2000; Switzerland Longitudinal N=12 | **Population:** 12 men with SCI; mean(SD) age 32.4(9) yrs, range 23-50 yrs at follow-up. **Methodology:** Monitoring changes in structural and geometric properties of the tibia and cortical bone. **Outcome Measures:** Structural and geometric properties of the tibia and cortical bone, assessed at 5 weeks post-injury and again at approx. 2 YPI. | 1. Trabecular and cortical bone, and geometric properties of tibia bone decreased within 2 YPI. <br> 2. Phase velocity propagation changed in swing tibia bone in 3 participants within 2 YPI. |
| Frey-Rindova et al. 2000; Switzerland Longitudinal N=29 | **Population:** 29 subjects with SCI (27M 2F); age range 19-57 yrs. **Methodology:** To evaluate changes in Trabecular and cortical bone mineral density (BMD). **Outcome Measures:** Trabecular and cortical BMD, evaluated at 1, 6, 12, and 24 months past injury. | 1. Trabecular BMD of radius and ulna decreased in persons with tetraplegia at 6 months (radius 19% less; ulna 6% less), and at 12 months (radius 28% less; ulna 15% less) post- injury. <br> 2. Cortical BMD of radius and ulna decreased in persons with tetraplegia at 12 months (radius 3% less; ulna 4% less) post-injury. <br> 3. Trabecular BMD of tibia was decreased at 6 months (5% less), and 12 months (15%) post-injury. |
| Kiratli et al. 2000; USA Cross-sectional with AB controls N SCI=246 N controls=188 | **Population:** 246 subjects with SCI (239M 7F); age range 21-78 yrs; YPI range 0.1-51. **Methodology:** Comparison of bone mineral density (BMD) throughout the femur and geometric properties at the femoral midshaft. **Outcome Measures:** BMD in various femoral regions. | 1. SCI group had lower BMD in all femoral regions (27%, 25%, and 43% for femoral neck, midshaft, and distal femur, respectively). <br> 2. Group with SCI had lower BMD in cortical area of femoral midshaft. |
| Bauman et al. 1999; USA Cross-sectional with AB control N SCI=8 N controls=8 | **Population:** Able-bodied (AB) twins of 8 men with complete paraplegia: mean(SD) ages 40.4(10) yrs, mean(SD) YPI 16(9). **Methodology:** Bone mineral content (BMC) and density (BMD) for total and regional skeletal bone mass. **Outcome Measures:** Dual-energy X-ray absorptiometry (DXA). | 1. Compared to twin controls, persons with SCI had significantly lower BMC, with predominant sites being the legs and pelvis. <br> 2. Duration of SCI, not age was associated to degree of leg bone loss in twin with SCI. |
| Lal 1998; USA Longitudinal N=53 | **Population:** 53 subjects with SCI (35M 18F); mean age 37 yrs, range 19-81 yrs at baseline. **Methodology:** Monitoring incidence of degenerative shoulder changes. **Outcome Measures:** Incidence of degenerative shoulder changes, accessed through X-ray at baseline and every 2 years after until 5-15 YPI. | 1. 72% of sample demonstrated radiological evidence of degenerative changes, but only 11% reported shoulder pain. <br> 2. Persons with increased age (> 30 yrs) had increased incidence of radiographic changes. <br> 3. Premature shoulder changes appear primarily in wheelchair users of advanced age in less than 10 yrs with predilection of Acromioclavicular |

| Author Year; Country<br>Score<br>Research Design<br>Total Sample Size | Methods | Outcome |
|---|---|---|
| | | joint. |
| Szollar et al. 1998;<br>USA<br>Cross-sectional with AB controls<br>N SCI=176<br>N controls=62 | **Population:** 176 men with SCI; mean age 41.2 yrs, range 20-59 yrs; YPI range 0.8-34.<br>**Methodology:** Comparison of bone mineral density (BMD), serum levels of calcium, calcitonin, biochemical markers of bone formation, and parathyroid hormone (PTH).<br>**Outcome Measures:** BMD of the lumbar spine, femoral neck, Ward's triangle, and the greater trochanter, serum levels of calcium, calcitonin, biochemical markers of bone formation, and parathyroid hormone (PTH). | 1. Spine BMD remained stable above fracture threshold in the 20-39 yr. and in the 30-49 yr. age groups.<br>2. In all groups, there was progressive decrease in BMD at proximal femur, and began 1-9 YPI. For the 20-39 yr. age group, this was significant for all three areas. For the 30-49 yr. age group, this progressed at a slower rate, reaching threshold at 10-19 YPI for all three areas.<br>3. PTH levels remained below the reference range, with a slight gradual increase after 1 YPI. Results suggest parathyroid dysfunction- related osteoporosis. |
| Szollar et al. 1997a;<br>USA<br>Cross-sectional with AB controls<br>N SCI=135<br>N controls=69 | **Population:** 135 subjects with SCI, mean(SD) age 48.8(1.3) yrs, range 20-78 yrs. 69 AB individuals, mean(SD) age 51.1(1.7) yrs, range 24-76 yrs.<br>**Methodology:** Both groups were stratified according to age and compared; SCI patients were grouped according to neurologic group within the various age categories.<br>**Outcome Measures:** Bone mineral density (BMD) in the lumbar spine, femoral neck, Ward's triangle, and the greater trochanter. | 1. Lumbar spine BMD of the 40-59 yr old and the aged 60+ SCI patients were significantly higher than AB counterparts<br>2. Femoral region BMD of the 20-39 yr old and 40-59 yr old patients were all significantly lower than AB counterparts<br>3. Hip region BMD loss occurred starting at 1 YPI, plateaus at 19 YPI and then improves.<br>4. Spine BMD in patients never decreased significantly and started increasing as YPI increasing.<br>5. Femoral neck and Ward's triangle BMD decreased after 1 YPI. After 19 YPI, slight increase in both regions. |
| Szollar et al. 1997b;<br>USA<br>Cross-sectional with AB controls<br>N SCI=263<br>N controls=92 | **Population:** 263 men with SCI; mean(SD) age 48.8(1.3) yrs, range 20-78 yrs; YPI range 0.8-53. Age and gender matched AB controls.<br>**Methodology:** Comparison of bone mineral density (BMD) of the lumbar spine, femoral neck, Ward's triangle, and the greater trochanter with AB controls.<br>**Outcome Measures:** BMD of the lumbar spine, femoral neck, Ward's triangle. | 1. Lumbar spine BMD was stable with a nonsignificant decrease in persons with tetraplegia at 1-5 YPI in the 20-39 yr. old group. Lumbar spine BMD maintained in all other SCI groups, increasing with age, regardless of age at injury or level of injury.<br>2. Persons injured less than 1 yr. had comparable BMD to AB controls.<br>3. Persons aged 20-39 yrs. old who were injured more than 1 YPI had lower BMD in the femoral region than AB matched controls and 20-39 yr olds injured less than 1 YPI. |
| Chow et al. 1996;<br>UK<br>Cross-sectional with AB controls | **Population:** 31 subjects with SCI (19M 12F); age range 19-60 yrs; mean(SD) YPI 5.87(10.21) yrs, range 5 wks-36 yrs; age and gender matched AB reference | 1. Ultrasonic properties at the calcaneus were lower in group with SCI.<br>2. After 1 YPI, BMD in femoral neck |

| Author Year; Country<br>Score<br>Research Design<br>Total Sample Size | Methods | Outcome |
|---|---|---|
| N SCI=31 | population.<br>**Methodology:** Comparison of bone mineral density (BMD) of right heal, lumbar spine, and proximal femur region (femoral neck, Ward's triangle, trochanteric and inter-trochanteric), and of bonestructure (stiffness).<br>**Outcome Measures:** BMD of right heel, lumbar spine, and proximal femur region (femoral neck, Ward's triangle, trochanteric and inter-trochanteric); bone structure. | was lower in the group with SCI compared to AB reference population. |
| Bauman et al. 1995;<br>USA<br>Cross-sectional with AB controls<br>N SCI=100<br>N controls=50 | **Population:** 100 men with SCI, mean(SD) age 51(14) yrs; mean(SD) YPI 20(13), range 1-48 yrs. 50 age and gender matched controls.<br>**Methodology:** Comparison of serum calcium (Ca), phosphorus (PO4), albumin, alkaline phosphatase (Alk P), and parathyroid hormone (PTH) with serum 25-hydroxyvitamin D [25(OH)D].<br>**Outcome Measures:** serum levels of calcium (Ca), phosphorus (PO4), albumin, alkaline phosphatase (Alk P), and parathyroid hormone (PTH) with serum 25-hydroxyvitamin D [25(OH)D]. | 1. Approximately ⅓ of group with SCI were vitamin D deficient, which was a higher percentage than AB controls.<br>2. Mean serum 25(OH) D was higher in the group with SCI compared to AB controls. |
| Wilmet et al. 1995;<br>Belgium<br>Longitudinal<br>N SCI=31 | **Population:** 31 subjects with SCI (24M 7F) with T2 – L3 paraplegia, mean age 32.5 yrs, range 17.5-65.5 yrs.<br>**Methodology:** Total body and regional bone mineral content (BMC) and soft-tissue composition assessed at 5, 10, 20, 30, 40, and 50 weeks post-injury.<br>**Outcome Measures:** Dual-energy X-ray absorptiometry (DXA) and soft tissue phantom. | 1. Rapid BMC loss in paralyzed areas of approx. 4% per month in trabecular bone and approx. 2% per month in areas with mainly compact bone.<br>2. Lean muscle mass decreased during first months post-injury in the legs while fat content increased. |
| Pentland & Twomey 1994;<br>Canada<br>Cross-sectional with AB controls<br>N SCI=52<br>N controls=52 | **Population:** 52 men with complete paraplegia (T2-L5, mean age 44 yrs, mean YPI 17) and 52 age- and activity level-matched AB males.<br>**Methodology:** Bilateral upper limb physical functions were compared between the paraplegic and AB groups.<br>**Outcome Measures:** Concentric isokinetic average torque for shoulder, elbow flexion/extension, shoulder adduction and eccentric shoulder adduction, grip strength, shoulder and elbow active ROM, upper limb pain. | 1. AB had greater bilateral shoulder flexion and SCI greater bilateral elbow extension.<br>2. Impairment and activity level were better predictors of strength in 9/14 muscles tested, whereas age was a better predictor in AB group.<br>3. Shoulder pain related to time since injury, not age; pain experienced by majority of subjects with paraplegia (58-60%). |

| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| Vaziri et al. 1994; USA Cross-sectional with AB controls N SCI=40 N controls=14 | **Population:** 40 men with SCI; age range 25-69 yrs; YPI range 3-50 yrs. **Methodology:** Comparison of serum levels of parathormone (PTH), calcitonin, vitamin D (calcitriol), 25 hydroxy (OH) vitamin D, 1,25 (OH)2, ionized calcium (Ca++), and phosphorous. **Outcome Measures:** serum levels of parathormone (PTH), calcitonin, vitamin D (calcitriol), 25 hydroxy (OH) vitamin D, 1,25 (OH)2, ionized calcium (Ca++), and phosphorous. | 1. Plasma PTH was lower in the group with SCI compared to AB controls, despite equivalent concentrations of Ca++. 2. Plasma calcitrol was lower in the group with SCI compared to AB controls, and lower in persons with tetraplegia vs. those with paraplegia. |
| Catz et al. 1992; Israel Longitudinal N=9 | **Population:** 9 C3-T11 patients; age at enrollment: mean 37.5 yrs, range 24-67 yrs; AB controls from another study. **Methodology:** Lumbar spine dimensions assessed twice over 10 yr interval. **Outcome Measures:** Lumbar anteroposterior (AP) radiographs. | 1. The normal aging process, including the horizontal spreading of the lumbar vertebral bodies and narrowing of the lumbar spinal canal, is not accelerated by spinal cord injury and may be retarded by relative immobilization. |
| Finsen et al. 1992; Norway Cross-sectional with AB controls N SCI=19 N controls=19 | **Population:** 19 men with SCI; median age at injury 20 yrs, range 15-64 yrs; median YPI 4, range 7 mos-33 yrs; age and gender matched AB controls. **Methodology:** Comparison of bone mineral density (BMD) of lower and upper extremities, and of biochemical and bone markers. **Outcome Measures:** BMD of lower and upper extremities and of biochemical and bone markers. | 1. SCI group had a significant BMD decrease in the metaphysis (45%) and diaphysis (26%) of tibia, while a barely significant difference of distal forearm was detected. 2. SCI group had lower levels of serum creatinine, and higher levels of alanine aminotransferase, serum phosphate, follicle stimulating hormone, and sex hormone binding globulin (SHGB). 3. Total testosterone was equivalent but when divided by SHGB, higher in the group with SCI. |
| Garland et al. 1992; USA Longitudinal N=45 | **Population:** 45 men with complete SCI; mean(SD) age 28.1(0.78) yrs – 25; mean(SD) days post-injury 114.1(8.6). **Methodology:** Assessment of total bone mass (TBM) and bone mineral density (BMD) at different times post-injury. **Outcome Measures:** TBM and BMD assessed at 114.1(8.6) days post-injury and again at 468.9(21) days post-injury. | 1. TBM of the pelvis and legs decreased between initial and follow-up assessment. 2. BMD of the distal femur and proximal tibia decreased between initial and follow-up assessment. |
| Biering-Sorensen et al. 1990; Denmark Longitudinal N SCI=8 | **Population:** 8 subjects (6M 2F) with complete paraplegia (1 with L1 incomplete paraplegia; mean(SD) age 24.4(3.9) yrs. **Methodology:** Bone mineral content (BMC) from lumbar spine, femoral neck and shaft, proximal tibia and distal forearm assessed at 43 days, and 5-13 up to 31-53 months post - injury. **Outcome Measures:** Dual photon absorptiometry (DPA). | 1. Lumbar spine and distal forearm BMC in pts did not change. 2. BMC in lower extremities (femoral bone and proximal tibia) decreased. |

**Discussion**

In general, the evidence (see Table 5) supports the notion that the musculoskeletal system undergoes obvious external signs of premature aging except for a few areas. Many studies found that there was rapid bone loss, and particularly for the pelvis and lower limbs within the acute stage post-SCI (Garland et al. 1992; Biering-Sorensen et al. 1990; Wilmet et al. 1995; Dauty et al. 2000; de Bruin et al. 2000; Frey-Rindova et al. 2000; Garland et al. 2004; Frotzler et al. 2008, Dudley-Javoroski & Shields, 2010; Dionyssiotis et al. 2011). Further, this loss may be greater for females with SCI (Garland et al. 2001b) and is evident in both bone mineral density (BMD; amount of matter per cubic centimeter of bones) and content (BMC; bone mass). Similarly, there are bone geometric changes (Finsen et al. 1992; de Bruin et al. 2000; Giangregorio et al. 2005) that occur, which may be independent of chronological age and YPI (Slade et al. 2005).

Some of the findings are mixed with regards to the duration of decline. One study found that bone mass continues to decline throughout the chronic phase (Finsen et al. 1992), whereas another study reporting a rapid loss with stabilization after approximately 2 years (Dudley-Javorski & Shields 2010). A cross-sectional study with AB controls (Eser et al. 2004) and a longitudinal analysis of the same cohort of persons with complete SCI (Frotzler et al. 2008) found that tibial and femoral bone geometry and density properties reach a new steady-state within 3-8 YPI, with the time frame depending on bone parameter and skeletal site.

The use of peripheral quantitative computed tomography (pQCT) is viewed as a superior approach for investigating changes in BMD and BMC compared to dual energy X-ray absorptiometry, DXA), but there are some unresolved issues with the use of this technology in people with SCI (Dudley-Javorski & Shields 2010). A mixed cross-sectional and longitudinal study by Dudley-Javorski & Shields (2010) who used two approaches for studying declines in BMD via pQCT found BMD values of their SCI subjects (n = 15) fell below the lowest range of control values (n = 10), suggesting that subjects lost an average of 1.7% BMD per month within the first two years post-SCI. However, their subjects (N=4) who were followed longitudinally starting at approximately 2 years demonstrated no BMD decline over time. There is a need to better understand anatomical variations related to bone adaptive processes in order to account for SCI-related bone losses (Rittweger et al. 2010). As such, further refinement into bone assessment are needed to help clarify some of the mixed findings noted in the literature.

There are also a number of other factors that contribute to bone loss post-SCI. For instance, endocrine changes may be contributing to the losses in bone density (Dauty et al. 2000; Szollar et al. 1998; Finsen et al. 1992; Vaziri et al. 1994; Bauman et al. 1995). It is thought that altered bone structure and microarchitecture due to SCI (de Bruin et al. 2000; Eser et al. 2004; Giangregorio et al. 2005; Kiratli et al. 2000; Slade et al. 2005; Frotzler et al. 2008) leads to impaired calcium and phosphate metabolism and the parathyroid hormone (PTH)-vitamin D axis (Finsen et al. 1992; Vaziri et al. 1994; Bauman et al. 1995; Szollar et al. 1998; Dauty et al. 2000). For instance, Bauman and colleagues (1995) noted that the reduction in the bioavailability of vitamin D in persons with SCI is similar to that found in AB elderly persons. These changes have been shown to contribute to premature onset of osteoporosis and increased risk for fracture in total and regional sites following SCI when compared to the AB population (Garland et al. 1992; Szollar et al. 1997a; Szollar et al. 1997b; Dauty et al. 2000; Kiratli et al. 2000; Garland et al. 2001b; Vlychou et al. 2003; Eser et al. 2004; Giangregorio et al. 2005; Frotzler et al. 2008, Dudley-Javoroski & Shields, 2010), which may be more related to YPI than chronological age (Bauman et al. 1999; Garland et al. 2001b).

Age of SCI onset, however, may be an influential factor on the extent of the decline in bone loss (Garland et al. 2001b; Kiratli et al. 2000; Szollar et al. 1997a). For instance, the findings by Szollar and colleagues (1997a) provide evidence that the BMD of persons with SCI are significantly lower than the AB population, but that YPI (i.e., older adults injured at a young age) may be more influential on BMD changes in specific areas (i.e. femoral and trochanter regions), although older males may not be as severely affected. Persons who were 60 years or older had comparable levels to their age-

matched AB controls in their BMD whereas persons in the younger age categories had significant differences in their femoral regions at different intervals (Szollar et al. 1997a). For instance, younger adults with SCI (20-39 year olds) had significantly lower BMD at 1-5 YPI and at 10-19 YPI in the femoral regions of their neck and trochanter when compared to their AB controls, and the mid-age group (40-59 year olds) only had lower BMD at 10-19 YPI in the femoral neck and trochanter regions. These findings possibly allude to premature aging occurring at specific intervals post-injury, most notably in the first year, in the femoral region in younger persons with SCI, and are consistent with the other identified studies (Garland et al. 1992; Biering-Sorensen et al. 1990; de Bruin et al. 2005; Frey-Rindova et al. 2000; Wilmet et al. 1995; Chow et al. 1996; Szollar et al. 1997a; Szollar et al. 1997b; de Bruin et al. 2000; Kiratli et al. 2000; Eser et al. 2004; Frotzler et al. 2008). It may be that age-related factors become less important on changes in bone mass when an individual reaches a certain chronological age threshold (i.e. 60 years). At this point, other factors (i.e. immobilization) affecting bone mass may become more prominent. In general, all of these changes provide additional support that premature aging is occurring.

Gender also is an influential factor on bone loss. Garland and colleagues (2001b) provide evidence that women with a complete SCI incur a rapid bone loss in the knee, resulting in a BMD that is approximately 40% to 45% of the AB population, and that this loss is greater than the loss seen in males with comparable injuries. Unlike the findings by Szollar and colleagues (1997a), the pattern of bone loss of the hip was linear regardless of the age at the time of injury. The findings by Bauman and colleagues (1999), which used a cross-sectional monozygotic twin design, also shows evidence that duration of injury may be more closely associated to bone loss than current age. Although lifestyle habits such as smoking and alcohol intake were examined and found not to be significant, the sample in Bauman et al. (1999) study was quite small, and relatively young.

As well, a study by Slade and colleagues (2005) which compared bone loss at the knee between AB and SCI women who were pre- and post-menopausal concluded that although age and estrogen effects could not be independently discerned, it was unloading (lack of weight bearing) that resulted in the deterioration of trabeculae that occurs early post-injury. Given that SCI is less common in women, more studies are needed to further our understanding of the interaction between gender, SCI, and aging plays on bone loss.

Interestingly, the lumbar spine BMD of persons with SCI appears to increase with age regardless of YPI. Szollar and colleagues (1997a) interpreted this finding as either being representative of the lumbar spine becoming the primary weight-bearing region or that neuropathic osetoarthropathy (i.e. spectrum of bone and joint destructive processes associated with neurosensory deficit) may have caused diffused increased radiodensity of the spinal column. The finding that BMD and BMC of the spine remains unaffected or increases is consistent with several other of the identified studies (Biering-Sorensen et al. 1990; Dauty et al. 2000; Chow et al. 1996; Garland et al. 2001b; Szollar et al. 1997b; Szollar et al. 1998), and are complementary to the findings by Catz and colleagues (1992). Based on their findings, Catz et al. (1992) concluded that an SCI injury does not accelerate the aging process of the lumbar spine, and that it may even prevent some expected spinal bone changes since no significant differences were detected between their group with SCI and their AB matched control group. However, they noted that a limitation of their study was that 10 years might be too short a duration to detect any significant effects. As well, the sample size was small and consisted of a heterogeneous group of spinal cord etiologies (i.e. non-traumatic). Finally, one study (Amsters & Nitz 2006) found that postural changes, such as thoracic kyphosis, might also be independent of age and YPI.

With regard to the upper extremities, the musculoskeletal system appears to decline with YPI (Siddall et al. 2003; Jensen et al. 2005, Akbar et al. 2010), with the incidence of shoulder pain increasing over time. However, the role of chronological age may also be influential (Lal et al. 1998; Kivimäki et al. 2008). The incidence of degenerative shoulder changes (Lal 1998) may be higher in persons who are

older than 30 years and are less than 10 YPI, suggesting that degenerative changes may occur earlier than previously thought in persons with SCI.

In addition to the lumbar spine, there are other areas of the musculoskeletal system that are not negatively affected by aging. For instance, handgrip strength may increase with YPI in males with paraplegia relative to AB controls (Petrofsky & Laymon 2002). This may be due to the use of manual wheelchairs, as well as to age-related changes in muscle fibre composition, and/or to a reduction in intramuscular pressure (Petrofsky & Laymon 2002). As well, older males with paraplegia (45 years and older) may have comparable levels of upper extremity strength to AB controls (Pentland & Twomey 1994).

## Conclusion

*There is Level 4 evidence from 9 longitudinal studies (Biering-Sorensen et al. 1990; Garland et al. 1992; Wilmet et al. 1995; de Bruin et al. 2000; Frey-Rindova et al. 2000; Garland et al. 2004; de Bruin et al. 2005; Frotzler et al. 2008, Dudley-Javorski & Shields, 2010) and Level 5 evidence from 15 studies (Chow et al. 1996; Szollar et al. 1997a; Szollar et al. 1997b; Szollar et al. 1998; Bauman et al. 1999; Dauty et al. 2000; Kiratli et al. 2000; Garland et al. 2001b; Vlychou et al. 2003; Eser et al. 2004; Giangregorio et al. 2005; Slade et al. 2005; Dudley-Javorski & Shields, 2010; Rittweger et al. 2010; Dionyssiotis et al. 2011) that there is a rapid loss of bone in the hip and lower extremities following SCI.*

*There is Level 2 evidence (Frotzler et al. 2008) and Level 5 evidence (Eser et al. 2004) that tibial and femoral bone geometry and density properties reach a new steady-state within 3-8 year post injury, with the time frame depending on bone parameter and skeletal site.*

*There is Level 5 evidence from three studies (Szollar et al. 1997a; Szollar et al. 1998; Garland et al. 2001b) that older males and females with SCI may not experience as rapid of a decline in bone mass compared to AB controls.*

*There is Level 5 evidence from two studies (Bauman et al. 1999; Garland et al. 2001b) that year YPI may be more associated with bone loss after SCI than chronological age.*

*There is Level 5 evidence (Slade et al. 2005) that there are differences in bone geometric indices and in structural properties in the lower extremities of women with SCI compared to the AB women.*

*There is Level 5 evidence from five studies (Finsen et al. 1992; Vaziri et al. 1994; Bauman et al. 1995; Szollar et al. 1998; Dauty et al. 2000) suggesting that there are impaired biochemical and bone markers in persons with SCI compared to AB controls that persons with SCI are at greater risk for fracture due to the premature development of osteoporosis.*

*There is Level 2 evidence from a longitudinal study with AB controls (Catz et al. 1992), Level 4 evidence from a longitudinal study (Biering-Sorensen et al. 1990), and Level 5 evidence from five studies (Chow et al. 1996; Szollar et al. 1997a; Szollar et al. 1997b; Szollar et al. 1998; Garland et al. 2001b) that premature aging does not occur in the lumbar spine after SCI. The possibility that the lumbar spine becomes the primary weight-bearing region, along with immobilization, may serve to protect age-related bone loss changes to this region.*
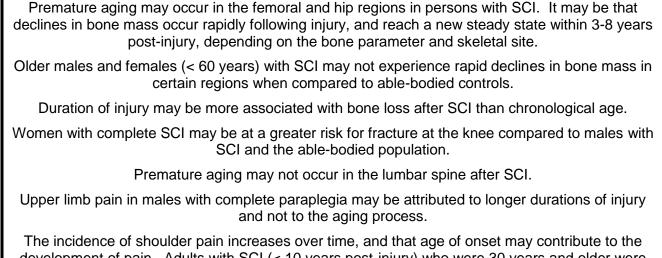
*There is Level 5 evidence (Amsters & Nitz 2006) that persons with SCI, regardless of age or YPI, had increased thoracic kyphosis compared to AB controls.*

*There is Level 5 evidence from two studies (Pentland & Twomey 1994; Petrofsky & Laymon 2002) that decreased hand grip strength does not occur in men with complete paraplegia and that continual wheelchair use may retard this aging process.*

*There is Level 5 evidence (Pentland & Twomey 1994) that upper limb pain in males with complete paraplegia who use manual wheelchairs may be attributed to longer YPI and not to chronological age.*

*There is Level 2 evidence from two longitudinal studies (Siddall et al. 2003; Jensen et al. 2005) showing that the incidence of shoulder pain increases over time in persons with SCI.*

*There is Level 2 evidence from a longitudinal study (Lal 1998) and Level 5 evidence (Kivimäki et al. 2008) that highlights chronological age having an important influence on developing shoulder pain.*

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Premature aging may occur in the femoral and hip regions in persons with SCI. It may be that declines in bone mass occur rapidly following injury, and reach a new steady state within 3-8 years post-injury, depending on the bone parameter and skeletal site.

Older males and females (< 60 years) with SCI may not experience rapid declines in bone mass in certain regions when compared to able-bodied controls.

Duration of injury may be more associated with bone loss after SCI than chronological age.

Women with complete SCI may be at a greater risk for fracture at the knee compared to males with SCI and the able-bodied population.

Premature aging may not occur in the lumbar spine after SCI.

Upper limb pain in males with complete paraplegia may be attributed to longer durations of injury and not to the aging process.

The incidence of shoulder pain increases over time, and that age of onset may contribute to the development of pain. Adults with SCI (< 10 years post-injury) who were 30 years and older were more likely to report shoulder pain over time than those who were less than 30 years of age.

Premature aging may not occur in hand grip strength in men with complete paraplegia. Rather, continual wheelchair use may retard the aging process in relation to handgrip strength.

Regardless of age or years post-injury, persons with SCI may have increased thoracic kyphosis than the able-bodied population.

Persons with SCI may have reduced lung capacity compared to able-bodied controls, but this reduction is due to SCI and not aging.

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### 3.4 Respiratory System

As a consequence of SCI, especially injury to the cervical and upper thoracic parts of the spinal cord, functioning of the respiratory muscles is disrupted, and leads to lowered lung volume parameters (Linn et al. 2000), in addition to other respiratory complications, such as decreases in compliance of the chest wall, changes in breathing patterns, sleep-disordered breathing (SDB), and ventilator dependency.

For individuals with SCI who have impaired autonomic function and impaired inspiratory muscle weakness, SDB may occur (Bonekat et al. 1990). In general, the incidence of SDB, characterized by sleep apnea, is estimated to be at least twice that reported in the general population (Schilero et al.

2009). Respiratory complications lead to significant morbidity and mortality in people with SCI (DeVivo et al. 1993; Cotton et al. 2005).

Among the general population, age associated changes in the respiratory system involve loss of elastic recoil of the lung. Similarly, among individuals with SCI, decreases in the compliance of the chest wall, and strength of the respiratory muscles are observed (Janssens et al. 1999; Janssens 2005). Complications resulting from SCI may therefore hold important respiratory implications as people age.

In this section, 5 longitudinal studies and 4 cross-sectional studies (see Table 6) on the respiratory system after SCI are reviewed.

**Table 6: Respiratory System**

| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| Postma et al. 2013; The Netherlands Prospective longitudinal N=180 | **Population:** 180 persons with SCI (73.9% male); mean (SD) age at start of active rehab (yrs): 39.7(13.7); mean (SD) YPI at start of active rehab (days): 101.8(62.1); Lesion level: 38.9% tetraplegia; Completeness: 66.7% motor complete (AIS A and B) **Methodology:** Pulmonary function (PF) was determined at the start of rehabilitation, at discharge, and 1 and 5 years after discharge. **Outcome Measures:** Forced vital capacity (FVC), forced expiratory volume in 1 second ($FEV_1$). | 1. Overall, FVC improved a mean of 5.1% over the 5 yrs of observation. There was no change in $FEV_1$. 2. There was no observed change in FVC or $FEV_1$ from discharge to year 1, nor from year 1 to year 5. |
| Tamplin et al. 2011; Australia Cross-sectional with AB controls SCI N=6 Control N=6 | **Population**: 6 individuals (4M 2F) with SCI; motor-complete C5-C7 tetraplegia; YPI >1 yr; age range 28-62 yrs. 6 AB age-matched controls. **Methodology**: Participants directed through phonatory exercises, standardized reading passages, and familiar songs. **Outcome Measures:** Maximal inspiratory and expiratory flow rates, timed lung volumes, surface electromyographic activity from accessory respiratory muscles, sound pressure levels during vocal tasks, Voice Handicap Index, Perceptual Voice Profile, ventilator function, upper airway function. | 1. Participants with tetraplegia had smaller lung capacities, reduced respiratory pressures, and significantly greater vocal impairment. 2. Significantly higher peak amplitude from participants with tetraplegia during loud and soft speech compared to control. 3. Control participants had wider dynamic range compared to participants with tetraplegia. 3. Control able to sustain vowel for longer than participants with SCI. |
| Ovechkin et al. 2010; USA Cross-sectional with AB controls N SCI=18 N Control=14 | **Population:** 18 subjects with SCI (15M 3F); 8 motor-complete, 10 motor-incomplete; ranging from C3 to L2. 14 AB controls (9M 5F). **Methodology:** Comparison of respiratory muscle control between SCI subjects and AB controls through PFT (standard spirometry). **Outcome Measures:** Pulmonary function test (PFT); respiratory motor control assessment (RMCA) by surface electromyographic recording (sEMG). | 1. Similarity index values relating individuals with SCI and the control group were developed. 2. Values for inspiratory and expiratory tasks were consistent with the control group. 3. Altered multi-muscle patterns in the SCI group produced values that trended lower for inspiratory tasks, and significantly lower for expiratory tasks. |
| Berlowitz et al. 2005; USA Longitudinal | **Population:** 30 subjects with acute tetraplegia (25M 5F); mean age 33.7, range 18-69 yrs. **Methodology:** Measured the incidence of | 1. At 2 weeks, 60% had SDB; at 4 weeks, 62%; at 13 weeks, 62%; at 26 weeks, 83%; at 52 weeks, 62%. |

| Author Year; Country<br>Score<br>Research Design<br>Total Sample Size | Methods | Outcome |
|---|---|---|
| N=30 | sleep disordered breathing (SDB), and identified the relationship between SDB and previously postulated predictors.<br>**Outcome Measures:** Apnea-Hyopnea Index; Incidence of sleep disordered breathing (SDB); overall respiratory function. | 2. All participants had reduced respiratory function compared with normative population values. |
| Biering-Sorensen & Biering-Sorensen 2001; Denmark<br>Cross-sectional with AB controls<br>N SCI=408<br>N controls=339 | **Population:** 408 subjects with SCI (331M 77F); mean(SD) age 42.5(14.1) yrs, range 17-86 yrs; mean(SD) YPI 12.1(6.3), range 2.5-45.1 yrs; age and gender matched AB controls.<br>**Methodology:** Self-administered questionnaire.<br>**Outcome Measures:** Nordic Sleep Questionnaire (NSQ) containing 21 questions. | 1. Subjects with SCI snored more often, louder, for more years, and started at younger ages compared to AB controls. |
| Bach & Wang 1994; USA<br>Longitudinal<br>N=10 | **Population:** 10 subjects (9M 1F) with tetraplegia; mean(SD) age 41(12.3) range 34-77 yrs; mean(SD) YPI 7.7(5.8), range 6mos-19 yrs.<br>**Methodology:** Comparison of oxygen desaturation.<br>**Outcome Measures:** Oxygen desaturation, assessed through pulse oximetry. | 1. At baseline, 6 subjects had desaturation below 90%. At follow-up, 5 subjects had an increased number of transient nocturnal oxygen desaturations. |
| Cahan et al. 1993; Australia<br>Cross-sectional with AB controls<br>N SCI=16<br>N controls=12 | **Population:** 16 men with tetraplegia; mean(SD) age 49(15) yrs, range 23-64 yrs; mean(SD) YPI 14(10), range 1-32 yrs; age and gender matched AB controls.<br>**Methodology:** Comparison of oxygen desaturation.<br>**Outcome Measures:** Pulse oximetry. | 1. 6 patients with tetraplegia had lower oxygen saturation levels below the normative range, indicative of SDB. |
| Loveridge et al. 1992; Canada<br>Longitudinal<br>N=6 | **Population:** 6 men with acute SCI; mean(SD) age 30(11) yrs; for persons with tetraplegia; mean age 32.6 yrs, range 21-50 yrs; mean time post-injury 38.6 months.<br>**Methodology:** Comparison of lung function and breathing patterns**.**<br>**Outcome Measures:** Lung function parameters including, force vital capacity, inspiratory capacity, residual volume, forced expiratory capacity, functional residual capacity, and maximum inspiratory mouth pressure; Breathing pattern indicators including, Inspiratory time, tidal volume, and expiratory time; assessed in both sitting and supine positions, at 2, 6, and >12 months post-injury. | 1. Seating position resulted in greater stress on the respiratory system and breathing patterns in the group with tetraplegia compared to the AB control group.<br>2. Over time, breathing patterns of the group with tetraplegia improved and were comparable to those of the AB control group. |
| Wicks & Menter 1986; USA<br>Longitudinal<br>N=134 | **Population:** 134 subjects with tetraplegia (118M 16F).<br>**Methodology:** Review of patients' medical records over 10 yrs in order to determine the number of patients who could be weaned off mechanical ventilation and to assess their long-term survival rate.<br>**Outcome Measures:** Medical records between1974-1983; mortality rates, ventilation status. | 1. Individuals over 50 yrs of age had less successful weaning attempts and higher mortality rates than younger individuals despite similar levels of injury. |

**Discussion**

Several of the identified studies highlight that SDB and other respiratory complications are higher in persons with SCI than in the general population and appear to increase with age (see Table 6). In a five-year longitudinal study to assess changes in SDB, Bach and Wang (1994) measured oxygen desaturation, which is characteristic of sleep apnea, in 10 individuals with tetraplegia; six individuals had oxygen desaturation below 90%. At the five-year follow-up, 5 of the 10 individuals had increased patterns of oxygen desaturation, leading to the conclusion that oxygen desaturation is common among people with tetraplegia and increases with age. In another longitudinal study (Berlowitz et al. 2005) sleep apnea, defined as an apnea-hypopnea index (AHI) of >10 events per hour, was found in 62% of the sample in the first month, peaking at 83% at 13 weeks, and falling to 68% and 62% at weeks 26 and 52 respectively.

Snoring is another important indicator of sleep apnea and appears to be age related. In a large case-control study, 29% of men (N = 331) and 21% of women with SCI (N = 77) snored daily or almost daily compared to 18.2% of the control group (N = 339) representing the normal population of Denmark (Biering-Sorensen & Biering-Sorensen 2001). In addition, those who snored daily or almost daily in the SCI group were significantly older than those with SCI who snored less frequently.
After SCI, there are temporal changes in pulmonary functioning. Forced vital capacity (FVC), inspiratory capacity (IC), and maximum inspiratory mouth pressure (Pimax) are lowered in the acute stage of SCI, and then gradually improve over time. In a five-year longitudinal study, Postma et al. (2013) showed improvements to FVC. Loveridge and colleagues (1992) showed that seated positioning imposes greater stress on the respiratory system in the acute stages of SCI than the supine position. While breathing patterns in the supine position at all measured time points one-YPI were comparable to the controls (N = 18), breathing patterns in the seated position had to be adjusted in order to maintain minute ventilation. Over time, however, improved breathing patterns were observed in the seated position, so much so that differences initially observed between the seated and supine positions became insignificant. Such improved breathing pattern is speculated to be due to increased accessory muscle function, improved chest wall stability, thoraco-abdominal coupling, or a combination of these factors over time.

An increasingly shallow breathing pattern resulting from a lack of deep breaths, and other factors associated with SCI such as obesity and decreased chest wall compliance, may lead to hypercapnia, or excessive amounts of carbon dioxide in the blood, and possibly ventilatory failure (Bach & Wang 1994). Despite these results from this prospective longitudinal study, it is unclear if breathing patterns change as a result of the injury or due to aging with SCI. The former may be the case as the study followed adjustments only during the first YPI.

Sustaining a SCI often leads to an initial respiratory insufficiency and necessitates a need for long-term mechanical ventilation. In some instances, individuals may be weaned from the ventilator. Wicks et al. (1986) conducted a 10-year retrospective study of ventilator-dependent patients with tetraplegia (N = 134) to determine factors associated with weaning and long-term survival rate. Despite similar levels of injury, patients over 50 years of age had a 20% mortality rate compared to 6% for those younger than 50, and that ventilator weaning is less successful for those over the age of 50. This suggests that ventilator-dependency among SCI individuals who are older than 50 possess a much greater risk of negative health outcomes (Wicks & Menter 1986).

Although there are additional factors that can affect respiratory health long-term for the individual with SCI (i.e. level and completeness), there are several preventative activities that can be done to minimize the aging of the respiratory system, such as not smoking, minimizing exposure to polluted air, and controlling body weight (Wilmot & Hall 1993). Further research is needed to better understand SDB in persons aging, especially in terms of their implications for for cardiovascular health.

**Conclusion**

*There is Level 4 evidence from two longitudinal studies (Bach & Wang 1994; Berlowitz et al. 2005) support that SDB may either increase or persist with the aging process.*

*There is Level 2 evidence from a longitudinal study with AB controls (Loveridge et al. 1992) that seated breathing patterns are compromised immediately post injury but recover over time. As well, persons with tetraplegia do not take deep breaths as often as AB individuals.*

*There is Level 4 evidence from a longitudinal study that adults over the age of 50 who are aging with ventilator dependency are at greater risk of death and are less likely to be weaned from their ventilators than younger adults aging with a ventilator (Wicks & Menter 1986).*

*There is Level 4 evidence from one longitudinal study (Postma et al. 2013) that forced vital capacity improves 5 years after inpatient rehabilitation.*

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Sleep disordered breathing may increase or persist with the aging process in persons with SCI.

Seated breathing patterns after tetraplegia appear compromised early post-injury but may recover over time.

Adults who are older (50 years +) and ventilator dependent have a higher mortality rate and lower weaning rate than adults who are younger and who are ventilator dependent.

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## 3.5 Nervous System

Characteristics of an aging nervous system include diminished strength and reaction time (Fozard et al. 1994; Lynch et al. 1999), loss of vibratory sense (Knox 1994), reduced fine coordination and agility (Pathy 1985), slowing of motor unit recruitment patterns (Tax et al. 1990), declining function of basal ganglia (Roth & Joseph 1994) and cerebellar systems (Bickford et al. 1999), and deterioration of gait (Greenhouse 1994). A number of anatomical and functional changes occur with aging, including deficits in long-term potentiation (the normal enhancement in signal transmission between two neurons when stimulated together), decline in expression of neurotrophic factors which promote neuronal survival and dendritic branching, and reduction in brain volume in some regions due to a decrease in synaptic density (Mora 2013). With the exception of neurons from a few areas, there is no significant loss of neurons during the normal process of aging (Mora 2013). Aging also impacts the peripheral and autonomic systems, which respectively result in a progressive loss of nerve conduction velocity (Verdú et al. 2000), and impaired temperature regulation (Collins et al. 1977) and baroreceptor reflexes (Duke et al. 1976).

In SCI, there is a lack of longitudinal evidence regarding the nervous system other than studies that evaluate neurological complications such as chronic pain (see Table 8). Neuropathic chronic pain following SCI is a complex issue and results from the abnormal processing of sensory input due to damage to the nervous system (Cardenas & Rosenbluth 2001). It is often difficult to identify a specific stimulus or cause for neuropathic syndromes (Scadding 2003). Although this pain can be identified by site (region of sensory disturbance) and by features (sharp, shooting, electric, burning, stabbing), individuals may find it difficult to describe the quality of neuropathic pain (Scadding 2003). Typically, neuropathic pain is present at or below the level of lesion, and is constant but fluctuates in intensity depending on the individual's emotional state or level of fatigue. SCI-related studies that have examined factors associated with the development of pain have yielded mixed results. With regards to age, some studies have found an association between chronological age and pain (e.g. Burke 1973; Anke et al. 1995; Stormer et al. 1997; Dalyan et al. 1999; Siddall et al. 1999; Putzke et al. 2000), whereas others have found none (e.g. Subbarao et al. 1995; Rintala et al. 1998; Curtis et al. 1999).

Overall, the dearth of literature on the nervous system is relatively surprising given the implications of how age may influence the recovery process following injury. New sensory and motor deficits in persons with SCI of more than 20 YPI (Whiteneck et al. 1992) may occur due to an age-related dropout of anterior horn cells and loss of myelinated tracts (Charlifue et al. 2002). As well, it is important to determine whether or not further deterioration in the autonomic nervous system occurs in the later decades of life, which hold implications for the gastrointestinal and genitourinary systems (Lammertse 1993).

In this section, 4 longitudinal studies (see Table 7) on the nervous system after SCI are reviewed.

**Table 7: Nervous System**

| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| Jensen et al. 2005; USA Longitudinal N=147 | **Population:** 147 subjects with SCI (110M 37F); mean(SD) age at follow-up 48.8(13.0) yrs, range 21-88 yrs; mean(SD) YPI at follow-up 16.6(10.4), range 3.2-57.4 yrs. **Methodology:** Examined the change in the prevalence and intensity of pain over time (range 2-6 yrs) between assessments. **Outcome Measures:** Brief Pain Inventory Interference scale; Bodily Pain scale; SF-36; Mental Health scale. | 1. Overall, the change or intensity in the prevalence of pain over time was not significant. |
| Rintala et al. 2004; USA Longitudinal N=96 | **Population:** 96 subjects with SCI (69M 27F); Phase I: *Males*: mean(SD) age 40.5(12.5) yrs, range 23-70 yrs; mean(SD) YPI 11.1(8.8). *Females:* mean(SD) age 37.0(10.8) yrs, range 21-61 yrs; mean(SD) YPI 10.4(7.2). **Methodology:** Assessed the consistency of pain at three (women) and four (men) measurement points across 10 years. **Outcome Measures:** Self-report pain characteristics. | 1. Of the 96 participants, approx. half the males and three-quarters of females reported consistent pain across all measurement points. |
| Siddall et al. 2003; Australia Longitudinal N=73 | **Population:** 73 subjects with SCI (60M 13F); mean age at baseline 40 yrs, range 21-81 yrs; mean time post-injury at baseline < 6 mos. **Methodology:** Assessed the prevalence, onset, and severity of pain. **Outcome Measures:** Pain intensity via numeric scale; Psychological distress; Von Korff chronic pain disability to assess pain interference on daily activities; assessed at less than 1 YPI and again at 5 YPI. | 1. Persons with neuropathic pain early following injury were likely to continue to experience ongoing and severe pain. |
| Putzke et al. 2002a; USA Longitudinal N=270 | **Population:** 270 subjects with SCI (210M 60F); mean(SD) age at 1 YPI 36.8(14.3) yrs. **Methodology:** Examined factors that contribute to pain interference. **Outcome Measures:** Short-form 12, at 1 and 2 YPI. | 1. Age effect for pain interference was detected. Youngest group with SCI who reported no pain interference at both year 1 and year 2, and the oldest group being those reporting pain interference at both year 1 and year 2. |

## Discussion

The most robust finding was that presence of pain at an earlier time point appears to be the best predictor of future pain, and that it likely does not change significantly over time (Jensen et al. 2005; Siddall et al. 2003; Putzke et al. 2002a; Rintala et al. 2004). A limitation of most studies was the lack

of clear assessments of the type and characteristics of pain being experienced by participants. For instance, Putzke and colleagues (2002a) do not report on the quality (e.g. frequency, intensity, duration) or pain type (e.g. neuropathic, nociceptive, etc.) of their sample. Although their findings suggested that age of onset may be an important factor, pain is a complex issue that involves the interaction of biological, psycho-social, and environmental factors.

In general, there are considerable gaps in knowledge regarding how the nervous system changes with aging with an SCI. Although it was identified as an issue of importance more than a two decades ago (Lammertse 1993), research on the nervous system still remains incomplete and speculative at best.

### Conclusion

***There is Level 4 evidence (Putzke et al. 2002a; Siddall et al. 2003; Rintala et al. 2004; Jensen et al. 2005) that the early onset of SCI-related pain is likely to be maintained over time, with some evidence indicating that the degree of interference experienced might be impacted by age of onset (Jensen et al. 2005).***

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Younger persons (< 30 years) may have less pain interference at one and at two years post-injury than older persons (> 60 years).

Previous reports of pain interference after SCI, irrespective of age, may be predictive of later pain interference.

</div>

### 3.6 Skin and Subcutaneous Tissues

Skin undergoes structural and physiological changes resulting from both the natural aging process and being exposed to damaging environmental elements. Over a lifetime, skin is observed to progressively degenerate. Most notable are the changes and deterioration in the structure of the skin which are due to losses and/or a disordering of collagen, the protein primarily responsible for the tensile strength of skin, and elastin fibres (Farage et al. 2009). The elderly therefore, have an increased susceptibility to skin injuries such as pressure ulcers, and a decreased healing response.

Pressure ulcers are common among individuals with SCI, and typically occur over boney prominences, such as the ischial tuberosities and malleoli. Damage to the skin and underlying tissue caused by pressure, shearing, and/or friction due to continuous sitting are the primary causes of pressure ulcers. As collagen metabolism increases as a result of SCI, these individuals may be more susceptible to pressure ulcers than non-SCI individuals (Claus-Walker & Halstead 1982a; Claus-Walker & Halstead 1982b). As a result of the combined effects of pressure, from sitting, and reduced skin integrity, due to collagen degradation, it is estimated that 85% of individuals with SCI will experience a pressure ulcer in their lifetime (Gunnewicht 1995). Given that the mean cost of healing a wound is approximately $50,000, which translates into an annual cost of 3.6 billion dollars in the United States (Beckrich & Aronovitch 1999), there is a strong need to understand age-related changes to the skin following SCI in order to help minimize the occurrence of wounds.

In this section, 2 longitudinal studies and 2 cross-sectional studies (see Table 8) on skin and subcutaneous tissues after SCI are reviewed.

## Table 8: Skin and Subcutaneous Tissues

| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| Park et al. 2011; South Korea Cross-Sectional with AB controls N SCI=48 N control=48 | **Population:** 48 men with SCI (C4 or below); 48 age-matched AB controls, divided into 4 groups: Subgroup 1 – complete somatic SCI patients with sympathetic paralysis; Subgroup 1a - incomplete somatic SCI patients with sympathetic paralysis; Subgroup 2 – SCI patients with any AIS whose sensory neurologic level of injury were low enough to preserve normal sympathetic integrity of the measured dermatomes; Subgroup 3 – healthy controls for each anatomical group. For each of the subgroups there was a shoulder group (SG) and thigh group (TG). **Methodology:** Comparison of biomechanical skin properties using a Cutometer MPA 580 (Courage & Khazaka Electronic GmbH) at 2 body regions of the non-dominant side: the anterior shoulder (C4 sensory dermatome) and the middle of the midial thigh (L2 sensory dermatome). **Outcome Measures:** skin distensibility; skin elasticity; and skin viso elasticity. | 1. In each anatomical group, sympathetic paralyzed subgroups regardless of somatic sensory completeness showed lower value of skin distensibility, and higher values of elasticity and viscoelasticity compared to other subgroups. 2. Age and YPI had significant impact on the biomechanical skin properties. |
| Rodriguez & Garber 1994; USA Longitudinal N=62 | **Population:** 62 men with SCI; with at least 1 past Stage II pressure ulcer; age range 22-49 yrs; YPI < 1 yr. **Methodology:** Monitored changes in skin metabolism for 2 years in relation to pressure ulcer symptoms. **Outcome Measures:** 24hr urine sample every 4-6 weeks used to determine concentrations of glu-gal Hyl, gal Hyl, calcium, and creatinine. | 1. Approximately ¼ of subjects developed pressure ulcers over the 2 year period. 2. Subjects with sustained elevated concentration of glu-gal Hyl (more than 100 μmole/g creatinine) were significantly more likely to develop pressure ulcers over the 2 years 3. More smokers than non-smokers developed ulcers. 4. The majority of persons who developed ulcers had injuries of T6 and above. |
| Vaziri et al. 1992; USA Longitudinal N=31 | **Population:** 21 men with SCI and pressure ulcers and 10 males with SCI and without pressure ulcers (SCI-control); mean(SD) age 53(13) yrs, range 25-79 yrs. 32 AB controls. **Methodology:** Examined the concentration of plasma fibronectin and its related proteins and its relationship to the healing of pressure ulcers over 8 weeks. **Outcome Measures:** Concentration of plasma fibronectin, fibrinogen, plasminogen, α2antiplasmin and Factor XIII, measured using immunoelectrodiffusion. | 1. 10 of the 21 participants in the study group showed near complete healing of pressure ulcer within five weeks; these individuals were classified as fast healers, and the other 11 as poor healers. 2. Plasma fibronectin concentration was higher in the fast healers, compared to the slow healers, the SCI control, and the AB control 3. There is a significant correlation between plasma fibronectin concentration and the severity of pressure ulcers in the study group. |
| Rodriguez & Claus-Walker 1984; USA Cross-sectional with AB | **Population:** 10 men with SCI; age range 14-50 yrs; time post-injury < 6 mos.; age and gender matched AB controls. **Methodology:** Comparison of skin | 1. Although not statistically significant, the concentration of Glu-gal Hyl and gal Hyl were consistent, whereas the group |

| Author Year; Country<br>Score<br>Research Design<br>Total Sample Size | Methods | Outcome |
|---|---|---|
| controls<br>N SCI=10<br>N controls=5 | degradation.<br>**Outcome Measures:** Glu-gal Hyl and gal Hyl from urine samples. | with SCI had a very wide range of values. |

## Discussion

Over a 2 year period, one-quarter of individuals with SCI experienced a pressure ulcer (Rodriguez & Garber 1994). Understanding how skin changes post-SCI is important, not only because of the implication of pressure ulcers, but because of other non-life threatening skin complications that commonly occur after SCI, which include local fungal infection, seborrheic dermatitis, and chronic acne vulgaris (Rubin-Asher et al. 2005; Stover et al. 1994). As well, attenuated immune response following SCI facilitates skin infections and lack of cutaneous sensation increases the incidence of pressure ulcers.

Park and colleagues (2011) found that the biomechanical skin properties were significantly altered following SCI in men, and these changes were directly influenced by regional sympathetic denervation rather than somatic sensory denervation. They found that age significantly correlated with all biomechanical skin parameters in their AB controls. However, in men with motor and sensory complete SCI, YPI rather than age was shown to be the most important factor influencing skin changes. Since the amount of dermal thickening is positively correlated with YPI, Park et al. (2011) hypothesized that the thickening process following SCI may be strong enough to overwhelm the impact of aging on biomechanical skin properties.

## Conclusion

***There is Level 2 evidence (Vaziri et al. 1995) suggesting that plasma fibronectin, as an indicator of wound healing, may rise in SCI male patients with fast healing ulcers but not in SCI patients with poor healing ulcers.***

***There is Level 5 evidence that the biomechanical skin properties are significantly influenced by sympathetic paralysis rather than somatic sensory paralysis. Furthermore, in men with complete SCI, YPI may be the influential factor on the biomechanical properties of the skin (Park et al. 2011).***

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Males with SCI have higher levels of collagen metabolite, glu-gal Hyl, than the able-bodied population, which may be a sign of premature aging of the skin. Further work is needed to conclusively demonstrate this.

Behavioural factors play a stronger role in the development of pressure ulcers in persons with SCI than either age or YPI.

In men with complete SCI, YPI may be the influential factor on biomechanical properties of the skin.

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## 3.7 Genitourinary and Gastrointestinal Systems

There are several normative age-related changes of the genitourinary and gastrointestinal systems that can lead to serious health problems for the elderly. With regard to the genitourinary system, there is a progressive and structural breakdown of the kidneys with age, and problems with urinary continence that results from decreased bladder capacity and compliance, and an increase in involuntary bladder contractions (Aldwin & Gilmer 2004). In males, enlargement of the prostate also

contributes to incontinence (Dubeau 1997), and prostate cancer is one of the primary causes of death (McClain & Gray 2000).   Although urinary tract infections (UTIs) increase with age, women are at greater risk, with the incidence in males only approaching that of women when they are 60 years or older (Foxman 2002).  Unlike the genitourinary system, the gastrointestinal system retains much of its regular function, and it is unclear whether the few normal changes do affect the health of the older population.  Some potential issues include slowing in large intestine motility, and diminished gut motility, with an increase in water resorption in the colon, which contributes to hard stool and increased risk of constipation, rectal fissures, hemorrhoids, and diverticular diseases (Wilson et al. 1997).

In persons with SCI, the effects of neurogenic bladder may compound the effects of aging in persons with SCI (Madersbacher & Oberwalder 1987) since bladder management techniques, such as the use of indwelling catheters, may contribute to the occurrence of common complications such as UTIs (Charlifue et al. 1999) and for a higher risk of developing bladder cancer (Groah et al. 2002).  Similarly, neurogenic bowel may also compound aging after SCI given that persons with SCI often have higher rates of bowel-related complications compared to the general population (Cosman et al. 1993).

In this section, 9 longitudinal studies and 13 cross-sectional studies (see Table 9) on the genitourinary and gastrointestinal systems after SCI are reviewed.

## Table 9: Genitourinary and Gastrointestinal Systems

| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| Alexandrino et al. 2011; Brazil Cross-sectional with AB comparison group N SCI=24 N controls=24 | **Population:** 24 men with SCI (Type A complete n=22, type C incomplete n=1, type D incomplete n=1); mean(SD) age 36.25(10.24) yrs; mean(SD) YPI 9.5(5.8), range 0.6-20 yrs; 24 age matched controls; mean(SD) age 36.5(10.31) yrs. **Methodology:** Seminal zinc is considered to be a marker of prostate function. This study compared of seminal zinc concentration (SZC) between the SCI group and control group. Seminal zinc was determined by atomic absorption. **Outcome Measures:** seminal zinc concentration. | 1. Significant difference between groups; Mean SZC in study group is 85.20 mg l$^{-1}$ and 147.16 mg l$^{-1}$ in control group. |
| Faaborg et al. 2011; Denmark Longitudinal N=22 | **Population:** Group A: n=12 (8M 4F); mean age range 37.7-67.2 yrs; complete SCI N=4. Group B: n=10 (7M 3F); mean age range 29.7-71.9 yrs; complete SCI N=8. **Methodology:** Assessed gastrointestinal transit times (GITTs) and colonic dimension changes in Group A; at 1 year after injury and again 12.8 years later; and Group B; at 18.7 years after injury and again 12.2 years later. **Outcome Measures:** GITTs, colonic diameters. | 1. Decrease in rectosigmoid transit time from 1-13 years after SCI (Group A). 2. No other significant changes in GITT and segmental colonic transit times. 3. No statistically significant changes in colonic dimension. |
| Ancha et al. 2010; USA Cross-sectional N SCI=8 N controls=6 | **Population:** 8 men with SCI (tetraplegia (C5 or below) n=3, paraplegia (T5 or below) n=5; < 2 spontaneous bowel movements/wk; mean(SD) age 59(13) yrs, mean(SD) YPI 13(4); 6 gender matched AB | 1. HAPC were absent in individuals with SCI during pre-sleep, sleep and post-sleep. 2. HAPC were significantly increased after awakening in the control group. 3. The MI was lower in the SCI group during |

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| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| | controls, mean(SD) age 57(10) yrs. **Methodology:** Comparison of high amplitude propagating contractions (HAPC) and other measures of motility by fixing a manometric probe to the colonic wall at the splenic flexure. Measurements pre-sleep phase (1hr before sleep), sleep phase, and post-sleep phase. **Outcome Measures:** High amplitude propagating contractions (HAPC), Motility index (MI), and number of waves were measured. | pre- and post-sleep than in the controls.<br>4. There was a sleep-induced depression of colonic motility in both the groups. |
| Kalpakjian et al. 2010; USA Prospective cohort N=128 | **Population:** 62 women with SCI (injury levels C6 through T12; >36 months post-injury). 66 gender matched AB controls; 45-60 years of age. **Methodology:** Self-report surveys collected 4 times (9 mos apart) over 4 years. Monthly diaries indicate day of bleeding, heaviness of blood flow, absence of period. **Outcome Measures:** Mid Life Symptom Checklist, monthly diaries, self-report surveys. | 1. No significant differences between women with and without SCI for menopause status.<br>2. No significant group differences for vaginal dryness, sleep problems or fatigue.<br>3. Significant increase in bother ratings in vaginal dryness across menopause transition (premenopause vs. late postmenopause (PM); 1.30(0.6) vs. 1.73(1.1) (%).<br>4. Women with SCI had significantly greater bother of diminished sexual arousal, somatic symptoms and bladder infections, and less bother of vasomotor symptoms. |
| Savic et al. 2010; UK Longitudinal N=282 | **Population:** 282 individuals with traumatic SCI injured prior to 1971; age at injury 15-55 yrs; mean age at enrollment 52.7 yrs; 86.7% males; 29.2% tetra ABC, 49.8% Para ABC, 21.0% Incomplete injuries. **Methodology:** Full physical assessment, diagnostic procedures, detailed medical and psychosocial interview, retrospective medical records review. **Outcome Measures:** Medical History and Current Status; battery of outcomes including quality of life, depression, pain, and environmental factors. | 1. Most frequently reported medical problems: urinary tract infection (UTI), upper extremity pain, fatigue, pressure sores, constipation, and bowel accidents.<br>2. Pressure sore prevalence remained stable.<br>3. No significant change over time in number of patients with UTIs (48% in 1993, 54% in 1996, 48% in 1999, 2002, 2006).<br>4. Number of UTIs requiring treatment went down significantly; 3.9 persons in 1990 to 1.2 in 2006.<br>5. Bowel evacuation methods changed significantly over time – increase manual evacuation, colostomy methods in 2006. |
| Emmanuel et al. 2009; UK Cross-sectional N=55 | **Population:** 55 complete SCI subjects (45M 10F); mean age 36 (range 19-68); mean time post-injury 34 months (range 13-134). **Methodology:** Comparison of rectal muscosal blood flow. **Outcome Measures:** Whole gut transit times; rectal electrosensitivity; stimulated defecation; laser Doppler studies of rectal mucosal blood flow; symptoms of constipation. | 1. 35 subjects (27M 8F, mean age 36, range 20-68) are symptomatically constipated, representing 75% of the subjects with lesion above T5 and 55% of those with lesion below T5.<br>2. 32 subjects who were symptomatically constipated had slow whole gut transit.<br>3. Transmucosal rectal electrical sensation was abnormally high in all SCI subjects, being significantly greater in those complaining of constipation (67.3mA in constipation, vs. 41.6mA in non-constipation SCI, vs. 36mA in control.<br>4. 71% of subjects with lesion above T5, and 61% of those below T5 were unable to expel a water-filled balloon and showed paradoxical sphincter contraction. |

| Author Year; Country<br>Score<br>Research Design<br>Total Sample Size | Methods | Outcome |
|---|---|---|
| | | 5. SCI subjects had significantly lower mucosal blood flow than asymptomatic SCI subjects (183 vs. 267 FU); SCI subjects with lesion above T5 had significantly lower resting blood flow than AB control, while SCI below T5 were similar to the control. |
| Faaborg et al. 2008;<br>Denmark<br>Longitudinal<br>N=159 | **Population:** 159 subjects who participated in a survey in 1996 and a follow-up in 2006; mean age 37 yrs (range 15-70 yrs), mean YPI 10 (range 0-48 yrs), 63 cervical, 40 thoracic, and 56 lumbar.<br>**Methodology:** Assessed colorectal function over a 10 yr period.<br>**Outcome Measures:** A questionnaire consisting of 34 items describing constipation, obstructed defecation, fecal incontinence and impact on quality of life (QoL) or social activities. | 1. All items regarding symptoms of constipation increased significantly.<br>2. The number of correspondents reporting fecal incontinence at least once monthly decreased from 32 (22%) to 26 (17%).<br>3. More correspondents report that their QoL or social activities were restricted by colorectal dysfunctions in general (39 vs. 60) and constipation (20 vs. 30). |
| Shim et al. 2008;<br>South Korea<br>Cross-sectional with AB controls<br>N SCI=31<br>N controls=31 | **Population:** 31 men with SCI, median age 58 yrs, range 45-81 yrs; median YPI 32, range 5-55 yrs; age and gender matched AB controls.<br>**Methodology:** Comparison of serum prostate specific antigen (PSA).<br>**Outcome Measures:** Serum levels of PSA; digital rectal examination; transrectal ultrasonography. | 1. No differences in PSA levels and prostate volume parameters between group with SCI and AB controls. |
| Alexandrino et al. 2004;<br>Brazil<br>Cross-sectional with AB controls<br>N SCI=44<br>N controls=44 | **Population:** 44 men with SCI, mean(SD) age 33.98(9.12) yrs, range 18-58 yrs; age and gender matched AB controls.<br>**Methodology:** Comparison of total serum prostate specific antigen (PSA) and seminal PSA.<br>**Outcome Measures:** Serum and seminal levels of PSA. | 1. No differences in total PSA levels between group with SCI and AB controls.<br>2. Total seminal PSA was lower in the SCI group compared to AB controls. |
| Scott et al. 2004;<br>USA<br>Cross-sectional with AB controls<br>N SCI=636<br>N controls=20949 | **Population:** 636 men with SCI; ages ≥50; 945 men with prostate cancer and 20,949 AB controls.<br>**Methodology:** Comparison of incidence and characteristics of prostate cancer.<br>**Outcome Measures:** SCI, cancer registry, and outpatient databases. | 1. 1.7% of SCI group had been diagnosed with prostate cancer compared to 4.4% of AB controls.<br>2. Average serum prostate specific antigen (PSA) level at diagnosis was significantly higher in the group with SCI compared to AB controls.<br>3. Group with SCI and prostate cancer (7; 63.6%) had locally advanced (stage T3) or metastactic prostate cancer compared to AB population (267; 29.1%). |
| Pannek et al. 2003;<br>Germany<br>Cross-sectional with AB controls<br>N SCI=100<br>N controls=575 | **Population:** 100 men with SCI; mean(SD) age 53.7(11.3) yrs, range 35-71; age and gender matched AB controls.<br>**Methodology:** Comparison of prostate size and serum prostate specific antigen (PSA).<br>**Outcome Measures:** Prostate size; serum levels of PSA. | 1. No differences in prostate size or PSA levels between group with SCI and AB controls.<br>2. Mean serum PSA level in the AB controls was found to increase with age, but shown to be of a lesser extent in persons with SCI. |
| Pramjudi et al. 2002; | **Population:** 366 men with SCI; age range | 1. No differences in PSA levels between |

| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| USA Cross-sectional with AB controls N SCI=366 N controls=371 | 40-79 yrs (40-49 yrs, 50-59 yrs, 60-69 yrs, 70-79 yrs); age and gender matched AB controls. **Methodology:** Comparison of serum prostate specific antigen (PSA). **Outcome Measures:** serum levels of PSA. | group with SCI and AB controls. |
| Konety et al. 2000; USA Cross-sectional with AB controls N SCI=79 N controls=501 | **Population:** 79 men with SCI; age range 40-89 yrs (40-49 yrs, 50-59 yrs, 60-69 yrs, 70-79 yrs, 80-89 yrs); age and gender matched AB controls. **Methodology:** Comparison of serum prostate specific antigen (PSA). **Outcome Measures:** Serum levels of PSA. | 1. No differences in PSA levels between group with SCI and AB controls. |
| Krogh et al. 2000; Denmark Cross-sectional with AB controls N SCI=26 N controls=24 | **Population:** 26 subjects with SCI (11M 15F); age range 17-69 yrs; YPI range 11-24 days **Methodology:** Comparison of total gastrointestinal transit times (GITT) and segmental colorectal transit times (CTT). **Outcome Measures:** GITT and CTT. | 1. GITT and CTT are significantly prolonged in SCI patients than in AB controls. |
| Lynch et al. 2000; New Zealand Cross-sectional with AB controls N SCI=467 N controls=467 | **Population:** 467 subjects with SCI (384M 83F); mean age 43.5 yrs, range 15-89; mean YPI 14, range 0.7-42.1 yrs. 467 age and gender matched AB controls. **Methodology:** Comparison of bowel functioning. **Outcome Measures:** Mean Fecal Incontinence Score, Bowel motion frequency, Haemorrhoidectomy, Time at toilet, Assistance at toilet. | 1. Group with SCI had higher rates of fecal incontinence, less frequent bowel motion, spent longer times on the toilet, and required more assistance. |
| Sekar et al. 1997; USA Longitudinal N=1114 | **Population:** 1114 subjects with SCI (915M 199F); mean(SD) age 31.25(13.79) yrs, range 1-87 yrs at injury. **Methodology:** Evaluation of the effects of different bladder management on long term renal function who were followed for at least 10 YPI. **Outcome Measures:** Total and individual kidney effective renal plasma flow (ERPF). | 1. A decreasing trend in mean ERPF was detected over time after injury, except for a slight reversal at 10 YPI. |
| MacDiarmid et al. 1995; New Zealand Longitudinal N=44 | **Population:** 44 subjects with SCI (31M 13F); mean age 36 yrs, range 13-79 yrs. **Methodology:** Reviewed the urological complications in patients treated with suprapubic catheterization at 12 to 15 mos post-injury. **Outcome Measures:** Urodynamic studies and ultrasound. | 1. None of the patients had renal deterioration, vesicoureteral reflux or bladder carcinoma. 2. Incidences of incontinence, urinary tract infections, and calculi were acceptable. |
| Dewire et al. 1992; USA Longitudinal N=57 | **Population:** 57 men with cervical SCI. **Methodology:** Comparison of incidence of urological complications and renal deterioration in SCI patients with and without a chronic indwelling urinary catheter from baseline to 10 YPI. | 1. No significant difference found between patients with and without chronic indwelling urinary catheters. |

| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| | **Outcome Measures:** Patients' medical records excretory urogram. | |
| Lamid et al. 1988; USA Longitudinal N=32 | **Population:** 32 men with SCI; mean age at injury: 29.72 yrs, range 19-66 yrs. **Methodology:** Medical chart review of annual visits from SCI patients with vesicoureteral reflux until 12 YPI. **Outcome Measures:** Medical records with information on bladder function, including radiological and laboratory examinations. | 1. The majority of refluxes developed 1-2 YPI, and some disappeared spontaneously without causing damage to the urinary tract.<br>2. After 4 YPI, the number of refluxes increased and progressed to grade II and IV, causing kidney damage with caliectasis. |
| Menardo et al. 1987; Italy Cross-sectional with AB controls N SCI=11 N controls=37 | **Population:** 11 subjects with SCI (8M 3F); age range 17-63 yrs; YPI range 2 mos-15 yrs. 37 age matched AB controls. **Methodology:** Comparison of transit of contents through the large bowel **Outcome Measures:** Gastrointestinal transit times (GITT). | 1. Compared to AB controls, GITT was lower in all patients with paraplegia.<br>2. Flow contents through the left colon were markedly lower in group with SCI compared to AB controls, and transit of contents in 8 persons with SCI were decreased, and below the normal range of the AB controls. |
| Viera et al. 1986; USA Longitudinal N=99 | **Population:** 99 subjects with SCI (77M 22F); age range 14-65 yrs at injury. **Methodology:** Investigated the effect of current bladder management techniques on renal function at 6 to 60 mos post-injury. **Outcome Measures:** Serum creatinine; Excretory urogram; Determination of short renal clearance of iothalamate. | 1. In the indwelling catheter group (n=9), bladder calculi occurred in 3 patients at 7, 28, and 44 mos post-injury, and were the only group to develop bladder stones.<br>2. Excretory urogram abnormalities tended to occur earlier in the intermittent self-catheterization group (first 18 mos) than in the bladder re-training group (third yr). |
| Kuhlemeier et al. 1984b; USA Cross-sectional with AB controls N SCI=400 N controls=287 | **Population:** 400 subjects with SCI (160 acute and 240 chronic); age range 16-60 yrs, YPI range for chronic 6-53 months. **Methodology:** Comparison of renal function. **Outcome Measures:** Total and individual kidney effective plasma flow. | 1. Both individual and global kidney effective plasma flows were decreased in the acute SCI group for persons who were 21-50 yrs old, but no difference existed for persons younger than 20 or older than 50. |

## Discussion

From the list of identified studies on the genitourinary system (see Table 9), there are four longitudinal studies (Viera et al. 1986; DeWire et al. 1992; MacDiarmid et al. 1995; Sekar et al. 1997) suggesting there are no differences in renal function over time among persons using various bladder management techniques. However, the samples of these studies did incur typical SCI-related complications such as UTIs and bladder stones, and there were some indications of renal decline. For instance, Lamid (1988) found that after 4 YPI, the number of vesicoureteral refluxes increased and progressed to grades II and IV, which caused kidney damage with caliectasis in 27 of 32 patients with SCI followed over 12 YPI. Finally, Sekar and colleagues (1997) reported that renal function (as measured by total and individual kidney effective renal plasma flow; ERPF) decreased over time in their SCI sample (N = 1114) with a slight reversal occurring at 10 YPI. A methodological strength of the study was the assessment of ERPF, which is thought to be a more sensitive measure of kidney function than serum creatinine (Kuhlemeier et al. 1984a). Based on the findings of the identified studies, it may be that significant declines in renal function occur approximately at 5 YPI.

Work regarding age of onset and the genitourinary system is also needed as the findings of a cross-sectional study by Kuhlemeier and colleagues (1984b) suggests that persons with acute SCI (N = 160) who were younger than 20 or older than 50 had comparable levels of individual and global kidney effective plasma flows compared to AB controls (N = 287), whereas persons with between 21-51 had impaired renal function.

Overall, the risk for prostate cancer appears to be lower in persons with SCI due to impaired testosterone levels, but prostate cancer screening should be encouraged given the possibility that males with SCI who do develop prostate cancer may have poorer outcomes than AB males (Scott et al. 2004).

With regard to women with SCI (n = 62), Kalpakjian and colleagues (2010) found that they experience greater symptom bother in certain areas related to menopause compared to AB controls (n = 66). Specifically, women with SCI reported greater bother of somatic symptoms, bladder infections, and diminished sexual arousal. However, the patterns of symptoms, transitioning through menopause, and age at final menstrual period transitions were comparable between groups. Overall, the authors concluded that in important ways, women with SCI appear to experience menopause similarly to their peers.

Although bowel function is clearly impaired in persons with SCI compared to AB controls, one study (Lynch et al. 2000) demonstrated that continence deteriorates with increasing age in an AB population (N = 467) but does not change with increasing age in persons with SCI (N = 467). This supports a Level 4 study that found that gastrointestinal transit times and colonic dimensions neither change during the first decade nor within the second decade post-SCI (Faaborg et al. 2011). However, a 10-year longitudinal study (Faaborg et al. 2008) suggests persons with SCI do incur an increase in constipation-related symptoms over time. One possible reason for this occurrence is due to the evidence that high amplitude propagating contractions (HAPC) are absent in persons with SCI compared to AB controls (Ancha et al. 2010). HAPC are often associated with colonic mass movements and are thought to be a precursor of bowel evacuation. Thus it is an important factor in the occurrence of difficulty with evacuation post-SCI. Conversely, the need for assistance from medications or persons does not change, while fecal incontinence decreases. It may be that bowel dysfunction worsens over time for persons with SCI but three studies (Menardo et al. 1987; Krogh et al. 2000; Emmanuel et al. 2009) provide evidence that level of injury plays a primary role in the extent of bowel dysfunction. At this time, the SCI evidence on aging and the gastrointestinal system is limited, but attention to bowel symptoms should be incorporated into routine follow-up procedures and education (Charlifue et al. 2002).

**Conclusion**

*There is Level 4 evidence (Viera et al. 1986; DeWire et al. 1992; MacDiarmid et al. 1995; Sekar et al. 1997) that there are no differences in renal functioning up to 4 YPI using various bladder management techniques with some decline occurring beyond that time.*

*There is Level 4 evidence (Lamid et al. 1988) that repeated episodes of vesicoureteral reflux can cause kidney damage as early as four YPI in some persons with SCI.*

*There is Level 4 evidence (Sekar et al. 1997) that renal plasma flow declines until 10 YPI after SCI, at which time a slight reversal occurs.*

*There is Level 5 evidence (Kuhlemeier et al. 1984b) that suggests age of SCI onset may be an important factor related to renal function, with persons with SCI who are under 20 and older than 50 having comparable renal function to AB controls, whereas persons between those ages have impaired functioning compared to the general population.*

*There is Level 5 evidence (Lynch et al. 2000) demonstrating a deterioration in bowel continence with increasing age in an AB population but no change with age in persons with SCI.*

*There is Level 4 evidence (Faaborg et al. 2008) suggesting persons with SCI do incur an increase in constipation-related symptoms and decrease in fecal incontincence over time.*

*There is Level 4 evidence (Faaborg et al. 2011) that gastrointestinal transit times and colonic dimensions do not change over time in persons with SCI.*

*There is Level 5 evidence from three studies (Menardo et al. 1987; Krogh et al. 2000; Emmanuel et al. 2009) that level of injury, and not necessarily age or YPI, plays a primary role in the extent of bowel dysfunction.*

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Various bladder management techniques (indwelling catheterization versus intermittent catheterization) may not impact renal functioning in persons with SCI over time.

Repeated episodes of vesicoureteral reflux can cause kidney damage as early as four years post-injury.

After SCI, renal plasma flow declines until 10 years post-injury, at which time, a slight reversal occurs.

Age of onset may play a role in minimizing renal decline, with adults who are under 20 and older than 50 having comparable renal functioning to the able-bodied population, while those between those ages have impaired functioning.

Bowel incontinence increased with age in the able-bodied population but does not change in persons with SCI.

Persons with SCI may experience an increase in constipation-related symptoms and decrease in fecal incontinence over time.

Level of injury, and not age or years post-injury, plays a primary role in the extent of bowel dysfunction.

---

### 3.8 Secondary Complications of Multiple Systems

Most individuals with SCI will develop a variety of secondary complications (Jensen et al. 2013). Common complications include pain, bowel and bladder regulation problems, muscle spasms, fatigue, esophageal symptoms, osteoporosis, cardiovascular disease, diabetes, and respiratory complications or infections (Jensen et al. 2013). As secondary health conditions negatively affect community re-integration and quality of life, the influence of the aging process on these conditions is important to consider in their management. While specific conditions have been described in previous sections (e.g. pain, bowel and bladder regulation, genitourinary and gastrointestinal problems, bone, cardiovascular disease and endocrine problems, and respiratory complications) the below section describes studies with general measures of secondary health complications or multiple health conditions, including physical and mental health (e.g. depression, fatigue and spasticity).

In this section, 1 systematic review (see Table 10) and 5 longitudinal studies (see Table 11) on secondary health complications after SCI are reviewed.

## Table 10: Systematic Review of Secondary Complications of Multiple Systems

| Author Year; Country Date included in the review Total Sample Size Level of Evidence Type of study Score | Methods Databases | Outcome |
|---|---|---|
| Jensen et al. 2013; USA  Reviewed published articles from 1986 to 2011  N=92  **Level of Evidence:** Methodological quality not assessed  **Type of study:** Not specified  AMSTAR: 3 | **Method:** Searches of electronic databases for studies published in English from 1986–2011 that provided information regarding the prevalence, course or associations with age and duration of secondary health conditions in human adults (>18 yrs of age) with SCI. No interventions studied. **Outcome Measures:** any findings regarding the frequency or prevalence, severity, time course, and/or age and duration of effects of a health condition. **Databases:** PubMed, CINAHL, PsycINFO. | 1. The findings show that individuals with SCI experience a number of secondary health conditions, many of which occur at a higher rate in those with SCI than the normative population. 2. The most common conditions or symptoms are pain, bowel and bladder regulation problems, muscle spasms, fatigue, esophageal symptoms and osteoporosis. 3. A number of these conditions – including cardiovascular disease, diabetes, bone mineral density loss, fatigue and respiratory complications or infections – occur with higher frequency in older individuals or those with longer SCI duration, relative to younger individuals or those with shorter SCI duration. 4. There is a lack of longitudinal research examining the natural course of health conditions in individuals aging with SCI – the findings from limited studies are often inconsistent, with only cardiovascular disease and weight (as measured by BMI) showing increases over time. |

In this scoping review that examined the association between age and secondary health complications post SCI, Jensen et al. (2013) report seven key findings (i.e. evidence that is reported in at least two studies): 1) bladder problems are not associated with duration of injury; 2) spasms are not associated with duration of injury; 3) cardiovascular disease is more prevalent in older individuals; 4) diabetes is more prevalent in older individuals; 5) bone mineral density loss is higher in both older individuals and in individuals with longer duration of injury; 6) fatigue is more commonly reported by older individuals; and 7) respiratory complications/infections are more prevalent in older individuals.

The authors concluded that older age and longer SCI duration are associated with more frequent and severe health conditions. These findings support the belief that premature aging may be occurring in individuals with SCI.

The following reviews additional papers studying aging and secondary health complications after SCI.

## Table 11: Aging and Secondary Health Complications after SCI

| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| Ullrich et al. 2013; USA | **Population:** 286 veterans with SCI (97% male): Age (yrs): mean 53; Duration of injury | 1. 20% of the sample showed both elevated pain and depression at Year 1. |

| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| Retrospective longitudinal N=286 | (yrs): mean 17; Type of SCI: 49% paraplegia, 38% low tetraplegia, 13% high tetraplegia; 46% complete. **Methodology:** 3 standardized annual psychological evaluations given to participants were reviewed. Administrative databases were used to collect SCI specialty care utilization data. Participants were categorized as having elevated pain, elevated depression, both elevated pain and depression, or neither elevated, using cut-off scores on the pain and depression scales. **Outcome Measures:** Center for Epidemiological Studies Depression Scale (CES-D), Numerical Rating Scale (NRS) for pain, medical comorbidities, SCI specialty care utilization. | 59% of participants had either elevated pain or depression or both at Year 1. 2. Pain scores were stable over time. 3. Depression scores improved over 3 years, but persons with elevated pain and depression showed less improvement on depression scores than did persons with depression alone. 4. Persons with pain and depression tended to utilize more SCI specialty care (number of SCI outpatient visits, number of psychologist visits, inpatient admissions). |
| Pershouse et al. 2012; Australia Longitudinal N=270 | **Population:** 270 persons with traumatic SCI (81% male); mean (SD) age in yrs: 43.3(11.4), range 20-76; mean (SD) age at injury in yrs: 27.3(9.7). **Methodology:** Data were collected via telephone interviews and written questionnaires annually over 5 years, between 2004 and 2008, across 6 strata comprising participants grouped according to time since injury (<5y, 5–9y, 10–14y, 15–19y, 20–24y, ≥25y). **Outcome Measures:** Secondary Conditions Surveillance Instrument (SCSI) | 1. There was a significant increase in secondary conditions with increasing time since injury. |
| Saunders et al. 2012; USA Prospective longitudinal N=801 | **Population:** 801 adults with traumatic SCI; mean (SD) age in yrs at Time 1 of survey: 44.8(13.8); mean (SD) YPI in yrs at Time 2: 23(10.6). **Methodology:** There were 2 data collection time points: the first between 2002 and 2004 (Time 1) and second between 2007 and 2009 (Time 2). There were 1543 participants at Time 1 and of those, 993 participated at Time 2; Using information from participants who had valid depression scores at both time points (n=801), change in probable major depression (PMD) status was assessed between the two time points. **Outcome Measures:** Older Adult Health and Mood Questionnaire (OAHMQ). | 1. 22.1% of participants had probable major depression (PMD) at Time 1 and 20.2% at Time 2. 2. Of those who had PMD at Time 1, 55.7% had PMD at Time 2. Between the two time points, the most change occurred in the group with clinically significant symptomatology. 3. Demographic factors (race-gender, age, time since injury) and health behaviours (pain medication use, hours out of bed, days out of the house, exercise) were significantly associated with PMD over time. 4. Socio-economic factors (income, education) were significantly related to depression but were not significant after controlling for behavioural factors. |
| Hitzig et al. 2010; Canada Longitudinal N=344 | **Population:** 344 subjects with SCI (293M 51F); 62 incomplete tetraplegia, 81 complete tetraplegia, 92 incomplete paraplegia, 109 complete paraplegia; age range 24-86 yrs; YPI 7-58. **Treatment:** AT Jousse Long-Term Follow-Up Questionnaire administered over the telephone during 1995-1997 (time 1) and 2003-2004 (time 2). Data collected on socio- | 1. Secondary health conditions (spasticity, pressure ulcers, bladder infections, kidney problems, cardiac problems, high blood pressure, respiratory complications, arthritis/joint pain, chronic pain, and psychological stress) increased significantly over time except for bowel problems, which decreased. 2. Mean health status at Time 1 |

| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| | demographics, mortality, impairment, health status, secondary health concerns and mobility. **Outcome Measures:** Chi square analyses, dependent samples t-test. | decreased significantly by Time 2. |
| Charlifue et al. 1999; USA Longitudinal N enrolled=439 N final=315 | **Population:** 315 individuals with SCI, mean(SD) age 37.1(0.6) yrs, mean(SD) YPI 9.3(0.2). **Methodology:** Subjects studied initially at their 5th, 10th, and 15th anniversaries post-injury and subsequently 5 yrs later at their 10th, 15th, and 20th anniversaries post-injury. **Outcome Measures:** Physical and psychosocial status. | 1. Para AIS ABC group reported significantly more fatigue between Time 1 and 2. Tetra AIS ABC group reported an increase in the need for physical assistance but had fewer reports of constipation, bladder stones and bleeding. |

## Discussion

Premature aging with a number of different organ systems appears to lead to the higher prevalence of a number of secondary health conditions compared to the normative population (Jensen al. 2013). Of concern is that more medical attention is required over time to address these secondary health complications (Krause et al. 2013). As with the general population (Roy 1986; Gaston-Johansson et al. 1996; Poluri et al. 2005), issues of fatigue and pain can limit the independence of a person with SCI. Fatigue can be defined as an overwhelming sense of tiredness, lack of energy and often a feeling of total exhaustion (Herlofson & Larsen, 2002). Fatigue after SCI is a prevalent issue (Gerhart et al. 1999; McColl et al. 2003; McColl et al. 2004; Fawkes-Kirby et al. 2008). The findings on the associations between age and fatigue after SCI have been somewhat conflicting. For example, one study found that males with SCI reported an increased fatigue with increasing age (Pentland et al., 1995), whereas some have found greater reports of fatigue in younger persons with SCI with short durations of injury (McColl et al. 2003).

Both pain and fatigue have been both found to negatively impact on several domains of function and QoL (Rintala et al. 1998; Ingles et al. 1999; Herlofson & Larsen 2002). As well, there is some evidence of a relationship between fatigue and pain after SCI (Fawkes-Kirby et al. 2008). When examined together, the study by Charlifue and colleagues (1999) and by Putzke and colleagues (2002a) highlight chronological age as a factor that mediates the expression and/or onset of change. In the study by Charlifue et al. (1999), the youngest and oldest group reported no significant changes in fatigue between Time 1 and Time 2. Similarly, in the study by Putzke et al. (2002a) the youngest and oldest group reported the least amount of pain interference between Year 1 and Year 2; however, overall, older individuals were significantly more likely to report pain in both years than younger individuals with SCI. In terms of the influence of pain and the interference of pain on QoL over time, Putzke et al. (2002a) found that those individuals who experienced increased interference over time had decreased life satisfaction scores, whereas those whose interference subsided had increased life satisfaction. Similarly, Stensman (1994) observed over 5 years that individuals with variable pain experienced fluctuating global QoL, those with constant pain experience consistently low QoL, and those with no or little pain had consistently high or improvements to an initially low QoL over time.

The finding by Charlifue and colleagues (1999) that increasing age is associated with increased fatigue and additional physical assistance is congruent with other studies examining the effects of long-term SCI (e.g. Gerhart et al. 1993; Thompson, 1999; Liem et al. 2004). A limitation noted by Charlifue et al. (1999) was that their sample was relatively 'young' (M = 37.1 years), and none having lived with their SCI for more than 20 years (M = 9.3), and may not have aged enough to significantly

affect overall health and functional status. However, the consistent findings for increased fatigue between Time 1 and Time 2 do highlight that there is a consistent physical decline occurring. Charlifue and colleagues (1999) recognized the systematic changes in their sample (i.e. improved health but declining functionality) but attributed them to external factors such as less contact with the healthcare system, funding changes, which lead to fewer participants reporting particular outcomes. As well, they noted the need for increased physical assistance over time in their sample may have reflected attitude changes in rehabilitation practice where maintaining functionality is preferred over complete physical independence. Although the strength of the study is its provision of several perspectives to aging with a SCI, an alternative analysis strategy might have helped to provide a more cohesive model of how the factors assessed related to one another. For instance, the increases in physical assistance between Time 1 and Time 2 were often accompanied with improvements in health but also with increases in fatigue. Reporting on associations (or lack of) between these variables may have provided additional support for their conclusions.

**Conclusions**

*There is Level 3 evidence (Jensen et al. 2013) from a scoping review that cardiovascular disease, diabetes, bone mineral density loss, fatigue and respiratory complications or infections occur with higher frequency in older individuals or those with longer SCI duration, relative to younger individuals or those with shorter SCI duration.*

*There is Level 4 evidence (Ullrich et al. 2013) from one longitudinal study that co-occurrence of pain and depression is common among persons who have lived with SCI for many years and remains stable over time. There is also evidence that comorbid pain and depression are associated with higher severity of conditions, more persistent conditions over time, and more utilization of SCI specialty health-care services.*

*There is Level 4 evidence (Hitzig et al. 2010; Pershouse et al. 2012) that secondary health complications increase over time in persons with SCI, (with the exception of bowel problems, which decrease).*

*There is Level 4 evidence from a longitudinal study (Charlifue et al. 1999) that fatigue and the need for physical assistance increases over time with SCI.*

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Fatigue and the need for physical assistance may increase over time with SCI.

The number of secondary health complications increase with more years post injury.

The incidence and severity of UTIs decrease over time in persons with SCI and prevalence of pressure sores remain stable.

The co-occurrence of pain and depression is common in persons who have lived with SCI for many years.

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**4.0 Functional Independence**

Motor and sensory impairments after spinal cord injury cause a variety of functional impairments. Functional impairments are defined as restrictions that hinder an individual's ability to perform tasks or activities (Jette 2006). Functional tasks are often described in terms of basic activities of daily living such as walking, climbing stairs, bathing and grooming. With complete lesions, higher levels of injury cause greater motor and sensory impairment, which are associated with greater functional impairments (Aidinoff et al. 2011).  Incomplete lesions produce a more complicated pattern of motor and sensory impairments (Yilmaz et al. 2005). Individuals who have problems performing functional tasks frequently rely on a combination of assistive devices and assistance from others. Haisma et al. (2008) found that functional motor independence improved during in-patient rehabilitation and

remained relatively stable one year post-discharge. Given that functional independence is a strong, significant predictor of care needs over time (Cohen et al. 2012), it is extremely important to understand the long-term functional independence of individuals with spinal cord injury.

In this section, 1 systematic review (see Table 12) and 5 longitudinal studies (see Table 13) on functional independence after SCI are reviewed.

**Table 12: Systematic Review on Functional Independence**

| Author Year; Country Date included in the review Total Sample Size Level of Evidence Type of study Score | Methods Databases | Outcome |
|---|---|---|
| Al-Habib et al. 2011; Saudi Arabia<br><br>Reviewed published articles from 1966 to April 2008<br><br>N=10<br><br>**Level of Evidence:** Class 1 and 2:<br><br>**Type of study:** 3 retrospective cohort 1 retrospective analysis of an RCT 3 observational 3 RCT<br><br>AMSTAR: 6 | **Method:** Literature search for published English articles that explored clinical factors associated with neurological and functional outcomes following traumatic SCI in adults. No intervention. Outcome measures include ASIA classification, FIM, SCIM and SF36.<br><br>**Databases:** MEDLINE and EMBASE. | 1. Patient related Predictors:<br>   Level 2 Evidence:<br>   - Motor recovery (as measured by ASIA) and functional recovery (as measured by SCIM) decreases with advancing age for complete SCI patients.<br>   - Age is not a significant predictor when incomplete SCI were included in the analysis. |

In this systematic review, the authors report that motor and functional recovery decreases with advancing age for complete SCI. They also report no association between recovery and age for individuals with incomplete SCIs. Only three studies were included in this review that examined the association with age. This may indicate a dearth of evidence on the impact of aging on functional independence, and that the results should be interpreted with caution.

**Table 13: Aging and Functional Independence**

| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| Cohen et al. 2012; USA Retrospective longitudinal N=11685 | **Population:** 11685 persons with SCI (9071M, 2614F); Available number of subjects at follow up: Year 1=9644, Year 5=5323, Year 10=2763, Year 15=1144, Year 20=191.<br>**Methodology:** Data from the National Spinal Cord Injury Statistical Center database (1988–2010) were analyzed. The authors | 1. All outcomes were statistically associated with higher FIM scores at discharge.<br>2. Each one-point increment in FIM was associated with improvements in: probability of institution care at discharge (-0.34%) and at follow-up (-0.13%), FIM score at follow-up (0.76 |

| Author Year; Country<br>Score<br>Research Design<br>Total Sample Size | Methods | Outcome |
|---|---|---|
| | investigated the association between motor FIM at rehabilitation discharge and residential status, survival and outcomes at 1, 5, 10, 15 and 20 years follow-up, including FIM, residential status, hospitalizations, days hospitalized in previous year, daily paid and total care and paid hours worked. Regression controlled for injury completeness, neurological level, demographic characteristics and temporal effects.<br>**Outcome Measures:** FIM, residential status, hospitalizations, days hospitalized in previous year, daily paid and total care and paid hours worked. | points), hospitalizations and days hospitalized/year (-0.0044 and -0.071, respectively), probability of needing paid assistance (-0.72%) or any assistance (-0.85%) and probability of paid work (0.41%).<br>3. Survival rates after discharge (Kaplan-Meyer) were: 88.7% for 5 yrs, 82.2% for 10 yrs, 76.5% for 15 yrs and 73.5% for 20 yrs. |
| Pershouse et al. 2012;<br>Australia<br>Retrospective longitudinal<br>N=270 | **Population:** 270 persons with traumatic SCI (81% male); mean (SD) age in yrs: 43.3(11.4), range 20-76; mean (SD) age at injury in yrs: 27.3(9.7).<br>**Methodology:** Data were collected via telephone interviews and written questionnaires annually over 5 years, between 2004 and 2008, across 6 strata comprising participants grouped according to time since injury (<5y, 5–9y, 10–14y, 15–19y, 20–24y, ≥25y).<br>**Outcome Measures:** motor subscale of FIM (mFIM) | 1. There was a significant decrease in activity as measured by the mFIM for higher functioning individuals<br>2. Activity limitations significantly increased with duration of injury. |
| Mitchell & Adkins 2010;<br>USA<br>Longitudinal with AB controls<br>N SCI=26<br>N controls=38 | **Population:** 26 individuals with SCI, mean(SD) age at baseline 50.3(11.2) yrs, mean(SD) YPI at baseline 25.2(14.2); YPI >5 yrs, no cognitive impairment. 38 age matched AB controls, mean(SD) age at baseline 50.4(11.5) yrs.<br>**Methodology:** Data collection at two time periods 5 years apart from 1999 - 2002, and 2004 -2007.<br>**Outcome Measures:** Self-related health (SRH). Potential predictors of SRH included: aging, Self-report Activities of Daily Living (ADL) and independent activities of daily living (IADL); 4-point pain severity scale; Fatigue Severity Subscale from the Fatigue Assessment Instrument; The Older Adult Health and Mood Questionnaire. | 1. Over time, the SCI group differed significantly from comparison group on the following measures: lower score on ADLs and lower score on IADLs.<br>2. Strong decrease in IADLs over the 5 years for SCI subjects (baseline vs. follow-up mean=4.42 vs.2.42) control group (6.95 vs. 6.45). |
| Amsters et al. 2005;<br>Australia<br>Longitudinal<br>N=84 | **Population:** 84 persons with SCI (70M, 14F) who sustained injury >20 yrs previously and were >15 yrs old at time of injury; mean (SD) age in yrs: 52(9.3), range 40-78; mean (SD) DOI in yrs: 28(6.2), range 20-51; mean (SD) age at onset in yrs: 24(7.2), range 15-49.<br>**Methodology:** Motor subset scores of the Functional Independence Measure (FIM) and a single scale measuring mobility aids status (MAIDS) were collected via telephone | 1. A significant number of participants (n=45) perceived that their function had increased between the discharge and mid points and had subsequently decreased between the mid and current points (n=39). Age, age at onset and duration of injury did not significantly differ between those who experienced functional improvement, remained unchanged or declined. |

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| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| | interview with participants for three points in time – post discharge from initial rehabilitation (discharge point), approx. 10 YPI (mid point), and currently (current point). **Outcome Measures:** Motor subset scores of FIM (included items on self care, sphincter control, mobility, and locomotion), single scale measuring mobility aids status (MAIDS). | 2. More individuals experienced functional improvement between the discharge and mid points for Mobility, Locomotion, and Self Care while significantly more individuals experienced functional decline between the mid and current points for Mobility, Locomotion, and Self Care.<br>3. Participants also reported an increasing dependence on mobility aids between the mid point and the current point.<br>3. Those who reported functional decline between the mid and current points were significantly older than those who did not report functional decline but did not differ in duration of injury or age at onset. |
| Hall et al. 1999; USA Longitudinal N: at rehab admission (3971); Discharge (4033); 1 year post-injury (903); 2 years post-injury (712); 5 years post-injury (570) | **Population:** Data drawn from SCI Model Systems National Database. Total number of cases for each time point are listed left. Inclusion criteria include, >16 years old, AIS A/B/C, admitted to inpatient rehabilitation within 60 days after injury. **Methodology:** FIM scored by observation at inpatient rehabilitation admission and discharge. Follow-up ratings obtained mostly by interview of the client, either by phone or in person. **Outcome Measures:** FIM motor and cognition subscales | 1. FIM motor items were consistent with level of injury and neurological status, providing information on functional independence across a continuum.<br>2. Trends over years 1, 2, and 5 were stable for both motor and cognition subscales. FIM motor gains were greatest between admission and discharge, and gains continued through 1 year after injury, but at a much-decreased rate.<br>3. No difference in FIM mean motor gain scores between those whose neurological level did or did not improve between inpatient rehab admission and discharge. Gains remained the same for those who improved from grade A to B or C. However, statistically significant greater gains were seen for those who improved from B to C, B to D or C to D. |

## Discussion

All the studies report some decline in functional independence over time, although interestingly, Amsters et al. (2005) found that individuals with SCI perceived functional improvements in the first 10 years post-injury and then a subsequent decline. This study recalls from recall bias as individuals were asked to recall their function up to 10 years post-injury.

## Conclusions

***There is level 4 evidence from one retrospective longitudinal study (Pershouse et al. 2012) that functional independence decreases with more years post injury for individuals who were higher functioning at one year.***

***There is Level 5 evidence from one longitudinal study (Amsters et al. 2005) that individuals with SCI (≥20 YPI) perceive functional improvements up to 10 YPI and subsequent functional decline and greater dependence on mobility aids after 10 or more YPI.***

> Functional independence decreases with more years post injury.

## 5.0 Quality of Life and Community Reintegration

In the general population, advancing into older adulthood is a period when individuals are faced with a unique array of physical, functional, and environmental stressors. This is no different for individuals aging with a traumatic SCI, who are now living an average of 30 to 40 years post-injury (YPI) (Samsa et al. 1993). As more individuals with SCI survive into their second, third, and even later decades, living with a disability becomes a life-long process for persons with SCI (Hallin et al. 2001).

Given the evidence in the previous sections of this chapter indicating that SCI represents a model for premature aging in some body systems (e.g. cardiovascular and endocrine, musculoskeletal, immune, and respiratory systems), the physical and functional declines associated with natural aging are likely to present more quickly among individuals with SCI. Such knowledge of these effects of aging however is insufficient for rehabilitation purposes without any indication of how individuals perceive the aging-related changes and how they adapt their lifestyles in response to such changes (Charlifue et al. 2010).

A key goal of rehabilitation is to enable successful community reintegration and high QoL. QoL describes the well-being and life satisfaction of an individual, and is a multi-factorial construct, which includes but is not limited to self-assessments of interpersonal relationships and social support, physical and mental health, environmental comfort, and a host of psycho-social factors (Kaplan & Erickson 2000). Community reintegration is an important construct shown to be predictive of life satisfaction in persons with SCI (e.g. Pierce et al. 1999; Richards et al. 1999; Putzke et al. 2002b; Tonack et al. 2008; Kemp & Bateham 2010). Community reintegration has been defined as returning to family and community life, engaging in normal roles and responsibilities, and actively contributing to one's social groups and to society as a whole (Dijkers 1998). Thus successful reintegration involves resuming occupations or activities deemed important to the individual and society (i.e. self-care, employment, leisure, etc.; Yasui & Berven 2009). Environmental factors (e.g. social, institutional, cultural or physical) can either create barriers or facilitate reintegration, which impacts QoL (Anderson 2004).

In the general population, older adults frequently experience physical declines (Branch & Jette 1983) that may limit their activities of daily living (e.g., Hoyer et al. 1999), and negatively impact community reintegration and QoL. Similarly, both physical and mental health factors influence QoL in persons with SCI. For instance, poor physical health, secondary health conditions (e.g. pressure ulcers, pain, etc.), depression and stress have all been shown to negatively affect QoL (Craven et al. 2012).

With regards to aging, however, there are some mixed findings in relation to community reintegration and QoL, even within the same studies. Some studies reports that life satisfaction, QoL and community reintegration (at least in some domains) improve with years post-SCI (e.g. Zarb et al. 1990; Pentland et al. 1995; Westgren & Levi, 1998; Dijkers 1999; Tonack et al. 2008), whereas other studies indicate older age is associated with poorer community reintegration and QoL (e.g. Krause & Crewe 1990; Eisenberg & Saltz 1991; Whiteneck et al. 1992; Tonack et al. 2008). The discrepancies with aging and QoL tend to be more evident in cross-sectional analyses whereas longitudinal studies "mostly show relatively high and stable levels of QoL over long periods of time" (Kemp & Ettelson 2001, p. 119; Savic et al. 2010). An additional point to consider is that these differences may arise due to the use of different instruments, which may not all assess the same underlying QoL construct.

In this section, one systematic review (see Table 14), twenty-five longitudinal studies and two cross-sectional studies (See Table 15) on community reintegration and QoL after SCI are reviewed.

**Table 14: Systematic Review on Quality of Life and Community Reintegration**

| Author Year; Country Date included in the review Total Sample Size Level of Evidence Type of study Score | Methods Databases | Outcome |
|---|---|---|
| Sakakibara et al. 2012; Canada<br><br>Reviewed published articles from 1980 to 2011<br><br>N=21<br><br>Level of Evidence: Modified Sackett scale (all were level 4)<br><br>Type of study: Longitudinal<br><br>AMSTAR: 7 | **Methods:** Electronic databases were searched for peer-reviewed published studies reporting on age-related QoL changes over time in adults with traumatic SCI; data from relevant studies were transcribed into data extraction forms and analyzed by years post injury (YPI) and chronologic age. No interventions studied. Outcome measures include various QoL measures ex: Satisfaction with Life Scale (SWLS), Quality of Life Index (QLI), Life Satisfaction Questionnaire (LSQ).<br><br>**Databases:** MEDLINE/PubMed, CINAHL, EMBASE and PsycINFO. | 1. In individuals with advanced YPI, overall QoL is consistently reported as good or excellent over time, however, with variations in different QoL domains.<br>2. In 4 studies with samples with mean ages in the late teens and 20s and 5 or less YPI, both overall QoL and various domains of QoL were shown to significantly increase with age.<br>3. 7 studies found individuals first assessed in their 20s (YPI ranging from 6-15 yrs) improved employment after 25 yrs of follow-up, but decreased satisfaction with social and sex lives, and general health. Similarly for individuals first assessed in their 30s, employment satisfaction increased but satisfaction with social and sex life, family relationships, recreational and life opportunities, emotional adjustment and control over life all diminished after a 9 year follow-up.<br>4. 3 studies reported on individuals with at least 16 YPI and showed that although life satisfaction was variable over the yrs, after 16 yrs the reported life satisfaction was higher than at earlier follow-ups. |

**Table 15: Quality of Life and Community Reintegration**

| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| Krause & Bozard 2012; USA Prospective Longitudinal N=64 | **Population:** 64 participants with traumatic SCI (88% male, 12% female); mean (SD) age at follow-up in yrs: 61.5(7.2); mean (SD) YPI in yrs: 41.4(4.9).<br>**Methodology:** Participants were enrolled in 1973 from a specialty hospital in the Midwestern United States and assessed again approximately 35 years later. Data were collected by mailed survey.<br>**Outcome Measures:** The Life Situation Questionnaire. | 1. Overall, social participation decreased over time, although the sitting tolerance and hours spent in gainful employment increased.<br>2. Satisfaction with employment improved over time, whereas satisfaction with social life, sex life and health declined.<br>3. Self-reported adjustment improved, but the prediction of future adjustment in 5 yrs declined. |
| Pershouse et al. 2012; | **Population:** 270 persons with traumatic SCI | 1. Quality of life remained relatively |

| Author Year; Country<br>Score<br>Research Design<br>Total Sample Size | Methods | Outcome |
|---|---|---|
| Australia<br>Retrospective Longitudinal<br>N=270 | (81% male); mean (SD) age in yrs: 43.3(11.4), range 20-76; mean (SD) age at injury in yrs: 27.3(9.7).<br>**Methodology:** Data were collected via telephone interviews and written questionnaires annually over 5 years, between 2004 and 2008, across 6 strata comprising participants grouped according to time since injury (<5y, 5–9y, 10–14y, 15–19y, 20–24y, ≥25y).<br>**Outcome Measures:** World Health Organization Quality of Life-8 (WHOQOL-8); Community Integration Measure (CIM) | constant across the lifespan<br>2. Participation, as measured by the CIM, showed a significant increase with time since injury, but not when adjusted for the American Spinal Injury Association Impairment Scale, income level, and living situation. |
| van Leeuwen et al. 2012;<br>Switzerland<br>Prospective longitudinal<br>N=206 | **Population:** 206 persons with recently acquired SCI; Age: range 18-65 yrs<br>**Methodology:** measurements at the start of active rehabilitation, after 3 mos, at discharge, 1, 2, and 5 years after discharge.<br>**Outcome Measures:** Mental Health Index (MHI-5) | 1. Levels of mental health increased between the start of active rehabilitation and 3 mos later, remained stable thereafter, and increased again between 2 and 5 years after discharge.<br>2. Latent class growth mixture modeling revealed 5 mental health trajectories: (1) high scores (above 80) at all time-points (52%), (2) low scores (≤60) at all time-points (4%), (3) early recovery from 40 to scores above 70 (13%), (4) intermediate scores from 60 to scores above 70 (29%), and (5) severe deterioration of scores above 70 to scores below 30 (2%). |
| DeVivo & Chen 2011;<br>USA<br>Longitudinal<br>N=1591 | **Population:** 1591 individuals with paraplegia and tetraplegia, complete and incomplete; Mean age 39.5 yrs; Mean YPI 1.0.<br>**Methodology:** Subjects studied at seven time points at 1, 5, 10, 15, 20, 25, and 30 YPI.<br>**Outcome Measures:** Satisfaction with Life Scale. | 1. Life satisfaction consistently increased over the 30 years of observation. |
| Kalpakjian et al. 2011;<br>USA<br>Longitudinal<br>N=6141 | **Population:** 6141 individuals with paraplegia and tetraplegia, complete and incomplete; Mean age 39.0 yrs; Mean YPI 1.0; Male = 4864.<br>**Methodology:** Subjects studied at 1 to >5 time points at 1 and 5 YPI, and every 5 years after.<br>**Outcome Measures:** Satisfaction with Life Scale. | 1. Life satisfaction was shown to improve over time.<br>2. Life satisfaction of those separated or divorced increased over time and did so to a greater degree for women. |
| Van Leeuwen et al. 2011;<br>The Netherlands<br>Longitudinal<br>N=206 | **Population:** 206 subjects with SCI (153M 53F); Mean age 41.5 yrs, range 26.2-56.9.<br>**Methodology:** Subjects studied at six points in time (Beginning of rehabilitation; 3 months after beginning of rehabilitation; at discharge, 1 year post discharge, 2 years post discharge and 5 years post discharge).<br>**Outcome Measures:** Two study specific questions: 1) current life satisfaction; and 2) life satisfaction now vs prior to SCI. | 1. 56 subjects had consistently low, yet improving, life satisfaction.<br>2. 34 subjects had consistently high life satisfaction.<br>3. 63 subjects had intermediate scores.<br>4. 48 subjects improved their life satisfaction.<br>5. 5 subjects had deteriorating life satisfaction. |

| Author Year; Country<br>Score<br>Research Design<br>Total Sample Size | Methods | Outcome |
|---|---|---|
| Mitchell & Adkins 2010;<br>USA<br>Longitudinal with AB controls<br>N SCI=26<br>N controls=38 | **Population:** 26 individuals with SCI, mean(SD) age at baseline 50.3(11.2) yrs, mean(SD) YPI at baseline 25.2(14.2); YPI >5 yrs, no cognitive impairment. 38 age matched AB controls, mean(SD) age at baseline 50.4(11.5) yrs.<br>**Methodology**: Data collection at two time periods 5 years apart from 1999 - 2002, and 2004 -2007.<br>**Outcome Measures:** Self-related health (SRH). Potential predictors of SRH included: aging, Self-report Activities of Daily Living (ADL) and independent activities of daily living (IADL); 4-point pain severity scale; Fatigue Severity Subscale from the Fatigue Assessment Instrument; The Older Adult Health and Mood Questionnaire. | 1. SCI subjects and control group declined significantly in SRH overtime.<br>2. SRH ratings at follow-up significantly differed by group: decrease in excellent/very good category from 57.7% to 24.6% for the SCI group and decrease from 76.3% to 63.2% in control group.<br>3. Aging has greater influence on SRH in people with SCI than on those without a SCI.<br>4. Over time, the SCI group differed significantly from comparison group on all health measures: increase in health conditions, increase in fatigue, decrease in ADLs and decrease in IADLs. |
| Mortenson et al. 2010;<br>Canada<br>Longitudinal<br>N=93 | **Population:** 93 subjects with SCI (83M 10F); Mean age 39.6 yrs, range 18-78 yrs; Mean YPI >0.25 post discharge.<br>**Methodology:** Subjects studied at two time points between 1999 and 2003 (3 months and 15 months post discharge).<br>**Outcome Measures:** Quality of Life Index. | 1. No QoL differences were observed between time points.<br>2. Average QLI scores were 19.66 out of 30. |
| Savic et al. 2010;<br>Britain<br>Longitudinal<br>N=122 | **Population:** 122 subjects with SCI (103M 19F); Mean age 48.0 yrs; Mean YPI 26.8.<br>**Methodology:** Subjects studied at six points in time (1990; 1993; 1996; 1999; 2002; and 2006).<br>**Outcome Measures:** Life Satisfaction Index. | 1. 76% consistently rated good or excellent QoL over 16 years.<br>2. Differences in life satisfaction were observed over the 16 yr period.<br>3. Life satisfaction was highest in the final (2006) follow up. |
| Barker et al. 2009;<br>Australia<br>Cross-sectional<br>N=270 | **Population:** 270 individuals (220M 50F) with SCI **(**Tetraplegia = 107; Paraplegia = 100; Others=63); Mean age (range) = 43.0 (20-76); YPI (range) = 15.0 (9-21).<br>**Methodology:** Comparison of QoL between SCI and AB groups, and group differences were observed by age.<br>**Outcome Measures:** World Health Organization Quality of Life Assessment Instrument (WHOQOL)-Brief. | 1. QoL was lower than the Australian norm.<br>2. Overall, mean scores in each of the 4 domains (Physical health, Psychological health, Social Relationships, Environment) were lower for individuals with SCI.<br>3. Analyses by age group showed significant differences between SCI and norm data in all domains, with the exception of the 60s and over age group that differed in the Physical health domain only.<br>4. No differences were detected between people with SCI of different ages and times since injury. |
| Krause et al. 2009;<br>USA<br>Longitudinal<br>N=250 | **Population:** 250 individuals (142M 108F) with SCI **(**Tetraplegia = 133; Paraplegia = 117); Mean age = 42.5 yrs; YPI = 14.0.<br>**Methodology:** Subjects studied at two points in time 6 years apart.<br>**Outcome Measures:** Life Satisfaction Questionnaire. | 1. Differences in the satisfaction domain did not systematically or significantly increase or decrease over time. |
| Van Koppenhagen et al. | **Population:** 222 individuals with SCI | 1. Individuals unsatisfied with their life |

| Author Year; Country<br>Score<br>Research Design<br>Total Sample Size | Methods | Outcome |
|---|---|---|
| 2009;<br>The Netherlands<br>Longitudinal<br>N=222 | (Tetraplegia complete= 54, Paraplegia complete= 96, Other = 38); Mean age (range) = 41.5 yrs (18-65); YPI = <0.9; Male = 165.<br>**Methodology:** Subjects studied at four points in time (Beginning of rehabilitation; 3 months after beginning of rehabilitation; at discharge and 1 yr post discharge).<br>**Outcome Measures:** Two study specific questions: 1) current life satisfaction; and 2) life satisfaction now vs. prior to SCI. | decreased from 74.6% at time 1 to 49.3% at time 4.<br>2. Individuals with deterioration in life satisfaction after SCI decreased from 85.8% at time 1 to 75.3% at time 4.<br>3. There was a significant increase in life satisfaction total scores between times 1 and 3, and stable scores from times 3 to 4. |
| Krause & Coker 2006;<br>USA<br>Longitudinal<br>N initial=256<br>N final=78 | **Population:** 78 respondents with SCI, mean(SD) age 55.7(7.6) yrs and mean(SD) YPI 35.8(4.7) at follow-up; mean(SD) age at enrollment 35.1(13.9) yrs and mean(SD) YPI at enrollment 9.7(6.9).<br>**Methodology:** Subjects assessed 3 times over a 30-year period (1973, 1988, 2002).<br>**Outcome Measures:** Life Situation Questionnaire (LSQ). | 1. During the first 15-year period, an increase was seen in sitting tolerance, educational and employment outcomes, satisfaction with employment, and adjustment.<br>2. During the last 15 years, sitting tolerance decreased, the number of physician visits increased, and satisfaction with social life and sex life decreased. |
| Bushnik & Charlifue 2005;<br>USA<br>Longitudinal<br>N=63 | **Population:** 63 individuals, C1-C4, sustained at a mean(SD) age of 24.2(2.2) yrs; Mean(SD) age (yrs): phase 1 = 29.7(8.1), phase 2 = 37.4(8.4), phase 3 = 43.2(8.4); Mean(SD) YPI: phase 1 = 5.3(2.4), phase 2 = 13.1(2.5), phase 3 = 18.9(2.6).<br>**Methodology:** Subjects assessed 14-24 YPI over three phases of data collection. Phase 1: 1984-1985; Phase 2: 1992-1994; and Phase 3: 1997-1999.<br>**Outcome Measures:** Demographics, respiratory support, assistance with care, psychosocial data, and time utilization data. | 1. Over the three phases of data collection, most indicators of quality of life and community participation remained at high levels with little variability. For those indicators that changed, SCI itself and not necessarily a high level of injury, and/or the aging process accounted for the change over time. Economics and advances in technology were responsible for changes in other indicators. |
| Krause & Broderick 2005;<br>USA<br>Longitudinal<br>N initial=161<br>N final=95 | **Population:** 95 individuals with SCI, mean(SD) age 53.8(9.2) yrs and mean(SD) YPI 32.2(5.6) at follow-up.<br>**Methodology:** Subjects assessed twice over a period of 25 years (1974 and 1998).<br>**Outcome Measures:** Life Satisfaction Questionnaire (LSQ). | 1. Employment outcomes improved; rate and satisfaction increased.<br>2. Participants continue to adapt to aging with SCI (increasing adjustment scores), yet experience declines in health (increase in number of physician visits) and social activities (decrease in number of outings and visitors) that were associated with diminished satisfaction with particular areas of life (i.e. social and sex lives). |
| Charlifue & Gerhart 2004a;<br>USA<br>Longitudinal<br>N=178 | **Population:** 178 individuals with SCI, age 43-83 yrs, YPI 29-55 at final phase of study.<br>**Methodology:** Subjects evaluated at 3 yr intervals from 1990-1999.<br>**Outcome Measures:** Craig Handicap Assessment and Reporting Technique (CHART), Life Satisfaction Index (LSI-Z), Index of Psychological Well-Being (IPWB), Center for Epidemiological Studies | 1. Community reintegration decreased over time – a significant relationship between perceived life satisfaction and community integration was revealed. |

| Author Year; Country<br>Score<br>Research Design<br>Total Sample Size | Methods | Outcome |
|---|---|---|
| | Depression Scale (CES-D), Perceived Stress Scale (PSS). | |
| Charlifue & Gerhart 2004b;<br>USA<br>Longitudinal<br>N=189 | **Population:** 189 subjects with SCI; age (range) 43-83 yrs and YPI 29-55 at final phase of study.<br>**Methodology:** Subjects evaluated at 3 yr intervals from 1990-1999.<br>**Outcome Measures:** Life Satisfaction Index (LSI-Z), Index of Psychological Well-Being (IPWB), Center for Epidemiological Studies Depression Scale (CES-D), Perceived Stress Scale (PSS); Perceived Quality of Life. | 1. LSI-Z scores were significantly correlated with perceived quality of life 3 yrs later at all three data points.<br>2. Previous scores on perceived quality of life were correlated with perceived well-being 3 yrs later at all three data points.<br>3. Being male, older, longer injured, and having functionally complete tetraplegia were related to worse outcomes. |
| Bushnik 2002;<br>USA<br>Longitudinal<br>N=58 | **Population:** 58 individuals with complete high tetraplegia (C1-C4); Mean(SD) age (yrs): phase 1 = 29.5(8.4), phase 2 = 37.3(8.7), phase 3 = 43.0(8.7); Mean(SD) YPI: phase 1 = 4.8(2.2), phase 2 = 12.7(2.4), phase 3 = 18.5(2.4).<br>**Methodology:** Subjects assessed up to 24 YPI over three phases of data collection. Phase 1: 1984-1985; Phase 2: 1992-1994; Phase 3: 1997-1999.<br>**Outcome Measures:** High Tetraplegia Questionnaire (HQQ) consisting of questions regarding assistance with care, respiratory support, special equipment, and costs, participation in work and leisure activities; Modified Level of Free Time Activities Scale; Rosenberg Self-Esteem Scale (RSE). | 1. An association between access to modified vans and perceived QoL was revealed. The proportion of individuals who rated their lives as "good or excellent" was higher in all three phases for those with modified vans, reaching statistical significance in Phases 2 and 3.<br>2. No significant changes in equipment utilization nor self-esteem or subjective QoL across time periods.<br>3. Participation in at-home leisure activities (e.g. reading, listening to the radio) significantly decreased from Phase 1 to Phase 2.<br>4. Older individuals spent fewer hours per day out of bed and fewer days per week out of the house than younger participants in Phase 1. In Phase 3, older individuals participated in fewer leisure activities at home than younger participants.<br>5. Income increased over time for the sample. |
| Putzke et al. 2002b;<br>USA<br>Longitudinal<br>N=270 | **Population:** 270 subjects with SCI.<br>**Methodology:** Subjects studied at 1 and 2 years post-injury.<br>**Outcome Measures:** Life satisfaction, physical and mental health. | 1. Those developing pain (i.e. pain-free at year 1 and in pain at year 2) reported decreased life satisfaction, physical and mental health, whereas those resolving pain from year 1 to year 2 reported an increase in the same domains.<br>2. Change in pain interference status was unrelated to change in self-reported handicap. |
| Charlifue et al. 1999;<br>USA<br>Longitudinal<br>N enrolled=439<br>N final=315 | **Population:** 315 individuals with SCI, mean(SD) age 37.1(0.6) yrs, mean(SD) YPI 9.3(0.2).<br>**Methodology:** Subjects studied initially at their 5th, 10th, and 15th anniversaries post-injury and subsequently 5 yrs later at their | 1. Between time 1 and time 2, self-reports of constipation, bladder stones, rectal bleeding, and personal well-being scores decreased (indicating an increase in well-being). Participants also |

| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| | 10th, 15th, and 20th anniversaries post-injury. **Outcome Measures:** Physical and psychosocial status. | reported requiring more physical assistance. 2. Para AIS ABC group reported significantly more fatigue between Time 1 and 2. Tetra AIS ABC group reported an increase in the need for physical assistance but had fewer reports of constipation, bladder stones and bleeding. |
| Kemp & Krause 1999; USA Cross-sectional N SCI=177 N controls=62 | **Population:** 177 subjects with SCI; mean age at onset 25.5 yrs; mean age at enrollment 40.1 yrs. 62 healthy subjects; mean age at enrollment 63.7 yrs. **Methodology:** Comparison of life satisfaction and depression between the 2 groups. **Outcome Measures:** 10-item scale to evaluate life satisfaction. | 1. The AB comparison group had significantly greater satisfaction than the SCI group in life areas related to: health, health care, finances, friendship, emotional health, housing, work or time use, leisure, and overall life. |
| Charlifue et al. 1998; USA Longitudinal N=227 | **Population:** 227 individuals with SCI, YPI at enrollment >20, age (range) at injury 15-55 yrs, mean age 54.9 yrs and mean YPI 30.0 at final phase of study. **Methodology:** Subjects contacted twice over a 3-year period (1990 and 1993). **Outcome Measures:** Health and functional status (physical exams), self-perceived health, Functional Independence Measures (FIM), Craig Handicap Assessment and Reporting Technique (CHART), Life Satisfaction Index (LSI-Z), Index of Psychological Well-Being (IPWB), the Center for Epidemiological Studies Depression Scale (CES-D), Perceived Stress Scale (PSS), Current Problem Questionnaire. | 1. LSI-Z scores decreased over time. These were statistically significant only for the older age groups, those injured less than 30 yrs or more than 40 yrs, and those with complete paraplegia. 2. Those who scored high on the LSI-Z experienced higher social integration 3 yrs later. Those who drank more also had higher social integration scores. 3. Those who reported feeling generally healthy were only ¼ as likely to experience fatigue 3 yrs later, while those who reported fatigue previously were more than 5 times more likely to still feel fatigue 3 yrs later. |
| Krause 1998; USA Longitudinal N=114 | **Population:** 114 individuals (95M 19F) with SCI **(**Tetraplegia = 67, Paraplegia = 47); Mean age = 29.9 yrs; Mean YPI = 8.7. **Methodology:** Subjects studied at four points in time (1974; 1985; 1989; 1994). **Outcome Measures:** Life Situation Questionnaire (LSQ). | 1. Satisfaction with employment increased over 20 yrs. 2. Satisfaction with living arrangements improved at each time point, and general health worsened (n.s.). 3. Satisfaction with finances, social and sex lives worsened overall (n.s.). |
| Krause 1997; USA Longitudinal N initial=347 N final=235 | **Population:** 235 subjects with SCI, mean(SD) age at injury 23.1(9.1) yrs, mean(SD) age and YPI at last data collection point: 46.7(10.7) yrs and 23.6(7.4). **Methodology:** Subjects assessed twice over a 9-year period (1985, 1994). **Outcome Measures:** Life Situation Questionnaire (LSQ). | 1. Objective aspects of life situation remained stable (i.e. frequency of visitors and social outings, sitting tolerance) or increased (i.e. employment rate, hours worked) over the study period; however, subjective wellbeing diminished. 2. Participants were less satisfied with their lives, reported more problems with dependency, and were more pessimistic when predicting their future adjustment. 3. Increase in non-routine doctor |

| Author Year; Country Score Research Design Total Sample Size | Methods | Outcome |
|---|---|---|
| | | visits but decrease in the number of hospitalizations, reflecting both actual health and changes in health care practices. |
| Stensman 1994; Sweden Longitudinal N=17 | **Population:** 17 subjects with SCI (15M 2F); Mean age = 32.4 yrs; Mean YPI = 0.5. **Methodology**: Subjects studied at six time points at 0.5, 1, 2, 3, 4, 5 YPI. **Outcome Measures:** Single item to measure perceived QoL. | 1. 5 subjects had consistently high QoL. 2. 6 had low QoL between 0.5 and 3 yrs, and improvements thereafter. 3. 2 had variable QoL over time, influence by variable pain. 4. 4 had consistently low QoL, influenced by constant pain. |
| Krause 1992; USA Longitudinal N=135 | **Population:** 135 individuals (110M 25F) with SCI **(**Tetraplegia = 91; Paraplegia = 44); Mean age = 30.6 yrs; Mean YPI = 9.2. **Methodology:** Subjects studied at two points in time (1974; 1989). **Outcome Measures:** Life Situation Questionnaire (LSQ). | 1. Satisfaction with employment and finances increased. 2. Satisfaction with social life and general health decreased (n.s.). |
| Crewe & Krause 1990; USA Longitudinal N=154 | **Population:** 154 individuals (124M 30F) with SCI **(**Tetraplegia = 95; Paraplegia = 58); Mean age = 32.0; YPI = 10.0. **Methodology:** Subjects studied at two points in time points (1974; 1985). **Outcome Measures:** Life Situation Questionnaire. | 1. Satisfaction with employment increased over 11 yrs. 2. Satisfaction with living arrangements, finances, and social life (n.s). 3. Satisfaction with sex life remained the same, and satisfaction with general health worsened (n.s.). |

## Discussion

Aging is a complex process that does not only encompass biology. Environmental factors also change over time, which may be particularly important to persons with SCI, because they not only face physical limitations associated with their SCI, but also injury-related social and economic changes (Krause & Coker 2006). For example, in a series of papers reporting on the same cohort at different time points over a period of 30 years, there were significant improvements with satisfaction with employment and finances over time (Crewe & Krause 1990; Krause 1992; Krause 1998; Krause & Broderick 2005; Krause & Coker 2006), whereas satisfaction with both social and sexual relationships decreased (Krause 1997; Krause & Broderick 2005; Krause & Coker 2006). Similarly, Bushnik & Charlifue (2005) observed changes related to economics and technology, but not related to SCI or aging per se. For example, letter writing, which probably included emails, increased in the sample over time because home computing had likely become more common. Although not significant, the high percentage of persons who switched to a portable ventilator or pneumobelt from a fixed ventilator may have improved community reintegration for these individuals. As well, the finding that economic self-sufficiency steadily improved with time (e.g. Charlifue & Gerhart 2004a; Krause & Broderick 2005; Krause & Coker 2006) supports Bushnik's (2002) speculation that increased economic standing may improve community reintegration. In the case of Bushnik's (2002) sample, improved financial status enabled better access to adaptive equipment (e.g. modified vans).

Conversely, level of community reintegration for Charlifue & Gerhart's (2004a) sample did not significantly change over time, but this may have been due to sample differences between the studies and that the time between data collection intervals in the other studies reviewed were further apart. As well, the individuals in Gerhart and Charlifue's (2004a) study were at least 20 years post-injury when they entered the study. At 20 years post-injury, it is likely that routines and strategies for community

participation have been well-established, and are not likely to dramatically change over 3 year periods. However, an understanding of environmental factors is important for assessing QoL since there is evidence that an individual's adjustment over time is influenced by corresponding environmental changes (Krause & Sternberg 1997).

With regards to change in activity patterns, Bushnik and Charlifue (2005) attributed the changes to the natural progression of time utilization from external social activities associated with youth (e.g. card games with friends) to other activities (e.g. spending time with family). Further, the reported declines in activity by the SCI cohorts as they aged (e.g., Bushnik 2002, Charlifue and Gerhart 2004a, and Krause and Broderick 2005) might be similar to declines in activity patterns in the general population (Christensen et al. 1996; Bukov et al. 2002).

One of the main strengths of the studies by Krause (1997), Krause and Broderick (2005), and Krause and Coker (2006) is they assessed whether there were any differences between their current sample and those who were lost to follow-up. Based on these analyses, clear survivor effects emerged in both studies as the characteristics of respondents (persons who participated in both data collection periods) at Time 1 were younger, younger at age of SCI-onset, were less years post-injury, had higher levels of education, more likely to have cervical injuries, greater sitting tolerance, and had more social outings than non-respondents (persons who only participated in the first data collection period). These findings highlight that some care should be taken when interpreting the findings from these studies as it may only reflect survivors, and those who continued to participate.

The findings appear to provide some mixed evidence regarding the stability of QoL/life satisfaction over time. In some cases QoL/life satisfaction remained stable (i.e. Charlifue et al. 1998; Charlifue et al. 1999; Charlifue & Gerhart 2004b; Savic et al. 2010; Pershouse et al. 2012), or decreased over time (i.e. Krause 1997; Charlifue et al. 1998). Similarly, Mitchell & Adkins 2010 that aging has greater negative influence on self-rated health in people with SCI than on those without a SCI over time. In other studies QOL/ life satisfaction improved with over (Stensman 1994; Kemp & Krause 1999; Bushnik 2002; Putzke et al. 2002b; Bushnik & Charlifue 2005; Krause & Coker 2006; van Koppenhagen et al. 2009; DeVivo & Chen 2011; Kalpakjian et al. 2011; van Leeuwen et al. 2011). Likewise, mental health has also been reported to improve longitudinally (van Leeuwen et al. 2012).

The discrepancies in these studies may potentially be attributed to theoretical and methodological differences. For instance, the study by Charlifue et al. (1998) was the only study that explicitly provided a theoretical model for assessing life satisfaction. Specifically, Charlifue and colleagues (1998) framed aging with SCI within a global thesis of function, which took into account physical, psychological, and environmental factors. Several studies with lower levels of evidence predicting life satisfaction have used other models that incorporate a variety of domains thought to impact on QoL (i.e. Pierce et al. 1999; Richards et al. 1999; Tonack et al. 2008). Unfortunately, Charlifue et al. (1998) did not provide a clear rationale for including specific predictor variables in their models. A larger theoretical concern is the issue of response shift (also known as *recalibration*, *reprioritization*, and *reconceptualization;* Schwartz & Spangers 2000), which refers to a dynamic process where an individual undergoes simultaneous changes in their internal standards, values, and conceptualizations of QoL in response to health and physical functioning changes (Tate et al. 2002). Ambiguous or paradoxical findings can occur because of differences among people or changes within people regarding internal standards, values, or conceptualization of health-related QoL (Schwartz et al. 2007). As a result, the psychometric properties (e.g. validity and reliability) of measurement tools can be affected (Schwartz et al. 2007).

In terms of methodological differences, because the samples in each of the studies had different mean ages and YPI it is not surprising that there are discrepancies in reported QoL. However, when examining the QoL results by an aging parameter, YPI for example, a common finding was that regardless of age, individuals with relatively new SCI (i.e. ≤5 YPI) are more likely to experience

improvements to their QoL (Stensman 1994; Kemp & Krause 1999; Bushnik 2002; Putzke et al. 2002b; Bushnik & Charlifue 2005; Krause & Coker 2006; van Koppenhagen et al. 2009; DeVivo & Chen 2011; Kalpakjian et al. 2011; van Leeuwen et al. 2011) than individuals with longer term SCI (i.e. ≥6 YPI) who consistently report high and stable QoL levels (i.e. Charlifue et al. 1998; Charlifue et al. 1999; Charlifue & Gerhart 2004b; Savic et al. 2010). That is, after sustaining a traumatic SCI, the QoL of these individuals may be low and have more room to improve than those individuals with longer term SCI. In fact, Dijkers (2005) noted that the wellbeing after SCI reaches a plateau at the end of the adjustment period, which is estimated to last from two to five years (Dijkers 2005). Similarly, Whalley-Hammell (2007) reported that after a four year adjustment period, individuals with SCI feel as though as they live a normal life, and have the same problems as everyone else (Whalley-Hammell 2007). In this review, there one study however that observed no changes in QoL among individuals with ≤5 YPI (Mortenson et al. 2010). Mortenson et al. (2010) argued that the individuals may have already adjusted and experienced a response shift prior to the baseline assessment.

Although age of SCI onset does not appear to limit the potential high QoL, there are likely age-related factors that may potentially influence QoL. For example, in studies with samples with mean ages in the 20s, individuals were found to have greater improvements in life satisfaction and QoL if they were students, lived independently, had a lower level injury, had overcome past medical problems, and if they had accessible vans for transportation (Barker et al. 2009; Sakakibara et al. 2012). Among individuals in their 30s, both Putzke et al. (2002b) and Stensman (1994) found QoL to be influenced by amount of pain and interference with pain (Putzke et al. 2002b; Stensman 1994), and Kalpakjian et al. (2011) found the relationship between life satisfaction and YPI to vary depending on marital status and gender (Kalpakjian et al. 2011).

Furthermore, the nature of the control group can lead to different interpretations of the results.  A strength of Kemp and Krause‟s (1999) was the use of an able-bodied, and a control group with disability (i.e., polio) when examining issues of QoL after SCI as it provides some context to the extent of some problems for persons post-SCI (i.e. levels of depression). However, the characteristics of the control groups were significantly different to the group with SCI on some key factors. For instance, the able-bodied and polio groups were significantly older (p < 0.01) and had higher levels of education than the group with SCI (p < 0.05). As well, the polio group was comprised mostly of females, had a mean pediatric age of onset, was 50.9 years post-polio, and 90% were Caucasian, whereas the SCI group was comprised of mostly males from culturally diverse backgrounds, and who had an adult age of onset, and were only 14.5 years post-injury. This limitation was addressed in the study, but highlights that the findings should be interpreted with caution since many socio-demographic and historical factors may have influenced levels of depression and life satisfaction. Nonetheless, the finding that persons with SCI have lower QoL compared to the able-bodied population is consistent with other studies that did not meet the SCIRE inclusion criteria (Kemp & Ettelson 2001).

Finally, although a couple of studies reported declines in QoL over time (Krause 1997; Charlifue et al. 1998), subsequent papers focusing on the same cohorts at longer lengths of follow-up reported different results. For example, Charlifue et al. (1998) first reported that after 3 years of observation 76% of the sample consistently rated their overall QoL as either good or excellent, but that there were significant decreases in life satisfaction, as measured by the life satisfaction index (LSI), among older individuals, those with <30 YPI and >40 YPI, and those with complete paraplegia (Charlifue et al. 1998). At a follow up thirteen years later, Savic et al. (2010) similarly reported that 76% of the sample consistently reported overall QoL as good or excellent, with the highest life satisfaction reported at the last time point (Savic et al. 2010). Similarly, over two time points 9 years apart, Krause (1997) reported diminished satisfaction related to social and sex lives, as measured by the life situation questionnaire (LSQ)* (Krause 1997).  Lower satisfaction is corroborated in papers by Krause and Broderick (2005) and Krause and Coker (2006) which used observations from the same cohort at different lengths of follow-up (Krause & Broderick 2005; Krause & Coker 2006). However, these two papers in addition to Crewe and Krause (1990), Krause (1992), and Krause (1998), all reported

significant increases in satisfaction related to employment among the same cohort over various lengths of time (Crewe & Krause 1990; Krause 1992; Krause 1998). In general, the overall and common finding from studies that followed the same cohorts over time is that global QoL tends to remain high and stable over time but when considering specific areas of QoL, fluctuations exist with some domains increasing in importance (e.g. employment) and other decreasing (e.g. social and sex lives) (Krause & Bozard 2012).

*Note: Krause 1997 used a modified version of the LSQ. Using this version, the authors also observed significant declines in satisfaction related to family relationships, emotional adjustment and control over life.

**Conclusion**

*There is level 2 evidence from one longitudinal study with able-bodied controls (Mitchell & Adkins 2010) that aging has greater influence on self-rated health in people with SCI than on those without a SCI.*

*There is Level 4 evidence from four longitudinal studies (Bushnik 2002; Bushnik & Charlifue 2005; Krause & Broderick 2005; Krause & Coker 2006) that changes in environmental factors over time (i.e. economics; technology) may influence QoL in persons with SCI rather than the aging process per se.*

*There is Level 4 evidence from three longitudinal studies (Charlifue & Gerhart 2004a; Bushnik & Charlifue 2005; Krause & Bozard 2012) that community reintegration and social participation declines with age after SCI. However, these changes in community reintegration may be similar as compared to the aging general population.*

*There is Level 4 evidence from seven longitudinal studies (Crewe & Krause 1990; Krause 1992; Krause 1997; Krause 1998; Krause & Broderick 2005; Krause & Coker 2006; Krause & Bozard 2012) that selected domains of life satisfaction change (i.e. social life, sex life, and health decrease, and employment, finances, and adjustment increase) as one ages with an SCI.  It may be that these changes in satisfaction of certain domains are comparable to changes in the general population.*

*There is Level 5 evidence from one cross-sectional study (Kemp & Krause 1999) that age of SCI-onset may be an influential factor on life satisfaction.*

*There is Level 4 evidence from one longitudinal study (Charlifue & Gerhart 2004b) that previous perceptions of life satisfaction are predictive of later perceptions of life satisfaction.*

*There is Level 5 evidence from two cross-sectional studies (Kemp & Krause 1999; Barker et al. 2011) that life satisfaction is lower for persons with SCI compared to the general population.*

*There is Level 4 evidence from two longitudinal studies (Stensman 1994; Putzke et al. 2002a) that previous reports of pain interference after SCI, irrespective of age, are predictive of later pain interference.*

*There is level 4 evidence from 10 longitudinal studies that individuals with ≤5 YPI have the potential to improve their QoL (Stensman 1994; Kemp & Krause 1999; Bushnik 2002; Putzke et al. 2002b; Bushnik & Charlifue 2005; Krause & Coker 2006; van Koppenhagen et al. 2009; DeVivo & Chen 2011; Kalpakjian et al. 2011; van Leeuwen et al. 2011).*

*There is level 4 evidence from 4 longitudinal studies that individuals with longer term SCI (i.e., ≥ 6 YPI) consistently report high and stable QoL levels (Charlifue et al. 1998; Charlifue & Gerhart 2004b; Savic et al. 2010). Similarly, there is Level 4 evidence from one longitudinal study (Pershouse et al. 2012) that QoL remains stable across the lifespan even in those with long-duration SCI.*

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Selected domains of life satisfaction (i.e. social life and sex life) may decline as one ages with a SCI. Other domains (i.e., employment and finances) may improve as one ages with a SCI. It may be that these changes in satisfaction of certain domains are comparable to changes in the general population.

Changes in environmental factors over time (i.e. economics; technology) may influence QoL in persons with SCI rather than the aging process per se.

Community participation may decline with age after SCI. However, these changes in community participation may be similar to the aging general population.

Individuals with new SCI (i.e. ≤ 5YPI) consistently report improvements to their QoL, whereas, individuals with longer term SCI consistently report high and stable QoL over time.

Age of SCI-onset may be an influential factor on life satisfaction.

Previous perceptions of life satisfaction may be predictive of later perceptions of life satisfaction.

Aging has greater influence on self-rated health in people with SCI than those without a SCI.

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## 6.0 Summary

The majority of studies for all the systems provide some important findings regarding the role of chronological age (including age of SCI onset) and YPI, but there is still lack of clarity on how all of these factors affect (individually and in combination) the individual living with SCI over time, and further work is needed to determine if SCI is indeed a model for premature aging. It appears that the field of aging with SCI has yet to make significant advances since many of the issues and questions raised over 15 years ago (Whiteneck et al. 1993) are still relevant today.

In general, longitudinal designs are the preferred method for investigating aging, but a number of longitudinal aging-related studies of SCI are limited in scope and quality due to several methodological issues (Krause 2007). One limitation with longitudinal research designs are problems with retaining sufficient sample size over many years to observe long term changes with aging. Problems with attrition lead to another type of cohort effect, namely survivor effects. Survivor effects describe those individuals who may have outlived other members in their cohort due to some unusual advantage (e.g. environmental, physiological, Adkins 2001). Persons who remain in longitudinal studies often represent those who are healthier, wealthier, and better educated whereas persons with poorer functioning drop out or have died. Another limitation of longitudinal designs is the possibility that data collected at an earlier time point may become obsolete due to advances or changes in measurement. Longitudinal research is also considerably more resource intensive than cross-sectional studies in terms of cost and time.

Despite the challenges associated with longitudinal research, gaining an understanding of what changes a person with SCI may undergo over time is important to identify potential problems that can be anticipated and perhaps prevented in some cases. This in turn may contribute to continued levels of maximum independence and overall wellbeing. The field of aging with SCI has made some tremendous strides forward, but the dearth of knowledge in some areas highlights research opportunities that will help to resolve current challenges and more importantly provide information to fill many existing gaps.

*There is level 4 evidence that the 10 year survival rate post injury is 84-87% (Rabadi et al. 2013; Picklesimer et al. 2010).*

*There is Level 4 evidence (Frisbie et al. 2010) that the mortality rate post-SCI over a 10-year period may be 15.5% to 25.8%, and level 4 evidence (Cao et al. 2013) that the mortality rate is higher for individuals with SCI than the general population.*

*There is Level 4 evidence (Cao et al. 2013) that mortality may be higher for persons with SCIs at the C1-4 level than other spinal cord levels.*

*There is Level 4 (Frisbie 2010) to Level 5 evidence (Samsa et al. 1993) that the causes of death post-SCI are beginning to approximate those of the general population.*

*There is Level 5 evidence (Samsa et al. 1993; Cao et al. 2013) that life expectancy for males with SCI is lower than the general male population.*

*There is level 4 evidence (Rabadi et al. 2013) that older age at time of injury is a predictor of SCI-related mortality.*

*There is Level 5 evidence from one cross-sectional study (Bauman & Spungen 2001) that plasma homocysteine levels are higher in persons with SCI compared to the AB population, with the greatest discrepancy in older adults with SCI (> 50 years).*

*There is Level 5 evidence from nine cross-sectional studies (Zlotolow et al. 1992; Huang et al. 1993; Bauman & Spungen 1994; Bauman et al. 1996; Huang et al. 1998; Bauman et al. 1999; Demirel et al. 2001; Liang et al. 2007; Wang et al. 2007) that lipid profiles are altered after SCI which may contribute to the development of cardiovascular disease.*

*There is Level 4 evidence (Shiba et al. 2010) that physical capacity can be maintained long-term in male athletes with SCI.*

*There is Level 4 evidence from one longitudinal study (de Groot et al. 2013) that lipid profiles in adults with SCI remain stable during the 5 years after inpatient rehabilitation.*

*There is Level 4 evidence (Apstein & George 1998) that total cholesterol (TC), total glycerides (TG), and low-density lipoproteins (LDL) increased while LDL/high-density lipoproteins (HDL) ratios decreased for males with tetraplegia and paraplegia from the acute phase until 1 YPI. All lipid profiles were significantly depressed compared to controls.*

*There is Level 4 evidence (Apstein & George 1998) that persons with tetraplegia had low HDL and elevated LDL/HDL ratios, which places them at an increased risk for coronary artery disease.*

*There is Level 5 evidence (Wang et al. 2007) that C-reactive protein levels are higher in males with SCI, which could also account for the decreases in TC, LDL, and HDL. Elevated C-reactive protein levels may also partly explain why persons with SCI are at increased risk for accelerated atherogenesis.*

*There is Level 5 evidence (Orakzai et al. 2007) that persons with SCI have greater atherosclerotic burden compared to an AB reference population.*

*There is Level 5 evidence from two studies that men with complete paraplegia (Petrofsky & Laymon 2002) and with complete tetraplegia (Yamamoto et al. 1999) have an abnormal (absent) heart rate response to isometric exercise.*

*There is Level 5 evidence that men with complete tetraplegia demonstrate increased blood pressure (Yamamoto et al. 1999) response to isometric contraction.*

*There is Level 5 evidence (Wang et al. 1992: 63 men; Tsitouras et al. 1995; Shetty et al. 1993) that there is lower secretion of testosterone and human growth hormone levels in men with SCI compared to AB controls.*

*There is Level 5 evidence from two studies (Tsitouras et al. 1995; Bauman et al. 1994) that serum IGF-I levels are impaired in persons with SCI compared to the AB population, which may be a sign of premature aging.*

*There is Level 5 evidence from three studies (Bauman & Spungen 1994; Jones et al. 2004; Liang et al. 2007) that glucose tolerance is impaired after SCI, which may lead to an increased risk for premature diabetes mellitus.*

*There is Level 5 evidence (LaVela et al. 2006) that diabetes mellitus occurs prematurely in male veterans with SCI compared to AB individuals in the general population, but not veteran controls.*

*There is Level 5 evidence (Lewis et al. 2010) that men with SCI have slower plasma-free cortisol responses than AB controls.*

*There is Level 4 evidence from three longitudinal studies (de Groot et al. 2013 & 2010; Crane et al. 2011) that BMI increases significantly over time in persons with SCI.*

*Seven studies (Nuhlicek et al. 1988; Bauman et al. 1996; Bauman et al. 1999; Spungen et al. 2000; Jones et al. 2003; Jones et al. 2004; Emmons et al. 2011) provide Level 5 evidence that persons with SCI are likely to have higher levels of fat mass, and that age-related declines of lean tissue in males with SCI may occur at a significantly faster rate than the AB population.*

*There is Level 5 evidence from one monozygotic twin study (Bauman et al. 2004) that basal and resting energy expenditures are lower in males with SCI compared to their AB twin.*

*There is Level 5 evidence from one cross-sectional study (Hosier et al. 2012) that post-menopausal women with SCI have cardiometabolic risk profiles that are similar to those observed in women without SCI.*

*There is Level 4 evidence that persons with SCI have a prevalence of anemia and hypoalbuminemia (Frisbie 2010), which might serve as markers for infection.*

*There is Level 5 evidence (Campagnolo et al. 1994; Campagnolo et al. 1996; Furlan et al. 2006) that the immune function of persons with acute and chronic SCI is compromised compared to the able-bodied population, but there is no influence due to aging.*

*There is Level 4 evidence from 9 longitudinal studies (Biering-Sorensen et al. 1990; Garland et al. 1992; Wilmet et al. 1995; de Bruin et al. 2000; Frey-Rindova et al. 2000; Garland et al. 2004; de Bruin et al. 2005; Frotzler et al. 2008, Dudley-Javorski & Shields, 2010) and Level 5 evidence from 15 studies (Chow et al. 1996; Szollar et al. 1997a; Szollar et al. 1997b; Szollar et al. 1998; Bauman et al. 1999; Dauty et al. 2000; Kiratli et al. 2000; Garland et al. 2001b; Vlychou et al.*

*2003; Eser et al. 2004; Giangregorio et al. 2005; Slade et al. 2005; Dudley-Javorski & Shields, 2010; Rittweger et al. 2010; Dionyssiotis et al. 2011) that there is a rapid loss of bone in the hip and lower extremities following SCI.*

*There is Level 2 evidence (Frotzler et al. 2008) and Level 5 evidence (Eser et al. 2004) that tibial and femoral bone geometry and density properties reach a new steady-state within 3-8 year post injury, with the time frame depending on bone parameter and skeletal site.*

*There is Level 5 evidence from three studies (Szollar et al. 1997a; Szollar et al. 1998; Garland et al. 2001b) that older males and females with SCI may not experience as rapid of a decline in bone mass compared to AB controls.*

*There is Level 5 evidence from two studies (Bauman et al. 1999; Garland et al. 2001b) that YPI may be more associated with bone loss after SCI than chronological age.*

*There is Level 5 evidence (Slade et al. 2005) that there are differences in bone geometric indices and in structural properties in the lower extremities of women with SCI compared to the AB women.*

*There is Level 5 evidence from five studies (Finsen et al. 1992; Vaziri et al. 1994; Bauman et al. 1995; Szollar et al. 1998; Dauty et al. 2000) suggesting that there are impaired biochemical and bone markers in persons with SCI compared to AB controls that persons with SCI are at greater risk for fracture due to the premature development of osteoporosis.*

*There is Level 2 evidence from a longitudinal study with AB controls (Catz et al. 1992), Level 4 evidence from a longitudinal study (Biering-Sorensen et al. 1990), and Level 5 evidence from five studies (Chow et al. 1996; Szollar et al. 1997a; Szollar et al. 1997b; Szollar et al. 1998; Garland et al. 2001b) that premature aging does not occur in the lumbar spine after SCI. The possibility that the lumbar spine becomes the primary weight-bearing region, along with immobilization, may serve to protect age-related bone loss changes to this region.*

*There is Level 5 evidence (Amsters & Nitz 2006) that persons with SCI, regardless of age or YPI, had increased thoracic kyphosis compared to AB controls.*

*There is Level 5 evidence from two studies (Pentland & Twomey 1994; Petrofsky & Laymon 2002) that decreased hand grip strength does not occur in men with complete paraplegia and that continual wheelchair use may retard this aging process.*

*There is Level 5 evidence (Pentland & Twomey 1994) that upper limb pain in males with complete paraplegia who use manual wheelchairs may be attributed to longer YPI and not to chronological age.*

*There is Level 2 evidence from two longitudinal studies (Siddall et al. 2003; Jensen et al. 2005) showing that the incidence of shoulder pain increases over time in persons with SCI.*

*There is Level 2 evidence from a longitudinal study (Lal 1998) and Level 5 evidence (Kivimäki et al. 2008) that highlights chronological age having an important influence on developing shoulder pain.*

*There is Level 4 evidence from two longitudinal studies (Bach & Wang 1994; Berlowitz et al. 2005) support that SDB may either increase or persist with the aging process.*

*There is Level 2 evidence from a longitudinal study with AB controls (Loveridge et al. 1992) that seated breathing patterns are compromised immediately post injury but recover over time. As well, persons with tetraplegia do not take deep breaths as often as AB individuals.*

*There is Level 4 evidence from a longitudinal study that adults over the age of 50 who are aging with ventilator dependency are at greater risk of death and are less likely to be weaned from their ventilators than younger adults aging with a ventilator (Wicks & Menter 1986).*

*There is Level 4 evidence from one longitudinal study (Postma et al. 2013) that forced vital capacity improves 5 years after inpatient rehabilitation.*

*There is Level 4 evidence (Putzke et al. 2002a; Siddall et al. 2003; Rintala et al. 2004; Jensen et al. 2005) that the early onset of SCI-related pain is likely to be maintained over time, with some evidence indicating that the degree of interference experienced might be affected by age of onset (Jensen et al. 2005).*

*There is Level 2 evidence (Vaziri et al. 1995) suggesting that plasma fibronectin, as an indicator of wound healing, may rise in SCI male patients with fast healing ulcers but not in SCI patients with poor healing ulcers.*

*There is Level 5 evidence that the biomechanical skin properties are significantly influenced by sympathetic paralysis rather than somatic sensory paralysis. Furthermore, in men with complete SCI, YPI may be the influential factor on the biomechanical properties of the skin (Park et al. 2011).*

*There is Level 4 evidence (Viera et al. 1986; DeWire et al. 1992; MacDiarmid et al. 1995; Sekar et al. 1997) that there are no differences in renal functioning up to 4 YPI using various bladder management techniques with some decline occurring beyond that time.*

*There is Level 4 evidence (Lamid et al. 1988) that repeated episodes of vesicoureteral reflux can cause kidney damage as early as four YPI in some persons with SCI.*

*There is Level 4 evidence (Sekar et al. 1997) that renal plasma flow declines until 10 YPI after SCI, at which time, a slight reversal occurs.*

*There is Level 5 evidence (Kuhlemeier et al. 1984b) that suggests age of SCI onset may be an important factor related to renal function, with persons with SCI who are under 20 and older than 50 having comparable renal function to AB controls, whereas persons between those ages have impaired functioning compared to the general population.*

*There is Level 5 evidence (Lynch et al. 2000) demonstrating a deterioration in bowel continence with increasing age in an AB population but no change with age in persons with SCI.*

*There is Level 4 evidence (Faaborg et al. 2008) suggesting persons with SCI do incur an increase in constipation-related symptoms and decrease in fecal incontinence over time.*

*There is Level 4 evidence (Faaborg et al. 2011) that gastrointestinal transit times and colonic dimensions do not change over time in persons with SCI.*

*There is Level 5 evidence from three studies (Menardo et al. 1987; Krogh et al. 2000; Emmanuel et al. 2009) that level of injury, and not necessarily age or YPI, plays a primary role in the extent of bowel dysfunction.*

*There is Level 3 evidence (Jensen et al. 2013) from a scoping review that cardiovascular disease, diabetes, bone mineral density loss, fatigue and respiratory complications or infections occur with higher frequency in older individuals or those with longer SCI duration, relative to younger individuals or those with shorter SCI duration.*

*There is Level 4 evidence (Ullrich et al. 2013) from one longitudinal study that co-occurrence of pain and depression is common among persons who have lived with SCI for many years and remains stable over time. There is also evidence that comorbid pain and depression are associated with higher severity of conditions, more persistent conditions over time, and more utilization of SCI specialty health-care services.*

*There is Level 4 evidence (Hitzig et al. 2010; Pershouse et al. 2012) that secondary health complications increase over time in persons with SCI, (with the exception of bowel problems, which decrease).*

*There is Level 4 evidence from a longitudinal study (Charlifue et al. 1999) that fatigue and the need for physical assistance increases over time with SCI.*

*There is level 4 evidence from one retrospective longitudinal study (Pershouse et al. 2012) that functional independence decreases with more years post injury for individuals who were higher functioning at one year.*

*There is Level 5 evidence from one longitudinal study (Amsters et al. 2005) that individuals with SCI (≥20 YPI) perceive functional improvements up to 10 YPI and subsequent functional decline and greater dependence on mobility aids after 10 or more YPI.*

*There is level 2 evidence from one longitudinal study with able-bodied controls (Mitchell & Adkins 2010) that aging has greater influence on self-rated health in people with SCI than on those without a SCI.*

*There is Level 4 evidence from four longitudinal studies (Bushnik 2002; Bushnik & Charlifue 2005; Krause & Broderick 2005; Krause & Coker 2006) that changes in environmental factors over time (i.e. economics; technology) may influence QoL in persons with SCI rather than the aging process per se.*

*There is Level 4 evidence from three longitudinal studies (Charlifue & Gerhart 2004a; Bushnik & Charlifue 2005; Krause & Bozard 2012) that community reintegration and social participation declines with age after SCI. However, these changes in community reintegration may be similar as compared to the aging general population.*

*There is Level 4 evidence from seven longitudinal studies (Crewe & Krause 1990; Krause 1992; Krause 1997; Krause 1998; Krause & Broderick 2005; Krause & Coker 2006; Krause & Bozard 2012) that selected domains of life satisfaction change (i.e. social life, sex life, and health decrease, and employment, finances, and adjustment increase) as one ages with an SCI. It may be that these changes in satisfaction of certain domains are comparable to changes in the general population.*

*There is Level 5 evidence from one cross-sectional study (Kemp & Krause 1999) that age of SCI-onset may be an influential factor on life satisfaction.*

*There is Level 4 evidence from one longitudinal study (Charlifue & Gerhart 2004b) that previous perceptions of life satisfaction are predictive of later perceptions of life satisfaction.*

*There is Level 5 evidence from two cross-sectional studies (Kemp & Krause 1999; Barker et al. 2011) that life satisfaction is lower for persons with SCI compared to the general population.*

*There is Level 4 evidence from two longitudinal studies (Stensman 1994; Putzke et al. 2002a) that previous reports of pain interference after SCI, irrespective of age, are predictive of later pain interference.*

*There is level 4 evidence from 10 longitudinal studies that individuals with ≤5 YPI have the potential to improve their QoL (Stensman 1994; Kemp & Krause 1999; Bushnik 2002; Putzke et al. 2002; Bushnik & Charlifue 2005; Krause & Coker 2006; van Koppenhagen et al. 2009; DeVivo & Chen 2011; Kalpakjian et al. 2011; van Leeuwen et al. 2011).*

*There is level 4 evidence from 4 longitudinal studies that individuals with longer term SCI (i.e., ≥ 6 YPI) consistently report high and stable QoL levels (Charlifue et al. 1998; Charlifue & Gerhart 2004b; Savic et al. 2010). Similarly, there is Level 4 evidence from one longitudinal study (Pershouse et al. 2012) that QoL remains stable across the lifespan even in those with long-duration SCI.*

## 7.0 References

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