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SPINAL CORD INJURY REHABILITATION EVIDENCE

Sexual and Reproductive Health Following Spinal Cord Injury

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Key Points:

- After an SCI it is still possible to have and enjoy sex.
- The degree of sexual dysfunction varies significantly among people with SCI and depends on the level and the severity of injury.
- People with lesions at T6 and above must be aware that sexual stimulation, especially orgasm and ejaculation, as well as childbirth increases the risk of developing Autonomic Dysreflexia (AD).

- <u>Assessment</u>
- There is no one measurement tool that adequately assesses the complex issue of sexual health and satisfaction after SCI. For an assessment to be comprehensive, neurological bases for sexual health dysfunction are necessary (such as The International Standards of Neurological Classification of Spinal Cord Injury (ISNCSCI) or The International Standards to Document Remaining Autonomic Function after SCI (ISAFSCI).

- <u>Sexual and Reproductive Health in Men with SCI</u>
- In general, the majority of men can attain an erection after SCI either through the psychogenic (T11-L2) or reflexogenic (S2-S4) pathways, depending on the level and completeness of injury.
- Phosphodiesterase Type 5 Inhibitors (PDE5i – e.g., Viagra®, Cialis®) can be used safely and effectively for treatment of erectile dysfunction (ED) in men with SCI and are recommended as first-line treatment.
- Intracavernosal (penile) injectable medications (ICI) are very effective for the treatment of ED in men with SCI and may be used with careful dose titration and some precautions. Medically sanctioned vacuum erection devices (VED), penile rings, perineal training, mechanical devices, and penile prostheses all may be effective in enhancing erectile function in men with SCI. Surgical options should be reserved for cases where other ED treatments fail.
- Sperm retrieval can be problematic after SCI. Semen quality in men with chronic SCI is reported to have decreased motility and viability, although total numbers of sperm tend to remain high.
- Prostatic massage alone is a safe and easy alternative way to retrieve semen in some men with SCI above T10. The least invasive sperm retrieval method should be tried first (i.e. penile vibrostimulatory stimulation (PVS) in the clinic setting to monitor for autonomic dysreflexia) followed by the more invasive of electroejaculation procedure (EEP). PVS is most successful in men with SCI above T10.

- <u>Sexual and Reproductive Health in Women with SCI</u>
- Multiple laboratory-based studies have documented the presence of sexual arousal and orgasm in women with SCI.
- Generally, women with SCI are less likely to achieve orgasm than able-bodied women, and time to orgasm is significantly increased compared to able-bodied controls. The ability to achieve orgasm, however, seems unrelated to the pattern or degree of neurological impairment in women with lesions down to T5 level.
- Amenorrhea may occur immediately following injury, lasting 4-5 months on average, but fertility is generally not affected once regular menstrual cycle resumes.
- Women with SCI are able to conceive, carry and deliver a baby; however, there is an increased frequency of complications during pregnancy, labour and delivery, including AD, bladder problems, spasticity, pressure sores, and problems with mobility.

- Sexual Behaviour/Activity/Satisfaction after SCI
- Frequency of sexual activity, desire for sexual activity and sexual satisfaction all tend to decrease after SCI in both men and women.
- A 2004 survey of 681 people with SCI found that regaining sexual function was rated the highest priority for the majority of people with paraplegia, and the 2nd highest priority for those with tetraplegia, after restoration of hand and arm function.
- Bladder and bowel management problems (incontinence/UTI's) have a negative impact on sexual activity and satisfaction in both men and women after SCI. Continent urinary diversion in women with tetraplegia may result in improved self-image, quality of life, and greater sexual satisfaction.
- For both men and women with SCI, psychological barriers to engaging in sexual activity include: feeling unattractive, low self-esteem, low sexual desire, lack of confidence in sexual ability and ability to satisfy a partner, lowered body image, and difficulty meeting a partner.

- Education and Counselling
- Surveys of people who have completed rehabilitation after SCI have expressed a need for more education and counselling on sexual health concerns. Some recent research reported that few people with SCI receive information or are satisfied with the levels of education about pregnancy or sexual health.
- Research shows that patients expect their health care professionals to bring up sexuality and sexual health, but health care professionals can be reluctant to do so because of their lack of knowledge, fear of offending the patient, or discomfort in asking questions that address sexual concerns.
- A number of studies in this area show that training in sexual health can make a positive difference in knowledge, attitudes, and willingness to bring up sexual health issues in health care professionals.
- As sexual health can be complex and multi-faceted, the authors present a Sexual and Fertility Rehabilitation Framework – a multidisciplinary approach to addressing the multi-faceted needs of people after SCI.

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Sexual and Reproductive Health Following Spinal Cord Injury

1.0 Executive Summary

After an SCI it is still possible to have and enjoy sex. Sexual health is a significant component of a person's overall health and wellbeing.[1] SCI can have direct or indirect effects on sexual functioning; ability to engage in sexual activities; sexual intimacy and relationships; sexual self-view, and fertility and reproductive health.

Both men and women typically retain some sexual function after SCI depending on the level and completeness of injury (e.g. genital arousal, erection, ejaculation). The degree of sexual dysfunction varies significantly among people with SCI and depends on the level and the severity of injury.[2,3,4] People with lesions at T6 and above must be aware that sexual stimulation, especially orgasm and ejaculation, as well as childbirth and lactation increases the risk of developing Autonomic Dysreflexia (AD).

Assessment

There is no one measurement tool that adequately assesses the complex issue of sexual health and satisfaction after SCI.[9] For an assessment to be comprehensive, neurological bases for sexual health dysfunction are necessary. (For a list of Outcome Measures validated for SCI in Sexual Health, visit: https://scireproject.com/outcome-measures/list-sci/).

The international community of SCI experts have collaborated to develop a number of 'gold standard' resources/assessments in order to facilitate better care in SCI. Three of the most important with regards to Sexual Health include:

1) The International Standards of Neurological Classification of Spinal Cord Injury (ISNCSCI) is a comprehensive assessment of motor function and sensation to determine the level and completeness of injury (an estimation of sexual functioning can be based on these findings).

2) The International Standards to Document Remaining Autonomic Function after SCI (ISAFSCI)[10] was designed to describe the diagnosis (supraconal, conal or cauda equina) of the spinal cord lesion and to document the impact of the injury on the components of autonomic response, including sexual response.

3) The International SCI Data Sets on Male Sexual Function and Female Sexual and Reproductive Function - These data sets are agreed upon as measures/indicators that both clinicians and researchers would need regarding SCI and Sexual Health. They are meant to establish a standard of data collection/clinical intake that is valid anywhere in the world.

Sexual and Reproductive Health in Men with SCI

In general, the majority of men can attain an erection after SCI either through the psychogenic (T11-L2) or reflexogenic (S2-S4) pathways, depending on the level and completeness of injury. However, these erections are often unreliable or inadequate for sexual intercourse with difficulties experienced in maintaining an erection.[5,6] Phosphodiesterase Type 5 Inhibitors (PDE5i – e.g., Viagra®, Cialis®) can be used safely and effectively for treatment of erectile dysfunction (ED) in men with SCI and are recommended as first-line treatment.

Intracavernosal (penile) injectable medications (ICI) are very effective for the treatment of ED in men with SCI and may be used with careful dose titration and some precautions. Medically sanctioned vacuum erection devices (VED), penile rings, perineal training, and mechanical devices all may be effective in enhancing erectile function in men with SCI. Surgical options such as penile prosthesis should be reserved for cases where other ED treatments fail. Intrauethreal and topical agents are not effective for treatment of erectile dysfunction in men with SCI.

Ejaculation is rare after SCI, but more common with incomplete than complete SCI. Orgasm (poorly defined in the literature), is self reported to occur less than 50% of the time for men after SCI. Orgasm is most likely to occur with ejaculation than without ejaculation, and in men with incomplete versus complete lesions. Attempts to improve the chance of ejaculation and orgasm include using PVS, mididrone, and sensory substitiution or microsurgery of the sensory nerves in men with low lesions.

Sperm retrieval can be problematic after SCI. Semen quality in men with chronic SCI is reported to have decreased motility and viability, although total numbers of sperm tend to remain high.[7,8] Prostatic massage alone is a safe and easy alternative way to retrieve semen in some men with SCI above T10. The least invasive sperm retrieval method should be tried first (i.e. penile vibrostimulatory stimulation (PVS) in the clinic setting to monitor for autonomic dysreflexia) followed by the more invasive of electroejaculation procedure (EEP). PVS is most successful in men with SCI above T10. The use of oral midrodrine to encourage ejaculation may also improve chance of orgasm and/or sperm retrieval.

Sexual and Reproductive Health in Women with SCI

Multiple laboratory-based studies have documented the presence of sexual arousal and orgasm in women with SCI.[11-16] Women with SCI are less likely to achieve orgasm than able-bodied women, and time to orgasm is significantly increased compared to able-bodied controls.[17] The ability to achieve orgasm, however, seems unrelated to the pattern or degree of neurological impairment in women with lesions down to T5 level.[13] On the other hand, women with LMN lesions affecting S2 –S5 segments were less likely to achieve orgasm compared with women who had other types of SCI lesion.[17]

Amenorrhea may occur immediately following injury, lasting 4-5 months on average, but fertility is generally not affected once regular menstrual cycle resumes.[18,19] Few studies exist that specifically address women's health and pregnancy after SCI, but they show that women with SCI are able to conceive, carry and deliver a baby despite an increased frequency of complications during pregnancy, labour and delivery.[18,20-23]

Women with SCI are able to conceive, carry and deliver a baby; however, there is an increased frequency of complications during pregnancy, labour and delivery, including AD.[3,18,20,21,24] Bladder problems, spasticity, pressure sores, autonomic dysreflexia and problems with mobility can pose a threat to the pregnant woman with SCI.[18,25,26]

Sexual Behaviour/Activity/Satisfaction after SCI

Frequency of sexual activity, desire for sexual activity and sexual satisfaction all tend to decrease after SCI in both men and women.[6,18,27-32]

A 2004 survey of 681 people with SCI found that regaining sexual function was rated the highest priority for the majority of people with paraplegia, and the 2nd highest priority for those with tetraplegia, after restoration of hand and arm function.[33]

Bladder and bowel management problems (incontinence/UTI's) have a negative impact on sexual activity and satisfaction in both men and women after SCI.[18,27,34-44] Continent urinary diversion in women with tetraplegia may result in improved self-image, quality of life, and greater sexual satisfaction.

For both men and women with SCI, psychological barriers to engaging in sexual activity include: feeling unattractive, low self-esteem, low sexual desire, lack of confidence in sexual ability and ability to satisfy a partner, lowered body image, and difficulty meeting a partner.[31,32,34,42,45-49]

Population-based studies have shown that the prevalence and predictors of sexual difficulties are closely associated with diminished quality of life (QOL).[50]

Education and Counselling

Surveys of people who have completed rehabilitation after SCI have expressed a need for more education and counselling on sexual health concerns. Some recent research reported that few people with SCI receive information, are satisfied with the levels of education about pregnancy or sexual health, and that most expect medical staff to start the conversation about sexuality rather than having to initiate it.[51,52]

A variety of health professionals (e.g., psychologists, physical therapists, nurse, physician, sexual health clinician) may be involved in treating these domains, as well as discussing the impact of SCI on aspects of sexual function. In fact, research shows that patients expect their health care professionals to bring up sexuality and sexual health, but health care professionals can be reluctant to do so because of their lack of knowledge, fear of offending the patient, or discomfort in asking questions that address sexual concerns.[53]

People with disabilities often express their sexual health concerns to the people they feel most comfortable with, so it is recommended that all persons working in SCI understand its effects on

sexual function.[54] A number of studies in this area show that training in sexual health can make a positive difference in knowledge, attitudes, and willingness to bring up sexual health issues in health care professionals.[55-59]
As sexual health can be complex and multi-faceted, the authors present a Sexual and Fertility Rehabilitation Framework – a multidisciplinary approach to addressing the multi-faceted needs of people after SCI.

2.0 Introduction
Spinal cord injury (SCI) causes significant disruption to many areas of a person's life, including sexual health. Both men and women typically retain some sexual function after SCI depending on the level and completeness of injury (e.g. genital arousal, erection, ejaculation). The degree of sexual dysfunction varies significantly among people with SCI and depends on the level and the severity of injury (Sipski et al. 1997; Ekland et al. 2008; Sipski et al. 2006). Sexual health has physiological, psychological and social dimensions that can change throughout the lifespan; it is considered a basic human right by the World Health Organization and it is a significant component of a person's overall health and wellbeing (Butler 2004). Population-based studies have shown that the prevalence and predictors of sexual difficulties are closely associated with diminished quality of life (QOL) (Laumann 1999).

The effects of a SCI on sexual functioning; ability to engage in sexual activites; sexual intimacy and relationships; sexual self-view, and fertility/reproductive health can be categorized in the following way (adapted with permission from Stevenson and Elliott, 2007):

1. Direct effects of the SCI on motor, sensory and autonomic pathways which alter sexual response specifically: genital sensation; arousal (erection in men and vaginal lubrication and engorgement in women); ejaculation in men, and sensation of orgasm in men and women) Typically, people with SCI below L2 are capable of psychogenic arousal (sensory stimulation including dreams or fantasies), whereas those with lesions above T11 are capable of reflexogenic arousal (direct touch or stimulation – e.g., urinary care in a man with tetraplegia may cause an erection) (Biering-Sorensen et al. 2015).
2. Indirect effects of the SCI such as sensory or motor alterations, bladder and bowel changes, spasticity, fatigue, psychological issues such as anxiety/depression/post traumatic stress disorder, chronic pain, autonomic dysreflexia, and alterations in sexual self-view.
3. Iatrogenic effects of treatment (e.g. surgery and/or side effects of medications).
4. Contextual influences, such as the effect of a SCI on relationships, one's roles and responsibilities in the family unit of culture, and the situational and societal components of the ups and downs of living with a SCI.

In 2004, Anderson et al. surveyed 681 participants (approximately 25% were female) asking what "gain of function" was most important to their quality of life. For the majority of individuals with paraplegia, regaining sexual function was rated the highest priority. For those with tetraplegia, sexual function was rated as the second highest priority, after restoration of hand and arm function. Yet, insufficient medical research has been performed in SCI to provide a great deal of evidence-based information to guide clinical sexual health practice (Biering-Sorensen & Sonksen 2001; Deforge et al. 2005). Several authors have highlighted the lack of attention given to this area and the resulting dissatisfaction within the SCI community (Tepper 1992; Tepper et al. 2001; Anderson 2004; Kennedy 2006). Thus, current sexual health clinical practice has limitations as it is primarily based on results from case reports and observational studies (with some areas like erectile dysfunction in men with SCI having a larger body of evidence). Adding to the problem is the fact that rehabilitation professionals may feel uncomfortable discussing sexual issues and are inadequately trained to do so (Herson et al. 1999; Booth et al. 2003; Post et al. 2008).

This review summarizes the main research findings to provide some recommendations for sexual and reproductive clinical practice based on evidence existing currently. In areas where evidence is lacking, recommendations based on case reports, expert opinion and observational studies are also indicated.

3.0 Systematic Review

Table 1: Systematic Reviews on Sexual Health Following SCI

Author Year; Country Dates included in the review Total sample size Level of evidence Type of study Score	**Methods Databases**	**Outcomes**
Consortium for Spinal Cord Medicine 2010; USA Reviewed published and unpublished articles between Jan 1995 and Sept 2007 N=145 **Level of evidence:** Methdological quality assessed using criteria from the Centre for Evidence-based Medicine in Oxford **Type of studies:** RCTs assessed using the Jadad Quality Score Assessment AMSTAR=5	**Method:** Searched for all articles describing sexual and reproductive health in people with SCI. Reviews and meta-analyses were excluded, as were studies with a paediatric population. Only English studies were considered. **Databases:** Medline, PreMedline, Cinahl, SocioFile, PsycInfo, and Cochrane Library.	A panel of experts reviewed the literature and created a clinical practice guideline to provide information for SCI clinicians, individuals with SCI and their partners. Some important points include: • understanding the importance of sexuality and reproduction to the individual, and conveying the appropriate information in a timely manner • obtain a sexual history and assessment • provide information on sexual education and on maintaining sexual well-being • discuss with the individual any relevant physical and practical considerations (bladder/bowel, skin care, secondary medical complications, optimal position for sexual activity) • discuss the effect of injury on sexual function, responsiveness and expression with the individual with SCI and their partner; and • discuss dysfunction and fertility issues as needed.
Davidson et al. 2016 Canada Systematic Review AMSTAR= 5 N=29	**Methods:** The first search used two sets of key words including ‘‘sexuality, orgasm, ejaculation, sexual arousal, and masturbation’’ and ‘‘cardiovascular measures, blood pressure, arterial pressure, cardiovascular, and hypertension.” The search was limited to the English language published articles from 1948-2012 to source original articles, practice guidelines, and review articles. 11 studies for able-bodied persons met the criteria and 18 studies for SCI patients met inclusion criteria, making 29 articles in total. **Databases:** Embase, PubMed and Medline	1. In able-bodied persons, sexual activity resulted in modest increases in systolic blood pressure peaking at orgasm (males of 163mm Hg and females of 142mm Hg) and returning to baseline shortly afterward. 2. In persons with SCI, results varied from minimal changes to significant elevations in systolic blood pressure because of episodes of autonomic dysreflexia, especially in those with high thoracic and cervical lesions. 3. Peak systolic blood pressure in these individuals was measured to be as high as 325mm Hg. In the SCI population, more intense stimuli (including penile vibrostimulation and electroejaculation) tended to result in a greater increase in systolic blood pressure compared with self-stimulation.

Author Year; Country Dates included in the review Total sample size Level of evidence Type of study Score	Methods Databases	Outcomes
		4. Studies that used continuous versus intermittent monitoring were more likely to report greater changes in systolic blood pressure. 5. In able-bodied persons, sexual activity results in modest increases in blood pressure. 6. In those with SCI, intense stimulation and higher injury levels result in a higher likelihood of autonomic dysreflexia and elevated blood pressure. 7. Because of rapid changes in blood pressure, continuous monitoring is more advantageous than intermittent measurement, because the latter may miss peak values.
Lombardi et al. 2015 Italy Systematic Review AMSTAR = N=12	Review study. **Method:** A MEDLINE search was done to retrieve relevant papers published in English from 1999 to 2014. Papers of interest were all ED interventions for humans other than oral phosphodiesterase type 5 inhibitors (PDE5Is). **Databases:** MEDLINE – PubMed, Embase and OVID.	1. Twelve studies were selected. One article documented that 76% of subjects reached satisfactory sexual intercourse (SI) using intracavernosal injection of vasoactive medications (papaverine and prostaglandin E1). One study regarding perineal training showed a significant increase (P<0.05) in penile tumescence in 10 individuals with preserved sacral segment. Two studies reported contrasting results on erectile function (EF) using various dosages of oral fampridine (25-40 mg). Furthermore, 95.1% of patients on fampridine 25 mg experienced drawbacks. Disappointing findings were found with intraurethral alprostadil (125-1000 µg) and sublingual apomorphine 3 mg. Two studies concerning penile prosthesis reported valid SI more than 75% of the time with a mean follow-up of 11 years, although around 15% of individuals showed side effects. As for surgical treatments, 88% of males submitted to Brindley sacral anterior root stimulator after sacral dorsal rhizotomy achieved valid erection up to 8 years following the procedure. Three studies documented the impact of definitive sacral neuromodulation implant (Medtronic, Minneapolis, MN, USA) also on EF. After surgery, 20-37.5% of patients with ED recovered normal EF. 2. CONCLUSIONS: 3. Data are scant on the efficacy of ED treatments for SCL subjects who did not respond to PDE5Is. Further research should investigate the effects of any SCL treatments even when they are not

Author Year; Country Dates included in the review Total sample size Level of evidence Type of study Score	Methods Databases	Outcomes
		strictly used for neurogenic sexual dysfunction.
Courtois et al. 2012; Canada Reviewed published articles from 1948 to 2011 N=37 **Level of evidence:** methodological quality not assessed **Type of studies:** Not described AMSTAR=2	**Method:** search using autonomic dysreflexia (AD) and spinal cord injury (SCI) to find literature on the acute or prophylactic treatment of AD in the context of sexual activities; included all levels of evidence (randomized placebo control studies, case reports, literature reviews) and all years of publication; articles were read to assess whether they mentioned only a procedural management of AD or whether they specifically investigated a treatment of AD. **Databases:** MEDLINE.	***1.*** 37 papers on the specific treatment of autonomic dysreflexia (AD) showed nifedipine, prazosin, captopril and clonidine are candidates in the context of sexual activities; sildenafil and prostaglandins have given inconclusive results. ***2.*** Prazosin has an initial hypotensive effect therefore treatment should begin 12h before intercourse. This makes it less ideal for spontaneous sexual activities. ***3.*** Nifedipine remains the most widely studied and significant treatment of AD whether in acute or prophylactic conditions. ***4.*** Recent concerns suggest increased cardiovascular risks with sublingual nifedipine in non-SCI populations, but negative long-term effects have not been reported in the SCI population.

4.0 Sexual Health Assessment

People with SCI, the same as able-bodied individuals, should have sexual health care examinations, including genital/prostate examination for men, and genital/pelvic examination and menstrual function assessment for women. Relevant medical, surgical, psychological and relationship status information should be obtained, as well as any sexual issues prior to SCI. Medication that could interfere with sexual functioning (e.g., antidepressants, antispasmodics and opioids) should also be considered during an examination of sexual health (Alexander et al. 2017). There may be secondary health conditions common in people with SCI that have sexual ramifications (e.g., spasticity, pressure sores on the pelvis, buttocks or genitals, low testosterone in men, and bowel and bladder dysfunction) and they need to be considered by care professionals when providing health examinations (Alexander et al. 2017). Furthermore, contraception options and fertility wishes should be discussed.

4.1 Data assessment tools for sexual function

There is no one measurement tool that adequately assesses the complex issue of sexual health and satisfaction after SCI (Abramson et al. 2008). For an assessment to be comprehensive, neurological bases for sexual health dysfunction are necessary. (For a list of Outcome Measures validated for SCI in Sexual Health, visit: https://scireproject.com/outcome-measures/list-sci/).

The international community of SCI experts have collaborated to develop a number of ‘gold standard’ resources/assessments in order to facilitate better care in SCI. Three of the most important developments with regards to Sexual Health include:

1) The International Standards of Neurological Classification of Spinal Cord Injury (ISNCSCI) is a comprehensive assessment of motor function and sensation that is available after SCI. The ISNCSCI

is important not only to determine the level of injury and completeness, but to provide estimation of sexual functioning based on these findings. (For complete information on the ISNCSCI, how to administer, and statistical properties, go to: https://scireproject.com/outcome-measures/outcome-measure-tool/american-spinal-injury-association-impairment-scale-ais-international-standards-for-neurological-classification-of-spinal-cord-injury/).

2) The International Standards to Document of Remaining Autonomic Function after SCI (ISAFSCI) (Krassioukov et al. 2012) was designed to describe the diagnosis (supraconal, conal or cauda equina) of the spinal cord lesion and to document the impact of the injury on the components of autonomic response, including sexual (Worksheet available for free download at: http://asia-spinalinjury.org/wp-content/uploads/2016/02/Auto_Stan_Worksheet.pdf). The patient's ability to experience arousal, orgasm, ejaculation (male) or sensation of menses (female) are rated on a scale of 0 (no function), 1 (impaired function) or 2 (normal). If a patient is not experiencing these sexual functions (based on the level and completeness of his/her injury,) the clinician should investigate factors which may be interfering, e.g., medication or spasticity.

3) The International SCI Data Sets on Male Sexual Function and Female Sexual and Reproductive Function
These data sets are agreed upon as measures/indicators that both clinicians and researchers would need regarding SCI and Sexual Health. They are meant to establish a standard of data collection/clinical intake that is valid anywhere in the world. Complete instructions for data collection, data sheet and training cases are available at: http://www.iscos.org.uk/international-sci-female-sexual-and-reproductive-function-data-sets http://www.iscos.org.uk/international-sci-male-sexual-function-data-sets.

5.0 Sexual and Reproductive Health in Men with SCI
SCI can be a risk factor for abnormally lower levels of testosterone (the main male hormone for sexual function and libido). In one study, 46% of men with SCI were identified as having low serum total testosterone concentrations (total testosterone <11.3 nmol/l), which is higher than seen with the age-related decline in total serum testosterone concentrations found in the general population (Baumann et al. 2014). Furthermore, the prevalence of testosterone deficiency was significantly greater in participants with motor complete (AIS A and B) injuries compared with those with motor incomplete (AIS C, D, and E) injuries, and in those taking narcotic medications for pain management (Durga 2011). Other additional factors which can lower testosterone after SCI include a concomitant brain injury, being obese, having diabetes or the metabolic syndrome, and having untreated sleep apnea (Morales et al. 2010). After SCI, reduction in serum testosterone can also lead to loss of muscle mass and gain of fat mass - a body composition that is already a problem after SCI. Body composition also plays a part in the development of pressure ulcers since muscle is better able to disperse pressure from the bony prominences than fat or skin.

5.1 Male Erectile Response and Enhancement
In general, the majority of men can attain an erection after SCI either through the psychogenic (T11-L2) or reflexogenic (S2-S4) pathways, depending on the level and completeness of injury. However, these erections are often unreliable or inadequate for sexual intercourse with difficulties experienced in maintaining an erection (Alexander et al. 1993; Courtois et al. 1993). Treatments for erectile dysfunction (ED) in men with SCI have advanced considerably in recent years with the availability of phosphodiesterase type 5 inhibitors (PDE5i) taken as a tablet orally. However, other methods are still being used when oral medication is ineffective or unaffordable. There is stronger evidence for treatment of erectile dysfunction than other areas of sexuality in SCI, primarily due to the advent of the PDE5i and their effectiveness in this population.

Therapies for erectile dysfunction (ED) include:

1. Oral medications, which indirectly relax the penile smooth muscle and enhance an erection attained by sexual stimulation, such as the oral phosphodiesterase 5 inhibitors [PDE5i] sildenafil (Viagra®), vardenafil (Levitra®) and tadalafil (Cialis®). Avanafil (Stendra®) is available in the USA and potentially soon in Canada.
2. Intracavernosal injectable medications, which directly relax the penile smooth muscle creating an erection (prostaglandin E1 penile injections [Caverject® or compounded] and other injectable combinations of papaverine and phentolamine)
3. Topical agents for penile smooth muscle relaxation (prostaglandin, minoxidil, papaverine and nitroglycerine)
4. Intraurethral preparation of prostaglandin E1 (MUSE®)
5. Mechanical methods, such as vacuum devices and penile rings
6. Surgical penile implants
7. Behavioural methods (perineal muscle training)
8. Psychological and sex therapy (non-medicinal) adjunct to medical therapies after SCI

All methods except penile implants are clinically reversible. The use of implantable sacral stimulators to assist an erection via stimulation of S2 and S3 anterior roots has not been well explored due to its limited use in those with complete SCI lesions (Brindley et al. 1989). The detrimental effects on erectile function of baclofen and baclofen pumps are noted, but they appear to be clinically reversible with baclofen discontinuation.

Table 2: Systematic Reviews on Erectile Response and Function

Author Year; Country Dates included in the review Total sample size Level of evidence Type of study Score	**Methods Databases**	**Outcomes**
DeForge et al. 2006; Canada Review of published and unpublished articles between 1966 and 2003 N=49 <u>Level of evidence</u> Jadad Scale – RCTs Newcastle-Ottawa Scale – Non RCTs <u>Type of studies</u> Not reported AMSTAR=7	**Methods:** Studies reporting on the effectiveness of erectile interventions in adolescents and adults with SCI. Interventions included devices (e.g. penile ring), prescription medications (oral, cream, injections) surgery, hormones, and behavioural (e.g. masturbation). **Databases:** MEDLINE, PreMEDLINE, CINAHL, Cochrane Central Register of Controlled Trials, SocioFile, PsycINFO.	1. Penile injection and sildenafil were successful in 90% and 79% of men respectively. Differences of efficacy not statistically significant. 2. No clear differences of efficacy between injections of papaverine, phentolamine, and prostaglandin E1. 3. High satisfaction rate of penile implants with 10% complications.
Rizio et al. 2012; USA Reviewed published articles from 2000 to August 2010 N=10	**Method:** Studies reporting on the efficacy and satisfaction of oral phosphodiesterase type 5 inhibitors (PDE5i) to treat ED secondary to SCI. Studies (any research design and language) using the International Index of Erectile Function (IIEF) as an outcome measure and done on more than 20 men with SCI were included. **Databases:** PubMed, CINAHL.	**1.** Statistically significant improvement of erectile function with the use of PDE5i's. Sildenafil, tadalafil, and vardenafil were equally effective. **2.** Improved sexual function satisfaction with all three. **3.** Tadalafil has a longer time duration effectiveness, which allows for more spontaneity in the sexual experience.

Author Year; Country Dates included in the review Total sample size Level of evidence Type of study Score	Methods Databases	Outcomes
Level of evidence: not reported Type of studies n/a AMSTAR=6		**4.** Minimal adverse effects noted: headache, flushing, and mild hypotension were most common.
Lombardi et al. 2012; Italy Reviewed published articles from Medline and PubMed up until June 2011 N=28 (21 for SCI) Level of evidence Reliability of studies assessed but method not specified Type of studies All clinical trials AMSTAR=4	**Method:** Searched for all clinical studies reporting efficacy/safety on treatments of at least 4 weeks with PDE5i in human patients with central neurological disorders suffering from ED. Only full-text articles were included; single case-reports and articles examining the effect of a single dose of PDE5 were excluded. No language restrictions were imposed. **Databases:** MEDLINE and PubMed	**1.** PDE5i represent first line ED therapy for SCI patients. **2.** Sildenafil, tadalafil, and vardenafil all significantly improved erectile function in SCI patients. **3.** PDE5i efficacy was documented for SCI patients for up to 10 years; treatment resistance did not occur. **4.** The most frequent predicable factor for PDE5i success and efficacy at low dosage was the presence of upper motoneuron lesion.
Martin et al. 2013; USA Reviewed published articles from July 2001-July 2011 N=12 (1 SCI) Level of evidence Methodological quality not assessed Type of studies Not described AMSTAR=3	**Method:** Searched using keywords “cost, budget, expenditure, resource use, economic, pharmacoeconomic, productivity, work loss, willingness to pay” to identify relevant economic publications in English on sildenafil in ED. Only studies with at least 20 patients were included. Relevant narrative reviews were included if published between 2007-2011. Conference abstracts were also examined for content. **Databases:** Medline and Embase	**1.** Only one study, Mittman et al. 2001, included patients with SCI. This study was a cost-utility analysis conducted in Canada, comparing sildenafil to transurethral suppository, intracavernous injections (ICI), vacuum erection device (VED), penile prosthesis surgery (PPS). 2. The annual cost of sildenafil was CAN$1,534, which was cheapter than costs associated with alprostadil intracavernous injections ($1908), alprostadil transurethral suppositories ($2613) and surgery ($7875) but more expensive than triple mix: alprostadil/papaverine/phentolamine ($858) and VED ($730). **3.** Sildenafil is the dominant economic strategy for SCI patients as sildenafil is less expensive and has a higher utility than the other treatments.
Lombardi et al. 2009; Italy Reviewed published articles from 1998 to 2008	**Method:** 18 internationally published clinical studies that enrolled SCI males treated with at least one of the PDE5 inhibitors and analyzed to evaluate how much the release of PDE5 inhibitors changed the management	1. 705 participants used sildenafil, 305 vardenafil and 224 tadalafil. Median age was <40 yrs. Only one study excluded tetraplegic individuals.

Author Year; Country Dates included in the review Total sample size Level of evidence Type of study Score	Methods Databases	Outcomes
N=18 Level of evidence methodological quality not assessed Type of studies RCT (n=7), case series (n=4), non-randomized CT (n=3), prospective CT (n=2), pre-post (n=1), review (n=1) AMSTAR=3	of erectile dysfunction (ED) in men with SCI and what remains to be seen of their potential or limits. **Databases:** Information not provided.	2. For measures of erectile dysfunction (ED) evaluated, 11 out of 13 studies reported significant statistical improvement with PDE5 inhibitors vs. placebo or erectile baseline. 3. The most frequent predicable factor for the therapeutic success of PDE5 inhibitors was upper motoneuron lesion. 4. Statistical impact on ejaculation success rates was shown in at least one paper for all PDE5 inhibitors. 5. Overall 15 patients (7 using sildenafil) discontinued the therapies due to drawbacks. Only one sildenafil study reported a follow-up max. of 24 mos.
Derry et al. 2002; UK Non-systematically reviewed articles from 1998 to 2001 N=6 Level of evidence methodological quality not assessed Type of studies RCT (n=2), Prospective case series (n=4) AMSTAR=2	**Method:** Search for articles examining efficacy and safety of sildenafil treatment of erectile dysfunction (ED) in men with SCI. **Databases:** Information not provided.	1. For general efficacy the proportion of patients who reported improved erections and ability to have intercourse was as high as 94%. Up to 72% of intercourse attempts were successful. 2. For measures of erectile function, 5 of 6 studies showed statistically significant improvements among sildenafil-treated vs. placebo-treated patients. 3. Incidence of adverse events from all causes in patients treated with sildenafil ranged from 10% to 42%. The most commonly reported adverse events were headache, facial flushing, nasal congestion, dyspepsia and visual disturbances. 4. Existing evidence suggests oral sildenafil is a highly effective and well-tolerated treatment for ED associated with SCI.
Brison et al. 2013; USA Reviewed publications relevant to the field of vacuum erection devices N=5 (SCI) Level of evidence Methodological quality not assessed Type of studies Not described AMSTAR=1	**Method:** searched for all publications related to vacuum erection devices (VEDs). **Databases:** Not mentioned.	**1.** 5 studies investigating the effects of VEDs in SCI patients showed that VEDs are a viable alternative for treatment of ED in the SCI population. VEDs are well tolerated, and improve erectile function and sexual satisfaction. **2.** 70% of men using the VED reported normal International Index of Erectile Function-Erectile Function domain (IIEF-EF) scores after treatment, compared with 0^ before treatment. Men using sildenafil or penile injections comparatively reported 90% normal IIEF scores. **3.** In a 20 patient study, 93% of men reported rigidity sufficient for vaginal penetration after 3 months use with the VED.

Author Year; Country Dates included in the review Total sample size Level of evidence Type of study Score	Methods Databases	Outcomes
		4. The most common complaint was premature loss of penile rigidity during intercourse
Todd 2011; UK Reviewed published studies from 1950-2005 N=not stated Level of evidence Methodological quality not assessed Type of studies 1 case report, 1 case series, other studies not described AMSTAR=1	**Method:** Searched using key terms priapism, penile erection or clitorism plus spinal injury. Only English articles were included. **Databases:** Oldmedline (1950-1965), Medline (1966-2005) and PubMed.	**1.** There is a very restricted literature that has reported priapism in patients with SCI. One study reported 6 patients with priapism following acute SCI; all patients had AIS A lesions. Another study described a patient undergoing posterior spinal fixation for a fracture of L2 who awoke with priapism and a complete motor and sensory paraplegia that was a consequence of a large epidural haematoma. **2.** Priapism has been reported following spinal shock. Typically, priapism that follows acute traumatic SCI is high-flow (non-ischaemic) priapism (blood within the corpus is arterial in nature). **3.** Following traumatic SCI, priapism usually settles rapidly without specific treatment required. **4.** Priapism occurs at the moment of complete motor and sensory paraplegia, it does not occur following a delay.
Lombardi et al. 2015 Italy AMSTAR=9 Non-systematically reviewed articles from 1998 to 2001 N=6 Level of evidence methodological quality not assessed Type of studies RCT (n=2), Prospective case series (n=4) AMSTAR=2		Review study. **OBJECTIVES:** Alternative treatments to oral phosphodiesterase type 5 inhibitors (PDE5Is) in individuals with spinal cord lesions (SCLs) and erectile dysfunction (ED). **SETTING:** Italy. **METHODS:** Research clinical trials (1999-2014). **RESULTS:** Twelve studies were selected, 6 documenting conservative treatments and 6 documenting surgical treatments. One article documented that 76% of subjects reached satisfactory sexual intercourse (SI) using intracavernosal injection of vasoactive medications (papaverine and prostaglandin E1). One study regarding perineal training showed a significant increase ($P<0.05$) in penile tumescence in 10 individuals with preserved sacral segment. Two studies reported contrasting results on erectile func tion (EF) using various dosages of oral fampridine (25-40 mg). Furthermore, 95.1% of patients on fampridine 25 mg experienced drawbacks. Disappointing

Author Year; Country Dates included in the review Total sample size Level of evidence Type of study Score	Methods Databases	Outcomes
		findings were found with intraurethral alprostadil (125-1000 µg) and sublingual apomorphine 3 mg. Two studies concerning penile prosthesis reported valid SI more than 75% of the time with a mean follow-up of 11 years, although around 15% of individuals showed side effects. As for surgical treatments, 88% of males submitted to Brindley sacral anterior root stimulator after sacral dorsal rhizotomy achieved valid erection up to 8 years following the procedure. Three studies documented the impact of definitive sacral neuromodulation implant (Medtronic, Minneapolis, MN, USA) also on EF. After surgery, 20-37.5% of patients with ED recovered normal EF. **CONCLUSIONS:** Data are scant on the efficacy of ED treatments for SCL subjects who did not respond to PDE5Is. Further research should investigate the effects of any SCL treatments even when they are not strictly used for neurogenic sexual dysfunction.

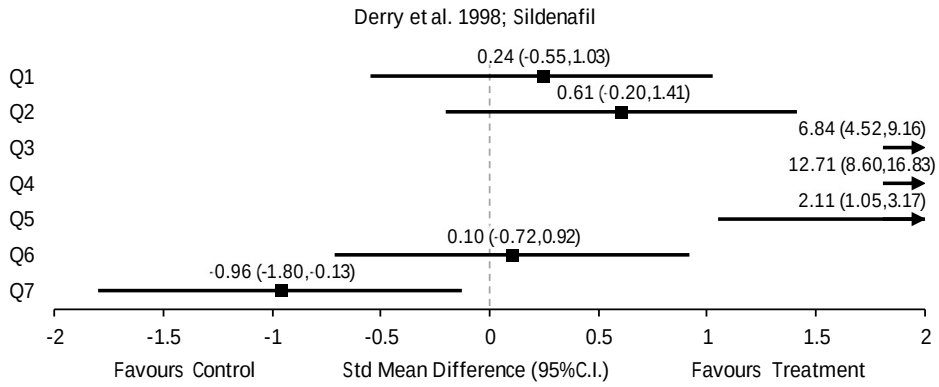
5.1.1 Phosphodiesterase Type 5 Inhibitors (PDE5i) and Other Oral Agents

Erection is initiated by smooth muscle relaxation of the corpora cavernosa (erectile bodies) of the penis and depends on the nitric oxide-cyclic guanosine monophoshpate [cGMP] pathway. The PDE5i are selective inhibitors of type 5 (cGMP specific) phosphodiesterase, which in turn delay breakdown of cGMP, prolonging and enhancing the erectile response. Apomorphine is a dopamine-receptor agonist important in the control of sexual functioning, whereas 4–aminopyridine is a K^+ channel-blocking agent noted for increasing neurotransmitter release at neuronal sites and enhancing conductivity in demyelinated axons. Most clinicians recommend that men with SCI, regardless of their level of injury, be offered a trial of PDE-5 inhibitors (Rizio et al. 2012).

Table 3: Effects of Phosphodiesterase Type 5 Inhibitors (PDE5i) and Other Oral Agents

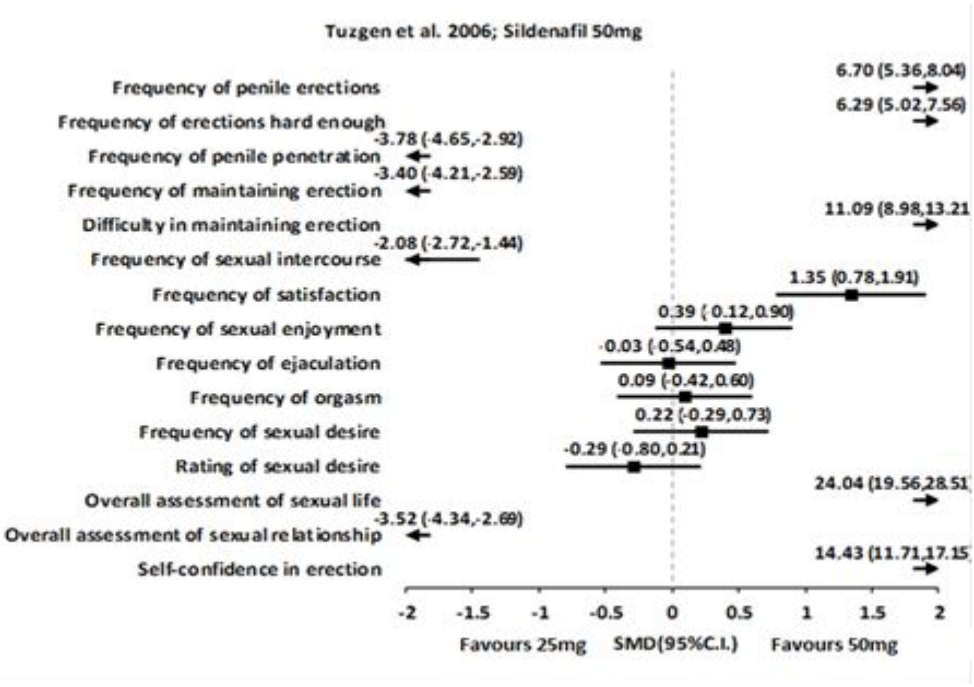
Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Khorrami et al. 2010; Iran RCT Level 1 PEDro=9 N=105	**Population:** 105 men with SCI who had neurogenic erectile dysfunction; all with paraplegia; mean age 47.6 (range 40-55); divided into those with upper motor neuron (UMN) injuries (n=72) and those with lower motor neuron (LMN) injuries (n=33). **Treatment:** Sildenafil 50mg 45min before start of sexual intercourse, increased to 100mg if not effective, for treatment group (n=45 from UMN and n=14 from LMN);	1. 37 (82%) of the 45 UMN participants who took sildenafil had a favourable response, compared to 7 (26%) of the 27 placebo UMN participants. 2. 4 (28.5%) of the 14 LMN participants who took sildenafil had a favourable response, compared to 5 (26%) of the 19 LMN participants who had placebo. 3. Side effects include headache (n=8), flushing (n=4) and gastro-intestinal discomfort (n=3).

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	placebo for control group (n=27 from UMN and n=19 from LMN). **Outcome Measures:** International Index of Erectile Function (IIEF5) questionnaire; if subject scored more than 15 points on the IIEF5, then treatment considered effective, if less than 15 then inadequate.	
Giuliano et al. 2008; USA RCT Level 1 PEDro=9 N=418	**Population:** 418 men with SCI over 18 yrs old with resulting erectile dysfunction for over 6 months, and in a stable heterosexual relationship for over 1 month, randomized to vardenafil (n=207) or placebo (n=211). **Treatment:** Vardenafil (placebo for controls) for 12 weeks; dosage for the first 4 weeks was 10mg, and subsequently adjusted individually to 20 or 5mg. **Outcome Measures:** Success of ejaculation; International Index of Erectile Function (IIEF) scores; Global Confidence Question (GCQ); Psychological General Well-Being Index (PGWBI); Centre for Epidemiological Studies – Depression (CES-D) score; Rosenberg Self-Esteem Score (RSES); Mental Health Summary of the SF-36 Health Survey.	1. Success rate of ejaculation was significantly higher in the vardenafil group compared to control (19% vs. 10%). 2. The IIEF orgasmic function domain score (questions 9 and 10) increased from 2.9 to 4.0 in vardenafil group, compared to 3.0 to 3.4 in control. 3. The GCQ score increased from 2.5 to 3.5 in the vardenafil group, compared to from 2.6 to 2.9 in control (significant difference). 4. No significant difference between vardenafil and control groups in the PGWBI, the CES-D, RSES, or SF-36 mental health domain scores before and after treatment.
Ergin et al. 2008; Turkey RCT with crossover Level 1 PEDro=8 N=50	**Population:** 50 men with SCI, over 19 yrs old, with associated erectile dysfunction but had some psychogenic or reflexogenic erectile function. **Treatment:** 50mg of sildenafil (placebo for controls) 1 hr before sexual activity, for 6 weeks; this was followed by a 2-week washout period, after which the patient was switched to the alternate treatment for another 6 weeks. **Outcome Measures:** International Index of Erectile Function (IIEF); Life-Satisfaction Check List (LISAT-8); Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS); Global Efficacy Assessment questionnaire.	1. Sildenafil produced greater improvements than placebo in following areas: satisfaction with sex life and sexual relationship (IIEF questions 13 and 14), EDITS score, erective function and overall sexual satisfaction. 2. No difference between the 2 groups with regard to total IIEF scores. 3. No difference between the 2 groups with regard to intercourse satisfaction or sexual desire. 4. No reports of AD symptoms in patients undergoing treatment. 5. Participants with incomplete injuries showed improvement in 7/11 measures whereas participants with complete injuries showed improvement in 3/11 measures.
Derry et al. 1998; UK RCT Level 1 PEDro=8 Initial N=27 Final N=26	**Population:** 27 men, treatment n=12, placebo n=14; Age: mean 32-34 yr; Injury level: T6-L5, AIS: A-D but must have partial reflexogenic erection to vibrostimulation. **Treatment:** Randomized to receive 50mg of sildenafil or placebo not more than 1/day, approx 1 hr before sexual activity. **Outcome Measures**: Efficacy and safety of sildenafil, sexual function questionnaire.	1. 75% on sildenafil and 7% on placebo reported that treatment improved erections. 2. Significant improved satisfaction with sex life reported by sildenafil group. 3. Mean number of grade 3-4 erections was 1.8/wk for sildenafil group, 0.4/wk for placebo patients.
	Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- and post-intervention data	

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	 Q1: frequency of sexual desire; Q2: rating of sexual desire; Q3: frequency of waking with erection; Q4: frequency of stimulated erections; Q5: frequency of erections hard enough for sex; Q6: frequency of erections lasting long enough; Q7: satisfaction with sex life	
Giuliano et al. 2007; France RCT Level 1 PEDro=7 N=186	**Population:** 186 men with SCI; Age: mean 38 yrs, range 18-66; Level of injury: cervical 15.6%, thoracic 62.0%, lumbosacral 22.3%; Impairment grade: 69% AIS A; Erectile dysfunction (ED) at least 6 months. **Treatment:** Tadalafil 10-20mg for 12 wks or placebo, 1 tablet 1 hr before each attempt at intercourse, not more than 1 dose/day, at wks 4 and 8 dose maintained or titrated up/downwards (10 or 20mg). **Outcome measures:** International Index of Erectile Function (IIEF)/Erectile Function (EF) domain, Sexual Encounter Profile (SEP), adverse events.	1. IIEF/EF: Tadalafil group improved (13.5 to 22.6) compared to placebo group (13.0 to 13.6). 2. Tadalafil group compared to placebo reported greater mean per-patient percentage of successful penetration attempts (75.4% vs 41.1%), greater percentage improved erections (84.6% vs 19.5%), and greater ejaculatory frequency. 3. Adverse events: headache (8.5% vs 4.5%) and UTI (7.7% vs 6.8%).
Giuliano et al. 1999; UK RCT (cross-over) Level 1 PEDro=7 N=178	**Population:** 178 men, Age: mean 38 yrs, Impairment: 53% complete. **Treatment:** Sildenafil 25, 50, or 100mg or placebo, 1hr before sexual activity for 6 weeks followed by a 2-week washout before cross-over. **Outcome Measures:** Efficacy and safety of oral sildenafil, International Index of Erectile Function (IIEF), event log data.	1. IIEF: 83% reported improved erections with sildenafil vs. 12% on placebo. 2. Ability to achieve & maintain erection, satisfaction of sexual intercourse, & satisfaction of sexual relationship with partner significantly improved with sildenafil over placebo. 3. Ejaculation and orgasm frequency improved in sildenafil group over placebo.
Maytom et al. 1999; UK RCT Level 1 PEDro=7 N=27	**Population:** 27 men; Age: range 21-49 yrs; Impairment grade: AIS A (n=14), B (n=3), C (n=5), D (n=5); Level of injury: T6-L5. **Treatment:** Single dose sildenafil 50mg or matching placebo (part I) in random order followed by at least a 3 day washout period before cross-over treatment (part II) for 28 days. **Outcome Measures**: Efficacy and safety of sildenafil, duration & rigidity of erections, self-report diary data.	1. Part I: 65% had erections (defined as >60% rigidity) on sildenafil, 8% with placebo. 2. Part II: 75% on sildenafil & 7% on placebo reported improved erections. 3. Sexual Satisfaction: the sildenafil group were more satisfied with their sex lives.
Potter et al. 1998; USA	**Population:** 26 men; Age: mean 40.6 yrs; Injury level: C4-T12, tetraplegia (n=19),	1. No significant results related to sexual function.

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
RCT Level 1 PEDro=7 Initial N=29 Final N=26	paraplegia (n=10), incomplete. **Treatment:** Fampridine-SR or placebo 12.5mg for first week, 17.5 mg for 7 days, 1 week washout before cross-over. **Outcome Measures:** Safety and efficacy of oral Fampridine-SR, patient satisfaction, quality of life, sensory and motor scores, Ashworth.	2. 5 fampridine-SR patients reported erection improvement; however 4 placebo patients also reported erection improvement.
Cardenas et al. 2014 US and Canada RCT PEDro=6 Study SCI-F301 N=213 Study SCI-F302 N=204	**Population:** Patients with incomplete chronic SCI from two identical double-blinded, placebo-controlled studies (SCI-F301 and SCI-F302), from 45 and 33 centres, respectively, in the US and Canada. Both patient populations were balanced at baseline rendering comparability of patient populations. SCI-F301: Placebo (n=98): Mean age: 40.1 yr; Gender: males=85, females=13. Fampridine-SR (n=114): Mean age: 41.6 yr, Gender: males=100, females=14. SCI-F301: Placebo (n=100): Mean age: 40.5 yr. Fampridine-SR (n=103): Mean age: 41.3 yr. **Intervention.** Patients were randomly assigned to either fampridine-SR 25 mg or placebo, twice daily for 2 wk in addition to a 2 wk titration, 12 wk of stable dosing, 2 wk of downward titration and 2 wk of untreated follow-up. Within treatment groups, patients were further stratified by concomitant antispasmodic medication within the two treatment groups. **Outcome Measures:** Ashworth Spasticity Scale (AS) scores for bilateral knee flexors and extensors, Subject Global Impression (SGI), Penn Spasm Frequency Scale (SFS), International Index of Erectile Function (IIEF), Bowel and Bladder assessments, Sexual function.	1. There were no significant between-treatment differences except for an improvement among men treated with fampridine-SR on two IIEF domains, erectile function (p=0.016) and orgasmic function (p=0.032) in SCI-F301.
Cardenas et al. 2007; USA RCT Level 1 PEDro=6 N=91	**Population:** 72 men (19 female) with SCI; Injury level: C4-T10, AIS C-D; Age: mean 38-42 yrs, range 19-67; Time since injury at least 1 yr. **Treatment:** Fampridine-SR 25mg 2 times per day or fampridine-SR 40mg 2 times per day for 8 wks (2-wk dose titration, 4 wks at fixed target dose, 2-wk downward titration) or placebo. **Outcome Measures:** International Index of Erectile Function (IIEF), adverse events.	1. IIEF: non-significantly improved scores for fampridine-SR 25mg and 40mg 2 times per day vs placebo. 2. Erection frequency: significantly improved for fampridine-SR 25mg group vs placebo. 3. Adverse events: fampridine-SR 40mg: increased incidence of abdominal pain, dizziness, insomnia, paresthesia, nervousness, and anxiety vs placebo; fampridine-SR 25mg: increased incidence of pain vs placebo.
Del Popolo et al. 2004; Italy RCT Level 1	**Population:** 30 men, Age: range 21-60 yrs; Injury level: cervical (n=9), above T10 (n=6), below T10 (n=10); Time since injury: 6-12 months.	1. Tadalafil allowed normal sexual functioning up to 24hr post dosing compared to sildenafil.

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
PEDro=6 N=30	**Treatment:** Randomized to sildenafil (4 doses 50mg) or tadalafil (4 doses 10 mg). To attempt intercourse on 4 separate occasions: within 4h of 1st tablet, 12h of 2nd tablet, 24h of 3rd and 24-36h after 4th tablet. Cross-over after 2 wk wash-out. **Outcome Measures**: Safety, time/duration effectiveness, Sexual Encounter Profile.	
Giuliano et al. 2006; USA RCT Level 1 PEDro=6 N=418	**Population:** 418 men, treatment n=207, placebo n=211; Age: range 18-80 yrs; Injury level: below T12 (n=94), at or above T12 (n=307). **Treatment:** Randomized to 12 wks of vardenafil (10mg for the first 4 wks) or placebo. 1 tablet 1 hr before each attempt at intercourse, not more than 1/day. At wks 4 and 8, dose maintained or titrated increasing or decreasing 1 step (to 5 or 20 mg). **Outcome Measures:** Efficacy and tolerability of vardenafil, Erectile Function Domain Scores (from International Index of Erectile Function), Sexual Encounter Profile.	1. EF domain scores in the vardenafil group improved significantly (22.0 from 11.6) compared to the placebo group (13.5 from 12.1). 2. Over 12 weeks of treatment, mean per-patient penetration (76% vs 41%), maintenance (55% vs 22%), and ejaculation success rates (19% vs 10%) on vardenafil were significantly greater vs the placebo group.
Hultling et al. 2000; Australia RCT (cross-over) Level 1 PEDro=6 N=178	**Population:** 178 men with SCI; Age: mean 38 yrs, range 19-63 yrs. **Treatment:** Sildenafil upward and downward titration with variable dose of 25mg 1hr pre-sexual activity to a maximum of 100mg. Doses adjusted by 25mg/wk during 6-wk period. Randomized to 6-wk flexible dosing, 2 wk washout, then 6-wk placebo or vice versa. **Outcome Measures:** Efficacy of sildenafil citrate, IIEF (Q13,14), Medical Outcomes Survey, SF-12, Psychological General Well-Being Index.	1. Increase in overall satisfaction with sex life (49% over baseline). 2. Sexual relationship with partner (increased 34% over baseline) with sildenafil. 3. "Impact of erectile problems" assessing emotional distress improved 23% above baseline.
Tuzgen et al. 2006; Turkey RCT Level 1 PEDro=6 N=60	**Population:** 60 Men with SCI; Age: mean 35.2 yrs, range 25-45; Impairment: AIS A (n=28), AIS B (n=8), AIS C (n=7), AIS D (n=17); Mean time since injury: 53.5 months. **Treatment:** Sildenafil 25mg or sildenafil 50mg for 4 wks, 1 hr before sexual activity. **Outcome measures:** International Index of Erectile Function (IIEF) - Erectile Function (EF), Intercourse Satisfaction (IS), Overall Satisfaction (OS), Orgasmic Function (OF), and Sexual Desire (SD); adverse events.	1. Improved reflexogenic erectile response in both groups. 2. Significant improvement in erections, frequency of sexual intercourse, satisfaction, enjoyment, sexual desire, overall sex life, sexual relationship, and self-confidence in erections at both the low and the high dosage. 3. There were no significant differences between the low dose and the high dose groups. . 4. There were 13 and 16 adverse events recorded in the low dose and high does group respectively. Main adverse events: headache, dyspepsia and rash.
	Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- and post-intervention data	

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
		
Hultling 1999; Sweden RCT Level 1 PEDro=5 N=178	**Population:** Men with SCI and partner; Age: mean 30 yrs, range 19-63 yrs. **Treatment:** Sildenafil flexible-dose 25-100mg (on demand) for 6 wks (cross-over with 4-wk washout period). **Outcome measures:** ability to have intercourse, partner perception of ability to achieve erection and ability to maintain erection.	1. Men: improved ability to achieve erections and to have intercourse was reported by 83% and 80% of men, respectively, compared to the placebo group with 10% reporting improvements. 2. The number of successful attempts at intercourse improved in the sildenafil group. 3. Partner perception: improved ability to achieve and maintain erections with sildenafil.
Yildiz et al. 2011; Turkey Prospective, one-way crossover, dose-controlled study Level 2 N=31	**Population:** Men with erectile dysfunction secondary to SCI**.** **Treatment:** Day 1**-** Group 1: visual and auditory sexual stimulus (VASS) Group 2: VASS with 25 mg of intracavernosal papaverine; Group 3: after a wash-out period of papaverine on day 2, VASS with 50mg oral sildenafil on day 5. **Outcome Measures:** Peak (PSV) and end diastolic velocity (EDV) using penile color Doppler ultrasound.	1. There was a statistically higher PSV with papaverine (45.31(11.37)) or with sildenafil (41.59(15.55)) compared to control (22.25(7.54)). 2. There was no statistically significant difference between the PSV and EDV values of the papverine and sildenafil groups.
Lombardi et al. 2009a; Italy Pre-post Level 4 N=103	**Population:** 103 men with SCI and erectile dysfunction (mean age 39) **Treatment:** Tadalafil 10mg for 4 weeks; participants whose IIEF (ED) score were still less than 26 were treated with Tadalafil 20mg for 4 weeks; participants who responded well to the treatment (n=74) continued treatment and were included in a 6-month follow up. **Outcome Measures:** International Index of Erectile Function (IIEF15); Sexual Encounter Profile (SEP) question 2 and 3.	1. 38 out of 103 participants responded to 10mg of Tadalafil. 2. 36 participants subsequently responded to 20mg of Tadalafil. 3. 9 patients dropped out of the follow-up due to various reasons. 4. There was a statistically significant improvement in erectile function, sexual satisfaction, and SEP2-3 scores in the follow-up group.

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
		5. There was no significant difference in ejaculatory function.
Lombardi et al. 2009b; Italy Pre-post Level 4 N=113	**Population:** 113 participants with SCI and with erectile dysfunction (ED), median age 39 (range 21-67), mean time since injury 39 months (range 6-74 months); 74 participants had injury level above T12, and 70 were AIS A. **Treatment:** Sildenafil 50mg, increased to sildenafil 100mg for non-responsive participants. **Outcome Measures:** Sexual Encounter Profile Questions 2 and 3 (SEP2 and SEP3); International Index of Erectile Function (IIEF15) erectile domain score; both scales were used for Phase 1, and only IIEF15 was administered for Phase 2 (follow-up every 6 months for 10 years).	1. 75 participants reached an erectile domain score of at least 26 and answered "yes" for 75% of the time or more for SEP2 and 3; of these participants 48 responded to 50mg of sildenafil while the rest had increased to 100mg. 2. In responsive participants, the IIEF15 erectile domain score increased from 16-18 to above 25. 3. 34 of the 75 responsive participants stayed for Phase 2 of the study; erectile domain scores remained stable at above 25 for the duration of the 10-year follow-up.
Soler et al. 2009; France Pre-post Level 4 N=14	**Population:** Men who sustained an abnormal prolonged erection or priapism following an intracavernous injection of prostaglandin E1 to induce erection. **Treatment:** Oral midodrine following the failure of 30 minutes of cooling procedures using ice or ether, or penile vibrator stimulation. **Outcome measures:** evaluation of penile rigidity at 30 minutes, and 1, 3 and 6 hours post treatment.	1. All patients returned to flaccid penile state within 30-45 min after midodrine administration. 2. Oral midodrine well tolerated with few side effects and without increasing incidence of AD. 3. Complete erection could be induced again 6 months later by intracavernous injection in all treated patients.
Moemen et al. 2008; Egypt Pre-post Level 4 N=60	**Population:** 60 men with SCI and erectile dysfunction, at least 6 months post-injury, randomized into 3 groups of 20 (A, B, C). **Treatment:** Group A took sildenafil 50mg before sexual activity for 1 month; Group B were given intracorporal injection (ICI, 10 mg/ml prostaglandin E1 or 0.5 ml trimix) for 1 month and then took sildenafil for 1 month; Group C used vacuum constriction device (VCD) for 1 month and sildenafil for 1 month. **Outcome Measures:** International Index of Erectile Function – erectile function domain (IIEF-EF); Global Efficacy Assessment Questionnaire (GAQ); Hormonal Profile.	1. The improvement in the IIEF-EF score was 90% in all groups after sildenafil, 90% in Group B after ICI, and 70% in Group C after VCD. 2. Improvement in erection reached 100% in all groups according to the GAQ, but ability to penetrate reached 90% after sildenafil, 90% after ICI, and 70% after VCD. 3. There was a significant increase in testosterone in all groups after sildenafil treatment. 4. Participants in Group B reported that ICI resulted in more rigid erections than sildenafil, but 14 of the 20 participants preferred sildenafil due to easier administration; no participants in Group C was satisfied with VCD and preferred either ICI or sildenafil.
Soler et al. 2007; France Pre-post Level 4 N=240	**Population:** Men with SCI; Age: mean 32.6-36.2 yrs; tetraplegia (n=78), paraplegia (n=145), cauda equine (n=17); Impairment: AIS A (n=197), AIS B (n=19), AIS C (n=18), AIS D (n=6); Mean time since injury 91.5-112.4 months. **Treatment:** Sildenafil (50-100mg, n=120), tadalafil (10-20mg, n=66), and vardenafil (10-20mg, n=54) depending on	1. Good rigidity reported by 85% (sildenafil), 74% (vardenafil), and 72% (tadalafil) of the patients. 2. Mean duration of erection: 34 min (sildenafil), 28 min (vardenafil), 26 min (tadalafil). 3. IIEF: improved global and domain (EF, IS, and OS) scores for all groups; improved orgasmic function and ejaculation for sildenafil group.

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	efficacy/tolerability, follow-up at 3 months. **Outcome measures:** Quality of erection; duration of erection; International Index of Erectile Function (IIEF) - Erectile Function (EF), Intercourse Satisfaction (IS), Overall Satisfaction (OS), Orgasmic Function (OF), and Sexual Desire (SD); adverse events.	4. Initial dose sildenafil (50mg) effective in 55%, whereas vardenafil and tadalafil (10mg) ineffective in over 70%. 5. Adverse events: mild; 15% on sildenafil (headache, flushing, dizziness, dyspepsia); 14% on vardenafil (headache, dizziness); 6% on tadalafil (headache, back pain).
Kimoto et al. 2006; Japan Pre-post Level 4 N=32	**Population:** 32 men with SCI; Age: mean 37.5 yrs, range 20-64; Level of injury: T12-lumbar (n=10), cervical-T11 (n=22); Time since injury at least 6 months. **Treatment:** Vardenafil 10mg for 12 wks or vardenafil 10mg for 4 wks and then 20mg for 8 wks. **Outcome measure:** International Index of Erectile Function (IIEF)/Erectile Function (EF), success in penetration, success in maintaining erection during intercourse.	1. IIEF/EF: Improved in both the 10/10mg group (12.2 to 25.0) and the 10/20mg group (10.3 to 22.5); the 10/20mg group increased 5.0 points following up-titration. 2. Success in penetration: 10/20mg group: 56% at 4 wks, 76% at 8 wks, 83% at 12 wks; 10/10mg group: 88% at 4-12 wks. 3. Success in maintaining erection: 10/20mg group: 43% at 4 wks, 62% at 8 wks, 69% at 12 wks; 10/10mg group: 81% at 4-12 wks.
Gans et al. 2001; USA Pre-post Level 4 N=17	**Population:** 17 men with SCI; Age: mean 40.3 yrs, range 25-58; Injury level: cervical (n=4), thoracic (n=12), lumbar (n=1). **Treatment:** Sildenafil 25mg (dose increased in 25mg increments as needed), mean(SD) follow up of 5.3(2.2) months. **Outcome measures:** International Index of Erectile Function (IIEF) (abridged version), questions on aspects of sexual function.	1. IIEF scores improved significantly compared with baseline or previous therapies. 2. Of the 17 men, 94% recommended sildenafil to others. 3. One patient discontinued treatment due to hypotension.
Schmid et al. 2000; Switzerland Pre-post Level 4 N=41	**Population:** 41 men with SCI; Age: mean 36.5 yrs, range 20-63; Injury level: paraplegia (n=33, 23 incomplete, 10 complete), tetraplegia (n=8, 7 incomplete, 1 complete); Time since injury: mean 5.9 yrs, range 0.5-26. **Treatment:** Sildenafil 25-100mg as needed. **Outcome measures:** International Index of Erectile Function (IIEF) – Erectile Function (EF) and Intercourse Satisfaction (IS), response rate, ideal dose, adverse events.	1. Improved erections (grade 3-4) permitting sexual intercourse reported by 38 (93%) men. 2. 58% of men achieved good erectile function with sildenafil 50mg, 37% required 75-100mg, and 5% required only 25mg. 3. EF (9.2 to 25.5) and IS (4.5 to 10.5) significantly improved after sildenafil therapy. 4. Men with preserved reflexive or psychogenic erection responded well to sildenafil, while men without integrity of either sacral or thoraco-lumbar segments due to ischemic damage did not have a successful response. 5. Adverse events: 10% suffered side effects such as headache, dizziness or flushing.
Ohl et al. 2015; USA Retrospective Analysis Level 5 N=248	**Population**: 248 men (≥ 18 years, mean age=37.7 years) with traumatic spinal cord injuries (≥ 6 months duration, 136/248 complete SCI) and erectile dysfunction attributed to SCI and in a stable heterosexual relationship (≥ 6 months). **Treatment**: Participants were randomized and treated sequentially with sildenafil and placebo in two treatment phases. The starting dose was 50 mg, taken one hour before sexual activity. Subsequent dose adjustments to 100 mg or 25 mg based on patients' tolerability during the 6 week treatment phase.	1. Average changes from baseline to week 6 in the IIEF Q3 (frequency of penetration), Q4 (maintaining erection after penetration), and Q9 (frequency of ejaculation) scores significantly improved with sildenafil vs. placebo (all $P<0.01$). 2. Treatment preference for sildenafil vs placebo was 96% vs 4% in the overall population ($P<0.001$). 3. The most common all-cause adverse events with sildenafil were headache (16.1%) and urinary tract infection (UTI) (11.6%)

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	Outcome Measures: The International Index of Erectile Function (IIEF) questions and percent successful attempts at intercourse were analyzed for sildenafil vs. placebo using analysis of covariance (ANCOVA) models.	

Discussion

Over 2000 men with SCI have been investigated in 14 RCTs and 9 prospective case series (pre-post) studies using oral agents for ED. The evidence supports the use of PDE5i as the first-line of treatment in men with ED secondary to SCI. Sildenafil (Viagra®) being the first available PDE5i has been more frequently studied to date than either vardenafil (Levitra®) or tadalafil (Cialis®). Avanafil (Stendra®) has not yet been assessed in the neurogenic population. Meta-analysis of case-series reports of sildenafil efficacy have shown a random effects pooled estimate of 79% success (with 95% CI from 68-90%) improving erectile function (EF) sufficient for intercourse at home (DeForge et al. 2006). Ergin et al. (2008) found that sildenafil was effective for improving erective function regardless of completeness of injury however the treatment showed wider impacts among individuals with incomplete injuries. Khorrami et al. (2010) found that sildenafil was more effective in upper motor neuron (UMN) versus lower motor neuron (LMN) injuries, with the latter being no more effective than that found with placebo.

In addition, in a cost-utility study of ED treatments in men with SCI (Mittmann et al. 2005), sildenafil has been shown to be preferred to non-oral treatments, as well as a cost-effective option with a calculated total annual cost (in 2005 dollars) of CAN $1,530 and incremental cost-utility ratio less than CAN $20,000 per QALY. Results from 3 large RCTs (Giuliano et al. 2006; 2007; 2008), as well as several case-series studies (Kimoto et al. 2006; Morgentaler et al. 2006; Soler et al. 2007), have shown similar efficacy for vardenafil and tadalafil compared to placebo, with reported improvements in erectile function (~10 points gain in IIEF/EF scores), success in penetration (~75%), maintenance and duration of erection (25-30 mins) and successful attempts at intercourse (~50-60%).

Only one small RCT (n=28) has directly compared the efficacy of different oral treatments in men with SCI (Del Popolo et al. 2004), comparing sildenafil (50mg) and tadalafil (10mg) in a randomized, blinded, cross-over design with washout. In this study, tadalafil significantly increased the percentage of successful intercourse attempts at 24 hours post dosing (68%), compared to sildenafil (18%) and 2 out of 5 partcipants, both with LMN incomplete lumbar lesions, not responding to sildenafil responded to tadalafil. The increased duration of action of tadalafil, providing for more spontaneous rather than planned “on-demand” sexual activity, has also been noted as a benefit by other authors (Giuliano et al. 2007; Soler et al. 2007). Two newer studies with higher participant numbers (Khorrami et al 2010; Ergin et al 2008) have expanded on the effectiveness of PDE5i depending on completeness of injury and whether it is UMN or LMN. There is also lack of effectiveness of PDE5i where there is extensive ischemic damage involving both thoraco-lumbar and sacral cord segments (Schmid et al. 2000). In general, a lesion above the sacral spinal tract and a higher reflexive erection are predictable favorable parameters for a positive response to all PDE5i (Lombardi 2009a; Soler 2007; Schmid 2000; Sanchez Ramos 2001. It appears that efficacy is maintained with the use of PDE5i over time, and tachphylaxis (a decrease in the response to a drug after repeated doses over a short time period) is rare (Lombardi et al 2009b).

The importance of correct dose titration has been emphasized by various studies, with over 50% of patients responding to sildenafil at a dose of 50 mg (Soler et al. 2007) and even as low as 25mg in some (Tuzgen et al. 2006), whereas around 50-70% of patients will require the higher dose (20mg

instead of 10mg) of vardenafil and tadalafil (Giuliano et al. 2006; 2007; Soler et al. 2007; Lombardi et al. 2009a). Kimoto et al. (2006) reported a 5-point increase in IIEF/EF score following up-titration of Vardenafil from 10 to 20mg. Soler et al. (2007) reported a significant improvement in ejaculation and orgasm only in the group taking sildenafil, while others (Giuliano et al. 2006,) have reported overall improvement in ejaculatory function with vardenafil (19% compared to 10% in placebo), particularly in those with incomplete lesions (29% compared to 15%). A recent study (Lombardi et al 2009a) on tadalfil failed to show a significant improvement in the ejaculatory and orgasmic parameter, however, the improvement in IIEF to > 26 (normal) was apparent in the majority of the men with SCI in the study. With the long acting tadalafil, over 80% of participants on either 10 or 20 mg of tadalafil were able to achieve successful intercourse within 24 hours of taking the drug, and approximately 65% were still able to have successful intercourse after 24 hours had passed (however the percentage of men attempting intercourse within versus after 24 hours were approximately 67% versus 33% respectively).

Headache (8-15%) and flushing (3-14%) were noted to be the most common side effects for men with SCI using PDE5i, followed by dyspepsia, nasal congestion, dizziness, visual disturbances and infrequently back pain. Urinary tract infection was also found to be a common adverse event, along with headache, in one sildenafil study (Ergin et al. 2008). Priapism and symptoms of dysreflexia are not reported in the SCI population after PDE5i use (Maytom 1999, Giuliano 1999, Gans 2001). Despite some concerns, cases of symptomatic hypotension requiring withdrawal of medication have rarely been reported with PDE5i (Gans et al. 2001; Giuliano et al. 2006; Lombardi et al 2009a). Garcia-Bravo et al. (2006) noted that patients with neurological impairment above T6 level had often been systematically excluded from earlier studies due to potential risks of autonomic dysreflexia and, more particularly, concern about inducing hypotension. This small study demonstrated significant reductions in blood pressure in individuals with a higher SCI lesion (n=12) compared to patients with neurologic levels below T5 (n=10) up to 4 hours after taking sildenafil (50mg dose). Although a maximum drop of 26mmHg (mean change of 17.5mmHg) in systolic and 17mmHg (mean 11mmHg) in diastolic BP was observed, none of these patients with high-level SCI reported hypotensive symptoms. Although not a primary question in their study, Sheel et al. (2005) also noted a significant hypotensive effect of sildenafil being present in a group of 8 participants with tetraplegia. Data supports an adequate tolerance of sildenafil in men with high-thoracic level paraplegia. However, despite a general absence of clinical reports of symptomatic postural hypotension associated with other PDE5i use, these studies suggest that men with tetraplegia may be at risk of significant hypotension during orthostatic challenges and some caution should be exercised in this group after taking PDE5i.

Three studies (2 RCTs and 1 case series) have trialed oral medications other than PDE5i for men with SCI. In a RCT assessing safety and efficacy of fampridine-SR in persons with established incomplete SCI (AIS grades C or D), Cardenas et al. (2007) reported strong trends for improved IIEF scores and increased erection frequency and firmness, ability to maintain erections and levels of sexual desire for fampridine-SR compared to placebo groups. However, adverse events were frequently reported, including pain, dizziness, insomnia, nervousness, paresthesia and one seizure, with 24% of patients discontinuing this trial, particularly those taking higher dose (40mg b.i.d.) of fampridine-SR. This study used considerably higher doses of fampridine-SR than an earlier exploratory trial (Potter et al. 1998) in 26 men with incomplete SCI, and reported statistical improvement in Global Assessment of Patient Satisfaction, but only five patients (19%) reported stronger, more frequent and better sustained erections. Apomorphine, a relatively successful medication in men without SCI, was used for 22 men with SCI and noted to have an overall low rate of response for erectile dysfunction, with 41% experiencing side effects (headache, nausea, tiredness) (Strebel et al. 2004).

Conclusion

There is level 1a evidence (from 9 RCTs, excluding 2 reporting outcomes of a previous trial: Derry et al. 1998; Giuliano et al. 1999; Hultling et al. 2000; Del Popolo et al. 2004; Giuliano et al. 2006; Tuzgen et al. 2006; Giuliano et al. 2007; Ergin et al. 2008; Khorrami et al. 2010) that

supports the use of PDE5i as a safe and effective treatment for erectile dysfunction in men with SCI.

Phosphodiesterase Type 5 Inhibitors (PDE5i) can be used safely and effectively for treatment of erectile dysfunction (ED) in men with SCI and are recommended as first-line treatment.

A lesion above the sacral spinal tract and a higher reflexive erection are predicable favorable parameters for a positive response to all PDE5i.

5.1.2 Intracavernosal Injections (ICI) utilizing Penile Medications

An intracavernosal (or intracavernous) injection is an injection into the base of the penis. This is often used to administer medications including alprostadil (prostaglandin E1 [PGE1]), Bimix (a combination of papaverine and phentolamine), and Trimix (a combination of papaverine, phentolamine and PGE1), to treat erectile dysfunction in adult men. This treatment can generate an erection in patients with SCI by direct cavernosal vasorelaxation, therefore bypassing theneurotransmission signals (release of nitric oxide from the nerve endings) requisite to initiate erection. Self-administration is an issue for the subset of SCI patients with poor hand function (Ibrahim et al. 2016).

Table 4: Effects of Intracavernosal Injections (ICI) utilizing Penile Medications

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Renganathan et al. 1997; India RCT Level 1 PEDro=4 N=28	**Population:** 28 men, Age: range 16-60 yrs. **Treatment:** Randomized to transdermal nitroglycerine or intracavernous injection of papaverine, two week washout, cross-over. **Outcome Measures:** Effectiveness of transdermal nitroglycerin vs. intracavernous injection of papaverine.	1. Erectile index for papaverine was significantly higher than that of nitroglycerine. 2. 93% who received papaverine had a complete response vs. 61% who received nitroglycerine. 3. 32% of patients had complications with papaverine vs 21% with nitorglycerine.
Yildiz et al. 2011; Turkey Prospective, one-way crossover, dose-controlled study Level 2 N=31	**Population:** Men with erectile dysfunction secondary to SCI**.** **Treatment:** Control: Received visual and auditory sexual stimulus (VASS). Treatment1- VASS with 25 mg of undiluted intracavernosal papaverine. Treatment 2 – Same participants as treatment 1, followed by 72 hour washout period **and** VASS with 50 mg of oral sildenafil on day 5. **Outcome Measures:** Peak systolic velocity (PSV), end diastolic velocity (EDV) for each cavernous artery.	1. There was a statistically higher PSV with papaverine (45.31(11.37)) or with sildenafil (41.59(15.55)) compared to control (22.25(7.54)). 2. There was no statistically significant difference between the PSV and EDV values of the papverine and sildenafil groups.
Soler et al. 2009; France Pre-post Level 4 N=14	**Population:** Men who sustained an abnormal prolonged erection or priapism following an intracavernous injection of prostaglandin E1 to induce erection. **Treatment:** Oral midodrine following the failure of 30 minutes of cooling procedures using ice or ether, or penile vibrator stimulation.	1. All patients returned to flaccid penile state within 30-45 min after midodrine administration. 2. Oral midodrine was well tolerated with few side effects and without increasing incidence of AD. 3. Complete erection could be induced again 6 months later by intracavernous injection in all treated patients.

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	Outcome measures: evaluation of penile rigidity at 30 minutes, and 1, 3 and 6 hrs post treatment.	
Moemen et al. 2008; Egypt Pre-Post Level 4 N=60	**Population:** 60 men with SCI and erectile dysfunction, at least 6 months post-injury, randomized into 3 groups of 20 (A, B, C). **Treatment:** Group A took sildenafil 50mg before sexual activity for 1 month; Group B were given intracorporal injection (ICI, 10 mg/ml prostaglandin E1 or 0.5 ml trimix) for 1 month and then took sildenafil for 1 month; Group C used vacuum constriction device (VCD) for 1 month and sildenafil for 1 month. **Outcome Measures:** International Index of Erectile Function – erectile function domain (IIEF-EF); Global Efficacy Assessment Questionnaire (GAQ); Hormonal Profile.	1. 90% of people in all groups showed improvement of erection as measured by IIEF-EF after sildenafil. 90% showed improvement in Group B after ICI, and 70% in Group C after VCD. 2. Improvement in erection reached 100% in all groups according to the GAQ, but ability to penetrate reached 90% after sildenafil, 90% after ICI, and 70% after VCD. 3. There was a significant increase in testosterone in all groups after sildenafil treatment. 4. Participants in Group B reported that ICI resulted in more rigid erections than sildenafil, but 14 participants preferred sildenafil due to easier administration; no participants in Group C was satisfied with VCD and preferred either ICI or sildenafil.
Zaslau et al. 1999; USA Pre-post Level 4 N=37	**Population:** 37 men, Age: mean 43.7 years, range 24-72 yrs, Level of injury: C3-L4. **Treatment:** Intracavernosal injection (ICI) of papaverine & prostaglandin E1 (PGE1); Dosage was titrated until satisfactory erection obtained. **Outcome Measures:** Safety & efficacy of intracavernosal injection therapy, satisfaction.	1. 28 patients (76%) responded to injection. 2. 21% ejaculated during >50 % of sexual encounters. 3. At 3 months: 77% were moderately or extremely satisfied with therapy. 4. 85% rated their intracavernosal injection - produced erections as good or excellent. 5. 60% on intracavernosal injection reported almost always or always being able to have successful intercourse.
Tang et al. 1995; Republic of China Post-test Level 4 N=15	**Population:** Men with SCI; Age: mean 38.5 yrs, range 25-50; Injury level: cervical (n=1), thoracic (n=6), lumbar (n=8); Time since injury: mean 6.3 yrs. **Treatment:** Intracavernosal Prostaglandin E1 (IC PGE1) 5µg (up to 20µg) until full erection lasting 20 minutes. **Outcome measures:** Schramek grade of erection, blood pressure, heart rate.	1. All men achieved a rigid (grade 5) functional erection lasting at least 20 mins (mean 59.1 min), except 1 found to have venogenic impotence. 2. Grade of erection improved significantly post-treatment. 3. No significant dosage effect of PGE1 in the difference between pre- and post treatment. 4. No systemic side effects or other complications, however, 2 men complained of pain at injection site.
Hirsch et al. 1994; USA Pre-post Level 4 N=27	**Population:** 27 men (14 SCI, 7 multiple sclerosis, 6 discogenic disease); Age: (SCI) mean 31.5 yrs, range 22-39. **Treatment:** Intracavernosal Prostaglandin E1 (IC PGE1) 2.5µg initially, increased in 2.5µg increments, with a mean maintenance dose of 6.2 µg. **Outcome measures:** Continued home	1. Rate of voluntary cessation in men with SCI at 28 months was 43%. 2. Main reason for voluntary cessation among men with SCI was urinary diversion, adrenal tumor, loss of interest, insurance difficulties. 3. Self-administered IC PGE1 was safe and efficacious, with all patients completing

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	use or cessation of PGE1 at 28 months and reasons for cessation.	protocol reporting excellent rigidity and no discontinuations due to inadequate erectile response or pain.
Costa et al. 1993; France Pre-post Level 4 N=12	**Population:** Men with SCI; Age: mean 34 yrs, range 25-43; Injury level: C6-L1; Impairment: complete; Previous successful treatment with intracavernosal injection (ICI) of 20mg moxisylyte. **Treatment:** ICI of 20mg moxisylyte diluted in 0.4, 0.8, 1.2, and 2.0 ml solvent. **Outcome measure:** Rigidity of penis at 5-10-15-20-30 min after injection, abdomino-penile angle, penis length, and circumference of penis at same times, duration of erection, blood pressure (BP), heart rate (HR), adverse events.	1. Penile rigidity, abdomino-penile angle, length, circumference, and duration of erection were unaffected by dilution/change in volume of solvent. 2. Mean maximal values for rigidity ranged from 2.33-2.58/3 and lasted between 47-62.5 min. 3. No priapism or prolonged erections were noted.
Kapoor et al. 1993; India Post-test Level 4 N=101	**Population:** 101 men with SCI; Age: range 20-51 yrs; Injury level: C4-L4, 65 paraplegia, 36 tetraplegia. **Treatment:** Intracavernosal injection (ICI) of papavarine hydrochloride. **Outcome Measures:** Erectile rigidity, duration of erection.	1. Satisfactory erection sufficient for penetration was possible in 98 patients. 2. 78 participants had good erection within 10 minutes, 13 within 20 minutes, 7 within 30 minutes. 3. Older patients required higher dose. 4. Erections lasted from < 1 hour to >4 hours.
Bodner et al. 1992; USA Post-test Level 4 N=58	**Population**: 58 men; Age: range 19-68 yrs; Injury level: cervical (n=19), thoracic (n=32), lumbar (n=17); Impairment grade: 44 complete, 14 incomplete, 19 cervical, 32 thoracic, 17 lumbar, (53%) dropped out. **Treatment**: 7.5mg papaverine, titrated to dosage that produced adequate erection, evaluated every week during titration period, then every 2 months. **Outcome Measures:** Erectile rigidity, complications.	1. Rigid erections in 45 patients (90%). 2. 53% of participants dropped out of program, usually after 1st injection or during titration period. 3. Main complication was prolonged erection necessitating aspiration and epinephrine injection.
Earle et al. 1992; Australia Post test Level 4 N=22 (14)	**Population:** Men with SCI; Age: mean 35.2 yrs, range 20-45; Injury level: cervical (n=3), thoracic (n=8), lumbosacral (n=3). **Treatment:** Intracavernosal self-injection (ICI) of papaverine 2-20mg or papaverine 40mg + phentolamine 0.5 mg or prostaglandin E1 1-20µg. **Outcome measures:** Achieve erection, patient acceptance (continued use of method), partner satisfaction and complications.	1. Full erection was achieved by 19 out of 22 men. 2. Out of 14 men who took part in survey, 12 reported continued use and satisfaction with self-injection (8 using papaverine, 1 using, papaverine + phentolamine and 3 using prostaglandin E1). 3. Partners of men with SCI responded positive in half of the cases. Two men stopped ICI due to partner disapproval. 4. Complications included blood in urethra, prolonged erection and bruising at injection site.
Sidi et al. 1987; USA Post-test Level 4 N=66	**Population:** 66 men with SCI, Age: range 18-61 yrs. **Treatment:** Intracavernosal injection of papaverine hydrochloride and	1. 52 participants had functional erections. 2. In response to plain papaverine 20/30 responded with functional erections. 3. 4 participants had sustained erections that had to be drained.

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	phentolamine mesylate (n=22), papaverine hydrochloride alone (n=44). **Outcome Measures:** Erection quality.	4. 71% continued to use method.
Beretta et al. 1986; Italy Post-test Level 4 N=22	**Population:** 22 men, Age: range 18-52 yrs. **Treatment:** 20-30mg papaverine. **Outcome Measures:** Effectiveness of papaverine.	1. 20/22 participants were able to achieve an erection with complete rigidity with a mean duration of 4.1 hrs. 2. 20 participants who were successful at intercourse were offered training in self injection, but only 10 accepted. 3. 7/22 lasting >5 hrs controlled with ethilefrine and aspiration of corpus.

Discussion

The technique of penile intracavernosal injection (ICI) of vasoactive medications, such as papaverine, phentolamine and prostaglandin E1 (PGE1) alone or in combination, has been used to treat ED in men with SCI for over 20 years. Despite this, there is only one RCT study (Renaganathan et al. 1997) in this area, comparing administration of intracavernosal papaverine with transdermal nitroglycerin. Patients who received ICI of papaverine were statistically more likely to have a complete response (erection) than those patients who received nitroglycerine (93% vs 61%).

Results from other non-RCTs support greater efficacy of ICI medications than PDE5i with a meta-analysis of 11 non-comparative case-series reports showing a random effects pooled estimate of 90% success rate (95% CI from 83-97%) achieving a satisfactory erection with intracavernosal injections (DeForge et al. 2006). Moemen et al. (2008) found a similar success rate of satisfactory erection with ICI but this was also comparable to the success rate of PDE5i found in the same participants. Participants also noted that erections were firmer on ICI than PDE5i. It is clear that there is a dose response to the efficacy of ICI, with combination therapy introduced for synergistic effect as well as for possible economic reasons. Yildiz et al. (2011) reported that the efficacies of ICI of papaverine were similar to orally administered sildenafil citrate at all neurological lesion levels and severity in paraplegic men within the first year after SCI. In general, lower ICI doses were required in neurogenic patients, but the combination of SCI with co-morbidity such as diabetes or hypertension decreased the efficacy of injections (Sidi et al. 1987; Zaslau et al. 1999).

Complication rates with ICI have been reported to range from 15-32% (Lloyd & Richards 1989; Dietzen & Lloyd 1992; Renaganathan et al. 1997; Moemen et al. 2008), with the caveat that accumulated clinical experience and choice of vasoactive medication/s with judicious adjustment of dosage reduce the risks substantially. The most common side effects of ICI are transient, such as pain and swelling at the injection site. The more serious side effect of priapism (or prolonged erection) has typically been reported with use of papaverine and can be treated with aspiration of blood from corpora with injection of an alpha-adrenergic medication (Sidi et al. 1987; Bodner et al. 1992). A reported long-term complication of ICI is fibrosis (scarring of the tunica albuginia), the risk of which can be reduced by lowering frequency of injections and minimising medication dose. Hirsch et al. (1994) noted evidence of sub-clinical corporal fibrosis in 2 out of 27 patients using ICI PGE1 with monitoring by quarterly penile ultrasound scans over 18 months.

Several small case series studies using intracavernosal injection of PGE1 (Hirsch et al. 1994; Tang et al. 1995) or PGE1 in combination with papaverine (Zaslau et al. 1999) have confirmed safety and efficacy in over 50 men with SCI without incidence of priapism. Soler et al. (2009) reported controversial results where some patients developed priapism after PGE1 administration, but it was easily treated by orally administered midodrine. Tang reported full functional erections with ICI PGE1 lasting an average duration of 59 minutes (range 30-120 mins) in 14 out of 15 men with 8 of them (7

with incomplete T4-L5 lesions and 1 with a complete L1 lesion) able to ejaculate. Prior to the availability of PDE5i, ICI had a high acceptance rate (70-86%) in the SCI population (Sidi et al. 1987; Earle et al. 1992; Watanabe et al. 1996), although longer term discontinuation has been reported in approximately 30-40%. Intracavernosal injection is also an option to consider in patients taking nitrate medications, where there are concerns about drug interactions with PDE5i.

Conclusion

There is level 2 evidence (from 1 low quality RCT; Renganathan et al. 1997) that supports the use of ICI as treatment for erectile dysfunction in men with SCI.

Intracavernosal (penile) injectable medications (ICI) are very effective for the treatment of ED in men with SCI and may be used with careful dose titration and some precautions.

5.1.3 Topical Agents

Topical agents to treat erectile dysfunction are applied to the penis or perineal regions and have included hormone-derived medications, as well as vasodilators.

Table 5: Effects of Topical Agents

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Kim et al. 1995; USA Prospective controlled trial Level 2 N=20	**Population:** 13 men with SCI, 7 non-SCI **Age:** range 19-73 yrs, Duration of erectile dysfunction: range 0.6-27 yrs. **Treatment:** Papaverine gel or placebo gel, dose range: 133-500mg. **Outcome Measures:** Safety and efficacyof topical papaverine gel.	For SCI patients (n=12) 1. 3 patients with papaverine gel had full erections, but full erections also occurred with placebo gel.
Kim et al.1995; USA Pre-post Level 4 N=10	**Population:** Men with SCI (n=9), 1 arterial insufficiency; Age: mean 33 yrs, range 19-50; Injury level: cervical (n=4), thoracic (n=5) **Treatment:** Topical prostaglandin E1 to penis, scrotum, and perineum. **Outcome measures:** Color flow Doppler Ultrasound for cavernous artery diameter and peak systolic flow velocity, vital signs: systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), clinical erection, adverse events.	1. Mean cavernous artery diameter increased from 0.09 to 0.11 cm. 2. Mean peak systolic flow velocity increased from 15.4 to 22.8 cm/sec. 3. Clinical erections were observed in 2 men. 4. Vital signs were unaffected by PGE1. 5. No adverse events.
Chancellor et al. 1994; USA Post-test Level 4 N=18	**Population**: 18 men with SCI, Age: range 19-65 yrs, Level of injury: C7-L3 (15 thoracic). **Treatment:** Minoxidil spray, papaverine injection, or vacuum constriction device (VCD). **Outcome Measures:** Erectile response.	1. Papaverine injections increased median rigidity 77% (range 30-100%). Rigidity was significantly less with minoxidil. 2. Vacuum constriction device changed rigidity a median of 57% (range 30-80%). 3. No difference between vacuum constriction device and papaverine. 4. Patient subjective rating scale was significantly lower for minoxidil than vacuum constriction device or papaverine. 5. Physicians' subjective ratings were significantly lower for minoxidil than other treatments.

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Beretta et al. 1993; Italy Post-test Level 4 N=15	**Population:** 15 men, age range: 20-38 yrs, Level: T2-L5. **Treatment**: Prostaglandin E1 and 2% Minoxidil solution. **Outcome Measures:** Erectile response.	1. 4 patients had complete responses, 5 had partial, 6 had no response. 2. 9 patients with complete/partial response continued to use minoxidil at home for 1 month. 3. 26.6% obtained an erectile response sufficient for vaginal penetration.
Sonksen et al. 1992; Denmark Post-test Level 4 N=17	**Population:** 17 men, age range: 19-51 yrs, level: C2-L4, 13 complete, 4 incomplete. **Treatment:** Transiderm-Nitro plaster (10mg/24hrs), which contains 50mg glyceryl trinitrate. **Outcome Measures:** Erectile response.	1. 5 patients had complete responses (full rigidity), 7 had partial responses (some rigidity and/or increase in penile circumference), and 5 had no response (no noticeable erection). 2. Erection duration (complete response): 20-45 min. 3. 5 (29%) had erections sufficient for vaginal penetration.

Discussion

There are no RCT studies in this area. Topical agents that cause vasodilation, such as minoxidil, PGE1, papaverine and nitroglycerine, are generally safe yet found to be effective only in a minority of patients (providing an erection sufficient for vaginal penetration in 22-29%), most likely due to inadequate absorption through the tunica albuginia. Kim & McVary (1995), although showing a significant increase in mean cavernous artery diameter and mean peak systolic flow velocity with topical application of PGE1, reported a clinically useful erection in only 2 out of 9 participants. One study found topical minoxidil spray to be significantly less effective than comparative treatments with papaverine ICI or a vacuum constriction device. Use of topical agents to treat ED seem to have little if any role to play in the SCI population, particularly in view of the efficacy and reliability of PDE5i and ICI.

Conclusion

There is level 2 evidence (from 1 non-randomized controlled trial; Kim et al. 1995) that shows that the use of topical agents is <u>not</u> effective or reliable as a treatment for erectile dysfunction in men with SCI.

Topical agents are not effective or reliable for the treatment of erectile dysfunction in men with SCI.

5.1.4 Intraurethral Preparations and other Medications

The application of intraurethral prostaglandin E1 (alprostadil) can be done by a urologist or self-administered to the distal male urethra via a drug deliver system. It appears to produce cavernosal vasodilation to initiate erection.

Table 6: Effects of Intraurethral Preparations and other Medications

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome

Strebel et al. 2004 Switzerland Post-test Level 4 N=22	**Population:** All 22 patients had a chronic SCI lasting a median (range) of 63 (7–156) months; 11 had an UMN lesion (six complete, five incomplete), eight a LMN (seven complete, one incomplete) and three a mixed lesion. **Treatment:** Eight tablets of apomorphine sublingual (SL) 3 mg, as a primary or secondary treatment for erectile dysfunction (ED) **Outcome Measures:** International Index of Erectile Function questionnaire, patient diaries. A neurophysiological evaluation included somatosensory evoked potentials of the pudendal nerve, palmar and plantar sympathetic skin responses and bulbocavernous reflex recordings.	1. There were no significant correlations for electrophysiological or urodynamic findings and treatment success. 2. Seven patients had some response and reported that the drug helped them to obtain an erection, but only two reported erections sufficient for intercourse and would agree to continue apomorphine SL as their standard treatment; all the others reported being disappointed. Nine patients reported side-effects.
Bodner et al. 1999; USA Post-test Level 4 N=15	**Population**: 15 men; Age range: 30-70 yrs, Injury level: 7 tetraplegia, 8 paraplegia. **Treatment:** Intraurethral alprostadil (125-1000µg); MUSE (medicated transurethral system for delivery of alprostadil to the male urethra). **Outcome Measures:** Efficacy of intraurethral prostaglandin E1.	**1.** 12 achieved grade 1-3 erections, 3 achieved grade 4 erections. **2.** All could achieve grade 5 erections with intracavernosal injections therapy. The three that achieved grade 4 erections all tried MUSE at home and were dissatisfied.

Discussion

There are no RCT studies in this area. In a series of 15 men with SCI, Bodner et al. (1999) found that the use of intraurethral alprostadil (PGE1) was ineffective in sustaining an adequate erection, and without a penile ring to sustain any increase in penile circumference (tumescence), patients experienced hypotension from the medication. Based on the evidence to date, such studies do not appear to be worth pursuing.

Conclusion

There is level 4 evidence (from a post-test study; Bodner et al. 1999) which suggests that the use of intraurethral preparations is not effective as treatment for erectile dysfunction in men with SCI.

There is level 4 evidence (from a pre-post study; Strebel et al. 2004) that found some success using apomorphine SL to facilitate erections.

Intraurethral preparations are not effective for treatment of erectile dysfunction in men with SCI. Limited evidence suggests apomorphine SLmay facilitate erections in men with SCI.

5.1.5 Mechanical Methods: Vacuum Devices and Penile Rings

Vacuum device is a pump machine consists of a plastic cylinder with an aperture at one end that is placed over the penile shaft, the other end is a pump mechanism that is used to generate negative pressure within the cylinder to draw venous and arterial blood into the erectile tissue. The erection is maintained by placing a constricting ring around the base of the penis and can slow down the speed at which blood leaves the penis.The constriction ring should not remain on for more than 30 – 45 minutes.

Table 7: Effects of Vacuum Devices and Penile Rings

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Moemen et al. 2008; Egypt Pre-post Level 4 N=60	**Population:** 60 men with SCI and erectile dysfunction, at least 6 months post-injury, randomized into 3 groups of 20 (A, B, C) **Treatment:** Group A took sildenafil 50mg before sexual activity for 1 month; Group B were given intracorporal injection (ICI, 10 mg/ml prostaglandin E1 or 0.5 ml trimix) for 1 month and then took sildenafil for 1 month; Group C used vacuum constriction device (VCD) for 1 month and sildenafil for 1 month **Outcome Measures:** International Index of Erectile Function – erectile function domain (IIEF-EF); Global Efficacy Assessment Questionnaire (GAQ); Hormonal Profile	1. 90% of people in all groups showed improvement of erection as measured by IIEF-EF after sildenafil. 90% showed improvement in Group B after ICI, and 70% in Group C after VCD. 2. Improvement in erection reached 100% in all groups according to the GAQ, but ability to penetrate reached 90% after sildenafil, 90% after ICI, and 70% after VCD. 3. There was a significant increase in testosterone in all groups after sildenafil treatment. 4. Participants in Group B reported that ICI resulted in more rigid erections than sildenafil, but 14 participants preferred sildenafil due to easier administration; no participants in Group C was satisfied with VCD and preferred either ICI or sildenafil.
Denil et al. 1996; USA Post-test Level 4 N=20	**Population:** 20 men with SCI; Age range 20-50 yrs: 13 complete, 7 incomplete. **Treatment:** Vacuum erection device (VED). **Outcome Measures:** Safety and efficacy of vacuum erection device, patient & partner satisfaction.	1. At 3 months, 93% of the men and 83% of the women reported rigidity sufficient for vaginal penetration. 2. At 6 months, 14 couples were regularly using device at least 1/wk. 3. At 6 months, 41% of the men and 45% of the women were satisfied with the device. 4. 60% of men and 42% of women indicated an improvement of the sexual relationship.
Chancellor et al. 1994; USA Post-test Level 4 N=18	**Population**: 18 men; Age: range 19-65 yrs; Level of injury: C7-L3, 15 thoracic. **Treatment:** Minoxidil spray, papaverine injection, or vacuum constriction device (VCD). **Outcome Measures:** Erectile response.	1. Vacuum constriction device changed rigidity a median range of 57% range (30-80%). 2. No difference between vacuum constriction device and papaverine. 3. Patient subjective rating scale was significantly lower for minoxidil than vacuum constriction device or papaverine. 4. Physician subjective ratings (from 0 to 10) were significantly lower for minoxidil than other treatments on erectile response.
Heller et al. 1992; Israel Pre-post Level 4 N=30	**Population**: 30 men with neurological impairment, 10 paraplegia, 2 tetraplegia, 7 paraparesis, 7 hemiplegia, 2 multiple sclerosis, 2 autonomic neuropathy. **Treatment:** Vacuum tumescence constriction therapy (VTCT). **Outcome Measures:** Device usage, frequency of coitus.	1. 17 (57%) of 30 patients bought vacuum tumescence constriction therapy device. 2. 83% very satisfied at follow-up. 3. 53% using device at follow-up.

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Zasler & Katz 1989; USA Post-test Level 4 N=20	**Population:** 20 men with SCI; Age: range 21-65 yrs; Level of injury: C4-L2. **Treatment:** Each patient was custom fitted for the synergist erection system. **Outcome Measures:** Efficacy of the synergist erection system.	1. Snap-gauge (a device used to measure circumferential penile expansion and rigidity) assessment correlated significantly with subjective reports of erectile capability. 2. 15 men and 14 women rated the quality of coitus as very good to excellent compared to previous best since injury.

Discussion

There are no RCT studies in this area, but level 4 pre-post studies noted that the vacuum constriction device (VCD) or vacuum erection device (VED) is an acceptable alternative for ED therapy in men with SCI who may not tolerate other methods and whose hand function can warrant its use (unless a partner applies it). Premature loss of rigidity, petechiae and penile skin edema, lack of spontaneity, uncomfortable erections and a 'cold penis" all were cited as unwanted side effects. For safe practice, it is recommended that the maximum vacuum pressure should not exceed 250 mmHg (to prevent petechiae and ecchymosis) and the penile ring placed at the base of the penis to trap blood does not remain on for more than 30-45 minutes. An alternative vacuum device (Synergist) is a vacuum device within a silicone sheath that remains on the penis that can be used for longer periods of time due to the absence of constricting bands and a much lower vacuum pressure (8-20 mmHg), and which most patients found satisfying. Denil et al. (1996) reported on 20 couples where 93% of men with SCI and 83% of their female partners reported sufficient penile rigidity for intercourse obtained by the use of a vacuum device after 3 months, but by 6 months less than half the couples were satisfied with the device. Most side effects were temporary and minor. In the Moemen et al. (2008) study, while vacuum device therapy was the least favored option as opposed to ICI or PDE5i, 70% had a normal IIEF-EF score with its use. The authors suggested that the range in variation in patient response to this option might be related to acceptability of the vacuum device by the patient or his partner.

Conclusion

There is level 4 evidence (Moemen et al. 2008; Denil et al. 1996; Chancellor et al. 1994; Heller et al. 1992; Zasler and Katz 1989) that supports the use of medically sanctioned vacuum constriction devices and penile rings as treatment for erectile dysfunction in men with SCI.

Medically sanctioned vacuum erection devices (VED) and penile rings may be used for treatment of erectile dysfunction in men with SCI.

5.1.6 Surgical Penile Implants

Surgical implantation of a penile prosthesis is one option for erectile dysfunction which involves inserting an implant into the erectile tissue. Different types exist including malleable (semi-rigid) and inflatable (hydraulic).

Table 8: Penile Implants and other Surgery

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Overgoor et al. 2015; The Netherlands	**Population**: 30 low spinal lesion (T12 (incomplete) to sacral) patients (mean age=29.5 years, range=13-59 years), 13 with spina bifida and 17 with a spinal cord injury.	1. Neither Self-report of RE nor BCR testing can independently predict which surgery protocol should be used (7 patients reported RE, 4 of which had

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Case series Level 4 N=30	**Treatment**: Researchers wanted to test whether self-report of reflex erections (RE) or bulbocavernosus reflex (BCR) testing was sufficient to determine whether patients should have unilateral or bilateral (surgery) to maximize sexual function. **Outcome Measures**: The integrity of the sacral-reflex-arc and DNP function was tested pre-operatively using bilateral needle electromyography (EMG)–bulbocavernosus reflex (BCR) measurements, and an interview about reflex erections (RE) ability.	positive bilateral BCR; 9 patients had positive BCR, 4 of which had RE.) 2. No significant association between BCR function and RE.
Overgoor et al. 2014 The Netherlands Case series Level 4 N=40	**Population**: 40 low-spinal lesion men with no penile but intact groin sensation **Methodology**: The "TOMAX" (TO MAX-imize sensation, sexuality, and quality of life) procedure restores genital sensation in men with low spinal lesions, improving sexual health, as shown previously. It connects the dorsal nerve of the penis to the intact ipsilateral ilioinguinal nerve, unilaterally or bilaterally. This study reports on the technical aspects based on 43 TOMAX nerve transfers. 43 nerve transfers were performed on the participants. **Outcome Measures**: Data on patient selection, surgical history, anatomy of the ilioinguinal nerve and dorsal nerve of the penis, unilateral or bilateral surgery, surgical technique, complications, and patient information were collected prospectively.	1. Regardless of origin, all patients with no penile but good groin sensation are eligible for the procedure, provided the ilioinguinal nerve is not damaged because of former inguinal surgery or absent because of anatomical variations. 2. Selection of a unilateral or bilateral procedure depends on the presence or absence of reflex erections and bulbocavernosus reflex. 3. Preliminary experience with the first three bilateral cases shows that it is technically feasible, with encouraging results. The surgical technique has evolved (described in detail, including video) to enhance outcome and reduce complications. 4. The TOMAX procedure can then be used to restore erogenous penile sensation and improve the quality of sexual health in patients with absent penile but good groin sensation.
Kim et al. 2008; Korea Case series Level 4 N=48	**Population:** 48 participants with SCI and erectile dysfunction, mean age 58.9 (range 39-74). **Treatment:** malleable penile prosthesis insertion. **Outcome Measures:** Subjective satisfaction questionnaire; possibility of intercourse.	1. 38 (79.2%) of the participants reported some degree of satisfaction with their prosthesis. 2. Intercourse was possible in 44 participants. 3. Complications occurred in 8 participants: 4 had infections, 2 had erosion towards the urethra and glans, 1 experienced pain due to the insertion of an overly large prosthesis, and 1 was dissatisfied with the small size of the inserted prosthesis.
Zermann et al. 2006; Germany Case series Level 4 N=245	**Population:** Men with neurological impairment, n=197 with SCI; Age: mean 40.8 yrs, range 17-75; Injury level: paraplegia (n=188), tetraplegia (n=57); Diagnostic groups: urinary management (n=134), erectile dysfunction (ED) (n=60),	1. Sexual intercourse was possible in 83.7% of individuals with penile prosthesis for ED. 2. 67% of female were satisfied with result of their partner's treatment. 3. Adverse events: infection rate 5%,

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	urinary management and ED (n=51). **Treatment:** Penile prosthesis: semirigid Jonas (n=147), self-contained inflatable AMS Hydroflex or AMS Dynaflex (n=113), and inflatable 3-piece AMS 700 CX (n=33). **Outcome Measures:** Sexual intercourse success, treatment satisfaction, secure condom fixation, urinary management, adverse events.	perforation rate 18.1% (semi-rigid Jonas), 2.4% (self-contained inflatable Dynaflex), and 0% (inflatable 3-piece AMS 700), respectively.
Gross et al. 1996; Germany Case series Level 4 N=209	**Population:** Men with SCI; Age: mean 39.9 yrs, range 16-72; Injury level: paraplegia (n=128), tetraplegia (n=38); Impairment: erectile dysfunction (n=49), penile retraction (n=113), both (n=47). **Treatment:** Penile prosthesis. **Outcome measures:** Use of prosthesis, satisfaction with sexual intercourse, adverse events.	1. Use of prosthesis: 83 out of 96 men with ED used prosthesis at 5 yrs after surgery. 2. Satisfactory sexual intercourse was reported by 84% of men with ED. 3. Adverse events: perforation in 7% of men: 9.4% occurred with semi-rigid prosthesis vs 2.7% of semi-flexible prosthesis, infection in 5.6% leading to removal of prosthesis.
Collins & Hackler 1988; USA Post-test Level 4 N=63	**Population**: 63 men with SCI. **Treatment:** Penile implantation of semi-rigid device or Mentor inflatable prosthesis. **Outcome Measures:** Penile implantation functionality.	1. 53 patients with a semi-rigid implant, 44 currently have functional prosthesis (83% overall success rate). 2. 10 patients received inflatable penile prostheses: 4 were lost, 2 had successful reimplantation. 3. Overall complication rate in the 63 patients=33% (lost prosthesis). 4. After reimplantation, 52/63 patients had functional device, resulting in 82% ultimate success rate.
Iwatsubo et al. 1986; Japan Case series Level 4 N=37	**Population:** Men with SCI, Age: mean 42 yrs, range 21-63, Injury level: tetraplegia (n=10), paraplegia (n=23), cauda equina lesions (n=4). **Treatment:** Shirai-type silicone implants; follow up from 6-46 months. **Outcome measures:** Impact on sexual function, adverse events.	1. Impact on sexual function: 15 (41%) men reported improvement, 18 (48%) men reported no sexual benefit, 4 (11%) men were dissatisfied. 2. Adverse events: extrusion of prosthesis due to infection (n=2) and removal due to causalgia in LE (n=1), posterior migration of prosthesis (n=1).
Green & Sloan 1986; USA Observational Level 5 N=40	**Population:** 40 men; Age range: 21-60 yrs, Impairment grade: AIS A (n=31), B-D (n=9). **Treatment**: Penile prosthesis. **Outcome Measures:** Sexual questionnaire.	1. 31 patients have intercourse regularly and pleased with decision to have device. 2. 4 patients dissatisfied all had semi-rigid implant.

Discussion

There are no RCT studies in this area. Penile prostheses have been used for over 25 years to treat ED, penile retraction (or a combination of both) or for improvement in urinary management in selected men with SCI. Generally, for ED, this option is only considered after failure of more conservative treatments, including ICI of vasoactive substances, vacuum devices and, more recently, oral PDE5i. Five case-series reports and one cohort study in over 500 men with SCI have revealed a high level of satisfaction with the use of penile prostheses for the treatment of ED, making intercourse possible in almost 85%, as well as resolution of urinary management issues in 90% of patients. In addition, in one study (Zermann et al. 2006), 67% of females interviewed were satisfied with results of treatment of

their partner's ED. Inflatable prostheses (although more expensive) are often preferred over semi-rigid malleable prosthesis as the semi-rigid prosthesis is more difficult to conceal due to the permanence of the erection. These factors, although affecting preference, have not altered the overall satisfaction rates associated with malleable prostheses (Kim et al. 2008). It has been suggested that the insertion of smaller diameter prosthesis in patients performing clean intermittent catheterizations is more appropriate to reduce the resistance at the time of catheter insertion and potential urethral erosion.

However, serious complications may occur in about 10% of patients, including infection (4-8%) and perforations depending on implant type (9-18% of semi-rigid devices vs 0-2.7% of semi-flexible/inflatable devicesResults of two larger studies (Gross et al. 1996; Zermann et al. 2006) have shown that improvements over the last 10 years in device design (with the introduction of softer implant materials), surgical approach (infrapubic rather than subcoronal) and infection control measures (broad-spectrum antibiotic prophylaxis and whole body disinfection) have dramatically reduced the likelihood of these complications occurring. Under these improved circumstances, implantation of a penile prosthesis appears to be a relatively safe and viable option, perhaps best reserved for when reversible ED therapies have failed or for those men (or their partners) who find other alternatives, such as intracavernosal injections unacceptable. This decision requires careful consideration in view of the fact that if explanation of penile prosthesis is necessary, the person may no longer be a candidate for other treatment options, such as ICI or a VCD, due to possible extensive penile damage and scarring.

Conclusion

There is level 4 evidence (Kim et al. 2008; Zermann et al. 2006; Gross et al. 1996) which suggests the use of penile prostheses as treatment for erectile dysfunction (ED) in men with SCI when other ED treatments have failed.

Penile prostheses may be effective for treatment of erectile dysfunction in men with SCI, however, should generally be reserved for situations where all reversible erectile dysfunction treatments have failed.

5.1.7 Intrathecal Baclofen Pump and Sacral Root stimulation

An intrathecal baclofen pump is a device for treatment of severe spasticity. This medical device is placed under the skin during a surgery (generally under abdominal skin) and is used to deliver baclofen directly into the intrathecal space surrounding the spinal cord. Baclofen stimulates GABA-B receptros and acts as a skeletal muscle relaxant.

For Sacral anterior root stimulation (SARS) implantation, a laminectomy is performed between S2-L4 to expose the sacral nerve roots of S2-S4 and possibly S5 (Worsoe et al. 2013). Anterior and posterior nerve roots are distinguished using intraoperative stimulation (Worsoe *et al.,* 2013; Creasey *et al.,* 2001). Then the sleeved electrodes are placed bilaterally along the S2-4 anterior roots and sutured onto the target nerves (Creasey *et al.,* 2001). Meanwhile, the S2-5 posterior root nerves are sacrificed through a bilateral rhizotomy. This procedure enables urinary continence during stimulation, maintenance of bladder capacity, and reduces the risk of AD by abolishing the reflex arcs mediated by these nerves (Valles *et al.,* 2009; Creasey *et al.,* 2000). The electrode cables are then subcutaneously tunneled between the costal margin and iliac crest and connected to a subcutaneous transmitter box in the anterior abdominal wall (Creasey *et al.,* 2001). The transmitter box and subsequently the stimulation can be activated by the patient using a wireless receiver block.

Table 9: Intrathecal Baclofen Pump and Sacral Root stimulation

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Lombardi et al. 2008 (males) Italy Prospective Comparison trial Level 2 N=54	**Population:** 54 males with SCI (mean age 42.8) suffering from Lower Urinary Tract Symptoms (LUTS) and concomitant erectile impairment. Group A - 30 neurogenic patients, (mean age 41.3; range 27–69), all showing at least partial peripheral or central preservation of the upper motor neuron. 6 had incomplete SCI, 3 had myelitis, 1 had MS, 2 had disk herniation, and 2 had peripheral polyneuropathy. Group B consisted of 24 idiopathic patients (mean age 44.6; range 27–62). **Treatment:** To evaluate if sacral neuromodulation (SNM) using the InterStim system improves erectile function. Stimulation consisted of continuous pulses with a frequency of 20 Hz. **Outcome Measures:** the five-item version of the International Index of Erectile Function (IIEF-5) A score of IIEF-5 equal to or higher than 25% compared to baseline indicated remarkable clinical enhancement. Three months after permanent implantation, the IIEF-5 was completed again. Those who benefited significantly in erectile function completed the IIEF-5 semiannually. A final checkup was performed in July 2007.	1. In the first post-SNM visit, there was a significant improvement in the median IIEF-5 score of group A (Neurogenics) (from 14.6 (range 11–18) to 18 (range 12–23) using the Wilcoxon test (P<0.02). 2. The patients' history revealed that erectile impairment was concomitant to LUTS (Fisher test P=0.008) in 12 neurogenic subjects compared to two idiopathic subjects. 3. Overall, 22 out of 52 males (42.3%) showed erectile impairment according to the IIEF-5. More precisely, 14 out of the 29 neurogenic patients (48.2%) and 8 out of the 23 idiophatic patients (34.7%) showed erectile impairment.
Lombardi et al. 2008 (females) Italy Prospective Comparison trial Level 2 N=31	**Population:** 31 women, 17 of whom had neurogenic bladder dysfunction with permanent SNM implanted. Group A comprised 18 neurogenic individuals, with mean age of 37.4 years (range 23–48). All of them showed at least partial peripheral or central preservation of the upper motoneuron confirmed with appropriate neurophysiologic investigations. Group B comprised 15 idiopathic females, with mean age of 37.4 years (range 25–46). All neurological diseases were excluded in these subjects using appropriate neurophysiologic tests such as anal sphincter electromyography. **Treatment:** To evaluate if SNM improves sexual function in females treated with SNM for lower urinary tract dysfunction. **Outcome Measures:** Improvement in blood sexual function as measured by the Female	1. Four out of 11 participants showed clinically significant improvement in sexual health (an increase of 60% of the total score or of one FSFI domain, or 50% improvement on the FSDS). 2. Mean duration of sexual improvement was 23 months. 3. The positive effects regarding sexuality may be due either to enhancement of LUTS or to the direct stimulation of the sacral roots (S3).

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	Sexual Function Index (FSFI) and the Female Sexual Distress Score (FSDS).	
Sievert et al. 2010 Germany Case control Level 3 N=16	**Population:** N: 16 Level: all thoracic; all complete; all AIS Score A Etiology: traumatic Experimental Group N: 10 Age: Mean 30.5 years, Range 19-38 years Control Group – N: 6 Age: Mean 36.5 years, Range 27-47 years **Treatment:** Sacroneuromodulation Stimulation (SNS) (Interstim- I & II) bilaterally implanted at the third sacral foramen. Control group was people with SCI given an antimuscarinic medication prescription with no stimulation. Follow-up schedule: 3 and 6 months, then every 6 months thereafter. **Outcome Measures:** bowel movement details (participant diaries), laxative use, and QOL questionnaire	1. The group with Sacral Neuromodulators (experimental group) reported sufficient colon movement without oral laxatives 2. People in the Stimulation group reported higher QoL than the controls: more independent and "normal social participation". 3. With additional Interstim- II programming, two patients experienced improved erectile function that permitted satisfying sexual intercourse.
Calabrò et al. 2014 Italy Pre-post Level 4 N=20	**Population**: 20 men (mean age 34.85±10.27 years) affected by severe spasticity due to SCI (10), vascular (3), degenerative (6) and congenital (1)d origins; level of lesion C4 - T10 with a mean disease duration of 6.1±4.45 years **Treatment**: Implantation of a Synchromed pump with port and a drug administration device (DAD) with a 20mL reservoir. Intrathecal baclofen was administered through the pump and port system (mean dose of 75±25 mg/day). **Outcome Measures:** All patients underwent neurological and sexological tests using the International Index of Erectile Function (IIEF) and the Diagnostic Impotence Questionnaire (DIQ) before pump implantation and approximately 2 months after implantation. All participants underwent specific clinical scales to evaluate force, muscle tone, cognition and mood, and specific sexual questionnaires, including a semi-structured interview.	**1.** Decrease in the IIEF median scores before and after implantation. **2.** Spasticity, spasms, and patient's perception of their own quality of life (QoL) improved after ITB administration but with a worsening of sexual functions. **3.** Found a correlation between ITB dosage and IIEF scores (ρ=-0.60; $P < 0.05$). **4.** Before implantation, 55% of participants declared difficulties to achieve or maintain an erection, whereas after the pump implant 80% of the sample suffered from erectile dysfunction.
Lombardi et al. 2011 Italy Pre-post Level 4 N=75	**Population:** N: 75 men (8 completed NBS outcomes) Level: incomplete Duration: > 6 months	**1.** Individuals (6) with neurogenic erectile dysfunction had a 37.4% improvement in IIEFS score and engaged in sexual intercourse without needing oral phosphodiesterase 5 inhibitor.

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	Treatment: using sacral neuromodulation (SNM) implanted at third sacral foramen. and comparing: before (14 day baseline) vs. after implantation . Follow-ups after: 1, 3, and 6 months then every 6 months after that. **Outcomes:** SF-36 QoL questionnaire, frequency of incontinence, frequency of evacuations, duration of evacuations, Wexner fecal incontinence and constipation questionnaires, pad usage, anorectal manometry and International Index of Erectile Function (IIEFS; male sexual function questionnaire)	
Jones et al. 2008; USA Pre-post Level 4 N=7	**Population:** 7 men with SCI (mean age 36.7 yrs) with positive bulbocavernous reflex and reported history of sexual activity since injury. **Treatment:** Implantation of intrathecal baclofen pump. **Outcome Measures:** Brief Sexual Function Inventory (BFSI) questionnaire; perception of spasticity questionnaire, developed by Schwartz et al.; SF-36 Health Survey.	**1.** Generally unchanged rating of perceived sexual functioning, sexual relationships, and ejaculation post-implant. **2.** Modest to drastic improvements in the participants' perception of problems with sexual functioning. **3.** In 3 participants, there was a relationship between baclofen dosage and perceived sexual function; as baclofen dosage increased, BFSI scores related to erections deteriorated. **4.** Significant improvement in the spasticity scores from pre- to post-implant. **5.** Improved health status score in all but 1 subject.
Denys et al. 1998 France Pre-Post Level 4 N=5	**Population: 3** female and 14 male participants. Time between injury and operation ranged from 1 to 15 years. All had a complete lesion of the spinal cord: in 16 cases situated between T1 and T10; in one patient at C5. **Treatment:** Implantation of intrathecal baclofen pump (average dose of 290(68.3) µg/day). **Outcome Measures:** yes or no questions (ability to sustain reflexive & psychogenic erections, obtain ejaculation without electrical, vibratory, pharmacologic stimulation); visual analog scale for penile rigidity; recall of maximal duration of stable erection (minutes); modification of libido.	**1.** Ability to sustain erections was not affected by treatment. **2.** 3/5 participants reported decreased rigidity after treatment. **3.** 4/5 participants reported decreased erection duration after treatment while 1 subject reported increased duration after treatment. **4.** One subject who had the ability to obtain ejaculation without electrical, vibratory or pharmological stim before treatment was no longer able after treatment. This ability returned after baclofen withdrawal.
Van der Aa et al. 1995 Netherlands Post-test Level 4 N=17	**Population:** 5 men with SCI (mean age 35.8 yrs); all participants with sacral reflexes and reflexive bladder. **Treatment:** Implantation of the Finetech-Brindley bladder controller (Sacral anterior neuromodulator)	1. A sustained full erection can be achieved in all our male patients using continous stimulation; in 12 patients by stimulation of the $2 anterior roots; in 2 patients by stimulating the $3 anterior roots. There is no interference with bladder emptying.

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	Outcome Measures: Four days after surgery, bladder capacity, continence, and sexual function were measured.	

Discussion

Implantation of a Sacral Anterior Root Stimulator (Brindley et al. 1982) for bladder control usually entails rhizotomy of posterior sacral roots to improve bladder capacity and compliance and reduce reflex incontinence and possibly sphincter spasticity, but in so doing has the disadvantage in men with SCI of abolishing reflex erection, and ejaculation when present. While not the primary indication for implantation, continuous stimulation of S2 or S3 anterior roots has been shown to achieve a sustained and full erection in all of a series of 14 men with complete SCI lesions between C5 –T10 level (Van der Aa et al. 1995). Vignes et al (2001) reported that 60 percent of men with complete SCI were able to achieve an erection by continuous stimulation of S2 roots.

We found 3 studies (Lombardi et al. 2008; Lombardi et al. 2011; Sievert et al. 2010) that used Sacroneuromodulation Stimulation (SNS) in an effort to correct lower urinary tract dysfunction and that also measured sexual function. Proportions of participants in each study recovered erectile function and/or genital arousal; though more research with larger sample sizes are needed.

Concerns have been raised about the impact of intrathecal baclofen (a drug to control spasticity) on sexual function among men with SCI. Baclofen may have an effect on sexual function presumably secondary to the inhibition of visceral afferent input to the lumbosacral spinal cord (Steers et al. 1992). Jones et al. (2008) reported that although there was minimal impact on sexual function after baclofen pump implantation, there was a possible dose response between baclofen and sexual function (ie, higher the dose to control spasticity, poorer the erection function). Four out of seven participants noted a decrease in perceived sexual function following an increase in baclofen dosages, although some were utilizing PDE5i as well, and one subject reported a dramatic improvement in rating of sexual function with increase and later tapering in baclofen dose. Denys et al (1998) reported similar inconsistent findings leading the authors to conclude that the effects of baclofen on sexual function seem to be transitory and reversible with withdrawal or reduction in dose. More recently, Calabro et al. (2014) found that before implantation, 55% of participants declared difficulties to achieve or maintain an erection, whereas after the pump implant 80% of the sample suffered from erectile dysfunction.

Conclusion

There is level 2 evidence (Lombardi et al. 2008) that Sacral neuromodulator stimulation can improve erectile function while simultaneously improving lower urinary tract dysfunction.

There is level 4 evidence (Denys et al. 1998; Jones et al. 2008; Calabro et al. 2014) that implantation of intrathecal baclofen pump, while effective in managing spasticity, may cause difficulties with erection and sexual function.

There is level 4 evidence (Lombardi et al. 2008) that implanting a sacral neuromodulator can improve sexual health and ability to achieve and maintain erection in men with SCI.

Implantation of an intrathecal baclofen pump, while effective in managing spasticity, may cause difficulties with erection and sexual function.

Implantation of a Sacral Anterior Root Stimulator usually entails rhizotomy of posterior sacral roots to improve bladder capacity and reduce incontinence, but has the disadvantage in men with SCI of compromising reflex erection and ejaculation.

Continuous stimulation of S2 or S3 anterior roots has been shown to achieve a sustained and full erection in men with complete SCI lesions between C5 –T10.

5.1.8 Perineal Muscle Training

Perineal muscle training (or pelvic-floor exercises) has been used with some success in men with erectile dysfunction (but without spinal cord injury).

Table 10: Effects of perineal muscle training

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Courtois et al. 2001; Canada Pre-post Level 4 N=10	**Population:** 10 men, age range 25-52 yrs. **Treatment**: Perineal training combined with biofeedback and home exercises. **Outcome Measures:** Tumescence (penile circumference).	**1.** Perineal training resulted in significant differences in tumescence. **2.** After treatments were stopped there was a decrease in penile circumference that was statistically significant from the treatment increase.

Discussion

This study (n=10) is worth mentioning since it focuses on the relatively successful use of perineal muscle training exercises to improve penile rigidity in those men with some capacity for voluntary pelvic floor contraction. The approach of maximizing the physiological potential before introducing pharmacological or mechanical intervention is an approach often forgotten in rehabilitation (Elliott 2003).

Conclusion

There is level 4 evidence (from 1 pre-post study; Courtois et al. 2001) suggesting that perineal training may result in improvement in erectile function in men with SCI who have some voluntary pelvic floor muscle contraction.

Perineal training may enhance erectile function in men with SCI who have some voluntary pelvic floor muscle contraction.

5.1.9 Summary: Treatment for ED

Overall, relatively few RCTs of therapies for ED have been performed in the SCI population, with the notable exception of PDE5i use. That said, however, and not withstanding the issues with research designs, there is much that can still be gleaned from these case series and pre-post studies regarding differences between the efficacy, practicality and safety of each method to help guide individual decision-making and choice.

PDE5i is recommended as the first choice for treatment of erectile dysfunction in SCI, as its effectiveness has been shown to be excellent in the SCI population (about 70 - 80% success). The longer acting tadalafil may be advantageous in those men where sildenafil failed or for those wishing for more spontaneous activity (longer action of up to 24-36 hours versus 1-4 hours with Viagra and Levitra). In general, PDE5i works best on those with UMN lesions in comparison to those with LMN lesions whose nitric oxide release at the nerve end terminal may not be as consistent. A lesion above

the sacral spinal tract and a higher reflexive erection are predicable favorable parameters for a positive response to all PDE5i. Effectiveness of sildenafil in men with LMN is reported to be between 28% -50% (Del Popolo et al. 2004, Khorrami 2009). Short term side effects are approximately the same as with able-bodied men (headache and flushing between 10-15%, dyspepsia about 5% and visual disturbances noted in higher doses), but caution should be used in differentiating the side effects of the PDE5i with those seen with autonomic dysreflexia (AD) - especially the presence of headache so as not to ignore the symptoms of AD. The use of PDE5i is contraindicated in men taking nitrates, and should be used with relative caution in men with symptomatic hypotension and/or tetraplegia due to the native hypotensive effect of PDE5i. Long term side effects have not been evaluated in the SCI population, but it appears tachyphylaxis is rare.

At the present time, there is not enough evidence to suggest either sublingual apomorphine or oral fampridine-SR are useful in the SCI population for the treatment of ED. Injectable medications have better efficacy (90%) than PDE5i, but are more invasive, and have a higher risk of short term side effects, especially prolonged erection in the SCI population (Deforge et al. 2004a). Careful teaching of correct injection technique and dose titration can largely eliminate this problem. PGE1, papaverine and phentolamine all require refrigeration, with PGE1 being the least stable at room temperature (Deforge et al. 2004b). Prolonged use of papaverine is more likely to cause cavernosal fibrosis due to its low pH of 3-4, and therefore is more commonly used in conjunction with other medications (commonly phentolamine or atropine). Injection with any of these medications can cause subcutaneous hematomas, cavernosal or tunica fibrosis (usually small and reversible with time) or mild edema. The use of intraurethral prostaglandin (MUSE®) and topical preparations have not been that successful in the SCI population and therefore are rarely used. Penile implant surgery is reserved now for those men with failed or unacceptable reversible methods (ICI, oral therapy or vacuum device), although some men with difficulties attaching external drainage devices may find penile implants helpful.

Conclusions

Oral PDE5i is the first line treatment for ED in men with SCI, with the more invasive but successful use of ICI being used most often in men who do not respond to the oral medications. Mechanical devices such as vacuum devices and rings may be effective but are not as favoured by consumers. Surgical prostheses should be reserved for refractory cases. Other therapies (e.g., nitrogycerine, intraurethral and topical application of PGE1 and papaverine, sublingual apomorphine, and oral fampridine) have not proven viable when compared to the more established therapies.

The use of PDE5i for treatment of ED in men with SCI is effective, safe and popular, followed by the more invasive but highly effective method of intracavernosal injection.

The use of mechanical devices may be effective but are less popular, and surgical options should be reserved for cases where other ED treatments fail.

5.2 Sensation, Ejaculation and Orgasm in Men with Spinal Cord Injury

Ejaculation, the process of external semen expulsion, is primarily a sympathetic phenomenon (involving the spinal cord segment between T10-L2). Internally, there is a pathway for sperm to be transported from the testicles with accessory fluids before being expelled out the end of the penile urethra (antegrade ejaculation) (Krassioukov and Elliott, 2017). Ejaculatory disorders (most often the lack of both seminal emission and antegrade ejaculation called anejaculation) are highly prevalent (reported at over 90%) so fertility can be a major issue for men with SCI (Elliott, 2002). Ejaculation is most likely to occur naturally in men with incomplete conus or cauda equina lesions, and men with lesions higher than T6; ejaculation is least likely to occur naturally in men with complete supraconal lesions (Comarr, 1985; Ibrahim et al. 2016). Retrograde ejaculation can also occur, most often in men with sphincterotomy or who have a suprapubic catheter (Ibrahim et al. 2016).

Much of our existing knowledge of ejaculation and orgasmic sexual satisfaction is derived either from self-report surveys or indirectly reported in the fertility literature, thus further research is needed. Not surprisingly, there are no RCT studies in this area, with only one study performing laboratory evaluation of these altered responses in men with SCI (Sipski et al. 2006). Orgasm, in particular, is a phenomenon that is not well defined, either clinically or neurophysiologically, being generated via cerebral, body or genital sources of stimulation, and usually is self-described by participants only in terms of being either similar or different in comparison to their pre-injury experience. Sipski et al. (2006) report that the preservation of light touch and pinprick sensation in the T11-L2 dermatomes is helpful in predicting which people with SCI can achieve psychogenic arousal.

A study by Phelps et al. (1983) found 42% of 50 male veterans with SCI reported orgasm. Alexander et al. (1993) showed in their series that the majority of 38 men with SCI could not ejaculate, with the exception of those with an incomplete paraplegia of whom 75% could ejaculate in some fashion. Despite this, they reported that in the group with complete SCI lesions, 50% of the men with tetraplegia and 25% of those with paraplegia reported that they could have some sort of orgasm, and of those that could, 38% with tetraplegia and 67% with paraplegia reported it was not accompanied by ejaculation. For the men with incomplete SCI lesions, 66% of the men with tetraplegia said they could have orgasm (of which 50% said it was accompanied by ejaculation) and 75% of those with paraplegia reported they could have some kind of orgasm that was always accompanied by ejaculation. There was a significant correlation between the ability to have an orgasm and ejaculation, as was the ability to ejaculate and having an erection firm enough for penetration.

Similarly, a recent laboratory study of 45 men with SCI and 6 able-bodied controls (Sipski et al. 2006) demonstrated that 79% of the men with incomplete lesions and 28% of those with complete lesions achieved orgasm in the laboratory setting (historically, these men reported post-injury orgasmic ability to be 84% and 50%, respectively). Independent significant predictors of orgasm in the laboratory were completeness of injury and prior history of orgasm post-injury. Those men with lower motor neuron lesions affecting the sacral segments (n=4) had no historical or laboratory experience with orgasm. They also reported that although orgasm and ejaculation were likely to occur together, the presence of orgasm was not necessarily connected with presence of ejaculation.

Table 11: Systematic Review on Sensation, Ejaculation and Orgasm in Men with SCI

Author Year; Country Dates included in the review Total sample size Level of evidence Type of study Score	**Methods Databases**	**Outcomes**
Chéhensse et al. 2013; France Reviewed published articles from 1955 to 2012 N=45 Level of evidence Methodological quality not assessed Type of studies All cross-sectional studies 36 retrospective	**Method:** searched for all published articles examining the occurrence of antegrade rhythmic forceful or dribbling ejaculation as a function of the neurological characterization of the lesion. All levels of evidence were included. **Databases:** MEDLINE, EMBASE, EBSCOhost, Cochrane Library	**1.** Ejaculation occurred in response to (i)masturbation or coitus; (ii) penile vibratory stimulation (PVS) followed by masturbation; (iii)acetylcholinesterase (AchE) inhibitors followed by masturbation in: (i)11.8%; (ii)47.4%; (iii)54.7% of patients with complete SCI (i)33.2%; (ii)52.8%; (iii)78.1% of patients with incomplete SCI **2.** Ejaculation in response to PVS or AchE inhibitors prior to masturbation was rhythmic forceful in 97.9% of patients with complete lesion strictly above segments S2-S4. Complete lesion of the S2-S4

Author Year; Country Dates included in the review Total sample size Level of evidence Type of study Score	Methods Databases	Outcomes
AMSTAR=3		segments precluded the occurrence of rhythmic forceful ejaculation. **3.** Controlling for the number of the injured segments between T12 and L2, the ejaculation rate sharply decreased when the lesion extended to the L3 segment and below. **4.** The spinal sympathetic and parasympathetic centres are crucial for emission and the somatic centre for expulsion. **5.** The spinal segments between L2 and S2 are more than a pathway to connect the ejaculation centres; L3-L5 segments likely harbour a spinal generator of ejaculation.

Table 12: Effects of Interventions to improve Ejaculation or Orgasm

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Overgoor et al. 2013; The Netherlands Pre-post Level 4 N=30	**Population:** 30 men (SCI n=12, Spina bifida n=18) with no penile sensation but good groin sensation. **Treatment:** TOMAX (TO MAX-imize sensation, sexuality and quality of life) procedure that involved microsurgical connection of the sensory ilioinguinal nerve to the dorsal nerve of the penis unilaterally. **Outcome measures:** sensitivity testing, bulbocavernosus testing, Hospital Depression and Anxiety Scale (HADS), Symptom Checklist (SCL-90-R), Groninger Arousability Scale (GAS), Visual Analogue Scale (VAS).	1. Participants became more sexually active with their partners and with more satisfaction. 2. Postoperative (11-24 months) glans sensation increased from absence to having sensations. 3. All patients retained the preoperative ability to have an erection and ejaculations. *4.* Participants reported having more open and meaningful sexual relationships with their partners.
Courtois et al. 2011; Canada Cohort Level 2 N=89	**Population:** Men who achieved ejaculation with (n=50) or without (n=39) experiencing autonomic dysreflexia (AD). **Treatment:** Ejaculation was obtained through natural stimulation, vibrostimulation or vibrostimulation combined with midodrine (5-25 mg). **Outcome measures:** Questionnaire inquiring about the physiological responses related to orgasm to test the hypothesis that orgasm is related to AD in individuals with SCI.	**1.** Significantly more sensations were described at ejaculation than with sexual stimulation alone. **2.** Men with SCI who experienced AD at ejaculation reported significantly more cardiovascular, muscular, autonomic and dysreflexic responses than those who did not.
Borisoff et al. 2010; Canada Pre-post Level 4 N=3	**Population:** 3 males (mean age = 38, range 34-42) with SCI ≥1 year. **Treatment:** Sexual self-stimulation while using a novel sensory substitution device that mapped the stroking motion of the hand to a congruous flow of electrocutaneous	**1.** Each participant reported an increased level of sexual pleasure compared to baseline after a few training sessions. **2.** No difference found on the ejaculation questionnaire scores.

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	sensations on the tongue. Erection-enhancing drugs administered as needed. **Outcome measures:** Solitary Masturbation Orgasm Questionnaire (Mah and Binik); SCI Ejaculation Questionnaire (Courtois et al.); Sexual Sensations Questionnaire (SSQ).	
Soler et al. 2008; France Pre-Post Level 4 N=158	**Population:** 158 participants with SCI who failed to ejaculate from penile vibratory stimulation (PVS). **Treatment:** Oral midodrine, starting at 7.5mg in participants with tetraplegia and 15mg with paraplegia. **Outcome Measures:** Ejaculation; orgasm.	1. With midodrine, ejaculation was obtained in 102 men (64.6%). 2. 93 (59%) participants reported orgasm with both midodrine and PVS, compared to 14 patients with only PVS. 3. Participants with upper motor neuron injury and incomplete lesions experienced significantly more often orgasm.
Courtois et al. 2014 Canada Retrospective Study Level 5 N=33	**Population**: 34 males (mean age= 41 years, age range= 19-65 years) with SCI who have been consulted for sexual dysfunctions over the past 20 years, lesions varied from L5-S1 and S4-S5, average delay since injury= 10 years **Treatment:** None **Outcome Measures:** Occurrence of psychogenic and reflexogenic erection and ejaculation since injury, and test for perineal reflexes (bulbocavernosus reflex, anal reflex, cremasteric reflex)	**1.** 31/33 patients maintained natural ejaculations, but 18 complained of premature ejaculation (PE) and five of spontaneous ejaculations. **2.** 14 patients complained of dribbling ejaculation, and 27 of non-climactic ejaculation (13 no sensation, 10 some sensation, 4 painful sensation). **3.** Medical assessments showed absent or diminished anal sensation in 28 patients, absent or diminished anal reflexes in 21, absent or diminished bulbocavernosus reflexes in 20, but 12/13 positive cremasteric reflex. **4.** Urodynamics showed 12/20 areflex and 2/20 hyperactive bladders
Soler et al. 2016 France Post test Level 4 N=33	**Population:** 33 males with anejaculation during sexual stimulation; mean age=29.0±9.1 years; mean time since the onset of the neurological disorder was 6.6±6.4 years; 19 have complete motor lesion (AIS A or B), 1 had incomplete motor lesion (AIS C). **Treatment** Penile vibratory stimulations were carried out following bladder catheterization and instillation of a pink buffering medium (Ferticult) and then PVS. If they failed to ejaculate, PVS was combined with oral midodrine 5mg up to 30mg until the patient ejaculated. The urethra was then milked manually to ensure that as much semen as possible was collected. Two-step catheterization was then performed: a catheter was inserted through the urethral sphincter into the prostatic urethra to aspirate its content, and then bladder catheterization was performed to collect the Ferticult. The procedure was repeated in some patients after at least 1 week.	**1.** A total of 42 trials were obtained from 22 patients. Sperms were found in the prostatic urethra in 21 samples (50%) from 12 patients (11 with spinal cord injury, 1 with diabetes). **2.** The colour of all 21 prostatic urethra sperm samples differed from the Ferticult. **3.** Sperm motility was greater in 8 samples, sperm count was higher in 10 and pH was different in 10, compared with the bladder samples. **4.** The higher overall quality of the sperm allowed cryopreservation in 10 prostatic urethra samples compared with only 5 bladder samples. **5.** Four of the five patients who underwent repeated trials had a reproducible pattern of prostatic urethra ejaculation **6.** The presence of sperm in the prostatic urethra most probably results from ‘ejaculation dyssynergia’, a lack of coordination between bladder neck and external sphincter.

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	Outcome Measures: Type of ejaculation, quality of sperm, antegrade/retrograde fraction, prostatic urethra fraction, motility, viability, and pH of sperm.	**7.** Sperm from the prostatic urethra should be systematically sought to improve the outcome of assisted reproduction.
Leduc et al. 2015; Canada RCT Level 1 PEDRO=8/11 N=20	**Population**: 20 men with traumatic SCI (level C4-T9) of at least one year duration, and anejaculation. **Treatment**: Participants were randomized into two groups, Group M and Group P where group M received an oral administration of flexible sham-midodrine (7.5-22.5 mg max) followed by PVS, and group P received oral administration of (placebo) followed by PVS. Intervention occurred once a week for a maximum of 3 weeks or until ejaculation occurred. **Outcome Measures**: Ejaculation, and measurement of AD.	**1.** Treatment of anejaculation after SCI with midodrine and PVS did not result in a better rate of antegrade ejaculation in 10 men than in 10 men treated with a placebo and PVS. **2.** One participant (10%) from group M reached ejaculation and two participants (20%) from group P reached ejaculation. **3.** Autonomic dysreflexia occurred in three patients (none of which ejaculated) during PVS.
Castle et al. 2014 United States Case series Level 4 N=30	**Population**: 30 anejaculatory males with SCI who were unable to ejaculate by sexual intercourse or masturbation, level of injury T10 and rostral. **Treatment**: The Viberect-X3 (Reflexonic, Frederick, MD, USA) was applied to 30 consecutive anejaculatory men with SCI whose level of injury was T10 and rostral. All patients received one trial of penile vibratory stimulation (PVS) with Viberect-X3. All patients were familiar with PVS and had been administered one or more previous trials with an alternate device. Prior to PVS, participants whose level of injury was T6 or rostral were administered 10–40mg nifedipine sublingually to manage autonomic dysreflexia. Viberect-X3 was administered. **Outcome Measures:** Ejaculatory success rate, time to ejaculation, volume of ejaculate, blood pressure, adverse events.	**1.** The ejaculatory success was 77% (23/30) slightly lower than previously published PVS success rates. **2.** No adverse events occurred, and there were no malfunctions of the device.

Discussion

Microsurgery of the sensory nerves to the penis is one promising treatment for improving sensation and orgasm in men with low spinal cord lesions (Overgoor et al. 2013). A sensory substitution technology trained patients over 20 sessions to map tongue sensations to sensory perceptions of the genitalia (Borisoff et al. 2010) and is one other possible therapeutic avenue for sexual rehabilitation.

One study (Soler et al. 2008) examined the effect of midodrone, an oral selective alpha-adrenoceptor agonist, which is mainly used as a treatment for orthostatic hypotension, on orgasm among 158 individuals with SCI who failed to ejaculate at home and when using penile vibratory stimulation. Soler et al. (2008) found that midodrine combined with penile vibratory stimulation produced orgasm in 59% of participants compared to 9% with vibratory stimulation alone, and orgasm was significantly related (84%) to the presence of either antegrade or retrograde ejaculation. Orgasm was experienced more

among individuals with incomplete injuries (vs complete) and among individuals with upper motor lesions (vs lower motor lesions). It is important to note that the sympathomimetic effect results in a significant increase in both systolic and diastolic blood pressure, and caused several patients to develop intense autonomic dysreflexia that required medical attention. It is theorized that orgasmic sensations, with or without ejaculation, are related to somatic responses of vibrostimulation and perceived sensations of autonomic dysreflexia, and that orgasm appears to be a reflex partly under cerebral influence and could therefore be learned and practiced (Courtois et al. 2004; Elliott 2002). In research on the efficacy of the Viberect-X3 for treatment of anejaculation in men with SCI, we conclude that the device is safe and effective for inducing ejaculation in men with SCI.

Conclusions

There is level 4 evidence (Overgoor et al. 2013) that microsurgery of the sensory nerves to the penis may be one treatment for improving senation and organism in men.

There is level 4 evidence (Borisoff et al. 2010) that sensory substitution training may be one therapeutic avenue for sexual rehabilitation.

There is level 4 evidence (Soler et al. 2008) that oral midrodrine may improve orgasm and ejaculation in men with SCI and level 4 evidence that PVS and midrodrine induces ejaculation in anejaculatory males with SCI.

There is level 1b evidence (Leduc et al. 2015) that oral midrodrine and PVS does not result in a better rate of antegrade ejaculation in men with traumatic SCI.

There is level 5 evidence (Courtois et al. 2014) that 53% of patients complained of premature ejaculation and 15% complained of spontaneous ejaculation.

Promising options (but with limited evidence) exist for improving the chance of reaching orgasm in men with SCI include microsurgery of the sensory nerves to the penis and sensory substitution training.

The use of oral midrodrine to encourage ejaculation may also improve chance of orgasm.

5.3 Male Fertility

Male fertility after SCI is often compounded by the difficulties of erectile dysfunction, as well as retrograde ejaculation or anejaculation. Ejaculation is a complex process involving coordinated activity of the sympathetic (smooth muscle) and somatic (striated muscle) nervous system controlling prostate and seminal vesicles, bladder neck/sphincter, pelvic floor and urethra. Few men with SCI are able to ejaculate with partner sexual practices alone and require medical assistance to obtain sperm. This sperm is then used for intravaginal/intrauterine insemination or other assisted reproductive technology (ART) interventions. Although most of the male fertility studies describe issues of retrieval, sperm quality, reproductive technology, pregnancy and live births within a single study, the tabled studies have been sorted into the topics of sperm retrieval, sperm quality and pregnancy based on the primary focus of the paper, although overlap does occur.

Table 13: Systematic Reviews on Male Fertility

Author Year; Country Dates included in the review Total sample size Level of evidence Type of study Score	Methods Databases	Outcomes
DeForge et al. 2005; Canada Reviewed published and unpublished articles between 1966 and 2003 N=66 <u>Level of evidence</u> Jadad Scale – RCTs Newcastle-Ottawa Scale – Non RCTs <u>Type of studies</u> Not specified AMSTAR=7	**Methods:** Literature search for published and unpublished studies from databases and selected annual proceedings, of any research design or language, that enrolled male, adult/adolescent populations with SCI reviewing fertility interventions with pre- and post-intervention fertility measures Interventions included electrical and vibrational stimulation, testicular biopsy, intracytoplasmic sperm injection (ICSI) and in vitro fertilization (IVF). Outcome measures included sperm quality and pregnancy and live birth rates. **Databases:** MEDLINE, PreMEDLINE, CINAHL, Cochrane Central Register of Controlled Trials, SocioFile, and PsycINFO.	**1.** Systematic review restricted to male fertility post-SCI, as there were no case-series studies investigating fertility issues such as pregnancy rates, live births and complications or obstetrical management issues in females after SCI. **2.** Ejaculation interventions in the last decade resulted in response rates of 95% (95% confidence intervals (CI) 91%, 99%), with 100% response rate reported in several recent publications. **3.** A total of 13 studies (1993–2001) yielded pregnancy rates of 51% (95% CI 42%, 60%) in partners of SCI males. Of these, 11 studies (1993–2003) yielded live birth rates of 41% (95% CI 33%, 49%), an improvement overtime. **4.** Reproductive success limited by prevailing low semen quality in SCI males. **5.** Sperm freezing would probably not enhance fertility unless the sperm were to be frozen almost immediately after injury.
Patki et al. 2008; UK Reviewed published articles from PubMed and Medline, dates not mentioned N=not stated Level of evidence Methodological quality not assessed Type of studies Not described AMSTAR=0	**Method:** Searched using the key words: spinal cord injuries, fertility, sexual dysfunction, and spermatogenesis, for articles on the effects of SCI on semen parameters that may contribute to poor motility and poor viability. **Databases:** PubMed and Medline	**1.** The distinguishing character of poor semen quality in men with SCI is abnormal sperm motility and viability, not the sperm count which remains comparable to the age-matched population. The cause of this asthenozoospermia appears be multifactorial, but not related to time since injury, elevated scrotal temperature, method of bladder management or method of ejaculation. **2.** Although abnormal hormonal levels in urine and blood have been reported in many studies, this does not seem to be the primary cause of infertility because equal numbers of studies report normal findings. **3.** 2 studies reported a decrease in sperm motility in men with SCI associated with elevated scrotal temperatures. However, a more recent study contradicted this, finding no correlation between scrotal temperature and semen parameters. **4.** Men with SCI have elevated levels of reactive oxygen species in semen which is associated with a decrease in fertility. **5.** Seminal plasma from men with SCI decreases sperm motility.

Author Year; Country Dates included in the review Total sample size Level of evidence Type of study Score	Methods Databases	Outcomes
		6. Axonemal defects and abnormalities of flagella were identified in the majority of patients with SCI.

5.3.1 Sperm Retrieval

The two methods of sperm retrieval most commonly used are penile vibrostimulation (PVS) and the electroejaculation procedure (EEP). PVS is performed using a specialized vibrator placed on the penis to induce reflex ejaculation, whereas EEP uses a rectal probe to deliver electrical current to the periprostatic nerves, eliciting seminal emission. In the first months after injury, semen can only be attained by EEP, since PVS is not effective until spinal shock has resolved.

Table 14: Sperm Retrieval

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Raviv et al. 2013; Israel Case control Level 3 N=32 (couples)	**Population:** 32 couples with male partner with SCI referred to IVF after repeated trials of electroejaculation (EEJ) or penile vibratory stimulation (PVS) and full andrological evaluation; mean(SD) time since injury until assisted reproductive procedure 7.6(2.1) yrs, range 5–16; Patient subgroups: obstructive azoospermia (n=19), non-obstructive azoospermia (n=6), severe oligozoospermia (n=7). **Treatment:** Testicular sperm aspiration (TESA) for sperm extraction. Open testicular sperm extraction (TESE) was performed only after a negative TESA attempt. **Outcome measures:** clinical pregnancy and live birth rates.	1. A total of 106 testicular procedures were performed. Sperm was found in 95 cycles (89.6%). 2. Average metaphase II (MII) oocyte number was 11.0(4.2), an average of 5.1(2.3) oocytes became normally fertilized after Intra Cytoplasmic Sperm Injection (ICSI) (fertilization rate 57.1%). 3. On average, 2.7(1.2) embryos were replaced. The clinical pregnancy rate was 32/106 (30.2%) per cycle and 19/32 (59.3%) per couple. The live birth rate was 62.5% (20/32).
Kathiresan et al. 2012; USA Case series Level 4 N SCI=444 N controls=61	**Population:** 444 men with SCI with no known causes of infertility other than SCI; level of injury: 176 cervical, 193 T1-T10, 70 T11-caudal; 115 complete, 126 incomplete. Controls: 61 able-bodied (AB) men, healthy with no history of infertility. **Treatment:** Retrospective chart review of Male Fertility Research Program participants from 1991 to 2011. Sperm retrieval methods included masturbation, penile vibratory stimulation (PVS), and electroejaculation (EEJ). **Outcome measures:** sperm retrieval method (masturbation, PVS, EEJ), semen volume, sperm concentration, sperm motility, total sperm count.	1. Sperm retrieval method in SCI participants: masturbation (n=43), PVS (n=243), EEJ (n=158). Sperm retrieval method in AB control group: masturbation (n=61). 2. 8.1% (43 of 528 SCI participants) retained ability to ejaculate by masturbation. 3. Sperm motility was significantly higher in the SCI-masturbation group (36.9%) than the PVS group (25.9%) or EEJ group (15.0%), but lower compared with a control group of 61 non-SCI healthy men who collected their semen by masturbation (58.0%). 4. The SCI-masturbation group had similar antegrade sperm concentration as the PVS group, and control group, but significantly higher than the EEJ group.
Qiu et al. 2012; China	**Population:** 26 infertile men with SCI (primary infertility present in 9), mean(SD)	1. The rate of sperm DNA fragmentation was higher in the PVS group than in the

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Pre-post Level 4 N SCI=26 N controls=16	age 33.8(2.9) yrs, mean(SD) DOI 8.6(3.0) yrs (range 1-11 yrs), level of injury: C5-C6 (n=4), T2-T12 (n=22), mean(SD) yrs of infertility 6.8(4.2) yrs; Controls: 16 non-SCI fertile donors (all had previously fathered at least one child), mean(SD) age 32.9(2.1) yrs. **Treatment:** Collection of semen samples in SCI men using penile vibratory stimulation (PVS) (n=14), percutaneous vasal sperm aspiration (PVSA) (n=12); collection of semen samples in non-SCI donors all by masturbation (n=16). **Outcome measures:** sperm vitality and DNA integrity, sperm chromosomal aneuploidy.	percutaneous vassal sperm aspiration (PVSA) group. 2. Aneuploidy rates for SCI patients were 1.5 to 1.6-fold higher for chromosomes 13, 18, and 21, and were 2.3- to 2.4-fold higher for chromosomes X and Y than for the control group.
Sonksen et al. 2012; Denmark Case control Level 3 N=140	**Population:** 140 SCI men with anejaculation and their healthy female partners (presenting for infertility treatment between 1988 and 2008); Age: SCI men (median 30 yrs, range 22–44), female partners (median 28 yrs, range 19–39 yrs); DOI: median 7 yrs (range 1–22), Level of lesion: C2 to T9. **Treatment:** Men who obtained antegrade ejaculation by penile vibratory stimulation (PVS) and had motile sperm in the ejaculate were offered the possibility of PVS combined with vaginal self-insemination at home. Couples were instructed to perform PVS and to instill the ejaculate intravaginally. **Outcome measures:** Pregnancy rate per couple, number of live births, total motile sperm count and time to pregnancies.	1. Median total motile sperm count: 29 million (range 1–92 million). 2. 60 of the 140 couples (43% pregnancy rate) achieved 82 pregnancies. 3. 72 of the pregnancies resulted in live births with delivery of 73 healthy babies. 4. Median time to first pregnancy was 22.8 months (range 6.0–98.4). No complications were reported.
Brackett et al. 2009; USA Case series Level 4 N=500	**Population:** 500 men with SCI (3,152 semen retrieval procedures); mean(SD) age 34.1(0.4) yrs (range 17-63); mean (SD) DOI: 10.0(0.3) yrs; Level of injury: 203 cervical, 123 T1-T6, 150 T7-T12, 20 ≤ L1,4 unknown. **Treatment:** review of research data from Jan 1991 to Apr 2009 from SCI participants in a male fertility research program. Semen retrieval methods were performed according to ability: masturbation, if not then penile vibratory stimulation (PVS), if not then electroejaculation (EEJ). **Outcome measures:** semen retrieval methods: masturbation, PVS, EEJ; semen analysis: total sperm count, motility.	1. Of the 500 men 9% could ejaculate by masturbation. 2. Penile vibratory stimulation (PVS) was successful in 86% of patients with a T10 or rostral injury level. 3. Electroejaculation (EEJ) was successful in most cases of failed PVS (91.9% responded to EEJ). 4. Sperm obtained without surgical sperm retrieval, in 97% of patients completing the treatment algorithm. 5. Total motile sperm counts exceeded 5 million in 63% of cases.
Hibi et al. 2008; Japan Post-test Level 4 N=8	**Population:** 8 participants with cervical SCI and neurogenic anejaculation (age 26-46 yrs, mean 35.6). **Treatment:** Retrograde vasal sperm aspiration (ReVSA). **Outcome Measures:** Presence of motile sperm.	1. Motile sperm was recovered in all participants who underwent ReVSA (11 procedures total). 2. The retrieved sperm concentration was 109.4(64.7) × 10^6 /mL (range 31.2-156.3 × 10^6 /mL). 3. The retrieved motility of sperm was 69.8% (16.8) (range 50-91%). 4. Clinical pregnancies were achieved in 8 cases (7 couples).

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Kanto et al. 2008; Japan Case control Level 3 N = 56	**Population:** 22 men with SCI (age 21-41); data on 34 men with obstructive azoospermia was obtained retrospectively as control **Treatment:** Testicular sperm extraction (TESE); if unsuccessful, microdissection TESE was performed, followed by intracytoplasmic injection (ICSI) **Outcome Measures:** Fertilization; pregnancy	**1.** TESE successfully retrieved sperm in 19 participants with SCI. **2.** ICSI resulted in a fertilization rate of 236 of 364 (64.8%) in SCI couples and 14/19 achieved pregnancy. **3.** In couples with obstructive azoospermia, ICSI resulted in a fertilization rate of 435 of 567 (77%) and 29/34 achieved pregnancy. **4.** Pregnancy rate was significantly higher for couples with SCI using fresh testicular sperm-ICSI compared to frozen-thawed sperm-ICSI
Arafa et al. 2007; Eqypt Post-test Level 4 N=69	**Population:** Men with SCI; Age: mean 36.6 yrs, SD=18.34; Injury level: at or below T10 (n=34), above T10 (n=35); Time since injury: mean 11.03 yrs, SD=7.80; anejaculatory. **Treatment:** Prostatic massage thru the rectum to push the sperm out through the ejaculatory ductal system. **Outcome Measures:** Semen retrieval.	**1.** Semen retrieval by prostatic massage was successful in 22 men (31.9%). **2.** Semen retrieval by prostatic massage was higher for men with a SCI above T10 than below T10 (81.8% vs 18.2%).
Brackett et al. 2007; USA Pre-post Level 4 N=297	**Population:** Men with SCI; Age: range 17-60 yrs; Injury level: cervical (n=109), T1-T10 (n=131), T11 or below (n=45), unknown (n=12); Time since injury: range 0.2-44.6 yrs. **Treatment:** Penile vibratory stimulation using 1 vibrator, or if this failed, 2 vibrators applied to glans penis using sandwich method. **Outcome Measures:** Semen retrieval.	**1.** 49% of all men ejaculate with 1 vibrator; 57% of men whose injury level was at or above T10 responded to 1 penile vibratory stimulation vs. only 15% with a level of injury at or below T11. **2.** Of failures with 1 vibrator, 22 % responded to penile stimulation with 2 vibrators.
Soler et al. 2007; France Pre-post Level 4 N=158	**Population:** Men with SCI; Age: mean 29.5-33.2 yrs; Level of injury: tetraplegia (group 1, n=55), paraplegia at or above T6 (group 2, n=52), paraplegia T7-T10 (group 3, n=23), paraplegia T11 and below (group 4, n=28); anejaculation, failed to respond to penile vibratory stimulation (PVS). **Treatment:** PVS and midodrine 7.5-30mg (tetraplegia) or 15-30mg (paraplegia) 30 to 120 mins before stimulation, ED was treated with PDE5i or intracavernosal prostaglandin injection. **Outcome Measures:** Number of ejaculations, blood pressure (BP), average dose for success.	**1.** Percentage successful ejaculation following midodrine was 64.6% (62%, 69%, 46%, and 79% in groups 1 to 4 respectively). **2.** Individuals with upper motor lesions above T10 and complete lesions had more success. **3.** Average dose required was 18.6mg. **4.** Midodrine induced mild increase in mean arterial BP (max. 10mmHg) and reduced heart rate with PVS in all patients. **5.** Individuals with tetraplegia have highest increase in SBP (more than 200mmHg in 20% of cases).
Kolettis et al. 2002; USA Post-test Level 4 N=27	**Population:** Men with SCI (n=27), 9 couples; Injury level: cervical (n=10), thoracic (n=16), lumbar (n=1). **Treatment:** Electrical stimulation (12-18V, 400-600mA for 30 second bursts) followed by intrauterine insemination or IVF. **Outcome Measures:** Seminal parameters, ejaculation rates, cycle function, pregnancy rates.	1. Ejaculation rates: 43/112 were antegrade ejaculations (38%), 24/112 were retrograde ejaculations, 45/112 were both antegrade and retrograde ejaculations (40%) and 2/112 were not able to ejaculate (2%). 2. Pregnancy rate: 3/9 couples achieved pregnancy, 2 or which resulted in live births and both were twins.

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Le Chapelain et al. 1998; France Case series Level 4 N=44	**Population:** Men with SCI; Age: mean 28.5 yrs, range: 19-49 yrs; Injury level: C4-L2, tetraplegia (n=17), paraplegia (n=22); Impairment: 8 complete, 9 incomplete. **Treatment:** Retrospective analysis of vibratory stimulation, electroejaculation or subcutaneous physostigmine (a reversible acetylcholine esterase antagonist) (at least 2 sessions). **Outcome Measures**: Ejaculation, conception, sperm count, motility.	**1.** 30/39 patients produced an ejaculation. **2.** Greater success rate among participants with tetraplegia (96%), then T1-T10 (73%), then T11-L2 (42%). **3.** Vibratory stimulation produced significantly higher volumes of sperm than electroejaculation, and better sperm quality. **4.** Among 10 couples who wanted children, 3 pregnancies resulted and 2 births of healthy children.
Lochner-Ernst et al. 1997; Germany Post-test Level 4 N=219	**Population:** 219 men; 51 participants with tetraplegia, 161 with paraplegia; Mean time since injury: 11.9 yrs. **Treatment:** Supranuclear patients were treated by vibrostimulation. When this failed, further treatment was applied: physostigmine medication and vibrostimulation, electroejaculation, physostigmine with electroejaculation (EE), surgical approaches. Infranuclear patients were treated by EE. **Outcome Measures:** Semen retrieval and pregnancy success.	1. Vibrostimulation in supranuclear lesions was successful in 133 patients, and in 5 more after physostigmine injection. 2. EE was successful in all 7 infranuclear lesions and in 4 supranuclear patients failing with vibrostimulation. 8 more supranuclear patients responded to EE and physostigmine. 3. Surgical retrieval was applied in 27 patients. 4. In 109 patients who wanted children, 73 pregnancies in 46 couples, leading to 54 births and 16 abortions.
Lim et al. 1994; Australia Post test Level 4 N=12	**Population:** Men with SCI; Age: mean 31 yrs, range 21-36; Injury level: C4-L2; Time since injury: mean 8 yrs, range 1-24 **Treatment:** Assisted ejaculation (electroejaculation (EE) or penile vibratory simulation (PVS)) using balloon catheter to tamponade the bladder neck. **Outcome measures:** Antegrade ejaculation, semen analysis including volume, sperm concentration, morphology, percentage of motile sperm, adverse events, impact of catheter and lubrications on sperm.	1. Antegrade ejaculations were collected on all occasions. 2. No urine contamination of sperm and no sperm were found in post-ejaculate urine. 3. Silicone catheters had minimal effect on sperm motility and viability. 4. Lubricant gels adversely affect sperm quality.
Sonksen et al. 1994; Denmark Post-test Level 4 N=66	**Population:** Men with SCI and erectile dysfunction; Age: range 18-44 yrs; Time since injury: 0.6-39 yrs, Level of injury: C2-L1. **Treatment:** Vibrator (multicept ApS) and Relax (Nordic Light) vibrators. Different amplitudes were tested. **Outcome Measures:** Ejaculation responses.	1. Similar ejaculation responses when using frequencies of 80-100Hz and amplitude of 1mm. 2. At 100Hz and 2.5mm amplitude there were significantly higher ejaculation rates than amplitude of 1mm. 3. Ejaculation occurred in 58/66 men (88%).
Leduc et al. 1992; Canada Post-test Level 4 N=37	**Population:** 37 men with SCI; Age: mean 29.5 yrs, range 19-61; 15 cervical (9 complete, 6 incomplete), 22 thoracic (20 complete, 2 incomplete), Time since injury: range 3 months-23 yrs. **Treatment**: 10mg nifedipine for autonomic dysreflexia, 40mg butylbromure hyoscine subcutaneously to limit some of the parasympathetic side effects of physostigmine, and then 2-4mg	1. 54% of cases resulted in antegrade ejaculation. 2. 46 samples showed mean normal count but low motility rate (28%). 3. Fresh unwashed sperm artificial insemination performed in 6 couples with 3 successful pregnancies.

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	physostigmine subcutaneously 30 mins later and followed by masturbation by female partner. **Outcome Measures**: Ejaculation responses, pregnancies.	
Rawicki & Hill 1991; Australia Post-test Level 4 N=39	**Population:** 39 men; Injury level: C4-L5. **Treatment:** Electroejaculation (EE), vibration ejaculation (VE), and subcutaneous physostigmine (PS). **Outcome Measures:** Seminal emission, pregnancies, conception.	1. Semen obtained from 21 of 24 men with a lesion at T8 or above, and from 4 of 11 men with lesions below T10. 2. 8 pregnancies from 6 couples.
Beretta et al. 1989; Italy Post-test Level 4 N=102	**Population:** 102 men; Age: mean 25.6 yrs; Injury level: cervical-sacral lesions, above T11 (n=58), thoracolumbar lesions (n=36), sacral (n=8); Mean time since injury 6.1yrs. **Treatment:** Simple vibrator applied to the penis for ejaculatory response. 15 patients who wanted to conceive a child, received instruction in home use of vibrator. **Outcome Measures:** Ejaculation frequency, sperm quality.	1. Penile vibrators triggered ejaculation in 72 patients (70.5%). 2. 11 other patients showed 'weak' ejaculation with poor contractions of perineal muscles. 3. Stimulation ranged from 30 sec-20 min. Of 15 'home-use' patients, increase in sperm concentration and steep decrease in abnormal spermatozoa over 3 months. 4. 6 couples had homologous artificial insemination, 3 pregnancies resulted.
Brindley et al. 1989; UK Post-test Level 4 N=8	**Population:** 7 SCI, 1 primary anorgasmia, Age: range 27-37 yrs; Level of injury: C5-T9, 5 complete; Time since injury: 2-15 yrs. **Treatment:** Implantation of radio-linked hypogastric plexus stimulator device. **Outcome Measures:** Seminal emission and erection (with use of implant).	1. Post-implant, all patients achieved external emission of semen, volume between 1-5ml in 4 patients, only a drop or two drops in 3 patients (but good quantities obtained later). 2. 5 pregnancies (2 live births) in the partners of 4 patients. Implants functioned for years without deterioration in performance.
Ohl et al. 1989; USA Post-test Level 4 N=48	**Population:** 48 men with SCI; mean age 31yrs, range 20-53 yrs; 15 cervical, 29 thoracic, 4 lumbar; YPI 4 months-34 yrs; 56% complete, 44% incomplete. **Treatment:** Rectal probe electroejaculation (EE). **Outcome Measures:** Semen retrieval and sperm quality.	1. 10 million sperm obtained in 71% of participants (n=34). 2. Age and interval since injury had no effect on outcome. 3. Higher success among participants with paraplegia (90% ejaculated successfully) and in those using intermittent catheterization for bladder management compared to cervical or lumbar patients (successful ejaculation in 60% and 50%, respectively). 4. Indwelling urethral catheters and high pressure reflex voiding had a negative impact on EE results.
Halstead et al. 1987; USA Post-test Level 4 N=12	**Population:** 12 men with SCI; Age: range: 23-38 yrs; Injury level: C5-C6 (n=4), T3-T12 (n=7), L1 (n=1); paraplegia (n=8), tetraplegia (n=4); Impairment grade: AIS A (n=7), b (n=1), C (n=3), D (n=1). Time since injury: range 0.5-18 yrs. **Treatment:** Rectal probe electroejaculation on 38 occasions. **Outcome Measures:** Ejaculation response	1. Antegrade ejaculation occurred in 9 patients with improvement in % motility and total live sperm count on repeated stimulations in 5 patients. 2. Significant retrograde ejaculation occurred in 1 patient. 3. Sperm acceptable for artificial insemination from 4 patients.

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	and sperm quality.	
Brindley 1984; England Post-test Level 4 N=81	**Population:** 81 men with SCI, mostly complete. **Treatment:** Application of a vibrator of 80 Hz and 2.5mm amplitude to the lower surface of the glans penis, electroejaculation (EE). **Outcome Measures:** Semen retrieval.	1. Required duration <20min (usually <3min) in 48/81 men with SCI. 2. Vibrator failed in 19/81 who lacked reflex hip flexion on scratching soles of feet and in 14 others. Vibrator failed in 11/12 men with injuries <6 months duration. 3. From 21/34 men for whom the vibrator failed, semen cold be obtained by electroejaculation (EE). 4. 11 pregnancies reported. 9 healthy children born.
Chapelle et al. 1983; France Post-test Level 4 N=20	**Population**: Injury level: T6-L4; Time since injury: >6 months. **Treatment:** Physostigmine (PS) followed by intraspinal injection of neostigmine (ISN) (0.25-0.5mg) or PSC (2mg physostigmine sulfate injected 30min after 40mg N-buthylhyocine) several weeks later. **Outcome Measures**: Ejaculation.	1. Initial PS application successful in 5/20 patients. 3 patients successful in subsequent tests. 12 not successful. 2. Only successful if T12-L2 segments are intact.
Brindley 1981; UK Post-test Level 4 N=89	**Population:** Men with SCI (n=84); Injury level: C6-L1 or below; ejaculatory failure. **Treatment:** Electro-ejaculation (EE) technique with glove-finger electrode. **Outcome measures:** Successful EE defined as: external success (liquid containing spermatozoa trickled from meatus), retrograde success (no external spermatozoa but at least $5x10^6$ spermatozoa in urine), definite failure (no liquid at meatus or no external spermatozoa or < $5x10^6$ spermatozoa in urine), external failure (no semen externally and no urine specimen provided), pain prevented (at the only attempt at EE, stimulation was less than strength needed for success due to pain).	1. EE technique resulted in external success in 43% of men, retrograde success in 17% of men, and definite failure in 24% of men, with remaining 16% uncertain due to external failure without urine confirmation or being prevented by pain.
Cechova et al. 2014 Czech Republic Post Test Level 4 N=20	**Population**: 20 males (mean age=30.8 years old, age range=20-44 years old); level of injury 13 cervical and 7 thoracic; average time since injury to PVS= 64 months; 7 patients had PVS for more than 3.5 years and 13 patients had PVS less than 3.5 years. **Treatment**: Participants were divided into two groups: Group 1 had 7 patients who were more than 3.5 years since their injuries and Group 2 had 13 patients who were less than 3.5 years since injury. PVS was performed using the Ferticare Multicept. **Outcome Measures:** Evaluate the effectiveness and safety of penile vibrostimulation (PVS), semen quality, sperm count, sperm motility, and further	1. Ejaculation was achieved in 11 (55 %) patients [9 (82%) of patients with cervical SCI & 2 (18%) patients with thoracic SCI] 2. Success rate of PVS in patients less than 3.5 years since injury was 77 % in comparison with 14 % in patients over 3.5 years since injury. 3. When comparing semen quality in first and second PVS, total sperm count and number of sperm with progressive motility increased. 4. Fertilization was not successful despite high sperm concentration (213 x 106/ml). The plan is to use it in vitro fertilization. In 1 patient the ejaculate was successfully used for fertilization. 5. Autonomic dysreflexia during PVS

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	utilization of the ejaculate in men with SCI.	occurred in 7 patients, in 6 with cervical and 1 patient with thoracic SCI. Symptoms of autonomic dysreflexia resolved within three minutes.
Chehenesse et al. 2016 France Case Series Level 4 N=384	**Population**: 384 participants with SCI; level of injury C5-L4. **Treatment**: None. A retrospective analysis of a cohort of men with complete SCI. **Outcome Measures:** Successful ejaculation with PVS	1. Successful ejaculation with PVS was reported in 47.4% of patients 2. Ejaculation success with PVS was high when any of the C5–T6 spinal segments was injured (50-67% success). 3. Ejaculation success with PVS decreased when lesions were more caudal, reaching a minimum for the subsample with complete L4 injury of 2.6% versus a minimum of 12% when any of the sacral segments was injured.

Discussion

There are no RCT studies in this area. One of the largest studies of its kind (n=500 men with SCI) (Brackett et al. 2009) determined that semen could be obtained from most men with SCI without surgical procedures. The studies have mainly reported cumulative ejaculatory success rates and suitability of using techniques such as vibrostimulation, electroejaculation, subcutaneous physostigmine (a reversible acetylcholine esterase antagonist) and operative sperm retrieval for assisted reproduction (Dahlberg et al. 1995; Nehra et al. 1996; Brinsden et al. 1997; Chung et al. 1997; Lochner-Ernst et al. 1997; Le-Chapelain et al. 1998; Hibi et al. 2008; Kanto et al. 2008). Simple prostatic massage alone has been successfully used to obtain sperm in 32% of 69 men with SCI, typically those with lesions above the T10 level (Arafa et al. 2007).

When using PVS, the vibrator parameters of frequency and, in particular, amplitude, have been shown to be important variables to optimize outcomes. The application of a specialized vibrator, with settings of approximately 70-100 Hz with 2.5-3.5 mm amplitude (Brindley 1984; Sonsken et al. 1994; Ohl et al. 1997) on the penis (usually frenulum) produces antegrade, retrograde, and some mixed semen samples. After each interval, it is important to examine the penile skin for early detection of skin abrasions or edema, which will warrant termination of the stimulation session (Sinha et al. 2017). Vibrostimulation worked most reliably in men with lesions above T10, those men with SCI who had a reflex hip flexion with scratching the soles of the feet and with injuries over 6 months in duration (Brindley 1984; Sonsken et al. 1994; Lochner-Ernst et al. 1997; Sonsken et al. 1997) or in patients with incomplete lesions (Taylor et al. 1999). Recent research has shown greater success with PVS in patients less than 3.5 years since injury vs. more than 3.5 years since injury (77% in comparison with 14%; Cechova et al. 2014). A retrospective chart review found that successful ejaculation with PVS was greater when any of the C5–T6 spinal segments was injured (50-67% success) and was less likely when lesions were more caudal (complete L4 injury of 2.6%; 12% when any of the sacral segments was injured; Chehenesse et al. 2016).

Vibrostimulation application for 30 sec to 20 minutes (most occurring in less than 3 min) resulted in ejaculation in 60% to 100% of patients (Beretta et al. 1989; Rawicki & Hill 1991; Sonksen et al. 1994; Rutkowski et al. 1995; Chung et al. 1997; Sonksen et al. 1997). Several recent studies have reported methods to “salvage” some of the ejaculatory failures with PVS. Brackett et al. (2007) reported success in recovering semen in an additional 22% of men with SCI who failed on several occasions to respond to high amplitude PVS with 1 vibrator, as well as 38% of inconsistent responders, using a technique that sandwiched the glans penis between two vibrators presumably by increasing afferent input.

PVS paired with midodrine has mixed results in producing ejaculation in men with SCI. Soler et al. (2007) reported that 65% of 158 men who failed to respond to PVS alone were able to ejaculate when treated with midodrine (average dose of 18.7 mg) 30-120 minutes prior to applying PVS. They found antegrade ejaculation was more frequent in patients with complete (73%) and UMN (89%) lesions; moderate increases in blood pressure (MAP ~10mmHg) were induced by midodrine in comparison to PVS alone, with 13 patients (11 with tetraplegia) recording systolic BP > 200mmHg. Midodrine plus PVS was well-tolerated and salvaged approximately 66% of cases that did not respond to PVS alone (Soler *et al*., 2007; Courtois *et al*., 2008). In contrast, a recent double-blind, randomized, placebo-controlled study found no improvement in ejaculation success rates by PVS combined with midodrine vs. a placebo (Leduc *et al*., 2015).
In a 12-week, multicenter, double blinded, placebo-controlled study; 418 men with SCI were randomized to vardenafil (*n* = 207) or placebo (*n* = 211) and ejaculation success was assessed using the International Index of Erectile Function (IIEF). The results of this study showed a significantly greater ejaculation success rate with vardenafil when compared to placebo (19% vs. 10%) (Giuliano *et al*., 2008).

When vibrostimulation fails, obtaining semen by electroejaculation (Taylor et al. 1999) is a possibility, particularly for people with lower lesions (Ohl et al. 2001). Since an ejaculate was almost always attainable by penile vibratory stimulation or electroejaculation, the need for surgical aspiration was rare (Dahlberg et al. 1995; Lochner-Ernst et al. 1997; Shieh et al. 2003). Retrograde ejaculation of semen into the bladder, which frequently accompanies EEP and affects sperm quality, can be prevented by simply applying a technique of gentle bladder neck tamponade (Lim et al. 1994) using a non-toxic all-silicone Foley catheter and the balloon filled with 10mls of saline. Controlling severity of autonomic dysreflexia with nifedipine allowed for better sperm retrieval using electroejaculation technique (VerVoort et al. 1988; Lucas et al. 1991; Brackett et al. 2002; Elliott & Krassioukov 2006). Electroejaculation is considered more invasive and painful than penile vibratory stimulation for men with incomplete SCI, and patients prefer penile vibratory stimulation if sperm quality was equal between the two techniques (Ohl et al. 1997). A small minority of men (4–5%) will require anesthesia during EEJ, owing to their retained pelvic sensation (Brackett et al., 2010).
Vibrostimulation has been shown to also induce pronounced levels of autonomic dysreflexia (Sheel et al. 2005; Claydon et al. 2006), especially in men with tetraplegia with increases of +70-90mmHg in mean arterial pressure (SBP ~190±20mg, DBP ~130±10mg, SBP ~150±10mg), reduced heart rate (–5-10 bpm) and cardiac arrhythmias. This requires careful monitoring during vibratory stimulation and screening for safe home use as AD was often silent in nature.

The use of physostigmine injections alone or in conjunction with both vibrostimulation and electroejaculation has largely dropped out of use since the mid-1990s in favour of newer and more successful technology (Chapelle et al. 1983; Leduc et al. 1992). An implantable hypogastric nerve stimulator (radio-controlled) was also successful in yielding semen with sperm (not necessary all motile), but has not undergone further development (Brindley et al.1989).

Operative sperm retrieval should be reserved for those men who fail conservative sperm retrieval methodology. Operative retrieval commits a couple to expensive higher-level interventions such as intracytoplasmic sperm injection (ICSI), where a single sperm is injected directly into the egg to force fertilization. Such high level interventions with operative sperm retrieval, i.e. using fresh testicular sperm (Kanto et al. 2008) or aspirated retrograde vasal sperm (Hibi, 2008) in an ICSI cycle, do result in better conception rates per cycle from the male SCI population. However, decisions regarding method of retrieval and insemination must also include a cost-benefit ratio (Ohl, 2009).
Conclusion
There is level 4 evidence (Beretta et al. 1989; Sonksen et al. 1994; Le Chapelain et al. 1998; Brackett et al. 2007, 2009; Kathiresan et al. 2012; Qiu et al. 2012; Sonksen et al. 2012;

Chehenesse et al. 2016; Cechova et al. 2014) that semen retrieval may be assisted by vibrostimulation in men with lesions above T10.

There is level 4 evidence (Soler et al. 2007) that Midodrine may be an effective and safe adjunct to penile vibratory stimulation in men not responding to penile vibratory stimulation alone who are not at risk for significant autonomic dysreflexia.

There is level 4 evidence (Brindley 1984; Halstead et al. 1987; Ohl et al. 1989; Lochner-Ernst et al. 1997; Le Chapelain et al. 1998; Kolettis et al. 2002) that semen retrieval may be assisted by electroejaculation in men who failed vibrostimulation.

There is level 4 evidence (Brindley et al. 1989) that surgical aspiration may be used to retrieve sperm if vibrostimulation and electroejaculation are not successful.

There is level 4 evidence (Arafa et al. 2007) that prostatic massage thru the rectum to push the sperm out through the ejaculatory ductal system is one technique to retrieve semen in some men and is more successful with lesions above T10.

There is level 4 evidence (Lim et al. 1994) that the use of a balloon catheter to tamponade the bladder neck may be effective in obtaining antegrade samples in men who normally deliver retrograde samples.

There is level 4 evidence (Hibi et al. 2008) that retrograde vasal sperm aspiration can retrieve sperm of sufficient motility to afford pregnancy.

There is level 3 evidence (Kanto et al. 2008) that testicular sperm extraction followed by intracytoplasmic injection is an effective way to induce pregnancy, with fresh sperm giving better results than frozen-thawed sperm.

Prostatic massage alone is a safe and easy alternative way to retrieve semen in some men with SCI above T10 but yields low sperm numbers.

The least invasive sperm retrieval method should be tried first (i.e. penile vibrostimulatory stimulation (PVS) in the clinic setting to monitor for autonomic dysreflexia) followed by the more invasive of electroejaculation procedure (EEP).

PVS is most successful in men with SCI above T10.

EEP can be done on men with any level of SCI but may require anesthetic.

Sperm aspiration can also be performed in either a clinic or operating room setting.

5.3.2 Sperm Quality

Unfortunately, semen quality is also noted to decline after SCI (Deforge et al. 2005). Semen obtained by EEP in the first 2-3 days after injury was scant, but had normal quality by 6-10 days post-injury (Mallidis et al. 1994). After approximately 2 weeks semen quality deteriorates to levels approaching those observed in males with chronic SCI. After 6 months to 1 year, there is no relationship between duration of injury and sperm quality (Sarkarati et al. 1987). Semen quality in men with chronic SCI is reported to have decreased motility and viability, although total numbers of sperm tend to remain high (Brackett et al. 1997b; Ibrahim et al. 2009). Sperm DNA damage, which is another method of assessing semen quality, has also been shown to be higher among men with SCI when compared to able-bodied controls (Brackett et al. 2008). The following studies investigate the effects of various factors on sperm quality, including: repeated ejaculations, different methods of bladder management,

antegrade versus retrograde ejaculation, vibratory stimulation versus electroejaculation, surgical extraction, heat and alterations to seminal plasma. In their chapter on fertility after SCI in the book Spinal Cord Injury Rehabilitation, Brackett and Ibrahim (2009) also provide a review of other areas related to sperm quality.

Table 15: Sperm Quality

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Hamid et al. 2006; UK PEDro=6 RCT Level 1 N=32	**Population:** Men with SCI; Age: mean 40.3-37.1 yrs, range 23-48; Level of injury: above T10; Time since injury: mean 4.8-7.0 yrs, range 0.7-19. **Treatment:** Weekly penile vibratory ejaculation (PVE) for 3 months vs PVE at baseline and at 3 months. **Outcome Measures:** Sperm morphology, forward progression, and motility.	**1.** Morphology and forward progression improved in the group with weekly PVE. **2.** Motility improved in the group with weekly PVE but did not reach statistical significance.
Brackett et al. 2002; USA PEDro=5 RCT Level 2 N=12	**Population:** Mean age=36.2 yrs, > 2 yrs post-injury, C4-T11. **Treatment:** Electroejaculation was performed with the Seager Model 14 electroejaculation unit. A total of 99 electroejaculation trials were administered 4-8 weeks apart according to a random schedule. Each trial consisted of continuous or interrupted current delivery. **Outcome Measures:** Semen quality.	1. For anterograde ejaculation, interrupted current produced greater semen volume (2 vs .9 ml), total sperm count (130 vs 79 million) and number of motile sperm (34 vs 25 million) compared to continuous current delivery. 2. In retrograde fractions, total sperm count was higher for continuous (113.6 million) than for interrupted delivery (29 million). 3. Retrograde sperm motility was lower than anterograde sperm motility regardless of the method used.
Giulini et al. 2004; Italy PEDro=5 RCT Level 2 N=34	**Population:** 34 couples (males with SCI), 21-37 yrs (females), 28-46 yrs (males), paraplegia, tetraplegia, C6-L1. **Treatment:** The male partner was randomly assigned to single transrectal electroejaculation or multiple (baseline, 1-month, 3- month) transrectal electroejaculation before intracytoplasmic sperm injection (ICSI). **Outcome Measures:** Sperm concentration, morphology, and motility.	**1.** Electroejaculation was successful in 32 of 34 cases. The rate of normal sperm morphology was not different between groups. **2.** The mean sperm concentration and rate of total sperm motility increased at 1- and 3-month in multi-transrectal electroejaculation group. **3.** A fertilization rate of 63.6% was observed and the pregnancy rate per patient was significantly higher in multi-transrectal electroejaculation group.
Kathiresan et al. 2012; USA Case series Level 4 N SCI=444 N controls=61	**Population:** 444 men with SCI with no known causes of infertility other than SCI; level of injury: 176 cervical, 193 T1-T10, 70 T11-caudal; 115 complete, 126 incomplete. Controls: 61 able-bodied (AB) men, healthy with no history of infertility. **Treatment:** Retrospective chart review of Male Fertility Research Program participants from 1991 to 2011. Sperm retrieval methods included masturbation, penile vibratory	1. Sperm retrieval method in SCI participants: masturbation (n=43), PVS (n=243), EEJ (n=158). Sperm retrieval method in AB control group: masturbation (n=61). 2. Sperm motility was significantly higher in the SCI-masturbation group (36.9%) than the PVS group (25.9%) or EEJ group (15.0%), but lower compared with a control group of 61 non-SCI healthy men who

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	stimulation (PVS), and electroejaculation (EEJ). **Outcome measures:** sperm retrieval method (masturbation, PVS, EEJ), semen volume, sperm concentration, sperm motility, total sperm count.	collected their semen by masturbation (58.0%). 3. The SCI-masturbation group had similar antegrade sperm concentration as the PVS group, and control group, but significantly higher than the EEJ group.
Qiu et al. 2012; China Pre-post Level 4 N SCI=26 N controls=16	**Population:** 26 infertile men with SCI (primary infertility present in 9), mean(SD) age 33.8(2.9) yrs, mean(SD) DOI 8.6(3.0) yrs (range 1-11 yrs), level of injury: C5-C6 (n=4), T2-T12 (n=22), mean(SD) yrs of infertility 6.8(4.2) yrs; Controls: 16 non-SCI fertile donors (all had previously fathered at least one child), mean(SD) age 32.9(2.1) yrs. **Treatment:** Collection of semen samples in SCI men using penile vibratory stimulation (PVS) (n=14), percutaneous vasal sperm aspiration (PVSA) (n=12); collection of semen samples in non-SCI donors all by masturbation (n=16). **Outcome measures:** sperm vitality and DNA integrity, sperm chromosomal aneuploidy.	1. The number of round cells per millilitre of semen obtained from the penile vibratory stimulation (PVS) group was between 1 million and 12 million. 2. The rate of sperm DNA fragmentation was higher in the PVS group than in the percutaneous vassal sperm aspiration (PVSA) group.
Caremel et al. 2011; Canada Case series Level 4 N=11	**Population:** 11 men with SCI; mean age 29 yrs (range 21-40); 11 complete C5-T6; mean DOI 74 mos, (range 18-163 mos). **Treatment:** cystoscopic intradetrusor botulinum neurotoxin A injections were performed with 300 units of Botox (n=10) or 1000 units of Dysport (n=3) for overactive bladder. Two patients received two BT injections at 7 months interval using different dosages, were therefore treated as independent tests. Ejaculation tests were done pre- and post-BT injections using penile vibrator stimulation or electroejaculation combined as needed with oral midodrine and/or intracavernous injection or phosphodiesterase inhibitors. **Outcome Measures:** Ejaculation type and volume, sperm count, mobility, vitality.	1. Anterograde ejaculations dropped from 77% pre-BT to 54% post-BT. The proportion of retrograde ejaculation or anejaculation increased from 23% pre-BT to 46% post-BT. There was a statistically significant drop in average volume of semen from 1.8 mL pre-BT to 1 mL post-BT. 2. Sperm mobility, sperm count and vitality were unaffected by Botox treatment, though vitality showed trend for improvement. 3. Semen culture improved following Botox treatment with 72% of semen samples infected pre-BT compared with 29% post-BT.
McGuire et al. 2011; Ireland Case series Level 4 N=31	**Population:** 31 men, 29 with acquired spinal cord injury (complete lesion (n=18), incomplete lesion (n=11). Injury levels: C3-C7; T1-T5; T11-L3), 2 with congenital spinal abnormality. **Treatment:** Electroejaculatory stimulation (EES) done with Seager model rectal probe; n= 27 (87%) underwent EES once, n=4 (13%) underwent EES several times. **Outcome measures:** The Mann-Whitney U test, semen analysis (volume, density, motility, normal morphology and live sperm); pregnancy rate.	1. Of the 25 patients whose partners underwent insemination with the EES semen, 9 (36%) became pregnant. All pregnancies resulted in live births. 2. 1 patient developed autonomic dysreflexia necessitating stopping EES before obtaining any ejaculate. No other side effects or complications were reported. 3. Semen analysis findings in 15 patients showed that mean semen volume and mean density were

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
		within the normal World Health organization reference ranges. 4. 30 patients produced antegrade, retrograde, or both types of ejaculate. 5. Only 1 patient failed to produce any ejaculate.
Ibrahim et al. 2009; USA Prospective controlled trial Level 2 N=24	**Population:** 12 men with traumatic SCI and 12 able-bodied men as controls. **Treatment:** Sperm sample from each subject was divided into 4 groups: Group 1: no treatment; Group 2: added phosphate buffered saline (PBS); Group 3: monoclonal antibodies (MAB) against target cytokines IL-6, IL-1β, and TNF-α; Group 4: receptor interference agents (RI) against the same cytokines. **Outcome Measures:** Sperm concentration; sperm motility; sperm viability; Sperm DNA damage (DFI).	1. The mean sperm motility and viability was significantly lower in the SCI group compared to the controls. 2. The sperm from the SCI group had a significantly higher DFI than the controls. 3. After treatment with MAD or RI, the DFI decreased slightly in 70% of samples (difference not significant). 4. No difference in viability between treatment groups was found. 5. Sperm motility of treatment groups was not compared.
Hibi et al. 2008; Japan Post-test Level 4 N=8	**Population:** 8 participants with cervical SCI and neurogenic anejaculation (age 26 – 46, mean 35.6). **Treatment:** Retrograde vasal sperm aspiration (ReVSA). **Outcome Measures:** Presence of motile sperm.	1. Motile sperm was recovered in all participants who underwent ReVSA (11 procedures total). 2. The retrieved sperm concentration was 109.4(64.7) × 10^6 /mL (range 31.2-156.3 × 10^6 /mL). 3. The retrieved motility of sperm was 69.8(16.8)% (range 50-91%). 4. Clinical pregnancies were achieved in 8 cases.
Kanto et al. 2008; Japan Case control Level 3 N=56	**Population:** 22 men with SCI (age 21-41); data on 34 men with obstructive azoospermia was obtained retrospectively for control. **Treatment:** Testicular sperm extraction (TESE); if unsuccessful, microdissection TESE was performed, followed by intracytoplasmic injection (ICSI) **Outcome Measures:** Fertilization; pregnancy.	1. TESE successfully retrieved sperm in 19 participants with SCI. 2. ICSI resulted in a fertilization rate of 236 of 364 (64.8%) in SCI couples and 14/19 achieved pregnancy. 3. In couples with obstructive azoospermia, ICSI resulted in a fertilization rate of 435 of 567 (77%) and 29/34 achieved pregnancy. 4. Pregnancy rate was significantly higher in couples with SCI using fresh testicular sperm-ICSI compared to frozen-thawed sperm-ICSI.
Brackett et al. 2007; USA Pre-post Level 4 N SCI=11 N controls=5	**Population:** 11 men with SCI and 5 able-bodied men; Age: mean(SD) range 31.9(2.3)-30.7(3.6) yrs; Level of injury: C4 to T11; mean(SD) time since injury 9(2.0) yrs. **Treatment:** Agents added to sperm to neutralize cytokines (IL-1beta, IL-6, and TNF-alpha) at the receptor level. **Outcome Measures:** Percentage sperm motility.	1. Significantly improved sperm motility in men with SCI when there was interference with receptors to all 3 cytokines. No significant improvement when only 1 or 2 cytokines neutralized. 2. Neutralizing agents had no effect in able-bodied men.
Das et al. 2006; UK	**Population:** 16 men with SCI; Age: median 37 yrs, range 24-46; Level of injury: C4-L1;	1. No improvement in sperm volume, motility, or total motile count in

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Case series Level 4 N=16	Impairment: complete (n=9), incomplete (n=7); Time since injury: median 12.5 yrs, range 5-43. **Treatment:** Repeated electro-ejaculation (3 successive EE at 2-4 week intervals). **Outcome measures:** Semen volume, sperm concentration, sperm motility, sperm variability, and total motile sperm concentration.	successive samples.
Salsabili et al. 2006; Iran Case series Level 4 N SCI=89 N controls=49	**Population:** 89 men with SCI and 49 able-bodied men; mean(SD) age: (SCI) 34(3.7) yrs, (AB controls) 36(4.76) yrs; Injury levels C4-L2, all complete; Time since injury range 11-18 yrs. **Treatment:** 1) Semen collection by electro-ejaculation (EE), masturbation penile vibratory stimulation (PVS) or percutaneous epididymal sperm aspiration (PESA); 2) Intracytoplasmic sperm injection (ICSI). **Outcome measures:** Quality and quantity of sperm, including sperm count, volume, PH, density, motility, viscosity, and white blood cells.	1. EE was the most commonly used method of semen retrieval in men with SCI (78.7%). 2. Normal form, motility, and viability were significantly lower in men with SCI than neurologically intact men. 3. In men with SCI, there was no difference in sperm parameters produced by EE and other methods of sperm collection. 4. Rate of oocytes fertilization in SCI group by EE/ICSI was 60%.
Cohen et al. 2004 USA Pre-Post Level 4 N = 17	**Population:** 17 men with SCI, mean age 35.2 yrs. **Treatment:** Antegrade semen specimens from all participants split into 8 groups. Group 1: no treatment. Group 2 to 8: semen treated with different combinations of monoclonal antibodies to IL1-β, IL6, and TNF-α. **Outcome Measures:** mean sperm motility.	1. Sperm motility increased in all groups 2-8 but increase attained significance only in group 8 (group receiving antibodies against all 3 cytokines). 2. Groups with pretreatment sperm motility between 11-30% showed greatest improvement after treatment.
Monga et al. 2001; USA Prospective controlled trial Level 2 N=12	**Population:** 7 participants with SCI, 5 fertile age matched donors, age range=27-54 yrs, 5 to 31 yrs post-injury, C4-C7, 5 incomplete, 2 complete. **Treatment:** Electrovibratory stimulation. **Outcome Measures:** semen quality.	**1.** The majority of sperm (65%) exhibited degenerative changes and significant axonemal defects. **2.** A significant percentage of sperm (65%) demonstrated disappearance of fiber doublets. **3.** Incubation of normal sperm with seminal fluid of participants with SCI induced a significant 43% decrease in motility within 15 min.
Brackett et al. 2000; USA Prospective controlled trial Level 2 N=26	**Population:** 12 men with SCI, 14 able-bodied controls; Age (men with SCI): range 29-40 yrs; Injury level: C4-L1; Mean time since injury: 14.6 yrs; Able-bodied controls all had vasectomy and biological children. **Treatment:** 1) sperm retrieved by electrical stimulator or vibratory stimulation for participants with SCI, 2) sperm retrieval before exposure to the seminal and prostatic fluids during vasectomy surgery in controls and vas aspiration surgery in participants with SCI. **Outcome Measures:** Sperm quality.	1. Sperm was obtained from 9/12 patients with SCI and 12/14 non-SCI patients having a vasectomy. 2. Aspirated sperm had greater motility (54.4%) and viability (74.1%) compared to ejaculated sperm (14.1%) motility and viability (26.1%) among patients with SCI. 3. Controls showed no difference between aspirated and ejaculated sperm.

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
		4. The seminal plasma in men with SCI is likely abnormal and toxic to sperm.
Mallidis et al. 2000; Australia Post-test Level 4 N=9	**Population:** 9 men; Age: mean 28 yrs, range 22-36 yrs. **Treatment:** Electroejaculation using CGS Electroejaculator with progressively increasing sine wave current at 20 Hz over 4 consecutive days. **Outcome Measures:** Semen quality.	1. Mean sperm motility increased 23% on days 2 and 3; however, sperm concentration and volume decreased. 2. In 3 of 7 patients sperm motility still remained low. 3. Major gains in sperm motility and viability were achieved by day 2 with some improvements in day 3 for three patients.
Chen et al. 1999; USA Post-test Level 4 N=14	**Population:** 14 men; Age: range 25-41 yrs, Injury level: 8 cervical, 6 thoracic; Impairment grade: Frankel A (n=8), B (n=4), and C (n=2); Hip flexion reflex in 13 (93%) and spasticity in 12 (86%). **Treatment:** Antegrade sample obtained using Ling vibrator. Bladder catheterized for collection of any retrograde ejaculate. Vibratory stimulation at clinic every 2-4 wks. **Outcome Measures:** Sperm quality.	**1.** Antegrade specimens collected in 51 trials (84%) and retrograde specimens obtained in all 61 trials (100%). **2.** Non-statistically significant trend toward higher sperm counts in the antegrade samples (mean=74.1 million) than in retrograde (40 million). **3.** No difference in sperm motility and morphology between antegrade and retrograde specimens. **4.** Fructose and zinc were present in all antegrade and retrograde specimens.
Brackett et al. 1997a; USA Prospective controlled trial Level 2 N=77	**Population:** 77 males, 45% cervical, 51% thoracic, 4% lumbar. **Treatment:** 1) vibration (n=23), 2) electroejaculation (n=44) or 3) underwent both procedures (n=10). **Outcome Measures:** Sperm quality.	**1.** Increased motile sperm with vibratory stimulation compared to electroejaculation. **2.** No difference in total sperm count.
Brackett et al. 1997b; USA Prospective controlled trial Level 2 N=19	**Population:** 10 men with SCI, 9 age-matched men without SCI; Age: mean 33.1 yrs; Injury level: C4-C5 (n=5), T5-T6 (n=4), T12 (n=1); Time since injury 11.4 yrs. **Treatment:** Electroejaculator (Seager model 14, 1-10 Volts) or laboratory stimulation. Specimens stored at room temperature (23°C) or body temperature (37°C). **Outcome Measures:** Semen quality, fertility rates.	1. Heat did not affect rate of degradation in motility in control specimens, but body temperature reduced sperm motility in SCI specimens compared to room temperature.
Ohl et al. 1997; USA Prospective controlled trial Level 2 N=11	**Population:** All males. **Treatment:** n=5 FertiCare Clinic Vibrator (2.5 mm, 100Hz, for 3 min) or electroejaculation (Seager model 11). **Outcome Measures:** Sperm quality.	1. No difference in antegrade sperm count, but penile vibratory stimulation specimens had greater motility, viability and motile sperm count compared to EE. 2. No difference in sperm functional assessment (mucus or sperm penetration assay).

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
		3. Electroejaculation was more painful and less preferred than penile vibratory stimulation.
Brackett et al. 1996; USA Prospective controlled trial Level 2 N=26	**Population:** 12 men with SCI; Age: range 18-42 yrs; Injury level: thoracic; Time since injury: range 3-28 yrs; Age matched controls (n=14). **Treatment:** Vibratory stimulation (SCI) or masturbation (controls). Effect of SCI seminal plasma was tested on control sperm and vice versa. **Outcomes Measures:** Seminal parameters.	1. At 5 minutes, seminal plasma from men with SCI reduced motility of sperm from control. 2. Seminal plasma from controls improved motility of sperm from men with SCI. 3. At 60 minutes the values were not different from each other.
Matthews et al. 1996; USA Case control Level 3 N=40	**Population:** 18 men with SCI and 22 men without SCI; Injury level: 2 cervical, 15 thoracic, 1 lumbar, 33 of 40 men were in a relationship with a female. **Treatment:** Retrospective review of electrical stimulator with rectal stimulation followed by intrauterine insemination (126 cycles in n=33) or in vitro fertilization (n=7 total 14 cycles). **Outcome Measures:** Fertility rates, seminal parameters, ejaculatory rates, cycle function, pregnancy rates.	1. Motile sperm were obtained in 95% of men. Semen quality improved with subsequent rectal probe ejaculation in 23/35 men. 2. Antegrade ejaculations produced greater percentage sperm motility in 59% of procedures in which both types of ejaculation were obtained in a patient. 3. However, total motile sperm in retrograde samples exceeded antegrade in 57% of the cases. 4. Pregnancy rate: 15/33 couples achieved pregnancy (45%), of which, 10/15 were achieved through intrauterine insemination. 5. Pregnancies leading to live birth were recorded in 5/7 couples undergoing IVF.
Rutkowski et al. 1995; Australia Case series Level 4 N=70	**Population:** 70 men with SCI, Age: mean 30 yrs, range 19-59 yrs; Injury level: C1-C8 (n=36), T1-T9 (n=19), T1-T9 (n=15), T10-L2 (n=15); Mean time since injury: 6 yrs. **Treatment:** Vibroejaculation at 10-50Hz, 3 cycles for 45seconds (n=36) or electroejaculation (n=34). **Outcome Measures:** Seminal parameters, type of catheterization, method of ejaculation.	1. Neurological level and method of bladder management were found to be significant variables that influenced 70% of the patients' sperm sample quality. 2. As neurological level became more caudal, motile sperm decreased. Use of a catheter greatly increased the number of motile sperm. 3. Intermittent self-catheterization was superior to suprapubic catheter or no catheter (reflex voiding).
Padron et al. 1994; USA Pre-post Level 4 N SCI=9 N controls=10	**Population:** 9 men with SCI and 10 able-bodied men; Age: (SCI) mean 30.2 yrs, SEM=1.2, (controls) mean 24.3 yrs, SEM=3.6; Injury level: cervical 33%, thoracic 55%, lumbar 11%; Time since injury >1yr. **Treatment:** Cryopreservation of sperm by liquid nitrogen vapor only (V) vs vapor for 12 minutes followed by submersion into liquid nitrogen (V+N2) vs direct submersion into liquid nitrogen (N2). **Outcome measures:** Mean percent motility in fresh sperm samples, post-thaw percent	1. Mean percent motility of fresh sperm samples for participants with SCI (21.0%) was lower than for control participants (55.7%). 2. After thawing, the mean percent drop in motility for men with SCI was 64.7% (V), 74.5% (V+N2), and 81.6% (N2) respectively, with no difference between control and men with SCI by method of freezing. 3. Vapor only as a freezing method was superior to V+N2 and N2 for retention of sperm motility in both

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	and grade of motility.	control and men with SCI.
Wang et al. 1992; Taiwan Post-test Level 4 N=25	**Population:** 25 men; Age: range 19-43 yrs; Injury level: C5-T12, all complete. **Treatment:** Pharmacologic: meperidine and diazepam; Device: Electroejaculation using Seger model 12 (max 60 stimulations). Bladder was emptied and then 20ml of Hams F-10 solution was instilled. **Outcome Measures:** Seminal parameters, sperm motility, sperm quality and quantity, ejaculation rate.	1. 21/25 retrograde, 12/21 antegrade ejaculations. 2. Poor sperm mobility in most cases, no motile Spermatozoa in 6/21. 3. No correlation in sperm quality and quantity with method of bladder management, age, level of injury or time after injury. 4. Sperm quality declines after stimulations are repeated more than once a week.
Siösteen et al. 1990; Sweden Post-test Level 4 N=32	**Population:** 32 men; Age: range 18-40 yrs; Injury level: C4-L1, 23 tetraplegia, 9 paraplegia, 5 incomplete, 27 complete **Treatment:** Vibrator stimulation (29/32 participants with hip flexion reflex) or electrostimulation (3 participants), 4-6 months of 'at-home' treatment, 1x/week stimulation. **Outcome Measures:** Semen quality.	1. Initial stimulation yielded semen in 29 men (91%; 22 had antegrade and 7 retrograde ejaculation). 2. 16 with antegrade ejaculation started 4-6 months of home stimulation which resulted in a rise of semen volume and fructose and acid phosphatase levels in seminal plasma (improved function of the seminal vesicles and prostate). 3. % motile sperm was low (before and after treatment period). 4. 11 men (69%) showed normal or nearly normal penetration tests after the period of regular stimulation.
Chapelle et al. 1988; France Prospective controlled trial Level 2 N=148	**Population:** 135 men with SCI and 13 age matched controls; Age (men with SCI): range 18-47 yrs; Impairment grade: complete. **Treatment:** 0.2mg physostigmine. **Outcome Measures:** Ejaculation rates and procreation, level of injured metamers, testicular volume.	1. 75/135 patients ejaculated after pharmacologic intervention. 2. Only 3/75 who could ejaculate had lesions T12-L2 lesions and testicle volume was significantly lower in patients with injured T12 segments.
Halstead et al. 1987; USA Post-test Level 4 N=12	**Population:** 12 men with SCI; Age: range 23-38 yrs; Injury level: C5-C6 (n=4), T3-T12 (n=7), L1 (n=1), paraplegia (n=8), tetraplegia (n=4); Impairment grade: AIS A (n=7), B (n=1), C (n=3), D (n=1); Time since injury: range 0.5-18 yrs. **Treatment:** Rectal probe electroejaculation on 38 occasions. **Outcome Measures:** Ejaculation response and sperm quality.	1. Anterograde ejaculation occurred in 9 patients with improvement in % motility and total live sperm count on repeated stimulations in 5 patients. 2. Significant retrograde ejaculation occurred in 1 patient. 3. Sperm acceptable for artificial insemination from 4 patients.

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Sarkarati et al. 1987; USA Post-test Level 4 N=34	**Population:** 34 men with SCI; Age: range 16-36 yrs; Injury level: 14 cervical (3 complete, 11 incomplete), 13 thoracic T1-T9 (all complete), 7 T10-L3 (3 complete, 4 incomplete). **Treatment:** Vibratory stimulation and/or electrostimulation. **Outcome Measures:** Ejaculation response, semen quality.	1. Semen obtained during first 6 months after injury was not of a quality consistent with successful fertilization, owing to poor motility. 2. Semen quality and motility were better in patients who had been injured for more than 6 months. 3. Repeated electro-ejaculation did not improve the quality of semen.
da Silva et al. 2016 Brazil Case Control Level 3 N=23	**Population**: 23 individuals; 12 SCI patients (mean age=38±10 years) and 11 controls; level of injury ranged from C4 –T6. **Treatment**: Antegrade semen specimens were collected using penile vibratory stimulation (PVS). Controls collected semen by masturbation in specific sterile containers after at least 3 days, but not longer than 7 days, of ejaculatory abstinence. **Outcome Measures:** Sperm concentration (millions of sperm/ml ejaculate), total sperm count, sperm motility (% with forward progression), seminal white blood cell (WBC) concentration (millions of WBC/ml ejaculate).	**1.** Alpha-2-macroglobulin (A2M) is three times more abundant in the seminal plasma (SP) of SCI patients but no direct correlation between motility and A2M levels were observed. **2.** Approximately 41% of all characterized protease inhibitors elevated in SCI are members of the largest family - the serpin family - 12 serpins were quantified and it was observed that SERPINB9 and SERPINB13 were exclusively identified in the SP of SCI patients. **3.** SERPINA5, the main serpin in human SP (seminal concentrations ranging between 150–200g/ml) **4.** (35–37) is three times more abundant in SCI. **5.** Results indicate no relationship between sperm motility and the concentration of leukocytes in the semen of men with SCI. **6.** Antibiotics used to treat UTIs resulted in little or no change to the semen parameters of SCI patients suggesting that noninfectious causes of an inflammatory response in the semen may be of more importance than previously thought.
Krebs et al. 2015; Switzerland Cross-Sectional Level 5 N=16	**Population**: 16 men with SCI and suffering from anejaculation. 28 semen samples underwent long term cryopreservation of more than 3 years and total sperm motility of >5% or viability of >10%. **Treatment**: None. Semen quality analysis both prior to and after a median of 11 years of cryopreservation. **Outcome Measures:** Semen quality, motility, and viability.	**1.** Cryopreservation resulted in a decrease in total sperm motility (median=2.5%, 95% CI 0-4%) and viability (median=7%, 95% CI 6-13%). Long-term cryopreservation of semen from SCI men results in essentially immotile sperm with minimal viability. **2.** Complete SCI had a negative effect on sperm viability ($\rho<0.0001$) and tetraplegia had a negative effect on pre-cryopreservation sperm viability and post-cryopreservation motility ($\rho<0.035$). **3.** There were no differences between the semen parameters of samples collected early (up to 3 weeks) after

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
		SCI, those collected later, or those collected using assisted ejaculation techniques.
Ibrahim et al. 2014; USA Prospective Controlled Trial Level 2 N=32	**Population**: Semen samples from 32 men with SCI (mean age=38 years; level of injury C3 to L1; mean time post-injury=14 years) were collected. All participants were past the period of spinal shock (≥ 12 months) and were in general good health with no active urinary tract infections. **Treatment**: Semen was obtained using the standard methods of penile vibratory stimulation (PVS) or electroejaculation (EEJ), where each subject served as their own control. Each sample was divided and treated with a vehicle control, normal goat IgG-control, or with a polyclonal antibody against ASC. **Outcome Measures:** Sperm concentration, total motile sperm count (TMSC), and four grades of sperm motility using the World Health Organization (WHO) method.	1. After treatment with anti-ASC polyclonal antibody, mean sperm motility signiticantly increased from 11.5% (95% CI, 6.3-16.7) to 18.3% (95% CI, 11.8-24.8). 2. 30 patients showed improvement in sperm motility, one patient showed no change in sperm motility, and one had a small decrease in sperm motility. 3. Samples treated with the IgG control did not show significant changes in sperm motility. 4. Improvements were most pronounced in the subgroup whose starting sperm motility ranged from 6-40% and whose mean motility improved from 13.3% (95% CI, 9.3-17.3) to 23.9% (95% CI, 14.7-23.0).
Ibrahim et al. 2015; USA Prospective Controlled Trial Level 2 N=45	**Population**: 30 men with spinal cord injury and 15 age-matched control participants. **Treatment**: None. **Outcome Measures:** the present study measured serum concentrations of inhibin B and anti-Mullerian hormone (AMH).	**1.** Serum concentrations of inhibin B and testosterone were significantly lower in the spinal cord injury group compared to the control group. (22.6±3.2% vs. 63.6±2.8%) **2.** A statistically significant negative relationship was observed between serum concentrations of inhibin B and follicle stimulating hormone in both the spinal cord injury group and the control group, and between inhibin B and luteinizing hormone in the spinal cord injury group only. **3.** A significant positive relationship was also observed between inhibin B and sperm concentration in the spinal cord injury group. **4.** Although serum concentrations of inhibin B were significantly lower in the spinal cord injury group than in controls, inhibin B and anti-Mullerian hormone serum concentrations did not provide an additional diagnostic tool for male infertility in this population.
	Population: 18 men with SCI who ejaculated regularly by penile vibratory stimulation (PVS) or ejaculation.	1. Probenecid treatment resulted in improved sperm motility in 17 of 18

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Ibrahim et al. 2015; USA Pre-Post Level 4 N=18	**Treatment**: Probenecid was administered in phases. Phase 1 had participants receive 250 mg orally twice a day for 1 week. Phase 2 had participants who completed phase 1 with no complications were given 500 mg orally twice a day for 3 weeks. Semen was analyzed at three time points: Pre-treatment (Pre-Rx), 1-2 days before Phase 1; Post-treatment (Post-Rx), 1-2 days after completion of Phase 2; Follow-up (F/U), 4 weeks after completion of Phase 2. **Outcome Measures:** sperm motility	men, where sperm motility increased from 18% to 25% 2. Linear sperm motility increased rapidly significantly after 4 weeks of treatment (5% vs 16%) and continued after the end of treatment (5% vs. 15%). 3. The improvement in motility continued 4 weeks after end of probenecid treatment but did not reach statistical significance (18% vs. 22%).
Ibrahim et al. 2017; USA Pre-post Level 4 N=20	**Population**: 20 men with SCI who ejaculated regularly by penile vibratory stimulation (PVS) or ejaculation. **Treatment**: Probenecid was administered for 4 weeks (250 mg twice a day for 1 week, followed by 500 mg twice a day for 3 weeks). Semen quality was assessed at three time points: pre-treatment, post-treatment (immediately after the 4-week treatment), and follow-up (4 weeks after the last pill was ingested). **Outcome Measures:** Sperm motility	1. Sperm motility improved in each subject after 4 weeks of oral probenecid. The mean percent of sperm with progressive motility increased from 19% to 26% ($P < 0.05$) and the mean percent of sperm with rapid linear motility went from 5% to 17%, ($P<0.001$). (the improvement continued into the four week follow up period). 2. Similar improvements were seen in the total motile sperm count (15 million, 28 million, and 27 million at pre-treatment, post-treatment, and follow-up, respectively), but sperm concentration was not significantly different at pre-treatment, post-treatment, and follow-up, (52 million, 53 million and 53 million).

Discussion

Results from studies have varied, however, in general have shown similar reductions in sperm parameters in antegrade and retrograde samples, except for decreased motility in non-alkalinized retrograde samples and one study which showed antegrade samples were better in motility and viability than retrograde samples (Ohl et al. 1997). There is also some evidence to suggest that vibratory stimulus seems to produce better semen quality samples than electroejaculation in terms of motility (Ohl et al. 1997; Le Chapelain et al. 1998). Semen quality appeared to improve with repeated ejaculations in some series (Matthews et al. 1996; Giulini et al. 2004; Hamid et al. 2006), and not in others (Sarkarati et al. 1987; Das et al. 2006). It has been suggested that parameters improve with consecutive days of electroejaculation (Mallidis et al. 2000). Once-weekly vibrator stimulation resulted in an increase of semen volume and of fructose and acid phosphatase levels in the seminal plasma (suggesting improved function of the seminal vesicles and prostate) (Siosteen et al. 1990), whereas other investigators reported that too frequent ejaculation caused semen quality to deteriorate (Wang et al. 1992). The possibility of improvement in semen parameters appears to be related to consistency of ejaculations over a regulated time period. One study found improved sperm motility after 3 months of weekly PVS performed by patients at home (Beretta *et al*., 1989). The majority of studies, however, found no statistically significant improvement in sperm motility after regular ejaculation by PVS or EEJ (Siosteen *et al*., 1990; Sonksen *et al*., 1999; Das *et al*., 2006; Hamid *et al*., 2006).

Poor sperm motility may be due in part to the seminal plasma secondary to disturbed nervous systems and anejaculation (Brackett et al. 2000; 2007), and there may also be alterations in testicular

function or morphological anomalies in the sperm (Chapelle et al. 1988; Elliott et al. 2000; Monga et al. 2001). Sperm aspirated from the vas prior to exposure to seminal fluid in men with SCI had significantly better motility (54% vs 14%) and greater viability (74% vs 26%) in comparison to sperm retrieved from same group by VS or EE (Brackett et al. 2000). These researchers had previously demonstrated an inhibitory effect of SCI seminal plasma on normal sperm motility, as well as improvement of SCI sperm motility when prepared with normal seminal plasma (Brackett et al. 1996). In addition, the same group (Brackett et al. 2007; Cohen et al. 2004) have recently shown that cytokines in the semen of men with SCI may play a key role in inhibiting sperm motility, with inactivation of the relevant receptors leading to improved sperm motility. Both studies (Cohen et al. 2004; Brackett et al. 2007) examined the effect of treating semen with different combinations of antibodies on motility and both found that sperm motility significantly increased with the combination of antibodies that acted against all 3 relevant cytokines. In a prospective controlled trial, Ibrahim et al. (2008) found no damage to sperm treated with cytokine inhibitors and suggested that further studies investigating cytokine inhibitors as a therapy for low sperm mobility are warranted. Probenecid has shown promising results to improve sperm motility (Ibrahim et al. 2017).

Once ejaculated, sperm motility in men with SCI declines rapidly, and storing at body temperature (in a 37°C incubator) may exacerbate this (Brackett et al. 1997b). Bladder management also seems to affect sperm quality, with low pressure emptying by clean intermittent catheterization improving semen quality over indwelling catheterization, reflex voiding or straining (Ohl et al. 1989; Rutkowski et al. 1995). Ibrahim et al (2014, 2015) found that slight improvements in sperm motility were achieved after treatment with anti-ASC polyclonal antibody (mean sperm motility increased from 11.5% to 18.3%) and after Probenecid treatment (sperm motility increased from 18% to 25%).

Padron et al. (1994) showed a similar reduction in sperm motility (65%) in men with SCI to normal with thawing after cryopreservation, preferring the vapor only method. Krebs et al. (2015) found that complete tetraplegia has a negative effect on pre-cryopreservation sperm viability and post-cryopreservation motility, and that there were no differences between the semen parameters of samples collected early (up to 3 weeks) after SCI, those collected later, or those collected using assisted ejaculation techniques. Given this and reported reliability of retrieval methods, there seems no point in cryopreserving semen for later insemination unless collected acutely within the first 1-2 week window while sperm quality is still normal (Mallidis et al. 1994).

Botox treatment for detreusor dyssynergia has beneficial and detrimental effects on ejaculation function (Caremel et al. 2011). The detrimental effects involve retrograde ejaculation and reduced semen volume, which result from reduce contraction of the smooth muscle sexual accessory due to the toxin. A beneficial effect is improved semen quality due to the reduced contamination of the semen by urinary infection.

Conclusion

There is level 2 evidence (Brackett et al. 1997a; Ohl et al. 1997) that using a penile vibratory stimulus produces samples with better sperm motility than from electrostimulation.

There is level 2 evidence (from 1 weak RCT; Brackett et al. 2002) that sperm obtained by antegrade samples has better motility than retrograde samples and that interrupted current produces higher sperm motility than continuous current.

There is level 4 evidence (Rutkowski et al. 1995) that bladder management by clean intermittent catheterization (with low pressure filling and emptying) may improve semen quality over indwelling catheterization, reflex voiding or straining.

There is level 4 evidence (Caremel et al. 2011) that botox injections to the overactive bladder may reduce semen volume, but increase semen quality.

There is level 4 evidence (Hibi et al. 2008) that retrograde vasal sperm aspiration can retrieve sperm of sufficient motility to afford pregnancy.

There is level 2 evidence that SCI sperm quality can be improved by placing sperm from SCI in able-bodied seminal plasma (Brackett et al. 1996), and that aspirated sperm from the vas deferens has better motility than that ejaculated (Brackett et al. 2000), demonstrating the etiology of poor semen quality may lie within the seminal plasma in men with SCI. These techniques have not been studied clinically with respect to pregnancy rates.

There is level 4 evidence (Cohen et al. 2004; Brackett et al. 2007) that interference with receptors to all 3 cytokines in semen can improve sperm motility.

There is level 2 evidence (Ibrahim et al. 2009) that monoclonal antibodies and receptor interference agents do not change the degree of DNA fragmentation in sperm from participants with SCI.

There is level 3 evidence (Kanto et al. 2008) that testicular sperm extraction followed by intracytoplasmic injection is an effective way to induce pregnancy, with fresh sperm giving better results than frozen-thawed sperm.

There is Level 2 evidence (Ibrahim et al 2014, 2015) that found slight improvements in sperm motility were achieved after treatment with anti-ASC polyclonal antibody (mean sperm motility increased from 11.5% to 18.3%) and after Probenecid treatment (sperm motility increased from 18% to 25%).

There is Level 5 evidence (Krebs et al. 2015) that found complete tetraplegia has a negative effect on pre-cryopreservation sperm viability and post-cryopreservation motility, and that there were no differences between the semen parameters of samples collected early (up to 3 weeks) after SCI, those collected later, or those collected using assisted ejaculation techniques.

Midodrine may be an effective and safe adjunct to PVS in men not responding to PVS alone who are not at risk for significant autonomic dysreflexia.

PVS results in better sperm quality than that obtained by EEP.

Balloon catheters to tamponade the bladder neck may be effective in securing antegrade ejaculate samples.

Botox injections to the overactive bladder may reduce semen volume, but increase semen quality due to decreased urinary tract infection rate. Antegrade samples have better sperm motility than that found in retrograde samples.

Electroejaculation with interrupted current produces better sperm motility than with continuous current.

Bladder management with clean intermittent catheterization may improve semen quality over indwelling catheterization, reflex voiding or straining.

SCI sperm quality improves by processing in able-bodied seminal plasma.

Aspirated sperm has better motility following sperm retrieval procedures than ejaculated sperm which is more exposed to the toxic seminal vesicle components

Sperm motility may improve by neutralizing receptors to various cytokines in semen.

Use of ejaculated sperm or aspirated sperm for reproductive purposes requires a cost- benefit analysis.

5.3.3 Male Fertility and Resulting Pregnancy

Unfortunately, after SCI, semen quality declines necessitating assistive reproductive technologies to compensate for the alterations (Elliott 2003). Pregnancy rates are lower than the general population but have been much improved since the advent of in vitro fertilization (IVF) and intracytoplasmic injection (ICSI).

Table 16: Fertility and Resulting Pregnancy

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Bechoua et al. 2013; France Case Series Level 5 N=19	**Population**: 19 men with SCI (6 quadriplegics, 13 paraplegics, mean age=25.2±5.6 years) who underwent sperm cryopreservation from 1995 to 2011. **Treatment**: Two groups were outlined based on sperm retrieval method: antegrade ejaculation group (n=10) and surgical sperm retrieval (SSR) group (n=9). **Outcome Measures:** Samples was analyzed according to the guidelines of the World Health Organization. Pregnancy outcomes in the 8 couples who chose to undergo Intra Cytoplasmic Sperm Injection (ICSI) were assessed.	**1.** Fertilization rates were 57 and 55% in the antegrade ejaculation and SSR groups respectively. **2.** The embryo's cleavage rates were 90 and 93% in the antegrade ejaculation and SSR groups respectively. **3.** Within the 8 couples that received ICSI, 5 couples achieved pregnancy. **4.** Pregnancy rates per couple were 50% and 75% in the antegrade ejaculation and SSR groups respectively.
Leduc 2012; Canada Case series Level 5 N=31 (couples)	**Population:** 31 couples with male partners with SCI and fertility disorder as result from SCI; mean(SD) age: SCI men 29.7(4.8) yrs, range 23-48, female partners 29.3(4.8) yrs, range 25-41; mean(SD) DOI: 7.6(6) yrs,	1. Among the 10 couples treated with intravaginal insemination, 9 pregnancies occurred among 7 couples. 2. No pregnancies resulted from intrauterine insemination (2 cases).

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	range 1-29; 10 cervical, 20 thoracic, 1 lumbar. **Treatment:** Semen samples obtained by manual stimulation (n=10, including 6 treated by sc physostigmine), penile vibratory stimulation (PVS) (n=4), electroejaculation (EEJ) (n=5), and testicular sperm extraction (n=12). Assisted reproductive technique (ART) selected according to sperm parameters (IVI, IUI, IVF). **Outcome measures:** Sperm parameters (count, motility), number of pregnancies, births, and paternities, pregnancy rate/cycle.	3. Among the 18 couples treated with IVF, 12 pregnancies were reported among 10 couples. 4. The pregnancy rate/cycle was 43%. 5. Following these assisted reproductive techniques (ARTs) the pregnancy rate reached 55%. 6. Overall 20 men with SCI (64% of the group) became fathers to at least one child.
Kathiresan et al. 2011; USA Retrospective analysis Level 5 N=82	**Population**: 82 male patients with SCI and their female partners; mean(SD) age 36.1(0.7) yrs, mean time after injury 0.8 yrs (range 0.7-34.0 yrs). **Treatment**: 45 couples performed intravaginal insemination (IVI); intrauterine insemination (IUI) was performed in 57 couples. **Outcome Measures:** Method of sperm retrieval, sperm quality, occurrence of pregnancy, live birth, pregnancy rate (PR), pregnancy losses, multiple gestations, total motile sperm count (TMSC).	1. Of the 45 couples with IVI, 17 couples had 20 pregnancies with 3 couples achieving pregnancy twice (16 through penile vibratory stimulation; 1 through electroejaculation; and 3 through masturbation). Eighteen live births occurred. 2. Average time from male partner's first semen analysis to time of pregnancy was 6.9(1.25) mos. The mean antegrade TMSC in men achieving vs. not achieving pregnancy was not statistically significant: 90.1(30.8) million (range 2.6-425.7 million) vs. 76.5(21.0) million (range 0.3-544.5 million). 3. 57 couples underwent IUI, where 14 couples had 19 pregnancies and 21 live births (1 twin and 1 triplet pregnancy occurred, both by IUI cycles stimulated by gonadotropins). Cycle fecundity was 7.9% (19 pregnancies of 241 cycles). Semen collected by PVS (6 pregnancies) and EEJ (13).
McGuire et al. 2011; Ireland Retrospective review (case series) Level 5 N=31	**Population:** 31 men (mean age 35 yrs, range 24-49), 29 with acquired spinal cord injury (complete lesion (n=18), incomplete lesion (n=11). Injury levels: C3-C7; T1-T5; T11-L3), 2 with congenital spinal abnormality. **Treatment:** EES done with Seager model rectal probe. Electroejaculatory stimulation (EES) – n= 27 (87%) underwent EES once, n= 4 (13%) underwent EES several times. **Outcome measures:** The Mann-Whitney U test, semen analysis (volume, density, motility, normal morphology and live sperm); pregnancy rate	1. Of the 25 patients whose partners underwent insemination with the EES semen, 9 (36%) became pregnant. All pregnancies resulted in live births. 2. One patient developed autonomic dysreflexia necessitating stopping EES before obtaining any ejaculate. No other side effects or complications were reported. 3. 30 patients produced antegrade, retrograde, or both types of ejaculate
Hibi et al. 2008; Japan Post-test Level 4 N=8	**Population:** 8 participants with cervical SCI and neurogenic anejaculation (age 26-46 yrs, mean 35.6). **Treatment:** Retrograde vasal sperm aspiration (ReVSA). **Outcome Measures:** Presence of motile sperm.	**1.** Motile sperm was recovered in all participants who underwent ReVSA (11 procedures total). **2.** The retrieved sperm concentration was 109.4(64.7) × 10^6 /mL (range 31.2-156.3 × 10^6 /mL).

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
		3. The retrieved motility of sperm was 69.8%(16.8) (range 50-91%). **4.** Clinical pregnancies were achieved in 8 cases.
Kanto et al. 2008; Japan Case control Level 3 N=56	**Population:** 22 men with SCI (age 21-41); data on 34 men with obstructive azoospermia was obtained retrospectively for control. **Treatment:** Testicular sperm extraction (TESE); if unsuccessful, microdissection TESE was performed, followed by intracytoplasmic injection (ICSI). **Outcome Measures:** Fertilization; pregnancy.	1. TESE successfully retrieved sperm in 19 participants with SCI. 2. ICSI resulted in a fertilization rate of 236 of 364 (64.8%) in SCI couples and 14/19 achieved pregnancy. 3. In couples with obstructive azoospermia, ICSI resulted in a fertilization rate of 435 of 567 (77%) and 29/34 achieved pregnancy. 4. Pregnancy rate was significantly higher in couples with SCI using fresh testicular sperm-ICSI compared to frozen-thawed sperm-ICSI.
Engin-Üstün et al. 2006; Turkey Case series Level 4 N=44	**Population:** Men with SCI and partner; median age 26.0-29.5 yrs, range 20-31; 4 cervical, 38 thoracic, 2 lumbar. **Treatment:** Retrieval by electro-ejaculation (EE), testicular sperm extraction (TESE) or prostatic massage (PM). **Outcome Measures**: Fertilization rate,pregnancy rate, live birth rate, sperm counts, sperm motility.	**1.** Fertilization, pregnancy and live birth rates were same between 3 methods. **2.** Sperm count and sperm motility were the same between EE and PM method.
Shieh et al. 2003; Taiwan Post-test Level 4 N=10	**Population:** 10 men with SCI and partner; Age: range 27-37 yrs; Injury level: C6-T12, 9 incomplete and 1 complete, 9 paraplegia & 1 tetraplegia; Time since injury: range 4-20 yrs. **Treatment:** If semen sample from electroejaculation (EE) was of fair quality, then 3 cycles of intrauterine insemination prior to intracytoplasmic sperm injection treatment (ICSI). If semen samples were poor, ICSI was suggested. If no sperm from EE, surgical retrieval of sperm was performed. **Outcome Measures:** Pregnancy rates.	**1.** 7 clinical pregnancies achieved, 2 of which ended with spontaneous abortion. 1 couple accomplished pregnancy by ICSI with cryopreserved sperm from vasal aspiration. **2.** The fertilization and pregnancy rates of ICSI cycles using sperm from men with SCI were comparable to men without SCI. **3.** One couple attained pregnancy by using donor sperm. **4.** The cumulative successful pregnancy rate per couple was 80%.
Heruti et al. 2001; Israel Post-test Level 4 N=84	**Population:** 84 men with SCI, 49 couples; Age: range 19-45 yrs; Injury level: cervical (34.5%), thoracic (59.5%), lumbar (5.9%); Impairment grade: AIS A (n=63), B (n=15), C (n=5), D (n=1); Time since injury: range 4 months-34 yrs. **Treatment:** Electroejaculation followed by intrauterine insemination for 3 trials (10million sperm/cc). If this did not result in fertilization, intracytoplasmic sperm injection and IVF. **Outcome Measures:** Volume, sperm count, motility, morphology, total motile sperm count, conception.	1. Ejaculation occurred in 98.6% of patients, with sperm in 88% of patients and enough viable sperm in 54.8%. 2. Antegrade semen parameters had significantly better sperm count, morphology and motility than retrograde samples. 3. No significant improvements were seen in seminal parameters after repeated ejaculations. 4. 69.2% overall pregnancy rate/couple. 33% (5/15) after intrauterine insemination, 70% (14/20) after IVF. 5. 26 live births (n=12 singletons, n=5 twins, n=1 triplets) and 4 abortions.

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Ohl et al. 2001; USA Post-test Level 4 N=121	**Population:** 121 couples (87 men with SCI and partner). **Treatment:** Electroejaculation followed by intrauterine insemination (IUI) was the route of sperm delivery. If not successful after 3-6 cycles of IUI, GIFT (gamete intrafallopian transfer) or IVF procedures were recommended. **Outcome Measures:** Pregnancy success and pregnancy outcomes.	**1.** 52/121 became pregnant, 39 by IUI alone. **2.** All patients undergoing IVF had significantly higher cycle fecundity than did those undergoing IUI. **3.** The rates of spontaneous abortion and multiple gestations were 23% and 12%, respectively.
Pryor et al. 2001; USA Prospective controlled trial Level 2 N=11	**Population:** 11 men with SCI and their partner; Injury level: tetraplegia. **Treatment:** Electrical stimulation or vibratory stimulation followed by 1) intrauterine insemination of partner 24 hour after Luteinizing Hormone surge (n=5), 2) 50 mg clomiphene citrate & hCG, followed by insemination after 32-34 hours (n=5), or 3) same as #2, except 38-40 hour delay (n=10). **Outcome Measures:** Fertility rates, seminal parameters.	1. No pregnancies with protocol 1 or 2. 6/10 patients became pregnant with protocol 3, which has the longest delay between drug administration and insemination.
Schatte et al. 2000; USA Post-test Level 4 N=17	**Population:** 10 men with SCI (7 non-SCI related anejaculation); mean age 38.9 yrs. **Treatment:** Electroejaculation and intracytoplasmic sperm injection (ICSCI) and results compared to 620 ICSI cycles for non-SCI male infertility with normal ejaculation. **Outcome Measures:** Pregnancy rate.	1. ICSI resulted in a median fertilization of 60%, 15% pregnancies per cycle and 29% pregnancies per couple. 2. Pregnancy rates were lower for the anejaculation group compared to the severe male factor group.
Taylor et al. 1999; Australia Post-test Level 4 N=19	**Population:** 19 men with SCI; Age: range 24-44 yrs; Injury level: C4-C9 (n=9), T4-T12/L1 (n=10), 12 complete and 7 incomplete; Time since injury: range 1-24 yrs. **Treatment:** Sperm was extracted through vibrator application or electroejaculation followed by assisted reproductive treatments (intrauterine insemination, gamete intrafallopian transfer, in vitro fertilization and embryo transfer, intracytoplasmic sperm injection). **Outcome Measures:** Seminal parameters, pregnancy rates (intrauterine insemination, gamete intrafallopian transfer, intracytoplasmic sperm injection).	**1.** 14/19 achieved at least 1 pregnancy. **2.** Methods used: Intrauterine insemination 12% (11/92), gamete Intrafallopian transfer 38.9% (8/18), intracytoplasmic sperm injection 19.2% (5/21). **3.** In patients with incomplete lesions vibratory stimulation was more frequently successful (4/7) 53%. **4.** Complete lesions required more advanced procedures to achieve pregnancy, (7/12) 58% required electroejaculation.
Brinsden et al. 1997; UK Post-test Level 4 N=35	**Population:** 35 men with SCI and their female partners; Age: (men) range 24-47 yrs, (female) range 21-43 yrs; Injury level: C5-L1; Time since injury: range 1-27 yrs. **Treatment:** Trans-rectal electroejaculation with in-vitro fertilization. 71 IVF cycles were used. **Outcome Measures:** Pregnancies, fertilization rate, motile sperm count.	1. Pregnancy rates: 18 total (14 were fresh embryo transfers, 4 were frozen embryo transfers). 2. Pregnancy rate per treatment cycle was 21.2% (18/35). 3. Overall clinical pregnancy rate per stimulated IVF treatment was 25.4% (18/71).

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Chung et al. 1997; USA Post-test Level 4 N=27	**Population:** 24 men with SCI, 3 men with retroperitoneal dissection; Age: range 4-48 yrs; Time since injury: range 3-25 yrs. **Treatment:** Electrostimulation and nifidepine (10mg) for prophylaxis of autonomic dysreflexia. **Outcome Measures:** Ejaculation rates, pregnancy rates, seminal parameters.	1. 7 pregnancies in 13 couples with a total of 56 intrauterine insemination, 2 spontaneous abortions, 4 live births, 1 ongoing twin pregnancy.
Hultling et al. 1997; Sweden Post-test Level 4 N=25	**Population:** 22 men with SCI and female partner; Age (men): range 25-51 yrs, (female): range 21-38 yrs; Injury level: C2-L3; Time since injury: range 3-33 yrs. **Treatment:** Vibratory or electrical stimulation followed by IVF. **Outcome Measures:** Conception.	**1.** Pregnancy rate: 16/25 pregnancies occurred leading to 11 deliveries. **2.** n=9 singletons, n=2 sets of twins; n=4 miscarriages during the first or second trimester (1 case of intrauterine death in week 31 of gestation). **3.** Pregnancy occurred in all groups of patients in the AIS scale A-D from injuries from C2-L2. **4.** Clinical pregnancy rate was 31% and the cumulative pregnancy rates up to four cycles were 56%.
Sonksen et al. 1997; Denmark Case series Level 5 N=28	**Population:** 28 men with SCI and female partner; Age (men): range 24-43 yrs, (female): mean 29 yrs, range 19-39 yrs; Injury level: C2-L4; Time since injury: range 1-22 yrs. **Treatment:** Males with SCI: vibratory stimulation or electroejaculation. Female partners: assisted reproductive techniques (vaginal self-insemination at home, intrauterine insemination, in vitro fertilization with or without intracytoplasmic sperm injection). **Outcome Measures:** Ejaculation rates, seminal parameters, pregnancy rates.	**1.** All men were able to ejaculate, 22 by vibratory stimulation (all with lesion above T10), 6 by electroejaculation. **2.** 4/16 achieved pregnancy and had healthy babies. This was achieved by home vibratory stimulation and self-insemination within 2 years. **3.** All couples that had children had significantly higher median motile sperm per ejaculate (105 million vs. 10 million). **4.** Overall 9/28 couples (32%) achieved 10 pregnancies with a delivery of 9 healthy babies.
Nehra et al. 1996; USA Case Series Level 4 N=78	**Population:** 78 men with SCI (33 couples); Age: range 23-44 yrs; Injury level: 37 cervical, 41 thoracic. **Treatment:** Retrospective review of electrical stimulation followed by cervical self-insemination, intrauterine insemination, in vitro fertilization, or gamete intrafallopian transfer. **Outcome Measures:** Sperm quality, pregnancy rates.	**1.** Vibratory stimulation achieved ejaculation in 20/37 cervical patients, 14/26 at or above T10 and 0/15 below T10. **2.** Pregnancy rates: 17/27 achieved pregnancy (10 with vibratory stim, 7 with electroejaculation). **3.** 5/8 achieved self-home insemination with PVS. **4.** 17/27 couples were successful at conception (5 self-insemination, 5 intrauterine insemination and 7 assisted reproductive techniques). **5.** 20 live births in 14 couples.
Brackett et al. 1995; USA Case series Level 4 N=23	**Population:** 23 (21 with SCI) men and partner; Age: range 26-42 yrs; Injury level: cervical (n=7), thoracic (n=12), lumbar (n=2); Time since injury: range 2-28 yrs. **Treatment:** Vibrostimulation or electro-ejaculation with ovulation induction by clomiphene citrate or gonadotropins and intrauterine insemination (IUI).	**1.** Six pregnancies (7 live births) occurred in 60 cycles of IUI (cumulative pregnancy rate 26%). **2.** Six couples who failed after a total of 33 IUI cycles, and 1 couple with no previous IUI cycles initiated 10 cycles of in vitro fertilization, resulting in 5 pregnancies (pregnancy rate 71%): 1

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	Outcome measures: Pregnancy and live births.	live birth, 1 ongoing pregnancy, 1 ectopic pregnancy, 2 spontaneous abortions.
Dahlberg et al. 1995; Finland Post-test Level 4 N=63	**Population:** Men with SCI and 35 female partners; Age: range 21-42 yrs; Level of injury: C1-C5 to L1-L2. **Treatment:** Sperm was extracted through vibrator application, drug application (Nifidepine 10-30mg), and electroejaculation or sperm aspiration from the vas deferens. Sperm was then introduced by insemination or IVF. **Outcome Measures:** Live births.	**1.** Fertility rates: of 35 males seeking pregnancy, 29 could produce viable sperm. **2.** Live births: n=24 children from 18/35 couples). Miscarriages: n=4.
Pryor et al. 1995; USA Post-test Level 4 N=6	**Population:** 6 men with SCI; Age: range 30-35 yrs: Injury level: C4-C7; Time since injury: 6-18 yrs. **Treatment:** Vibratory stimulation (using 4,200rpm for 5-45min, with 5 min breaks every 5 min) followed by intrauterine inseminations. **Outcome Measures:** Pregnancy rates.	**1.** Pregnancies occurred in 5/6 of the partners. 2 partners delivered healthy boys, 1 partner miscarried at 9 wks. **2.** One couple has completed second vibratory stimulation without conception and will try again.
Hultling et al. 1994; Sweden Post-test Level 4 N=12	**Population:** 12 men with SCI and female partner; Age: range 27-38 yrs; Injury level: C4-L3; Time since injury: range 4-33 yrs. **Treatment:** Vibratory stimulation and, if necessary, physostigmine and/or electroejaculation followed by IVF. **Outcome Measures:** Seminal parameters, pregnancy rates.	1. Pregnancy rates: 7 pregnancies in 6 couples, 3 spontaneous abortions, 2 live births, 2 ongoing pregnancies.
Buch & Zorn 1993; USA Post-test Level 4 N=18	**Population:** 18 men with SCI; Age range 22-43 yrs; Injury level: C5-T12; Impairment grade: AIS A (n=12), B-D (n=6); Time since injury: range 2-22 yrs. **Treatment:** Rectal probe electroejaculation (RPE). **Outcome Measures:** Sperm retrieval, sperm quality, live births.	**1.** After fertility testing, 6/18 men proceeded to use RPE in effort to conceive. Sperm obtained in 16/18 cases. **2.** Ejaculate total sperm count=306 million (good), but motility (22%) was poor. **3.** Adequate sperm retrieval after processing yielded normal sperm penetration assay in 4/16 (25%) cases in which sperm was obtained. **4.** Live births in 2/6 couples attempting conception.
Lucas et al. 1991; UK Post-test Level 4 N=14	**Population:** 12 men with SCI, 2 men without SCI (diabetes); mean age 34.6 yrs, range 25-46; Injury level: C5-T10. **Treatment:** Electrical stimulator (up to 35V, 900mA, 50Hz). **Outcome Measures:** Fertility rates, seminal parameters, pregnancy rates.	**1.** Seminal parameters: volume obtained: a few drops to 5.5ml, % of progressive motility: 0-60%, and sperm concentration: 0-260 million/ml. **2.** 1 pregnancy recorded (father: T10 paraplegia, 8 yrs post-injury, 54million/ml, 30% motility) resulted in a singleton with no genetic abnormalities.

Discussion

Pregnancy rates of partners of men with SCI, although somewhat dependent on sperm motility, are improved consistently with higher levels of reproductive assisted technology. Fertility rates improve

progressively with the use of assisted reproductive technology (ART) and more advanced techniques, as follows:

- At home (intercourse or vaginal insemination)
- Intrauterine insemination
- In vitro fertilization (IVF)
- IVF + intracytoplasmic sperm injection (ICSI).

Reports have varied in their description of pregnancy rates, using either pregnancy rate per couple or pregnancy rate per insemination method. In general, reported as per couple, there has been considerable improvement in rates over the last 20 years due to better technology (Brinsden et al. 1997; Schatte et al. 2000). In collation of reports by many authors, there appears to be an average 30-50% pregnancy rate and a 40% live birth rate (Beretta et al. 1989; Hultling et al. 1994; Dahlberg et al. 1995; Chung et al. 1997; Hultling et al. 1997; Heruti et al. 2001; Sheih et al. 2003; Giulini et al. 2004). Cumulative pregnancy rates could go as high as 80% (Sheih et al. 2003). The number of attempts varied greatly, with pregnancy unlikely to occur after 5 attempts of any method (recognizing that some couples advanced on the continuum of increasing ART). Cycle fecundity rate (chance of pregnancy per cycle) for intrauterine insemination is <15%, whereas for IVF/ICSI it is between 25-40%. In one study, it was felt that delayed timing of intrauterine insemination resulted in significantly improved pregnancy rates in female partners of men with tetraplegia (Pryor et al. 2001). While fresh semen samples were preferred, cryopreserved semen samples were used successfully for IVF technology. Cryopreservation of embryos to be replaced at a later date is also useful (Buch & Zorn 1993). Multiple gestations were more frequent with IVF/ICSI. Testicular aspiration has been used less commonly, since it commits the man and his partner to IVF/ICSI procedures. One case control study however, found that pregnancy rates among couples using testicular aspirated sperm from males with SCI were comparable to the rates among couples using the same procedure from able-bodied controls with obstructive azoospermia (Kanto et al. 2008). The use of retrograde vasal sperm aspiration has also shown to be a reliable method for consistent sperm recovery such that a high pregnancy rate and cryopreservation of excess sperm for future use was possible (Hibi 2008).

Estimates of the feasibility of and effort required to pursue biological fatherhood after SCI are emerging. This cumulative evidence and substantial clinical experience suggest starting with an appropriate clinical assessment of neurological impairment, physical health, bladder management and risk factors for the man (i.e. autonomic dysreflexia), as well as fertility history and blood work for the female partner. Assessment of sperm retrieval methods follows with evaluation of the resultant semen samples retrieved. Female intervention is determined by her fertility factors and by the quality of semen available. The least invasive and least expensive insemination options are pursued after weighing invasiveness and risk of sperm retrieval and semen quality. Men with SCI stand a good chance (>50%) of becoming biological fathers when they have access to specialized clinics and care. Recently, Bechoua et al. (2013) found fertilization rates of 55-57%, embryo cleavage rates of 90-93%, and pregnancy rates of 50-75% when using antegrade ejaculation or surgical sperm retrieval (SSR).

Conclusion

There is level 3 (Kanto et al. 2008), level 4 evidence (Buch and Zorn 1993; Hultling et al. 1994; Brackett et al. 1995; Dahlberg et al. 1995; Pryor et al. 1995; Nehra et al. 1996; Brinsden et al. 1997; Chung et al. 1997; Hultling et al. 1997; Sonksen et al. 1997; Taylor et al. 1999; Schatte et al. 2000; Heruti et al. 2001;Ohl et al. 2001; Shieh et al. 2003; Hibi 2008, McGuire et al. 2011; Kathiresan et al. 2011; Leduc 2012) and level 5 (Bechoua et al. 2013) evidence that men with SCI have a good chance of becoming biological fathers with access to specialized care utilizing reproductive assisted technology.

Men with SCI should have realistic expectations of becoming a biological father.

Depending on semen quality and female factors, a progression from intravaginal insemination to assisted techniques such as intrauterine insemination, in vitro fertilization (IVF) to IVF plus intracytoplasmic sperm injection (ICSI) is recommended.

At home intravaginal insemination has revealed pregnancy rates of 40-50%, with cumulative pregnancy rates as high as 90%

6.0 Sexual and Reproductive Health in Women with SCI

For many years the sexual and reproductive health of women with SCI was not studied. Although fewer intervention trials exist on this topic, there are observational studies of clinical importance, which provide information as well as serve to highlight the major sexual and reproductive health issues that exist for women with SCI.

Table 17: Systematic Reviews on Female Sexual and Reproductive Health

Author Year; Country Dates included in the review Total sample size Level of evidence Type of study Score	**Methods Databases**	**Outcomes**
Ghidini & Simonson 2011; USA Reviewed published articles from 1990 to 2010 N=13 Level of evidence methodological quality not assessed Type of studies Case control (n=1), Case series (n=12) AMSTAR=3	**Method:** Literature search for peer-reviewed original articles published in English concerning pregnancy in women with SCI; references selected based on relevance to effects of pregnancy on SCI and the outcome of pregnancy in women with SCI. **Databases:** PubMed, MEDLINE, The Cochrane Library.	1. Worsened spasticity, autonomic dysreflexia, urinary tract infections, and thrombosis are reported more often than expected during pregnancy in women with SCI. 2. SCI increases the risk of obstetric complications such as preterm delivery, low birth weight, and rates of admission to the neonatal intensive care unit. 3. The only case-control study on the subject found that women who became pregnant after SCI had nearly double the rates of preterm delivery as those who became pregnant before SCI. 4. The rate of Caesarean sections and the incidence of post-partum depression are higher among with SCI than expected in the general obstetric population.
Pannek and Bertschy 2011; Switzerland Reviewed published articles from PubMed and Medline with no date restrictions N=14 Level of evidence Assessed using the Oxford Center of Evidence-Based Medicine criteria Type of studies 1 prospective cohort,	**Method:** Searched for studies published in English or German on the urologic management of pregnant women with SCI. **Databases:** Medline and PubMed	**1.** SCI was cervical in 34.7%, thoracic in 61.2% and lumbar in 4.1% of the pregnant women. **2.** 34.7% used indwelling catheters, 25% performed intermittent catheterization, 11.5% used the Credé maneuver and 28.8% voided spontaneously. **3.** Urinary tract infections (UTIs) were more common in women with indwelling catheters (100%) than in those performing intermittent catheterization (38.5%), using the Credé technique (17%) or voiding spontaneously (53.3%). **4.** A total of 64% of the patients had at least one symptomatic UTI during pregnancy. **5.** A single study with 66 patients, of which 40% had an indwelling catheter, reported leakage around the catheter in 15% of patients, bladder spasms being so

Author Year; Country Dates included in the review Total sample size Level of evidence Type of study Score	Methods Databases	Outcomes
9 retrospective case series, 4 case reports AMSTAR=3		significant that catheters were expelled in 9.1% and there was a necessity to change the mode of bladder management in 25%.
Lombardi et al. 2010; Italy Reviewed published articles from 1993 to 2009 N=not stated Level of evidence Methodological quality not assessed Type of studies Not described AMSTAR=1	**Method:** Searched for internationally published studies from the PubMed database with keywords related to female SCI sexual function. Searches were also done with oneco-morbidity or one behaviour risk factor together with SCI female or female sexual dysfunction. **Databases:** PubMed	**1.** Females with complete tetraplegia require special attention immediately at initial recovery as sexual intercourse is much more difficult for them compared with other women with SCI mainly because of autonomic dysreflexia and urinary incontinence. **2.** Sexual satisfaction increases as duration of injury increases. The likelihood of a woman with SCI taking part in a sexual relationship also increases as duration of injury increases. **3.** 40-80% of women continued to be sexually active after injury, but much less so than before injury. The ability to reach orgasm decreased significantly after injury. **4.** One paper reported that sildenafil has no significant benefit on sexuality.

6.1 Sexual Response in Women with SCI

Though it is true that women with SCI have clinically significant impairment in arousal and orgasm, women with complete SCI have been self-reporting orgasm that seemed physiologically impossible (Richards et al. 1997). Multiple laboratory-based studies have documented the presence of sexual arousal and orgasm in women with SCI (Whipple & Komisaruk 2002; Komisaruk et al. 2004, Sipski et al. 1995, 2000, 2004, 2005). Following SCI, women may attain genital sexual arousal through a psychogenic and/or a reflex pathway. Preservation of T11–L2 sensory dermatomes is associated with psychogenically mediated genital vasocongestion and lubrication (Sipski et al. 1997; Sipski et al. 2001). The ability to achieve reflexogenic genital congestion and orgasm depends on the presence of an intact sacral reflex arc (Sipski et al. 1997; Sipski et al. 2001). The vagus nerve has also been hypothesized to serve as a pathway that bypasses the spinal cord and thereby may facilitate those responses (Komisaruk et al. 2004).

Women with SCI are less likely to achieve orgasm than able-bodied women, and time to orgasm is significantly increased compared to able-bodied controls (Sipski et al. 2001). The ability to achieve orgasm, however, seems unrelated to the pattern or degree of neurological impairment in women with lesions down to T5 level (Sipski et al. 1995). On the other hand, women with LMN lesions affecting S2 –S5 segments were less likely to achieve orgasm compared with women who had other types of SCI lesion (Sipski et al. 2001).

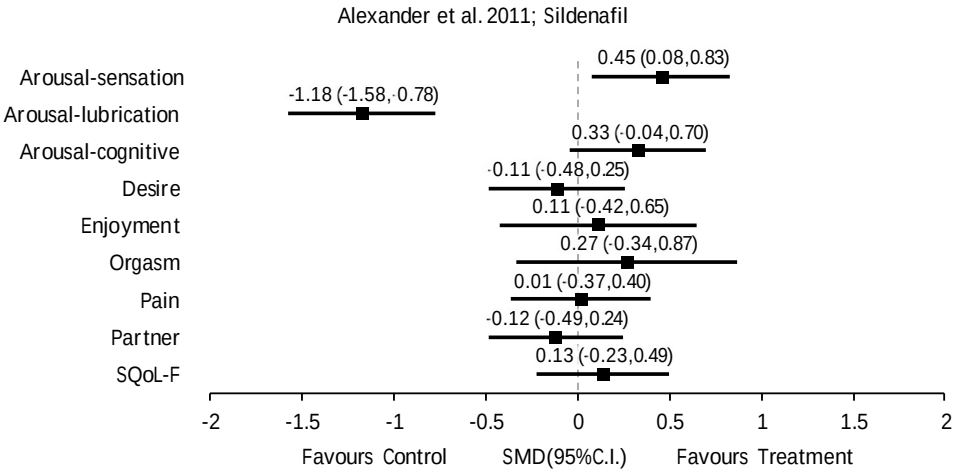
Similar cardiovascular responses were found in women with SCI compared to able-bodied controls at time of orgasm (Sipski et al. 1995; Sipski et al. 1996). Another study found only significant increase in blood pressure, but not in heart rate, in women with complete SCI above T10 level in response to self-stimulation, however, not all women stimulated to orgasm (Whipple et al. 1996). Greater knowledge about sexuality seems to be related to sexual responsiveness (Sipski et al. 1995).

A number of treatments to improve sexual responsiveness in women with SCI have been explored over the past decade. Two therapies were based on the assumption that psychogenic genital vasocongestion is under control of the sympathetic nervous system and that sympathetic activation may lead to enhanced sexual arousal (Sipski et al, 2000, 2004). Positive feedback was shown to increase psychogenic arousal in women with SCI, and furthermore, increased genital arousal in those women who had preservation of sensory function in the T11-L2 dermatomes (Sipski et al. 2000). In another study, anxiety-eliciting videos were used to elicit sympathetic activation (Sipski et al. 2004). Anxiety pre-exposure resulted in a small increase in genital responsiveness to erotic stimulation in participants with impaired, but not absent, ability to achieve psychogenic genital vasocongestion (those with T11-L2 sensory score < 23). While these two studies help to understand the role of the sympathetic nervous system in mediating sexual arousal in women with SCI, clinical application of these two approaches has yet to be determined. Sipski et al. (2005) studied the effect of vibratory stimulation on sexual arousal in women with SCI. Vibratory clitoral stimulation resulted in increased genital responsiveness as compared with manual clitoral stimulation, although the differences were not statistically significant. One randomized controlled trial tested the effect of sildenafil 50mg versus placebo on sexual responsiveness (Sipski et al. 2000). Sildenafil administration improved subjective measures of sexual arousal with borderline objective measures. The effect was most evident under optimal stimulation conditions (manual combined with visual).

Further studies are required to investigate augmenting sexual arousal responses in women with SCI by combining psychological, physical/physiological and pharmacological approaches.

Table 18: Sexual Response in Women with SCI

Author Year; Country Score Research Design Total Sample Size	**Methods**	**Outcome**
Alexander et al. 2018 RCT Level 1 PEDro = N = 23 (11 w/SCI)	**Population:** 23 women (18 MS, 5 SCI) completed the study including 13 of 16 and 10 of 15 randomized to the 2 conditions. **Treatment:** A 12-week trial of the use of a clitoral vacuum suction device (CVSD) versus vibratory stimulation (V) to treat orgasmic dysfunction in women with multiple sclerosis (MS) or spinal cord injury (SCI). **Outcome Measures:** Female Sexual Function Inventory (FSFI) and Female Sexual Distress Scale (FSDS) including subscales.	1. There were statistically significant increases in total FSFI score (p=.011), desire (p=.009), arousal (p=.009), lubrication (p=.008), orgasm (p=.012), and satisfaction (p=.049), and a significant decrease in distress as measured by FSDS (p=.020) in subjects using the CVSD. 2. In participants who used V, there was a statistically significant increase in the orgasm subscale of the FSFI (p=.028). 3. Participants using the CVSD maintained improvements 4 weeks after treatment, but participants using V did not have significant differences between baseline and follow-up on any measures. 4. CVSD is safe and efficacious to treat female neurogenic sexual dysfunction related to MS and SCI. V is also safe and efficacious for female neurogenic orgasmic dysfunction; however, results were limited to the active treatment period.
Alexander et al. 2011; Sweden PEDro=9 RCT Level 1	**Population:** 129 females (mean age=37 years, range=19-62 years); 86 (67%) with female sexual arousal disorder (FSAD) resulting from paraplegia/tetraplegia for >12months. Patients from clinical practice sites in North America, Europe, Australia, and	**1.** There is no statistically significant difference in satisfactory sexual activities between baseline and end of treatment (EOT). **2.** No statistically significant difference between sildenafil and placebo in questionnaire data, Total score on the SQoL-F increased for both

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
N=129	South Africa. Mean sensory score was 133 and the mean motor score was 59. **Treatment:** Double-blind, placebo-controlled, flexible-dose design; after 4 week, treatment free, run-in period (baseline) patients randomized to receive either oral sildenafil 50mg as needed or a matching placebo for 12 weeks. Dose adjustments were allowed once, either increasing to 100 mg or decreasing to 25 mg. **Outcome measures:** event log for sexual activity, study dosing, and sexual satisfaction; Sexual Function Questionnaire (SFQ); Sexual Quality of Life Questionnaire-Female (SQoL-F); global efficacy question (GEQ); Sexual Distress Question.	groups, but the difference was not statistically significant. **3.** GEQ and SDQ results favoured sildenafil but were not statistically significant. 55% of the sildenafil group compared with 38% of the placebo group report improvement in GEQ.
	Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- and post-intervention data 	
Sipski et al. 2000; USA PEDro=6 RCT Level 1 N=19	**Population:** Age range: 25-45 yrs, 19 females, 13 complete, 6 incomplete, length of injury range=15-457mos. **Treatment:** Random assignment to sildenafil (50mg) or placebo on day 1 and the alternate medication on day 2. One hour after drug, participants underwent two 12-minute periods of audiovisual stimulation, followed by two 12-minute periods of audiovisual plus manual clitoral stimulation, each separated by 6-minute baseline periods. The identical protocol was administered on the subsequent day with the alternate medication. **Outcome Measures:** Subjective arousal, vaginal pulse amplitude.	1. Significant increases in subjective arousal were observed with both drug and sexual stimulation conditions. 2. Borderline significant effect of drug administration on vaginal pulse amplitude, an objective measure of vaginal arousal, was noted. 3. Findings suggest that sildenafil may partially reverse sex dysfunction in women with SCI.
Sipski et al. 2005 USA	**Population:** Women with SCI (n=46) and 11 non-disabled/control women; Age: Mean	1. Increased arousal from both manual and vibratory stimulation in both groups. No

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
PEDro=4 RCT Level 1 N SCI=46 N controls=11	(SCI) 35.1 yrs, SD=7.9, (control) 34.3 yrs, SD=8.2; Injury level: C5-S3; Lesion level: upper motor neuron (UMN) (n=32), lower motor neuron (LMN) (n=14); Time since injury: mean 127 months, range 15-494. **Treatment:** Vibratory stimulation vs manual stimulation. **Outcome Measures:** Vaginal pulse amplitude (VPA), levels of arousal.	difference in arousal level between vibratory and manual clitoral stimulation in women with SCI. 2. In participants with SCI, VPA increased (non-significant) more from vibratory clitoral stimulation compared to manual stimulation. 3. No impact on VPA or arousal levels by completeness of injury or by UMN vs LMN injury.
Sipski et al. 1995 USA Matched Controlled Trial Level 2 N=34	**Population:** Women with SCI (n=25) and 9 non-disabled/control women; Age: Mean (SCI) 32 yrs, SD=7.9, (control) 34 yrs, SD=8.2; Injury level: Cervical = 20, Thoracic = 5. Time since injury: mean 98 months, range 10-242. **Treatment:** Participants attempted to perform stimulation to orgasm in a controlled laboratory-based setting. **Outcome Measures:** Dependent Variables included: vaginal pulse amplitude, heart rate, respiration rate, blood pressure, subjective arousal and subscores on the Derogatis Sexual Functioning Inventory (DSFI).	1. All able-bodied participants achieved orgasm whereas 52% of SCI participants achieved orgasm. 2. Degree and type of SCI did not significantly relate to participants' ability to achieve orgasm, and there were no significant differences ($p > .05$) between subject groups on any of the dependent measures. 3. Participants with no lower extremity function took significantly longer than able-bodied participants to achieve orgasm. 4. Results of DSFI revealed that able-bodied participants acknowledged greater sexual satisfaction than the participants with SCI. 5. No consistent characteristics were identified that would allow prediction of which women with SCI would be able to experience orgasm.
Celik et al. 2014 Turkey Cross-Sectional Level 5 N=26	**Population**: 26 women (mean age 32.96±8.23 years, range=22-50 years), mean time post injury=168±88.73 months'; level of injury: 24 paraplegia, 2 tetraplegia **Treatment:** None **Outcome Measures:** Demographic questionnaires regarding marital status before and after SCI, sexual experience, pregnancy, miscarriages and abortions, and family members of the patients. Female Sexual Function Index (FSFI) and Beck Depression Inventory (BDI) were also administered.	1. 8 participants had regular sexual intercourse while one married woman did not have any sexual relationship after SCI. 2. 24 people received no information about pregnancy or sexual health after SCI. 2 people only received information when actively requested. All women were willing to receive information about sexuality after SCI. These patients expected the doctors to start the conversation about sexuality rather than asking about it. 3. FSFI revealed 5 of the 8 sexually active patients had sexual dysfunction. 4. BDI scores depicted that 3 out of the 8 sexually active patients had depression, whereas 14 out of 18 sexually inactive patients had depression.
Hajiaghababaei et al. 2014 Iran	**Population**: 105 women (mean age 41.0 years); AIS A-E, lesion level 8.6% cervical, 42.9% thoracic, 21.9% lumbar-sacral; etiology of SCI 80% car accident, 11.4% impact of object on body, 8.6% fall. **Treatment**: None **Outcome Measures:** Sociodemographic information, Female Sexual Function Index,	1. Women with SCI reported significantly higher levels of sexual dysfunction compared with normal controls. 2. 88% of SCI patients reported at least 1 type of sexual dysfunction, whereas only 37% of healthy controls reported sexual dysfunction. 3. Lack of vaginal lubrication was reported more frequent in SCI patients compared with controls.

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Cross-sectional study Level 5 N=105	Hospital Anxiety and Depression Scale, and Female Sexual Distress Scale-Revised questionnaire.	4. Women with SCI reported a significantly higher level of sexual distress compared with healthy women. 5. Sexual dysfunction was observed to be significantly higher in older patients, those with less education, patients with complete lesions, those with sexual distress and patients who were anxious and depressed.
Merghati-Khoei et al. 2017 Iran Case-control study Level 3 N=62 (31 SCI)	**Population**: 62 women; 31 women with SCI (mean age 35.42±6.51) and 31 case controls (mean age 33.77±4.02 years); mean time since injury 36.32±19.21 months; 13 AIS A, 10 AIS B, 5 AIS C, 3 AIS D; most common cause was traffic injuries (74.2%), falls (19.3%), surgery side effect (6.5%). **Treatment:** None **Outcome Measures**: Socio-demographic and reproductive traits questionnaire, Sexual Quality of life-Female (SQOL-F), Female Sexual Function Index (FSFI) and Spinal Cord Independence Measure (SCIM).	1. The SCI group performed worse in scores of quality of life, SQOL-F, and FSFI domains (except satisfaction). 2. In the case group, there was a significant positive correlation between SCIM score and the mean score of and SQOL-F, suggesting that higher levels of independence correlate with better sexual function and quality of sexual life in women with SCI. 3. Although our participants showed low sexual dysfunction, they tended to report moderate to poor quality of sexual life. 4. Results from regression models indicated that spinal cord injury, participant's education, occupation and duration of SCU were variables most affecting the quality of sexual life e.g., proportional regression showed that women with SCI had 4.2 times the odds of being in the poor or moderate quality of sexual life category, compared with the good quality.
Moreno-Lozano et al. 2016 Mexico Cross-Sectional Level 5 N = 295	**Population:** 83 women with SCI (mean age 42.8±15.87 years); mean time since SCI 65.16±117.65 months; 40 AIS A, 10 AIS B, 12 AIS C, 19 AIS D, and 2 AIS E; level of injury: 16 cervical, 26 high thoracic level, 34 low thoracic, and 7 lumbar. **Treatment:** None **Outcome Measures:** AIS, Female Sexual Function Index (FSFI, Modified Ashworth Scale for spasticity, Spinal Cord Independence Measure III Score. Other variables such as neurologic level, time since injury, age, relationship status, socioeconomic status, spasticity, use of antispasticity drugs, education level, antidepressant medication, offspring, work activities and neuropathic pain were also considered.	1. There is a high percentage of sexual dysfunction among women with SCI in this study (81.9%). 2. The study showed a negative correlation between age and the FSFI questionnaire (-0.384). 3. Results showed that the younger the person is, the better sexual function they have, and offspring decreased sexual function and work activities increased it.
	Population: 20 women (mean age=46 years, age range=27-77 years); average time since SCI=19.5 years; 11 had paraplegia and 9 had tetraplegia; 60% obtained SCI via car	1. Regardless of participants' personal definitions of sexual intimacy, 15 (75%) reported wanting to be more sexually active than they currently were.

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Fritz et al. 2015 USA Observational Level 5 N=20	accidents and 20% were obtained from gunshot wounds. **Treatment**: None **Outcome Measures:** In-depth qualitative interview re: sexual and reproductive health experiences of 20 women with SCI. Questions about overall health and physical functioning, accessibility of doctor offices, interactions with health care providers, gynecological health-seeking behaviors, sexuality and sexual behavior, and complementary and alternative medicine use.	2. The lack of bowel and bladder control was especially problematic for women who were developing new intimate relationships. 3. Participants believed that women with SCI "age faster" than able-bodied women and that they experienced age-related barriers to sex at an earlier age than their able-bodied peers. 4. Lack of support and education about sexual activity also contributed to the challenges faced by participants in our study. Only 1 woman received any education regarding sexual activity. 5. The life stage of participants and their level of adjustment to their injury affected how ready and interested they were in education about sexual intimacy and the types of concerns they reported about their sexual lives. 6. Ultimately, SCI can greatly alter a person's sexual identity and sexual self-esteem. Identity and self-esteem issues can further complicate a person's efforts to date potential partners or develop new intimate relationships.

Discussion

A survey of 105 women with SCI in Iran found that women with SCI reported significantly higher levels of sexual dysfunction compared with normal controls. Of all the participants in this study, 88% of SCI patients reported at least 1 type of sexual dysfunction, whereas only 37% of healthy controls reported sexual dysfunction. Lack of vaginal lubrication was reported more frequent in SCI patients compared with controls. Women with SCI reported a significantly higher level of sexual distress compared with healthy women (Hajiaghababaei et al. 2014). A US interview study with women with SCI reported that the lack of bowel and bladder control was especially problematic for women who were developing new intimate relationships (Fritz et al. 2015).

Vibratory and manual clitoral simulation in women with SCI improved sexual arousal (Sipski et al. 2005). Small studies (Sipski et al. 2000) have evaluated the use of sildenafil (Viagra) 50 mg in women with SCI and reported promising increases in subjective arousal especially when combined with manual and visual stimulation. However, a larger study (Alexander et al. 2011) with a sample size of 126 found that sildenafil lacked clinically meaningful benefits for women with SCI, as found similarly with other populations of women.

Conclusions

There is level 1b (Alexander et al. 2011) evidence that sildenafil does not result in clinically meaningful benefits in women who have sexual arousal disorder as a result of SCI.

There is level 2 evidence (from 1 weak RCT; Sipski et al. 2005) that supports the use of manual and vibratory clitoral stimulation to increase genital responsiveness in women with SCI.

There is level 5 evidence (Moreno-Lozano et al. 2016; Hajiaghababaei et al. 2014; Fritz et al. 2015) that women with SCI reported significantly higher levels of sexual dysfunction and sexual distress compared with able-bodied controls.

Sildenafil does not appear to result in clinically meaningful benefits in women who have sexual arousal disorder as a result of SCI.

Manual and vibratory clitoral stimulation may increase genital responsiveness in women with SCI.

6.2 Gynecological Health

Table 19: Gynecological Health

Author, Year; Country Score Research Design Total Sample Size	Methods	Outcome
Cramp et al. 2014 Canada Observational Study Level 5 N=7	**Population**: 7 women (age range= 24-61 years); AIS A-D, level of injury C5-L3. **Methodology**: Each participant completed an in-depth interview (average 85mins). **Outcome Measures:** 13 themes regarding sexuality, 10 themes regarding urinary incontinence (UI) on sexuality.	1. Themes regarding sexuality: fear of rejection, fear that their partners would leave them for able bodied women, fear of being hurt, disappointment to assume a more passive role during sex due to loss of mobility, more planning required, need to "fake orgasm" to please their partners. 2. Themes regarding the impact of urinary incontinence on sexuality: fear UI during sexual activity, fear of darker/odorous urine during bladder infection, preparations involving a pee pad, causes some women to withdraw from sexual activities. 3. Intimacy and the sexual experience were negatively affected by UI as a result of SCI, and by an excessive concern about autonomic dysreflexia.

There are conflicting reports on the occurrence of dysmenorrhea post-injury. Jackson and Wadley (1999) and Comarr et al. (1966) found a decrease and absence, respectively, whereas Axel et al. (1982) found the majority of women had no change in menstrual discomfort. Other gynecological problems reported by women with SCI include an increase in the incidence of urinary tract infections and vaginal yeast infections (Jackson & Wadley 1999). One qualitative study found a common pattern of diarrhea frequently occurring in conjunction with menstruation, leading to bowel accidents during transfers, and in turn to bladder and vaginal infections (Pentland et al. 2002). In terms of health promotion behaviour of women with SCI, women were found to be less likely to have routine mammograms and annual Papanicolaou smears (Nosek 1996; Jackson & Wadley 1999; Lavela et al. 2006) than women without disabilities; however, they had a similar practice of breast self-exam (Jackson & Wadley 1999). Inadequate knowledge of women with SCI regarding health care risks and health care needs, reliance on caregivers to facilitate preventative health practices and perceived access to competent health care providers were the main identified factors that had an impact on preventative health practices among these women (Persaud 2003).

Amenorrhea may occur immediately following injury, lasting 4-5 months on average (Jackson & Wadley 1999; Axel 1982). It is commonly believed that despite this initial delay in menstruation following traumatic SCI, fertility in women is unaffected. However, as DeForge et al. (2005) point out, there are no controlled studies comparing fertility rates with non-SCI cohorts and thus, there may be unknown effects of SCI on the rate of miscarriages and live births in couples trying to conceive. Jackson and Wadley (1999) found 70.3% of sexually active women use some form of contraception after injury and that fewer women used the birth control pill compared to before the injury.

Limited evidence suggests that comprehensive gynaecologic services may improve women's health behaviors, with no studies to date specifically on female contraception and SCI.

6.3 Pregnancy and Labour

In North America, women represent approximately a third of the SCI population (Ackery et al. 2004). Approximately 3,000 American women of childbearing age are affected by SCI (Cross et al. 1992). The ability of women to have children is not usually affected once their menstrual cycle resumes (Jackson & Wadley 1999). Few studies exist that specifically address women's health and pregnancy after SCI, but they show that women with SCI are able to conceive, carry and deliver a baby despite an increased frequency of complications during pregnancy, labour and delivery (Baker & Cardenas 1996; Jackson & Wadley 1999; Morton et al. 2013; Iezzoni et al. 2015; Bertschy et al. 2016).

Table 20: Pregnancy and Labour

Author, Year; Country Score Research Design Total Sample Size	Methods	Outcome
Bertschy et al. 2016 Switzerland Retrospective Interview study Level 5 N=17	**Population**: 17 women who are mothers with SCIs who gave birth over to 23 children over the last 15 years (age range= 18-54 years), mean age of SCI= 21yo, mean age of giving birth= 33yo, 13 paraplegic and 4 tetraplegics **Treatment**: None. Descriptive study of the most frequent secondary medical problems during the pregnancies of women with SCI. **Outcome Measures:** The questionnaire specifically asked about skin problems, bowel function, UTI frequency, mode of delivery, decubital ulcers, hospital admissions, medication changes, respiratory tract problems, and changes in neurogenic lower urinary tract dysfunction symptoms. In addition, patients were asked whether they took prophylactic measures against UTIs, decubitis, and deep vein thrombosis.	**1.** All participants practiced independent bladder management. 3 women changed their bladder management techniques during pregnancy. 5 women reported an increased bladder evacuation frequency during pregnancy, and 6 women reported a new onset or increase in incontinence. **2.** 10/17 women performed prophylactic measures against deep vein thrombosis where 9/10 of them used compressive stockings. No incidences of deep vein thrombosis were diagnosed during pregnancy. **3.** 10 women were hospitalized during the course of their pregnancies. Aside from urinary tract infections/ pyelonephritis, women were hospitalized for falls, hypertension, pneumonia, preeclampsia, pre-term labour or tachycardia. **4.** Although medical complications are not infrequent during pregnancy in women with SCIs, pregnancy and delivery in this group of women are possible without posing intolerable risks to the mothers or the children. **5.** 5 women had vaginal births (1 required general anesthesia) while 11 women underwent caesarean sections (8 general and 3 epidural anesthesia).
Iezzoni et al. 2015 USA Observational Study Level 5	**Population**: 22 women (34.8±5.3years); most were white, well-educated, and higher income; 8 had SCI, 4 had cerebral palsy, 10 had other conditions; 18 used wheeled mobility aids. **Treatment:** None **Outcome Measures:** Interviews.	**1.** Some women's obstetricians had height adjustable examination tables, which facilitated transfers for physical examinations. Other women had difficulty transferring onto fixed height examination tables and were examined while sitting in their wheelchairs.

N=22 (8 SCI)		**2.** Family members and/or clinical staff sometimes assisted with transfers; some women reported concerns about transfer safety. **3.** No women reported being routinely weighed on an accessible weight scale by their prenatal care clinicians. A few were never weighed during their pregnancies.
Iezzoni et al. 2015 USA Observational Study Level 5 N=22 (8 SCI)	**Population**: 22 women (34.8±5.3years); most were white, well-educated, and higher income; 8 had SCI, 4 had cerebral palsy, 10 had other conditions; 18 used wheeled mobility aids. **Treatment:** None **Outcome Measures:** Functional impairment-related complications during pregnancy.	**1.** 14 had cesarean deliveries (8 elective). **2.** Impairment-related complications during pregnancy included: falls; urinary tract and bladder problems; wheelchair fit and stability problems that reduced mobility and compromised safety; significant shortness of breath, sometimes requiring respiratory support; increased spasticity; bowel management difficulties; and skin integrity problems (this was rare, but many women greatly increased skin monitoring during pregnancy to prevent pressure ulcers). **3.** Women with mobility disabilities appear to experience problems relating to their functional impairments. **4.** Pre-conception planning and in-depth discussions during early pregnancy could potentially assist women with mobility disabilities to anticipate and address these difficulties.
Iezzoni et al. 2015; USA Cross-sectional study Level 5 N=1907	**Population**: 1907 women with traumatic SCI (age range=18-49 years). **Treatment**: None **Outcome Measures:** Data included SCI clinical details, functional impairments, participation measures, depressive symptoms, life satisfaction, and hospitalizations in the last year relating to pregnancy or its complications.	**1.** 2% of participants were hospitalized during the past 12 months for a reason related to pregnancy), which differedsignificantly by the years elapsed since injury. **2.** The highest rate occurred 15 years post injury (3.7%). **3.** Younger age at injury was associated with current pregnancy ($P<0.0001$). **4.** Those reporting pregnancy were more likely to be married or partnered, have sport-related SCI, have higher motor scores, and have more positive psychosocial status scores.

Bladder problems, spasticity, pressure sores, autonomic dysreflexia and problems with mobility can pose a threat to the pregnant woman with SCI (Baker et al. 1992; Jackson & Wadley 1999; Skrowronski & Hartman 2008). Frequent and sometimes lengthy hospital admissions during pregnancy can occur due to these and other reasons (Skrowronski & Hartman 2008). Impairment-related complications during pregnancy may include: falls; urinary tract and bladder problems; wheelchair fit and stability problems that reduced mobility and compromised safety; significant shortness of breath, sometimes requiring respiratory support; increased spasticity; bowel management difficulties; and skin integrity problems (Iezzoni et al. 2015). Although medical complications do happen during pregnancy in women with SCIs, pregnancy and delivery in this group of women are possible without posing intolerable risks to the mothers or the children (Bertschy et al.

2016). Population-based studies that determine the proportion of pregnancies and healthy births among women with or without SCI would be useful information (Horner-Johnson et al. 2016). Obstetric outcomes include higher rates of Cesarean-sections and increased incidence of low birth-weight babies (Jackson & Wadley 1999; Morton et al. 2013).

6.3.1 Pregnancy, Labour and Autonomic Dysreflexia

The below section is presented with tables in full in the Autonomic Dysreflexia chapter (see section on Prevention of AD during Pregnancy and Labour), but is presented in condensed form here.

There are increasing numbers of women with SCI who have healthy babies (Cross et al. 1992). However, during labor and delivery, women with SCI are at high risk of developing uncontrolled AD (Sipski 1991; Sipski & Arenas 2006).

Recognition and prevention of this life threatening emergency is critical for managing labour in women with SCI (McGregor & Meeuwsen 1985). The majority of women with SCI above T10 experience uterine contractions with only abdominal discomfort, an increase in spasticity and AD (Hughes et al. 1991). Numerous observational studies, case reports and expert opinions recommend adequate anesthesia in women with SCI during labor and delivery despite the apparent lack of sensation. However, there are only five studies (n=54) (Ravindran et al. 1981; Hughes et al. 1991; Cross et al. 1991; Cross et al. 1992; Skowronski & Hartman 2008) with observational evidence recording the management specific to AD during labour. The American College of Obstetrics and Gynecology emphasized that it is important that obstetricians caring for these patients be aware of the specific problems related to SCI (American College of Obstetrics and Gynecology 2002).

Autonomic dysreflexia is aggressively managed using sublingual nifedipine or intramuscular clonidine during labour, but pre-emptive epidural anaesthesia before or during labour is preferred: the latter can also be used in the postpartum period (Skrowronski & Hartman 2008). Difficulties exist because medications that lower blood pressure can potentially cause acute hypotension, which in turn may affect fetal bloodflow. Since labour can go undetected, regular monitoring of uterine tone and cervical dilation and effacement is important (Skrowronski & Hartman 2008). It should be noted that the acute onset of AD in labor can be difficult to distinguish from preeclampsia, but that making the correct diagnosis and initiating appropriate therapy can be life-saving (Pereira 2003).

Gap: The Influence of SCI on Breastfeeding
Source of evidence: **The Influence of Spinal Cord Injury on Breastfeeding Ability and Behaviour. Holmgren, Lee, Hocaloski, Hamilton, Hellsing, Elliott, Hultling & Krassioukov 2018 (in press). Journal of Human Lactation. 22 May 2018, 34(3):556-565**
Intro Although fertility is typically not affected, little is known about the challenges faced by women with SCI both during and after, including breastfeeding (Alexander, Aisen, Alexander, & Aisen, 2017). Lactation dysfunction following disability has been noted in the literature (Charlifue, Gerhart, Menter, Whiteneck, & Scott Manley, 1992; Morton et al., 2013); however, the extent of lactation dysfunction and influence of SCI on breastfeeding ability and behaviour is not well understood.

Study

To assess differences in breastfeeding experience and challenges, researchers in Stockholm, Sweden and Vancouver, Canada conducted a retrospective self-report study with mothers with SCI; participants were divided into two groups for analytic purposes – high-level SCI (Injury at T6 or above (n=18)) and low-level SCI (Injury below T6 (n=20)).

They found three significant differences between the mothers with high-level SCI and the mothers with low-level SCI:

- Women with high-level SCI breastfed exclusively (i.e., without formula supplementation) for an average of 2.78 months, a significantly shorter period of time than the mothers than in the low-level SCI group who breastfed exclusively for an average of 6.45 months.

- More women with high-level injury (14 or 77.8%) reported insufficient milk production or ejection versus women with low-level injury (7 or 35%).

- 39% of women with high-level SCI experienced an episode of Autonomic Dysreflexia (AD) whereas none of the women in the low-level SCI group experienced an episode of AD.

Management

Though this is the first study comparing breastfeeding in mothers with high-level or low-level SCI, there are some clinical implications we can draw from the work to date:

1) Mothers with SCI are capable of breastfeeding, but there may be significant barriers or problems with: disrupted lactation, impaired milk ejection, mobility challenges and AD. Clinicians should be aware of these difficulties and considerations for high-level versus low-level SCI.

2) Clinicians should be prepared to provide education and appropriate support (e.g., nursing pillows) to facilitate positioning during breastfeeding, a difficulty reported by most women in the study, regardless of their level of injury.

3) There is a need for more in-depth and longitudinal research to be conducted with mothers with SCI, particularly research that addresses blood pressure, AD and SCI. Blood pressure in people with SCI is lower than their able-bodied counterparts, especially when the SCI is cervical or high thoracic (Phillips & Krassioukov, 2015). As AD is typically initiated by any stimulus below the injury level, it is possible that an infant's suckling, breast engorgement or mastitis would be sufficient to trigger an AD episode.

The benefits of breastfeeding for the infant are well-known, but researchers have shown that mothers also experience benefits from breastfeeding including: higher levels of oxytocin, lower levels of blood pressure, lower rates of post-partum hemorrhage, and reduced maternal risk of ovarian and breast cancer (Johnston and Amico 1986; Light et al. 2000; Jonas et al. 2008; Ebina and Kashiwakura 2012; Chowdhury et al., 2015; Feng, Chen, & Shen, 2014; Horta & Victora, 2013b; Saxton, Fahy, Rolfe, Skinner, & Hastie, 2015; Victora et al., 2016). It would be useful to have evidence that showed if the benefits of breastfeeding for mothers with SCI outweighed the risks, particularly from a cardiovascular perspective.

Conclusion

There is level 4 evidence (Skowronsky and Hartman 2008) that women with SCI may give birth vaginally. With vaginal delivery or when Cesarean or instrumental delivery is indicated, adequate anesthesia (spinal or epidural) is needed to reduce the episodes of AD associated with birth.
There is level 4 and 5 evidence (from 2 case series and 2 observational studies) (Cross et al. 1992; Hughes et al. 1991; Cross et al. 1991; Showronski and Hartman 2008) that epidural anesthesia is preferred and effective for most patients with AD during labour and delivery.

Adequate anesthesia (spinal or epidural) is needed for vaginal, Cesarean, or instrumental delivery.

Epidural anesthesia is preferred and effective for most women with AD during labour and delivery.

6.4 Menopause

Little has been published on women's experience of menopause post-SCI. In their observational study, Dannels and Charlifue (2004) report presence of typical peri-menopausal symptoms in women with SCI, but at a lower rate compared to the general population. The authors hypothesize that symptoms could be mimicking those related to SCI, or that there is a lack of communication about peri-menopause between providers and women with SCI (Dannels & Charlifue 2004). Jackson and Wadley (1999) also found a lower frequency of menopausal symptoms post-injury, but higher than those women who had undergone menopause pre-injury. Conversely, Kalpakjian et al. (2010) reported that women with SCI transitioning through menopause experienced greater somatic symptoms, bladder infections, and diminished sexual arousal compared to women without SCI. Numerous clinical questions remain unanswered; particularly a lack of information and support for the gynecological health needs of women with SCI (Pentland et al. 2002). Given that obtaining access to gynecological and obstetric care is also a challenge for many women with SCI, it raises the question of whether women with SCI are receiving adequate sexual and reproductive health care (Nosek et al. 1996; Jackson & Wadley 1999).

7.0 Sexual Behaviour, Activity, and Satisfaction in Spinal Cord Injured Men and Women

There is a growing body of SCI literature on aspects of sexuality beyond genital sexual functioning and fertility. A large-scale (350 respondents over 4 European countries) cross-sectional questionnaire identified sexual activity as the area of greatest unmet need for persons with SCI (Kennedy et al. 2006). This is even more disconcerting given the importance placed on sexuality by men and women with SCI (Anderson 2004). Few intervention trials exist in this area, but a number of observational studies offer insight into post-injury sexual adjustment in terms of sexual behaviour and sexual satisfaction, including what factors are perceived as contributing to or hindering sexual satisfaction. A summary of these findings follows.

7.1 Sexual Behaviour

Table 21: Systematic Reviews on Sexual Behaviour

Author Year; Country Dates included in the review Total sample size Level of evidence Type of study Score	Methods Databases	Outcomes
Cramp et al. 2014 Canada Systematic Review AMSTAR= N=40	**Methods:** The first search used the following search terms ‘‘spinal cord injury, women, and sexuality”. Articles were included if they were published in 1990 or more recently, had a term related to sexuality or sexual function in the title, were written in English, and were available in full text. Forty articles were accepted and are included in this review. **Databases**: PubMed	**1.** A woman’s relationships, sexual desires, frequency of participation in sexual activities, the types of sexual activities she participates in, stimulation and arousal, orgasm and sexual satisfaction, as well as psychological influences on image and esteem have all been shown to be affected by SCI **2.** Spinal cord injury and its related consequences have a greater effect on the marital status of women than men and the marriage rate is considerably lower for women with SCI than for men with SCI. **3.** Women’s sexual desire and the frequency of sexual activity has been found to decrease after SCI **4.** The ability for a woman with SCI to become sexually aroused and to experience orgasm seems to occur less frequently after injury, but also seems to depend on the lesion level and completeness and on the type of stimulation that is used to induce the response. **5.** Women with SCI will typically experience a decrease in sexual satisfaction after injury. **6.** Having an active and satisfying sexual life after injury is associated with improved quality of life. **7.** After SCI, two types of neurogenic bladder exist, those being overactive and hypotonic bladders

1. Fisher et al. (2002) showed a significant increase in sexual activity between discharge from inpatient rehabilitation and 6-months later, while no further changes were found in the remaining 18 month followup and they suggested that the first 6 months post-discharge are optimal for sexual health interventions.
2. For women with SCI, psychological barriers to engaging in sexual activity include: feeling unattractive, low self-esteem, low sexual desire, lack of confidence in sexual ability and ability to satisfy a partner, and difficulty meeting a partner (Julia & Othman 2011; Kreuter et al. 2011; Kreuter et al. 2008).
3. Physical problems women with SCI cite as barriers to sexual activity include: impaired genital sensation, difficulty with positioning oneself, bowel and bladder problems, and vaginal lubrication (Julia & Othman 2011; Kreuter et al. 2011; Otero-Villaverde et al. 2015).
4. For women, longer duration of injury and lower level of injury (not extent of injury) were significant positive predictors of participation in sexual intercourse (Jackson & Wadley 1999).
5. For men, level and extent of injury have not been found to affect frequency of sexual activity (Alexander 1993).

6. The preferred type of sexual activity for men and women changes after injury. Preferred activities for women are kissing, hugging and touching, instead of penile-vaginal intercourse (Sipski & Alexander 1993) and for men, oral sex, kissing and hugging (Alexander et al. 1993).
7. Males reported engaging in masturbation significantly more often than females whereas females indicated being involved in intimate touching more often than males (Mona et al. 2000).

8. Males with SCI used condoms during penile-vaginal intercourse more often than females with SCI with their male partners. (Mona et al. 2000).
9. Both women and men remain interested in sexual activity after SCI, but level of desire and activity levels decrease (Charlifue et al. 1992; Alexander et al. 1993; Julia & Othman 2011; Miranda et al. 2016 (Alexander 1993; White et al. 1993; Jackson & Wadley 1999; Fisher et al. 2002, Lysberg & Severinsson 2003; Cardoso et al. 2008; Julia & Othman 2011; Kreuter et al. 2011).

7.1.1 Body Image and Acceptance

Table 22: Body Image and Acceptance

Author, Year; Country Score Research Design Total Sample Size	Methods	Outcome
Bailey et al. 2015 Canada Observational/Qualitative Level 5 N=9	**Population**: 9 individuals (5 females & 4 males, age range= 21-63 years), type of injury C3-T7 (AIS A-D, complete & incomplete SCI), years post injury 4-36 years **Treatment:** None **Outcome Measures:** Interview consisting of open-ended questions to determine participants' overall body image, how participants themselves defined body image, positive body image, and negative body image.	1. The following main categories were found: body acceptance, body appreciation and gratitude, social support, functional gains, independence, media literacy, broadly conceptualizing beauty, inner positivity influencing outer demeanour, finding others who have a positive body image, unconditional acceptance from others, religion/spirituality, listening to and taking care of the body, managing secondary complications, minimizing pain, and respect. 2. Unique characteristics (i.e., resilience, functional gains, and independence) were also reported demonstrating the importance of exploring positive body image in diverse groups.
Merghati-Khoei et al. 2017 Iran Qualitative Study Level 5 N=53	**Population**: 53 individuals with SCI; 41 men (mean age 24.4 ± 5.7 years) and 12 women (mean age 29.5 ± 8.3 years); duration of SCI for men (46.0 ±41.6 months) and for women (97.3 ± 99.6 months) **Treatment:** None **Outcome Measures**: Semi-structured Interview to understand how people with SCI understand marriage.	1. "Attractiveness," "able body for breadwinning," "sexually active," and "reproduction" were dominant concepts ('outer' scenarios) for how Iranian adults with SCI understood marriage. 2. The participants' inner scenarios (beliefs) revealed that marriage would be welcomed if a potential partner accepted them as a "whole person" regardless of their SCI condition. Adults with SCI do not ignore or reject marriage, however it was a lower life priority due to major health concerns that they had internalized.
Smith et al. 2015 USA Cross-sectional Study Level 5 N=218	**Population:** 218 individuals consisting of 120 males and 98 females (mean age=58, 7years); 38% had SCI. **Treatment:** None	1. Consistent with studies of able-bodied adults, sexual function was the strongest predictor of satisfaction. 2. Depression also predicted sexual satisfaction for women.

	Outcome Measures: Patient Reported Outcomes Measurement Information System's (PROMIS) sexual function item bank measuring sexual function, sexual satisfaction, and use of aids for sexual activity; PROMIS Pain Interference - Short Form; Patient Health Questionnaire-9 (PHQ-9); Mobility was measured with the 6-point Gross Motor Function Classification System	3. Use of aids for sexual activity varied by disability type and was generally associated with better function. 4. Lowest levels of sexual satisfaction were reported by men with SCI. 5. Depression may negatively impact sexual satisfaction in women, beyond contributions of sexual dysfunction, and effective use of sexual aids may improve function in this population.
Bozan et al. 2015 Turkey Observational Level 5 N=50	**Population**: 50 individuals- 29 male and 21 female patients; 10 had tetraplegia and 40 had paraplegia. **Treatment:** None **Outcome Measures:** Participants were asked to rate how significant each dysfunction (walking disorder, urinary incontinence, fecal incontinence, and sexual dysfunction) was in their view.	1. 50% of male participants and 36% of female participants had urinary incontinence 2. 46% of males and 32% of females had fecal incontinence. 3. All participants had at least impaired walking, with complete inability to walk in a certain proportion of patients. 4. 22% of males and 24% of female patients required walking-aids for walking. All male patients and 16 female patients reported sexual dysfunction. 5. Male patients regarded inability to walk as the most significant dysfunction, followed by sexual dysfunction, absence of voluntary defecation, and absence of voluntary urination. 6. In females, inability to walk and absence of voluntary urination were placed equal level of importance, followed by the loss of voluntary defecation. Interestingly, no female patients included sexual dysfunction in the ranking. 7. The observed gender difference in the perceived significance of dysfunction because of SCI may be due to anatomical, cultural and social factors.

Four studies have recently been published examing body image, acceptance and SCI. Qualitative studies indicate that people with SCI have concerns about their body, its appearance, and its functionality that are particular to sexual behaviour. Studies also indicate that physical dysfunction, in particular loss of bowel and bladder control and inability to walk, pose specific problems for people with SCI, their sexual functioning, and their body image acceptance.

7.2 Sexual Satisfaction

1. Sexual satisfaction is reportedly lower in both men and women after SCI (Alexander et al. 1993; Fisher et al. 2002; Reitz et al. 2004; Kennedy et al. 2006; Sharma et al. 2006; Mendes et al. 2008).
2. In an exploratory study of comparing African-American men and women with SCI, authors found that the women reported greater satisfaction with their sex lives than the men (Krause et al. 2004).
3. A comparison study of women with and without SCI, found that married women with SCI are as sexually satisfied as their able-bodied counterparts (Black et al. 1998).
4. In a study involving South Asian women with SCI, the women reported lack of sexual satisfaction more often than the men (Sharma et al. 2006). Conversely, in a survey study of Italian men and women with SCI, men reported significantly lesser satisfaction with sexual life post-injury than women (Sale et al. 2012).

5. Moreno et al. (1995) included sexual parameters in their report of outcome of continent urinary diversion with a catheterizable umbilical stoma in women with tetraplegia (n=3). They found that sexual satisfaction improved in the 2 women who were sexually active and body image improved in all 3 women.

Table 23: Sexual Satisfaction and Activity
Systematic Reviews

Author Year; Country Dates included in the review Total sample size Level of evidence Type of study Score	Methods Databases	Outcomes
Sunilkumar et al. 2015 India Systematic Review AMSTAR= N=19	**Methods:** Search key words and phrases: SCI and sexuality, paraplegia and sexuality, paraplegia and sexual functioning, Indian males and SCI, Indian males and paraplegia and sexual attitudes, and males and SCI and sexual functioning. Inclusion criteria included: English language, Indian male population with sexuality issues, all age groups history of a SCI with resultant paraplegia. The search yielded 457 articles but only 19 were specifically related to male views on sexuality. **Databases:** Cumulative Index to Nursing and Allied Health Literature (CINAHL), Medline, Applied Social Sciences Index and Abstracts (ASSIA), and Google Scholar.	1. 6 areas related to the topic of sexual functioning, SCI, and paraplegia were identified: sexual stigmatization, physiological barriers to sexual satisfaction, clinical aspects of sexual functioning, biomedical approaches to sexual dysfunction, partner satisfaction, and lack of accessibility to sexual education. **2.** SCI and sexual functioning affects a large segment of the male Indian population, yet most current research focuses on quantitative measurement with the emphasis on ejaculatory dysfunction, orgasm impairment, incontinence, and other physiological dysfunction.

Other Studies
Table 24: Other Studies on Sexual Health

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Cobo Cuenca et al. 2014; Spain Case Control Level 3 N=165 (85 SCI)	**Population**: 165 men with sexual dysfunction SD: Group A 85 with SCI (mean age= 35.61±8.13 years) and Group B 80 without SCI (mean age=46.31±10.69 years); duration of lesion 26.45±8.72 years; neurological level of injury 16 cervical, 46 thoracic, and 23 lumbar; 59 AIS A and 26 AIS B/C/D. **Treatment:** None **Outcome Measures:** The Sexual Health Evaluation Scale, the Fugl-Meyer Life Satisfaction Questionnaire scale (LISAT-8), the Hospital Anxiety and Depression Scale, the Evaluation of the Sexual Health Scale, and the Rosenberg's Self-esteem Scale.	1. In the SCI group, 89.4% (76) showed erectile dysfunction and 75.2% (64) reported anejaculation. 2. In the non-SCI group, 96.8% (75) showed erectile dysfunction and 58.7% (47) had disorders of sexual desire. 3. All of the participants reported a high general QOL and a high satisfaction with their QOL but their satisfaction with their sexual lives was only at the acceptable level. 4. Social QOL was significantly higher in the SCI group than the non-SCI group. 5. The QOL, self-esteem, and anxiety and depression levels are significantly correlated. 6. Sexuality and employment status are the areas where men with spinal cord injuries report less satisfaction.
Miranda et al. 2016 Brazil Cross-sectional Study Level 5 N=295	**Population**: 295 men (mean age 40.7±14.5 years) with SCI for more than 1 year (median time since SCI= 3.6 years; range= 1.6-7.0 years). **Treatment**: None **Outcome Measures**: Performance in various domains of sexual function was evaluated using the Male Sexual Quotient (MSQ) questionnaire and Sexual Health Inventory for Men (SHIM) questionnaires.	1. The prevalence of sexual dysfunction was as follows: decreased sexual desire (28.8%), lack of confidence for partner seduction (38.3%), dissatisfaction with sexual foreplay (48.8%), frustration with partner's sexual satisfaction (54.6%), inability to obtain an erection (71.0%), difficulty maintaining erection (67.8%), lack of full erections (64.4%), problems with ejaculatory control (89.4%), inability to achieve orgasm (74.5%), and overall sexual intercourse dissatisfaction (51.1%). 2. Only 70 men (23.7%) had an MSQ score >60, which represents highly or partially satisfied individuals; only 71 individuals (24.1%) had good erectile function or mild dysfunction based on the SHIM questionnaire (SHIM >17). 3. The Pearson correlation coefficient revealed a strong correlation between the MSQ and the SHIM (r=.826; 95% CI, .779 -.864).

Sunilkumar et al. 2015 India Qualitative Study Level 5 N=7	**Population:** 7 men living with SCI/paraplegia **Treatment:** None **Outcome Measures:** Semi-structured and open-ended interviews regarding participant perspective of living with SCI in India.	1. 7 themes emerged through qualitative methods**:** 1) recalling an active sexual life, 2) disconnection with sexual identity, 3) incongruence between a sense of physical and emotional capability, 4) isolation of spouse or sexual partner, 5) social readjustment of spouse, 6) perceived physical barriers to improved sexual functioning, and 7) coping and attempting ways of sexual integration. 2. All patients were sexually active prior to injury and all desired a healthy and active sexual life. A huge gap existed between sexual desire and physical capability, and quality of life (physiological, social, existential, emotional) has been compromised for both patient and family, causing anxiety, distress, and sadness. 3. There is a significant burden of added responsibility placed on the participants' spouses in that she must find a way of coping and attempting ways of sexual re-integration.
Otero-Villaverde et al. 2015 Spain Observational Study Level 5 N=32	**Population:** 32 women (mean age=29.8 years, range 13.9-59 years); most common cause of SCI trauma (72%); degree of disability 44% AIS A, 19% AIS B, 9% AIS C, and 28% AIS D **Treatment:** None. **Outcome Measures:** Spinal Cord Independence Measure (SCIM) version III.	1. The only factors that we found to be related to sexual activity were not having a stable partner (P=0.017) and a lack of sensation in the genital area (P=0.039). 2. When comparing the group of women who were sexually active with those who were not, variables such as age, neurological level, time since the SCI, ASIA or Spinal Cord Independence Measure score, urinary incontinence, chronic pain and spasticity were not related to sexual activity. 3. The median score on the SCIM scale was 68.7. 80% of the women maintained a stable relationship at the time of the SCI, and 9 of these (37.5%) subsequently lost their partner.

Pakpour et al. 2016; Iran Cross-sectional study Level 5 N= 93	**Population**: 93 men with SCI (mean age=37.8 years, age range=19-63 years, mean post-injury time=4.6 years). **Treatment**: None **Outcome Measures:** Levels of anxiety and depressive mood were assessed using the Hospital Anxiety and Depression Scale. Religious coping strategies were measured using the 14-Items Brief Coping Questionnaire. Erectile function was measured using the International Index of Erectile Function (IIEF).	1. SCI patients reported more positive religious coping than negative religious coping and higher levels of anxiety than depressive mood. 2. Multivariate regression analyses indicated that age, education, the American Spinal Injury Association impairment scale, anxiety, positive religious coping, negative religious coping and the duration of injury were all independent factors influencing erectile function in SCI patients.
Akman et al. 2015; Turkey Observational Study Level 5 N=47	**Population**: 47 men with spinal cord injuries (age range = 20-62 years, mean age = 35.2 years, mean time since injury=6.3±4.0 years) who were out of the spinal shock period and had their injury for more than 6 months. **Treatment**: None **Outcome Measures:** Social status, sexual activities, abilities, sexual education after injury, and erectile function evaluated by the International Index of Erectile Function-5 (IIEF-5) questionnaire.	1. 28 patients had lesions located above T10, 15 had lesions between T11 and L2, and 4 had lesions at the cauda equina. 2. Mean IIEF-5 score of group was 5.3 ± 4.1. 3. 61.7% of patients reported sexual activity and 93.6% reported some degree of erection. 4. 87.3% of men in this study had moderate to severe erectile dysfunction.

Table 25: Summary Table re: Issues affecting Sexual Satisfaction and/or Activity

Issues perceived to affect sexual satisfaction and/or sexual activity	Positive or Negative Impact	Reported in men/women or both	Studies supporting
Age (<18 years or >30 years old)	(–)	Women	Kreuter et al. 1994; Westgren et al. 1997; Ferreiro-Velasco et al. 2005
Time since injury	(+)	Both, Men	Black et al. 1998; Tepper et al. 2001; Anderson et al. 2007; Lombardi et al. 2008; Pakpour et al. 2016; Choi et al. 2015
Severity of injury	(–)	Both, Men	Mona et al. 2000; Anderson et al. 2007; Kreuter et al. 2008; Sale et al. 2012; Pakpour et al. 2016
Bladder management problems (incontinence/UTI's)	(–)	Both, Women	White et al. 1993; Richards et al. 1997; Jackson & Wadley 1999; Benevento & Sipski 2002; Blok & Holstege 1999; Anderson et al. 2007; Kreuter et al. 2008; Biering-Sorensen et al. 2012; Sale et al. 2012; Moreno et al. 1995; Bozan et al. 2015; Otero-Villaverde et al. 2015
Spasticity	(–)	Both, Women	Jackson & Wadley 1999; Anderson et al. 2007; Biering-Sorensen et al. 2012, Otero-Villaverde et al. 2015
Fecal incontinence	(–)	Both, Women	Charlifue et al. 1992; White et al. 1993; Richards et al. 1997;

Issues perceived to affect sexual satisfaction and/or sexual activity	Positive or Negative Impact	Reported in men/women or both	Studies supporting
			Kreuter et al. 2008; Biering-Sorensen et al. 2012; Bozan et al. 2015
Autonomic dysreflexia/Blood Pressure	(–)	Women	Charlifue et al. 1992; Jackson & Wadley 1999; Anderson et al. 2007
Pressure ulcers and pain	(–)	Both, Women	Biering-Sorensen et al. 2012; Otero-Villaverde et al. 2015
Sexual self esteem	(+)	Both	Mona et al. 2000
Making a female partner pregnant	(+)	Men	Biering-Sorensen et al. 2012
Altered body image	(–)	Both, Women	Bozan et al. 2015; Smith et al. 2015; Bailey et al. 2015; Merghati-Khoei et al. 2017; Richards et al. 1997; Elkland & Lawrie 2004; Reitz et al. 2004; Kreuter et al. 2008
Altered genital sensation	(–)	Women, Men	Richards et al. 1997; Anderson et al. 2007; Kreuter et al. 2008, Miranda et al. 2016; Otero-Villaverde et al. 2015; Akman et al. 2015
Sexual desire	(+)	Both, Men	Phelps et al. 2001; Reitz et al. 2004; Miranda et al. 2016
Lack of a partner	(–)	Women	Jackson & Wadley, 1999; Kreuter et al. 2008; Otero-Villaverde et al. 2015
Quality of intimate relationship/relationship satisfaction	(+)	Both/Men	Jackson & Wadley 1999; Phelps et al. 2001; Reitz et al. 2004, Lombardi et al. 2008; Smith et al. 2015
Repertoire of sexual behaviour	(+)	Men, Women	Richards et al. 1997; Phelps et al. 2001
Partner as caregiver	(–)	Women	Kreuter et al. 1996; Black et al. 1998; Pentland et al. 2002
Perceived partner satisfaction	(+)	Men, Women	Phelps et al. 2001; Ekland & Lawrie 2004; Miranda et al. 2016
Partner's understanding of sexual needs	(+)		Kreuter et al. 1996
Level of social and vocational activity; outgoing personality; acceptance of the disability**	(+)		Kreuter 2000
Inadequate vaginal lubrication	(–)	Women	Charlifue et al. 1992; Jackson & Wadley 1999; Anderson et al. 2007
Ability to move	(+)	Both	Reitz et al. 2004; Anderson et al. 20à7; Kreuter et al. 2008; Bozan et al. 2015

Issues perceived to affect sexual satisfaction and/or sexual activity	Positive or Negative Impact	Reported in men/women or both	Studies supporting
Mental well-being	(+)	Both, Men	Reitz et al. 2004; Kreuter et al. 2008, Smith et al. 2015, Pakpour et al. 2016
Sexual education and counselling	(+)	Women, Men, Both	White et al. 1993; Westgren et al. 1997; Hess et al. 2007; Valtonen et al. 2006; New et al. 2016; Akman et al. 2015
Peer support	(+)	Women, Both	Richards et al. 1997; Fisher et al. 2002; Pentland et al. 2002; Ekland & Lawrie 2004
Sexual arousal	(–)	Men	Cardoso et al. 2008; Miranda et al. 2016
Orgasm intensity	(–)	Men	Cardoso et al. 2008; Miranda et al. 2016

**correlates positively with partner availability thereby indirectly related to sexual satisfaction

Discussion

Research shows that sexual function is important to people after SCI. A systematic review of 24 studies of health and life priorities for persons with SCI determined that motor function, bowel, bladder and sexual function emerged as the top four functional recovery priorities (Simpson et al. 2012). Two individual studies using community samples showed that the most common significant problem for people with SCI was sexual dysfunction (reported at 41% - New 2016; and 60.8% Park et al. 2016).

Despite the importance of sexual adjustment to overall quality of life, there have been few studies addressing this topic and few investigating the effectiveness of interventions on sexual satisfaction and adjustment to SCI. A number of studies have reported that the frequency of sexual activity and desire for sexual activity decreases after injury in both men and women (Julia & Othman 2011; Kreuter et al. 2011). The issues that are perceived to affect sexual satisfaction and/or sexual activity are multi-faceted. However, common barriers to sexual satisfaction from the effects of SCI include bladder and bowel problems, as well as other impairments resulting from the severity of injury (e.g., spasticity, lack of mobility) (Biering-Sorensen et al. 2012; Moreno et al. 1995; Anderson et al. 2007). Researchers suggest that improving sexual satisfaction, information and specific programs during rehabilitation can help women with SCI explore and investigate new erotic possibilities, thereby improving their self-esteem and social relationships (Otero-Villaverde et al. 2015).

Sexual dysfunction following SCI may take many forms, including: decreased sexual desire, lack of confidence, dissatisfaction with sexual foreplay or intercourse, frustration with partner's sexual satisfaction, inability to obtain or maintain a full erection or to achieve orgasm, and problems with ejaculatory control.

Common barriers to sexual satisfaction include bladder and bowel problems, as well as other SCI-related impairments (e.g., spasticity, lack of mobility).

Continent urinary diversion in women with tetraplegia may result in improved self-image, quality of life, and greater sexual satisfaction.

8.0 Sexual Education and Counselling

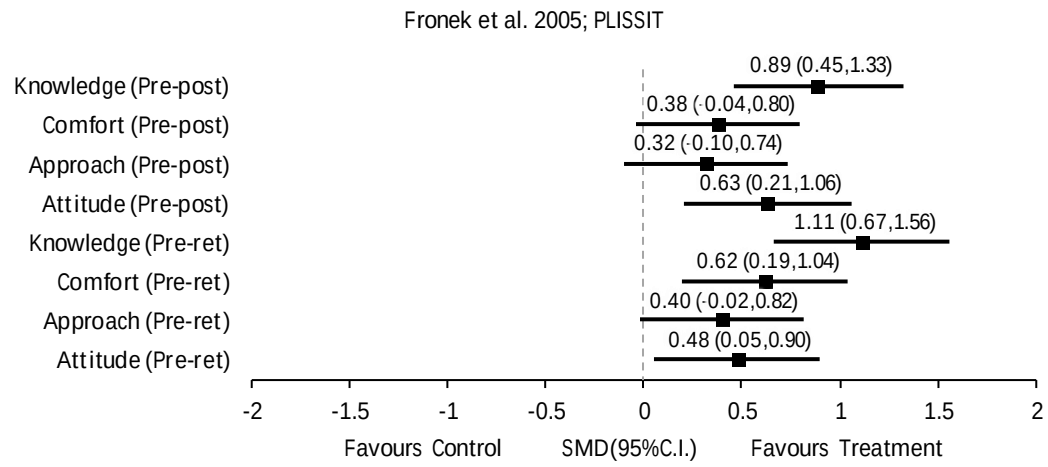
8.1 Sexual Health Education for SCI Clinicians

A spinal cord injury can have consequences on many different domains, which in term can affect sexual health. A variety of health professionals (e.g., psychologists, physical therapists, nurse, physician, sexual health clinician) may be involved in treating these domains, as well as discussing the impact of SCI on aspects of sexual function. In fact, research shows that patients expect their health care professionals to bring up sexuality and sexual health, but health care professionals can be reluctant to do so because of their lack of knowledge, fear of offending the patient, or discomfort in asking questions that address sexual concerns (Althof et al. 2013).

People with disabilities often express their sexual health concerns to the people they feel most comfortable with, so it is recommended that all persons working with people with SCIs understand the effects of SCI on sexual function (Biering-Sorenson et al. 2013, p. 613). Education and support to health professionals is critical to ensure that these professionals are able to comfortably and knowledgably address relevant patient concerns about sexual health.

Table 26: Sexual Health Education for SCI Clinicians

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Fronek et al. 2005; Australia RCT PEDro=6 Level 1 N=89 2011; 2 year follow-up N=37	**Population:** Staff from an SCI rehab service; Treatment group (n=44): 31 nurses, 1 medical practitioner, 6 allied health staff, 6 community staff; Control group (n=45): 32 nurses, 2 medical practitioners, 5 allied health staff, 6 community staff; Previous sexuality training: yes (n=25), no (n=50); Previous SCI sexuality training: yes (n=18), no (n=57). 2 year follow-up population: 25 from treatment group, 12 from control group; nurses (n=23), medical practitioners (n=1), allied health staff (n=3), community staff (n=10). **Methods:** Staff members were randomized to treatment or control groups across disciplines. A consumer driven sexuality training program was developed then delivered in a series of 1-day workshops to the treatment group. Focus groups and written questionnaires were conducted at the 2 yr follow-up. **Outcome Measures:** KCAASS (Knowledge, Comfort, Approach and Attitudes towards Sexuality Scale); focus group discussion at 2-year follow-up with written feedback to open-ended questions on the KCAASS.	1. Significant improvement in all domains (knowledge, comfort, approach, and attitude) for treatment group compared to control group. 2. Significant changes in all domains (knowledge, comfort, approach, and attitude) were maintained at 3-month follow-up. **At 2 year follow up:** 3. No significant between-group differences in knowledge, comfort, or attitudes (training of the control group at the 4 month period equalized the groups). 4. Significant within group changes in the treatment group on knowledge, comfort, and approach. 5. Significant change over time in both treatment and control groups on attitude subscale.
	Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- to post-intervention data and pre-intervention to retention/follow-up data	

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
		
Sawyer et al. 1983; USA PEDro=5 RCT Level 1 N=22	**Population:** 22 graduates in rehabilitation counselling. **Methods:** participants were randomized to experimental (micro-counselling) and control groups (didactic lecture) to test the effectiveness of this training approach in counsellors' ability to respond appropriately to sexual concerns expressed by SCI women. Micro-counselling group (n=11) was shown a videotape modelling specific counselling skills followed by discussion, demonstration, and role-play. Didactic lecture group (n=11) had traditional lecture and classroom discussion. **Outcome Measures:** micro-counselling interaction rating scale (developed using the same response cues that appeared on the video model).	1. A main training effect was found when comparing the experimental and control groups, and in regard to pre- vs. post-testing a significant main effect was found. 2. The micro-counselling group differed significantly in the pre-and post-test. 3. On the post-test the groups differed significantly with the largest gain demonstrated by the micro-counselling group and little change demonstrated by the didactic lecture group.
Simpson et al. 2006 New Zealand Prospective Controlled trial with pre- and post-evaluation Level 2 N = 99	**Participants:** 74 rehabilitation staff and a control group of 25 other staff members. **Treatment:** Two workshops were held at major rehabilitation centres in New Zealand (control group did not attend). **Outcomes:** The Sex Attitude Scale, as well as a knowledge test, a self-rating inventory of skills and clinical activity, and a single-item measure of the degree of staff comfort.	1. Workshop participants showed significant increases in knowledge, skills and comfort after the workshop, and a number of these gains were maintained at the six-month follow-up. 2. There was an associated increase in reported staff activity (for the treatment group only) addressing patient/client sexual health concerns in the six months to follow-up, compared to a similar time period preceding the workshop.
Fronek et al. 2011 Australia Follow-Up study Level 4 N=37	**Population:** 37 of the original 89 participants from Fronek et al. 2005 who completed all three previous assessments. 23 nurses, 1 medical practitioner, 3 allied health staff and 10 community staff. **Treatment:** None - follow-up of trainees in Fronek et al. 2005.	1. For the experimental group, 2 year follow-up scores did not differ significantly from scores at post-training or 3 month follow-up for Knowledge, Comfort and Approach subscales. Attitude scores were significantly lower at 2 year follow-up than at post-training. 2. For the control group, Knowledge and Attitude scores were significantly higher at 2 year follow-up than at 3-month follow-up.

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	Outcomes: The KCAASS was administered approximately 4 months later (no significant differences re: scores on the KCAASS between those who participated at 2 year follow-up and those who did not). Focus group - participants were asked to comment about the benefits and challenges of the training.	3. From the focus group, participants said that the multidisciplinary rehabilitation setting 'helped to understand views of others' and 'foster respect of other team members'. It was suggested that 'self-directed learning packages' or a 'combination of learning options' would be useful to update staff.
Burch 2008; USA Pre-post Level 4 N=402	**Population:** 402 health care professionals who provided services to SCI patients. PTs (n=176), OTs (n=93), speech therapists (n=46), PT assistants (n=22), OT assistants (n=8), nurses (n=50), physicians (n=7). **Methods:** A pre-intervention questionnaire to assess levels of knowledge, attitudes, and self-efficacy providing care to SCI persons who may be LGBT. Videotape for health care professionals on providing services to LGBT persons was shown and a post-briefing diversity-training questionnaire was given. **Outcome Measures:** pre- and post-intervention questionnaires on knowledge, attitudes, and self-efficacy.	1. 317 strongly agreed that watching the videotape increased their confidence levels in providing services for people who may be LGBT. 2. Effect of the training program: - Increased knowledge: Strongly agree (SA; 18.2%), Moderately agree (MA; 63.9%), Agree (A; 14.9%), Moderately disagree (MD; 3%) - Increased Attitudes: SA (24.6%), MA (65.9%), A (9%), MD (0.5%) - Increased Self-efficacy: SA (78.9%), MA (12.9%), A (6.7%), MD (1.5%)
Tepper 1997; USA Pre-post Level 4 N=18	**Population:** 18 staff who worked ≥50% of the time in SCI rehabilitation; nurses (n=10), psychologists (n=2), OTs (n=1), physiatrists (n=1); Time working in SCI rehab: 9 months to 22 years. **Methods:** An interdisciplinary continuing education and training curriculum addressing the provision of comprehensive sexual health care for professionals was implemented as a 3-day experiential, massed-learning pilot workshop. **Outcome Measures:** For evaluating the workshop: 1) matched pre- and post-test (summative evaluation) 2) participant journals, 3) participant observation by research assistant, 4) Objective Structured Clinical Examination (OSCE), 5) post-workshop program evaluation (formative evaluation) 6) 5 month follow-up (questionnaire and phone interview).	1. The workshop significantly increased tested knowledge of the sexual response cycle and the possible effect of SCI, staff self-assessed comfort, knowledge, and skill from pre- to post-test. 2. Behavioural changes reported post-workshop: - Incorporated some definable change in provision of sexual health care to patients (yes=17, attributed: 1.65) - Sought additional information about effects of SCI on sexual function (yes=16, no=1, attributed: 1.65) - Showed greater comfort in talking with patients about their sexual questions/concerns (yes=17, attributed: 1.59) - Improved skills in providing comprehensive sexual health care (yes=17, attributed: 1.82) - Increased skills in identifying sexual concerns (yes=15, no=2, attributed: 1.31)
Cole & Stevens 1975; USA Pre-post Level 4 N=199	**Population:** 199 SCI professionals; counsellors (n=142), social workers (n=9), nurses (n=8), psychologists (n=7), OTs (n=6), physicians (n=2), speech therapists (n=1), clergy (n=1), other (n=23). **Methods:** Creation and implementation of a 1-day seminar on sexual function in SCI for rehabilitation professionals. **Outcome Measures:** questionnaires pre- and post-seminar.	1. Did sexual counselling with their clients: - No (n=138), Yes (n=61) - Inappropriate to their work (n=14) - 50 expected to do sexual counselling, 13 of them not doing it 2. Post-seminar evaluation (n=132): - Beneficial/somewhat beneficial (95%) - Not beneficial (5%) - Harmful/somewhat harmful (3%) - Not harmful (97%)

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
		3. 87% felt a program like the seminar should be part of professional training for rehab professionals, 13% had reservations/opposed the idea.
Held et al. 1975 USA Pre-Post Level 4 N= 95	**Population**: 1st Sample = 76 people with SCI/their partners; 2nd Sample = 119 Rehabilitation professionals; 3rd Sample = 51 Rehabilitation professionals). 51% men, 49% women. **Treatment**: Sexual attitude and Sexual counselling workshops for spinal cord injured adults, their partners and rehabilitation professionals. Slides, films, panels and large/small group discussions. The 3rd workshop (sexual history taking/sexual counseling) included an interview demonstration and practice for participants in small groups. **Outcome Measures:** 1st sample – (post- only) asked participants did they enjoy, learn, and would they recommend. 2nd sample – (pre-post) asked about involvement in sexual counseling and education and how the seminar affected. 3rd sample – survey re: attitudes towards sexual activities completed before and 6 weeks after the workshop.	1. 1st sample – 96% were glad they attended, 92.1% thought the workshop was worthwhile, 82.8% stated that they personally benefitted, 90.8% would recommend the program to others. 2. 2nd sample - 97.3% reported that the workshop had given them ideas. 3. 3rd sample –67.3% frequently had the opportunity to do sex counseling, 100% thought that they should, but only 51% did it sometimes. Only 18% felt effective, 54% felt uncomfortable, and 4% felt ineffective. 63% said they had no specific training and limited experience; 4% said they were trained and experienced. 4. 3rd sample – 96% said the workshop had been a good learning experience. Participants were significantly more accepting towards 4 of the 9 listed sexual behaviors and who they were appropriate for after the workshop.
Milligan & Petchers 1988 USA Pre-Post Level 4 N =609	**Participants:** 609 participants completed pre-test and post-test questionnaires (response rate = 73.5%). 123 participants answered the follow-up telephone survey (15%). Trainees included physicians, nurse practitioners, clinic assistants, social workers, educators, and residential program managers. **Treatment:** 37 different workshops on aspects of sexual health, including one workshop specifically on issues re: the physically disabled. **Outcomes:** Pre/post-test measuring knowledge and skills. Follow-up interviews, asking whether workshops resulted in improved knowledge and skills on the job and how they used/disseminated information on the job.	1. Participants significantly improved knowledge and skills after series of training workshops. 2. Specific workshop on sexuality and the physically disabled – participants showed no significant difference in knowledge or skills after training. 3. Follow up questionnaire indicated that the majority of respondents: gained new knowledge, improved understanding, dealt better with problems, informally shared information, and had the opportunity to use what was learned, but took no action and delivered no different services based on attending the workshops.
Giannoten et al. 2006 Netherlands Pre-Post Level 4 N=302	**Population:** 302 rehabilitation professionals attended at least one training session. Participants were nurses (36.2%) physicians (15.1%), occupational therapists (14.3%), physical therapists (13.6%), psychologists and social workers (9.3%), speech/language therapists (2.5%), and other disciplines (8.9%). Their (mean) experience in rehabilitation was 9.1 years and 11.2% had attended post-study courses in sexology before.	1. All professional groups said that they needed training in sexuality (Doctors, 71%; Nurses 92%; PTs/OTs/SLPs 71%). 2. Mean general opinion of the training was between ‘moderately good’ and ‘good’, and only a small percentage of participants expressed a negative opinion on the usefulness of the training.

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	Treatment: The training consisted of seven modules (based on the PLISSIT model) and was offered in six sessions of three hours. Lectures, discussions, role-playing, and simulation of cases/team meetings, and homework consisting of talking about sex with their rehabilitation patients. **Outcomes:** Each participant completed 3 questionnaires (pre-, post-, and 3-4 months after training) and a Dutch translation of the KCAASS.	3. Knowledge, recognizing problems and communication skills all improved significantly after training, and improvements were generally maintained at follow-up.
Post et al. 2008 Netherlands Pre-Post Level 4 N=283	**Participants:** 283 Participants were nurses (35.2%), physicians (14.3%), physical therapists (14.0%), occupational therapists (13.7%), psychologists and social workers (10.2%), and other disciplines (12.6%). Mean age was 39 years, 83% were female and their mean experience in rehabilitation was 9.1 years (same sample as Giannoten, 2006). **Treatment:** The training for physicians, psychologists, and social workers was three units of 3 h each and for the other disciplines two units of 3 h each. The training used exercises on actively ''talking sex'' and role-playing exercises with volunteer patients. **Outcomes:** Each participant completed 3 questionnaires (pre-, post-, and 3-4 months after training) and a Dutch translation of the KCAASS (same measures as Gianotten et al. 2006).	1. Multivariate testing showed significant differences between disciplines and significant improvement between the first and second measurement. 2. Physicians improved on all KCAASS subscales, the group of other disciplines improved in Knowledge, Comfort, and Approach, Occupational therapists improved in Knowledge and Approach, psychologists/social workers and nurses improved only in Knowledge, and physical therapists did not show any change at all. 3. 88.8% had not taken courses in sexology before this training; despite this 81.7% of participants felt that discussing sexual concerns with patients was part of their job (Range - 99.5% physicians- 60.5% physical therapists). 4. The duration of the training was judged ''good'' by 76.5% of participants and the possibilities to apply the lessons learned were judged positively (moderately, good or very good) by most groups.
Pieters et al. 2017 Netherlands Pre-Post Level 4 N = 74	**Participants:** 74 participants completed the pre- and post-test questionnaires. Participants included 13 medical (doctors, nurses, physician assistants), 13 psychosocial (5 psychologists, 7 social workers, 1 chaplain), and 48 paramedical (24 physiotherapists, 18 occupational therapists, one cognitive therapist, one dietician, four speech therapists). **Treatment:** Training, based on the PLISSIT model, consisted of six half-day sessions and multiple modules, including some disability-specific sexual health information. Interactive teaching, exercises, role-playing, presentation of sexual aids, and information delivery. **Outcomes:** A pretest-posttest design used the Dutch adaptation of the KCAASS, as well as two questionnaires where participants would rate the number of times sexual issues were discussed	1. The number of times that sexuality was discussed with patients increased significantly after the training. Rehabilitation staff received more questions from patients, initiated speaking about sexuality with their patients, and discussed sexual health during meetings much more frequently. 2. After finishing the training, participants reported that they "recognized sexual problems" more frequently (36.4% to 59.7%), "gave permission to talk about sexual problems with patients" (66.2%), "gave advice or specific suggestions" (31.2%), and "exchanged relevant information with colleagues" (29.9% to 48.3%), but that there was still no difference in the number of referrals. 3. Staff's knowledge, attitude and skills and comfort increased significantly after receiving the training, as measured by the KCAASS.

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	and how good they were at recognizing and treating problems.	4. There were no differences between professional groups, except PTs/OTs who initiated sexuality discussions compared to the other groups.
Chubon 1981 USA Pre-Post Level 4 N=15	**Participants:** 15 students from graduate programs and rehabilitation agencies in the Greater Pittsburgh area, representing the fields of rehabilitation counseling, special education, social work, counselor education, psychology, and physical therapy. **Treatment:** A full 2 credit elective course including broad range of topics re: Sexual Health, including the Impact of Spinal Cord Injury. Information delivery, modeling, small group/class discussions, role play, films, all intended to aid with desensitizing students. **Outcomes:** State-Trait Anxiety Inventory Form, Irvine Sexual Attitude and Knowledge Inventory, Marlowe-Crowne Social Desirability Scale, Personal logbooks, a course evaluation survey, and a multiple choice exam for testing knowledge.	1. There were significant increases in knowledge levels and in sexual attitudes toward greater acceptance, both with regard to sexuality in general and of handicapped persons. 2. The students indicated that the course content met their needs and was of value to them both professionally and personally. 3. No differences in pre-course scores, and attitudes or knowledge levels, between sexes or married/single students, between age and any of the experimental measure scores. Anxiety and social desirability scores were all inside of the norm.
Mims et al. 1974 USA Pre-post Level 4 N = 143	**Participants:** 143 Medical, Nursing and Health/Social sciences students at graduate and undergraduate level. **Treatment:** 5 days of didactic sessions, films, role plays, and small group discussions on topics of human sexuality including sex and the handicapped. **Outcome:** Sex Knowledge and Attitude test (SKAT)	1. The total group Knowledge scores and 3 of 4 Attitudinal subscales increased significantly from pre- to post. 2. Med students increased Knowledge scores and 2 of 4 Attitude scales; Nursing students increased Knowledge scores and 3 of 4 Attitude scales; Other students increased Knowledge scores and 1 of 4 Attitude scales. 3. There were no differences between Medical and Nursing students on Knowledge or Attitude scores.
Cohen et al. 1994 Canada Pre-Post Level 4 N = 164	**Participants:** 164 Undergraduate students in 4 programs at McMaster University – Medicine, Nursing, PT and OT – completed the course and both pre-and post-tests. **Treatment:** A two-day interprofessional workshop in sexuality using lectures, audiovisuals, and small group discussions. **Outcome:** The Sexual Opinion Survey (SOS) and a 46 item sexual knowledge test were administered pre- and post-workshop.	1. No differences between 4 groups in either pre- or post-test scores. 2. Total group and Nursing group improved attitudes and comfort significantly from pre- to post-training. 3. Total group, Nursing and Physiotherapy showed significant increases in knowledge from pre- to post-training.
Cohen et al. 1996 Canada Follow-up (Post evaluation 18 months later) Level 4 N = 76	**Participants:** 76 students from the OT/PT, Nursing, or Medical programs that originally took part in Cohen 1994. **Treatment:** None (18 month follow-up to Cohen et al. 1994).	1. Significant gains reported from post-workshop to follow-up on Knowledge and Attitude scores. 2. Participants reporting additional sexuality education showed significantly higher Attitude scores from post-workshop to 18 month follow-up.

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	Outcome: 3 questionnaires to assess Sexual Attitude, Comfort and Knowledge (same questionnaires as Cohen 1994), plus asking participants if they had participated in any additional education re: sexual health.	
Hay et al. 1996 Canada Follow-up (Post Evaluation 18 months later) Level 4 N = 30	**Participants:** 30 Occupational and Physical Therapy students. 90% female with an average age 25 (some of the same participants from Cohen et al. 1994). **Treatment:** None (follow-up to workshop reported in Cohen et al. 1994). **Outcomes:** Same measures on Sexual Attitudes, Comfort, and Knowledge as assessed during original workshop collected at 18 month follow-up.	1. No differences between OT and PT students on any of the three measures (attitudes, comfort, knowledge) in the 18 month follow-up results. 2. No differences between the 11 students who reported additional sexuality education on any of the three measures. 3. There were no changes from the post workshop results to the 18 month follow-up.
Neistadt 1986 USA Cross-Sectional Level 5 N = 288	**Participants:** 288 students from Boston school of OT at Tufts university who have taken the sexuality counseling module. **Treatment:** Three sessions of 3-hour each devoted to the knowledge areas and skills re: sexual health including the ways in which various disabilities might influence sexual functioning. **Outcomes:** Post-course evaluation	1. 100% of the students felt the module was a pertinent part of their academic program at BSOT. Many reported using the information and skills they gained in the module during their fieldwork experiences. 2. (For 48 students taking the course 1 year prior to publication) 100% met course objectives in Anatomy, Comfortableness in discussion, Development, and Sexual Acting out; 95.8% met objectives in Counseling strategies and the Sexual response cycle, 89.6% met objectives in Sexuality and Disability, and 68.8% met course objectives in Neurological control.
Cole, 1973 USA Cross-sectional Level 5 N= 55	**Population:** 55 participants, 20% paraplegic, 20% quadriplegic; 15% spouses of people with SCI; 45% = health professionals/friends of participants. Age = 16-59 (range). Time since injury – Range = 2-15+5 years; (90% more than 3 years since injury). **Treatment:** A 2-day program for people with SCI and able-bodied persons was developed to deal with sexual attitudes. Slides, speakers, panels and films were sequenced to introduce progressively more explicit and anxiety-evoking sexual material (e.g., pornography), as well as specific content re: aspects of human sexuality of the spinal cord injured person. **Outcomes:** Pre-workshop questionnaire assessed sexual knowledge, attitudes, and behaviors of the participants. A post-training evaluation asked if participants were glad they attended, and if it had been helpful or harmful.	1. 90% of the paraplegics and 80% of the quadriplegics indicated that never or seldom did the hospital staff initiate discussions re: the sexual implications of spinal cord injury. 2. 50% of male/female quadriplegics to 87% of able-bodied males agreed or strongly agreed that an active sex life is important to personal happiness of people with SCI. 3. 98% of respondents said the workshop had been helpful, 2% said it had no effect, and no one said it had been harmful. 4. 98% of the participants agreed that a program dealing with human sexuality should be offered on a voluntary basis for all spinal cord injured adults. 5. Able-bodied and disabled participants agreed that addressing sexual health should be offered during the first hospitalization/certainly within the first 6 months after injury.
Katzman 1990 USA	**Participants:** 78 nursing students – 73 female, 5 male	1. One participant said: "This class has led me to believe in sexual health care by nurses. I would have been content to leave it to the

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Qualitative (Description of class and quotes from students only) Level 5 N = 78	**Treatment:** A course focusing on the effect of illness, disability, and medical treatment on sexual functioning, as well as sex education of patients and clients. **Outcomes:** Post-course interview with participants.	doctors or social workers who I thought were taking care of it…I was not aware of how little attention was given to patients' sexual concerns by any health professional until I started looking for it. I now believe that nurses, more than anyone, can help bring about positive changes in these areas." 2. Another student said: "I think more resources for sexuality teaching should be available for nurses. I have cared for many patients who could have used this type of intervention, but I was not prepared to give it."
Blanchard, 1976 USA Qualitative Level 5 N=56	**Population:** 56 nursing staff completed the program. **Treatment:** 4 meetings of 1.25 hours each dealing with a) personal taboos that prevent people from developing a healthy therapeutic attitude towards sexuality; b) misconceptions about sex and of vocabulary; c) identification of the sexual problems of the spinal cord injured patient; and d) how the knowledge gained could be used to help SCI patients. **Outcomes:** Evaluated the program by interviewing individual participants.	Participants reported that after the program they: - enjoyed the class and felt it was worthwhile, though it was stressful at times, and that some participants became uncomfortable when peers freely shared sex experiences. - could respond with a calm and positive attitude when patients asked about sexual functioning. - appreciated having more factual knowledge to pass on to patients. - found that patients learned about the program's existence and felt freer to ask the nurses about sex. - Found that nursing staff who did not participate were now interested in taking the program. - Head nurses felt that other health disciplines should also be knowledgeable re: sexual rehabilitation.

Discussion

One randomized controlled trial demonstrated that one-day workshops could improve clinician knowledge, comfort, approach, and attitude towards sexual health counselling (Fronek et al. 2005; 2011). Another RCT (Sawyer et al. 1983) found that an interactive session on microcounselling would improve clinician's ability to respond appropriately to sexual concerns of patients. One prospective controlled trial and multiple pre-post studies have shown that Sexual Health workshop participants show significant increases in knowledge, skills and comfort after workshops, and a number of these gains are maintained at three-month, six-month, and two year follow-up (Simpson et al. 2006, Giannoten et al. 2006, Tepper 1997, Chubon 1981, Mims et al. 1974, Cohen et al. 1994, 1996, Fronek et al. 2011).

Conclusion

There is level 1b evidence from 1 RCT (Fronek et al. 2005; 2011), level 2 evidence (Simpson et al. 2006) and level 4 evidence (Giannoten et al. 2006, Tepper 1997, Chubon 1981, Mims et al. 1974, Cohen et al. 1994, 1996) that educational workshops can improve clinician knowledge, comfort and attitudes towards sexual health counselling.

There is level 2 (Simpson et al. 2006) and level 4 evidence (Fronek et al. 2011, Giannoten et al. 2006) that gains can be in knowledge, attitudes, and comfort in addressing sexual health issues are maintained at six-month follow-up.

There is level 2 evidence from 1 poor quality RCT (Sawyer et al. 1983) that microcounselling sessions can improve clinician's ability to respond appropriately to sexual concerns of patients.

Interactive educational workshops can improve clinician knowledge and attitudes towards sexual health counselling, that these knowledge gains can be maintained over time, and that clinicians improve their ability to respond appropriately to the sexual concerns of patients.

8.2 Sexual Education and Counselling for People with SCI

Sexual rehabilitation is recognized as an important component of the overall rehabilitation program for patients with SCI; however, retrospective studies identify a gap between services desired by patients and the services actually provided (White et al. 1993; McAlonan 1996; Tepper 1999). As far back as 1982, Schuler compared five sexual rehab programs for persons with SCI, and urged clinicians to evaluate the sexual rehab services provided (Schuler 1982). Though the ideal timing for sexual education for SCI patients has not been determined, Fisher et al. (2002) showed a significant increase in sexual activity between discharge from inpatient rehabilitation and 6-months later, and they suggested that the first 6 months post-discharge are optimal for sexual health interventions.

Table 27: Sexual Education and Counselling for SCI Patients

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Pebdani et al. 2013 USA Longitudinal Study (part of bigger study) Level 2 N=253	**Population:** 253 individuals consisting of 159 males (mean age 48.74±14.81 years) and 94 females (44.32±13.12 years); years since diagnosis males 13.75±10.53 years, females 12.79±9.63 years; level of injury C1-S5. **Treatment:** None **Outcome Measures:** Questions regarding family planning, the effect of SCI on family planning, where they received advice and information about SCI and pregnancy, SCI and fertility, and attitudes towards having children.	1. Approximately 50% were diagnosed with SCI prior to family planning. 2. Over half of the women in the sample had not spoken with a physician about SCI and pregnancy. 3. 60% of the women in the sample had been pregnant at some point in their lives. 4. Half of the men had fathered a child. 5. 13.4% reported that fertility issues had been discussed with a fertility specialist. 6. 7.1% reported that they or their partner had taken part in an infertility evaluation. 7. 4.3% reported that either they or their partner had received fertility treatment. 8. 2 women and 1 man reported that they or their partner had an abortion partially because of their SCI
Hess et al. 2007; USA Pre-post N=4	**Demographics:** 4 men with SCI; age range 35-55 yrs; time since injury 10-23 yrs; 3 with traumatic SCI, 1 with transverse myelitis; All with paraplegia: 2 complete, 2 incomplete (AIS B and AIS C). **Methods:** Patients referred to an outpatient SCI sexuality program and seen by an interdisciplinary team (nurse, physician, and psychologist); completed a pre-evaluation questionnaire and post-evaluation clinic visit questionnaire regarding their satisfaction with both sexual function and the clinic experience. **Outcome Measures:** pre- and post-visit satisfaction with sexual function and clinic experience.	1. Patients were very satisfied with their clinic experience. All stated they would recommend the clinic to others and would themselves return with new issues regarding their sexuality. 2. Despite patients' reporting insufficient knowledge about sexual function, all rated their clinic visit positively, and felt their questions had been answered and their emotional wellbeing appropriately addressed in a respectful environment.

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Schopp et al. 2002; USA Pre-post Level 4 N=28	**Demographics:** 28 women with SCI; mean age 40 yrs, range 17-59. **Methods:** Participants accessing comprehensive gynaecologic and reproductive health care services at a SCI women's health clinic; surveyed immediately prior to 1st clinic visit, and at 3- and 12-month follow-ups; participants mailed a set of baseline questionnaires approx. 3 weeks before their scheduled exam date; subsequent assessments conducted by phone and mail. **Outcome Measures:** measures of health-promoting behaviours (breast self-exams, exercise, reducing fat intake, increasing fibre intake and mammography); SCI-adapted General Health subscale of the US. Short-Form-36 (SF-36); Satisfaction with Life Scale (SWLS); Brief Symptom Inventory (BSI).	1. With exception of exercise, frequencies of health promoting behaviours increased across the 3 time periods. 2. Trend toward increased willingness to engage in monthly breast self exams from baseline to 3 months, and trend toward increased willingness to receive a mammogram between baseline and 12 month follow-up.
Cushman 1998; USA Observational (questionnaire) Level 5 N=50 (25 SCI)	**Demographics:** 50 patients who had participated in an inpatient rehab program; 25 SCI (16 M 9 F); mean(SD) age 41.8(20.8) yrs, range 16-74; mean time since injury 126.1 days; mean time in inpatient rehab 85.5 days. **Methods:** SCI patients were involved in a nursing education program, which included a group-oriented information sharing session and written information as part of a self-instruction program. Information presented centred on physiological aspects of sexual functioning, also included body image and attitudes regarding sexuality. **Outcome measures:** patient perceptions of sexual information and support provided.	1. 80% of SCI respondents felt access to information about sexuality was available to them. 2. 72% of SCI patients felt the amount of information or discussion about sexuality they received was sufficient. 3. 36% reported having received or reviewed written materials regarding sexuality. 4. 52% indicated that someone had volunteered information regarding sexuality to them.
Charlifue et al. 1992; USA Observational (survey) Level 5 N=231	**Demographics:** 231 women with SCI; mean age 32.7 yrs; mean age at injury 21.5 yrs; 112 quadriplegic (72% complete), 119 paraplegic (77% complete). **Methods:** Women who had initial rehab at a hospital centre in Colorado contacted by phone to participate in a comprehensive survey that examined demographic characteristics, menstrual and female hygiene history, pregnancy and child bearing, and sexuality. **Outcome measures:** sexual health needs, concerns, and support.	1. Over half the women reported the sexuality information provided for them during rehab was inadequate; however those whose rehab was after 1977 had higher levels of satisfaction (coincided with the establishment of a weekly women's group at the treatment centre).
New et al. 2016 Australia	**Population:** 152 individuals; 115 with traumatic SCI and 37 with non-traumatic spinal cord dysfunction (SCDys). Those with SCI were more likely to be male (72%), younger (median age 46) and have tetraplegia (48%) compared with those with SCDys (male=49%, P=0.008; median age 58). Median time since onset of spinal cord damage was 11 years. Most (95%)	1. There was no difference between SCI and SCDys regarding satisfaction or preferred modes of presentation. 2. People with SCDys were less likely to report receiving sexuality education during rehabilitation (SCDys n=11, 30%; SCI n=61, 53%; P=0.03). Interviews suggested that this may be gendered, as only two women recalled receiving

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Mixed methods comprehensive survey & semi structured interviews Level 5 N = 152	respondents were exclusively heterosexual, and 5% were gay, lesbian or bisexual. **Treatment:** None **Outcome Measures:** Demographic information, as well as questions regarding education participants received during their initial inpatient admission and the consequences of spinal cord damage for their sexuality.	sexual education, whereas men often received this as part of continence management. 3. Only 18% were satisfied or very satisfied with sexual education and information received, and 36% were dissatisfied or very dissatisfied. 4. Preferred modes for receiving sexuality information included sexuality counsellor, recommended internet sites, peer support workers, staff discussion, written information and DVD.
Choi et al. 2015; Korea Cross-sectional Survey Level 5 N=139	**Population**: 139 men (mean age=43.3 years, age range=16-69) with motor-complete spinal cord injuries (mean time since injury=14.4±7.7 years). **Treatment**: None **Outcome Measures:** sexuality, sexual satisfaction, socioeconomic factors, medical conditions, rehabilitation services.	1. 90 participants (65%) were sexually active. 2. A period of 21-25 years since injury, compared to 5 years since injury, and experience with sexual rehabilitation education was positively associated with sexual activity. 3. Among the group that was sexually active, 8 (8.9%) were sexually satisfied, and 56 (62.2%) were sexually unsatisfied. 4. Lower levels of education were significantly correlated with sexual dissatisfaction.
Valtonen et al. 2006; Sweden Observational (survey) Level 5 N=231 (190 SCI)	**Demographics:** 190 adults with SCI (144 M, 46 F) and 41 persons with menigomyelocele (MMC); SCI participants: mean age 46.6 yrs, range 21.8-74.2; Level of injury: 87 cervical, 60 thoracic, 39 lumbar/sacral. **Methods:** mail-out questionnaire on aspects of health and functioning. All SCI participants had been treated in the Spinal Injuries Unit in a university hospital in Goteborg, Sweden. **Outcome measures:** satisfaction with sexual life, self-assessed sufficiency of sexual counselling.	1. 69% of men and 59% of women with SCI reported that they had received enough sexual counselling. 2. Those who reported the amount of sexual counselling as sufficient showed higher satisfaction with their sexual life than the others. 3. In all subgroups, those who considered the sexual counselling they had received as sufficient were more satisfied with their sexual life than the others.

Discussion

Surveys of people who have completed rehabilitation after SCI have expressed a need for more education and counselling on sexual health concerns. Some recent research reported that few people with SCI receive information, are satisfied with the levels of education about pregnancy or sexual health, and that most expect medical staff to start the conversation about sexuality rather than having to initiate it (New et al. 2016; Celik et al. 2014).

There are only two pre-post studies that have evaluated a specific sexual health program after SCI. In Hess et al. (2007), four men received an outpatient SCI sexuality program staffed by an interdisciplinary team; they rated their visits as positive, but analysis of sexual satisfaction or knowledge was not done (i.e., level 5 evidence). Schopp et al. (2002) investigated the effect of comprehensive gynecologic services on the health behaviour of women with SCI. The authors note a trend towards desired behavioural improvement in one outcome measured, namely, increased willingness to receive a mammogram. The other outcome measure (adoption of health-promoting behaviours) was not shown to change.

Observational studies suggest that those who receive sexual counselling or educational services may have higher levels of sexual satisfaction (Charlifue et al. 1992; Valtonen et al. 2006). In addition to physical challenges, SCI can alter a person's sexual identity and sexual self-esteem, further complicating a person's efforts to date potential partners or develop new intimate relationships (Fritz et al. 2015).

Conclusion

There is level 5 evidence (Hess et al. 2007) that a sexual health program may be positively received by patients with SCI.

There is level 4 evidence (Schopp et al. 2002) which suggests that comprehensive gynecologic services may improve women's health behaviours.

There is some evidence, although limited, to show that participation in sexual health programs improves sexual health outcomes.

8.3 Clinical Focus - Multidisciplinary Approach to Sexual and Fertility Rehabilitation

By Dr. Stacy Elliott, MD, FRCP(C)

Source: Elliott S, Hocaloski S and Carlson M. A Multidisciplinary Approach to Sexual and Fertility Rehabilitation: The Sexual Rehabilitation Framework. Topics in Spinal Cord Injury Rehabilitation 2017; 23:49–56.

Many studies have identified improvement in sexual function as a priority for persons with spinal cord injury (SCI). Due to the various secondary sensory, motor, and autonomic consequences following SCI and due to the complexity of sexuality per se, this area can be overwhelming to many health care professionals. The literature indicate that sexual and fertility rehabilitation must be addressed in a biopsychosocial manner and include various disciplines. The Sexual Rehabilitation Framework (SRF) is a user-friendly and simplified way to proactively address the major biopsychosocial areas of sexuality and to create a plan of action for the person with SCI. It is an adjunct tool to the full sexual history, and it encourages all disciplines involved in SCI rehabilitation to address the issue of sexual function in the same manner as they would other activities of daily living.

Eight areas included in the SRF are:

- Sexual drive/interest,
- Sexual functioning,
- Fertility and contraception,
- Factors associated with the condition,
- Motor and sensory influences,
- Bladder and bowel influences,
- Sexual self-view and self-esteem, and
- Partnership issues.

The use of the SRF is encouraged in both inpatient and outpatient settings. Multidisciplinary or interdisciplinary team work is encouraged in sexual and fertility rehabilitation to move clinicians toward providing proactive and comprehensive care for individuals with SCI or other chronic disabilities. To assess and manage sexual issues, single or multiple disciplines can be recruited to suit the needs each individual client. Health care providers can include physicians, nurses, occupational therapists, physiotherapists, recreational therapists, psychologists, and social workers. Peer experience around sexuality can also be invaluable, but will depend on the availability of peer programs or counselors. In its simplest form, the SRF can be a checklist that covers the sexual areas and notes how one area can affect another area. The SRF is contextualized within the 3 principles of sexual rehabilitation16:

• Maximize the remaining capacities of the total body before relying on medications or aids (learning new body maps, breathing, visualization methods, mindfulness exercises),
• Adapt to residual limitations by utilizing specialized therapies (use of vibrators, mobility devices, training aids, phosphodiesterase type 5 inhibitors, vacuum device aids), and
• Stay open to rehabilitative efforts and new forms of sexual stimulation, with a positive and optimistic outlook.

For an example of what a variety of professionals would be responsible for in a multidisciplinary approach, refer to figure X below.

PATIENT IDENTIFIER:
26 year old C 6 complete SCI male
1 year post injury
Current Meds: Baclofen

SEXUAL REHABILITATION FRAMEWORK MULTIDISCIPLINARY WORKING SHEET EXAMPLE

REFERRAL (■ = RECCOMENDED)

SEXUAL AREA	SEXUAL CONCERN	MD	RN	PT	OT	PSYCH	SW	RT	OTHER
SEXUAL INTEREST	decreased secondary to sex changes and depression?	■				■			
SEXUAL FUNCTION	ED Anejaculation Anorgasmia	ED meds	■		adapt vibrator				Sexual health clinician/ therapist
FERTILITY & CONTRACEPTION	Curious	Urologist	■						Sperm retrieval Fertility clinic
FACTORS AFFECTING:									
Fatigue		check T							
Pain									
AD	with arousal	BP med							Physiatrist
Depression	untreated	■				■			Watch SSRI effect
Medications		■							
Cultural/Religious									
Other	social isolation							■	
MOTOR & SENSORY	Spasm Hypersensitivity at level of injury Positioning	meds?	■	■	■				Skin care needs improving
BLADDER & BOWEL	catheter use with sex?		■						Continence nurse
SEXUAL SELF-VIEW & SELF-ESTEEM	"lost manhood" Diff. adjustment to WC living Substance abuse Poor social supports				■	■	■		Peer counselling Vocational rehab
RELATIONSHIP ISSUES	Sirgle, gay (pre-injury partner left)					■		■	Wants to find a partner

SPECIFIC CONCERNS:

1) untreated depression affecting sexual function but SSRI could worsen it

2) watch for AD with ejaculation attempts

3) check testosterone since depressed & fatigued

Sexual Health Clinicians/Sex Therapists (SHC/ST): The role of sexual health clinicians (usually nurses) specially trained in sexuality and chronic illness/disability and those of community sexual therapists (often psychologists) goes beyond providing permission to discuss the area of sexuality and normalizing and validating client's concerns. SHC/STs are trained to take full sexual histories and to provide more specific information related to a client's particular concern. With or without other disciplines, they can intervene with therapeutic options (i.e., looking at erection enhancement options, fertility procedures, and techniques to address anejaculation and/or premature ejaculation, ways to experience pleasure in the context of limited or decreased sensation, mindfulness work). Specialized training and knowledge in sexuality and disability are required in this role. Occupational therapists

(OTs): OTs are in an excellent position to normalize sexual health as part of rehabilitation and assist in specifics for sexual activity, such as adaptive sexual devices, environmental controls, and adapted clothing.

Physiotherapists (PTs): A PT is often the first clinician that clients see in community, and he or she can be very effective in opening the conversation, normalizing sexual health rehabilitation as part of overall rehabilitation, and connecting individuals to necessary supports.

Psychologists and counselors: Depression, anxiety, loss and grief, role changes, and relationship discord are common post SCI and can have a significant effect on sexual health (sexual drive, relationships, etc).

Social Workers (SW): In the context of sexual rehabilitation, the SW is able to work with the client or group to seek out individual resources as well as sources of support and resources in the community to support clients to attain their goals for their sexual health/relationships.

Recreational therapists (RTs): An RT could teach a client new or adaptive ways of expressing themselves through activities such as sports, art, exercise, and dance. This could affect a person's sense of his or her sexual self in the world and how he or she is seen as a sexual person by others.

Vocational Rehabilitation Therapists: Loss of employment following an injury can be devastating to a person's sense of self. As a result, confidence and self-esteem, including sexual self-esteem, can be negatively impacted. Supporting a person to return to previous employment, train for a new occupation, or assume a volunteer role is important for re-establishing a sense of purpose, accomplishment, and wholeness to a person's life.

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EFFECT OF REPEATED EJACULATION ON SEMEN QUALITY IN SPINAL CORD INJURED MEN

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Abbreviations

AchE	acetylcholinesterase
AD	autonomic dysreflexia
AIS	ASIA Impairment Scale
ART	assisted reproductive technology
BP	blood pressure
BSI	Brief Symptom Inventory
BT	botox
CES-D	Centre for Epidemiological Studies - Depression scale
cGMP	cyclic guanosine monophosphate
CI	confidence interval
DBP	diastolic blood pressure
DOI	duration of injury
ED	erectile dysfunction
EDITS	Erectile Dysfunction Inventory of Treatment Satisfaction
EEJ/EEP	electroejaculation procedure
GAS	Groninger Arousability Scale
GCQ	Global Confidence Question
HADS	Hospital Anxiety and Depression Scale
HR	heart rate
ICI	intracavernosal injectable medications
ICSI	intracytoplasmic sperm injection
IIEF	International Index of Erectile Function
IVF	in vitro fertilization
IUI	intrauterine insemination
IVI	intravaginal insemination
KCAASS	Knowledge, Comfort, Approach and Attitudes towards Sexuality Scale
LMN	lower motor neuron
PDE5i	phosphodiesterase type 5 inhibitors
PGE1	prostaglandin E1
PGWBI	Psychological General Well-Being Index
PPS	penile prosthesis surgery
PR	pregnancy rate

PS	physostigmine
PVS	penile vibrostimulatory stimulation
PVSA	percutaneous vassal sperm aspiration
QOL	quality of life
RCT	randomized controlled trial
RSES	Rosenberg Self-Esteem Score
SBP	systolic blood pressure
SD	standard deviation
SCL-90-R	Symptom Checklist
SEP	Sexual Encounter Profile
SF-36	Short Form-36
SR	self-report
SSQ	Sexual Sensations Questionnaire
TESA/TESE	testicular sperm aspiration/extraction
TMSC	total motile sperm count
UMN	upper motor neuron
VAS	Visual Analogue Scale
VCD	vacuum constriction device
VED	vacuum erection device
VTCT	vacuum tumescence constriction therapy