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DeForge et al. 2006; Canada Review of published and unpublished articles between 1966 and 2003 N=49 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 Level of evidence: not reported Type of studies n/a AMSTAR=6	**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. **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	**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.

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AMSTAR=4		
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 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	**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 of erectile dysfunction (ED) in men with SCI and what remains to be seen of their potential or limits. **Databases:** Information not provided.	1. 705 participants used sildenafil, 305 vardenafil and 224 tadalafil. Median age was <40 yrs. Only one study excluded tetraplegic individuals. 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	**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

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Level of evidence methodological quality not assessed Type of studies RCT (n=2), Prospective case series (n=4) AMSTAR=2		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. **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		Review study.

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Italy 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=6		**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 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.

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Chochina et al. 2016; France Reviewed published studies up to November 2014 N=23 Level of evidence methodological quality was assessed using the Institute of Health Economics (IHE) checklist for case series and Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) check list for studies with studies with any other designs. Type of studies Retrospective case series (N=14), NR clinical trial (N=4), Prospective case series (N=1), Open randomized crossover clinical trial (N=1), Crossover randomized clinical trial (N=2) AMSTAR=9	**Method:** Searched for papers involving the use of intracavernous injections (ICI), regardless of drug, for men with SCI and ED. Literature restricted to English, French and Spanish. **Databases:** PubMed-Medline, Cochrane Library, Embase, EBSCO, and Web of Science..	**1.** ICIs resulted in successful erection in 88% (95% CI = 83%-92%) of patients with SCI. **2.** Satisfactory erection was obtained with papaverine (mean dosing = 17 mg) in 91%, with alprostadil (PGE1) (mean dosing = 12 mcg) in 80%, with bi-mix of papaverine (mean dosing = 15 mg) and phentolamine (mean dosing = 0.4 mg) in 93%, with moxisylite (mean dosing = 22 mg) in 83% and with tri-mix (mean dosing = papaverine 4 mg, phentolamine 0.02 mg, PGE1 1.5 mg) in 100%. **3.** Age, type of drug, doses, level and extent of injury, time since injury, and persistence of transience of erections were not predictive of response to ICI. **4.** Overall complication rate was 13.3%, specifically 2% for PGEI, 0% for moxisylite, and 13% for papaverine. **5.** Combination of papaverine with phentolamine led to highest complication rate of 30%. **6.** Main side effects of ICIs were ecchymosis (5%), prolonged erection ($\geq$3 hours; 4%) and priapism ($\geq$4 hours; 3%).