Table 3b. Effects of Phosphodiesterase Type 5 Inhibitors (PDE5i)

Author Year; Country **Score** **Research Design** **Total Sample Size**	**Methods**	**Results**
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); placebo for control group (n=27 from UMN and n=19 from LMN). **Outcome Measures:** International Index of Erectile Function (IIEF5) questionnaire; if the participant scored more than 15 points on the IIEF5, then treatment was considered effective, if less than 15 then inadequate.	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).
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-	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.

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	Esteem Score (RSES); Mental Health Summary of the SF-36 Health Survey.	
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.
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%).

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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 than the placebo group.
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 dose group respectively. Main adverse events: headache, dyspepsia and rash.
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. **Treatment:** Randomized to sildenafil (4 doses 50mg) or tadalafil (4 doses 10 mg). To attempt	1. Tadalafil allowed normal sexual functioning up to 24hr post dosing compared to sildenafil. 2. 19 out of 28 patients (67.9%), compared to five out of 28 patients (17.9%) with sildenafil, while we did not observe a significant difference in up to

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PEDro=6 N=28	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.	12h.
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 the 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.
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. 4. Ejaculation and orgasm frequency improved in the sildenafil group over placebo.
Hultling 1999 Sweden RCT Level 1	**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	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.

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PEDro=5 N=178	period). **Outcome measures:** ability to have intercourse, partner perception of ability to achieve erection and ability to maintain erection.	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.
Ohl et al. 2015 USA Case-control Level 3 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**: Retrospective analysis of RCT. 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. **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.	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%).
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	1. 38 out of 103 participants (37%) responded to 10mg of Tadalafil. 2. 36 participants (35%) subsequently responded to 20mg of Tadalafil. 3. 9 patients (8%) 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.

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	Index of Erectile Function (IIEF15); Sexual Encounter Profile (SEP) question 2 and 3.	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.
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.