

Invited review

# Efficacy and satisfaction rates of oral PDE5is in the treatment of erectile dysfunction secondary to spinal cord injury: A review of literature

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**Concept:** Decreased sexual function is a major concern of men with spinal cord injuries (SCIs). Treatment of erectile dysfunction (ED) through oral pharmacotherapies has been proven to be an effective way to address and treat this concern.

**Objective:** To find an efficacious and satisfactory treatment ED secondary to SCI through the compilation of studies that utilized the International Index of Erectile Function (IIEF) when testing phosphodiesterase V inhibitors (PDE5i).

**Method:** Ten articles, which used the IIEF to study satisfaction and/or efficacy of PDE5is sildenafil, tadalafil, and vardenafil in the treatment of ED were reviewed and analyzed. Through the use of a self-made grading scale the value of each article was determined for this research.

**Results:** Sildenafil, tadalafil, and vardenafil all have been proven to be effective in treating ED in men with SCI. While sildenafil is the most thoroughly studied ED treatment for patients with SCI, tadalafil has a longer time duration effectiveness, which allows for more spontaneity in the sexual experience. Minimal adverse effects have been noted in patients with SCI using these medications; headache, flushing, and mild hypotension are the most common. In articles that study satisfaction, patients show great improvement over baseline with the use of these medications.

**Conclusion:** Although there is a need for further research on the safety in long-term use of tadalafil and vardenafil, comparative studies done on all three medications show no statistically significant difference in effectiveness or satisfaction. New medications and treatment options, such as avanafil, are being studied in hope of continued improvement of sexual function in men with SCI.

**Keywords:** Spinal cord injuries, Erectile dysfunction, Phosphodiesterase V inhibitors, Sildenafil, Tadalafil, Vardenafil

## Introduction

A study of 286 men with spinal cord injury (SCI) stated that, 'their SCI had altered their sexual sense of self and that improving sexual function would improve their quality of life (QoL).'<sup>1</sup> A major contributor to this altered sense of self is the varying degrees of erectile dysfunction (ED) experienced secondary to their injury. There are many factors that affect their ED including level of injury (LOI) and degree of completeness of injury (American Spinal Injury Association (ASIA) impairment score). Two types of erections are noted in men after SCI, psychogenic and reflex. Psychogenic erections are caused by thoughts, smells, images, etc. The ability to achieve

these a psychogenic erection is maintained in patients whose LOI is below L3. Reflex erections are due to direct physical stimulation of the genitalia. The ability to achieve this type of erection is disrupted in patients with injuries from S2 to S4.<sup>2</sup> Erections are a result of the parasympathetic innervation of the penis, which utilize the nitric oxide-cGMP (cyclic guanosine monophosphate) pathway. This pathway relaxes cavernosal smooth muscle allowing for increased blood flow and in turn creating an erection.

Owing to the overwhelming interest patients with SCI have in sexual function, which includes ED, it is important for clinicians working with this population to be aware of the options that are available to improve sexual function.<sup>3</sup> In recent years, the preferred method of treatment for ED has been oral pharmacotherapies, specifically phosphodiesterase V inhibitors (PED5i)

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(sildenafil, tadalafil, and vardenafil). This study will attempt to determine the appropriateness of this treatment in men with ED secondary to SCI by answering the following questions through a review of literature:

1. What is the efficacy of oral PDE5i used to treat ED in men with SCI?
2. What is the satisfaction level of men who used oral PDE5i to treat ED secondary to a SCI?

### *Conceptual framework*

To provide the highest quality of care for men with SCI who have ED, it is important to be knowledgeable about caring for patients with SCI as well as being aware of the sensitive nature of caring for patients with sexual dysfunction. The permission, limited information, specific suggestions, intensive therapy (PLISSIT) model will be used for the conceptual framework for this literature review as it is geared toward interventions related to sexuality, and is designed to identify various levels of services depending on the needs of individuals.<sup>4</sup> The model is broken down into four levels: permission, limited information, specific suggestions, and intensive therapy.

The different phases/levels of the model are used to assist in creating and deepening a trusting relationship between the provider and patient. The permission level of the PLISSIT model refers to creating an environment where the patient feels comfortable talking about sexuality and their sexual problems. This first level of the model is appropriate when working with any patient dealing with sexual dysfunction due to the personal nature of care being provided. Limited information is the next level of this model that focuses on patients having a full understanding of the impact their injury has on their sexual function. This is achieved through answering any questions the patient has and correction any misinformation they have received about their sexual function. During this phase of the model, it is imperative for the healthcare provider to continue to build a trusting relationship with their patients and provide any information that they are willing to receive.

In continuing to grow their relationship through the limited information phase the provider is preparing their patient for the next phase, specific suggestions. In this phase the provider utilizes the information gained about the patient's dysfunction, lifestyle, and needs during the previous phases to make treatment suggestions that are appropriate to that specific patient (i.e. PDE5i vs. vacuum constrictive devices). The knowledge the provider gained of their patient's dysfunction, lifestyle, and needs during the previous

phases will allow them to make suggestions that are appropriate for this patient. The continued guidance and care provided to the patient are part of the intensive therapy phase. In this phase the patient will continue to work with the provider to find the appropriate care and make changes in treatment as they are needed.

### *Medications studied*

To date, the medications that have been the most intensively studied for the treatment of ED in patients with SCI are PDE5i; sildenafil, tadalafil, and vardenafil.<sup>5</sup> These three medications work by selectively blocking the PDE5 enzyme, which breaks down cGMP. Therefore, blocking of PDE5 allows for an increased presence of cGMP, which increases cavernosal blood flow through smooth muscle relaxation which in-turn creates prolonged erectile function. Although all three drugs have comparable pharmacodynamic effects, they have different pharmacokinetics, which may have some bearing on how satisfactory patients find each drug. Sildenafil and vardenafil have terminal half-lives of approximately 4–5 h; tadalafil's half-life is much longer at 17.5 h.<sup>6</sup> By reviewing literature of the efficacy and satisfaction of patients' experiences taking these medications, we hope to assist healthcare providers in the specific suggestion phase of the PLISSIT model.

## **Methods**

### *Eligibility criteria*

For this research, articles considered for inclusion were limited to studies that were done on at least 20 men with SCI. Articles of any research design and language of publication were also put into consideration. The criterion for the date of publication was no earlier than 2000 and no later than August 2010. Interventions investigated in these articles included oral pharmacotherapies for the treatment of ED secondary to SCI.

### *Literature search strategies*

Articles were collected from several databases including PubMed and CINAHL. Key words used when searching the databases included: 'spinal cord injuries and sexual dysfunction' (CINAHL = 59 hits; PubMed = 79 hits), 'spinal cord injuries and erections' (CINAHL = 5; PubMed = 24 hits), 'spinal cord injuries and sildenafil' (CINAHL = 27 hits; PubMed = 31 hits), 'spinal cord injury and tadalafil' (CINAHL = 2 hits; PubMed = 8 hits), 'spinal cord injury and vardenafil' (CINAHL = 4 hits; PubMed = 8 hits), and 'avanafil' (CINAHL = 2 hits; PubMed = 7 hits).

### Scoring key

For the purposes of this literature review a scoring key was created to help analyze the collected articles. Articles were rated on a 25-point scale that assesses the relevance of these articles to the questions posed above. The scoring key is broken into two domains; population and content. The population domain aims to ensure that the results are valid across all SCI men no matter LOI or ASIA impairment score. Therefore the population domain is graded on the three areas – sample size, number of LOI, and ASIA scores included. Articles would receive a score of 0–4 in these domains. For sample size the scoring is as follows: 0 points = <25 participants; 1 point = 25–50 participants; 2 points = 50–74 participants; 3 points = 75–100 participants; and 4 points = >100 participants. LOI inclusion is given by the following scores; 0 points = no LOI specified; 1 point = 2 groups (e.g. servical vs. thoracic, lumbar, and sacral); 2 points = 3 groups (e.g. cervical vs. thoracic vs. lumbar–sacral); 4 points = 4 or more groups (e.g. cervical vs. thoracic vs. lumbar vs. sacral). ASIA scoring points were awarded in much the same way: 0 points = no difference in ASIA impairment score was accounted for, 1 point = 2 groups (e.g. A vs. B–D), 2 points = 3 groups (e.g. A vs. B vs. C–D), 4 points = all ASIA impairment scores accounted for.

Articles are also scored based on their content which includes: use of the International Index of Erectile Function (IIEF) = 3 points; discussion of efficacy = 2 points; discussion of satisfaction = 5 points; and statistical significance of findings = 5 points. The use of the IIEF proved vital to this research because it provides a universal and standardized language with which to discuss ED. Satisfaction and statistical significance of findings are given the most weight in this scoring key due to their importance in assessing the validity of the

articles for this research. The implied inclusion of efficacy in a satisfaction rating is the foremost reason why satisfaction is weighted more heavily than efficacy. Statistical significance is also given the highest value to ensure the validity of the information being reported.

Two different routes were taken to validate the use of this scoring key. First, the scoring key was created with the input and approval of other health care professionals. Their opinion was sought in the assigning of scores and categories analyzed within each domain. Along with looking to others in the professional community to validate the use of this scoring key all of the articles were scored by two separate reviewers. All articles had matching scores giving this scale 100% inter-rater reliability (Table 1).

When analyzing the articles utilizing the scoring key, articles with total scores of 10 or less were excluded. Articles with low scores did not contribute to answering the posed research questions and were therefore excluded. Of the articles collected, 10 articles fulfilled the minimum score requirement. The article by Soler was the most appropriate to this research due to the inclusion of all three medications, use of the IIEF and study of both reported efficacy and satisfaction.<sup>7</sup> Although Anderson's article had the lowest score out of the 10 articles analyzed, it turned out to be crucial in our analysis because it provides a view of the satisfaction of the general population of men with SCI whether or not they are employing these medications to treat their ED.<sup>1</sup>

### International Index of Erectile Function

Articles that are focused on in this literature review utilize all or part of the IIEF as a way of evaluating the effectiveness and satisfaction of patients in the studies. The use of this questionnaire is important to this review because it gives common language with

**Table 1** Scores for the 10 article that are included in this research and a breakdown of the points received in each domain

Article	Drugs	Participants	LOI	ASIA score	IIEF	Effectiveness	Satisfaction	Significant difference	Total
Anderson <i>et al.</i> <sup>1</sup>	None	4	2	1	0	0	5	0	12
Del Popolo <i>et al.</i> <sup>11</sup>	Tadalafil, sildenafil	1	2	2	3	2	5	5	20
Ergin <i>et al.</i> <sup>10</sup>	Sildenafil	2	0	3	3	2	5	5	20
Gans <i>et al.</i> <sup>5</sup>	Sildenafil	0	2	0	3	2	5	5	17
Giuliano <i>et al.</i> <sup>14</sup>	Tadalafil	4	1	1	3	2	0	5	16
Hulding <i>et al.</i> <sup>12</sup>	Sildenafil	4	0	0	3	2	5	5	19
Lornardi <i>et al.</i> <sup>18</sup>	Tadalafil	4	2	2	3	2	5	5	23
Moemen <i>et al.</i> <sup>16</sup>	Sildenafil	2	3	2	3	2	5	5	22
Sanchez-Ramos <i>et al.</i> <sup>13</sup>	Sildenafil	4	1	3	3	2	0	5	18
Soler <i>et al.</i> <sup>7</sup>	Sildenafil, tadalafil, vardenafil	4	2	3	3	2	5	5	24

The article by Soler received the highest score and Anderson received the lowest while still being included in this research.

which to discuss and compare the results in the articles being reviewed. The IIEF is not only important to this research but in all research looking at erectile function. Self-report is considered to be a more effective way of evaluating sexual function than laboratory-based studies. Prior to the creation of the IIEF many of the questionnaires that were being used were limited for several reasons including 'excessive length or complexity, an overly narrow or restrictive focus, inadequate psychometric, cultural or linguistic validation.'<sup>8</sup> The IIEF consists of 15 questions that cover five domains of erectile function: erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction. The IIEF has undergone rigorous testing to ensure validity and consistency. As of 2008, the IIEF had been used in more than 60 studies and 50 clinical trials; it has continued to be utilized throughout studies analyzing erectile function in all populations.

Many of the articles being reviewed not only look at the IIEF as a whole but also focuses on scores in specific domains; especially the satisfaction domain. Questions 13 and 14 of the scale are used to assess satisfaction. Question 13 asks, 'How satisfied have you been with your overall sex life?' and Question 14 asks, 'How satisfied have you been with your sexual relationship with your partner?' Studies that specifically look at this domain are important for this review because of its focus on patient satisfaction in the use of PDE5i.

Although the IIEF does serve an important purpose in studying the treatment for ED in SCI men, it has some shortcomings when being used with this population. The IIEF does not differentiate between psychogenic and reflexogenic erections and other varying effects that SCI has on erectile function. Another issue noted in using the IIEF with this population is the focus on ejaculatory function in the questionnaire. Ejaculation is often altered if not eliminated in SCI men and therefore, data collected on this domain may be skewed and inappropriate for this population.<sup>9</sup> There are some issues with this scale that are non SCI-specific. The scale only looks at the patient's sexual experience for the 4 weeks prior to filling out the questionnaire. Along with the time constraints, patients need to have a consistent sexual partner to be able to fully answer the questionnaire. The studies analyzed for this literature review accommodate these restrictions by only taking subjects who are in long-term relationships and also include patients using medications for 4-week periods. Despite the shortcomings of the IIEF when assessing erectile function in this population, there is currently no better measure.

## Results

The 10 articles reviewed fit the criteria required for this literature review. All articles showed a statistically significant improvement in erectile function over baseline and/or compared to placebo with the use of these PDE5i.

### *Efficacy*

Based on the IIEF questionnaire, the efficacy of a drug is determined by the ability to achieve an erection rigid enough for penetration, the ability to maintain an erection to completion of intercourse, and how often a patient is able to penetrate their partner (reliability). Sildenafil, tadalafil, and vardenafil have all proven to be effective in the treatment of ED. All articles that were analyzed showed there was a significant difference in the IIEF score after taking a PDE5i compared to the baseline or placebo.

Sildenafil is the oldest and most researched PDE5i being used to treat ED.<sup>6</sup> The studies being reviewed all showed an improvement in erectile function over baseline and compared to placebo when patients took sildenafil. No matter the LOI or ASIA impairment score, patients who took sildenafil reported a higher IIEF score in sexual stimulation and intercourse compared to those who took a placebo.<sup>10</sup> Sildenafil has also been found to prolong the duration of an erection compared to the baseline. In the article by Gans, the mean baseline duration of erection was 8.4 minutes, but was increased to 10 minutes following use of sildenafil.<sup>5</sup> Patients who took sildenafil were also found to be more confident in their ability to achieve and maintain an erection rigid enough for penetration. The mean score for the IIEF question concerning their confidence in the ability to maintain an erection increased from 1.6 to 3.8 ( $P < 0.05$ ).<sup>4</sup> Compared to tadalafil and vardenafil no significant difference was found in the efficacy of sildenafil. Although patients found all three medications efficacious, a study by Soler showed that patients are more likely to have improved function with lower doses of sildenafil than tadalafil or vardenafil. This is an important difference due to patients being more likely to experience adverse effects of the medications at higher doses of the medications.

As previously stated, tadalafil and vardenafil have also shown to improve erectile function over baseline and compared to placebo regardless of ASIA impairment score or LOI. The improved erectile function experienced with tadalafil has been shown to continue 12–24 hours post-dosing due to the previously discussed increased time duration effectiveness. In a study that compared the time duration effectiveness of tadalafil



vs. sildenafil in 12–24 hours post-dosing, 67.9% of patients who took tadalafil had successful intercourse whereas only 17.9% of those taking sildenafil were able to. At this time it has not been studied how vardenafil compares to tadalafil in time duration effectiveness for men with SCI, but the known pharmacokinetics of this medication lead to the conclusion that its results would be comparable to that of sildenafil. As well as having an extended time-duration effectiveness compared with sildenafil, in the same study, tadalafil was also shown to be more effective in the treatment of patients with lower motor neuron (LMN) injuries. In this study 40% of patients with LMN injuries unable to achieve a satisfactory erection with sildenafil were able to do so with tadalafil<sup>11</sup> (Table 2) (Fig. 1).

### Satisfaction

Patients showed increased satisfaction over baseline with all the medications studied (Table 4). The increased satisfaction of patients taking sildenafil, tadalafil, and vardenafil is comparable based on patients' answers to Q13 (overall satisfaction with sex life) and 14 (overall satisfaction with sexual relationship with partner) of the IIEF. In an article by Soler that compared the three medications, there was no significant difference between the satisfaction reported by patients<sup>7</sup> (Fig. 2).

As seen with efficacy, sildenafil is the oral pharmacotherapy that has undergone the most rigorous study when looking at how satisfied patients were with their ED treatment. Sildenafil showed a significant improvement in satisfaction over placebo and baseline. In a two-way crossover study by Hultling *et al.*,<sup>12</sup> the mean score for Q13 and Q14 improved by 49 and 34%, respectively, with the use of sildenafil. This improvement in satisfaction was not only a statistically significant over baseline but also placebo, which had a 1% decrease for Q13 and 2% increase for Q14. A study by Sanchez-Ramos not only had patients comment on their satisfaction with sildenafil but also asked their partners about their satisfaction level. There was a statistically significant increase in satisfaction in the sexual experience for both the patients and their partners when they began using sildenafil.<sup>13</sup>

Tadalafil and vardenafil also showed increased sexual satisfaction over baseline. In Soler *et al.* patients taking vardenafil and tadalafil rated their satisfaction (combined score of Q13 and Q14) significantly higher when using these therapies over baseline. Patients' scores improved from at mean of 2.5–6.7 for vardenafil and 3.2–7.5 for tadalafil. The aforementioned increased time-duration effectiveness of tadalafil could provide patients with increased satisfaction with their sexual

experience due to the spontaneity it allows them (Table 3) (Fig. 2).

### Adverse effects

Minimal adverse effects were reported in the articles we reviewed. Of the 739 patients studied in the 10 articles, only 102 patients reported any adverse effects, most of which were mild. Headache, flushing, hypotension, nasal congestion, and dyspepsia were the most commonly noted adverse reactions. These side effects are not only found in men with SCI but also in men without SCI who have ED. It should be noted that of the 102 patients who experienced any adverse effects of these medications, only 14 found them to be severe enough to drop from the study. In the vast majority of cases many patients found these side effects manageable. Acknowledging these findings is important to the study of the satisfaction of these medications because weighing the benefit vs. the adverse effects is at the core of finding the satisfaction rates of any treatment (Table 4).

In the studies by Ergin and Guiliano, patients reported increased incidences of urinary tract infections (UTIs) in men taking PDE5i over placebo. There were 11 patients (7.7%) taking tadalafil who reported having UTIs, while compared to 3 (6.8%) who were taking placebo.<sup>14</sup> The number of patients who reported having UTIs when they took sildenafil were statistically similar to those who took placebo.<sup>9</sup> In studies of men without SCI treating ED with PDE5i patients did not report UTI as a side effect.<sup>6,15</sup> Owing to this reaction being specific to the SCI population it may be attributable to some difference in lifestyle and more studies would need to be conducting for any conclusive explanation of these findings (Table 4).

### Discussion

#### *What is the efficacy of oral pharmacotherapies used to treat ED in men with SCI?*

Studies conducted over the past 10 years on the oral pharmacotherapies used to treat ED in SCI men have shown that these medications are highly effective. All studies have shown a statistically significant increase in IIEF scores. sildenafil, tadalafil, and vardenafil showed no difference in their effectiveness, although tadalafil has an increased time-duration effectiveness. In a study comparing the time-duration effectiveness of tadalafil and sildenafil 67.9% of patients who took tadalafil were able to have successful intercourse 12–24 hours after taking their dose compared to 17.9% who took sildenafil. Tadalafil has also shown to have greater success in treating ED of men with LMN injuries.<sup>11</sup> Despite tadalafil's increased time-duration

**Table 2 A breakdown of the included articles that study efficacy.**

Article	Drug	IIEF score before treatment (drug)	IIEF score before treatment (placebo)	IIEF score after treatment (drug)	IIEF score after treatment (placebo)	Conclusion
Del Popolo <i>et al.</i> <sup>11</sup>	Sildenafil, tadalafil	Mean baseline 11.25	N/A	15.75 (sildenafil); 17.82 (tadalafil)	N/A	Tadalafil significantly increased the percentage of successful intercourse attempts at 24 hours (19/28) patients, compared to 5/28 (sildenafil). Tadalafil allowed a majority of men in this trial to achieve normal sexual functioning at up to 12–24 hours after taking the drug compared to sildenafil
Ergin <i>et al.</i> <sup>10</sup>	Sildenafil	First treatment phase: 34.3; second treatment phase: 30.1	First treatment phase: 30.4; second treatment phase: 30.7	First treatment phase: 34.0; second treatment phase: 43.0	First treatment phase: 28.9; second treatment phase: 26.9	Sexual stimulation and intercourse rates were significantly higher with sildenafil than with placebo. Sildenafil produced greater improvements than placebo in satisfaction with sex life and sexual relationship. Erectile response rates after treatment with sildenafil have been reported to be generally higher in patients with incomplete vs. complete SCI and in men with upper vs. lower motor neuron lesions
Gans <i>et al.</i> <sup>5</sup>	Sildenafil	2.5	N/A	3.7	N/A	Scores from IIEF questionnaire were all significantly increased after sildenafil use. Before sildenafil use, the mean duration of erection was 8.4 minutes. After sildenafil, mean duration of erection was increased to 10 minutes. Oral sildenafil appears to be a safe effective option for the treatment of ED in patients with SCI. Sildenafil improved erectile function and subjectively improved erectile function compared to previous therapies patients have used
Giuliano <sup>14</sup>	Tadalafil	13.5	13	22.6	13.6	Tadalafil significantly improved erectile function compared with placebo as seen by IIEF scores. Also, 75.4% of the patients taking tadalafil had successful attempts with penetration compared to 41.1% of the patients taking the placebo. Of the patients taking tadalafil, 47.6% had successful sexual intercourse attempts, while only 16.8% for patients taking the placebo. Through the study, researchers were able to show that tadalafil was efficacious regardless of severity and level of SCI, degree of REF, and severity of ED.
Moemen <sup>16</sup>	Sildenafil	16.03 (sildenafil only); 15.3 (ICI, sildenafil after); 15.5 (vacuum, sildenafil after)	N/A	27.7 (sildenafil only); 27.5 (ICI, sildenafil after); 27.7 (vacuum, sildenafil after)	N/A	The improvement of erection was 90% after sildenafil therapy.

*Continued*

Table 2 Continued

Article	Drug	IIEF score before treatment (drug)	IIEF score before treatment (placebo)	IIEF score after treatment (drug)	IIEF score after treatment (placebo)	Conclusion
Sánchez-Ramos <sup>13</sup>	Sildenafil	12.5 (responders)	N/A	24.8 (responders)	N/A	88.2% of men with ED due to spinal cord injury treated with sildenafil reported an improvement in ED. A dose of 50 mg of sildenafil was required by 69.8% of patients to achieve efficacy, whereas the remaining 30.2% required a dose of 100 mg. 57.4% of the patients achieved successful sexual intercourse on the first attempt. PDE5 inhibitors are effective in treating ED. Sildenafil was associated with a higher percentage of rigidity and longer duration of erection than vardenafil and tadalafil. 2/3 of the patients on tadalafil in the study reported a duration of action longer than 24 h. This can give more spontaneity, allowing patients to decide when to engage in sexual intercourse with a partner.
Soler <sup>7</sup>	Sildenafil, tadalafil, vardenafil	14.0 (sildenafil); 15.8 (vardenafil); 18.6 (tadalafil)	N/A	26.8 (sildenafil); 28.7 (vardenafil); 28.4 (tadalafil)	N/A	

Results of efficacy are based on IIEF scores pre and post treatment as well as in comparison with placebo medications.

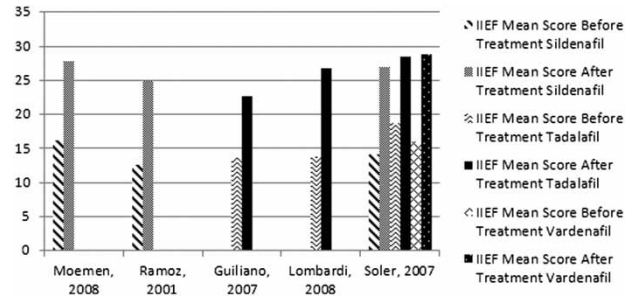


Figure 1 A comparison of the IIEF scores of sildenafil, tadalafil, and vardenafil. Differences noted between medications as well as pre- and post-dosing of individual medications.

effectiveness, sildenafil requires lower dosing for most patients to be effective and increased dosing can lead to increased adverse effects.

In a study by Soler *et al.*, it was found that sildenafil was effective at its minimal dose, 50 mg, in 55% of patients. This study also found that 70% of patients taking tadalafil and vardenafil needed the maximal dose, 20 mg, for these drugs to be effective. The authors hypothesized that this may indicate that sildenafil is more effective in treating ED.<sup>7</sup>

### What is the satisfaction of oral pharmacotherapies used to treat ED in men with SCI?

As with efficacy all three of these medications have been shown to improve satisfaction with sexual function over baseline and compared to placebo. Sildenafil, the most studied drug of the three, has also been shown to be more satisfactory than other ED treatment options.<sup>4</sup> In a study that compared sildenafil to intracorporal injections (ICI) and vacuum constriction devices (VCD), sildenafil was the most preferred method of treatment even though ICI produced a more rigid erection. Sildenafil was chosen over the other two for multiple reasons;

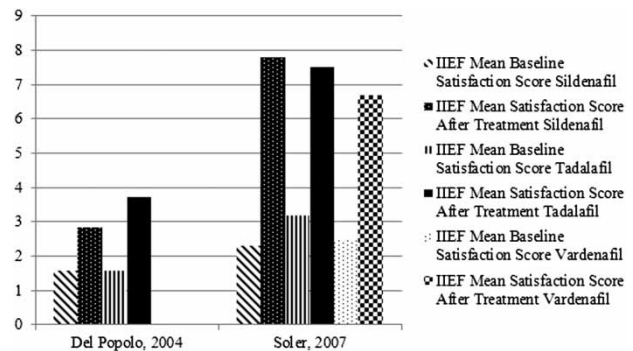


Figure 2 A comparison of satisfaction ratings based on the mean score of IIEF Q13 and 14 pre- and post-treatment for sildenafil, tadalafil, and vardenafil.

**Table 3 A description and results of articles that include satisfaction rates.**

Title	Overview	Satisfaction findings	Conclusion
Del Popolo <i>et al.</i> <sup>11</sup>	Double blinded cross over study comparing sildenafil and tadalafil. Compared time/duration effectiveness, and QoL effects of 10 mg tadalafil vs. 50 mg sildenafil. The patients were split into two groups 1/2 received sildenafil for the first 4 weeks and half received tadalafil. They then had a 2-week wash out period and then switched drugs	Q13 tadalafil = 3.46; sildenafil = 2.96; Q14 tadalafil = 3.71; sildenafil = 3.71	Tadalafil had better results in time/duration and satisfaction. Patients were able to have an erection in the period 24–36 hours post-taking tadalafil. They also reported higher levels of satisfaction in Q13 and Q14 of IIEF
Ergin <i>et al.</i> <sup>10</sup>	Two way cross over study of sildenafil vs. placebo. Patients are given either sildenafil or a placebo for 6 weeks and then have a 2-week wash out period and then switch to the other for 6 weeks	Patients reported an increase from a baseline of 2.5–3.2 and 2.8–4.2 in answer to Q14 of IIEF. This is a <i>P</i> 0.002	Patients were more satisfied with their sexual experience when taking sildenafil than when using a placebo
Hultling <i>et al.</i> <sup>12</sup>	A multi-centered, randomized, double-blind, flexible dose, placebo controlled sildenafil study. Patients were randomized to two groups. They either received 6 week of sildenafil or placebo and then had a 2-week wash out period and then switched	Q13: sildenafil = 49% increase over baseline; placebo = 1% decrease from baseline Q14: sildenafil = 34% increase over baseline; placebo = 2% increase over baseline	Patients showed a statistically significant increase in satisfaction over baseline when using sildenafil. Sildenafil also proved to be significantly more satisfactory than placebo
Moemen <sup>16</sup>	Study of the efficacy and preference for different ED treatment options (ICI, VCD and Sildenafil) for men. 60 patients were split into three separate groups. Group A took Sildenafil as needed for 1 month; 1 hr before planned sexual activity and not more than 1 time per day. Group B was first given ICI for 1 month and then shifted to Sildenafil for 1 month. Group C was given VCD for one month and then shifted to Sildenafil for 1 month.	Patients had more rigid erections than men taking Sildenafil but of the men in Group B 14/20 said they would rather take Sildenafil because the route of administration is easier. VCD also produced erections rigid enough for intromission but they reported a lack of satisfaction and would rather use Sildenafil or ICI.	Sildenafil is the most generally preferred and accepted treatment option for ED. The other treatment options (ICI and VCD) should still be considered when Sildenafil is not suitable or not preferred by the patient.
Sánchez-Ramos <sup>13</sup>	An open, before-after study. Patients and their partners filled out questionnaires about the effectiveness and satisfaction with the use of Sildenafil.	Sexual Satisfaction: Baseline = 7.3; Final = 10.7; Overall Satisfaction: Baseline = 6.1; Final = 8.0	Both patients and their partners found the medication to increase their satisfaction with their sexual experiences.
Soler <sup>7</sup>	Patients were treated with flexible doses of Sildenafil (N = 120), Tadalafil (N = 54) and Vardenafil (N = 66) in clinic trials. Efficacy was self-assessed by patients using IIEF.	Q 6-8 of IIEF Baseline 6.5 Sildenafil 9.8 Baseline 4.6 Vardenafil 8.6 Baseline 6.0 Tadalafil 8.5 Q 13-14 of IIEF Baseline 2.3 Sildenafil 7.8 Baseline 2.5 Vardenafil 6.7 Baseline 3.2 Tadalafil 7.5 All of these results are significant from baseline but not from each other.	Sildenafil ratings were slightly (but not significantly) higher than the other two drugs but Tadalafil had a longer duration and allowed for more flexibility in use. The authors suggest use of Sildenafil due to the need for further study of the other two drugs and the need for higher dosage of the other two drugs.

Satisfaction findings are based on answers to Q13 and 14 of IIEF, which make up the Sexual Satisfaction domain.

men felt that the erections they had with VCD were not rigid enough and did not look natural. Patients taking ICI were not satisfied with the route of administration and so were more willing to take sildenafil. Patient satisfaction with the route of administration of a drug is important because this can deter them from using the medication (no matter the efficacy) and therefore, limit the improvement of their sexual experience.<sup>16</sup>

The increased time-duration effectiveness of tadalafil can have both positive and negative affects on patient satisfaction with this medication. This increase allows for a more spontaneous sexual experience and allows the patients and their partner to decide when to engage in intercourse. Although the spontaneity allowed with this medication can increase satisfaction, the increased time-duration effectiveness can make



**Table 4 Adverse reactions experienced by patients included in the studies reviewed**

Article	Adverse reactions	# of patients with adverse reactions	Drop outs
Del Popolo <i>et al.</i> <sup>11</sup>	N/A	N/A	6/178
Ergin <i>et al.</i> <sup>10</sup>	H/A, mild UTI	N/A	N/A
Gans <i>et al.</i> <sup>5</sup>	Hypotension	1/17	1/17
Giuliano <i>et al.</i> <sup>14</sup>	H/A, UTI, upper abdominal pain, muscle spasticity	50/129	4/129
Hultling <i>et al.</i> <sup>12</sup>	N/A	N/A	2/30
Lomardi <i>et al.</i> <sup>18</sup>	H/A, flushing	10/65	0/65
Moemen <i>et al.</i> <sup>16</sup>	H/A, flushing, dyspepsia, hypotension, nasal congestion	N/A	0/60
Sánchez-Ramos <i>et al.</i> <sup>13</sup>	H/A, flushing, GI discomfort, nasal congestion, visual disturbances	41/170	1/170
Soler <i>et al.</i> <sup>7</sup>	None	0/90	0/90

How many patients of those included in the studies experienced these adverse reactions and how many patients dropped out.

patients more sensitive to excessive stimulation. The increased sensitivity can lead to unwanted mechanical erections, which can be both embarrassing and inconvenient for the patient and decrease satisfaction with this medication. For this reason providers and patients should be cautious in the use of penile sheaths and tight clothing while taking this drug.<sup>7</sup>

#### Provider implications

Improved sexual function is a highly important to men with SCI. As patient advocates healthcare professionals need to be educated on topics that are highly concerning to their patients. With this knowledge healthcare providers will be able to assist their patients in making informed decisions about their treatment and also ensure that they are receiving care that is appropriate for their needs. In using the PLISSIT model when caring for these patients, healthcare providers will ensure that patients are receiving the most efficacious and satisfactory treatment of their sexual dysfunction. In the SS phase, the provider can discuss the use of PDE5i to their patient to treat their sexual dysfunction. The information obtained about the patient in the P and LI phases will give the provider an insight into the patient's needs and assist them in suggesting the appropriate treatment during the SS phase of treatment. If the provider knows that the patient and their partner are looking to increase spontaneity in their sexual experience, then tadalafil would be the medication they would prescribe for their patient. In the IT phase, the provider will be ensuring that the patient is able to have a satisfactory sexual experience with their chosen treatment option. If this is not the case or the patient is experiencing adverse effects from the treatment, the provider would then work with the patient to find a more appropriate treatment option. For example, if the patient prescribed tadalafil is having increased unwanted mechanical erections, then the provider may have the patient try sildenafil or vardenafil.

#### Further research

Along with the continued study of the current oral medications available, especially tadalafil and vardenafil, research is being done on new drugs to treat ED. A new PDE5i, avanafil is currently being researched for the general population. Preliminary studies show that avanafil is more selective than the three major PDE5i being used at this time. These studies have also shown avanafil to have lower hemodynamic effects and patients experienced less hypotension and tachycardia than with sildenafil. Udenafil, SLx-2101, and mirodenafil are also PDE5i that are starting preliminary trials. Other non-PDE5i are also being studied in the general population. These include bremelanotide, topical administrations of alprostadil, and new ICI injections.<sup>17</sup>

As discussed earlier, the IIEF is a very important tool in the study of sexual function, and still leaves much to be desired for the SCI population. The IIEF gives a common language to those studying sexual function in the able-bodied population, but it does not account for some the differences in sexual and erectile function of men with SCI. There is a need for future research into creating a standardized and appropriate language to discuss the erectile function of these patients. Any future metric used to grade erectile function in men with SCI would need to account for the change in ejaculatory function secondary to their injury, as well as differentiating the different types of erection (psychogenic vs. reflexogenic) these patients can achieve.

#### Conclusion

Sildenafil, tadalafil, and vardenafil have proven to be comparably efficacious and satisfactory in the treatment of ED in men with SCI. As more studies are conducted on tadalafil and vardenafil new data, especially about tadalafil's time-duration effectiveness, they may become more popular treatment options.<sup>18</sup> New drugs

and treatment options may help improve the treatment of ED in this population.

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