www.medscape.com

Patients' Preference in the Treatment of Erectile Dysfunction

A Critical Review of the Literature

A Martin Morales; M Casillas; C Turbi

Posted: 02/28/2011; Int J Impot Res. 2011;23(1):1-8. © 2011 Nature Publishing Group

Abstract and Introduction

Abstract

The increase in the number of safe and effective ED treatments highlights the importance of patients' preference when choosing a therapeutic option. Several studies assessing these preferences are now available in published literature. This article aims to review and discuss the studies on patients' preference and the data concerning the reasons for preference for one PDE-5 inhibitor over another. A PubMed search was conducted for manuscripts published within the last 10 years containing the search items ED, preference, sildenafil, tadalafil or vardenafil. Selected articles were discerningly reviewed and summarized (design, limitations and relevance). The articles selected were peer reviewed publications on patients' preference and ED published in medical literature since 2000. Preference studies that include either two (tadalafil and sildenafil) or three PDE-5 inhibitors (tadalafil, sildenafil and vardenafil), showed that the majority of the patients preferred tadalafil versus either vardenafil or sildenafil. As the treatment of ED has evolved, patients' preference has become an important aspect of ED therapy, 52–65% of patients prefer tadalafil versus 12–20% vardenafil or 8–30% sildenafil. All founded studies have serious limitations, particularly in terms of dosing differences. Preference for tadalafil was mainly because of the longer duration of action that increases patients' freedom in sexual life. There is a consistency in patients' preference for tadalafil over sildenafil or vardenafil across the studies reviewed.

Introduction

ED is one of the most prominent sexual health concerns among men aged 40–80 years, and has a prevalence rate ranging from 13 to 28%.[1] ED is defined as the consistent or recurrent inability of a man to attain and/or maintain penile erection sufficient for sexual activity.[2] ED affects men both physically and psychologically, and has a strong affect on both partners, causing emotional distress and impairment in self-esteem, interpersonal relationships and quality of life.[3] The introduction of easy to use oral PDE-5 inhibitors has revolutionized the treatment and management of ED. Patients have more treatment choices than ever before, and therapy can be better tailored to a patient's and his partner's sexual attitudes and patterns of activity.

Sildenafil (sildenafil citrate), tadalafil and vardenafil (vardenafil HCl) are the three oral PDE-5 inhibitors widely available. These drugs have shown their effectiveness, tolerability and safety in men with ED of varying severity and resulting from diverse causes.[4–12] It is widely accepted that there are no significant differences in PDE-5 inhibitor safety and efficacy. PDE-5 inhibitors differ mainly in half-life (that is, sildenafil and vardenafil ~4 h and tadalafil ~17.5 h), known duration of action and dietary effects on absorption.[13–15]

In ED, where the patients' subjective perception is very important, the objective of treatment should not only be 'organ focused', that is, facilitating the erection, but should also be 'patient-outcome oriented'. Patients' satisfaction with sexual intercourse, their overall sex lives and ED treatments may represent reliable predictors of key patient-related treatment outcomes, in addition to pharmacological efficacy and safety.[16]

The acknowledgement that the patient has an important role in therapeutic decisions for ED has fueled interest in the concept of patients' preference. In a traditional management model, physicians make treatment decisions, whereas in the preference-based paradigm, patients choose the treatments that best conform to their values,[17–20] and are involved on the potential outcomes (favorable and adverse) of each treatment alternative. As clinicians, researchers and patients try to comprehend the differences between the available treatment options for ED, it is important to discuss the study methodology and potential bias that may influence the results of patients' preference studies in order to provide an accurate and balanced assessment of treatment attributes for patients and their partners to make an informed decision on their preferred therapy.[21]

Various study designs, including randomized, open label, observational, double blind and crossover, have been used in research on patients' preference for one PDE-5 inhibitor over another. Few guidelines to establish an 'ideal' preference study in order to minimize confounding factors have been published.[22] The requirements and differences in the drug instructions make it very difficult for all studies to follow these guidelines and to constitute a 'perfect' flaw's free study, but every single study conducted on

preference had a rationale and provided important information. However, many of these studies have several flaws because of the methodological pitfalls. Though none of the studies are perfect, a consistency can be found in the information conveyed by them. This article focuses on the studies dealing with patients' preference on ED treatments.

Materials and Methods

A PubMed search was conducted for manuscripts published within the last 10 years with the search items ED, preference, sildenafil, tadalafil or vardenafil. We did not look at studies comparing oral treatments with intracavernous injection therapy. The identified articles were screened for relevance to the field of sexual medicine and likely interest to sexual health specialists. We selected only studies published in peer-reviewed journals, and eliminated those that could be retrieved just as abstracts/posters publications. We also eliminated the per-country sample articles related to another published study. Selected articles were critically reviewed and summarized. This review focuses on the preference of patients with ED for one drug over another.

Results

Looking at studies comparing one to one drug, we found two randomized, double-blind trials, one observational and three open-label studies, that compared tadalafil with sildenafil, but unfortunately we did not find any study comparing vardenafil with sildenafil or with tadalafil. We also found one randomized trial, one open-label and one observational study, which analyzed the three different PDE-5 inhibitors.

Preference Studies: Tadalafil versus Sildenafil

Data on two randomized, double-blind, one observational and three open-label studies that compared tadalafil with sildenafil are illustrated in Table 1.

Table 1. Preference studies on tadalafil and sildenafil

Study design	Population (N)	Drug dosage (mg)		Preference (%)		Preference evaluation	Industry sponsored
		Tadalafil	Sildenafil	Tadalafil	Sildenafil		
EC double blind, crossover of two periods[23]	215	20	50	66	34	TPQ	Yes
Randomized EC, double blind, crossover of four arms[24]	219	20	50, 100	73	27	DPA	Yes
Open-label EC, crossover of two periods[25]	367 (291 completed)	10, 20	25, 50, 100	71	29	TPQ	Yes
EC multicenter, open label, a crossover of one arm[26]	155	20	25, 50, 100	90.5	9.5	TPQ	Yes
Open-label EC, crossover of single arm[27]	160	20	NS	73.7	26.3	TPQ	Yes
Observational, multicenter, partners preference included[28]	2425 295[b]	NS	NS	59[a] 70[c]	28[a] 17[c]	TPQ	Yes

Abbreviations: DPA, drug preference assessment; EC, experimental control; NS, not specified; TPQ, treatment preference question.
[a]Patients who plan to change from tadalafil to sildenafil.
[b]Couples included in the study.
[c]Patients who plan to change from sildenafil to tadalafil.

Randomized, Double-blind Studies The first randomized, double-blind, crossover study was conducted to assess naive patients' preference for tadalafil 20 mg or sildenafil 50 mg to be taken as needed up to once daily.[23] Patients (*N*=215) with ED were randomized to the tadalafil–sildenafil sequence (*N*=109) or to the sildenafil–tadalafil sequence (*N*=106) for 4 weeks and then crossed over. Out of 190 patients who completed the study, 66.3% preferred tadalafil and 33.7% preferred sildenafil. These preferences were similar regardless of the age of the patients, time of evolution of ED and sequence of treatment. The strengths of

the study were its double-blind design and inclusion of naive patients, which guaranteed less bias. The main limitations of the study were exclusion of men ≥66 years of age, dose differences in the drugs used, which precluded maximal dose of sildenafil, and the short duration of the study.

Another multicenter, randomized, double-blind, crossover study with four treatment arms: in the first two arms, for analyzing treatment preference, 219 patients were randomized to tadalafil 20 mg or sildenafil 50 mg (each of the drug with its corresponding dosing instructions) and the second two arms to assess dosing instructions, 46 patients were randomized to tadalafil 20 mg, with either tadalafil or sildenafil dosing instructions.[24] Patients following sildenafil dosing instructions were offered to upward titration after 4 weeks of treatment. After 12 weeks patients crossed over, followed by a 12-week extension period when patients chose their double-blind preferred treatment. In the drug preference assessment, of the total patients (*N*=181) who completed the study, 73% preferred tadalafil over sildenafil (*P*<0.001). This outcome was consistent in all subgroups of patients analyzed, despite comorbidities, before use of sildenafil, or the order in which treatments were received. In the dosing instruction preference assessment, 24 of 36 (67%) patients preferred tadalafil with its dosing instructions (*P*=0.046). Dosage of both drugs and titrations of the sildenafil dose constitute the main limitations of the study, even though subgroup analysis minimized those considerations.

Randomized Open-label Studies An open-label, randomized crossover study was conducted to assess the preference, efficacy and tolerability of sildenafil and tadalafil with the appropriate dose needed in PDE-5-naive patients with ED.[25] The study duration was 24 weeks (12 weeks on each treatment, during which patients could titrate, up or down the dose (25–50 or 100 of sildenafil, 10–20 of tadalafil) to find their optimum dose) with an 8-week extension phase, in which the patient could choose the treatment. Of the total patients (*N*=291) who completed both treatments, 70.8% preferred tadalafil versus 29.2% who opted for sildenafil (*P*<0.001). This preference was not affected by ED severity and etiology, age, dosage and treatment sequence. The main limitation of the study was its open-label design, which was because of the difference in dosing instructions and pharmacokinetic characteristics of the two drugs.

In patients (*N*=155) on a stable fixed dose of 25, 50 or 100 mg sildenafil (at least 6 weeks and up to 24 weeks), an open-label, crossover, single-arm study was conducted with tadalafil 20 mg (3 weeks), and then drug preferences were obtained.[26] Of the 94.8% (*n*=147) of patients who completed the study, the majority of patients opted for tadalafil (90.5%), and only a few patients opted for sildenafil (9.5%) (*P*<0.001). The proportion of patients who preferred tadalafil remained the same, regardless of age, ED severity and etiology, and the dose of sildenafil previously received. The doses of each drug were held constant throughout the trial. The open-label design constitutes the main limitation for this study.

In another Korean open-label study,[27] 160 men (mean age 55 years), who were taking sildenafil for at least 6 weeks before study entry (45.6% of patients with 50 mg dose and 54.4% with 100 mg dose), were enrolled. Following the screening, patients continued sildenafil treatment for 4 weeks, and then were switched to tadalafil (20 mg dose) for 8 weeks with a 1-week-washout period in between and with their treatment of choice during an extension phase. In all, 73.7% of patients elected to take tadalafil, whereas 26.3% chose sildenafil (*P*<0.001). In this particular study, this preference might be influenced by a broader window of opportunity available for sexual activity. The limitations include potential bias, as they might identify the drug because of the differences in dosing instructions, or it is possible that patients might have preferred whichever treatment they received last. Finally, the issue of imbalance between groups was attempted to be addressed by adjusting for baseline confounders. It is possible that these baseline corrections might not fully address the potential biases of this open-label study.

Observational Studies In a leading study, it was reported that partner preference is equally important to patients' preference in the treatment of ED.[28] In an observational, multicenter study on patients who were planning to switch from tadalafil to sildenafil or vice versa, designed to determine both the patient's and their partner's preference, a total of 2425 patients and 295 couples participated in this study. The preference for one treatment over another was assessed by the physician, the patients themselves and their partners. In all three cases, the response showed a similar pattern of preference, with a significantly higher proportion toward tadalafil (59–76%) versus sildenafil (9–29%), regardless of the order in which the change was made (from sildenafil to tadalafil or from tadalafil to sildenafil). The constraints of the study were in its observational design, which limited the number of evaluations and the amount of information gathered.

Preference Studies: Tadalafil versus Sildenafil or Vardenafil

The data from one randomized, one open-label and one observational study, which analyzed the three different PDE-5 inhibitor treatments, tadalafil, sildenafil and vardenafil are presented in Table 2.

Table 2. Preference studies on tadalafil, sildenafil and vardenafil

Study	Population	Drug dosage (mg)	Preference (%)	Preference	Industry

design	(N)	Tadalafil	Vardenafil	Sildenafil	Tadalafil	Vardenafil	Sildenafil	None	evaluation	sponsored
Randomized, open label of three periods[29]	90	20	20	100	52.2	20	27.7	0	EDITS	No
Open label, crossover of three periods[30]	186 (145 completed)	20	20	100	55	17	27	0	TPQ	No
A 6-month, pan-European, prospective, observational study[31]	4026[a]	NS	NS	NS	64.5	12	7.8	0[b]	Switches of treatment	Yes

Abbreviations: EDITS, erectile dysfunction inventory for treatment satisfaction; NS, not specified; TPQ, treatment preference question.
[a]Patients naive to phosphodiesterase-5 inhibitor and who completed the study were analyzed.
[b]Remaining patients were on other inhibitors.

Randomized, open-label studies In a prospective, randomized, open-label study of three periods, sequential administration of the three PDE-5 inhibitors was carried out, and patients' preference was analyzed for sildenafil (100 mg), vardenafil (20 mg) or tadalafil (20 mg) for the treatment of ED.[29] In this study, 90 men, aged ≥18 years, with a clinical ED of at least 6 months' duration and naive to PDE-5 inhibitor treatment, were enrolled. Patients were randomly assigned to one of the six groups with different possible sequences. Patients were prescribed to take at least six tablets of each drug in its corresponding period. Of the total patients (*N*=90) who completed the study, 52% preferred to continue with tadalafil, 28% opted to continue with sildenafil and 20% chose vardenafil. Out of the 47 patients who chose tadalafil, 11 because of intense and longer lasting erection, 3 chose it because of flexibility in time, 5 because of the feeling that they could have intercourse the following day and 25 because of the same quality erection on the second day as the first. Out of the 25 patients who chose sildenafil, 21 did because of intense and longer lasting erection, 3 because it had fewer site effects and one because erection occurs more quickly. Out of the 18 patients who chose vardenafil, 16 chose it because of intense and longer lasting erection, one because erection occurs more quickly and one because it had fewer site effects. Potential limitations of this study were that it was conducted in only one center with a small sample.

Another study was designed for patients to individually identify the treatment they preferred after administration of the three PDE-5 inhibitors.[30] Patients were provided with the prescribed drugs (sildenafil 100 mg, tadalafil 20 mg and vardenafil 20 mg) for administration on demand (eight doses of each drug). A total of 186 patients were included in the study. Of the total patients (*n*=145) who responded to treatment and completed the study, 55% showed their preference for a long-response period drug, tadalafil, and 44% showed preference for drugs with a shorter response period (sildenafil: 27%; vardenafil: 17%). The difference was not statistically significant ($P<0.300$). In all, 1% the patients did not show preference for any of the treatments. However, the study is limited by several methodological flaws, which include a lack of treatment sequence randomization, the grouping of the sildenafil and vardenafil into a single group of short-acting agents, the limitation of sildenafil and vardenafil, exposure to four as opposed to eight tablets with tadalafil and the lack of a washout period between different treatment phases.

Observational Study Hatzichristou *et al.* [31] described patterns of treatment changes with the PDE-5 inhibitors tadalafil, sildenafil and vardenafil, and variables associated with those treatment changes, during the 6-month, prospective, pan-European Erectile Dysfunction Observational Study. This study enrolled 8047 men with ED, who began or changed ED therapy as part of their routine healthcare. Patients could change ED treatment at any time during European Erectile Dysfunction Observational Study. Data were collected at baseline and at 3 (±1) and 6 (±1) months. ED treatment-naive patients (*n*=4026) were prescribed a PDE-5 inhibitor at baseline and analyzed by complete follow-up. Most patients, regardless of which PDE-5 inhibitor they were prescribed at baseline, continued on that same PDE-5 inhibitor throughout the study. Continuation rates were ~89% in the tadalafil cohort, versus 63–64% in the sildenafil and vardenafil cohorts. The variables most strongly associated with increased risk of switching were prescription of sildenafil or vardenafil, versus tadalafil, at baseline (odds ratios 4.43 and 4.14, respectively; $P<0.0001$). Of patients who switched from tadalafil to another treatment, nearly 25% had switched back to tadalafil by study end. In contrast, of patients who switched

from sildenafil or vardenafil, <10% from each cohort had switched back to their original treatment by study end. The data suggest that tadalafil treatment in treatment-naive patients with ED may increase their likelihood of treatment continuation. These findings should be interpreted conservatively because of the observational nature of the study. A limitation of European Erectile Dysfunction Observational Study was that data were collected only at baseline, and at 3 (±1) and 6 (±1) months. However, patients could switch treatment at any time during the study, and for this reason, the recorded rates of switching may actually be underestimated and, conversely, the recorded rates of continuation overestimated. Another limitation was that the sample of patients was not random, and indeed in many ways it was self-selected, as too were the investigators.

Reasons and Factors that may Affect Patients' Preference

Because there are several effective and safe oral PDE-5 inhibitors for the treatment of ED, various factors important to both the patients and his partner, such as biological, social, psychological and/or cultural factors, will influence the treatment choices made.[27] It has been established that patients' preference depends on three factors, that is, personal characteristics, such as age, duration of ED, frequency and dynamics of sexual relations, and the characteristics of their partners, such as age, menopausal status, level of interest in sexual activity and medication profile. Medication features of interest include efficacy in terms of quality of erection, consistency of effects, rapid onset of action, long duration of action, side-effect profile and route of administration.[3] Understanding the reasons for ED treatment preferences might enhance patient compliance and satisfaction as well.[28] Non-medical (lifestyle) factors might shape patients' and partners' attitudes toward ED treatments, including convenience, cost, ease of administration and 'naturalness' in promoting erection.[32]

Although several previous studies have focused on determining patient treatment choices,[24,26,33] the reasons surrounding these treatment choices have not been fully explored. The psychological and interpersonal relationship scales was developed to incorporate outcomes, such as time concerns, spontaneity and sexual self-confidence, which are not assessed in existing measures of sexual function. This is another approach to identify some of the possible reasons as to why patients have preferences for one form of treatment over another. A statistically significant decrease in the mean psychological and interpersonal relationship scale time concern domain scores was observed when patients switched from sildenafil to tadalafil, indicating that patients were less concerned about time in relation to sexual activity while taking tadalafil, as compared with when they were taking sildenafil. Together, these results suggest that time concerns seem to have a role in patient decisions regarding ED treatment type.[27] Furthermore, other studies have shown that the sequence in which treatments are given (that is, sildenafil followed by tadalafil or vice versa) does not seem to affect the treatment preference of the patient.[24,25]

In a *post hoc* analysis,[34] baseline characteristics and post-baseline measurements were carried out to identify factors associated with patients' preference. No baseline characteristics were identified that prospectively distinguished patients' preference for tadalafil or sildenafil. The baseline characteristics included age, race, ED etiology/duration, basal metabolic rate, smoking status, alcohol consumption, vital signs and comorbid medical conditions, as well as baseline scores for international index of erectile function, psychological and interpersonal relationship scales domains, and for sexual encounter profile.[12,25,35–37] When baseline characteristics were considered individually, the only significant factor (P=0.01) associated with the treatment preference of the patient was the presence or absence of comorbid hyperlipidemia (in patients without hyperlipidemia, 73% preferred tadalafil versus 26.6 who preferred sildenafil and in patients with hyperlipidemia 51.4% preferred tadalafil versus 48.6% who preferred sildenafil). Patient differences in time concerns, dosage choice, intercourse satisfaction, treatment tolerability, number of sexual attempts and satisfaction with erection hardness were the set of factors most significantly associated with treatment preference, and the preference observed for tadalafil (71%) or sildenafil (29%) might be substantially accounted for by differences in these factors during the tadalafil and sildenafil treatment periods.[34] Among patients naive to PDE-5 inhibitors, ~70% preferred tadalafil regardless of whether they received sildenafil or tadalafil as their first PDE-5 inhibitor.[34]

The preference for tadalafil decreased to <50%, only for patients with large differences in efficacy in favor of sildenafil, suggesting that additional factors are playing a role in driving the preference toward tadalafil.[34] This is consistent with the identification of psychosocial outcomes and treatment tolerance as factors significantly associated with preference. Patient's perception of side-effect severity appeared comparable for the tadalafil and sildenafil treatment periods, regardless of treatment preference. The few patients with severe side-effects after treatment with one drug would tend to prefer the other drug.[34]

Partner's Preference

The potential influence of female partners on ED patients' treatment-seeking behaviors and treatment outcomes is well documented.[38,39] Taking into account the importance not only of patients' preference, but partners' opinion, a single-center, open-label, crossover study was published, in which 100 heterosexual couples in stable relationships with male partners having ED were randomly assigned to receive sildenafil or tadalafil for a 12-week phase.[40] Female participants were interviewed for their preference and their reasons at baseline, midpoint and at the end of the study. A total of 79.2% of the women preferred their

partners' use of tadalafil, whereas 15.6% preferred sildenafil. Preference was not affected by age or treatment order randomization. Women preferring tadalafil reported feeling more relaxed, experiencing less pressure and enjoying more natural or spontaneous sexual experiences as reasons for their choice. Women preferring sildenafil focused on satisfaction and drug effectiveness for their partners.[40] A limitation because of the community context of the study was the direct-to-consumer advertising of ED medication that occured in New Zealand and may have generated expectations in the participants. Despite this, many couples did not know that tadalafil was used to treat similar problems as sildenafil, and most were unfamiliar with the generic names of either drug, as well as their cost. Most couples thought that both medications might be expensive. In asking whether participants would continue to use these medications, it was recognized that, for many, cost was a potential barrier and a number of the women confirmed this.

Discussion

All available PDE-5 inhibitors have demonstrated their efficacy and safety profiles in patients with ED. It has been proposed that, such as safety and efficacy trials, randomized, double-blind, crossover-controlled trials should be the gold standard for evaluating patients' preference for ED treatments.[21,22] In terms of methodology, there is no perfect head-to-head study, and no meta-analysis has been published to date, but a large amount of data have been generated with clear scientific evidence that goes beyond the individual limitations of each single study.

The main limitation of these studies arises from the design itself. As we have seen, there is a broad range of approaches that have tried to cover all aspects, some more experimentally oriented as per methodology, others sticking to observational settings trying to mimic the real daily clinical practice. Nevertheless, none of them provide the highest level of evidence at this point. Another commonly cited limitation is the non-equivalent doses used between drugs. Differences in dosing recommendations may have influenced patient and provider blinding and thereby compromised results. Nevertheless, there is no study that had established the equivalence between the three PDE-5 inhibitors. Most of the studies were conducted with the most commonly prescribed doses in real clinical practice, and so, the studies aimed to mimic the daily conditions in clinics. The period, in which a patient is taking the drug is also an important factor, which limits the evaluation of the results. Studies having short treatment periods influence the results and this feature may be considered as a limitation of the study.[23]

Different drug instructions result in potential bias, which is commonly mentioned in preference studies. Clearly, it is very difficult to blind drugs which have different pharmacokinetic profiles and, therefore, different dosing and instructions on how to take the study medication in relation with food, and the flexibility on timing for sexual intercourse. Some studies have tried to minimize this effect using placebo or assessing dosing instructions.[24] But we cannot obviate that differentiation between these drugs results from their inherent characteristics, which make them different in their effect on each single patient's need.

On the other hand, when most of these studies were conducted, tadalafil and vardenafil were just launched so they could be considered as 'new' drugs, which may have introduced any kind of bias in the results, that is, interest to try a new treatment. In addition, most of the studies were industry sponsored, although the two independent studies that compared the three drugs contributed with similar results.

The mentioned limitations do not invalidate the studies, although it becomes necessary to take them into account in the interpretation of the data. In fact, having restrictive conditions in a study is, by itself, a clear bias that sometimes makes the generalization of data more difficult. To our knowledge, the weight or impact of the potential bias associated with each study design is neither completely known nor addressed.

However, what we really can see across the studies is a consistent trend of the results, independently of the specific design, bias or approach. According to the preference studies published to date in randomized, double-blind and open-label designs, with both naive and non-naive patients, and with dosage differences, the majority of patients preferred tadalafil over sildenafil. Among the patients who had the opportunity to try a cycle of therapy with tadalafil, 66–90% decided to continue their treatment with tadalafil, or switch to tadalafil.

Patients on tadalafil may be less concerned about the time between dosing and intercourse, likely because of longer period of responsiveness for tadalafil[11] and the drug can be taken without regard to food intake,[13] in contrast to sildenafil and vardenafil, for which heavy-fat meals have been shown to decrease the extent and slow the rate of absorption.[14,41] The fact that convenience, simplicity and naturalness are traits that men value in an ED treatment[32] could, therefore, have contributed to more tadalafil patients being satisfied with their treatment, thereby resulting in less patients switching from tadalafil, as compared with sildenafil or vardenafil.[31] The importance of the patient's perception and needs, and the consistency of the data from the studies analyzed, should be considered when the patients are given different treatment options, keeping in mind that the real objective should be the 'normalization' of patient's sexual life and reach the ultimate goal of restoration of both erection and perception.

Although a high level of evidence does not exist on this issue, analysis of the literature shows a consistent trend in patients' preference for tadalafil over sildenafil or vardenafil, mainly because of longer duration of action, that improves patients' perception of freedom in sexual life.

References

1. Laumann EO, Nicolosi A, Glasser DB, Paik A, Gingell C, Moreira E *et al*. Sexual problems among women and men aged 40–80 y: prevalence and correlates identified in the Global Study of Sexual Attitudes and Behaviors. *Int J Impot Res* 2005; 17: 39–57.
2. Lewis RW, Fugl-Meyer KS, Bosch R, Fugl-Meyer AR, Laumann EO, Lizza E *et al*. Epidemiology/risk factors of sexual dysfunctions. *J Sex Med* 2004; 1: 35–39.
3. Hedelin H, Ströberg P. Treatment for erectile dysfunction based on patient-reported outcomes: to every man the PDE5 inhibitor that he finds superior. *Drugs* 2005; 65: 2245–2251.
4. Mirone V, Fusco F, Rossi A, Sicuteri R, Montorsi F. Tadalafil and vardenafil vs sildenafil: a review of patient-preference studies. *BJU Int* 2009; 103: 1212–1217.
5. Bai WJ. Tadalafil for erectile dysfunction: excellent safety and tolerance. *Zhonghua Nan Ke Xue* 2009; 15: 92–95.
6. Zhang K, Zhu JC. A decade's evidence review of sildenafil citrate. *Zhonghua Nan Ke Xue* 2009; 15: 3–6.
7. Shindel AW. 2009 update on phosphodiesterase type 5 inhibitor therapy part 2: updates on optimal utilization for sexual concerns and rare toxicities in this class. *J Sex Med* 2009; 6: 2352–2364.
8. Hatzimouratidis K, Burnett AL, Hatzichristou D, McCullough AR, Montorsi F, Mulhall JP. Phosphodiesterase type 5 inhibitors in postprostatectomy erectile dysfunction: a critical analysis of the basic science rationale and clinical application. *Eur Urol* 2009; 55: 334–347.
9. Eardley I, Lee JC, Guay AT. Global experiences with vardenafil in men with erectile dysfunction and underlying conditions. *Int J Clin Pract* 2008; 62: 1594–1603.
10. Hellstrom WJ, Gittelman M, Karlin G, Segerson T, Thibonnier M, Taylor T *et al*. Vardenafil for treatment of men with erectile dysfunction: efficacy and safety in a randomized, double-blind, placebo-controlled trial. *J Androl* 2002; 23: 763–771.
11. Brock GB, McMahon CG, Chen KK, Costigan T, Shen W, Watkins V *et al*. Efficacy and safety of tadalafil for the treatment of erectile dysfunction: results of integrated analyses. *J Urol* 2002; 168: 1332–1336.
12. Goldstein I, Lue TF, Padma-Nathan H, Rosen RC, Steers WD, Wicker PA. Oral sildenafil in the treatment of erectile dysfunction. Sildenafil Study Group. *N Engl J Med* 1998; 338: 1397–1404.
13. Forgue ST, Patterson BE, Bedding AW, Payne CD, Phillips DL, Wrishko RE *et al*. Tadalafil pharmacokinetics in healthy subjects. *Br J Clin Pharmacol* 2006; 61: 280–288.
14. Nichols DJ, Muirhead GJ, Harness JA. Pharmacokinetics of sildenafil after single oral doses in healthy male subjects: absolute bioavailability, food effects, and dose proportionality. *Br J Clin Pharmacol* 2002; 53: S5–S12.
15. Stark S, Sachse R, Liedl T, Hensen J, Rohde G, Wensing G *et al*. Vardenafil increases penile rigidity and tumescence in men with erectile dysfunction after a single oral dose. *Eur Urol* 2001; 40: 181–188.
16. Carson C, Giuliano F, Goldstein I, Hatzichristou D, Hellstrom W, Lue T *et al*. The 'effectiveness' scale—therapeutic outcome of pharmacologic therapies for ED: an international consensus panel report. *Int J Impot Res* 2004; 16: 207–213.
17. Weinstein JN. The missing piece: embracing shared decision making to reform health care. *Spine (Phila Pa 1976)* 2000; 25: 1–4.
18. Kaplan RM. Shared medical decision-making: a new paradigm for behavioral medicine—1997 presidential address. *Ann Behav Med* 1999; 21: 3–11.
19. Blumenthal D. Part 1: quality of care—what is it? *N Engl J Med* 1996; 335: 891–894.
20. Katz JN. Patient preferences and health disparities. *JAMA* 2001; 286: 1506–1509.
21. Mulhall JP, Montorsi F. Evaluating preference trials of oral phosphodiesterase 5 inhibitors for erectile dysfunction. *Eur Urol* 2006; 49: 30–37.
22. Mulhall JP. Understanding erectile dysfunction medication preference studies. *Curr Opin Urol* 2004; 14: 367–373.
23. Govier F, Potempa AJ, Kaufman J, Denne J, Kovalenko P, Ahuja S. A multicenter, randomized, double-blind, crossover study of patient preference for tadalafil 20 mg or sildenafil citrate 50 mg during initiation of treatment for erectile dysfunction. *Clin Ther* 2003; 25: 2709–2723.
24. von Keitz A, Rajfer J, Segal S, Murphy A, Denne J, Costigan T *et al*. A multicenter, randomized, double-blind, crossover study to evaluate patient preference between tadalafil and sildenafil. *Eur Urol* 2004; 45: 499–507.
25. Eardley I, Mirone V, Montorsi F, Ralph D, Kell P, Warner MR *et al*. An open-label, multicentre, randomized, crossover study comparing sildenafil citrate and tadalafil for treating erectile dysfunction in men naïve to phosphodiesterase 5 inhibitor therapy. *BJU Int* 2005; 96: 1323–1332.
26. Ströberg P, Murphy A, Costigan T. Switching patients with erectile dysfunction from sildenafil citrate to tadalafil: results of a European multicenter, open-label study of patient preference. *Clin Ther* 2003; 25: 2724–2737.

27. Ahn TY, Lee SW, Kim SW, Yang DY, Park NC, Min KS *et al*. Treatment preferences in men with erectile dysfunction: an open label study in Korean men switching from sildenafil citrate to tadalafil. *Asian J Androl* 2007; 9: 760–770.
28. Lee J, Pommerville P, Brock G, Gagnon R, Mehta P, Krisdaphongs M *et al*. Physician-rated patient preference and patient- and partner-rated preference for tadalafil or sildenafil citrate: results from the Canadian 'Treatment of erectile dysfunction' observational study. *BJU Int* 2006; 98: 623–629.
29. Tolrà JR, Campaña JM, Ciutat LF, Miranda EF. Prospective, randomized, open-label, fixed-dose, crossover study to establish preference of patients with erectile dysfunction after taking the three PDE-5 inhibitors. *J Sex Med* 2006; 3: 901–909.
30. Ströberg P, Hedelin H, Ljunggren C. Prescribing all phosphodiesterase 5 inhibitors to a patient with erectile dysfunction-a realistic and feasible option in everyday clinical practice—outcomes of a simple treatment regime. *Eur Urol* 2006; 49: 900–907.
31. Hatzichristou D, Haro JM, Martin-Morales A, von Keitz A, Riley A, Bertsch J *et al*. Patterns of switching phosphodiesterase type 5 inhibitors in the treatment of erectile dysfunction: results from the Erectile Dysfunction Observational Study. *Int J Clin Pract* 2007; 61: 1850–1862.
32. Hanson-Divers C, Jackson SE, Lue TF, Crawford SY, Rosen RC. Health outcomes variables important to patients in the treatment of erectile dysfunction. *J Urol* 1998; 159: 1541–1547.
33. Eardley I, Wright P, MacDonagh R, Hole J, Edwards A. An open-label, randomized, flexible-dose, crossover study to assess the comparative efficacy and safety of sildenafil citrate and apomorphine hydrochloride in men with erectile dysfunction. *BJU Int* 2004; 93: 1271–1275.
34. Eardley I, Montorsi F, Jackson G, Mirone V, Chan ML, Loughney K *et al*. Factors associated with preference for sildenafil citrate and tadalafil for treating erectile dysfunction in men naïve to phosphodiesterase 5 inhibitor therapy: *post hoc* analysis of data from a multicentre, randomized, open-label, crossover study. *BJU Int* 2007; 100: 122–129.
35. Padma-Nathan H, McMurray JG, Pullman WE, Whitaker JC, Saoud JC, Ferguson KM *et al*. On-demand IC351 (Cialis) enhances erectile function in patients with erectile dysfunction. *Int J Impot Res* 2001; 13: 2–9.
36. Porst H, Rosen R, Padma-Nathan H, Goldstein I, Giuliano F, Ulbrich E *et al*. The efficacy and tolerability of vardenafil, a new, oral, selective phosphodiesterase type 5 inhibitor, in patients with erectile dysfunction: the first at-home clinical trial. *Int J Impot Res* 2001; 13: 192–199.
37. NIH Consensus Conference. Impotence. NIH consensus development panel on impotence. *JAMA* 1993; 270: 83–90.
38. Althof SE, Eid JF, Talley DR, Brock GB, Dunn ME, Tomlin ME *et al*. Through the eyes of women: the partners' perspective on tadalafil. *Urology* 2006; 68: 631–635.
39. Fisher WA, Rosen RC, Eardley I, Sand M, Goldstein I. Sexual experience of female partners of men with erectile dysfunction: the female experience of men's attitudes to life events and sexuality (FEMALES) study. *J Sex Med* 2005; 2: 675–684.
40. Conaglen HM, Conaglen JV. Investigating women's preference for sildenafil or tadalafil use by their partners with erectile dysfunction: the partners' preference study. *J Sex Med* 2008; 5: 1198–1207.
41. Rajagopalan P, Mazzu A, Xia C, Dawkins R, Sundaresan P. Effect of high-fat breakfast and moderate-fat evening meal on the pharmacokinetics of vardenafil, an oral phosphodiesterase-5 inhibitor for the treatment of erectile dysfunction. *J Clin Pharmacol* 2003; 43: 260–267.

Conflict of interest
Dr Martin-Morales has served on advisory boards and lectured on behalf of Bayer, Lilly, Pfizer, Johnson and Johnson, Abbott, Schering, Ipson and Sanofi. Marta Casillas and Carmen Turbi are currently full-time Lilly employees.

Acknowledgements
We thank the collaboration of Smita Agarwal, from Primo Scientific, for her editorial assistance in the writing of the manuscript.

Int J Impot Res. 2011;23(1):1-8. © 2011 Nature Publishing Group