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REVIEW

An assessment of patient-reported outcomes for men with erectile dysfunction: Pfizer's perspective

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Patient-reported outcomes (PROs) for men with erectile dysfunction (ED) have blossomed in the published literature and at professional conferences. These outcomes have been central to study the science of ED itself and to evaluate efficacy of treatment for men with ED. In this review article we highlight and distinguish among seven key PROs: the International Index of Erectile Function, for sexual function including erectile function; the Sexual Health Inventory for Men (SHIM), for diagnosis of ED; the Quality of Erection Questionnaire, for satisfaction with quality of erections; the Erectile Dysfunction Inventory of Treatment Satisfaction, for personal evaluation of treatment received; the Self-Esteem And Relationship questionnaire, for emotional well-being; the Erection Hardness Score (EHS), for targeting erection hardness and the Sexual Experience Questionnaire, for erection (both function and quality), individual satisfaction and couples satisfaction. Depending on the purpose of the investigation, all seven PROs have merit for use in clinical trials and at least deserve consideration in clinical practice. The SHIM and the EHS, given their aims and brevity, deserve special consideration in clinical practice. As a unit these seven PROs complement and supplement each other. Which ones to choose in a particular undertaking depends on the objective or purpose of a given study. These PROs acknowledge that sexual dysfunction and its treatment have multiple dimensions. Each of these instruments represents a significant contribution to sexual medicine research and, when used judiciously and appropriately, can help to provide optimal patient care and management.
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Introduction

The Institute of Medicine's report 'Crossing the Quality Chasm' suggests that optimal medical care should be safe, effective (evidence-based), efficient, equitable, timely and patient centered.[1] The inclusion of 'patient centered' in this list highlights the importance of the patient's perspective when providing medical care. Medical intervention, in some cases, may not be justifiable in the absence of patient bother and may be of questionable success in the absence of patient satisfaction, improvement in subjective symptoms and improved quality of life. In addition, patient centered implies involvement of the patient in decision-making and self-management.

Patient-reported outcomes (PROs) have been used in clinical trials for more than 20 years.[2] At least three major reasons exist for the acceptance of PROs. First, in recent years, the patient's perception of functioning and well-being has been increasingly acknowledged as relevant by different stakeholders, including patients and health-care providers.

Second, many PROs are the result of careful development, including rigorous assessment, such that 'their reliability may be superior to widely accepted clinical outcomes that have not been formally validated.'[3] Despite the fact that PROs are valid and essential, they differ in important ways from objective clinically determined end points such as survival—for example, PROs require the patient's active participation and therefore nonresponse may affect the results. The differences inherent in PROs necessitate unique design and analytic methods.[3–4]

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Third, PROs are prime candidates for inclusion into a medicine's label claim and for promotional use and, in doing so, may help to get the medicine approved or lend distinction to a pharmaceutical sponsor's medical product. In fact, as of this writing, the Food and Drug Administration has released a draft guidance to support labeling claims of patient-reported measures in medical product development,[5] and an entire journal issue has been devoted to the topic.[6–13]

An important purpose of clinical trials is 'to communicate information about the risks and benefits of new therapies to physicians, patients, and their families' so as to inform individual healthcare decisions in the clinical practice setting.[2] PROs are key to treatment decision-making, including shared decision-making, which can improve patient self-management. As summarized by the PRO Harmonization Group Meeting at the Food and Drug Administration, 'The patient's perspective is a key element in medical diagnosis and treatment' and 'PRO data are essential for evidence-based practice.'[2]

Over the past decade in particular, there has been an explosion in PROs that have been developed and validated to evaluate treatment and to monitor patients with chronic conditions.[14–15] As in other fields like asthma and arthritis, the field of erectile dysfunction (ED) research has witnessed accelerated growth and application of PROs developed and validated to evaluate treatment effect in clinical trials and monitor patient change in clinical practice.

In clinical trials of ED, PRO instruments such as self-administered questionnaires and per-event patient diaries are the preferred assessments.[16] The International Index of Erectile Function (IIEF)—and especially its Erectile Function (EF) domain—is widely accepted as the standard PRO to assess erectile function of men in clinical trials of ED.[16–19] Other well-known PROs in clinical trials include the Sexual Health Inventory for Men (SHIM),[20–21] Quality of Erection Questionnaire (QEQ),[22–23] the Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS),[24] the Self-Esteem And Relationship questionnaire (SEAR)[25–27] and the Erection Hardness Score (EHS).[28–30] A recent member to the list of PROs is the Sexual Experience Questionnaire (SEX-Q).[31]

In clinical practice, the SHIM and EHS have been valuable, respectively, in the diagnosis and treatment of ED. In addition, given that ED may be a marker for occult cardiovascular disease, the SHIM and EHS (as well as other PROs) may be useful in the identification of men at risk. The hallmarks of recommended outcomes to evaluate effectiveness of ED treatment in clinical practice are 'simple, quick, inexpensive, and efficient'.[32]

Of course, the seven PROs highlighted above are not the only ones applied in the treatment and management of ED. Others exist and include (but are not limited to) the Erection Quality Scale,[33–34] the Treatment Satisfaction Scale,[35] Psychological and Interpersonal Relationship Scales,[36] the Sexual Life Quality Questionnaire,[37] the Erectile Dysfunction-Effect on Quality of Life,[38] the Psychological Impact of Erectile Dysfunction instrument[39] and the Sexual Encounter Profile.[40]

In this review, though, we restrict our attention to seven specific PROs—IIEF, SHIM, QEQ, EDITS, SEAR, EHS, SEX-Q—as they have earned recognition in the published literature and at professional conferences, and are the ones that having been involved with their development and validation we are most familiar with. Although the development of these measures was sponsored by Pfizer Inc, as part of the sildenafil clinical trial program, they were designed and intended for any therapeutic intervention of ED and have become part of the science of ED research. These measures have achieved or, in the case of the SEX-Q, expected to achieve broad acceptance throughout the sexual health research community. These outcomes have matured with the field of sexual medicine.

With these seven PROs to choose from, researchers and practitioners in sexual medicine are offered a choice of instruments developed and validated to meet their varying objectives. With the opportunity to select an appropriate PRO for a given purpose, however, researchers and practitioners also run the risk of choosing a PRO that is not intended or ill-suited for their real purpose. How do the seven PROs compare and contrast? What are their intended and correct uses? In this review article, we highlight key psychometrics (measurement) properties of the seven PROs and provide a guidance to distinguish among these PROs so that they can be applied appropriately to the situation.

International index of erectile function

The IIEF was created to overcome several limitations of then-existing self-reported measures of erectile function, including excessive length or complexity, overly restrictive focus and inadequate psychometric, cultural or linguistic properties. The development of the IIEF, led by an international consortium of experts, included an extensive review of the literature and of existing questionnaires in addition to detailed interviews of men with ED and their partners.[16–19]

The IIEF meets psychometric criteria for test reliability and validity, has a high degree of sensitivity and specificity and correlates well with other measures of treatment outcome, such as global assessments of treatment efficacy and quality of life.[16–19] The final IIEF instrument consists of 15 questions (Q), is self-administered and is designed primarily

for use in clinical trials. It has five domains: EF (Q 1–5, 15), Orgasmic Function (Q 9, 10), Sexual Desire (Q 11, 12), Intercourse Satisfaction (Q 6–8) and Overall Satisfaction (Q 13, 14), each addressing a unique dimension of sexual function (Table 1). Responses to each question are based on a man's experience over the past 4 weeks using an ordinal scale (0–5 or 1–5, depending on the question), with lower values indicating more sexual dysfunction.

For men in a stable relationship who report no sexual activity, a coded response of 0 is taken to be the most dysfunctional response. A domain score is computed by summing the responses to its individual items. The IIEF is considered the gold standard among questionnaires in male sexual functioning, regardless of treatment intervention or population studied, and has had a tremendous impact on the field of ED research. It is widely accepted by both regulatory agencies and scientific journals as a valid and reliable measure of sexual functioning in men. The IIEF has been linguistically and culturally validated in 32 languages.

Important limitations of the IIEF include its prime focus on EF and its limited assessment of other sexual functions, such as orgasm and sexual desire. No etiological classification can be derived from the IIEF scores, nor does it assess distress. In addition, the IIEF is not designed to distinguish between different kinds of sexual desire disorder or between premature ejaculation and other orgasmic disorders. The IIEF focuses on heterosexual activity (including vaginal intercourse) and may be less suitable in assessing treatment outcome for individuals whose primary sexual activity is not heterosexual intercourse.

In the IIEF and in other questionnaires described here, the term 'sexual activity' includes intercourse, caressing, foreplay and masturbation; 'sexual intercourse' is defined as penetration of the partner; 'sexual stimulation' includes situations like foreplay with partner, looking at erotic pictures and so on and 'ejaculate' is defined as the ejection of semen from the penis (or feeling of this).

Erectile function domain of the IIEF

The six-item EF domain, consisting of Q 1–5 and Q 15, is the cornerstone of the IIEF and was designed primarily to assess changes in EF over time and efficacy of drug therapy. Two items, Q 3 and Q 4, were specifically designed to assess major components of EF: the ability to achieve penetration and the ability to maintain an erection, respectively. In addition to assessing treatment efficacy in clinical trials, the EF domain was also evaluated to assess severity grades of ED. Such a staging system could aid in defining the patient population for a clinical trial, measure responder rates associated with ED treatment, improve patient care and support claims for reimbursement.

Among men in a stable relationship—those who had the regular opportunity to engage in sexual activity—who attempted sexual intercourse and activity in the past 4 weeks, levels of ED severity on the EF domain have been classified as follows: normal (no ED; score, 26–30); mild ED (22–25); mild-to-moderate (17–21); moderate (11–16) and severe (6–10).[19,41–42] For men in a stable relationship whose ED is so poor that they do not even attempt sexual activity, the severe ED scores range from 1 to 10. Validity and reliability of this diagnostic classification was confirmed in a separate independent study comparing ED severity as determined using the EF domain with a single-item self-assessment of ED severity before and after ED treatment.[42]

Sexual health inventory for men

Although the 15-item IIEF is the gold-standard measure for the assessment of EF in clinical research, it is not ideal for use in clinical practice because of its length. In clinical practice, patients may be reluctant to raise the topic of sexual health with clinicians. Routine use of an inventory to assess this potential problem can help open communications on the sensitive topic of ED. The SHIM[20–21] is designed for clinical practice and is an abridged 5-item version of the 15-item IIEF (Table 2). The five items selected for the SHIM were based on their ability to identify the presence or absence of ED consistent with the definition of ED by the National Institutes of Health (NIH), namely, as the inability to attain or maintain an erection sufficient for satisfactory sexual performance.[43]

The SHIM asks men to respond to five specific questions about sexual functioning over the previous 6 months, a time period suggested in the current NIH guideline. The SHIM contains four items from the erection function domain of the IIEF (Q 2, erection firmness; Q 4, maintenance frequency; Q 5, maintenance ability; Q 15, erection confidence) and one item on intercourse satisfaction (Q 7). Responses to the five questions are summed with a possible score range from 1 to 25. Patients who score 21 or less may be at high risk of ED. Grades of ED severity using SHIM scores are as follows: normal (no ED), score 22–25; mild ED, 17–21; mild-to-moderate, 12–16; moderate, 8–11 and severe, 1–7 (among men who had the opportunity to engage in sexual activity and intercourse but whose sexual functioning is so poor that they do not even bother to attempt sexual activity and intercourse; otherwise the scores for severe ED are from 5 to 7).[20–21]

When administering the SHIM, clinicians should ask patients about their desire and opportunity for sexual activity to ensure that low scores are truly indicative of severe ED. This simple tool provides a basis for discussing potential problems caused by

Table 1 International Index of Erectile Function (United States—English version)

	Question	*Response options*
Over the past 4 weeks		
Q1:	How often were you able to get an erection during sexual activity?	0 = No sexual stimulation 1 = Almost never/never 2 = A few times (much less than half the time) 3 = Sometimes (about half the time) 4 = Most times (much more than half the time) 5 = Almost always/always
Q2:	When you had erections with sexual stimulation, how often were your erections hard enough for penetration?	0 = No sexual stimulation 1 = Almost never/never 2 = A few times (much less than half the time) 3 = Sometimes (about half the time) 4 = Most times (much more than half the time) 5 = Almost always/always
Q3:	When you attempted sexual intercourse, how often were you able to penetrate (enter) your partner?	0 = Did not attempt intercourse 1 = Almost never/never 2 = A few times (much less than half the time)
Q4:	During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?	3 = Sometimes (about half the time) 4 = Most times (much more than half the time) 5 = Almost always/always
Q5:	During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?	1 = Did not attempt intercourse 2 = Extremely difficult 3 = Difficult 4 = Slightly difficult 5 = Not difficult
Q6:	How many times have you attempted sexual intercourse?	0 = No attempts 1 = One to two attempts 2 = Three to four attempts 3 = Five to six attempts 4 = Seven to ten attempts 5 = Eleven + attempts
Q7:	When you attempted sexual intercourse, how often was it satisfactory for you?	0 = Did attempt intercourse 1 = Almost never/never 2 = A few times (much less than half the time) 3 = Sometimes (about half the time) 4 = Most times (much more than half the time) 5 = Almost always/always
Q8:	How much have you enjoyed sexual intercourse?	0 = No intercourse 1 = No enjoyment 2 = Not very enjoyable 3 = Fairly enjoyable 4 = Highly enjoyable 5 = Very highly enjoyable
Q9:	When you had sexual simulation or intercourse, how often did you ejaculate?	0 = No sexual stimulation/intercourse 1 = Almost never/never
Q10:	When you had sexual stimulation or intercourse, how often did you have the feeling of orgasm or climax?	2 = A few times (much less than half the time) 3 = Sometimes (about half the time) 4 = Most times (much more than half the time) 5 = Almost always/always
Q11:	How often have you felt sexual desire?	1 = Almost never/never 2 = A few times (much less than half the time) 3 = Sometimes (about half the time) 4 = Most times (much more than half the time) 5 = Almost always/always
Q12:	How would you rate your level of sexual desire?	1 = Very low or none at all 2 = Low 3 = Moderate 4 = High 5 = Very high

Table 1 (Continued)

	Question	*Response options*
Q13:	How satisfied have you been with your overall sex life?	1 = Very dissatisfied 2 = Moderately dissatisfied 3 = About equally satisfied and dissatisfied
Q14:	How satisfied have you been with your sexual relationship with your partner?	4 = Moderately satisfied 5 = Very satisfied
Q15:	How do you rate your confidence that you could get and keep an erection?	1 = Very low 2 = Low 3 = Moderate 4 = High 5 = Very high

other diseases, especially emerging or asymptomatic diseases. In addition to being a diagnostic aid to supplement patient history and examination in clinical practice, the SHIM can serve as part of inclusion criteria in a clinical trial to confirm ED status (SHIM scores of 21 or less) or to enroll a specific study subpopulation (for example, mild to moderate ED with SHIM scores between 8 and 21 inclusive).

Thousands of primary care physicians worldwide have used the SHIM as a diagnostic tool or simple office screening measure for ED. A 5-year review on the SHIM revealed that it is a useful, quick and inexpensive tool that can complement clinical judgment for the diagnosis, treatment and management of ED.[21]

Quality of erection questionnaire

The QEQ was designed to solely and specifically evaluate men's satisfaction with the quality of their erections (Table 3). In clinical trials, besides an item-level analysis, the QEQ is evaluated chiefly as a total score based on responses to all of its six items. For use in clinical trials, the QEQ total score is transformed onto a 0–100 scale, with higher score meaning higher quality of erections. The reference period is the past 4 weeks.

The QEQ was developed through in-depth qualitative interviews of men with ED in the United States and Australia. An exploratory methodology study was conducted on 65 men with ED. Subsequently, the psychometric properties were confirmed in a larger data set of 558 men with ED from two combined clinical trials.[23] The QEQ demonstrated excellent convergent and known-groups validity. Additional analysis indicated high internal consistency (Cronbach's α, 0.92). Item analysis demonstrated a singular or one-dimensional concept—quality of erections—and suggested that satisfaction with hardness may be the key driver for satisfaction with overall quality of erections ($r = 0.8$). The smaller exploratory study likewise demonstrated good test–retest reliability ($r = 0.82$).

The results of two clinical trials for the treatment of men with ED, one of which was double blind and placebo controlled (DBPC), suggest that the QEQ is a responsive, sensitive and robust instrument to detect changes in satisfaction with erection quality.[22] It is anticipated that the QEQ will find a role in clinical practice because it is the only PRO instrument that solely and specifically assesses the key concept of satisfaction with quality of erections from the individual patient perspective. Others either exclude quality of erection in terms of patient satisfaction or include it as a minor component.[22–23] The QEQ is a potentially useful measure for monitoring and evaluating treatment in those who are bothered by, or concerned about, their EF. In the clinical practice setting, the original (untransformed) QEQ score may be sufficient.

Erectile dysfunction inventory of treatment satisfaction

Because satisfaction with treatment is important to treatment adherence, the EDITS was developed as a distinct and fundamental measure for men treated for their ED.[24] It was developed to assess satisfaction with ED therapies and to explore the impact of satisfaction on treatment continuation. This PROs has been used to evaluate patients' satisfaction with therapies such as sildenafil, apomorphine, intracavernosal injections and penile prosthesis;[44–46] for the treatment of ED of varied etiologies, including Peyronie's disease;[47] and following therapy for prostate cancer.[48] Results of open-label trials and DBPC trials have demonstrated that the EDITS is responsive to treatment for men with ED.[49–50]

The patient version of EDITS consists of 11 items, scored from 0 (low satisfaction) to 4 (high satisfaction), and an EDITS index score is calculated by multiplying the mean score of all 11 items by 25, which yields a total score ranging from 0 (lowest satisfaction) to 100 (highest satisfaction) (Table 4). The EDITS index is administered at post-baseline treatment visits. An abbreviated version, published in the original EDITS publication,[24] was developed for the partners of men with ED. In addition to being informative in clinical trials, the EDITS can be

Table 2 Sexual Health Inventory for Men

Over the past 6 months

1. How do you rate your confidence that you could get and keep an erection?

Very low	Low	Moderate	High	Very high
1	2	3	4	5

2. When you had erections with sexual stimulation, how often were your erections hard enough for penetration (entering your partner)?

No sexual activity	Almost never or never	A few times (much less than half the time)	Sometimes (about half the time)	Most times (much more than half the time)	Almost always or always
0	1	2	3	4	5

3. During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?

Did not attempt intercourse	Almost never or never	A few times (much less than half the time)	Sometimes (about half the time)	Most times (much more than half the time)	Almost always or always
0	1	2	3	4	5

4. During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?

Did not attempt intercourse	Extremely difficult	Very difficult	Difficult	Slightly difficult	Not difficult
0	1	2	3	4	5

5. When you attempted sexual intercourse, how often was it satisfactory for you?

Did not attempt intercourse	Almost never or never	A few times (much less than half the time)	Sometimes (about half the time)	Most times (much more than half the time)	Almost always or always
0	1	2	3	4	5

Score: Add the numbers corresponding to questions 1–5. If your score is 21 or less, you may want to speak with your doctor.

helpful in clinical practice by providing health care professionals with insight into how well the treatment for ED is meeting treatment expectations.

Self-esteem and relationship questionnaire

Instead on centering on the degree or extent of erectile or sexual function (IIEF, SHIM), quality of erections (QEQ) or treatment satisfaction (EDITS), the SEAR questionnaire was developed and validated to center on the emotional well-being of men with ED and who take ED medication. The development of the SEAR questionnaire consisted literature review, focus groups and medical specialists who identified a slew of potential items. Subsequently, data were then collected from 98 ED men and 94 controls who assisted in final item selection and psychometric evaluation. A detailed review article on the SEAR questionnaire is published elsewhere.[27]

Briefly, the 14 chosen items on SEAR questionnaire clustered into two domains: Sexual Relationship Satisfaction (items 1–8) and Confidence (items 9–14), the latter comprising Self-Esteem (items 9–12) and Overall Relationship Satisfaction (items 13–14) subscales (Table 5). As with the QEQ, the SEAR questionnaire has its constituent item responses summed to arrive at an individual's actual raw score for each domain and subscale, as well as his overall score, and the corresponding actual raw score is then transformed onto a 0–100 scale: transformed score = 100 × ((Actual raw score−Lowest possible raw score)/Possible raw score range). Higher scores indicate a more favorable response (0 = least favorable, 100 = most favorable). Each item pertains to the past 4 weeks. The questionnaire has been linguistically and culturally validated into 27 languages from the questionnaire's original United States English version.

The resulting 14-item SEAR questionnaire showed validity through factor analysis, item-level discriminant validity tests, convergent validity, divergent validity, discriminant validity (among different severity levels of ED, as well as between ED and no ED groups) and clear and considerable responsiveness to known treatment benefit (sildenafil).[25–26] The SEAR questionnaire also showed reliability through internal consistency and test–retest reliability.[25–26]

The validity of the SEAR questionnaire was bolstered when it, as a measure of psychosocial benefit, indicated a tangible relationship with treatment satisfaction (EDITS) among men with ED treated with sildenafil.[51] This research also underscores the relevance of assessing the psychosocial attributes and impact of ED in men undergoing treatment.

Mean SEAR scores between subjects with ED at baseline and control subjects without ED were statistically different from 0 and not statistically equivalent.[52] On the other hand, mean SEAR scores between ED subjects after treatment and control

Table 3 Quality of Erection questionnaire

The following questions ask about the quality of your erections over the past 4 weeks:

1. You had erections hard enough for penetration of your partner:
   5. Almost always or always
   4. More than half the time
   3. About half the time
   2. Less than half the time
   1. Almost never or never

2. Your ability to keep your erection to completion of sexual intercourse was:
   5. Very satisfactory
   4. Somewhat satisfactory
   3. Neither satisfactory nor unsatisfactory
   2. Somewhat unsatisfactory
   1. Very unsatisfactory

3. The length of time (from when you started sexual activity) until your erection was hard enough to participate in sexual intercourse was:
   5. Very satisfactory
   4. Somewhat satisfactory
   3. Neither satisfactory nor unsatisfactory
   2. Somewhat unsatisfactory
   1. Very unsatisfactory

4. The length of time you were able to be erect during intercourse was:
   5. Very satisfactory
   4. Somewhat satisfactory
   3. Neither satisfactory nor unsatisfactory
   2. Somewhat unsatisfactory
   1. Very unsatisfactory

5. The hardness of your erection was:
   5. Very satisfactory
   4. Somewhat satisfactory
   3. Neither satisfactory nor unsatisfactory
   2. Somewhat unsatisfactory
   1. Very unsatisfactory

6. The overall quality of your erection was:
   5. Very satisfactory
   4. Somewhat satisfactory
   3. Neither satisfactory nor unsatisfactory
   2. Somewhat unsatisfactory
   1. Very unsatisfactory

subjects were statistically equivalent and not statistically significant from 0.[52] The results indicated that sildenafil is associated with normalization of relationship satisfaction, confidence and self-esteem. In separate research, a 10-point change was proposed as a minimal clinically meaningful improvement for most SEAR components (Sexual Relationship Satisfaction, Confidence, Self-Esteem, Overall Score); the data did not support such a confident recommendation for Overall Relationship Satisfaction.[53]

In two separate DBPC trials of men with ED, treatment with sildenafil demonstrated that the SEAR questionnaire is a responsive (within-group change), sensitive (between-group change) and robust (stable) instrument to detect changes related to sexual relationship satisfaction, confidence and particularly self-esteem after successful treatment.[54–55] Changes in SEAR scores also showed a moderate-to-high positive correlation with IIEF scores.

Open-label extension sildenafil after DBPC placebo significantly improved EF, self-esteem, confidence and relationship satisfaction.[56] Following an initial 12 weeks of DBPC sildenafil therapy for ED, improvements were sustained for an additional 9 months. The positive correlations between EF and self-esteem, confidence and relationship satisfaction suggest that improved EF can improve longer term psychosocial quality of life. Although designed primarily for application in clinical trials, the SEAR questionnaire may be a worthwhile tool as an assessment of emotional well-being of patients in clinical practice as well, both at diagnosis of ED and during treatment for ED.

Erection hardness score

Erection hardness is a fundamental component of EF and is a very specific and easily monitored

Table 4 The EDITS index (patient version)

1.	Overall, how satisfied are you with this treatment?	Very satisfied 0	Somewhat satisfied 1	Neither satisfied nor dissatisfied 2	Somewhat dissatisfied 3	Very dissatisfied 4
2.	During the past 4 weeks, to what degree has the treatment met your expectations?	Completely 0	Considerably 1	Halfway 2	A little 3	Not at all 4
3.	How likely are you to continue using this treatment?	Very likely 0	Moderately likely 1	Neither likely nor unlikely 2	Moderately unlikely 3	Unlikely 4
4.	During the past 4 weeks, how easy was it for you to use this treatment?	Very easy 0	Moderately easy 1	Neither easy nor difficult 2	Moderately difficult 3	Difficult 4
5.	During the past 4 weeks, how satisfied have you been with how quickly the treatment works?	Very satisfied 0	Somewhat satisfied 1	Neither satisfied nor dissatisfied 2	Somewhat dissatisfied 3	Very dissatisfied 4
6.	During the past 4 weeks, how satisfied have you been with how long the treatment works?	Very satisfied 0	Somewhat satisfied 1	Neither satisfied nor dissatisfied 2	Somewhat dissatisfied 3	Very dissatisfied 4
7.	How confident has this treatment made you feel about your ability to engage in sexual activity?	Very confident 0	Somewhat confident 1	It has had no impact 2	Somewhat less confident 3	Very much less confident 4
8.	Overall, how satisfied do you believe your partner is with the effects of this treatment?	Very satisfied 0	Somewhat satisfied 1	Neither satisfied nor dissatisfied 2	Somewhat dissatisfied 3	Very dissatisfied 4
9.	How does your partner feel about your continuing to use this treatment?	My partner absolutely wants me to continue 0	My partner generally prefers me to continue 1	My partner has no opinion 2	My partner generally prefers me to stop 3	My partner absolutely wants me to stop 4
10.	How natural did the process of achieving an erection feel when you used this treatment over the past 4 weeks?	Very natural 0	Somewhat natural 1	Neither natural nor unnatural 2	Somewhat unnatural 3	Very unnatural 4
11.	Compared to before you had an erection problem, how would you rate the naturalness of your erection when you used this treatment over the past 4 weeks in terms of hardness?	A lot harder than before I had an erection problem 0	Somewhat harder than before I had an erection problem 1	The same hardness as before I had an erection problem 2	Somewhat less hard than before I had an erection problem 3	A lot less hard than before I had an erection problem 4

outcome that has been used in many clinical trials as a supplement to other measures, often as part of a sexual activity event log.[28] The EHS is a targeted self-reported measure that classifies erection hardness on a single-item scale. Two versions of the EHS have appeared in the literature. One version of the EHS, perhaps the better known one, has four response categories: penis is (1) larger but not hard, (2) hard but not hard enough for penetration, (3) hard enough for penetration but not completely hard and (4) completely hard and fully rigid. A second version is a five-category scale that keeps those same four grades and adds the grade 0 category 'penis does not enlarge' as the lowest level (Table 6). For the five-category version, the first two categories (penis does not enlarge and penis is larger but not heard) are often combined and subsequent analyses are based using a four-point ordinal scale (with the first two of five categories combined).

The EHS was validated formally in a data set of 307 men with ED from a multinational sildenafil trial with a 2-week screening phase, a 6-week DBPC

Table 5 Self-Esteem And Relationship questionnaire

During the past 4 weeks

1. I felt relaxed about initiating sex with my partner
2. I felt confident that during sex my erection would last long enough
3. I was satisfied with my sexual performance
4. I felt that sex could be spontaneous
5. I was likely to initiate sex
6. I felt confident about performing sexually
7. I was satisfied with our sex life
8. My partner was unhappy with the quality of our sexual relations
9. I had good self-esteem
10. I felt like a whole man
11. I was inclined to feel that I am a failure
12. I felt confident
13. My partner was satisfied with our relationship in general
14. I was satisfied with our relationship in general

Response options

Almost always/always
Most times (much more than half the time)
Sometimes (about half the time)
A few times (much less than half the time)
Almost never/never

Scoring

All questions except questions 8 and 11 are scored as 1 = almost never/never, 2 = a few times (much less than half the time), 3 = sometimes (about half the time), 4 = most times (much more than half the time) and 5 = almost always/always. Questions 8 and 11 were reverse scored with 5 = almost never/never, 4 = a few times (much less than half the time), 3 = sometimes (about half the time), 2 = most times (much more than half the time) and 1 = almost always/always. Thus, a higher score signified a more favorable response for all 14 items.

treatment phase and a 6-week open-label extension.[30] The EHS indicated good test–retest reliability, acceptable quality and distribution of responses, known-group validity against the IIEF (including clear differentiation between normal and impaired EF), moderate-to-strong convergent validity with the QEQ and prespecified domains of the IIEF. Moreover, the EHS resonated with high responsiveness to known treatment benefit. Psychometric analyses, therefore, support the use of the EHS as a simple, reliable and valid tool for the assessment of erection hardness in clinical research trials as well as by physicians who would like to help their male patients reach their optimal erection potential.

An international panel of experts in urology, psychology and primary care was convened to evaluate retrospective data from worldwide phase 2, 3 and 4 clinical trials, involving over 10 000 men with ED, as well as data from recent prospective studies. The panel evaluated the role of erection hardness in defining the response to treatment with phosphodiesterase type 5 inhibitor therapy.[29] As with the study attesting to the psychometric merits of the EHS,[30] this compilation of evidence-based data supported a significant positive correlation of the EHS with the QEQ and the EF domain of the IIEF, as well as with other IIEF domains.

Table 6 Erection Hardness Score

How would you rate the hardness of your erection?

0: Penis does not enlarge
1: Penis is larger but not hard
2: Penis is hard but not hard enough for penetration
3: Penis is hard enough for penetration but not completely hard
4: Penis is completely hard and fully rigid

Significant positive correlations were also found between erection hardness and psychosocial measures such as self-esteem, confidence and relationship satisfaction (assessed by the SEAR questionnaire), and between erection hardness and satisfaction with medical treatment (assessed by EDITS).[29] A shift in most frequent erection from EHS 3 (hard enough for penetration but not fully hard) at baseline to EHS 4 (completely hard and fully rigid) at the end of treatment was accompanied by significant improvements in intercourse and relationship satisfaction, psychosocial benefits and satisfaction with ED treatment. This research suggests that achievement of grade 4 erection hardness may be the optimal goal of ED treatment. Consequently, the EHS may be useful in monitoring the progress of men with ED in achieving this treatment goal with ED therapy in clinical practice.

Sexual experience questionnaire

The development of the SEX-Q was motivated by the absence of a single, brief measure that assesses elements of function and health-related quality of life with respect to the sexual experience in men with ED. The SEX-Q was psychometrically analyzed with two data sets.[31] A randomized, DBPC trial of flexible-dose sildenafil for ED treatment provided the final clinical trial data set (213 men enrolled) and the interim clinical trial data set (165 men enrolled). The survey data set consisted of 902 respondents to a United States community health survey, of whom two-thirds had ED and one-third did not.

The original candidate list of 15 items on the SEX-Q was reduced to 12 items in three domains (Erection, Individual Satisfaction and Couples Satisfaction) (Table 7). The Erection domain of the SEX-Q is described by items 1–6 and encompasses both EF and erectile quality, the Individual Satisfaction domain by items 7–9, and the Couples Satisfaction domain by items 10–12. Individual items of the SEX-Q are scored on a five-point ordinal scale from 1 to 5 (higher score is better, except for item 3, which is reverse scored). The raw score for each domain and the total raw score are transformed onto a 0–100 scale, where higher scores are more favorable, using the equation: $100 \times ((\text{Average value of the items}) - 1)/4$, where 1 is the lowest possible score in

original units and 4 is the score range in original units. The reference period is the past 4 weeks.

These domains revealed good quality responses for all items; a strong factor structure; excellent internal consistency; good test–retest reliability; clear known-group validity across the severity groups; moderate-to-strong convergent validity against the IIEF, SEAR and QEQ; and high treatment responsiveness.[31] The estimated clinically important difference ranged from 16.0 to 22.3 across domains.[31]

The SEX-Q is the first questionnaire to solely and exclusively combine functional and health-related quality-of-life concepts (Erection, Individual Satisfaction and Couples Satisfaction domains) into a brief questionnaire. Doing so may allow for a more encompassing and less burdensome evaluation of the sexual experience, making it a potentially useful measure in clinical trial research as well as in clinical practice.

Guidelines for using PROs

The seven PROs highlighted and described in this article complement and supplement each other, because each of them emphasizes a related yet distinct central element that characterizes ED and its treatment. Collectively, this assembly of PROs embraces an array of key attributes that addresses the condition of ED so as to provide a comprehensive and an accurate profile of men treated and managed for their ED. Because these measures inform and color the condition of ED with shades of gray rather than a pure black or white assessment, though, we provide guidance to further distinguish and discern among the PROs so that researchers and practitioners apply these PROs judiciously and responsibly for a given purpose. Such clarification is intended to avoid confusion and misuse of these PROs in ED research.

International index of erectile function

Accepted by regulatory agencies and scientific journals, the IIEF is a standard instrument for evaluating the efficacy of therapeutic intervention in men with ED in clinical trials. The IIEF encapsulates principal facets of sexual function: EF, orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction. Of these, the EF domain of the IIEF is the most relevant to gauge sexual function and is best suited to quantify EF as a specific measure of erectile performance and activity (frequency). EF scores can be measured as mean changes from baseline and mean scores at follow-up as well as proportions in each of the ED severity groups and proportions of men who change from one ED severity group to another. The EF domain is also well suited as part of inclusion criteria to confirm that men have ED (EF score of 25 or less) or to study a specific subpopulation (for example, those with mild or moderate ED verified with scores between 11 and 25 inclusive) in clinical trials.

Sexual health inventory for men

The SHIM can substitute for the erection function domain of the IIEF to confirm that the enrolled sample has ED (SHIM score of 21 or less) or to study a specific subpopulation (for example, those with mild or moderate ED verified with scores between 8 and 21 inclusive) in clinical trials. While the EF domain is well placed to diagnose the presence and severity of ED in clinical trials, the SHIM is well suited to diagnose the presence and severity of ED in clinical practice.

Quality of erection questionnaire

Quality of erections is among the concepts reflected in the SHIM and its parent, the IIEF. Unlike the SHIM or IIEF, however, the QEQ focuses solely on evaluating and monitoring satisfaction with the quality of erections, which includes as its key driver the capability to enable hard erections. Quality of erections in terms of hardness *per se* is addressed only by a single item on the IIEF and SHIM (Q 2: when you had erections with sexual intercourse, how often where your erections hard enough for penetration?) and satisfaction with quality of erections is not addressed at all. Quality of erection, a primary attribute sought in a treatment for ED, as measured by the QEQ can be considered a specific subset of EF, that is, a subset that targets satisfaction with the quality of erections. The QEQ was designed primarily as a tool in clinical trials for evaluating and monitoring treatment in men who are bothered by, or concerned about, their EF. Being brief (six items) and easy to use, this tool merits consideration in clinical practice as well.

Erectile dysfunction inventory of treatment satisfaction

Satisfaction with treatment is a unique form of satisfaction, and the EDITS has successfully measured it for men with ED. The concept of treatment satisfaction is intentionally subjective, trying to capture an individual's personal evaluation of the treatment received. This evaluation includes feelings about the efficacy of treatment, side effects, ease of use, naturalness and impact on the partner. For example, it is possible that although a treatment may produce an excellent erection, a patient may rate the treatment as unsatisfactory because the erection was artificially induced, painful to create, failed to enhance the patient's sense of sexual confidence or masculinity, or was not acceptable to the partner. Recognizing this, EDITS as a measure of treatment satisfaction distinguishes itself from other PROs in

Table 7 The sexual experience questionnaire

Instructions

For each of the following questions, place an "X" in the one box that best describes your answer.

Over the past 4 weeks,

1. How often were you able to maintain an erection for as long as you wanted to?

Never or Almost Never	Rarely	Sometimes	Usually	Always or Almost Always
❒	❒	❒	❒	❒

2. During sexual intercourse, how often were you able to penetrate your partner?

Never or Almost Never	Rarely	Sometimes	Usually	Always or Almost Always
❒	❒	❒	❒	❒

3. How much have you worried about whether you could get an erection?

Not at All Worried	A Little Worried	Somewhat Worried	Very Worried	Extremely Worried
❒	❒	❒	❒	❒

4. How confident were you that you could get an erection when you wanted to?

Not at all Confident	A Little Confident	Somewhat Confident	Confident	Very Confident
❒	❒	❒	❒	❒

5. How satisfied were you with the hardness of your erections?

Very Dissatisfied	Dissatisfied	Equally Satisfied and Dissatisfied	Satisfied	Very Satisfied
❒	❒	❒	❒	❒

6. How satisfied were you with the duration of your erections?

Very Dissatisfied	Dissatisfied	Equally Satisfied and Dissatisfied	Satisfied	Very Satisfied
❒	❒	❒	❒	❒

7. How satisfied were you with your level of sexual desire?

Very Dissatisfied	Dissatisfied	Equally Satisfied and Dissatisfied	Satisfied	Very Satisfied
❒	❒	❒	❒	❒

8. How satisfied were you with your overall sexual activity?

Very Dissatisfied	Dissatisfied	Equally Satisfied and Dissatisfied	Satisfied	Very Satisfied
❒	❒	❒	❒	❒

9. How much pleasure did you get from sexual activity?

No Pleasure	Little Pleasure	Some Pleasure	Much Pleasure	Great Pleasure
❒	❒	❒	❒	❒

10. How confident were you that you could satisfy your partner during sexual activity?

Not at all Confident	A Little Confident	Somewhat Confident	Confident	Very Confident
❒	❒	❒	❒	❒

11. How often did you achieve mutual satisfaction with your partner?

Never or Almost Never	Rarely	Sometimes	Usually	Always or Almost Always
❒	❒	❒	❒	❒

12. How satisfied were you with your ability to control the timing of your ejaculations?

Very Dissatisfied	Dissatisfied	Equally Satisfied and Dissatisfied	Satisfied	Very Satisfied
❒	❒	❒	❒	❒

ED by asking questions such as to what degree has the treatment met expectations, likelihood of continuing treatment, how easy was it to use this treatment and the naturalness of the erection when using the treatment. While designed primarily for clinical trials, EDITS can aid in clinical practice in choosing among treatment alternatives.

Self-esteem and relationship

Successful treatment for ED is multi-faceted and involves emotional well-being and fulfillment in addition to sexual function, EF, quality of erections and treatment satisfaction. Sexual dysfunction can compromise overall quality of life and foster anxiety. Sexual dysfunction can be especially damaging to self-esteem and can contribute to relationship difficulties, diminishing mental health or psychological well-being in men with ED. A successful treatment for ED, regardless of the specific therapy, should therefore be associated with improvement in emotional and relational areas, as well as sexual ones. The SEAR questionnaire targets the psychosocial attributes of self-esteem and confidence, along with the accompanying attributes of sexual relationship satisfaction and overall relationship satisfaction, to quantify the emotional side of sexual dysfunction and to encompass a richer, fuller understanding of how treatment may benefit men with ED beyond sexual performance and activity. While designed primarily for clinical trials, the SEAR questionnaire may be considered as an adjunct measure in clinical practice.

Erection hardness score

In comparison with most other PROs for evaluating erections in men with ED (such as the IIEF, SHIM, QEQ, EDITS and SEAR), the EHS assesses erections at the time of the sexual encounter with a daily event log (rather than relying on patient recall at the time of the clinical visit). And only the EHS concretely and concisely pinpoints erection hardness. Erection hardness is a fundamental component of EF and can be considered, like quality of erections, as another distinct subtype of EF. Another attractive and distinctive quality of the single-item EHS is its simple, meaningful and forceful interpretation whereby treatments can be compared with respect to discrete grades of erectile hardness that are easily understood. This lucid interpretation has appeal in not only clinical trials, where the EHS has received most of its attention, but also in clinical practice. As an easily monitored single question, the EHS is a practical measure that can be tied to a therapeutic goal.

Sexual experience questionnaire

In the focus groups and qualitative interviews that drive questionnaire development, men with ED have attested to different forms of satisfaction they seek and consider relevant to their condition. Among them are intercourse and orgasmic satisfaction, captured by IIEF; treatment satisfaction, captured by EDITS and sexual relationship and overall satisfaction, captured by the SEAR questionnaire. The SEX-Q captures couples satisfaction (when a man also considers his partner) and individual satisfaction (when a man considers mainly himself) as complementary though separate variants of satisfaction. The erection domain of the SEX-Q embodies EF (akin to the EF domain of the IIEF) plus satisfaction with quality of erections (akin to the QEQ). This domain, then, unites EF and quality into one general concept called 'erection.' The SEX-Q therefore consolidates certain aspects of function and quality as well as satisfaction into one instrument and, in doing so, may engender a focused and convenient evaluation of the sexual experience with the objective of measuring EF and quality along with individual and couples satisfaction. For these objectives, the SEX-Q is a potentially useful measure for application in clinical trials research, the primary setting of the SEX-Q. The questionnaire may also bring value in clinical practice.

Summary

Patient-reported outcomes empower patients to participate in the efficacy (in clinical trials) and effectiveness (in clinical practice) of therapy. Responses from patients allow them to partner with researchers and health care providers to help achieve optimal patient care and management. Although it is beyond the scope of this review article to detail all possible PROs used in ED, we acknowledge that other PROs not sponsored, developed, or validated by Pfizer Inc are also noteworthy and deserve a review themselves.

In this review we highlighted six specific PROs—IIEF, SHIM, QEQ, EDITS, SEAR and EHS—that have matured with the field of ED research and one related, new PRO (SEX-Q) with expectations for increase use. One or more of these PROs may be relevant to address specific questions. While it is true that they share some overlapping features or concepts, it is also true that each PRO is distinct and tailored to a given objective.

In this review we describe the aforementioned seven PROs, detail their questions and categorical responses, and highlight their similarities and differences so that researchers and practitioners can choose among them judiciously and appropriately for a specific endeavor. Each of these PROs originated from clinical trials research and is applicable there, depending on the research objective. All of them at least deserve consideration in clinical practice but the SHIM and EHS are especially convenient and practical tools.

The IIEF is intended mainly for clinical trials research and has become the standard instrument to

assess treatment efficacy and sexual function. In particular, the EF domain of the IIEF has proven to be the par excellence measure to gauge ED in particular and to assess treatment efficacy in clinical trials. The SHIM is intended chiefly as a useful diagnostic tool for health care providers to quickly assess men's sexual function and open communication channels with their patients. This communication between physicians and patients serves to treat not only sexual function, such as ED, but also presents the opportunity to discuss other men's health issues.

The QEQ is a specialized tool that targets satisfaction with quality of erection, rather than erectile functioning more broadly. The EDITS questionnaire is a valid instrument for assessing satisfaction with treatment, which can be one of the most important indicators of long-term treatment continuation. The SEAR questionnaire addresses emotional well-being—self-esteem and confidence and certain types of satisfaction (sexual, overall)—in men with ED and allows evaluation of possible psychosocial improvements with therapeutic intervention. The EHS is dedicated to measure erection hardness, a key and specific component of EF, in clinical trials and clinical practice so that patients, researchers and clinicians can monitor the effect of therapy with regard to erection hardness. Finally, the SEX-Q is designed to capture the sexual experience in terms of erection (both function and hardness), individual satisfaction and couples satisfaction.

Conclusion

As a unit the seven PROs described here—the IIEF, SHIM, QEQ, EDITS, SEAR, EHS and SEX-Q—complement and supplement each other. They acknowledge and embrace the multiple dimensions of sexual dysfunction and its treatment by measuring the variant aspects of sexual dysfunction. Each of these instruments represents a significant contribution to sexual medicine research and, when used judiciously and appropriately, can help to provide optimal patient care and management.

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