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Evidence-Based Unified Definition of PE

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REVIEWS

An Evidence-Based Unified Definition of Lifelong and Acquired Premature Ejaculation: Report of the Second International Society for Sexual Medicine Ad Hoc Committee for the Definition of Premature Ejaculation

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ABSTRACT

Introduction. The International Society for Sexual Medicine (ISSM) Ad Hoc Committee for the Definition of Premature Ejaculation developed the first evidence-based definition for lifelong premature ejaculation (PE) in 2007 and concluded that there were insufficient published objective data at that time to develop a definition for acquired PE.
Aim. The aim of this article is to review and critique the current literature and develop a contemporary, evidence-based definition for acquired PE and/or a unified definition for both lifelong and acquired PE.
Methods. In April 2013, the ISSM convened a second Ad Hoc Committee for the Definition of Premature Ejaculation in Bangalore, India. The same evidence-based systematic approach to literature search, retrieval, and evaluation used by the original committee was adopted.
Results. The committee unanimously agreed that men with lifelong and acquired PE appear to share the dimensions of short ejaculatory latency, reduced or absent perceived ejaculatory control, and the presence of negative personal consequences. Men with acquired PE are older, have higher incidences of erectile dysfunction, comorbid disease, and cardiovascular risk factors, and have a longer intravaginal ejaculation latency time (IELT) as compared with men with lifelong PE. A self-estimated or stopwatch IELT of 3 minutes was identified as a valid IELT cut-off for diagnosing acquired PE. On this basis, the committee agreed on a unified definition of both acquired and lifelong PE as a male

sexual dysfunction characterized by (i) ejaculation that always or nearly always occurs prior to or within about 1 minute of vaginal penetration from the first sexual experience (lifelong PE) or a clinically significant and bothersome reduction in latency time, often to about 3 minutes or less (acquired PE); (ii) the inability to delay ejaculation on all or nearly all vaginal penetrations; and (iii) negative personal consequences, such as distress, bother, frustration, and/or the avoidance of sexual intimacy.

Conclusion. The ISSM unified definition of lifelong and acquired PE represents the first evidence-based definition for these conditions. This definition will enable researchers to design methodologically rigorous studies to improve our understanding of acquired PE. **Serefoglu EC, McMahon CG, Waldinger MD, Althof SE, Shindel A, Adaikan G, Becher EF, Dean J, Giuliano F, Hellstrom WJG, Giraldi A, Glina S, Incrocci L, Jannini E, McCabe M, Parish S, Rowland D, Segraves RT, Sharlip I, and Torres LO. An evidence-based unified definition of lifelong and acquired premature ejaculation: Report of the second International Society for Sexual Medicine Ad Hoc Committee for the Definition of Premature Ejaculation. Sex Med 2014;2:41–59.**

Key Words. Premature Ejaculation; Definition; Lifelong Premature Ejaculation; Acquired Premature Ejaculation; Intravaginal Ejaculatory Latency Time; Ejaculatory Control; Sexual Satisfaction; Personal Distress; Interpersonal Distress; Negative Personal Psychological Consequences

Introduction

Research into the treatment and epidemiology of premature ejaculation (PE) is heavily dependent on how PE is defined. The medical literature contains several univariate and multivariate operational definitions of PE [1–10]. Each of these definitions characterizes men with PE using all or most of the accepted dimensions of this condition: ejaculatory latency, perceived ability to control ejaculation, reduced sexual satisfaction, personal distress, partner distress, and interpersonal or relationship distress. In the last decade, substantial progress has been made in the development of evidence-based methodology for epidemiologic and drug treatment research on PE through the use of objective (intravaginal ejaculatory latency time, IELT) and subjective (patient-reported outcome, PRO) validated measures.

At one time, the definitions of PE given in the American Psychiatric Association's (APA's) *Diagnostic and Statistical Manual of Mental Disorders* (DSM) were largely accepted by the medical community with little discussion, despite having no evidence-based medical support [11–13].

Following the introduction of evidence-based PE pharmacotherapy, the validity of the DSM definitions was the subject of debate, with a substantial polarization of opinion. The inclusion of words such as "persistent," "recurrent," "minimal," and "shortly after" rendered the DSM definitions vague, ambiguous, and lacking in objective and quantitative criteria [14–16]. Concerns about the validity and application of the DSM-IV-TR definition were also expressed by regulatory agencies such as the United States Food and Drug Administration, which regarded the lack of evidence-based criteria as an obstacle in interpretation and assessment of data from clinical trials of experimental drugs for PE.

The absence of a specific ejaculation time cutoff point to operationalize "shortly after penetration or before the person wishes" has led to ambiguous application of the DSM criteria for PE in epidemiological and clinical research [17–20]. Giuliano et al. reported the IELT of men with DSM-IV-TR-diagnosed PE to range from 0 seconds (*ante portas* ejaculation) to almost 28 minutes, with 44% of subjects having an IELT ≥2 minutes and 25% ≥4 minutes [20]. This study demonstrates that a subject diagnosed with PE according to DSM-IV-TR criteria has a 44% chance of not having PE if a PE diagnostic threshold IELT of 2 minutes, as suggested by community-based normative IELT trial, is used [21].

Waldinger et al., in a number of studies in cohorts of heterosexual men with lifelong PE with prospective stopwatch IELT measurement, showed that about 90% of men seeking treatment for lifelong PE ejaculated within 1 minute after penetration, and about 10% ejaculated between 1 and 2 minutes [17]. These data were confirmed by McMahon in a retrospective questionnaire analysis of a large cohort of men with lifelong PE [22]. These data support the proposal that lifelong PE is characterized by an IELT of less than or about 1 minute after vaginal penetration.

In October 2007, the International Society for Sexual Medicine (ISSM) responded to these concerns and convened a meeting in Amsterdam of the

ISSM Ad Hoc Committee for the Definition of Premature Ejaculation. The committee included 21 international experts in PE who were charged with the development of the first contemporary, evidence-based definition of lifelong PE. Evidence-based definitions seek to limit errors of classification and thereby increase the likelihood that existing and newly-developed therapeutic strategies are truly effective in carefully selected dysfunctional populations [4]. After critical evaluation of the published data, the committee unanimously agreed that the constructs that are necessary to define lifelong PE are time from penetration to ejaculation, inability to delay ejaculation, and negative personal consequences from PE. The following definition was agreed upon [10]:

> Lifelong PE is a male sexual dysfunction characterized by the presence of all of these criteria: (i) ejaculation that always or nearly always occurs prior to or within about 1 minute of vaginal penetration; (ii) the inability to delay ejaculation on all or nearly all vaginal penetrations; and (iii) negative personal consequences such as distress, bother, frustration, and/or the avoidance of sexual intimacy.

The committee was, however, unable to identify sufficient published objective data to craft an evidence-based definition of acquired PE.

In April 2013, the International Society for Sexual Medicine (ISSM) convened a second ISSM Ad Hoc Committee for the Definition of Premature Ejaculation in Bangalore, India. The brief of the committee was to evaluate the current published data and attempt to develop a contemporary, evidence-based definition of acquired PE and/or a single unifying definition of both acquired and lifelong PE.

This article chronicles the development of current definitions of PE and details their strengths and weaknesses. Included are critiques of the evidence in support of the constructs of ejaculatory latency, ejaculatory control, sexual satisfaction, and personal distress. The epidemiology, etiology, and presenting symptoms of lifelong and acquired PE are compared, and a new, unifying definition for both acquired and lifelong PE is proposed.

Definition Development Process

The second Ad Hoc ISSM Committee for the Definition of Premature Ejaculation was supported by an unrestricted research grant from Johnson & Johnson. However, ISSM required complete independence from industry during the development of the new definition of PE. There were no industry representatives at the meeting, and there was no attempt by industry to influence any part of the development process at any time. The same evidence-based systematic approach to literature search, retrieval, and evaluation used in the original meeting was adopted [23].

The Committee was chosen by peer recommendation and comprised 19 experts appointed to achieve a balance of opinion, knowledge, gender, and geography. These 19 included several of the world's most highly recognized experts on PE and comprised 6 psychologists or psychiatrists, 8 urologists, 2 sexual health physicians, 1 primary care physician, 1 endocrinologist, and 1 radiation oncologist. All of the attendees were ISSM members. The meeting was organized, chaired, and facilitated by the current ISSM president, Chris G. McMahon.

The Need for an Evidence-Based Definition of Acquired Premature Ejaculation

The lack of consensus as to what constitutes acquired PE has continued to hamper clinical practice and basic and clinical research into the etiology and management of this condition. The results of epidemiological and drug treatment clinical trials on PE are only reliable, interpretable, and capable of being generalized to patients when consistent objective physiological measures or sensitive, validated outcome assessment instruments are used as study endpoints in well-defined and consistent populations where lifelong PE, acquired PE, and PE with comorbid ED are treated as separate PE subtypes [24].

The original Ad Hoc Committee for the Definition of Premature Ejaculation concluded that there was insufficient published evidence to propose an evidence-based definition of acquired PE [10]. The committee anticipated that future studies would generate sufficient data to develop an evidence-based definition for acquired PE. The committee suggested that a post hoc review of baseline data from Phase 3 dapoxetine drug trials might provide preliminary exploratory data on the dimensions of acquired PE that might assist in future research and the development of an evidence-based definition for acquired PE. These data were interpreted as suggesting that men with acquired PE have similar IELTs and report similar levels of ejaculatory control and distress to men with lifelong PE, raising the possibility of a single unifying definition of PE [25].

However, as acquired PE generally manifests later in life and is likely to have a different etiology [26], it may be that the presenting patient characteristics and/or symptoms reported by men with acquired PE differ from those of men with lifelong PE. Additional information regarding differential symptomatology and/or sexual history experiences in men with acquired PE may facilitate the development of a definition and assist in the diagnosis of acquired PE. A more accurate definition may improve design of research and assist in selecting the best treatments for this PE subtype.

Operationalization of PE Variables and Constructs

The original Ad Hoc Committee for the Definition of Premature Ejaculation agreed that errors of PE diagnosis and classification can be minimized by the development and clinical application of a multivariate definition that captures and operationalizes (i.e., develops into an identifying measure, procedure, or operation) the key PE constructs of rapidity of ejaculation, perceived lack of ejaculatory self-efficacy or control, and negative personal and interpersonal consequences (e.g., distress) [10].

The committee determined that operationalization was inherently difficult and that the constructs were interrelated and potentially confounded by each other and by multiple other variables [10,27]. The following measures were identified as adequately but not precisely capturing the essence of each construct [10,27]:

1. Rapidity of ejaculation (patient estimation or stopwatch measurement).
2. Perceived ejaculatory control (improvements in ejaculation latency time during attempts to delay ejaculation or by the measurement of the subjective feeling of ejaculatory control using patient report or validated single-item or multi-item multidomain PE inventories).
3. Negative personal consequences (patient report or measurement using validated single-item or multi-item multidomain PE inventories of sexual or global levels of distress, bother, frustration, anxiety, depression, confidence, self-esteem and quality of life).

The ISSM Definition of Lifelong and Acquired PE

Members of the second Ad Hoc Committee for the Definition of Premature Ejaculation unanimously agreed that lifelong and acquired PE are distinct and different demographically and etiologically. However, they can be jointly defined, in part, by the constructs of time from penetration to ejaculation, inability to delay ejaculation, and negative personal consequences from PE. The committee agreed that the presence of these mutual constructs was sufficient justification for the development of a single unifying definition of both lifelong and acquired PE. Finally, the committee determined that the presence of a clinically significant and bothersome reduction in latency time, often to about 3 minutes or less, was an additional key defining dimension of acquired PE.

The second ISSM Ad Hoc Committee for the Definition of Premature Ejaculation defined PE (lifelong and acquired) as a male sexual dysfunction characterized by the following:

1. Ejaculation that always or nearly always occurs prior to or within about 1 minute of vaginal penetration (lifelong PE) or a clinically significant and bothersome reduction in latency time, often to about 3 minutes or less (acquired PE).
2. The inability to delay ejaculation on all or nearly all vaginal penetrations.
3. Negative personal consequences, such as distress, bother, frustration, and/or the avoidance of sexual intimacy.

The Committee agreed that published objective evidence on PE is limited to studies of men with PE engaging in vaginal intercourse. There is insufficient information to objectively define problematic early ejaculation in the context of oral sex, anal sex, and same-gender sexual activity.

History of Definitions of PE

During the period of 1920 to 1960, the absence of any scientific publications proposing a definition of PE reflects the scarcity of prevalence data. Based upon the limited published literature, a man was considered to suffer from PE when he ejaculated within seconds or within about a minute of vaginal penetration [28]. In the 1970s, despite an absence of any empirical data, Masters and Johnson rejected this ejaculation latency proposal and defined PE as a man's inability to satisfy his female partner in more than 50% of sexual events [1]. In spite of their noteworthy accomplishments, Masters and Johnson's definition was seriously flawed in that the diagnosis was determined by the female partner's response rather than the sexual function of the man. Additionally, their rejection of the ejaculation time criterion has led to a debate on "objective criteria" and "subjective criteria" for PE [29]. Typical "objective" criteria include the

ejaculation latency time and the number of penile thrusts. "Subjective" criteria are measures of self-efficacy including "diminished feelings of control" and "ejaculation at moments without wishing it."

These opposing constructs have served as the framework for the development of the various definitions proposed in the DSM by the APA [12,13].

DSM Definitions of PE

The first official definition of PE was established in 1980 by the APA in the DSM-III [30]. PE was defined as "ejaculation that occurs before the individual wishes it, because of recurrent and persistent absence of reasonable voluntary control of ejaculation and orgasm during sexual activity" [30]. However, because of disagreement on the criterion of "reasonable voluntary control," this criterion was removed in the subsequent DSM-III-R and DSM-IV definitions [31,32] and replaced by the criterion of a "short ejaculation time." The DSM-IV-TR defined PE as a "persistent or recurrent ejaculation with minimal sexual stimulation before, on, or shortly after penetration and before the person wishes it," stating that "the clinician must take into account factors that affect the duration of the excitement phase such as age, novelty of the sexual partner or situation, and recent frequency of sexual activity" and requiring for the diagnosis that "the disturbance causes marked distress or interpersonal difficulty" [32]. As such, the DSM-III definition involves the criterion of control but not that of time, whereas subsequent DSM-III-R, DSM-IV, and DSM-IV-TR definitions involved the criterion of time but not that of control [12,13].

DSM-5 Definition of PE

Based upon the same data that supported the ISSM definition of lifelong PE, the recently published DSM-5 definition of PE now includes an objective ejaculatory latency criterion. The DSM-5 defines PE by four major criteria [33]:

A. A persistent or recurrent pattern of ejaculation occurring during partnered sexual activity within approximately 1 minute following vaginal penetration and before the person wishes it.
B. The symptom in Criterion A must have been present for at least six months and must be experienced on almost all or all (approximately 75%–100%) occasions of sexual activity (in identified situational contexts or if generalized, in all contexts)
C. The symptom in Criterion A causes clinically significant distress in the individual.
D. The sexual dysfunction is not better explained by a nonsexual mental disorder or as a consequence of severe relationship distress or other significant stressors and is not attributable to the effects of a substance/medication or another medical disorder.

The DSM-5 definition of PE requires clinicians to specify whether PE is lifelong or acquired and whether it is generalized or situational. In addition, the DSM-5 definition of PE distinguishes between mild PE (ejaculation occurring within approximately 30 seconds to 1 minute of vaginal penetration), moderate PE (ejaculation occurring within approximately 15–30 seconds of vaginal penetration), and severe PE (ejaculation occurring prior to sexual activity, at the start of sexual activity, or within approximately 15 seconds of vaginal penetration).

ICD-10 Definition of PE

The World Health Organization'S 1992 International Classification of Diseases (ICD-10) defines PE as "the inability to control ejaculation sufficiently for both partners to enjoy sexual interaction" and as "an inability to delay ejaculation sufficiently to enjoy lovemaking, and manifest as either of the following: (i) occurrence of ejaculation before or very soon after the beginning of intercourse (if a time limit is required: before or within 15 seconds of the beginning of intercourse); and (ii) ejaculation occurs in the absence of sufficient erection to make intercourse possible" [3]. The ICD-10 uses both the criterion of "control" and that of a "very short" ejaculation time, defining the latter as a maximum of 15 seconds after penetration. Although the ICD-10 provides an objective definition of PE, evidence to support a latency cutoff of 15 seconds was not provided [12,13]. Furthermore, the ICD-10 use of the criterion of ejaculation occurring within 15 seconds restricts the application of the criterion of control [12,13].

Classification of PE

In 1943, Schapiro [34] proposed a classification of PE into two types, types B and A. Type B (the

"sexually hypertonic" or "hypererotic" type) represented a consistent tendency to ejaculate rapidly from the first act of intercourse, and type A (the "hypotonic" type) was associated with the development of ED. In 1989, Godpodinoff [35] renamed these types as lifelong (primary) and acquired (secondary) PE. Over the years, other attempts to specify subtypes have occurred (e.g., global vs. situational PE, PE due to the effect of a substance, etc.).

Community-based normative IELT research and observational studies of men with PE demonstrated that IELTs of less than 1 minute have a low prevalence of about 2.5% in the general population. However, a much higher percentage of men with IELT greater than 1 minute report PE [19–21,36].

In order to take account of this disparity, Waldinger and Schweitzer [13,29] proposed a new classification of PE in which four PE subtypes are distinguished on the basis of the duration of the IELT, frequency of complaints, and course in life. In addition to lifelong PE and acquired PE, this classification includes variable PE and subjective PE. Men with variable PE occasionally experience an early ejaculation. It should not be regarded as a disorder, but as a natural variation of the ejaculation time in men [37]. On the other hand, men with subjective PE complain of PE while actually having a normal or even extended ejaculation time [37]. The complaint of PE in these men is probably related to psychological and/or cultural factors. In contrast, the consistent early ejaculations of lifelong PE suggest an underlying neurobiological functional disturbance, whereas the early ejaculation of acquired PE is more related to underlying medical and/or psychological and interpersonal causes. Serefoglu et al. [38,39] confirmed the existence of these four PE subtypes in a cohort of men in Turkey. Recently, Zhang et al. [40] and Gao et al. [41], using a similar methodology, confirmed similar prevalence rates of the four PE subtypes in China to that reported by Serefoglu et al. [38,39]. This new classification and continued research into the diverse phenomenology, etiology, and pathogenesis of PE is expected to provide a better understanding of the four PE subtypes [29]. Although the etiologies of lifelong and acquired PE differ, the presence of shared dimensions such as a lack of ejaculatory control and the presence of negative personal consequences suggest a potential for a single unifying definition of both lifelong and acquired PE. With continued research into the two other PE subtypes, variable PE and subjective PE, it may be appropriate to expand this unifying definition in the future.

The Rationale for the ISSM Definition of Lifelong PE

The multivariate, evidence-based ISSM definition of lifelong PE captures the key PE constructs of ejaculatory latency, perceived ejaculatory control, and the presence of negative personal consequences from PE [10].

Rationale for Inclusion of Ejaculatory Latency

Operationalization of PE using the length of time between penetration and ejaculation (IELT) forms the basis of most current clinical studies on PE [42]. IELT can be measured by a stopwatch or estimated (Table 1). Several authors report that estimated and stopwatch IELT correlate reasonably well or are interchangeable in assigning PE status when estimated IELT is combined with PROs [44,46].

Several studies suggest that 80–90% of men seeking treatment for lifelong PE ejaculate within 1 minute [17,22,43]. Waldinger et al. reported IELTs <30 seconds in 77% and <60 seconds in 90% of 110 men with lifelong PE, with only 10% ejaculating in between 1 and 2 minutes [17]. These data are consistent with normative community IELT data, support the notion that IELTs of less than 1 minute are statistically abnormal, and confirm that an IELT cutoff of 1 minute will capture 80–90% of treatment-seeking men with lifelong PE [21]. Further qualification of this cutoff to "about 1 minute" affords the clinician sufficient flexibility to also diagnose PE in the 10–20% of PE-treatment-seeking men who ejaculate within 1–2 minutes of penetration without unnecessarily stigmatizing the remaining 80–90% of men who ejaculate within 1–2 minutes of penetration but have no complaints of PE.

Rationale for Inclusion of Perceived Ejaculatory Control

The ability to prolong sexual intercourse by delaying ejaculation and the subjective feelings of ejaculatory control comprise the complex construct of ejaculatory control. Virtually all men report using at least one cognitive or behavioral technique to prolong intercourse and delay ejaculation, with varying degrees of success, and many young men reported using multiple different techniques [48]. Voluntary delay of ejaculation is most likely

Table 1 Findings of key publications regarding time to ejaculation in PE

Study	Summary of primary findings
Waldinger et al. 1998 [17]	• 110 men with lifelong PE whose IELT was measured by the use of a stopwatch • 40% of men ejaculated within 15 seconds, 70% within 30 seconds, and 90% within 1 minute
McMahon 2002 [22]	• 1,346 consecutive men with PE whose IELT was measured by the use of a stopwatch/wristwatch • 77% of men ejaculated within 1 minute
Waldinger et al. 2007 [43]	• 88 men with lifelong PE who self-estimated IELT • 30% of men ejaculated within 15 seconds, 67% within 30 seconds, and 92% within 1 minute after penetration • Only 5% ejaculated between 1 and 2 minutes
Waldinger et al. 2005 [21]	• Stopwatch IELT study in a random unselected group of 491 men in 5 countries • IELT had a positively skewed distribution • Application of 0.5 and 2.5 percentiles as disease standards; 0.5 percentile equated to an IELT of 0.9 minutes and 2.5 percentile to an IELT of 1.3 minutes
Althof 1995 [44]	• IELT estimations for PE men correlate reasonably well with stopwatch-recorded IELT
Pryor et al. 2005 [45]	• IELT estimations for PE men correlate reasonably well with stopwatch-recorded IELT
Rosen et al. 2007 [46]	• Self estimated and stopwatch IELT as interchangeable • Combining self-estimated IELT and PROs reliably predicts PE
Porst et al. 2010 [25]	• Stopwatch IELT was slightly (but significantly) greater for patients with acquired PE vs. lifelong PE (0.9 vs. 0.7 minutes, $P < 0.001$)
McMahon et al. 2013 [47]	• Stopwatch IELT was significantly greater for patients with acquired PE vs. lifelong PE (0.9 vs. 0.7 minutes, $P < 0.001$)
Serefoglu et al. 2010 [38]	• Self-estimated IELT was lowest in men with lifelong PE and highest in men with subjective PE • Lifelong PE: 20.47 ± 28.90 seconds (2–120 seconds); acquired PE: 57.91 ± 38.72 seconds (90–180 seconds); variable PE: 144.17 ± 22.47 seconds (120–180 seconds); subjective PE: 286.67 ± 69.96 seconds (180–420 seconds); $P = 0.001$
Zhang et al. 2013 [40]	• Self-estimated IELT follows a continuum among the four PE syndromes • Mean self-estimated IELT of 1.65 ± 0.82 minutes in acquired PE patients
Gao et al. 2013 [41]	• Self-estimated IELT follows a continuum among the four PE syndromes • Mean self-estimated IELT of 1.84 ± 1.02 minutes in acquired PE patients

exerted either prior to or in the early stages of the emission phase of the reflex but progressively decreases until the point of ejaculatory inevitability [49,50].

Several authors have suggested that an inability to voluntarily delay ejaculation defines PE (Table 2) [54–57]. Patrick et al. reported ratings of "very poor" or "poor" for control over ejaculation in 72% of men with PE, compared to 5% in a group of normal controls [19]. Lower ratings for control over ejaculation were associated with shorter IELT with "poor" or "very poor" control

Table 2 Findings of key publications regarding ejaculatory control in PE

Study	Summary of primary findings
Grenier and Byers 1997 [48]	• Relatively weak correlation between ejaculatory latency and ejaculatory control ($r = 0.31$) • Ejaculatory control and latency are distinct concepts
Grenier and Byers 2001 [51]	• Relatively poor correlation between ejaculatory latency and ejaculatory control, sharing only 12% of their variance, suggesting that these PROs are relatively independent
Waldinger et al. 1998 [17]	• Little or no control over ejaculation was reported by 98% of subjects during intercourse • Weak correlation between ejaculatory control and stopwatch IELT ($P = 0.06$)
Rowland et al. 2000 [52]	• High correlation between measures of ejaculatory latency and control ($r = 0.81$, $P < 0.001$)
Patrick et al. 2005 [19]	• Men diagnosed with PE had significantly lower mean ratings of control over ejaculation ($P < 0.0001$) • 72% of men with PE reported ratings of "very poor" or "poor" for control over ejaculation, compared with 5% in a group of normal controls • IELT was strongly positively correlated with control over ejaculation for subjects ($r = 0.51$)
Giuliano et al. 2007 [20]	• Men diagnosed with PE had significantly lower mean ratings of control over ejaculation ($P < 0.0001$) • "Good" or "very good" control over ejaculation in only 13.2% of PE subjects compared to 78.4% of non-PE subjects • Perceived control over ejaculation had a significant effect on intercourse satisfaction and personal distress • IELT did not have a direct effect on intercourse satisfaction and had only a small direct effect on personal distress
Patrick et al. 2007 [53]	• Effect of IELT upon satisfaction and distress appears to be mediated via its direct effect upon control
Rosen et al. 2007 [46]	• Control over ejaculation and subject-assessed level of personal distress are more influential in determining PE status than IELT • Subject reporting "very good" or "good" control over ejaculation is 90.6% less likely to have PE than a subject reporting "poor" or "very poor" control over ejaculation

Table 3 Findings of key publications regarding the negative personal consequences of PE

Study	Summary of primary findings
Patrick et al. 2005 [19]	• Using the validated Premature Ejaculation Profile, 64% of men in the PE group vs. 4% in the non-PE group reported personal distress
Giuliano et al. 2007 [20]	• On the Premature Ejaculation Profile, 44% of men in the PE group vs. 1% of men in non-PE group reported personal distress
Rowland et al. 2007 [61]	• Men in highly probable PE group reported greater distress vs. men in non-PE group on Premature Ejaculation Profile scale • On the Self-Esteem and Relationship Questionnaire, men with highly probable PE had lower mean scores overall for confidence and self-esteem vs. non PE men
Rowland et al. 2004 [60]	• 30.7% of probable PE group, 16.4% of possible PE group, 7.7% of non-PE group found it difficult to relax and not be anxious about intercourse
Porst et al. 2007 [62]	• Depression reported by 20.4% of PE group vs. 12.4% of non-PE group • Excessive stress in 28% of PE group vs. 19% of non-PE group • Anxiety in 24% of PE group vs. 13% of non-PE group
McCabe 1997 [63]	• Sexually dysfunctional men, including those with PE, scored lower than sexually functional men on all measures of intimacy on the Psychological and Interpersonal Relationship Scale
Symonds et al. 2003 [64]	• 68% reported self-esteem affected by PE; decreased confidence during sexual encounters • Anxiety reported by 36% (causing PE or because of it) • Embarrassment and depression also cited as due to PE
Dunn et al. 1999 [65]	Strong association of PE with anxiety and depression on the Hospital Depression and Anxiety Scales
Hartmann et al. 2005 [66]	58% of PE group reported partner's behavior and reaction to PE was positive, and 23% reported it was negative
Byers et al. 2003 [67]	Men with PE and their partners reported slightly negative impact of PE on personal functioning and sexual relationship but no negative impact on overall relationship

reported by 67.7%, 10.2%, and 6.7% of subjects with IELT <1 minute, >1 minute, and >2 minutes respectively. However, Grenier and Byers failed to demonstrate a strong correlation between ejaculatory latency and subjective ejaculatory control [48,51]. Several authors report that diminished control is not exclusive to men with PE and that some men with a brief IELT report adequate ejaculatory control and vice versa, suggesting that the dimensions of ejaculatory control and latency are distinct concepts [19,48,58]. Furthermore, there is a greater variability in changes in control compared with IELT in men treated with SSRIs [59]. Contrary to this, several authors have reported a moderate correlation between the IELT and the feeling of ejaculatory control [19,20,46,52]. Rosen et al. reported that control over ejaculation, personal distress, and partner distress were better predictors of PE status than IELT [46]. In addition, the effect of IELT upon satisfaction and distress appears to be mediated via its direct effect upon control [53]. However, despite conflicting data on the relationship between control and latency, the balance of evidence supports the notion that the inability to delay ejaculation appears to differentiate men with PE from men without PE [19,20,60].

Rationale for Inclusion of Negative Personal Consequences

Several authors have reported an association between PE and negative psychological outcomes in men and their female partners (Table 3) [19,20,60–72]. Patrick et al. reported significant differences in men with and without PE in the PRO measures of personal distress (64% vs. 4%) and interpersonal difficulty (31% vs. 1%), suggesting that this personal distress has discriminant validity in differentiating men with and without PE [19]. The personal and/or interpersonal distress, bother, frustration, and annoyance that results from PE may affect men's quality of life and partner relationships, their self-esteem, and their self-confidence, and can act as an obstacle to single men forming new partner relationships [19,20,60–72]. McCabe reported that sexually dysfunctional men, including men with PE, scored lower on all aspects of intimacy (emotional, social, sexual, recreational, and intellectual) and had lower levels of satisfaction compared with sexually functional men ($P < 0.001$ or $P < 0.01$) [63]. Rowland et al. showed that men with PE had significantly lower overall health-related quality of life, total Self-Esteem and Relationship Questionnaire scores, and lower confidence and self-esteem compared to non-PE groups [61]. Men with PE rated their overall health-related quality of life lower than men without PE ($P \leq 0.001$).

Rationale for Exclusion of Sexual Satisfaction

Men with PE report lower levels of sexual satisfaction compared with men with normal ejaculatory latency. Patrick et al. reported ratings of "very poor" or "poor" for sexual satisfaction in 31% of

subjects with PE compared with 1% in a group of normal controls [19]. However, caution should be exercised in assigning lower levels of sexual satisfaction solely to the effect of PE, and contributions from other difficult-to-quantify issues such as reduced intimacy, dysfunctional relationships, poor sexual attraction, and poor communication should not be ignored. This is supported by the report of Patrick et al. that despite reduced ratings for satisfaction with shorter IELTs, a substantial proportion of men with an IELT <1 minute report "good" or "very good" satisfaction ratings (43.7%). The current data are limited but suggest that sexual satisfaction is of limited use in differentiating PE subjects from non-PE subjects, and it was not included in the ISSM definition of PE [19].

Epidemiology and Pathophysiology of Acquired PE

Prevalence of Acquired PE

The previous lack of a standardized definition and specific operational criteria for PE has limited evidence-based research into the epidemiology, pathogenesis, characteristics, dimensions, and psychological burden of this condition. As a result, different authors report conflicting prevalence rates for PE (Table 4) [7,36–39,64,74,76,79,80,83–85,87–90,92–95,98,100–105]. There appears to be a substantial disparity between the incidence of PE in epidemiological studies, which rely upon either patient self-report of PE and/or inconsistent and poorly validated definitions of PE [19,20,74], and that suggested by community-based stopwatch studies of the IELT [21]. Furthermore, few researchers have focused on the epidemiology and characteristics of acquired PE.

Data from the Global Study of Sexual Attitudes and Behaviors (GSSAB), an international survey investigating the attitudes, behaviors, beliefs, and sexual satisfaction of 27,500 men and women aged 40–80 years, reported the global prevalence of PE (based on subject self-report) to be approximately 30% across all age groups [74]. Perception of "normal" ejaculatory latency varied by country and differed between patients and their partners [106]. A core limitation of the GSSAB survey stems from the fact that the youngest participants were aged 40 years, an age when the incidence of PE might be different from that in younger males [101].

Fasalo et al. reported that 2,658 of 12,558 men (21.2%) attending a free andrological consultation self-diagnosed PE, the majority describing acquired PE (14.8%), with 4.5% describing lifelong PE [78]. In contrast, Serefoglu et al. [38] reported that the majority of PE treatment-seeking patients described lifelong PE (62.5%) rather than acquired PE (16.1%). Similar findings were reported by Zhang et al., who found that the majority of 1,988 Chinese outpatients described lifelong PE (35.6%) or acquired PE (28.07%) [40]. These data provide evidence that lifelong and acquired PE patients comprise the majority of the patients who seek treatment for the complaint of ejaculating prematurely. In addition, there appears to be a disparity between the incidence of the various PE subtypes in the general community and in men actively seeking treatment for PE (Table 5).

Consistent with this notion, Serefoglu et al. subsequently reported an overall PE prevalence of 19.8%, comprising lifelong PE (2.3%), acquired PE (3.9%), variable PE (8.5%), and subjective PE (5.1%) [38]. Using similar research methodology, Gao et al. reported that 25.80% of 3,016 Chinese men complained of PE, with similar prevalences of lifelong PE (3.18%), acquired PE (4.84%), variable PE (11.38%), and subjective PE (6.4%) [41]. Of particular interest is the report of Serefoglu et al. [38] that men with acquired PE were more likely to seek medical treatment than men with lifelong PE (26.53% vs. 12.77%). This finding was confirmed by Gao et al., who demonstrated that acquired PE patients were more likely to seek (17.12% vs. 14.58%) or plan to seek (36.30% vs. 27.08%) treatment for their complaints, compared with men with lifelong PE [41]. These data suggest that the prevalence of acquired PE in the community is approximately 4% among sexually active adults and that these patients are more likely to seek medical treatment (Table 5). The reasons for increased treatment-seeking behavior in men with acquired PE compared with men with lifelong PE are unclear. It is possible that men with lifelong PE may reach a degree of accommodation to their rapid ejaculation, whereas the additional psychological burden imposed by the bothersome change in ejaculatory latency in acquired PE may prompt treatment seeking.

Etiology of Acquired PE

Acquired PE is most commonly due to sexual performance anxiety [66], psychological or relationship problems [66], or ED [77] and is occasionally due to prostatitis [107], hyperthyroidism [108], or withdrawal/detoxification from prescribed [109] or recreational drugs [110].

Table 4 Findings of key publications on the prevalence of premature ejaculation

Study	Method of data collection	Method of sample recruitment	Specific operational criteria	Prevalence rate	Number of men
Dunn et al. 1998 [73]	Mail	General practice registers—random stratification	Having difficulty with ejaculating prematurely	14% (past 3 months) 31% (lifetime)	617 618
Laumann et al. 1999 (National Health and Social Life Survey) [74]	Interview	NA	Climaxing/ ejaculating too rapidly during the past 12 months	31%	1,410
Fugl-Meyer et al. 2002 [75]	Interview	Population register	NA	9%	1,475
Rowland et al. 2004 [60]	Mailed questionnaire	Internet panel	DSM-IV	16.3%	1,158
Nolazco et al. 2004 [76]	Interview	Invitation to outpatient clinic	Ejaculating fast or prematurely	28.3%	2,456
Laumann et al. 2005 (Global Study of Sexual Attitudes and Behaviors) [77]	Telephone-personal interview/ mailed questionnaires	Random (systematic) sampling	Reaching climax too quickly during the past 12 months	23.75% (4.26% frequently)	13,618
Fasolo et al. 2005 [78]	Clinician-based	Invitation to outpatient clinic	DSM-IV	21.2%	12,558
Stulhofer et al. 2005 [79]	Interview	Stratified sampling	Often ejaculating in less than 2 minutes	9.5%	601
Porst et al. 2007 (Premature Ejaculation Prevalence and Attitudes) [62]	Web-based survey (self-report)	Internet panel	Control over ejaculation, distress	22.7%	12,133
Shindel et al. 2008 [80]	Questionnaire	Male partners of infertile couples under evaluation	Self report premature ejaculation	50%	73
Brock et al. 2009 [81]	Telephone interview	Web-based survey	DSM-III Control Distress	16% 26% 27%	3,816
Traeen et al. 2010 [82]	Mailed questionnaire and Internet	Web interview and randomization	NA	27%	11,746 and 1,671
Son et al. 2010 [83]	Questionnaire	Internet panel (≤60 years)	DSM-IV	18.3%	600
Amidu et al. 2010 [84]	Questionnaire	NA	NA	64.7%	255
Liang et al. 2010 [85]	NA	NA	ISSM	15.3%	1,127
Park et al. 2010 [86]	Mailed questionnaire	Stratified sampling	Suffering from PE	27.5%	2,037
Vakalopoulos et al. 2010 [87]	One-on-one survey	Population-based cohort	ED Lifelong PE	58.43% 17.7%	522
Hirshfeld et al. 2010 [88]	Web-based survey	Online advertisement in the USA and Canada	Climaxing/ejaculating too rapidly during the past 12 months	34%	7,001
Christensen et al. 2011 [89]	Interview and questionnaire	Population register (random)	NA	7%	5,552
Serefoglu et al. 2011 [39]	Interview	Stratified sampling	Complaining about ejaculating prematurely	20.0%	2,593
Son et al. 2011 [83]	Questionnaire	Internet panel	Estimated IELT ≤5 minutes, inability to control ejaculation, distress	10.5%	334
Tang and Khoo 2011 [90]	Interview	Primary care setting	PEDT ≥9	40.6%	207
Mialon et al. 2012 [91]	Mailed questionnaire	Convenience sampling (18–25 years old)	Control over ejaculation, distress	11.4%	2,507
Shaeer et al. 2012 [92]	Web-based survey	Online advertisement in Arabic countries	Ejaculation before the person wishes to ejaculate at least sometimes	83.7%	804
Shindel et al. 2012 [93]	Web-based survey	Online advertisement targeted to MSM and distribution of invitation to organizations catering to MSM	PEDT ≥9	8–12%	1,769
McMahon et al. 2012 [94]	Computer-assisted interviewing, either online or in person and self-completed	NA	PEDT ≥11 Self-reported (always/nearly-always)	16% 13%	4,997
Lotti et al. 2012 [95]	Interview	Men seeking medical care for infertility	PEDT ≥9	15.6%	244
Zhang et al. 2013 [96]	Interview	Random stratified sample of married men aged 30–60	Self-reported premature ejaculation	4.7%	728
Lee et al. 2013 [97]	Interview	Stratified random sampling	PEDT ≥11 Self-reported PE IELT <1 minute	11.3% 19.5% 3%	2,081 1,035
Shaeer 2013 [98]	Web-based survey	Online advertisement in the United States	PEDT ≥11 Self-reported any PE Self-reported PE “always” or “mostly”	50% 78% 14%	1,133
Gao et al. 2013 [41]	Interview	Random stratified sample of monogamous heterosexual men in China	Self-reported premature ejaculation	25.8%	3,016
Hwang et al. 2013 [99]	Survey of married couples	Married heterosexual couples in Korea	Estimated IELT <2 minutes PEDT ≥11	21.7% 12.1%	290
Vansintejan et al. 2013 [100]	Web-based survey	Online and flyer advertisements to Belgian MSM (only HIV^+ men in this study)	IPE score ≤50% of total possible IPE score ≤66% of total possible	4% 18%	72

NA = not applicable; MSM = men who have sex with men; PEDT = Premature Ejaculation Diagnostic Tool; IPE = Index of Premature Ejaculation

Table 5 Distribution of patients with the complaint of PE according to PE syndromes in the general population and outpatient clinics in Turkey and China

General male population					
Study	Population (n)	Lifelong PE (%)	Acquired PE (%)	Variable PE (%)	Subjective PE (%)
Serefoglu et al. 2011 [39]	2,593	2.3%	3.9%	8.5%	5.1%
Gao et al. 2013 [41]	3,016	3.2%	4.8%	11.4%	6.4%
Outpatient clinic					
Study	PE patients (n)	Lifelong PE (%)	Acquired PE (%)	Variable PE (%)	Subjective PE (%)
Fasolo et al. 2005 [78]	2,658	21.4%	69.8%	Not specified: 8.8%	
Serefoglu et al. 2010 [38]	261	62.5%	16.1%	14.5%	6.9%
Zhang et al. 2013 [40]	1988	35.7%	28.1%	12.7%	23.5%

Psychological and Relationship Problems

Psychological and relationship factors that may result in acquired PE include the effect of early experience and sexual conditioning, anxiety, sexual technique, the frequency of sexual activity, and psychodynamic factors [71,111]. Several authors have suggested that anxiety activates the sympathetic nervous system and reduces the ejaculatory threshold, leading to an earlier emission [54,112]. Hypoactive sexual desire may lead to acquired PE because of an unconscious desire to abbreviate unwanted penetration [111]. Similarly, diminished sexual desire can be a consequence of chronic and frustrating PE [10]. Female sexual dysfunctions, such as anorgasmia, hypoactive sexual desire, sexual aversion, sexual arousal disorders, and sexual pain disorders such as vaginismus [112], may also be related to acquired PE.

Comorbid Erectile Dysfunction

Recent data demonstrate that as many as half of subjects with ED also experience PE [62,78]. Subjects with ED may either require higher levels of stimulation to achieve an erection or intentionally "rush" intercourse to prevent early detumescence of a partial erection, resulting in ejaculation with a brief latency [9]. This may be compounded by the presence of high levels of performance anxiety related to their ED, which serve only to worsen their prematurity and erectile function.

Prostate Disease

Acute and chronic lower urogenital infection, prostatodynia, and chronic pelvic pain syndrome (CPPS) are associated with ED, PE, and painful ejaculation [113–115]. Several studies report PE as the main sexual disorder symptom in men with chronic prostatitis or CPPS, with a prevalence of 26–77% [116]. The pathophysiologic link between chronic prostatitis, ED, and PE is unknown. Prostatic inflammation may result in altered sensation and modulation of the ejaculatory reflex, but evidence in support of this hypothesis is lacking [115–117]. Antibiotic treatment of microbiologically confirmed bacterial prostatitis in men with acquired PE resulted in a 2.6-fold increase in IELT and improved ejaculatory control in 83.9% of subjects [117].

Hyperthyroidism

The majority of patients with thyroid hormone disorders experience sexual dysfunction. Studies suggest a significant correlation between PE and suppressed thyroid-stimulating hormone (TSH) values in a selected population of andrological and sexological patients. The 50% prevalence of PE in men with hyperthyroidism fell to 15% after treatment with thyroid hormone normalization [108]. Hyperthyroidism is relatively rare in men, with a prevalence of 0.2% reported in a community-based study, and is more common in men over 60 years of age [118]. It is very uncommon in the population who present for treatment of PE, and routine TSH screening is not recommended unless clinically indicated [119].

Comparison of Characteristics of Acquired PE and Lifelong PE

Lifelong PE is a syndrome characterized by a cluster of core symptoms including early ejaculation at nearly every intercourse—within 30–60 seconds in the majority of cases (80%) or in between 1 and 2 minutes (20%)—with every or nearly every sexual partner and from the first sexual encounter onwards [17,22]. Acquired PE differs in that sufferers develop early ejaculation, which is often situational, after having previously had normal ejaculation experiences. The main distinguishing features between the presentations of these two syndromes are the time of onset of symptoms and that there is a reduction in previously normal ejaculatory latency in acquired PE.

Table 6 Demographic, IELT, and PRO data from the post hoc analysis of five Phase 3 dapoxetine trials

	McMahon et al. 2013 [47,120]							
	Overall		IIEF-EF 21–25		IIEF-EF 25–26		Porst et al. 2010 [25]	
Parameter	Acquired PE	Lifelong PE	Acquired PE	Lifelong PE	Acquired PE	Lifelong PE	Acquired PE	Lifelong PE
Age (years), mean	52.2	45.5	53.3	46.5	51	44.5	41.9	39.7
IELT (min), mean	1.205	0.99	1.26	0.99	1.16	0.99	1.07	0.9
IELT <1 minute	39.5%	57.0%	35%	60%	44%	54%	45%	58%
IELT 1–2 minutes	58.5%	41.5%	64%	38%	53%	45%	55%	41%
Control								
Very poor	28.0%	47.5%	23%	44%	33%	51%	35%	47%
Very poor + poor	80.5%	92.5%	81%	93%	80%	92%	90%	94%
Satisfaction								
Very poor	16.0%	29.0%	17%	30%	15%	28%	21%	22%
Very poor + poor	52.0%	76.5%	56%	79%	48%	74%	71%	66%
Distress								
Quite a bit + extremely	66.0%	83.5%	63%	83%	69%	84%	72%	71%
Interpersonal difficulty								
Quite a bit + extremely	37.0%	58.0%	40%	65%	34%	51%	42%	37%

IIEF-EF = International Index of Erectile Function erectile function domain

Although men with lifelong and acquired PE appear to share the dimensions of short ejaculatory latency, reduced or absent perceived ejaculatory control, and the presence of negative personal consequences from PE, they remain distinct and different demographic and etiological populations [25].

Demographic Differences Between Lifelong and Acquired PE

Consistent with the predominant organic etiology of acquired PE, men with this complaint are usually older [25,38–41,47,78]. Fasolo et al. reported that the mean age of men with acquired PE was greater compared with that of patients with lifelong PE (50 vs. 39 years) [78]. Both Serefoglu et al. [38] and Zhang et al. [40] confirmed this finding that men with acquired PE were significantly older than men with other PE syndromes.

Porst et al. reported the results of an integrated analysis of baseline characteristics and treatment outcomes from Phase 3 dapoxetine trials in men with acquired or lifelong PE (n = 2,228) who met the DSM-IV-TR criteria for PE, had an IELT ≤2 minutes in ≥75% of intercourse episodes and had mild or no ED (International Index of Erectile Function [IIEF] score ≥21) [25]. Statistical analysis was limited to comparison of baseline IELT and Premature Ejaculation Profile responses between subjects with acquired PE and lifelong PE with or without ED.

Although formal statistical analysis of baseline demographics was not reported, a slight age-related trend was observed. Subjects with acquired PE, especially those with mild ED, were noted to be slightly older than men with lifelong PE (Table 6). This is consistent with the increased incidence of ED in acquired PE and the epidemiology of ED. Predictably, the overall mean IIEF domain scores in men with acquired PE were slightly lower compared with those in men with lifelong PE. Men with acquired PE appear less likely to experience early ejaculation during solitary masturbation and are more likely to benefit from behavioral treatment, consistent with a syndrome associated with situational anxiety symptoms [25,47]. Porst et al. concluded that with the exception of time of onset, duration of PE, and incidence of ED, the characteristics of men with acquired and lifelong PE were sufficiently similar in terms of demographics, sexual history, and PE symptomatology to preclude their use in discriminating between lifelong and acquired PE.

A post hoc analysis of baseline demographic data from the COUPLE study, a Phase 3 randomized clinical trial of the efficacy and safety of flexible-dose dapoxetine (30/60 mg) in men with either lifelong or acquired PE and comorbid ED who were simultaneously and successfully being treated with a phosphodiesterase type 5 inhibitor drug (IIEF erectile function score ≥21), also confirmed that men with acquired PE and comorbid ED were older than men with lifelong PE and comorbid ED (Table 6) [47].

Differences in Comorbidities Between Lifelong and Acquired PE

Godpodinoff [35] noted that 81% of secondary (acquired) PE patients had "demonstrable organic

causes" for their PE, whereas 18% demonstrated no organic causes but were involved in disturbed or triangular relationships. Recent studies have suggested that in some men neurobiological and genetic variations could contribute to the pathophysiology of lifelong PE [26,29,121–123], but the etiology of acquired PE can be either psychological or organic, the latter etiology commonly being associated with other comorbid diseases [66,77,107–110]. Men with acquired PE have a higher incidence of ED and other comorbid diseases, as well as cardiovascular risk factors [38–41,78].

Serefoglu et al. [39], Zhang et al. [40], and Gao et al. [41] reported that patients with acquired PE had a higher mean BMI and a greater incidence of comorbid diseases, including hypertension, sexual desire disorder, diabetes mellitus, chronic prostatitis, and ED, compared with patients with lifelong, variable, and subjective PE.

Porst et al. reported the presence of comorbid ED in 15% and 24% of the lifelong and acquired PE subgroups, respectively [25]. Overall, the mean IIEF domain scores were similar for the lifelong and acquired subgroups for erectile function (27.9 vs. 27.1), orgasmic function (8.9 vs. 8.6), sexual desire (7.7 vs. 7.5), intercourse satisfaction (8.2 vs. 7.8), and overall satisfaction (5.1 vs. 5.1). Predictably, slightly lower IIEF domain scores for the orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction domains were observed in men with mild ED. However, this post hoc analysis has several limitations imposed by the design of the original Phase 3 studies that restrict additional analysis of other factors that may have discriminatory relevance. These limitations include (i) the use of the authority-based DSM-IV-TR to diagnose PE; (ii) the lack of a standardized method used to differentiate lifelong and acquired PE; (iii) the application of IELT selection criteria based upon normative IELT data for men with lifelong PE, which may have filtered out more substantial differences in average IELT that may exist between these two subtypes in the general population; and (iv) the exclusion of men with moderate or severe ED (IIEF erectile function domain score <21), chronic prostatitis, or no available information regarding hyperthyroidism.

The inclusion of men with moderate or severe ED in the trials comprising the Porst et al. study [25] might have resulted in a statistically significant age trend consistent with the epidemiology of ED, in which prevalence is known to increase with age, and statistically different overall IIEF domain scores. The greater disparity in age between these two PE subgroups observed in the COUPLE study, which enrolled men with more severe ED, supports this speculation [47].

Differences in IELT Between Lifelong and Acquired PE

Porst et al. reported that both the arithmetic (1.1 vs. 0.9 minute, $P < 0.001$) and geometric (0.9 vs. 0.7 minute, $P < 0.001$) mean IELTs were slightly (but significantly) greater for patients with acquired PE [25]. Several authors have confirmed this preliminary finding by demonstrating that self-estimated IELT is longer in men with acquired PE compared with those with lifelong PE [38,40,41,47].

The post hoc analysis of the COUPLE data confirms a statistically significantly longer IELT in men with acquired PE and comorbid ED compared with men with lifelong PE with comorbid ED (52.2 years vs. 45.5 years) (Table 6) [47]. Serefoglu et al. [39] reported that self-estimated IELT was lowest in men with lifelong PE and highest in men with subjective PE (lifelong PE 20.47 ± 28.90 seconds [2–120 seconds]; acquired PE 57.91 ± 38.72 seconds [90–180 seconds]; variable PE 144.17 ± 22.47 seconds [120–180 seconds]; subjective PE 286.67 ± 69.96 seconds [180–420 seconds, $P = 0.001$]). Gao et al. [41] and Zhang et al. [40] confirmed that self-estimated IELT follows a continuum among the four PE syndromes and reported a mean self-estimated IELT of 1.65 ± 0.82 minutes and 1.84 ± 1.02 minutes, respectively, in acquired PE patients. These data suggest 3 minutes as a valid cutoff for either self-estimated or stopwatch IELT for the diagnosis of acquired PE.

Differences in PRO Between Lifelong and Acquired PE

Both Porst et al. [25] and McMahon et al. [47] reported that the majority of patients with acquired and lifelong PE, regardless of comorbid ED, reported perceived control over ejaculation as "poor" or "very poor," levels of satisfaction with intercourse as "fair" or worse, and levels of personal distress as at least "moderate." The COUPLE data demonstrate that men with lifelong PE and comorbid ED have less control, less satisfaction, more distress, and more interpersonal difficulty than men with acquired PE and comorbid ED (Table 6) [47,120].

These findings conflict with the reports of Patrick et al. [19] and Serefoglu et al. [39], who observed better satisfaction with sexual intercourse and less interpersonal difficulty in the lifelong PE subgroup compared with the acquired PE subgroup. However, caution should be exercised in assigning lower levels of sexual satisfaction solely to the effect of PE, and contributions from other difficult-to-quantify issues such as reduced intimacy, dysfunctional relationships, poor sexual attraction, and poor communication should not be ignored. This is supported by the report of Patrick et al. that despite reduced ratings for satisfaction with shorter IELTs, a substantial proportion of men with an IELT <1 minute report "good" or "very good" satisfaction ratings (43.7%).

In conclusion, men with lifelong and acquired PE appear to share the dimensions of short ejaculatory latency, reduced or absent perceived ejaculatory control, and the presence of negative personal consequences. Although there are limited published reports, these studies, supported by expert opinion, suggest that self-estimated IELT appears higher in men with acquired PE compared with those with lifelong PE and that a self-estimated or stopwatch IELT of 3 minutes is a valid IELT cutoff for diagnosing acquired PE. Men with acquired PE are older, have higher incidences of ED, comorbid disease, and cardiovascular risk factors, and report less sexual satisfaction and more interpersonal difficulty compared with patients with lifelong PE. Further observational studies in men with acquired PE are required to validate the 3-minute IELT cutoff and other patient characteristics.

Conclusion

Although the 2007 ISSM definition of lifelong PE represents a major development in the application of evidence-based methodology in the field of sexual medicine, its application in clinical practice is restricted by its limitation to men with lifelong PE. Research into the epidemiology, etiology, features, and treatment of acquired PE has been limited by the lack of an evidenced-based definition. An urgent need for standardization of the methodology for observational, intervention, and intervention preference trials in PE continues to exist. The lack of an evidence-based definition promotes errors of classification, resulting in poorly defined study populations and in less reliable and harder-to-interpret data that are difficult to generalize to patients.

The unified ISSM definition of lifelong and acquired PE represents an evidence-based definition for these conditions. This definition should form the basis for both the office diagnosis of lifelong PE and the design of observational and interventional clinical trials in PE. It is limited to men engaging in vaginal intercourse because there are few studies on early ejaculation in the context of oral sex, anal sex, and same-gender sexual activity between men.

The evidence suggests that the multivariate evidence-based unified ISSM definition of lifelong and acquired PE will reduce errors of diagnosis and classification by providing the clinician with a discriminating diagnostic tool. The IELT cutoff of about 1 minute captures the 90% of men with lifelong PE who actively seek treatment and ejaculate within 1 minute but also affords the clinician sufficient flexibility to also diagnose lifelong PE in the 10% of men seeking treatment for lifelong PE who ejaculate within 1–2 minutes of penetration.

The Committee reiterated that the 1-minute IELT cutoff point should not be applied in the most absolute sense, as about 10% of men seeking treatment for lifelong PE have IELTs of 1–2 minutes. The phrase "within about 1 minute" must be interpreted as giving the clinician sufficient flexibility to diagnose PE also in men who report an IELT as long as 90 seconds. Similarly, a degree of flexible clinical judgement is key to the recognition and interpretation of a bothersome change in ejaculatory latency with reduction of premorbid latency to ≤3 minutes in men with acquired PE. Men who report these ejaculatory latencies but describe adequate control and no personal negative consequences related to their rapid ejaculation do not merit the diagnosis of PE.

This definition intentionally includes a degree of diagnostic conservatism and flexibility for several reasons. First, a conservative and flexible definition will provide more realistic figures for prevalence of the dysfunction. Second, it will help to establish PE as a bona fide sexual dysfunction rather than a lifestyle condition where men are simply seeking to enhance their sexual function. Third, it will help to ensure greater confidence in the efficacy of new and existing treatments and strengthen the likelihood that regulatory agencies might approve new efficacious and safe compounds for this dysfunction [27].

We wish to thank the ISSM for its leadership in assembling and encouraging the committee members in the development of the evidence-based definition of lifelong and acquired PE. We

anticipate that this definition will promote and assist further research into the prevalence of both lifelong and acquired PE, as well as the development of new tools and PROs for both the diagnosis and assessment of treatment outcomes and the development of new pharmacological and psychological treatments.

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Conflict of Interest:

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Stanley Althof	Allergan—Consultant, Advisory Board, Principal Investigator Abvie—Consultant Eli Lilly—Consultant Ixchelsis—Consultant Menarini—Speaker Palitan—Advisory Board Plethora—Consultant Sprout—Advisory Board, Consultant Trimel—Principal Investigator
Chris McMahon	Johnson & Johnson—Consultant, Principal Investigator, Advisory Board Member, Speaker Menarini Group—Principal Investigator, Advisory Board Member, Speaker Bayer Schering—Investigator, Advisory Board, Speaker Plethora Solutions—Advisory Board, Speaker Ixchelsis—Consultant
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Wayne J.G. Hellstrom	American Medical Systems—Consultant or Advisor Andromedical—Consultant or Advisor Auxilium—Meeting Participant, Lecturer, Consultant, Investigator, Advisor Allergan—Consultant or Advisor, Scientific Study or Trial Coloplast—Consultant or Advisor, Investigator Cook—Consultant or Advisor, Lecturer Endo—Consultant or Advisor, Investigator, Lecturer Johnson & Johnson—Consultant or Advisor, Meeting Participant or Lecturer, Investigator Lilly, USA—Consultant or Advisor, Lecturer; NIH—Board Member, Officer, Trustee Slate—Pharmaceutical—Lecturer, Advisor, and Investigator Theralogix—Board Member, Officer, Trustee VIVUS—Advisor/Consultant, Investigator, Lecturer
Annamaria Giraldi	Eli Lilly: Speaker Emotional Brain: Advisory Board Apricus Bioscience: Advisory board
Sidney Glina	Principal Investigator for Lilly, Astra Zeneca Speaker for Pfizer, Lilly, Bayer Advisory Board: Lilly, Besins
Luca Incrocci	No conflicts to report
Emmanuele Jannini	Bayer—Consultant, Speaker, Investigator Besins—Consultant, Speaker, Investigator Lilly—Consultant , Speaker, Investigator Menarini—Consultant , Speaker, Investigator Pfizer—Consultant, Speaker, Investigator
Marita McCabe	Menarini—Advisory Board
Sharon Parish	Emotional Brain—Advisory Board Shinogi—Advisory Board Apricus—Advisory Board Strategic Science and Technology—Advisory Board Pfizer—Advisory Board
David Rowland	No conflicts to report
Robert Segraves	Advisor and Investor S1Biopharm
Ira Sharlip	Speaker and consultant to Pfizer and Lilly; Consultant to Absorption Pharmaceuticals and Plethora
Luiz Otavio Torres	Speaker for Bayer, Janssen, Lilly, Pfizer, GSK. Member of the advisory board for Lilly

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