American Urological Association

Education and Research, Inc.

Premature Ejaculation

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Guideline on the Pharmacologic Management of Premature Ejaculation

Acknowledgements and Disclaimers: AUA Guideline on the Management of Premature Ejaculation (PE)

This document was written by the Erectile Dysfunction Guideline Update Panel of the American Urological Association Education and Research, Inc., which was created in 1999. The Practice Guidelines Committee (PGC) of the AUA selected the committee chairs. Panel members were selected by the chairs. Membership of the committee included urologists with specific expertise on this disorder. The mission of the committee was to develop recommendations, that are analysis-based or consensus-based, depending on panel processes and available data, for optimal clinical practices in the diagnosis and treatment of premature ejaculation. This document was submitted for peer review to 57 urologists and other health care professionals. After the final revisions were made, based upon the peer review process, the document was submitted to, and approved by the PGC and the Board of Directors of the AUA. Funding of the committee was provided by the AUA. Committee members received no remuneration for their work. Each member of the committee provided a conflict of interest disclosure to the AUA.

This report is intended to provide medical practitioners with a consensus of principles and strategies for the treatment of premature ejaculation. The report is based on current professional literature, clinical experience and expert opinion. It does not establish a fixed set of rules or define the legal standard of care and it does not pre-empt physician judgment in individual cases. The medical therapies currently employed in the management of PE have not been approved by the U.S. Food and Drug Administration (FDA) for this specific indication. Thus, doses and dosing regimens may deviate from that employed for FDA-approved indications, and this difference should be considered in the risk-versus-benefit assessment. Physician judgment must take into account variations in resources and in patient needs and preferences.

I. Introduction

The three major forms of male sexual dysfunction are ejaculatory dysfunction, erectile dysfunction (ED), and decreased libido (hypoactive sexual desire disorder). While survey findings vary considerably, most epidemiological studies suggest that premature ejaculation (PE) (Although the terms *early ejaculation* and *rapid ejaculation* recently have been suggested as more accurate descriptions of this disorder, to prevent confusion, the common name *premature ejaculation* will be used throughout this document.) may be the most common male sexual disorder. Data from the National Health and Social Life Survey have revealed a prevalence of 21% in men ages 18 to 59 in the United States[1]. Using various definitions, other studies report prevalences ranging from less than 5%[2] to greater than 30%[3, 4, 5].

A universally accepted definition of PE has yet to be established. Masters and Johnson (1970)[6] proposed one of the earliest definitions that focused on the inability to delay ejaculation long enough for the woman to achieve orgasm fifty percent of the time, assuming that PE is the sole cause of the female anorgasmia. Kaplan (1974)[7] first suggested that PE is primarily a problem of voluntary control over timing of ejaculation, a concept on which the current definition is based. The American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (4th ed., Text Revision) (DSM-IV TR) (2000)[8] defines PE with an added emphasis on the emotional and interpersonal impact of ejaculation that occurs earlier than the male desires. Premature ejaculation has been subclassified into two forms: a primary (lifelong) form that begins when a male first becomes sexually active and a secondary (acquired) form[9, 10]. The present guidelines and recommendations are based on the following definition, which assumes the absence of partner sexual dysfunction:

Premature ejaculation is ejaculation that occurs sooner than desired, either before or shortly after penetration, causing distress to either one or both partners.

The exact etiology of PE is unknown. Psychological/behavioristic and biogenic etiologies have been proposed. Consequently, the treatment of PE has encompassed psychological, behavioral, and pharmacologic interventions. Current treatments are largely based upon logical solutions (decreasing sensory input), behavior modification therapies, and observations of drug side effects (those with serotonin reuptake inhibiting activity). This guideline will address only pharmacologic therapies, as other therapies are not routinely prescribed by our target audience.

To facilitate informed treatment decisions by physicians and their patients, recommendations on the use of medications currently available in the United States are provided. The majority of the recommendations contained herein are based on a consensus of expert opinion following review of the literature. In some cases, expert consensus is supplemented with a focused review of the limited data. This guideline does not preempt physician judgment in individual cases. Variations in patient subpopulations, physician experience, and available resources necessarily will influence choice of clinical strategy. Adherence to the recommendations presented in this document cannot assure a successful treatment outcome.

For ease of review, the recommendations are bolded and followed by supporting text. The evidence supporting the recommendations is summarized in Appendices 1 to 3.

II. Methods

The Erectile Dysfunction Guideline Update Panel (hereafter the Panel) of the American Urological Association (AUA) was convened in April 2000 at the request of the AUA Board of Directors. The Practice Guidelines Committee of the AUA selected the Panel Co-chairmen, and the full Panel roster was assembled by invitation to experts in the field. The Panel evaluated several topics for possible guideline development. Premature ejaculation was selected because of its high prevalence and the availability of a defining body of literature.

Using the MEDLINE® database with MeSH headings related to ejaculatory dysfunction, initial literature searches were performed limiting papers to reports of human studies published in English-language journals between 1966 and January 2001. Only a small number of articles provided outcomes data on PE. Additional studies were identified from references cited in these articles and from recommendations of individual Panel members. The MEDLINE search was last updated in October 2002. Even after the final literature search was completed, however, the Panel continued to scrutinize key references that were identified up until the peer review process.

From a review of abstracts, the Panel chairs selected articles with potentially usable information. Selected papers were reviewed in detail, and relevant data on efficacy and adverse events were extracted and listed in evidence tables (see Appendix 1). Only papers with outcomes data that were relevant to PE, involving pharmacologic treatments generally available in the United States, were included in the evidence tables. If the study was seriously flawed, the article was not considered. Summary tables of adverse event rates and effects of various treatments on latency were created to supplement the data captured in the evidence tables (see Appendices 2 and 3). A

complete list of the 51 references that met all inclusion criteria is available in Appendices 4 and 5. The full Panel reviewed the evidence and summary tables at successive meetings.

Three major limitations were encountered in the evaluation of the evidence that precluded the ability to combine outcomes data and to perform study outcomes comparisons:

- The lack of standardization in studying PE. Clinical trials employ a variety of definitions, entry criteria, physiological measurements and psychometric instruments for evaluation.
- The lack of agreement in quantifying the amount of stimulation that patients experienced. Time to ejaculation is a function of many factors, not the least of which is the nature of the stimulation. The same stimulus may be excessive for one man but elicit little excitement in another. Furthermore, the lack of a consistent stimulus (partner variables, nature of sexual activity, presence or absence of foreplay, preference for single or multiple stimuli) precludes a rigorous experimental design.
- The lack of consistency and accuracy in measurements of time to ejaculation and other outcomes. The most common outcome parameter, time to ejaculation, is either recorded at the time or documented later by recall. These measurements lack accuracy but generally are useful when applied consistently within a single study. Application across multiple studies in a meta-analysis is problematic because any methodological differences will compromise the ability to make a valid comparison. Other common outcome measures concern patient and partner satisfaction. A variety of assessment tools are used, and there is no assurance of comparability between studies.

The Panel determined that a meta-analysis was inappropriate due to the disparate outcome measures and populations in the existing studies. The amount of variation between studies also made other less rigorous forms of outcome estimation inaccurate. The Panel's recommendations were developed either solely by consensus or by consensus combined with a review of the available, though limited, evidence. Unless otherwise noted, the statistics cited in this document are derived from the evidence tables.

After this guideline was written, it was reviewed and approved by each member of the Panel and submitted for peer review by 57 physicians. Based on the results of peer assessment, revisions were made and the guideline was forwarded to the Panel again, to the Practice Guidelines Committee, and the Board of Directors of the AUA, all of which rendered approval.

III. Evaluation of the Patient With Premature Ejaculation

Premature ejaculation is a self-reported diagnosis. A sexual history in which the patient uses language that explicitly communicates the circumstances of the condition is the fundamental basis of assessment with time to ejaculation as the most important feature. The opinion of a partner can provide a significant contribution to clinician understanding. A complete description is essential in distinguishing PE from ED, i.e., the inability to attain or maintain an erection, because these conditions frequently coexist. Moreover, some men are unaware that loss of erection after ejaculation is normal; thus, they may erroneously complain of ED when the actual problem is PE.

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Recommendation 1:

The diagnosis of PE is based on sexual history alone. A detailed sexual history should be obtained from all patients with ejaculatory complaints.

[Based on Panel consensus.]

When obtaining the patient's history, several important sexual and psychological characteristics should be assessed: frequency and duration of PE, relationship to specific partners, occurrence with all or some attempts, degree of stimulus resulting in PE, nature and frequency of sexual activity (foreplay, masturbation, intercourse, use of visual clues, etc.), impact of PE on sexual activity, types and quality of personal relationships and quality of life, aggravating or alleviating factors, and relationship to drug use or abuse. Laboratory or physiological testing is not required unless the history and a physical examination reveal indications beyond uncomplicated PE.

Recommendation 2:

In patients with concomitant PE and ED, the ED should be treated first.

[Based on Panel consensus.]

Another priority of assessment should be determining whether ED is a concurrent problem. Many patients with ED develop secondary PE, perhaps due to either the need for intense stimulation to attain and maintain an erection or due to the anxiety associated with difficulty in attaining and maintaining an erection. Premature ejaculation may improve in patients when concomitant ED is effectively treated.

IV. Treatment of Premature Ejaculation

Recommendation 3:

The risks and benefits of all treatment options should be discussed with the patient prior to any intervention. Patient and partner satisfaction is the primary target outcome for the treatment of PE.

[Based on Panel consensus.]

As outlined above, the treatments for PE range from psychological and behavioral therapies to pharmacologic therapies. While pharmacologic therapies are the focus of this guideline, other types of interventions may be considered. The patient plays a central role in determining the need for treatment. The patient and possibly his partner can be reassured that PE is a common and treatable disorder. Information on the risks and benefits of all therapeutic options should be presented to the patient (and partner) so that an educated treatment choice may be made by the patient in consultation with the physician. Premature ejaculation is not a life-threatening condition; therefore, safety should be a primary consideration. Some treatments, such as neurectomy and penile prosthesis implantation, have risks that far outweigh their benefits. In addition, none of the medical therapies currently employed in the management of PE have been approved by the U.S. Food and Drug Administration (FDA) for this specific indication. Thus, doses and dosing regimens frequently deviate from that employed for FDA-approved indications, and this difference should be considered in the risk-versus-benefit assessment of pharmacologic therapy.

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Efficacy of Proposed Treatments

The preponderance of evidence together with Panel consensus strongly suggest that patients can benefit from the use of several oral or topical medications. At the dosages used in the management of PE, these treatments have been shown to have safety profiles that generally are appropriate to support their use.

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Recommendation 4:

Premature ejaculation can be treated effectively with several serotonin reuptake inhibitors (SRIs) or with topical anesthetics. The optimal treatment choice should be based on both physician judgment and patient preference.

[Based on Panel consensus and review of data.]

Oral Medication — Antidepressants

Several antidepressants known to cause anorgasmia and delayed ejaculation have been evaluated in the management of PE. These antidepressants include SRIs, the majority of which are selective (SSRIs) — fluoxetine, paroxetine, and sertraline — and the tricyclic antidepressant clomipramine (Table 1). The SRIs have been successfully utilized in the management of PE. As a group, in clinical trials, the SRIs have provided significant benefit over placebo. Studies have suggested that nefazodone, citalopram, and fluvoxamine are ineffective for the treatment of PE and may be more suitable than other SSRIs for treatment of depression in men *not* wanting ejaculatory impairment.

Table 1. Medical therapy options for the treatment of premature ejaculation[*]

Oral Therapies	Trade Names[†]	Recommended Dose [‡§]
Nonselective serotonin reuptake inhibitor		
Clomipramine	Anafranil®	25 to 50 mg/day or 25 mg 4 to 24 h pre-intercourse
Selective serotonin reuptake inhibitors		
Fluoxetine	Prozac®, Sarafem®	5 to 20 mg/day
Paroxetine	Paxil®	10, 20, 40 mg/day or 20 mg 3 to 4 h pre-intercourse
Sertraline	Zoloft®	25 to 200 mg/day or 50 mg 4 to 8 h pre-intercourse
Topical Therapies		
Lidocaine/prilocaine cream	EMLA® Cream	Lidocaine 2.5%/prilocaine 2.5% 20 to 30 minutes pre-intercourse

[*]This list does not reflect order of choice or efficacy.
[†]Trade names listed may not be all-inclusive.
[‡] Peak plasma concentrations occur 2 to 8 hours (h) postdose and half-lives range from 1 to 3 days.
[§]Titrate doses from low to high based on response.

Dosing

Various doses and dosing regimens of the SRIs have been evaluated in efficacy and safety studies of PE. Some studies have employed continuous daily dosing while others use a situational dosing regimen whereby the medication is only taken prior to sexual activity. Different situational dosing regimens also have been assessed, varying timing of the dose prior to sexual activity to the time of peak plasma concentrations of the prescribed agent. The limited data on situational dosing suggest that this regimen may be of use to some men because of the theoretical advantage that less of the drug will be used. In general, though, these SRIs have been designed for continuous usage, and their benefits in the treatment of depression are better established after a period of consistent drug administration. Conversely, continuous administration may foster a problem with patient compliance.

Whether continuous or situational dosing is more effective in the management of PE is unclear. The optimal interval for situational dosing before intercourse has not been established and the onset of action of these SRIs for this indication is unknown. However, all Panel members utilize a situational dosing regimen in their practices, and some initiate therapy with daily dosing (loading period). The choice of regimen often is based upon the frequency of sexual activity by the patient.

Duration of Therapy

Therapy for PE most likely will be needed on a continuing basis. There is no clear consensus as to whether SRIs will effect an eventual cure of PE, allowing for discontinuation of the medication, or whether SRIs will be required for life. The Panel members' experience is that PE usually returns upon discontinuing therapy.

Dosing of Specific Serotonin Reuptake Inhibitors

Doses of fluoxetine ranging from 5 to 20 mg/day (see Table 1) are reported to be more effective in delaying ejaculation and enhancing patient/partner satisfaction than placebo. A regimen in which the dose is increased after 1 week (to 40 mg/day or to 60 mg/day) also has been used with success [11, 12]. In addition, there is evidence that a clinically beneficial effect may be observed at daily doses as low as 5 mg[13].

Both daily administration of paroxetine at 10, 20 and 40 mg/day and episodic administration at 20 mg 3 to 4 hours prior to intercourse (see Table 1) have been shown to increase ejaculatory latency[14, 15, 16]. Due to the limited number of patients evaluated in these trials, the benefit of

increasing the dose to 40 mg/day has not been established. The majority of evidence shows effectiveness with 20 mg daily dosing, thus supporting a general suggestion that this dose of paroxetine provides the greatest benefit in remediating PE.

Sertraline, either given in daily doses of 25, 50, 100 or 200 mg or situationally in doses of 50 mg at 5 p.m. (4 to 8 hours before intercourse) (see Table 1), has been shown to increase ejaculatory latency[17]. Higher doses may increase efficacy, but logic suggests that higher doses may be associated with increased frequency of ED and decreased libido. Studies to date, though, have been too small to substantiate this conclusion about dose-related side effects.

Clomipramine, a tricyclic antidepressant with SRI effects, has improved ejaculatory latency and other measures of PE when prescribed at doses of 25 and 50 mg/day or 25 mg 4 to 24 hours prior to intercourse (see Table 1). Adverse event rates and the beneficial effects of clomipramine appear to be dose-related[18].

Adverse Effects

Although the adverse effects of the SRIs have been well described in the management of clinical depression, the following facts should be considered when weighing the risks of prescribing these agents for the patient with PE:

- First, men being treated for PE often are different from those being treated for depression, and the adverse effects of these medications have not been well assessed in settings other than depression. However, from evidence gathered to date, it appears that the adverse event profiles of the SRIs reported in the treatment of PE are

similar to those reported in patients being treated for depression. The type and rate of occurrence of side effects appear to be acceptable to most patients and typically include nausea, dry mouth, drowsiness, and reduced libido (see Appendices 1 and 2). Isolated cases of more serious complications, such as mania[19] and withdrawal symptoms, and potential drug interactions also have been associated with the use of SRIs. Pharmacodynamic drug interactions resulting in a "serotonergic syndrome" characterized in mild cases by headache, nausea, sweating, and dizziness and in severe cases by hyperthermia, rigidity, delirium, and coma have been reported rarely with concomitant use of monoamine oxidase inhibitors, lithium, sumatriptan and tryptophan. Pharmacokinetic interactions resulting in alterations in drug blood levels have been reported with the concomitant administration of agents that, like the SRIs, also are metabolized by the cytochrome P450 isoenzyme system or are bound to plasma proteins. Clinically significant pharmacokinetic interactions may rarely occur with the use of anticonvulsants, benzodiazepines, cimetidine, tricyclic antidepressants, antipsychotic agents, tolbutamide, antiarrhythmics, and warfarin especially in the elderly patient.

- Second, doses that are effective in the treatment of PE usually are lower than those recommended in the treatment of depression, suggesting that the frequency and severity of adverse events also could be less.
- Third, because two drug administration regimens, continuous daily dosing and situational dosing, are employed in the treatment of PE, adverse event profiles may differ among patients depending on the regimen prescribed.

The experience with SRIs, as reflected in the evidence tables, and the familiarity of Panel members to date with these medications in this clinical setting suggest that the level of adverse effects is acceptable for the benefit derived in the patient with PE.

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Topical Anesthetic Agents

Topical anesthetic agents may be applied to the penis prior to intercourse to delay ejaculation. After topical application, these agents have been used either with or without a condom. The condom may be removed prior to sexual intercourse and the penis washed clean of any residual active compound. Lidocaine/prilocaine cream (2.5 g) applied for 20 to 30 minutes prior to intercourse (see Table 1) has been shown to increase latency time. No significant side effects have been noted. Prolonged application of topical anesthetic (30 to 45 minutes) has been reported to result in loss of erection due to numbness of the penis in a significant percentage of men[20]. The reduction of penile sensation may limit the acceptability of this method of treatment. Diffusion of residual topical anesthetic on the penis into the vaginal wall also may result in numbness in the partner[21]. Topical anesthetics are contraindicated in patients who are either allergic themselves or have partners who are allergic to any component of the product.

Other Pharmacologic Therapies

Other pharmacologic therapies have been described in the treatment of PE in patients without ED. Intracorporal injection of a vasoactive agent, such as alprostadil, and the administration of sildenafil citrate, therapies effective in the management of ED, have been found to increase latency in patients with PE in a few small studies[22, 23]. A recent study of 80 men without concomitant ED found that the administration of a combination of sildenafil citrate and

paroxetine on a situational basis enhanced the efficacy of paroxetine alone, although there was an increase in the frequency of the side effects of headache and flushing[24]. Underlying these interventions is the hypothesis that pharmacologic maintenance of a rigid erection reduces the patient's need to rush to orgasm.

Because ejaculation involves the sympathetic nervous system, adrenergic blockade has been proposed as a treatment for delaying or inhibiting ejaculation. One clinical trial did show modest efficacy with alfuzosin and terazosin[25]. Phenoxybenzamine and propranolol also have been studied, but the Panel did not believe the evidence was sufficient to support a recommendation for their use[26, 27, 28].

V. Future Research

Deficiencies and inconsistencies in the design of and lack of reporting standards for clinical studies on PE have hindered attempts to identify best practices. Future research efforts using well-planned and well-executed randomized, controlled trials are needed to:

- Determine ejaculation latency time in the general population;
- Develop a consensus on the definition of PE;
- Develop standardized, validated instruments to measure outcomes (i.e., patient/partner satisfaction and bother, ejaculatory latency);
- Determine more precisely the efficacy and risks of drug therapies;
- Determine ideal dosing regimens for SRIs (i.e., daily versus situational dosing regimens and whether loading is necessary prior to situational dosing);
- Determine the optimal treatment duration and how or whether to discontinue therapy;

- Determine the long-term acceptability of therapeutic agents to patients;
- Determine the efficacy of combining pharmacologic and behavioral approaches to therapy; and
- Identify the age-specific prevalence of PE.

Other authors[29, 30] have made recommendations for reporting results in this field that should be considered by investigators studying PE.

VI. Conclusions

A common male sexual disorder, PE traditionally has been treated with psychotherapy or behavioral therapy. This guideline is the first to address the pharmacologic treatment of PE. Although not approved by the FDA for this indication, oral antidepressants and topical anesthetic agents have been shown to delay ejaculation in men with PE and have minimal side effects when used for the treatment of PE. Treatment with oral antidepressants should be started at the lowest possible dose that is compatible with a reasonable chance of success. The choice of additional therapy is based on the patient and partner reports of efficacy, side effects, and acceptance of the therapy as well as on a regular review of alternative approaches. Support and education of the patient and, when possible, the partner are an integral part of PE therapy.

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Pharmacologic Treatment of Premature Ejaculation (PE) Appendices

Appendix 1

Evidence Tables: Pharmacologic Treatment of Premature Ejaculation

1-A Fluoxetine

1-B Paroxetine

1-C Sertraline

1-D Clomipramine

1-E Topical Anesthetics

1-F Adrenergic Blockers

1-G Miscellaneous Treatments

Appendix 2

Summary Tables: Adverse Event Rates by Pharmacologic Treatment

Appendix 3

Summary Tables: Effects of Pharmacologic Treatment on Latency

Appendix 4

Articles Selected for Review: Sorted by Author

Appendix 5

Articles Selected for Review: Sorted by ProCite Reference Number

Pharmacologic Treatment of Premature Ejaculation (PE)

Appendix 1-A. Evidence Tables: Fluoxetine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Atan, 2000 (795257) Controlled Trial Turkey N=43	n=26: age 27 (range, 21-36) With RE and without ED, substance abuse, infections, diabetes, thyroid disease, hypotension or loss of libido. Patients had normal psychiatric consultations.	Fluoxetine 20 mg/day for 1 week followed by 40 mg/day for 7 weeks	Cured: 8 (30.8%) Improved: 11 (42.3%) Failure: 7 (26.9%) Side effects: Nausea 3 Headache 1 Insomnia 2 Total pts with side effects: 6	There is no indication of randomization in the article.
	n=17: age 31 (range,19-48) With PE and without ED, substance abuse, infections, diabetes, thyroid disease, hypo tension or loss of libido. Patients had normal psychiatric consultations.	Fluoxetine 20 mg/day and local application of lidocaine ointment to the glans 20 min. prior to intercourse.	Cured: 9 (52.9%) Improved: 5 (29.4%) Failure: 3 (17.6%) Side effects: Nausea 1 Headache 4 Insomnia 0 Total pts with side effects: 5	
Haensel, 1998 (900017) Crossover RCT Netherlands N=40	n=9: age 41.9±4.6 (range, 26-64) Patients with premature ejaculation BL: 73±22 sec	Treatments included placebo or fluoxetine (5 mg/day for two weeks followed by 10mg/day for two weeks). All patients had both treatments in a random order. Each treatment lasted 4 weeks with a 4-week washout in between.	Latency increase with fluoxetine 190% (CI: 80-450%; p=.13) but combined groups 1 and 3 reached sig. (p=.007) 6/7 pts increased latency with fluoxetine 1/7 decreased latency	All patients received both therapies. Groups were significantly different (p<.01) on age, Zung depression scale, erectile function, and pretreatment latency. Treatment dose is much less than other fluoxetine studies. Article also has data on response erotic stimuli with and without vibratory stimulus.
	n=7: age 54.6±3.7(range, 40-70) Patients with erectile dysfunction BL: 360±91 sec		4/6 pts. decreased latency with fluoxetine, 1/6 increased and 1/6 inability to ejaculate	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-A. Evidence Tables: Fluoxetine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Haensel, cont.	n=9: age 51.2±2.7(range, 41-65) Patients with premature ejaculation and erectile dysfunction BL: 89±22 sec		Significant increase in latency with fluoxetine over placebo (p=.03) 6/8 increased latency with fluoxetine 1/8 decreased 1/8 unchanged	Side effects of fluoxetine: Dry mouth 3 Incr. Libido 2 Loose stools 2 Slight palpitations 1 Penile pain 1 Dizziness 1 Altered sleep 2 Sweating 1 Side effects of placebo: Increased libido 1 Decreased libido 1 Burning on micturation 1 Change in stools 1
	n=15: age 41.3±2.0 Normal controls BL: 535±116 sec		7/15 increased latency with fluoxetine, 8/15 decreased latency	
Kara, 1996 (12110) RCT Turkey N=40	All patients married age 15-50, ½ of whom had latencies (average of 3) < 2 min n=7 (Initially n=9, but 2 discontinued due to side effects)	Fluoxetine 20 mg/day for 1 week Fluoxetine 40 mg/day thereafter	Initial latency: 25±12.6 sec 4 wk latency: 180±99.5 sec Side effects: Headache (discontinued) 1 Nausea 2 Insomnia (discontinued) 1	Article gives patient ages, spouse ages, and length of marriage by groups. Change in latency status significant for fluoxetine but not for controls.
	All patients married age 15-50, ½ of whom had latencies (average of 3) < 2 min. n =7 (Initially n=8, but 1 dropped from efficacy analysis for not following directions)	Placebo 1 tablet/day for 1 week 2 tablets/day thereafter	Initial latency: 30±8.6 sec 4 wk latency: 60±46.9	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-A. Evidence Tables: Fluoxetine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Kim, 1998 (12047) Crossover RCT Korea N=53	n=37: age 44 (range, 30-60) 53 heterosexual patients enrolled; 37 completed the study. Reasons for withdrawal: loss to follow-up (5), no efficacy (fluoxetine 3, sertraline 1, placebo 1) and no efficacy plus side effects (clomipramine 1). One patient was excluded from analysis because of delayed (>30 min) ejaculation with sertraline or clomipramine.	Baseline – no treatment	Latency: 46±41 sec Patient Satisfaction: Satisfied 0% Moderate 0% Dissatisfied 100% Partner Satisfaction: Satisfied 0% Moderate 22.2% Dissatisfied 77.8%	Article gives patient ages, spouse ages, and length of marriage by groups. Change in latency status significant for fluoxetine but not for controls. All patients received each therapy and placebo for 4 weeks with a 4-week washout between therapies. Order of administration was randomized.
		Placebo 1 capsule/day first week and 2/day thereafter	Latency: 2.27±3.78 min Patient Satisfaction: Satisfied 19.4% Moderate 27.8% Dissatisfied 52.8% Partner Satisfaction: Satisfied 11.1% Moderate 36.1% Dissatisfied 52.8% Side effects: Drowsiness 2 Dry mouth 0 Reduced Potency 3 Nausea 1 Vomiting 0 Other 3 Total pts with side effects: 7	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-A. Evidence Tables: Fluoxetine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Kim, cont.		Clomipramine 25 mg/day for first week, 50 mg/day thereafter	Latency: 5.75±6.68 min Patient Satisfaction: Satisfied 25.0% Moderate 38.9% Dissatisfied 36.1% Partner Satisfaction: Satisfied 19.4% Moderate 38.9% Dissatisfied 41.7% Side effects: Drowsiness 6 Dry mouth 2 Reduced Potency 3 Nausea 4 Vomiting 0 Other 3 Total pts with side effects: 13	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-A. Evidence Tables: Fluoxetine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Kim, cont.		Fluoxetine 20 mg/day for first week, 40 mg/day thereafter	Latency: 2.30±2.08 min Patient Satisfaction: Satisfied 25.0% Moderate 38.9% Dissatisfied 36.1% Partner Satisfaction: Satisfied 19.4% Moderate 38.9% Dissatisfied 41.7% Side effects: Drowsiness 6 Dry mouth 2 Reduced Potency 3 Nausea 4 Vomiting 0 Other 3 Total pts with side effects: 13	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-A. Evidence Tables: Fluoxetine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Kim, cont.		Sertraline 50 mg/day for first week, 100 mg/day thereafter	Latency: 4.27±5.69 min Patient Satisfaction: Satisfied 41.7% Moderate 36.1% Dissatisfied 22.2% Partner Satisfaction: Satisfied 30.6% Moderate 38.9% Dissatisfied 30.6% Side effects: Drowsiness 7 Dry mouth 4 Reduced Potency 3 Nausea 2 Vomitting 0 Other 0 Total pts with side effects: 12	
Lee, 1996 (12112) CS Korea N=11	11 pts with stable hetero-sexual relationships meeting DSM III-R requirements for PE. 14 pts originally recruited with 3 drop outs not analyzed (2 from car wreck, 1 for non-compliance). Mean age 39.6±10.4 (range, 24-62). Duration of illness 12.9±7.8 (3-24)	Baseline – no treatment	Median latency: Pre treatment .91±.050 min YSFI II Scale: Sexual des. 40±24 Erect. Qual. 29±33 Anx. For RE 70±27 Ejac. Satis. 45±29 Partn. Ejac. Sat. 25±18 Overall Sex sat. 46±17 Partn. Ovr. Sat. 24±17	It appears that patient is assessing partner satisfaction on this scale

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-A. Evidence Tables: Fluoxetine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Lee, cont.		2 wk washout followed by fluoxetine 20mg/day for 1-2 weeks titrated to 60mg/day based on tolerance. 8 week total trial	Median latency: Post-treatment 9.64±7.0 min YSFI II Scale: Sexual des. 55±21* Erect. Qual. 35±30 Anx. For RE 52±24* Ejac. Satis. 65±18 Partn.Ejac.Sat. 54±17* Overall sex sat. 64±19 Partn. Ovr. Sat. 53±13* *P<.05 Side effects: Nausea and other GI 4 Extremity tingling 1 Dizziness 1 All side effects disappeared in 2-3 weeks after treatment ceased.	
Murat Basar, 1999 (12003) RCT Turkey N=57	n=26: age 27±1.1 (range, 21-36) Exclusion criteria: loss of libido; erection failure; alcohol or substance abuse; mental retardation; thyroid disease orthostatic hypotension; previous use of drugs for PE; recent myocardial infarction, uncontrolled diabetes, urogenic infections	Fluoxetine 20 mg/day for 1 week, 40 mg/day later	Cured 8 (30.8%) Improved 11 (42.3%) Failure 7 (29.6%) Side effects: Nausea 3 Headache 1 Insomnia 2	Cured and improved not defined. Authors concluded no significant difference between the two treatments.

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-A. Evidence Tables: Fluoxetine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Murat Basar, cont.	n=31: age 34±1.7 (range, 21-45) Same exclusion criteria as above.	Sertraline 50 mg/day	Cured 12 (38.78%) Improved 10 (32.3%) Failure 9 (29.0%) Side effects: Nausea 2 Mouth dryness 6	
Raju, 1997 (500001) Letter-CS India N=44	N=44; age 31±6; without clinically detectable organic etiology, and ejaculation prior to intromission or within 10-20 strokes, usually less than 1 min		Total GRISS score Before 10.7±4 After 3.2±2 Side effects included glossitis, vague headache, and lack of concentration	The scale used is not clear since the article describes a 0-5 point scale, but reports larger values. No numbers given for complications
Waldinger, 1998 (12044a) RCT Netherlands N=51	After prescreening exclusions, 60 patients enrolled; 51 completed the study; 6 withdrew due to adverse events and 3 for lack of efficacy			This article describes two RCTs, the first of which is a 5-arm study. 6-week data are recorded here; graphs of intermediate results are presented in the paper.
	n=10: age 38±7, partner age 36±7 BL: 21±12 sec	Fluoxetine 20 mg/day	Latency at 6 weeks: 211±251 sec Absolute change: 189±244 sec	
	n=10: age 44±10, partner age 43±10 BL: 15±17 sec	Fluvoxamine 100 mg/day	Latency at 6 weeks: 55±70 sec Absolute change: 42±57 sec	
	n=11: age 41±8, partner age 39±8 BL: 16±10 sec	Paroxetine 20 mg/day	Latency at 6 weeks: 476±1146 sec Absolute change: 458±1142 sec	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-A. Evidence Tables: Fluoxetine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Waldinger, cont.	n=11: age 40±9, partner age 38±10 BL: 21±12 sec	Sertraline 50 mg/day	Latency at 6 weeks: 117±87 sec Absolute change: 96±84 sec	
	n=9: age 45±4, partner age 41±5 BL: 19±15 sec	Placebo	Latency at 6 weeks: 29±25 sec Absolute change: 10±18 sec	
Yilmaz, 1999 (12032) RCT Turkey N=40	n=20: age 37.3 (range, 24-58)	Fluoxetine 20 mg/day for 1 month	Latency: Pre 1.2±1.0 min Post 6.6±7.7 min	40 of 48 patients enrolled. Latency was average reported by patient and not verified. Study also reports data on penile sensory thresholds.
	n=20: age 36.5 (range, 22-56)	Placebo	Latency: Pre 1.1±1.3 min Post 4.8±1.0 min	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-B. Evidence Tables: Paroxetine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Abdel-Hamid, 2001 (700014) Crossover RCT Egypt N=51	n=31: age 34.09±4.29 (range, 27-42) Heterosexual, married at least 1 year, with primary PE and willing to have intercourse twice a week. Patients did not have history of psychiatric illness, current physical illness, previous surgery or drug known to affect sexual function, current substance abuse, or ED. Patients each received each of 5 treatments for 4 weeks separated by 2-week washout periods. The treatments were ordered randomly in a double blind manner. BL (med.): 1(0.5-1.5) min Baseline anxiety (med.): 12 (5-25)	Clomipramine 25 mg, 3-5 hrs before planned coitus and not more than twice/week	Results at 4 weeks: Median latency 4 (1-8) min Median anxiety score 11 (4-22) min Median sexual satisfaction score 11 (0-25) min 2 patients dropped out for lack of efficacy and 1 for side effects and lack of efficacy. Side effects: Dry mouth 3 Anorexia 0 Nausea 1 Headache 0 Flushing 0 Drowsiness 1 Sleepiness 2 Nasal congestion 0 Yawning 0 Total patients with side effects: 7/28	Study also included a normal control group of 20 patients who were not treated but supplied anxiety scores of 3.7±2.7 (range 1-9) vs. 12.7±5.8 (range 5-25) for the PE subjects. Study contains blinding problems because the Masters and Johnson pause squeeze technique cannot be blinded.

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-B. Evidence Tables: Paroxetine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Abdel-Hamid, cont.		Paroxetine 20 mg, 3-5 hrs before planned coitus and not more than twice/week	Results at 4 weeks: Median latency 4(2-10) min Median anxiety score 9(5-23) min Median sexual satisfaction score 12(0-29) min 2 patients dropped out for lack of efficacy. Side effects: Dry mouth 2 Anorexia 0 Nausea 1 Headache 0 Flushing 0 Drowsiness 0 Sleepiness 0 Nasal congestion 0 Yawning 2 Total patients with side effects: 5/29	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-B. Evidence Tables: Paroxetine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Abdel-Hamid, cont.		Sertraline 50 mg, 3-5 hrs before planned coitus and not more than twice/week	Results at 4 weeks: Median latency 3(1-10) min Median anxiety score 11(5-22) min Median sexual satisfaction score 10(0-31) min 2 patients dropped out for lack of efficacy. Side effects: Dry mouth 0 Anorexia 1 Nausea 1 Headache 0 Flushing 0 Drowsiness 1 Sleepiness 0 Nasal congestion 0 Yawning 0 Total patients with side effects: 3/29	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-B. Evidence Tables: Paroxetine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Abdel-Hamid, cont.		Sildenafil 50 mg, 3-5 hrs before planned coitus and not more than twice/week	Results at 4 weeks: Median latency 15(5-30) min Median anxiety score 8(4-15) min Median sexual satisfaction score 30(17-34) min 2 patients dropped out for side effects. Side effects: Dry mouth 0 Anorexia 0 Nausea 0 Headache 2 Flushing 2 Drowsiness 0 Sleepiness 0 Nasal congestion 1 Yawning 0 Total patients with side effects: 5/28	
		Masters and Johnson pause squeeze technique	Results at 4 weeks: Median latency 3(1-7) min Median anxiety score 12(5-21) min Median sexual satisfaction score 6(0-22) min 2 patients dropped out for lack of efficacy.	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-B. Evidence Tables: Paroxetine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Ludovico, 1996 (12118) CS Italy N=32	n=32: mean age 28 BL: < 1 min (14 ejaculated before penetration)	Paroxetine 20 mg/day for two months.	Latency: 15-20 min Side effects: Severe sensory confusion 1 (withdrew) Sleepiness 14 Mild sensory confusion 21 Side effects disappeared after 15-20 days. PE recurred in 28 patients 2-3 weeks after cessation of therapy.	This is a prospective clinical series. No detailed data given.
McMahon, 1999 (12005) CS Australia N=94	n=94 Heterosexual patients in stable relationships with no other sexual disorders. BL: < 1 min Group A: n=61: age 40 (range, 22-61) Mean latency 0.4 min, 37 with lifelong PE, 6 severe (never had intravaginal ejaculation) Group B: n=33: age 37 (range, 18-56) Mean latency 0.4 min, 18 with lifelong PE, 4 severe	Group A, Phase 1: Paroxetine 20 mg/day for 4 weeks.	Latency 4.5 min Side effects: Anejaculation 5 (1 withdrawal) Drowsiness & anorexia 1 Minor GI upset 2 Reduced libido 3 Inhibited orgasm 3 Ejaculation restored for anejaculation patients with lower dose.	Also data on frequency of intercourse.

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-B. Evidence Tables: Paroxetine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
McMahon, cont.		Group A, Phase 2: Paroxetine 20 mg single dose 3-4 hrs before intercourse (Phase II for Group A patients with success in Phase I above) for 4 weeks	Latency 3.9 min No side effects	
		Group B: Paroxetine 20 mg single dose 3-4 hrs before intercourse for 4 weeks	Latency 1.5 min No side effects	
McMahon, 1999 (12020a) Crossover RCT Australia N=26	n=26: mean age 39.5 19 patients with primary PE, 3 never ejaculated vaginally. Average latency = 0.3 min The two groups each had 13 patients.	Paroxetine 20 mg, 3-4 hrs before intercourse for 4 weeks. 3-week washout followed by placebo 3-4 hrs before intercourse for 4 weeks.	Pretreatment latency 0.3min Paroxetine latency at 4 weeks 3.2 min Placebo latency at 4 weeks 0.45 min No side effects with either pill.	First of two studies in one article. Study is single blind only. Also data on intercourse frequency.
		Placebo, 3-4 hrs before intercourse for 4 weeks. 3-week washout followed by paroxetine 20 mg 3-4 hrs before intercourse for 4 weeks.	Pretreatment latency 0.3 min Placebo latency at 4 weeks 0.6 min Paroxetine latency at 4 weeks 3.5 min No side effects with either pill.	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-B. Evidence Tables: Paroxetine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
McMahon, 1999 (12020b) Crossover RCT Australia N=42	n=42: mean age 40.5 32 patients with primary PE, 10 never ejaculated vaginally. Average latency 0.5 min The two groups each had 21 patients.	Paroxetine 10 mg/day for 3 weeks, followed by paroxetine 20 mg 3-4 hrs before intercourse for 4 weeks, followed by 3-week washout, then placebo daily for 3 weeks followed by placebo 3-4 hrs before intercourse for 4 weeks.	BL: 0.5 min Results at the end of each section: Paroxetine daily latency 4.3 min Paroxetine PRN latency 5.8 min Placebo daily latency 0.9 min Placebo PRN latency 0.6 min	Second of two studies in one article. Study is single blind only. Side effects were not listed by group and were as follows: Paroxetine Daily: Anorexia 1 Anejaculation 3 GI upset 3 Reduced libido 2 Placebo Daily: Erectile dysfunction 2 Placebo PRN: Headache 1
		Placebo daily for 3 weeks, then placebo 3-4 hrs before intercourse for 4 weeks. 3-week washout followed by paroxetine 10 mg/day for 3 weeks followed by paroxetine 20 mg 3-4 hrs before intercourse for 4 weeks	BL: 0.5 min Results at the end of each section: Paroxetine daily latency 3.3 min Paroxetine PRN latency 6.1 min Placebo daily latency 0.8 min Placebo PRN latency 1.1 min	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-B. Evidence Tables: Paroxetine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Salonia, 2002 (500005) CT Italy N=80	N=40; mean age 34 (range, 19-46); primary PE 29, secondary PE 11, never ejaculated vaginally 8	10 mg/day paroxetine for 21 days, followed by 20 mg 3-4 hrs before intercourse for 6 months	Latency: Baseline .33±.04 3 mo 3.7±..10 6 mo 4.2±.03 Side effects: Anejaculation 1/40 GI upset/nausea 5/40 Headache 4/40 Decr. Libido 2/40 Flushing 0/40	Analysis of IIEF data showed significant differences at 6 months only in intercourse satisfaction and overall satisfaction.
	N=40; mean age 36 (range 21-47); primary PE 33, secondary PE 7, never ejaculated vaginally 12	10 mg/day paroxetine for 21 days, followed by 20 mg 3-4 hrs plus 50 mg sildenafil before intercourse for 6 months	Latency: Baseline .35±.05 3 mo 4.5±..07 6 mo 5.3±.02 Side effects: Anejaculation 1/40 GI upset/nausea 6/40 Headache 8/40 Decr. Libido 1/40 Flushing 6/40	
Waldinger, 2001 (795220) RCT Netherlands N=30	n=15: age 38±11 Married or in a relationship for 15±10 years BL: 22±15 sec	Paroxetine 20 mg/day for 6 weeks	Geometric mean latency by week (sec): 0 17.58 1 34.17 2 57.27 3 116.00 4 141.16 5 170.50 6 152.28	Randomized blinded controlled trial of a superselective SSRI vs. paroxetine. Also data on intercourse frequency, which rose with paroxetine and fell with citalopram.

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-B. Evidence Tables: Paroxetine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Waldinger, cont.	n=15: age 39±8 Married or in a relationship for 24±10 years BL: 24±10 sec	Citalopram 20 mg/day for 6 weeks	Geometric mean latency by week (sec): 0 20.68 1 33.80 2 43.30 3 40.44 4 33.07 5 44.21 6 42.82	
Waldinger, 2001 (795222) RCT Netherlands N=48	n=12: age 38±10 Married for 15±12 years with primary PE	Placebo, morning and evening	Geometric mean latency by week (sec): 0 15.1 1 20.8 2 19.3 3 19.1 4 23.6 5 18.8 6 18.1	All patients had a 1-month baseline and were prohibited from using condoms or topical anesthetics through the study. Study was randomized and blinded. Patients used stopwatches to measure latency.
	n=12: age 40±7 Married for 17±7 years with primary PE	Paroxetine 20 mg/day, morning and evening	Geometric mean latency by week (sec): 0 17.1 1 36.7 2 71.1 3 119.2 4 88.3 5 146.0 6 107.9	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-B. Evidence Tables: Paroxetine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Waldinger, cont.	n=12: age 41±9 Married for 15±9 years with primary PE	Sertraline 50 mg/day, morning and evening	Geometric mean latency by week (sec): 0 13.9 1 25.2 2 38.6 3 33.8 4 42.7 5 58.1 6 50.3	
	n=12: age 35±6 Married or in a relationship for 12±8 years with primary PE	Nefazodone 400 mg/day, morning and evening	Geometric mean latency by week (sec): 0 16.8 1 19.1 2 14.2 3 25.6 4 28.4 5 15.6 6 17.9	
Waldinger, 1998 (12044a) RCT Netherlands N=51	After prescreening exclusions, 60 patients enrolled; 51 completed the study; 6 withdrew due to adverse events and 3 for lack of efficacy			This article describes two RCTs, the first of which is a 5-arm study. 6-week data are recorded here; graphs of intermediate results are presented in the paper.
	n=10: age 38±7, partner age 36±7 BL: 21±12 sec	Fluoxetine 20 mg/day	Latency at 6 weeks: 211±251 sec Absolute change: 189±244 sec	
	n=10: age 44±10, partner age 43±10 BL: 15±17 sec	Fluvoxamine 100 mg/day	Latency at 6 weeks: 55±70 sec Absolute change: 42±57 sec	
	n=11: age 41±8, partner age 39±8 BL: 16±10 sec	Paroxetine 20 mg/day	Latency at 6 weeks: 476±1146 sec Absolute change: 458±1142 sec	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-B. Evidence Tables: Paroxetine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Waldinger, cont.	n=11: age 40±9, partner age 38±10 BL: 21±12 sec	Sertraline 50 mg/day	Latency at 6 weeks: 117±87 sec Absolute change: 96±84 sec	
	n=9: age 45±4, partner age 41±5 BL: 19±15 sec	Placebo	Latency at 6 weeks: 29±25 sec Absolute change: 10±18 sec	
Waldinger, 1998 (12044b) RCT Netherlands N=32	n=24 with latency ≤ 1min: age 46±6 (range, 31-45) BL: 18±13 sec (range, 1-46)	12 randomized to paroxetine 20 mg/day and 12 to placebo 1 paroxetine and 3 placebo patients dropped out	Paroxetine treated latency increased 580% (CI 314-1025%). No statistically significant increase in placebo group.	Study notes paroxetine had no clinically significant effects on libido or erectile function and no statistically significant differences between paroxetine and placebo on other side effects (unspecified).
	n=8 with latency > 1 min: age 47±3 (range 43-53) BL: 82±27 sec (range, 57-130)	5 patients randomized to paroxetine 20 mg/day and 3 to placebo 1 placebo patient dropped out	Paroxetine treated latency increased 596% (CI 225-1388%). No significant increase in placebo group.	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-B. Evidence Tables: Paroxetine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Waldinger, 1997 (12088) RCT Netherlands N=34	n=17: age 44 (range, 23-57) All patients in stable heterosexual relationship with primary PE and no ED, substance or alcohol abuse, mental disorders, physical illnesses, use of medications, or history of sexual abuse of the patient or partner. SCL-90 depression and fear scores similar to normal population.	Paroxetine 20 mg/day for 8 weeks. 2 capsules/day (1 placebo).	BL: 13 3 wk latency: 300 8 wk latency: 300 2 patients discontinued for anejaculation and frequent yawning. 1 patient discontinued 2nd pill (placebo) for yawning, perspiration, and fatigue. At 8 weeks, 6 patients still had yawning, perspiration, dry mouth, fatigue and/or nausea. One patient had slight reduction in erectile function at 8 weeks.	Study also contains partner data and estimates of latency, which matched the patients' estimates. Latency estimates are medians not mean. Patients who dropped were not included in the latency results, but authors said including them did not change results.
	n=17: age 43 (range 32-55) All patients in stable heterosexual relationship with primary PE and no ED, substance or alcohol abuse, mental disorders, physical illnesses, use of medications, or history of sexual abuse of the patient or partner. SCL-90 depression and fear scores similar to normal population.	Paroxetine 40 mg/day for 8 weeks. 2 capsules/day both paroxetine.	BL: 10 3 wk latency: 240 8 wk latency: 540 4 patients discontinued 2nd capsule for anejaculation, yawning, fatigue and perspiration. One also experienced reduced libido and dry mouth. Reducing dose reduced symptoms. At 8 weeks 7 patients still had yawning, perspiration, dry mouth, fatigue and/or nausea.	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-B. Evidence Tables: Paroxetine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Waldinger, 1994 (12172) RCT Netherlands N=17	n=8: age 41 (range, 27-48) 7 with primary PE and 1 with secondary. 2 patients dropped out. One in the first week and one in the third because of latencies > 30 min Reducing dose to 20 mg yielded latency of 7 min, but patient was excluded from analysis.	Paroxetine 20 mg/day first week and 40 mg/day for 5 more weeks.	Latency – patient assessment: Initial 30 (3-4) sec 3 wks 7.5 (3-20) min 6 wks 10 (5-20) min Latency – partner assessment: Initial 10 (3-30) sec 3 wks 8.5 (2-17.5) min 6 wks 10.0 (5-17.5) min	Data on number of thrusts are also available in the study. Study stated there were no statistically significant differences in side effects at any time point.
	n=9: age 38 (range, 30-47) 7 with primary PE and 2 with secondary. One patient dropped out in the first week.	Placebo, 1 capsule/day for first week and 2 per day for 5 more weeks.	Latency – patient assessment: Initial 15 (5-90) sec 3 wks 20 (5-120) sec 6 wks 15 (5-120) sec Latency – partner assessment: Initial 30 (5-90) sec 3 wks 23 (5-60) sec 6 wks 33 (10-90) sec	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-C. Evidence Tables: Sertraline treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Abdel-Hamid, 2001 (700014) Crossover RCT Egypt N=51	n=31: age 34.09±4.29 (range, 27-42) Heterosexual, married at least 1 year, with primary PE and willing to have intercourse twice a week. Patients did not have history of psychiatric illness, current physical illness, previous surgery or drug known to affect sexual function, current substance abuse, or ED. Patients each received each of 5 treatments for 4 weeks separated by 2-week washout periods. The treatments were ordered randomly in a double blind manner. BL (med.): 1 (0.5-1.5) min Baseline anxiety (med.): 12 (5-25) min	Clomipramine 25 mg, 3-5 hrs before planned coitus and not more than twice/week	Results at 4 weeks: Median latency 4 (1-8) min Median anxiety score 11 (4-22) min Median sexual satisfaction score 11 (0-25) min 2 patients dropped out for lack of efficacy and 1 for side effects and lack of efficacy. Side effects: Dry mouth 3 Anorexia 0 Nausea 1 Headache 0 Flushing 0 Drowsiness 1 Sleepiness 2 Nasal congestion 0 Yawning 0 Total patients with side effects: 7/28	Study also included a normal control group of 20 patients who were not treated but supplied anxiety scores of 3.7±2.7(range 1-9) vs. 12.7±5.8 (range 5-25) for the PE subjects. Study contains blinding problems because the Masters and Johnson pause squeeze technique cannot be blinded.

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-C. Evidence Tables: Sertraline treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Abdel-Hamid, cont.		Paroxetine 20 mg, 3-5 hrs before planned coitus and not more than twice/week	Results at 4 weeks: Median latency 4 (2-10) min Median anxiety score 9 (5-23) min Median sexual satisfaction score 12 (0-29) min 2 patients dropped out for lack of efficacy. Side effects: Dry mouth 2 Anorexia 0 Nausea 1 Headache 0 Flushing 0 Drowsiness 0 Sleepiness 0 Nasal congestion 0 Yawning 2 Total patients with side effects: 5/29	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-C. Evidence Tables: Sertraline treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Abdel-Hamid, cont.		Sertraline 50 mg, 3-5 hrs before planned coitus and not more than twice/week	Results at 4 weeks: Median latency 3 (1-10) min Median anxiety score 11 (5-22) min Median sexual satisfaction score 10 (0-31) min 2 patients dropped out for lack of efficacy. Side effects: Dry mouth 0 Anorexia 1 Nausea 1 Headache 0 Flushing 0 Drowsiness 1 Sleepiness 0 Nasal congestion 0 Yawning 0 Total patients with side effects: 3/29	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-C. Evidence Tables: Sertraline treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Abdel-Hamid, cont.		Sildenafil 50 mg, 3-5 hrs before planned coitus and not more than twice/week	Results at 4 weeks: Median latency 15 (5-30) Median anxiety score 8 (4-15) Median sexual satisfaction score 30 (17-34) 2 patients dropped out for side effects. Side effects: Dry mouth 0 Anorexia 0 Nausea 0 Headache 2 Flushing 2 Drowsiness 0 Sleepiness 0 Nasal congestion 1 Yawning 0 Total patients with side effects: 5/28	
		Masters and Johnson pause squeeze technique	Results at 4 weeks: Median latency 3 (1-7) Median anxiety score 12 (5-21) Median sexual satisfaction score 6 (0-22) 2 patients dropped out for lack of efficacy.	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Pharmacologic Treatment of Premature Ejaculation (PE)

Appendix 1-C. Evidence Tables: Sertraline treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Balbay, 1997 (12063) CS N=22	n=22: age 26-53 With undefined PE. 4 patients lost to follow-up.	Oral sertraline 50 mg/day for 2 weeks.	Efficacy: Completely satisfied 14/16 Not completely satisfied 2/16 Side effects: Patients reported 5/18 2 patients discontinued due to unspecified side effects	Study also has data on patient condition based on whether the patient was satisfied. Minimal data are available – side effects not defined, efficacy measure soft and patient condition not well defined.
Basar, 1999 (12003) RCT Turkey N=57	n=26: age 27±1.1 (range, 21-36) Exclusion criteria: loss of libido; erection failure; alcohol or substance abuse; mental retardation; thyroid disease orthostatic hypotension; previous use of drugs for PE; recent myocardial infarction, uncontrolled diabetes, urogenic infections	Fluoxetine 20 mg/day for 1 week 40 mg/day later	Cured 8 (30.8%) Improved 11 (42.3%) Failure 7 (29.6%) Side effects: Nausea 3 Headache 1 Insomnia 2	Cured and improved not defined. Authors concluded no significant difference between the two treatments.
	n=31: age 34±1.7 (range, 21-45) Same exclusion criteria as above.	Sertraline 50 mg/day	Cured 12 (38.78%) Improved 10 (32.3%) Failure 9 (29.0%) Side effects: Nausea 2 Mouth dryness 6	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-C. Evidence Tables: Sertraline treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Biri, 1998 (12033) RCT Turkey N=37	n=37: age 31.1 (range, 21-54) Patients with latencies < 1 min during previous 6 months. No impotence.	Sertraline 50 mg/day for 4 weeks, 22 patients	Latency: Initial 40.93±12.6 Treated 325.4±261.7 Side effects: Headache 6/22 Sleepiness 6/22 Diarrhea 3/22 Dry mouth 2/22 PE recurred in 19 patients 4 weeks after cessation of treatment.	
		Placebo for 4 weeks, 15 patients	Latency: Initial 43.53±20.2 Treated 114.4±93.7 Side effects: Headache 3/15 Sleepiness 3/15 Diarrhea 1/15 Dry mouth 0/15	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Pharmacologic Treatment of Premature Ejaculation (PE)

Appendix 1-C. Evidence Tables: Sertraline treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Chia, 2002 (500002) CS Singapore N=87	N=52; without neurological disease or depression, with primary PE. 12 age 20-30, 24 age 30-40, 14 age 40-50, 2 age 50-60.	Sertraline 50 mg 4 hours prior to intercourse for 6 months	Latency (sec) Baseline 46 6 months 247.2 Treatment failures 3/52 Sexual Satisfaction (mean of 5 pt scale) Baseline .81 6 months 2.21 Side effects Dizziness 3/52 Nausea 2/52 Dry mouth 1/52	
	N=35; without neurological disease or depression, with ED treated successfully with sildenafil. Pts with PE prior to ED excluded. 3 age 20-30, 13 age 30-40, 11 age 40-50, 8 age 50-60.		Latency (sec) Baseline 34.6 6 months 111.6 Treatment failures 7/35 Sexual Satisfaction (mean of 5 pt scale) Baseline .51 6 months 1.17 Side effects Dizziness 4/35 Nausea 3/35 Dry mouth 1/35	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-C. Evidence Tables: Sertraline treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Kim, 1999 (12013) CS Korea N=24	n=24: age 32.5 (range, 27-52) Patients with primary PE. Latency < 1 min at least 50% of time. Patients had one stable partner, were not receiving psychotropic medication, were not depressed, or did not have any other medical disease or symptoms. Reasons for withdrawal: 6 patients were excluded from efficacy analysis due to drop out (3 non-compliance, 2 unknown, 1 intercurrent illness).	Pretreatment	Latency 23±19 sec Patient satisfaction (0-5) 0.8±0.8 Partner satisfaction 1.1±0.7 Side effects not linked to dose schedule: Delayed ejaculation 1 Fatigue 2 Numbness in extremities 1 No withdrawals due to side effects.	
		Sertraline 50 mg/day for 2 weeks	Latency 5.9±4.2 min Patient satisfaction (0-5) 3.8±1.2 Partner satisfaction 3.2±1.6	
		Sertraline 50 mg at 5 pm on days when intercourse was anticipated (4-8 hrs before intercourse). Dose titrated up to 100 mg in 3rd week if needed. Total of 4 or 6 weeks (not clear).	At 2 weeks: Latency 5.1±3.8 min Patient satisfaction (0-5) 3.4±1.0 Partner satisfaction 3.1±1.4 At 4 weeks: Latency 4.5±2.7 min Pt. satisfaction (0-5) 3.2±0.7 Partner satisfaction 3.3±1.2	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
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Appendix 1-C. Evidence Tables: Sertraline treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Kim, 1998 (12047) Crossover RCT Korea N=53	n=37: age 44 (range, 30-60). 53 heterosexual patients enrolled; 37 completed the study. Reasons for withdrawal: loss to follow-up (5), no efficacy (fluoxetine 3, sertraline 1, placebo 1) and no efficacy plus side effects (clomipramine 1). One patient was excluded from analysis because of delayed (> 30 min) ejaculation with sertraline or clomipramine.	Baseline – no treatment	Latency: 46±41 sec Patient Satisfaction: Satisfied 0% Moderate 0% Dissatisfied 100% Partner Satisfaction: Satisfied 0% Moderate 22.2% Dissatisfied 77.8%	All patients received each therapy and placebo for four weeks with a 4-week washout between therapies. Order of administration was randomized.
		Placebo 1 capsule/day first week and 2/day thereafter.	Latency: 2.27±3.78 min Patient Satisfaction: Satisfied 19.4% Moderate 27.8% Dissatisfied 52.8% Partner Satisfaction: Satisfied 11.1% Moderate 36.1% Dissatisfied 52.8% Side effects: Drowsiness 2 Dry mouth 0 Reduced Potency 3 Nausea 1 Vomiting 0 Other 3 Total pts with side effects: 7	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-C. Evidence Tables: Sertraline treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Kim, cont.		Clomipramine 25 mg/day for first week, 50 mg/day thereafter	Latency: 5.75±6.68 min Patient Satisfaction: Satisfied 25.0% Moderate 38.9% Dissatisfied 36.1% Partner Satisfaction: Satisfied 19.4% Moderate 38.9% Dissatisfied 41.7% Side effects: Drowsiness 6 Dry mouth 2 Reduced Potency 3 Nausea 4 Vomiting 0 Other 3 Total pts with side effects: 13	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-C. Evidence Tables: Sertraline treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Kim, cont.		Fluoxetine 20 mg/day for first week, 40 mg/day thereafter	Latency: 2.30±2.08 min Patient Satisfaction: Satisfied 25.0% Moderate 38.9% Dissatisfied 36.1% Partner Satisfaction: Satisfied 19.4% Moderate 38.9% Dissatisfied 41.7% Side effects: Drowsiness 6 Dry mouth 2 Reduced Potency 3 Nausea 4 Vomiting 0 Other 3 Total pts with side effects: 13	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-C. Evidence Tables: Sertraline treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Kim, cont.		Sertraline 50 mg/day for first week, 100 mg/day thereafter	Latency: 4.27±5.69 min Patient Satisfaction: Satisfied 41.7% Moderate 36.1% Dissatisfied 22.2% Partner Satisfaction: Satisfied 30.6% Moderate 38.9% Dissatisfied 30.6% Side effects: Drowsiness 7 Dry mouth 4 Reduced Potency 3 Nausea 2 Vomitting 0 Other 0 Total pts with side effects: 12	
McMahon, 1998 (12057) Crossover RCT Australia N=37	n=19: age 40 Heterosexual in stable relationships without other sexual disorders or other physical or psychological ailments. BL: < 1 min	Sertraline 50 mg/day for 4 weeks, washout for 4 weeks, placebo for 4 weeks. Patients asked to not use condoms or anesthetics.	Latency: Initial 0.3 min After sertraline 3.4 min After washout 0.6 min After placebo 0.5 min Frequency of intercourse: Initial 0.6/wk After sertraline 3.3/wk After washout 1.6/wk After placebo 1.0/wk	Single blind study. Overall patient age range (19-70). In patients who had not previously achieved intra-vaginal ejaculation, 5/8 achieved it for the first time with sertraline. 29/35 who completed the study continued sertraline open label after the study. Stage withdrawal of the drug

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-C. Evidence Tables: Sertraline treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
McMahon, cont.	n=18: age 42 Heterosexual in stable relationships without other sexual disorders or other physical or psychological ailments. BL: < 1 min	Placebo for 4 weeks, washout for 4 weeks, sertraline 50 mg/day for 4 weeks. Patients asked to not use condoms or anesthetics.	Latency: Initial 0.3 min After placebo 0.5 min After washout 0.5 min After sertraline 3.0 min Frequency of intercourse: Initial 0.4/wk After placebo 0.8/wk After washout 0.5/wk After sertraline 3.1/wk	every 4 weeks allowed 20/29 to discontinue treatment after a mean of 7.3 months and maintain ejaculatory control with mean latency of 4.1 according to authors. Sertraline side effects: Anejaculation, withdrawal: 2 Drowsiness, anorexia: 1 GI upset: 2 No ED, reduced libido, or reduced orgasmic intensity. One patient had minor ED on placebo.
McMahon, 1998 (12037) CS Australia N=46	n=46: age 42 (range, 22-63) All heterosexual in stable relationships with no other sexual disorders. 36 had primary PE and 10 had secondary. 6 men had severe PE, who had never achieved vaginal ejaculation. Each patient received each dose for 3 weeks followed by a 3week washout period. The doses were given in increasing order. BL: 1.0 min (range, 0 to 5 min).	Setraline 25 mg/day for 3 weeks.	Latency: 7.6 (0-20) min Anejaculation: 0 Intravaginal ejaculation in 4/6 severe cases Adverse events: Anorexia 0 Anxiety 0 Dizziness 1 Drowsiness 0 Dyspepsia 0 Erectile dysfunction 0 Reduced libido 0	Study also includes data on intercourse frequency.

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-C. Evidence Tables: Sertraline treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
McMahon, cont.		Setraline 50 mg/day for 3 weeks.	Latency: 13.1 (7-anej) min Anejaculation: 4 Intravaginal ejaculation in all 6 severe cases Adverse events: Anorexia 1 Anxiety 0 Dizziness 0 Drowsiness 1 Dyspepsia 1 Erectile dysfunction 0 Reduced libido 0	
		Setraline 100 mg/day for three weeks	Latency : 16.4 (7-anej) min Anejaculation: 10 Intravaginal ejaculation in all 6 severe cases Adverse events: Anorexia 2 Anxiety 2 Dizziness 0 Drowsiness 2 Dyspepsia 2 Erectile dysfunction 2 Reduced libido 2	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-C. Evidence Tables: Sertraline treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Mendels, 1995 (12139) RCT N=52	n=52: age 25-52 Heterosexual with only 1 partner in the last 6 months. Reasons for exclusion: Patients taking psychotropic medications, depressed (> 14 on Hamilton scale), receiving therapy for sexual dysfunction or with significant medical disease or symptoms. 4 patients excluded from analysis: 1 sertraline without baseline data, 1 sertraline dropped out in the first 3 weeks, 2 placebo dropped out in first 3 weeks. BL: < 1 min on at least 50% of tries in last 6 months.	Sertraline 50 mg/day titrated from 50 to 200 mg/day during weeks 1-3. Total 8 weeks and 26 patients. Mean final dosage 121 mg/day. 2-week washout titrating down to 0 mg/day.	Efficacy (min): Latency (n=22) Baseline 0.98±1.15 Endpoint 5.43±5.62 Change 3.58±3.82 Ejaculation during foreplay (n=24) Baseline 3 During treatment 1 Patient satisfaction (n=24) 0-4 Baseline 1.42±1.10 Endpoint 2.42±1.28 Change 1.00±1.47 Partner satisfaction (n=19) 0-4 Baseline 1.53±0.90 Endpoint 2.58±1.22 Change 1.05±1.18 Side effects (n=26): Any adverse event 17 Discontinued due to AE 0 Diarrhea 6 Anejaculation 5 Dry mouth 4 Fatigue 4 Headache 3 Dizziness 3 Insomnia 3 Nausea 3 Somnolence 2 Dyspepsia 2 Flatulence 2	The data reporting in this study is unclear and this extraction attempts to summarize the results. Latency, patient satisfaction, and ejaculation during foreplay based on patients' assessment. Partner satisfaction based on partner assessment. Article contains data on many variables from both patient and partner assessment as well as global clinical impression from health care provider.

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-C. Evidence Tables: Sertraline treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Mendels, cont.		Placebo 50 mg/day titrated from 50 to 200 mg/day during weeks 1-3. Total 8 weeks and 26 patients. Mean final dosage 145 mg/day. 2-week washout titrating down to 0 mg/day.	Efficacy (min): Latency (n=22) Baseline 1.10±1.35 Endpoint 1.85±3.68 Change 1.22±3.86 Ejaculation during foreplay (n=24) Baseline 4 During treatment 8 Patient satisfaction (n=24) Baseline 1.83±1.20 Endpoint 1.88±1.39 Change 0.04±1.60 Partner satisfaction (n=20) Baseline 1.65±1.14 Endpoint 2.10±1.37 Change 0.45±1.57 Side effects (n=26): Any adverse event 16 Discont. due to AE 2 Diarrhea 1 Anejaculation 0 Dry mouth 2 Fatigue 0 Headache 3 Dizziness 1 Insomnia 1 Nausea 1 Somnolence 3 Dyspepsia 1 Flatulence 1	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-C. Evidence Tables: Sertraline treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Waldinger, 2001 (795222) RCT Netherlands N=48	n=12: age 38±10 Married for 15±12 years with primary PE.	Placebo, morning and evening	Geometric mean latency by week (sec): 0 15.1 1 20.8 2 19.3 3 19.1 4 23.6 5 18.8 6 18.1	All patients had a 1-month baseline and were prohibited from using condoms or topical anesthetics through the study. Study was randomized and blinded. Patients used stopwatches to measure latency.
	n=12: age 40±7 Married for 17±7 years with primary PE.	Paroxetine 20 mg/day, morning and evening	Geometric mean latency by week (sec): 0 17.1 1 36.7 2 71.1 3 119.2 4 88.3 5 146.0 6 107.9	
	n=12: age 41±9 Married for 15±9 years with primary PE.	Sertraline 50 mg/day, morning and evening	Geometric mean latency by week (sec): 0 13.9 1 25.2 2 38.6 3 33.8 4 42.7 5 58.1 6 50.3	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-C. Evidence Tables: Sertraline treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Waldinger, cont.	n=12: age 35±6 Married or in a relationship for 12±8 years with primary PE.	Nefazodone 400 mg/day, morning and evening	Geometric mean latency by week (sec) 0 16.8 1 19.1 2 14.2 3 25.6 4 28.4 5 15.6 6 17.9	
Waldinger, 1998 (12044a) RCT Netherlands N=51	After prescreening exclusions, 60 patients enrolled; 51 completed the study; 6 withdrew due to adverse events and 3 for lack of efficacy			This article describes two RCTs, the first of which is a 5-arm study. 6-week data are recorded here; graphs of intermediate results are presented in the paper.
	n=10: age 38±7, partner age 36±7 BL: 21±12 sec	Fluoxetine 20 mg/day	Latency at 6 weeks: 211±251 sec Absolute change: 189±244 sec	
	n=10: age 44±10, partner age 43±10 BL: 15±17 sec	Fluvoxamine 100 mg/day	Latency at 6 weeks: 55±70 sec Absolute change: 42±57 sec	
	n=11: age 41±8, partner age 39±8 BL: 16±10 sec	Paroxetine 20 mg/day	Latency at 6 weeks: 476±1146 sec Absolute change: 458±1142 sec	
	n=11: age 40±9, partner age 38±10 BL: 21±12 sec	Sertraline 50 mg/day	Latency at 6 weeks: 117±87 sec Absolute change: 96±84 sec	
	n=9: age 45±4, partner age 41±5 BL: 19±15 sec	Placebo	Latency at 6 weeks: 29±25 sec Absolute change: 10±18 sec	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-C. Evidence Tables: Sertraline treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Wise, 1994 (12173) Letter/CR N=1	n=1: age 43 Patient with primary PE and no intercourse for 6 months due to wife's frustration with PE.	Sertraline 50 mg/day	Latency 6-10 min Patient and wife satisfied.	This letter is a case report about a single patient who refused sexual therapy (partially because wife refused).

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-D. Evidence Tables: Clomipramine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Abdel-Hamid, 2001 (700014) Crossover RCT Egypt N=51	n=31: age 34.09±4.29 (range, 27-42) Heterosexual, married at least 1 year, with primary PE and willing to have intercourse twice a week. Patients did not have history of psychiatric illness, current physical illness, previous surgery or drug known to affect sexual function, current substance abuse, or ED. Patients each received each of 5 treatments for 4 weeks separated by 2 week wash-out periods. The treatments were ordered randomly in a double blind manner. BL (med.): 1 (0.5-1.5) min Baseline anxiety (med.): 12 (5-25)	Clomipramine 25 mg, 3-5 hrs before planned coitus and not more than twice/week	Results at 4 weeks: Median latency 4 (1-8) min Median anxiety score 11 (4-22) min Median sexual satisfaction score 11 (0-25) min 2 patients dropped out for lack of efficacy and 1 for side effects and lack of efficacy. Side effects: Dry mouth 3 Anorexia 0 Nausea 1 Headache 0 Flushing 0 Drowsiness 1 Sleepiness 2 Nasal congestion 0 Yawning 0 Total pts with side effects: 7/28	Study also included a normal control group of 20 patients who were not treated but supplied anxiety scores of 3.7±2.7(range 1-9) vs. 12.7±5.8 (range 5-25) for the PE subjects. Study contains blinding problems because the Masters and Johnson pause squeeze technique cannot be blinded.

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-D. Evidence Tables: Clomipramine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Abdel-Hamid, cont.		Paroxetine 20 mg, 3-5 hrs before planned coitus and not more than twice/week	Results at 4 weeks: Median latency 4 (2-10) min Median anxiety score 9 (5-23) min Median sexual satisfaction score 12 (0-29) min 2 patients dropped out for lack of efficacy. Side effects: Dry mouth 2 Anorexia 0 Nausea 1 Headache 0 Flushing 0 Drowsiness 0 Sleepiness 0 Nasal congestion 0 Yawning 2 Total pts with side effects: 5/29	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-D. Evidence Tables: Clomipramine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Abdel-Hamid, cont.		Sertraline 50 mg, 3-5 hrs before planned coitus and not more than twice/week	Results at 4 weeks: Median latency 3 (1-10) min Median anxiety score 11 (5-22) min Median sexual satisfaction score 10 (0-31) min 2 patients dropped out for lack of efficacy. Side effects: Dry mouth 0 Anorexia 1 Nausea 1 Headache 0 Flushing 0 Drowsiness 1 Sleepiness 0 Nasal congestion 0 Yawning 0 Total pts with side effects: 3/29	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-D. Evidence Tables: Clomipramine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Abdel-Hamid, cont.		Sildenafil 50 mg, 3-5 hrs before planned coitus and not more than twice/week	Results at 4 weeks: Median latency 15 (5-30) Median anxiety score 8 (4-15) Median sexual satisfaction score 30 (17-34) 2 patients dropped out for side effects. Side effects: Dry mouth 0 Anorexia 0 Nausea 0 Headache 2 Flushing 2 Drowsiness 0 Sleepiness 0 Nasal congestion 1 Yawning 0 Total pts with side effects: 5/28	
		Masters and Johnson pause squeeze technique	Results at 4 weeks: Median latency 3 (1-7) Median anxiety score 12 (5-21) Median sexual satisfaction score 6 (0-22) 2 patients dropped out for lack of efficacy.	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-D. Evidence Tables: Clomipramine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Althof, 1995 (12146) Crossover RCT Cleveland N=15	n=15: age 38±8.94 (range, 23-56) All patients in stable relationships (married or cohabitating) recruited through newspaper ads. All had primary PE with latency < 4 min and in good physical health without history of mental illness, not taking prescription meds, ED less than 10% of time, and no substance or alcohol dependency in last 2 years. BL: < 4 min	Each patient had a run-in period long enough for 3 attempts at coitus. 3 treatment periods were each set long enough to anticipate 5 attempts. The treatment periods were separated by 1-week washout. At the end was a run-out equivalent to the run-in. 3 treatments were used in random order: Clomipramine 25 mg/day Clomipramine 50 mg/day Placebo 1/day	Latency: Run-in 81 sec 25mg/day clomipramine 202 sec 50mg/day clomipramine 419 sec Placebo (from graph) 137 sec Run-out (from graph) 80 sec Side effects (days with effect): Placebo Nausea 4 Clomipramine 25 mg/day Dry mouth 7 Feeling different 8 Constipation 1 Clomipramine 50 mg/day Dry mouth 33 Feeling different 21 Constipation 18 Dizziness 10 Nausea 8 Sleep disturbance 6 Fatigue 4 Hot flashes 4 Headache 3 Ears ringing 3 Moist mouth 1 Decreased concentration 1	Satisfaction scores are only on a graph. Study also lists data on a symptom checklist 90-R results.

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-D. Evidence Tables: Clomipramine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Assalian, 1988 (105301) CR (5) Canada N=5	n=5: age 39.6 (range, 26-52) Patients were reported as individual case reports. 4 had primary PE and 1 had secondary.	All were started on clomipramine 25 mg/day. 1 patient partially complied by only taking the tablet when sexual activity was anticipated. Another patient took the dose only on Friday, Saturday, and Sunday when sex was possible. 1 patient reduced to 10 mg/day due to sleepiness.	All patients reported significant delay and heightened control over ejaculation. 2 patients had side effects including daytime sedation, dry mouth, and constipation.	No real data are supplied. Results and side effect data are not clear in this study.
Eaton, 1973 (105303) CS England N=13	n=13: age 35 (range, 19-58) 11 in stable relationships, 2 with multiple partners. 11 with primary PE (but 1 had a period of normal response in the past). 7 had some ED and 5 had some loss of libido. Most had some amount of anxiety and/or depression.	Clomipramine 25 mg/day titrated up to 75 mg/day in 25 mg steps every 2 weeks	12/13 responded "positively" in 2 weeks to 2 months. Side effects included dyspepsia, dry mouth and perspiration.	No numbers for side effects or definition of PE or positive response given.
Girgis, 1982 (12409) Crossover RCT Egypt N=50	n=50: age 34.5±8.2 (range, 19-57) Married with history of PE from 1 months to 17 years. Patients in good health with normal libido and erection, no diabetes, pyuria or prostatitis.	Clomipramine 10 mg bid (12.00 and 18.00 hrs) for 6 weeks followed by placebo bid for 6 weeks	n=22 (Initially 25 patients but 3 dropouts.) Number of satisfactory sexual performances: Clomipramine 161/317 Placebo 163/313 No side effects observed.	Dropouts were for no apparent reason. There was no washout.

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-D. Evidence Tables: Clomipramine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Girgis, cont.		Pacebo bid (12.00 and 18.00 hrs) for 6 weeks followed by clomipramine 10 mg bid for 6 weeks.	n=17 (Initially 25 patients but 8 dropouts.) Number of satisfactory sexual performances: Clomipramine 106/216 Placebo 73/228 No side effects observed.	
Goodman, 1980 (13710) Crossover RCT England N=20	n=10: age 28 (range, 18-43) 4 with primary PE and 3 with secondary PE. 2 with occasional ED. All patients offered or trained in squeeze technique without success. 3 withdrawals from study – net 7 patients.	Clomipramine 10 mg/day increasing up to 40 mg/day for 1 month. Second month clomipramine at doses up to 150 mg/day.	At 4 weeks 2/7 were better. At 8 weeks 3/7 were better. At 16 weeks 1 was cured (no further treatment needed), 2 better using clomipramine occasionally and the rest not better.	This study is difficult to decode. There are no numeric outcomes, only subjective terms like better or no better. Side effects are listed in a divided table that makes it unclear which drug or group they apply to.
	n=10: age 30 (range, 22-41) 7 with primary PE and 2 with secondary PE. 3 with occasional ED. All patients offered or trained in squeeze technique without success. 1 withdrawal from study – net 9 patients.	Placebo 10 mg/day increasing up to 40 mg/day for 1 month. Second month clomipramine at doses up to 150 mg/day.	At 4 weeks 4/9 were better. At 8 weeks 5/9 were better. At 16 weeks 6 were better (2 using clomipramine occasionally, 4 using it regularly), 2 were better but stopped using clomipramine due to side effects and 1 was not better.	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-D. Evidence Tables: Clomipramine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Haensel, 1996 (10696) Crossover RCT Netherlands N=22	n=8: age 42.2 (range, 31-62) Patients with SMD-IV criteria for primary premature ejaculation, heterosexual, with dysfunction for at least 6 months, willingness to attempt coitus or masturbation at least once a week, no concomitant psychiatric disease, previous surgery or drug use that would affect sexual function.	Patients in all three groups were given two treatments in crossover. The treatments were 25 mg of clomipramine 12-24 hrs before anticipated sexual activity (coitus or masturbation) and placebo. Patients received each treatment for 3 weeks and were crossed over to the alternate treatment for 3 weeks. Patients were randomized as to order with 13 beginning with clomipramine and 9 with placebo.	Latency: (n=6) Pretest 1.4±.3 Clomipramine 2.8±.6 Placebo 1.7±.3 Approximately 2 min placebo, 8 min clomipramine: Number of thrusts (n=6) Pretest 1.9±0.4 Clomipramine 4.0±0.0 Placebo 3.3±0.5 Orgasm sooner than desired (n=8) Pretest 1.0±0.0 Clomipramine 4.0±0.8 Placebo 1.1±0.1	There is no mention of this being a double-blind trial. The lack of washout and the fact that more patients began with clomipramine may have impacted results. A variety of other scores and frequencies were also listed in the article. Latency and number of thrusts were scored on unusual scales: Latency(min) Score <1 1 1-3 2 4-6 3 7-10 4 11-15 5 >15 6 Number of thrusts Score <5 1 6-10 2 11-20 3 >20 4 Orgasm sooner than desired was scored on a 1 – 7 scale
	n=6: age 41.2 (range, 26-52) Patients with SMD-IV criteria for secondary premature ejaculation who also had erectile dysfunction. These patients were heterosexual, with dysfunction for at least 6 months, willingness to attempt coitus or masturbation at least once a week, no concomitant psychiatric disease, previous surgery or drug use that would affect sexual function.		Latency: (n=5) Pretest 1.0±0.0 Clomipramine 1.2±0.2 Placebo 1.2±0.2 Approximately 2 min with either treatment: Number of thrusts (n=5) Pretest 1.5±0.5 Clomipramine 1.8±0.4 Placebo 1.5±0.4 Orgasm sooner than desired (n=6) Pretest 1.2±0.2 Clomipramine 1.8±0.5 Placebo 1.8±0.8	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-D. Evidence Tables: Clomipramine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Haensel, cont.	n=8: age 40.5 (range, 26-52) recruited through word of mouth healthy normal controls		Latency: (n=5) Pretest 3.7±0.3 Clomipramine 3.6±0.2 Placebo 3.8±0.2 Approx. 9 min placebo and 11 min clomipramine: Number of thrusts (n=6) Pretest 3.7±0.3 Clomipramine 3.7±0.3 Placebo 4.0±0.0 Orgasm sooner than desired (n=7) Pretest 5.3±0.6 Clomipramine 5.6±0.6 Placebo 5.7±0.5	1 – always, 7 – never Side effects, not broken down by group, included: Dry mouth 4 Fatigue or low energy 8 Dizziness 3 Nausea, headache, yawning 1 9/14 patients discriminated drug from placebo
Kim, 1998 (12047) Crossover RCT Korea N=53	n=37: age 44 (range; 30-60). 53 heterosexual patients enrolled; 37 completed the study. Reasons for withdrawal: loss to follow-up (5), no efficacy (fluoxetine 3, sertraline 1, placebo 1) and no efficacy plus side effects (clomipramine 1). One patient was excluded from analysis because of delayed (>30 min) ejaculation with sertraline or clomipramine.	Baseline – no treatment	Latency: 46±41 sec Patient Satisfaction: Satisfied 0% Moderate 0% Dissatisfied 100% Partner Satisfaction: Satisfied 0% Moderate 22.2% Dissatisfied 77.8%	All patients received each therapy and placebo for 4 weeks with a 4-week washout between therapies. Order of administration was randomized.

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-D. Evidence Tables: Clomipramine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Kim, cont.		Placebo 1 capsule/day first week and 2/day thereafter	Latency: 2.27±3.78 min Patient Satisfaction: Satisfied 19.4% Moderate 27.8% Dissatisfied 52.8% Partner Satisfaction: Satisfied 11.1% Moderate 36.1% Dissatisfied 52.8% Side effects: Drowsiness 2 Dry mouth 0 Reduced Potency 3 Nausea 1 Vomiting 0 Other 3 Total pts with side effects: 7	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-D. Evidence Tables: Clomipramine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Kim, cont.		Clomipramine 25 mg/day for first week, 50 mg/day thereafter	Latency: 5.75±6.68 min Patient Satisfaction: Satisfied 25.0% Moderate 38.9% Dissatisfied 36.1% Partner Satisfaction: Satisfied 19.4% Moderate 38.9% Dissatisfied 41.7% Side effects: Drowsiness 6 Dry mouth 2 Reduced Potency 3 Nausea 4 Vomiting 0 Other 3 Total pts with side effects: 13	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-D. Evidence Tables: Clomipramine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Kim, cont.		Fluoxetine 20 mg/day for first week, 40 mg/day thereafter	Latency: 2.30±2.08 min Patient Satisfaction: Satisfied 25.0% Moderate 38.9% Dissatisfied 36.1% Partner Satisfaction: Satisfied 19.4% Moderate 38.9% Dissatisfied 41.7% Side effects: Drowsiness 6 Dry mouth 2 Reduced Potency 3 Nausea 4 Vomiting 0 Other 3 Total pts with side effects: 13	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-D. Evidence Tables: Clomipramine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Kim, cont.		Sertraline 50 mg/day for first week, 100 mg/day thereafter	Latency: 4.27±5.69 min Patient Satisfaction: Satisfied 41.7% Moderate 36.1% Dissatisfied 22.2% Partner Satisfaction: Satisfied 30.6% Moderate 38.9% Dissatisfied 30.6% Side effects: Drowsiness 7 Dry mouth 4 Reduced Potency 3 Nausea 2 Vomitting 0 Other 0 Total pts with side effects: 12	
Montorsi, 1995 (500007) RCT, Italy N=40	N=17 with available partner, without ED, penile defects with PE at least 50% of time	Placebo for 8 weeks followed by clomipramine 50 mg/day given at bedtime for 8 weeks	Placebo response Complete 1/17 Partial 2/17 Failure 14/17 Overall complication rate 10% Clomipramine response Complete 5/17 Partial 6/17 Failure 6/17	Dropouts due to side effects: tremor in 5, nausea in 2 – not clear which group. Overall clomipramine complication rate (both groups) is 40%. The 3 month data is with all patients taking clomipramine.

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-D. Evidence Tables: Clomipramine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Montorsi, cont.	N=16 with available partner, without ED, penile defects with PE at least 50% of time	Clomipramine 50 mg/day given at bedtime for 8 weeks (presumably continued for at least 3 months)	Clomipramine response Complete 4/16 Partial 4/16 Failure 8/16	Complete 8/33 Partial 9/33 Failure 16/33 Complete response is ability to control ejaculation at least 90% of the time. Partial response is controlled at least 70% of the time.
Rowland, 2001 (795018) CS US N=4	n=4: age 53.5 (range, 44-72) Out of 13 who failed with 25 mg. Clomipramine PRN who were in stable relationships. Other 9 had either moved out or were no longer in stable relationships with a willing partner. PE persisted for 7.5 (3-10) years with BL: ≤1 min	Patients received increasing daily doses of clomipramine of 10, 20, and 30 mg/day for 3 weeks for each dose. Data were also reported from a previous study with these patients where they received 25 mg PRN or placebo.	Latency in sec (mean): Baseline 25.5 10 mg 50.65 (median from graph) 20 mg 91.5 30 mg 221.0 Ejaculatory control (0-10 increasing scale): Baseline 4.0 10mg 4.5 20mg 5.9 30mg 6.2	This is a very small study that shows that daily dosing may salvage some patients who fail PRN dosing. Patients were failures from article 12022.

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-D. Evidence Tables: Clomipramine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Segraves, 1993 (12219) RCT Czech. Rep. N=29	n=10: age 44.7±7.5 Recruited by newspaper ad. Requirements include age 21-65, and no history of psychiatric disorder, current substance abuse, significant illness, or use of psychotropic drugs. 8 were married and 7 had primary PE.	25 mg clomipramine to take 6 hrs prior to coitus. After 2 attempts patients could double dose in the absence of side effects or unsatisfactory ejaculatory delay. Trial continued for a total 10 attempts at coitus.	At 25 mg: 7/10 had latency ≥ 2 min Mean at 25 mg, 6.1 min At 50 mg: 8/10 had latency ≥ 2 min 6/7 men increased latency by 2 min or more by spousal estimate. Rating of libido, erections, ejaculation timing and quality, and overall satisfaction significantly increased. Side effects: Mild nausea 3 Drowsiness 3 Diarrhea 1 Transient ED 2	9 patients (out of 29) dropped out and were not included in the analysis, but it is not clear which groups they were in. Only data for completers was supplied. Numbers lacking for some outcomes.

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-D. Evidence Tables: Clomipramine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Segraves, cont.	n=10: age 47.2±10.2 Recruited by newspaper ad. Requirements include age 21-65, and no history of psychiatric disorder, current substance abuse, significant illness, or use of psychotropic drugs. 6 were married and 8 had primary PE.	25 mg placebo to take 6 hrs prior to coitus. After two attempts patients could double dose in the absence of side effects or unsatisfactory ejaculatory delay. Trial continued for a total 10 attempts at coitus.	At 25mg: 0 men had latency ≥ 2 min Mean at 25mg, 51 sec At 50 mg: 2 men had latency ≥ 2 min 2/5 men increased latency by 2 min or more by spousal estimate. Rating of libido, erections, ejaculation timing and quality, and overall satisfaction were unchanged. Side effects: Mild nausea 1 Drowsiness 1 Constipation 2	
Strassberg, 1999 (12022) Crossover RCT Salt Lake City N=34	n=23: age 46.3±11.738 PE patients recruited from newspaper ads of which 28 completed the study. 5 of these were dropped because the studies indicated placebo latencies greater than 3 min Patients had no history of psychiatric disorder, no current substance abuse, no current relevant medications, no previous surgery or drug use known to impact sexual function, and in a stable heterosexual relationship.	Patients each received 2 treatments for 2 weeks with no apparent washout. Treatment 1: 25 mg (2 capsules) of clomipramine taken 4 hrs before coitus. Treatment 2: 2 capsules of placebo taken similarly. Patients were randomized to sequence.	Latency: (n=22) Placebo 52±45 sec Clomipramine 229±286 sec Control over ejaculation: (n=16) (1-10 scale) Placebo 2.70±1.84 Clomipramine 5.08±2.45	This article contains many complex statistical analyses, showing that clomipramine increased latency and control for the patients with PE. The study included lab studies with arousing videos and vibrators, but only the at home diary data is included under outcomes here.

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-D. Evidence Tables: Clomipramine treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Strassberg, cont.	n=13: age 45.6±7.3 15 normal control patients recruited from newspaper ads of which 13 completed study. 2 of these were dropped because the studies indicated placebo latencies less than 150 sec Patients had no history of psychiatric disorder, no current substance abuse, no current relevant medications, no previous surgery or drug use known to impact sexual function, and in a stable heterosexual relationship.		Latency: (n=4) Placebo 491±245 sec Clomipramine 665±307 sec Control over ejaculation: (n=4) (1-10 scale) Placebo 8.25±1.5 Clomipramine 8.5±1.0	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-E. Evidence Tables: Topical anesthetic treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Atan, 2000 (795257) Controlled Trial Turkey N=43	n=26: age 27 (range, 21-36) With PE and without ED, substance abuse, infections, diabetes, thyroid disease, hypotension or loss of libido. Patients had normal psychiatric consultations.	Fluoxetine 20 mg/day for 1 week followed by 40 mg/day for 7 weeks	Cured: 8 (30.8%) Improved: 11 (42.3%) Failure: 7 (26.9%) Side effects: Nausea 3 Headache 1 Insomnia 2 Total patients with side effects: 6	There is no indication of randomization in the article.
	n=17: age 31 (range,19-48) With PE and without ED, substance abuse, infections, diabetes, thyroid disease, hypo tension or loss of libido. Patients had normal psychiatric consultations.	Fluoxetine 20 mg/day and local application of lidocaine ointment to the glans 20 min prior to intercourse	Cured: 9 (52.9%) Improved: 5 (29.4%) Failure: 3 (17.6%) Side effects: Nausea 1 Headache 4 Insomnia 0 Total patients with side effects: 5	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-E. Evidence Tables: Topical anesthetic treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Atikeler, 2002 (500006) RCT Turkey N=40	N=10, age 29.4 (range, 20-40) with latency less than 1 minute and married or with constant partner for more than 2 years and no organic causes.	Placebo cream used at least 5 times (range 5-8)	Mean latency 1.01 min	
	N=10, age 29.4 (range, 20-40) with latency less than 1 minute and married or with constant partner for more than 2 years and no organic causes.	Prilocaine-lidocaine cream applied and left in place under a condom for 20 min and removed—used at least 5 times (range 5-9)	Mean latency 6.71 min in 8 patients. One patient still had 1 min latency and one patient increased to 3-5 min. Overall average latency 6.5 min	
	N=10, age 29.4 (range, 20-40) with latency less than 1 minute and married or with constant partner for more than 2 years and no organic causes.	Prilocaine-lidocaine cream applied and left in place under a condom for 30 min and removed—used at least 5 times (range 5-9)	Mean latency 8.71 min in 4 patients while 6 patients complained of erection loss due to numbness and delayed ejaculation	
	N=10, age 29.4 (range, 20-40) with latency less than 1 minute and married or with constant partner for more than 2 years and no organic causes.	Prilocaine-lidocaine cream applied and left in place under a condom for 45 min and removed—used at least 5 times (range 5-9)	All patients complained of erection loss due to numbness and delayed ejaculation	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Pharmacologic Treatment of Premature Ejaculation (PE)

Appendix 1-E. Evidence Tables: Topical anesthetic treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Berkovitch, 1995 (12140) CS Canada N=11	n=11: age 36±7 (range, 26-44) All patients heterosexual and married or in stable relationship without ED or risk factors for ED or extensive drug or alcohol use.	Lidocaine-prilocaine cream 2.5 mg dose applied to glans and shaft and covered with a condom for 30 min After that time the condom could be removed at the patient's option.	Patients estimated latency and graded it as follows: Excellent 5 Better than usual 4 Unsatisfied 2 Patients rating excellent used the cream 8.4±1.7 times with latency 15-20 min Patients rating better used the cream 5±0.41 time with latency 5-10 min One unsatisfied patient complained of numbness despite 20 min latency and spousal satisfaction. The other unsatisfied patient had no meaningful improvement.	
Damrau, 1963 (105302) CS New Jersey N=13	n=13: age 31.2 (range, 22-39) 11 with ejaculation prior to intromission, 1 with immediate ejaculation and 1 with 1 min latency. Duration of condition 2.7 years (range, 0.5-5).	Ethyl aminobenzoate cream (3%) to glans and prepuce, wiped off after 5 min	PE "corrected" in all cases. Latency 1.6 (range, 0.5-5). Duration of anesthesia mean 25.2 min (range, 10-50).	Study also reports some data on the use of the cream on normal volunteers.

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-E. Evidence Tables: Topical anesthetic treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Slob, 2000 (500003) CS Netherlands N=15	N=15; age 43±11(range, 21-64) Estimated latency between 1-2 min with less than 8 thrusts with ejaculation prior to intromission 31% of the time. 11/15 patients experienced ejaculation prior to intromission at some times. Full erections 92% of the time.	Lidocaine-prilocaine cream (1/2 tube) applied for 10 min contained with condom, then removed. Patients given 5 tubes and 12 condoms.	Latency 489±465 Sense of control 4.7±3.1 3 pts reported inability to reach orgasm on some occasions with the cream	Patients were own controls in an unblended crossover.
		Coitus without cream or intervention. Patients asked to report on 2-3 encounters.	Latency 115±142 Sense of control 2.5±2.2 No patients reported inability to achieve orgasm	

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-F. Evidence Tables: Adrenergic blockade treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Beretta, 1986 (12350) CS Italy N=15	n=15: age 34 (range, 20-55) All patients with primary PE who refused psychological treatment (at least initially).	Phenoxybenzamine 10 mg/day	Outcomes given by patient. 7 patients ejaculated ante portam before treatment but only 4 did so after treatment. The other 3 had an average latency of 15 min after treatment. Average pretreatment latency of 8 patients who ejaculated intravaginally pretreatment was 1.38 min pretreatment and 5.63 min post-treatment. Of these 8 patients, 3 had no change in latency. Patients report of sexual response: Improved 8 No variation 5 Worsened 2 Partner satisfaction: Improved 8 No variation 5 Worsened 2 Two patients reported dry ejaculation	Also data on semen volume.

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-F. Evidence Tables: Adrenergic blockade treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Cavallini, 1995 (12160) Crossover RCT Italy N=101	n=101: age 34.3 (range, 21-63)	Patients received alphuzosine (2x3 mg/day, terazosine (1 mg/day up to 5 mg once a day), vitamin C 2x500 mg/day (placebo). The patients were in 3 groups which received treatment in 1 of the following 3 orders: 1. Alphuzosine, terazosine, placebo 2. Terazosine, placebo, alphuzosine 3. Placebo, alphuzosine, terazosine	Results deemed positive if patients and spouses agreed they were satisfied. Alphuzosine: 1st administered 14/30 2nd administered 16/31 3rd administered 13/30 Terazosine: 1st administered 15/30 2nd administered 16/30 3rd administered 17/31 Placebo: 1st administered 4/31 2nd administered 10/30 3rd administered 8/30 Side effects: Alphuzosin: 5/90 (3 hypotension, 2 withdrawals, 1 hypotension plus epigastralgia) Terazosine: 3/90 (2 hypotension leading to withdrawal, 1 headache) Placebo: 1/90 (weak epigastralgia)	No washout periods between treatments and terazosine followed by alphuzosine directly twice, but the reverse never happened. Only 3 of 6 possible orders were used. 6 patients were excluded from analysis because patients and spouses disagreed about results. It is not clear which groups they came from. Dosages did not match (terazosine 1/day, others bid) so blinding was compromised. Side effect numbers do not add up and refer to withdrawals at various stages in the study. It is not clear how this was handled in the results statistics.

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-F. Evidence Tables: Adrenergic blockade treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Cooper, 1984 (12387) Crossover RCT Canada N=12	n=12: age 28 (range, 18-58) Patients with PE for mean 4.2 years (range, 1-12.5). Patients also had chronic anxiety for at least 6 months scoring > 9 on the somatic scale of the Hamilton Anxiety Rating Scale.	Patients each had a 4 week run-in followed by a 4 week treatment (either propranolol 120 mg/day or placebo), 4 week washout, 4 week treatment with the alternate treatment, and a 4 week run-out. Patients were randomly assigned to treatment sequence.	Latency, mean (min): Run-in 1.5 Placebo 1.7 Wash-out 1.5 Propranolol 1.7 Run-out 1.6 Overall satisfaction, mean (0-100 scale): Run-in 51.7 Placebo 51.7 Wash-out 50.3 Propranolol 52.5 Run-out 52.2	Also data about erectile quality, blood pressure, pulse rate, Hamilton rating scale. No real impact in any case. Not all subjects were able to meet the projected goal of intercourse 2x per week.

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-F. Evidence Tables: Adrenergic blockade treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Shilon, 1984 (12371) CS Israel N=9	n=9: age 36.3±7.7 (range, 28-50) All patients with undefined premature ejaculation.	Patients were treated with phenoxybenzamine. Patients received increasing doses of 10, 20, and 30 mg/day, but the study is not clear whether there was a washout period, or even the sequence of doses. Presumably the doses were escalated based on results. Duration of treatment ranged from 7 to 150 days. All patients received 10 mg. 7 also received 20 mg and 3 of those received 30 mg.	Premature Ejaculation Baseline: 9/9 10 mg : No improvement 5/9 Slight improvement 2/9 Good 2/9 20 mg: No improvement 1/7 Slight improvement 1/7 Good 4/7 Excellent 1/7 Wife's response: Baseline: Unsatisfied 7/9 Satisfied 2/9 10 mg.: Unsatisfied 2/9 No improvement 5/9 Slight improvement 1/9 Good 1/9 20 mg.: No improvement 2/7 Satisfied 4/7 Good 1/7 30 mg.: Satisfied 2/2 Zero semen volume 10 mg 4/9 20 mg 6/7 30 mg 2/2	Erection quality: 2 patients with fair erection at baseline progressed to good erections on any drug dose. One patient with good erections at baseline had fair erections on 10 mg/day and 20 mg/day and good erections at 30 mg/day. Most other patients had significant reductions in semen volume.

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 1-G. Evidence Tables: Miscellaneous treatment studies

Reference*	Study Population†	Treatment Regimen	Outcomes	Comments
Brown, 2000 (105252) CR New York N=1	n=1: age 31 Patient with acute prostatitis who also had unreported PE for three years. BL: 1-2 minutes.	Ciprofloxacin 500 mg bid for 30 days (for prostatitis)	After treatment: Latency 6-15 Increase persisted after treatment discontinued.	Individual patient report of an incidental finding after ciprofloxacin therapy.
Fein, 1990 (900015) CS Florida N=16	n=8 Complaining of life-long PE, ejaculating prior to or immediately on vaginal penetration. Reasons for withdrawal: 8 patients declined to participate in the study due to an unwillingness to have penile injections.	Penile injection with 0.2 ml of papaverine 30 mg/ml and phentolamine 1mg/ml	Success was defined as having an erection of sufficient length for satisfactory intercourse regardless of ejaculation. All patients were successful with doses ranging from 0.1 to 0.4 ml. Three patients said they were cured and having successful intercourse with no PE. Other 5 continuing injections. No side effects reported in 14 months of treatment.	All 16 patients trained in Masters and Johnson squeeze technique, gluteal muscle contraction technique, mental divergence and 15 min masturbation exercise with no success.

*Author, year/(Procite number)/Study Design/Location/N=Total patients
†age=mean±standard deviation in years
BL=baseline latency ; RCT=randomized controlled trial
CI = confidence interval

Appendix 2. Summary Tables: Adverse Event (AE) Rates by Pharmacologic Treatment

Clomipramine

Reference	Description/Comments	No. of AE's	No. of Patients	Rate
Anorexia				
700014	25 mg 3-5 hrs before coitus, not > 2 x per week	0	31	0.0%
Diarrhea				
12219	25 mg 6 hrs prior to coitus	1	10	10.0%
Dizziness				
10696	25 mg 12-24 hrs prior to sexual activity	3	22	13.6%
Drowsiness				
12047	25 mg/day for 1 week, 50 mg/day later	8	53	15.1%
12219	25 mg 6 hrs prior to coitus	3	10	30.0%
700014	25 mg 3-5 hrs before coitus, not > 2 x per week	1	31	3.2%
Dry mouth				
10696	25 mg 12-24 hrs prior to sexual activity	4	22	18.2%
12047	25 mg/day for 1 week, 50 mg/day later	12	53	22.6%
700014	25 mg 3-5 hrs before coitus, not > 2 x per week	3	31	9.7%
Erectile dysfunction - transient				
12219	25 mg 6 hrs prior to coitus	2	10	20.0%
Fatigue or low energy				
10696	25 mg 12-24 hrs prior to sexual activity	8	22	36.4%
Flushing				
700014	25 mg 3-5 hrs before coitus, not > 2 x per week	0	31	0.0%
Headache				
700014	25 mg 3-5 hrs before coitus, not > 2 x per week	0	31	0.0%
Nasal congestion				
700014	25 mg 3-5 hrs before coitus, not > 2 x per week	0	31	0.0%
Nausea				
12047	25 mg/day for 1 week, 50 mg/day later	3	53	5.7%
500007	50 mg/day given at bedtime for 8 weeks	2	33	6.1%
700014	25 mg 3-5 hrs before coitus, not > 2 x per week	1	31	3.2%
Nausea - mild				
12219	25 mg 6 hrs prior to coitus	3	10	30.0%
Nausea, headache, yawning				
10696	25 mg 12-24 hrs prior to sexual activity	1	22	4.5%
Other				
12047	25 mg/day for 1 week, 50 mg/day later	2	53	3.8%
Potency - reduced				
12047	25 mg/day for 1 week, 50 mg/day later	5	53	9.4%
Sleepiness				
700014	25 mg 3-5 hrs before coitus, not > 2 x per week	2	31	6.5%
Tremor				
500007	50 mg/day given at bedtime for 8 weeks	5	33	15.1%
Vomiting				
12047	25 mg/day for 1 week, 50 mg/day later	2	53	3.8%
Yawning				
700014	25 mg 3-5 hrs before coitus, not > 2 x per week	0	31	0.0%

Appendix 2. Summary Tables: Adverse Event (AE) Rates by Pharmacologic Treatment

Fluoxetine

Reference	Description/Comments	No. of AE's	No. of Patients	Rate
Altered Sleep				
900017	5 mg/day for 2 weeks, 10 mg/day for 2 weeks	2	40	5.0%
Dizziness				
12112	20 mg/day for 1-2 weeks, titrated to 60 mg/day	1	11	9.1%
900017	5 mg/day for 2 weeks, 10 mg/day for 2 weeks	1	40	2.5%
Drowsiness				
12047	20 mg/day for 1 week, 40 mg/day later	6	53	11.3%
Dry mouth				
12047	20 mg/day for 1 week, 40 mg/day later	2	53	3.8%
900017	5 mg/day for 2 weeks, 10 mg/day for 2 weeks	3	40	7.5%
Extremity tingling				
12112	20 mg/day for 1-2 weeks, titrated to 60 mg/day	1	11	9.1%
Headache				
12003	20 mg/day for 1 week, 40 mg/day later	1	26	3.8%
12110	20 mg/day for 1 week, 40 mg/day later	1	9	11.1%
795257	20mg/day for 1 week then 40mg/day	1	26	3.8%
Insomnia				
12003	20 mg/day for 1 week, 40 mg/day later	2	26	7.7%
12110	20 mg/day for 1 week, 40 mg/day later	1	9	11.1%
795257	20mg/day for 1 week then 40mg/day	2	26	7.7%
Libido - increased				
900017	5 mg/day for 2 weeks, 10 mg/day for 2 weeks	2	40	5.0%
Loose stools				
900017	5 mg/day for 2 weeks, 10 mg/day for 2 weeks	2	40	5.0%
Nausea				
12003	20 mg/day for 1 week, 40 mg/day later	3	26	11.5%
12047	20 mg/day for 1 week, 40 mg/day later	4	53	7.5%
12110	20 mg/day for 1 week, 40 mg/day later	2	9	22.2%
795257	20mg/day for 1 week then 40mg/day	3	26	11.5%
Nausea and other GI				
12112	20 mg/day for 1-2 weeks, titrated to 60 mg/day	4	11	36.4%
Other				
12047	20 mg/day for 1 week, 40 mg/day later	3	53	5.7%
Palpitations - slight				
900017	5 mg/day for 2 weeks, 10 mg/day for 2 weeks	1	40	2.5%
Penile pain				
900017	5 mg/day for 2 weeks, 10 mg/day for 2 weeks	1	40	2.5%
Potency - reduced				
12047	20 mg/day for 1 week, 40 mg/day later	3	53	5.7%
Sweating				
900017	5 mg/day for 2 weeks, 10 mg/day for 2 weeks	1	40	2.5%
Vomiting				
12047	20 mg/day for 1 week, 40 mg/day later	0	53	0.0%

Appendix 2. Summary Tables: Adverse Event (AE) Rates by Pharmacologic Treatment

Fluoxetine/Lidocaine

Reference	Description/Comments	No. of AE's	No. of Patients	Rate
Headache				
795257	Fluoxetine 20mg/day + topical lidocaine cream	4	17	23.5%
Insomnia				
795257	Fluoxetine 20mg/day + topical lidocaine cream	0	17	0.0%
Nausea				
795257	Fluoxetine 20mg/day + topical lidocaine cream	1	17	5.9%

Appendix 2. Summary Tables: Adverse Event (AE) Rates by Pharmacologic Treatment

Paroxetine

Reference	Description/Comments	No. of AE's	No. of Patients	Rate
Anejaculation				
12005	20 mg/day for 4 weeks	5	61	8.2%
12020	10 mg/day for 3 weeks; followed by 20mg 3-4 hrs prior to intercourse	3	42	7.1%
500005	10 mg/day for 21 days, followed by 20 mg 3-4 hrs before intercourse for 6 months	1	40	2.5%
500005	10 mg/day for 21 days, followed by 20 mg 3-4 hrs plus 50 mg sildenafil before intercourse for 6 months	1	40	2.5%
Anejaculation and frequent yawning				
12088	20 mg/day for 8 weeks	2	17	11.8%
Anejaculation, yawning, fatigue, perspiration				
12088	40 mg/day for 8 Weeks	4	17	23.5%
Anorexia				
12020	10 mg/day for 3 weeks; followed by 20mg 3-4 hrs prior to intercourse	1	42	2.4%
700014	20 mg 3-5 hrs before coitus, not > 2 x per week	0	31	0.0%
Any side effect				
12005	20 mg single dose 3-4 hrs prior to intercourse	0	37	0.0%
12020	20 mg single dose 3-4 hours before coitus for 4 weeks	0	13	0.0%
Decreased Libido				
500005	10 mg/day for 21 days, followed by 20 mg 3-4 hrs before intercourse for 6 months	2	40	5.0%
500005	10 mg/day for 21 days, followed by 20 mg 3-4 hrs plus 50 mg sildenafil before intercourse for 6 months	1	40	2.5%
Drowsiness				
700014	20 mg 3-5 hrs before coitus, not > 2 x per week	0	31	0.0%
Drowsiness & anorexia				
12005	20 mg/day for 4 weeks	1	61	1.6%
Dry mouth				
12088	40 mg/day for 8 Weeks	1	17	5.9%
700014	20 mg 3-5 hrs before coitus, not > 2 x per week	2	31	6.5%
Erectile function - slight reduction				
12088	20 mg/day for 8 weeks	1	17	5.9%
Flushing				
500005	10 mg/day for 21 days, followed by 20 mg 3-4 hrs before intercourse for 6 months	0	40	0.0%
500005	10 mg/day for 21 days, followed by 20 mg 3-4 hrs plus 50 mg sildenafil before intercourse for 6 months	6	40	15.0%
700014	20 mg 3-5 hrs before coitus, not > 2 x per week	0	31	0.0%
GI upset				
12020	10 mg/day for 3 weeks; followed by 20mg 3-4 hrs prior to intercourse	3	42	7.1%
500005	10 mg/day for 21 days, followed by 20 mg 3-4 hrs before intercourse for 6 months	5	40	12.5%
500005	10 mg/day for 21 days, followed by 20 mg 3-4 hrs plus 50 mg sildenafil before intercourse for 6 months	6	40	15.0%
GI upset - minor				
12005	20 mg/day for 4 weeks	2	61	3.3%
Headache				
700014	20 mg 3-5 hrs before coitus, not > 2 x per week	0	31	0.0%
500005	10 mg/day for 21 days, followed by 20 mg 3-4 hrs before intercourse for 6 months	4	40	10.0%
500005	10 mg/day for 21 days, followed by 20 mg 3-4 hrs plus 50 mg sildenafil before intercourse for 6 months	8	40	20.0%

Appendix 2. Summary Tables: Adverse Event (AE) Rates by Pharmacologic Treatment

Paroxetine

Reference	Description/Comments	No. of AE's	No. of Patients	Rate
Libido - reduced				
12005	20 mg/day for 4 weeks	3	61	4.9%
12020	10 mg/day for 3 weeks; followed by 20mg 3-4 hrs prior to intercourse	2	42	4.8%
12088	40 mg/day for 8 Weeks	1	17	5.9%
Nasal congestion				
700014	20 mg 3-5 hrs before coitus, not > 2 x per week	0	31	0.0%
Nausea				
700014	20 mg 3-5 hrs before coitus, not > 2 x per week	1	31	3.2%
Orgasm - inhibited				
12005	20 mg/day for 4 weeks	3	61	4.9%
Sensory confusion - mild				
12118	20 mg/day for 2 months	21	32	65.6%
Sensory confusion - severe				
12118	20 mg/day for 2 months	1	32	3.1%
Sleepiness				
12118	20 mg/day for 2 months	14	32	43.8%
700014	20 mg 3-5 hrs before coitus, not > 2 x per week	0	31	0.0%
Yawning				
700014	20 mg 3-5 hrs before coitus, not > 2 x per week	2	31	6.5%
Yawning, perspiration, dry mouth, fatigue, nausea				
12088	20 mg/day for 8 weeks	6	17	35.3%
12088	40 mg/day for 8 Weeks	7	17	41.2%

Appendix 2. Summary Tables: Adverse Event (AE) Rates by Pharmacologic Treatment

Placebo

Reference	Description/Comments	No. of AE's	No. of Patients	Rate
Anejaculation				
12139	145 mg/day mean final dosage	0	26	0.0%
Any side effect				
12020	Placebo for 4 weeks after 3 week washout	0	13	0.0%
12139	145 mg/day mean final dosage	16	26	61.5%
Burning on micturation				
900017	5 mg/day for 2 weeks, 10 mg/day for 2 weeks	1	40	2.5%
Change in stools				
900017	5 mg/day for 2 weeks, 10 mg/day for 2 weeks	1	40	2.5%
Constipation				
12219	25 mg 6 hrs prior to coitus	2	10	20.0%
Diarrhea				
12033	Placebo	1	15	6.7%
12139	145 mg/day mean final dosage	1	26	3.8%
Discontinued due to AE				
12139	145 mg/day mean final dosage	2	26	7.7%
Dizziness				
12139	145 mg/day mean final dosage	1	26	3.8%
Drowsiness				
12047	1 capsule day for 1 week, 2 per day later	2	53	3.8%
12219	25 mg 6 hrs prior to coitus	1	10	10.0%
Dry mouth				
12033	Placebo	0	15	0.0%
12047	1 capsule day for 1 week, 2 per day later	0	53	0.0%
12139	145 mg/day mean final dosage	2	26	7.7%
Dyspepsia				
12139	145 mg/day mean final dosage	1	26	3.8%
Erectile dysfunction				
12020	Placebo daily	2	42	4.8%
Erectile dysfunction - minor				
12057	Placebo	1	18	5.6%
Fatigue				
12139	145 mg/day mean final dosage	0	26	0.0%
Flatulence				
12139	145 mg/day mean final dosage	1	26	3.8%
Headache				
12020	Placebo PRN	1	42	2.4%
12033	Placebo	3	15	20.0%
12139	145 mg/day mean final dosage	3	26	11.5%
Insomnia				
12139	145 mg/day mean final dosage	1	26	3.8%
Libido - decreased				
900017	5 mg/day for 2 weeks, 10 mg/day for 2 weeks	1	40	2.5%
Libido - increased				
900017	5 mg/day for 2 weeks, 10 mg/day for 2 weeks	1	40	2.5%

Appendix 2. Summary Tables: Adverse Event (AE) Rates by Pharmacologic Treatment

Placebo

Reference	Description/Comments	No. of AE's	No. of Patients	Rate
Nausea				
12047	1 capsule day for 1 week, 2 per day later	1	53	1.9%
12139	145 mg/day mean final dosage	1	26	3.8%
Nausea - mild				
12219	25 mg 6 hrs prior to coitus	1	10	10.0%
Other				
12047	1 capsule day for 1 week, 2 per day later	3	53	5.7%
Potency - reduced				
12047	1 capsule day for 1 week, 2 per day later	3	53	5.7%
Sleepiness				
12033	Placebo	3	15	20.0%
Somnolence				
12139	145 mg/day mean final dosage	3	26	11.5%
Vomiting				
12047	1 capsule day for 1 week, 2 per day later	0	53	0.0%

Appendix 2. Summary Tables: Adverse Event (AE) Rates by Pharmacologic Treatment

Topical Anesthetics

Reference	Description/Comments	No. of AE's	No. of Patients	Rate
Delayed ejaculation				
500006	Prilocaine-lidocaine cream applied and left in place under a condom for 30 min and removed – used at least 5 times (range 5-9)	6	10	60.0%
500006	Prilocaine-lidocaine cream applied and left in place under a condom for 45 min and removed – used at least 5 times (range 5-9)	10	10	100.0%
Inability to reach orgasm				
500003	Lidocaine-prilocaine cream (1/2 tube) applied for 10 min, contained with condom, then removed. Patients given 5 tubes and 12 condoms.	3	15	20.0%
Numbness				
500006	Prilocaine-lidocaine cream applied and left in place under a condom for 30 min and removed – used at least 5 times (range 5-9)	6	10	60.0%
500006	Prilocaine-lidocaine cream applied and left in place under a condom for 45 min and removed – used at least 5 times (range 5-9)	10	10	100.0%

Sertraline

Reference	Description/Comments	No. of AE's	No. of Patients	Rate
Anejaculation				
12037	25 mg/day for 3 weeks	0	46	0.0%
12037	100 mg/day for 3 weeks	10	46	21.7%
12037	50 mg/day for 3 weeks	4	46	8.7%
12139	121 mg/day mean final dosage	5	26	19.2%
Anejaculation & withdrawal from study				
12057	50 mg/day for 4 weeks	2	19	10.5%
Anorexia				
12037	50 mg/day for 3 weeks	1	46	2.2%
12037	100 mg/day for 3 weeks	2	46	4.3%
12037	25 mg/day for 3 weeks	0	46	0.0%
700014	50 mg 3-5 hrs before coitus, not > 2 x per week	1	31	3.2%
Anxiety				
12037	25 mg/day for 3 weeks	0	46	0.0%
12037	50 mg/day for 3 weeks	0	46	0.0%
12037	100 mg/day for 3 weeks	2	46	4.3%
Any side effect				
12139	121 mg/day mean final dosage	17	26	65.4%
Delayed ejaculation				
12013	50mg/day for 2 weeks / 50 mg at 5 pm when intercourse	1	24	4.2%
Diarrhea				
12033	50 mg/day for 4 weeks	3	22	13.6%
12139	121 mg/day mean final dosage	6	26	23.1%
Discontinued due to AE				
12139	121 mg/day mean final dosage	0	26	0.0%
Dizziness				
12037	25 mg/day for 3 weeks	1	46	2.2%
12037	50 mg/day for 3 weeks	0	46	0.0%
12037	100 mg/day for 3 weeks	0	46	0.0%
12139	121 mg/day mean final dosage	3	26	11.5%
500002	50 mg 4 hours prior to intercourse for 6 months, pts with primary PE	3	52	5.8%
500002	50 mg 4 hours prior to intercourse for 6 months, pts with ED treated successfully with sildenafil	4	35	11.4%
Drowsiness				
12037	100 mg/day for 3 weeks	2	46	4.3%
12037	25 mg/day for 3 weeks	0	46	0.0%
12037	50 mg/day for 3 weeks	1	46	2.2%
12047	50 mg/day for 1 week, 100 mg/day later	7	53	13.2%
700014	50 mg 3-5 hrs before coitus, not > 2 x per week	1	31	3.2%
Drowsiness & anorexia				
12057	50 mg/day for 4 weeks	1	19	5.3%
Dry mouth				
12003	50 mg/day	6	31	19.4%
12033	50 mg/day for 4 weeks	2	22	9.1%
12047	50 mg/day for 1 week, 100 mg/day later	4	53	7.5%
12139	121 mg/day mean final dosage	4	26	15.4%
500002	50 mg 4 hours prior to intercourse for 6 months, pts with primary PE	1	52	1.9%
500002	50 mg 4 hours prior to intercourse for 6 months, pts with ED treated successfully with sildenafil	1	35	2.9%
700014	50 mg 3-5 hrs before coitus, not > 2 x per week	0	31	0.0%

Appendix 2. Summary Tables: Adverse Event (AE) Rates by Pharmacologic Treatment

Sertraline

Reference	Description/Comments	No. of AE's	No. of Patients	Rate
Dyspepsia				
12037	50 mg/day for 3 weeks	1	46	2.2%
12037	100 mg/day for 3 weeks	2	46	4.3%
12037	25 mg/day for 3 weeks	0	46	0.0%
12139	121 mg/day mean final dosage	2	26	7.7%
Erectile dysfunction				
12037	25 mg/day for 3 weeks	0	46	0.0%
12037	50 mg/day for 3 weeks	0	46	0.0%
12037	100 mg/day for 3 weeks	2	46	4.3%
12057	50 mg/day for 4 weeks	0	19	0.0%
Fatigue				
12013	50mg/day for 2 weeks / 50 mg at 5 pm when intercourse	2	24	8.3%
12139	121 mg/day mean final dosage	4	26	15.4%
Flatulence				
12139	121 mg/day mean final dosage	2	26	7.7%
Flushing				
700014	50 mg 3-5 hrs before coitus, not > 2 x per week	0	31	0.0%
GI upset				
12057	50 mg/day for 4 weeks	2	19	10.5%
Headache				
12033	50 mg/day for 4 weeks	6	22	27.3%
12139	121 mg/day mean final dosage	3	26	11.5%
700014	50 mg 3-5 hrs before coitus, not > 2 x per week	0	31	0.0%
Insomnia				
12139	121 mg/day mean final dosage	3	26	11.5%
Libido - reduced				
12037	25 mg/day for 3 weeks	0	46	0.0%
12037	100 mg/day for 3 weeks	2	46	4.3%
12037	50 mg/day for 3 weeks	0	46	0.0%
12057	50 mg/day for 4 weeks	0	19	0.0%
Nasal congestion				
700014	50 mg 3-5 hrs before coitus, not > 2 x per week	0	31	0.0%
Nausea				
12003	50 mg/day	2	31	6.5%
12047	50 mg/day for 1 week, 100 mg/day later	2	53	3.8%
12139	121 mg/day mean final dosage	3	26	11.5%
500002	50 mg 4 hours prior to intercourse for 6 months, pts with primary PE	2	52	3.8%
500002	50 mg 4 hours prior to intercourse for 6 months, pts with ED treated successfully with sildenafil	3	35	8.6%
700014	50 mg 3-5 hrs before coitus, not > 2 x per week	1	31	3.2%
Numbness in extremities				
12013	50mg/day for 2 weeks / 50 mg at 5 pm when intercourse	1	24	4.2%
Orgasmic intensity - reduced				
12057	50 mg/day for 4 weeks	0	19	0.0%
Other				
12047	50 mg/day for 1 week, 100 mg/day later	0	53	0.0%
Potency - reduced				
12047	50 mg/day for 1 week, 100 mg/day later	3	53	5.7%
Sleepiness				
12033	50 mg/day for 4 weeks	6	22	27.3%
700014	50 mg 3-5 hrs before coitus, not > 2 x per week	0	31	0.0%

Appendix 2. Summary Tables: Adverse Event (AE) Rates by Pharmacologic Treatment

Sertraline

Reference	Description/Comments	No. of AE's	No. of Patients	Rate
Somnolence				
12139	121 mg/day mean final dosage	2	26	7.7%
Vomiting				
12047	50 mg/day for 1 week, 100 mg/day later	0	53	0.0%
Yawning				
700014	50 mg 3-5 hrs before coitus, not > 2 x per week	0	31	0.0%

Appendix 2. Summary Tables: Adverse Event (AE) Rates by Pharmacologic Treatment

Sildenafil

Reference	Description/Comments	No. of AE's	No. of Patients	Rate
Anejaculation				
500005	10 mg/day paroxetine for 21 days, followed by 20 mg 3-4 hrs plus 50 mg sildenafil before intercourse for 6 months	1	40	2.5%
Anorexia				
700014	50 mg 3-5 hrs before coitus, not > 2 x per week	0	31	0.0%
Decreased libido				
500005	10 mg/day paroxetine for 21 days, followed by 20 mg 3-4 hrs plus 50 mg sildenafil before intercourse for 6 months	1	40	2.5%
Drowsiness				
700014	50 mg 3-5 hrs before coitus, not > 2 x per week	0	31	0.0%
Dry mouth				
700014	50 mg 3-5 hrs before coitus, not > 2 x per week	0	31	0.0%
Flushing				
500005	10 mg/day paroxetine for 21 days, followed by 20 mg 3-4 hrs plus 50 mg sildenafil before intercourse for 6 months	6	40	20.0%
700014	50 mg 3-5 hrs before coitus, not > 2 x per week	2	31	6.5%
GI upset/nausea				
500005	10 mg/day paroxetine for 21 days, followed by 20 mg 3-4 hrs plus 50 mg sildenafil before intercourse for 6 months	6	40	15.0%
Headache				
500005	10 mg/day paroxetine for 21 days, followed by 20 mg 3-4 hrs plus 50 mg sildenafil before intercourse for 6 months	8	40	15.0%
700014	50 mg 3-5 hrs before coitus, not > 2 x per week	2	31	6.5%
Nasal congestion				
700014	50 mg 3-5 hrs before coitus, not > 2 x per week	1	31	3.2%
Nausea				
700014	50 mg 3-5 hrs before coitus, not > 2 x per week	0	31	0.0%
Sleepiness				
700014	50 mg 3-5 hrs before coitus, not > 2 x per week	0	31	0.0%
Yawning				
700014	50 mg 3-5 hrs before coitus, not > 2 x per week	0	31	0.0%

Appendix 3-A. Summary Tables: Citalopram treatment studies

Treatment Groups	Treatment regimen			Number of Patients	Latency in Seconds			
	Week	Dosage	Treatment Duration		Mean	SD	Min	Max
Waldinger, M. D., Zwinderman, A. H., Olivier, B. SSRIs and ejaculation: a double-blind, randomized, fixed-dose study with paroxetine and citalopram. J Clin Psychopharmacol 2001 Dec; 21: 556-60. (ProCite no. 795220)								
1	Baseline		6 weeks	15	21*			
	1	10 mg/day			34			
	2	20 mg/day			43			
	3	20 mg/day			40			
	4	20 mg/day			33			
	5	20 mg/day			44			
	6	20 mg/day			43			
	* Geometric means							

Appendix 3-B. Summary Tables: Clomipramine treatment studies

Treatment Groups	Treatment regimen			Number of Patients	Latency in Seconds			
	Week	Dosage	Treatment Duration		Mean	SD	Min	Max
Abdel-Hamid, I. A., El Naggar, E. A., El Gilany, A. H. Assessment of as needed use of pharmacotherapy and the pause-squeeze technique in premature ejaculation. Int J Impot Res. 2001 Feb; 13: 41-5. (ProCite no. 700014)								
1	Baseline			31	60		30	90
	Overall/ entire time period	25 mg 3-5 hrs before coitus, not > 2 x per week	4 weeks + 2 week washout	28	240		60	480
		Crossover design - 2-week washout period						
Althof, S. E., Levine, S. B., Corty, E. W., Risen, C. B., Stern, E. B., Kurit, D. M. A double-blind crossover trial of clomipramine for rapid ejaculation in 15 couples. J Clin Psychiatry. 1995 Sep; 56: 402-7. (ProCite no. 12146)								
1	Baseline			15	81			
	Overall/ entire time period	1-4 week run-out period 3 intercourse attempts	1-4 weeks	15	80			
		Crossover design, time points vary to allow for normal pattern of intercourse attempts						
	Overall/ entire time period	25 mg/day for 2-7 weeks 5 intercourse attempts	2-7 weeks	15	202			
	Overall/ entire time period	50 mg/day for 2-7 weeks 5 intercourse attempts	2-7 weeks	15	419			
Kim, S. C., Seo, K. K. Efficacy and safety of fluoxetine, sertraline and clomipramine in patients with premature ejaculation: a double-blind, placebo controlled study. J Urol 1998 Feb; 159: 425-7. (ProCite no. 12047)								
1	Baseline			53	46	41		
	Overall/ entire time period	25 mg/day for 1 week, 50 mg/day later	4 weeks	37	345	401		
		Crossover design - 4-week washout period						
Montorsi, F., Guazzoni, G., Trimboli, F., Rigatti, P., Pizzini, G., Miani, A. Clomipramine for premature ejaculation: a randomized, double blind, placebo controlled study. Acta Urol Ital. 1995; 1: 5-6. (ProCite no. 500007)								
1	Baseline							
	Overall/ entire time period	50 mg/day given at bedtime for 8 weeks (following 8 weeks placebo treatment)	8 weeks	17				
		Only efficacy outcome is 5 (29.4%) complete response, 6 (35.3%) partial response, 6 (35.3%) failure						
2	Baseline							
	Overall/ entire time period	50 mg/day given at bedtime for 8 weeks (presumably continued for at least 3 months)	8 weeks	16				
		Only efficacy outcome is 4 (25.0%) complete response, 4 (25.0%) partial response, 8 (50.0%) failure						

Appendix 3-B. Summary Tables: Clomipramine treatment studies

Treatment Groups	Treatment regimen			Number of Patients	Latency in Seconds			
	Week	Dosage	Treatment Duration		Mean	SD	Min	Max
Rowland, D. L., De Gouveia Brazao, C. A., Koos Slob, A. Effective daily treatment with clomipramine in men with premature ejaculation when 25 mg (as required) is ineffective. BJU Int. 2001 Mar; 87: 357-60. (ProCite no. 795018)								
1	Baseline		9 weeks	4	26			
	3	1 mg/day for 3 weeks then 20 mg/day for 3 weeks*		4	51			
	6	1 mg/day for 3 weeks then 20 mg/day for 3 weeks		4	92			
	9	1 mg/day for 3 weeks then 20 mg/day for 3 weeks		4	221			
	These are patients who failed 25 mg clomipramine PRN * This value is a median from a graph							
Segraves, R. T., Saran, A., Segraves, K., Maguire, E. Clomipramine versus placebo in the treatment of premature ejaculation: a pilot study. J Sex Marital Ther. 1993 Fall; 19: 198-200. (ProCite no. 12219)								
1	Overall/ entire time period	25 mg 6 hrs prior to coitus, could double dose to 50 mg after 2 attempts at coitus and no side effects	10 attempts at coitus	10	366			
Strassberg, D. S., de Gouveia Brazao, C. A., Rowland, D. L., Tan, P., Slob, A. K. Clomipramine in the treatment of rapid (premature) ejaculation. J Sex Marital Ther 1999;25:89-101. (ProCite no. 12022)								
1	Overall/ entire time period	25 mg 4 hrs precoitus	2 weeks	22	229	286		
	PE patients – crossover design, no washout – 2 weeks drug, then 2 weeks placebo and vice-versa							
2	Overall/ entire time period	25 mg 4 hrs precoitus	2 weeks	4	665	307		
	Normal controls - crossover design, no washout period - 2 weeks drug, then 2 weeks placebo and vice-versa							

Appendix 3-C. Summary Tables: Fluoxetine treatment studies

Treatment Groups	Treatment regimen			Number of Patients	Latency in Seconds			
	Week	Dosage	Treatment Duration		Mean	SD	Min	Max
Atan, A., Basar, M. M., Aydoganli, L. Comparison of the efficacy of fluoxetine alone vs. fluoxetine plus local lidocaine ointment in the treatment of premature ejaculation. Arch Esp Urol. 2000 Nov; 53: 856-8. (ProCite no. 795257)								
1	7	20 mg/day for 1 week, 40 mg/day later	7 weeks	26				
		Only efficacy outcome is 8 (30.8%) cured, 11 (42.3%) improved, 7 (26.9%) failed						
Haensel, SM, Klem, Tmal, Hop, WJC and Slob, AK Fluoxetine and Premature Ejaculation. J Clinical Psychopharmacology. 1998; 18: 1-6. (ProCite no. 900017)								
1	Baseline (pts with PE only)		4 weeks	9	73	22		
	Overall/ entire time period	5 mg/day for 2 weeks, 10 mg/day for 2 weeks		9				
		(Latency increase 180% with Confidence Interval 80%-450%)						
2	Baseline (pts with ED only)		4 weeks	7	360	91		
	Overall/ entire time period	5 mg/day for 2 weeks, 10 mg/day for 2 weeks		7				
		(1/6 increase latency, 4/6 decrease)						
3	Baseline (pts with ED and PE)		4 weeks	9	89	22		
	Overall/ entire time period	5 mg/day for 2 weeks, 10 mg/day for 2 weeks		9				
		(6/8 increase latency, 1/8 decrease, 1/8 no change)						
4	Baseline (Normal controls)		4 weeks	15	535	116		
	Overall/ entire time period	5 mg/day for 2 weeks, 10 mg/day for 2 weeks		15				
		(7/15 increase latency, 8/15 decrease latency)						
		All groups had Fluoxetine and Placebo in random order – 4-week washout period						
Kara, H., Aydin, S., Yucel, M., Agargun, M. Y., Odabas, O., Yilmaz, Y. The efficacy of fluoxetine in the treatment of premature ejaculation: a double-blind placebo controlled study. J Urol. 1996 Nov; 156: 1631-2. (ProCite no. 12110)								
1	Baseline		4 weeks	9	25	13		
	4	20 mg/day for 1 week, 40 mg/day later		7	180	100		
Kim, S. C., Seo, K. K. Efficacy and safety of fluoxetine, sertraline and clomipramine in patients with premature ejaculation: a double-blind, placebo controlled study. J Urol 1998 Feb;159: 425-7. (ProCite no. 12047)								
2	Baseline		4 weeks	53	46	41		
	Overall/ entire time period	20 mg/day for 1 week, 40 mg/day later		37	138	125		
		Crossover design - 4-week washout period						
Lee, H. S., Song, D. H., Kim, C. H., Choi, H. K. An open clinical trial of fluoxetine in the treatment of premature ejaculation. J Clin Psychopharmacol. 1996 Oct; 16: 379-82. (ProCite no. 12112)								
1	Baseline		8 weeks	14	55	3		
	8	20 mg/day for 1-2 weeks, titrated to 60 mg/day later		11	578	420		
		2 week washout before active drug						

Appendix 3-C. Summary Tables: Fluoxetine treatment studies

Treatment Groups	Treatment regimen			Number of Patients	Latency in Seconds			
	Week	Dosage	Treatment Duration		Mean	SD	Min	Max
Raju, G. A. R., Naidu, M. U. R., Ramesh T., Schobha, J. C. Evaluation of fluoxetine in premature ejaculation. Indian Journal of Pharmacology. 1997; 29: 204-5. (ProCite no. 500001).								
1	Baseline		4 weeks	44	10.7	4		
	Overall/ entire time period	20 mg/day in the morning for 4 weeks		44	3.2	2		
		Crossover design - 4-week washout period, Mean and SD – Total GRISS Score						
Waldinger, M. D., Hengeveld, M. W., Zwinderman, A. H., Olivier, B. Effect of SSRI antidepressants on ejaculation: a double-blind, randomized, placebo-controlled study with fluoxetine, fluvoxamine, paroxetine, and sertraline. J Clin Psychopharmacol. 1998 Aug; 18: 274-81. (ProCite no. 12044)								
1	Baseline		6 weeks	10	21	12		
	6	20 mg/day		10	211	251		
Yilmaz, U., Tatlisen, A., Turan, H., Arman, F., Ekmekcioglu, O. The effects of fluoxetine on several neurophysiological variables in patients with premature ejaculation. J Urol. 1999 Jan; 161: 107-11. (ProCite no. 12032)								
1	Baseline		4 weeks	20	72	60		
	4	20 mg/day for 1 week, 40 mg/day later		20	396	462		

Appendix 3-D. Summary Tables: Fluoxetine/Lidocaine treatment studies

Treatment Groups	Treatment regimen			Number of Patients	Latency in Seconds			
	Week	Dosage	Treatment Duration		Mean	SD	Min	Max
Atan, A., Basar, M. M., Aydoganli, L. Comparison of the efficacy of fluoxetine alone vs. fluoxetine plus local lidocaine ointment in the treatment of premature ejaculation. Arch Esp Urol. 2000 Nov; 53: 856-8. (ProCite no. 795257)								
2	7	Fluoxetine 20 mg/day + local lidocaine cream	7 weeks	17				
Only efficacy outcome is 9 (52.9%) cured, 5 (29.4%) improved and 3 (17.6%) failed.								

Appendix 3-E. Summary Tables: Fluvoxamine treatment studies

Treatment Groups	Treatment regimen			Number of Patients	Latency in Seconds			
	Week	Dosage	Treatment Duration		Mean	SD	Min	Max
Waldinger, M. D., Hengeveld, M. W., Zwinderman, A. H., Olivier, B. Effect of SSRI antidepressants on ejaculation: a double-blind, randomized, placebo-controlled study with fluoxetine, fluvoxamine, paroxetine, and sertraline. J Clin Psychopharmacol. 1998 Aug; 18: 274-81. (ProCite no. 12044)								
2	Baseline		6 weeks	10	15	17		
	6	100 mg/day		10	55	70		

Appendix 3-F. Summary Tables: Nefazodone treatment studies

Treatment Groups	Treatment regimen			Number of Patients	Latency in Seconds			
	Week	Dosage	Treatment Duration		Mean	SD	Min	Max
Waldinger, M. D., Zwinderman, A. H., Olivier, B. Antidepressants and ejaculation: a double-blind, randomized, placebo- controlled, fixed-dose study with paroxetine, sertraline, and nefazodone. J Clin Psychopharmacol. 2001 Jun; 21: 293-7. (ProCite no. 795222)								
4	Baseline		6 weeks	12	17*			
	1	400 mg/day morning and evening			19			
	2	400 mg/day morning and evening			14			
	3	400 mg/day morning and evening			26			
	4	400 mg/day morning and evening			28			
	5	400 mg/day morning and evening			16			
	6	400 mg/day morning and evening			18			
		* Geometric means						

Appendix 3-G. Summary Tables: Paroxetine treatment studies

Treatment Groups	Treatment regimen			Number of Patients	Latency in Seconds			
	Week	Dosage	Treatment Duration		Mean	SD	Min	Max
Abdel-Hamid, I. A., El Naggar, E. A., El Gilany, A. H. Assessment of as needed use of pharmacotherapy and the pause-squeeze technique in premature ejaculation. Int J Impot Res. 2001 Feb; 13: 41-5. (ProCite no. 700014)								
2	Baseline			31	60		30	90
	Overall/ entire time period	20 mg 3-5 hrs before coitus, not > 2 x per week	4 weeks + 2 week washout	29	240		120	600
		Crossover design - 2-week washout period						
Ludovico, G. M., Corvasce, A., Pagliarulo, G., Cirillo-Marucco, E., Marano, A., Pagliarulo, A. Paroxetine in the treatment of premature ejaculation. Br J Urol. 1996 Jun; 77: 881-2. (ProCite no. 12118)								
1	Baseline (latency < 1 min.)		2 months	32				
	8	20 mg/day		32			900	1200
McMahon, C. G., Touma, K. Treatment of premature ejaculation with paroxetine hydrochloride. Int J Impot Res. 1999 Oct; 11: 241-245; discussion 246. (ProCite no. 12005)								
1	Baseline			61	24			
	4	20 mg/day	4 weeks	61	270			
	8	20 mg single dose 3-4 hrs precoitus	4 weeks	53*	234			
		* Only included responders to first 4-week trial						
2	Baseline			33	24			
	4	20 mg single dose 3-4 hrs precoitus	4 weeks	33	90			
McMahon, C. G., Touma, K. Treatment of premature ejaculation with paroxetine hydrochloride as needed: 2 single-blind placebo controlled crossover studies. J Urol. 1999 Jun; 161: 1826-30. (ProCite no. 12020)								
Study a								
1a	Baseline			13	18			
		Crossover design - drug, 3-week washout, then placebo						
	4	20 mg single dose 3-4 hrs precoitus	4 weeks	13	192			
2a	11	20 mg single dose 3-4 hrs precoitus	4 weeks	13	210			
Study b								
1b	Baseline			21	30			
	3	10 mg/day	3 weeks	21	258			
	7	20 mg single dose 3-4 hrs precoitus	4 weeks	21	348			
2b	13	3-week washout, then 20 mg/day for 3 weeks	6 weeks	21	198			
	17	20 mg single dose 3-4 hrs precoitus	4 weeks	21	366			

Appendix 3-G. Summary Tables: Paroxetine treatment studies

Treatment Groups	Treatment regimen			Number of Patients	Latency in Seconds			
	Week	Dosage	Treatment Duration		Mean	SD	Min	Max
Salonia, A., Maga, T., Columbo, R., Scattoni, V., Briganti, A., Cestari, A., Guazzoni, G., Rigati, P., Montorsi, F. A prospective study comparing paroxetine alone versus paroxetine plus sildenafil in patients with premature ejaculation. J Urol. 2002 Dec; 168: 2486-9. (ProCite no. 500005)								
1	Baseline			40	.33	.04		
	12	10 mg/day for 21 days, followed by 20 mg 3-4 hrs before intercourse	3 months	40	3.7	.10		
	24	10 mg/day for 21 days, followed by 20 mg 3-4 hrs before intercourse	6 months	40	4.2	.03		
2	Baseline			40	.35	.05		
	12	10 mg/day paroxetine for 21 days, followed by 20 mg 3-4 hrs plus 50 mg sildenafil before intercourse	3 months	40	4.5	.07		
	24	10 mg/day paroxetine for 21 days, followed by 20 mg 3-4 hrs plus 50 mg sildenafil before intercourse	6 months	40	5.3	.02		
Waldinger, M. D., Zwinderman, A. H., Olivier, B. SSRIs and ejaculation: a double-blind, randomized, fixed-dose study with paroxetine and citalopram. J Clin Psychopharmacol 2001 Dec; 21: 556-60. (ProCite no. 795220)								
1	Baseline		6 weeks	15	18*			
	1	20 mg/day			34			
	2	20 mg/day			57			
	3	20 mg/day			116			
	4	20 mg/day			141			
	5	20 mg/day			170			
	6	20 mg/day			152			
		* Geometric means						
Waldinger, M. D., Zwinderman, A. H., Olivier, B. Antidepressants and ejaculation: a double-blind, randomized, placebo- controlled, fixed-dose study with paroxetine, sertraline, and nefazodone. J Clin Psychopharmacol. 2001 Jun; 21: 293-7. (ProCite no. 795222)								
2	Baseline		6 weeks	12	17*			
	1	20 mg/day morning and evening			37			
	2	20 mg/day morning and evening			71			
	3	20 mg/day morning and evening			119			
	4	20 mg/day morning and evening			88			
	5	20 mg/day morning and evening			146			
	6	20 mg/day morning and evening			108			
		* Geometric means						

Appendix 3-G. Summary Tables: Paroxetine treatment studies

Treatment Groups	Treatment regimen			Number of Patients	Latency in Seconds			
	Week	Dosage	Treatment Duration		Mean	SD	Min	Max
Waldinger, M. D., Hengeveld, M. W., Zwinderman, A. H., Olivier, B. Effect of SSRI antidepressants on ejaculation: a double-blind, randomized, placebo-controlled study with fluoxetine, fluvoxamine, paroxetine, and sertraline. J Clin Psychopharmacol. 1998 Aug; 18: 274-81. (ProCite no. 12044)								
Study a								
3a	Baseline		6 weeks	11	16	10		
	6	20 mg/day		11	476	1146		
Study b								
1b	Baseline (BL < 60 sec)		6 weeks	12	18	13		
	6	20 mg/day		11	92			
		(latency increase 580%)						
3b	Baseline (BL > 60 sec)		6 weeks	5	82	27		
	6	20 mg/day		5	602			
		(latency increase 596%)						
Waldinger, M. D., Hengeveld, M. W., Zwinderman, A. H. Ejaculation-retarding properties of paroxetine in patients with primary premature ejaculation: a double-blind, randomized, dose-response study. Br J Urol. 1997 Apr; 79: 592-5. (ProCite no. 12088)								
1	Baseline		8 weeks	17	13			
	3	20 mg/day		14	300			
	8	20 mg/day		14	300			
2	Baseline		8 weeks	17	10			
	3	20 mg/day		13	240			
	8	20 mg/day		13	540			
Waldinger, M. D., Hengeveld, M. W., Zwinderman, A. H. Paroxetine treatment of premature ejaculation: a double-blind, randomized, placebo-controlled study. Am J Psychiatry. 1994 Sep; 151: 1377-9. (ProCite no. 12172)								
1	Baseline		6 weeks	8	30			
	3	20 mg/day for 1 week, 40 mg/day for 5 weeks		8	450		180	1200
	6	20 mg/day for 1 week, 40 mg/day for 5 weeks		8	600		300	1200
		Latency assessed by patient						

Appendix 3-H. Summary Tables: Pause/Squeeze treatment studies

Treatment Groups	Treatment regimen			Number of Patients	Latency in Seconds			
	Week	Dosage	Treatment Duration		Mean	SD	Min	Max
Abdel-Hamid, I. A., El Naggar, E. A., El Gilany, A. H. Assessment of as needed use of pharmacotherapy and the pause-squeeze technique in premature ejaculation. Int J Impot Res. 2001 Feb; 13: 41-5. (ProCite no. 700014)								
5	Baseline			31	60		30	90
	Overall/ entire time period		4 weeks + 2 week washout	29	180		60	420
		Crossover design – 2-week washout period (Study unclear about washout period for this group)						

Appendix 3-I. Summary Tables: Phenoxybenzamine treatment studies

Treatment Groups	Treatment regimen			Number of Patients	Latency in Seconds			
	Week	Dosage	Treatment Duration		Mean	SD	Min	Max
Beretta, G., Chelo, E., Fanciullacci, F., Zanollo, A. Effect of an alpha-blocking agent (phenoxybenzamine) in the management of premature ejaculation. Acta Europaea Fertilitatis. 1986 Jan-Feb; 17: 43-5. (ProCite no. 12350)								
1	Baseline			8	83			
	Overall/ entire time period	10 mg/day		8	338			

Appendix 3-J. Summary Tables: Placebo treatment studies

Treatment Groups	Treatment regimen			Number of Patients	Latency in Seconds			
	Week	Dosage	Treatment Duration		Mean	SD	Min	Max
Althof, S. E., Levine, S. B., Corty, E. W., Risen, C. B., Stern, E. B., Kurit, D. M. A double-blind crossover trial of clomipramine for rapid ejaculation in 15 couples. J Clin Psychiatry. 1995 Sep; 56: 402-7. (ProCite no. 12146)								
1	Overall/ entire time period	1 capsule/day for 2-7 weeks – 5 intercourse attempts	2-7 weeks	15	137			
		Crossover design, time points vary to allow for normal pattern of intercourse attempts						
Biri, H., Isen, K., Sinik, Z., Onaran, M., Kupeli, B., Bozkirli, I. Sertraline in the treatment of premature ejaculation: a double-blind placebo controlled study. Int Urol Nephrol. 1998; 30: 611-5. (ProCite no. 12033)								
2	Baseline		4 weeks	15	44	20		
	4	Placebo control		15	114	94		
Cooper, A. J., Magnus, R. V. A clinical trial of the beta blocker propranolol in premature ejaculation. J Psychosom Res. 1984; 28: 331-6. (ProCite no. 12387)								
1	Overall/ entire time period	Placebo	4 weeks	12	102			
Kara, H., Aydin, S., Yucel, M., Agargun, M. Y., Odabas, O., Yilmaz, Y. The efficacy of fluoxetine in the treatment of premature ejaculation: a double-blind placebo controlled study. J Urol. 1996 Nov; 156: 1631-2. (ProCite no. 12110)								
1	Baseline		4 weeks	8	30	9		
	4	1 capsule/day for 1 week, 2 capsule/day later		7	60	47		
Kim, S. C., Seo, K. K. Efficacy and safety of fluoxetine, sertraline and clomipramine in patients with premature ejaculation: a double-blind, placebo controlled study. J Urol 1998 Feb;159:425-7. (ProCite no. 12047)								
4	Baseline			53	46	41		
	Overall/ entire time period	1 capsule/day for 1 week, 2 capsule/day later	4 weeks	37	136	227		
		Crossover design - 4-week washout period						
Montorsi, F., Guazzoni, G., Trimboli, F., Rigatti, P., Pizzini, G., Miani, A. Clomipramine for premature ejaculation: a randomized, double blind, placebo controlled study. Acta Urol Ital. 1995; 1: 5-6. (ProCite no. 500007)								
1	Baseline							
	Overall/ entire time period	8 weeks placebo treatment	8 weeks	17				
		Only efficacy outcome is 1 (5.9%) complete response, 2 (11.8%) partial response, 14 (82.3%) failure						
McMahon, C. G., Touma, K. Treatment of premature ejaculation with paroxetine hydrochloride as needed: 2 single-blind placebo controlled crossover studies. J Urol. 1999 Jun; 161: 1826-30. (ProCite no. 12020)								
Study a								
1a	11	Placebo for 4 weeks after 3 week washout	4 weeks	13	27			
2a	Baseline			13	18			
	4	Placebo for 3 weeks, then 3 week washout	4 weeks	13	36			
Study b								
1b	13	3 week washout, then placebo daily for 3 weeks	6 weeks	21	54			
	17	Placebo 3-4 hours before coitus for 4 weeks	4 weeks	21	36			
2b	Baseline			21	30			
	3	Placebo daily for 3 weeks	3 weeks	21	48			
	7	Placebo 3-4 hours before coitus for 4 weeks	4 weeks	21	66			

Appendix 3-J. Summary Tables: Placebo treatment studies

Treatment Groups	Treatment regimen			Number of Patients	Latency in Seconds			
	Week	Dosage	Treatment Duration		Mean	SD	Min	Max
McMahon, C. G. Treatment of premature ejaculation with sertraline hydrochloride: a single-blind placebo controlled crossover study. J Urol. 1998 Jun; 159: 1935-8. (ProCite no. 12057)								
1	12	Placebo for 4 weeks, Crossover design - 4-week washout	4 weeks	19	30			
2	Baseline			18	18			
	4	End of placebo	4 weeks	18	30			
		Crossover design - 4-week washout						
	8	Washout for 4 weeks	4 weeks	18	30			
Mendels, J., Camera, A., Sikes, C. Sertraline treatment for premature ejaculation. J Clin Psychopharmacol. 1995 Oct; 15: 341-6. (ProCite no. 12139)								
2	Baseline		8 weeks	26	66	81		
	8	145 mg/day mean final dosage, 50 mg/day titrated to 200 mg/day during weeks 1-3		22	111	221		
Segraves, R. T., Saran, A., Segraves, K., Maguire, E. Clomipramine versus placebo in the treatment of premature ejaculation: a pilot study. J Sex Marital Ther. 1993 Fall; 19: 198-200. (ProCite no.12219)								
2	Overall/ entire time period	25 mg 6 hrs prior to coitus	10 attempts at coitus	10	51			
		(Could double dose to 50 mg after 2 attempts at coitus and no side effects)						
Strassberg, D. S., de Gouveia Brazao, C. A., Rowland, D. L., Tan, P., Slob, A. K. Clomipramine in the treatment of rapid (premature) ejaculation. J Sex Marital Ther 1999; 25:89-101. (ProCite no. 12022)								
1	Overall/ entire time period	25 mg taken 4 hr precoitus	2 weeks	22	52	45		
		PE patients – crossover design, no washout – 2 weeks drug, then 2 weeks placebo and vice-versa						
2	Overall/ entire time period	25 mg taken 4 hr precoitus	2 weeks	4	491	245		
		Normal controls - crossover design, no washout period - 2 weeks drug, then 2 weeks placebo and vice-versa						
Waldinger, M. D., Zwinderman, A. H., Olivier, B. Antidepressants and ejaculation: a double-blind, randomized, placebo- controlled, fixed-dose study with paroxetine, sertraline, and nefazodone. J Clin Psychopharmacol. 2001 Jun; 21: 293-7. (ProCite no. 795222)								
1	Baseline		6 weeks	12	15*			
	1	Placebo morning and evening			21			
	2	Placebo morning and evening			19			
	3	Placebo morning and evening			19			
	4	Placebo morning and evening			24			
	5	Placebo morning and evening			19			
	6	Placebo morning and evening			18			
		* Geometric means						

Appendix 3-J. Summary Tables: Placebo treatment studies

Treatment Groups	Treatment regimen			Number of Patients	Latency in Seconds			
	Week	Dosage	Treatment Duration		Mean	SD	Min	Max
Waldinger, M. D., Hengeveld, M. W., Zwinderman, A. H., Olivier, B. Effect of SSRI antidepressants on ejaculation: a double-blind, randomized, placebo-controlled study with fluoxetine, fluvoxamine, paroxetine, and sertraline. J Clin Psychopharmacol. 1998 Aug; 18: 274-81. (ProCite no. 12044)								
Study a								
5a	Baseline			9	19	15		
	6	Placebo control	6 weeks	9	29	25		
Study b								
2b	Baseline			12	18			
	6	Placebo control	6 weeks	9				
		(no sig. increase in latency)						
4b	Baseline			3	82	27		
	6	Placebo control	6 weeks	2				
		(no sig. increase in latency)						
Waldinger, M. D., Hengeveld, M. W., Zwinderman, A. H. Paroxetine treatment of premature ejaculation: a double-blind, randomized, placebo-controlled study. Am J Psychiatry. 1994 Sep; 151: 1377-9. (ProCite no. 12172)								
2	Baseline		6 weeks	9	15		5	90
	3	1 capsule/day for 1 week, 2 capsule/day for 5 weeks		8	20		5	120
	6	1 capsule/day for 1 week, 2 capsule/day for 5 weeks		8	15		5	120
		Latency assessed by patient						
Yilmaz, U., Tatlisen, A., Turan, H., Arman, F., Ekmekcioglu, O. The effects of fluoxetine on several neurophysiological variables in patients with premature ejaculation. J Urol. 1999 Jan; 161: 107-11. (ProCite no. 12032)								
2	Baseline		4 weeks	20	66	78		
	4	Placebo control		20	288	60		

Appendix 3-K. Summary Tables: Propanolol treatment studies

Treatment Groups	Treatment regimen			Number of Patients	Latency in Seconds			
	Week	Dosage	Treatment Duration		Mean	SD	Min	Max
Cooper, A. J., Magnus, R. V. A clinical trial of the beta blocker propranolol in premature ejaculation. J Psychosom Res. 1984; 28: 331-6. (ProCite no. 12387)								
1	Baseline			12				
	4	Run-in period	4 weeks		90			
	8	Washout period	4 weeks		90			
	Overall/ entire time period	120 mg/day			102			

Appendix 3-L. Summary Tables: Sertraline treatment studies

Treatment Groups	Treatment regimen: Week	Dosage	Treatment Duration	Number of Patients	Latency in Seconds: Mean	SD	Min	Max
Abdel-Hamid, I. A., El Naggar, E. A., El Gilany, A. H. Assessment of as needed use of pharmacotherapy and the pause-squeeze technique in premature ejaculation. Int J Impot Res. 2001 Feb; 13: 41-5. (ProCite no. 700014)								
3	Baseline		4 weeks + 2 week washout	31	60		30	90
	Overall/ entire time period	50 mg/3-5 hrs before coitus, not > 2 x per week		29	180		60	600
		Crossover design - 2-week washout period						
Biri, H., Isen, K., Sinik, Z., Onaran, M., Kupeli, B., Bozkirli, I. Sertraline in the treatment of premature ejaculation: a double-blind placebo controlled study. Int Urol Nephrol. 1998; 30: 611-5. (ProCite no. 12033)								
1	Baseline		4 weeks	22	41	13		
	4	50 mg/day		22	325	262		
Chia, S. J. Management of premature ejaculation - a comparison of treatment outcome in patients with and without erectile dysfunction. Int J Androl. 2002; 25: 301-5. (ProCite no. 500002)								
1	Baseline (pts with primary PE)		6 months	52	46			
	Overall/ entire time period	50 mg 4 hours prior to intercourse for 6 months		52	247.2			
2	Baseline (pts with ED only)		6 months	35	34.6			
	Overall/ entire time period	50 mg 4 hours prior to intercourse for 6 months		35	111.6			
		(Pts with ED treated successfully with sildenafil. Pts with PE prior to ED excluded)						
Kim, S. W., Paick, J. S. Short-term analysis of the effects of as needed use of sertraline at 5 PM for the treatment of premature ejaculation. Urology. 1999 Sep; 54: 544-7. (ProCite no. 12013)								
1	Baseline			18	23	19		
	2	50 mg/day	2 weeks		354	252		
	4	50 mg/day at 5 pm on days when intercourse planned, dose titrated to 100 mg in week 3 if needed	2 weeks		306	228		
	6	50 mg/day at 5 pm on days when intercourse planned	2 weeks		270	162		
Kim, S. C., Seo, K. K. Efficacy and safety of fluoxetine, sertraline and clomipramine in patients with premature ejaculation: a double-blind, placebo controlled study. J Urol. 1998 Feb; 159: 425-7. (ProCite no. 12047)								
3	Baseline			53	46	41		
	Overall/ entire time period	50 mg/day for 1 week, 100 mg/day later	4 weeks	37	256	341		
		Crossover design - 4-week washout period						
McMahon, C. G. Treatment of premature ejaculation with sertraline hydrochloride. Int J Impot Res. 1998 Sep; 10: 181-4; discussion 185. (ProCite no. 12037)								
1	Baseline		15 weeks	46	60		0	300
	3	25 mg/day			456		0	1200
	6	Washout						
	9	50 mg/day (4 pts w anejaculation)			786		420	
	12	Washout						
	15	100 mg/day (10 pts w anejaculation)			984		420	

Appendix 3-L. Summary Tables: Sertraline treatment studies

Treatment Groups	Treatment regimen			Number of Patients	Latency in Seconds			
	Week	Dosage	Treatment Duration		Mean	SD	Min	Max
McMahon, C. G. Treatment of premature ejaculation with sertraline hydrochloride: a single-blind placebo controlled crossover study. J Urol. 1998 Jun; 159: 1935-8. (ProCite no. 12057)								
1	Baseline		4 weeks	19	18			
	4	50 mg/day		19	204			
	8	Washout		19	36			
2	12	50 mg/day		18	180			
		Crossover design - 4-week washout period						
Mendels, J., Camera, A., Sikes, C. Sertraline treatment for premature ejaculation. J Clin Psychopharmacol. 1995 Oct; 15: 341-6. (ProCite no. 12139)								
1	Baseline		8 weeks	26	59	69		
	8	121 mg/day mean final dosage		22	326	337		
		* 50 mg/day titrated to 200 mg/day during weeks 1-3						
Waldinger, M. D., Zwinderman, A. H., Olivier, B. Antidepressants and ejaculation: a double-blind, randomized, placebo- controlled, fixed-dose study with paroxetine, sertraline, and nefazodone. J Clin Psychopharmacol. 2001 Jun; 21: 293-7. (ProCite no. 795222)								
3	Baseline		6 weeks	12	14*			
	1	50 mg/day morning and evening			25			
	2	50 mg/day morning and evening			39			
	3	50 mg/day morning and evening			34			
	4	50 mg/day morning and evening			43			
	5	50 mg/day morning and evening			58			
	6	50 mg/day morning and evening			50			
		* Geometric means						
Waldinger, M. D., Hengeveld, M. W., Zwinderman, A. H., Olivier, B. Effect of SSRI antidepressants on ejaculation: a double-blind, randomized, placebo-controlled study with fluoxetine, fluvoxamine, paroxetine, and sertraline. J Clin Psychopharmacol. 1998 Aug; 18: 274-8. (ProCite no. 12044)								
4	Baseline		6 weeks	11	21	12		
	6	50 mg/day		11	117	87		

Appendix 3-M. Summary Tables: Sildenafil treatment studies

Treatment Groups	Treatment regimen			Number of Patients	Latency in Seconds			
	Week	Dosage	Treatment Duration		Mean	SD	Min	Max
Abdel-Hamid, I. A., El Naggar, E. A., El Gilany, A. H. Assessment of as needed use of pharmacotherapy and the pause-squeeze technique in premature ejaculation. Int J Impot Res. 2001 Feb; 13: 41-5. (ProCite no. 700014)								
4	Baseline		4 weeks + 2 week washout	31	60		30	90
	Overall/ entire time period	50 mg 3-5 hrs before coitus, not > 2 x per week		29	900		300	1800
		Crossover design – 2-week washout period						
Salonia, A., Maga, T., Columbo, R., Scattoni, V., Briganti, A., Cestari, A., Guazzoni, G., Rigati, P., Montorsi, F. A prospective study comparing paroxetine alone versus paroxetine plus sildenafil in patients with premature ejaculation. J Urol. 2002 Dec; 168: 2486-9. (ProCite no. 500005)								
2	Baseline			40	.35	.05		
	12	10 mg/day paroxetine for 21 days, followed by 20 mg 3-4 hrs plus 50 mg sildenafil before intercourse	3 months	40	4.5	.07		
	24	10 mg/day paroxetine for 21 days, followed by 20 mg 3-4 hrs plus 50 mg sildenafil before intercourse	6 months	40	5.3	.02		

Appendix 3-N. Summary Tables: Topical anesthetic treatment studies

Treatment Groups	Treatment regimen			Number of Patients	Latency in Seconds			
	Week	Dosage	Treatment Duration		Mean	SD	Min	Max
Atikeler, M. K., Gecit, I., Senol, F. A. Optimum usage of priocaine-lidocaine cream in premature ejaculation. Adnrologia. 2002; 34: 356-9. (ProCite no. 500006)								
	Baseline		Used at least five times (range 5-9)	40	< 1 min			
1	Overall/ entire time period	Placebo cream		10	1.01 min			
2	Overall/ entire time period	Prilocaine-lidocaine cream applied and left in place under a condom for 20 min and removed		10	6.5 min			
3	Overall/ entire time period	Prilocaine-lidocaine cream applied and left in place under a condom for 30 min and removed		10	8.71 min *			
4	Overall/ entire time period	Prilocaine-lidocaine cream applied and left in place under a condom for 45 min and removed		10	**			
*Group 3 - Mean latency 8.71 min in 4 patients, 6 patients complained of erection loss due to numbness and delayed ejaculation ** Group 4 - All patients complained of erection loss due to numbness and delayed ejaculation								
Slob, A. K., van Berkel, A., van der Werff ten Bosch, J. J. Premature ejaculation by local penile anesthsia in an uncontrolled clinical replication study. J Sex Res. 2000 Aug; 37: 244-7. (ProCite no. 500003)								
1	Baseline			15	1-2 min			
	Overall/ entire time period	Lidocaine-prilocaine cream (1/2 tube) applied for 10 min contained with condom, then removed.	Patients given 5 tubes and 12 condoms.		489	465		
		3 pts reported inability to reach orgasm on some occasions with cream						
	Overall/ entire time period	Coitus without cream or intervention.	Patients asked to report on 2-3 encounters.		115	142		
		No patients reported inability to reach orgasm						

Appendix 4. Summary Tables:

Articles Selected for Review: Sorted by Author

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Appendix 4. Summary Tables:

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Appendix 5. Summary Tables:

Articles Selected for Review: Sorted by ProCite Reference Number

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