Complementary and Alternative Medicine for Management of Premature Ejaculation: A Systematic Review

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ABSTRACT

Introduction: Premature ejaculation (PE) is defined as ejaculation within 1 minute (lifelong PE) or 3 minutes (acquired PE), inability to delay ejaculation, and negative personal consequences. Management includes behavioral and pharmacologic approaches.

Aim: To systematically review effectiveness, safety, and robustness of evidence for complementary and alternative medicine in managing PE.

Methods: Nine databases including Medline were searched through September 2015. Randomized controlled trials evaluating complementary and alternative medicine for PE were included.

Main Outcome Measures: Studies were included if they reported on intravaginal ejaculatory latency time (IELT) and/or another validated PE measurement. Adverse effects were summarized.

Results: Ten randomized controlled trials were included. Two assessed acupuncture, five assessed Chinese herbal medicine, one assessed Ayurvedic herbal medicine, and two assessed topical “severance secret” cream. Risk of bias was unclear in all studies because of unclear allocation concealment or blinding, and only five studies reported stopwatch-measured IELT. Acupuncture slightly increased IELT over placebo in one study (mean difference [MD] = 0.55 minute, \( P = .001 \)). In another study, Ayurvedic herbal medicine slightly increased IELT over placebo (MD = 0.80 minute, \( P = .001 \)). Topical severance secret cream increased IELT over placebo in two studies (MD = 8.60 minutes, \( P < .001 \)), although inclusion criteria were broad (IELT < 3 minutes). Three studies comparing Chinese herbal medicine with selective serotonin reuptake inhibitors (SSRIs) favored SSRIs (MD = 1.01 minutes, \( P = .02 \)). However, combination treatment with Chinese medicine plus SSRIs improved IELT over SSRIs alone (two studies; MD = 1.92 minutes, \( P < .00001 \)) and over Chinese medicine alone (two studies; MD = 2.52 minutes, \( P < .00001 \)). Adverse effects were not consistently assessed but where reported were generally mild.

Conclusion: There is preliminary evidence for the effectiveness of acupuncture, Chinese herbal medicine, Ayurvedic herbal medicine, and topical severance secret cream in improving IELT and other outcomes. However, results are based on clinically heterogeneous studies of unclear quality. There are sparse data on adverse effects or potential for drug interactions. Further well-conducted randomized controlled trials would be valuable.

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INTRODUCTION

Premature ejaculation (PE) in men is characterized by short ejaculatory latency during intercourse. PE can be lifelong (primary; present since first sexual experiences) or acquired (secondary; beginning later). The International Society for Sexual Medicine (ISSM; 2014) defines PE as a combination of (i) ejaculation usually occurring within approximately 1 minute of vaginal penetration (for lifelong PE) or a clinically significant decrease in latency time, often to no longer than approximately 3 minutes (for acquired PE);
(ii) inability to delay ejaculation; and (iii) negative personal consequences such as distress, bother, frustration, and/or avoidance of sexual intimacy. PE has also been defined by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (2013) as ejaculation usually occurring within approximately 1 minute of vaginal penetration and before the individual wishes it and causing clinically significant distress. Estimating the prevalence of PE is not straightforward because of the difficulty in defining what constitutes clinically relevant PE. Surveys have estimated the prevalence of self-reported early ejaculation as 20% to 30%. However, these estimates are likely to include men who have some concern about their ejaculatory function but do not meet the current diagnostic criteria for PE. It has been suggested that the prevalence of lifelong PE according to the ISSM and the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition definitions (with an ejaculatory latency of approximately 1 minute) is unlikely to exceed 4%. Men with PE are more likely to report lower levels of sexual functioning and satisfaction and higher levels of personal distress and interpersonal difficulty than men without PE. They also might rate their overall quality of life as lower than that of men without PE. In addition, their partner’s satisfaction with the sexual relationship has been reported to decrease with increasing severity of the condition.

Management of PE can involve a range of interventions. These include systemic drug treatments such as selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants, phosphodiesterase type 5 inhibitors, and analgesics and topical anesthetic creams and sprays that are applied directly to the penis shortly before intercourse. Behavioral therapies also can be useful. These can include psychosexual or relationship counseling for men and/or couples to address psychological and interpersonal issues that could be contributing to PE. Behavioral therapies also can include physical techniques to help men develop sexual skills to delay ejaculation and improve sexual self-confidence, such as the “stop-start” technique, “squeeze” technique, and sensate focus. There are sparse data on whether and for how long effectiveness is maintained after cessation of treatment (drug or behavioral) and whether repeat treatments are effective. Many interventions currently used for PE are not approved for this use, and men might choose to self-treat, with several remedies being available through the internet. Some complementary and alternative medicines (CAMs) have been evaluated in randomized controlled trials (RCTs) for the management of PE. However, there are no existing systematic reviews evaluating CAMs for management of PE. Our aim was to systematically review the effectiveness, safety, and robustness of evidence for CAM therapies in the management of PE.

METHODS

Review Methods

This work was undertaken as part of a systematic review for the UK National Institute for Health Research Health Technology Assessment Programme, which assessed a wide range of interventions for management of PE. The review followed the general principles recommended in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The review protocol is available from the Health Technology Assessment Programme website and is registered on the PROSPERO database (registration number CRD42013005289). The PRISMA checklist is provided in Supplementary Appendix 3.

Definition of CAM

CAM has been defined by the Cochrane Collaboration as “a broad domain of healing resources that encompasses all health systems, modalities, and practices and their accompanying theories and beliefs, other than those intrinsic to the politically dominant health system of a particular society or culture in a given historical period.” In addition, many CAM therapies are based on a traditional model of health and well-being, and many (although not all) are designed to treat the whole patient as opposed to a specific condition, whereas some (although not all) involve the use of traditional or natural therapies. Therefore, CAM is defined in this study as therapies for PE that have typically not been provided within conventional Western health care systems and that appear on the list of CAM therapies collated by the Cochrane Collaboration.

Literature Searches

The following databases were searched from inception to September 2015: Medline; Embase; Cumulative Index to Nursing and Allied Health Literature (CINAHL); the Cochrane Library including the Cochrane Systematic Reviews Database (CDSR), the Cochrane Controlled Trials Register (CCRT), the Database of Abstracts of Reviews of Effects (DARE), and the Health Technology Assessment database; the ISI Web of Science including the Science Citation Index and the Conference Proceedings Citation Index—Science. The Medline search strategy is provided in Appendix 1. The search strategy was designed to identify any articles tagged with the Medical Subject Headings ejaculation or premature ejaculation plus articles whose title or abstract included one of the terms premature, early, or rapid within three words of ejaculation or climax or the term ejaculation praecox/precox. These were combined with search filters to identify RCTs, reviews, and guidelines. It should be noted that the search was undertaken as part of a wider project assessing different treatments for PE, and for this reason the search was not specific to complementary therapies. The US Food and Drug Administration website and the European Medicines Agency website also were searched. Existing systematic reviews and relevant studies also were checked for eligible studies.

Eligibility Criteria

RCTs were eligible for inclusion if they compared CAM therapies for management of PE against placebo, waitlist, no treatment, or another therapy or assessed combination treatment.
CAM is defined as therapies for PE that have typically not been provided within conventional Western health care systems and that appear on the list of CAM therapies collated by the Cochrane Collaboration.15

Studies were included if they reported intravaginal ejaculatory latency time (IELT) and/or any of the following PE outcome measurements:

- Premature Ejaculation Profile (PEP)16
- Index of Premature Ejaculation (IPE)17
- Premature Ejaculation Diagnostic Tool (PEDT)18
- Arabic Index of Premature Ejaculation (AIPE)19
- Chinese Index of Premature Ejaculation—5 (CIPE-5)20
- International Index of Erectile Function (IIEF)21

Five of these measurements (PEP, IPE, PEDT, AIPE, and CIPE) were referenced in the update of the ISSM PE guidelines.6 Of these, PEP and IPE have been validated as tools to measure changes in PE outcomes.16,17 and CIPE also has been evaluated as a PE outcome measurement.20 The PEDT and AIPE have been validated as tools for diagnosing PE18,19 and have been used as outcome measurements in PE trials. In addition, the IIEF was validated for measuring changes in outcomes in erectile dysfunction, but some dimensions overlap with PE and have been used to measure outcomes in PE studies.21 Adverse effects also were summarized. Poorly defined outcomes, such as “percentage of patients showing improvement,” were not included in this review.

Data Extraction and Synthesis

One reviewer performed data extraction of each study; all numerical data were checked by a second reviewer. Results were presented as forest plots where data permitted, and meta-analyses were undertaken using RevMan software.22 Assessment of publication bias by visual inspection of funnel plots was planned when at least 10 RCT comparisons were available.23

Assessment of Methodologic Quality of Studies

Methodologic quality of included RCTs was assessed using the Cochrane Collaboration risk-of-bias assessment criteria.24 Completeness of outcome data was considered low risk if the percentage of randomized participants excluded from the primary analysis was smaller than 30%.25 Selective reporting was considered low risk if IELT or ejaculatory latency was reported and all outcomes referred to in the study methods were reported. Overall risk of bias for each study was classed as “low” or “high” if they were rated as such for each of three key domains: allocation concealment, blinding of outcome assessment, and completeness of outcome data; otherwise, overall risk of bias was classed as “unclear.”

RESULTS

Quantity of Evidence

The searches identified 2,455 citations (as part of a wider project assessing different treatments for PE). Fourteen studies were examined at the full-text stage. Ten RCTs evaluating a complementary therapy for PE were included in the review.26—35 The PRISMA flowchart is presented in Appendix 2. The four studies excluded at the full-text stage are described below, with reasons for exclusion.

Characteristics of Included Studies

Details of the included study characteristics are presented in Table 1; details include specific acupuncture points and herbal remedies used. Two studies (one in Turkey26 and one in China27) assessed acupuncture provided daily for 4 weeks and twice weekly for 4 weeks, respectively. Each study used a set range of acupuncture points (with some overlap but some differences between studies). Five studies assessed a 2- to 8-week course of oral Chinese herbal medicine; all were conducted in China.28—32 One study conducted in India assessed Ayurvedic medicine (Indian herbal medicine) given for 2 months.33 Two Korean studies assessed four to five treatments with “severance secret” (SS) cream,34,35 an extract of nine natural products that is applied to the penis 1 hour before intercourse and washed off before intercourse. SS cream is believed to work by localized desensitizing effects to decrease penile hypersensitivity.34

The number of analyzed participants was 50 to 200 for all studies, with the mean and median numbers being 98. Comparators included placebo (four studies),26,29,33—35 treatment as usual (one study),32 an SSRI (five studies),26—29,31 and/or a combination of CAM and drug treatment (three studies).28,30,31 Nine of the 10 studies assessed IELT26,28—35; five by stopwatch,26,28,29,34,35 one by questionnaire,32 and three did not report the method of IELT assessment.30,31 Additional outcome measurements reported included the PEDT (three studies)26,28,29, the CIPE-5 (two studies)27,32, and the IIEF (one study).31

Three studies included men with lifelong PE,30,34,35 one included men with only acquired PE,28 four included men with lifelong PE and men with acquired PE,26,29,31,33 and two did not report this information.27,31 Participants had an IELT no longer than 1 minute (most or all the time) in two studies,28,33 an IELT no longer than 2 minutes (most or all the time) in five studies,26,29—32 an IELT no longer than 3 minutes in two studies,34,35 and IELT inclusion criteria were not reported in one study.27 In four studies, patient or partner satisfaction also had to be below 30% or below 50%.32—35 In some studies, the inclusion criteria were not consistent with the ISSM definition of PE. For example, one study of Chinese herbal medicine recruited men with acquired PE, but they had to have an IELT shorter than 1 minute in at least 50% of attempts28 (whereas the ISSM widens the definition of acquired PE to IELT ≤ 3 minutes36). Also, two studies of SS cream stated that participants had lifelong PE but were required only to have an IELT shorter than 3 minutes (plus patient or partner satisfaction below 30% or 50%)34,35 rather than no longer than 1 minute according to the ISSM definition of lifelong PE.5
| Study; country; center, n | Duration (n), IELT assessment | Treatments and comparators | CAM treatment details | PE definition | Lifelong and acquired |
|--------------------------|-------------------------------|-----------------------------|----------------------|---------------|----------------------|
| **Acupuncture**          |                               |                             |                      |               |                      |
| Sunay et al, 2011; Turkey; 1 | 4 wk (n = 90, a = 90), stopwatch | Acupuncture 2×/wk; paroxetine 20 mg/d; sham acupuncture 2× weekly | Acupuncture 2×/wk using points Zusanli (ST 36), Hegu (LI 4), Taixi (KI 3), Taichong (LR 3), Yintang (EX-HN 3), Zhongji (CV 3) | IELT ≤ 2 min in >70% of attempts | Lifelong 66%, acquired 34% |
| Chen, 2009; China; 1     | 4 wk (n = 111, a = 111), method NR | Acupuncture daily; citalopram 20 mg/d | Acupuncture: 2 groups of acupoints on alternate days: day 1, Xinshu (BL 15), Ganshu (BL 18), Pishu (BL 20), Shenshu (BL 23); day 2, Guanyuan (CV 4), Zhongji (CV 3), Sanyinjiao (SP 6), Taixi (KI 3), Taichong (LR 3) | NR | NR |
| **Chinese herbal medicine** |                               |                             |                      |               |                      |
| Li and Lu, 2015; China; 1 | 4 wk (n = 120, a = 119), stopwatch | Chinese medicine (Qilin pills) 6 g 2×/d; sertraline 50 mg/d; Chinese medicine + sertraline | Chinese medicine (Qilin pills) containing Chinese raspberry (fu pen zi), horny goat weed (yin yang huo), Polygonum multiflorum (he shou wu), Herba ecliptae (mo han lian), Cynomonium (suo yang), Astragalus (huang qi), Chinese yam (shan yao), immature tangerine peel (qing pi), mulberry fruit spike (sang shen), turmeric tuber (yu jin), Chinese red sage (dan shen), white peony root (bai shao) | IELT < 1 min in >50% of attempts + TCM definition of “secondary non-consolidated kidney qi PE” | Acquired (>3 mo) of attempts + TCM definition of “secondary non-consolidated kidney qi PE” |
| Xu et al, 2014; China; 1  | 8 wk (n = 218, a = 200), stopwatch | Chinese medicine (mycelium of Cordyceps sinensis C4); sertraline 50 mg/d | Chinese medicine (mycelium of Cordyceps sinensis C4) | IELT ≤ 2 min in ≥75% of attempts | Acquired and lifelong (n = NR) |
| Xu et al, 2012; China; 1  | 4 wk (n = 68, a = 68), method NR | Chinese medicine (Yimusake 50 mg/d); Chinese medicine + trazodone 50 mg/d | Chinese medicine (Yimusake 50 mg/d) | IELT < 2 min | Lifelong |
| Sun et al, 2010; China; 2 | 4 wk (n = 114, a = 114), method NR | Chinese medicine (Yimusake 1.5 g/d); fluoxetine 20 mg/d; Chinese medicine + fluoxetine | Chinese medicine (Yimusake 1.5 g/d) | IELT < 2 min | NR |

(continued)
| Study; country; center, n | Duration (n), IELT assessment | Treatments and comparators | CAM treatment details | PE definition | Lifelong and acquired |
|--------------------------|-------------------------------|----------------------------|----------------------|---------------|-----------------------|
| Song et al,32 2007; China; 2 | 15 d (n = 68, a = 68), questionnaire | Chinese medicine (Uighur) 2×/d; treatment as usual | Chinese medicine (Uighur) 2×/d | IELT ≤ 2 min, partner satisfaction < 50% | Acquired and lifelong (n = NR) |
| Ayurvedic herbal medicine | Kulkarni and Chandola,33 2013; India; 1 | 2 mo (n = 55, a = 50), method NR | Ayurvedic herbal medicine 2×/d + psychological counseling; placebo + psychological counseling | Ayurvedic herbal medicine 2×/d: Stambhanakaraka Yoga containing Tulsi beeja (Occimum sanctum Linn), Akarakaraha (Anacyclus pyrethrum Linn), Mishri (sugar) | IELT ≤ 1 min, partner satisfaction < 50% | Acquired and lifelong (n = NR) |
| Topical herbal SS cream | Choi et al,34 2000; Korea; 3 (crossover) | 5 applications (n = 125, a = 106), stopwatch | SS cream (0.20 g applied 1 h before intercourse); placebo | SS cream: extracts of 9 natural products applied to glans penis 1 h before intercourse and then washed off (Ginseng radix alba, Angelicae gigantis radix, Cistanches herba, Zanthoxyl fructus, Torlidis semen, Asiasari radix, Caryophylli flos, Cinnamonomi cortex, Bufonis venenum) | IELT < 3 min AND patient and partner satisfaction < 30% | Lifelong |
| Choi et al,35 1999; Korea; 1 (crossover) | 4 applications (1 of each dose; n = 73, a = 50), stopwatch | SS cream (0.05, 0.10, 0.15, or 0.20 g applied 1 h before intercourse); placebo | SS cream: extracts of 9 natural products as above | IELT < 3 min and/or patient satisfaction < 50% | Lifelong |

a = analyzed number; CAM = complementary and alternative medicine; IELT = intravaginal ejaculatory latency time; n = randomized number; NR = not reported; PE = premature ejaculation; SS = secret severance; TCM = traditional Chinese medicine.
Four studies were excluded at the full-text stage. Two studies of Chinese medicine were excluded because they did not report on IELT or any validated or widely used PE outcome measurement. A study of Ayurvedic herbal medicine was excluded because it was not randomized (patients self-selected to the intervention or control group) and the other study of Ayurvedic herbal medicine was excluded because it did not report on IELT or any validated or widely used PE outcome measurement.

### Risk of Bias in Included Studies

The risk of bias within included studies is presented in Table 2. Five studies reported the method of randomization, whereas the other five did not report the method but did state that the study was randomized. Allocation concealment was unclear in all studies. Blinding of participants and personnel was reported as being undertaking in five studies. Blinding of outcome assessment was unclear in all studies except one, which reported that this was blinded. All studies except one were considered at low risk of bias for completeness of outcome data, with eight studies including at least 90% of randomized patients in the primary analysis and the two studies of SS cream including 85% and 68%, respectively. All studies scored a low risk for selective reporting except for one that did not report on IELT. Of the nine studies reporting on IELT, this was measured by stopwatch in five studies, by questionnaire in one study, and the method of IELT assessment was not reported in three studies. In summary, all 10 studies were classed as having an overall unclear risk of bias because of unclear reporting of allocation concealment (all 10 studies) and unclear blinding of participants and personnel (five studies).

### Table 2. Risk of bias in included studies

| RCT; country | Random sequence generation | Allocation concealment | Blinding of participants and personnel | Blinding of outcome assessment | Completeness of outcome data* (n/N, % included in primary analysis) | Selective reporting† | Overall risk‡ |
|--------------|---------------------------|------------------------|----------------------------------------|-------------------------------|-------------------------------------------------|---------------------|--------------|
| Acupuncture  |                           |                        |                                        |                               |                                                 |                     |              |
| Sunay et al,26 2011; Turkey | Low                        | Unclear                | Low (partial blinding)               | Unclear                      | Low (90/90, 100%)                                 | Low                 | Unclear      |
| Chen,27 2009; China | Unclear                   | Unclear              | High                                  | Unclear                      | Low (111/111, 100%)                               | High (no IELT)     | Unclear      |
| Chinese herbal medicine |                           |                        |                                        |                               |                                                 |                     |              |
| Li and Lu,28 2015; China | Low                       | Unclear                | High                                  | Unclear                      | Low (119/120, 99%)                               | Low                 | Unclear      |
| Xu et al,29 2014; China | Low                       | Unclear                | Low (68/68, 100%)                    | Unclear                      | Low (200/218, 92%)                               | Low                 | Unclear      |
| Xu et al,30 2012; China | Unclear                   | Unclear                | High                                  | Unclear                      | Low (68/68, 100%)                                | Low                 | Unclear      |
| Sun et al,31 2010; China | Unclear                   | Unclear                | High                                  | Unclear                      | Low (114/114, 100%)                              | Low                 | Unclear      |
| Song et al,32 2007; China | Low                       | Unclear                | High                                  | Unclear                      | Low (68/68, 100%)                                | Low                 | Unclear      |
| Ayurvedic herbal medicine |                           |                        |                                        |                               |                                                 |                     |              |
| Kulkarni and Chandola,33 2013; India | Unclear                   | Unclear                | Low (50/55, 91%)                    | Unclear                      | Low                                             | Low                 | Unclear      |
| Topical herbal SS cream |                           |                        |                                        |                               |                                                 |                     |              |
| Choi et al,34 2000; Korea | Unclear                   | Unclear                | Low (106/125, 85%)                   | Unclear                      | Low                                             | Low                 | Unclear      |
| Choi et al,35 1999; Korea | Low                       | Unclear                | Low (50/73, 68%)                     | Low                           | High                                            | Low                 | Unclear      |

IELT = intravaginal ejaculatory latency time; SS = secret severance.

*Completeness of outcome data was classed as low risk if fewer than 30% randomized participants were excluded from the primary analysis.

†Selective reporting was classed as low risk if IELT or ejaculatory latency was reported and all outcomes referred to in study methods were reported.

‡Overall risk of bias was classified as low or high if rated as such for each of three key domains: allocation concealment, blinding of outcome assessment, and completeness of outcome data; otherwise, overall risk of bias was classed as unclear.
| Studies, n | Treatment | Comparator | Duration | Reference | Outcome | Participants, n | MD (95% CI), P value | Favors |
|-----------|-----------|------------|----------|-----------|---------|----------------|----------------------|--------|
|           |           |            |          |           |         |                |                      |        |
| Acu vs placebo |           |            |          |           |         |                |                      |        |
| 1         | Acu 2x/wk | Sham acu   | 4 wk     | Sunay 2011 | IELT (stopwatch) | 60       | MD = 0.55 (NR), .001 MD = NR (NR), .001 | Acu vs placebo |
|           |           |            |          |           | PEDT    | 60              |                      |        |
| Acu vs drug |           |            |          |           |         |                |                      |        |
| 2         | Acu 2x/wk | Paroxetine 20 mg/d | 4 wk | Sunay 2011 | IELT (stopwatch) | 60       | MD = −0.28 (NR), .001 MD = NR (NR), NS | Drug over acu |
|           |           |            |          |           | PEDT    | 60              |                      |        |
|           |           | Acu daily  | Citalopram 20 mg/d | 4 wk | Chen 2009 | CIPE-5 | 111       | MD = 1.44 (0.02 to 2.86), .05 | Acu over drug |
| CM vs TAU |           |            |          |           |         |                |                      |        |
| 1         | CM (Uighur 2x/d) | TAU | 15 d     | Song 2007 | IELT (questionnaire) | 68       | MD = 1.57 (1.11 to 2.03), .000001 CM over TAU |
|           |           |            |          |           | CIPE-5   | 68              |                      |        |
| CM vs drug |           |            |          |           |         |                |                      |        |
| 3         | CM (Qilin pills 6 g 2x/d) | Sertraline 50 mg/d | 4 wk | Li 2015 | IELT (stopwatch) | 79       | MD = −0.64 (−1.58 to −0.30), .18 Not sig (drug vs CM) |
|           |           |            |          |           | PEDT    | 79              |                      |        |
|           | CM (mycelium of cordyceps sinensis C4) | Sertraline 50 mg/d | 8 wk | Xu 2014 | IELT (stopwatch) | 200      | MD = −1.70 (−2.12 to −1.28), <.01 Not sig (drug vs CM) |
|           |           |            |          |           | PEDT    | 200             |                      |        |
| CM + drug vs drug alone |           |            |          |           |         |                |                      |        |
| 2         | CM (Qilin) + sertraline | Sertraline 50 mg/d | 4 wk | Li 2015 | IELT (stopwatch) | 79       | MD = 2.05 (0.83 to 3.27), .001 Combined over drug |
|           |           |            |          |           | PEDT    | 79              |                      |        |
|           | CM (Yimusake) + fluoxetine | Fluoxetine 20 mg/d | 4 wk | Sun 2010 | IELT (method NR) | 76       | MD = 1.90 (1.47 to 2.33), <.00001 Combined over drug |
|           |           |            |          |           | Satisfaction (IIEF) | 76       | MD = 3.00 (2.46 to 3.54), <.00001 Combined over drug |

(continued)
| Studies, n | Treatment | Comparator | Duration | Reference | Outcome | Participants, n | MD (95% CI), P value | Favors |
|-----------|-----------|------------|----------|-----------|---------|----------------|----------------------|--------|
| 3         | CM (Qilin) + sertraline | CM (Qilin 6 g 2x/d) | 4 wk     | Li 2015   | IELT (stopwatch) | 80 | MD = 2.69 (1.57 to 3.81), <.00001 | Combined over CM |
|           |           |            |          |           | PEDT | 80 | MD = 1.30 (0.63 to 1.97), .0001 | Combined over CM |
|           | CM (Yimusake) + fluoxetine | CM (Yimusake 1.5 g/d) | 4 wk     | Sun 2010  | IELT (method NR) | 76 | MD = 2.50 (2.08 to 2.92), <.00001 | Combined over CM |
|           |           |            |          |           | Satisfaction (IIEF) | 76 | MD = 3.90 (3.32 to 4.48), <.00001 | Combined over CM |
|           | CM (Yimusake 50 mg/d) + trazodone 50 mg/d | CM (Yimusake 50 mg/d) | 4 wk     | Xu 2012   | IELT (method NR) | 68 | MD = 0.08 (–0.19 to 0.35), .56 | Not sig (combined vs. CM) |
| 1         | Ayurvedic med + counselling | Placebo + counselling | 2 mo     | Kulkarni 2013 | IELT (method NR) | 50 | MD = 0.80 (0.32 to 1.28), .001 | Ayurveda + counselling over placebo + counselling |
| 2         | SS cream (0.2 g/h prior) | Placebo (crossover) | 5 app    | Choi 2000 | IELT (stopwatch) | 106 | MD = 8.47 (6.52 to 10.42), <.001 | SS cream over placebo |
|           | SS cream (0.2 g/h prior) | Placebo (crossover) | 1 app    | Choi 1999 | IELT (stopwatch) | 50 | MD = 8.79 (6.41 to 11.17), <.001 | SS cream over placebo |

**Acu** = acupuncture; **app** = applications; **CI** = confidence interval; **CIPE** = Chinese Index of Premature Ejaculation; **CM** = Chinese medicine; **IELT** = intra-vaginal ejaculatory latency time; **IIEF** = International Index of Erectile Function; **MD** = mean difference; **NR** = not reported; **PEDT** = Premature Ejaculation Diagnostic Tool; **TAU** = treatment as usual.
Assessment of Effectiveness and Safety

Effectiveness results are presented in Table 3 and adverse effects are presented in Table 4. Further details of effectiveness (including results data per study group) are presented in Table 5.

Acupuncture

Two RCTs (one in Turkey\textsuperscript{26} and one in China\textsuperscript{27}) assessed acupuncture provided daily for 4 weeks and twice weekly for 4 weeks, respectively. Each study used a standardized range of acupuncture points for all patients. There was some overlap, but also some differences, between the acupuncture points used in the two studies (Table 1). There were no studies of individualized acupuncture treatment (where different points are used per patient based on clinical examination).

One study compared acupuncture against sham acupuncture (N analyzed = 60) and reported a small but significant improvement in stopwatch-measured IELT for acupuncture over sham (mean difference (MD) = 0.55 minute, \(P = .001\)) and a significant improvement in PEDT score (\(P = .001\); Table 3).\textsuperscript{26} These two studies showed mixed results when comparing acupuncture against drug treatment with an SSRI (paroxetine or citalopram, each given daily for 4 weeks),\textsuperscript{26,27} with IELT favoring drug treatment in the one study reporting this (N = 60; MD = −0.28, \(P = .001\)),\textsuperscript{26} a PEDT score showing no

### Table 4. Adverse effects

| Study, country, duration (n) | Treatments | AEs |
|-----------------------------|------------|-----|
| **Acupuncture**             |            |     |
| Sunay et al,\textsuperscript{26} 2011, Turkey, 4 wk (n = 90, a = 90) | Acupuncture 2×/wk, paroxetine 20 mg/d, sham acupuncture 2×/wk | No AEs observed (although no formal evaluation of AEs) |
| Chen,\textsuperscript{27} 2009, China, 4 wk (n = 111, a = 111) | Acupuncture daily, citalopram 20 mg/d | NR |
| **Chinese herbal medicine** |            |     |
| Li and Lu,\textsuperscript{28} 2015, China, 4 wk (n = 120, a = 119) | CM (Qilin pills 6 g 2×/d), sertraline 50 mg/d | CM: no AEs reported Sertraline: mild transient AEs (gastrointestinal discomfort in 3, headache and dizziness in 2); 1 patient receiving only sertraline discontinued because of erectile dysfunction |
| Xu et al,\textsuperscript{29} 2014, China, 8 wk (n = 218, a = 200) | CM (mycelium of Cordyceps sinensis C4), sertraline 50 mg/d | CM: 7/61 (11.5%) developed mild AEs (dizziness in 2, decreased libido in 1, gastrointestinal discomfort in 4), no discontinuations Sertraline: 52/157 (33.1) developed mild AEs (dizziness in 30, decreased libido in 12, other); 3/157 (1.9%) discontinued because of severe dizziness |
| Xu et al,\textsuperscript{30} 2012, China, 4 wk (n = 68, a = 68) | CM (Yimusake 50 mg/d), CM + trazodone 50 mg/d | CM alone: no AEs CM + trazodone: minor AEs (headache in 2, dry mouth in 1, constipation in 1) |
| Sun et al,\textsuperscript{31} 2010, China, 4 wk (n = 114, a = 114) | CM (Yimusake 1.5 g/d), fluoxetine 20 mg/d, CM + fluoxetine | Number of AEs with CM + fluoxetine were not significantly different from CM or fluoxetine alone (included nausea, dizziness, headache, flushing, somnolence) |
| Song et al,\textsuperscript{32} 2007, China, 15 d (n = 68, a = 68) | CM (Uighur) 2×/d, treatment as usual | NR |
| **Ayurvedic herbal medicine** |            |     |
| Kulkarni and Chandola,\textsuperscript{33} 2013, India, 2 mo (n = 55, a = 50) | Ayurvedic medicine + counseling, placebo + counseling | NR |
| **Topical herbal SS cream** |            |     |
| Choi et al,\textsuperscript{34} 2000, Korea, 6 applications (n = 125, a = 106) | SS cream (0.20 g 1 h before intercourse), placebo | SS cream: mild burning sensation in 15% of applications, mild pain in 4% of applications, effects resolved < 1 h |
| Choi et al,\textsuperscript{35} 1999, Korea, 4 applications (n = 73, a = 50) | SS cream (0.05, 0.10, 0.15 or 0.20 g 1 h before intercourse), placebo | SS cream: mild burning sensation in 15% of applications, mild pain in 0.04% of applications |

\(a = \text{number analyzed}; \text{AE} = \text{adverse effect}; \text{CM} = \text{Chinese medicine}; n = \text{number randomized}; \text{NR} = \text{not reported}; \text{SS} = \text{secret severance}.)
| Study, country | Treatment | Comparator | Duration | Outcome | Participants analyzed, n | Results per group, mean (SD) | MD (95% CI), P value | Favors |
|---|---|---|---|---|---|---|---|---|
| **Acupuncture vs placebo** | Sunay et al, 2011, Turkey | Acu 2×/wk | Sham acu | 4 wk | IELT (stopwatch) PEDT | 60 | acu: 1.10 (NR), sham acu: 0.55 (NR) †, acu: −4.0, sham acu: 0.0 ‡ | 0.55 (NR), .001 NR (NR), .001 | Acu over sham Acu over sham |
| **Acupuncture vs drug** | Sunay et al, 2011, Turkey | Acu 2×/wk | Paroxetine 20 mg/d | 4 wk | IELT (stopwatch) PEDT | 60 | acu: 1.10 (NR), paroxetine: 1.38 (NR) †, acu: −4.0, paroxetine: −5.0 ‡ | −0.28 (NR), .001 NR (NR), NS | Drug over acu Acu vs drug NS |
| | Chen, 2009, China | Acu daily | Citalopram 20 mg/d | 4 wk | CIPE-5 | 111 | acu: 12.56 (3.84), citalopram: 11.12 (3.77)* | 1.44 (0.02—2.86), .05 | Acu over drug |
| **CM vs TAU** | Song et al, 2007, China | CM (Uighur 2×/d) | TAU | 15 d | IELT (questionnaire) CIPE-5 | 68 | CM: 2.73 (1.25), TAU: 1.16 (0.58)*, CM: 15.80 (3.60), TAU: 10.85 (3.18) | 1.57 (1.1—2.03), <.00001, 4.95 (3.34—6.56), <.00001 | CM over TAU CM over TAU |
| **CM vs drug** | Li and Lu, 2015, China | CM (Qilin pills 6 g 2×/d) | Sertraline 50 mg/d | 4 wk | IELT (stopwatch) PEDT | 79 | CM: 3.23 (1.84), sertraline: 3.87 (2.43)*, CM: 5.1 (1.8), sertraline: 4.9 (1.7)* | −0.64 (−1.58 to 0.30), .18, −0.20 (−0.97 to 0.57), .61 | CM vs drug NS CM vs drug NS |
| | Xu et al, 2014, China | CM (mycelium of Cordyceps sinensis C4) | Sertraline 50 mg/d | 8 wk | IELT (stopwatch) PEDT | 200 | CM: 1.4 (0.7), sertraline: 3.1 (2.3)*, CM: 14.8 (3.5), sertraline: 11.0 (4.9)* | −1.70 (−2.12 to −1.28), <.01, −3.8 (−5.01 to −2.59), <.01 | Drug over CM Drug over CM |
| | Sun et al, 2010, China | CM (Yimuzae 1.5 g/d) | Fluoxetine 20 mg/d | 4 wk | IELT (method NR) satisfaction (IIEF) | 76 | CM: 5.2 (0.87), fluoxetine: 5.8 (0.94)*, CM: 10.3 (1.26), fluoxetine: 11.2 (1.09)* | −0.60 (−1.01 to −0.19), .004, −0.90 (−1.43 to −0.37), .0009 | Drug over CM Drug over CM |

(continued)
| Study, country       | Treatment                        | Comparator               | Duration | Outcome                  | Participants analyzed, n | Results per group, mean (SD) | MD (95% CI), P value | Favors                      |
|----------------------|----------------------------------|--------------------------|----------|--------------------------|--------------------------|-----------------------------|------------------------|-----------------------------|
| **CM + drug vs drug alone** |                                 |                          |          |                          |                          |                             |                        |                             |
| Li and Lu, 2015, China | CM (Qilin pills) + sertraline 50 mg/d | Sertraline 50 mg/d       | 4 wk     | IELT (stopwatch) PEDT     | 79                       | CM + sertraline: 5.92 (3.11), sertraline: 3.87 (2.43)* | 2.05 (0.83–3.27), .001 | Combined over drug          |
|                      | Li and Lu, 2015, China           | CM (Qilin pills) +       |          | IELT (method NR) satisfaction (IIEF) | 76                       | CM + fluoxetine: 7.7 (0.98), fluoxetine: 5.8 (0.94)* | 1.90 (1.47–2.33), <.00001 | Combined over drug          |
| Sun et al, 2010, China | CM (Yimusake) + fluoxetine 20 mg/d | Fluoxetine 20 mg/d       | 4 wk     | IELT (method NR) satisfaction (IIEF) | 76                       | CM + fluoxetine: 14.2 (1.31), fluoxetine: 14.2 (1.31), CM: 10.3 (1.26)* | 2.50 (2.08–2.92), <.00001 | Combined over CM            |
|                      | Xu et al, 2012, China            | CM (Yimusake) + trazodone 50 mg/d |          | IELT (method NR) | 68                       | CM + trazodone: 3.05 (0.60), CM: 2.97 (0.54)* | 0.08 (0.01 to 0.19) | Combined vs CM NS           |
| **Ayurvedic herbal medicine vs placebo** |                                 |                          |          |                          |                          |                             |                        |                             |
| Kulkarni and Chandola, 2013, India | Ayurvedic medicine + counseling | Placebo + counseling     | 2 mo     | IELT (method NR)         | 50                       | Ayurveda: 1.85 (0.91), placebo: 1.05 (0.82)* | 0.80 (0.32–1.28), .001 | Ayurveda + counseling over placebo + counseling |
significant difference (P value not reported),
and a CIPE-5 score favoring acupuncture in the other study (N = 111; P = .05). One study reported that no adverse effects were observed (although there was no formal evaluation of these),
and the other study did not report adverse effect data (Table 4).

In summary, the available data indicate that acupuncture might be slightly more effective than placebo (sham) in treating PE, although this is based on only one study of unclear quality.

### Chinese Herbal Medicine

Five RCTs (all conducted in China) assessed a 2- to 8-week course of oral Chinese herbal medicine. Each study used the same herbal medicine(s) for all patients. There were no studies of individualized Chinese medicine (where different herbs are used per patient based on clinical examination). The specific Chinese medicines used differed among studies. One study used Qilin pills (a combination of herbs; Table 1) at a dose of 6 g twice daily; one used mycelium of Cordyceps sinensis C4; two used Yimusake (one at 50 mg/d and one at 1.5 g/d); and one used Uighur twice daily.

Results for Chinese medicine are presented in Table 3 and Figures 1 and 2. One study favored Chinese medicine (Uighur) over treatment as usual (N analyzed = 68),
reporting significant differences in IELT measured by questionnaire (MD = 1.57 minutes, 95% CI = 1.11–2.03, P < .00001) and CIPE-5 score (P < .00001; Table 3 and Figure 1). Three studies compared Chinese medicine against drug treatment with an SSRI (fluoxetine or sertraline, each given daily for 4–8 weeks).

Of these, two studies significantly favored SSRIs over Chinese medicine (mycelium of Cordyceps sinensis C4 or Yimusake) for IELT (one measured by stopwatch) and PEDT and IIEF scores, whereas the third study showed no significant difference in stopwatch-measured IELT or PEDT score between the SSRI and Chinese medicine (Qilin pills; Table 3). A meta-analysis of IELT across all three studies significantly favored drug treatment with SSRIs (total N = 355; pooled MD = 1.01 minutes, 95% CI = 0.18–1.84, P = .02; Figure 1), with a high level of heterogeneity (I^2 = 86%, P = .0007).

Two studies compared Chinese medicine (Qilin pills or Yimusake) plus SSRI (fluoxetine or sertraline) against SSRI alone. These studies (total N = 155) significantly favored combination treatment over SSRI alone for IELT (one measured by stopwatch; pooled MD = 1.92 minutes, 95% CI = 1.51–2.32, P < .00001) with low heterogeneity (I^2 = 0%, P = .82); PEDT and IIEF scores also favored combination treatment (P < .001 for the two comparisons; Table 3 and Figure 2).

The same two studies compared Chinese medicine (Qilin pills or Yimusake) plus SSRI (fluoxetine or sertraline) against Chinese medicine alone. These studies (total N = 156) significantly favored combination treatment over Chinese medicine alone for IELT (one measured by stopwatch; pooled MD = 2.52,
95% CI = 2.13–2.91, P < .00001) with low heterogeneity (I² = 0%, P = .76); PEDT and IIEF scores also favored combination treatment (P < .0001 for all comparisons). Results favoring combination treatment over drug or Chinese medicine alone (for IELT and PEDT) remained significant 1 month after treatment ended in the one study reporting this.28 A third study (N = 68) comparing Chinese medicine (Yimusake) plus a serotonin antagonist and reuptake inhibitor (trazodone) against Chinese medicine alone30 showed no significant difference in IELT (measurement method not reported; MD = 0.08, 95% CI = −0.19 to 0.35, P = .56; Table 3 and Figure 2).

Four of five studies reported data on adverse effects (Table 4).28–31 For patients receiving Chinese medicine alone, two studies reported that no adverse effects were observed (one of Qilin pills 6 g twice daily28 and one of Yimusake 50 mg/d30). One study reported adverse effects in 12% of patients receiving mycelium of Cordyceps sinensis C4 (including gastrointestinal discomfort, dizziness, and decreased libido),29 whereas one study reported that the number of adverse effects did not differ significantly among Chinese medicine alone (Yimusake 1.5 g/d), fluoxetine alone, and combination treatment.31

In summary, across studies of Chinese medicine, one study favored Chinese medicine over treatment as usual.15 A meta-analysis of three studies favored SSRI treatment over Chinese medicine.28,29,31 Two studies favored Chinese medicine plus SSRIs over SSRIs alone or Chinese medicine alone.28,31

Ayurvedic Medicine

One RCT conducted in India (N analyzed = 50) assessed a 2-month course of Ayurvedic medicine (Indian herbal medicine) plus psychological counseling compared with placebo plus

| Study or Subgroup | Treatment Mean | SD | Total | Comparator Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI | Mean Difference IV, Random, 95% CI |
|-------------------|---------------|----|-------|----------------|----|-------|--------|----------------------------------|----------------------------------|
| 10.3.1 Chinese med + SSRI vs. SSRI |               |    |       |                |    |       |        |                                  |                                  |
| Li 2015 CM+sert vs. sert | 5.92 | 3.11 | 40 | 3.87 | 2.43 | 40 | 11.1% | 78 | 2.05 [0.83, 3.27] |                                  |
| Sun 2010 CM+fluox vs fluox | 7.7 | 0.98 | 38 | 5.6 | 0.94 | 38 | 88.9% | 78 | 1.90 [1.47, 2.33] |                                  |
| Subtotal (95% CI) | 78 | 78 | 100.0% | 1.92 [1.51, 2.32] |                                  |
| Heterogeneity: Tau² = 0.00; Chi² = 0.05, df = 1 (P = .82); I² = 0% |                                  |                                  |
| Test for overall effect: Z = 9.23 (P < .000001) |                                  |                                  |
| 10.3.5 Chinese med + SSRI vs. Chinese med |               |    |       |                |    |       |        |                                  |                                  |
| Li 2015 CM+sert vs CM | 5.92 | 3.11 | 40 | 3.23 | 1.84 | 40 | 12.2% | 78 | 2.69 [1.57, 3.81] |                                  |
| Sun 2010 CM+fluox vs CM | 7.7 | 0.98 | 38 | 5.2 | 0.87 | 38 | 87.8% | 78 | 2.50 [2.08, 2.92] |                                  |
| Subtotal (95% CI) | 78 | 78 | 100.0% | 2.52 [2.13, 2.91] |                                  |
| Heterogeneity: Tau² = 0.00; Chi² = 0.10, df = 1 (P = .76); I² = 0% |                                  |                                  |
| Test for overall effect: Z = 12.66 (P < .000001) |                                  |                                  |
| 10.3.8 Chinese med + SARI vs. Chinese med |               |    |       |                |    |       |        |                                  |                                  |
| Xu 2012 CM+trazo vs CM | 3.05 | 0.6 | 36 | 2.97 | 0.54 | 32 | 100.0% | 36 | 0.08 [-0.19, 0.35] |                                  |
| Subtotal (95% CI) | 36 | 36 | 100.0% | 0.08 [-0.19, 0.35] |                                  |
| Heterogeneity: Not applicable |                                  |                                  |
| Test for overall effect: Z = 0.58 (P = .56) |                                  |                                  |

Test for subgroup differences: Chi² = 120.89, df = 2 (P < .000001), I² = 98.3%
psychological counseling. Ayurvedic medicine showed a small but significant improvement in IELT (measurement method not reported; MD = 0.80 minutes, 95% CI = 0.32–1.28, P = .001; Table 3). Adverse effects were not reported.

SS Cream
Two crossover RCTs conducted in Korea compared SS cream against placebo. These two RCTs showed significant effects on stopwatch-measured IELT (total N = 156; pooled MD = 8.60 minutes, 95% CI = 7.09–10.10, P < .001) with low heterogeneity (I² = 0%, P = .84; Table 3 and Figure 3). The two studies used a single-group crossover design in which each patient received four or five applications of SS cream and one of placebo. One study used different doses of SS cream; only the results for the maximum dose (0.2 g) are presented. Patients might have had less severe PE than those in some other studies because the inclusion criterion was an IELT shorter than 3 minutes (combined with low partner satisfaction in one study). Adverse effects included a mild burning sensation in 15% of patients (the two studies) and mild pain in 0.04% to 4% of patients (Table 4).

Summary
The included studies evaluated the effectiveness of acupuncture, Chinese herbal medicine, Ayurvedic herbal medicine, and topical SS cream in improving IELT and other outcomes. Overall risk of bias was unclear in all cases because of unclear allocation concealment and/or blinding. Studies were clinically heterogeneous and stopwatch-measured IELT was reported in only 5 of 10 studies. Acupuncture increased IELT over placebo (one study; MD = 0.55 minute, P = .001), Ayurvedic herbal medicine increased IELT over placebo (one study; MD = 0.80 minute, P = .001). Topical SS cream improved IELT over placebo in two crossover studies (MD = 8.60 minutes, P < .001), although inclusion criteria were broad (IELT < 3 minutes), and there were mild irritant effects in some patients. SSRI treatments were more effective on IELT than Chinese herbal medicine (three studies; MD = 1.01 minutes, P = .02). However, combination treatment with Chinese medicine plus SSRIs improved IELT over SSRIs alone (two studies; MD = 1.92 minutes, P < .00001) or Chinese medicine alone (two studies; MD = 2.52 minutes, P < .00001). Adverse effects were not consistently assessed but where reported were generally mild. There were sparse data on the potential for drug interactions.

DISCUSSION
Our systematic review is (to our knowledge) the first to evaluate CAM for PE. All studies were classed as having an overall unclear risk of bias because of limited reporting. Blinding of participants and personnel was difficult in many studies because of the nature of the interventions, although a few studies used placebo. However, because most studies included an active control group (eg, drug treatment), any placebo effect might be expected to occur in the two groups. It was not possible to conduct a formal test for publication bias or produce funnel plots because of the small number of studies in each analysis. However, all but three studies were conducted in single centers, and single-center trials tend to show larger treatment effects than multicenter trials, possibly because of a lower likelihood of publication if the result is negative (publication bias), lower methodologic quality, and/or more selected patients.

Regarding outcomes, 9 of 10 included studies assessed IELT but only five reported on stopwatch-measured IELT. Because IELT tends to be positively skewed, it has been suggested that studies should report geometric (rather than arithmetic) mean IELT. None of the included studies reported geometric mean IELT, although two studies used the Mann-Whitney U-test for between-group differences because of non-normal distribution of data. Additional outcomes included PEDT, CIPE-5, and IIEF scores. Although it is important that clinical studies assess non-IELT outcomes in addition to IELT, there is a need for greater agreement on which measurements are most robust. Duration of the interventions was 2 to 8 weeks in all studies (or one to five applications for SS cream). Only one study (of Chinese medicine) provided follow-up data beyond the end of treatment and reported that differences remained significant 1 month after treatment ended. For most interventions, it was not clear how long the effects might last or whether repeat treatments were effective. This is an issue for all PE treatments.

An interesting point relates to the nature of CAM therapies. In clinical practice, many CAM therapies involve a holistic approach based on the patient’s overall pattern of health. It can
be difficult to determine how much of the treatment effect is due to the specific treatment (acupuncture, herbs) and how much is due to the patient-therapist interaction and other aspects (eg, lifestyle advice). Some researchers believe the patient-therapist interaction and other aspects of treatment should be controlled for, whereas others argue that they are a valid element of treatment. A related issue is whether CAM therapies are individualized to the patient (eg, in clinical practice, two patients with PE might receive different herbal remedies or acupuncture points depending on their overall symptom picture). All studies included in this review used a standardized treatment across patients within a study (same set of acupuncture points or same Chinese herbal preparation), although treatments varied among studies. Although standardized treatment protocols increase reproducibility, effectiveness of CAM therapies could be compromised by this approach.

None of the included therapies are commonly provided for PE by Western government health services. This has implications for access and use of these therapies. Acupuncture, Chinese medicine, and Ayurvedic medicine might be available from private practitioners, whereas SS cream currently has limited availability outside Korea. Pragmatically, because there are so many CAM therapies available, it seems unlikely that they will all undergo further evaluation in large-scale studies. Therefore, it might be reasonable to summarize that the CAM therapies reviewed here have some (although limited) evidence for effectiveness in treating PE, and that they might provide another option for patients who favor a mind-body approach or who wish to avoid long-term pharmacologic treatment. It would need to be borne in mind that the effectiveness evidence is not conclusive, and care would need to be taken to monitor for adverse effects and to consider the potential for herb-drug interactions.

Regarding further research, it would be useful to see further RCTs in a Western setting for any of the included treatments, because all had some (limited) evidence of effectiveness in PE. It would be useful to conduct comparisons against placebo, no treatment, existing therapies (drug or behavioral treatment), and combination treatment. To increase consistency and facilitate meta-analyses, future studies should recruit men meeting the ISSM definition of PE, measure stopwatch-assessed IELT, and report additional outcomes using validated instruments. Additional areas for further study could include optimum duration of therapy and how effects might best be maintained in the long term.

CONCLUSIONS

There is preliminary evidence for effectiveness of some CAM therapies in PE. However, results are based on clinically heterogeneous, mostly single-center studies of unclear quality. Acupuncture, Ayurvedic medicine, and SS cream improved IELT and other outcomes over placebo based on limited data. Chinese herbal medicine was not as effective as SSRIs, whereas combination treatment with Chinese medicine plus SSRIs improved outcomes over either therapy alone. Adverse effects were not consistently assessed, although where reported they were generally mild, and there were sparse data on the potential for drug interactions. Further well-conducted RCTs of all treatments would be valuable.

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SUPPLEMENTARY DATA
Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.esxm.2016.08.002.

APPENDIX 1. MEDLINE SEARCH STRATEGY

Medline search strategy
1. exp Ejaculation/
2. exp Premature Ejaculation/
3. (premature$ adj3 ejaculat$).ti,ab.
4. (early adj3 ejaculat$).ti,ab.
5. (rapid adj3 ejaculat$).ti,ab.
6. (rapid adj3 climax$).ti,ab.
7. (premature$ adj3 climax$).ti,ab.
8. (ejaculat$ adj3 pr?ecox).ti,ab.
9. or/1-8.

Filter 1: Randomized Controlled Trials
10. Randomized Controlled Trials as Topic/
11. randomized controlled trial/
12. Random Allocation/
13. Double Blind Method/
14. Single Blind Method/
15. clinical trial/
16. clinical trial, phase i.pt.
17. clinical trial, phase ii.pt.
18. clinical trial, phase iii.pt.
19. clinical trial, phase iv.pt.
20. controlled clinical trial.pt.
21. randomized controlled trial.pt.
22. multicenter study.pt.
23. clinical trial.pt.
24. exp Clinical Trials as topic/
25. or/10-24
26. (clinical adj trial$).tw.
27. ((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw.
28. PLACEBOS/
29. placebo$.tw.
30. randomly allocated.tw.
31. (allocated adj2 random$).tw.
32. 26 or 27 or 28 or 29 or 30 or 31
33. 25 or 32
34. case report.tw.
35. letter/
36. historical article/
37. 34 or 35 or 36
38. 33 not 37

Filter 2: Reviews
10. review.ab.
11. review.pt.
12. meta-analysis.ab.
13. meta-analysis.pt.
14. meta-analysis.ti.
15. or/10-14
16. letter.pt.
17. comment.pt.
18. editorial.pt.
19. or/16-18

20. 15 not 19

Filter 3: Guidelines
10. guideline.pt.
11. practice guideline.pt.
12. exp Guideline/
13. health planning guidelines/
14. 10 or 11 or 12 or 13